

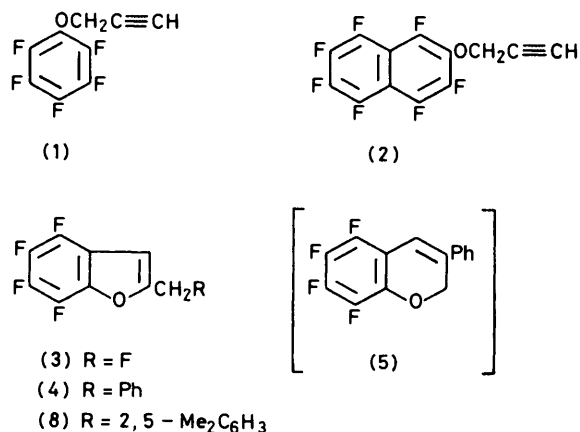
Partially Fluorinated Heterocyclic Compounds. Part 13.¹ The Formation of Some Furan Derivatives from Polyfluoroaryl Prop-2-ynyl Ethers

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Pentafluorophenyl prop-2-ynyl ether (1) undergoes isomerisation to 2-fluoromethyl-4,5,6,7-tetrafluorobenzo[*b*]-furan (3) on distillation *in vacuo* over silica at 370 °C. The ether (1) undergoes reaction with benzene and *p*-xylene at 140 °C to give the 2-arylmethyl-4,5,6,7-tetrafluorobenzo[*b*]furan derivatives (4) and (8) respectively, while 1,3,4,5,6,7,8-heptafluoro-2-naphthyl prop-2-ynyl ether (2) reacts with the same solvents at 140 °C to give the corresponding 2-arylmethyl-4,5,6,7,8,9-hexafluoronaphtho[2,1-*b*]furan derivatives (9) and (10) respectively.

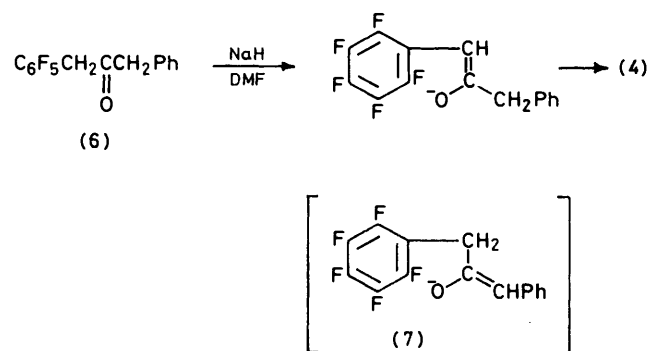
THE vapour-phase pyrolyses of polyfluoropyridyl¹ and pentafluorophenyl² prop-2-ynyl ethers have been shown to give a variety of products *via* an initial Claisen rearrangement followed by an internal Diels–Alder reaction. In an extension of this work concerning Claisen rearrangements with aromatic substrates containing fluorine in *ortho*- and *para*-positions as blocking groups (*i.e.* replacing hydrogen, which would lead to enolisation of the rearranged material) we report now the chemistry of some related prop-2-ynyl ethers: the pentafluorophenyl derivative (1)^{2c} and the 1,3,4,5,6,7,8-heptafluoro-2-naphthyl derivative (2) prepared from 1,3,4,5,6,7,8-heptafluoro-2-naphthol³ and prop-2-ynyl bromide. It is noteworthy that the first internal Diels–Alder intermediate to be isolated from a Claisen rearrangement utilised 2,6-dimethylphenyl prop-2-ynyl ether.⁴

Distillation of pentafluorophenyl prop-2-ynyl ether (1) through a silica tube packed with quartz wool at 370 °C gave a complex tarry product from which was isolated 2-fluoromethyl-4,5,6,7-tetrafluorobenzo[*b*]furan (3) (8%) as the major component. The structure of this material, suggested by its simple ¹H and ¹⁹F n.m.r. spectra, was confirmed by the halogen-exchange reaction of 2-bromomethyl-4,5,6,7-tetrafluorobenzo[*b*]furan⁵ with caesium fluoride in sulpholan.



The reaction of the ether (1) with benzene in a sealed tube at 140 °C for 116 h gave HF and a complex mixture from which was isolated one compound (28%). In the absence of model compounds, the elemental analysis,

mass spectral, and n.m.r. data (¹H and ¹⁹F) of this material could be interpreted in terms of two possible isomers (4) and (5) whose formation could be rationalised mechanistically. However, the problem was resolved by an unambiguous synthesis of (4) from pentafluorobenzyl benzyl ketone (6) [from benzyl chloromethyl ketone⁶ and pentafluorophenylcopper⁷] and sodium hydride in dimethylformamide (Scheme 1);⁸ even if the enolate formed initially was (7), cyclisation and a proto-



SCHEME 1

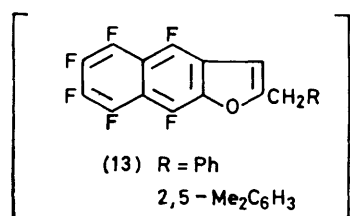
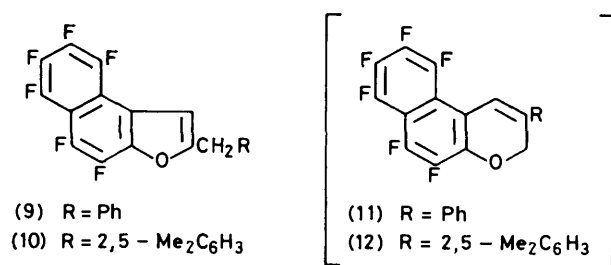
tropic shift in acid during the work-up procedure would give (4).⁹

When pentafluorophenyl prop-2-ynyl ether (1) and *p*-xylene were heated under reflux for 118 h, 2-(2,5-dimethylbenzyl)-4,5,6,7-tetrafluorobenzo[*b*]furan (8) (21%) was formed, the structure of which was assigned from its ¹H n.m.r. spectrum on the basis of the chemical shifts of its CH₂ and vinylic CH groups which were essentially identical with those found in (4).

1,3,4,5,6,7,8-Heptafluoro-2-naphthyl prop-2-ynyl ether (2) reacted with benzene at 140 °C over 21 h and with *p*-xylene at reflux temperature over 20 h to give (9) (64%) and (10) (73%) respectively. The structures of these compounds were assigned to the furan derivatives and not to the respective 2*H*-pyran derivatives (11) and (12), again on the basis of the similarity of the chemical shifts of their CH₂ and vinylic CH groups in the ¹H n.m.r. spectra to the corresponding absorptions in (4). The small deviation of each absorption to lower fields is expected from the larger diamagnetic anisotropy effect of a naphthalene ring on substituents as compared with

the effect of a benzene ring. The presence of only *one* large *peri* J_{F-F} coupling constant (*ca.* 60 Hz) in the products was consistent only with the structures (9) and (10); the isomeric products (13) would have had *two* large *peri* J_{F-F} coupling constants.

These experiments show that the prop-2-ynyl ethers of polyfluoroaromatic systems behave quite differently from the corresponding prop-2-enyl ethers. Previously, substrates having *ortho* halogens in aryl prop-2-ynyl ethers when heated in *n*-decane have been shown in each case to give 2-halomethylbenzo[*b*]furan derivatives among the products.¹⁰ Thus 2,6-dichlorophenyl prop-2-ynyl ether gave 2-chloromethyl-7-chlorobenzo[*b*]furan and 3,8-dichloro-2*H*-1-benzopyran as the main products; 2,4,6-tribromophenyl prop-2-ynyl ether gave 2-bromo-methyl- and 2-methyl-benzo[*b*]furan; and 1-chloro-(bromo)-2-naphthyl prop-2-ynyl ether gave 2-chloro-(bromo)methylnaphtho[2,1-*b*]furan accompanied in the

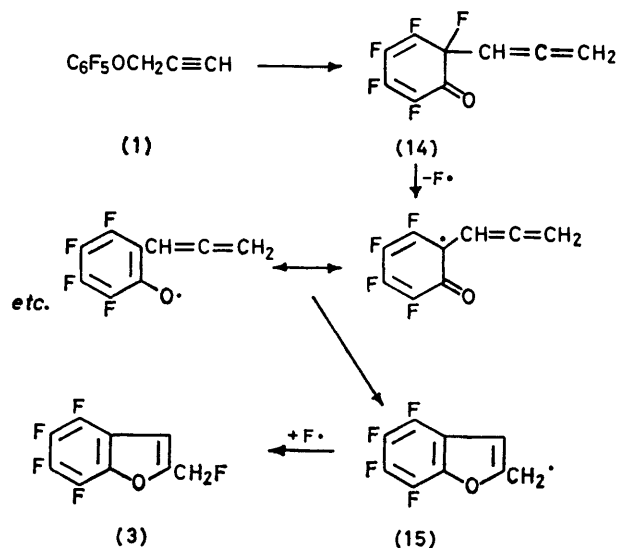


case of the 1-bromo-compound by 2-methylnaphtho[2,1-*b*]furan. Homolytic cleavage of the C-Cl(Br) bond in the initially formed Claisen rearrangement product was proposed to account for the products in these reactions.

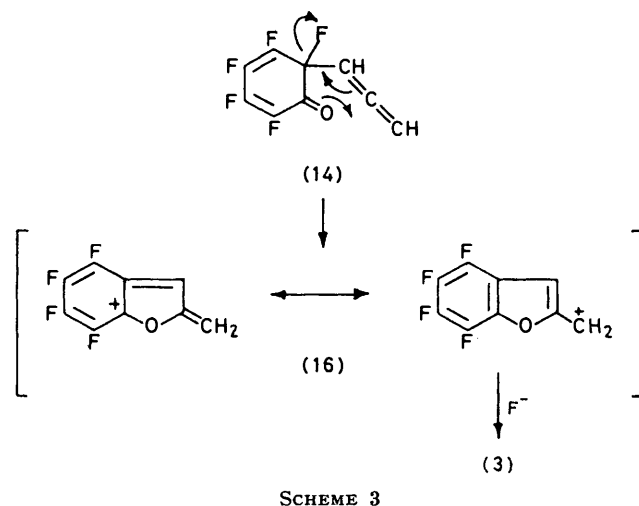
In order to account for the formation of 2-fluoromethyl-4,5,6,7-tetrafluorobenzo[*b*]furan (3) from pentafluorophenyl prop-2-ynyl ether (1), an analogous isomerisation mechanism can be written (Scheme 2). This remarkable *vapour phase* reaction requires that following the homolytic cleavage of the aliphatic C-F bond in the Claisen rearrangement product (14), there is a close association between the fluorine atom and the accompanying radical during and following the cyclisation stage. Furthermore, the formation of the 2-arylmethyl derivatives (4) and (8) from the reaction of (1) in benzene and *p*-xylene respectively can be rationalised on the basis of a homolytic substitution mechanism. This necessitates attack on the aromatic solvent by the cyclised radical (15) followed by abstraction of

hydrogen from the intermediate complex by the fluorine atom.

An alternative heterolytic process* for the formation



of the 2-fluoromethyl compound (3) from (14) is shown in Scheme 3. This mechanism also requires a close association between the departing fluorine (as fluoride ion) and the associated organic moiety (16) (a carbocation in this case) in the *vapour phase*. Electrophilic substitution of hydrogen in benzene and *p*-xylene would then give compounds (4) and (8) respectively. On the evidence presently available it is not possible to distinguish between this mechanism and the mechanism proceeding *via* homolytic cleavage of the aliphatic C-F bond.



The formation of the 2-arylmethyl-4,5,6,7,8,9-hexafluoronaphtho[2,1-*b*]furan derivatives (9) and (10) from 1,3,4,5,6,7,8-heptafluoro-2-naphthyl prop-2-ynyl ether

* We acknowledge the comments of a referee for this suggestion.

(2) with benzene and *p*-xylene, respectively, must proceed through 1,3,4,5,6,7,8-heptafluoro-1-(propa-1,2-dienyl)naphthalen-2-one [the corresponding 2-(prop-2-enyl) ether rearranges to the stable 1,3,4,5,6,7,8-heptafluoro-1-(prop-2-enyl)naphthalen-2-one¹¹] and again mechanisms involving both homolytic and heterolytic rupture of the aliphatic C-F bond in this intermediate can be proposed to rationalise the reaction pathway.

EXPERIMENTAL

1,3,4,5,6,7,8-Heptafluoro-2-naphthyl Prop-2-ynyl Ether (2).—1,3,4,5,6,7,8-Heptafluoro-2-naphthol³ (14.02 g), anhydrous potassium carbonate (15.70 g), prop-2-ynyl bromide (15.65 g, 80% w/w solution in toluene), and dry acetone (150 ml) were refluxed under nitrogen for 22 h. The mixture was acidified with hydrochloric acid (2M) and extracted with ether. The extracts were dried (MgSO₄), the solvent evaporated off, and the residue distilled *in vacuo* to give the ether (2) (13.31 g, 83%), b.p. 94–97 °C at 0.05 mmHg, m.p. 33–34 °C (Found: C, 50.8; H, 0.7. C₁₃H₃F₇O requires C, 50.6; H, 0.97%); M⁺, 308.

Pyrolysis of Pentafluorophenyl Prop-2-ynyl Ether (1).^{2c}—The ether (1) (5.42 g) was distilled over 10 min from a heated vessel through a silica tube (58 × 1.4 cm) packed with quartz wool heated to 370 °C, into a trap cooled in liquid air connected to a high-vacuum system (0.001 mmHg). The major component in the tarry product was isolated by chromatography on silica (120 × 3.4 cm) (light petroleum [b.p. 40–60 °C] as eluant) followed by preparative t.l.c. on silica (same solvent) to give 2-fluoromethyl-4,5,6,7-tetrafluorobenzo[b]furan (3) (0.41 g, 8%), b.p. 28–29 °C at 0.05 mmHg (Found: C, 48.4; H, 1.7. C₉H₃F₅O requires C, 48.7; H, 1.4%); M⁺, 222; δ_F (CDCl₃) 147.3, 160.3, 161.7, 164.1, and 211.4 (t, -CH₂F) (upfield from internal CFCl₃); δ_F (CDCl₃) 5.42 (d, -CH₂F), and 7.02 (vinylic CH); J_{gem-F,H} 48.0 Hz.

2-Fluoromethyl-4,5,6,7-tetrafluorobenzo[b]furan (3).—2-Bromomethyl-4,5,6,7-tetrafluorobenzo[b]furan⁵ (1.35 g) and dry caesium fluoride (2.9 g) were stirred in dry sulpholan (10 ml) under nitrogen at 90 °C for 3 h. The mixture was diluted with water and extracted with diethyl ether. The extracts were dried (MgSO₄), the solvent evaporated off and the residue distilled *in vacuo* to give the benzofuran (3) (0.77 g, 73%), b.p. 28–29 °C at 0.05 mmHg, identical (i.r. spectrum) with the material prepared above.

Reactions of Pentafluorophenyl Prop-2-ynyl Ether (1) with Aromatic Hydrocarbons.—(a) With benzene. The ether (1) (3.1 g) and benzene (20 ml) were sealed in a 50-ml tube under reduced pressure (0.05 mmHg) and heated at 140 °C for 116 h. On opening the tube, hydrogen fluoride was evolved. The solvent was evaporated off and the residue was chromatographed on silica (118 × 3.4 cm) (CCl₄ as eluant) to give a crude product (1.08 g, 28%) which after preparative t.l.c. on silica (CCl₄ as eluant) gave 2-benzyl-4,5,6,7-tetrafluorobenzo[b]furan (4), b.p. 103–105 °C at 0.05 mmHg (Found: C, 64.0; H, 2.9. C₁₅H₅F₄O requires C, 64.3; H, 2.9%); M⁺, 280; δ_F (CDCl₃) 148.5, 162.4, 163.4, and 165.4 (upfield from internal CFCl₃); δ_H (CDCl₃) 4.08 (s, CH₂), 6.42 (m; vinylic CH), and 7.3 (C₆H₅).

(b) With *p*-xylene. The ether (1) (5.65 g) and *p*-xylene (100 ml) were heated under nitrogen for 118 h during which time HF was evolved. The solvent was distilled *in vacuo*, the residue was chromatographed on silica (114 × 3.4 cm) (CCl₄ as eluant) and the enriched product, after preparative

t.l.c. on silica (same solvent), gave 2-(2,5-dimethylbenzyl)-4,5,6,7-tetrafluorobenzo[b]furan (8) (1.68 g, 21%), b.p. 120–126 °C at 0.05 mmHg (Found: C, 66.1; H, 4.1. C₁₇H₁₂F₄O requires C, 66.2; H, 3.9%); M⁺, 308; δ_F (CDCl₃) 148.3, 162.0, 163.2, and 165.1 (upfield from external CFCl₃); δ_H (CDCl₃) 2.33 (s, 2 × CH₃), 4.07 (m, CH₂), 6.38 (m, vinylic CH), and 7.10 (m, C₆H₅).

Reactions of 1,3,4,5,6,7,8-Heptafluoro-2-naphthyl Prop-2-ynyl Ether (2) with Aromatic Hydrocarbons.—(a) With benzene. The ether (2) (2.12 g) and benzene (20 ml) were heated together in a sealed tube at 140 °C for 21 h and the crude product (95% pure by ¹H n.m.r.) (1.70 g, 64%) was isolated by chromatography as before. The material was sublimed at 100 °C at 0.05 mmHg and crystallised from ethanol to give 2-benzyl-4,5,6,7,8,9-hexafluoronaphtho[2,1-b]furan (9), m.p. 98.5–100 °C (Found: C, 62.4; H, 2.1. C₁₉H₈F₆O requires C, 62.3; H, 2.2%); M⁺, 366; δ_F (CDCl₃) 146.6–147.4 (br m), 151.9 (m), and 158.8–159.7 (br m) upfield from internal CFCl₃ in the ratio 2 : 1 : 3 respectively, *peri* J_{F-F} 60 Hz; δ_H (CDCl₃) 4.21 (s, CH₂), 6.95 (m, vinylic CH), and 7.34 (C₆H₅).

(b) With *p*-xylene. The ether (2) (2.86 g) and *p*-xylene (50 ml) were heated under reflux for 20 h and the product was isolated as before by chromatography to give the crude product (90% pure by ¹H n.m.r.) (2.98 g, 73%). Recrystallisation of this material from ethanol gave 2-(2,5-dimethylbenzyl)-4,5,6,7,8,9-hexafluoronaphtho[2,1-b]furan (10), m.p. 116–117 °C (Found: C, 64.0; H, 3.2. C₂₁H₁₂F₆O requires C, 64.0; H, 3.0%); M⁺, 394; δ_F (CDCl₃) 145.5–146.5 (br m), 151.4 (m), and 158.0–158.9 (br m) (upfield from internal CFCl₃) in the ratio 2 : 1 : 3 respectively, *peri* J_{F-F} 61 Hz; δ_H (CDCl₃) 2.32 (s, 2 × CH₃), 4.17 (s, CH₂), 6.83 (m, vinylic CH), and 7.05 (m, C₆H₅).

2,3,4,5,6-Pentafluorobenzyl Benzyl Ketone (6).—Bromopentafluorobenzene (26 g) in dry tetrahydrofuran (200 ml) at -70 °C under nitrogen, was treated with *n*-butyl-lithium in hexane (65 ml; 1.54M) over 30 min at ≤ -60 °C. Diethyl ether (100 ml) was added and the mixture was stirred for 4 h at -70 °C. Copper(I) iodide (20 g) was added, and the temperature was maintained at -70 °C for 5 h, after which the solution was warmed to 0–5 °C when benzyl chloromethyl ketone⁶ (4.21 g) was added. After stirring for 12 h at 20 °C all the solvents were removed by distillation at 12 mmHg, dry diglyme (80 ml) was added, and the mixture was maintained at 100 °C for 5 h. The mixture was cooled, diluted with diethyl ether (100 ml) and shaken with saturated NH₄Cl solution. The organic phase was dried (MgSO₄), the solvents were evaporated off, and the black residue was separated by chromatography on dry silica (120 × 3.5 cm) using CHCl₃ as eluant to give the crude product (1.75 g, 5%). Recrystallisation (×4) from light petroleum (b.p. 60–80 °C) gave the ketone (6) (0.50 g), m.p. 75.5–76.5 °C (Found: C, 59.8; H, 3.1. C₁₅H₅F₅O requires C, 60.0; H, 3.0%); M⁺, 300.

Reaction of 2,3,4,5,6-Pentafluorobenzyl Benzyl Ketone (6) with Sodium Hydride in Dimethylformamide.—The ketone (6) (0.41 g) was treated with sodium hydride (0.06 g; 80% dispersion in oil) in dimethylformamide (5 ml) for 1 h at reflux temperature. The mixture was cooled, diluted with diethyl ether, and washed with sulphuric acid (2M). The dried (MgSO₄) ethereal layer was evaporated and the residue after preparative t.l.c. on silica using CCl₄ as solvent, gave 2-benzyl-4,5,6,7-tetrafluorobenzo[b]furan (4) (0.28 g, 73%), identical (i.r. spectrum) with the material prepared from (1) in benzene.

We thank the S.R.C. for an award (to D. I. W.) and Dr. B. S. Furniss for suggesting the synthesis of compound (6).

[0/1473 Received, 26th September, 1980]

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