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PARTIALLY FLUORINATED HETEROCYCLIC COMPOUNDS. PART 17 [1]. THE PREPARATION OF FUSED 2H-PYRAN DERIVATIVES FROM POLYFLUOROARYL AND -HETEROARYL PROP-2-ENYL ETHERS WITH POTASSIUM FLUORIDE VIA AN ELECTROCYCLISATION REACTION. A NOVEL [1,5] SIGMATROPIC PROTON SHIFT DURING THE REACTION OF PENTAFLUOROPHENYL PROP-2-ENYL SULPHIDE WITH POTASSIUM FLUORIDE

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SUMMARY

A new synthesis of fused 2H-pyran derivatives via an electrocyclisation reaction is described which is based on a novel route to o-quinomethide-type precursors. These transient materials are formed by the dehydrofluorination (with KF) in dipolar aprotic solvents of the Claisen rearrangement intermediates produced by the thermolyses of polyfluoroaryl and -heteroaryl prop-2-enyl ethers. 5,6,7,8-Tetrafluoro-2H-1-benzopyran (4) is formed from the C_6F_5-ether (1) in refluxing DMF while 5,6,7,8,9,10-hexafluoro-2H-naphtho[2,1-b]pyran (6) is obtained from the 2-naphthyl ether (5) in sulpholane at 155-162°. The 2,4,5,6-tetrafluoro-3-pyridyl ether (8) in sulpholane at 182° gave a mixture of 6,7,8-trifluoro-2H-pyrano[3,2-b]pyridine (10) (34%) and 5,6,8-trifluoro-2H-pyrano[2,3-c]pyridine (12) (1%), but 2,3,5,6-tetrafluoropyridyl ether underwent dealkylation to the 4-hydroxypyridine. The o-quinodimethide intermediate from pentafluorophenylprop-2-enyl sulphide (13) isomerised via a novel [1,5] sigmatropic proton shift before cyclisation to 4,5,6,7-tetrafluoro-2-methylbenzo[b]thiophen (14).

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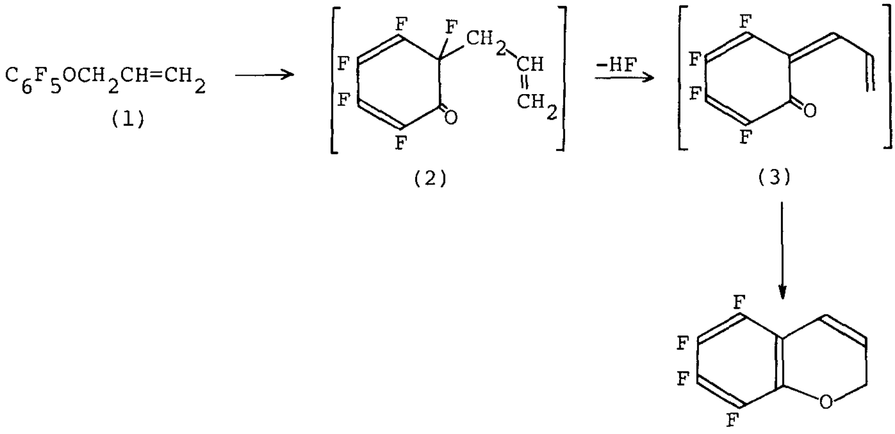
INTRODUCTION

In an earlier paper [2], a potentially simple route to 5,6,7,8-tetrafluoro-2H-1-benzopyran (4) was conceived whereby the thermolysis of pentafluorophenyl prop-2-enyl ether (1) to the Claisen rearrangement intermediate (2) would be followed first by elimination of hydrogen fluoride and then electrocyclisation of the o-quinomethide-type material (3) (Scheme 1). However, pyrolytic elimination of HF from



Scheme 1

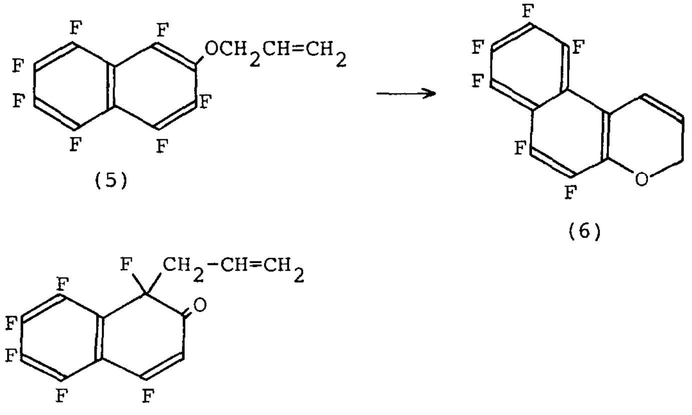
(4)

(2) failed to take place even at 480°: products arose from internal Diels-Alder reactions of the dienone (2) [2,3]. This paper records a successful method for the dehydrofluorination of (2) and the subsequent formation of (4), and its application to other polyfluoroaryl and -heteroaryl prop-2-enyl ethers. One example of the reaction using a prop-2-enyl sulphide is also given.

RESULTS AND DISCUSSION

Pentafluorophenyl prop-2-enyl ether (1) treated with potassium fluoride in dimethylformamide at reflux temperature for 4 h. gave the 2H-1-benzopyran derivative (4) in 48% yield. The structure of this material was deduced from its simple ^{19}F and ^{1}H n.m.r. spectra.

1,3,4,5,6,7,8-Heptafluoro-2-naphthyl prop-2-enyl ether (5) [4] reacted with potassium fluoride in sulpholane at 155-162° over 4 h. to give (6) in 41% yield (Scheme 2). The ^{19}F n.m.r. spectrum showed the presence of only one large



(5)

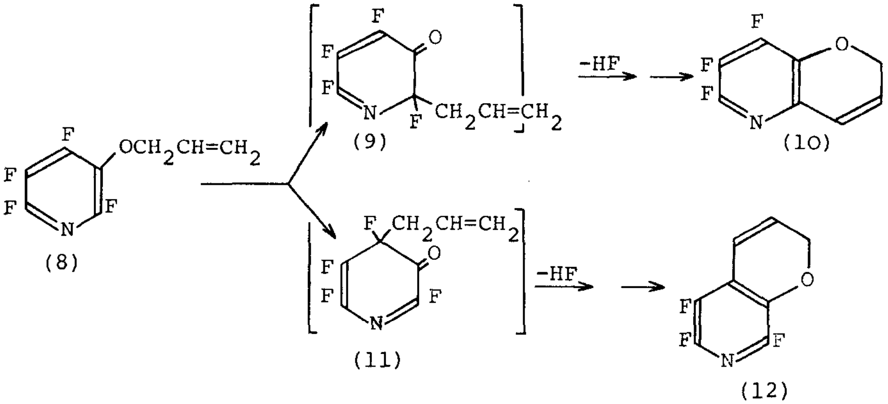
(6)

(7)

Scheme 2

peri J_{F-F} coupling constant (J_{8F-9F} 64 Hz) demonstrating that the reaction must have proceeded via the 1-(prop-2-enyl)naphthalen-2-one derivative (7).

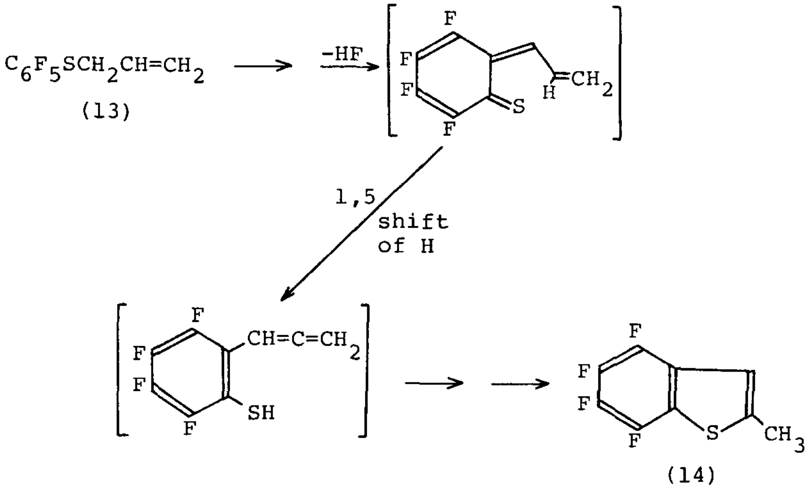
No viable products were obtained from the reaction of 2,4,5,6-tetrafluoro-3-pyridyl prop-2-enyl ether (8) [5] with potassium fluoride in sulpholane at 140-180° in conventional glass apparatus, presumably because of the hydrolysis of intermediates containing a -N=CF-group by water formed from the attack of eliminated HF with the glass [6]. When the reaction was carried out in a sealed nickel tube at 182° for 4 h., two products were formed. The major product (34%) was identified as the 2*H*-pyran derivative (10) from its ^{1}H n.m.r. spectrum and from its ^{19}F n.m.r. spectrum which showed three fluorine absorptions, only one of which was at low field (92.7 p.p.m.) and therefore on a carbon adjacent to the nitrogen atom. The minor component (1%) was the isomer (12) which had two low field fluorine absorptions (at 93.9 and 97.3 p.p.m.) out of a total of three. These results are summarised in Scheme 3, which also shows the respective Claisen rearrangement intermediates. The most interesting feature of this reaction is the fact that the major product in the reaction (10) arises from the [3,3] sigmatropic shift of the prop-2-enyl group onto the adjacent carbon <u>nearest</u> to the nitrogen, which contrasts with the vapour phase reaction at 185^{o} for 112.8 h. in which the prop-2-enyl group migrated to the adjacent carbon farthest away from the nitrogen [5], demonstrating in a spectacular way the role of the solvent on the course of the reaction.



Scheme 3

Treatment of 2,3,5,6-tetrafluoro-4-pyridyl prop-2-enyl ether [5] with potassium fluoride in sulpholane in a sealed nickel tube at 137-140^{o} for 17 h. failed to give any 2*H*-pyran derivative. Extensive decomposition occurred during the reaction and the only compounds isolated were unchanged starting material (9%) and 2,3,5,6-tetrafluoro-4-hydroxypyridine (10%) [7], the de-alkylation product from the parent ether.

Finally, an attempt was made to prepare the sulphur analogue of (4) from pentafluorophenyl prop-2-enyl sulphide (13) [8]. Reaction of (13) with potassium fluoride in sulpholane in a sealed nickel tube at 191-192^{o} for 22 h. gave a complex mixture of products from which was isolated 4,5,6,7-tetrafluoro-2-methylbenzo[b]thiophen (14) (9%) which had been prepared previously [9]. The formation of this compound can be rationalised by invoking the following sequence of reactions (Scheme 4):

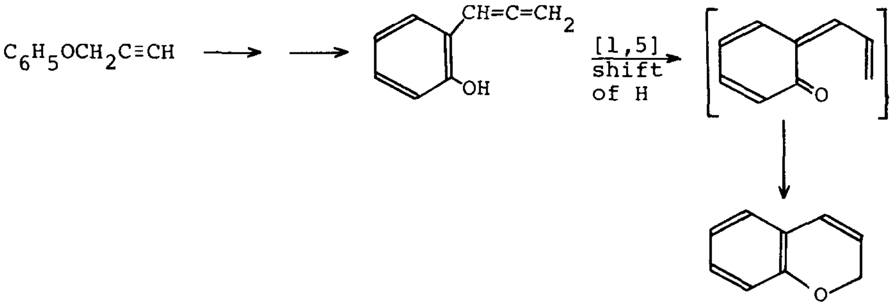


(13)

(14)

Scheme 4

This [1,5] sigmatropic shift appears to be the first example of the migration of a *vinylic* hydrogen to a terminal heteroatom. Previously a related reaction in the opposite direction was invoked to account for the formation of 2*H*-1-benzopyran [10] (Scheme 5).



Scheme 5

EXPERIMENTAL

^{1}H (60 MHz) and ^{19}F n.m.r. (56.4 MHz) were obtained with a Varian EM360L spectrometer. Chemical shifts δ_F are upfield from internal CFCl$_3$; δ_H are downfield from internal TMS.

Reactions of polyfluoroaryl and -heteroaryl prop-2-enyl ethers with potassium fluoride

(a) Use of pentafluorophenyl prop-2-enyl ether (1) [2]

The ether (1) (5.17 g) and anhydrous KF (3.33 g) were heated together in dry dimethylformamide (DMF) under reflux for 4 h. After being cooled, the mixture was fractionally distilled through a 6" vacuum-jacketed column first to remove the solvent, while the material boiling up to 80°/ 0.05 mm solidified in the condenser. Recrystallisation of this crude product (2.28 g, 48%) from methanol with external cooling gave 5,6,7,8-tetrafluoro-2*H*-1-benzopyran (4), m.p. 44.0 - 45.5° [Found: C, 52.7; H, 1.8; M$^+$, 204. $C_9H_4F_4O$ requires C, 52.9; H, 2.0%; M, 204]. δ_F (CDCl$_3$) 151.2 (doublet of doublets), 157.7 (triplet), 164.0 (doublet of doublets) and 169.1 p.p.m. (triplet) with intensities in the ratio 1:1:1:1 respectively; δ_H (CDCl$_3$) 4.87 (CH$_2$ at position 2); 5.90 (doublet of triplets, vinylic C-H at position 3, J_{3H-4H} 10 Hz; J_{2H-3H} 3.5 Hz) and 6.58 p.p.m. (doublet, vinylic C-H at position 4).

(b) Use of 1,3,4,5,6,7,8-heptafluoro-2-naphthyl prop-2-enyl ether (5) [4]

The ether (5) (2.07 g), anhydrous KF (0.87 g) and dry sulpholane (10 ml) were heated together at 155-162° for 4 h. The mixture was diluted with water, acidified (2M HCl), and extracted with ether. The extracts were washed with water, dried (MgSO$_4$) and the residue sublimed at 95°/0.05 mm to give crude product (0.80 g, 41%). Recrystallisation of the sublimate from light petroleum [b.p. 60-80°] gave 5,6,7,8,9,10-hexafluoro-2*H* naphtho[2,1-b]pyran (6), m.p. 98.5 - 100.0° [Found: C, 54.0; H, 1.0; M$^+$, 290. $C_{13}H_4F_6O$ requires

C, 53.8; H, 1.4%; M, 290]. δ_F ($CDCl_3$) 142.3 (doublet of doublets, peri $J_{8F,9F}$ 64 Hz), 144.2 (triplet), 147.1 (doublet of triplets, a peri fluorine), 156.9 (overlapping multiplets), and 160.1 p.p.m. (triplet) with intensities in the ratio 1:1:1:2:1 respectively; δ_H ($CDCl_3$) 4.90 (CH_2 at position 2), 5.86 (doublet of triplets, vinylic C-H at position 3, J_{3H-4H} 10 Hz; J_{2H-3H} 4 Hz) and 7.13 p.p.m. (doublet, vinylic C-H at position 4).

(c) Use of 2,4,5,6-tetrafluoro-3-pyridyl prop-2-enyl ether (8) [5]

The ether (8) (5.48 g), anhydrous KF (3.23 g) and dry sulpholane (25 ml) were heated together in a sealed nickel tube (capacity: 85 ml) at 182° for 4 h. The crude reaction product, worked up as in (b) was distilled in vacuo at 95°/ 0.05 mm. The semi-solid distillate (1.8 g, 36%) was examined by ^{19}F n.m.r. spectroscopy and was shown to consist mainly of two isomers containing three fluorine atoms in the ratio 95:5. The major component, isolated by crystallisation of the mixture from methanol with external cooling was 6,7,8-trifluoro-2*H*-pyrano[3,2-b]pyridine (10), m.p. 38.5 - 40.5° [Found: C, 51.4; H, 1.9; N, 7.5; M^+, 187. $C_8H_4F_3NO$ requires C, 51.3; H, 2.1; N, 7.5%; M, 187]. δ_F ($CDCl_3$) 92.7 (a broad doublet of doublets), 143.6 (a sharp doublet of doublets) and 162.0 p.p.m. (a sharp doublet of doublets) with intensities in the ratio 1:1:1 respectively; δ_H ($CDCl_3$) 4.93 (CH_2 at position 2), 6.00 (doublet of triplets, vinylic C-H at position 3, J_{3H-4H} 10 Hz; J_{2H-3H} 3 Hz) and 6.35 p.p.m. (doublet, vinylic C-H at position 4).

The minor component, isolated from the mother liquors from the crystallisation of the original mixture as the faster moving component on thick layer chromatography on silica using 80% CCl_4:20% $CHCl_3$ ($^v/v$) as eluent and after recrystallisation from methanol with external cooling, was 5,6,8-trifluoro-2*H*-pyrano[2,3-c]pyridine (12) m.p. 46 - 46.2° [Found: C, 51.4; H, 1.7; N, 7.4. $C_8H_4F_3NO$ requires C, 51.3; H, 1.9; N, 7.5%]. δ_F ($CDCl_3$) 93.9 (a broad doublet of doublets), 97.3 (a broad doublet of doublets) and 153.7

p.p.m. (a sharp doublet of doublets) with intensities in the ratio 1:1:1 respectively; δ_H ($CDCl_3$) 4.93 (CH_2 at position 2), 6.14 (doublet of doublets, vinylic C-H at position 3, J_{3H-4H} 10 Hz; J_{2H-3H} 3.5 Hz), and 6.67 p.p.m. (doublet, vinylic C-H at position 4).

(d) Use of 2,3,5,6-tetrafluoropyridyl prop-2-enyl ether [5]

The ether (1.14 g), anhydrous KF (1.02 g) and dry sulpholane (10 ml) were heated together in a nickel tube at 137 - 140° for 17 h. The mixture was worked up as in (c) and the crude product (0.18 g) was examined by ^{19}F n.m.r. spectroscopy and shown to contain approximately equal amounts of unreacted starting material (9%) and 2,3,5,6-tetrafluoro-4-hydroxypyridine (10%) [7].

(e) Use of pentafluorophenyl prop-2-enyl sulphide (13) [8]

The sulphide (13) (1.89 g), anhydrous KF (1.91 g) and dry sulpholane (10 ml) were heated together in a sealed nickel tube at 191 - 192° for 22 h. The mixture was treated with water, extracted with ether, the extracts dried ($MgSO_4$) and the solvent evaporated. The residual brown oil (1.09 g) shown by ^{19}F n.m.r. spectroscopy to be a complex mixture of products was distilled and the distillate (0.63 g) was separated by chromatography on silica (15" x 1") using light petroleum [b.p. 40 - 60°] as eluent. The fastest moving (and major) component was 4,5,6,7-tetrafluoro-2-methylbenzo-[b]thiophen (14) (0.15 g, 9%) identified by i.r. spectroscopy by comparison with the i.r. spectrum of an authentic sample [9].

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