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THE PREPARATION AND THERMOLYSIS REACTIONS OF ALLYL 3,4,5,6,7,8-HEXAFLUOROQUINOLIN-2-YL ETHER, ALLYL 2,3,5,6,7,8-HEXAFLUOROQUINOLIN-4-YL ETHER AND ALLYL 3,4,5,6,7,8-HEXAFLUOROISOQUINOLIN-1-YL ETHER.

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SUMMARY

Sodium allyl oxide reacted with 2,3,4,5,6,7,8-heptafluoroquinoline to give allyl 3,4,5,6,7,8-hexafluoroquinolin-2-yl ether (7) and allyl 2,3,5,6,7,8-hexafluoroquinolin-4-yl ether (8) in the ratio 3.4:1 respectively, and with 1,3,4,5,6,7,8-heptafluoroisoquinoline to give allyl 3,4,5,6,7,8-hexafluoroisoquinolin-1-yl ether (9). Thermolyses of (7) and (9) in tetralin at 212°C gave the Claisen rearrangement products (10) and (12) in which nitrogen is the migration terminus, in slow reactions over 48 h, whereas the isomerisation of (8) to (11) in which carbon is the migration terminus, was complete within 2.5 h at 147.5°C. Compound (11) is very susceptible to hydrolysis, giving with undried toluene, the dione (13) containing half a molecule of solvent toluene.

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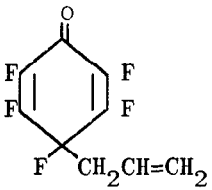
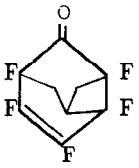
INTRODUCTION

The presence of fluorine rather than hydrogen in the ortho-positions of polyfluoroaromatic and -heteroaromatic allyl ethers provides the structural pre-requisite for the formation of de-aromatised products in thermally promoted Claisen Rearrangement reactions. The initially formed materials may undergo further reactions depending on the experimental conditions employed. Thus allyl pentafluorophenyl ether gave 2,3,4,5,6-pentafluoro-4-allyl-2,5-cyclohexadiene (1) by vapour phase pyrolysis at 365^{o} via a Cope rearrangment of the presumed Claisen rearrangement product formed initially [1], whereas with the ether in the vapour phase at 137-141^{o} for 13 days, the same Claisen rearrangement product gave the tricyclic compound (2) via an internal Diels-Alder reaction [2]. Under similar relatively low temperature conditions



(1)



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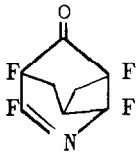

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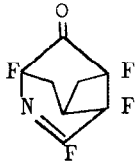
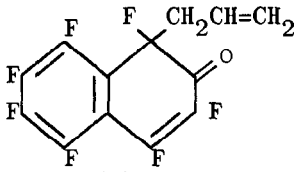


(4)

the heterocylic compounds allyl 2,3,5,6-tetrafluoro-4-pyridyl ether and allyl 2,4,5,6-tetrafluoro-3-pyridyl ether gave (3) and (4) respectively [3]. Claisen rearrangement products themselves have been isolated from thermolysis reactions of allyl 1,3,4,5,6,7,8-heptafluoro-2-naphthyl ether which gave (5) [4] and allyl 2,5,6-trifluoropyrimidin-4-yl ether which gave (6) [5].



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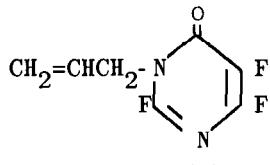
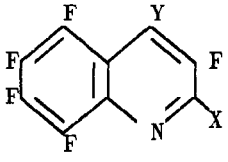


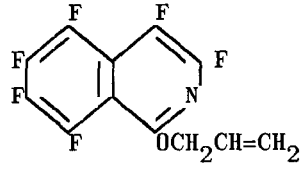
(6)

It was of interest to examine the thermolysis reactions of other fused bicyclic aromatic and -heteroaromatic allyl ethers, and the first obvious candidate would be allyl 2,3,4,5,6,7,8-heptafluoro-1-naphthyl ether, to complement the study on the 2-naphthyl ether [4]. Unfortunately this material is not available by nucleophilic substitution reactions involving octafluoronaphthalene. However bicyclic analogues of pentafluoropyridine are well known, namely 2,3,4,5,6,7,8-heptafluoroquinoline and 1,3,4,5,6,7,8-heptafluoroisoquinoline [6], and their known behaviour towards nucleophiles [7] ensured that two α-allyl ethers [allyl 2,3,5,6,7,8-hexafluoroquinolin-4-y ether (8) and allyl 3,4,5,6,7,8-hexafluoroisoquinolin-1-yl ether (9)] and one β-allyl ether (allyl 3,4,5,6,7,8-hexafluoroquinolin-2-yl ether) (7) would be accessible. This paper reports the preparation and thermolysis reactions of these isomers.



(7) X = $OCH_2CH=CH_2$, Y = F

(8) X = F, Y = OCH_2-CH=CH_2



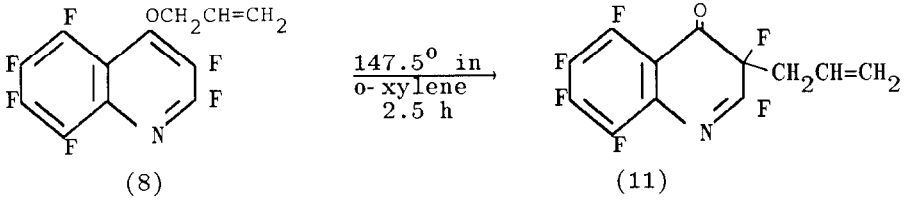
(9)

RESULTS AND DISCUSSION

2,3,4,5,6,7,8-Heptafluoroquinoline was reacted with an equimolar amount of sodium allyl oxide in allyl alcohol to give a mixture of the 2- and 4-allyl ethers (7) and (8) respectively in the ratio of 3.4:1, exactly the same proportions for fluorine replacement at these sites as that reported previously for the reaction with sodium methoxide [7]. The two compounds were readily separated by flash chromatography on silica, and their structures were determined by ^{19}F nmr spectroscopy. Compound (7) (isolated in 67% yield) did not have a low field absorption due to a 2-F (found at 71.3 ppm in the parent) and it did show the large peri coupling (47 Hz) between the 4-F and 5-F. On the other hand, compound (8) (isolated in 20% yield) did have a low field absorption at 76.2 ppm and no large peri coupling was present in the spectrum.

Treatment of 1,3,4,5,6,7,8-heptafluoroisoquinoline with an equimolar amount of sodium allyl oxide gave the 1-allyl ether (9) (84%), again identified by the absence of a low field absorption due to 1-F in the ^{19}F nmr spectrum (found at 61.8 ppm in the parent), and the presence of only one large peri coupling constant ($J_{4\text{-}F,5\text{-}F}$ 50 Hz).

Previously allyl 1,3,4,5,6,7,8-heptafluoro-2-naphthyl ether had been isomerised to compound (5) in mixed xylenes at 130-135° over 2.5 h [4]. When individual solutions of allyl 3,4,5,6,7,8-hexafluoroquinolin-2-yl ether (7), allyl 2,3,5,6,7,8-hexafluoroquinolin-4-yl ether (8) and allyl 3,4,5,6,7,8-hexafluoroisoquinolin-1-yl ether (9) in o-xylene were heated at 147.5° for 2.5 h, the isomerisation of (8) to (11) was complete (Scheme 1) as shown by ^{19}F n.m.r. whereas no reaction occurred

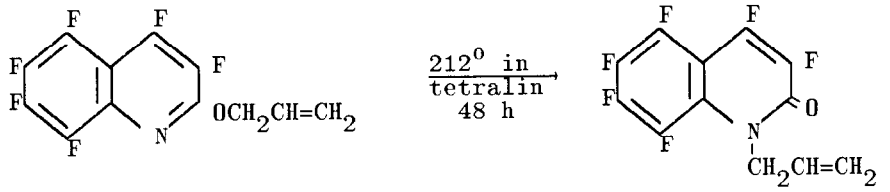


(8) (11)

Scheme 1

with either (7) or (9) under these conditions nor when the reaction time was extended to 24 h (Table). When the compounds (7) and (9) were heated separately in tetralin at 212° and the courses of the reactions followed by ^{19}F nmr spectroscopy, after 2.5 h, the proportion of unchanged (7) to its isomerised product (10) was 73:27 respectively, while after 24 h the ratio of (7):(10) was 25:75. The isoquinoline compound (9) was marginally less reactive than the quinoline compound (7): after 2.5 h, the proportion of unchanged (9) to its isomerised product (12) was 85:15 respectively while after 24 h it was 30:70; after 87 h complex mixtures resulted from both reactions.

Preparative scale experiments were carried out on both allyl ethers (7) and (9) in refluxing tetralin over 48 h and their respective rearrangement products (10) (69%) and (12) (45%) were isolated by flash chromatography on silica (Scheme 2). The

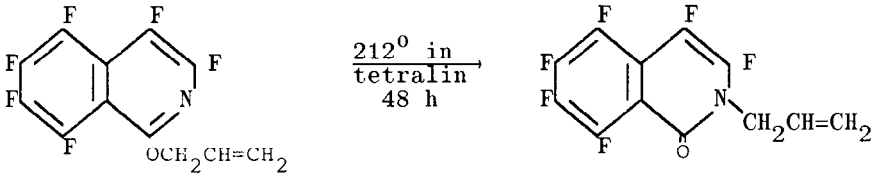


(7) (10)

Scheme 2

TABLE

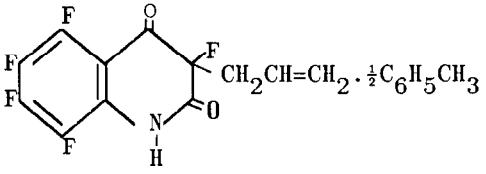
Compound	Time in o-xylene at 147.5°C		Time in tetralin at 212°C	
	2.5 h	24 h	2.5 h	24 h
(7)	No reaction	No reaction	73 parts (7) 27 parts (10) + others	25 parts (7) 75 parts (10) + others
(8)	100% conversion to (11)			
(9)	No reaction	No reaction	85 parts (9) 15 parts (12)	30 parts (9) 70 parts (12) + others



(9) (12)

Scheme 2

product (11) from the isomerisation of the 4-allyl ether (8) required special handling for its isolation, as the 2-F was very susceptible to hydrolysis: crystallisation from undried toluene gave the analogous dione containing half a molecule of solvent of crystallisation (13) (45%).



(13)

The products isolated from the thermolysis reactions of the three allyl ethers described in this paper all arise from Claisen rearrangement reactions, though a further Cope rearrangement could have taken place with (11) (to give an N-allyl functionality) and with (12) (to give a CF-allyl functionality). Of critical importance in determining the migration terminus for each of the rearrangement reactions is the chemical shift of the aliphatic CH_2 of the allyl group in the ^1H nmr spectra, since it has been established in work with allyl polyfluoropyrimidyl ethers [5] that these differ significantly in the two environments, viz. 2.81-2.95 ppm for CF-CH_2 and 4.40-4.64 ppm for N-CH_2 [8]. The thermolysis

of compounds (7) and (9) gave products containing a CH_2 group at 5.09 and 4.70 ppm respectively showing that nitrogen is the migration terminus in each case [compounds (10) and (12) respectively]. However, the thermolysis of the 4-allyloxy compound (8) gave a product in which the CH_2 group occurred at 2.95 ppm, characteristic of carbon as the migration terminus and is therefore assigned the structure (11). Furthermore, the chemical shift of the aliphatic CH_2 group at 2.90 ppm in (13), the hydrolysis product from (11), is entirely consistent with the initial rearrangement to carbon.

It is of interest to compare the conditions required to promote the thermal rearrangement reactions of fluorine-containing compounds described in this paper, with those used for the analogous hydrogen containing materials. Allyl quinolin-2-yl ether rearranges at 250°C over 1 h with no solvent present [9] [cf. 212°C over 48 h in tetralin for (7)]; allyl quinolin-4-yl ether rearranges at 200°C over 1.5 h in 1-methylnaphthalene [10] [cf. 147.5°C over 2.5 h in o-xylene for (8)]; and allyl isoquinolin-1-yl ether rearranges at 250°C over 5 h with no solvent present [11] [cf. 212°C over 48 h in tetralin for (9)]. Previously it had been observed that allyl 2-naphthyl ether rearranged at 194° over 2 h in NN-dimethylaniline [12], whereas allyl 1,3,4,5,6,7,8-heptafluoro-2-naphthyl ether isomerised to (5) at 130-135°C over 2.5 h in mixed xylenes [4]. However, it is clearly evident that these Claisen rearrangement reactions need to be carried out under standardised reaction conditions (temperature, time, solvent and concentration) to determine whether polyfluoro substitution has any significant effect on the rates of reaction.

EXPERIMENTAL

^{1}H (250 MHz) and ^{19}F (235.34 MHz) nmr spectra were obtained on a Brüker AC250 spectrometer. Chemical shifts are downfield from internal $SiMe_4$ (δ_H) or upfield from internal $CFCl_3$ (δ_F).

Reaction of 2,3,4,5,6,7,8-heptafluoroquinoline with sodium allyl oxide in allyl alcohol

2,3,4,5,6,7,8-Heptafluoroquinoline (5.02g; 19.7 mmol) in dry allyl alcohol (50 ml) was treated over 30 min with sodium allyl oxide in allyl alcohol (7.2 ml, 2.76 M; 19.9 mmol), the internal temperature being maintained between 8° and 12.5°C. The mixture was poured into water at 0°C, the solution acidified with sulphuric acid (4 M) and extracted with ether. The solvents were evaporated from the dried ($MgSO_4$) extracts and the residue (5.70 g) was shown by ^{19}F nmr to consist mainly of three components: unreacted 2,3,4,5,6,7,8-heptafluoroquinoline (7.5%), and 2- and 4-substituted allyl ethers, 71.5% and 21% respectively. The mixture was separated by flash chromatography on silica [7" x 2", 40-63 μm silica gel 60 (E.Merck 9385)] using CCl_4 as eluant. Two components were isolated: allyl 3,4,5,6,7,8-hexafluoroquinolin-2-yl ether (7) (3.85 g, 67%), nc mp 41-41.3°C [from light petroleum (bp 40-60°C)] (Found: C, 49.03; H, 1.50; N, 4.77%. $C_{12}H_5F_6NO$ requires C, 49.16; H, 1.72; N, 4.78%); $\delta_F(CDCl_3)$ 132.5 (dd, 4-F), 147.7 (m, 5-F), 151.1 (complex t), 154.0 (complex t), 159.4 (complex t) and 160.9 ppm (complex m) in the ratio 1:1:1:1:1:1, $J_{4\text{-}F,5\text{-}F}$ 47 Hz; $\delta_H(CDCl_3)$ 5.12 (d, CH_2), 5.39 (d, one H of $=CH_2$), 5.55 (d, other H of $=CH_2$), and 6.16 (m, -CH=); and the more slowly eluting component, allyl 2,3,5,6,7,8-hexafluoroquinolin-4-yl ether (8) (1.157 g, 20%), nc mp 51.5-52°C

[from light petroleum (bp 40-60°C)] (Found: C, 49.20; H, 1.66; N, 4.75%. $C_{12}H_5F_6NO$ requires C, 49.16; H, 1.72; N, 4.78%); $\delta_F(CDCl_3)$ 76.2 (d, 2-F), 143.8 (complex t), 149.9 (complex t), 153.1 (complex t), 157.4 (complex t) and 159.1 ppm (d, 3-F) in the ratio 1:1:1:1:1:1; $\delta_H(CDCl_3)$ 5.12 (bm, CH_2), 5.40 (d, one H of $=CH_2$), 5.54 (d, other H of $=CH_2$), and 6.10 (m, -CH=).

Reaction of 1,3,4,5,6,7,8-heptafluoroisoquinoline with sodium allyl oxide in allyl alcohol

1,3,4,5,6,7,8-Heptafluoroisoquinoline (5.16 g, 20.2 mmol) in dry allyl alcohol (35 ml) was treated over 20 min with sodium allyl oxide in allyl alcohol (7.4 ml, 2.76 M; 20.4 mmol) the internal temperature being maintained at -2°C to 1°C. After a further 45 min at 2°C, the mixture was worked up as in the previous experiment and the crude product (5.759 g), shown by ^{19}F nmr to consist mainly of two components: unreacted 1,3,4,5,6,7,8-heptafluoroisoquinoline (8%) and its 1-allyl ether (92%), was separated as before by flash chromatography on silica using CCl_4 as eluant to give allyl 3,4,5,6,7,8-hexafluoroisoquinolin-1-yl ether (9) (4.97 g, 84%), nc mp 49-50.5°C [from light petroleum (bp 40-60°C)] (Found: C, 49.13; H, 1.47; N, 4.96%. $C_{12}H_5F_6NO$ requires C, 49.16; H, 1.72; N, 4.78%); $\delta_F(CDCl_3)$ 98.3 (d, 3-F), 136.7 (complex m, 8-F), 147.5 (dt, 5-F), 148.7 (complex t, 6-F), 156.6 (complex t, 7-F) and 165.2 ppm (dd, 4-F) in the ratio 1:1:1:1:1:1, $J_{4\text{-}F,5\text{-}F}$ 50 Hz, $J_{3\text{-}F,4\text{-}F}$ 15 Hz; $\delta_H(CDCl_3)$ 4.99 (bm, CH_2), 5.36 (d, one H of $=CH_2$), 5.53 (d, other H of $=CH_2$), and 6.12 (m, -CH=).

Semi-kinetic thermolyses of allyl 3,4,5,6,7,8-hexafluoroquinolin-2-yl ether (7), allyl 2,3,5,6,7,8-hexafluoroquinolin-4-yl ether (8) and allyl 3,4,5,6,7,8-hexafluoroisoquinolin-1-yl ether (9)

Each of the allyl ethers (7), (8) and (9) was dissolved in dry o-xylene in an nmr tube and the ^{19}F nmr spectrum was determined. The samples were then immersed in refluxing o-xylene for specific times after which the ^{19}F nmr spectra were determined and the integrated spectra measured. For the less reactive allyl ethers, the experiments were repeated in tetralin solutions which were heated in refluxing tetralin. The results of these reactions are shown in the Table: the products from the isomerisation of the allyl ethers (7), (8) and (9) are (10), (11) and (12) respectively.

Thermolysis of allyl 3,4,5,6,7,8-hexafluoroquinolin-2-yl ether (7) in tetralin

The allyl ether (7) (0.168 g) was heated in freshly distilled tetralin (10 ml) under reflux in an atmosphere of nitrogen for 48 h. The ^{19}F nmr spectrum of the solution showed the presence of unreacted starting material (7) (5 parts), the major product (10) (95 parts) and unidentified material (ca. 17 parts). The solvent was removed by distillation in vacuo at 0.05 mmHg with an external water bath at $\leq 35^{o}C$ and the major product isolated from the mixture by flash chromatography on silica (6.5" x 1.5") using chloroform as eluant to give 1-allyl-3,4,5,6,7,8-hexafluoroquinolin-2(1H)-one (10) (0.116 g, 69%) nc mp 66-67°C [from light petroleum (bp 40-60°C)] (Found: C, 49.11; H, 1.65; N, 5.03%. $C_{12}H_5F_6NO$ requires C, 49.16; H, 1.72; N, 4.78%); $\delta_F(CDCl_3)$ 132.5 (dd, 4-F), 143.2 (d, 5-F), 147.6 (complex t),

149.2 (complex t), 151.8 (m, 3-F) and 161.0 ppm (t), in the ratio 1:1:1:1:1:1, $J_{4\text{-}F,5\text{-}F}$ 71 Hz; $\delta_H(CDCl_3)$ 5.09 (N-CH_2), 5.14 (d, one H of =CH_2), 5.25 (d, other H of =CH_2), and 5.96 (m, -CH=).

Thermolysis of allyl 3,4,5,6,7,8-hexafluoroisoquinolin-1-yl ether (9) in tetralin

The allyl ether (9) (1.483 g) was heated in freshly distilled tetralin (20 ml) under reflux in an atmosphere of nitrogen for 48 h. The ^{19}F nmr spectrum of the solution showed the presence of unreacted starting material (9) (9 parts), the main product (12) (91 parts) and unidentified material (ca. 43 parts). The solvent was removed as in the previous experiment and the major product isolated from the mixture by flash chromatography on silica (8" x 2") using chloroform as eluant to give 2-allyl-3,4,5,6,7,8-hexafluoroisoquinolin-1(2H)-one (12) (0.663 g, 45%) nc mp 64.5-65.5°C [from light petroleum (bp 40-60°C)] (Found: C, 49.42; H, 1.61; N, 4.63%. $C_{12}H_5F_6NO$ requires C, 49.16; H, 1.72; N, 4.78%); $\delta_F(CDCl_3)$ 123.0 (m, 3-F), 136.9 (m), 146.3 (overlapping ddd), 147.0 (dddd, 5-F), 156.1 (tdd) and 179.8 ppm (d, 4-F) in the ratio 1:1:1:1:1:1, $J_{4\text{-}F,5\text{-}F}$ 49 Hz; $\delta_H(CDCl_3)$ 4.70 (bm N-CH_2), 5.28 (d, one H of =CH_2), 5.34 (s, other H of =CH_2), and 5.92 (m, -CH=).

Thermolysis of allyl 2,3,5,6,7,8-hexafluoroquinolin-4-yl ether (8) in o-xylene

The allyl ether (8) (0.0946 g) and dry o-xylene (0.5 ml) were sealed in an nmr tube and immersed in boiling o-xylene (148°C) for 2.5 h. The ^{19}F nmr of the solution showed that the ether (8) had

been completely converted to the product (11). The contents of the nmr tube were transferred under dry nitrogen into a sublimation apparatus, the solvent was removed by freeze-drying and the residue was sublimed in vacuo at 50^{o}/0.05 mmHg. Thereafter, all the manipulations were carried out under dry nitrogen to give 3-allyl-2,3,5,6,7,8-hexafluoroquinolin-4(3)-one (11) nc mp 58.5-60^{o}C (Found: C, 49.31; H, 1.58; N, 4.65%. $C_{12}H_5F_6NO$ requires C, 49.16; H, 1.72; N, 4.78%); $\delta_F(CDCl_3)$ 42.2 (d, 2-F), 136.9 (overlapping dt), 141.3 (complex t), 144.3 (complex t), 152.9 (complex t) and 174.3 ppm (overlapping dt); $\delta_H(CDCl_3)$ 2.95 (CF-CH_2), 5.29 (overlapping protons, =CH_2) and 5.59 (m, -CH=).

Compound (11) was exceedingly prone to hydrolysis, simply on contact with undried solvents. Recrystallisation of the hydrolysed product from toluene gave 3-allyl-3,5,6,7,8-pentafluoroquinolin-2,4(1H,3H)-dione associated with half a molecule of toluene (13) (0.049 g, 45%) nc mp 196.5-198.5^{o}C (Found: C, 55.00; H, 2.77; N, 3.80%. $C_{12}H_6F_5NO_2 \cdot \frac{1}{2}C_6H_5CH_3$ requires C, 55.20; H, 2.99; N, 4.15%); $\delta_F(d^6$-acetone) 141.7 (m), 147.1 (m), 154.7 (m), 165.7 (m) and 180.5 (m); $\delta_H(d^6$-acetone) 2.31 (s, CH_3) and 7.20 (m) due to toluene; 2.9 (dd CF-CH_2), 5.2 (m, =CH_2) and 5.77 (-CH=) J_{CF,CH_2} 21 Hz; the toluene to dione ratio was 1:2.

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