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# TRIS(2,2,2-TRIFLUOROETHYL)AMINE AND ITS REACTIONS WITH HALOGENS

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## SUMMARY

The reaction of $NH_3$ with $C_4F_9SO_2OCH_2CF_3$ has been shown to yield, depending on the molar ratio, $F_3CCH_2NH_2$, $(F_3CCH_2)_2NH$ and the novel tertiary amine $(F_3CCH_2)_3N$ (III). Halogenation of (III) with $Br_2$ and $Cl_2$ at the $\alpha$-position formed $(F_3CCH_2)_2NCBrHCF_3$ , $F_3CCH_2N(CBrHCF_3)_2$ and $N(CClHCF_3)_3$ . Compound (III) was found to be extremely toxic with a strong anesthetic effect accompanied by convulsions.

## INTRODUCTION

Selective routes to incompletely fluorinated tertiary amines are not known, as commonly used methods like electrochemical or direct fluorination yield preferentially perfluorinated material. Partially fluorinated amines like $(F_3CCH_2)_3N$ are suitable for selective halogenation and halide exchange reactions, the products $(F_3CCF_2)_nN(CHFCF_3)_{3-n}$ ( n = 0,1,2 ) in mind being potentially reactive precursors for perfluorovinyl amines $(F_3CCF_2)_nN(CF{=}CF_2)_{3-n}$ ( n = 0,1,2 ) . Two routes starting from readily available material seemed to be possible for the synthesis of $(F_3CCH_2)_3N$:

i) the reduction of $(F_3CCH_2)_2NCOCF_3$ (I) with $LiAlH_4$ by analogy to the formation of $(H_3CCH_2)_3N$ [1],
ii) the alkylation of $NH_3$ with 2,2,2-trifluoroethylesters of strong acids by analogy to the synthesis of $(F_3CCH_2)_2NH$ from $p\text{-}H_3CC_6H_4SO_2OCH_2CF_3$ and $F_3CCH_2NH_2$ [2].

We have investigated both routes and report in the following on our results.

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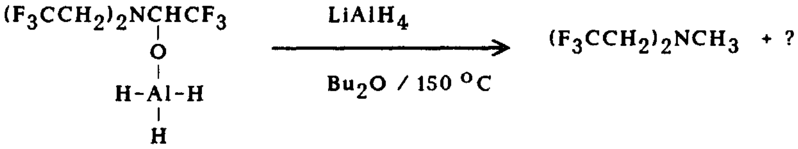
## RESULTS

When (I), which we obtained from $(F_3CCH_2)_2NH$ and $F_3CCOCl$ in $NBu_3$ according to eq. (1), was reacted with $LiAlH_4$ ,

$$(F_3CCH_2)_2NH + F_3CCOCl \xrightarrow[-[HNBu_3]^+ Cl^-]{+NBu_3} (F_3CCH_2)_2NCOCF_3 \qquad (1)$$

a hydridoaluminate complex was formed. Its hydrolysis yielded unstable $(F_3CCH_2)_2NCH(OH)CF_3$ , which decomposed under the reaction conditions to form $(F_3CCH_2)_2NH$ and $F_3CC(OH)_2H$. If the reaction mixture was refluxed in $Bu_2O$, the carbon-carbon bond was cleaved, and $(F_3CCH_2)_2NCH_3$ (II) was obtained in 46 % yield according to eq. (2).



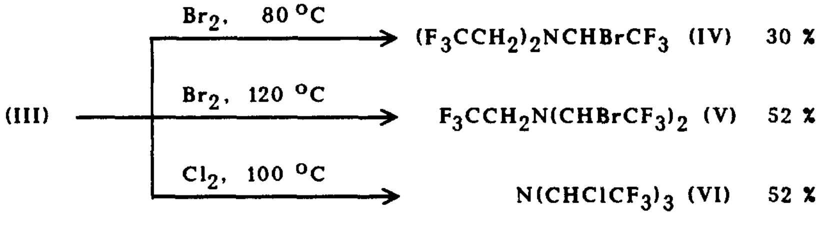
$$(F_3CCH_2)_2NCH(O{-}AlH_3)CF_3 \xrightarrow[Bu_2O\ /\ 150\ ^oC]{LiAlH_4} (F_3CCH_2)_2NCH_3 + ? \qquad (2)$$

The fate of the terminal $CF_3$ group, however, is not known.
Because a synthesis of $(F_3CCH_2)_3N$ (III) was not possible according to route (i), we investigated pathway (ii). Although it has been reported that $(F_3CCH_2)_2NH$ has been obtained by reacting $p\text{-}H_3CC_6H_4SO_2OCH_2CF_3$ with $F_3CCH_2NH_2$, formation of (III) has not been observed. We found that (III) is conveniently prepared from $NH_3$ and $C_4F_9SO_2OCH_2CF_3$ at 210 °C . If $C_4F_9SO_2OCH_2CF_3$ and $NH_3$ are reacted in a 3 : 1 ratio, $(F_3CCH_2)_2NH$ and (III) are obtained in nearly equal amounts according to eq. (3).

$$6\,NH_3 + 5\ C_4F_9SO_2OCH_2CF_3 \xrightarrow[4\ d]{210\ ^oC} \begin{array}{l} (III) + (F_3CCH_2)_2NH + 4\ NH_4^+ \\ + [F_3CCH_2NH_3^+] + 5\,[C_4F_9SO_3^-] \end{array} \qquad (3)$$

Unlike $F_3CCH_2NH_2$ and with some restrictions $(F_3CCH_2)_2NH$, (III) does not form a salt with the sulfonic acid formed in the course of the reaction. Thus (III) can be separated from other reaction products by condensation in vacuo. With the assistance of a base the above reaction could, in principle, be brought to completion, but no base was found which was less nucleophilic than $(F_3CCH_2)_2NH$.

Selective halogenation of (III) was achieved by treatment with $Br_2$ and $Cl_2$, and $(F_3CCH_2)_2NCHBrCF_3$ (IV), $F_3CCH_2N(CHBrCF_3)_2$ (V) and $N(CHClCF_3)_3$ (VI) were formed in reasonable yields according to eq. (4).



(4)

Bromination of all three $F_3CCH_2$ groups could not be achieved. On the other hand, the chlorination reaction could not be directed selectively to mono- and dichlorinated species.

## PROPERTIES

Compounds (I) to (VI) are colorless liquids at ambient temperature which, except for (I) and (IV), are resistant to hydrolysis. The tertiary amines (III), (IV),(V) and (VI) are poor bases; that is, they form no salts with strong acids like $F_3CSO_2OH$ or adducts with strong Lewis acids like $BBr_3$.

Warning! The amine (III) was found to be extremely toxic, and inhalation of a few mg caused sudden loss of consciousness accompanied by heavy convulsions. In this respect, (III) shows a related but obviously stronger effect than $(F_3CCH_2)_2O$, which has been used as a convulsive agent [ Indoklon® (Ohio Med. ) ] for the therapy of mental disorders [3]. As (III) is odorless, it must be handled in a well ventilated area.

Table 1 lists the NMR data of (I) to (VI). The two possible isomers of (V), racem- (RR,SS) and meso- (RS), are formed in a 8 : 1 ratio and exhibit quite different NMR spectra. The $CH_2$ group of racem- (V) appears as an AB spin system. At -40 °C, rotation around the N-CHBr bond is hindered, and two signals are observed for the CHBr groups. In contrast, only one signal is observed for the CHBr and $CH_2$ groups of meso-(V). For (VI), which exists in even more isomeric forms, only signals of the main component are given in Table 1.

TABLE 1

NMR spectra of compounds (I) to (VI) , δ in [ppm], J in [Hz]

| | (I) | (II) | (III) | (IV) | (V) racem/meso | (VI) |
|---|---|---|---|---|---|---|
| $^1H$ | | | | | | |
| δ $C\underline{H}_3$ | | 2.66 | | | | |
| δ $F_3CC\underline{H}_2$ | 4.19<br>4.25 | 3.22 | 3.46 | 3.28<br>3.48 | 3.10<br>3.74 / 3.64 | |
| δ $F_3CC\underline{H}$ | | | | 5.57 | 5.56 / 5.70 | 5.8 |
| $^{19}F$ | | | | | | |
| δ $\underline{F}_3CCH_2$ | -69.7<br>-70.0 | -71.0 | -71.5 | -70.8 | -70.2 / -69.2 | |
| δ $\underline{F}_3CCH$ | | | | -72.7 | -73.5 / -72.5 | -76.2 |
| δ $\underline{F}_3CCO$ | -68.5 | | | | | |
| $^{13}C$ | | | | | | |
| δ $F_3\underline{C}CH_2$ | 123.3<br>123.9 | 125.6 | 125.5 | 123.6 | 123.1 / 123.4 | |
| δ $F_3\underline{C}CH$ | | | | 120.6 | 120.7 / 120.9 | 122.2 |
| δ $F_3C\underline{C}H_2$ | 48.6<br>46.9 | 57.5 | 55.5 | 55.0 | 52.3 / 50.6 | |
| δ $F_3C\underline{C}H$ | | | | 72.5 | 65.5 / 64.2 | 70.1 |
| δ $F_3\underline{C}CO$ | 115.9 | | | | | |
| δ $F_3C\underline{C}O$ | 158.4 | | | | | |
| δ $H_3\underline{C}$ | | 43.0 | | | | |
| $^1J$ $(\underline{F}_3\underline{C}CH_2)$ | 280.0<br>280.0 | 281.7 | 280.7 | 278.5 | 278.2 / 279.4 | |
| $^1J$ $(\underline{F}_3\underline{C}CH)$ | | | | 279.0 | 279.5 / 281.6 | 280.4 |
| $^1J$ $(\underline{F}_3\underline{C}CO)$ | 286.6 | | | | | |
| $^2J$ $(\underline{F}_3C\underline{C}H_2)$ | 35.1<br>35.8 | 31.4 | 33.3 | 35.0 | 34.7 / 35.5 | |
| $^2J$ $(\underline{F}_3C\underline{C}H)$ | | | | 37.0 | 39.7 / 38.3 | 39.4 |
| $^2J$ $(F_3CC\underline{H}\underline{H})$ | | | | 16.4 | 16.3 | |
| $^3J$ $(\underline{F}_3CC\underline{H}_2)$ | 7.8<br>8.4 | 9.3 | 8.8 | 8.2 | 8.2 / 8.3 | |
| $^3J$ $(\underline{F}_3CC\underline{H})$ | | | | 5.9 | 5.7 | |
| $^1J$ $(F_3C\underline{C}\underline{H}_2)$ | 142.7<br>143.6 | 136.7 | 138.7 | | 141.4 | |
| $^1J$ $(F_3C\underline{C}\underline{H})$ | | | | | 162.5 | 162.3 |
| $^2J$ $(\underline{F}_3C\underline{C}O)$ | 38.1 | | | | | |
| $^1J$ $(\underline{H}_3\underline{C}N)$ | | 135.9 | | | | |
| $^2J$ $(F_3\underline{C}C\underline{H}_2)$ | 5.4<br>5.3 | 4.6 | 4.6 | | 6.6<br>3.7 / 4.9 | |
| $^2J$ $(F_3\underline{C}C\underline{H})$ | | | | | 5.4 / 5.3 | 5.4 |
| $^3J$ $(C\underline{H}_2N\underline{C})$ | 3.8 | 4.8 | 4.1 | | | |
| $^3J$ $(\underline{C}H_2NC\underline{H})$ | | 4.3 | | | 4.7 | |
| $^6J$ $(\underline{F}_3CCH_2/C\underline{F}_3)$ | 4.9 | | | 2.0 | 2.8 / 4.2 | |

Table 2 lists the specific fragments in the mass spectra of (I) to (VI), which have in common fragment m/e = 178 $(F_3CCHNCHCF_3)^+$ with different intensities, while the peaks m/e = 83 $(F_3CCH_2)^+$ and m/e = 110 $(F_3CCH_2NCH)^+$ are missing for (VI). The fragment $(F_3CCHX)^+$ (X=Cl,Br) is the basis peak for (VI) and strong for (V) too. Elimination of Br, Cl, $CF_3$ and F from the ion $M^+$ is important. For (IV), the elimination of $CF_2Br$ to form m/e = 212 (77) $((F_3CCH_2)_2NCHF)^+$ is dominant.

TABLE 2

EI mass spectra, m/e and relative intensities (%) of selected fragments

| | (I) | (II) | (III) | (IV) | (V) | (VI) |
|---|---|---|---|---|---|---|
| $M^+$ | 277(13) | 195(21) | 263(10) | | | 365(1) |
| $(M-X)^+$ X=F | 258(18) | | 244(2) | 322(2) | 400(1) | 436(1) |
| X=Cl | | | | | | 330(81) |
| X=Br | | | | 262(100) | 340(100) | |
| $(M-CF_3)^+$ | 208(100) | 126(100) | 194(100) | 272(5) | 350(1) | 296(17) |
| $(M-C_2F_5)^+$ | 158(17) | 76(27) | 144(38) | | | |
| $(F_3CCHNCHCF_3)^+$ | (7) | (2) | (14) | (17) | (47) | (70) |
| $(F_3CCH_2NCH)^+$ | (13) | (23) | (12) | (46) | (21) | |
| $(F_3CCHX)^+$ X=H | (18) | (8) | (11) | (36) | (15) | |
| X=Cl | | | | | | (100) |
| X=Br | | | | (10) | (92) | |

## EXPERIMENTAL

### Synthesis of the novel compounds (I)-(VI).

N-Bis(2,2,2-trifluoroethyl)-trifluoroacetamide (I) 20 g (151 mmol) $F_3CCOCl$ were slowly passed through a solution of 21 g (116 mmol) $(F_3CCH_2)_2NH$ in 150 ml $NBu_3$ at room temperature. The reaction mixture was distilled, and 25 g (I), bp. 120 °C, were obtained. Yield 78 %.

$C_6H_4F_9NO$. Required/found; %C, 26.00/26.25; %H, 1.46/1.60; %N, 5.06/5.16;
IR /Raman : 2990m/3065w, 2950w/3045w, 2920w/3000m, 1749s/1735s, 1185vs/1180w, 1130vs/1130m, 840m/835vs, -/785vs.

**N-Bis(2,2,2-trifluoroethyl)-methylamine (II)** 17.0 g (61 mmol) (I) were added to a suspension of 6.0 g (160 mmol) $LiAlH_4$ in 300 ml $Bu_2O$ at room temperature. The reaction mixture was refluxed for 16 h, and following addition of another 6 g of $LiAlH_4$, refluxing was continued for 8 h. Then (II) was distilled from the reaction mixture together with 100 ml of $Bu_2O$ and fractionated over a 50 cm slit tube column, bp. 81 °C. Yield 5.5 g (46 %). $C_5H_7F_6N$. Required/found; %C, 30.77/30.94; %H, 3.62/3.50; %F, 58.42/58.5;
IR /Raman : 2990m/2980m, 2970m/2960m, 2945m/2930sh, 2920m/-, 2905m/2905m, 2880m/2880sh, 2845/2850m, 1168vs/1160w, 1115vs/1120w, 832m/835vs, -/818vs.

**Tris(2,2,2-trifluoroethyl)amine (III)** 3.57 g (210 mmol) $NH_3$ and 237.5 g (620 mmol) $C_4F_9SO_2OCH_2CF_3$ were sealed in a thick-walled glass ampoule and heated to 210 °C for 4 days. Volatile reaction products were removed in vacuo. Their fractionation over a 30 cm Vigreux column yielded 4.1 g $(F_3CCH_2)_2NH$ (23 mmol), bp. 78 °C , 7.0 g (III) (27 mmol) , bp. 109 °C , and 129 g $C_4F_9SO_2OCH_2CF_3$ (340 mmol) , bp. 141 °C . The residue mainly contained $NH_4^+[C_4F_9SO_3^-]$ and small amounts of $[F_3CCH_2NH_3^+][C_4F_9SO_3^-]$.
IR /Raman : 3000w/3005w, 2970w/2975w, 2940/2950sh, 1165vs/1165w, 1122vs/1122w, 832m/832vs, -/821vs.

**Bis(2,2,2-trifluoroethyl)-1,2,2,2-bromotrifluoroethyl-amine (IV) and (2,2,2-trifluoroethyl)-bis(1,2,2,2-bromotrifluoroethyl)-amine (V)**

1.8 g (6.8 mmol) (III) and 3.3 g (21 mmol) $Br_2$, dissolved in 15 ml $CCl_4$, were heated to ~ 80 °C for 5h with UV radiation. (IV) was purified by repeated trap to trap distillation and collected in a -35 °C trap. Yield 0.7 g (30 %). Similarly, (V) was obtained from 3.4 g (13 mmol) (III) and 2.6 ml (48 mmol) $Br_2$ in 30 ml 1,2,4 - trichlorobenzene at 120 °C. Distillation of the reaction mixture yielded 2.8 g (52 %) (V), bp. 174 - 176 °C.

IR /Raman :(IV) 3050w/3030w, 2970w/2950w, 1292vs/1285w, 1183vs/-, 1170vs/1165w, 1130vs/1130sh, 1115vs/1110w, 837s/836s, 745m/745s, 690s/690vs, -/308vs, -/294 vs.

(V) 3050w/3030w, 2950w/2950w, 1287vs/1287w, 1205vs/1210w, 1180vs/1184w, 1157vs/1158w, 1130vs/1125sh, 1115vs/1112w, 837s/838m, 735m/735vs, 700m/698vs, -/317vs, -/295vs.

Tris(1,2,2,2-chlorotrifluoroethyl)amine (VI) 5.7 g (22 mmol) (III) were chlorinated for 1 h at room temperature with UV radiation. Then the temperature was raised to 100 °C and the reaction continued for 5 h. Distillation of the reaction mixture yielded 4.1 g (52 %) (VI), bp. 149 °C.

IR /Raman: 3035w/3030w, 1299vs/1300w, 1215vs/1210w, 1140vs/1140w,
772m/772vs, -/357vs, -/305s.

No elemental analyses of (III) to (VI) were performed because of the indicated or possible toxicity of the material.

## Physical measurements

| | |
|---|---|
| Mass spectra: | Varian MAT 311A ; EI; 70 eV. |
| NMR spectra: | $^1H$ and $^{13}C$ Bruker AC 250 ; $^{19}F$ Varian EM 390;<br>$^1H$ at 250.13 MHz, int. std. TMS, $^{19}F$ at 84.67 MHz, int. std. $CFCl_3$, $^{13}C$ at 62.9 MHz, int. std. $CDCl_3$ = 77.0 ppm. |
| Raman spectra: | Cary 82, excitation $Kr^+$ 647.1 nm, liquid samples. |
| IR spectra: | Perkin-Elmer 580B, 400 - 4000 $cm^{-1}$, 18. 7 cm gas cells, KBr windows, ± 2 $cm^{-1}$. |

## ACKNOWLEDGEMENT

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