Journal of Fluorine Chemistry, *25* (1984) 47–56

STEREOCHEMISTRY OF NUCLEOPHILIC ADDITIONS TO HEXAFLUORO-2-BUTYNE

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SUMMARY

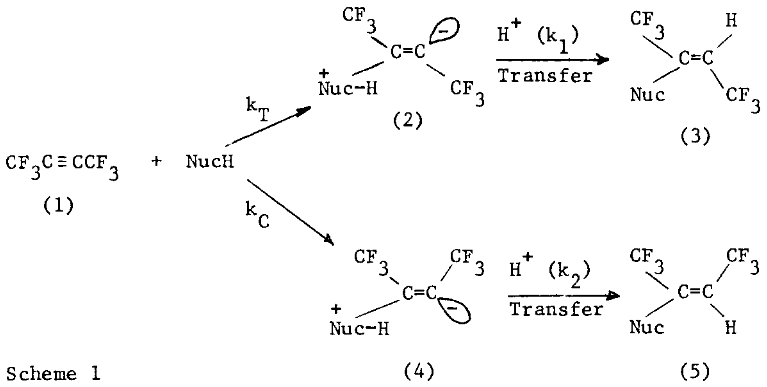
Base-catalysed additions of alcohols to F-2-butyne (1) give mainly products of trans-addition while cis-addition predominates in uncatalysed additions of alcohols carried out in a diluent. The stereochemistry of addition of diethylamine is very dependent on the solvent used and cis- or trans-addition may predominate. Stepwise and concerted mechanisms are advanced to account for these observations. Nucleophilic addition of sulphur to (1) gives F-tetramethylthiophene (68%) and hydration gives $CF_3CH_2COCF_3$ (91%).

RESULTS AND DISCUSSION

Although nucleophilic additions to hexafluoro-2-butyne (1) are well established [1,2], relatively little is known about the factors affecting stereochemistry of addition. Where the stereochemistry has been investigated, mainly trans-addition products (3) are described. Here, however, we probe the influence of steric requirements of the nucleophile and effects of charge and solvent on the stereochemistry of addition (Scheme 1).

Base-catalysed additions of alcohols to hexafluoro-2-butyne (1) proceed very readily and results of a series of reactions is described in Table 1. In all cases ca. 90% trans-addition occurs but there is some indication that alcohols with larger steric requirements give more cis-product (5).

0022-1139/84/$3.00



Scheme 1

TABLE 1

Base catalysed additions of alcohols to hexafluoro-2-butyne

NucH	Solvent	Temperature, °C	% *trans* (3)
CH_3OH	-	20	96
$n-C_3H_7OH$	-	20	92
$n-C_4H_9OH$	-	20	89
$n-C_4H_9OH$	-	117	86
$n-C_4H_9OH$	sulpholan	117	92
$2-C_4H_9OH$	-	20	91
$t-C_4H_9OH$	-	20	86

The effect is, however, relatively small. Uncatalysed additions of alcohols required very high temperatures, e.g. 95° for methanol and even higher temperatures for the more sterically demanding t-BuOH and *ca.* 90% *trans*-addition was obtained in each case (Table 2) i.e. closely resembling the base-catalysed processes. In contrast, however, use of diethyl ether or sulpholan as diluent gave more *cis*-addition (5) than *trans*-addition products (6).

Additions of diethylamine are shown in Table 3. Reactions occurred very readily and ether and sulpholan were used as separate solvents. The contrast between results with these solvents is quite significant, *cis*-additio (5) predominating with ether and mainly *trans*-addition (3) occurring with sulpholan.

TABLE 2

Uncatalysed additions of alcohols to hexafluoro-2-butyne

NucH	Solvent	Temperature, °C	% *trans* (3)
CH_3OH	-	95	92
$n\text{-}C_4H_9OH$	-	95	90
$n\text{-}C_4H_9OH$	ether	95	†
$n\text{-}C_4H_9OH$	ether	150	27
$n\text{-}C_4H_9OH$	sulpholan	100	†
$n\text{-}C_4H_9OH$	sulpholan	150	30
$t\text{-}C_4H_9OH$	-	95	†
$t\text{-}C_4H_9OH$	-	150	90

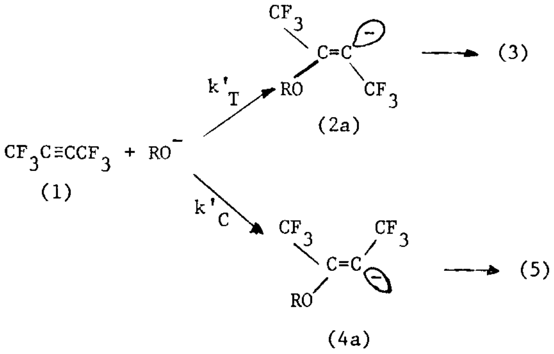
† No detectable reaction.

TABLE 3

Additions of diethylamine to hexafluoro-2-butyne

Solvent	Temperature, °C	% *trans* (3)
ether	2	40
sulpholan	2	61

Base-catalysed additions of alcohols to (1) occur readily and lead to preferential formation of *trans*-addition products (3) either when carried out using the corresponding alcohol or sulpholan as solvent. There is a slight increase in the proportion of *cis*-addition (5) with increasing steric requirements of the alcohol and this may be attributed to interactions with adjacent trifluoromethyl, which makes (2a) less stable relative to (4a) (Scheme 2). It is not easy to envisage a realistic mechanism for direct equilibration of vinyl anions and, indeed, calculations carried out for the vinyl anion itself indicate that the barrier to inversion is large [3].

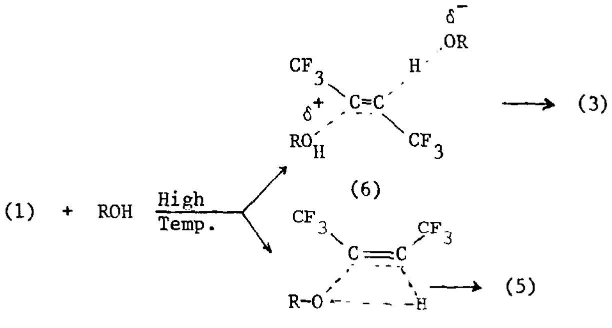


Scheme 2

Therefore it seems reasonable to discount direct interconversion of either (2a) and (4a) or (2) and (4), as processes leading to both (3) and (5). If this conclusion is valid, then the ratios of products, (3)/(5) represents the ratio of rate constants k'_T/k'_C for the addition process.

The addition of diethylamine may be represented by Scheme 1 where, again, the products (3) and (5) represents the ratio of the rate constant for addition k_T/k_C. In this case, however, the products are markedly affected by solvent. In sulpholan (high dielectric constant) trans-addition (2) is preferred whereas in ether cis-addition (4) is preferred. We can attribute this change to differences in charge separation in the Zwitterionic intermediates (2) and (4). Charge separation is greater in the trans-isomer (2) and its formation should be assisted by a solvent of higher dielectric constant. However, we must not overlook the fact that diethylamine is a sterically demanding nucleophile and increased steric demand will destabilise (2) relative to (4).

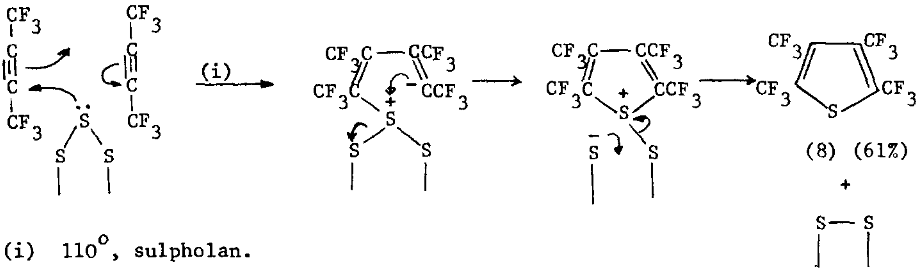
The mechanism of the uncatalysed additions of alcohols to (1) apparently differs from that of addition of diethylamine. In the addition of alcohols, use of either sulpholan or ether as solvent led to preferential formation of the product of cis-addition. In contrast, however, uncatalysed addition of neat alcohols gives principally, products of trans-addition (3). These results indicate, therefore, an essentially concerted process for the uncatalysed addition of alcohols, as outlined in Scheme 3. Addition via (6) involves concerted transfer of a proton from another molecule of alcohol, whereas addition via (7) involves intramolecular transfer of a proton. Obviously, dilution would then favour (7) over (6).



Scheme 3

The results described above form evidence that cis-addition to (1) may be increased, in some cases, by one or more of the following factors: (a) increasing the steric requirement of the nucleophile, (b) using a neutral nucleophile and therefore generating Zwitterionic intermediates, or (c) use of a solvent of low dielectric constant.

Consistent with these conclusions, we have discovered at least one all-cis nucleophilic addition to hexafluoro-2-butyne (1) i.e. the reaction of sulphur, suspended in sulpholan. Krespan [4] has synthesised perfluorotetramethylthiophene (8) by reaction of sulphur with (1) at 200°C and concluded that the process involves reaction of an intermediate dithietene with (1), probably in a free-radical process. We find that reaction with sulphur will occur at 110°C in sulpholan giving (8), surprisingly readily. No other sulphur heterocycles were detected and we conclude that a different process operates under our conditions, from that operating under the conditions used by Krespan. Indeed, it seems reasonable to conclude that a nucleophilic cyclisation process operates, as shown in Scheme 4, the cis-addition occurring because sulphur is both a bulky and a neutral nucleophile.



(i) 110°, sulpholan.

Scheme 4

Since we were able to effect uncatalysed reaction between alcohols and (1) we attempted a corresponding uncatalysed hydrolysis. Cullen and Dawson [5] have previously described base catalysed addition of water to (1) giving the ketone (9) but only as a minor product. We now find that uncatalysed addition of water to (1) occurs using sulpholan as solvent at 110^{o}C in a nickel tube giving the ketone (9) in very high yield. Further work is progressing with this interesting ketone.

$$\underset{(1)}{CF_3C{\equiv}CCF_3} + H_2O \xrightarrow{(i)} \underset{(9)}{CF_3CH_2COCF_3} \quad (91\%)$$

(i) 110^{o}, sulpholan

EXPERIMENTAL

^{19}F n.m.r. spectra were measured using a Varian EM 360L or A56/60 spectrometer, with trichlorofluoromethane as external reference; upfield shifts are quoted as positive. Gas chromatography was carried out using columns packed with 30% silicone gum rubber SE-30 on chromosorb P (Column O) or 20% diisodecyl-phthalate on chromosorb P (Column A). Mass spectra were recorded on a V.G. Micromass 12 B linked with g.l.c.

Addition of nucleophiles to hexafluorobut-2-yne

Alcohols (a) Reaction conditions

Most of the addition reactions were performed in Carius tubes but nickel tubes were used for reactions above 100^{o}C. Hexafluorobut-2-yne (1) was sealed in the tube with an excess of the alcohol and the tube was either heated or allowed to stand at room temperature for approximately 20h. The catalysed reactions were carried out by dissolving the appropriate amount of sodium in the alcohol in order to give a solution containing 4-5% of the alkoxide. Catalysed reactions at elevated temperatures were carried out at atmospheric pressure, the hexafluorobut-2-yne being introduced into the reaction vessel from a variable reservoir. The products were not isolated but were studied by ^{19}F n.m.r. and m.s.-g.l.c. spectroscopy on the crude reaction mixture. Isomer ratios were determined by identification of the resonances due to the CF_3 groups and noting that $J_{CF_3-CF_3}$ (trans) << $J_{CF_3-CF_3}$ (cis).

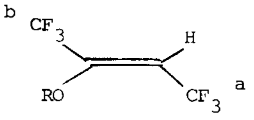
(b) Base catalysed reactions

Alcohol (g, mmol)	Solvent (g)	(1) (g, mmol)	Temp °C	Recovered (1) (g)	% *trans*
CH_3OH					
5.1, 160	-	6.0, 37	20	0.0	96
$n-C_3H_7OH$					
8.1, 135	-	4.0, 25	20	0.0	92
nC_4H_9OH					
9.0, 120	-	5.3, 33	20	0.0	89
15.8, 214	-	6.8, 42	117	0.0	86
5.2, 70	Sulpholan (25.0)	3.8, 23	117	0.0	92
$2-C_4H_9OH$					
4.6, 62	-	2.4, 15	20	0.0	91
$t-C_4H_9OH$					
9.9, 130	-	4.0, 25	20	2.2	86

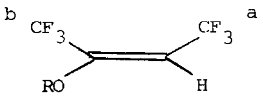
(c) Uncatalysed reactions

Alcohol (g, mmol)	Solvent (g)	(1) (g, mmol)	Temp °C	Recovered (1) (g)	% *trans*
CH_3OH					
4.5, 140	-	4.5, 28	95	0.0	92
$n-C_4H_9OH$					
8.0, 11.0	-	6.1 , 38	95	3.7	70
1.8, 24	Ether, (6.5)	5.5, 34	95	5.5	-
3.5, 47	Ether, (14.2)	10.0, 62	150	7.5	27
1.8 24	Sulpholan (12.7)	5.8, 36	100	5.8	-
1.2, 16	Sulpholan (9.0)	4.8, 28	150	3.4	30
$t-C_4H_9OH$					
18.6, 251	-	4.2, 26	95	4.2	-
9.8, 130	-	3.0, 19	150	2.5	90

The following were identified: (Z) and (E)-2-methoxy-1,1,1,4,4,4-hexafluorobut-2-ene (by comparison of ^{19}F n.m.r. spectra with those of a known sample [1]); (Z)-2-n-propoxy-1,1,1,4,4,4-hexafluorobut-2-ene (nc) (Found: M^+-CH_3, 207. $C_7H_8F_6O$ requires M^+-CH_3, 207; δ_F 59.0 (3 F, d, J 7.5 Hz, F_a) and 71.5 (3 F, s, F_b); (E)-2-n-propoxy-1,1,1,4,4,4-hexafluorobut-2-ene (nc) δ_F 55.1 (3 F, m, F_a) and 69.8 (3 F, q, J 10 Hz, F_b); (Z)-2-n-butoxy-1,1,1,4,4,4-hexafluorobut-2-ene (nc) (Found: M^+-CH_3 207. $C_8H_{10}F_6O$ requires $M-CH_3$, 207; δ_F 58.9 (3 F, d, J 7.5 Hz, F_a) and 71.5 (3 F, s, F_b); (E)-2-n-butoxy-1,1,1,4,4,4-hexafluorobut-2-ene (nc), δ_F 55.0 (3 F, m, F_a) and 69.7 (3 F, q, J 10 Hz, F_b); (Z)-2-secbutoxy-1,1,1,4,4,4-hexafluorobut-2-ene (nc) (Found: $M^+-C_2H_5$, 207. $C_8H_{10}F_6O$ requires $M-C_2H_5$, 207; δ_F 59.5 (3 F, d, J 7.5 Hz, F_a) and 70.0 (3 F, s, F_b); (E)-2-sec-butoxy-1,1,1,4,4,4-hexafluorobut-2-ene (nc), δ_F 54.6 (3 F, m, F_a) and 69.9 (3 F, q, J 10.5 Hz, F_b); (Z)-2-tert-butoxy-1,1,1,-4,4,4-hexafluorobut-2-ene (nc) (Found: M^+-H, 235. $C_8H_{10}F_6O$ requires M-H, 235; δ_F 59.5 (3 F, d, J 7.5 Hz, F_a) and 70.1 (3 F, s, F_b); (E)-2-tert-butoxy-1,1,1,4,4,4-hexafluorobut-2-ene (nc) δ_F 61.5 (3 F, m, F_a) and 68.2 (3 F, m, F_b).



(Z)



(E)

R = $n-C_3H_7-$, $n-C_4H_9-$, $C_2H_5(CH_3)CH-$ and $(CH_3)_3C-$

(d) Attempted equilibrium reactions

(i) A portion of the mixture obtained from the uncatalysed reaction of n-butanol with (1) in sulpholan at 150°C was stirred at 20°C with an equal volume of a 5% solution of sodium n-butoxide in n-butanol. The ratio of isomers was found to remain unaltered over a period of 48h.

(ii) The above experiment was repeated using a Carius tube at 150°C for 48h. On cooling to 20°C and opening the tube, no isomerisation was found to have occurred.

Diethylamine [2]

The reactions were carried out at 22°C and at atmospheric pressure, the hexafluoro-2-butyne being introduced into the reaction vessel from a variable reservoir. Reaction was allowed to proceed for 1½h. The products were isolated only in the case of sulpholan (85% yield). Isomer ratios were determined from the ^{19}F n.m.r. spectra, as before.

Solvent (10 ml)	Dielectric Constant	Et_2NH (g, mmol)	(1) (g, mmol)	% *trans*
Cyclohexane	2	2.1, 28.8	4.8, 29.6	34
Diethyl Ether	4.3	1.85, 25.3	4.1, 25.3	40
Sulpholan	44	1.94, 26.6	4.3, 26.5	61
Acetonitrile	38	2.1, 28.8	4.8, 29.6	89

Sulphur

A suspension of sulphur (3 g, 93.8 mmol) in sulpholan (40 ml) was stirred at 110°C under an atmosphere of hexafluorobut-2-yne (1) (6.0 g, 37 mmol). After 5 days, (1) (2.5 g) was recovered and volatile material was transferred at 80°C under vacuum to a cold trap. The resultant liquid was shown by g.l.c. (Column O; 170°C) to consist of one component, identified as tetrakistrifluoromethylthiophene (8) (2.4 g, 61%) b.p. 134°C, (lit. value 134-5°C [4]). Analysis: Found: C, 26.89; F, 64.26; S, 9.29%, M^+, 356 (for ^{32}S). $C_8F_{12}S$ requires C, 26.97; F, 64.04; S, 8.99%; M, 356 (for ^{32}S).

Water

Water (2.2 g, 120 mmol), hexafluorobut-2-yne (1) (10.9 g, 67 mmol) and sulpholan (10 g) were sealed in a Carius tube and shaken at 110°C for 114h. On opening the tube, (1) (5.0 g) was recovered and volatile material was transferred under vacuum to a cold trap. The resulting liquid was dried (P_2O_5) and transferred under vacuum to give a colourless liquid which was shown to be a single component by g.l.c. (Column A; 70°C) and identified as 1,1,1,4,4,4-hexafluorobutan-2-one (9) (5.9 g, 91%) b.p. 56°C (lit. value 54.2°C at 747 mm Hg [5]). Analysis: Found: C, 26.55; H, 1.08; F, 63.49%; M^+-19, 161. $C_4H_2F_6$ requires C, 26.67; H, 1.11; F, 63.33%; M-19, 161.

REFERENCES

1 E.K. Raunio and T.G. Frey, J. Org. Chem., 36 (1971) 345.

2 R.N. Haszeldine, J. Chem. Soc, (1952) 3490.

3 J.M. Lehn, B. Munsch and Ph. Millie, Theor. Chim. Acta., 16 (1970) 351; D.T. Clark, Annual Reports Chem. Soc. B, 68 (1971) 43.

4 C.G. Krespan, J. Am. Chem. Soc., 83 (1961) 3434.

5 W.R. Cullen and D.S. Dawson, Can. J. Chem., 45 (1967) 2887.