Synthetic Methods and Reactions XV[1]. Convenient Dediazoniative Hydrofluorination and Halofluorination of Diazoalkanes and Diazoketones in Pyridinium Polyhydrogen Fluoride Solution

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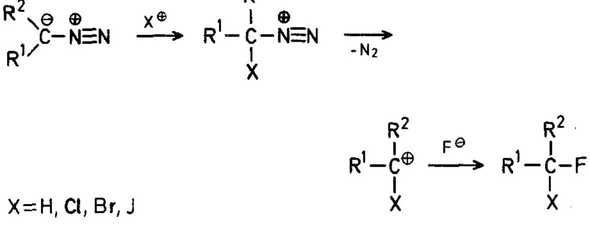
The chemistry and preparative utility of diazoalkanes have been thoroughly reviewed[2]. The preparation of halogenated alkanes by the reaction of a diazoalkane with hydrogen halides was first utilized by Curtius[3a] in 1888 in the reactions of diazomethane. Pechmann extended these reactions to include molecular iodine[3b]. Wolff later reported the reaction of diazoacetates with iodine to form the diiodomethyl acetate[4]. Subsequently Arndt and Eistert reported the reaction of diazoketones to form haloketones[5]. The preparation of fluoro-[6], chloro-[7], bromo-[8], and iodo-substituted[9] ketones from diazoketones has been studied by various investigators.

We report now a convenient, improved preparation of α-halogenated ketones from diazoketones as well as the preparation of haloalkanes from diazoalkanes by their reactions with halide ions in 70% polyhydrogen fluoride/pyridine solution[10] at 0°. Data for the halogenation and hydrohalogenation of diazoalkanes and diazoketones are summarized in the Table. Diazomethane, prepared from nitrosomethyl urea[2c,2g,11], diazoketones prepared from acyl chlorides and diazomethane[2c,12], phenyldiazomethane prepared from benzylhydrazine[13], and commercially available diazoalkanes were reacted with alkali halides and/or *N*-halosuccinimides in polyhydrogen fluoride/pyridine solution. The reaction of aliphatic diazo compounds is considered to involve initial electrophilic attack on the diazoalkane followed by concommitant loss of nitrogen and nucleophilic attack on the incipient carbocation by fluoride ion.



Typical are the preparations of ethyl bromofluoroacetate, α-fluoroacetophenone and α-bromo-α-fluoroacetophenone.

Ethyl Bromofluoroacetate:

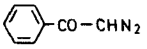
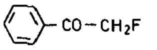
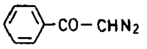
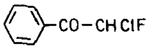
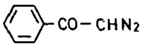
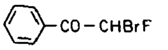
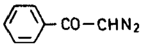
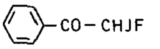
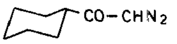
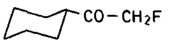
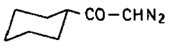
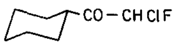
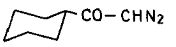
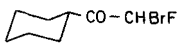
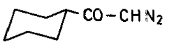
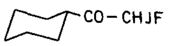
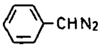
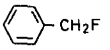
Into a well stirred solution of 70% hydrogen fluoride/pyridine (20 ml) and ether (20 ml) was added *N*-bromosuccinimide (5.31 g, 0.03 mol) at 0°. Ethyl diazoacetate (2.3 g, 0.02 mol) dissolved in ether (10 ml) was then added in 10 min and the reaction mixture was held at 0° for 20 min. The mixture was poured into ice/water and extracted with ether. The ether layer was washed with water, aqueous sodium hydrogen carbonate, water, and dried over anhydrous sodium sulfate. The ether was evaporated and the product obtained by distillation; yield: 1.9 g (50%); b.p. 68°/34 torr.

$C_4H_6BrFO_2$	calc.	C 26.0	H 3.2	Br 42.9	F 10.3
(184.9)	found	26.2	3.3	41.3	10.3

α-Fluoroacetophenone:

In a polyethylene bottle 70% hydrogen fluoride/pyridine (100 ml) was magnetically stirred at −15°. Diazoacetophenone (7.0

Table. Dediazoniative Hydrofluorination and Halofluorination of Diazoalkanes and Diazoketones in Polyhydrogen Fluoride/Pyridine Solution

Diazoalkane	Halide	Product	Yield (%)	M.p.	B.p
	-		32		50°/0.15 torr
	Cl		49	45°	—
	Br		63	55°	—
	J		62	70–72°	
	-		50	—	27°/0.4 torr
	Cl		95	—	70°/1.2 torr
	Br		38	—	30°/0.1 torr
	J		80	—	45°/0.9 torr
$C_2H_5-CO-CHN_2$	-	$C_2H_5-CO-CH_2F$	40	—	50°/5 torr
$C_2H_5-CO-CHN_2$	Cl	$C_2H_5-CO-CHClF$	50	—	40°/15 torr
$C_2H_5-CO-CHN_2$	Br	$C_2H_5-CO-CHBrF$	32	—	49°/2.4 torr
$C_2H_5-CO-CHN_2$	J	$C_2H_5-CO-CHJF$	80	—	170°/4 torr
$C_2H_5O-CO-CHN_2$	–	$C_2H_5O-CO-CH_2F$	40	—	117–118°
$C_2H_5O-CO-CHN_2$	Cl	$C_2H_5O-CO-CHClF$	30		100°
$C_2H_5O-CO-CHN_2$	Br	$C_2H_5O-CO-CHBrF$	50	—	68°/34 torr
$C_2H_5O-CO-CHN_2$	J	$C_2H_5O-CO-CHJF$	50	—	68–72°/14 torr
	–		70		145° (decomp.)

g, 0.05 mol, prepared by the method of Eistert) in ether (250 ml) was added while the temperature of the reaction mixture (determined by a teflon jacketed thermometer) was not allowed to exceed 0°. The mixture was then allowed to warm to room temperature over a period of 2 h with continued stirring. The product was isolated by extraction of the reaction mixture with pentane (350 ml). Remaining hydrogen fluoride was removed by treatment with anhydrous potassium fluoride and sodium sulfate. Evaporation of the solvent gave the product, α-fluoroacetophenone; yield: 3.5 g (51% based on benzoyl chloride); b.p. 62°/0.5 torr.

C_8H_7FO	calc.	C 69.5	H 5.0	F 14.0
(138.1)	found	68.9	4.9	14.4

The product α-fluoroacetophenone must be carefully freed from acid as it condenses with itself readily.

α-Bromo-α-fluoroacetophenone:

N-Bromosuccinimide (12 g, 0.07 mol) was dissolved in 70% hydrogen fluoride/pyridine (100 ml) with magnetic stirring in a polyethylene bottle at −15°. α-Diazoacetophenone (7.0 g, 0.05 mol) in ether (250 ml) was then added in the manner described above. The product was isolated as described previously; yield: 6.2 g (63%); m.p. 70–72° (recrystallized from petroleum ether).

C_8H_6BrFO	calc.	C 44.4	H 2.7	F 8.7	Br 36.5
(217.0)	found	44.8	2.8	9.1	36.4

All products had expected ^1H- and ^{19}F-N.M.R. spectra and gave satisfactory elemental analyses.

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