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TRISTRIFLUOROMETHYLMETHANE TAKES UP DEUTERIUM FROM A NEUTRAL MEDIUM FASTER THAN DO 1H-PERFLUOROBICYCLO-[2,2,2]OCTANE AND -[2,2,1]HEPTANE: ARE INDUCTIVE EFFECTS STILL A SUFFICIENT EXPLANATION OR IS A CONCEPT SUCH AS NEGATIVE HYPERCONJUGATION NECESSARY AFTER ALL? *

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SUMMARY

Mixtures of tristrifluoromethylmethane(I) and 1H-undecafluorobicyclo[2,2,1]heptane(II), and of I and 1H-tridecafluorobicyclo-[2,2,2]octane(III) were kept for approximately 19 days in hexadeuteroacetone/deuterium oxide (9:1) at 50°C. Uptakes of deuterium as measured by mass spectrometry were ca. 70% into I, not detectable with II, and ca. 12% into III. If this reaction is mechanistically similar to base-catalysed proton exchange, the acyclic system(I)is much more acidic than the bridgehead species (II). This result revives again the possibility that fluorine hyperconjugation (no-bond resonance) could be significant in aliphatic organofluorine chemistry.

INTRODUCTION

One of the most important aspects of contemporary fluorocarbon chemistry is the use [1-7] of fluorocarbanions as synthetic intermediates, pioneered by Miller [1]. They are usually generated for synthetic purposes by addition of fluoride ion to perfluoroalkenes. An alternative approach [5-7] is from the corresponding carbon acid, a fluorocarbon hydride; under the influence of a strong base, hydrogen is replaced by a potentially electrophilic species, probably *via* an intermediate fluorocarbanion. Synthetically, this process is limited by the inherent instability of most fluorocarbanions [7,6], which decompose to fluoroalkenes and fluoride ion more rapidly than they react with electrophiles.

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However, the relationship of acid strength to structure in saturated fluorocarbon hydrides is of great interest. For monohydroperfluorides, Andreades showed [7] that as perfluoroalkyl substituents progressively replace fluorine at the carbanionic centre, the acidity increases in the order:

$$CF_3H < CF_3(CF_2)_5CF_2H < (CF_3)_2CFH < (CF_3)_3CH \text{ (I)}$$

Though Andreades himself [7] explained this effect by no-bond resonance, it is now more usually ascribed [e.g. 4,5,8,9] to destabilisation of carbanions in which I-π electronic repulsion can arise between the negative charge and any fluorines carried directly on carbon bearing that charge.

Accepting I-π effects, however, there has also been much discussion [3,4,7-10] on whether saturated fluorocarbanions are stabilized only by partial delocalisation of their negative charge by inductive electron attraction, or whether charge spreading is enhanced further by no-bond resonance effects (negative hyperconjugation). This concept postulates that the carbanionic ground state involves not only the normal covalent structure but also contributors such as IV (and eight other equivalent species). This ascribes slight ionic characte to each of the fluorines carried on carbons next to the carbanionic centre. If the effect is real, and applies to carbanions from monohydroperfluoroalkanes, it should be at its maximum in the anion from tristrifluoromethylmethane (I) with 9 possible hyperconjugative contributors. Roberts, et al [11] first postulated the effect in organofluorine chemistry, to explain results from benzotrifluoride derivatives. Though, intuitively, many must have felt that no-bond resonance contributors lack plausibility somewhat, the concept has been widely used, and many authors have invoked it at some stage to explain aspects of reactivity [e.g. 12]. Andreades interpreted his results that way [7].

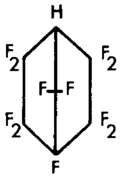
The review by Holtz [9] gave a critical survey of the quantitative data put forward in support of the concept of negative hyperconjugation and marshalled convincing arguments against its existence, concluding that inductive effects alone need be invoked. Though much other evidence was presented, a major argument deployed was based on the acidities determined by Streitwieser, Holtz et al [13,14] for bridgehead polyfluorides 1H-undecafluorobicyclo[2,2,1]heptane(II) and 1H-tridecafluorobicyclo-[2,2,2]-octane(III).

These compounds were synthesised and their chemistry studied here [15,16], and were supplied by us to Streitwieser.

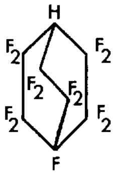
Elimination of fluoride ion from the carbanions arising from II and III is inhibited, since the resultant double bond is at a bridgehead position in "violation"of Bredt's rule [17]. Such "bridgehead olefins" can be formed [15,16,18], as transient reactive intermediates, but only under forcing conditions. Therefore, for similar steric arguments, significant enhancement of the stability of a bridgehead carbanion by involvement of resonance contributors of type V appears unlikely. Whatever the significance of IV, V should not contribute to the carbanion from II.

$(CF_3)_3CH$

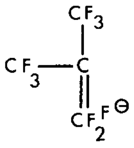
I



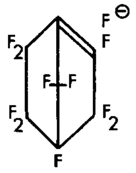
II



III



IV



V

Streitwieser and Holtz [14] determined pKa values for II and III of 20.5 and 18.3 (± 0.3) respectively. Calculations [9,14] based on Andreades'results [7] for I gave a pKa value around 21. Hence there appeared no need to invoke any special effects such as C-F no-bond resonance (fluorine hyperconjugation). From work based on different types of compound, others [8,19] have reached similar conclusions.

Some uncertainties still exist however. As was pointed out by Streitwieser and Holtz [14], the pKa for I was based on a single kinetic measurement,approximate, and not measured by them. This experiment, under conditions different from those used for the bridgehead compounds, was of course by Andreades [7], who himself had estimated a pKa of about 11 for I. Further, the hydride being studied, as was stated by Andreades [7], was subject to rapid concomitant dehydrofluorination. So far as we are aware, simultaneous or competition experiments, involving any bridgehead compound and I together, have not been undertaken as yet.

Further confusion was added to this involved story when polyfluoronorbornyl mercury compounds were studied [20]. A polarographic reduction technique applied to a mercurial (Rf_2Hg) had been proposed by Butin et al [21] as a measure of the acidity of the corresponding fluorohydrocarbon (RfH). When results on our mercurials were applied to the calibration graph of Butin et al, a pKa of 16 was given [20] for undecafluoride II, which must be compared with the pKa of 7 determined by Butin et al themselves for I [21]. Again, the compounds were not measured together. The difference between the pKa values for II, as determined by polarography and base exchange, was disappointing, but possibly acceptable, particularly since in our hands the former method had some experimental problems. However, I had a much lower polarographic pKa value than that obtained for II, whereas by base exchange they had broadly similar pKa values. This was most disturbing. We [20], and Streitwieser et al [14] have expressed reservations about the polarographic technique. However, as we pointed out [20], if both techniques are measuring the same acidity effect, the results are irreconcilable.

Clearly, direct comparison of I and II was called for, but since the ready dehydrofluorination of I makes for difficulties in basic media, an exchange process under essentially neutral conditions was highly desirable.

Exchange of H for D occurs with I in ethanol-O-D [7]. Also, as we had found earlier, exchange occurs with III in hexadeuteroacetone containing some deuterium oxide though, significantly, with II none could be detected [16b].

RESULTS

We developed the latter reaction further, and used it to make direct comparisons between I, II, and III. Hexadeuteroacetone containing 10% by volume of deuterium oxide dissolved I, II and III, and exchange of deuterium for hydrogen then occurred. Tables 1 and 2 record the percentage of uptake of deuterium into the polyfluorides, as determined by mass spectrometry, when mixtures of I and II, and of I and III, respectively, were kept together in the same sample of the $(CD_3)_2CO/D_2O$ solvent system.

The results are very clear-cut and surprising. After 450 hours at 50°C, the isolated products had deuterium contents as follows: from I over 70%, from II none detectable, from III 12%. Ratios of

TABLE 1

Deuteration of Mixtures of Tristrifluoromethylmethane(I) and 1H-Undecafluorobicyclo[2,2,1]heptane(II) in Hexadeuteroacetone - Deuterium Oxide (9:1 by volume, respectively; 0.5 cm^3)

Experiment No.	Temp. ^{o}C	Time (hours)	Compound	Amount Used (g)	Amount Recovered (g)	Deuterium Uptake (%)
1	50	20	I	0.055	0.05	6.5
			II	0.073	0.05	0*
2	50	140	I	0.055	0.04	22
			II	0.073	0.06	0*
3	50	262	I	0.055	0.05	50
			II	0.073	0.06	0*
4	50	450	I	0.055	0.05	71
			II	0.073	0.06	0*

*The maximum uptake in any of these runs was 0.3%; i.e. within the experimental uncertainty.

rate coefficients are k_I/k_{III} approx. 10, and k_I/k_{II} at least 60 and most probably >100.

Clearly in this process, tristrifluoromethylmethane (I) exchanges significantly more rapidly than the bicyclo-octane (III) and very much more so than the norbornane (II). Though we do not claim a high order of accuracy for the actual figures obtained, the deuterium uptakes for the three compounds are so different that the overall result is quite unambiguous. We prefer not to calculate pKa values from these results however. For one thing, there is obvious doubt whether the systems used were subject to catalysis by glass, though if it did occur it should have affected both compounds equally. We also considered the possibility that the norbornane II was not exchanging with D_2O because it was reacting preferentially with hexadeuteroacetone to give a tertiary alcohol. This latter reaction should not be happening since recoveries of II were reasonable, and in earlier work no product of this type could be detected [15b].

TABLE 2

Deuteration of Mixtures of Tristrifluoromethylmethane(I) and 1H-Tridecafluorobicyclo[2,2,2]octane(III) in Hexadeuteroacetone-Deuterium Oxide (9:1 by volume, respectively; 0.5 cm^3)

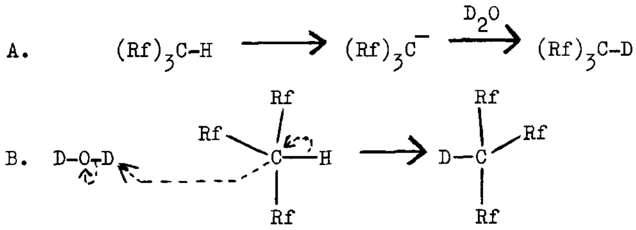
Experiment No.	Temp. °C	Time (hours)	Compound	Amount Used (g)	Amount Recovered (g)	Deuterium Uptake (%)
5	50	20	I	0.055	0.05	7.8
			III	0.086	0.06	1.0
6	50	140	I	0.055	0.05	44
			III	0.086	0.07	8.4
7	50	262	I	0.055	0.04	62
			III	0.086	0.07	9.1
8	50	450	I	0.055	0.04	72
			III	0.086	0.06	12

DISCUSSION

Some mechanistic speculation is called for, following these new observations. The obvious first question is whether these neutral exchanges are of the same mechanistic type as the base-catalysed exchanges used for the previous quantitative work [7,13,14]. Two extreme mechanistic situations are possible [cf. 22, p. 137].

From the results in Table 1, the rate coefficient for the exchange with Compound I may be calculated as $k_I/S^{-1} = (7.64 \pm 0.58) \times 10^{-7}$ (values quoted are appropriate pseudo first order rate coefficients and uncertainties are standard errors). Assuming that an uptake of deuterium of 2% would just have remained undetected in Compound II, then k_{II}/S^{-1} would be 1.3×10^{-8}, and $k_I/k_{II} \geqslant 60$. If, as seems likely, the level of uptake into II, just not detectable, was no greater than 1%, then k_{II}/S^{-1} would be 6.1×10^{-9} and $k_I/k_{II} \geqslant 125$.

From the results in Table 2, for Compound I, $k_I/S^{-1} = (8.06 \pm 0.97) \times 10^{-7}$ and for Compound III, $k_{III}/S^{-1} = (7.81 \pm 1.75) \times 10^{-8}$, and $k_I/k_{III} = 10.3 \pm 2.6$.



A is a unimolecular process (SE1) passing through a discrete carbanionic intermediate. B is a bimolecular concerted process (SE2).

Each process would take place in a solvent cage and other neighbouring molecules of D_2O and of CD_3-CO-CD_3 would be involved in aspects of the overall sequence.

If our present series of neutral deuterium exchanges proceed preferentially by something close to mechanism type B, this could explain the much readier reaction of tristrifluoromethylmethane (I) relative to the bicyclic compounds (II and III), if a 'backside' approach of the D_2O reagent was required. This would be analogous to the situation for SN2 reactions in classical chemistry, our bridgehead species being less reactive for reasons corresponding to those applying to SN reactions involving hydrocarbon-based bridgehead compounds with halogeno- or tosyloxy-substituents [23]. Altogether, this postulate is not too convincing. If it does hold, however, how many more reactions of weak carbon acids operate by similar mechanisms?

However, if a mechanism similar to B operates without the steric requirement of a 'backside' approach, or if mechanism A applies, another reason for the lower reactivity of II and III may be postulated. For electronic and/or steric reasons, II and III may form stable complexes with the co-solvent hexadeuteroacetone much more readily than does I. Reaction with D_2O to give deutero-compounds could then be inhibited for II and III, though no new isolatable compound need be formed from any $(CD_3)_2CO$ complex. One experiment using C_2H_5OD alone as the solvent and deuterium source suggests that this is not in fact the correct explanation of these results. Nevertheless, it is difficult to entirely rule out the involvement of solvent effects of some sort. Gas-phase acidity measurements are needed here.

It is still perhaps most likely that our neutral deuterium exchanges approximate to mechanistic type A, involving an effectively carbanionic intermediate as base-catalysed proton exchanges are usually thought to do. If this is so, there are of course the usual reservations that we are measuring kinetic acidities [cf. 22,24]. Nevertheless, it seems quite probable that tristrifluoromethylmethane (I) is exceptional in its acidity. It is much more acidic than secondary and primary acyclic monohydropolyfluorides [7] and now seems to be significantly more so than the bicyclic species II and III. This might still be due entirely to inductive effects, related to the greater number of β-fluorines in I than in II or III, and Streitwieser [private communication] believes this to be the case. However it has been claimed [10] that fluorine and different perfluoroalkyl groups have very similar inductive effects.

Nevertheless, if the earlier results indicating a greater acidity of II and III relative to I were evidence against negative hyperconjugation [3,4,9,13,14,25], then these new observations must alter the balance of the argument. Any reservations about solvent effects, mechanistic type, etc., apply to both sets of observations. Reluctantly, therefore, and pace our collaborators Streitwieser and Holtz, we feel we must resurrect the concept of fluorine hyperconjugation (no-bond resonance) as a possible explanation of our results. It could be that, after all, it is involved in organofluorine chemistry, at least in negatively-charged species such as carbanions, where charge-spreading must surely occur if it can. It need not apply, necessarily, in neutral molecules. Representations formally by structures such as IV and V do not perhaps help; nothing as extreme as this need be involved. Need the postulate really be much more than a continuum extending beyond a simple inductive effect?

If a C-F bond assumes some ionic character, then the adjacent C-C bond presumably must acquire some alkene-like characteristics, by partial sharing of the anionic lone pair (if charge-spreading is to be effective). If all this is true, there must also be significant stereochemical demands involved, since the bridgehead compounds II and III are less acidic - for 'Bredt's rule' reasons.

A further implication would be that fluoroalkyl groups to which negative hyperconjugation applies should lose their fluorine more readily than normal ones, because their C-F bonds will have more ionic character. This can be argued for benzotrifluoride derivatives [11],and it is worth noting that Andreades' paper [7] suggests that the rate of dehydrofluorination relative to that of the corresponding exchange is greater with I than with the other hydrides studied. Strong bases cause no decomposition of II or III themselves. If however their lithio-derivatives are decomposed in refluxing diethyl ether, that derived from III is much more stable than that from II [16]. However, III is more acidic, and presumably the 'bridgehead olefin' derived from it is less strained than that from II; altogether, a complicated situation.

In a recent paper, negative hyperconjugation was invoked [26] to help explain the photoelectron spectrum of 1,1-difluoroallene: C_1-C_2 is, like in allene itself, an electron-rich double bond (ascribed to an I-π effect), whereas C_2-C_3 is electron-deficient, like the double bond in 3,3,3-trifluoropropene (ascribed to an energy-lowering effect on the orbitals with which the fluorines can negatively hyperconjugate). Perhaps both concepts have a place in organo-fluorine chemistry.

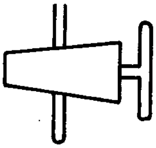
We are still uncertain whether fluorine hyperconjugation is a reality. However, as an explanation for our results it cannot now be ruled out, and more work is clearly necessary to settle an issue thought to have been resolved already.

EXPERIMENTAL

Materials: 1H-Undecafluorobicyclo[2,2,1]heptane(II) [15] and 1H-tridecafluorobicyclo[2,2,2]octane(III) [16] were from our own stocks. Tristrifluoromethylmethane(I) [27] was kindly supplied to us by Dr. D.C. England of Du Pont, having been made by reaction of perfluoroisobutene with caesium fluoride in dimethylformamide, followed by acidification [cf. 28]: ^{19}F NMR [7,28] and infrared [29] were as reported.

Solvent System: Hexadeuteroacetone (99.8%) and deuterium oxide (99.7%) in volume ratio of 9:1 respectively gave homogeneous solutions with I, II, and III, in significant quantities.

Experimental Conditions: Reaction vessels were Pyrex glass tubes (internal diameter 6 mm) made from taps, which were lubricated with silicone grease. When being filled, care was exercised to keep the air space above the liquid to a minimum. In a typical experiment I (0.055g) in solvent (0.25 cm^3)



was mixed with II (0.73g) in solvent (0.25 cm^3) and the mixture injected through the tap bore using a capillary pipette. The tap was closed and secured with copper wire, and the unit immersed in a heated water bath controlled thermostatically. After each run the tube contents were separated gas chromatographically, using a dinonyl phthalate/celite column (1:3) (210 cm x 4 mm internal diameter)in a Pye series 104 instrument equipped with a flame ionization detector. Nitrogen (flow rates 4.5 ℓ/hr.) was used as carrier gas. Detailed results are given in Tables 1 and 2.

Mass Spectrometry: Fluoro-compounds isolated were examined using an A.E.I. MS9 mass spectrometer. They were introduced at room temperature and the mass spectra recorded with an electron current of 400 μA and an electron voltage of 70V. The source temperature was 220°C. Since the molecule-ion peaks for these compounds were small, measurements were made on peaks $(M - 19)^+$. For precise measurement of the D:H ratio, the ion currents, due to the two isotopic species, were focussed in turn on the collector and the output read upon the collector meter. The value corresponding to the ion containing deuterium was corrected for the contribution due to the ^{13}C ion containing hydrogen.

Exchange in Ethanol-O-D: An experiment similar to those summarised in Table 1 was carried out using ethanol-O-D (without added D_2O) as solvent. After 20 hr. at 50°C the deuterium uptake was 4.7% into I and 0% into II.

Competition Involving II and III: An early experiment similar to Nos. 4 and 8 was carried out using a mixture of II and III. Uptakes of deuterium were 0% into II and 5% into III.

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