Journal of Fluorine Chemistry, 52 (1991) 229–234

Received: November 12, 1990; accepted: January 13, 1991

REACTION OF TETRAKIS(DIMETHYLAMINO)ETHYLENE WITH CF_2Br_2 IN THE PRESENCE OF SECONDARY AMINES, FORMATION OF N-TRIFLUOROMETHYL-DIALKYLAMINES

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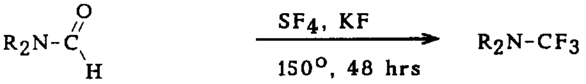
SUMMARY

N-trifluoromethylamines of the general formula R_2NCF_3 (R= Me (I), Et (II), i-Pr (III), i-Bu (IV); 2R = $(CH_3)_2C\text{-}(CH_2)_3\text{-}C(CH_3)_2$ (V) and $(CH_2)_6$ (VI)) have been obtained from the corresponding secondary amines R_2NH with the reagent combination tetrakis(dimethylamino)-ethylene/CF_2Br_2/$(CH_2)_4SO_2$ in moderate yields. The new N-trifluoromethylamines have been characterized by elemental analyses, multinuclear NMR and vibrational spectra and the mechanism of formation is discussed.

INTRODUCTION

Though N-trifluoromethylamines have been known for a long time and Et_2NCF_3 has been shown to convert alcohols into alkyl fluorides and carboxylic acids into acid fluorides [1], their synthesis afforded either expensive reagents like SF_4 [2], R_2NSF_3 [3] according to eq. (1) and (2) or the use of SbF_3 as fluorinating agent [4] (eq. (3)).



$$R_2N\text{-}C(=O)H \xrightarrow[150^{o},\ 48\ hrs]{SF_4,\ KF} R_2N\text{-}CF_3 \qquad (1)$$

$$R_2N\text{-}C(=S)\text{-}S\text{-}S\text{-}C(=S)\text{-}NR_2 \xrightarrow{R'_2N\text{-}SF_3} R_2N\text{-}CF_3 \qquad (2)$$

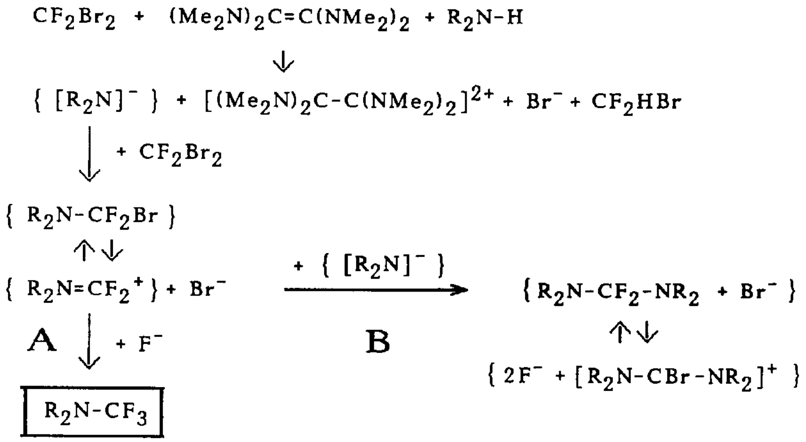
0022-1139/91/$3.50

$$R_2N{=}CCl_2^{+}\ Cl^{-} \xrightarrow{SbF_3} R_2N{-}CF_3 \qquad (3)$$

There is however no reaction known in which a secondary amine is directly N-trifluoromethylated. While studying reactions of tetrakis(dimethylamino)ethylene (TMAE) with various fluorinated methanes e.g. CF_2Br_2, we noticed that Me_2NCF_3 (I) was occasionally produced as a volatile by-product. A detailed investigation of the formation of I led us to a simple one pot synthesis for N-trifluoromethylamines of the general formula R_2NCF_3 (R = alkyl) starting from the corresponding secondary amine R_2NH.

RESULTS AND DISCUSSION

We found that traces of I and CF_2HBr were formed from CF_2Br_2 and TMAE, which was believed to be free of Me_2NH, but the amount of I formed increased if Me_2NH was added. Addition of Et_2NH as well as $(i\text{-}Pr)_2NH$ led to the formation of Et_2NCF_3 (II) and $(i\text{-}Pr)_2NCF_3$ (III) respectively. Optimizing the reaction conditions, we found that the yield of I - III was as high as 40 % based on the starting amine and that the best ratio between TMAE and the amine was about 2.2 / 1 . These observations can be explained by the following reaction scheme below.



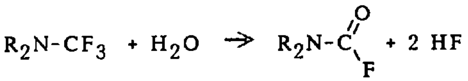
In the first step TMAE reduces CF_2Br_2 to Br^- and the intermediate CF_2Br^-. Acting as a strong base CF_2Br^-, abstracts the N-H proton forming CF_2HBr and an amide anion R_2N^-. This amide ion can react with further CF_2Br_2 to form a R_2NCF_2Br species. In polar solvents like $(CH_2)_4SO_2$, R_2NCF_2Br is in equilibrium with its ionic isomer $R_2N{=}CF_2^+\ Br^-$, which is easily fluorinated by F^- to form the final amine R_2NCF_3 (reaction pathway **A**).

While the source of the fluoride ions has not been verified, reaction path **B** appears to be a viable possibility. $R_2N{=}CF_2^+$ may well react with the amide R_2N^- forming $R_2NCF_2NR_2$. The latter could serve as the fluoride source since diaminofluoromethanes are known to dissociate. Assuming that only one fluoride ion is provided by $R_2NCF_2NR_2$, the yield of R_2NCF_3 cannot exceed 33 %, and if two F^- ions are provided the theoretical yield is 50 % of our starting amine respectively. The highest yield obtained (~50 % for V) is thus compatible with the reaction scheme. Addition of finely ground, dried KF also raised the yield of III from 45 % to 53 % and obviously suppresses reaction way **B**. The lower yields of I and II are mainly due to workup losses, that is repeated distillations.

The novel N-trifluoromethylation reaction appears to be limited to strongly basic secondary amines. Attempts to synthesize $CF_3N(CH_2CF_3)_2$ from $HN(CH_2CF_3)$ failed, but small amounts of the diamine $Me_2NCF_2N(CH_2CF_3)_2$ (VII) were obtained together with some unreacted starting material. The formation of VII can be explained by the reaction scheme as well. Obviously the amide $N(CH_2CF_3)_2^-$ is unable to react with CF_2Br_2 but adds irreversibly to $Me_2NCF_2^+$ or reacts with Me_2NCF_3 which is formed in small quantities from TMAE and CF_2Br_2 alone to yield VII.

PROPERTIES AND SPECTRA

The physical properties and NMR spectra of I-VII are set out in Table 1. All N-trifluoromethyldialkylamines I-VI are colorless liquids which hydrolyse to the corresponding formyl fluorides according to eq. (4).



$$R_2N\text{-}CF_3 + H_2O \rightarrow R_2N\text{-}C(=O)F + 2\,HF \qquad (4)$$

TABLE 1

Physical properties and NMR spectra of I - VII (δ in ppm, J in Hz)[a]

	I	II	III	IV	V	VI	VII
b.p. °C	20[b]	71[b]	109	143	171	133	
^{1}H							
δ (CH$_3$)	2.52	1.12	1.20	0.90	1.31		2.47
δ (CH$_2$)		2.96		2.60	~1.54	~1.58 ~2.98	3.62
δ (CH)			3.44	1.79			
^{3}J (HH)		7.2	6.9	6.7			
^{3}J (HF)							8.7
^{4}J (HF)	0.9	1.1		1.2			
^{5}J (HF)		0.6	0.9		1.6		
^{19}F							
δ (CF$_3$)	-69.7	-61.5	-52.8	-61.8	-39.0	-63.3	-70.7
δ (CF$_2$)							-81.0
^{13}C							
δ (CH$_3$)	35.93	13.19	21.71	20.12	29.90*		36.40
δ (CH$_2$)		40.43		57.12	16.77 42.71	26.84 28.58 46.06	
δ (CH)			45.63	27.75			
δ (C)					55.12		
δ (CF$_3$)	125.10	125.75	125.81	125.62	126.23	125.04	124.88
δ (CF$_2$)							126.37
^{1}J (CF)		253.7	254.0	253.2	259.1	252.7	250.6
							280.0
^{2}J (CF)							34.8
^{3}J (CF)	3.0	2.2		2.2		2.1	3.2
^{4}J (CF)			1.4		1.1 4.2*		

[a] In CDCl$_3$. ^{1}H: 250.13 MHz, internal standard CHCl$_3$ = 7.27 ppm. ^{19}F: 84.67 MHz, internal standard CFCl$_3$. ^{13}C: 62.90 MHz, internal standard CDCl$_3$ = 77.0 ppm.

[b] Ref. [2].

While I and II even attack glass at room temperature, V is less sensitive to hydrolysis and can be stored for several days in a sealed ampoule under the same conditions. In the proton spectra usually a small ^4J HF coupling indicates the presence of a CF_3 group and in V a rather large ^5J HF coupling of 1.6 Hz is obsereved for the CH_3 resonances. While all CF_3 resonances fall in the range between -70 and -50 ppm, V has an unusual value of -39.0 ppm. ^{13}C signals of carbons adjacent to nitrogen reveal a small ^3J CF coupling of ~ 2 Hz. The large ^4J CF coupling constant of 4.2 Hz in V is explained by the close proximity of the CH_3 groups to the CF_3 group.

EXPERIMENTAL

Dimethyltrifluoromethylamine (I), Diethyltrifluoromethylamine (II) Diisopropyltrifluoromethylamine (III), Diisobutyltrifluoromethylamine (IV) 2,2,6,6-tetramethyl-1-trifluoromethylpiperidine (V), 1-trifluoromethyl azacyloheptane (VI)

General procedure:
0.05 mol of the secondary amine was mixed with 50 ml CF_2Br_2 in 100 ml dry $(CH_2)_4SO_2$, and 0.11 mol (26 ml) TMAE were added dropwise within 15 min at room temperature. The reaction mixture was stirred for about 30 min, and the volatile reaction products were isolated by trap to trap distillation. I and II were collected in a -100°C and -78°C trap, respectively, together with unreacted CF_2Br_2 and CF_2HBr and further purified by low temperature distillation through a 30 cm slit tube column (FISCHER). While II was obtained analytically pure, I could not be completely separated from CF_2Br_2. Therefore this mixture was reacted with an excess of $CH_3OSO_2CF_3$ to form the quaternary salt $Me_3NCF_3^+$ $CF_3SO_3^-$ [5] which was used to determine the yield of I.
III stopped in a -65 °C trap while IV, V and VI were trapped at -45 °C and needed no further purification.
Yields : I 37 %, II 27 %, III 45 (53)*%, IV 35 %, V 50 %, VI 38 %.
*This yield was obtained in the presence of 0.05 mol dried KF.

IR$_{gas}$ cm^{-1}: III 1301 vs, 1255 vs, 1070 vs (ν CF_3)
IV 1250 vs, 1089 vs (ν CF_3)
V 1293 vs, 1270 vs, 1173s, 1089 vs (ν CF_3), 1052 vs
VI 1270 vs, 1090 vs (ν CF_3), 830 s

Elemental analyses:
III $C_7H_{14}NF_3$ Required/found; %C, 49.69/49.9; %H , 8.34/8.4; %N, 8.28/8.4.
IV $C_9H_{18}NF_3$ Required/found; %C, 54.81/54.6; %H , 9.20/9.3; %N, 7.10/7.0.
V $C_{10}H_{18}NF_3$ Required/found; %C, 57.40/57.2; %H , 8.67/8.8; %N, 6.69/6.9.
VI $C_7H_{12}NF_3$ Required/found; %C, 50.29/50.4; %H , 7.24/7.4; %N, 8.38/8.5.

ACKNOWLEDGEMENT

The author wishes to thank Prof. H. Bürger for support.

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