O_{28}

REACTION MECHANISMS OF FLUORINATION REACTION IN HF: PYRIDINE MIXTURES OF DIFFERENT MOLAR RATIO: REGIOSELECTIVITY AND STEREOSELECTIVITY OF FLUORINATION REACTIONS IN THIS MEDIUM

Sylvain Hamman, Claude G. Beguin*, Abderrahman Dahbi and Tahar Benaisa
University of Grenoble I, Department of Chemistry, BP 68, 38402 Saint Martin d'Hères (France)

For a convenient synthetic route for pure diastereoisomers of α-fluoro β-amines of following formula:

$PhCHFCH(NR'_2)R$

with R=D, Me, Ph and $NR'_2=NH_2$ or N⬡ we used the corresponding α-fluoro β-bromo compounds. The synthesis of these fluorobromo compounds was undertaken through two fluorination reactions in HF:pyridine mixture:

(i) fluorodehydroxylation of bromo-alcohols or amino-alcohols

PhCH(OH)CHBrR	R=D, Me, Ph
PhCH(OH)CH(N⬡)R	R=Me

(ii) fluorobromination (with N-bromosuccimide) of alkenes

PhCH=CHR	R=D, Me, Ph

The analyses of the first stereochemical results were so complex that the study became ; "Influence of the solvent composition mixture on the neighbouring group participation in the fluorination reactions". Bromine, amine and hydrogen groups are the studied neighbouring participating groups.

The configurations of the alcohols are mostly already known in the literature. The configurations of the corresponding fluoro compounds were unambiguously determined through the analysis of the vicinal coupling constants around the C_{α} C_{β} bond (J (HH), J (FH) and J (FC)).

The stereochemical results of fluorination reactions are shown according to the following graph: percentage of the e isomer versus x, the number of moles of HF to one mole of pyridine in the solvent mixture.

Interesting comparisons can be made with our previous results of fluorination of alkyl substituted alcohols giving substitution or transposition. The substitution is obtained for low HF content and transposition at high HF content.

Two conclusions can be made from the results.

a) The first one is from a synthetic point of view to obtain diastereoisomerically pure α-fluoro β-primary amines (e isomer or t isomer).

b) The second conclusion is from a mechanistical point of view.

Low HF content gives a low ionizing power medium and a low reactivity for the carbocation and so a long lifetime and so the equilibration to give the more stable carbocation has time to take place. The participation of the group Br, H, Ph, Br from NBS is late.

For high HF content, the ionizing power is large and early nucleophilic participation of the neighboring group prevents the equilibration of the carbocation and leads to a product retaining the structure of the initial product.