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Oxidation of primary alcohols to acyl fluorides using BrF_3

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Abstract

Aliphatic and alicyclic primary alcohols when treated with BrF_3 were rapidly oxidized to the corresponding acyl fluorides. The reaction is of an ionic nature. The main by-product was found to be the symmetrical ester which originates from the reaction between the acyl fluoride and unreacted starting alcohol.

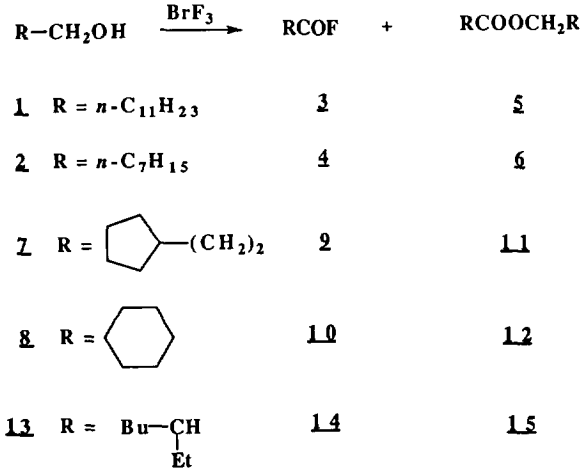
Keywords: Fluorine; Bromine trifluoride; Acyl fluorides; Oxidation; NMR spectroscopy; IR spectroscopy

1. Introduction

Most of the strongly oxidizing fluorinating agents contain the fluoroxy moiety and, apart from CF_3OF, they are usually prepared in situ using elemental fluorine just prior to a designed reaction [1]. The strong oxidizer bromine trifluoride, BrF_3, on the other hand, is a commercial reagent used quite frequently in inorganic transformations. Because of its higher than usual reactivity however, it generates unjustified fears, as did elemental fluorine two decades ago, and consequently many organic chemists shy away from it [2]. Recently, we have been able to show that when handled properly, this reagent can participate in some very interesting chemistry, especially in aromatic brominations [3] and the preparation of some compounds containing CF_2 and CF_3 groups [4]. In this work we have explored the reaction of BrF_3 with primary alcohols.

2. Results and discussion

Although, as mentioned above, bromine trifluoride is a commercial reagent, it can also be readily prepared by reacting a three molar ratio of fluorine with bromine at around 5 °C and then storing in a tightly closed Teflon vessel. For all reactions described below, a $CFCl_3$ solution of BrF_3 at 0 °C was made and added dropwise to either a chloroform or a $CFCl_3$ solution of a primary alcohol, using approximately 50% excess of BrF_3. An immediate reaction took place and two compounds could be isolated and identified, the major one being the corresponding oxidized acyl fluoride [5], while the minor proved to be the symmetrical ester which resulted from a secondary reaction of the acyl fluoride with the starting alcohol.



Thus, straight-chain normal alcohols such as dodecanol (**1**) and octanol (**2**) gave dodecanoyl and octanoyl fluorides (**3** and **4**) in good yield accompanied by small amounts of dodecyl dodecanoate (**5**) and octyl octanoate (**6**). Similar results were obtained with ring-containing compounds such as 3-cyclopentylpropanol (**7**) and cyclohexylmethanol (**8**) which formed the corresponding 3-cyclopentylpropanoyl fluoride (**9**) and cyclohexylacetyl fluoride (**10**) along with the corresponding esters **11** and **12**. The branched primary alcohol 2-ethyl-1-hexanol (**13**) behaved similarly to give the acyl fluoride **14** and the symmetrical ester **15**.

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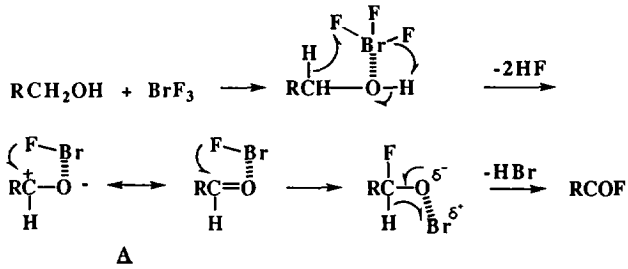
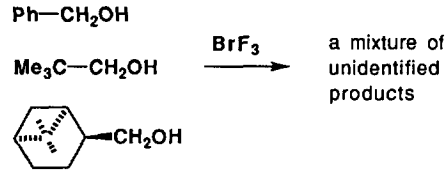
We believe that the whole process is mainly ionic in nature since radical scavengers such as dinitrobenzene and oxygen did not affect the outcome. Similarly, keeping the reaction in darkness or under irradiation of a 300 W sun lamp had no effect. In the past, we have noted that bromine trifluoride reacts immediately with oxygenated solvents such as water, acetone and THF [4]. This led us to believe that the first fast step of the reaction is indeed a complexation of the alcohol oxygen with the electrophilic bromine. The fluorine in BrF_3, which also can be electrophilic in nature, abstracts the hydride-like hydrogen α to the oxygen atom to eventually form a complex between the corresponding aldehyde and BrF (**A**). We have indeed identified corresponding aldehydes in the course of this reaction and also found that they could easily be further oxidized to the respective acyl fluorides. These facts well support the proposed mechanism.



A

Experiments employing reverse addition of the alcohol to BrF_3 did not reduce the amount of the symmetrical esters formed to any great extent, indicating that esterification of the starting alcohol with the acyl fluoride is at least comparable in rate to that of the oxidation of the alcohol.

It should be mentioned that fairly activated benzylic alcohols did not react cleanly, apparently because of bromination of the aromatic ring. The same was true with compounds which are more than usually sensitive to carbocation rearrangements, such as neopentyl alcohol and myrtanol.



We tried to react **2**, **8** and **13** with fluorine, but yields of the corresponding acetyl fluorides did not exceed 10%–15%.

3. Experimental details

^1H NMR spectra were recorded with Bruker AC-200 and AM-360 WB spectrometers with $CDCl_3$ as solvent and Me_4Si as internal standard. The ^{19}F NMR spectra were measured at 338.8 MHz and are reported in parts per million upfield from $CFCl_3$, which also served as internal standard. IR spectra were recorded as neat films, in $CHCl_3$ solution or in KBr pellets on a Nicolet 205 FT-IR spectrophotometer.

3.1. Preparation and handling of BrF_3

Although commercially available, we prepared our own BrF_3 simply by passing 0.58 mol of pure fluorine through 0.2 mol of bromine placed in a Teflon reactor at 0–10 °C. When no excess of bromine was present, the BrF_3 obtained was a pale yellow liquid and had a density of 2.5 with a melting point of 7–9 °C [6]. At that temperature the higher oxidation state derivative, BrF_5, did not form in any appreciable amounts [7], although we always used a small excess of bromine to keep the reagent from disproportionation to BrF_5 and also giving it a reddish colouration. We stored the reagent in Teflon containers for long periods. BrF_3 is a strong oxidizer and tends to react very exothermically with water and oxygenated organic solvents. **Work with BrF_3 should be conducted in a well-ventilated area and caution and common sense exercised.**

3.2. General alcohol oxidation procedure with BrF_3

BrF_3 [1.6 mol equiv^{-1} (usually ca. 15 mmol)] was dissolved in 30 ml of $CHCl_3$ and cooled to −5 °C. This solution was added dropwise (10–15 min) to a cold (10 °C) solution consisting of 10 mmol of alcohol in 50 ml of either $CHCl_3$ or $CFCl_3$. After the addition was complete, the reaction mixture was added to water, the organic layer separated as quickly as

Table 1

Compound	Yield (%)	*^{19}F NMR* (δ, ppm); ^1H NMR (δ, ppm)	IR (cm^{-1})	Ref.
3	65	*+44.92*; 2.49 (2H, dt, J_1 = 7.5 Hz, J_2 = 1 Hz)	1844	[8]
4	70	*+44.9*; 2.51 (2H, dt, J_1 = 7.5 Hz, J_2 = 1 Hz)	1844	[9]
5	20	2.26 (2H, t, J = 7.5 Hz); 4.03 (2H, t, J = 6.5 Hz)	1735	
6	15	2.29 (2H, t, J = 7.5 Hz); 4.06 (2H, t, J = 6.5 Hz)	1736	
9	70	*+44.9*; 2.52 (2H, dt, J_1 = 7.5 Hz, J_2 = 1 Hz)	1843	[a]
10	55	*+36.22*; 2.51 (1H, tt, J_1 = 10.5 Hz, J_2 = 4 Hz)	1834	[10]
11	15	2.31 (2H, t, J = 7.5 Hz); 4.05 (2H, t, J = 6.5 Hz)	1734	
12	20	2.29 (1H, tt, J_1 = 10.5 Hz, J_2 = 4 Hz); 3.87 (2H, d, J = 6.5 Hz)	1733	
14	85	*+39.9 (d, J = 5 Hz)*; 2.45 (1H, m)	1836	[b]
15	10	2.26 (1H, tt, J_1 = 9 Hz, J_2 = 5 Hz); 3.99 (2H, d, J = 6 Hz)	1732	

[a] This is a new acyl fluoride; b.p. 32 °C/1.3 mmHg; hydrolysis with KOH followed by acidification afforded the known 3-cyclopentylpropionic acid.

[b] This is a new acyl fluoride; b.p. 28 °C/1.3 mmHg; reaction with aniline afforded the corresponding known anilide, m.p. 89 °C.

possible, dried over $MgSO_4$ and the organic solvent evaporated. The acyl fluoride was then distilled under reduced pressure leaving the symmetrical esters as a distillation residue. The yields of the latter are based on GC only. The results are summarized in Table 1.

Acknowledgment

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