

Synthesis of Trifluorovinyl Ethers

by

Robert Daniel Lousenberg

A thesis submitted in conformity with the requirements
for the degree of Master of Science
Graduate Department of Chemistry
University of Toronto

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Robert Daniel Lousenberg

University of Toronto

ABSTRACT

Novel trifluorovinyl ethers (TFVEs, $\text{ROCF}=\text{CF}_2$), where R is a functionalized oligo-ether, were synthesized by two methods. In the first method, thermolysis of trimethylsilyl 2-alkoxy-2,3,3,3-tetrafluoropropionate esters in the gas phase yielded TFVEs. Variable temperature ^{19}F NMR spectroscopy of trimethylsilyl 2-alkoxy-2,3,3,3-tetrafluoropropionates suggests that these esters exist in an equilibrium between two structural conformations. In one conformation, there is intramolecular “interaction” of silicon with fluorine. The second is a random conformation. To some degree, this interaction may influence the outcome of the thermolysis reaction which is ultimately successful because of favorable reaction kinetics. In the second method, the TFVEs were synthesized by the reaction of a sodium alkoxide with tetrafluoroethylene (TFE). For alkoxides of limited solubility, the observed rate of reaction was determined to be rate-limited by the forward and reverse rates of solubility and the rate of reaction with TFE. Addition of 18-crown-6 was shown to significantly increase the rate of reaction.

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For Dawn and Cory.

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The major objective of the research presented in this thesis was the preparation of novel trifluorovinyl ethers (TFVEs, $\text{ROCF}=\text{CF}_2$, Figure 1.1) which might eventually be used as monomers for homo- or potentially copolymerization. It is anticipated that these polymers may have biomaterial applications. The TFVEs described herein have never been synthesized. The majority of this thesis (chapter 3) describes a novel synthetic route (and mechanism) to prepare these TFVEs.¹ Chapter 4 describes the preparation of the TFVEs by an existing method in which a sodium alkoxide is reacted with tetrafluoroethylene (TFE). Previously reported reaction times were long requiring very high TFE pressures and product yields were low. Kinetic factors affecting TFVE reaction rates were examined and a method to increase reaction rates at low TFE pressures was proposed. Finally, chapter 5 is a summary in which future work is proposed based on the results presented in this thesis.

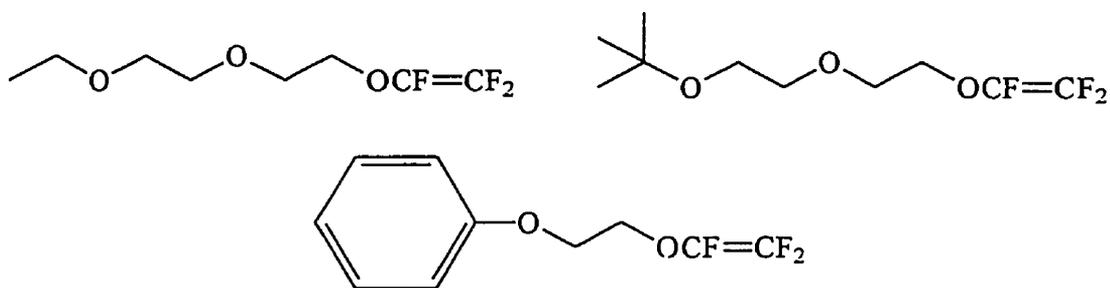


Figure 1.1. Functionalized oligo-ether trifluorovinyl ethers which may be used as monomers for polymer synthesis.

The decision to prepare functionalized oligo-ether trifluorovinyl ethers as monomers for potential polymer synthesis was based primarily on three considerations. Firstly, fluoropolymers such as expanded poly(tetrafluoroethylene) have been used with generally acceptable clinical success in biomaterial applications such as vascular grafts,² and peripheral nerve repair.³ Part of this success is a result of high chemical stability and a resistance to protein adsorption *in vivo*.⁴ Secondly, “the utilization of polyethylene glycol (PEG) substrates for biomaterial applications has grown increasingly important in recent years.”⁵ Material surfaces modified with PEG have been shown to have increased resistance to protein adsorption relative to the unmodified surface. It is anticipated that a functionalized oligo-ether pendant group within the bulk of a fluoropolymer

soluble/processable relative to conventional fluoropolymers. These considerations will be expanded upon in the following sections.

1.1 Fluoropolymer and PEG Biomaterials

Biological systems interact at the surfaces of implanted materials.⁶ Most implanted materials will quickly absorb a monolayer of many different proteins. These proteins will occupy many different conformational and orientational states. Cells arriving at the surface will respond in specific ways to the different conformational and orientational states of these proteins. Consequently a variety of cellular processes may be triggered. This can result in the recognition of the material as foreign by the immune system which can lead to isolation of the material from the rest of the biological system and ultimately in failure of the implant. For biomaterial applications, fluoropolymers have been found to be chemically and relatively biologically inert yet still adsorb proteins.

Surfaces of materials are being engineered with the intention of producing minimal and/or specific biological responses. Considerable research has focused on surface modification of fluoropolymers, such as poly(tetrafluoroethylene) or poly(tetrafluoroethylene-*co*-hexafluoropropylene). Fluoropolymer surfaces have been altered by chemical etching and other techniques such as microwave frequency generated plasmas. However fluoropolymers remain difficult to process into complex structures, are insoluble in common organic solvents, and require highly reactive species for surface modification.⁷

Researchers have also focused on the modification of material surfaces with PEG. The interest shown in PEG derives from its unique set of properties, such as having a lack of toxicity,⁸ a lack of immunogenicity,⁹ solubility in water, high mobility in water and large excluded volume in water.⁸ PEG modification renders the surface more hydrophilic, less protein and cell adsorptive¹⁰ and less recognizable by the immune system. However, there is no clear consensus on how PEG modified surfaces are better able to resist protein and cell adsorption. Hydration and mobility (i.e. “a brush effect”) factors may be responsible. Because of the hydration and mobility of the polymer chain, molecules such as proteins tethered to surfaces via PEG exhibit activity similar to

back to a material surface. Finally, surfaces modified with polyethylene oxide oligomers have also been shown to have an increased resistance to protein adsorption.¹⁰

1.2 Novel Fluoropolymers

It is anticipated that polymers from the monomers described herein can be synthesized and may eventually be shown to mimic the increased resistance to protein and cell adsorption seen with PEG and oligoethylene oxide modified surfaces as well as some of the chemical resistance of fluoropolymers. The pendant groups would be expected to impart dramatically different physical and chemical properties to the polymer relative to conventional fluoropolymers, possibly rendering them soluble in common organic solvents. However, with improved processability and solubility, there will undoubtedly be a considerable decrease in chemical resistance. This may not be a significant problem since what is required is chemical resistance *in vivo*. Conditions are such that it is anticipated that these polymers will perform satisfactorily.

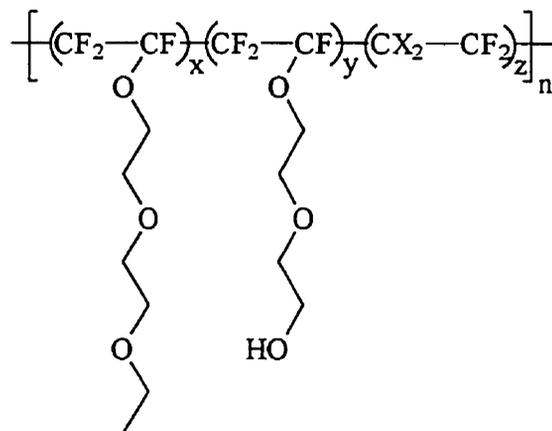


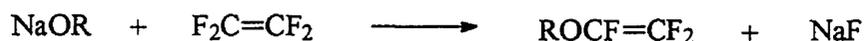
Figure 1.2. A copolymer when either x or y is zero or a possible terpolymer incorporating two oligoether TFVE monomers when both x and y are nonzero. X is H or F.

The TFVE monomers may also copolymerize with a gaseous comonomer such as 1,1-difluoroethylene or tetrafluoroethylene (TFE) (Figure 1.2). Copolymerization with different pressures of the comonomer would allow for varied molar ratios of the comonomer to be incorporated in the copolymer resulting in varied chemical and physical properties. For example, incorporation of high molar ratios of the comonomer may be expected to decrease the

would allow for further surface modification

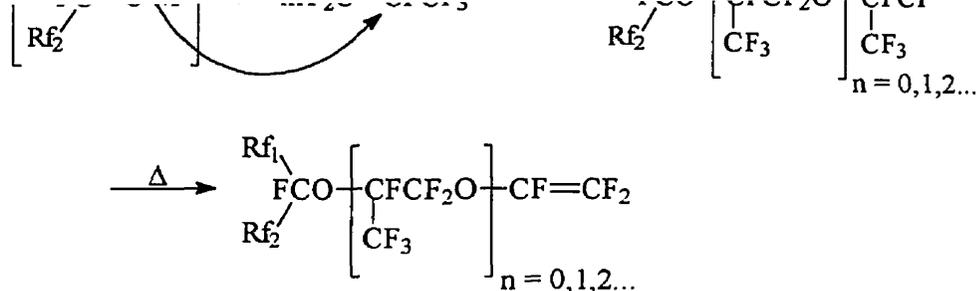
2.1 Monomer Synthesis

TFVEs have been previously synthesized by two principal synthetic routes which do not involve the use of elemental fluorine/chlorine or HF. For example, 1-methoxy-1,1,2-trifluoroethene was prepared by the reaction of sodium methoxide with tetrafluoroethylene.¹² This reaction was expanded to include ethyl, isopropyl and *tert*-butyl substituted TFVEs (Scheme 2.1).¹³ While straightforward in approach, this method required high pressure reaction equipment to achieve high tetrafluoroethylene pressures and long reaction times (and in one instance an explosion was reported).¹³ Also, the reported yields of TFVEs with aliphatic alkoxides (higher than ethoxide) are low, on the order of 10-30%.



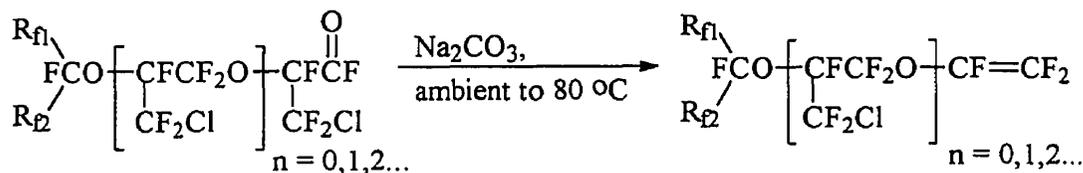
Scheme 2.1. Reaction of an aliphatic alkoxide with tetrafluoroethylene to form a trifluorovinyl ether. R (examples) = methyl, ethyl, isopropyl, and *tert*-butyl, or phenyl.

Alternatively, a synthesis of TFVEs (i.e. *perfluoroalkoxy*-1,1,2-trifluoroethenes) involved the reaction of a perfluoroacid fluoride^{14,15} or perfluoroketone^{14,16} with hexafluoropropene oxide (HFPO) in the presence of an alkali metal fluoride catalyst (e.g. potassium or cesium fluoride) to yield a 2-perfluoroalkoxy-2,3,3,3-tetrafluoropropionyl fluoride intermediate (Scheme 2.2). The alkali metal fluoride reacts with the perfluoroacid fluoride or perfluoroketone to form an intermediate perfluoroalkoxide which ring opens HFPO at the center atom (C2). Thermolysis of either this intermediate acid fluoride in the vapor phase over a metal oxide or thermolysis of the alkali metal salt of the corresponding carboxylic acid yielded the TFVE.^{14,17}



Scheme 2.2. Reaction of a perfluoroacid fluoride or perfluoroketone with hexafluoropropene oxide (HFPO) to yield a 2-perfluoroalkoxy-2,3,3,3-tetrafluoropropionyl fluoride. R_{f1} is perfluoroalkyl, R_{f2} is F or perfluoroalkyl, M is K or Cs. Thermolysis of the 2-perfluoroalkoxy-2,3,3,3-tetrafluoropropionyl fluoride yielded the TFVE. When HFPO is added as the limiting reagent to a solution of the perfluoroalkoxide, n is zero.

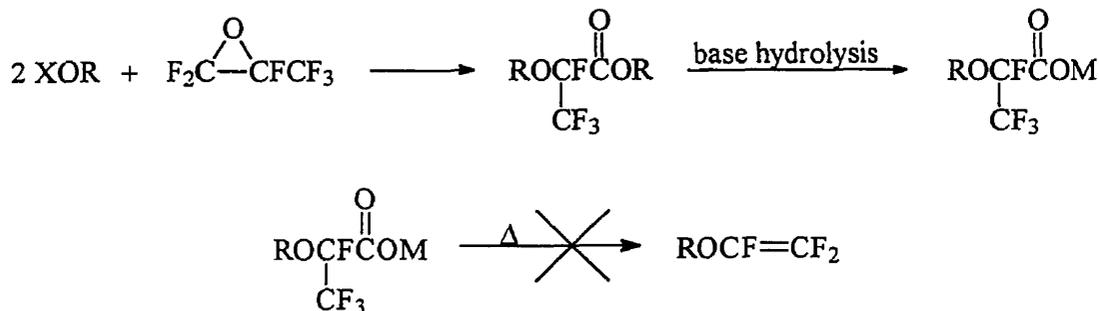
Thermolysis of the acid fluoride intermediate was a “fair yielding step at best.”²⁴ However, the yield was improved by using 3-chloroperfluoropropene oxide, instead of HFPO, producing a 2-perfluoroalkoxy-3-chloro-2,3,3-trifluoropropionyl fluoride intermediate (Scheme 2.3).¹⁸ The latter was reported to react with sodium carbonate at temperatures between ambient and 80 °C to form the TFVE in very high yields. However, 3-chloroperfluoropropene oxide is not commercially available.



Scheme 2.3. 2-Perfluoroalkoxy-3-chloro-2,3,3-trifluoropropionyl fluoride reacts with Na_2CO_3 under mild conditions to form the TFVE. R_{f1} is perfluoroalkyl, R_{f2} is F or perfluoroalkyl.

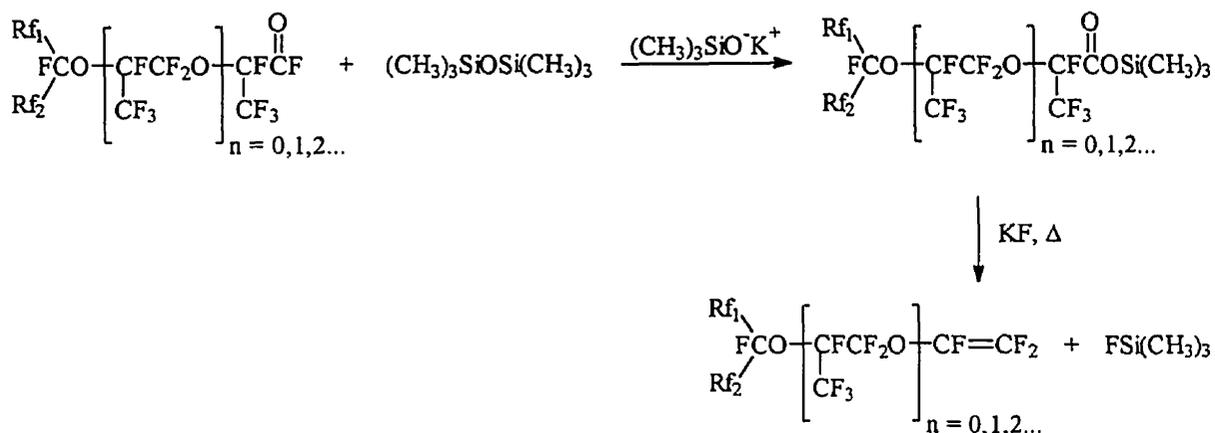
Substituted acid fluorides or fluoroketones have also been successfully reacted with HFPO and the resulting acid fluoride intermediates were converted to TFVEs.^{19,20} Published examples were prepared from the reaction of highly fluorinated or perfluorinated acid fluorides or ketones with HFPO. Fluorine or trifluoromethyl substitution appears to stabilize the fluoroalkoxide intermediate which reacts with HFPO (*cf.* Scheme 2.2).²¹ However, reaction of a hydrocarbon alcohol²² or alkoxide²³ with HFPO was shown to lead to an alkyl 2-alkoxy-2,3,3,3-tetrafluoropropionate ester (Scheme 2.4). The esters were base hydrolyzed to give the

hydrocarbon substituent and counterion.²³



Scheme 2.4. Reaction of an alcohol or alkoxide with HFPO. Thermolysis of the 2-alkoxy-2,3,3,3-tetrafluoropropionate salt resulted in negligible to low yields of TFVE depending on the hydrocarbon substituent and counterion. X is H or Na. M is Na, K, or Cs. R is alkyl.

Thermolysis of trimethylsilyl 2-fluoro/perfluoroalkoxy-2,3,3,3-tetrafluoropropionates in the presence of a fluoride ion catalyst (i.e. KF) has resulted in fluoro/perfluoroalkoxy TFVEs in nearly quantitative yields.²⁴ The thermolysis reaction was conducted in solution or more favorably in the gas phase at temperatures of 140 °C to 350 °C (Scheme 2.5). The trimethylsilyl esters were prepared in nearly quantitative yields from the 2-fluoro/perfluoroalkoxy-2,3,3,3-tetrafluoropropionyl fluorides (Scheme 2.2). The 2-perfluoroalkoxy-2,3,3,3-tetrafluoropropionyl fluorides were reacted with hexamethyldisiloxane in the presence of catalytic potassium trimethylsilanolate.



Scheme 2.5. Synthesis of trimethylsilyl 2-fluoro/perfluoroalkoxy-2,3,3,3-tetrafluoropropionates from appropriate fluorinated acid fluorides. Thermolysis of the trimethylsilyl 2-fluoro/perfluoroalkoxy-2,3,3,3-tetrafluoropropionates resulted in high yields of fluoro/perfluoroalkoxy TFVEs.

Fluorinated/perfluorinated TFVEs have been used commercially, “typically as co-monomers in highly fluorinated polymers.”²⁴ There has been no reported commercial use of hydrocarbon based TFVEs as monomers in the preparation of polymers. There is, however, some qualitative observations that these types of TFVEs will homopolymerize. It was reported that 1-methoxy-1,2,2-trifluoroethene would polymerize on standing at ambient temperature, while 1-ethoxy-1,2,2-trifluoroethene could be “polymerized to a balsam like mass with common free radical initiators.”¹³

Homo/copolymers from fluoro/perfluoro TFVEs are also prepared by free radical polymerization. The polymerization can be carried out in solution using organic solvents (i.e. fluorinated/perfluorinated solvents) but is more commonly done in an aqueous emulsion.²⁰ Free radicals on carbon bonded to fluorine are highly electrophilic and can abstract hydrogen atoms from nearly all hydrocarbons.²⁵ Consequently, high molecular weight fluoropolymers cannot be obtained in most organic solvents. Sources of radicals for the aqueous emulsion polymerizations are typically inorganic salts such as ammonium or potassium persulfate. Soluble organic initiators, such as perfluoropropionyl peroxide, have been used for non-aqueous polymerizations. Examples of the surfactants used to stabilize the emulsions are perfluoroaliphatic carboxylate salts such as ammonium or sodium perfluorooctanoate. Recently, it has been shown that perfluoro(propyl vinyl ether), $(F(CF_2)_3OCF=CF_2)$, can be copolymerized with TFE in supercritical carbon dioxide.²⁵

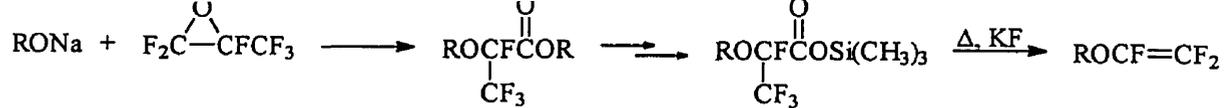
Fluoro/perfluoro TFVEs can dramatically alter the chemical and physical properties of the fluoropolymer while often retaining a fairly high chemical and/or thermal stability. For example, a component of PFA, a copolymer with TFE, is perfluoro(propyl vinyl ether). Perfluoro(propyl vinyl ether) lowers the melt viscosity of the copolymer. Consequently, PFA can be molded using conventional melt processing techniques which are not possible for poly(tetrafluoroethylene).²⁶ A component of Nafion[®] is a TFVE with a terminal sulfonic acid moiety $(CF_2=CFO(CF_2)_2SO_3H)$. This monomer dramatically alters the properties of Nafion[®] allowing for water uptake and ion conductivity.

As described in section 2.1, two primary methods for the preparation of TFVEs which do not require the use of elemental fluorine, HF, or other halogens have previously been documented in the literature. In one method, aliphatic alkoxides were reacted with TFE to form the desired TFVEs (*cf.* Scheme 2.1).^{12,13} However, there were several drawbacks which initially disfavored the use of this method. For example, the large excess of TFE used translated to high TFE pressures which required the use of expensive high pressure reaction equipment. Secondly, TFE is not presently commercially available and has to be synthesized. Yields of TFVEs prepared by this method were reported to be low.

In the second method, a fluoro/perfluoroketone or acid fluoride is reacted with hexafluoropropene oxide (HFPO) to yield an intermediate, 2-perfluoroalkoxy-2,3,3,3-tetrafluoropropionyl fluoride. Thermolysis of this intermediate resulted in a TFVE (*cf.* Scheme 2.2). However, there is no precedent in the literature for a reaction of an aliphatic acid fluoride with HFPO. It appears that fluorine or trifluoromethyl substitution alpha to the carbonyl is required to stabilize a fluoroalkoxide intermediate which then reacts with HFPO.²¹

2.3.1 Hypothesis

An alternate preparation of the desired TFVEs has been proposed and investigated (Scheme 2.6). The synthesis involved the reaction of the appropriate aliphatic sodium alkoxide (i.e. oligoether alkoxides) with HFPO to yield a 2-alkoxy-2,3,3,3-tetrafluoropropionate ester ($\text{ROCF}(\text{CF}_3)\text{CO}_2\text{R}$) as outlined in Scheme 2.4. However, it has been demonstrated that thermolysis of the corresponding 2-alkoxy-2,3,3,3-tetrafluoropropionate alkali metal salts results in negligible to low yields of TFVEs. Thus, it was proposed that the ester be converted to a trimethylsilyl 2-alkoxy-2,3,3,3-tetrafluoropropionate ester which would undergo gas phase vacuum thermolysis in the presence of potassium fluoride catalyst (KF) to possibly yield the desired TFVE. Although the thermolysis of this type of trimethylsilyl ester (as opposed to trimethylsilyl 2-*fluoro/perfluoroalkoxy-2,3,3,3-tetrafluoropropionates*) has been suggested,²⁴ these trimethylsilyl esters have never been synthesized.



Scheme 2.6. Proposed synthesis of the desired TFVEs. R is an aliphatic oligoether.

The proposed synthesis is more elaborate than a reaction of the alkoxide with TFE, but it can be accomplished with common and/or easily prepared laboratory equipment. However, the high pressure reaction equipment required for preparing and handling TFE became available. The desired TFVEs were also prepared by the reaction of the appropriate sodium alkoxide with TFE and the reaction mechanism was investigated.

As described in section 2.2, there is some precedent for polymerization of TFVEs of the type presented here. However, a thorough investigation of the homo/copolymerization characteristics of these monomers and properties of the polymers is beyond the scope of this thesis.

3.1 Results

The overall synthetic route is summarized in Figure 3.1. Two equivalents of a sodium alkoxide, **2**, react with HFPO to yield the ester, **5**, which is converted to the sodium carboxylate salt, **6**, and then to the trimethylsilyl ester, **7**, prior to thermolysis to the desired TFVE, **8**.

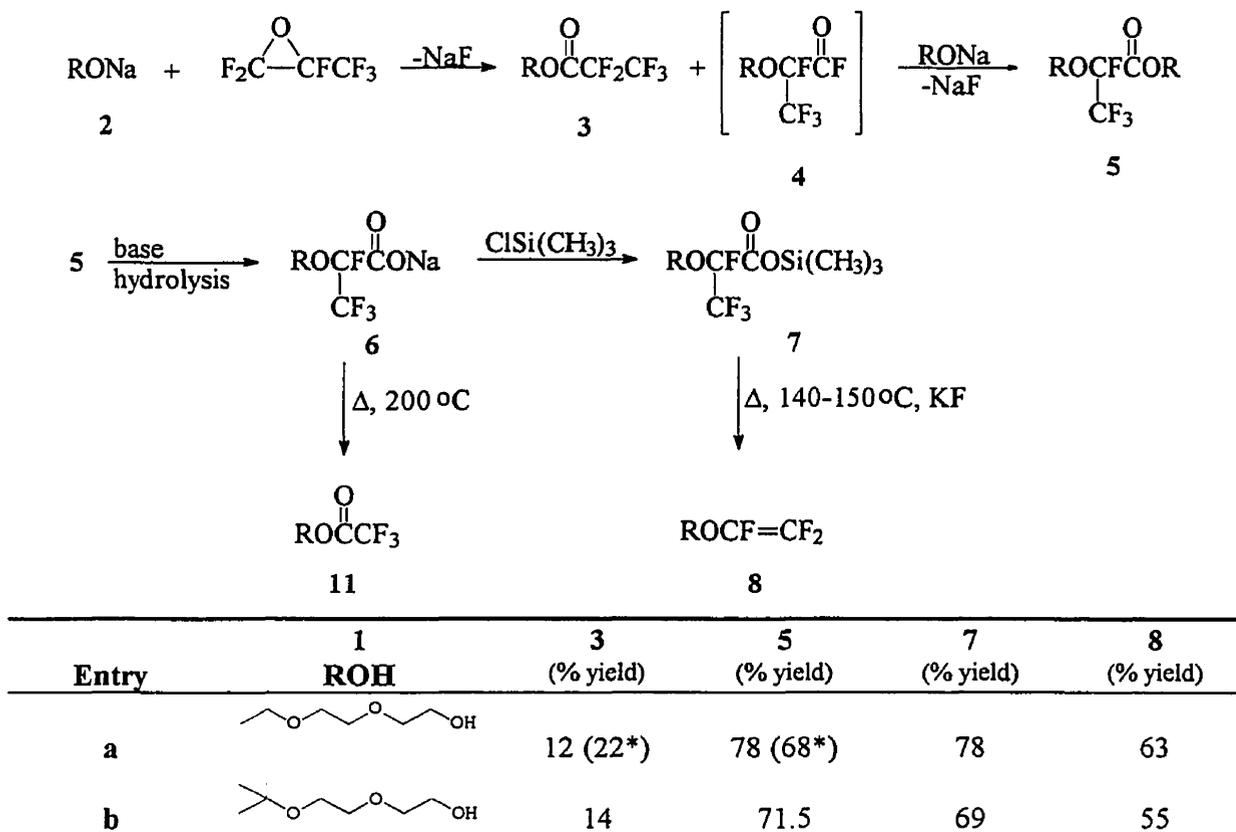
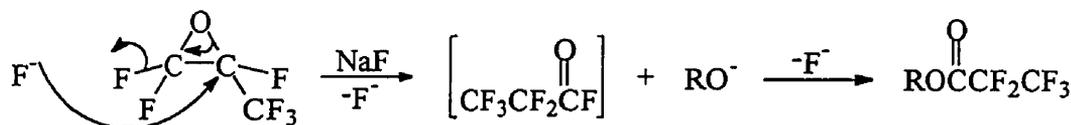


Figure 3.1. Reaction of a sodium alkoxide, **2**, with hexafluoropropene oxide (HFPO) produces an ester incorporating two equivalents of the alcohol, **5**. Hydrolysis of the ester and reaction of the sodium carboxylate salt, **6**, with trimethylsilyl chloride produces a trimethylsilyl ester, **7**, which forms the desired trifluorovinyl ether (TFVE), **8**, under thermolysis conditions. *Reaction started at -78°C .

The sodium alkoxide, **2**, was prepared (but not isolated) by reaction of the appropriate alcohol, **1**, with sodium hydride. The sodium alkoxide was required for reaction with HFPO because, unlike lower alcohols (i.e. methanol, ethanol) which react readily with HFPO, higher alcohols are

methylene chloride.²⁷ The mono-ether was obtained in 70% yield (96% purity by gas chromatography, GC) following vacuum distillation. A negligible amount of the bis(2-*tert*-butoxy-ethyl) ether was formed.

The reaction of the sodium alkoxide, **2**, with 0.59 to 0.75 equivalents of HFPO in anhydrous ethylene glycol dimethyl ether (DME) was exothermic, resulting in the formation of the ester, **5** and an perfluoropropionate ester, **3**. The ester, **5**, contains two equivalents of the alcohol per equivalent of HFPO (*cf.* Figure 3.1). Ring-opening of HFPO at the center carbon (C2) is favored by the electron withdrawing trifluoromethyl (CF₃) group.²² The mechanism likely involves formation of an acid fluoride intermediate, **4**, which reacts with a second equivalent of the alkoxide **2** to form **5**.



Scheme 3.1. Mechanism for the formation of the undesired trifluoroacetate ester, **3**. Reaction of fluoride ion (formed during the primary reaction of alkoxide with HFPO) at C2 of HFPO to yield perfluoropropionyl fluoride followed by reaction with the alkoxide to yield **3**. R is alkyl.

Formation of the perfluoropropionate ester, **3**, is likely a result of the fluoride ion (formed during the primary reaction of the alkoxide) reacting with HFPO at C2 to give perfluoropropionyl fluoride. Perfluoropropionyl fluoride reacts with the alkoxide to give **3** (Scheme 3.1). While HFPO has been shown to be stable to fluoride ion attack in *tert*-butyl alcohol, potassium *tert*-butoxide has been shown to react with HFPO in *tert*-butyl alcohol at 20 °C to form *tert*-butyl perfluoropropionate exclusively.²⁸ It was suggested that the alkoxide may be reacting at C1 due to steric hindrance at C2, followed by elimination of fluoride ion with rearrangement to yield **3**. However, this is unlikely given that C2 is a hard electrophilic center. HFPO has been shown to react with cesium fluoride to form perfluoropropionyl fluoride in ether solvents.²⁹ In the experiments described herein, the relative amount of **5** vs. **3** produced was controlled by temperature. For example, a reaction started at -78 °C, yielded 40 mol % (or 22% yield) of **3a** whereas one started at 0 °C yielded 18 mol % (or 12% yield) of **3a**.

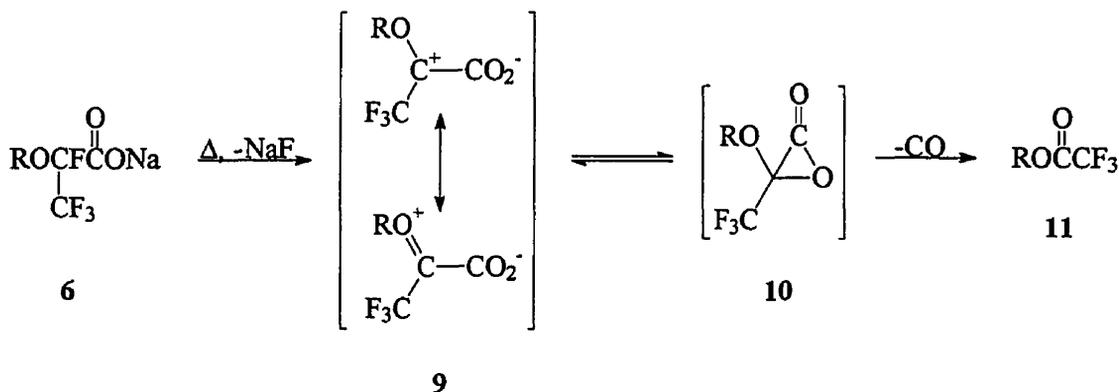
approximately 1.1 to 1.2 equivalents of sodium hydroxide. THF, water, and the majority of byproduct alcohol, **1**, were removed from the flask. The sodium carboxylate salt, dissolved in anhydrous diethyl ether, reacted with trimethylsilyl chloride (TMSCl) to produce the trimethylsilyl ester, **7**. The sodium salt, **6**, is sensitive to acidic conditions while **7** is susceptible to hydrolysis. To remove acidic species introduced from TMSCl and ensure complete dryness, sodium hydride was added before the addition of TMSCl to avoid conversion of **6** or **7** to the corresponding acid.

For purposes of characterization, pure sodium carboxylate salt, **6a**, was obtained in near quantitative yields by reaction of **7a** with an equivalent of sodium hydroxide in aqueous THF. (Otherwise, **6a** was prepared, but not isolated, from the ester **5a** prior to thermolysis.)

Thermolysis of **6a**, at 200 °C, resulted in the formation of a complex mixture of products. The yield was approximately 27% by mass and consisted primarily of a trifluoroacetate ester, **11a** (*cf.* Figure 3.1), as identified by GC analysis. The trifluoroacetate ester, **11a**, was isolated by vacuum fractional distillation and further characterized by HRMS.

The trimethylsilyl ester, **7**, was injected at a constant rate onto the evacuated pre-heated column as described in the experimental section. Although the thermolysis reaction is exothermic, the reaction column was heated to temperatures between 140 and 150 °C to both maintain volatility and ensure efficient passage of the trimethylsilyl ester through the column. GC analysis of the crude thermolysis product indicated that it consisted primarily of TFVE, fluorotrimethylsilane and a small amount of the trifluoroacetate ester, **11**. The fluorotrimethylsilane, and residual carbon dioxide were removed using aspirator vacuum followed by vacuum fractional distillation, resulting in TFVE, **8**, with yields of 55-63% from the trimethylsilyl ester, **7**.

Vacuum thermolysis of sodium 2-[2-(2-ethoxy-ethoxy)-ethoxy]-2,3,3,3-tetrafluoropropionate, **6a**, resulted in the formation of a trifluoroacetate ester, 2-(2-ethoxy-ethoxy)-ethyl trifluoroacetate, **11a**. Sodium or potassium carboxylate salts, similar to those described herein, have also been shown to yield the trifluoroacetate esters as the major product after thermolysis.²³ A unimolecular reaction pathway was proposed, similar to that shown in Scheme 3.2: sodium fluoride, eliminated alpha to the carbonyl, results in a zwitterionic intermediate which can exist in either open-chain, **9**, or cyclic, **10**, forms. Loss of carbon monoxide from **10** results in the observed trifluoroacetate ester, **11**. The alkyl substituent, which is relatively electron-rich compared to a fluoroalkyl substituent, may also stabilize the zwitterion, **9**, through resonance with the positive charge on the ether oxygen.

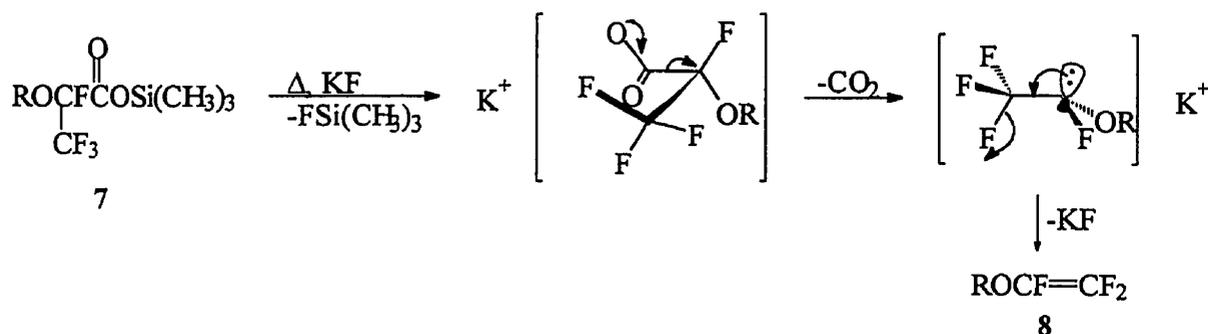


Scheme 3.2. Reaction pathway²³ which leads to a trifluoroacetate ester, **11**, from zwitterion, **9**, and cyclic, **10**, intermediates. The zwitterion intermediate, **9**, may be further stabilized by a resonance structure when R is alkyl as opposed to fluoroalkyl, with the positive charge on the oxygen atom.

In contrast to the mechanism described for the formation of the undesirable trifluoroacetate ester, **11**, from **6**, it is generally accepted that salts of 2-fluoroalkoxy-2,3,3,3-tetrafluoropropionates decarboxylate to form an intermediate carbanion which eliminates fluoride ion at the β -position to form the desired olefin (Scheme 3.3).¹⁸ These salts decarboxylate at temperatures of approximately 200 °C. In contrast, salts of 2-fluoroalkoxy-3-chloro-2,3,3-trifluoropropionates decarboxylate at temperatures between ambient and 80 °C,¹⁸ requiring dramatically less energy to form the olefin (through an intermediate carbanion if it exists) when chloride (a better leaving group) replaces fluoride (*cf.* Scheme 2.3).

Scheme 3.3. Generally accepted mechanism for the decarboxylation of 2-fluoro/perfluoroalkoxy-2,3,3,3-tetrafluoropropionate salts via a carbanion intermediate to TFVEs. R_f is fluoro/perfluoroalkyl.

The successful thermolysis of trimethylsilyl esters, **7**, to the desired TFVEs, **8**, is likely a result of favorable reaction kinetics. On contact with the potassium fluoride catalyst, desilylation occurs. Given that thermolysis of potassium 2-alkoxy-2,3,3,3-tetrafluoropropionates yielded undesired trifluoroacetate esters, **11**,²³ it is likely that decarboxylation is fast and well-advanced before a metal-oxygen bond can form (Scheme 3.4). The successful decarboxylation of alkali metal 2-methoxy-2,3,3,3-tetrafluoropropionates to form 1,1,1,2-tetrafluoroethyl methyl ether was shown to be inversely related to the strength of the metal oxygen bond.³⁰



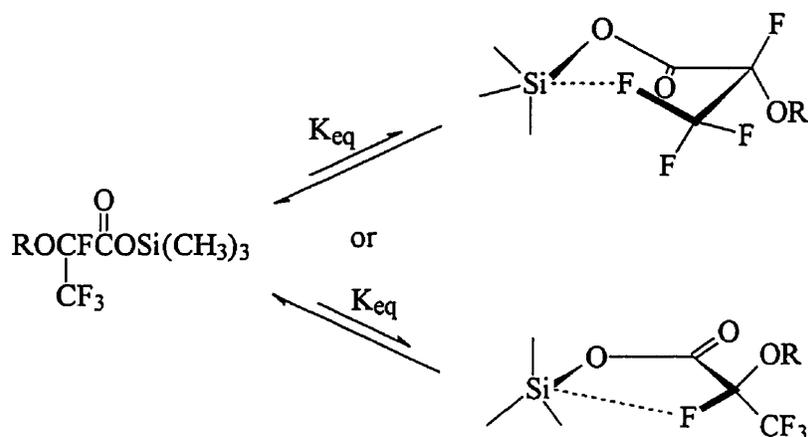
Scheme 3.4. Thermolysis of a trimethylsilyl ester, **7**, with desilylation occurring first. Decarboxylation occurs before a potassium oxygen bond can form resulting in a short-lived carbanion which eliminates fluoride ion to form the olefin. R is alkyl.

Decarboxylation likely results in formation of an intermediate carbanion which then eliminates fluoride ion to form the olefin (*cf.* Scheme 3.4) and not a concerted elimination of fluoride ion with decarboxylation. Although no direct observance of this type of carbanion has been reported in the literature, decarboxylation of alkali metal 2-methoxy-2,3,3,3-tetrafluoropropionates in protic solvents yielded 1,1,1,2-tetrafluoroethyl methyl ether, a stable hydride.³⁰

The thermolysis reaction may also be influenced by an intramolecular silicon-fluorine interaction as suggested by the ¹⁹F NMR spectrum of trimethylsilyl ester, **7**. The ¹⁹F NMR spectrum of **7a** in deuterated chloroform, for example, was expected to have a simple AX₃ pattern. However, two

and fluoromethylene (CF) respectively; and (2) a less intense doublet at -82.0 ppm and a broad, considerably less intense, singlet at -131.2 ppm also with an integration ratio of 3:1. Comparing this ^{19}F NMR spectrum to those of preceding intermediates, reaction byproducts and potential decomposition products of **7a** (i.e. the corresponding acid), it was suggested that the second set of peaks could also be attributed to the CF_3 and CF of **7a**. A similar ^{19}F NMR spectrum was observed for **7b**.

In order to justify the assignment of the two sets of peaks to the same fluorine atoms, an equilibrium between two different conformations of **7** is proposed: (1) a conformation with an intramolecular interaction between silicon and fluorine and (2) a conformation where there is no silicon-fluorine interaction (Scheme 3.5). Two possible interaction conformations can be rationalized; interaction of either CF or CF_3 with silicon through either a five- or six-membered ring, respectively.



Scheme 3.5. Proposed equilibrium between two structural conformations of trimethylsilyl 2-alkoxy-2,3,3,3-tetrafluoropropionates, **7**. The interaction between silicon and trifluoromethyl fluorine (6-membered ring) or silicon and methylene fluorine (5-membered ring) may influence the thermolysis mechanism.

The driving forces for the interaction conformation may include the high silicon-fluorine bond energy (43 kJ/mol), and the stability of the five- or six-membered ring. A potentially destabilizing shift of electron density from silicon onto oxygen may be partly offset by the stability of

It is more likely that the interaction of silicon is with CF fluorine through a five membered ring rather than with CF₃ fluorine through a six membered ring. In the ¹⁹F NMR spectrum of **7a**, both peaks attributed to CF₃ fluorine appear to be doublets. If silicon were interacting with CF₃ fluorine, these fluorines would likely be chemically inequivalent resulting in a more complex ¹⁹F NMR spectrum.

A ¹⁹F-²⁹Si Nuclear Overhauser Enhancement (NOE) NMR experiment where the enhancement of silicon while saturating each fluorine peak separately was attempted to determine relative proximity of each type of fluorine to silicon. The experiment was inconclusive, partly due to the low natural abundance of ²⁹Si. In fact, only one ²⁹Si peak was observed and the fine structure suggests that it is coupled to 9 equivalent protons (i.e. 3 equivalent methyl groups, Appendix 2, pp. 12). If it is assumed that the less intense set of fluorine peaks represent the interaction conformation, then a second ²⁹Si peak would likely not be observed without ²⁹Si enrichment.

To support the proposed equilibrium, the effect of temperature on relative ¹⁹F NMR peak areas was also studied. ¹⁹F NMR spectra were collected for **7a** (Appendix 3) over a temperature range of -30 °C (243 K) to 94 °C (367 K), the temperature being limited only by the boiling point of the NMR solvent (CDCl₃). Assuming that the less intense set of peaks represent the interaction conformation, the small to large peak area ratio³¹ may be expected to increase with increasing temperature if the equilibrium (*cf.* Scheme 3.5) is endothermic. As the temperature increases the equilibrium constant (K_{eq}) shifts towards the products.

Figure 3.2 is a 3-dimensional plot of the ¹⁹F NMR trifluoromethyl peaks of **7a** as a function of temperature with the intensities of the larger peaks held constant. As can be seen, a trend of increasing intensity for the smaller peaks with temperature may be observed. The trend becomes apparent when the small to large peak area ratio or equilibrium constant is correlated with temperature.

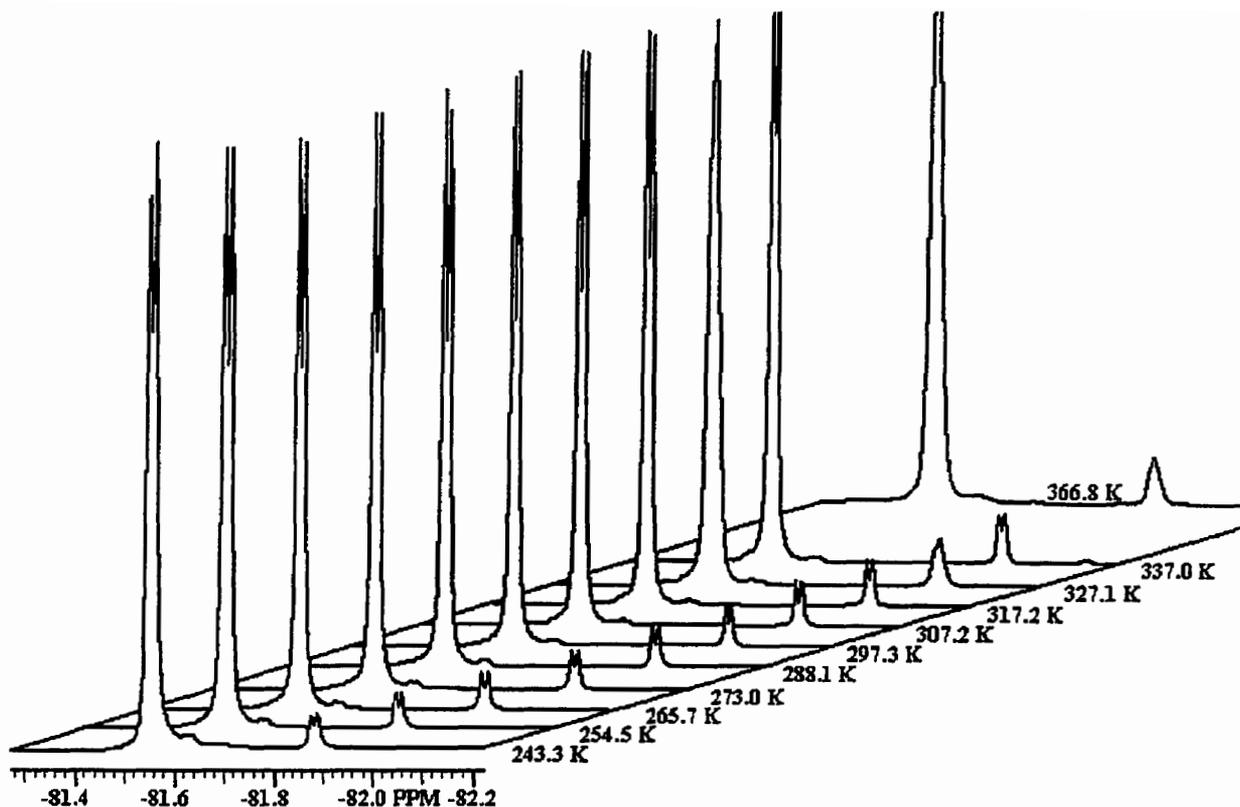


Figure 3.2. A 3-dimensional plot of the ^{19}F NMR trifluoromethyl peaks as a function of temperature. The intensities of the larger peaks are constant and a trend for the smaller peaks of increasing intensity with temperature may be observed.

As shown in Figure 3.3, a van't Hoff plot of $\ln K_{\text{eq}}$ versus $1/T$ appears linear (R^2 is 0.988); $\ln K_{\text{eq}}$ decreases as $1/T$ increases or K_{eq} increases with increasing temperature. Assuming a similar equilibrium exists in the gas phase as exists in the deuterated chloroform, K_{eq} is estimated at 0.10 for thermolysis temperatures. The standard enthalpy for the equilibrium described in Scheme 3.5 was calculated from the slope in Figure 3.3, $\Delta H^\circ = 3.0 \pm 0.1 \text{ kJ mol}^{-1}$, and the standard entropy from the intercept, $\Delta S^\circ = -12.1 \pm 0.4 \text{ J mol}^{-1} \text{ K}^{-1}$. The enthalpy and entropy data indicate that entropy dominates K_{eq} at temperatures higher than 250 K.

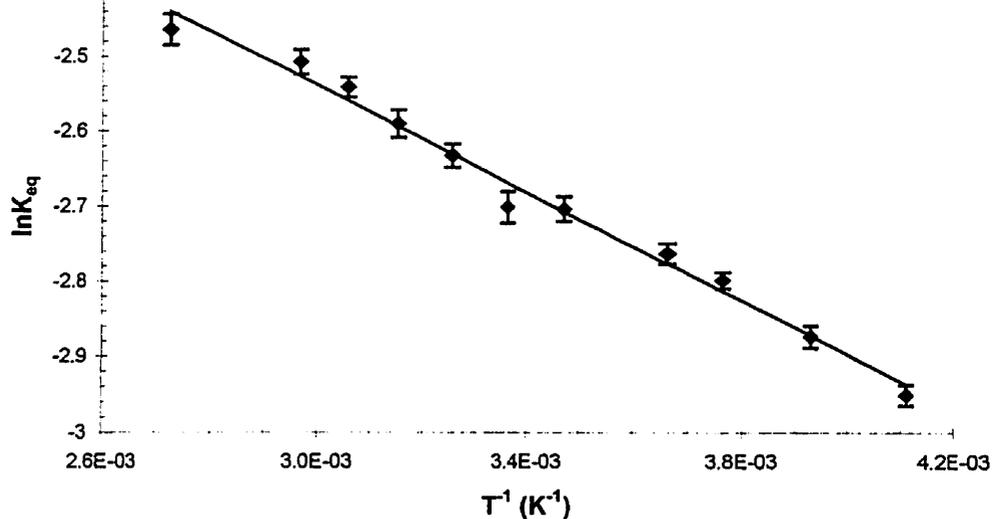
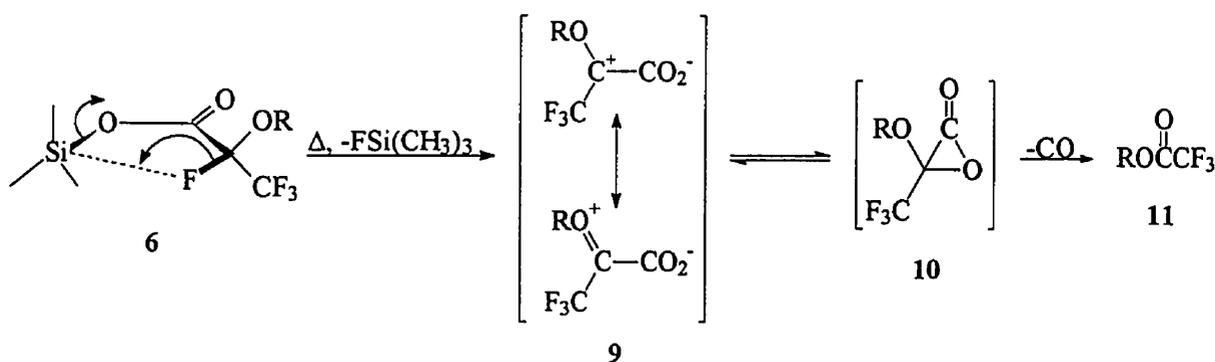


Figure 3.3. Plot of $\ln K_{eq}$ versus $1/T$ for the equilibrium defined in Scheme 9 for trimethylsilyl ester **7a** ($R^2 = 0.988$). From the slope, $\Delta H^\circ = 3.0 \pm 0.1 \text{ kJmol}^{-1}$. From the intercept, $\Delta S^\circ = -12.1 \pm 0.4 \text{ Jmol}^{-1}\text{K}^{-1}$.

The trimethylsilyl ester, **7**, is necessary for successful thermolysis to the desired TFVE, **8**. However, it is not clear that the proposed interaction conformation at thermolysis temperatures contributes significantly to the overall success. While the proposed silicon-fluorine interaction may serve to further weaken the silicon-oxygen bond, the concentration of the interaction conformation is relatively low (estimated at 9%) relative to the non-interaction conformation at thermolysis temperatures. In fact, interaction through a five-membered ring might account for the formation of the small amount of trifluoroacetate ester, **11**, that was observed (Scheme 3.6).

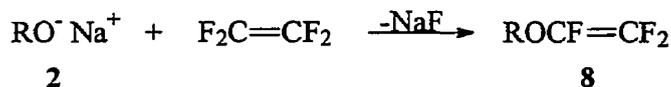


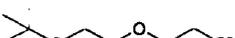
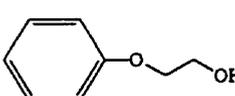
Scheme 3.6. Trifluoroacetate ester formation at 150 °C due to a weakened CF carbon-fluorine bond as a consequence of a silicon-fluorine interaction. R is alkyl ether.

trifluoroacetate ester, **11a** (based on recovered **7a**), was formed. In this instance, formation of trifluoroacetate ester, **11a**, has occurred at temperatures approximately 50 °C lower than that observed for formation from the sodium carboxylate salt, **6a** (*cf.* Scheme 3.2). Since carbon-fluorine (CF) bond breaking is the first step in the mechanism of trifluoroacetate ester formation, a silicon-fluorine interaction may cause this carbon-fluorine bond to break at lower temperatures leading to formation of the trifluoroacetate ester, **11**, by a mechanism similar to that from the sodium carboxylate salt, **6**.

4.1 Results

The sodium alkoxide, **2**, was prepared (but not isolated) by reaction with sodium hydride in diethyl ether under a nitrogen atmosphere. Tetrafluoroethylene (TFE) was prepared according to published methods³² and stored in a pressure cylinder prior to use. Reaction of the alkoxide with a constant pressure of TFE in a Parr 300 mL stainless steel reactor at pressures of approximately 50 psi resulted in the formation of TFVEs, **8**, as outlined in Figure 4.1.



Entry	1 ROH	8 (% yield)
a		62
b		56
c		39 37*

*Isolated yield with 4.4% (by weight) 18-crown-6 added to the solvent

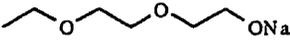
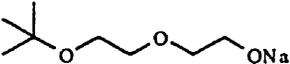
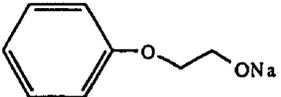
Figure 4.1. Reaction of a sodium alkoxide with tetrafluoroethylene to yield a TFVE.

4.2 Discussion

Somewhat surprisingly, the reaction of sodium alkoxides **2a**, **2b**, and **2c** with TFE resulted in respectable yields (*cf.* Figure 4.1) of TFVEs compared to reported yields from alkoxides higher than ethoxide. Reported TFE pressures were also considerably higher than the pressures used here. With a constant TFE pressure of approximately 50 psi, the reaction of **2a** was complete within 0.5 h and resulted in a 62% isolated yield of TFVE **8a**. In contrast the reaction of **2b** or **2c** at the same TFE pressure required up to 24 h and resulted in 56% and 39% isolated yields of **8b** and **8c**, respectively. The time needed to effectively complete the reaction of **8b** and **8c** also appeared to be proportional to the amount of alkoxide used in the reaction.

electronegativity, alkoxides **2a**, **2b** and **2c** are similar and it was expected that steric factors would not significantly affect reactivity. However, it was qualitatively observed that the solubility of **2a** in diethyl ether was considerably higher than **2b** or **2c**. The solubilities of **2a**, **2b**, and **2c** were determined quantitatively in ethylene glycol dimethyl ether (DME) (Table 4.1). Alkoxide solutions in which the clear supernatant solution was in equilibrium with the solid alkoxide, were prepared. The supernatant solution was sampled and the alkoxide was converted back to the corresponding alcohol. The weight fraction of alcohol/alkoxide in the supernatant was determined by gas chromatography with reference to an internal standard (naphthalene).

Table 4.1. Sodium alkoxide solubility in DME

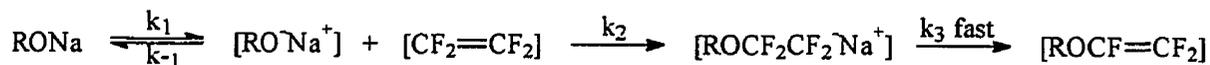
Entry	2 RONa	Solubility in DME* (Wt. fraction × 100 %)
a		31.5 ± 0.2
b		0.12 ± 0.01
c		0.043 ± 0.003 0.107 ± 0.003**

*Determined at temperatures between 25-27 °C. **Solubility with 4.4% w/w 18-crown-6 added to the solvent

To determine the extent to which alkoxide solubility affected the observed rate of reaction, a set of kinetic experiments were conducted in which the change in total weight fraction of sodium alkoxide as a function of time and constant TFE pressure was followed by gas chromatography. Initially, alkoxides **2a** and **2b** were to be used for the study. However, the peaks corresponding to alcohol, **1b**, and TFVE, **8b**, were coincident and could not be sufficiently resolved with any other temperature program. Thus, alkoxide **2c**, which also has a low but determinable solubility in DME, and resolvable peaks, was used in conjunction with **2a** for the study.

I have proposed that sodium alkoxides of limited solubility react with TFE in a stepwise fashion as outlined in Scheme 4.1. The observed rate of reaction was expected to be governed by the solubility of the alkoxide and the rate of reaction of the soluble alkoxide with TFE as will later be

to trap carbanion intermediates.³³ Here, the formation of a TFVE results from an intramolecular rearrangement of the carbanion with elimination of sodium fluoride. It was expected that k_3 would be considerably larger than k_2 and would not be rate-determining.



Scheme 4.1. Proposed reaction pathway for formation of a TFVE from a sodium alkoxide and TFE. Rate constants k_1 , k_{-1} , and k_2 are rate limiting and k_3 is considerably larger than k_2 . RONA is the insoluble alkoxide. $[\text{RO}^-\text{Na}^+]$ is the alkoxide in solution.

Sodium alkoxide, **2a**, was completely soluble at the concentrations used in the study. That is k_1 is considerably larger than k_{-1} . Thus, it was expected that k_2 would be strictly rate-determining and the reaction would be first order in **[2a]** and TFE. The rate constant, k_2 , would be second order overall. If the TFE pressure was held constant, first order kinetics were expected experimentally. A rate equation for the reaction of **2a** with TFE is as follows:

$$-\frac{d[\text{RO}^-\text{Na}^+]}{dt} = k_2[\text{RO}^-\text{Na}^+][\text{CF}_2=\text{CF}_2] = k_{2\text{obs}}[\text{RO}^-\text{Na}^+] \quad (4.1)$$

Figure 4.2 is a plot of the natural logarithm of the weight fraction of sodium alkoxide, **2a**, as a function of time at constant TFE pressure and temperature. Experimentally, it does appear that the reaction kinetics are first order. A best fit linear regression was determined (R^2 is 0.976). From the slope, a value for the observed rate constant, $k_{2\text{obs}}$ was determined to be $(4.1 \pm 0.1) \times 10^{-3} \text{ s}^{-1}$.

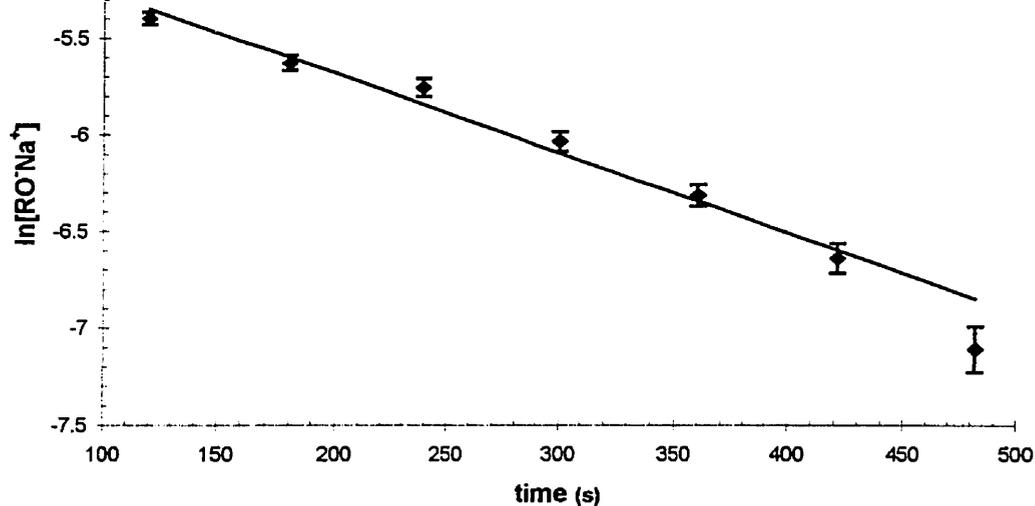


Figure 4.2. Plot of the natural logarithm of the experimentally observed weight fraction of alkoxide, [2a], as a function of time. The reaction was performed at a constant TFE pressure of 50 psi and a constant temperature of 26 °C.

For alkoxides of limited solubility, such as 2c, a rate equation is postulated as follows:

$$-\frac{d\text{RONa}}{dt} = k_1 - k_{-1}[\text{RO}^-\text{Na}^+] \quad (4.2)$$

Assuming a steady state for $[\text{RO}^-\text{Na}^+]$ gives:

$$\frac{d[\text{RO}^-\text{Na}^+]}{dt} = k_1 - k_{-1}[\text{RO}^-\text{Na}^+] - k_2[\text{RO}^-\text{Na}^+][\text{CF}_2=\text{CF}_2] = 0 \quad (4.3)$$

Rearrangement of equation 4.3 for $[\text{RO}^-\text{Na}^+]$ and substitution into equation 4.2 gives the following rate equation:

$$-\frac{d\text{RONa}}{dt} = k_1 - \frac{k_1 k_{-1}}{k_{-1} + k_2[\text{CF}_2=\text{CF}_2]} = k_1 \left[1 - \frac{1}{1 + \frac{k_2[\text{CF}_2=\text{CF}_2]}{k_{-1}}} \right] \quad (4.4)$$

Equation 4.4 implies that the rate of reaction is dependent on k_1 , k_{-1} , k_2 , and $[\text{CF}_2=\text{CF}_2]$ and predicts that the rate of decrease of the alkoxide weight fraction would be constant with time if the TFE pressure was constant. The time to complete the reaction would be proportional to the initial weight fraction of alkoxide. At a constant TFE pressure, $k_2[\text{CF}_2=\text{CF}_2]$ is equivalent to $k_{2\text{obs}}$, and an observed rate constant, k_{obs} , is equal to:

There are two special limits that can be calculated from equation 4.5. If $k_{2obs} \gg k_{-1}$, the observed rate of reaction, k_{obs} , is found to be equal to:

$$k_{obs} = \lim_{k_{2obs} \gg k_{-1}} \left[k_1 - \frac{k_1 k_{-1}}{k_{-1} + k_{2obs}} \right] = k_1 \quad (4.6)$$

Equation 4.6 predicts that the reaction would be subject to kinetic control and the observed rate would be equal to the forward rate of alkoxide solvation. However if $k_{-1} \gg k_{2obs}$, then k_{obs} is found to be equal to:

$$k_{obs} = \lim_{k_{-1} \gg k_{2obs}} \left[k_1 - \frac{k_1 k_{-1}}{k_{-1} + k_{2obs}} \right] = \frac{k_1 k_{2obs}}{k_{-1}} = K_{sol} k_{2obs} \quad (4.7)$$

Equation 4.6 predicts that the observed rate of reaction would be governed by the relative free energy difference between the insoluble/soluble alkoxide (a fast solubility equilibrium) and the rate of reaction of the soluble alkoxide with TFE.

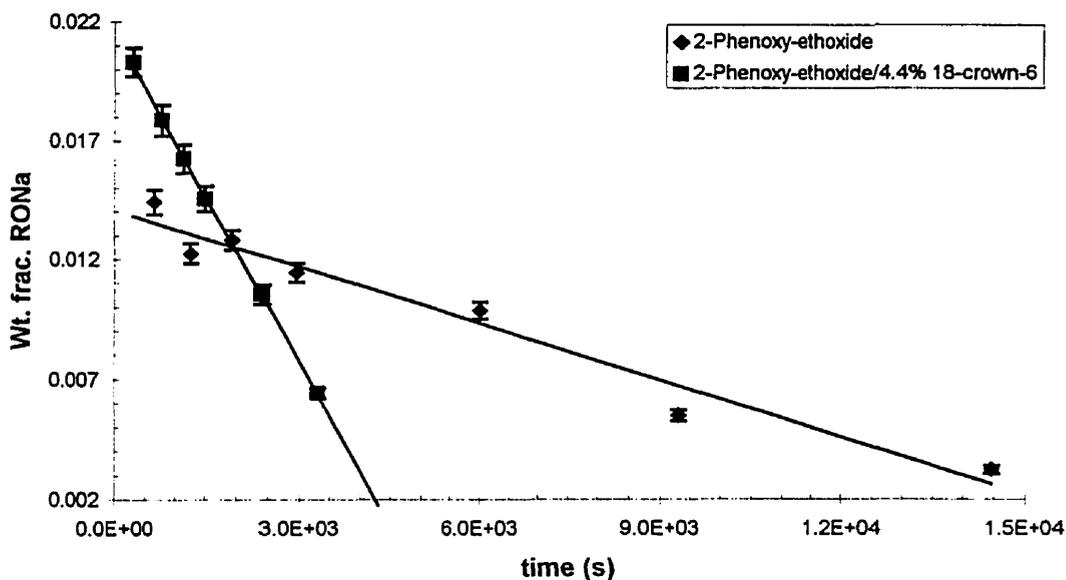


Figure 4.3. Plot of the experimentally observed weight fraction of sodium alkoxide, 2c, as a function of time. The observed rate of reaction is considerably increased with the addition of 4.4 % (by weight) 18-crown-6. Both reactions were performed at a constant TFE pressure of 50 psi and a constant temperature of 26 °C.

was constant with time. A best fit linear regression was determined (R^2 is 0.963). From the slope, a value for the observed rate constant, k_{obs} was determined to be $(7.9 \pm 0.7) \times 10^{-7} \text{ s}^{-1}$. A value for k_{-1} was calculated by substitution of $k_1 = K_{sol}k_{-1}$ into equation 3.5 and rearrangement for k_{-1} as follows:

$$k_{-1} = \frac{k_{obs}k_{2obs}}{K_{sol}k_{2obs} - k_{obs}} \quad (4.8)$$

It was assumed that k_{2obs} for **2c** is approximately the same as determined for **2a**. Using the solubility for **2c** shown in Table 4.1, a value for k_{-1} of $(3.3 \pm 0.6) \times 10^{-3} \text{ s}^{-1}$ was obtained from equation 4.8. The calculated value for k_1 was $(1.4 \pm 0.3) \times 10^{-6} \text{ s}^{-1}$. Experimentally, k_{-1} was the same order of magnitude as k_{2obs} , resulting in k_1 , k_{-1} , and k_{2obs} all being rate limiting. The observed reaction rate, k_{obs} , was approximately half the value of k_1 .

It would be desirable to increase the observed rate of reaction to reduce the reaction time without increasing TFE pressure or diluting the alkoxide. For alkoxide **2c**, increasing TFE pressure would increase k_{2obs} relative to k_{-1} and the observed reaction rate, at most, would double to the limiting value k_1 . The forward rate of solubility, k_1 , could be increased further by increasing temperature. However, the reaction becomes increasingly more dangerous as TFE pressure is increased and raising the temperature may accelerate the decomposition of the TFVE monomer. For sodium alkoxides with even lower solubility, this strategy would likely not work at all. If the overall alkoxide solubility could be increased, reaction rates may increase if k_1 and/or k_{-1} were increased relative to k_{2obs} .

There were two immediate possibilities for increasing alkoxide solubility. Firstly, a better solvent for the alkoxide could be used. Secondly, addition of a compound such as a crown ether which may act as a phase transfer catalyst and stabilize the sodium cation in solution, could be used. With regards to finding a better solvent than the ethers used in this study, there are very few that were stable to strongly basic conditions, able to solvate the alkoxide to some extent, offer a range of boiling points and relatively inexpensive. Thus, it was decided to investigate the reaction of **2c** with the addition of the crown ether, 18-crown-6.

Again, the observed rate of reaction appeared to be constant with time. However, it was considerably larger than the observed rate without 18-crown-6. A best fit linear regression was determined ($R^2 > 0.999$). From the slope, a value for the observed rate constant, k_{obs} was determined to be $(4.60 \pm 0.04) \times 10^{-6} \text{ s}^{-1}$. This was approximately 6 times the observed rate without 18-crown-6. Table 4.1 also shows that the solubility of **2c** had more than doubled.

As k_{-1} became larger than k_{2obs} , the value in the denominator of equation 4.8 became very small. Consequently, the experimental error was larger than the denominator and a value for k_{-1} or k_1 could not be calculated. However, a lower limit for k_{-1} was calculated using the experimental error for the denominator (calculated using the value for the solubility of **2c** with 18-crown-6 shown in table 4.1), and the value of k_{2obs} for **2a**, as follows:

$$k_{-1} \geq \frac{k_{obs}k_{2obs}}{\sigma} \quad (4.9)$$

From equation 4.9, a lower limit for k_{-1} was calculated ($k_{-1} \geq 0.11 \text{ s}^{-1}$). Similarly, a lower limit for k_1 was: $k_1 \geq 1.2 \times 10^{-4} \text{ s}^{-1}$. Since k_{-1} was estimated to be at least 27 times larger than k_{2obs} , equation 4.7 was used to calculate a new value of k_{2obs} . Using this equation, an experimental value of k_{2obs} was calculated to be $(4.3 \pm 0.1) \times 10^{-3} \text{ s}^{-1}$. This was identical to k_{2obs} for **2a** within error limits. The initial assumption that k_{2obs} was approximately the same for both **2a** and **2c** thus appeared to be valid.

Overall, the observed rate of reaction had been increased substantially without increasing TFE pressure or temperature. The reaction rate without 18-crown-6 was rate-limited by both the forward and reverse rates of alkoxide solubility and the rate of reaction of the soluble alkoxide with TFE. With 18-crown-6, the reaction was rate-limited by the rate of reaction of the soluble alkoxide with TFE and the relative free energy difference between the soluble/insoluble alkoxide. The 18-crown-6 not only reduced the difference in free energy as evidenced by the increased solubility of the alkoxide but also decreased the activation barrier for solvation as evidenced by the increased forward rate of solvation.

Two synthetic methods were demonstrated for the preparation of oligo-ether TFVEs. In the first method, the desired TFVEs were synthesized by the thermolysis of the appropriate 2-alkoxy-2,3,3,3-tetrafluoropropionate ester. In the second method, the desired TFVEs were synthesized from a reaction of the appropriate sodium alkoxide with TFE. For both reactions, there were advantages and disadvantages.

With TFVEs from trimethylsilyl 2-alkoxy-2,3,3,3-tetrafluoropropionate esters, the overall synthesis was fairly simple and could be done with readily obtainable or prepared equipment. However, 2 steps were required just to obtain the trimethylsilyl 2-alkoxy-2,3,3,3-tetrafluoropropionate esters. In combination, all three steps contributed to an overall yield which was approximately 30 to 40%. Also, each step resulted in a product of lower molecular weight than the previous intermediate. This fact, in combination with less than quantitative yields at each step, would disfavor a scale-up of the reaction.

In contrast, the reaction of an alkoxide with TFE could be done in one step. With the addition of a catalyst such as 18-crown-6, the reaction rate was increased and was practical at relatively low TFE pressures. Low TFE pressures are desirable since TFE has been known to violently disproportionate to tetrafluoromethane and carbon at pressures above 100 psi. Lower pressures also reduce the amount of excess and potentially wasted TFE. A factor disfavoring this reaction is that TFE is not commercially available and has to be synthesized.

For alkoxides that cannot be made sufficiently soluble, TFVE yields will be low and the reaction may not work at all. This may in part be due to side reactions such as a reaction of the alkoxide with the TFVE at high TFVE concentrations. Although the solubility of 2c and the observed rate of reaction with TFE were increased with 18-crown-6, the overall yield did not increase (*cf.* Figure 4.1). This may be the result of a proportional increase in the rate of side reactions. Overall, yields were as high as 62%. Ultimately, this method is better; at least for the synthesis of the desired TFVEs. Relatively large quantities will be required for future polymer synthesis and a one step reaction will require less time.

be investigated. It is anticipated that these monomers will homopolymerize. Initially, free radical aqueous emulsion polymerization will be investigated using ammonium or potassium persulfate as initiators, a buffering agent such as sodium hydrogen phosphate, and a surfactant such as sodium dodecyl sulfate (SDS). There is a possibility that the hydrophobic portion of the surfactant may not be compatible with monomers **8a** and possibly **8b**, since the former is to some degree hydrophilic. However, monomer **8c** could be used as a model system since it is somewhat similar in structure to substituted α,β,β -trifluorostyrenes.³⁴ α,β,β -Trifluorostyrenes are known to be compatible with surfactants such as SDS.

Another concern is the possibility that the propagating radical will be electrophilic to such a degree where it readily abstracts hydrogen from the monomer or the pendant group of the polymer. For this reason, the polymerization of TFE cannot be done in organic solvents.²⁵ It is likely that these TFVE monomers will not copolymerize with TFE to yield high molecular weight polymer. However, a comonomer such as 1,1-difluoroethylene may copolymerize to a desirable molecular weight.

If hydrogen abstraction is a problem during homopolymerization, the molecular weight of the resulting polymer will be low. It may be possible to increase the molecular weight of the homopolymer by reducing the rate of hydrogen abstraction relative to the rate of propagation. This might be done by lowering the temperature. A redox initiation system would be required to generate radicals at low temperatures.

Ultimately, if these TFVE monomers cannot be polymerized to a desirable molecular weight, a fluorinated TFVE such as $\text{CF}_2=\text{CFO}(\text{CF}_2)_2\text{CO}_2\text{CH}_3$ might be investigated. Once incorporated into a homo/copolymer, the methyl ester could be reduced to an alcohol. Although, this type of homo/copolymer does not have the desired oligo-ether pendant group, the alcohol as the alkoxide could be used to polymerize ethylene oxide at the surface of such a polymer.

6.1 Experimental Protocols

The reagents and solvents were purchased from Aldrich Chemical Company (Millwaukee, WI) and used as received unless otherwise stated. Anhydrous diethyl ether and Celite 545[®] were purchased from Fisher Scientific, (Toronto, Canada). Dry sodium hydride was prepared prior to use from a 60% dispersion in mineral oil by dispersion in pentane followed by filtration through a medium porosity glass frit funnel (4 times) and then dried under nitrogen. Hexafluoropropene oxide (HFPO, 97%) was purchased from PCR Chemicals (Gainesville, Florida) and used as received.

Compounds were initially characterized and the purity determined by gas chromatography (HP 6890, Hewlett Packard, Ontario) using a Restek Rtx-5 column (Chromatographic Specialties, Ontario, 0.530 mm × 15m with a 1.2 μm film thickness) with FID detector, helium carrier gas (35 cm/s) and a split ratio of ~25:1. A typical temperature profile held the initial temperature at 80 °C for 1 min., then ramped the temperature to 230 °C at 15 °C/min., and finally held the temperature at 230 °C for 4 min.

Most ¹H NMR spectra were taken on a 200 MHz Varian Gemini spectrometer using TMS as an internal reference standard and deuterated chloroform as the solvent. Fluorine (¹⁹F NMR) spectra were taken on a 300 MHz Varian Gemini spectrometer using CFCl₃ as an external reference standard and deuterated chloroform as the solvent. ²⁹Si and ¹⁹F NMR spectra for the NOE experiment were taken on a 400 MHz Unity spectrometer using deuterated chloroform as the solvent. Mass spectra were obtained on a Micromass 70-250S (double focusing) mass spectrometer, arrayed with a HP 5890 gas chromatograph (capillary column: J&W Scientific, DB-5ms, 30 m, 0.25 mm). High resolution data were obtained at 10,000 (10% valley) resolution. $2\sigma = 5.7$ ppm based on 27 measurements of the molecular ion of cholesterol.

The gas phase thermolysis apparatus consisted of a 1.9 cm by 43 cm borosilicate glass tube with B24 female inlet and B24 male outlet ground glass joints. A 1.3 cm by 2.3 m, 400 W heating tape

reducer to vacuum side arm adapter and receiver flask were attached to the outlet. The tube was packed with 40 g of approximately 3 mm dia. borosilicate glass beads held in place by Vigreux type indentations in the tube, 1.3 cm above the outlet. Suspended on the glass beads were approximately 2 to 3 g of potassium fluoride. The temperature was maintained by a temperature controller connected to a hose clamp thermocouple mounted on the outside of the heating tape and under the insulation. The internal temperature was monitored using a thermocouple mounted in the center of the tube through a port located halfway along the tube length.

6.2 Kinetic Experiments and Sodium Alkoxide Solubility

Sodium alkoxide solutions/dispersions for kinetic experiments were prepared in a 500 mL oven dried 3-neck round bottom flask under nitrogen with magnetic stirring. Approximately 2-3 g of the appropriate alcohol was slowly added with stirring to a two fold excess of sodium hydride in 150 mL of ethylene glycol dimethyl ether (DME). The alkoxide was stirred for an additional 3 h before addition to the reactor. The solubility of the sodium alkoxide was determined by preparing a saturated solution of the alkoxide and allowing it to equilibrate overnight.

The alkoxide solubility was measured by removing a sample of the clear supernatant solution. Immediately after removing the sample, the sample was accurately weighed. An approximately equivalent weight of an accurately known 0.2 % solution of naphthalene (internal standard) in DME was added followed by 1-2 drops of deionized water to convert the residual alkoxide to the alcohol. Samples were then analyzed by gas chromatography. The relative areas of the alcohol and internal standard were related by an FID response factor which was previously determined for each alcohol. The weight fraction of alkoxide was determined with the following equation:

$$\text{Wt. fraction RONa} = \frac{(\text{Area}_{\text{ROH}})(\text{Wt}_{\text{in.std}})(\text{Mw}_{\text{RONa}})}{(\text{Area}_{\text{in.std.}})(\text{Wt}_{\text{RONa}})(\text{Mw}_{\text{ROH}})} (\text{FID}_{\text{res. fac.}})([\text{in.std}]) \quad (6.1)$$

the alkoxide sample respectively. MW_{RONa} and MW_{ROH} are the molecular weights of the sodium alkoxide and alcohol respectively. $FID_{res.fac.}$ represents the relative GC flame ionization detector response factor determined by mass for the alcohol and internal standard. $[in.std]$ represents the concentration of the internal standard solution.

All kinetic experiments were conducted in a 300 mL Parr stainless steel pressure reactor. The reactor was pre-dried under vacuum for a minimum of 3 hours before the addition of reactants. The reactor contents were stirred overnight in the reactor before starting the experiment. The top of the reactor was briefly opened to atmospheric pressure (dry nitrogen purge) just before the start of the experiment to vent residual hydrogen gas. With vigorous mechanical stirring, the experiment was started by the addition of TFE gas to the reactor. The TFE pressure was maintained at a constant (50 ± 1) PSI throughout the duration of the experiment.

The first sample was taken no less than 5 minutes after the addition of TFE to ensure that all the saturated ether byproduct, $ROCF_2CF_2H$, had formed. Samples were removed at the appropriate time intervals through a valve connected to a dip tube into the reactor. Approximately 2-4 mL of the reactor contents were always removed before the actual sample was taken. The volume of sample taken for analysis was between 1 and 1.5 mL and the time was noted at this point. The sample was prepared for gas chromatography analysis and the weight fraction of sodium alkoxide determined as described above.

Experimental errors were estimated for masses and gas chromatography FID response values. Errors for calculated values were determined using widely known procedures for products, dividends, sums and differences. For values that were obtained from linear regressions, ANOVA statistics were used to calculate standard errors.

2-(2-*tert*-Butoxy-ethoxy)-ethanol [1b]. To a dry 500 mL, 3-neck round bottom flask that was fitted with a dry ice/acetone condenser under a static nitrogen purge were added 30.0 g (283 mmol) of diethylene glycol, 250 mL of methylene chloride, and 7.0 g of Amberlyst[®] 15 resin. With magnetic stirring, 19.0 g (337 mmol) of isobutene were slowly added and the reaction mixture was maintained at 30 °C. After 7 h, GC analysis indicated that 90% of the diethylene glycol had been converted to 2-(2-*tert*-butoxy-ethoxy)-ethanol and that very little (<1%) had been converted to di-(2-*tert*-butoxy-ethyl) ether. The reaction was stopped by removal of the Amberlyst[®] 15 resin by gravity filtration. The solvent was removed by rotary evaporation leaving a clear, oily liquid. 32.1 g (70% yield, >96% purity by GC) of 2-(2-*tert*-butoxy-ethoxy)-ethanol was isolated by vacuum fractional distillation (~0.05 mmHg, bp 36-37 °C). ¹H NMR: δ = 3.8-3.5 (m, 8H, CH₂), 3.0 (broad s, 1H, OH), 1.2 (s, 9H, C(CH₃)₃).

2-(2-Ethoxy-ethoxy)-ethyl 2-[2-(2-ethoxy-ethoxy)-ethoxy]-2,3,3,3-tetrafluoropropionate [5a]. To a dry 500 mL, 3-neck round bottom flask that was fitted with a 50 mL pressure equalizing addition funnel, mechanical stirrer, and a dry ice/acetone condenser under a nitrogen purge were added 3.6 g (150 mmol) of sodium hydride. Approximately 200 mL of anhydrous ethyleneglycol dimethyl ether (DME) were added by cannula to the flask. The reaction flask was cooled to ~0 °C and the dispersion stirred while 20.0 g (149 mmol) of 2-(2-ethoxy-ethoxy)ethanol were slowly added. In forming the alkoxide, hydrogen gas evolved and the resulting cloudy white solution was stirred for 1 h. The addition funnel was replaced with a septum through which 14.6 g (88.0 mmol) of HFPO were slowly added using a transfer needle. Since the reaction was very exothermic, care was taken to maintain the temperature at or below 30 °C. A cloudy pale yellow reaction mixture resulted and was stirred for an additional 3 h at room temperature. The reaction mixture was filtered through 1 cm of Celite 545[®] on a coarse porosity glass frit funnel (to separate sodium fluoride) and the supernatant was rotary-evaporated, leaving a yellow, oily, liquid that was vacuum distilled using a 10 cm Vigreux column. Two fractions were isolated: the first fraction (bp 43-45 °C, 0.05 mmHg) was identified as the byproduct ester, 2-(2-ethoxy-ethoxy)-ethyl perfluoropropionate (yield 3.8 g, 13%) and the second fraction (bp 112-114 °C, 0.04 mmHg) was identified as the desired product, 2-(2-ethoxy-ethoxy)-ethyl 2-[2-(2-ethoxy-ethoxy)-ethoxy]-

3.45 (m, 16H, OCH₂), 1.2 (t, 6H, CH₃); HRMS: (MH)⁺; calc. 395.1693; obs. 395.1705.

2-(2-*tert*-Butoxy-ethoxy)-ethyl 2-[2-(2-*tert*-butoxy-ethoxy)-ethoxy]-2,3,3,3-tetrafluoropropionate [5b]. To a dry 500 mL, 3-neck round bottom flask that was fitted with a 50 mL pressure equalizing addition funnel, mechanical stirrer, and a dry ice/acetone condenser under a nitrogen purge were added 3.3 g (140 mmol) of sodium hydride. Approximately 200 mL of anhydrous DME were added by cannula to the flask. 22.0 g (136 mmols) of 2-(2-*tert*-butoxy-ethoxy)-ethanol were slowly added to the cooled reaction flask (~0 °C) to form the alkoxide with evolution of hydrogen gas. The resulting cloudy white reaction mixture was stirred for 1 h to ensure complete formation of the alkoxide. The addition funnel was replaced with a septum through which 17.0 g (102 mmol) of HFPO were slowly added using a transfer needle and during which the reaction mixture was maintained below 30 °C. The slightly cloudy pale yellow reaction mixture that resulted was stirred for an additional 3 h. The reaction mixture was filtered through 1 cm of Celite 545[®] on a coarse porosity glass frit funnel (to separate sodium fluoride) and the supernatant was removed by rotary evaporation, leaving a yellow, oily liquid. The crude product was vacuum distilled using a short path distillation apparatus. Two fractions were isolated: the first fraction (bp 53-56 °C, 0.05 mmHg, yield 4.3 g, 14%) was identified by GC as a mixture of unreacted alcohol (0.3 g), and byproduct ester 2-(2-*tert*-butoxy-ethoxy)-ethyl perfluoropropionate (yield 4 g, 13%); and the second fraction (bp 132-134 °C, 0.04 mmHg) was identified as the desired product, 2-(2-*tert*-butoxy-ethoxy)-ethyl 2-[2-(2-*tert*-butoxy-ethoxy)-ethoxy]-2,3,3,3-tetrafluoropropionate (yield 21.8 g, 71.5%, >99% purity by GC). ¹⁹F NMR: δ = -81.7 (d, CF₃), -132.0 (broad m CF); ¹H NMR: δ = 4.5 (m, 2H CO₂CH₂), 3.95 (m, 2H CFOCH₂), 3.8-3.4 (m, 12H, OCH₂), 1.2 (s, 18H, C(CH₃)₃); HRMS: (M-CH₃)⁺; calc. 435.2006; obs. 435.1988.

Trimethylsilyl 2-[2-(2-ethoxy-ethoxy)-ethoxy]-2,3,3,3-tetrafluoropropionate [7a]. To a 300 mL, round bottom flask equipped with condenser and thermocouple side port were added 26.9 g (68.2 mmol) of 2-(2-ethoxy-ethoxy)-ethyl 2-[2-(2-ethoxy-ethoxy)-ethoxy]-2,3,3,3-tetrafluoropropionate and 175 mL of THF. With magnetic stirring, 3.4 g (85 mmol) of sodium hydroxide and 6.1 mL (340 mmol) of deionized water were added to the flask and maintained at 40 °C for 3 h during which the translucent reaction mixture became slightly yellow. GC analysis

tetrafluoropropionic acid sodium salt. Most of the THF and water were removed from the reaction mixture by rotary-evaporation. Any remaining water and most of the 2-(2-ethoxy-ethoxy)-ethanol (~80%) were removed by short path vacuum distillation (~0.05 mmHg, stillpot temperature <100 °C). After cooling the reaction pot to ambient temperature, approximately 125 mL of diethyl ether were added by cannula into the flask. The sodium salt dissolved with magnetic stirring to give a translucent, light amber solution. Sodium hydride (0.8g, 30 mmol) was added to the flask. With ice bath cooling, 15.0 g (138 mmols) of trimethylsilyl chloride were slowly added to the flask during which a slight exotherm and sodium chloride precipitation were observed. After 3 h of stirring at room temperature, the reaction mixture was filtered through 1 cm of Celite 545[®] on a medium porosity glass frit funnel. Most of the diethyl ether was removed by rotary-evaporation. The crude product was vacuum distilled using a 10 cm Vigreux column from which three fractions were isolated: the first fraction (bp 28-30 °C, 0.06 mmHg) was identified as 2-(2-ethoxy-ethoxy)-ethanol; the second fraction (bp 38-40 °C, 0.06 mmHg) was identified as 2-(2-ethoxy-ethoxy)-ethyl trimethylsilyl ether; and the third fraction (bp 56-57 °C, 0.04 mmHg) was identified as the desired product, trimethylsilyl 2-[2-(2-ethoxy-ethoxy)-ethoxy]-2,3,3,3-tetrafluoropropionate (yield 18.6 g, 78%, >97% purity by GC). ¹⁹F NMR (20 °C): $\delta = -81.6$ and -82.0 (d, CF₃), -131.2 and -131.7 (broad s, CF); ¹H NMR: $\delta = 3.9$ (m, 2H, CFOCH₂), 3.8-3.45 (m, 6H, OCH₂), 1.2 (t, 3H, CH₃), 0.4 and 0.15 (s, 9H, Si(CH₃)₃); HRMS: (M-H)⁺; calc. 349.1094; obs. 349.1086.

Trimethylsilyl 2-[2-(2-*tert*-butoxy-ethoxy)-ethoxy]-2,3,3,3-tetrafluoropropionate [7b]. To a 300 mL, round bottom flask equipped with a condenser and thermocouple side port were added 20.0 g (44.4 mmol) of 2-(2-*tert*-butoxy-ethoxy)-ethyl 2-[2-(2-*tert*-butoxy-ethoxy)-ethoxy]-2,3,3,3-tetrafluoropropionate and 130 mL of THF. Sodium hydroxide (2.11 g, 52.8 mmol) and 4.0 mL (220 mmol) of deionized water were added to the reaction flask with magnetic stirring and maintained at 40 °C overnight during which a translucent, pale yellow solution resulted. GC analysis of a sample indicated that the ester was converted to the sodium salt. Most of the THF and water were removed from the reaction mixture by rotary-evaporation. The remaining water and most of the 2-(2-*tert*-butoxy-ethoxy)-ethanol (~70%) were removed by short path vacuum distillation (~0.05 mmHg, stillpot temperature <100 °C). After cooling the reaction pot to ambient temperature, approximately 125 mL of diethyl ether were added by cannula into the flask.

hydrogen gas. Trimethylsilyl chloride (10.0 g, 92.0 mmols) was slowly added to the flask during which a slight exotherm and sodium chloride precipitation were observed. After 3 h of stirring at room temperature, the mixture was filtered through 1 cm of Celite 545[®] on a coarse porosity glass frit funnel. Most of the diethyl ether was removed by rotary-evaporation. The crude product was vacuum distilled using a 10 cm Vigreux column from which two fractions were isolated: the first fraction (bp 45-48 °C, 0.04 mmHg, yield 2.3 g) was identified as 2-(2-*tert*-butoxy-ethoxy)-ethyl trimethylsilyl ether and the second fraction (bp 71-73 °C, 0.04 mmHg) was identified as the desired product, trimethylsilyl 2-[2-(2-*tert*-butoxy-ethoxy)-ethoxy]-2,3,3,3-tetrafluoropropionate (yield 10.8 g, 69%, >96% purity by GC). ¹⁹F NMR (ambient temperature): $\delta = -81.6$ and -82.0 (d, CF₃), -130.6 and -131.7 (broad s, CF); ¹H NMR: $\delta = 3.9$ (m, 2H, CFOCH₂), 3.75-3.45 (m, 6H, OCH₂), 1.3 and 1.2 (s, 9H, C(CH₃)₃), 0.4 and 0.15 (s, 9H, Si(CH₃)₃); HRMS: (M-CH₃)⁺; calc. 363.1251; obs. 363.1237.

1-[2-(2-Ethoxy-ethoxy)-ethoxy]-1,2,2-trifluoroethene [8a]. Trimethylsilyl 2-[2-(2-ethoxy-ethoxy)-ethoxy]-2,3,3,3-tetrafluoropropionate (9.30 g, 26.5 mmol) was injected onto the pre-heated thermolysis column (140 °C, ~50 mL/min N₂ flow, ~0.2 mmHg) at a rate of ~0.2 mL/min using a 10 mL Gastight[®] syringe and syringe pump. The thermolysis was exothermic and the column temperature increased to ~160 °C during the injection. The product was collected for an additional 1 h after the injection was completed in a receiver flask cooled with liquid nitrogen. An oily, pale yellow liquid product (7.8 g) was collected. The crude product was fractionally distilled to give 3.58 g (63% yield, 95% purity by GC) of a product identified as 1-[2-(2-Ethoxy-ethoxy)-ethoxy]-1,2,2-trifluoroethene (bp 22 °C, 0.15 mmHg). ¹⁹F NMR: $\delta = -123.4$ (dd, 1F, $J = 56, 104$ Hz, CF), -130.2 (dd, 1F, $J = 104, 108$ Hz, CF), -135.1 (dd, 1F, $J = 56, 108$ Hz, CF); ¹H NMR: $\delta = 4.15$ (m, 2H, CFOCH₂), 3.75 (t, 2H, OCH₂), 3.7- 3.45 (m, 6H, OCH₂), 1.2 (t, 3H, CH₃).

1-[2-(2-*tert*-Butoxy-ethoxy)-ethoxy]-1,2,2-trifluoroethene [8b]. Trimethylsilyl 2-[2-(2-*tert*-butoxy-ethoxy)-ethoxy]-2,3,3,3-tetrafluoropropionate (11.8 g, 31.3 mmol) was injected onto the pre-heated thermolysis column (150 °C, ~50 mL/min N₂ flow, ~0.2 mmHg) at a rate of ~0.2 mL/min using a 10 mL Gastight[®] syringe and syringe pump. The thermolysis was exothermic and the column temperature increased to ~170 °C during the injection. The product was collected in a

distilled to give 4.2 g (55% yield, 95% purity by GC) of a product identified as 1-[2-(2-*tert*-Butoxy-ethoxy)-ethoxy]-1,2,2-trifluoroethene (bp 26 °C, 0.15 mmHg). ¹⁹F NMR: δ = -123.5 (dd, 1F, *J* = 56, 104 Hz, CF), -130.3 (dd, 1F, *J* = 104, 108 Hz, CF), -135.1 (dd, 1F, *J* = 56, 108 Hz, CF); ¹H NMR: δ = 4.15 (m, 2H, CFOCH₂), 3.75 (t, 2H, OCH₂), 3.65-3.45 (m, 4H, OCH₂), 1.2 (s, 9H, C(CH₃)₃); HRMS: (M-CH₃)⁺; calc. 227.0895, obs. 227.0892.

Sodium 2-[2-(2-Ethoxy-ethoxy)-ethoxy]-2,3,3,3-tetrafluoropropionate [6a]. To a 300 mL round bottom flask were added 9.33 g (26.6 mmol) of trimethylsilyl 2-[2-(2-ethoxy-ethoxy)-ethoxy]-2,3,3,3-tetrafluoro-propionate and 85 mL of THF. With magnetic stirring, 1.22 g (30.5 mmol) of sodium hydroxide followed by 2.52 mL (140 mmol) of deionized water were added to the reaction flask. After 1 h of stirring at room temperature, the reaction mixture was filtered through 1 cm of Celite 545[®] on a medium porosity frit funnel. Residual suspended small particulates were separated by centrifugation. Most of the THF and water were removed by rotary evaporation and final purification was done in a vacuum oven at 40 °C for 2 h to give a very viscous, pale yellow liquid. The yield of sodium 2-[2-(2-ethoxy-ethoxy)-ethoxy]-2,3,3,3-tetrafluoropropionate was 7.58 g (95%). ¹⁹F NMR: δ = -81.9 (broad s, CF₃), -131.8 (broad s, CF); ¹H NMR: δ = 4.2-3.4 (broad m, 10H OCH₂), 1.2 (m, 3H, CH₃).

2-(2-Ethoxy-ethoxy)-ethyl trifluoroacetate [11a]. To a 300 mL round bottom flask equipped with condenser and thermocouple side port were added 30.4 g (77.1 mmol) of 2-(2-ethoxy-ethoxy)-ethyl 2-[2-(2-ethoxy-ethoxy)-ethoxy]-2,3,3,3-tetrafluoropropionate, and 175 mL of THF. Sodium hydroxide (4.06 g, 102 mmol) and 7.13 mL (396 mmol) of deionized water were added to the flask with magnetic stirring and maintained at 40 °C for 3 h during which the reaction mixture became slightly yellow. The reaction mixture was filtered through 1 cm of Celite 545[®] on coarse porosity glass frit funnel. The majority of the THF and water were removed by rotary evaporation. 92% of the byproduct, 2-(2-ethoxy-ethoxy)ethanol, was removed by short path vacuum distillation (mantle temperature ~ 120 °C). The temperature of the heating mantle was increased to 200 °C and the resulting thermolysis product was collected in a receiver flask cooled by liquid nitrogen. An oily, pale yellow liquid was obtained (8.2 g, 27% w/w based on starting ester). GC analysis of a sample indicated that it was a complex mixture with one predominant,

ethyl trifluoroacetate. ^{19}F NMR: $\delta = -75.3$ (s, CF_3); ^1H NMR: $\delta = 4.5$ (t, 2H $\text{C}(\text{O})\text{CH}_2$), 3.8 (t, 2H OCH_2), 3.6-3.45 (m, 6H, OCH_2), 1.2 (t, 3H, CH_3); HRMS: MH^+ ; calc. 231.0844, obs. 231.0822.

Tetrafluoroethylene (TFE).³² To a cylindrical 7 cm dia. by 14 cm quartz flask with a 15 cm neck and B24 female ground joint was added 75.0g of poly(tetrafluoroethylene) powder. The flask was placed in a steel cored cylindrical (7.4 cm dia.) open top furnace to a depth of 16 cm and evacuated to a pressure of ~0.05 mmHg. The portion of the neck of the flask in the furnace was insulated with quartz wool. The furnace was heated and maintained at 620 °C. To control the bumping of the poly(tetrafluoroethylene) powder as TFE gas evolved, the flask was connected to the vacuum system by a 6 mm id. by 120 cm piece of Teflon[®] vacuum tubing. A restricting, uncompressed piece of quartz wool was placed at the junction of the tubing with the vacuum system to act as a filter. TFE gas was condensed into a cold trap cooled by liquid nitrogen. After 3 h, the furnace was allowed to cool and the quartz flask was isolated from the vacuum system. A pre-evacuated 300 mL stainless steel pressure cylinder containing approximately 2 g of (R)-(+)-limonene was cooled with liquid nitrogen and opened to the vacuum system. A valve with a rupture disk was used on the cylinder for safety. The vacuum pump was isolated from the vacuum system and the cold trap was allowed to warm up. TFE liquid (<-80 °C) was distilled under static vacuum into the pressure cylinder. When the distillation was complete, the pressure cylinder was isolated from the vacuum system, the cold trap was purged to atmospheric pressure and the pressure cylinder was allowed to warm up to room temperature at the back of a fumehood. The yield of TFE was 74.7 g or > 99%.

1-[2-(2-Ethoxy-ethoxy)-ethoxy]-1,2,2-trifluoroethene [8a]. To a oven dried 500 mL 3-neck round bottom flask purged with dry nitrogen were add 4.2 g (180 mmol) of sodium hydride. 150 mL of anhydrous diethyl ether was added by cannula to the flask. With magnetic stirring, 20.0 g (149 mmol) of 2-(2-ethoxy-ethoxy)ethanol were added to the cooled flask (~0 °C) with evolution of H₂ gas. After 3 h, the sodium alkoxide was transferred by cannula to the dry, pre-evacuated pressure reactor. The reactor contents were stirred overnight. Briefly, the reactor was vented to atmospheric pressure to vent residual H₂. TFE gas was admitted to the reactor and the pressure maintained at 50 psi. After 0.5 h, analysis of a sample by gas chromatography indicates that all the alkoxide had been consumed. The reactor was vented to atmospheric pressure, and the contents were poured into a 500 mL separatory funnel. Excess sodium hydride was reacted with

ether. The ether fractions were combined and dried over anhydrous magnesium sulfate. The solution was filtered by gravity and most of the diethyl ether was removed by rotary evaporation. The crude product was vacuum distilled using a 10 cm Vigreux column. One fraction was isolated (19.9 g, 62%, bp 39-41 °C, 1 mmHg, 94% purity by GC). ¹⁹F NMR: δ = -123.4 (dd, 1F, *J* = 56, 104 Hz, CF), -130.2 (dd, 1F, *J* = 104, 108 Hz, CF), -135.1 (dd, 1F, *J* = 56, 108 Hz, CF); ¹H NMR: δ = 4.15 (m, 2H, CFOCH₂), 3.75 (t, 2H, OCH₂), 3.7- 3.45 (m, 6H, OCH₂), 1.2 (t, 3H, CH₃).

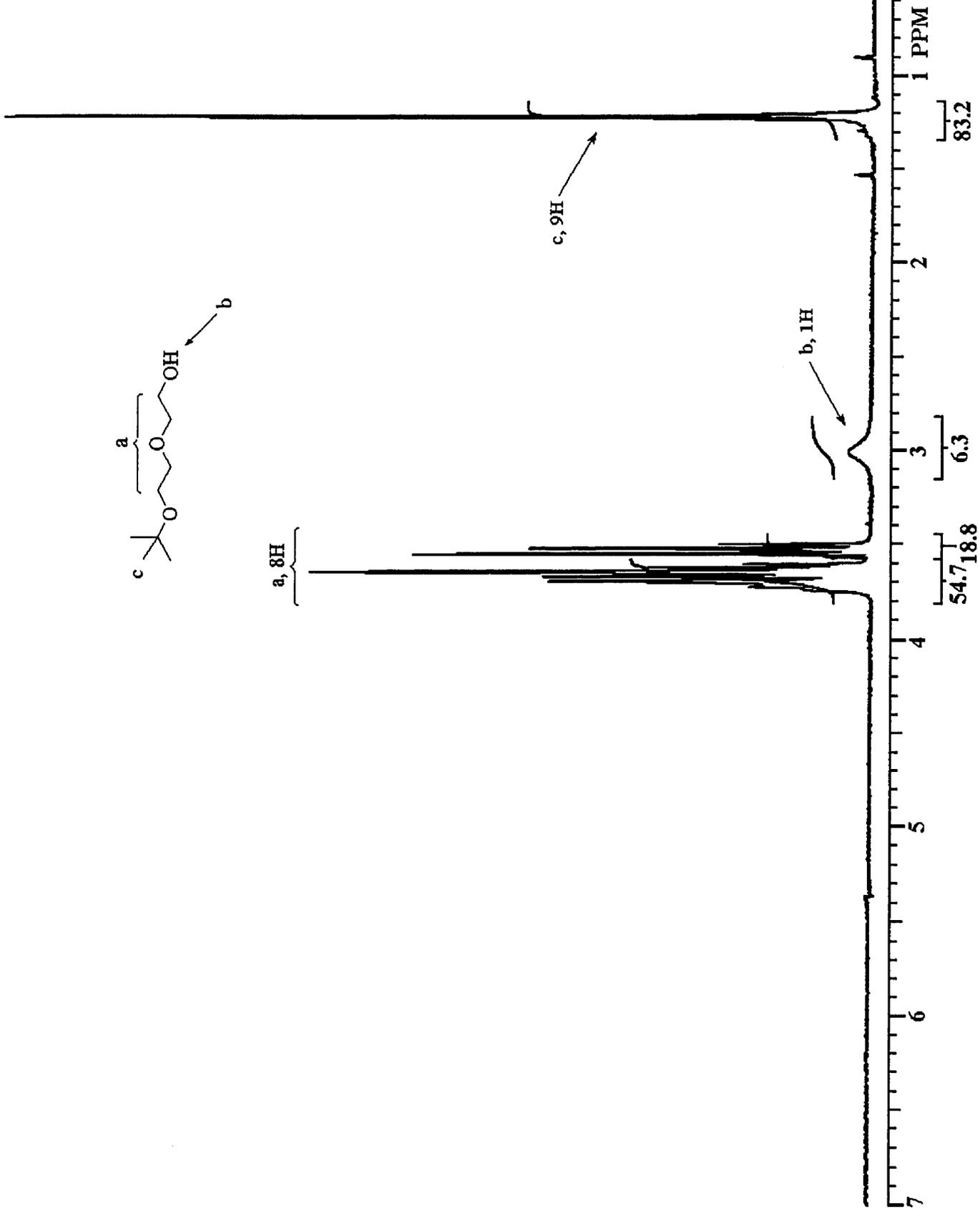
1-[2-(2-*tert*-Butoxy-ethoxy)-ethoxy]-1,2,2-trifluoroethene [8b]. To a oven dried 500 mL 3-neck round bottom flask purged with dry nitrogen were add 3.0 g (130 mmol) of sodium hydride. 150 mL of anhydrous diethyl ether was added by cannula to the flask. With magnetic stirring, 9.1 g (56 mmol) of 2-(2-butoxy-ethoxy)ethanol were added to the cooled flask (~0 °C) with evolution of H₂ gas. After 3 h, the sodium alkoxide was transferred by cannula to the dry, pre-evacuated pressure reactor. The reactor contents were stirred overnight. Briefly, the reactor was vented to atmospheric pressure to vent residual H₂. TFE gas was admitted to the reactor and the pressure maintained at 50 psi. After 24 h, the reactor was vented to atmospheric pressure, and the contents were poured into a 500 mL separatory funnel. Excess sodium hydride was reacted with 95 % ethanol before 250 mL of deionized water was added to the funnel. The diethyl ether layer was removed and the aqueous layer was extracted three times with 75 mL portions of diethyl ether. The ether fractions were combined and dried over anhydrous magnesium sulfate. The solution was filtered by gravity and most of the diethyl ether was removed by rotary evaporation. The crude product was vacuum distilled using a 10 cm Vigreux column. One fraction was isolated (7.6 g, 56%, bp 26-27 °C, 0.15 mmHg, ~95% purity by GC). ¹⁹F NMR: δ = -123.5 (dd, 1F, *J* = 56, 104 Hz, CF), -130.3 (dd, 1F, *J* = 104, 108 Hz, CF), -135.1 (dd, 1F, *J* = 56, 108 Hz, CF); ¹H NMR: δ = 4.15 (m, 2H, CFOCH₂), 3.75 (t, 2H, OCH₂), 3.65-3.45 (m, 4H, OCH₂), 1.2 (s, 9H, C(CH₃)₃).

1-(2-Phenoxy-ethoxy)-1,2,2-trifluoroethene [8c]. To a oven dried 500 mL 3-neck round bottom flask purged with dry nitrogen were add 2.1 g (88 mmol) of sodium hydride. 150 mL of anhydrous diethyl ether was added by cannula to the flask. With magnetic stirring, 8.8 g (64

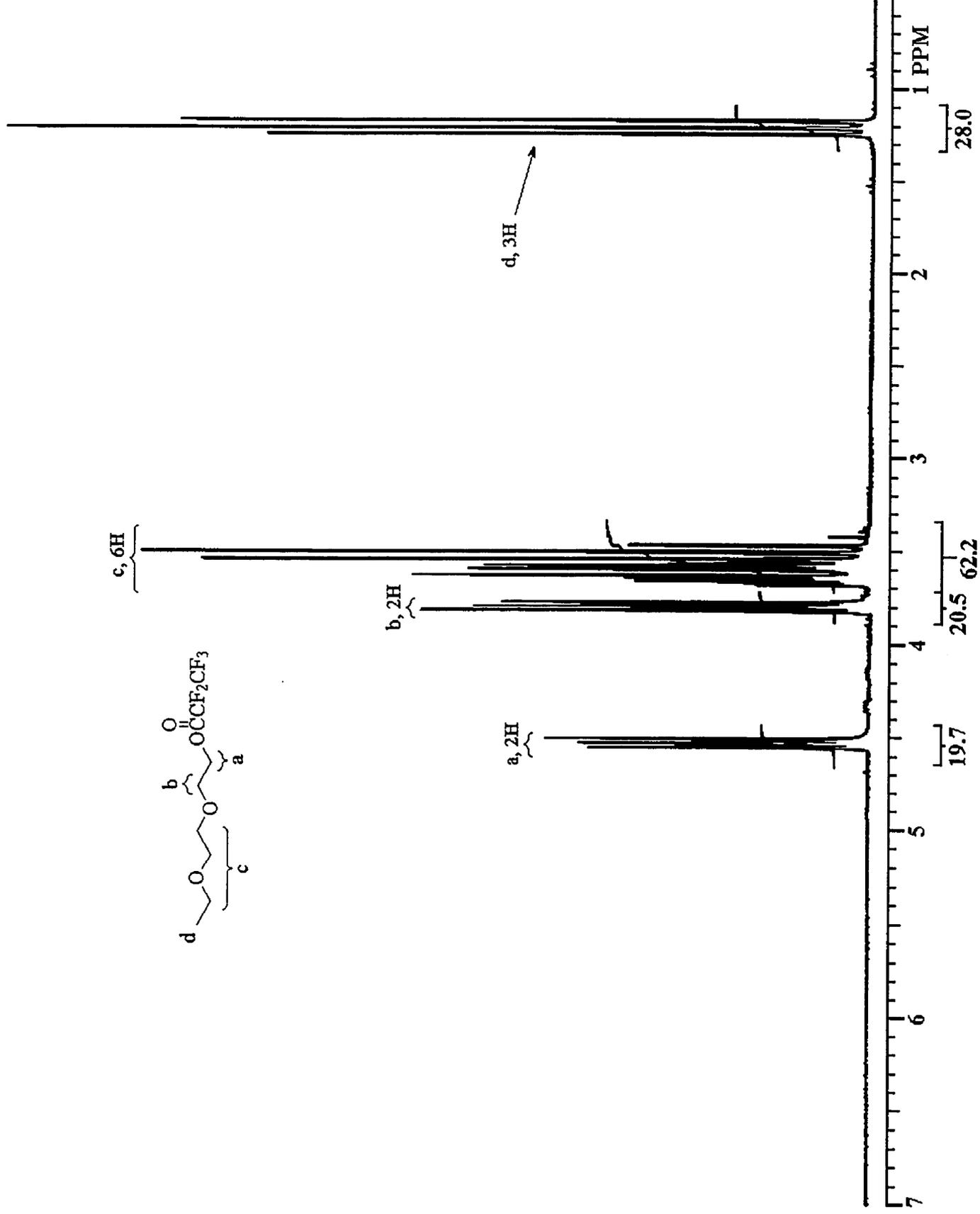
reactor contents were stirred overnight. Briefly, the reactor was vented to atmospheric pressure to vent residual H₂. TFE gas was admitted to the reactor and the pressure maintained at 50 psi. After 24 h, the reactor was vented to atmospheric pressure, and the contents were poured into a 500 mL separatory funnel. Excess sodium hydride was reacted with 95 % ethanol before 250 mL of deionized water was added to the funnel. The diethyl ether layer was removed and the aqueous layer was extracted three times with 75 mL portions of diethyl ether. The ether fractions were combined and dried over anhydrous magnesium sulfate. The solution was filtered by gravity and most of the diethyl ether was removed by rotary evaporation. The crude product was vacuum distilled using a 10 cm Vigreux column. One fraction was isolated (5.4 g, 39%, bp 35-27 °C, 0.15 mmHg, ~95% purity by GC). ¹⁹F NMR: δ = -122.9 (dd, 1F, J = 56, 103 Hz, CF), -129.6 (dd, 1F, J = 103, 108 Hz, CF), -135.1 (dd, 1F, J = 56, 108 Hz, CF); ¹H NMR: δ = 7.3 (m, 2H, PhH), 6.95 (m, 3H, PhH), 4.3 (t, 2H, CFOCH₂), 4.2(t, 2H, PhOCH₂).

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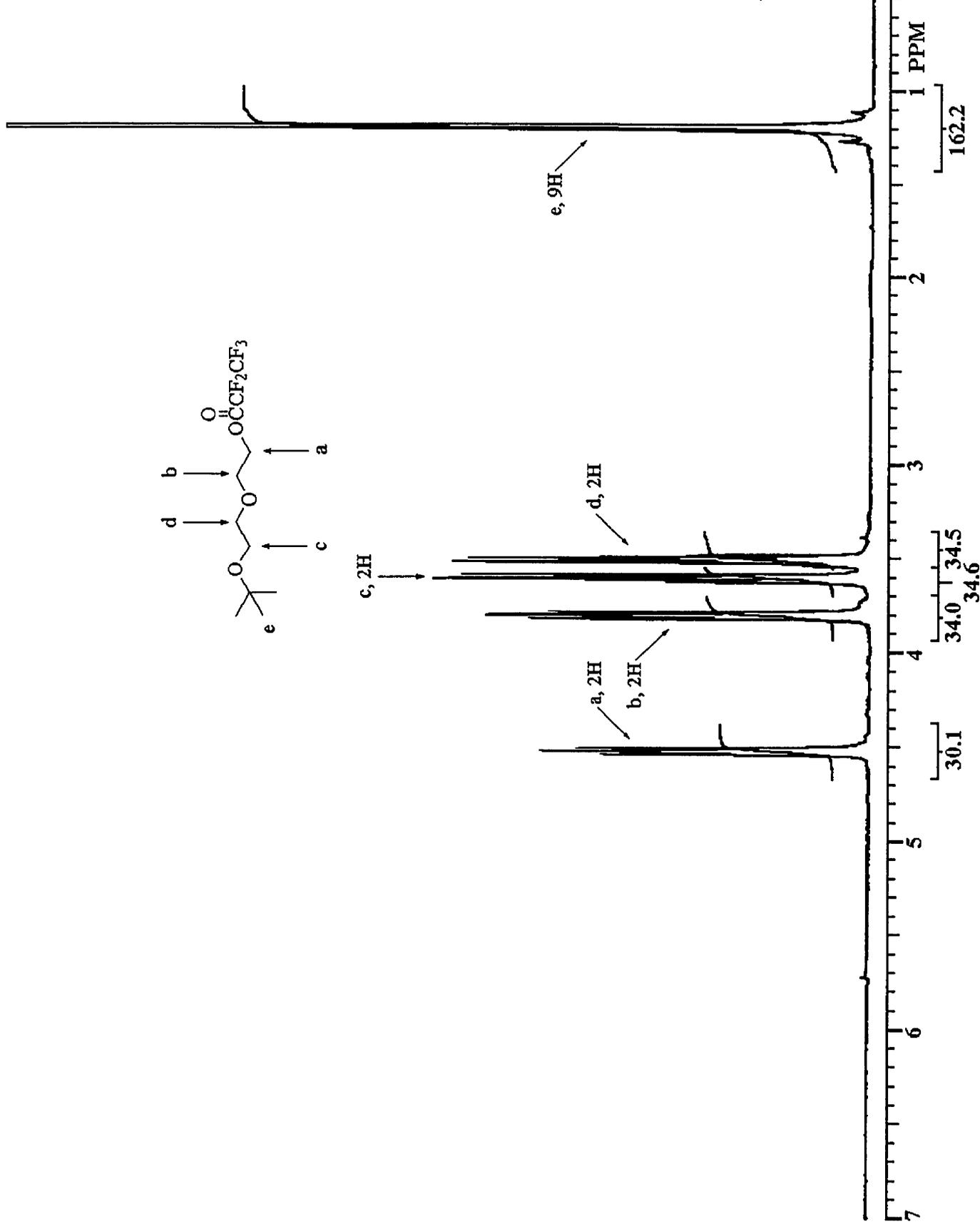
2-(2-*tert*-Butoxy-ethoxy)-ethanol [1b]
 ^1H 200 MHz NMR



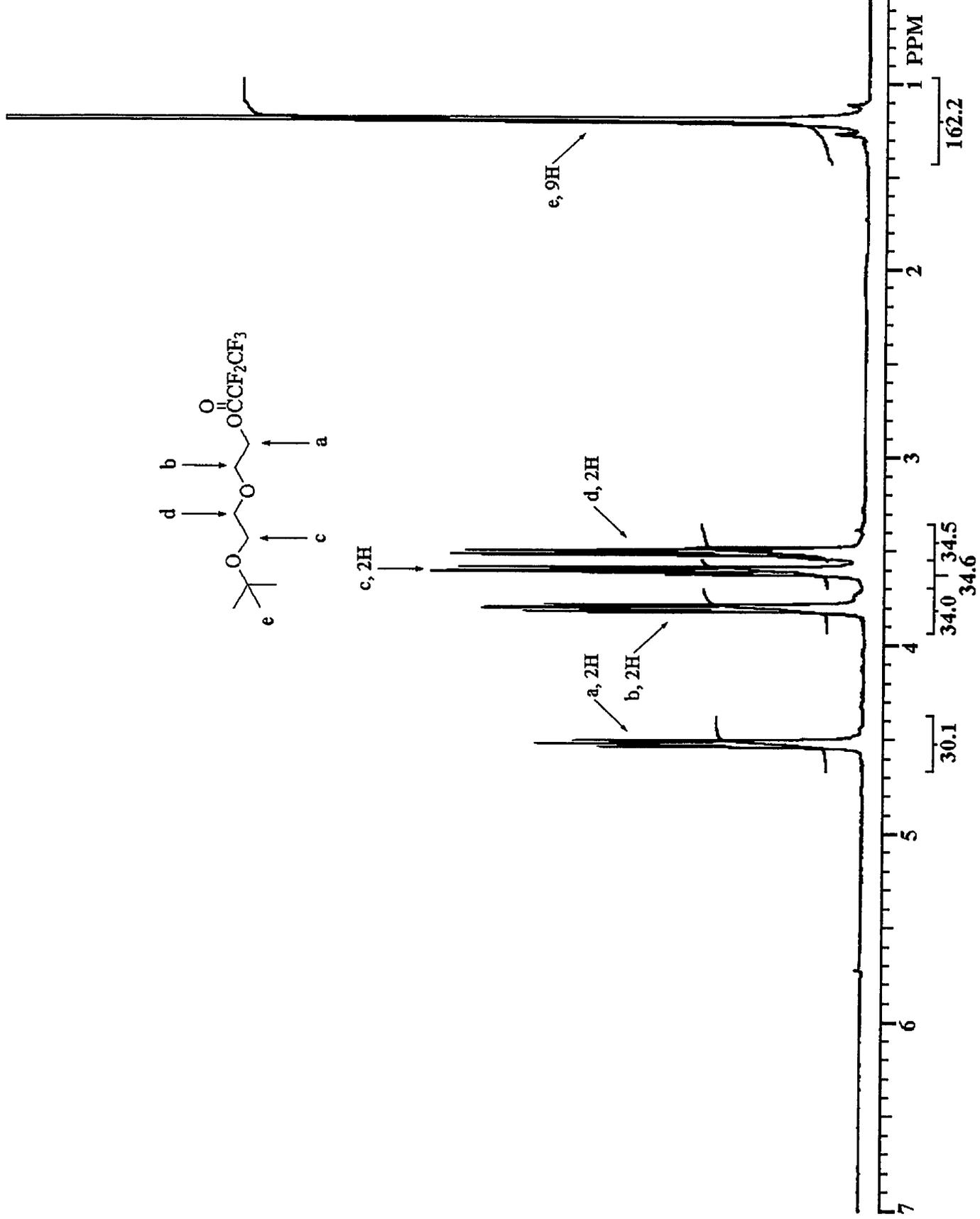
2-(2-Ethoxy-ethoxy)-ethyl pentafluoropropionate [3a]

¹H 200 MHz NMR

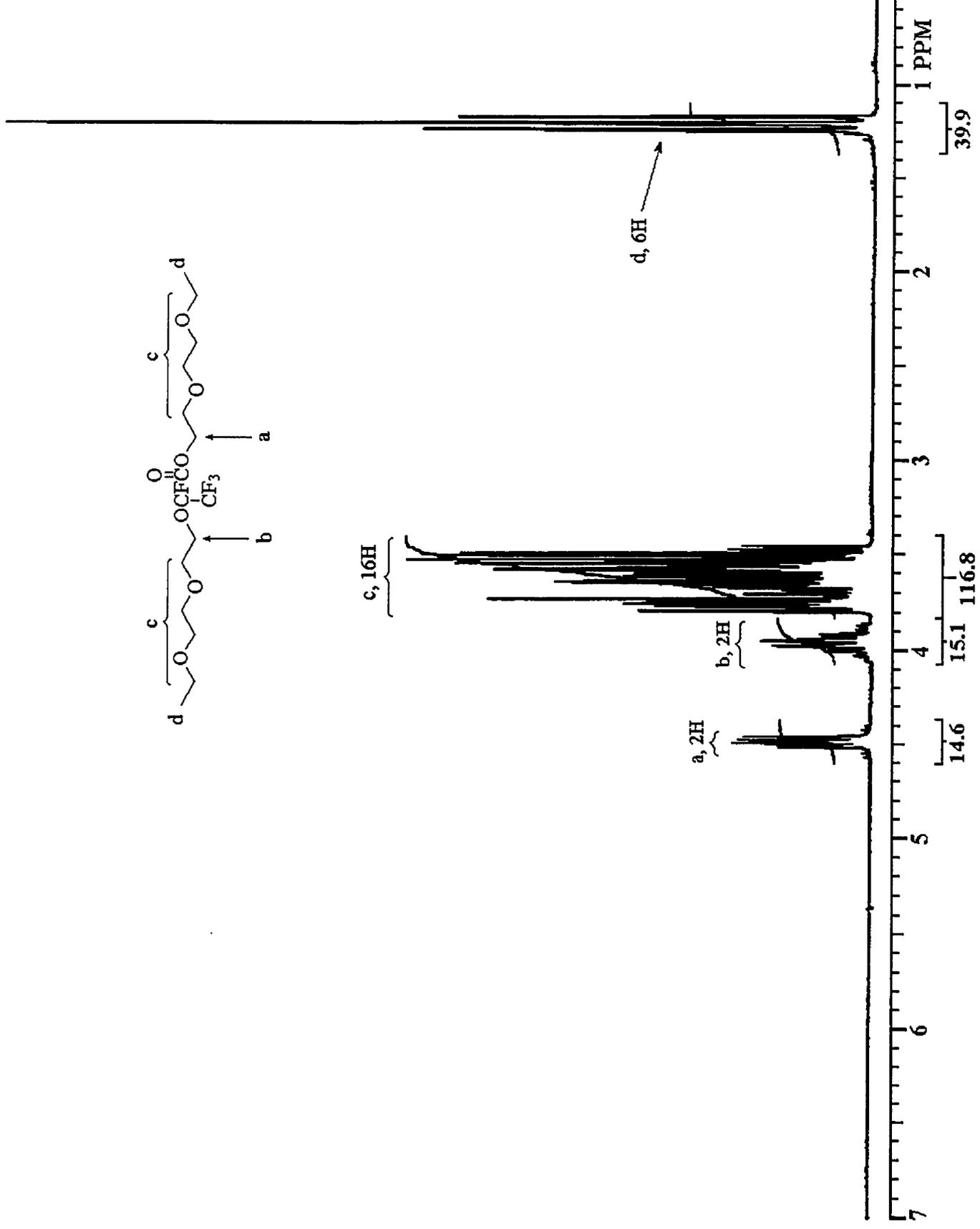
solvent: CDCl₃, reference: TMS



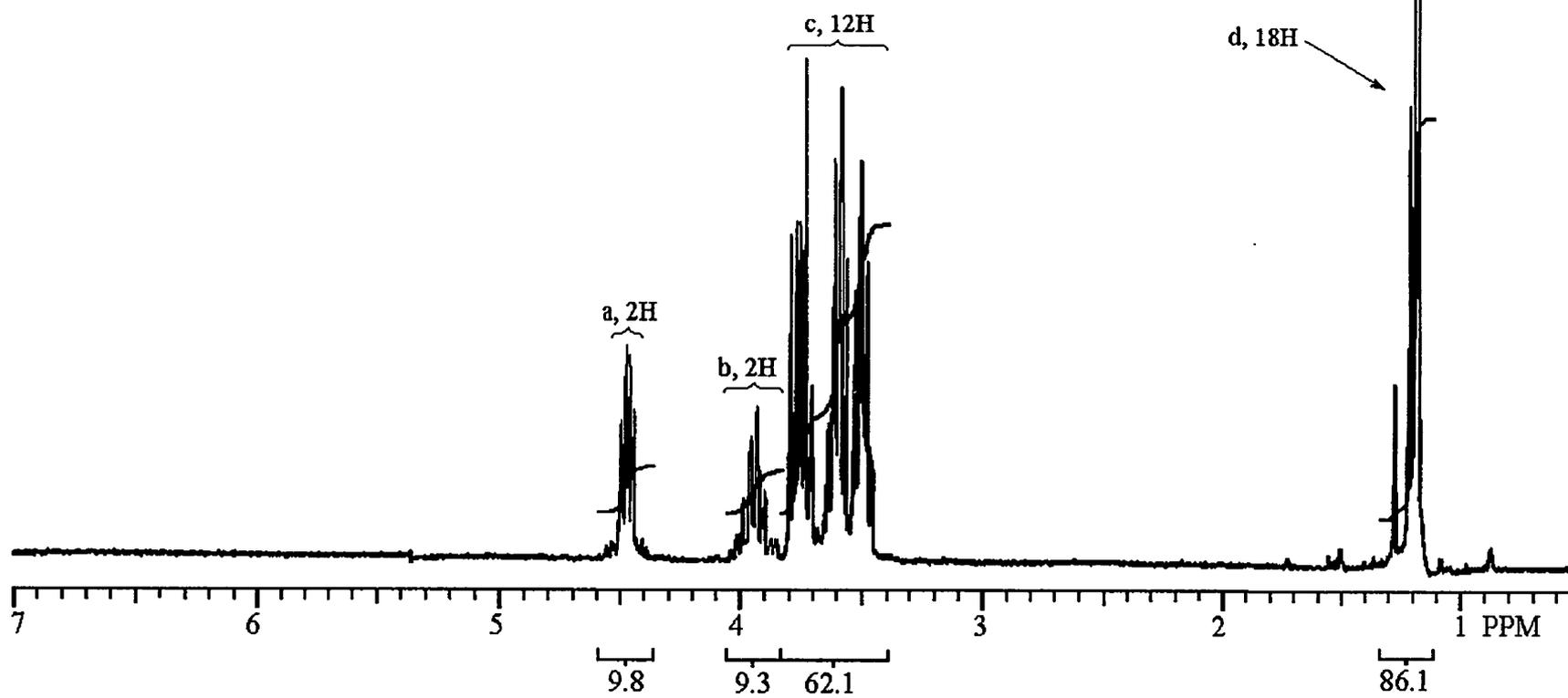
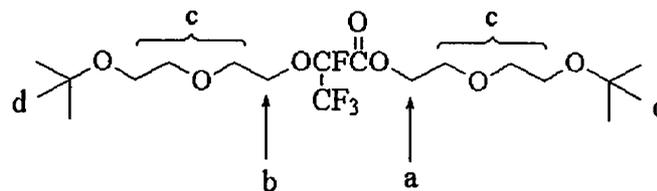
2-(2-*tert*-Butoxy-ethoxy)-ethyl pentafluoropropionate [3b]
 ^1H 300 MHz NMR



2-(2-*tert*-Butoxy-ethoxy)-ethyl pentafluoropropionate [3b]
¹H 300 MHz NMR

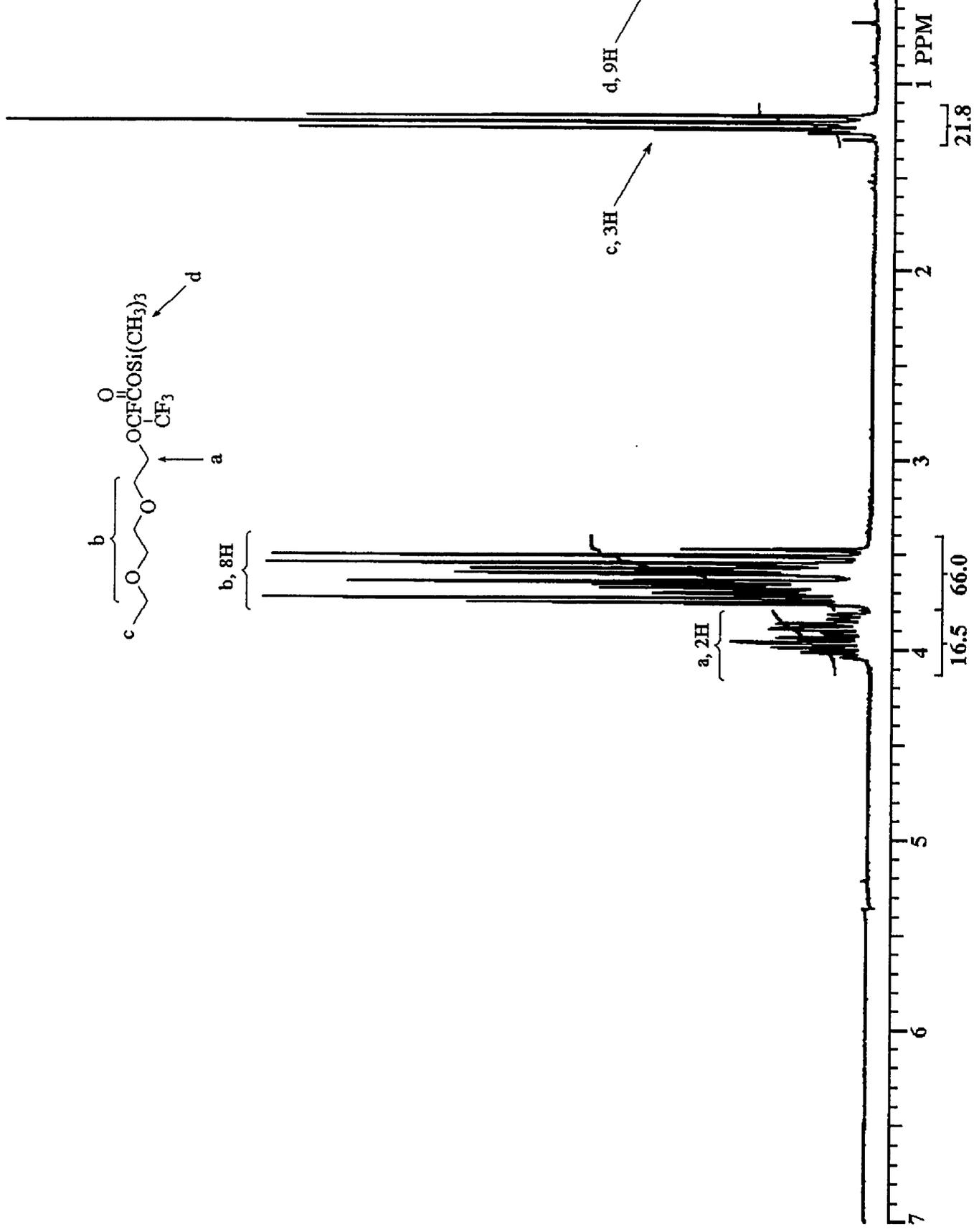


2-(2-Ethoxy-ethoxy)-ethyl 2-[2-(2-ethoxy-ethoxy)-ethoxy]-2,3,3,3-tetrafluoropropionate [5a]
¹H 200 MHz NMR

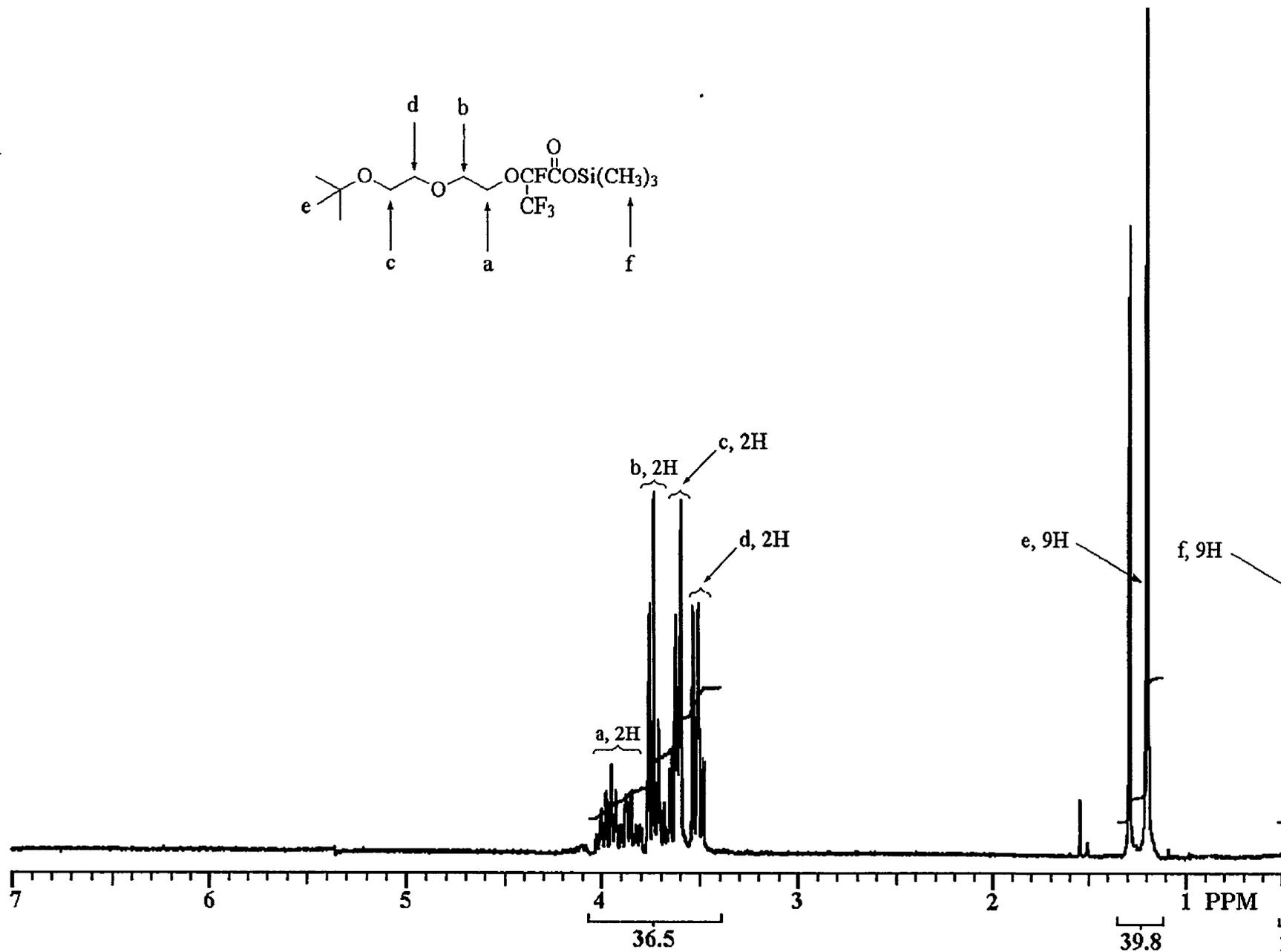
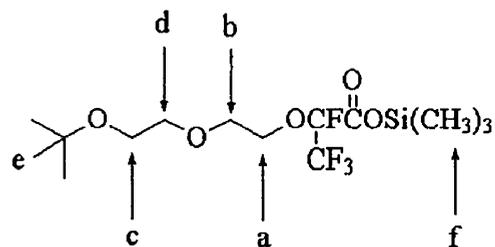


2-(2-*tert*-Butoxy-ethoxy)-ethyl 2-[2-(2-*tert*-butoxy-ethoxy)-ethoxy]-2,3,3,3-tetrafluoropropionate [5b]

^1H 200 MHz NMR



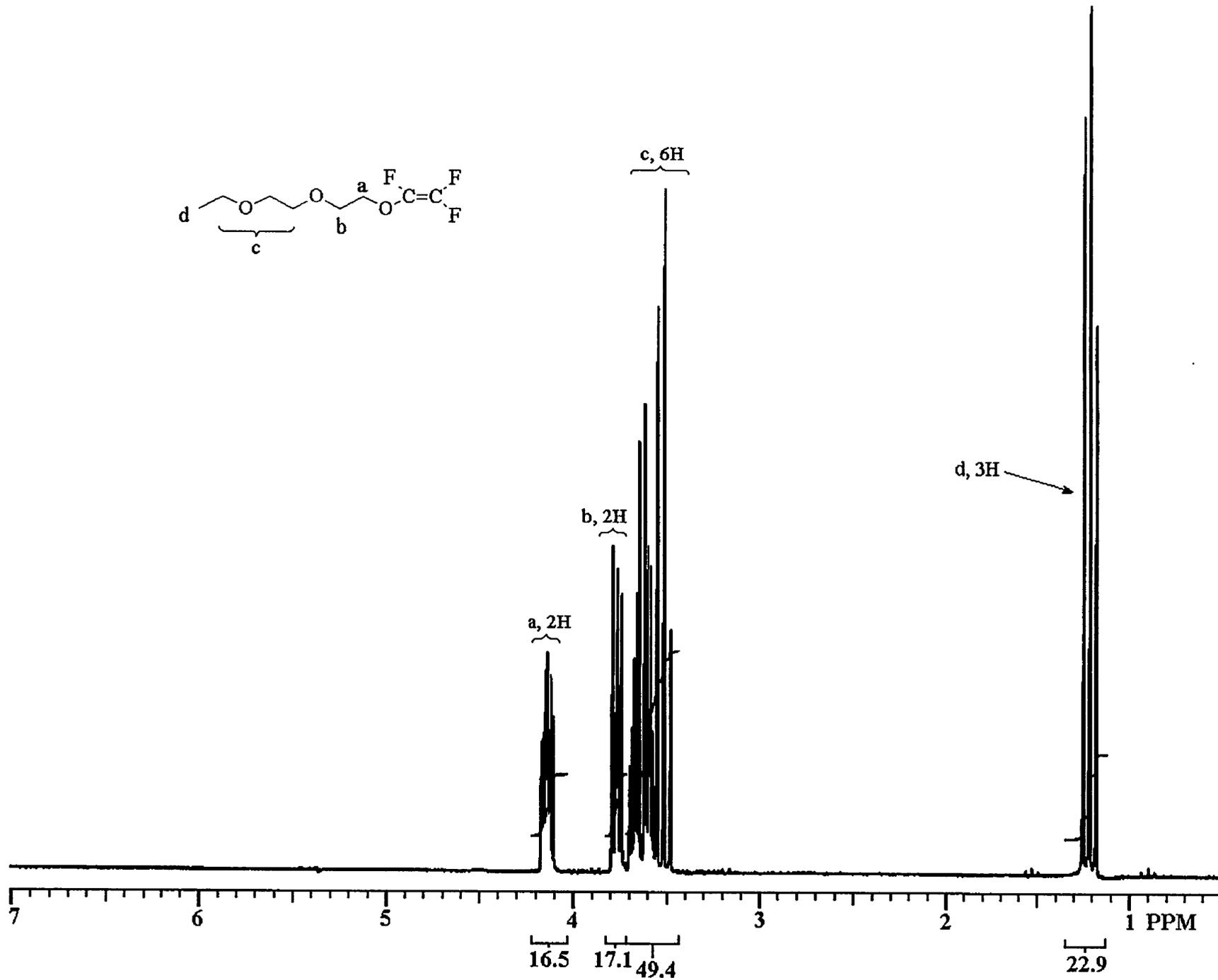
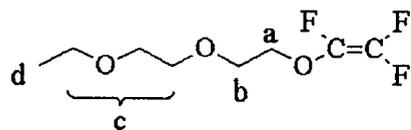
Trimethylsilyl 2-[2-(2-ethoxy-ethoxy)-ethoxy]-2,3,3,3-tetrafluoropropionate [7a]
¹H 200 MHz NMR



Trimethylsilyl 2-[2-(2-*tert*-butoxy-ethoxy)-ethoxy]-2,3,3,3-tetrafluoropropionate [7b]

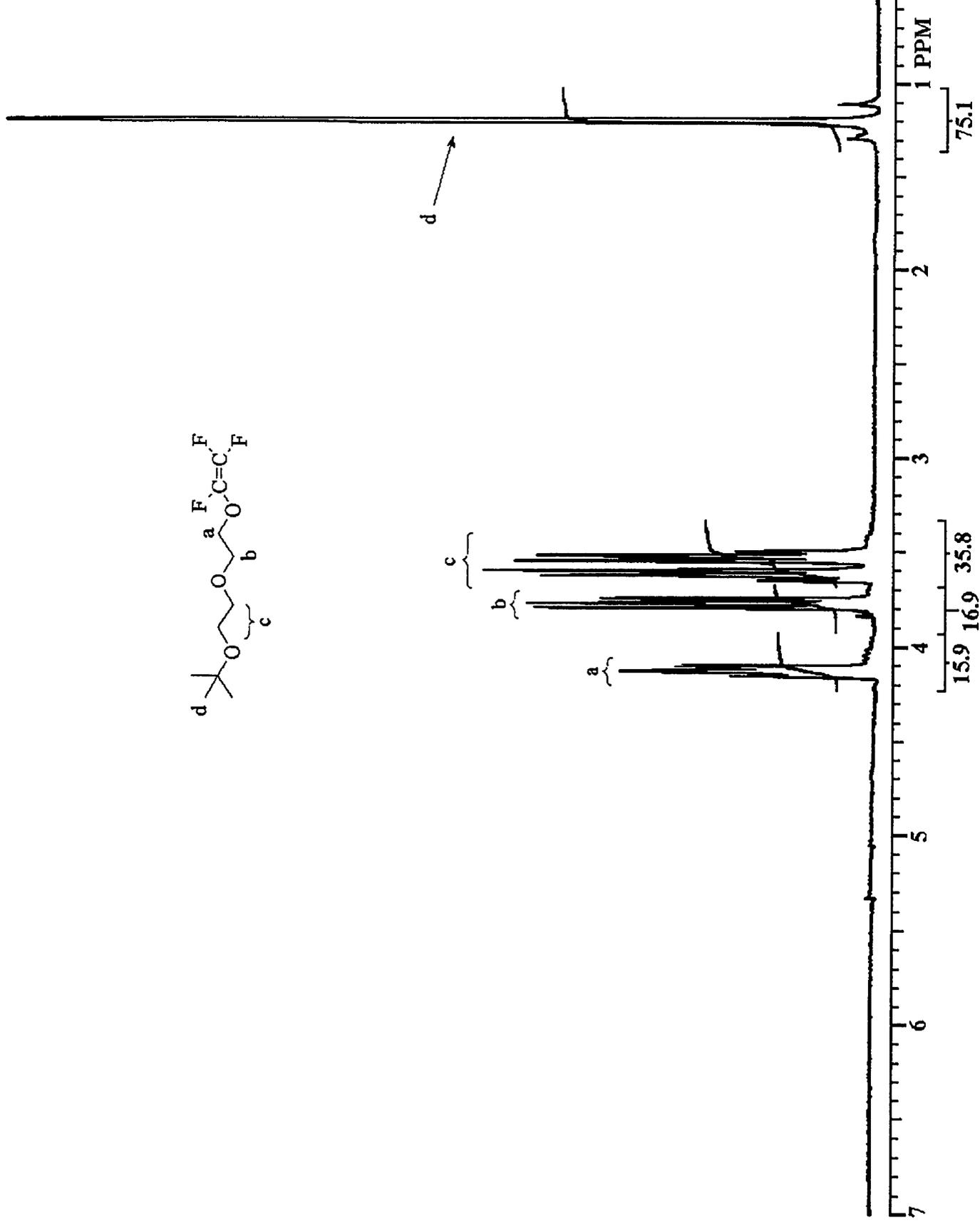
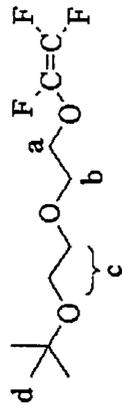
^1H 200 MHz NMR

solvent: CDCl_3 , reference: TMS

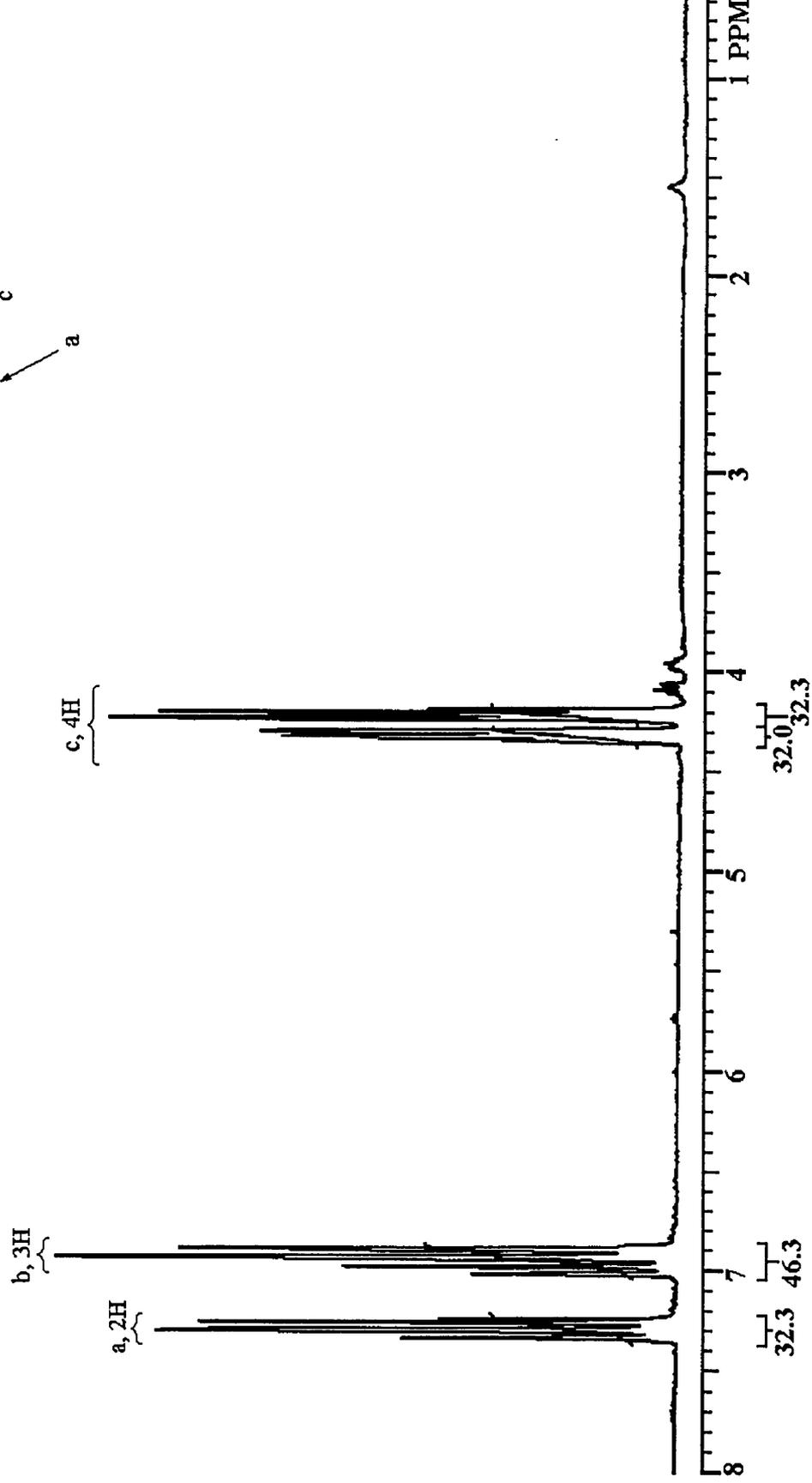
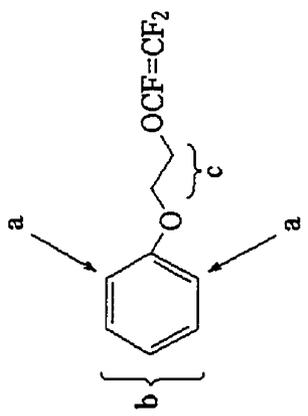


1-[2-(2-ethoxy-ethoxy)-ethoxy]-1,2,2-trifluoroethene [8a]

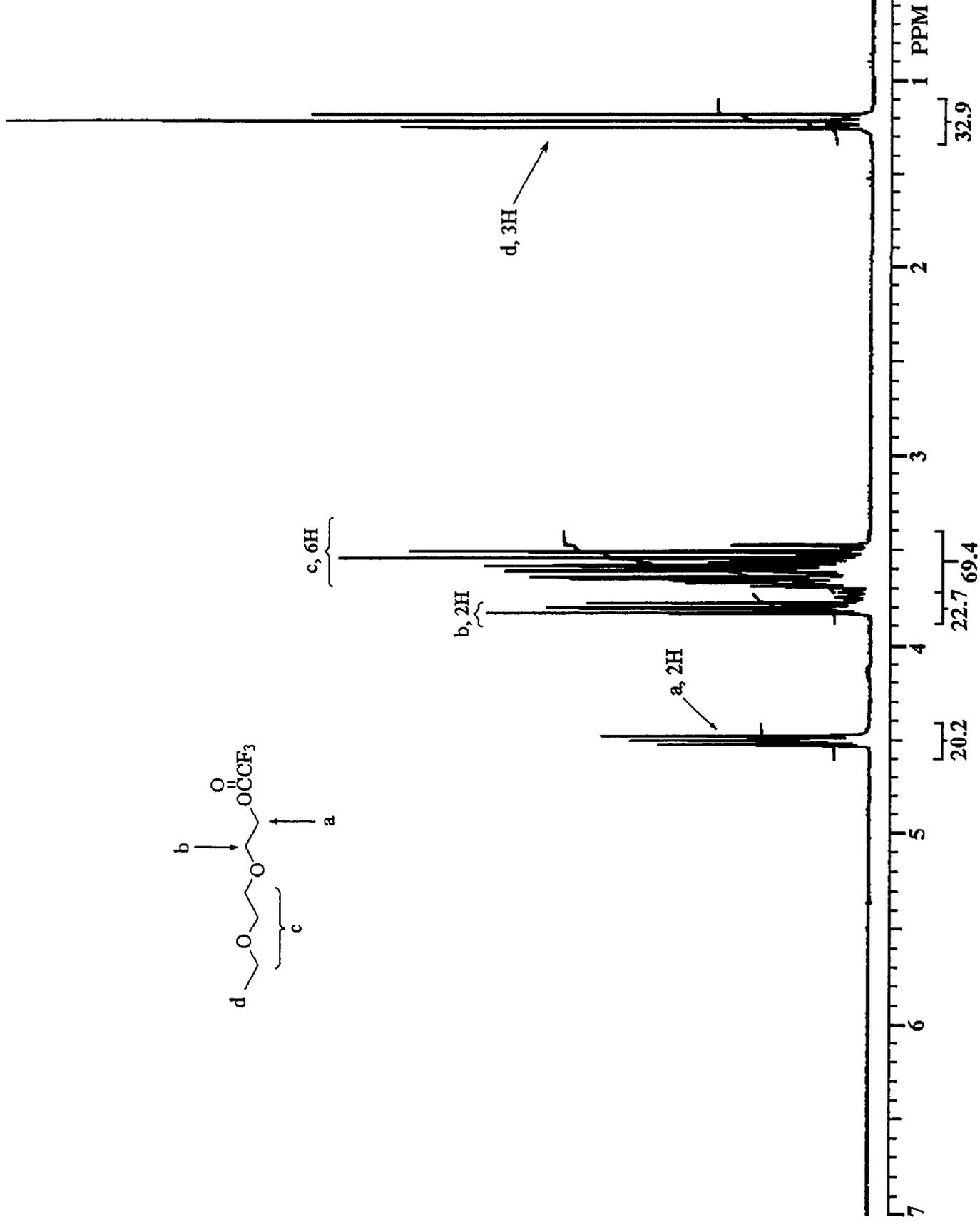
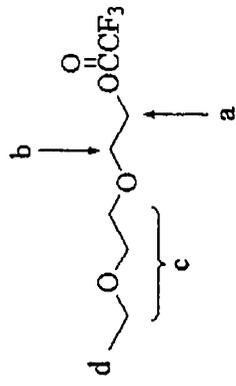
^1H 200 MHz NMR



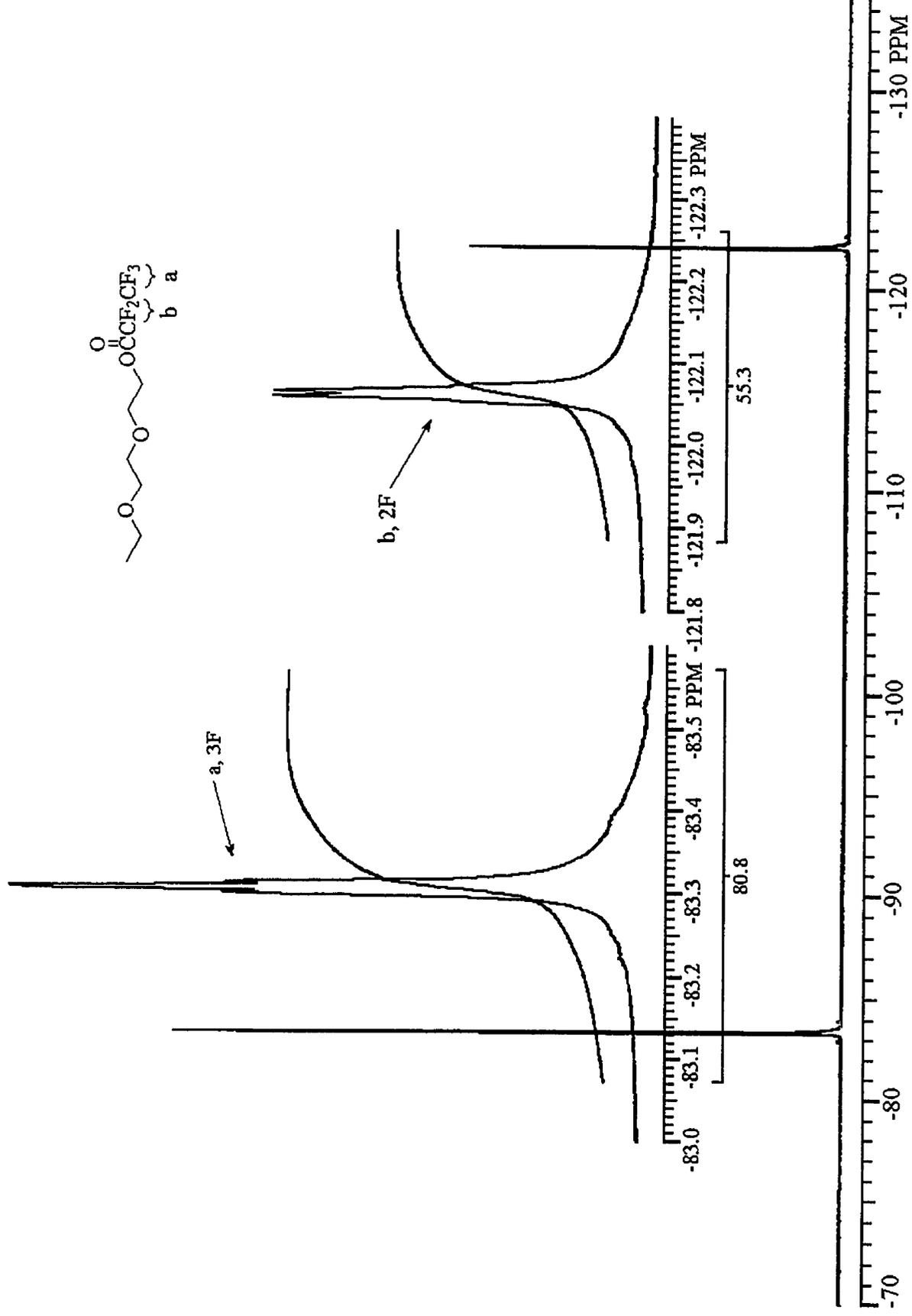
1-[2-(2-*tert*-Butoxy-ethoxy)-ethoxy]-1,2,2-trifluoroethene [8b]
 ^1H 200 MHz NMR



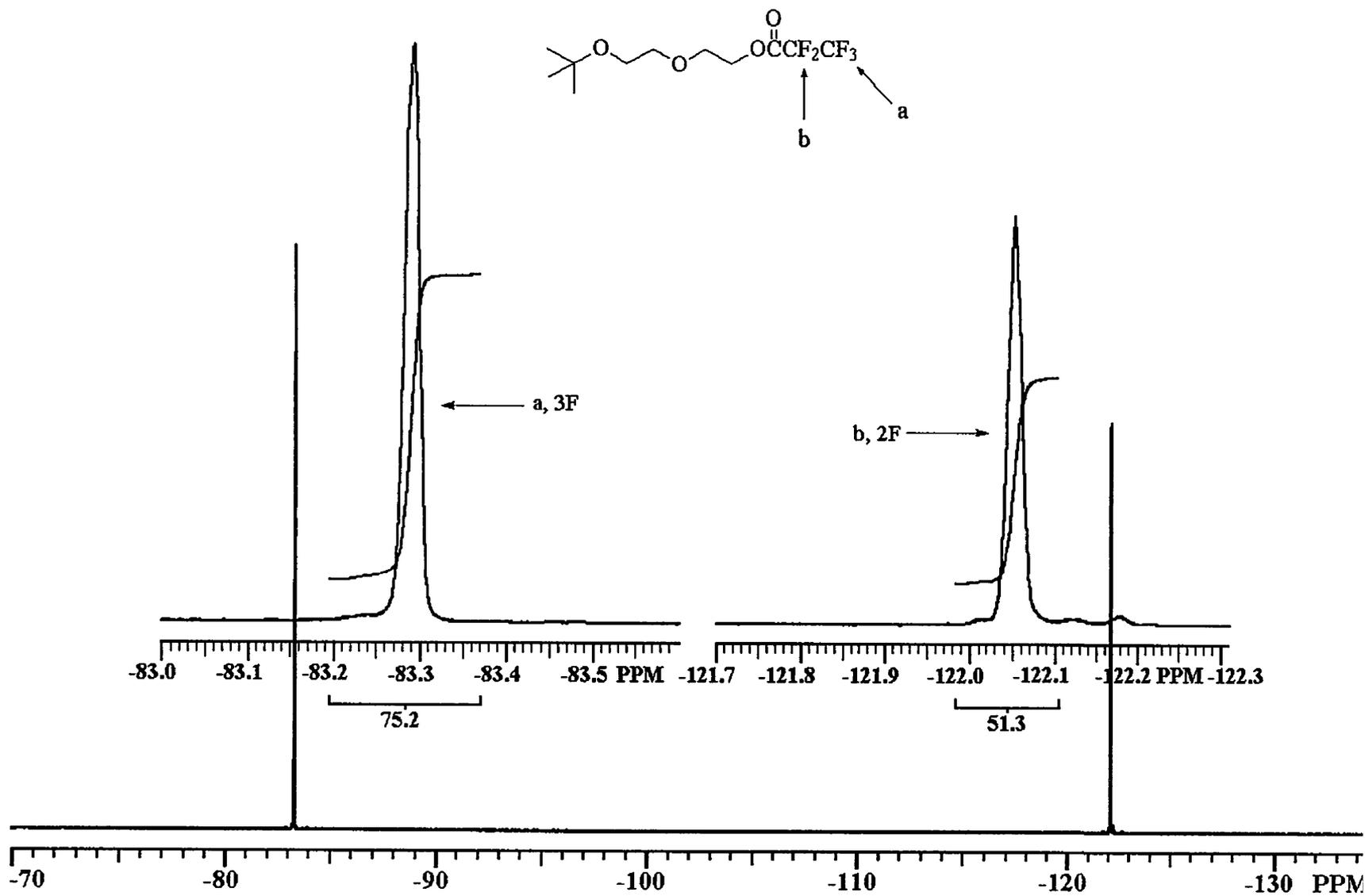
1-(2-Phenoxy-ethoxy)-1,1,2,2-trifluoroethane [8c]
¹H 200 MHz NMR



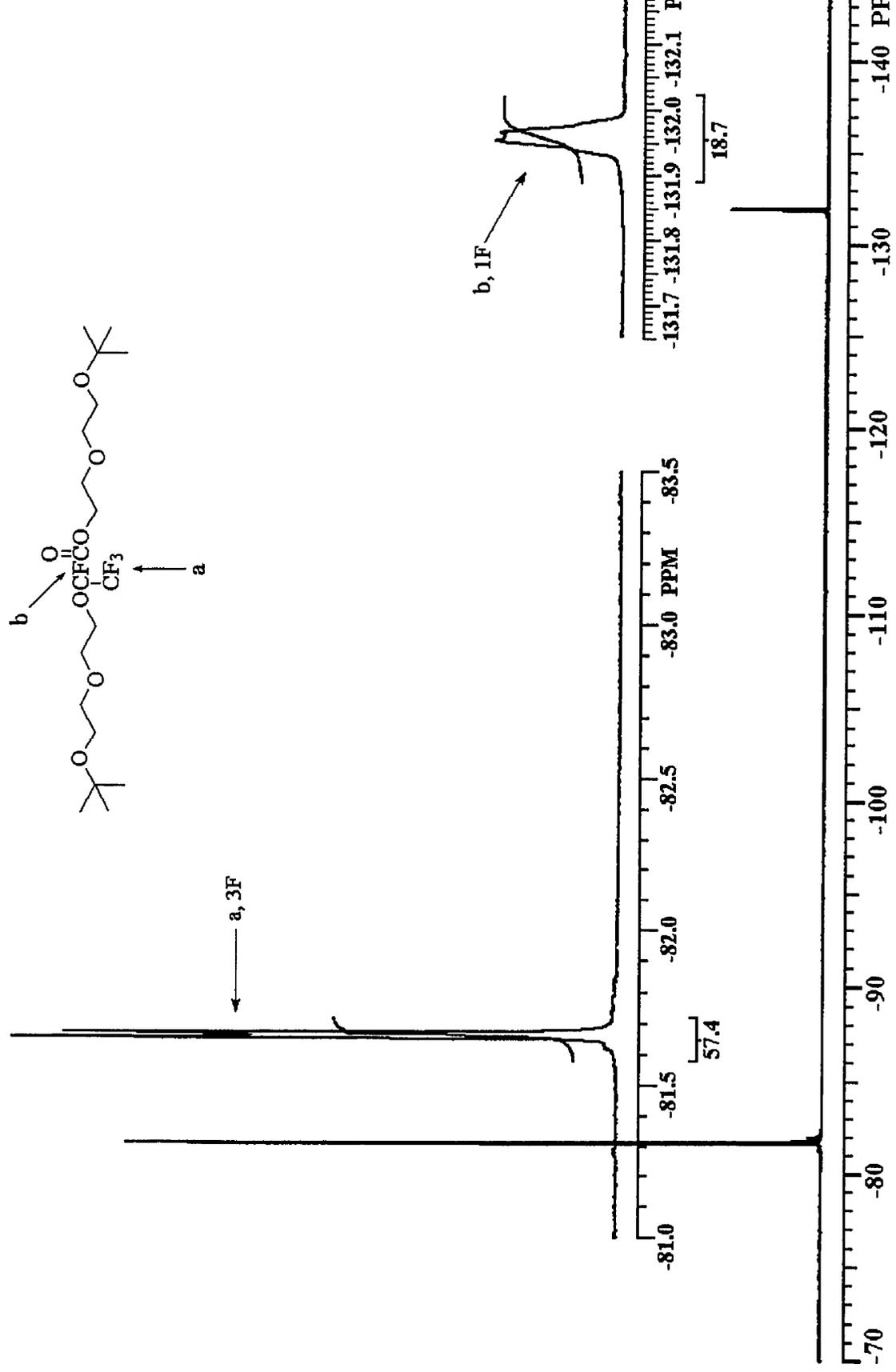
2-(2-Ethoxy-ethoxy)-ethyl trifluoroacetate [11a]
¹H 200 MHz NMR



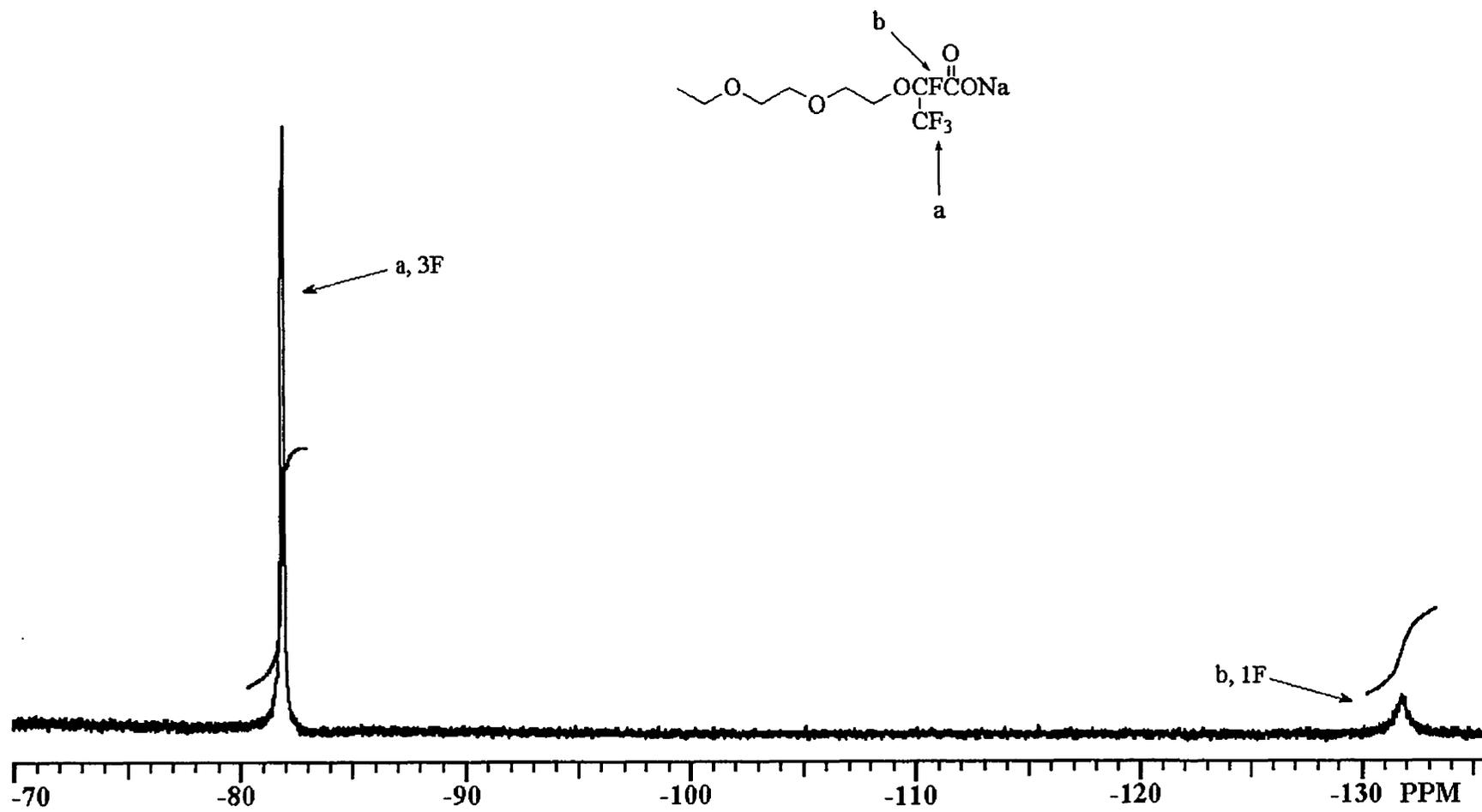
2-(2-Ethoxy-ethoxy)-ethyl pentafluoropropionate [3a]
¹⁹F 300 MHz NMR



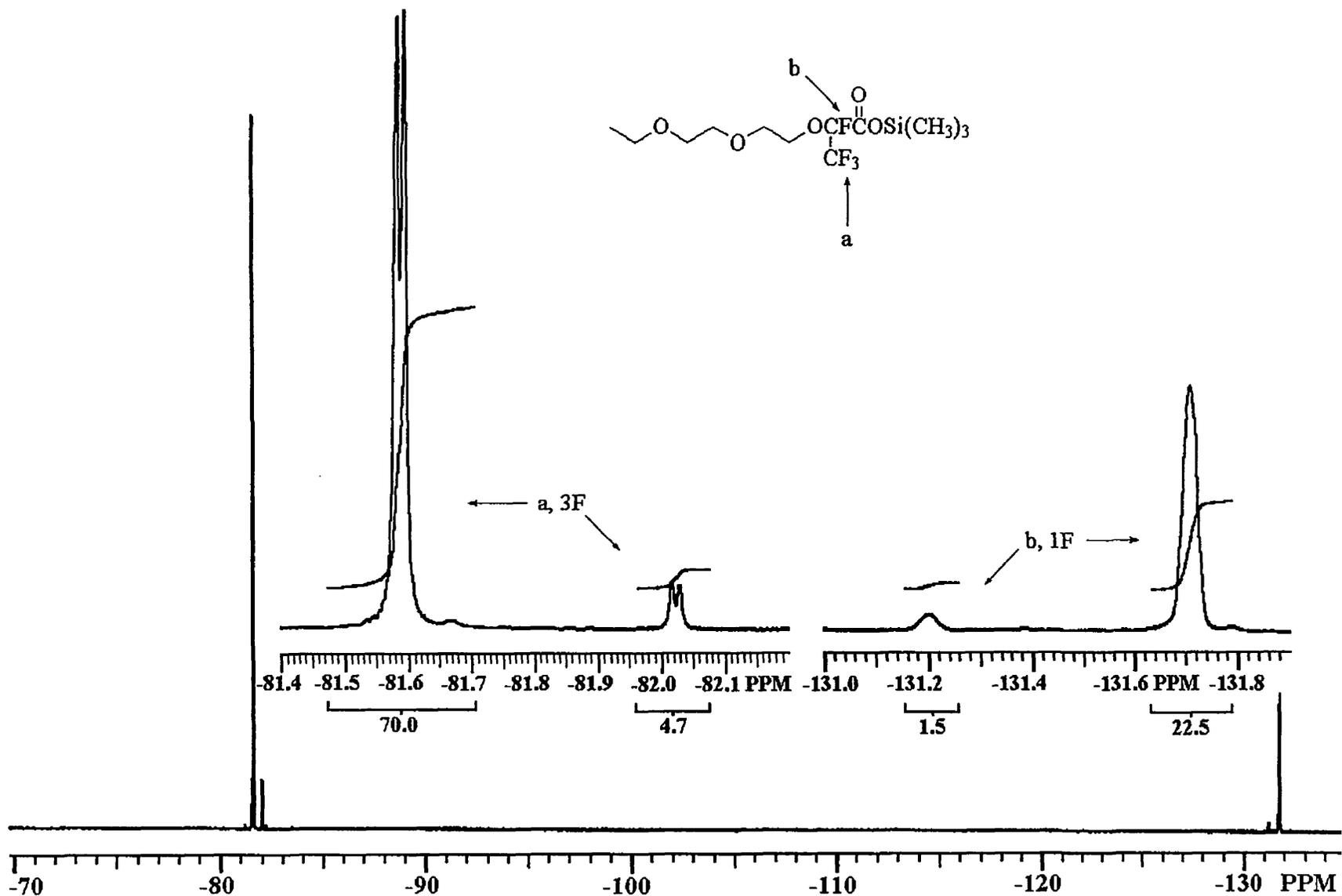
2-(2-*tert*-Butoxy-ethoxy)-ethyl pentafluoropropionate [3b]
 ^{19}F 300 MHz NMR



2-(2-*tert*-Butoxy-ethoxy)-ethyl 2-[2-(2-*tert*-butoxy-ethoxy)-ethoxy]-2,3,3,3-tetrafluoropropionate [5b]
¹⁹F 300 MHz NMR

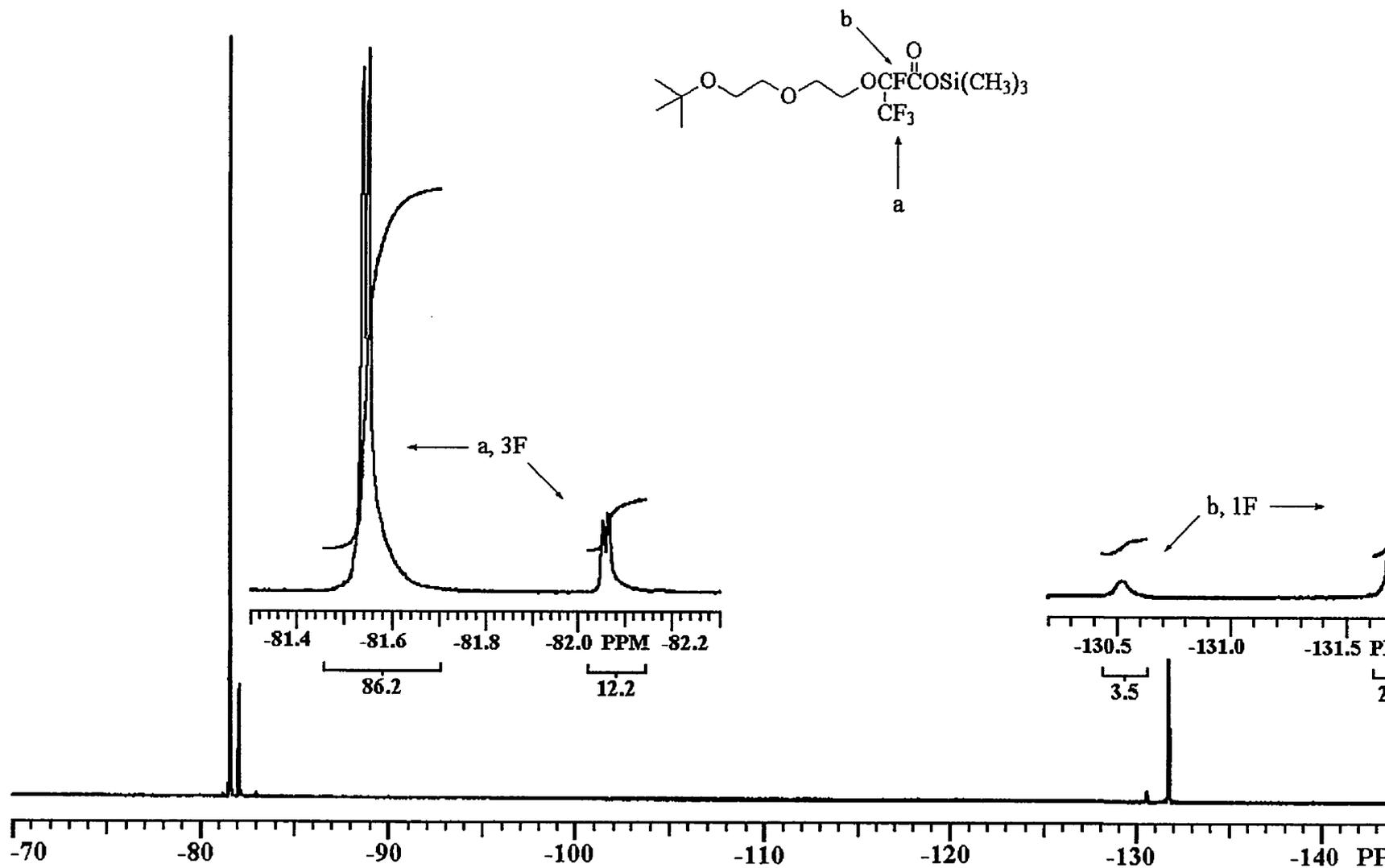


Sodium 2-[2-(2-ethoxy-ethoxy)-ethoxy]-2,3,3,3-tetrafluoropropionate [6a]
 ^{19}F 300 MHz NMR

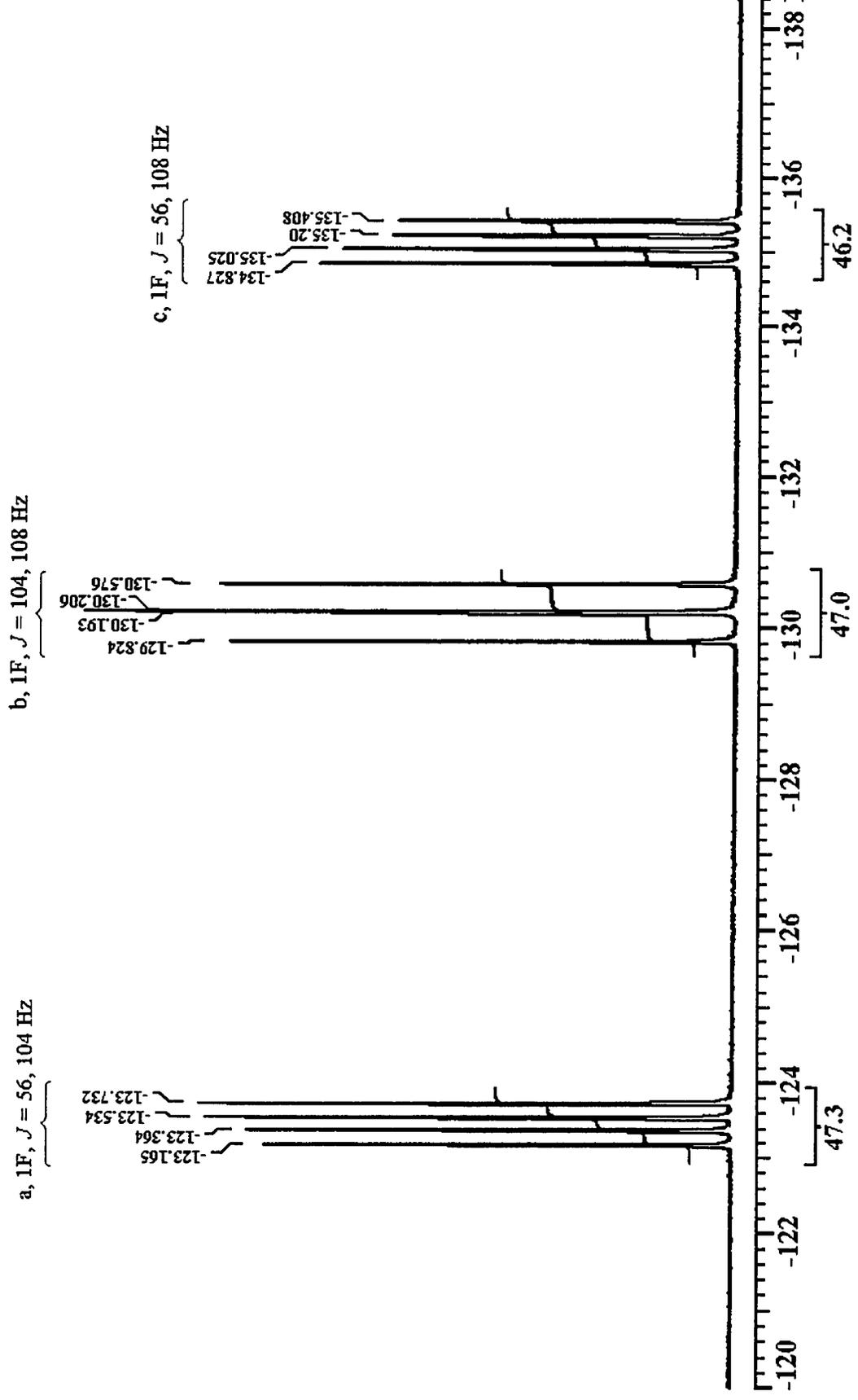
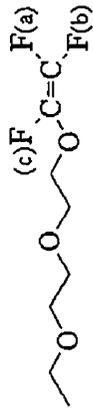


Trimethylsilyl 2-[2-(2-ethoxy-ethoxy)-ethoxy]-2,3,3,3-tetrafluoropropionate [7a]

^{19}F 300 MHz NMR



Trimethylsilyl 2-[2-(2-*tert*-butoxy-ethoxy)-ethoxy]-2,3,3,3-tetrafluoropropionate [7b]
 ^{19}F 300 MHz NMR



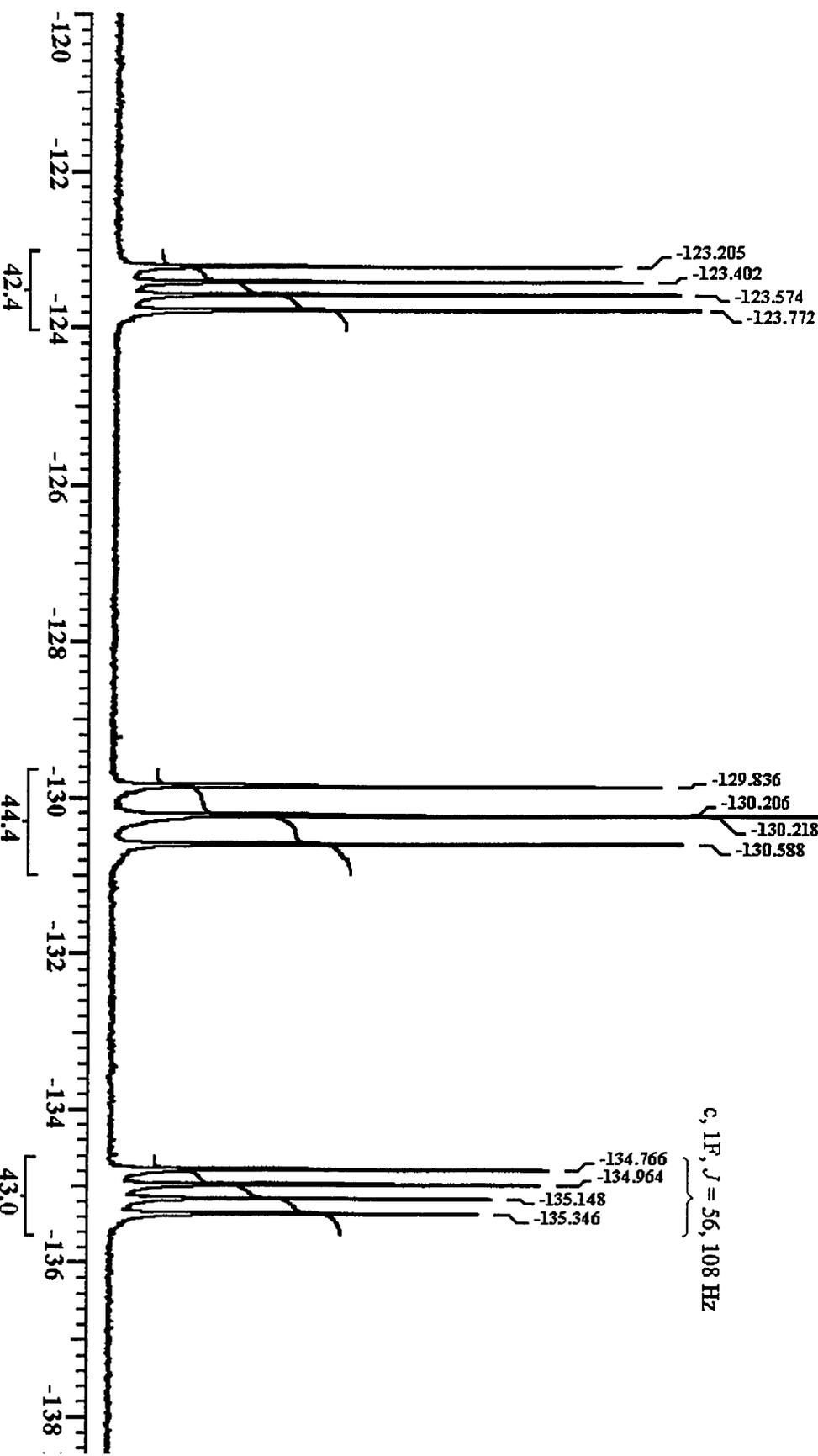
1[2-(2-Ethoxy-ethoxy)-ethoxy-1,2,2-trifluoroethene [8a]
¹⁹F 300 MHz NMR



a, $1F$, $J = 56, 104$ Hz

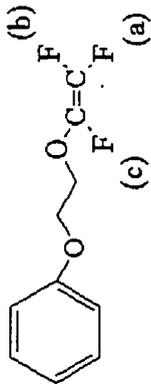
b, $1F$, $J = 104, 108$ Hz

c, $1F$, $J = 56, 108$ Hz



1-[2-(2-*tert*-Butoxy-ethoxy)-ethoxy]-1,2,2-trifluoroethene [8b]

^{19}F 300 MHz NMR



a, 1F, $J = 56, 103$ Hz

-122.652
-122.852
-123.017
-123.217

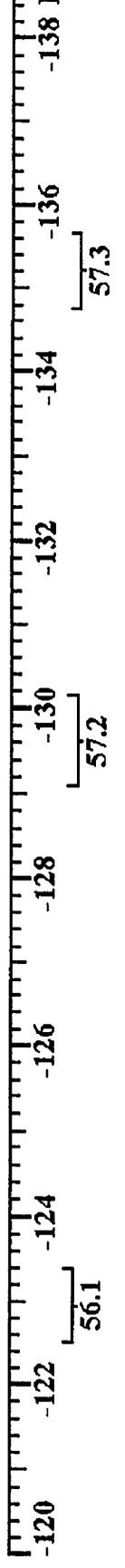
b, 1F, $J = 103, 108$ Hz

-129.195
-129.560
-129.578
-129.944

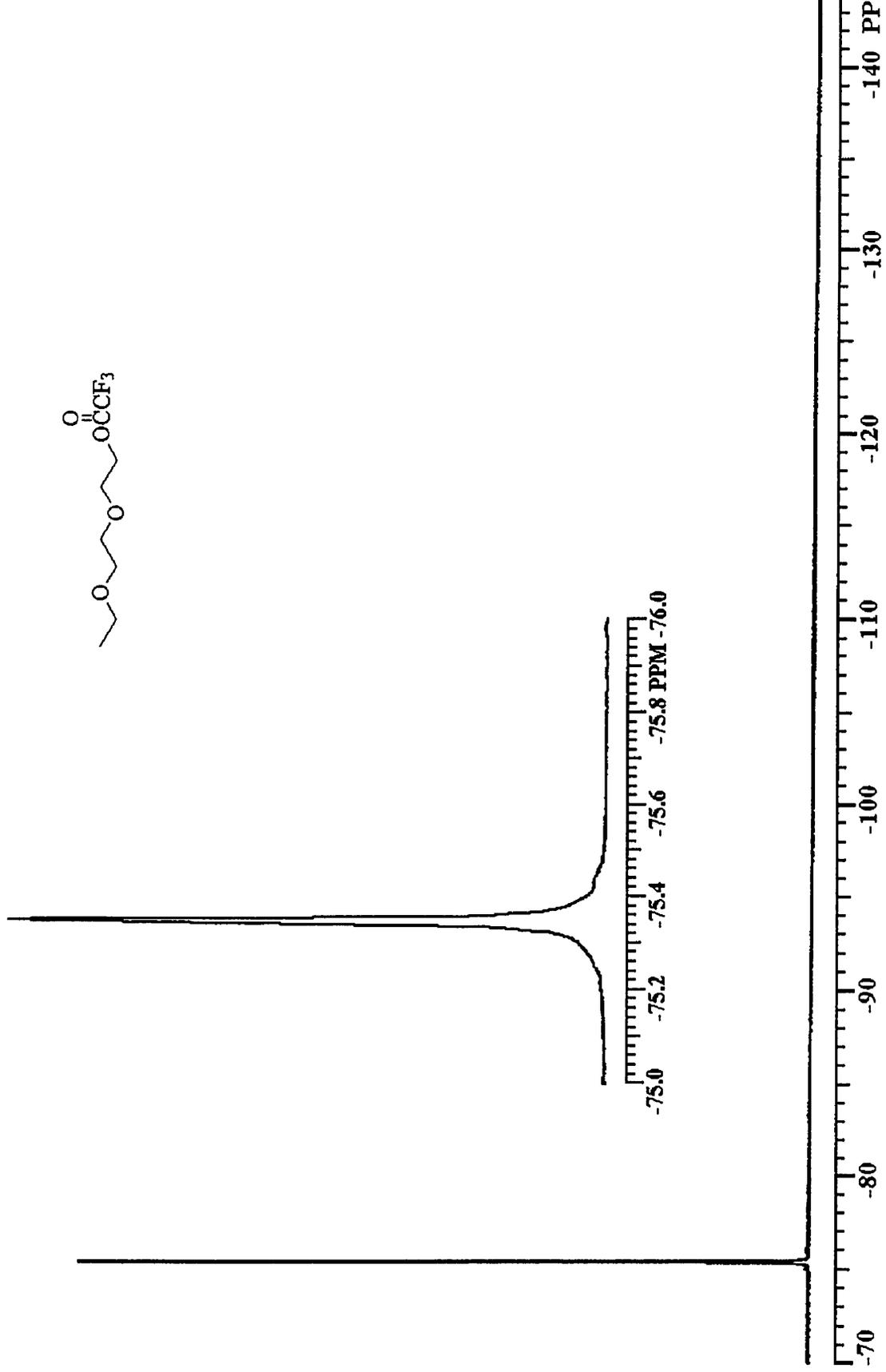
c, 1F, $J = 56, 108$ Hz

-134.900
-135.100
-135.283
-135.482

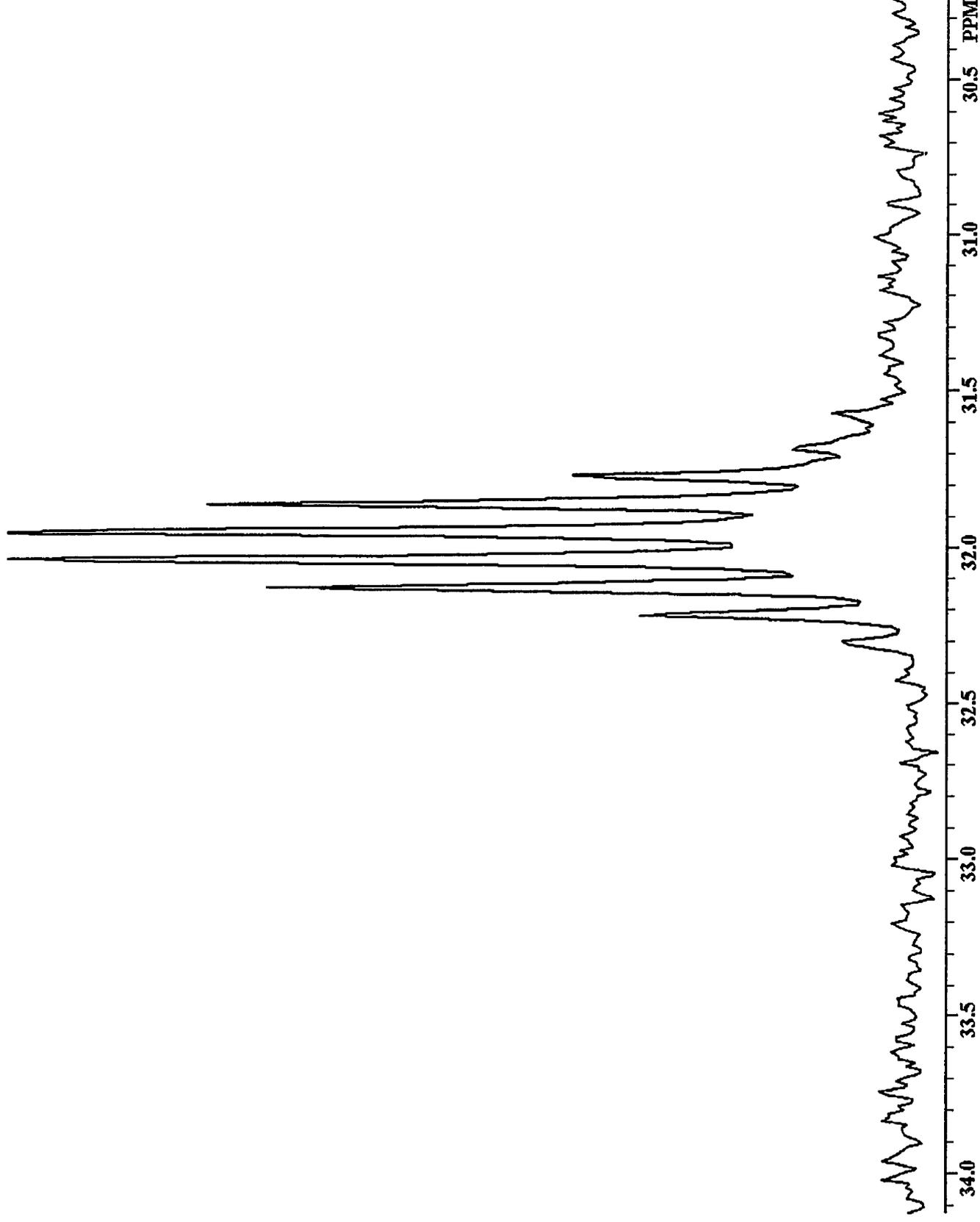
$\text{HCF}_2\text{CF}_2\text{O}$



1-(2-Phenoxy-ethoxy)-1,2,2-trifluoroethene [8c]
 ^{19}F 300 MHz NMR



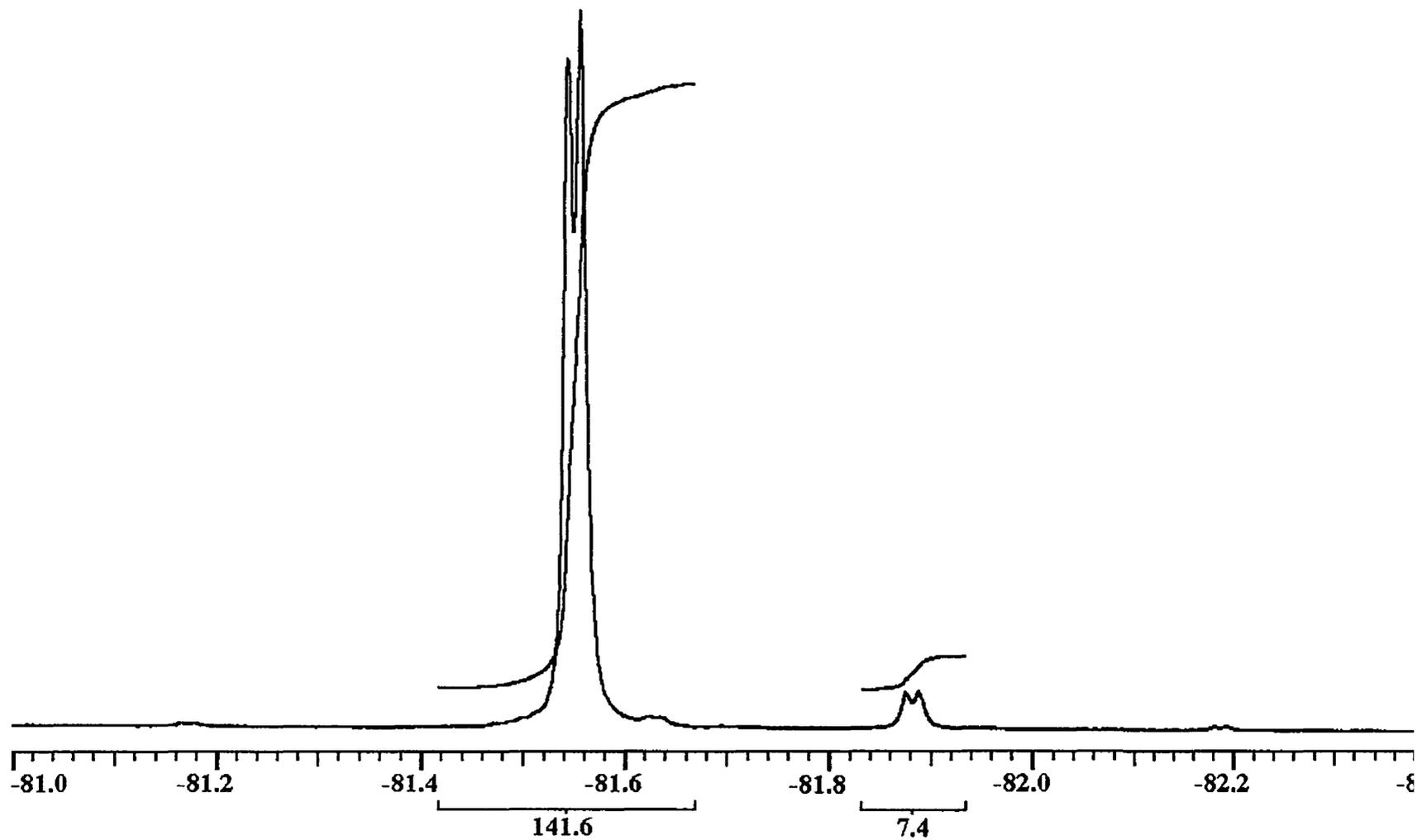
2-(2-Ethoxy-ethoxy)-ethyl trifluoroacetate [11a]
 ^{19}F 300 MHz NMR



Trimethylsilyl 2-[2-(2-ethoxy-ethoxy)-ethoxy]-2,3,3,3-tetrafluoropropionate [7a]

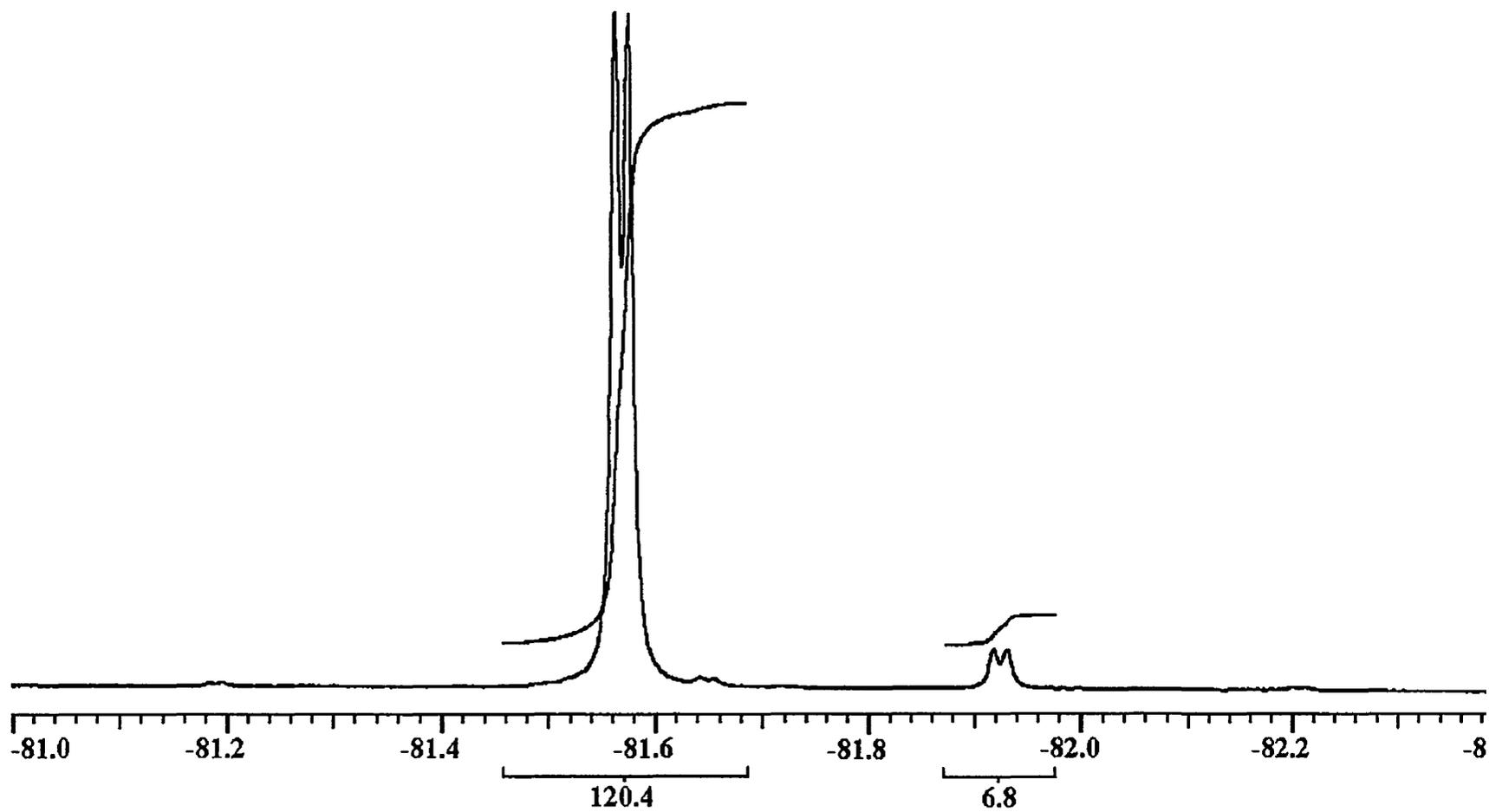
^{29}Si 400 MHz NMR

solvent: CDCl_3 , reference: TMS

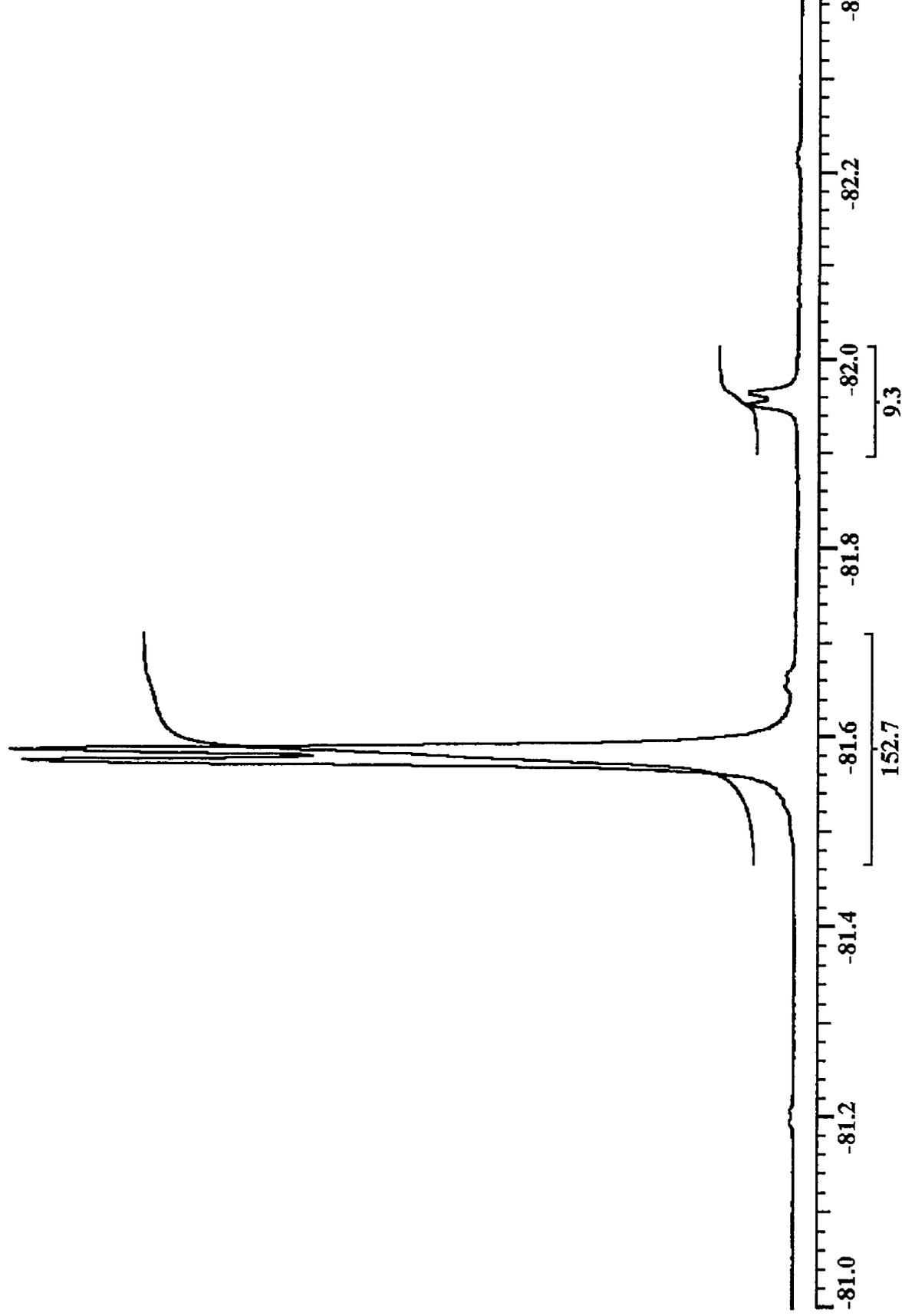


Trimethylsilyl 2-[2-(2-ethoxy-ethoxy)-ethoxy]-2,3,3,3-tetrafluoropropionate [7a]

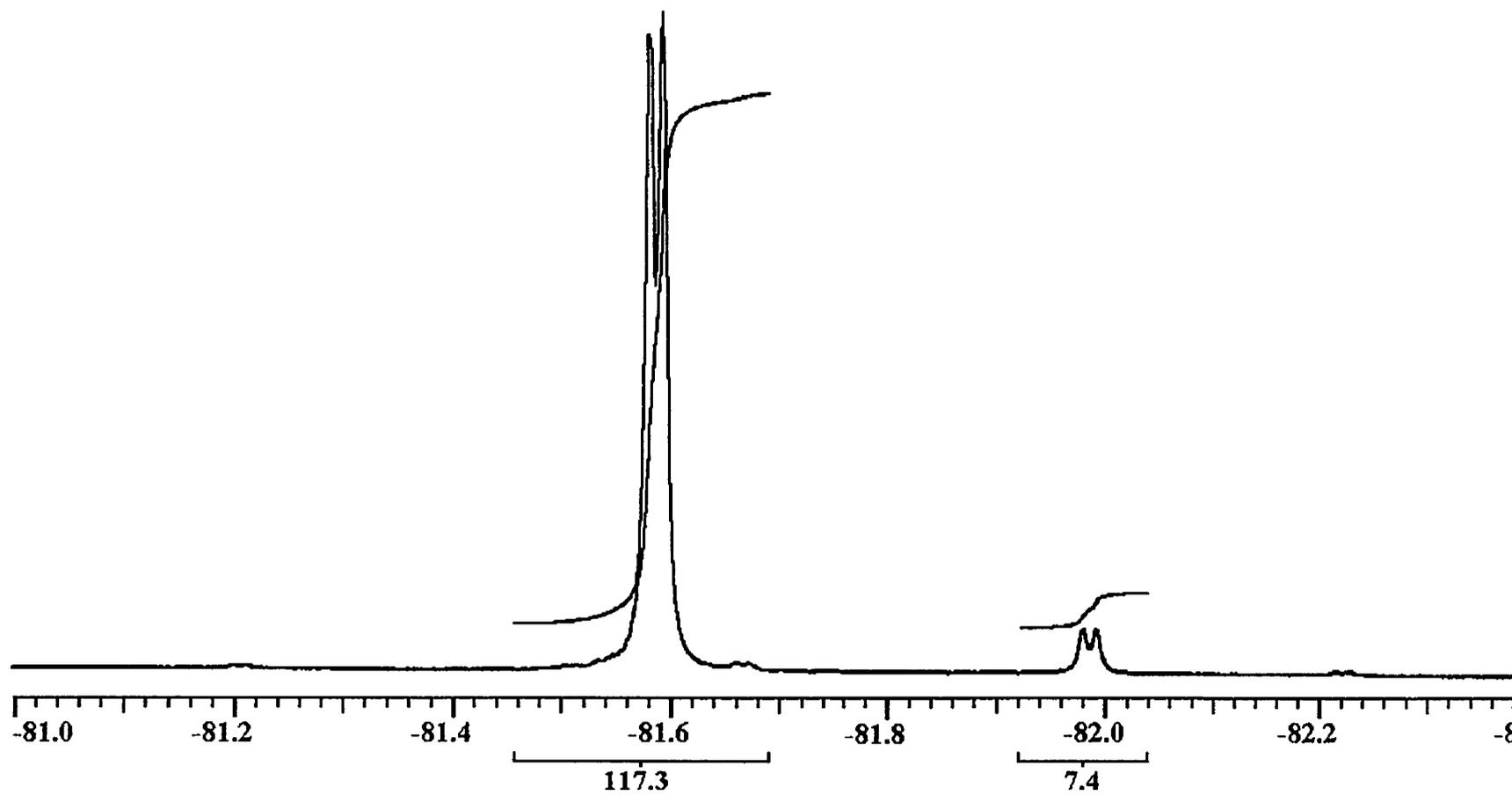
^{19}F 300 MHz Variable Temperature NMR, 243.3 K



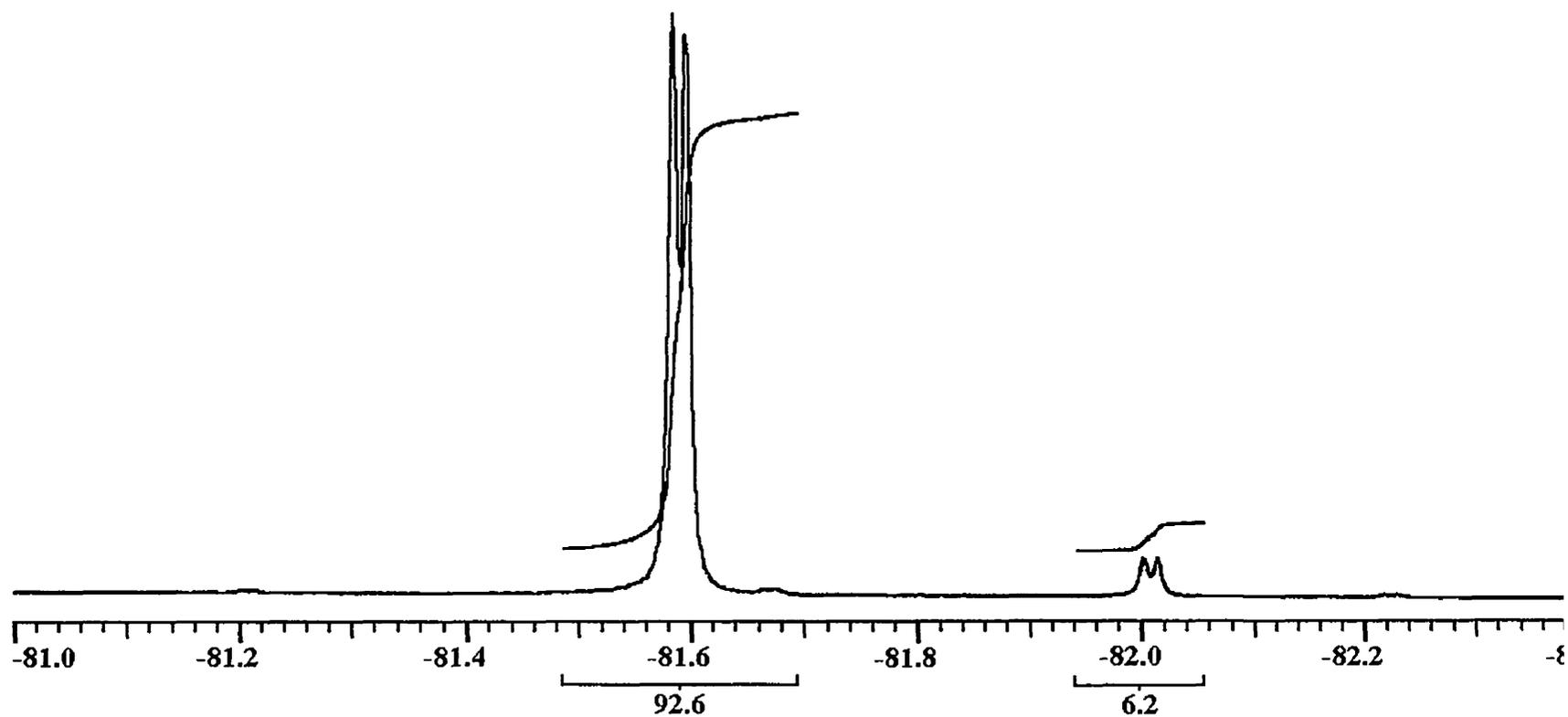
Trimethylsilyl 2-[2-(2-ethoxy-ethoxy)-ethoxy]-2,3,3,3-tetrafluoropropionate [7a]
 ^{19}F 300 MHz Variable Temperature NMR, 254.5 K



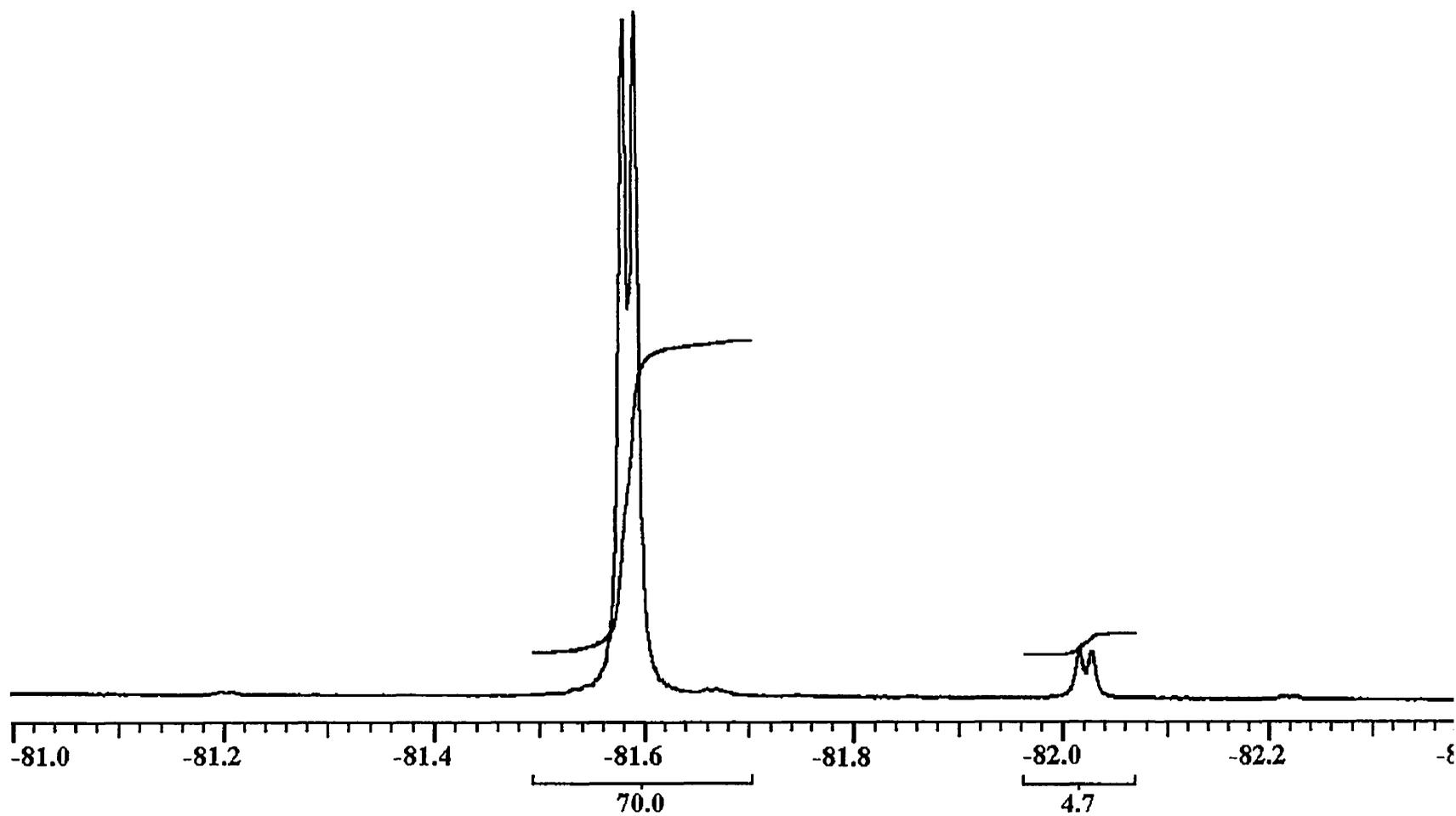
Trimethylsilyl 2-[2-(2-ethoxy-ethoxy)-ethoxy]-2,3,3,3-tetrafluoropropionate [7a]
 ^{19}F 300 MHz Variable Temperature NMR, 265.7 K



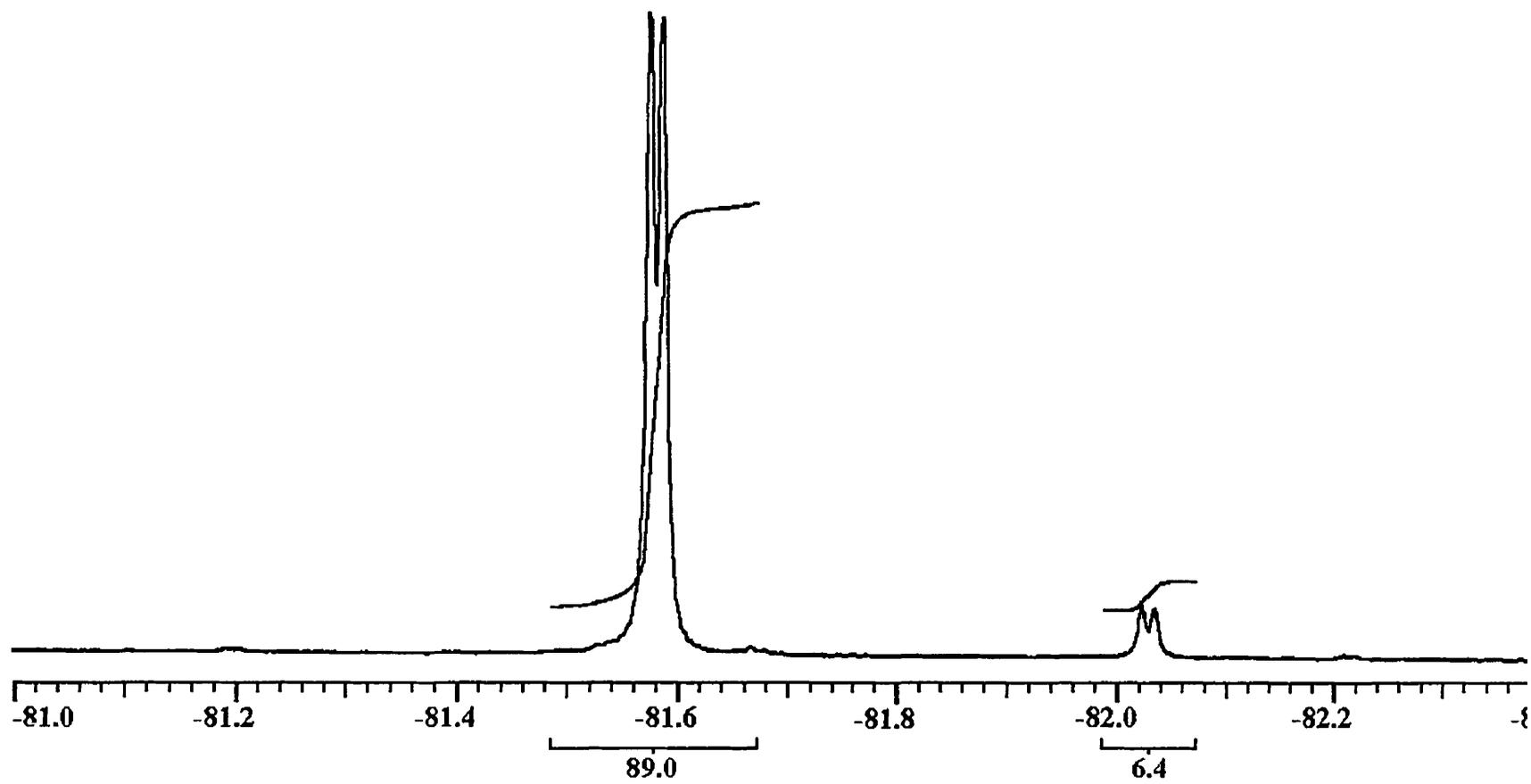
Trimethylsilyl 2-[2-(2-ethoxy-ethoxy)-ethoxy]-2,3,3,3-tetrafluoropropionate [7a]
 ^{19}F 300 MHz Variable Temperature NMR, 273.0 K



Trimethylsilyl 2-[2-(2-ethoxy-ethoxy)-ethoxy]-2,3,3,3-tetrafluoropropionate [7a]
 ^{19}F 300 MHz Variable Temperature NMR, 288.1 K

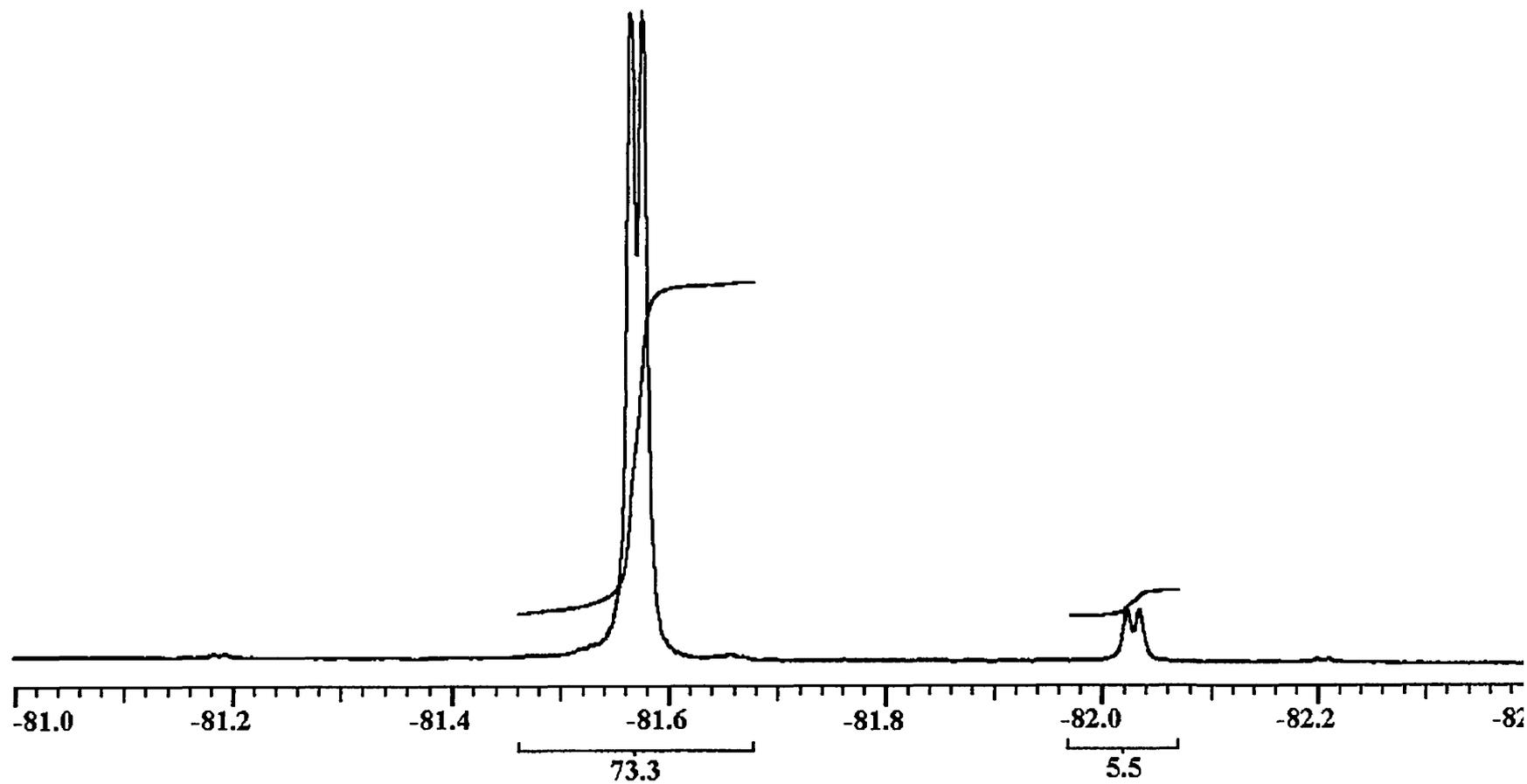


Trimethylsilyl 2-[2-(2-ethoxy-ethoxy)-ethoxy]-2,3,3,3-tetrafluoropropionate [7a]
 ^{19}F 300 MHz Variable Temperature NMR, 297.3 K

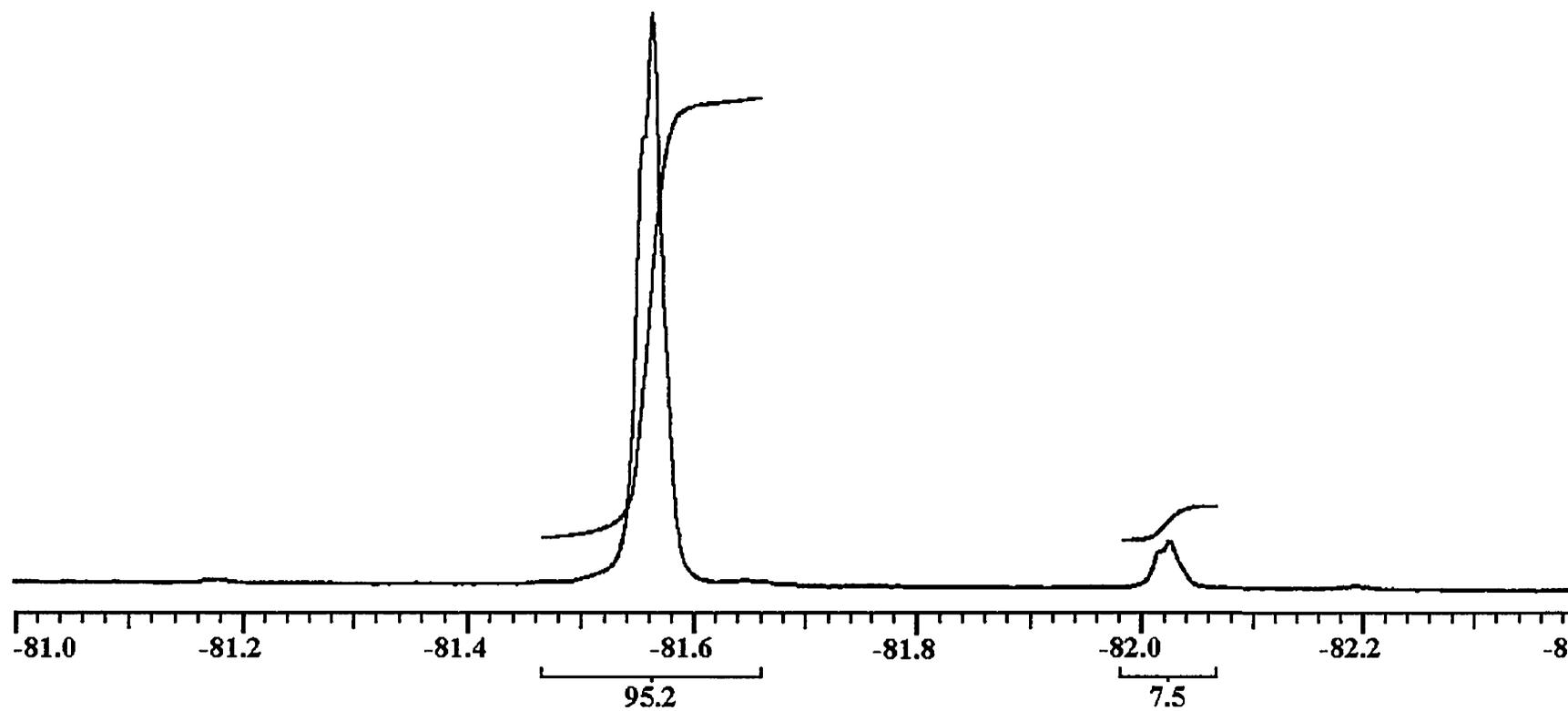


Trimethylsilyl 2-[2-(2-ethoxy-ethoxy)-ethoxy]-2,3,3,3-tetrafluoropropionate [7a]

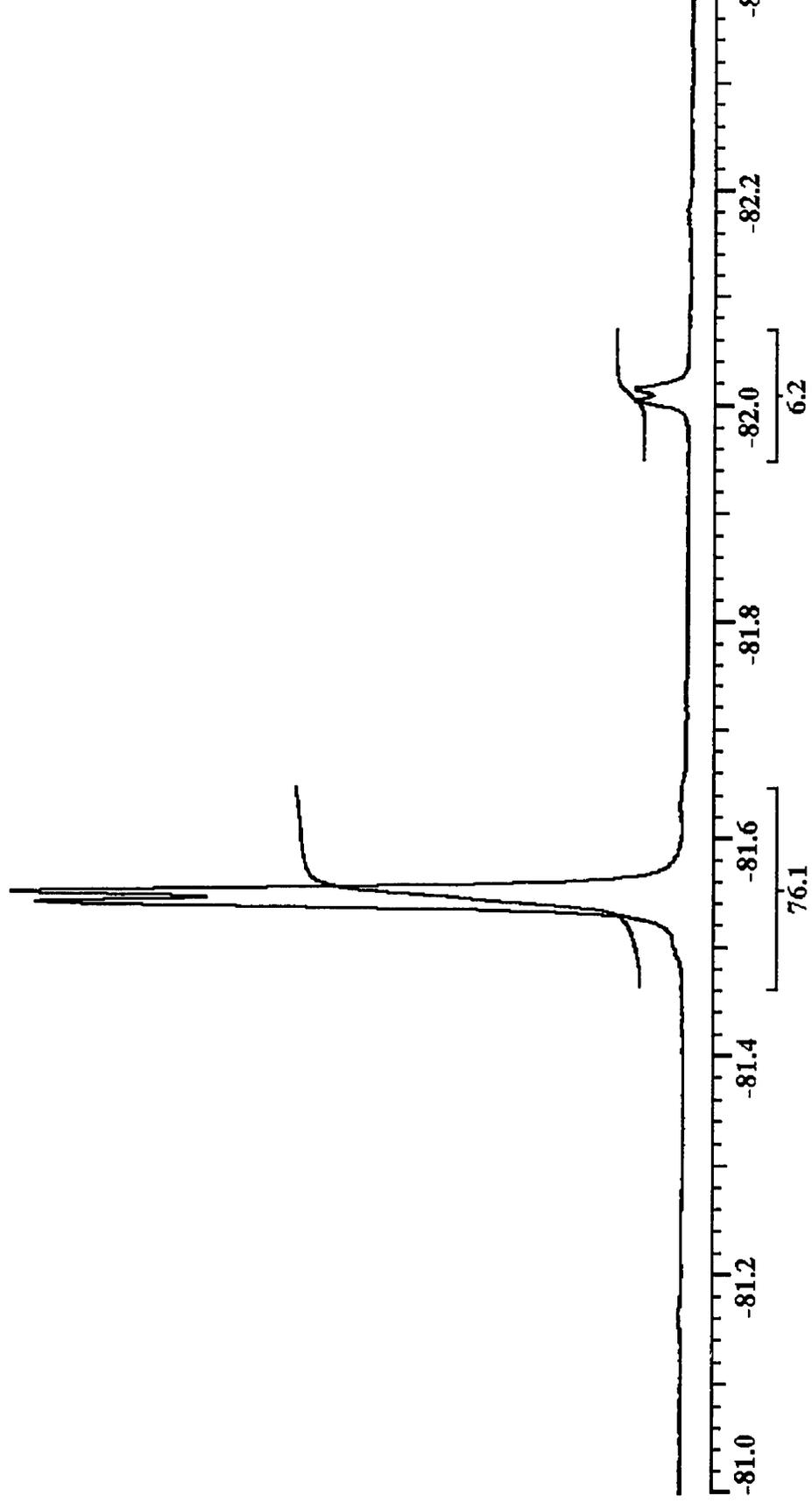
^{19}F 300 MHz Variable Temperature NMR. 307.2 K



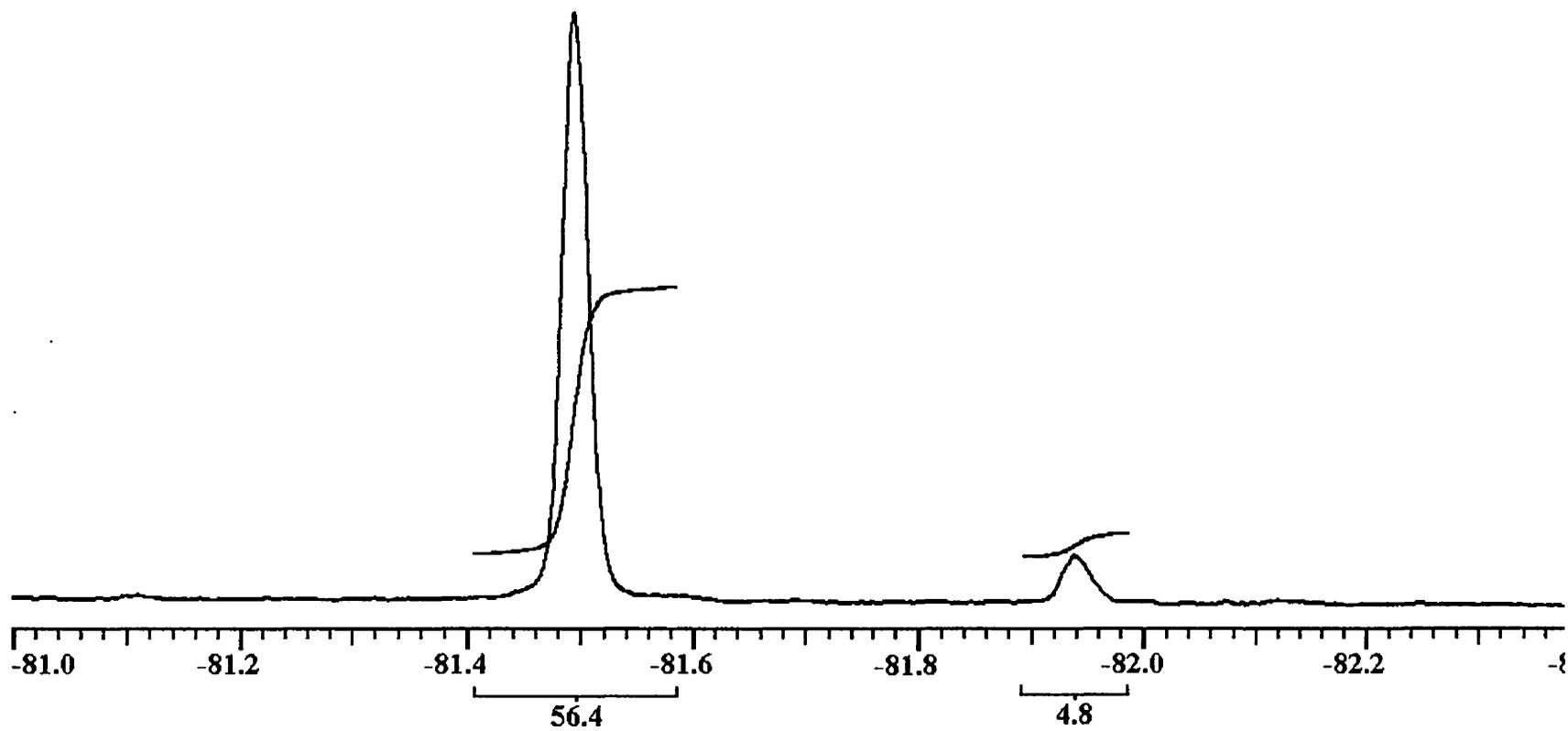
Trimethylsilyl 2-[2-(2-ethoxy-ethoxy)-ethoxy]-2,3,3,3-tetrafluoropropionate [7a]
 ^{19}F 300 MHz Variable Temperature NMR, 317.2 K



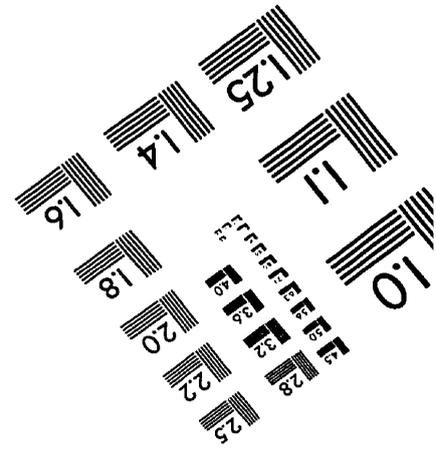
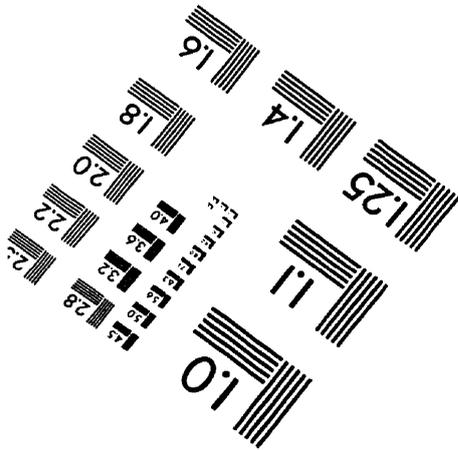
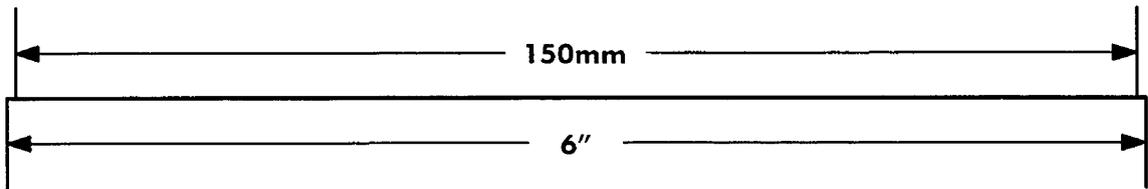
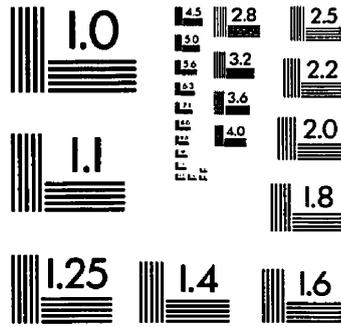
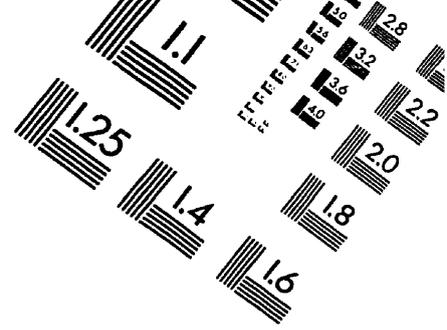
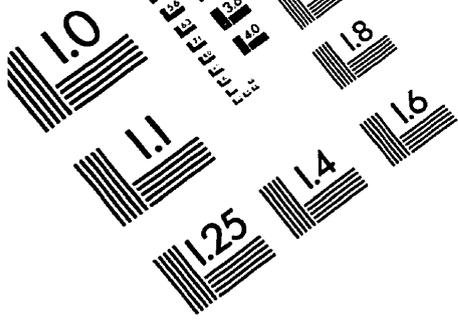
Trimethylsilyl 2-[2-(2-ethoxy-ethoxy)-ethoxy]-2,3,3,3-tetrafluoropropionate [7a]
 ^{19}F 300 MHz Variable Temperature NMR, 327.1 K



Trimethylsilyl 2-[2-(2-ethoxy-ethoxy)-ethoxy]-2,3,3,3-tetrafluoropropionate [7a]
 ^{19}F 300 MHz Variable Temperature NMR, 337.0 K



Trimethylsilyl 2-[2-(2-ethoxy-ethoxy)-ethoxy]-2,3,3,3-tetrafluoropropionate [7a]
 ^{19}F 300 MHz Variable Temperature NMR, 366.8 K



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1653 East Main Street
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Phone: 716/482-0300
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