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FREE RADICAL CHEMISTRY. PART 2 [1]. ADDITIONS OF DIMETHYLETHER TO F-CYCLOALKENES

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SUMMARY

γ-Ray and peroxide-initiated additions of dimethylether to F-cyclobutene, F-cyclopentene, and F-cyclohexene give mixtures of cis- and trans-adducts in each case, with a clear preference for trans-addition with F-cyclobutene. Selective bromination of the adducts occurs but the position of chlorination depends dramatically on solvent. Fluorination with cobalt trifluoride is very efficient.

INTRODUCTION

In pursuit of our interest [1] in the use of the carbon-hydrogen bond, in free-radical additions to unsaturated fluorocarbons, as a means of synthesising functional fluorocarbons, we describe here some additions of dimethylether to F-cycloalkenes. Although there is a significant literature concerning additions of various ethers to polyfluoro-alkenes and -cycloalkenes, surprisingly, the only report that we are aware of,

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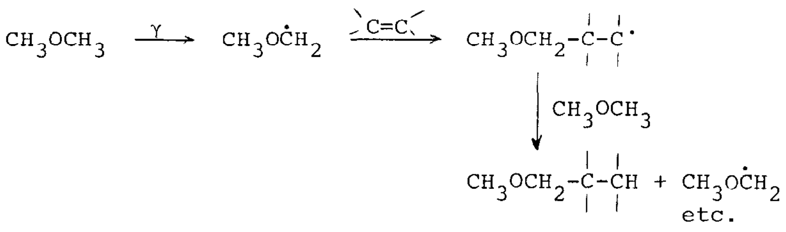


$$CH_3OCH_3 \xrightarrow{\gamma} CH_3O\dot{C}H_2 \xrightarrow{\rangle C=C \langle} CH_3OCH_2-\overset{|}{\underset{|}{C}}-\overset{|}{\underset{|}{C}}\cdot \xrightarrow{CH_3OCH_3} CH_3OCH_2-\overset{|}{\underset{|}{C}}-\overset{|}{\underset{|}{C}}H + CH_3O\dot{C}H_2 \text{ etc.}$$

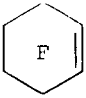
concerning dimethylether, involves co-pyrolysis or photolysis with F-propene [2,3]. In ethers where a choice of carbon-hydrogen bond is available for addition to fluorinated alkenes, reaction occurs at the bond alpha- to oxygen, analogous to the reaction of dimethylether shown schematically above. Hanford first described the peroxide-initiated additions of certain cyclic ethers to F-ethene, giving simple adducts as well as telomers [4]; reactions involving chlorofluoroethenes with diethylether, tetrahydrofuran (T.H.F.) [5,6], 1,4-dioxane [5], and dimethoxymethane [7] give both 1:1 and 2:1 adducts (two molecular proportions of fluorinated alkene and one of the ether); F-propene, F-2-methylpropene, and F-alkylvinylethers give both 1:1 and 1:2 adducts with various ethers [8-10]; and a cyclic product may be obtained from F-propene and phenylalkyl-ethers [11]. Ethers have also been added to a variety of poly-fluorocycloalkenes, the ethers include T.H.F. [9,12-14], 1,4-dioxane, and diethylether [12,13].

RESULTS AND DISCUSSION

Free-radical additions of dimethylether to F-cycloalkenes occur very readily using γ-ray initiation and we have also carried out corresponding reactions initiated by benzoyl peroxide for comparison. High yields were obtained in each case and the results are recorded in Table 1. A mixture of *trans-* and *cis-* isomers was obtained in each case (see later for discussion of stereochemical assignments) and it may be noted that the *trans*:*cis* ratios are very similar for comparable γ-ray and peroxide initiated reactions. A particularly interesting feature of the results, however, is the trend in the *trans*:*cis* ratio which increases very significantly with decreasing ring size.

TABLE 1

Additions of dimethylether to perfluorocycloalkenes

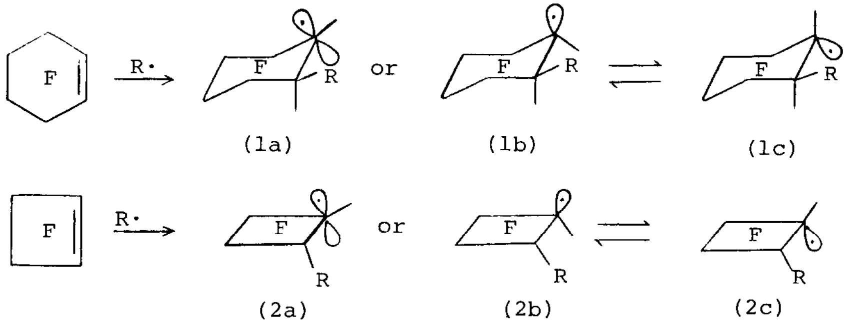
Cycloalkene		% Conversion[a]	Trans/Cis Ratio
	(γ)[b]	74	8.0
	(P)[c]	51	8.0
	(γ)	58	2.0
	(P)	51	1.8
	(γ)	78	0.7
	(P)	73	0.9

[a] Conversions to the 1:1 adduct.

[b] Induced by γ-rays at room temperature.

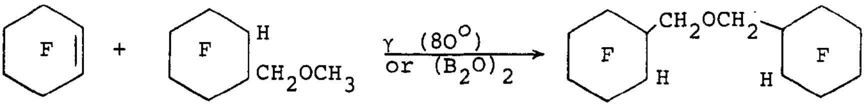
[c] Induced by benzoyl peroxide at ca. 85°C.

E.s.r. spectra of cycloalkylradicals have been interpreted on the basis of planar radical sites [15]. Therefore, the non-stereospecific additions to F-cycloalkenes could be accounted for on the basis of planar intermediate radicals (e.g. 1a, 2a) or through rapid interconversion of tetrahedral intermediates



(e.g. 1b, 1c and 2b, 2c) in which (1a and 2a) are the low-energy transition states. On the basis of results obtained with cyclopropyl systems [16] the effect of a fluorine atom attached at the radical site would probably favour the tetrahedral forms. The significant change in *trans*:*cis* ratio from F-cyclohexene (0.7) to F-cyclobutene (8.0) is most likely an indication that inversion of the cyclobutyl radicals (2b, 2c) is more difficult than the cyclohexyl radicals (1b, 1c). Where highly stereoselective radical addition to double bonds has been observed in hydrocarbon systems, then *anti*-addition is preferred [17]. Therefore, the most reasonable explanation of the trend in stereoselectivity shown in Table 1 is that *anti*-addition to F-cycloalkenes is preferred but the case of inversion of the resultant tetrahedral radical becomes slightly more difficult as ring-size decreases.

In the peroxide induced additions (conducted at 85°C) some of the 2:1 adducts were observed; none of these adducts were detected in the γ-ray induced processes at 18°C but at 80°C, these were formed. Only in the case of F-cyclohexene was this product (3) in sufficient yield (ca. 14%) for isolation.



(3) (14%)

Adducts (4) of dimethylether to F-cycloalkenes obviously react with F-cycloalkenes much less readily than dimethylether itself, even though the $-OCH_3$ group in (4) would seem relatively remote from the polyfluorocycloalkyl group (HR_F in 4). At this stage, it cannot be determined whether the effect of the poly-

$$CH_3OCH_3 \xrightarrow{\text{F-cycloalkene}} \underset{(4)}{H(R_F)CH_2OCH_3} \xrightarrow{\text{F-cycloalkene}} H(R_F)CH_2OCH_2(R_F)$$

fluorocycloalkyl group in (4) is to increase the bond dissociation energy of $-OCH_3$ in (4), relative to dimethylether, or to make the resultant radical more electrophilic, and therefore less reactive, in further reaction with electrophilic F-cycloalkenes. Intuitively, however, we prefer the latter explanation.

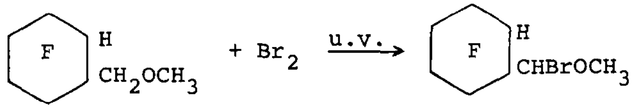
Structure derivation of adducts

In the first paper in this series [1] we described a partial analysis of the F-19 n.m.r. spectrum of the *cis*-isomer of the adduct of acetaldehyde to F-cyclohexene and the observed chemical shifts also agreed with calculated values for this isomer. Also, assignment of stereochemistry to acetaldehyde adducts of F-cyclobutene have been made on the basis of dipole moment measurements [12]. These, relatively firmly assigned structures enabled us to relate the stereochemistry of other adducts through a consideration of F-19 chemical shifts for CFR and CFH positions in the adducts. These correlated completely, the *trans*-isomers having resonances at lower field from the corresponding resonances of the *cis*-isomers.

The F-19 chemical shifts for the dimethylether adducts, shown in Table 2, confirm this approach because there is a correlation with the shifts reported earlier for other adducts [1], on the basis of the assignments given in Table 2. In this case, there is also a good correlation between these assignments and both boiling points and order of retention time on g.l.c. i.e. *cis*-isomers have the higher boiling points and longer retention times.

Further halogenation

We have carried out halogenation studies on a selection of the dimethylether adducts i.e. reactions with bromine, chlorine, and, in one case, cobalt trifluoride. The results are shown below and were, at first sight, very surprising in that



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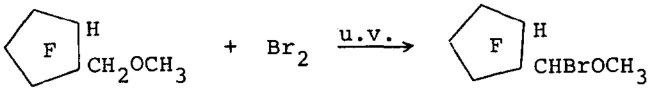
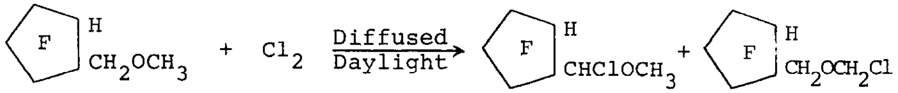


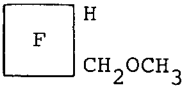
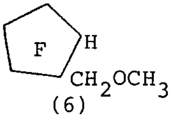
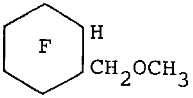
(6) (9)


(6) (10) (11)

Solvent	%	%
neat liquid	9	91
CCl_4	44	56
CS_2	77	23

TABLE 2

^{19}F n.m.r. data for CFR and CFH positions in dimethylether adducts

Adduct	Trans				Cis			
	B.p. (°C)	G.l.c.[a]	$^{19}F\delta$[b]		B.p. (°C)	G.l.c.[a]	$^{19}F\delta$[b]	
			CFR	CFH			CFR	CFH
 (5)	106	1	181	220	124	2	198	222
 (6)	121	1	181	212	127	2	193	227
 (7)	c	c	187	211	c	c	194	234

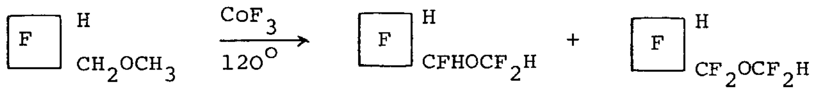
[a] Order of emergence from a column packed with 2-cyanoethylmethylsilicone (Column Z).

[b] p.p.m., measured from $CFCl_3$ as external reference, positive shifts to high field.

[c] Isomers could not be separated by g.l.c. or distilled apart; b.p. of mixture 143°C.

bromination and chlorination results with neat liquids each gave a high level of selectivity but this was reversed from bromination, to chlorination. The most substituted sites in the adducts are the -CFH- positions, which are not attacked by any of the halogenating agents used, and this may be attributed to the fact that the site is electrophilic, because of attached fluorine, therefore inhibiting to attack by electrophilic radicals. The next most substituted site, $-CH_2O-$ is attacked exclusively by bromine; this site will be more electrophilic, because of the attached fluorocarbon group, than $-OCH_3$ and the fact that the more electrophilic chlorine attacks $-OCH_3$ preferentially, may be attributed to this effect. Solvent effects on this reaction are, however, fascinating. Carbon disulphide as solvent is known to 'complex' with chlorine and produce more selective chlorinations while, in previous studies [18] carbon tetrachloride is considered a non-complexing solvent. Clearly, carbon disulphide interacts with chlorine in this system, leading to a less electrophilic radical and more nearly comparable to bromine. It is possible that the relevance of these solvents is that carbon disulphide functions as a weak Lewis acid while, at the other extreme, the neat partly fluorinated ether acts as a weak Lewis base. So far, however, there seems to have been little progress made in the literature at defining the nature of these obviously very important interactions between radical and solvent [19].

Fluorination of di-alkyl ethers have been investigated previously [20] and are usually accompanied by some fragmentation. Fluorination of (5), however, gave very smooth conversion to a mixture of (12) and (13) in high yield. Clearly, the presence of a fluorocarbon group in the molecule has led to a significant moderating effect on the reaction.



$$\boxed{F}\,\overset{H}{\underset{CH_2OCH_3}{}} \xrightarrow[120^{o}]{CoF_3} \boxed{F}\,\overset{H}{\underset{CFHOCF_2H}{}} + \boxed{F}\,\overset{H}{\underset{CF_2OCF_2H}{}}$$

(5) (12) (13)

EXPERIMENTAL

Irradiations by gamma-rays were achieved by exposure at room temperature to a ^{60}Co source, housed in a purpose-built chamber. Analogous reactions using benzoyl peroxide were carried out at 85°C. All addition reactions were performed using glass Carius tubes of ca. 100 cm^3 volume and the reactants were degassed before sealing under vacuum. Reactions of the adducts with chlorine and bromine were carried out using a Pyrex tube (volume ca. 40 cm^3) fitted with a Rotaflo tap and the reactants were degassed before closing the tube. Distillations were carried out using a Fischer-Spaltrohr MS200 apparatus. ^{19}F n.m.r. spectra were recorded with a Varian A56/60D spectrometer; chemical shifts are quoted with reference to external $CFCl_3$ (upfield positive). Isomer and product ratios were obtained from g.l.c. peak area measurements using a Varian Aerograph Model 920 gas density balance detector and the former also from ^{19}F n.m.r. integration of high field signals. Preparative-scale g.l.c. employed a Varian Aerograph Model 920 apparatus using columns packed with 30% silicone gum rubber SE-30 on chromosorb P (Column O), 20% di-isodecyl phthalate on chromosorb P (Column A) or 17% 2-cyanoethyl methyl silicone on the same support (Column Z). Boiling points were recorded by the Siwoloboff method or during distillation at atmospheric pressure and are uncorrected.

Addition to F-cyclohexene

(a) By gamma-ray initiation

A mixture containing F-cyclohexene (13.98 g, 53.4 mmol) and dimethylether (7.57 g, 165 mmol) was irradiated to a total dose of 1.5 x 10^7 rad. After the unchanged dimethylether had been distilled off at room temperature, the liquid remaining was distilled to give 1-methoxymethyl-2-hydro-decafluorocyclohexane (7) (12.78 g, 78%) as a mixture of isomers which could not be resolved during distillation or by any of the g.l.c. columns available (Found: C, 31.3; H, 2.3; F, 61.5%. Calc. for $C_8H_6F_{10}O$: C, 31.17; H, 1.95; F, 61.69%), b.p. 143°C.

(b) By benzoyl peroxide initiation

A mixture containing F-cyclohexene (15.4 g, 58.8 mmol), dimethylether (6.77 g, 147 mmol) and benzoyl peroxide (0.38 g) was heated at 85°C for 68 hours. Distillation as above gave (7) (10.2 g, 56%), b.p. 143°C, and from the pot residue a further amount of this compound (3.15 g, 17%) was separated by preparative-scale g.l.c. (Column Z, 200°C) as well as di-[(2'H-decafluorocyclohexyl)-methyl]-ether (3) (2.29 g, 14%) as an isomer mixture (Found: C, 29.6; H, 0.9; F, 66.3%. Calc. for $C_{14}H_6F_{20}O$: C, 29.47; H, 1.05; F, 66.66%), m.p. 81°C.

Addition to F-cyclopentene

(a) By gamma-ray initiation

A mixture containing F-cyclopentene (10.50 g, 49.5 mmol) and dimethylether (6.87 g, 149 mmol) was irradiated to a dose of 1.5×10^7 rad. After the unchanged dimethylether had been distilled off at room temperature, the remaining liquid was distilled to give 1-methoxymethyl-2-hydro-octafluorocyclopentane (6) (7.4 g, 58%) whose isomers could not be clearly separated during the distillation. Samples of the isomers were separated by preparative-scale g.l.c. (Column A, 145°C) and identified as, in order of elution, trans-1-methoxymethyl-2-hydro-octafluorocyclopentane (6, trans) (nc), b.p. 121°C, and cis-1-methoxymethyl-2-hydro-octafluorocyclopentane (6, cis) (nc), b.p. 127°C. The isomers were analysed as a mixture (Found: C, 32.4; H, 2.6; F, 58.7%. Calc. for $C_7H_6F_8O$: C, 32.56; H, 2.32; F, 58.91%).

(b) By benzoyl peroxide initiation

A mixture containing F-cyclopentene (10.3 g, 48.6 mmol), dimethylether (7.23 g, 157 mmol) and benzoyl peroxide (0.26 g) was heated at 85°C for 68 hours. Distillation as before gave (10) (6.33 g, 51%) as an isomer mixture and the two-to-one adduct was detected by mass spec./g.l.c. in the pot residue but not separated.

Addition to F-cyclobutene

(a) By gamma-ray initiation

A mixture containing F-cyclobutene (14.9 g, 93 mmol) and dimethylether (11.0 g, 239 mmol) was irradiated to a total dose of 1.23 x 10^7 rad. After the unchanged starting materials had been distilled off at room temperature, the liquid remaining was distilled to give 1-methoxymethyl-2-hydro-hexafluorocyclobutane (5) (14.20 g, 74%) whose isomers could not be cleanly separated during the distillation. Samples of the isomers were separated by preparative-scale g.l.c. (Column A, 135°C) and identified as, in order of elution, trans-1-methoxymethyl-2-hydro-hexafluorocyclobutane (5, trans) (nc), b.p. 106°C, and cis-1-methoxymethyl-2-hydro-hexafluorocyclobutane (5, cis) (nc), b.p. 124°C. The isomers were analysed as a mixture (Found: C, 34.4; H, 3.2; F, 54.5%. Calc. for $C_6H_6F_6O$: C, 34.62; H, 2.88; F, 53.85%).

(b) By benzoyl peroxide initiation

A mixture containing F-cyclobutene (11.9 g, 73.5 mmol), dimethylether (8.17 g, 178 mmol) and benzoyl peroxide (0.27 g) was heated at 80°C for 64½ hours. Distillation as above gave (5) (7.88 g, 5.1%) as an isomer mixture and the two-to-one adduct was detected by mass spec./g.l.c. in the pot residue but not separated.

Gamma-ray initiated reaction of 1-methoxymethyl-2-hydro-decafluorocyclohexane (7) with F-cyclohexene at 80°C

A mixture containing (7) (3.50 g, 11.4 mmol) and F-cyclohexene (1.7 g, 6.5 mmol) was irradiated to a total dose of 1.2 x 10^7 rad whilst being heated at 80°C. Volatile liquid (3.53 g) was gently evaporated from the reaction mixture at reduced pressure to leave a residue which was sublimed to give a white solid, identified by mass spectrometry as (3) (0.57 g, 15%). No addition occurred when a similar reaction was performed at room temperature.

Halogenation experiments

(a) Chlorination of 1-methoxymethyl-2-hydro-octafluorocyclopentane (6)

(i) Using no solvent. The tube containing a mixture of (6) (3.49 g, 13.5 mmol) and chlorine (1.10 g, 15.5 mmol) was wrapped in aluminium foil and kept in a dark place overnight. The colour due to chlorine persisted when the mixture was examined the following day but on allowing to stand in daylight the colour due to chlorine rapidly disappeared. A colourless liquid (3.92 g) was recovered which contained (6) and two major products. The latter were separated by preparative-scale g.l.c. (Column O, 190°C) and identified as, in order of elution, 1-methoxychloromethyl-2-hydro-octafluorocyclopentane (10) (0.2 g, 5%) as a mixture of isomers (Found: C, 29.0; H, 2.0; Cl, 12.5; F, 51.5%. Calc. for $C_7H_5ClF_8O$: C, 28.72; H, 1.71; Cl, 12.14; F, 51.97%) and 1-chloromethoxymethyl-2-hydro-octafluorocyclopentane (11) (2.00 g, 51%) as a mixture of isomers (Found: C, 29.0; H, 2.0; Cl, 12.5; F, 51.5%. Calc. for $C_7H_5ClF_8O$: C, 28.72; H, 1.71; Cl, 12.14; F, 51.97%), b.p. 163°C.

(ii) Using carbon tetrachloride as solvent. A mixture containing (6) (1.35 g, 5.3 mmol), chlorine (0.52 g, 7.4 mmol) and carbon tetrachloride (3.79 g, 24.3 mmol) was allowed to stand in daylight for several hours during which time the colour due to chlorine disappeared. From g.l.c. peak area measurements (Column O, 200°C), the ratio of (11):(10) in the reaction mixture was 56:43.

(iii) Using carbon disulphide as solvent. A mixture containing (6) (0.90 g, 3.5 mmol), chlorine (0.61 g, 9 mmol) and carbon disulphide (2.62 g, 34.5 mmol) was allowed to stand in daylight for several hours during which time the colour due to chlorine disappeared. From g.l.c. peak area measurements (Column O, 220°C), the ratio of (11):(10) in the reaction mixture was 23:77.

(b) Bromination of 1-methoxymethyl-2-hydro-octafluorocyclopentane (6)

A mixture containing (6) (4.41 g, 17.1 mmol) and bromine (3.70 g, 23.1 mmol) was irradiated for 2½ hours by an Hanovia high-pressure mercury vapour lamp. The liquid recovered (5.92 g) contained (6) and one major product, a sample of which was isolated by preparative-scale g.l.c. (Column O, 200°C) and identified as 1-methoxybromomethyl-2-hydro-octafluorocyclopentane (9) as a mixture of isomers (Found: C, 25.2; H, 1.5; Br, 24.4; F, 44.5%. Calc. for $C_7H_5BrF_8O$: C, 24.93; H, 1.48; Br, 23.74; F, 45.10%), b.p. 164°C.

(c) Bromination of 1-methoxymethyl-2-hydro-decafluorocyclohexane (7)

A mixture containing (7) (6.06 g, 19.7 mmol) and bromine (3.61 g, 22.6 mmol) was irradiated for $1^3/4$ hours by an Hanovia high-pressure mercury vapour lamp. Distillation of the recovered liquid gave the major product, identified as 1-methoxybromomethyl-2-hydro-decafluorocyclohexane (8) (5.88 g, 77%) as an isomer mixture (Found: C, 24.7; H, 1.1; Br, 21.3; F, 48.7%. Calc. for $C_8H_5BrF_{10}O$: C, 24.81; H, 1.29; Br, 20.67; F, 49.10%), b.p. 183°C.

(d) Fluorination of 1-methoxymethyl-2-hydro-hexafluorocyclobutane (5)

Compound (5) (4.32 g, 20.8 mmol) was passed dropwise in a stream of nitrogen (50 cm^3/min.) over a bed of cobalt trifluoride heated to 120°C during $1^3/4$ hours. After purging for a further half hour, a total of 4.3 g of colourless liquid was collected and found to be a mixture of two products. These were separated by preparative-scale g.l.c. (Column O, 110°C) and identified as, in order of elution, 1-difluoromethoxydifluoromethyl-2-hydro-hexafluorocyclobutane (13) (0.46 g, 8%) as an isomer mixture (Found: C, 25.9; H, 1.1. Calc. for $C_6H_2F_{10}O$: 25.71; H, 0.71%), b.p. 87°C, and 1-difluoromethoxyfluoromethyl-2-hydro-hexafluorocyclobutane (12) (0.92 g, 17%) as an isomer mixture (Found: C, 27.6; H, 1.1; F, 65.5%. Calc. for $C_6H_3F_9O$: C, 27.48; H, 1.15; F, 65.27%), b.p. 107°C.

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