

Received: May 4, 1976

SHORT COMMUNICATION

The Synthesis of Substituted  $\alpha$ -Chloro- $\beta$ -Fluoro-Ethylbenzenes by  
Fluorination of the Corresponding Alcohols in Polyhydrogen Fluoride/  
Pyridine Solution

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In our study of 2-fluoro-2-phenylethylamine, we required the following fluoroalkanes :  $p$   $ZC_6H_4CHFCH_2Cl$  (I). Several authors [1 - 7] have obtained the unsubstituted product ( $Z = H$ ) by different methods and in one case [6] the product with  $Z = F$ . As Olah [8] [9] has recently published a new method for the preparation of alkyl fluorides from alcohols in a polyhydrogen fluoride/pyridine solution, we tried to apply his method to the readily available corresponding alcohols  $p$   $ZC_6H_4CH(OH)CH_2Cl$  (II).

The fluorination procedure was carried out by dissolving the alcohols II in the polyhydrogen fluoride/pyridine solution (70 : 30 by weight) at room temperature (see experimental section). The end of the reaction is controlled by g.l.c. The yield of the transformation is almost quantitative. The reaction times necessary to effect the reaction are given in Table I. With electron donating substituents the general tendency is towards faster reaction. However, the following remarks can be made :

(i) Reaction rates did not vary when an alkaline fluoride was added to the polyhydrogen fluoride/pyridine solution. This result differs from Olah's observation [8] that alkyl fluorides could be



obtained from primary alcohols at room temperature only if the monomeric fluoride ion  $F^-$ , a stronger nucleophile than polymeric  $(HF)_x F^-$  were present. In our system, the addition of fluoride ion  $F^-$  had no effect. We suggest that this difference arises from the structure of the alcohols II (secondary and sterically hindered by the  $\alpha$  chloro substituent).

(ii) With the highly electron donating substituents ( $Z = CH_3$  and  $OCH_3$ ), better results were obtained in polyhydrogen fluoride/pyridine 60 : 40 solution. With  $Z = OCH_3$ , the product is not stable in the medium and polycondensation is observed.

(iii) With the highly electron-attracting substituents ( $Z = CN$ ,  $NO_2$ ) the exchange did not succeed. Several attempts using higher concentrations of  $HF$  or  $F^-$ , higher temperatures or longer reaction times failed. The alcohols were recovered unchanged from the reaction.

In conclusion, the method seems to adapt well to the fluorination of II when the Hammett coefficient for  $Z$  is within the interval  $-0.2$  to  $+0.4$ . For higher values the reactivity of the corresponding alcohol is too low. For lower values polycondensation of the fluorides occurs in the acidic reaction medium.

### Experimental

The chlorohydrins (II) were obtained by reduction of the corresponding  $\omega$ -chloroacetophenones (III) with sodium borohydride in an alcoholic medium (methanol or ethanol according to the solubility of the ketone). Compounds III were obtained by acylation of the corresponding substituted benzenes according to conventional procedures.

Alcohol (II) (0.1 mole) was added dropwise with stirring (Teflon coated magnetic stirring bar) at room temperature to the 70% hydrogen fluoride/30% pyridine reagent (50 g) in a Kel-F flask. The times necessary to effect the reaction were determined by g.l.c. (Inter-smat IGC 12) using a 1 m SE 30 column with helium as a vector gas (30 ml/min). The reaction mixture was then poured into 200 ml of cold water and extracted three times with 25 ml of ether. The ether layer was washed to neutrality with 10% potassium hydroxide solution, with pure water, and then with saturated sodium chloride solution. It was then dried with a sulfate. The solvent was evaporated and the product was isolated by distillation under reduced pressure.

The fluorides obtained are all colorless liquids. The stability varies and the effective yields after distillation are from 80% for stable compounds ( $Z = \text{Cl, Br}$ ) to 50%<sub>be</sub> for less stable ones ( $Z = \text{CH}_3$ ). The compound with  $Z = \text{OCH}_3$  could not be obtained. The compounds were stored at low temperature in the absence of light.

Microanalysis for C, H, Cl and F gave satisfactory results for all of the stable products ( $Z = \text{H, F, Cl, Br}$  and 2-4  $\text{Cl}_2$ ). The I.R. spectra (BECKMANN Acculab 4) and the  $^1\text{H}$  NMR spectra (PERKIN-ELMER R 24 A at 60 MHz) were in agreement with the assigned structures ( $2J_{\text{HF}} \sim 47,5 \text{ Hz}$  and  $3J_{\text{HF}} \sim 20 \text{ Hz}$ ). A detailed analysis of the  $^1\text{H}$ ,  $^{19}\text{F}$  and  $^{13}\text{C}$  spectra in order to determine the preferred conformation is in progress.

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