Journal of Fluorine Chemistry, *23* (1983) 219–228

Received: October 18, 1982; accepted: December 28, 1982

DIALKYL-α,α-DIFLUOROBENZYLAMINES AND DIALKYL(TRIFLUOROMETHYL)-AMINES - NOVEL FLUORINATING REAGENTS

Wojciech DMOWSKI and Maciej KAMIŃSKI

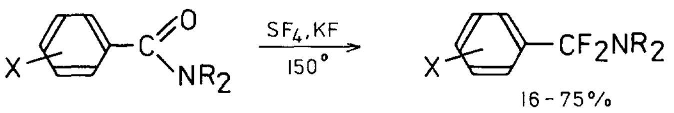
Institute of Organic Chemistry, Polish Academy of Sciences,
00-961 Warsaw (Poland)

SUMMARY

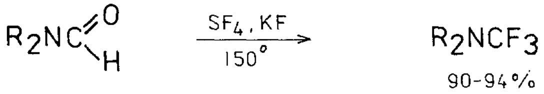
The use of α,α-difluorobenzyl(dimethyl)amine (DBDA) and diethyl(trifluoromethyl)amine (DTA) as fluorinating reagents to replace hydroxyl groups in alcohols and carboxylic acids by fluorine atoms has been studied. The results are compared with those reported for other fluoroamine reagents.

INTRODUCTION

Dialkyl-α-fluoroamines <u>e.g.</u> 2-chloro-1,1,2-trifluoroethyl-(diethyl)amine (FAR) [1,2] and diethyl-1,1,2,3,3,3-hexafluoropropyl amine [3] are known as mild fluorinating reagents. These amines are of particular value for selective substitution of fluorine atoms for hydroxyl groups in alcohols and carboxylic acids. In earlier papers [4,5] we reported facile synthesis of a number of α-fluoroamines <u>i.e.</u> dialkyl-α,α-difluorobenzyl amines and dialkyl(trifluoromethyl)amines in the reactions of sulphur tetrafluoride with N,N-dialkylbenzamides and N,N-dialkylformamides, respectively, in the presence of potassium fluoride.



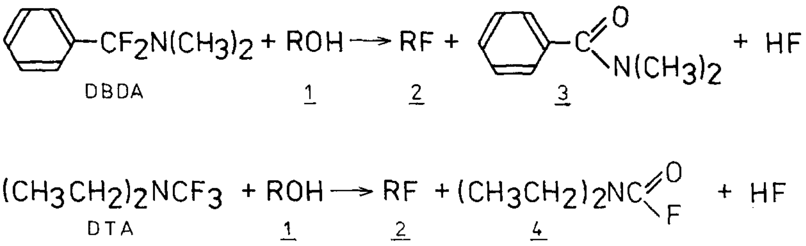
0022-1139/83/$3.00



The aim of the present work was to examine the usefulness of dialkyl-α,α-difluorobenzylamines and dialkyl(trifluoromethyl)amines as fluorinating reagents. From amongst a number of fluoroamines which have been synthetised [4,5] , α,α-difluorobenzyl(dimethyl)amine (DBDA) and diethyl(trifluoromethyl)amine (DTA) were chosen for these studies; the former because of the availability of the starting amide for its synthesis and the latter because of convenient boiling point (71 - 72°). Reactions of amines DBDA and DTA with simple primary, secondary, and tertiary alcohols and with carboxylic acids are reported.

RESULTS AND DISCUSSION

DBDA and DTA react with hydroxyl compounds 1 to give fluorinated products 2 and hydrogen fluoride and the reactant amines are converted to **N,N-dimethylbenzamide** 3 or **diethylfluoroformylamine** 4, respectively, according to the general schemes as follows:

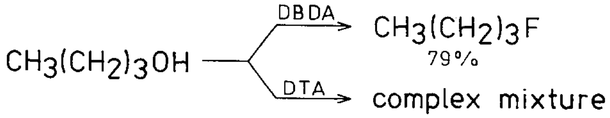


R=H , alkyl , acyl

In reactions involving DTA, particularly when carried out for longer time, fluoroformylamine 4 undergoes decomposition to give diethylamine trihydrofluoride $Et_2NH\cdot 3HF$, which is formed as a crystalline precipitate.

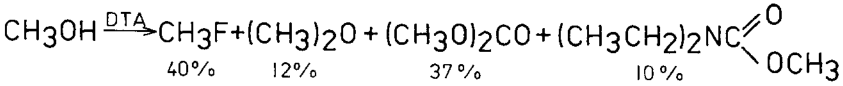
Reactions with alcohols

Results of reactions of DBDA and DTA with alcohols strongly depend on the nature of the alcohol and on the amine used. Primary alcohols,e.g. n-butyl alcohol, reacted with DBDA to give a high yield of 1-fluorobutane as the only product while reactions of n-butyl, n-octyl, 2,2,2-trifluoroethyl, and benzyl alcohols with DTA gave very complex mixtures of compounds.



$$CH_3(CH_2)_3OH \xrightarrow{DBDA} \underset{79\%}{CH_3(CH_2)_3F} \qquad CH_3(CH_2)_3OH \xrightarrow{DTA} \text{complex mixture}$$

Spectroscopic analysis of the gaseous mixture obtained from the reaction of methyl alcohol with DTA showed that it consisted of methyl fluoride and dimethyl ether; liquid products were found to contain dimethyl carbonate and methyl N,N-diethylcarbamate.

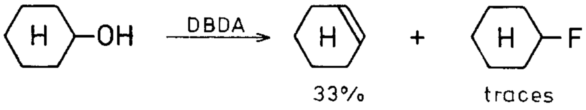


$$CH_3OH \xrightarrow{DTA} \underset{40\%}{CH_3F} + \underset{12\%}{(CH_3)_2O} + \underset{37\%}{(CH_3O)_2CO} + \underset{10\%}{(CH_3CH_2)_2NC(=O)OCH_3}$$

With iso-propyl alcohol the same results were obtained using either DBDA or DTA; 2-fluoropropane was obtained in a 74 - 75 % yield together with trace amounts of propene.

$$(CH_3)_2CHOH \xrightarrow[\text{or DTA}]{DBDA} \underset{74-75\%}{CH_3CHFCH_3} + \underset{\text{traces}}{CH_3CH{=}CH_2}$$

In contrast to iso-propyl alcohol, cyclohexyl alcohol gave fluorinated products neither with DBDA nor with DTA. The reaction with DBDA mainly gave the dehydration product, viz. cyclohexene; ^1H and ^{19}F NMR spectra of the crude reaction mixture revealed the presence of only trace amounts of cyclohexyl fluoride. A mixture obtained from the reaction with DTA was found to contain none of the expected products.



The reaction of tert-butyl alcohol with DBDA gave a 1.2 to 1 mixture of tert-butyl fluoride and 2-methylpropene, but in the reaction with DTA this ratio was as high as 3.5 to 1.

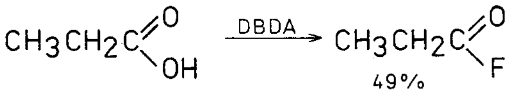
$$(CH_3)_3COH \longrightarrow (CH_3)_3CF + CH_3C(CH_3)=CH_2$$

with DBDA :	49%	41%
with DTA :	70%	20%

It is interesting to notice that tertiary alcohols rarely give tertiary fluorides in the reaction with FAR($CHClFCF_2NEt_2$); in most cases side reactions predominate [2] .

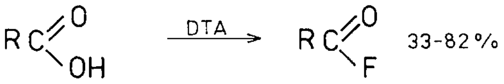
Reactions with carboxylic acids

Both fluoroamines DBDA and DTA react with carboxylic acids to give the corresponding acid fluorides. Thus, propionic acid reacted exothermally with DBDA to give a reasonable yield of propionyl fluoride.



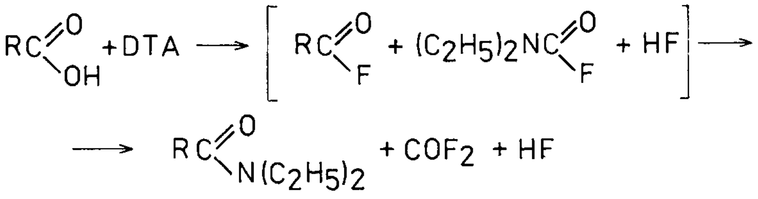
The reaction of DBDA with benzoic acid is of no preparative value because benzoyl fluoride cannot be separated by distillation from simultaneously formed N,N-dimethylbenzamide.

Results of the reactions of DTA with carboxylic acids depend on the volatility of the resultant acid fluorides. Gaseous fluorides i.e. acetyl, and trifluoroacetyl, which are immediately removed from the reaction mixture, were obtained with good yields, whereas less volatile propionyl fluoride was obtained with only moderate yield.



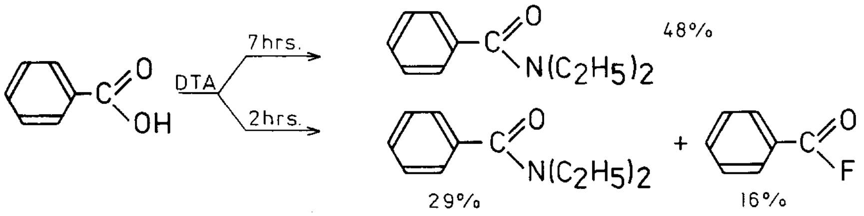
R = CH_3, CF_3, CH_3CH_2

n-Butyric and benzoic acids gave no acid fluorides in the reaction with DTA; instead, N,N-diethylbutyramide and N,N-diethylbenzamide were obtained, respectively. It has been proved in separate experiments that the expected non-volatile acid fluorides, n-butyryl and benzoyl (and also the acids themselves), undergo a metathetic reaction with diethyl-N-fluoroformylamine which is simultaneously formed to give the corresponding N,N-diethylamides.



R=n-C_3H_7, phenyl

The above consecutive reaction of non-volatile acid fluorides may be diminished to some extent by shortening the reaction time; thus, the reaction of benzoic acid with DTA gave after seven hours N,N-diethylbenzamide as the only aromatic product while after two hours a 1 to 2 mixture of benzoyl fluoride and the benzamide were formed.



Comparison of fluorinating properties of fluoroamines

α,α-Difluorobenzyl(dimethyl)amine (DBDA) and diethyl(trifluoromethyl)amine (DTA) showed, in general, fluorinating properties similar to that of 2-chloro-1,1,2-trifluoroethyl-diethylamine (FAR) and other α-fluoroamines, however, there are some differences in the behaviour of particular amines in reactions with hydroxyl compounds (Table 1). DBDA gave good

TABLE 1

Fluorination of alcohols and carboxylic acids with various fluoroamines

$$\mathrm{ROH} \xrightarrow{\text{fluoroamine}} \mathrm{RF}$$

R	Yields (mole %) of RF with:				Physical properties of RF	
	DBDA	DTA	FAR[a]	$CF_3CHFCF_2NEt_2$[b]	B.p.(°C)	^{19}F NMR[c]: ϕ_F(ppm), J(Hz)
CH_3		40				268.6(q), $^2J(HF)=42.5$
n-C_4H_9	79	0	67		32-33[d]	22.0(t), $^2J(HF)=47.6$
i-C_3H_7	74	75			ca. -10[e]	166.0(d,sept), $^2J(HF)=46.8$
t-C_4H_9	49	70		78		131.5(decet), $^3J(HF)=20.5$
CH_3CO		82	59		20-21[d]	-49.8(q), $^3J(HF)=7.2$
CF_3CO		68			ca. -60[f]	-14.5(q), and 62.0(d) , $^3J(FF)=6.1$
C_2H_5CO	49	33	40		42[g]	-41.5(s)
C_3H_7CO		0	46	61		
PhCO		16	90[b]	60		

[a] Reference [1,2] , [b] Reference [3]

[c] Chemical shifts are in ppm from internal CCl_3F, positive upfield (s - singlet, d - doublet, t - triplet, q - quartet)

[d] In agreement with reference [6] , [e] In agreement with reference [7] ,

[f] In agreement with reference [8] , [g] In agreement with reference [9]

results with primary and secondary alcohols. DTA seems to be a particularly useful reagent for fluorination of secondary and tertiary alcohols and for acetic acids, but is of no use for fluorination of primary alcohols and higher molecular weight carboxylic acids.

Neither DBDA nor DTA reacts with the carbonyl group of aldehydes, ketones, and carboxylic acids.

Other reactions

α,α-Difluorobenzylamines were reported to form crystalline 1 to 1 complexes with boron trifluoride [4] ; formation of such complexes was not observed with dialkyl(trifluoromethyl)amines.

Unlike fluoromethyl-dimethylamine $(CH_3)_2NCH_2F$ and difluoromethyl-dimethylamine $(CH_3)_2NCHF_2$, which were reported to add to perfluoroolefins [10] , attempted reactions of DBDA and DTA with hexafluoropropene and tetrafluoroethylene gave no addition products. However, similarly to the former amines, DBDA was found to be a good source of fluoride ion; at ambient temperature it effectively promoted oligomerisation of hexafluoropropene to give an almost quantitative mixture of dimers and trimers. In contrast, DTA was totally ineffective, even at elevated temperature.

EXPERIMENTAL

Boiling points (uncorrected) were determined by distillation. NMR spectra were recorded with a JEOL JNM-4H-100 spectrometer.

α,α-Difluorobenzyl(dimethyl)amine (DBDA) and diethyl(trifluoromethyl)amine (DTA) were prepared according to the previously described procedures [4,5] . Alcohols and carboxylic acids were pure grade commercial reagents.

Reactions of DBDA and DTA with alcohols

The reactions were carried out on a 0.1 mole scale in a three-necked glass flask fitted with a reflux condenser, dropping funnel, thermometer, and a magnetic stirring bar. The outlet of the reflux condenser was connected to a trap kept at -78°. An alcohol was placed in the reaction flask and, while stirring, an equimolar amount of the amine was added dropwise at 40°. Usually an exothermic reaction occurred and the reaction mixture was brought to reflux. After addition of the amine, the mixture was stirred for 15 minutes. Volatile alkyl fluorides, methyl, iso-propyl, tert-butyl, and alkenes which were evolved in the course of the reaction, were condensed in the cold trap; they were subjected to the NMR and MS analyses. Less volatile n-butyl fluoride was distilled off after the reaction had run to completion. Yields, boiling points, and ^{19}F NMR data of alkyl fluorides are given in Table 1 .

Distillation of the residue after removal of volatile products gave a 55 - 75 % yield of N,N-dimethylbenzamide (from DBDA) or diethyl(N-fluoroformyl)amine (from DTA); b.p. 90-92° (0.4 mmHg) [11] and 155° [5] , respectively.

Compounds obtained from the reaction of DTA with methyl alcohol were identified from ^{1}H NMR spectra of their mixtures by comparing chemical shifts of the CH_3 group signals of these compounds with the reported values [12] .

Reactions of DBDA and DTA with carboxylic acids

Reactions of DBDA with the acids were carried out as with alcohols. Reactions with DTA were carried out by dropwise addition of an acid to the refluxing amine. After addition, the reaction mixture was heated and stirred for one hour. Acetyl, and trifluoroacetyl fluorides were condensed in the cold trap and identified by the ^{19}F NMR and MS spectrometry. Propionyl and benzoyl fluorides were distilled off after the reaction had run to completion. Yields, boiling points and ^{19}F NMR data are given in Table 1. Distillation of mixtures obtained from the reactions of DTA with butyric and benzoic acids gave mostly

N,N-diethylbutyramide (b.p. 205-206° [13]) and N,N-diethylbenzamide (b.p. 154°/32mmHg [14]), respectively. Structure of the amides was confirmed by elemental analysis and MS and ^1H NMR spectra.

Identification of $(C_2H_5)_2NH.3HF$

A solid substance, which was usually formed in the reactions of DTA with alcohols and carboxylic acids, was separated and recrystallised from ethanol; m.p. 213-215°. Calculated for $C_4H_{14}F_3N$: F, 42.9 %. Found : F, 42.9 %. ^1H NMR : $\delta(CH_3)=1.45$, $\delta(CH_2)=3.32$ ppm, relative intensities being as 3 : 2 . When treated with an aqueous solution of sodium carbonate the compound released diethylamine which was identified as its hydrochloride (m.p. 222-223° [6]).

Reactions of benzoyl fluoride and benzoic acid with diethyl-(N-fluoroformyl)amine

Equimolar amounts of benzoyl fluoride or benzoic acid and the amine were refluxed for 10 hours. Distillation of the reaction mixture gave N,N-diethylbenzamide in a 38 and 18 % yield, respectively.

Attempted reactions of DBDA and DTA with perfluoroolefins

The amine (0.04 mole), and if required dimethylformamide (10 ml), were placed in a pressure glass tube of 100 ml capacity equipped with a Rotaflo valve. The reactor was then cooled in liquid nitrogen, evacuated, and an equimolar amount of olefin was condensed into the tube. After closing, the tube was allowed to warm to ambient temperature and then shaken mechanically for 72 hours. Upon this time the unreacted olefin was released by opening the valve and the residue was subjected to ^{19}F and ^1H NMR analysis.

From the reactions of DTA with tetrafluoroethylene and hexafluoropropene and of DBDA with tetrafluoroethylene only unreacted amines and olefins were recovered. In the reaction of DBDA with hexafluoropropene in dimethylformamide or without solvent the olefin was totally consumed (no pressure) and the reaction mixture consisted of two layers: an upper layer of the unchanged amine (and the solvent if used) and the lower layer of a mixture of hexafluoropropene dimers and trimers. The oligomers were identified by comparison of their GLC retentions (3% SE-52 oil on Chromosorb G) with those of the original samples.

ACKNOWLEDGMENT

This work has been supported by the Polish Academy of Sciences within the project MR-I-12 .

REFERENCES

1 N.N.Yarovenko, M.S.Raksha,Zh.Obshch.Khim., 29(1959) 2159

2 C.M.Sharts, W.A.Sheppard, Org.React., 21 (1972) 158

3 A.Takaoka, H.Iwakiri, N.Ishikawa, Bull.Chem.Soc.Japan, 52 (1979) 3377

4 W.Dmowski, M.Kamiński, Pol.J.Chem., in press

5 W.Dmowski, M.Kamiński, J.Fluorine Chem., preceeding paper

6 Dictionary of Organic Compounds,Eyre and Spottiswoode, London (1965) vol.3, p.1445

7 W.F.Edgell, L.Parts, J.Am.Chem.Soc., 77 (1955) 4899

8 N.Fukuhura, L.A.Bigelow, J.Am.Chem.Soc., 63 (1941) 788

9 J.H.Simons, Fluorine Chemistry, New York (1954) vol.2, p.276

10 I.L.Knunyants, N.I.Delyagina, S.M.Igumnov, Izv.Akad.Nauk S.S.S.R.,Ser.Khim., (1981) 851, 860

11 Von Braun, Chem.Ber., 36 (1913) 3625, 37 (1914) 2514

12 A.Zschunke, Kernmagnetische Resonanzspectroskopie in der organischen Chemie, Berlin (1971)

13 Beilsteins Handbuch der organischen Chemie,Berlin (1942), II, vol.4, p.604, and references therein

14 Beilsteins Handbuch der organischen Chemie,Berlin (1970), III, vol.9, p.1069, and references therein