



Reaction of tetramethylammonium fluoride with trifluoromethyltrimethylsilane

Dave J. Adams, James H. Clark^{*}, Liv B. Hansen, Victoria C. Sanders, Stewart J. Tavener

Department of Chemistry, University of York, Heslington, York YO10 5DD, UK

Received 1 July 1998; accepted 30 July 1998

Abstract

Tetramethylammonium fluoride reacts with either trifluoromethyltrimethylsilane or trimethylsilylacetonitrile in acetonitrile to form a pentacoordinate silicon species, which can act as a source of either fluoride or cyanomethyl carbanion, depending on substrate. © 1998 Elsevier Science S.A. All rights reserved.

Keywords: Ruppert's reagent; Trifluoromethane; TMAF; Fluorodenitration

1. Introduction

The use of Ruppert's reagent (trifluoromethyltrimethylsilane, Me_3SiCF_3) as a convenient source of trifluoromethide has received considerable attention in recent years for the trifluoromethylation of aldehydes and ketones [1]. This reagent is normally used in THF solvent, and is activated by use of a fluoride salt. The intermediate in these reactions is assumed to be a pentacoordinate silicon species, but this has not yet been confirmed/identified. Prakash [1] has studied the reaction between TMAF and Ruppert's reagent in CD_3CN , but reported only the formation of Me_3SiF and CF_3D .

Benzotrifluorides are important molecules for agricultural and pharmaceutical use due to the lipophilic and electron-withdrawing effects of the CF_3 group, but their synthesis generally involves the use of HF or SbF_3 , and so there is a need for new synthetic routes to these compounds [2,3].

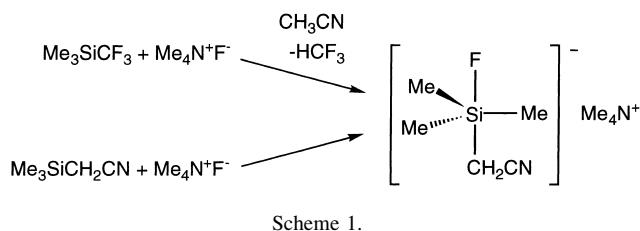
2. Results and discussion

We wanted to perform aromatic nucleophilic substitution using Ruppert's reagent as a source of trifluoromethide, with the aim of producing benzotrifluorides [4], but aromatic substitution reactions are best performed in solvents more polar than THF [5]. In the course of studying the activation of Ruppert's reagent in polar solvents, we observed that

addition of an equimolar quantity of Me_3SiCF_3 to a suspension of anhydrous tetramethylammonium fluoride (TMAF) in acetonitrile caused instantaneous dissolution of all the fluoride salt, even at room temperature. This is remarkable because TMAF has very limited solubility in acetonitrile, even at elevated temperatures (although it will react with the solvent over several days, forming the bifluoride salt [6]). It seems unlikely that this increased solubility is due to simple polarity effects because silanes are generally less polar than acetonitrile [7]. The dissolution is accompanied by an exotherm, and evolution of HCF_3 gas (^{19}F NMR: $\delta = -79$ ppm, d, $^2J_{\text{FH}} = 79$ Hz). ^{19}F NMR spectroscopy showed that the solution contains no other trifluoromethyl-containing compounds, indicating that all the [14] CF_3 is lost from the silane. Repeating the experiment in CD_3CN gave DCF_3 , demonstrating that the reaction involved deprotonation of the solvent. The reaction is noticeably slower in CD_3CN , suggesting a kinetic isotope effect. ^1H NMR spectroscopy reveals peaks at 0.03 (s, 9H) and -0.17 (s, 2H) ppm, consistent with methyl and $-\text{CH}_2\text{CN}$ groups attached to a silicon anion, respectively. It appears that attack by the fluoride at the silicon centre releases the strongly basic trifluoromethide anion ($\text{p}K_{\text{a}}$ of $\text{HCF}_3 = 31$ [8]), which deprotonates a neighbouring acetonitrile molecule. This in turn reattacks the silicon centre to form a pentacoordinate complex (Scheme 1). In contrast to Prakash's report [1], we observed no Me_3SiF .

Analysis of the solution by IR shows two pairs of CN stretches: one for the solvent ($2254, 2410 \text{ cm}^{-1}$), and another for the complex ($2174, 2124 \text{ cm}^{-1}$). At room temperature, the fluorine attached to the silicon cannot be

^{*}Corresponding author. Tel.: +44-1904-432-559; fax: +44-1904-432-516; e-mail: jhc1@york.ac.uk



observed by ^{19}F NMR spectroscopy, presumably due to rapid exchange between silicon centres: the pentacoordinate silicon has a vacant coordination site, so this will be facile. On cooling to -20°C , a broad peak appeared at -60 ppm. The Si–F bond could be seen at room temperature by solution IR (950 cm^{-1}), as this technique has a much faster timescale than NMR. The identity of the complex was confirmed by reacting authentic $\text{Me}_3\text{SiCH}_2\text{CN}$ (from Aldrich) with TMAF in acetonitrile, which produced a homogeneous solution with a ^1H NMR spectrum identical to that of the complex prepared from Me_3SiCF_3 . In the absence of fluoride and moisture, the silane is stable in acetonitrile for at least 24 h.

For successful preparation of the complex, it is necessary to use anhydrous TMAF. Replacement of anhydrous TMAF with TMAF· H_2O did not lead to dissolution of the fluoride salt, although the silane is hydrolysed to form hexamethyldisilylether. Addition of Me_3SiCF_3 to a suspension of dry KF in acetonitrile also caused dissolution of the fluoride salt. However, in this case, no complex was formed. Instead, fluorotrimethylsilane and HCF_3 were formed, presumably along with KCH_2CN . Evidently a larger cation is necessary to stabilise the pentacoordinate silicon complex.

Addition of excess Me_3SiCF_3 to the complex prepared from TMAF in solution causes evolution of stoichiometric [14] quantities of HCF_3 , and formation of $\text{Me}_3\text{SiCH}_2\text{CN}$ (Fig. 1). The complex is therefore an active source of fluoride, and there is facile transfer of the fluorine in the complex to the more electropositive silicon centre of the Me_3SiCF_3 . The complex is, in effect, catalysing the reaction between the silane and acetonitrile.

Addition of CFCl_3 to the solution as an internal reference for ^{19}F NMR spectroscopy caused a white solid to precipitate. This solid was soluble in water and gave a positive silver nitrate test, indicating the presence of chloride ion, and IR confirmed the identity of the action as Me_4N^+ . This shows that a halogen exchange reaction is occurring between the complex and CFCl_3 , although the identity of the halomethane product was not confirmed.

The complex was found to be an active source of $[\text{CH}_2\text{CN}]^-$, as well as fluoride, and reacted with a number of model substrates. Reaction with 2-chloro-6-nitrobenzonitrile at room temperature gave the fluorodenitration product, 2-chloro-6-fluorobenzonitrile as the only product (40% conversion): this is remarkable as fluorodenitration reactions usually require higher temperatures and more polar solvents [5]. This indicates that the complex is a

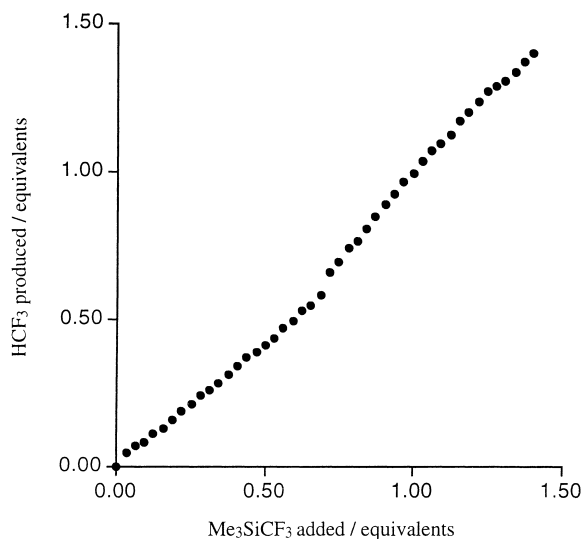


Fig. 1. Evolution of HCF_3 formed by reaction of Me_3SiCF_3 with acetonitrile, catalysed by the pentacoordinate silicon complex.

potent soluble fluoride source. No $-\text{CH}_2\text{CN}$ containing products (other than $\text{Me}_3\text{SiCH}_2\text{CN}$) were observed. However, no reactions occurred for the more demanding 1,3-dinitrobenzene and 3,5-dinitrobenzonitrile.

The complex reacts with benzophenone by nucleophilic attack at the carbonyl carbon, followed by elimination, forming $\text{Ph}_2\text{C}=\text{CHCN}$ (12% yield). The reaction between $\text{Me}_3\text{SiCH}_2\text{CN}$ and ketones in the presence of fluoride is known to give this product [9], although this was previously believed to follow a mechanism in which fluoride attack at the silicon centre formed Me_3SiF and $[\text{CH}_2\text{CN}]^-$. Our work suggests that the reactive species in this reaction may also be a pentacoordinate silicon containing species. Reaction of the complex with 4-nitrobenzophenone, which is activated towards fluorodenitration and attack at the carbonyl carbon, showed exclusive cyanomethylation at the carbonyl carbon, indicating that this is far more facile than fluorodenitration.

3. Experimental

All chemicals and solvents were purchased from Aldrich, except Me_3SiCF_3 and TMAF which were purchased from Apollo Scientific. All were used without further purification, except for KF, which was dried at 300°C for at least 24 h prior to use, and TMAF, which was dried by the method of Christie et al. [10].

Gas chromatography was carried out on a packed HP5 column in a Hewlett Packard HP6890 gas chromatography. GC–MS spectra were obtained on a DB5 capillary column in a Varian 3400 CX gas chromatograph interfaced to a Finnigan Mat Magnum mass spectrometer. Solution state NMR spectra were obtained on a JEOL 270 EX270 spectrometer (operating at 254 MHz for ^{19}F , referenced to HCF_3).

IR spectra were recorded on a Bruker Equinox 55 FT-IR spectrometer.

3.1. Reaction between TMAF and Me_3SiCF_3

TMAF (0.22 g, 2.3 mmol, anhydrous) was placed in a 50 ml round-bottomed flask under an argon atmosphere. Acetonitrile (10 ml, anhydrous) was added and the solution stirred. Using a microsyringe, Me_3SiCF_3 (0.34 ml, 2.3 mmol) was added. For the IR analysis, only 1.2 ml acetonitrile was used.

$^1\text{H-NMR}$ (CD_3CN): δ 0.03 (s), -0.17 (s) ppm; $^{19}\text{F-NMR}$ (CD_3CN , -20°C): δ -60 ppm; IR (CH_3CN solution, omitting solvent peaks) ν max (cm^{-1}): 3009 (s), 2964 (s) (C–H stretching); 2174 (s), 2124 (s) (C–N stretching); 1590 (s), 1490 (s) (C–H bending); 947 (s, Si–F stretching).

3.2. Reaction of complex with model substrates

For the reaction of the pentacoordinated complex with various substrates, a bulk solution was formed via the addition of TMAF (0.11 g, 1.18 mmol, anhydrous) in a 25 ml flask to acetonitrile (6 ml, anhydrous) under argon. Me_3SiCF_3 (175 μl , 1.18 mmol) was then added. Two ml of the above solution was then added to 2-chloro-6-nitrobenzotrile (0.0716 g, 0.39 mmol) and biphenyl (0.020 g, 0.13 mmol) in acetonitrile (3 ml, anhydrous) under argon at room temperature. The reaction was followed by GC. The reactions with benzophenone and 4-nitrobenzophenone were carried out similarly.

2-Chloro-6-fluorobenzotrile: MS (m/z , %) M^+ 155: 155 (100), 120 (18), 100 (12), 82 (8), 93 (5), 75 (4).

3,3-Diphenyl-2-propenenitrile: MS (m/z , %) M^+ 205: 205 (100), 165 (42), 178 (28), 190 (18), 51 (21), 76 (16), 88 (14), 102 (14).

3-Phenyl-3-nitrophenyl-2-propenenitrile: MS (m/z , %) M^+ 250: 250 (100), 203 (77), 176 (36), 165 (16), 155 (14), 77 (12), 220 (9), 151 (7).

3.3. Reaction of the pentacoordinated complex with Me_3SiCF_3

TMAF (0.11 g, 1.18 mmol, anhydrous) was added to acetonitrile (6 ml, anhydrous) under argon in a 25 ml flask. Me_3SiCF_3 (175 μl , 1.18 mmol) was added. This was connected to a pressure gauge (accuracy of 1 Torr) and the system sealed under argon. The pressure was read and a known amount of Me_3SiCF_3 added. The pressure was again read and more Me_3SiCF_3 added.

Acknowledgements

We thank the EPSRC Clean Technology Unit for funding through a ROPA award (SJT) and the Royal Academy of Engineering/EPSRC for a fellowship (to JHC). Thanks to Barbara Chamberlain for running the variable temperature ^{19}F NMR study.

References

- [1] G.K.S. Prakash, A.K. Yudin, Chem. Rev. 97 (1997) 757.
- [2] M.A. McClinton, D. McClinton, Tetrahedron 48 (1992) 6555.
- [3] J.H. Clark, D. Wails, T.W. Bastock, Aromatic Fluorination, CRC Press, Boca Raton, 1996.
- [4] D.J. Adams, J.H. Clark, L.B. Hansen, V.C. Sanders, S.J. Tavener, Perkin Trans. 1 (1998), 3081.
- [5] J.H. Clark, D.J. Macquarrie, J. Fluorine Chem. 35 (1987) 591.
- [6] K.O. Christe, W.W. Wilson, J. Fluorine Chem. 47 (1990) 117.
- [7] C. Reichardt, Solvents and Solvent Effects in Organic Chemistry, 2nd ed., VCH, Weinheim, 1988.
- [8] S. Andreades, J. Am. Chem. Soc. 86 (1964) 2003.
- [9] C. Palomo, J.M. Aizpurua, M.C. Lopez, B. Lecea, Perkin Trans. 1 (1989) 1692.
- [10] K.O. Christe, W.W. Wilson, R.O. Wilson, R. Bau, J. Feng, J. Am. Chem. Soc. 112 (1990) 7619.