PARTIALLY FLUORINATED HETEROCYCLIC COMPOUNDS.   PART 15 [1].
FURTHER PREPARATIONS OF FURAN DERIVATIVES FROM PENTAFLUORO-
PHENYL- AND 1,3,4,5,6,7,8-HEPTAFLUORO-2-NAPHTHYL PROP-2-YNYL
ETHERS.   THE ISOLATION OF THE CLAISEN REARRANGEMENT INTER-
MEDIATE 1,3,4,5,6,7,8-HEPTAFLUORO-1-(PROPA-1,2-DIENYL)-
NAPHTHALEN-2-ONE

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SUMMARY

    1,3,4,5,6,7,8-Heptafluoro-2-naphthyl prop-2-ynyl ether (5)
and boiling isopropylbenzene gives 1,3,4,5,6,7,8-heptafluoro-
1-(propa-1,2-dienyl)naphthalen-2-one (9) and two isomeric 2-
(isopropylbenzyl)-4,5,6,7,8,9-hexafluoronaphtho[2,1-b]furans
(11).   Di-(4,5,6,7,8,9-hexafluoronaphtho[2,1-b]furan-2-ylmethyl)
ether (17) and bis-(4,5,6,7,8,9-hexafluoronaphtho[2,1-b]furan-
2-yl)methane (18) are formed from (5) in $CF_2ClCFCl_2$ at 137°.
The solvolysis of 2-fluoromethyl-4,5,6,7,8,9-hexafluoronaphtho-
[2,1-b]furan (10) in water at 145-156° yields (17) (2%), (18)
(37%) and 4,5,6,7,8,9-hexafluoronaphtho[2,1-b]furan-2-ylmethyl
alcohol (19) (13%).   Pentafluorophenyl prop-2-ynyl ether (1)
reacts in either C_6F_6 or $CF_2ClCFCl_2$ at 140° to give di-(4,5,6,7-
tetrafluorobenzo[b]furan-2-ylmethyl) ether (15).   The major
product from the solvolysis of 2-fluoromethyl-4,5,6,7-tetra-
fluorobenzo[b]furan (2) in water at 140-142° is 4,5,6,7-tetra-
fluorobenzo[b]furan-2-ylmethyl alcohol (16) (87%) accompanied
by (15) (2.5%).

INTRODUCTION

In an earlier paper in this series, we described the flash vapour phase isomerisation of pentafluorophenyl prop-2-ynyl ether (1) at 370° to 2-fluoromethyl-4,5,6,7-tetrafluoro-benzo[b]furan (2) and the reactions of (1) with benzene at 140°, and with p-xylene at reflux temperature to give the furan derivatives (3) and (4) respectively [2]. 1,3,4,5,6,7,8-
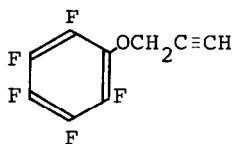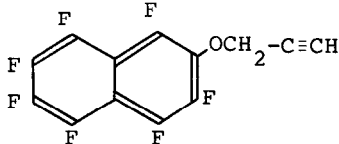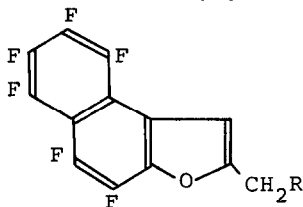

(1)
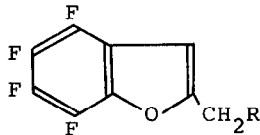
(2) R = F
(3) R = Ph
(4) R = 2,5-Me$_2$C$_6$H$_3$

(5)

(6) R = Ph
(7) R = 2,5-Me$_2$C$_6$H$_3$

Heptafluoro-2-naphthyl prop-2-ynyl ether (5) reacted similarly, but more efficiently, with benzene and with p-xylene to give compounds (6) and (7) respectively [2]. The formation of all these products was rationalised in terms of two plausible but indistinguishable reaction mechanisms involving the respective Claisen rearrangement intermediates (8) and (9): (i) a homolytic cleavage of the C-F bond; and
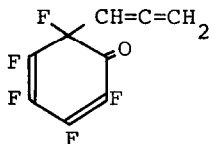
(8)
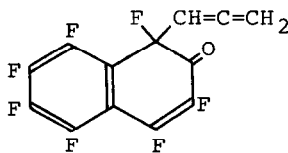
(9)
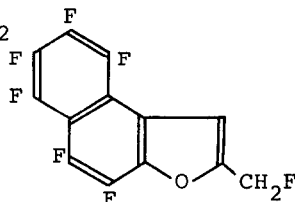
(10)

(ii) a heterolytic cleavage of the C-F bond occurring synchronously with cyclisation. These mechanisms are illustrated in Scheme 1 for compound (9).

Mechanism (i)

(9)

etc.

ArH

CH_2Ar + HF

ArH

etc.

Mechanism (ii)

(9)

SCHEME 1

In this Paper we describe the reaction of (5) with isopropyl-benzene, a molecule which could give products which might dif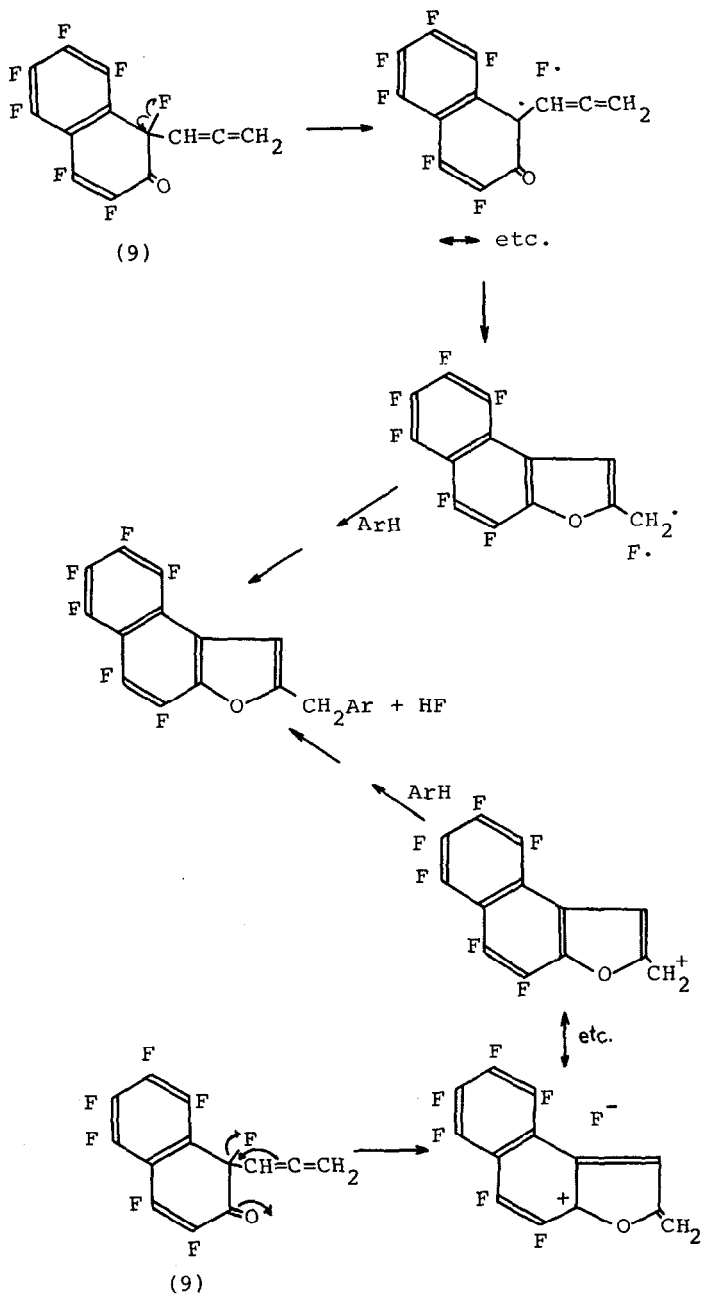ferentiate between the two reaction mechanisms proposed. The attempted isomerisations of (1) to (2) and of (5) to 2-fluoromethyl-4,5,6,7,8,9-hexafluoronaphtho[2,1-b]furan (10) in inert solvents are also described.

RESULTS AND DISCUSSION

1,3,4,5,6,7,8-Heptafluoro-2-naphthyl prop-2-ynyl ether (5) heated in refluxing isopropylbenzene for 24 hrs. gave the Claisen rearrangement product 1,3,4,5,6,7,8-heptafluoro-1-(propa-1,2-dienyl)naphthalen-2-one (9) (10%) and a mixture containing at least two isomers of the furan derivative (11)

(11)   (12)
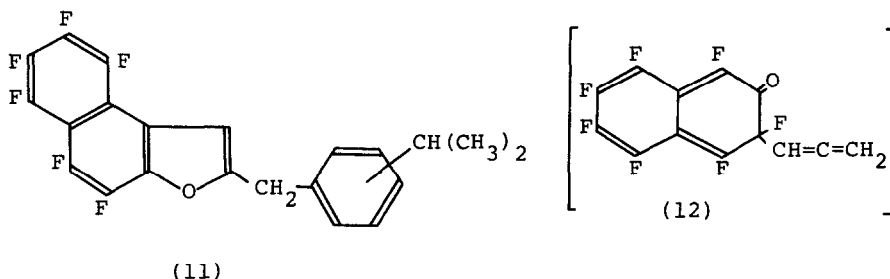
(42%). The structure of (9) was assigned on the basis of its ^{1}H and [19]F n.m.r. spectra and was distinguishable from the isomer (12) because of the presence of only <u>one</u> large <u>peri</u> J_{F-F} coupling constant ($J_{F-4,F-5}$ 68 Hz) [compound (12) would have had two large <u>peri</u> J_{F-F} values]. The [1]H n.m.r. spectrum of the mixture of furan derivatives (11) had absorptions for the 2-CH_2 and 3-H protons at similar values to those found previously for (6) and (7), but the presence of two isomers was deduced from the two singlet absorptions in the region for the 2-CH_2 protons: (2 parts at δ 4.14 and 1 part at δ 4.23). These absorptions <u>could</u> overlap that of the third possible isomer, though chromatography on silica failed to resolve the mixture. One isomer, having the 2-CH_2-protons at δ 4.14 was obtained pure by recrystallisation.

The [1]H n.m.r. of the crude reaction product was examined for products which could arise from a free radical reaction with the tertiary hydrogen of the isopropylbenzene, namely: compounds (13) and (14), their formation being determined by the particular sequence of the radical reactions (Scheme 2).
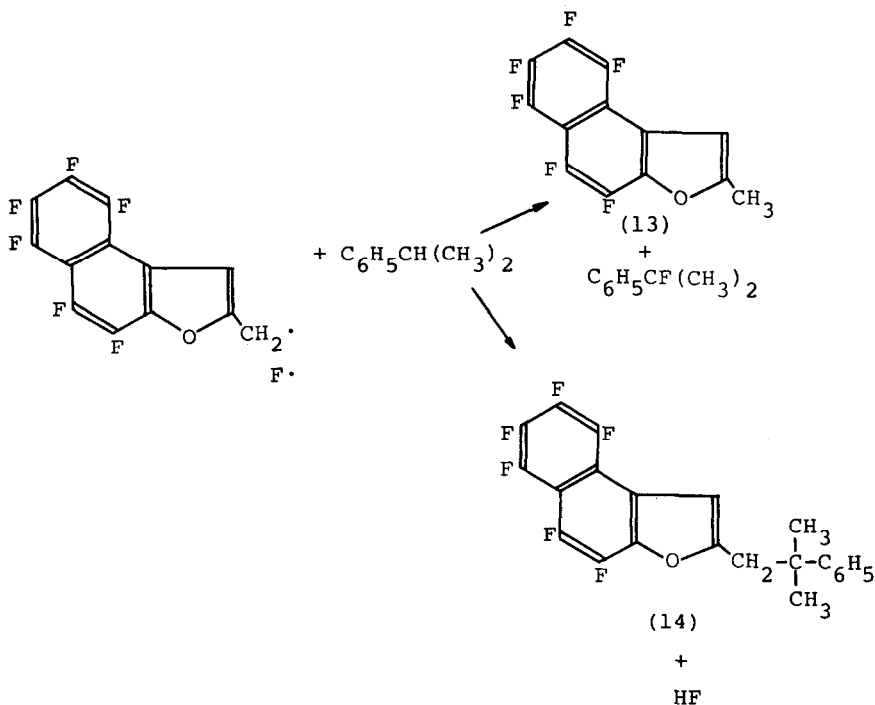
SCHEME 2

No sharp singlet absorptions were found in the high field region, which would be a feature of these compounds. Moreover, a careful [19]F n.m.r. examination of the recovered solvent did not reveal any fluorine incorporation. These results do not rule out a radical reaction for the initial cyclisation reaction, however, since it is not possible to predict the competitiveness of these reactions over radical substitution of the aromatic hydrogens.

We have re-examined the reactions of the prop-2-ynyl ether (5) with benzene and with p-xylene [2] and have found the

naphthalenone (9) (26%) in addition to the products described
previously, with benzene, but (9) was not detected in the
reaction with p-xylene.

Previously [2], the isomerisation of pentafluorophenyl
prop-2-ynyl ether (1) to 2-fluoromethyl-4,5,6,7-tetrafluoro-
benzo[b]furan (2) had been observed in a flash vapour-phase
pyrolysis reaction at 370° and it was of interest to
investigate the possibility of effecting the same transformation
in the liquid phase at much lower temperatures. Hexafluoro-
benzene was the first inert solvent to be used with the ether
(1) in a reaction carried out in a sealed tube at 140° for
118 hrs. Extensive decomposition occurred, hydrogen fluoride
was evolved from the reaction mixture, and the only product
isolated was di-(4,5,6,7-tetrafluorobenzo[b]furan-2-ylmethyl)
ether (15) (8%), a compound which was synthesised independently

(15)   (16)
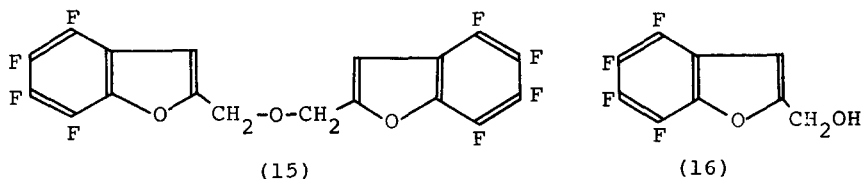
from 2-bromomethyl-4,5,6,7-tetrafluorobenzo[b]furan [3] and
sodium hydroxide solution (68% yield).

The obvious explanations for the formation of (15) and
the absence of the 2-fluoromethyl compound (2) was that either
water had been present during the reaction, or that any 2-
fluoromethyl compound formed in the reaction had been converted
into (15) during the work-up procedure. In order to test the
first of these possibilities the reaction was repeated with
rigorous precautions being taken to exclude water from the
reacting system. Using $CF_2ClCFCl_2$ as solvent the ether (1),
heated in a sealed tube at 140° for 119 hrs. underwent
extensive decomposition but only 45% of the reactant was
consumed. Surprisingly however, the ether (15) was again
formed [11% based on the consumption of (1)].

When the 2-fluoromethyl compound (2) was treated with
water in a sealed tube at 140 - 142° for 120 hrs., the
alcohol (16) was the major product (87%), accompanied by only

a small amount of ether (15) (2.5%). The HF produced during
this hydrolysis could act autocatalytically [4], with compound
(16) subsequently competing increasingly with water in the
solvolysis reaction to give (15). The HF could also catalyse
the self-condensation of (16) to the ether (15), since an
independent experiment with (16) and a vast excess of dilute
sulphuric acid in a sealed tube at 140° for 19 hrs. gave (15)
[5% based on 86% consumption of (16)] accompanied by extensive
decomposition products. Water had no effect at room temperature
on a solution of the 2-fluoromethyl compound (2) in anhydrous
$CF_2ClCFCl_2$ which had been saturated with HF, so that none of
compound (15) could have been formed from (1) via (2) during
the work-up procedure.

We now propose that water is actually _generated_ in the
reaction of (1) in the inert solvent. Hydrogen fluoride
formed during the decomposition of the reaction mixture would
attack the glass walls of the reaction vessel and generate
water. Consequently, the anhydrous environment of the reacting
system would be vitiated as the reaction proceeded. The
homolytic mechanism for the reaction of (8) would require the
prior formation of (2) for reaction with water to give (15),
though this would not be necessary if a heterolytic mechanism
operated.

1,3,4,5,6,7,8-Heptafluoro-2-naphthyl prop-2-ynyl ether (5)
heated in $CF_2ClCFCl_2$ in a sealed tube at 137° for 24 hrs.
[special attention having been paid to exclude all traces of
water from the reacting system] gave the naphthalenone (9)
slightly contaminated with unreacted ether (5), (12%), di-
(4,5,6,7,8,9-hexafluoronaphtho[2,1-b]furan-2-ylmethyl) ether
(17) (29%) and a totally unexpected product: bis-(4,5,6,7,8,9-

(17).

F F F F F F F F F F F F F F F F F F CH₂ O O F CH₂OH

(18)   (19)
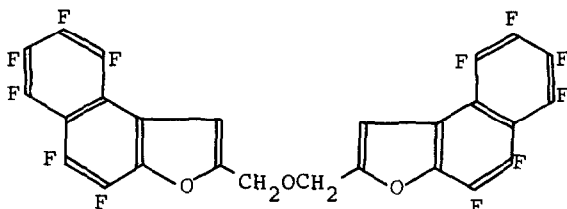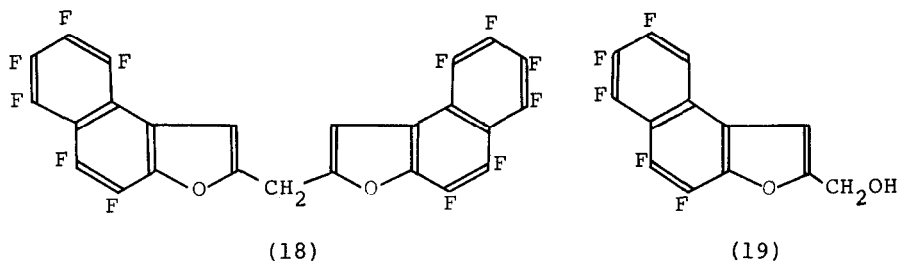
hexafluoronaphtho[2,1-b]furan-2-yl)methane (18) (25%). The
structures of (17) and (18) were assigned on the basis of
their simple [1]H n.m.r. spectra.

2-Fluoromethyl-4,5,6,7,8,9-hexafluoronaphtho[2,1-b]furan
(10), which was available from other work [5], when heated in
a sealed tube with water at 143 - 148° for 24 hrs. was only
partially consumed (52%) and gave the primary alcohol (19)
(56%) and the ether (17) (7%). However, under more forcing
conditions (145 - 156° over 39 hrs.), in addition to the
alcohol (19) (13%) and the ether (17) (2%), the major product
was the methane derivative (18) (37%). The formation of (17)
can be rationalised by invoking processes exactly analogous
to the ones described above for the formation of the ether (15)
from the 2-fluoromethyl compound (2), while the formation of
(18) is proposed to take place by the mechanism shown in
Scheme 3. The formation of the symmetrical methane derivative
is in accordance with the preferred electrophilic attack at the
2-position of a benzo[b]furan derivative [6], while the dis-
placement of formaldehyde (not detected experimentally) can be
related to the reverse reaction of this compound with aromatic
hydrocarbons in the presence of Lewis acids [7].

The conversion of compound (5) into the ether (17) and
the methane derivative (18) under initially anhydrous
conditions in $CF_2ClCFCl_2$ can be understood once more in terms
of the intervention of water produced during the progress of
the experiment as proposed earlier. Surprisingly, no product
analogous to the methane derivative (18) was found in the
solvolysis of 2-fluoromethyl-4,5,6,7-tetrafluorobenzo[b]furan
(2).

SCHEME 3

EXPERIMENTAL

Chemical shifts δ_H in the ^{1}H n.m.r. spectra are down-field from internal TMS. Chemical shifts δ_F are upfield from internal $CFCl_3$ reference. Thick layer chromatography separations were carried out on plates [silica (20 g), 18 x 18 cm.]. All descriptions of chromatographic separations follow the sequence in which the components were eluted, starting with the fastest moving component.

The reaction of 1,3,4,5,6,7,8-heptafluoro-2-naphthyl prop-2-ynyl ether (5) with isopropylbenzene

The ether (5) (1.48 g) and isopropylbenzene (10 ml) were heated under reflux for 24 h. The excess solvent was distilled in vacuo at 0.05 mm from the very dark product and was shown by F.T. ^{19}F n.m.r. spectroscopy (3000 scans) to contain no fluorine-containing material. The residue was partially separated by chromatography (silica, 90 x 2.5 cm, CHCl$_3$/CCl$_4$ 1:1 ^{V}/v), and the least strongly retained components were further separated by thick layer chromatography (CCl$_4$) and sublimation at 70°/0.05 mm to give two fractions: (i) 0.819 g and (ii) the sublimate (0.151 g). Fraction (i) was a mixture of at least two 2-(isopropylbenzyl)-4,5,6,7,8,9-hexafluoro-naphtho[2,1-b]furan compounds (11), present in the ratio of 2:1 as shown by the only non-overlapping signals at δ_H 4.14 and 4.23 p.p.m. respectively in the ^{1}H n.m.r. spectrum. Recrystallisation of this sample from petroleum ether [b.p. 40-60°] gave a <u>pure isomer</u>, m.p. 76.5 - 77.5° [Found: C, 64.9; H, 3.2; M$^+$, 408. C$_{22}$H$_{14}$F$_6$O requires C, 64.7; H, 3.5%; M, 408]. δ_F (CDCl$_3$) 144.0 - 145.9 (broad multiplet), 150.4 (multiplet), and 156.3 - 158.1 p.p.m. (broad multiplet) in the ratio 2:1:3 respectively; δ_H (CDCl$_3$) 1.26 (doublet 2 x CH$_3$), 2.88 (heptet, CH), 4.14 (singlet CH$_2$); 6.90 (multiplet 3-H), and 7.17 p.p.m. (singlet C$_6$H$_4$).

Fraction (ii) was recrystallised from petroleum ether [b.p. 40 - 60°] to give <u>1,3,4,5,6,7,8-heptafluoro-1-(propa-1,2-dienyl)naphthalen-2-one</u> (9), m.p. 81.0 - 81.5° [Found: C, 50.7; H, 1.0; M$^+$ 308. C$_{13}$H$_3$F$_7$O requires C, 50.7; H, 1.0%; M$^+$ 308]. δ_F (CDCl$_3$) 111.3; 142.3 (F-4); 144.2; 145.7 (F-5); 155.0; 155.9; and 158.3 p.p.m.; $J_{(F-4,F-5,peri)}$ 68 Hz. δ_H (CDCl$_3$) 4.96 (sharp multiplet, =CH$_2$), 6.88 p.p.m. (doublet, -CH=); $J_{(F-1,H-1)}$ 12 Hz.

The reactions of pentafluorophenyl prop-2-ynyl ether (1) in inert solvents

(i) In hexafluorobenzene. The ether (1) (4.18 g) and hexafluorobenzene (20 ml) were sealed in vacuo in a Carius tube (capacity 50 ml) and heated at 140° for 118 h. The reaction product was black and evolved HF. The solvent was evaporated in vacuo and the residue was chromatographed on silica (90 x 2.4 cm, CCl_4) to give a liquid (0.65 g) which later solidified. The i.r. spectra of the liquid and of a nujol mull of the solid were different* though solutions of the two samples in CS_2 had identical i.r. spectra. Sublimation of the solid at 80 - 90°/0.05 mm and recrystal- lisation from petroleum ether (b.p. 30 - 40°) gave di-(4,5,6,7- tetrafluorobenzo[b]furan-2-ylmethyl) ether (15), m.p. 55.5 - 56.5° [Found: C, 51.5; H, 1.2; M^+ 422. $C_{18}H_6F_8O_3$ requires C, 51.2; H, 1.4%; M, 422]. δ_F [$CDCl_3$] 147.3 (multiplet), 160.5 to 161.8 (broad multiplet), 164.1 p.p.m. (multiplet) with intensities in the ratio 1:2:1 respectively. δ_H[$CDCl_3$] 4.74 (singlet, two equivalent CH_2), 6.89 p.p.m. (multiplet, two equivalent 3-H).

(ii) In $CF_2ClCFCl_2$. The Carius tube was 'flamed-out' in vacuo and then filled at room temperature with nitrogen. The ether (1) (10.0 g) was placed in the tube and $CF_2ClCFCl_2$ (20 ml) was transferred in vacuo from P_2O_5 into the tube which was then sealed, and heated at 140° for 119 h. The products of the reaction, separated as in the previous experiment,were identified by i.r. and consisted of unreacted starting material (1) (5.52 g) and the ether (15) (0.46 g).

The hydrolysis of 2-bromomethyl-4,5,6,7-tetrafluorobenzo[b]- furan with aqeuous sodium hydroxide

The 2-bromomethyl compound [3] (1.45 g) and aqueous sodium hydroxide (20 ml, 2.5M) were heated under reflux for 18.5 h. The mixture was acidified with hydrochloric acid (2M),

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* Several examples of this phenomenon were found with compounds described in this paper. Some examples involved two solid samples, though their spectra in solution were always identical.

extracted with ether, the extracts dried (MgSO$_4$) and solvent
evaporated. The residue was separated by chromatography
(silica, 2.4 x 40 cm, CHCl$_3$/CCl$_4$ 1:1 ^{V}/v) to give the ether
(15) (0.75 g) identified by i.r.

The hydrolysis of 2-fluoromethyl-4,5,6,7-tetrafluorobenzo[b]-furan (2) with water

The 2-fluoromethyl compound (2) (0.1223 g) and water
(1.5 ml) were sealed under nitrogen in a Carius tube (2½" x ½")
and heated at 140 - 142° for 120 h. The contents of the tube
were extracted with ether, the extracts dried (MgSO$_4$) and the
solvent evaporated. The residue was separated by thick layer
chromatography (CHCl$_3$/CCl$_4$ 1:1 ^{V}/v) to give the ether (15)
(0.0030 g) (2.5%) identified by i.r., and 4,5,6,7-tetrafluoro-benzo[b]furan-2-ylmethyl alcohol (16) (0.1052 g) (87%), m.p.
51.5 - 52.5^O (after sublimation at 60°/0.05 mm). [Found: C,
49.1; H, 1.8; M$^+$ 220. C$_9$H$_4$F$_4$O$_2$ requires C, 49.1; H, 1.8%;
M$^+$ 220]. δ_F (CDCl$_3$) 147.2 (multiplet), 160.0 - 161.2 (broad
multiplet); 163.2 (multiplet) with intensities in the ratio
1:2:1 respectively. δ_H (CDCl$_3$) 2.40 (broad singlet, OH); 4.72
(singlet CH$_2$); 6.70 p.p.m. (multiplet, 3-H).

The acid-catalysed conversion of 4,5,6,7-tetrafluorobenzo[b]-furan-2-ylmethyl alcohol (16) to the ether (15)

The alcohol (16) (0.0994 g) and sulphuric (2 ml, 1M) were
heated in a Carius tube (2½" x ½") at 140° for 19 h. The
products, separated as in the previous experiment were
identified by i.r. and consisted of unchanged alcohol (16)
(0.0137 g) and the ether (15) (0.0040 g).

The reaction of 1,3,4,5,6,7,8-heptafluoro-2-naphthyl prop-2-ynyl ether (5) in CF$_2$ClCFCl$_2$

In this experiment, the Carius tube was initially baked in
an oven at ca. 120°, evacuated while hot, and then filled with
nitrogen at room temperature. The ether (5) (0.726 g) was
introduced into the tube which was then evacuated, and dry
CF$_2$ClCFCl$_2$ (20 ml) introduced by distillation from P$_2$O$_5$ using

a vacuum-line technique. The tube was sealed in vacuo and
heated at 137° for 24 h. The solvent was evaporated and the
residue sublimed at 50°/0.05 mm to give a solid (0.089 g),
identified by i.r. as the naphthalenone (9) slightly
contaminated with the unreacted ether (5). The solid remaining
was separated by thick layer chromatography (CHCl$_3$/CCl$_4$ 3:7 ^{V}/v)
into two fractions: (i) 0.166 g and (ii) 0.206 g. Fraction
(i), recrystallised from toluene was bis-(4,5,6,7,8,9-hexa-
fluoronaphtho[2,1-b]furan-2-yl)methane (18), m.p. 220.5 -
221.5° (Found: C, 53.4; H, 0.4; M$^+$ 564. C$_{25}$H$_4$F$_{12}$O$_2$ requires
C, 53.2; H, 0.7%; M$^+$ 564). δ_F (C$_6$D$_6$ at 85°) 144.0 - 146.6
(broad multiplet); 149.4 (multiplet); 156.8 - 159.0 p.p.m.
(broad multiplet) in the ratio 2:1:3 respectively; δ_H (C$_6$D$_6$ at
85°) 3.88 (singlet, CH$_2$) 6.85 p.p.m. (multiplet, 2 x 3-H).
Fraction (ii), recrystallised from petroleum ether [b.p. 100 -
120°] was di-(4,5,6,7,8,9-hexafluoronaphtho[2,1-b]furan-2-yl
methyl) ether (17), m.p. 159.5 - 160° (Found: C, 52.5; H, 0.9;
M$^+$ 594. C$_{26}$H$_6$F$_{12}$O$_3$ requires C, 52.5; H, 1.0%; M$^+$ 594). δ_F
(CDCl$_3$) 143.9 - 145.9 (broad multiplet); 148.7 (multiplet);
155.5 - 157.9 p.p.m. (broad multiplet) in the ratio 2:1:3
respectively; δ_H (CDCl$_3$) 4.87 (singlet, 2 x CH$_2$); 7.33 p.p.m.
(2 x 3-H).

The hydrolysis of 2-fluoromethyl-4,5,6,7,8,9-hexafluoronaphtho-
[2,1-b]furan (10)

     (i) The 2-fluoromethylcompound [5] (10) (0.0917 g) and
water (1 ml) were sealed under nitrogen in a Carius tube (2½"
x ½") and heated at 143 - 148° for 24 h. The contents of the
tube were extracted with ether, the extracts dried (MgSO$_4$) and
the solvent evaporated. The residue was separated by thick
layer chromatography (one plate, CHCl$_3$/CCl$_4$ 1:1 ^{V}/v) to give
two fractions. The first fraction was a mixture of two
components from which was sublimed (50°/0.01 mm) unreacted
starting material (10) (0.044 g), the residue being the ether
(17) (0.0033 g). Both compounds were identified by i.r. The
second fraction (0.0268 g) was sublimed at 96°/0.01 mm and
recrystallised from petroleum ether [b.p. 60-80°] with cooling
to give 4,5,6,7,8,9-hexafluoronaphtho[2,1-b]furan-2-ylmethyl
alcohol (19), m.p. 98.5 - 99° (Found: C, 51.1; H, 0.9; M$^+$

306. $C_{13}H_4F_6O_2$ requires C, 51.0; H, 1.3%; M^+ 306). δ_F (CDCl$_3$) 144.2 - 146.0 (broad multiplet); 149.2 (multiplet); and 155.8 - 158.0 p.p.m. (broad multiplet) in the ratio 2:1:3 respectively. δ_H (CDCl$_3$) 2.28 (singlet, OH); 4.87 (singlet, CH$_2$); and 7.20 (multiplet, 3-H).

(ii) Compound (10) (0.1726 g) and water (1.5 ml) were sealed under nitrogen in a Carius tube (2½" x ½") and heated at 145 - 156° for 39 h. The crude product was isolated as in the previous experiment and separated by thick layer chromatography (CHCl$_3$/CCl$_4$ 1:1 ^{V}/v) to give the methane derivative (18) (0.0591 g), the ether (17) (0.0033 g) and the alcohol (19) (0.0220 g), each compound being identified by i.r.

ACKNOWLEDGEMENT

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