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A NOVEL METHOD FOR PREPARATION OF VICINAL FLUORO-IODO COMPOUNDS USING ELEMENTAL FLUORINE

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Abstract: Elemental fluorine reacts with iodine at -75° and the resulting IF is reacted, without any isolation or purification, with olefins thus producing fluoro-iodo compounds in an excellent regio- and stereospecific mode.

The synthesis of fluorine containing compounds is mainly based on the use of nucleophilic, radical or electrophilic fluorinating reagents like pure KF, CoF_3, CF_3OF, just to mention a few. Thus, in sharp contrast to the other halogenating procedures, the use of the primary source of fluorine atoms namely, elemental fluorine itself, is strikingly avoided. This attitude, however, is changing rapidly. Only recently, elemental fluorine was employed in remarkably selective electrophilic fluorinations[1,2]. What is more, we have also shown recently that the fluorine molecule can be indirectly utilized to produce in situ a mixture of various fluoroxy compounds which can be used either as a single reagent[3] or as specialized agents like CF_3COOF and/or CF_3CF_2OF[4]. We wish to describe in this paper, a further development of the idea of using elemental fluorine indirectly in fluorination reactions.

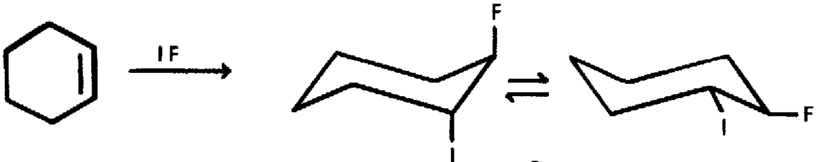
Iodine fluoride, IF, was synthesized by several groups from the corresponding elements under various conditions but it tends to disproportionate to IF_3 and eventually to IF_5 and iodine[5]. The main purpose of the synthesis, therefore, was not the evaluating of its synthetic potential but rather an investigation of its physical properties[6]. Only limited works on the addition of the elements of IF to double bonds exist in the literature. These works can be divided into two categories: a catalyst aided synthesis of IF from $IF_5 + I_2$ and its addition to perhalolefins[7]; b reactions between AgF and I_2 or between some N-iodo amide with anhydrous HF. The resulting mixtures act as an "IF" source when added to olefins[8].

It seems to us, that once a laboratory possesses an easy to assemble[1-4] fluorine line system, the above two methods which suffer from various limitations can efficiently be replaced by the following method. When a stream of nitrogen-diluted fluorine was passed through a cold solution (-75°) of an excess of iodine in $CFCl_3$ (Freon), practically all the fluorine reacts instantaneously with the iodine as evident from the fluorine free nitrogen gas leaving the reaction mixture. After the addition of the fluorine, a solution of 1-octene in Freon was introduced and an addition in a Markovnikov mode took place immediately across the double bond. We were able, thus, to isolate in 70% yield the previously unknown 1-iodo-2-fluoroctane (1,oil). Similar results were obtained also with 1-decene, thus producing the yet undescribed 1-iodo-2-fluorodecane (2,oil, 70% yield)

$$CH_3(CH_2)n-CH{=}CH_2 \xrightarrow{IF} CH_3(CH_2)n-CHF-CH_2I$$

1 n=5 ; 2 n=7

An endocyclic double bond as in cyclohexene also reacts smoothly. The product here, trans 1-fluoro-2-iodocyclohexane (3,oil,64% yield)[8], clearly demonstrates that the iodine, the electrophilic site of the reagent, forms first the iodonium ion which leads to the trans diaxial adduct. Trisubstituted olefins also react quite readily as can be seen from the reaction with p-1-menthene (4). The product, trans-1-fluoro-2-iodo-p-menthane(5,oil,45% yield) emphasizes the excellent regio- and stereospecifity of this reaction[9].



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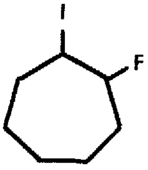

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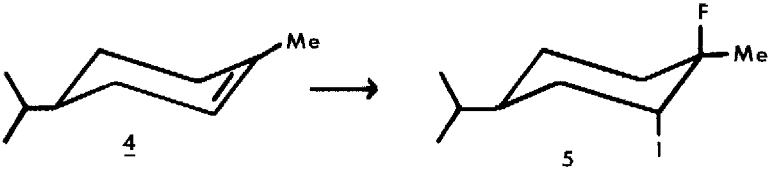

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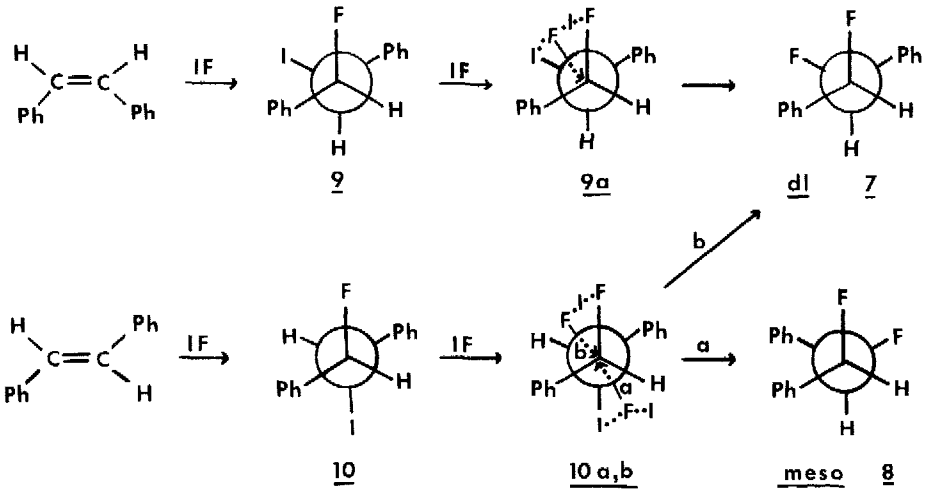
A double bond in a larger ring also did not present any special problems. Thus, cycloheptene reacts with IF to give 1-fluoro-2-iodocycloheptane (6, oil, 45% yield).

The iodo compounds are usually not very stable and although we have not made an attempt at this stage to isolate any pure by-products, spectral evidences indicate that they are mainly fluorolefins, difluorides and rearranged products caused by secondary reactions involving the iodine atom. What is more, in some cases if the iodo compounds are chromatographed slowly, hydrolysis can take place leading to the corresponding fluorohydrines.

Interesting and somewhat puzzling results were obtained when cis and trans stilbene were reacted with the in situ generated IF. Thus, while trans stilbene gives in almost quantitative yield a 1:1 mixture of dl and meso 1,2-difluoro-1,2-diphenylethane (7 and 8 respectively)[10], cis stilbene gives only the dl isomer 7 also in excellent yield. We believe that in the case of the cis isomer the first reaction is the usual anti addition of the IF producing the threo adduct. This adduct adopts the most stable conformation - 9. It has been established that fluoroiodo compounds are capable of forming I...F....I bridges[11], so an additional molecule of IF can be complexed between the two halogens (9a). The fluorine anion then attacks the partially positive relatively stable benzilic carbon on which the iodine was originally attached, leading to the stable 7.



With trans stilbene the picture is somewhat different. An anti addition of IF gives a stable erythro adduct 10. However the relative position of the halogen atoms in this stable conformation does not permit the same kind of complexation as in 9a. Instead, complexation of an IF molecule, with consecutive attack of fluoride, may occur either on the benzilic iodine (route a) thus producing the meso isomer 8, or on the benzilic fluorine (route b) thus permitting back side attack resulting in the stable dl isomer 7.

References and Notes

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9. The reaction between IF and p-menth-1-ene is typical to all other reactions. After a desired amount of fluorine (usually about 30 mmoles diluted with N_2, 3% V/V) is passed through the iodine solution in Freon at -75°, the olefin (about 15 mmols) is added at this temperature and stirred for 5 minutes. The reaction mixture is then poured into thiosulphate solution to decompose the excess iodine present. After washing the organic layer with water, drying and evaporating, the crude product is rapidly chromatographed on a column or purified if necessary, using HPLC technique. No special attempt was made to optimize the yields and they are based on the converted starting materials (usually about 80% conversion). It should also be noted, that provided there is an excess of iodine, the IF in the solution may be warmed up to 0°, apparently with no rapid disproportionation. Adding olefin at this temperature does not affect the yield and may even improve it slightly. The identification of the trans 1-fluoro-2-iodo-p-menthane (5) serves as a typical example: Mass spectrum: M/e = 284 (M^+), 264 (M^+ - HF), 138 (M^+ - IF). NMR: $\delta = 4.47$ ($CH_{eq}I$, dt, 1H, $J_{HH} = 2.5$ Hz, $J_{FH(vic)} = 9$ Hz), 1.59 ppm (d, 3H, $J_{MeCF} = 22$ Hz); F^{19} NMR: $\phi^* = 145.5$ ppm, m, $W^h/2 = 80$ Hz. The spectral data of the other described compounds is also in excellent agreement with the proposed structures. The combustion analyses of all new compounds are also in accordance with the proposed formulas.
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