Tetrahedron Vol. 47, No. 33, pp. 6725-6736, 1991
Printed in Great Britain

0040-4020/91 $3.00+.00
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Hexafluoroisopropanol as a Suitable Solvent for Rearrangements via Zwitterionic Intermediates

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(*Received in UK* 13 *May* 1991)

Key Words: Hexafluoroisopropanol; Zwitterionic intermediates; Solvent effects; Molecular mechanics.

Abstract. *Rearrangement of the tricarbonyl(cycloheptatriene)iron derivative* ***1*** *to* ***2*** *and* ***3*** *took place very readily in 1,1,1,3,3,3-hexafluoroisopropanol (HFIP) at room temperature. This finding is in striking contrast to the stability of* ***1*** *in MeOH under otherwise similar conditions. The isomerization processes which give rise to an equilibrium among* ***1****,* ***2*** *and* ***3*** *must involve zwitterionic intermediates of the type* ***4****, whose formation, consequently, is highly favored by HFIP. Heating* ***9*** *in HFIP brought about its rearrangement to* ***15****. We suggest that formation of the zwitterionic intermediate* ***12*** *triggers a rearrangement of the carbocyclic moiety which can take place as a result of the high polarity and low nucleophilicity of HFIP. The rearrangement* ***9*** *→* ***15*** *could not be achieved by using other polar solvents such as methanol or nitromethane. This observation once again demonstrates how suitable HFIP is as a medium for isomerizations* via *zwitterionic intermediates. The role of traces of free acid, present even in purified HFIP, is discussed.*

INTRODUCTION

Reactions (cycloadditions, cycloreversions, rearrangements etc.) *via* zwitterionic intermediates have been the subject of intense study over the last two decades in particular by Huisgen and coworkers.[1] The solvent of choice for these reactions are polar solvents such as acetonitrile. Alcohols (methanol, ethanol etc.) are very effective in promoting formation of zwitterions but, owing to their high nucleophilicity, they also often trap these intermediates.[1] Such a behavior, while making these solvents very useful for purpose of demonstrating the presence of a zwitterion along a reaction pathway, renders them quite useless if one wants to know the further fate of a dipolar intermediate. This drawback can be overcome by using highly ionizing[2] and highly dissociating[3] yet very little nucleophilic polyfluorinated alcohols.[2] In fact, the use of these solvents as ideal media for genuine S_N1 reactions largely free from nucleophilic solvent assistance is well established.[2] By contrast, the use of polyfluorinated alcohols as solvents for reactions involving zwitterionic intermediates is not a common practice. Here we report on examples which demonstrate how these solvents can promote massive acceleration in formation of zwitterionic intermediates with interesting mechanistic and synthetic results.

RESULTS AND DISCUSSION

In the context of our investigation on the mechanism of the reaction of 1,3-dipoles, in particular nitrile oxides, with 8-azaheptafulvenes and tricarbonyl(8-azaheptafulvene)iron derivatives[4] we needed to know what compounds could actually convert into each other via zwitterionic intermediates of the type **4** (Scheme 1). Compound **1**, prepared by cycloaddition of mesitonitrile oxide with tricarbonyl(8-azaheptafulvene)iron, was used as a precursor of **4a**. When **1** was dissolved in commercial 1,1,1,3,3,3-hexafluoro-2-propanol (HFIP) at room temperature (21°C) a very fast (< 3 minutes) reaction took place with formation of a mixture of **1**, **2** and **3** (9:71:20). The same equilibrium mixture was obtained starting from **2** and **3**. These reactions were very clean and compounds **1**, **2** and **3** could be isolated in almost quantitative yields by Silicagel column chromatography. Then we repeated isomerization of **1** under the same conditions but with HFIP carefully purified by distillation from calcium hydride.[5] Equilibration was not so fast as in commercial HFIP and it was complete after 15 minutes. Addition of 2% Et_3N to purified HFIP resulted in a markedly slower isomerization of **1** (as well as of **2** and **3**); it took ≥ 6 h (at 21°C) to reach the equilibrium however with the same ratio of **1**, **2** and **3** as in commercial HFIP.

The very fast reaction in the commercial solvent is certainly the result of acid catalysis by free acid (hydrofluoric acid) whose presence is clearly disclosed even by litmus paper. Somewhat surprising is the fact that this catalysis seems to be at work even after purification of HFIP with calcium hydride. Anyway, the results of the reaction in the presence of triethylamine clearly demonstrate that there is an intrinsic ability of HFIP to promote isomerization of **1**, **2** and **3** which can be traced back to its "polarity". Hydrogen bonding by HFIP certainly plays a major role in promoting the heterolysis of the C-O bond of **1** and in stabilizing the anionic moiety of **4**. As a matter of fact, hydrogen bonding effects are likely to be the underlying reason of the excellent ionizing and dissociating power of polyfluorinated alcohols.[2,3,6]

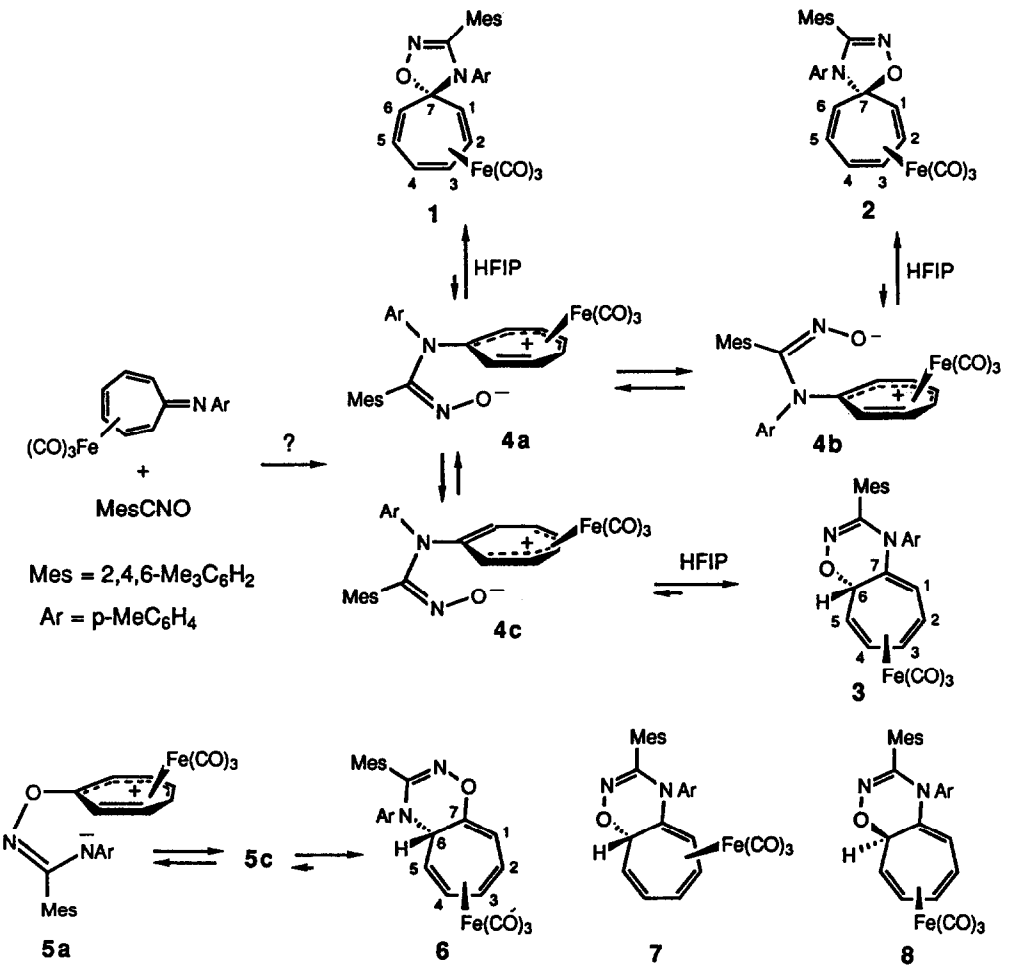
HFIP is a relatively "acidic" solvent (pK_A = 9.31).[3] However the behavior observed by us cannot directly be correlated with its acidity. Acetic acid, which is much more acidic (pK_A = 4.75)[7] than HFIP, displays a much lower ability than HFIP+Et_3N to promote isomerization of **1** (more than 24 h to reach the equilibrium).

Compound **1** did not appreciably convert into **2** and **3** when kept in dichloromethane, acetonitrile and methanol at 21°C for a month or at 60°C for 20 h. In methanol at 60°C longer reaction times (96 h) led to the appearance of small amounts of **2** (< 10%) whereas **3** could hardly be detected in this reaction mixture. In nitromethane a ≈50% conversion of **1** into **2** was reached after 1 month at 21°C or 20 h at 60° but in both reactions compound **3** was present only in very small amounts.[8] When anhydrous hydrochloric acid was bubbled through a solution of **1** in nitromethane isomerization **1** → **2** took place at once.

Even among common fluorinated solvents the behavior of HFIP is unique. Thus, only trace amounts of **3** could be detected when **1** was kept in CF_3CH_2OH (+2% Et_3N) (pK_A = 12.31 for trifluoroethanol)[3] at room temperature for five days. In commercial trifluoroethanol (once again owing to the presence of free acid) isomerization took place very readily to afford a slightly different equilibrium mixture (**1**:**2**:**3** = 11:73:16).

To conclude this part our results demonstrate that HFIP must be the solvent of choice if one wants to get a clean equilibrium **1** ⇄ **2** ⇄ **3** in a short time and, in particular, if one wants to prepare compound **3** in substantial amounts starting from **1** and **2**.

A single crystal X-ray analysis established beyond all doubt the structure of compound **1**, in particular the presence of a (diene)tricarbonyliron moiety with the tricarbonyliron group *anti* to the oxygen atom of the oxadiazoline ring (Figure 1). A (diene)tricarbonyliron moiety is present in all of the three compounds **1-3**. In fact, their NMR spectra (see Table 1) display the characteristic high field resonances of the terminal hydrogen and carbon atoms of such a system.[9] The ^1H and ^{13}C NMR spectra of compounds **1** and **2** are very similar clearly showing that also compound **2** must have a spiro structure, namely the *syn* one. The higher stability of **2** than **1** at the equilibrium is the result of lower steric congestion in the former with respect to the latter. ^1H and ^{13}C NMR data support the condensed structure **3**. The doublet at δ 5.02 (J = 4.2 Hz) can be assigned to H-6. The related carbon atom consistently gives rise to a doublet at δ 78.9. This latter observation allowed



SCHEME 1

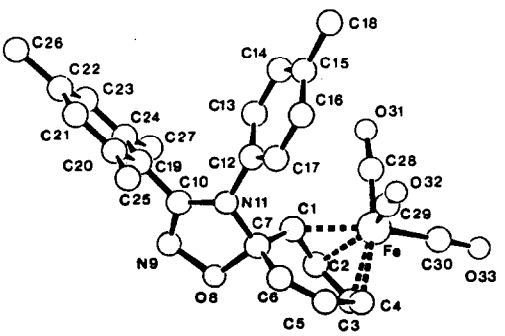


FIGURE 1. A perspective view of **1** showing the numbering scheme used in Tables 2-4.

Table 1. ^1H and ^{13}C NMR Data of Compounds **1-3** ($CDCl_3$).

	H-1	H-2	H-3	H-4	H-5	H-6
1	3.42 ddd	5.76 ddd	5.80 ddd	2.91 ddd	6.12 dd	5.53 ddd
2	3.20 ddd	5.27 ddd	5.40 ddd	2.72 dddd	6.11 dd	5.45 ddd
3	4.49 d	2.76 ddd	5.65 ddd	5.75 ddd	3.14 ddd	5.02 d

	$J_{1,2}$	$J_{2,3}$	$J_{3,4}$	$J_{4,5}$	$J_{5,6}$	$J_{1,6}$	$J_{4,6}$	$J_{1,3}$
1	8.0	4.7	7.5	8.0	10.8	2.5	0.8	1.5
2	7.8	4.7	7.5	8.3	10.8	2.5	0.8	1.4
3	8.4	7.5	4.7	7.5	4.2	-	-	-

	C-1	C-2	C-3	C-4	C-5	C-6	C-7
1	63.7 d	97.3 d	85.8 d	52.9 d	135.2 d	124.5 d	100.1 s
2	60.2 d	93.7 d	85.8 d	51.0 d	134.1 d	124.1 d	100.3 s
3	105.7 d	52.4 d	89.9 d	94.2 d	53.3 d	78.9 d	135.5 s

[a] ^1H NMR spectra were analyzed as first order spectra. Coupling relationships were established by systematic decoupling experiments. In the case of compounds **2** the reported J values were evaluated from the spectrum in C_6D_6 [δ 2.22 (ddd, H-4), 3.62 (ddd, H-1), 4.89 (ddd, H-3), 5.13 (ddd, H-2), 5.60 (ddd, H-6), 5.73 (dd, H-5).]. $J_{2,4} = 1.40$ in both **1** and **2**. $J_{2,4} = J_{3,5} = 1.3$ Hz in **3**.

[b] The signals of C-1, C-4, C-5 and C-6 of **1** and **2** as well as those of C-1 and C-6 of **3** were assigned on the basis of selective decoupling experiments. Assignment of C-7 in compound **3** is tentative owing to the presence of other five singlets in the range of 134-139 ppm. Also the choice between C-2 and C-3 of **1** and **2** as well as that between C-3, C-4 and C-2, C-5 of **3** is tentative. Carbon atoms of the carbonyl groups give rise to a broad singlet at δ 208 ppm.

us to confidently rule out a condensed structure of the type **6** in which the carbon atom at position 6 should resonate at ≤ 55 ppm. The vinyl proton (δ 4.49, J = 8.4 Hz) as well as the carbon atom (δ 105.7) at position 1 are shifted to high fields by the electron donating effect of the amino group at position 7. Finally, the observation that these two protons, H-1 and H-6, are coupled to the two high field terminal protons of the (diene)tricarbonyliron moiety (to H-2 and H-5, respectively) definitely establishes the connectivity of the groups in the cycloheptatriene moiety and rules out alternative structures such as **7**. Spectroscopic data have not allowed us to choose between *anti* **3** and *syn* **8** structures for this condensed derivative. Structure **3** is proposed as the more reasonable as it is less crowded than **8**. Moreover, when **3** is dissolved in HFIP/Et_3N at 21°C TLC analysis showed that there is a faster formation of *anti* **1** than *syn* **2**.

The proposed mechanism of interconversion of **1**, **2** and **3** is depicted in Scheme 1. Starting from **1** there is a fast and reversible formation of **4a** in which both charges are highly stabilized by conjugation. The two charged moieties are located in almost perpendicular planes with charges held in close proximity to each other in order to make the electrostatic work necessary to separate them as low as possible.[10] Moreover, it is well known that monosubstituted tropylium-$Fe(CO)_3^+$ species consist of rapidly interconverting structures which are known to be an iron-bound pentadienyl unit and a free double bond.[9] In the case of **4** formation of **3** provides evidence of the presence of the zwitterion **4c** in equilibrium with **4a**. Rotation around carbon-nitrogen bond in **4a** leads to formation of the *syn* zwitterion **4b** which collapses to **2**. Other details of the mechanism could be defined (see Experimental), in particular

i) formation of **2** from **1** is kinetically at least as fast as formation of **3**; ii) when **4a** is formed from **4b** in HFIP it prefers to collapse to **1** than to isomerize to **4c** and close to **3**.

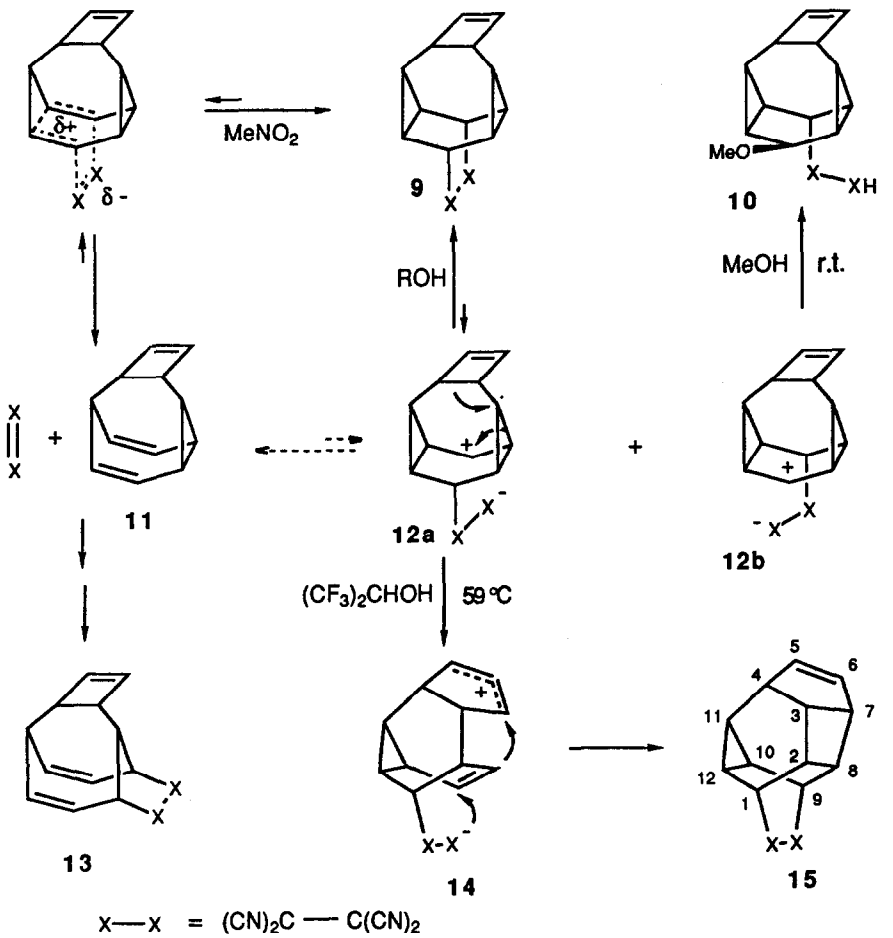
It should be stressed that we cannot definitely exclude the possibility that conversion of **1** and **2** into each other might involve carbon-nitrogen bond cleavage to form a zwitterion of the type **5** notwithstanding a

worse charge stabilization than in **4**. This mechanism can sound reasonable in the case of **2** if one assumes that cleavage of a bond *anti* to a $Fe(CO)_3$ group is favored over a *syn* one. However, we feel that zwitterion **5a** should collapse at least in part to **6** *via* **5c**. The absence of **6** in the isomerization reaction of **2** militates against formation of **5a**.

A similar problem to that discussed above, i.e. the behavior of the zwitterionic intermediate **12**, was of major concern to us during the study of the cycloaddition of TCNE to **11** (Scheme 2). We have already reported that **9** reacts slowly in methanol at r.t. to give **10**, i.e. the adduct of methanol to **12b**.[11] Upon heating in nitromethane (at 90°C) adduct **9** undergoes a retro-homo-Diels-Alder reaction with formation of **11** and TCNE which then gives rise to **13** via a two step $[(\pi 2+\sigma 2+\pi 2)+\pi 2)$cycloaddition.[11] Is a zwitterion of the type **12** an intermediate in the formation of **11** from **9**? To answer this question we decided to generate **12** in the non-nucleophilic HFIP. Heating compound **9** in purified HFIP (at 59° for 51 h) produced a new compound,i.e. **15** (65%),along with small amounts (≈ 4%)of **13**. Neither the reaction outcome nor the reaction time necessary to reach 100% conversion did change by using commercial HFIP. Disappointingly, in this reaction the presence of Et_3N brought about formation of tarry products. Actually, in HFIP + 2% Et_3N compound **9** disappeared without forming any characterizable reaction product.

The only relevant peaks present in the mass spectrum of **15** [m/z: 284 ($M^{+\cdot}$, 25%), 156 ($C_{12}H_{12}^{+\cdot}$, 28%), 155 ($C_{12}H_{11}^{+}$, 37%), 128 ($TCNE^{+\cdot}$, 23%), 91 ($C_7H_7^{+}$, 100%] are consistent with an electron impact induced homo-Diels-Alder cycloreversion with formation of a TCNE radical cation. This finding, while testifying that the $C(CN)_2$-$C(CN)_2$ moiety has survived unchanged during the isomerization, also suggests that a system formally derived from the cycloaddition of TCNE to a homodiene moiety is still present in **15**. Particularly informative is the ^1H NMR (500 MHz) spectrum of **15**: δ ($CDCl_3$) 1.42 (m, H-10, $J_{10,11} = J_{10,12}$ = 8.1 Hz, and $J_{9,10}$ = 4.8 Hz), 1.60 (dddd, H-12, $J_{1,12}$ = 4.4 Hz, $J_{2,12}$ = 1.6 Hz, and $J_{11,12}$ = 8.1 Hz), 1.82 (ddd, H-11, $J_{4,11}$ = 5.0 Hz), 2.71 (dd, H-8, $J_{2,8} \cong J_{7,8} \cong$ 8.0 Hz), 2.75 (m, H-3), 2.95 (m, H-2, $J_{1,2}$ = 5.6 Hz and $J_{2,3} \cong$ 8.0 Hz), 3.06 (dd, H-1), 3.20 (, H-9, $J_{8,9}$ = 1.6 Hz), 3.30 (ddd, H-4, $J_{3,4}$ = 8.8 Hz and $J_{4,5}$ = 2.5 Hz), 3.35 (ddd, H-7, $J_{6,7}$ = 3.3 Hz and $J_{3,7}$ = 8.0 Hz), 5.80 (dd, H-6, $J_{5,6}$ = 5.6 Hz) and 6.38 (dd, H-5). Systematic decoupling experiments as well as a 2D-COSY spectrum, allowed us to assign all signals to individual protons and to determine all relevant coupling relationships between them. Starting from the substituted cyclopropane moiety (whose presence is clearly disclosed by the three high field signals due to protons all coupled to each other) we could fully reconstruct the structure of **15**. Thus, one of the cyclopropyl proton (H-11) exhibits a vicinal coupling to an allylic proton (H-4) thus assuring the presence of the C-4, C-11 bond. Moreover, H-4 is located on a cyclopentene ring as demonstrated by the characteristic value of the coupling constant between the two olefinic protons (5.6 Hz to be compared to 5.1 Hz in cyclopentene) and by the fact that the two allylic protons (H-4 and H-7) are strongly coupled to the same aliphatic proton (H-3). The presence of the cyclobutane ring can be safely inferred from the fact that H-3 and H-7 are strongly coupled to two protons, H-2 and H-8 respectively, which in turn are vicinal coupled to each other. Assemblement of the remaining two CH groups and of the $C(CN)_2$-$C(CN)_2$ moiety leads finally to **15** which satisfactorily accounts for all of the ^1H NMR data reported above but one. In fact, at first sight, $J_{8,9}$ = 1.6 Hz may look too low for two protons located at vicinal positions and which appear to bear a similar geometric relationship to that between H-2 and H-1 ($J_{1,2}$ = 5.6 Hz). To reconcile this apparent inconsistency we performed molecular mechanics calculations on the proposed structure **15** using the MM2 (85) program.[12] In the optimized geometry (Figure 2) the dihedral angle between H-8 and H-9 was found larger (67°) than that between H-1 and H-2 (47°) and calculation of the coupling constants through the Altona equation[13] gave $J_{8,9}$ = 1.8 Hz and $J_{1,2}$ = 4.9 Hz in close agreement with the experimental values.[14]

A reasonable explanation for formation of **15** starts from **12** which evidently does not significantly decompose to **11** and TCNE. This finding supports our previous proposal of a concerted mechanism for the cycloreversion of **9** to **11** and TCNE in nitromethane.[11] The low nucleophilicity of HFIP assures long enough survival of the cationic center in **12** to allow its rearrangement to **14** which then ring closes to **15**. Rearrangement to **14** takes place only in **12a** in which cleavage of the cyclopropyl ring can be rearside assisted by the contemporary enlargement of the cyclobutane ring. While in MeOH only **12b** was trapped by



SCHEME 2

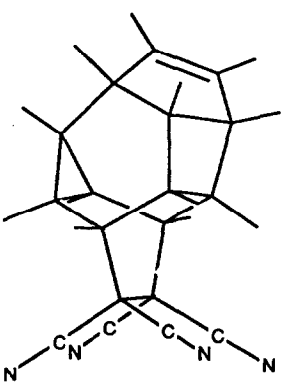


FIGURE 2. Optimized MM2 geometry of **15**.

MeOH, in HFIP only **12a** easily enters a rearrangement process.[15]

The mechanism reported in Scheme 2 is for an uncatalyzed reaction but it is quite clear that we cannot definitely rule out an acidic catalysis. However, the fact that passing from commercial HFIP to purified HFIP there was not any apparent relevant change in the reaction rate is not consistent with the latter hypothesis.

Moreover, a reaction carried out in nitromethane in the presence of HCl at ≈58° for 40 h led to a recovery of 70% of unaltered **9**. This latter finding and the whole of our observations make it evident that the polarity of HFIP plays a relevant role in opening the way to easy formation of products not obtainable in other solvents.

Conclusion

1,1,1,3,3,3-Hexafluoro-2-propanol lends itself as an interesting solvent for reactions with zwitterionic intermediates from both a mechanistic and synthetic standpoint. The presence (even in purified samples) of small amounts of free acid while compounding mechanistic studies may well make this solvent even more suitable as a medium for synthetic works. The particular and sometimes surprising behavior of "flustrates"[16] does hold even when they act as solvents.

EXPERIMENTAL

Melting points are uncorrected. Elemental analyses were made on a Carlo Erba CHN analyzer mod. 1106. IR spectra were measured as Nujol suspensions on a Perkin Elmer 157 spectrophotometer. ^1H and ^{13}C NMR Spectra were recorded as $CDCl_3$ solutions on a Bruker ACE spectrometer (operating at 300.3 and 75.5 MHz, respectively) with TMS as internal standard. The 2D-COSY experiment was performed on a Varian XL200 (at 200 MHz) and a spectrum of compound **15** was also recorded at 500 MHz (Bruker AM).Mass spectra were measured on a Finnigan MATT 8222 using the electron impact mode (75 eV). Thin layer chromatography was carried out on plates precoated with Silicagel 60 GF_{254} Merck. Spots were revealed either by spraying with 3% chromium (VI) oxide in sulfuric acid (50%) followed by heating at 120°C or under UV light (254 nm). Column chromatography was performed with Silicagel 60 (70-230 mesh) Merck eluting with cyclohexane-ethyl acetate mixtures. GC analyses were carried out with a Dani 6500, PTV injector, CP-Sil-19 CB (25 m) capillary column and carrier H_2.

Compound **1** was prepared by reaction of excess mesitonitrile oxide with tricarbonyl-(8-azaheptafulvene)iron in methanol. It was separated from other adducts by column chromatography (eluant, cyclohexane/AcOEt, 9:1). Experimental details for this reaction will be reported elsewhere. Methanol, methylene chloride, acetonitrile, triethylamine and nitromethane were purified and dried by standard methods. Hexafluoroisopropanol was distilled from calcium hydride, kept for 24 h over molecular sieves 3Å and redistilled from calcium hydride. A similar purification procedure was used for trifluoroethanol.

*Isomerization of **1**, **2** and **3**, respectively, in HFIP and TFE.*

Compound **1** (285 mg) was dissolved in commercial HFIP (5 mL) at room temperature (21-22°C) and after 3 minutes rapidly evaporated under reduced pressure. The oily yellow residue was column chromatographed (cyclohexane/AcOEt, 9:1, as eluant) to give in order of elution compound **2** (198 mg), **3** (56 mg) and **1** (24 mg) (Total yield: 97%). Compound **1**: orange prisms from methanol, m.p. 153-154°C dec.; ν_{max} 1970 and 2052 (s, CO) cm^{-1}. Found: C, 65.5; H, 4.9; N, 5.6. Calc. for $C_{29}H_{24}N_2O_4$ Fe: C, 65.3; H, 4.8; N, 5.6). Compound **2**: yellow needles from methanol, m.p. 155°C dec.; ν_{max} 1975 and 2044 (s, CO) cm^{-1}. (Found: C, 65.1; H, 5.0; N, 5.6). Compound **3**: orange-yellow prisms from petrol ether, m.p. 140°C dec.; ν_{max} 1970 and 2040 (s, CO) cm^{-1}. (Found: C, 65.6; H, 5.0; N, 5.4.) Longer reaction times (5, 10 and 15 minutes) did not appreciably change the reaction outcome and TLC analysis after 1 minute revealed that the ratio of **1**, **2** and **3** is already similar to the equilibrium ratio.

Under the same conditions compounds **2** and **3** led to very similar mixtures (i.e. **1**:**2**:**3** = 10:70:20 from **2** in 96% yield and 10:68:22 from **3** in 94% yield).

The reaction of **1** was then carried out in purified HFIP. A solution of **1** (200 mg) in purified HFIP (3 mL) was kept at 21 ± 0.5 °C for 30 minutes. Usual workup afforded a mixture of **1**, **2** and **3** in the ratio 10:69:21 (97% recovery). TLC analysis showed that the equilibrium was reached after ≥ 15 minutes. In a further experiment (at 21°C) isomerization of **1** was interrupted after 2 minutes by diluting the reaction mixture with a large amount of ethyl acetate. The solvent was removed rapidly under reduced pressure to give a mixture of **1**, **2** and **3** in the ratio 28:39:33 (column chromatography, 98% recovery). Under the very same conditions of this latter reaction compound **3** led to a mixture of **1**, **2** and **3** in the ratio 10:6:84 (97%). The results of these two latter reactions as well as those of the isomerization of **1** in HFIP/Et_3N (see below) clearly reveal that kinetic formation of **2** from **1** is at least as fast as that of **3**. We observed that the reaction in purified HFIP kept over molecular sieves and used without prior distillation was slower than that in purified distilled HFIP. Consequently, we decided to carry out reactions in the presence of a base to eliminate beyond all doubt adventitious acid catalysis. Solutions of **1**, **2** and **3**, respectively, in HFIP/Et_3N (98/2) were kept at 21°C and reactions monitored by TLC and ^1H NMR techniques. TLC analysis of the reaction of **1** (200 mg in 3 mL of solvent) showed that both **2** and **3** were already present in the reaction mixture after 2 minutes and that the intensity of the spot corresponding to **2** was slightly higher than that of **3**. After 1 h evaporation of the solvent and ^1H NMR analysis allowed us to quantitatively evaluate the product ratio: **1**:**2**:**3** ≈ 17.5:44.5:38. After ≈ 6 h it was difficult to appreciate changes in the product ratio of this reaction. After 24 h column chromatography led to isolation of **1**, **2** and **3** (16 mg, 133 mg and 40 mg, respectively, i.e. 8.5:70.5:21 in 95% total yield).

In the isomerization of **2** and **3** compound **1** could already be detected after two minutes whereas compound **2** in the reaction of **3** and compound **3** in the reaction of **2** were detected only after ≈ 10-15 minutes by TLC analysis. ^1H NMR analysis after 1 h (**1**:**2**:**3** ≈ 12:8:80 from **3** and **1**:**2**:**3** ≈ 5:92:3 from **2**) confirmed the TLC data. In particular they indicate that ring closure of **4a** to **1** is faster than isomerization to **4c** followed by ring closure to **3**. Column chromatography after 48 h led to recovery of 15 mg (15 mg) of **1**, 133 mg (130) of **2** and 39 mg (41 mg) of **3** from 200 mg of **2** (**3**).

Finally 200 mg of **1** were dissolved in commercial trifluoroethanol. Equilibration was fast (< 30 minutes) to give the equilibrium mixture (**1**:**2**:**3** = 11:73:16) in 98% yield. However, only trace amounts of **3** were present in a solution of **1** in TFE/Et_3N (98/2) after five days at room temperature (≈ 22°C).

*Isomerization of **1** in methanol, dichloromethane, acetonitrile, nitromethane and acetic acid.*

A solution of **1** (200 mg) in methanol, acetonitrile, nitromethane and dichloromethane (5-10 mL), respectively, was kept either at 21 ± 1 °C for a month or at 60° ± 1 °C (in sealed ampoules) for 20 h. In the reactions in MeOH, acetonitrile and dichloromethane, respectively, conversion of **1** into **2** and **3** was still at the very beginning whereas in the reaction in nitromethane ≈ 50% of **1** had already been converted into **2** and **3** but recovery yields (73-76%) are not as high as in the reactions reported above [at 21°C (60°C) 68 mg (74 mg) of **2**, 73 mg (76 mg) of **1** and 5 mg (4 mg) of **3**]. A solution of **1** (200 mg) in methanol was heated at 60°C for 96 h to give 156 mg of **1** and 14 mg of **2**. Into a solution of **1** in nitromethane gaseous hydrochloric acid was bubbled. Evaporation of the solvent and crystallization from methanol allowed us to isolate **2** in 70% yield.

Finally, a solution of **1** (100 mg) in glacial acetic acid (3 mL) was left at 21°C for 1 h. Then the reaction mixture was diluted with ethyl acetate and washed with a solution of sodium bicarbonate. ^1H NMR analysis of the crude product (99 mg) showed that conversion of **1** into **2** and **3** is much lower (**1**:**2**:**3** ≈ 80:12:8) than that in HFIP/Et_3N after the same time. It took more than 24 h to reach the equilibrium (ratio: **2** >> **3** ≈ **1** in acetic acid as judged from TLC analysis. Equilibration **1** ⇄ **2** ⇄ **3** in this solvent is also accompanied by formation of minor amounts of other products (not characterized) and by decomposition reactions.

Rearrangement of 9 to 15 in HFIP and nitromethane.

A solution of **9** (340 mg) in HFIP (either commercial or purified by distillation from calcium hydride, 7 mL) was heated under reflux for 51 h. After that time compound **9** had been totally consumed as judged by TLC and ^{1}H NMR analysis. The solvent was removed under reduced pressure and the red black residue column chromatographed (cyclohexane: AcOEt = 7:3 as eluant) to give, in order of elution compound **13** (12 mg, 3.5 %), compound **15** (221 mg, 65%) and a compound (≈ 15 mg) which we do not manage to characterize. These data are the average of several reactions in both purified and commercial HFIP. The only relevant difference observed between the reactions in the two media was that in commercial HFIP the red black color developed more rapidly than in purified HFIP. A GC analysis of the crude reaction mixture confirmed the product ratio reported above and disclosed the presence of small amounts of **11**. Compound **15** was purified as colorless prisms from ethyl acetate, m.p. 217-218°C. ν_{max} (Nujol) 2240 (w, C ≡ N), 743(s), 738(s) and 723(s) cm^{-1}. Compound **15** showed end absorption only in the UV spectrum. ^{13}C NMR ($CDCl_3$) δ 10.5(d), 13.6(d), 24.8(d), 25.4(d), 34.4(d), 35.7(d), 37.1(d), 37.9(d), 39.2(d), 41.0(s), 43.2(s), 45.8(d), 111.0(s), 111.6(s), 111.7(s), 111.8(s), 129.7(d), 144.3(d). (Found: C, 75.6; H, 4.5; N, 19.8. Calc. for $C_{18}N_{12}N_4$: C, 76.0; H, 4.3; N, 19.7). Compounds **13** and **15** heated in refluxing HFIP for 51 h were recovered unchanged (≥ 95%).

We also reinvestigated the reaction of **9** in nitromethane [60 mg of **9** in 3 mL of nitromethane heated in a sealed ampoule at 90°C for 39 h] in order to find out whether compound **13** is accompanied by **15** or not. GC analysis of the crude reaction mixture fully confirmed our previous results as far as formation of compound **13** as the only important reaction product is concerned. Compound **13** was isolated in 38% yield (23 mg). Moreover a peak, whose retention time corresponds to that of **15**, is present in the gas chromatogram but its intensity is ≈5% of that of **13** and we did not manage to isolate it.

In a solution of **9** in nitromethane anhydrous gaseous hydrochloric acid was bubbled and the resulting mixture heated in a sealed ampoule at 58 ± 1 °C for 40 h. The solution became slightly yellow. Evaporation of the solvent, column chromatography and crystallization from benzene led to recovery of **9** in 70% yield. GC showed the presence in the reaction mixture of minor amounts of **13** and **15**. Finally a solution of **9** in HFIP/Et_3N (98/2) was heated at ≈58°C in a sealed ampoule for 39 h. The reaction mixture became progressively brown black and no characterizable products could be isolated from it.

Crystal data and X-ray single crystal structure refinement of compound 1.

$C_{27}N_2O_4H_{24}Fe$, orange crystals from methanol, triclinic, space group Pl; a = 10.659 (1), b = 14.913 (2), c = 8.440 Å; α = 82.13 (1), β = 69.06 (1), γ = 74.44 (1) °; V = 1205.8 A^3, Z = 2; D_c = 1.337 g/cm^3; F(000) = 516; μ = 53.1 cm^{-1}. X-ray single crystal analysis and data collection performed on a Philips PW1100 four-circle diffractometer (monochromatic CuKα radiation, λ = 1.5418 Å). Unit-cell dimensions calculated by least-squares refinement of 25 rows in the ϑ range 2-40°; 2478 independent reflections (-9<h<9; -14<k<14; 0<l<8) measured in the ϑ range 2-50°, corrected for absorption[17] (max. = 1.51). Correction for intensity variation applied (max. = 3.0%). Structure solved by direct methods (MULTAN80);[18] full-matrix least-squares refinement on F performed with a locally rewritten version of the program ORFLS[19] on the 1847 reflections with I≥5σ(I). Scattering factors for neutral atoms from International Tables for X-ray Crystallography.[20] Refinement of the anisotropic atomic displacement parameters only for non-H atoms; the positions of the H atoms were calculated at convergence with program PARST,[21] inserted with an overall isotropic atomic displacement parameter = 5 Å^2 but not refined. At convergence, R_{all} = 6.9%, R_{obs} = 5.1%, S = 0.996; secondary extinction = 1.27 x 10^3; scale factor = 7.029; the final difference Fourier map did not show peaks higher than 0.4 el. A^{-3}. Atomic coordinates and equivalent isotropic atomic displacement parameters for non-H atoms in Table 2; bond distances in Table 3; bond angles in Table 4; Figure 1, drawn with program SCHAKAL,[22] illustrates the molecular structure and the atomic numbering. Lists of observed and calculated structure factors, anisotropic atomic displacement parameters for non-H atoms, fractional coordinates for H atoms and torsion angles have been deposited within the Cambridge Crystallographic Data Center.

Table 2. Atomic Fractional Coordinates (x 10^4) and Equivalent Isotropic Atomic Displacement Factors ($Å^2$) for non-Hydrogen Atoms.

	X/a	*Y/b*	*Z/c*	B_{eq}
C1	.0708 (5)	.1400 (3)	.5649 (6)	3.6 (2)
C2	.1063 (5)	.0789 (4)	.4315 (7)	4.3 (2)
C3	.2325 (5)	.0129 (4)	.3901 (7)	4.5 (2)
C4	.3213 (5)	.0078 (4)	.4858 (8)	4.8 (2)
C5	.2867 (5)	.0050 (3)	.6693 (7)	4.5 (2)
C6	.1713 (5)	.0465 (4)	.7859 (7)	4.3 (2)
C7	.0507 (5)	.1059 (3)	.7457 (7)	3.7 (2)
O8	-.0532 (3)	.0508 (2)	.7974 (4)	4.5 (1)
N9	-.1875 (4)	.1069 (3)	.8845 (5)	4.1 (2)
C10	-.1642 (5)	.1826 (3)	.9170 (6)	3.5 (2)
N11	-.0265 (4)	.1832 (3)	.8629 (5)	3.6 (1)
C12	.0231 (5)	.2669 (3)	.8427 (6)	3.8 (2)
C13	-.0333 (5)	.3475 (4)	.7700 (7)	4.6 (2)
C14	.0183 (6)	.4264 (4)	.7512 (8)	5.7 (2)
C15	.1295 (6)	.4233 (4)	.8006 (8)	5.2 (2)
C16	.1857 (6)	.3421 (5)	.8704 (8)	5.8 (2)
C17	.1346 (6)	.2631 (4)	.8914 (8)	5.1 (2)
C18	.1818 (7)	.5100 (5)	.7844 (9)	7.5 (3)
C19	-.2800 (5)	.2547 (3)	1.0151 (6)	3.8 (2)
C20	-.2897 (5)	.2710 (3)	1.1796 (7)	4.1 (2)
C21	-.4029 (6)	.3356 (4)	1.2717 (7)	5.1 (2)
C22	-.5062 (6)	.3842 (4)	1.2092 (8)	5.2 (2)
C23	-.4931 (5)	.3672 (4)	1.0481 (8)	5.2 (2)
C24	-.3826 (5)	.3031 (4)	.9481 (7)	4.2 (2)
C25	-.1825 (6)	.2195 (4)	1.2604 (7)	5.0 (2)
C26	-.6296 (7)	.4523 (5)	1.3159 (9)	7.7 (3)
C27	-.3771 (6)	.2864 (4)	.7719 (7)	4.9 (2)
Fe	.2628 (1)	.1455 (1)	.3785 (1)	3.9 (3)
C28	.1795 (7)	.2558 (4)	.3119 (8)	5.9 (3)
C29	.3517 (6)	.1855 (4)	.4893 (7)	4.8 (2)
C30	.3911 (6)	.1284 (4)	.1729 (8)	5.7 (2)
O31	.1204 (6)	.3289 (3)	.2826 (6)	8.7 (2)
O32	.4115 (4)	.2079 (3)	.5587 (5)	6.6 (2)
O33	.4693 (5)	.1156 (4)	.0376 (6)	8.6 (2)

Table 3. Bond Distances for non-Hydrogen Atoms.

	Uncorrected dist		Uncorrected dist
C1 - C2	1.426 (8)	C15 - C16	1.357 (8)
C1 - C7	1.498 (7)	C15 - C18	1.511 (10)
C1 - Fe	2.103 (5)	C16 - C17	1.390 (10)
C2 - C3	1.395 (6)	C19 - C20	1.405 (8)
C2 - Fe	2.050 (6)	C19 - C24	1.395 (8)
C3 - C4	1.430 (10)	C20 - C21	1.377 (7)
C3 - Fe	2.072 (6)	C20 - C25	1.518 (9)
C4 - C5	1.455 (9)	C21 - C22	1.377 (9)
C4 - Fe	2.153 (5)	C22 - C23	1.368 (10)
C5 - C6	1.325 (6)	C22 - C26	1.503 (8)
C6 - C7	1.473 (8)	C23 - C24	1.386 (7)
C7 - O8	1.462 (7)	C24 - C27	1.519 (9)
C7 - N11	1.485 (6)	Fe - C1	2.103 (3)

Table 3. Continue.

O8 - N9	1.437 (4)	Fe - C2	2.049 (9)
N9 - C10	1.302 (7)	Fe - C3	2.071 (9)
C10 - N11	1.375 (6)	Fe - C4	2.153 (3)
C10 - C19	1.471 (6)	Fe - C28	1.768 (6)
N11 - C12	1.448 (7)	Fe - C29	1.795 (7)
C12 - C13	1.363 (7)	Fe - C30	1.784 (6)
C12 - C17	1.375 (9)	C28 - O31	1.147 (7)
C13 - C14	1.396 (9)	C29 - O32	1.138 (9)
C14 - C15	1.379 (11)	C30 - O33	1.153 (7)

Table 4. Bond Angles (°) for non-Hydrogen Atoms.

C7 - C1 - Fe	124.9 (.4)	C10 - C19 - C24	120.0 (.5)
C2 - C1 - Fe	67.9 (.3)	C10 - C19 - C20	119.5 (.5)
C2 - C1 - C7	122.7 (.4)	C20 - C19 - C24	120.4 (.5)
C1 - C2 - Fe	71.9 (.3)	C19 - C20 - C25	122.8 (.5)
C1 - C2 - C3	119.4 (.5)	C19 - C20 - C21	118.2 (.5)
C3 - C2 - Fe	71.1 (.3)	C21 - C20 - C25	119.0 (.5)
C2 - C3 - Fe	69.4 (.3)	C20 - C21 - C22	122.8 (.5)
C2 - C3 - C4	118.6 (.5)	C21 - C22 - C26	121.0 (.6)
C4 - C3 - Fe	73.3 (.3)	C21 - C22 - C23	117.6 (.6)
C3 - C4 - Fe	67.2 (.3)	C23 - C22 - C26	121.4 (.6)
C3 - C4 - C5	128.6 (.5)	C22 - C23 - C24	122-9 (.6)
C5 - C4 - Fe	113.3 (.4)	C19 - C24 - C23	118.1 (.5)
C4 - C5 - C6	129.3 (.6)	C23 - C24 - C27	119.9 (.5)
C5 - C6 - C7	123.5 (.5)	C19 - C24 - C27	122.0 (.5)
C1 - C7 - C6	118.0 (.5)	C3 - Fe - C4	39.5 (.2)
C6 - C7 - N11	113.2 (.4)	C2 - Fe - C4	70.6 (.2)
C6 - C7 - O8	105.9 (.4)	C2 - Fe - C3	39.6 (.2)
C1 - C7 - N11	110.8 (.4)	C1 - Fe - C4	81.5 (.2)
C1 - C7 - O8	108.0 (.4)	C1 - Fe - C3	71.4 (.2)
O8 - C7 - N11	98.7 (.4)	C1 - Fe - C2	40.2 (.2)
C7 - O8 - N9	110.6 (.3)	C4 - Fe - C30	97.2 (.3)
O8 - N9 - C10	105.0 (.4)	C4 - Fe - C29	88.3 (.2)
N9 - C10 - C19	119.8 (.5)	C4 - Fe - C28	168.2 8.3)
N9 - C10 - N11	114.0 (.4)	C3 - Fe - C30	91.5 (.3)
N11 - C10 - C19	126.0 (.5)	C3 - Fe - C29	127.6 (.2)
C7 - N11 - C10	107.5 (.4)	C3 - Fe - C28	132.7 (.3)
C10 - N11 - C12	123.7 (.4)	C2 - Fe - C30	115.6 (.3)
C7 - N11 - C12	120.8 (.4)	C2 - Fe - C29	138.9 (.2)
N11 - C12 - C17	118.6 (.5)	C2 - Fe - C28	98.5 (.3)
N11 - C12 - C13	121.9 (.5)	C1 - Fe - C30	154.8 (.3)
C13 - C12 - C17	119.4 (.5)	C1 - Fe - C29	103.8 (.2)
C12 - C13 - C14	120.2 (.6)	C1 - Fe - C28	87.1 (.3)
C13 - C14 - C15	120.7 (.5)	C29 - Fe - C30	101.3 (.3)
C14 - C15 - C18	120.2 (.6)	C28 - Fe - C30	91.6 (.3)
C14 - C15 - C16	118.2 (.6)	C28 - Fe - C29	97.8 (.3)
C16 - C15 - C18	121.5 (.6)	Fe - C28 - O31	174.4 (.6)
C15 - C16 - C17	121.7 (.6)	Fe - C29 - O32	177.5 (.5)
C12 - C17 - C16	119.7 (.6)	Fe - C30 - O33	176.4 (.6)

Acknowledgment.
Financial support from MURST and CNR is gratefully acknowledged.

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