Journal of Fluorine Chemistry, 20 (1982) 419–424

Received: November 17, 1981

PRELIMINARY NOTE

SYNTHESIS OF VICINAL BROMO-FLUORO ORGANIC COMPOUNDS USING ELEMENTAL FLUORINE

MICHAEL BRAND and SHLOMO ROZEN*

Chemistry Department, Tel-Aviv University, Tel Aviv 69978,(Israel)

SUMMARY

The direct action of fluorine on bromine at -78° produces BrF which, without any isolation or purification, adds readily across various double bonds providing there is some hydrogen donor in the reaction mixture. Only trans addition of the elements of BrF was observed. When the reaction was applied to enons an easy elimination of HF can take place thus producing α-bromo enons.

In our previous work we described the reaction of some olefins with IF, a reagent which was prepared in situ by the action of F_2 on I_2[1]. The literature deals with several other fluorohalogens, among them the three known bromo-fluoro compounds, BrF, BrF_3 and BrF_5, although only the last two are well characterized[2]. However, because of the instability and the high reactivity of these compounds, they have hardly been employed in organic chemistry[3].

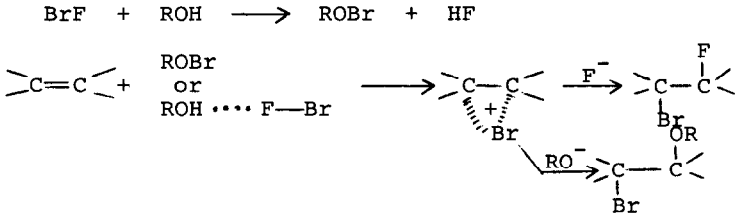
We wish to describe here for the first time, an efficient and convenient method of synthesizing vicinal bromo-fluoro compounds using the primary source of the fluorine atoms, namely elemental fluorine itself[4].

When a mixture of F_2/N_2 is bubbled through a cold (-78°C), dilute solution of Br_2 (20 mmolar) in $CFCl_3$(Freon) the bromine disappears and mainly BrF is produced. However, despite previous efforts, it seems that this compound cannot be isolated since it disproportionates easily to the very reactive BrF_3 and

0022-1139/82/0000-0000/$02.75 © Elsevier Sequoia/Printed in The Netherlands

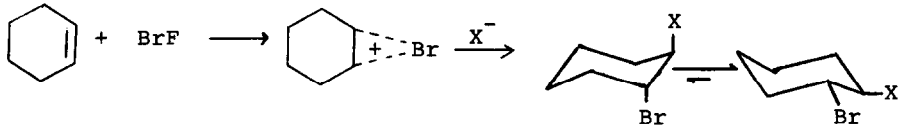
Br_2[2]. Still we hoped, as in our previous works, that we would be able to react olefins with the in situ prepared reagent without its isolation and purification[1,5]. When, however, several olefins were added to the resulting BrF suspension in Freon, very messy reactions took place and no bromo-fluoro adducts could be detected. It is apparent that BrF is much more reactive than IF or Br_2 and resembles F_2 itself[6].

Nevertheless, when the reaction of F_2 with Br_2 was performed in Freon and then commercial grade chloroform (which usually contains a little ethanol) was added followed by the olefin, the bromo-fluoro adducts could be obtained in good yields along with small amounts of bromo-ethyl ethers. When ethanol-free chloroform was used, again messy reactions took place, resembling the reaction observed in Freon only. Adding small amounts of ethanol to the Freon or replacing the ethanol by several other proton-donating compounds (i-PrOH, t-BuOH, succinimide and AcOH) had a similar taming effect on the very reactive BrF thus enabling the production of the bromo-fluoro adducts. It appears that a primary reaction takes place between the BrF and the proton-donating compound like an alcohol. Such a reaction can directly lead to small amount of hypobromite or forming hydrogen bonds with BrF thus enhancing its polarizability. In either case the positive halogen in the hypobromite can then react with the double bond to produce the well-known bromonium ion. This in turn will be attacked in the usual anti mode, either by the alkoxy residue to produce the minor ether component found in some cases, or by the fluoride ion resulting in the bromo-fluoro adduct.



We have reacted several types of olefins in this indirect way with BrF. In a typical experiment, about 1.6 gr. of bromine (10 mmol) was dissolved in 150 cc of cold Freon (-78°) and 8%

fluorine in nitrogen was passed through, till the color of the resulting suspension became pale yellow * , then 150 cc of cold $CHCl_3$ was added to the reaction mixture and stirred for about 15 minutes during which time a solution resulted. Subsequently, a cold solution (-78°) of 0.82 gr of cyclohexene (10 mmol) in $CHCl_3$ was added and after 15-20 minutes practically all the starting material had reacted. The reaction mixture was poured into dilute thiosulphate solution, washed with water, dried and evaporated. Two compounds were isolated by chromatography, trans-1-bromo-2-fluorocyclohexane(I) (oil, 61% yield) [4b] and trans-1-bromo-2-ethoxycyclohexane(II) (oil, 10% yield). The NMR spectra of both products show unequivocally that both substituents of the cyclohexane ring in I and II are in diequatorial position ** . This suggests that a bromonium is first formed which is followed by a trans diaxial attack of the fluoride anion.



$$RCH=CH_2 \xrightarrow{BrF} RCH(Br)-\overset{+}{C}H_2 \longrightarrow RCH(F)-CH_2Br + RCH(Br)-CH_2F$$

III R = $CH_3(CH_2)_9$ IV V

VI R = CH_2COOMe VII VIII

$$VII \xrightarrow{-HF} CHBr=CHCH_2COOMe;$$

IX

---

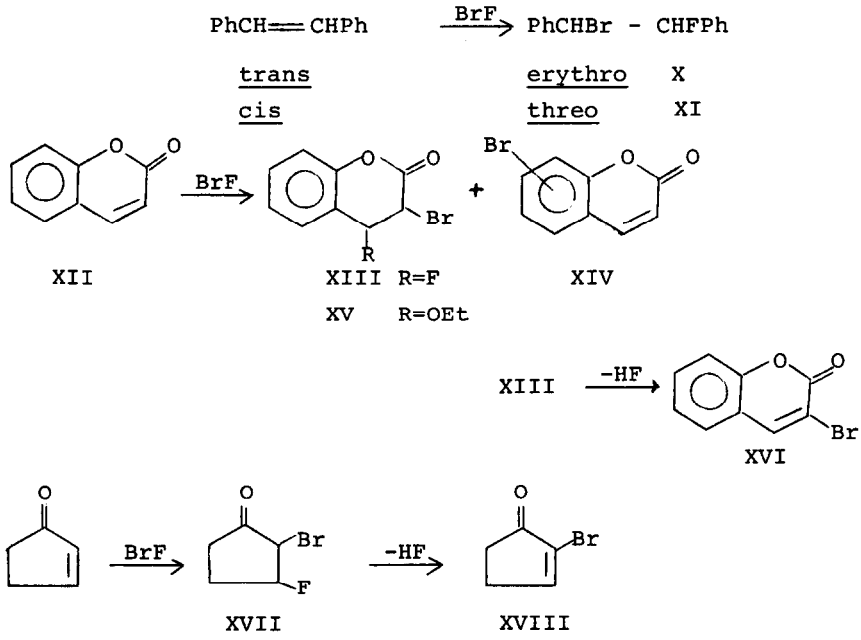
* Fluorine and probably BrF are, of course, strong poisons and very corrosive materials. An appropriate vacuum line in a well ventilated room should be constructed. The reaction itself can be carried out in glass vessels. For more details see ref. 5.

** The spectral data of all compounds described are in excellent agreement with the proposed structures. Unless otherwise stated, the combustion analyses of all fluorine containing compounds are also in accordance with the proposed formulas.

Performing the reaction in Freon, to which several drops of EtOH or i-PrOH were added, did not alter the results obtained with Freon-chloroform. Replacing these alcohols with t-BuOH, reduced the yield of II to 39%. An even larger reduction in yield occurred when the proton donor was succinimide or acetic acid - 21% and 18% yield, respectively. The lower yields obtained in the latter cases can be explained by the low solubility of these proton donors in the reaction mixture at -78°.

Similar results were obtained with terminal olefins. 1-Dodecene (III) was converted into two bromo-fluoro adducts. An attack on the more stable carbocation leads to compound IV (oil, 66% yield) while an attack from the less hindered side of the bromonium ion produces the isomer V (oil, 18% yield). When the alkyl group in IV was replaced by a methyl acetate residue as in methyl 3-butenoate (VI) and the crude mixture was rapidly chromatographed, again two bromo-fluoro compounds VII and VIII were formed (oils, 50% and 30% yield, respectively), together with small amounts (up to 10% each) of the corresponding bromo ethers as evident from the NMR spectra. It should be noted that if VII or VIII is subjected to slow chromatography, elimination of HF occurs to produce a bromo vinyl compound like IX.

Benzylic olefins like cis and trans stilbenes also reacted readily. An exclusive anti addition was observed, thus trans stilbene produced erythro α-bromo-β-fluoro bibenzyl (X) in 84% yield (m.p. 105°) while cis stilbene was converted to the respective threo isomer XI (65% yield, m.p. 65°)[7]. The stereochemistry of these two adducts can be evaluated from the coupling constants of the vicinal hydrogen atoms, J = 6.5 and 7.5 Hz for X and XI, respectively bearing in mind that such compounds have a slightly preferable gauche conformation [5b]. The only other by-product which was isolated in less than 20% yield from the reaction of cis stilbene was the corresponding bromo ether.



We have investigated the reaction of BrF with conjugated enones. Since the double bonds here are deactivated, longer reaction periods, up to 12 hours, were required. The resulting bromo-fluoro adducts proved to be quite labile so that analytical samples could not be obtained. These compounds are sensitive to chromatography and very easily lose HF, forming the stable α-bromo enones since the hydrogen geminal to the bromine is highly acidic. Thus the bromo-fluoro adducts could be obtained in about 90% purity. When cumarin (XII) was reacted with BrF at -78° for about 12 hours and then subjected to rapid chromatography, three main products could be isolated. The first proved to be the bromo-fluoro adduct XIII (50% yield greater than 90% purity). NMR δ= 7.46-6.96 (4H, m), 5.56 (1H, dd, J_1=49Hz, J_2=3.2Hz) 4.66 ppm (1H,dd,J_1=8Hz, J_2=3.2Hz); FMR:Ø*=147.5 ppm. IR; 1750 cm^{-1}; Mol.wt. (MS)=244.246. The second compound was an aromatic bromo cumarin XIV (25% yield, m.p.=150°) which undoubtedly resulted from the attack of the electrophilic bromine on the aromatic ring although at this stage the position of this

halogen on the aromatic ring can not be ascertained. The third product proved to be the corresponding bromo-ethoxy compound XV (15% yield). Prolonged chromatography or traces of HF from the reaction mixture results in the elimination of HF thus producing, quantitatively, 6-bromocumarin XVI[8]. 2-Bromo-3-fluoro cyclopentanone XVII (oil) is formed in 90% yield and isolated in almost pure form. As in the case of cumarin, XVII readily loses HF producing the 2-bromocyclopentenone (XVIII)[9] in quantitative yield.

1 Rozen, S; Brand, M., Tet. Lett. 1980, 21, 4543.

2 See for example: Naumann, D.; Lehmann, E., J. Fluorine Chem., 1975, 5, 307.

3 Pyridine complexes of BrF and BrF_3 have been prepared see ref. 2. A mixture of BrF_3 and Br_2 was reacted with perfluoro-olefins to produce mono-bromo-perfluoro alkanes, see Lo, E.S.; Readio, J.D.; Iserson, H., J. Org. Chem., 1970, 35, 2051.

4 Until now the main method for synthesis of bromo-fluoro compounds was the action of anhydrous HF and N-bromoamides on olefins, e.g. a. Hall, L.D.; Jones, D.L., Can. J. Chem. 1973, 51, 2902; b. Olah, G.; Masatomo, N.; Kerekes, I., Synthesis, 1973, 780.

5 See for example: a. Rozen, S.; Menahem, Y., J. Fluorine Chem., 1980, 16, 19.; b. Rozen, S.; Lerman, O., J. Org. Chem., 1980, 45, 672; c. Lerman, O; Rozen, S., ibid, 1980, 45, 4122.

6 In our experience F_2 does not add cleanly to most double bonds. See, however, Merritt, R. F.; J. Org. Chem., 1966, 31, 3871 and references therein.

7 Zupan, M.; Pollak, A., J. Chem. Soc. Perkin I, 1976, 971. It should also be noted that although relatively stable benzylic carbocations are involved in these reactions, in the absence of EtOH or other proton donors, messy reactions take place and no definite compounds could be isolated.

8 LeCorre, M.; Ann. Chim., 1968, 193.

9 Dunn, G.L.; DePasquo, V.J.; Hoover, J.R.E. J. Org. Chem., 1968, 33, 1454.