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MODE OF THE NUCLEOPHILIC REACTION OF \underline{F} -2,4-DIMETHYL-3-HEPTENE AND PHENOL

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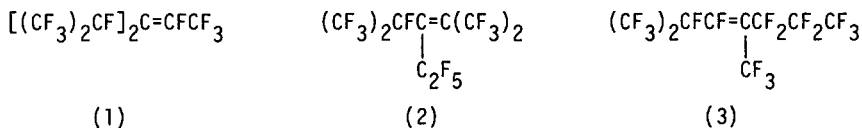
SUMMARY

Nucleophilic substitution on \underline{F} -2,4-dimethyl-3-heptene (3) by sodium phenoxide in diethyl ether gave 3-phenoxyated \underline{F} -2,4-dimethyl-4- (5) and -3-heptenes (6). In contrast, the reaction of (3) with phenol and triethylamine in dimethylformamide afforded 4-phenoxyated \underline{F} -2,4-dimethyl-3-heptene (7) as the major product. The reaction mechanisms are discussed.

INTRODUCTION

It is well known that \underline{F} -propene oligomerizes readily in the presence of a base or fluoride ion, giving a mixture of dimers and trimers [1-6]. While nucleophilic reactions of the dimers have been investigated by several workers [7-11], very little is known of the reactivities of the trimers.

Of the trimers, at present three isomers are known: \underline{F} -3-(1-methyl-ethyl)-4-methyl-2-pentene (1), \underline{F} -3-ethyl-2,4-dimethyl-2-pentene (2) and \underline{F} -2,4-dimethyl-3-heptene (3).



Some nucleophilic reactions of trimers (1) and (2), in particular with phenol, have been reported by Soviet chemists [12] and by these authors [13]. However, nothing is known about the reactivity of trimer (3), which can be prepared by the method recently reported by Martini [5].

We now wish to report some interesting results from nucleophilic reactions of (3), as the reaction mode of this trimer is somewhat different

from those of the other trimers, (1) and (2). The reaction with phenol was examined first, as it is known that phenol and perfluoroolefins usually react smoothly giving stable substitution products in which the ether linkage has no α -hydrogen atoms.

RESULTS AND DISCUSSION

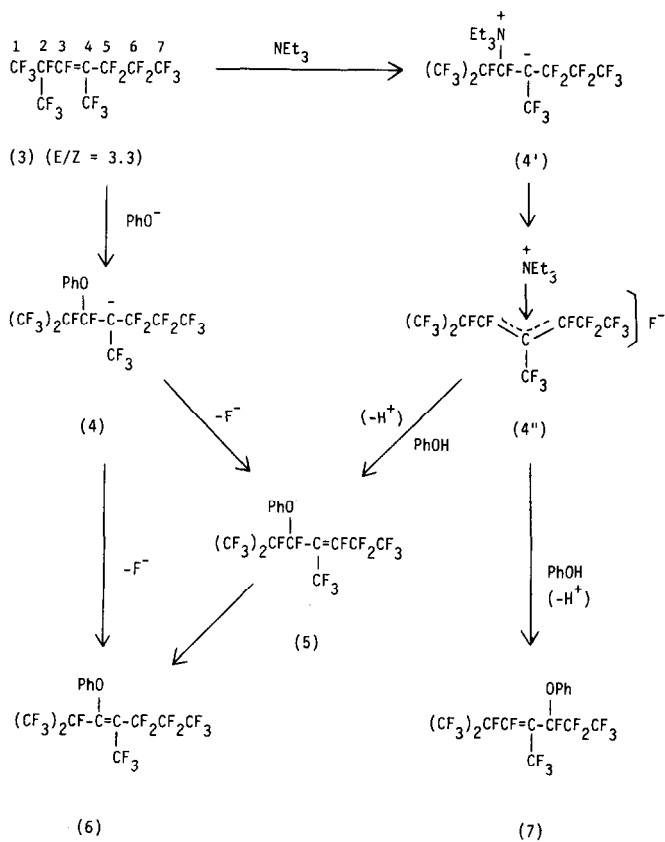
The reaction of (3) with sodium phenoxide

Sodium phenoxide readily reacted with (3) in various solvents at room temperature. In aprotic polar solvents such as dimethylformamide, dimethyl sulfoxide or acetonitrile, the reactions gave mixtures of di- and tri-phenoxyated products even when only one equimolar amount of sodium phenoxide was used. However, isolation of each of these poly-substituted products was not possible, and their structures were not elucidated.

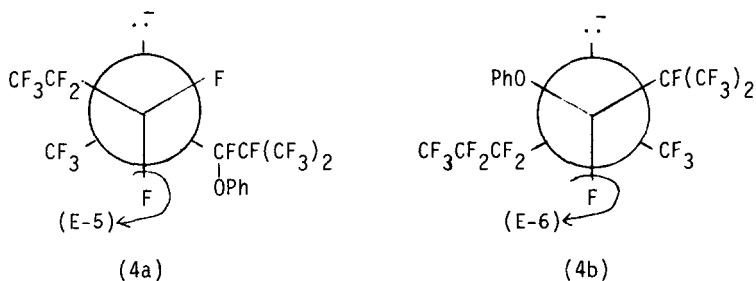
In less polar solvents, such as diglyme, tetrahydrofuran and especially diethyl ether, the reaction proceeded more moderately, and the monophenoxyated product was obtained as well as a considerable amount of polyphenoxyated product (TABLE 1).

The monophenoxyated product, obtained in 60% yield in diethyl ether, was composed of three isomers according to ^{19}F nmr analysis. Although these isomers were not separable, their structures were established by careful checking of the ^{19}F nmr spectra, as shown in TABLE 2. Thus, phenyl F-2,4-dimethyl-4-hepten-3-yl (5) and F-2,4-dimethyl-3-hepten-3-yl ethers (6) were obtained as major products, together with a small amount of phenyl F-2,4-dimethyl-3-hepten-5-yl ether (7). While the ^{19}F nmr signals for (6) were rather simple, those for (5) were very complex. However, the structure of (5) was able to be elucidated from the similarity of its chemical shifts and coupling constants with those of $(\text{CF}_3)_2\text{C}=\text{CFCF}_2\text{CF}_3$, a dimer of F-propene.

The formation of the main products (5) and (6) is quite reasonable. The first attack of phenoxide ion to (3) should take place at the 3-C position giving the carbanion (4), which is stabilized by the surrounding polyfluoroalkyl groups. Elimination of fluoride ion from the 5-position would lead to (5) whereas that from the 3-position would give (6). Comparing the thermodynamic stabilities of (5) and (6), the latter appeared to be more stable as it has no fluorine atoms in the α -positions to the double bond. In fact, we found that (5) is completely isomerized to (6) ($E/Z = 0.83$) by treating it with triethylamine for 30 min in dimethylformamide. Treatment for a prolonged time gave (6) ($E/Z = 0.32$). The predomi-



nant formation of (5) in the reaction of (3) and sodium phenoxide should then be ascribed to kinetic control. We presume that the trans-elimination of fluoride ion from (4) via the (4a) configuration giving (E-5) must be more likely than through the more crowded (4b) configuration giving (E-6).



The formation of (7) will be discussed later.

TABLE 1

$$\text{C}_9\text{F}_{18} (3) + \text{ArOH} \xrightarrow[22^\circ\text{C}]{\text{Solvent (30 mL)}} \text{C}_9\text{F}_{17}\text{OAr} (5), (6), (7) + \text{C}_9\text{F}_{16}(\text{OAr})_2$$

| Reagents (mmol) | Solvents | Time (h) | Yields (%) ^a & (E/Z) | | | | |
|--|-------------------|-------------|------------------------------------|----------|---|-------|----|
| | | | C ₉ F ₁₇ OAr | | C ₉ F ₁₆ (OAr) ₂ | | |
| | | | (5) | (6) | (7) | Total | |
| (3)(10) + PhONa(10) | Et ₂ O | 1 | 46 (2.4) | 12 (1.5) | 2 | 60 | 15 |
| " | THF | 1 | 35 (5.0) | 5 | 4 | 44 | 33 |
| " | Diglyme | 1 | 9 (5.9) | 3 | 3 | 15 | 57 |
| " | MeCN | 1 | 4 | — | — | 4 | 69 |
| " | DMF | 1 | — | — | — | — | 72 |
| " | DMSO | 1 | — | — | — | — | 67 |
| (3)(10) + PhONa(10)/Et ₃ N(50) | THF ^b | 1 | — | — | — | — | 20 |
| (3)(12) + PhOH(10)/Et ₃ N(10) | Et ₂ O | 3 | — | 39 (0.3) | 22 (∞) | 61 | — |
| " | THF | 3 | — | 2 | 56 (2.5) | 58 | — |
| " | MeCN | 3 | — | 5 | 86 (∞) | 91 | — |
| " | DMF | 3 | — | 6 | 86 (∞) | 92 | — |
| (3)(12) + p-NO ₂ C ₆ H ₄ OH(10)/Et ₃ N(10) | DMF | 3 | — | 7 | 87 (∞) | 94 | — |
| (3)(12) + p-MeCOC ₆ H ₄ OH(10)/Et ₃ N(10) | DMF | 3 | — | — | — | 9 | 74 |
| | DMF | 3 | — | 10 (0.3) | 35 (∞) | 45 | 33 |

a) While the total yields are those of the isolated products, the yields of (5), (6) and (7) are calculated based on the glc peak areas and the signal intensities of ¹⁹F nmr spectra.

b) THF (40 ml) was used.

TABLE 2

The ^{19}F nmr spectra of $\text{C}_9\text{F}_{17}\text{OPh}$.

| No. | Compound Structure | ^{19}F Chemical shifts (δ ppm) ^{a)} | Coupling constants (Hz) |
|-------|--------------------|--|---|
| (E-5) | | a) -27.5 (m) b) -5.3 (m) c) 5.5 (m) d) 11 (m) e) 26 (m) f) 38.8 (q, br) g) 98 (m) | $J_{ac}=4$ $J_{af}=20$ $J_{cd}=11$ $J_{ef}\approx 2$ |
| (Z-5) | | a) -20.3 (d, d, br) b) -5.7 (m) c) 5.5 (m) d) 9.7 (m) e) 26 (m) f) 35 (m) g) 98 (m) | $J_{ad}=23$ $J_{ae}=23$ |
| (E-6) | | a) -24.2 (d, br) b) -4.8 (d, q) c) 4.5 (t) d) 28.5 (q, q, br) e) 43.8 (q, br) f) 97.7 (q, br) | $J_{ab}=4$ $J_{bf}=8$ $J_{ad}=11$ $J_{cd}=11$ $J_{ae}=10$ $J_{af}=47$ |
| (Z-6) | | a) -18.5 (t, t) b) -4.6 (d, t) c) 4.4 (d, t) d) 18.2 (d, br) e) 40.5 (d, q, br) f) 98.9 (t, t, br) | $J_{ad}=11$ $J_{cd}=11$ $J_{ae}=11$ $J_{ef}=11$ $J_{bd}=5$ $J_{df}=55$ $J_{bf}=5$ $J_{ef}=42$ |
| (E-7) | | a) -24.5 (m) b) -3.0 (m) c) 2.9 (d) d) 9.1 (m) e) 31.4 (d, q, q, br) f) 46.9 (q, non equiv) g) 104.4 (d, q, sep) | $J_{ab}=2$ $J_{bd}=10$ $J_{ad}=9$ $J_{bz}=6$ $J_{ae}=28$ $J_{ce}=11$ $J_{af}=9$ $J_{de}=22$ $J_{ag}=48$ $J_{dg}=18$ |
| (Z-7) | | a) -20.2 (d, d, t) b) -3.0 (m) c) 2.8 (d) d) 5.1 (m) e) 26.0 (d, m) f) 44.8 (m) g) 101.5 (d, m) | $J_{ad}=13$ $J_{ae}=25$ $J_{af}=8$ $J_{ce}=11$ $J_{eg}=152$ |

a) Chemical shifts are given in δ ppm upfield from ext. $\text{CF}_3\text{CO}_2\text{H}$. All the measurements were carried out in neat.

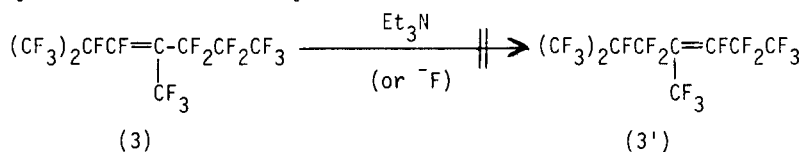
The reaction of (3) with phenol in the presence of triethylamine

As stated above, sodium phenoxide and (3) in polar solvents gave considerable amounts of diphenoxylated products. In order to increase the yield of monophenoxylated product, we carried out the reaction using phenol instead of sodium phenoxide and in the presence of triethylamine. Various solvents such as dimethylformamide, acetonitrile, tetrahydrofuran and diethyl ether were tried. In contrast to the results with sodium phenoxide, the reaction proceeded slowly even in polar solvents and afforded the monophenoxylated product in good yields (TABLE 1). Unexpectedly, the product was phenyl (E)-F-2,4-dimethyl-3-hepten-5-yl ether (E-7), with a small amount of (6), but none of (5) detected in the reaction mixture. The structure of (E-7) was established from its ^{19}F nmr spectra. In particular, the splitting patterns of CF_3 (-24.5 ppm) and $\text{CF}(\text{OPh})$ and the coupling constant between the latter and CF_3 (2.9 ppm) strongly supported the structure.

In diethyl ether, the reaction proceeded even more slowly, giving (7) which, however, contains some of the Z-isomer (E/Z = 2.7). This fact suggests that the Z-form isomerizes to E-form by the action of triethylamine. We confirmed this experimentally by observing that a mixture of (E-7) and (Z-7) was converted to pure (E-7) by treatment with triethylamine in dimethylformamide for 1.5 h.

In these reactions involving triethylamine, the pathway can be well explained as follows. The perfluoroolefin (3) is first attacked by triethylamine to form the carbanion (4'). Subsequent elimination of fluoride ion should occur from the 5-position, owing to the formation of a stable allylic complex (4''). In the third step, phenoxide ion would attack the 3- or 5-position of the complex. From the steric point of view, however, attack on the 5-position forming (7) rather than the 3-position forming (5), which isomerizes to (6), should occur preferentially.

There is another possible route from (3) to (7). If (3) was isomerized to (3') by the action of triethylamine, the latter might go on to (7) by phenoxy substitution. However, this pathway was excluded because the isomerization of (3) to (3') was not observed on treating (3) with triethylamine or KF in dimethylformamide.



When sodium phenoxide was allowed to react with (3) in the presence of triethylamine, the product was a mixture of (6) and (7) in the ratio 2 : 1. This fact suggests that there is considerable interaction between (3) and triethylamine even in the presence of sodium phenoxide.

When a more acidic phenol such as p-nitrophenol was used with triethylamine in the reaction on (3), di-substituted compounds were obtained as the major product (74%), even though p-nitrophenol is less nucleophilic than phenol. This implies that triethylamine reacted with p-nitrophenol rather than with (3), and the reaction proceeded as in the case with sodium phenoxide. p-Hydroxyacetophenone, of acidity intermediate to phenol and p-nitrophenol, gave a moderate composition of products, i.e., a mixture of mono-phenoxyated (45%) and di-phenoxyated compounds (33%).

EXPERIMENTAL

F-2,4-Dimethyl-3-heptene (3)

This perfluoroolefin was prepared by the oligomerization of F-propene by the method of Martini et al. [5]. The crude product was subjected to fractional distillation repeated three times. The purity of the final product determined by glc was over 97%.

The reaction of (3) with sodium phenoxide : Phenyl F-2,4-dimethyl-4-hepten-3-yl (5) (nc) and F-2,4-dimethyl-3-hepten-3-yl ethers (6) (nc)

Into a mixture of (3) (4.5 g, 10 mmol) and diethyl ether (20 ml) was added dropwise a suspension of sodium phenoxide (1.16 g, 10 mmol) in diethyl ether (10 ml) at 20 ± 2 °C over 5 min. After 55 min of stirring at that temperature, the reaction mixture was poured into dilute hydrochloric acid. The separating oil was extracted with diethyl ether and the ethereal solution was washed with a dilute aqueous solution of sodium hydroxide and then brine.

After drying over magnesium sulfate, the solvent was removed and the residue was subjected to distillation in vacuo yielding two fractions. The first fraction (3.16 g, 60%), b.p. 84 - 86 °C/10 mm, was a mixture of three isomers of the monophenoxyated compounds (5), (6), and (7), in the ratios 77 : 20 : 3 (from ^{19}F nmr). Found : C, 34.48; H, 0.97%. $\text{C}_{15}\text{H}_5\text{F}_{17}\text{O}$ requires C, 34.37; H, 0.96%.

The second fraction, a viscous oil (0.44 g, 15%) of b.p. 149 - 152 °C/10 mm, was a mixture of diphenoxylated products. Found : C, 42.06; H, 1.77%. $C_{21}H_{10}F_{16}O$ requires C, 42.16; H, 1.68%.

A mixture (0.5 g, 0.95 mmol) of monophenoxy derivatives (5), (6), and (7) obtained by the above reaction in diethyl ether was treated with triethylamine (0.1 g, 1 mmol) in dimethylformamide (2ml) at room temperature. In 30 min, (5) was completely isomerized to (6) (E/Z = 0.83).

A mixture of E and Z isomers (E/Z = 5.0) of (6) in dimethylformamide was treated with triethylamine at room temperature. An equilibrium mixture of E/Z = 0.32 was obtained after 12 h.

Reaction of (3) with phenols in the presence of triethylamine : Aryl F-2,4-dimethyl-3-hepten-5-yl ethers (7) (nc)

A solution of triethylamine (1.01 g, 10 mmol) was added dropwise into a mixture of (3) (5.4 g, 12 mmol), phenol (0.94 g, 10 mmol) and dimethylformamide (20 ml) over a period of 30 min at 20 ± 2 °C. After 2.5 h of stirring at that temperature, the reaction mixture was worked up as above. An oil (4.94 g, 94%), b.p. 84 - 86 °C/11 mm, composed of (7) and (6) in the ratio 93 : 7 was obtained. Found: C, 34.50; H, 1.09%. $C_{15}H_5F_{17}O$ requires C, 34.37; H, 0.96%.

A mixture of E and Z isomers (E/Z = 2.6) of (7) (0.5 g, 0.95 mmol) was treated with triethylamine (0.1 g, 1 mmol) in dimethylformamide (2 ml) at room temperature. After 1.5 h of stirring, the Z-isomer was found to have isomerized completely into E-isomer (^{19}F nmr).

When p-hydroxyacetophenone (1.36 g, 10 mmol) was allowed to react with (3) in the same manner, an oil (2.59 g, 46%), b.p. 127 - 129 °C/9 mm, composed of (7) and (6) (Ph = p-AcC₆H₄) in the ratio 77 : 23 (^{19}F nmr), was obtained. Found: C, 36.18; H, 1.29%. $C_{17}H_7F_{17}O_2$ requires C, 36.06; H, 1.25%.

The second fraction, a viscous oil (1.12 g, 33%) of b.p. 172 - 175 °C/1 mm, was a mixture of four diphenoxylated isomers (glc). Found: C, 44.22; H, 2.10%. $C_{25}H_{14}F_{16}O_4$ requires C, 44.01; H, 2.07%.

The similar reaction with p-nitrophenol gave an oily material containing crystals. This crude product was subjected to silica-gel column chromatography, using a 1 : 1 mixture of chloroform and hexane as eluent. The first elution, after evaporation of the solvent, gave an oily material (0.51 g, 9%) which was a mixture of five p-nitrophenoxylated isomers (glc). Found: C, 31.95; H, 0.84; N, 2.56%. $C_{15}H_4NF_{17}O_3$ requires C, 31.65; H, 0.71; N, 2.46%.

The second elution, after evaporation of the solvent and treatment with methanol, gave white crystals of a bis(p-nitrophenoxy) compound (2.54 g, 74%), m.p. 106 - 108 °C. Found: C, 36.49; H, 1.17; N, 4.06%. $C_{21}H_8N_2F_{16}O_6$ requires C, 36.64; H, 1.17; N, 4.07%.

The reaction of (3) with sodium phenoxide in the presence of NEt_3

After 30 min of magnetical stirring of a mixture of (3) (4.50 g, 10 mmol), triethylamine (5.05 g, 50 mmol) and tetrahydrofuran (30 ml), a suspension of sodium phenoxide (1.16 g, 10 mmol) in tetrahydrofuran (10 ml) was added dropwise at 22 ± 2 °C. The stirring was continued for 55 min at that temperature, and the reaction mixture was worked up as described above. Fractional distillation of the raw product gave mono- and diphenoxy compounds in 61 and 20% yields respectively.

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