Interaction of polyfluoroalkyl-containing aziridinyl ketones with hydrogen halides

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Polyfluoroalkyl-containing aziridinyl ketones, unlike their nonfluorinated analogs, react with hydrogen halides to give only α-halo-β-aminoketones or their hydrogen halide salts. Thermal decomposition of the latter in the case where Hal = Cl affords α-chlorovinyl ketones.

Key words: polyfluoroalkyl-containing aziridinyl ketones, α-halo-β-aminoketones, α-chlorovinyl ketones.

Aziridines are known to be cleaved by hydrogen halides to give β-haloalkylamines.[1] In the present work we have studied the reactions of HCl and HBr with polyfluoroalkyl-containing aziridinyl ketones (**1**) prepared by us previously[2] (characteristics of the compounds that have not been described previously are given in the Experimental section).

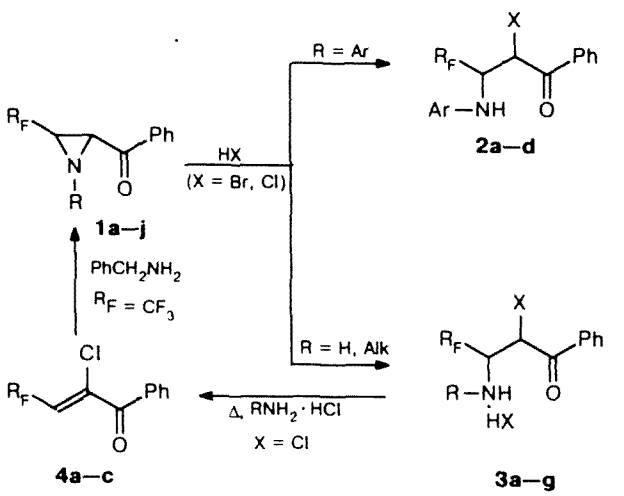
These reactions involving nonfluorinated aziridinyl ketones afford, as a rule, mixtures of hydrogen halide salts of α-halo-β-aminoalkylketones and α-aminoalkyl-β-haloketones in a ratio depending on the reaction conditions, in particular, on whether gaseous hydrogen halide or its aqueous solution is used.[3]

We found that the reaction of compound **1** with HCl and HBr is accompanied by cleavage of only the C(3)—N bond of the aziridine ring irrespective of the reaction conditions (Scheme 1). When R = H or Alk, hydrogen halide salts of α-halo-β-aminoketones (**3**) are obtained (Table 1). When R = Ar, the basicity of the amino group is insufficient for the formation of the salts, and, therefore, α-halo-β-aminoketones (**2**) are formed as free bases (Table 2). The yields were quantitative in both cases.

Compounds **3** were obtained as mixtures of two diastereomers in a 1:1 ratio (two H_α doublets in the ^1H NMR spectra (Table 1)). Free aminoketones **2** were isolated as single diastereomers.

Polyfluoroalkyl-containing β-aminoketones are stable only in the case where the amino group is unsubstituted or carries an aryl substituent. *N*-Alkylaminoketones decompose on attempted isolation.[2] In our case, the formation of the salts increases the stability of compounds **2**. However, when compounds **2** (X = Cl) are gradually heated to 240 °C, they abstract amine hydrochloride to give polyfluoroalkyl-containing α-chlorovinyl ketones (**4**) in nearly quantitative yields. On the one hand, this reaction is additional evidence for the α-position of the halogen in compounds **2**, and, on the other hand, it is a method for preparing compounds **4**, which, by analogy

Scheme 1



Compound	R_F	R	Compound	R_F	R	X
1a	CF_3	H	**3a**	CF_3	H	Cl
1b	CF_3	n-C_6H_{13}	**3b**	CF_3	n-C_6H_{13}	Cl
1c	CF_3	$HO(CH)_2$	**3c**	CF_3	$HO(CH)_2$	Br
1d	CF_3	Me	**3d**	CF_3	Me	Cl
1e	C_6F_{13}	$PhCH_2$	**3e**	C_6F_{13}	$PhCH_2$	Br
1f	$H(CF_2)_6$	Me	**3f**	$H(CF_2)_6$	Me	Cl
1g	C_8F_{17}	Me	**3g**	C_8F_{17}	Me	Cl
1h	HCF_2	Ph				
1i	C_3F_7	4-MeC_6H_4	**2a**	HCF_2	Ph	Cl
1j	CF_3	Ph	**2b**	C_3F_7	4-MeC_6H_4	Br
			2c	C_3F_7	4-MeC_6H_4	Cl
4a	CF_3	—	**2d**	CF_3	Ph	Cl
4b	C_8F_{17}	—				
4c	$H(CF_2)_6$	—				

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Table 1. Hydrogen halide salts of α-halo-β-aminoketones **3**

Compound	R_F	R	X	M.p./°C (with dec.)	IR, ν/cm^{-1}		^{1}H NMR (DMSO-d_6, δ)			
					C=O	NH·HX	H_α	H_β	NH_2X	R
3a	CF_3	H	Cl	176—180	1667	2833	6.42 d 6.91 d	4.87—5.02 m	7.37—8.06 m	7.37—8.06 m
3b	CF_3	n-C_6H_{13}	Cl	125—130	1695	2670	6.35 d 7.02 d	4.97—5.35 m	7.49—8.17 m	0.87 (m, CH_3), 1.22—1.50 (m, C_3H_6), 1.95—2.17 (m, CH_2), 3.31—3.50 (m, NCH_2)
3c	CF_3	$(CH_2)_2OH$	Br	105—109	1705	2650	6.35 d 6.92 d	5.37—5.57 m	7.52—8.22 m	3.59—3.75 (m, CH_2OH), 3.99—4.24 (m, NCH_2)
3d	CF_3	Me	Cl	247—249	1687	2673	6.41 d 6.58 d	4.42—4.79 m	7.57—7.95 m	2.30—2.59 (m, CH_3)
3e	C_6F_{13}	$PhCH_2$	Br	86—90	1690	2680	6.20 br.d	4.10—4.43 m	7.21—8.10 m	7.21—8.10 (m, Ph), 3.73—3.99 (m, CH_2)
3f	$H(CF_2)_6$	Me	Cl	112—116	1702	2714	6.17 br.d	4.87—5.23 m	8.02—8.12 m	2.28—2.46 (m, CH_3)
3g	C_8F_{17}	Me	Cl	129—134	1705	2710	6.33 br.d	4.32—4.76 m	9.17 br.s	2.40—2.70 (m, CH_3)

Table 2. α-Halo-β-aminoketones (**2**)

Compound	R_F	Ar	X	M.p./°C	IR, ν/cm^{-1}		^{1}H NMR ($CDCl_3$, δ)			
					N—H	C=O	H_α, d	H_β, m	NH	R
2a	HCF_2	Ph	Cl	107.0—107.5	3370	1672	5.26	4.38—4.74	4.11 br.s	6.71—7.26 m
2b	C_3F_7	4-$CH_3C_6H_4$	Br	125.5—126.0	3358	1680	5.59	4.78—5.04	5.42 br.s	2.25 s, 6.86 q
2c	C_3F_7	4-$CH_3C_6H_4$	Cl	133.0—133.4	3355	1678	5.53	4.80—5.09	4.80—5.09 m	2.25 s, 6.85 q
2d	CF_3	Ph	Cl	109.5—110.0	3380	1673	5.43	4.60—4.88	4.60—4.88 m	7.14—7.24 m

Table 3. α-Chlorovinyl ketones **4**

Compound	R_F	IR, ν/cm^{-1}	^{1}H NMR ($CDCl_3$, δ)			Isomer ratio	Yield (%)
		C=O, C=C	H_β	$J_{H_\beta R_F}$/Hz	Ph, m		
4a	CF_3	1675 1647	6.29 q 6.54 q	7.51 7.04	7.36—7.97	1.9:1	92
4c	C_8F_{17}	1676 1640	6.28 t 6.47 t	14.1 12.9	7.38—7.99	2.3:1	88
4d	$H(CF_2)_6$	1679 1635	6.29 t 6.42 t	14.0 12.7	7.39—8.00	1.6:1	86

with α-bromovinyl ketones, can be valuable synthons.[4] Unlike α-bromovinyl ketones existing as one isomer,[4] compounds **4** are formed as mixtures of geometrical isomers, which is indicated by the double set of signals

corresponding to the β-proton in their ^{1}H NMR spectra (Table 3). Compounds **4** like α-bromovinyl ketones react with amines to yield the corresponding aziridinyl ketones.

Experimental

IR spectra were recorded on a Specord 75 IR spectrophotometer (in films for liquids and in pastes in Vaseline oil for solids). The ^{1}H NMR spectra were recorded on a Tesla BS-567A spectrophotometer, 100 MHz.

3-Benzoyl-2-trifluoromethylaziridine (1a), m.p. 65.0—65.5 °C. Found (%): C, 55.65; H, 3.97; F, 26.38; N, 6.52. $C_{10}H_8F_3NO$. Calculated (%): C, 55.82; H, 3.75; F, 26.49; N, 6.51. IR (Vaseline oil), ν/cm^{-1}: 1667 (C=O); 3187 (NH). ^{1}H NMR ($CDCl_3$), δ: 2.25—2.49 (m, 1 H, NH); 2.62—2.86 (m, 1 H, H_β); 3.65 (dd, 1 H, H_α, $J_{H_\alpha H_\beta}$ = 2.53 Hz, $J_{H_\alpha NH}$ = 7.50 Hz); 7.46—8.11 (m, 5 H, COPh).

3-Benzoyl-2-difluoromethyl-1-phenylaziridine (1h), m.p. 122.0—122.5 °C. Found (%): C, 70.59; H, 4.80; F, 13.89; N, 4.94. $C_{16}H_{13}F_2NO$. Calculated (%): C, 70.32; H, 4.79; F, 13.90; N, 5.13. IR (Vaseline oil), ν/cm^{-1}: 1663 (C=O). ^{1}H NMR ($CDCl_3$), δ: 3.35—3.58 (m, 1 H, H_β); 4.22 (d, 1 H, H_α, $J_{H_\alpha H_\beta}$ = 2.35 Hz); 5.77 (td, 1 H, HCF_2, J_{HCF_2} = 52.0 Hz, $J_{HCF_2CF_2}$ = 4.8 Hz); 6.76—7.24 (m, 5 H, NPh); 7.39—8.06 (m, 5 H, COPh).

3-Benzoyl-1-(4-methylphenyl)-2-perfluoropropylaziridine (1i), m.p. 62.0—62.5 °C. IR (Vaseline oil), ν/cm^{-1}: 1672 (C=O). ^{1}H NMR ($CDCl_3$), δ: 2.19 (s, 3 H, CH_3); 3.74 (br.t, 1 H, H_β, $J_{H_\beta CF_2}$ = 10.1 Hz); 4.36 (d, 1 H, H_α, $J_{H_\alpha H_\beta}$ = 2.35 Hz); 6.66—7.00 (m, 4 H, NC_6H_4); 7.09—7.89 (m, 5 H, COPh).

3-Benzoyl-1-benzyl-2-perfluorohexylaziridine (1e), m.p. 55.0—55.5 °C. Found (%): C, 48.40; H, 2.82; F, 43.89; N, 2.46. $C_{22}H_{14}F_{13}NO$. Calculated (%): C, 47.58; H, 2.54; F, 44.47; N, 2.52. IR (Vaseline oil), ν/cm^{-1}: 1667 (C=O). ^{1}H NMR ($CDCl_3$), δ: 3.33 (br.t, 1 H, H_β, $J_{H_\beta CF_2}$ = 10.2 Hz); 3.88 (q, 2 H, CH_2, $J_{H_\alpha H_\beta}$ = 13.38 Hz); 3.89 (d, 1 H, H_α, $J_{H_\alpha H_\beta}$ = 2.58 Hz); 7.09—7.89 (m, 10 H, 2Ph).

3-Benzoyl-2-(1,1,2,2,3,3,4,4,5,5,6,6-dodecafluorohexyl)-1-methylaziridine (1f), oil. Found (%): C, 41.70; H, 2.62; F, 49.46; N, 2.85. $C_{16}H_{11}F_{12}NO$. Calculated (%): C, 41.66; H, 2.40; F, 49.43; N, 3.04. IR (film), ν/cm^{-1}: 1667 (C=O). ^{1}H NMR ($CDCl_3$), δ: 2.52 (s, 3 H, CH_3); 3.05 (td, 1 H, H_β, $J_{H_\beta CF_2}$ = 11.3 Hz); 3.85 (d, 1 H, H_α, $J_{H_\alpha H_\beta}$ = 2.58 Hz); 6.08 (tt, 1 H, HCF_2, J_{HCF_2} = 51.88 Hz, $J_{HCF_2CF_2}$ = 5.16 Hz); 7.42—8.12 (m, 5 H, COPh).

General procedure for the reactions of aziridinyl ketones 1 with gaseous hydrogen halides. A flow of dry hydrogen halide was passed through an ethereal solution of aziridinyl ketone **1** (the reaction was monitored by TLC). After that, if compounds **3** were obtained, the resulting precipitate was filtered off, washed with hexane on the filter, and dried in air. In the case of compounds **2**, the ether was evaporated, and the residue was recrystallized from hexane.

General procedure for the reactions of aziridinyl ketones 1 with hydrochloric or hydrobromic acid. A 2.5—3-fold molar excess of hydrochloric or hydrobromic acid was added to an acetone solution of aziridinyl ketone **1**, the mixture was kept for 2 h at −20 °C with shaking from time to time, and the solvent was evaporated to dryness. After that, to isolate compounds **3**, the residue was washed on the filter with hexane and dried in air. In the case of compounds **2**, the residue was recrystallized from hexane.

General procedure for thermal decomposition of compounds 3. Dry salt **3** was heated in an oil bath, the temperature being gradually increased to 240 °C, kept at this temperature for 10 min, cooled, triturated in hexane, and filtered through a layer of silica gel. Evaporation of the hexane gave compounds **4** as light yellow oils.

Reaction of 1-phenyl-4,4,4-trifluoro-2-chlorobut-2-en-1-one with benzylamine. Benzylamine (2.79 g, 26 mmol) was added to a solution of 1-phenyl-4,4,4-trifluoro-2-chlorobut-2-en-1-one **(4a)** (2.0 g, 8.5 mmol) in 20 mL of methanol, and the mixture was kept for 24 h, poured into water, and extracted with chloroform. The extract was dried with $MgSO_4$ and concentrated, and the residue was recrystallized from hexane to give 2.25 g (87%) of 1-benzyl-2-trifluoromethyl-3-benzoylaziridine **1** identical to an authentic sample.

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