Polymerization of 1,1,1-Trifluoroacetone with Aliphatic Secondary Amines. A Proton and Fluorine Magnetic Resonance Investigation

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The polymerization of 1,1,1-trifluoroacetone with aliphatic secondary amines is reported. The polymerization product is found to be a mixture of four diastereoisomers of the cyclic trimer, the structure of which has been determined using proton and fluorine magnetic resonance spectroscopy. The proportions of the isomers have been estimated to be 70:19:8:3 from the ^{19}F resonance spectrum. A comparative study of the reaction products of trifluoroacetone with metallic sodium and diethylamine is also discussed.

INTRODUCTION

1,1,1-Trifluoroacetone exhibits very interesting chemical behaviour due to the presence of the perfluoromethyl group. It is known to undergo autocondensation[1] in the presence of bases such as sodium ethoxide and sodamide giving the hydrate of 1,1,1,5,5,5-hexafluoro-2-hydroxy-2-methylpentan-4-one. Henne and Hinkamp[2] failed in their attempt to prepare trifluoromethylated butadienes from the reaction of 1,1,1-trifluoroacetone with sodium metal but instead isolated a cyclic trimer to which they assigned a substituted pyran structure. The same cyclic trimer was also isolated as a secondary product by Simmons and Wiley[3] when they reacted 1,1,1-trifluoroacetone with chlorohydrin in the presence of potassium carbonate. Trimerization of 1,1,1-trifluoroacetone has also been reported in the presence of fused[4] KOH and Mg-amalgam.[5] The trimer obtained from the Mg-amalgam polymerization was assigned a cyclohexane structure from its proton magnetic resonance spectrum.[5] The trimer obtained in most of these investigations, although claimed to have the same structure as reported by Henne and Hinkamp,[2] showed a different melting point and proton magnetic resonance spectrum. No useful information could be obtained from the ^{19}F magnetic resonance spectrum as it has been reported to be very complex.[3]

During our investigations of the solvent properties of 1,1,1-trifluoroacetone (TFA) in proton donor solvents,[6] a colourless crystalline solid was obtained with anhydrous diethylamine and dipropylamine. This product has been found to be a trimer of TFA. The structure of this trimer has been determined and substantiated by the proton and fluorine magnetic resonance spectra. The n.m.r. spectra of a number of its derivatives which help in making the assignments of n.m.r. lines are also reported. The isomerization of this trimer in the presence of various solvents such as acetone, ether, pyridine and diethylamine is also discussed. A re-investigation of the product obtained by the reaction of TFA with metallic sodium[2] is reported as well.

EXPERIMENTAL

1,1,1-Trifluoroacetone (TFA) was obtained from Aldrich Chemical Company, Inc. Diethylamine was distilled before use. The proton and fluorine magnetic resonance spectra were recorded on a Varian HR-n.m.r. spectrometer operating at 56.445 MHz. TMS was used as an internal reference for proton magnetic resonance (^{1}H n.m.r.) spectra while trifluoroacetic acid was used as an external reference for fluorine magnetic resonance (^{19}F n.m.r.) spectra. The infrared spectra were recorded on a Perkin-Elmer Model 21 spectrometer with a NaCl prism.

Reaction of TFA with diethylamine

A mixture of TFA and anhydrous diethylamine in molar ratios, cooled to 0 °C was allowed to stand overnight. The solid mass so obtained was recrystallized from chloroform solution m.p. 80 °C. The elemental analysis of this crystalline product and molecular weight determination corresponds to a molecular formula $(C_3H_3F_3O)_3(C_2H_5)_2NH$. The ^{19}F n.m.r. spectrum of this adduct in CD_3COCD_3 is a complicated pattern of 12 lines (Fig. 1). A close examination of the spectrum leads to the break up of the spectrum into four sets of three lines each. The intensities of the lines within the set are equal. The intensity ratios of the lines in the different sets are 70:19:8:3. The ^{1}H n.m.r. spectrum exhibits the usual quartet and triplet pattern for the methylene and methyl groups respectively of the diethylamine moeity, a sharp singlet at +6.4 ppm and two broadened lines in the methyl region.

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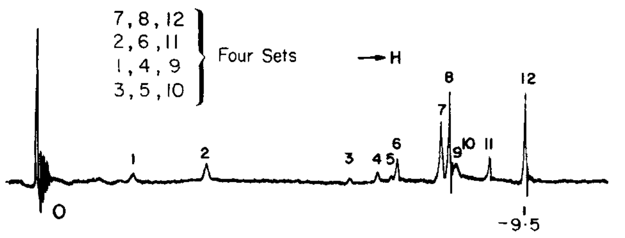


Figure 1. ^{19}F n.m.r. spectrum of the polymerization product of TFA with diethylamine in CD_3COCD_3.

Deamination of the adduct $(C_3H_3F_3O)_3(C_2H_5)_2NH$

Treatment of the adduct with 10% dilute HCl removed the amine moiety. The deaminated product was extracted with ether and was recrystallized from benzene–light petroleum. The elemental analysis and molecular weight determination (cryoscopic method) corresponds to a molecular formula for a trimer $(C_3H_3F_3O)_3$ m.p. in the range 98–100 °C. The ^{19}F n.m.r. spectrum is similar to that of the adduct but the ^{1}H n.m.r. spectrum shows the absence of the quartet, triplet and the singlet at +6.4 ppm, confirming the complete deamination of the trimer. The i.r. spectrum in CCl_4 shows C—F, C—H and C—OH bands but no C═O group.

Fractional crystallization of the trimer

The fractional crystallization of the trimer with benzene–light petroleum leads to the separation of the major component (70%) to the extent of 20% in the pure form (hereafter called the pure isomer) m.p. 117 °C. The chemical analysis and molecular weight determination (mol. wt = 338) correspond to a molecular formula for the trimer of TFA $[(C_3H_3F_3O)_3]$.

Dehydration of the pure isomer

The pure isomer was treated with concentrated H_2SO_4 and distilled. The product, a liquid, had a boiling point 58 °C. The chemical analysis corresponds to a molecular formula of $C_9H_5F_9O$ and absorbs two moles of bromine.

Preparation of the monoacetate from the pure isomer

The monoacetate of the pure isomer was prepared with acetic anhydride in the presence of pyridine. The white solid so obtained was recrystallized from acetone. The recrystallized material had m.p. 162 °C and the chemical analysis corresponds to one acetoxy group.

Preparation of the monomethoxy derivative of the pure isomer

The monomethoxy derivative was prepared with diazomethane in ether. The product so obtained was a yellow coloured liquid b.p. 140 °C. The chemical analysis corresponds to the presence of a single methoxy group.

Preparation of acetoxy–methoxy derivative of the pure isomer

The acetoxy–methoxy derivative was prepared from the monoacetate by treating with diazomethane in ether. The recrystallized sample had m.p. 71 °C.

The diacetoxy and dimethoxy derivatives could not be prepared.

Reaction of TFA with metallic sodium

Molecular sodium suspended in ether and TFA cooled to 0 °C were left overnight and the crude solid so obtained was treated with dilute HCl (20%) to remove the sodium. The white solid (Na-trimer) obtained by filtration was crystallized from benzene–light petroleum m.p. in the range 92–98 °C. The chemical analysis and molecular weight correspond to $(C_3H_3F_3O)_3$. Fractional crystallization of the Na-trimer lead to the separation of a major component to the extent of 20%, with a molecular formula corresponding to a trimer m.p. 117 °C.

The dehydration of the Na-trimer with concentrated H_2SO_4 gave a single product, a liquid, b.p. 58 °C. The methoxy derivative of the Na-trimer was also prepared by using diazomethane in ether.

Table 1. ^{1}H **n.m.r. and infrared data on the pure isomer and its derivatives**

Compound	^{19}F chemical shifts in ppm				^{1}H chemical shifts in ppm				Infrared absorption		Figure
									C═O	—OH	
Pure isomer	−7.7^{a}	−7.9	−9.7		+6.9	+6.2	+2.1	+1.8	No	Yes	2
Dehydrated isomer	−6.2	+2.9	+5.6			+6.0	+1.3		No	No	2
Monoacetoxy	−0.7	−7.8^{a}	−9.6		+7.4	+3.5	+2.1	+1.9	Yes	Yes	2
Monomethoxy	−2.2^{b}	−7.2^{a}	−7.5		+3.8	+3.6^{c}	+2.1	+1.8	No	Yes	2
Acetoxy–methoxy	−0.2	−2.4^{b}	−7.4^{a}		+3.5^{c}	+2.1	+1.7		Yes	No	2
Na-trimer	−7.6^{a}	−7.8	−9.9	70%	complex pattern				No	Yes	3
	−3.4	−6.8	−8.5	30%							
Major component of Na-trimer	−7.7^{a}	−7.9	−9.7		+6.9	+6.2	+2.1	+1.8	No	Yes	—
Dehydrated Na-trimer	−6.2	+2.9	+5.6			+6.0	+1.3		No	No	—
Monomethoxy	−1.9^{b}	−6.4	−6.4	70%	+3.5^{c}	+2.1	+1.5	+1.8	No	Yes	5
Derivative of Na-trimer	−2.0^{b}	−3.1	−5.2	30%							

^{a} Broad band. ^{b} Quartet. ^{c} Quartet.

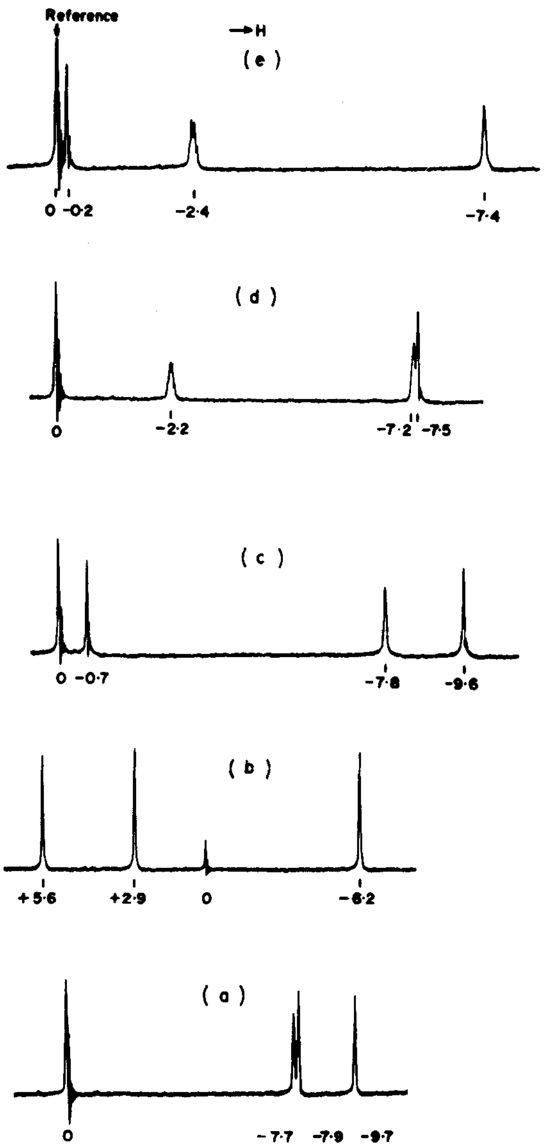


Figure 2. ^{19}F n.m.r. spectra of the pure isomer and its derivatives: (a) pure isomer; (b) dehydration product; (c) monoacetoxy; (d) monomethoxy; (e) acetoxy–methoxy.

The proton and fluorine chemical shifts and infrared data for the pure isomer, its derivatives and the sodium trimer are given in Table 1. Figures 2 and 3 show the ^{19}F n.m.r. spectra.

Solvent effect studies on the pure isomer and its monoacetate

The ^{19}F n.m.r. spectra of the pure isomer and its monoacetate in CD_3COCD_3 and ether change with time. In the pure isomer, in addition to the three bands at −7.7, −7.9, −9.7 ppm, three further bands of equal intensity appear at −6.1, −7.8 and −8.3 ppm (Fig. 4), which increase in intensity with time. This change is quite slow on the n.m.r. time scale and the equilibration time is about 80 h. The equilibrium concentrations of the two species are in the ratio 90:10. Similar ^{19}F n.m.r. spectra are observed for the pure isomer and its monoacetate in pyridine and diethylamine (Fig. 4), but the equilibrium is attained instantaneously. The ^{1}H n.m.r. spectra are quite complicated due to overlapping of the lines from both species and hence no information could be obtained. The solvent effect studies indicate that the rate of isomerization of the pure isomer and its monoacetate is slow in acetone and ether while it is very fast in pyridine and diethylamine. The infrared spectra of the pyridine and diethylamine solutions do not indicate absorption in the carbonyl region.

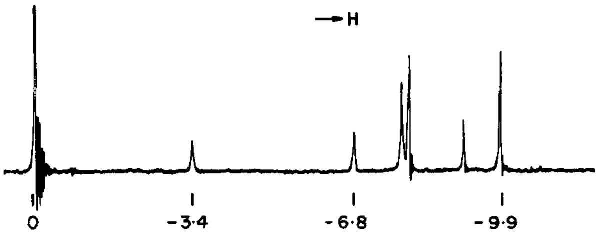


Figure 3. ^{19}F n.m.r. spectrum of the Na-trimer in CD_3COCD_3. Spectrum recorded immediately.

Solvent effect studies on methoxy, acetoxy–methoxy and dehydrated derivatives

The ^{19}F n.m.r. spectra are independent of solvent and time.

Solvent effect studies on the Na-trimer

The ^{19}F n.m.r spectra of the Na-trimer (70:30) in CD_3COCD_3 and ether initially exhibit six lines which in the course of time changes to a 12 line pattern. The equilibration time is about 120 h. Similar (12 line) ^{19}F

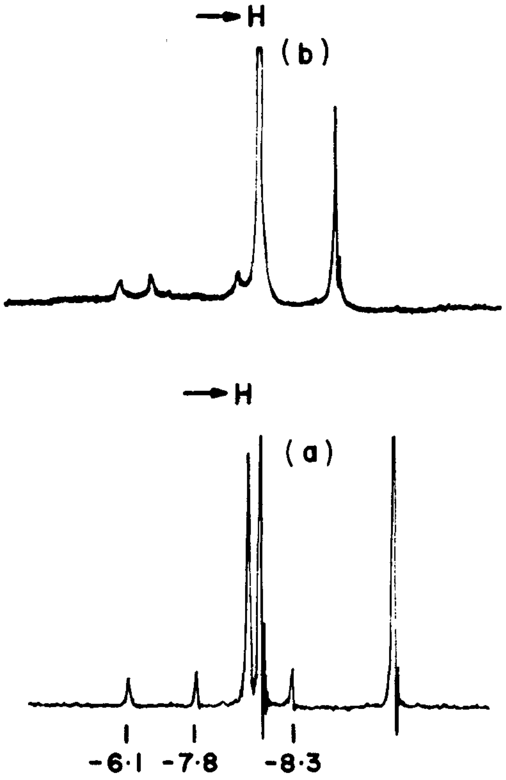


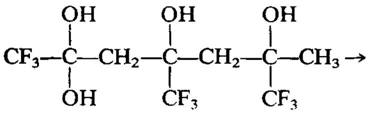
Figure 4. ^{19}F n.m.r. spectra of the pure isomer in (a) CD_3COCD_3 after 80 h; (b) diethylamine immediately.

n.m.r. spectra of the Na-trimer are obtained in pyridine and diethylamine but the equilibration is instantaneous. These spectra can be broken up into four sets of three lines each. The intensity ratio of the lines within the four sets is 70:19:8:3. The i.r. spectra of the equilibrated mixture in pyridine and diethylamine do not indicate absorption in the carbonyl region.

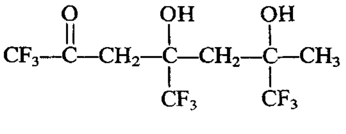
DISCUSSION

The pure isomer and the major component separated from the polymerization products of TFA with diethylamine and metallic sodium, respectively, have identical melting points and molecular weights, corresponding to a trimer of TFA, and give identical derivatives and ^{19}F n.m.r. ^{1}H n.m.r. and i.r. spectra. These results indicate the formation of the same major product. The ^{19}F n.m.r. spectrum of this major product suggests that there are three non-equivalent fluorine sites in the molecule, and that there are no magnetic nuclei in their vicinity since no coupling is observed. Considering these facts, as well as the information obtained from the i.r. spectra, the trimer could have any one of the following three structures.

1. Open chain structure

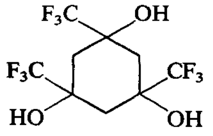


$CF_3-\underset{OH}{\overset{OH}{C}}-CH_2-\underset{CF_3}{\overset{OH}{C}}-CH_2-\underset{CF_3}{\overset{OH}{C}}-CH_3 \rightarrow$

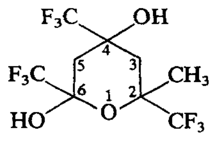


$CF_3-\overset{O}{\overset{\|}{C}}-CH_2-\underset{CF_3}{\overset{OH}{C}}-CH_2-\underset{CF_3}{\overset{OH}{C}}-CH_3$

2. Carbocyclic structure



3. Tetrahydropyran structure



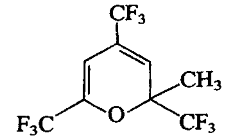
The carbocyclic structure is eliminated on the basis of dehydration studies with concentrated H_2SO_4 since it would have given rise to nonafluoromesitylene affording a single band in the ^{19}F n.m.r. and ^{1}H n.m.r. spectra.

The open chain structure is ruled out on the grounds that the major component, the pure isomer and its derivatives do not give an i.r. carbonyl absorption. Since the molecule has a large number of fluorine atoms it is quite likely that the open chain keto structure might exist as a hydrate,[7] but the absence of a C=O group in the i.r. spectrum of the dehydrated product rules out this possibility. All these facts lead to the trimer having a pyran structure.

Evidence for the tetrahydropyran structure

The pyran structure for the pure isomer is expected to give three bands in the ^{19}F n.m.r. spectrum. The CF_3 groups at the 2 and 6 positions are expected to have practically the same chemical shift, with one of the CF_3 groups relatively broadened due to coupling with the geminal CH_3 group. This is in agreement with the three bands of the experimental spectrum [Fig. 2(a)], where the absorption at −7.7 ppm is relatively broad.

The formation of the various derivatives and the OH i.r. absorption are also in conformity with the pyran structure. In the ^{19}F n.m.r. spectra of the dehydrated product [Fig. 2(b)], the downfield shift of two bands relative to trifluoroacetic acid suggests that two of the CF_3 groups are attached to double bonded carbon atoms.[8] This is also supported by the ^{1}H n.m.r. spectrum with a 2 proton ethylenic and a 3 proton methyl absorption at 6.0 ppm and 1.3 ppm, respectively. This is in conformity with the following structure of the dehydrated product.



The assignments of the three bands in the ^{19}F n.m.r. spectrum of the pure isomer is made from the analysis of the ^{19}F n.m.r. spectra of its various derivatives. The separation of the two closely placed bands (−7.7 and −7.9 ppm) in the ^{19}F n.m.r. spectrum of the pure isomer [Fig. 2(a)] on acetate formation [Fig. 2(c)] suggests that the acetyl group goes into the 6 position. On the other hand, the ^{19}F n.m.r. spectrum of the monomethoxy derivative suggests that the methoxy group is in the 4 position [Fig. 2(d)]. This 4-CF_3 group resonates at a lower field relative to the corresponding CF_3 group of the pure isomer and is a 1:3:3:1 quartet due to coupling with the geminal-OCH_3 group ($J = 2.0$ Hz). In the ^{19}F n.m.r. spectrum of the acetoxy–methoxy derivative [Fig. 2(e)], the band at −0.2 ppm is due to the CF_3 group on the carbon atom carrying the acetyl group and the band at - 2.2 ppm, a quartet, is due to the CF_3 group on the carbon atom carrying the methoxy group. Hence the broad band at −7.4 ppm is due to the CF_3 group on the carbon atom carrying the CH_3 group. Since the chemical shift of this band relative to trifluoroacetic acid remains practically constant, it is unambiguously assigned to the carbon atom which does not have an hydroxyl group as a substituent. Hence the three bands at −7.7, −7.9 and −9.7 ppm in the ^{19}F n.m.r. spectrum of the pure isomer are due to three non-equivalent CF_3 groups in positions 2, 6 and 4, respectively. Therefore, it is concluded that the trimer obtained in the polymerization of TFA with either diethylamine or sodium has the pyran structure 4,6-dihydroxy-2-methyl-2,4,6-trifluoromethyltetrahydropyran. The ^{1}H n.m.r. spectra of the pure isomer and its derivatives support this

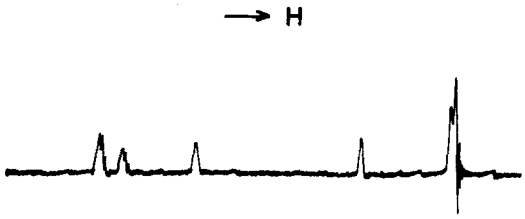
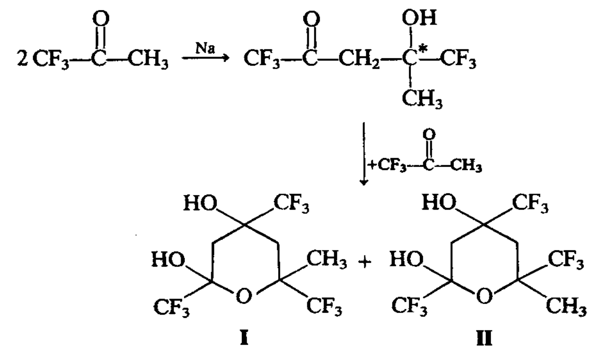


Figure 5. ^{19}F n.m.r. spectrum of the monomethoxy derivative of the Na-trimer.

structure and the bands at +1.8, +2.1 and +3.5 ppm can be assigned unambiguously to CH_3, CH_3–CO and CH_3O groups, respectively. The *gem* protons in the 3 and 5 positions exhibit AB type patterns which are difficult to assign, but the OH protons in some of the compounds can be recognized.

Second species in the Na-trimer

The ^{19}F n.m.r. spectrum of the Na-trimer indicates the presence of two species in the ratio of 70:30. Since the dehydration product of this mixture is a single product whose ^1H n.m.r. and ^{19}F n.m.r. spectra are similar to the dehydration product obtained from the pure isomer, it is possible that this trimer is a mixture of two isomers. The second isomer seems to have the same skeleton as the pure isomer because the ^{19}F n.m.r. spectrum corresponding to this species also shows three non-equivalent fluorine sites and also forms a methoxy derivative (Fig. 5). The pure isomer has three asymmetric carbon atoms and can in principle exist as 8 stereoisomers. However, in the reaction of TFA with metallic sodium, only two stereoisomers seem to have been formed (Fig. 3). These two isomers differ in the orientation of the CF_3 group on the C-2 and hence are a pair of enantiomers. This has been discerned from the observed shift of the broad band, which has been assigned to the CF_3 group on C-2, to lower field in the ^{19}F n.m.r. spectrum (Fig. 3) corresponding to 30% relative to the corresponding band in the major component (70%). The formation of these enantiomers can possibly be explained on the basis that during the trimerization of TFA with metallic sodium, the condensation of two molecules of TFA leads to the formation of hexafluorodiacetone alcohol which has one asymmetric carbon atom and hence can exist as a pair of enantiomers. The reaction of these enantiomers with one more molecule of TFA and cyclization can lead to two isomers having a different configuration on C-2. These two isomers are expected to give a single dehydration product and this is exactly what is observed. The large chemical shift difference observed for the CF_3 groups on C-2 in the two isomers is due to their spatial orientation being either axial or equatorial and hence supports the above argument for their being enantiomers. Such large chemical shift difference for axial and equatorial CF_3 groups have been observed in substituted cyclohexane derivatives. The configuration of the CF_3 groups on the remaining carbon atoms 2 and 4 could be either axial or equatorial, but they are more likely to be in the equatorial position because such a configuration is expected to be the most stable. It is not possible from n.m.r. data alone to say unequivocally that the major component (i.e. 70%) has all the CF_3 groups in the equatorial position. However, the configurational changes observed in different solvents for the major component and the Na-trimer (70:30 mixture) are discussed in the following section.



Comparison of Na-trimer and diethylamine-trimer

The solvent effect studies on the ^{19}F n.m.r. spectra of the pure isomer and the Na-trimer indicate some configurational changes. The ^{19}F n.m.r. spectrum of the Na-trimer in acetone, ether, diethylamine and pyridine exhibits a 12 line pattern (Fig. 6) which is very similar to the one obtained from the polymerization product of TFA with diethylamine. Since the 6 line ^{19}F n.m.r. spectrum of the Na-trimer changes to a 12 line pattern it is suggested that these solvents bring about a configurational change with different rates either on C-4 or C-6. If the configurational change had

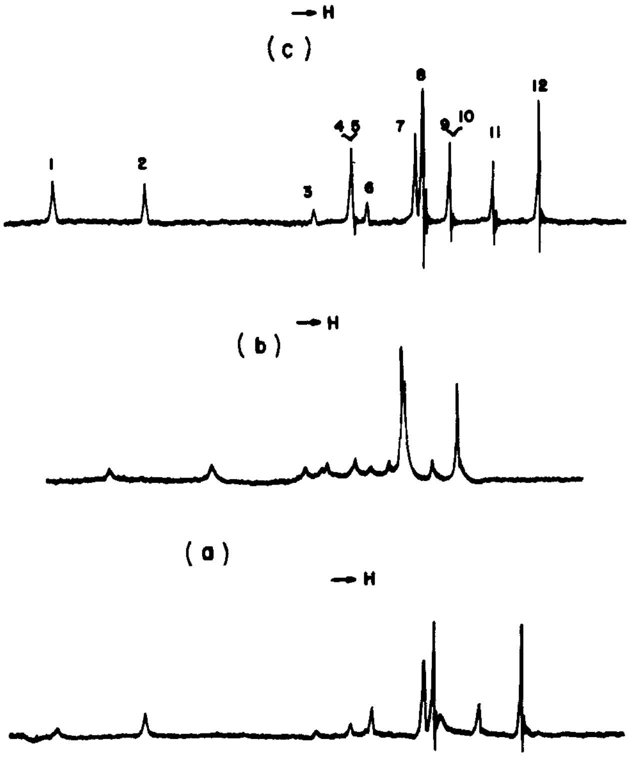
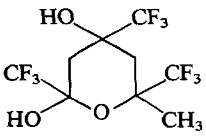


Figure 6. Comparison of ^{19}F n.m.r. spectra of Na-trimer and diethylamine-trimer: (a) diethylamine-trimer; (b) Na-trimer in diethylamine (immediately); (c) Na-trimer (50:50 in CD_3COCD_3 (after 20 days).

occurred on both carbon atoms, then the number of diastereomers would be more than actually observed. This configurational change, which is probably on C-6, is supported by the fact that the configurational change observed in the ^{19}F n.m.r. spectrum of the pure isomer leads to a species (10%) (Fig. 4) which is different from that observed as a second species in the ^{19}F n.m.r. spectrum of the Na-Trimer (30%). The structures of the species produced due to this configurational change are given below. The configurational change on C-4 seems to be precluded due to the formation of intramolecular hydrogen bonding between the ring oxygen and the hydroxyl group. This hydrogen bonding is possible only if the molecule exists in the boat conformation with the hydroxyl group in the axial position, and hence the CF_3 group would be in the equatorial position.



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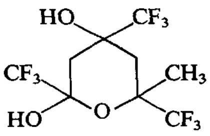

IV

Tetrahydropyran and its derivatives, by analogy with cyclohexane, can exist in chair or boat conformations.[10] The kinetic parameters of ring inversion of tetrahydropyran have been determined by the n.m.r. linewidth method.[11] The i.r. spectrum of the pure isomer has two bands corresponding to free (3500 cm^{-1}) and bonded (3340 cm^{-1}) hydroxyl groups. The relative intensities of these bands were independent of concentration which showed that the low frequency band is due to intramolecular hydrogen bonding. This could be between either the two hydroxyl groups or the -OH group in the 4 position and the ring oxygen leading to a boat conformation. The boat conformation has been reported to be stabilized by this type of hydrogen bonding.[12] It is rather difficult to say whether the pure isomer exists in the boat conformation or an equilibrium mixture of the chair and boat forms.

It is concluded that the polymerization products of TFA with diethylamine or dipropylamine and metallic sodium are identical and are a mixture of the diastereoisomers of the cyclic trimer. The proportions of the diastereoisomers are 70:30 and 70:19:8:3 in the sodium and diethylamine polymerizations, respectively.

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