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SELECTIVE FLUORINATION BY $C_{19}XeF_6$

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Summary : Selective fluorination by $C_{19}XeF_6$ of β-diketones and β-ketoesters is described. The ease of handling of this fluorinating reagent and high yields of mono fluorinated products obtained, show promise in organic synthesis.

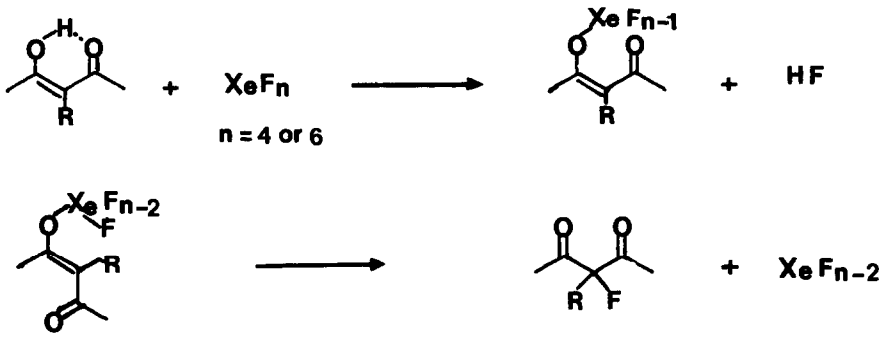
Among the three known fluorides of xenon, xenon difluoride has been employed extensively in the fluorinations of aromatic hydrocarbons[1], nitrogen-containing aromatic compounds[2], substituted alkenes[3] and alkynes[4]. Most of these reactions are catalyzed either by anhydrous HF or trifluoroacetic acid or BF_3-etherate. On the other hand xenon hexafluoride is a highly reactive fluorinating agent which is difficult to handle and reacts unselectively with organic molecules[5]. Its aggressive property is tamed by insertion into graphite. A lamellar compound of formula $C_{19}XeF_6$ was prepared by Selig et al.[6]. This graphite derivative is much more stable than free XeF_6 and gave mild fluorinations of aromatic systems[7].

We wish to present the results obtained by the reaction of $C_{19}XeF_6$ on other functional groups. We checked the fluorinating properties of $C_{19}XeF_6$ by stirring 1 mmole of the reagent with 1 mmole of an organic substrate in 20 ml anhydrous CH_2Cl_2 at room temperature under anhydrous conditions for 24 hrs. Under these conditions, there was no reaction with simple ketones such as octan-2-one, cyclohexanone, 5α-cholestan-3-one or camphor. Even 5α-cholestan-3-one enol acetate was unreactive. By contrast, β-diketones or β-ketoesters gave monofluoro-derivatives in moderate to good yields (Table 1). The reaction is very simple to carry out and does not need any special equipment. The product is recovered by filtration of graphite and solvent evaporation. We never observed any uncontrolled reaction but it is advisable to observe general precautions[6] for handling or storing the fluorinating reagent.

Fluorination of β-diketones has not been reported previously ; however, β-ketoesters have been fluorinated using perchloryl fluoride[8].

In the reactions of phenyl-substituted alkenes and alkynes with XeF_2, addition to the multiple bond takes precedence over aromatic substitution[2]. Similarly with $C_{19}XeF_6$, fluorination on a reactive methylene of an aromatic β-diketone predominates over the aromatic substitution. Thus, 2-acetyl tetral-1-one reacted with $C_{19}XeF_6$ to give 2-acetyl-2-fluoro-tetral-1-one as the major product and negligible amount of fluoroaromatic compound was formed. Also of interest are the formation of fluorouracil and fluorobarbituric acid. The fluorination of uracil, using XeF_2, to give 5-fluorouracil in 10 % yield, has been already reported[9].

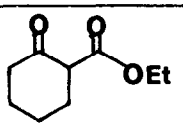
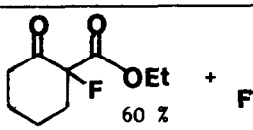
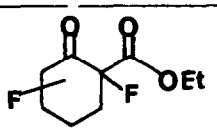
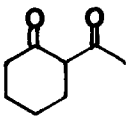
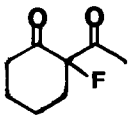
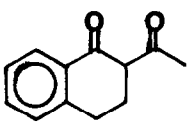
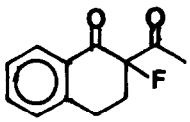
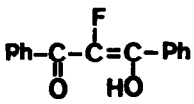
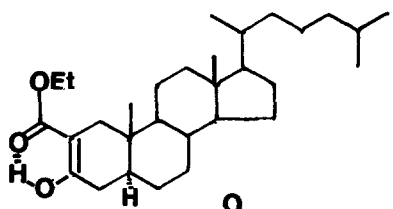
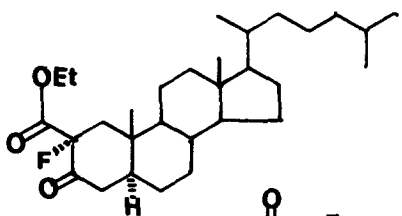
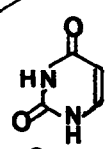
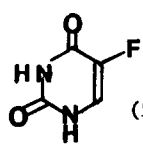
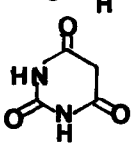
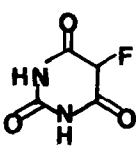
Though a simple formula $C_{19}XeF_6$ for this lamellar compound was derived from chemical analysis and weight increase the exact nature of the intercalated species is unknown. On the basis of wide line ^{19}F nmr measurements, a formula $(C^{+}_{9.5}\ F^{-})_2XeF_4$ was proposed[7]. Chemical behaviour of the noble gases fluorides is similar to corresponding halogen compounds[10]. This behaviour suggests the possibility that XeF_4 and XeF_6 follow the same reaction course as halogen fluorides. An intramolecular (cyclic) transfer of fluoride ion in bidentate anions has been suggested as one of the mechanisms of fluorination by perchloryl fluoride[11]. If the intercalated species is XeF_4, and considering the fact that XeF_4 shows a strong tendency to form XeF_3^{+} [10], we suggest the following sequence of reactions for the fluorinations :



Other possible mechanisms[12] cannot be ruled out presently, in the absence of definite evidence, and also this mechanism cannot be applied without any modification to the fluorination of uracil.

The insertion of XeF_6 into graphite greatly modifies its chemical properties, allowing control of its reactivity. This trend is not unprecedented and has already been found for several types of lamellar compounds[13]. We are currently checking the fluorinating properties of $C_{19}XeF_6$ on other functional groups and using it for fluorination of polyfunctional molecules of therapeutic interest.

Table 1

Compound	Conditions[a]	Products and yields[b]
	A	 60 % +  15 %
	A	 40 % + unidentified product without fluorine 30 %
	B	 60 %
Ph–CO–CH_2–CO–Ph	B	 + $[(PhCO)_2CH]_2$ 20 % 40 %
	A	 40 % [15]
	C	 90 % (5-fluorouracil)
	A	 68 %

[a] All the reactions were carried out using conventional glassware in a well-ventilated hood.

[b] Structures of all products were deduced from ^{1}H and ^{19}F nmr and mass spectra. Yields are reported for the isolated products.[14]

A Addition at room temperature, and stirring for 24 hrs.

B Addition was done at -196°C, allowed to warm to room temperature and stirred for 24 hrs.

C Suspension of uracil in excess of CH_2Cl_2 was added to 2 equ. of $C_{19}XeF_6$ at room temperature and stirred for 24 hrs.

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References and notes

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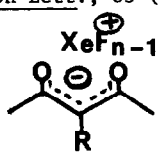
11) W A.Sheppard, Tetrahedron Lett., 83 (1969).

12) e.g., an ion pair of the type 

may be an intermediate in the reaction.

13) H.B.Kagan, Chemtech., 510 (1976).

14) No attempts were made to optimise the yields. However, in case of an aged reagent, it was necessary to use a little excess of the reagent to complete the reaction.

15) An α-orientation of F at C-2 is suggested in analogy with the perchloryl fluoride fluorination of 3-ethoxycholest-2-ene

S.Nakanishi, K Morita and E.V.Jensen, J.Am.Chem.Soc., 81, 5259 (1959).

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