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Microscale Preparation of Isotopically Enriched ^{37}ClHC=CHF

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ABSTRACT

Chlorination of 1-bromo-2-fluoroethylene followed by reductive dehalogenation of the produced 1-bromo-1,2-dichloro-2-fluoroethane selectively affords 1-chloro-2-fluoroethylene. This process is suitable to produce ^{37}Cl isotopically enriched ClHC=CHF on a convenient scale (3.8 mmol).

Key Words: Fluoroalkenes; Isotopic labeling; ClHC=CHF; Reductive dehalogenation.

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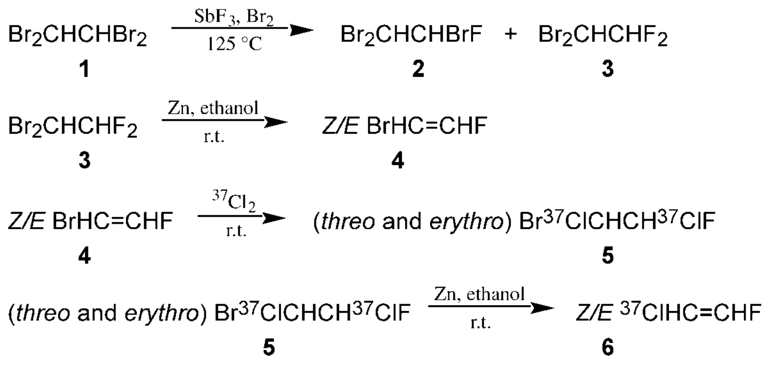
INTRODUCTION

Natural chlorine exists as a mixture of the two stable isotopes ^{35}Cl and ^{37}Cl, in abundance of 75.4% and 24.6%, respectively. These isotopes are incorporated into molecules and equilibria among isotopically substituted molecules (isotopomers) reflect the background isotopic ^{35}Cl/^{37}Cl ratio.

Recent literature contains some spectroscopic studies of gas-phase high-resolution infrared spectra of the natural *cis*-1-chloro-2-fluoroethylene, which are limited to the more abundant *cis*-^{35}ClHC=CHF isotopomer owing to the scarcity of the *cis*-^{37}ClHC=CHF in an ordinary specimen.[1–3] Therefore, isotopically enriched *cis*-^{37}ClHC=CHF has been regarded as necessary in order to obtain reliable spectroscopic parameters by measurements.[1–3]

Previously, many methods have been used to synthesise ClHC=CHF,[1–8] which are not suitable for the preparation of 37-chlorine isotopically enriched samples. At variance, this method, involving the ^{37}Cl-chlorination of 1-bromo-2-fluoroethylene to 1-bromo-1,2-(dichloro-^{37}Cl)-2-fluoroethane, followed by reductive 1,2-elimination of Br^{37}Cl, does afford a *Z-E* diastereoisomeric mixture of 1-(chloro-^{37}Cl)-2-fluoroethylene. Since the key intermediate reagent BrHC=CHF is not commercially available, it was prepared with a slight modification of the reported method (Sch. 1).[9,10]

Since hitherto, to the best of my knowledge, isotopically enriched ^{37}ClHC=CHF preparation has not been reported, this work describes a simple method able to afford this species on a convenient scale (3.8 mmol).



Scheme 1.

RESULTS

Fluorination of 1,1,2,2-tetrabromoethane (**1**) by $SbF_3{-}Br_2$ mixture ("Swarts reagent") gave a mixture of 1,1,2-tribromo-2-fluoroethane (**2**), 1,1-dibromo-2,2-difluoroethane (**3**) and unreacted **1**,[9,10] which was somewhat difficult to separate into its components. During fluorination in a closed reactor, the presence of the most volatile product **3** was periodically checked by gas-phase IR spectroscopy.[11] After separation, the more abundant and pure fluorinated ethane **3** was reacted with zinc in absolute ethanol to afford a cis–trans mixture of $BrHC{=}CHF$ (**4**). Traces of vinyl fluoride and acetylene were identified by IR spectroscopy[12,13] in the raw **4** into the reaction vessel. Vinyl fluoride formation may be attributed to the presence of $BrCH_2CHBrF$ in the sample of **3** owing to the fluorination of traces of $BrCH_2CHBr_2$ likely contained in the starting $Br_2CHCHBr_2$.

Since it has been reported that the *trans*-$BrHC{=}CHF$ is quite sensitive to polymerization even at room temperature,[14] **4** was stored under vacuum at −20°C in the dark and checked by IR spectroscopy just before the chlorination.[9,15]

At first, in order to perform exploratory syntheses with the most stable cis-isomer and natural chlorine, the two isomers of **4** were separated. Later on, as a cis-trans isomerization occurred during the first step of *cis*-$BrHC{=}CHF$ chlorination, the isomeric mixture **4** was used as reactant in the present preparation and $Br^{37}ClCHCH^{37}ClF$ (**5**) was obtained without olefin polymerization.

As far as the cis-trans isomerization of *cis*-$BrHC{=}CHF$ is concerned, its nature is similar to iodine-catalyzed gas-phase isomerization reported for other *cis*-1-2-dihaloethylenes.[16,17]

When, in a separated experiment, chlorination reaction of **4** was performed in the presence of air and light, the olefin oxidation was observed. This oxidation reaction should be similar to the chlorine-initiated photochemical oxidation previously reported for other halogenated ethylenes.[18,19] Therefore, in order to obtain $Br^{37}ClCHCH^{37}ClF$ (**5**), 37-Chlorine addition to $BrCH{=}CHF$ (**4**) was performed under vacuum and at minimized light level conditions.

The sample of (**5**) obtained by chlorination of **4** is a *threo* and *erythro* isomeric mixture of $Br^{37}ClCHCH^{37}ClF$. These diastereoisomers were characterized by NMR spectroscopy.[20,21] Gas-phase infrared data for **5**, not published in the literature, are reported in Experimental section. Furthermore, it was observed that 1,2-elimination reaction of **5** with zinc in absolute ethanol is totally selective and affords, as the only product, the requested compound $^{37}ClHC{=}CHF$ (**6**). It is known that the equilibrium composition of the $ClHC{=}CHF$ isomeric mixture is 70% cis- and 30% trans-isomer.[9]

In order to check ^{37}Cl enrichment in **6**, the $^{35/37}$Cl splitting was estimated from the *Q*-branches (central part) of the ν_8 and ν_7 gas-phase IR bands for the *cis*-isomer, where the isotope effect can be observed even with medium resolution IR spectroscopy.[5] In the IR spectrum of the natural *cis*-ClHC=CHF ν_8 and ν_7 show two *Q*-branches and for every band the most intense peak is located at a greater wavenumber. *Q*-branches of ν_8 and ν_7 for *cis*-^{35}ClHC=CHF are located at 655.7 and 811.6 cm^{-1}, while for *cis*-^{37}ClHC=CHF they are at 651.8 and 808.7 cm^{-1}, respectively. In the IR of **6** both ν_8 and ν_7 for the *cis*-isomer exhibit only one intense *Q*-branch at 651.8 and 808.7 cm^{-1}, respectively, which is consistent with an 95% abundance of ^{37}Cl incorporated into **6**. In summary, this convenient method for ^{37}ClHC=CHF preparation should be useful in the spectroscopic field.

EXPERIMENTAL

The expensive isotopically enriched Na^{37}Cl salt (95% stated isotopic enrichment) was obtained from Stable Isotopes Icon (Summit, NJ, USA). Br_2-CHCHBr$_2$ (98%), SbF$_3$ (99.8%), Br$_2$ (99%) and zinc dust (98%) were obtained by Sigma–Aldrich and used without further purification. Pure cis- and trans-isomers of the natural ClHC=CHF were prepared, separated and purified as reported previously.[7] All of the products prepared in the present research are known compounds and were characterized by comparison of their spectral data (NMR, IR) and Boiling Points with those reported in the literature.[4,5,9–12,14,15,20–22] Gaseous compounds were handled in a mercury-free vacuum line of known volume fitted with a manometer. Krytox (perfluoropolyether) LVP high-vacuum grease (E.I. Du Pont de Nemours) was used on stopcocks and joints coming to contact with chlorine. Proton NMR spectra were recorded on a Bruker AC 200 instrument. Survey midrange IR spectra were taken as vapors in a 16-cm gas cell, equipped with KBr windows, on a Bruker Vector 22 FT-IR spectrometer operating at 0.5 cm^{-1} resolution.

Preparation of *Z*- and *E*-1-bromo-2-fluoroethylene (4). (**1**) 116 g (0.336 mol) was treated with a mixture of SbF$_3$ 20 g (0.112 mol) and Br$_2$ 17.9 g (0.112 mol) in a closed steel reactor at 120–125°C for 23 hr. Into a separating funnel, the raw product was washed successively with 20% HCl, 20% L-tartaric acid, 30% $Na_2S_2O_3 \cdot 5H_2O$ and water, to remove the SbBr$_3$ and Br$_2$. The reaction mixture is more dense than water and so it lies below the aqueous layer. The separated organic phase was dried over anhydrous MgSO$_4$ and filtered. After fractionation, both **2** (10.6 g, 0.037 mol, 11%) b.p.$_{17}$: 74–84°C [lit.[9] b.p.$_{24}$: 74–78°C] and **3** (14.4 g, 0.064 mol, 19%) b.p.: 107°C [lit.[9,10] 107°C, 106.8°C] were obtained. Compound **3** (14.4 g, 0.064 mol) was treated with zinc dust in absolute ethanol at room temperature.

After 10 min, the reaction mixture was distilled to give **4** (7 g, 0.056 mol, 87%) b.p.: 25–39°C [lit.[10] 36.5°C]. *cis*-BrHC=CHF used in the exploratory chlorination reactions was obtained as follows: compound **4** was vacuum transferred into a coil of Pyrex tubing merged in a −105°C 1-propanol/liquid nitrogen slush bath. The coming out vapor from the coil was closely checked by IR spectroscopy[9,15] and collected into reservoirs using liquid nitrogen. *cis*- and *trans*-BrHC=CHF samples were trapped from −86°C to −80°C and from −98°C to −95°C, respectively. *cis*-BrHC=CHF b.p. 39.4°C [lit.[9,14] 39.5°C, 39.8°C], *trans*-BrHC=CHF b.p. 20°C [lit.[9,14] 20°C, 19.8°C].

Preparation of *Z*- and *E*-1-(chloro-^{37}Cl)-2-fluoroethylene (**6**). $^{37}Cl_2$ was prepared from Na^{37}Cl in vacuo,[23] by a slight modification of the reported method to produce radioactive $^{36}Cl_2$.[24] With a minimized light level in the room, compound **4** (0.473 g, 3.8 mmol) was chlorinated with dry gaseous $^{37}Cl_2$ 0.287 g (3.9 mmol) into an evacuated flask wrapped in aluminium foil. The reaction was performed at room temperature under vacuum by periodically adding small amounts of gaseous $^{37}Cl_2$ to the olefin **4**. The chlorine additions were accomplished by monitoring the halogen pressure in the vacuum line and then freezing the sample into the flask using liquid nitrogen. After 1 hr, product **5** was obtained in quantitative yield. B.p. 123.8–125°C [lit.[21] *threo*-1-bromo-1,2-dichloro-2-fluoroethane b.p. 123°C; 85% *erythro*- and 15% *threo*-1-bromo-1,2-dichloro-2-fluoroethane b.p. 126°C], IR (vapour) ν: 3014 w, 2988 w, 1346 w, 1285 w, 1174 w, 1122.5 m, 1091 (doublet) s, 1067.5 w, 1059 m, 1042 m, 813 s, 793 (doublet) s, 761.7 s, 701 m, 674.5 s, 565 w, 543 w cm^{-1}. Compound **5**, collected as liquid on the bottom of the flask, was vacuum transferred into an evacuated reservoir cooled to liquid nitrogen temperature and containing a zinc dust/absolute ethanol mixture. The reaction mixture was brought to room temperature and, after 10 min, the formed 1-(chloro-^{37}Cl)-2-fluoroethylene (**6**) was separated from the ethanolic mixture by trap-to-trap condensation under dynamic vacuum from −115°C to −95°C (Isopentane/liquid nitrogen slush bath). The other product, Zn Br^{37}Cl, was recovered from the residual solution by ethanol evaporation. (**6**) b.p. 10°C [lit.[4] 10–11°C]. ^{37}ClHC=CHF (**6**) yield was estimated at 79%, assuming ideal behavior for the gas.

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