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POLYFLUORO-COMPOUNDS BASED ON THE CYCLOHEPTANE
RING SYSTEM. PART 1. COMPOUNDS DERIVED FROM
TRIDECAFLUOROCYCLOHEPTANE

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SUMMARY

Partial fluorination of cycloheptane by cobaltic fluoride gave a mixture of polyfluorides, of which tridecafluorocycloheptane was present in significant proportions. With aqueous alkali this afforded dodecafluorocycloheptene, which with lithium aluminium hydride gave 1H-undecafluorocyclohept-1-ene. Each of these cyclo-olefins was oxidised to decafluoropimelic acid. Methanol/KOH reacted with dodecafluorocycloheptene to give mainly 1-methoxy-undecafluorocyclohept-1-ene together with ca 15% of the 3-methoxy-isomer, and some 1,2-dimethoxydodecafluorocyclohept-1-ene. The 1-methoxy-1-ene and cobaltic fluoride gave 1-methoxy- and 1-fluoromethoxy-tridecafluorocycloheptane: the former was demethylated by sulphuric acid to dodecafluorocycloheptanone. The dichloro-adduct of the perfluoro-olefin was reduced by lithium aluminium hydride to a complex mixture, from which 1H/2H- and 1H,2H/-dodecafluorocycloheptane were isolated.

INTRODUCTION

Series of papers from our Group have described the detailed chemistry of ranges of alicyclic fluoro-compounds derived from the cyclohexane [1] and cyclopentane systems [2]. As part of this general programme, we carried out extensive investigations into fluorocycloheptane chemistry, as yet unpublished apart from the isolation of perfluorocycloheptane(I) [3], and a preliminary note on the first successful syntheses of octafluorocyclohepta-1,3,5-triene and hexafluorotropone [4]. Alternative approaches

to fluoro-tropones and -tropolones gave other products [5;6]. This paper now reports the experimental details of the first stage of the investigations into polyfluorocycloheptane chemistry.

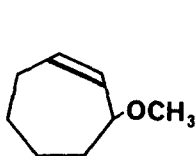
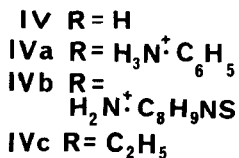
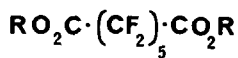
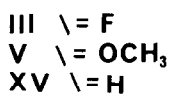
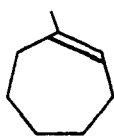
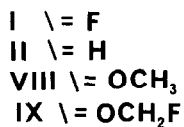
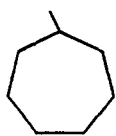
RESULTS AND DISCUSSION

The exhaustive fluorination of cycloheptane by cobaltic fluoride described earlier [3] gave tetradecafluorocycloheptane(I), but some rearrangement occurred to give significant proportions of perfluoromethylcyclohexane as well; fortunately, the two products were separable by glc. The ^{19}F nmr spectrum of perfluorocycloheptane had only one peak [3], indicating that the ring was flexible, and was interconverting rapidly. Hence, the diagnostic value of ^{19}F nmr spectroscopy has been more limited in fluorocycloheptane chemistry than for fluorocyclohexanes.

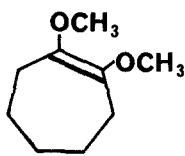
It was feared at first that the presence of many fluoro-methylcyclohexane isomers would prevent the isolation of reasonably pure samples of polyfluorocycloheptanes. Fortunately again, this was not too serious a problem; where complete separations could not be achieved, proportions of cyclohexanes present were very small.

Fluorinations of cycloheptane by cobaltic fluoride were done at lower temperatures (200-240°) than those used previously, and the products were separated by fractional distillation and glc. The first fraction contained the same two fluorocarbons as were present before [3], and they were followed in order of glc separations by some tridecafluoromethylcyclohexane isomers, already known [1]. Present in greater amount than any of these, however, was tridecafluorocycloheptane(II), like the fluorocarbon(I) a low-melting solid. The ^{19}F nmr spectrum of II was complex, but a most important feature was the complete absence of any absorption due to CF_3 groups. Further fluorination of the tridecafluoride(II) gave fluorocarbon I containing perfluoromethylcyclohexane (13%). High proportions of other higher-boiling polyfluorocycloheptanes were isolated from later fractions of the fluorination mixture, as will be described in later papers. These observations suggest that rearrangements of the cycloheptane rings to methylcyclohexanes occur mainly at the later stages of fluorination. This is different from the fluorinations of bicyclo-octanes [7], where the presence of some fluorine substituents in the precursors ensures the retention of the original carbon skeleton intact in the products.

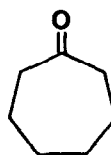
The tridecafluoride(II) was subjected to our dehydrofluorination technique routine at the time, refluxing with very concentrated aqueous potassium hydroxide, but clearly some deep-seated decomposition of the product occurred. Passage over heated sodium fluoride in a metal tube [1] gave the first samples of dodecafluorocycloheptene(III), which had a strong infrared double bond absorption at 1732 cm^{-1} . Subsequently, dehydrofluorinations of II with much more dilute alkali, present only in small excess, gave good conversions of II to III (See Scheme for structures).



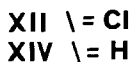
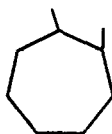
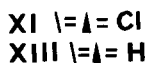
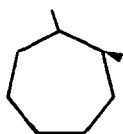
VI



VII



X



All unmarked
 bonds are to
 FLUORINE

S C H E M E

Cyclo-olefin III was subjected to some of our standard reaction procedures. Oxidation by potassium permanganate in acetone [8] gave decafluoropimelic acid(IV) characterised as amine salts, the diethyl ester and diamide. Methanol in the presence of potassium hydroxide gave with III a classical nucleophilic addition - elimination sequence [cf. 9]. The two expected methoxy-undecafluorocyclohept-1-enes were both formed, the 1-isomer (V), and the 3-isomer (VI), in a ratio of about 85:15. The 1-isomer (V) was isolated pure. Though the 3-isomer (VI) was identified unambiguously, a pure sample, completely free from V, could not be obtained. Also isolated pure, was 1,2-dimethoxydecafluorocyclohept-1-ene(VII), the product of a second attack on V. The proportions of products of 'inwards' (V), and 'outwards' (VI) elimination are in line with those from other perfluorocycloalkenes [9]. The structures of the two vinylic ethers (V and VII) were confirmed by oxidation to amine salts of decafluoropimelic acid (IV).

A crude mixed methoxylation product from III, with V and VI predominating, was fluorinated by cobaltic fluoride at ca 80° [cf. 10], to give mainly methoxytridecafluorocycloheptane(VIII), and fluoromethoxytridecafluorocycloheptane(IX). The methoxide VIII was demethylated by sulphuric acid to give the first synthesis of dodecafluorocycloheptanone(X). The photolysis of this ketone by colleagues has been reported already [11].

Perfluorocycloheptene(III) gave a dichloro-adduct, chiefly the cis-isomer (XII) containing around 5% of the trans (XI). The mixture was reduced by lithium aluminium hydride in ether. Side reactions involving double bond formation and further reduction occurred to a disappointing extent, but 1H/2H- (XIII) and 1H,2H/-dodecafluorocycloheptane(XIV) were major products and both were isolated and characterised. Stereochemical allocations were based on the Auwers-Skita rule [cf. 12], all examples of 1H/2H- polyfluorocycloalkanes in our previous work having significantly lower boiling points and glc retention times than the 1H,2H/- stereoisomers. The trans-dodecafluoride XIII was identical with a compound isolated from the fluorination product from cycloheptane, but the cis (XIV) could not be detected therein. Fluorinations produce greater proportions of trans-compounds with residual hydrogen left on opposite sides of cycloalkane rings, than of the cis-analogues [12]. Dehydrofluorinations with aqueous potash, to give the appropriate cyclo-alkenes, were done on 1H,2H/-octafluorocyclopentane [13], 1H/2H- and 1H,2H/-decafluorocyclohexane [14] and the pair of cycloheptanes (XIII and XIV). The 1H,2H/-cycloheptane

(XIV; cis) reacted to the greatest extent; the 1H,2H/-cyclopentane (cis), the 1H/2H-cycloheptane (XIII; trans) and the 1H,2H/-cyclohexane (cis) all reacted to about 50% but decreasingly in the order stated, whilst the 1H/2H-cyclohexane (trans) gave scarcely any olefinic products.

Perfluorocycloheptene(III) was reduced by lithium aluminium hydride in ether to give 1H-undecafluorocyclohept-1-ene(XV). The structure was proved by oxidation to salts of decafluoropimelic acid (IV).

EXPERIMENTAL

Apparatus This was as defined before [3]. For glc separations, column, temperature, and nitrogen flow rates are given in that order. ^{19}F nmr were measured on a Perkin Elmer R10 at 56.4 MHz (CCl_3F internal standard) and ^1H nmr on a Varian A60 relative to tetramethylsilane.

Fluorination of cycloheptane. This was first done in a 6 Kg reactor, cycloheptane (25 g) affording a product (P1) (55-60 g) at reactor temperatures of 130-140°. Re-fluorination of product (P1) (136.5 g) at 240° gave polyfluoro-mixture (P2) (116.3 g). After being washed with water and dried (MgSO_4) P2 showed 9 major peaks on analytical glc. Preparative glc (B, 80°, 57; 4 portions) of P2 gave the fractions corresponding to the first four peaks:- 1, 14.0 g; 2, 9.7 g; 3, 21.2 g; 4, 6.3 g. Peaks 2 and 4 were complex and each showed three maxima.

Fraction 1 by glc (C, 68°, 20) gave:- (i) perfluoromethylcyclohexane (3.1 g), and (ii) perfluorocycloheptane(I) (6.2 g), b.p. 81°, m.p. 40° [3] identified by ir.

Fraction 2 by glc (B, 76°, 54; 2 portions) gave:- (i) cis-2H-trifluoromethyldecafluorocyclohexane (1.4 g) [1]; (ii) a mixture of a 3H- and cis-4H-trifluoromethyldecafluorocyclohexane (3.6 g) [1]; (iii) tridecafluorocycloheptane (trace), all identified by ir.

Fraction 3 was tridecafluorocycloheptane(II) nc, b.p. 90-91°, m.p. ca 20° (Found: C, 25.6; H, 0.5. C_7HF_{13} requires C, 25.3; H 0.3%).

Fraction 4 by glc (A, 100° 17) gave:- (i) tridecafluorocycloheptane(II) (0.8 g) (ir): (ii) 1H/2H-dodecafluorocycloheptane(XIII) (1.2 g) identical with material prepared later: (iii) unidentified (trace): (iv) unidentified (2.35 g) (Found: C, 27.1; H, 0.8. Calc. for $\text{C}_7\text{H}_2\text{F}_{12}$ C, 26.8; H, 0.6%).

Subsequently, fluorinations were done in a 10 Kg reactor. Cycloheptane (180 g) in one pass at 200° gave around 400 g of product. Distillation (2292 g) through a 4' fractionating column packed with Dixon gauzes gave combined fractions (166 g) b.p. 89-92° largely tridecafluorocycloheptane(II), purified by glc separation as for fraction 2 above.

When tridecafluorocycloheptane(II) (3.0 g) in a stream of nitrogen (15 ℓ h⁻¹) was passed through the large cobalt trifluoride reactor at 280°, the products (50% recovery) were perfluoromethylcyclohexane (13%) and perfluorocycloheptane(I) (87%).

Dehydrofluorination of tridecafluorocycloheptane(II)

(a) By heated sodium fluoride. C₇HF₁₃ (II) (1.0 g) was passed during 1.5 h over sodium fluoride pellets [cf. 1] at 325° (N₂ flow 0.9 ℓ h⁻¹); the product (0.85 g) was collected at -180°. Separation (3.0 g) by glc (A, 101°, 18) gave:- (i) dodecafluorocycloheptene(III) nc (1.0 g), b.p. 79° (Found: C, 26.2. C₇F₁₂ requires C, 26.9%); ¹⁹F nmr, peaks centred at 114.5 (posn. 3 and 7), 127.3 (5), 128.9 (4 and 6), 141.4 (1 and 2) in intensity ratio 2:1:2:1; ir 1732 cm⁻¹ (C=C): (ii) starting material (1.1 g).

(b) By potassium hydroxide. C₇HF₁₃ (II) (3.3 g), potassium hydroxide (0.8 g), and water (15 cm³) were heated together at 100° in a sealed tube for 16 h. The product (ca 95%) was almost 99% olefin III, and glc separation as in (a) gave material identical with fraction a(i).

Derivatives of decafluoropimelic acid(IV). The standard oxidation procedure [8] applied to perfluorocycloheptene(III) afforded dianilinium decafluoropimelate(IVa) nc (70%), m.p. 174° (Found: C, 43.8; H, 3.5%; equiv., 262.5: C₁₉H₁₆F₁₀N₂O₄ requires C, 43.4; H, 3.1; equiv., 263.2), and thence the bis-S-benzylthiuronium salt(IVb) nc, m.p. 205-206° (Found: C, 41.1; H, 3.3. C₂₃H₂₂F₁₀N₄O₄S₂ requires C, 41.1; H, 3.3%).

When dodecafluorocycloheptene(III) (4.0 g) was oxidized as before, the ether extract was evaporated to give crude acid (IV) as an oil. Standard esterification with ethanol (15 cm³), sulphuric acid (2.0 cm³; s.g. 1.84) and refluxing for 3 h, gave diethyl decafluoropimelate(IVc) nc (1.65 g) b.p. 228-230°/752 mm (Found: C, 33.7; H, 2.6. C₁₁H₁₀F₁₀O₄ requires C, 33.35; H, 2.5%).

Passage of ammonia gas for 15 min through an ethanolic solution of the di-ester (IVc) gave decafluoropimeldiamide(IVd) nc (72%; from ethanol) m.p. 223-225° (Found: C, 25.0; H, 1.1. C₇H₄F₁₀N₂O₂ requires C, 24.9; H, 1.2%).

Reaction of dodecafluorocycloheptene(III) with methanol. Methanol (5 cm³) was added slowly to a stirred mixture of the olefin (III) (15.0 g) and potassium hydroxide (3.3 g). Reaction was vigorous and potassium fluoride was precipitated. After 1 h of stirring, water (100 cm³) was added, and the lower layer (14.0 g) was separated by glc (B, 100°, 65) to give:- (i) a trace of unreacted olefin: (ii) 1-methoxy-undecafluorocyclohept-1-ene(V) nc (5.7 g), b.p. 125° (Found: C, 29.7; H, 0.9. C₈H₃F₁₁O requires C, 29.6; H, 0.9%); ¹H nmr; doublet, centred at 3.71, J=2.4; ir 1692 cm⁻¹ (C=C): (iii) impure 3-methoxyundecafluorocyclohex-1-ene(VI) (1.0 g), ¹H nmr; singlet at 3.34; ir 1715 cm⁻¹ (C=C): (iv) 1,2-dimethoxydecafluorocyclohept-1-ene(VII) nc (2.0 g), b.p. 160° (Found: C, 32.1; H, 1.9. C₉H₆F₁₀O₂ requires C, 32.2; H, 1.8%); ¹H nmr singlet at 3.59; ir 1650 cm⁻¹ (C=C).

1-Methoxy-undecafluorocycloheptene(V) was oxidised as before to give dianilinium decafluoropimelate(IVa) (62%) and thence the bis-S-benzyl salt (IVb). The 1,2-dimethoxy-1-ene(VII) was oxidised and salt IVb isolated directly. All salts had correct m.p.s., with no depressions on admixture with authentic specimens.

Fluorination of the product of methoxylation of dodecafluorocycloheptene(III). Methoxylation of the olefin (III) (27.0 g) was done as described above but rather less heat allowed to develop. By glc, the product contained more III and less VII than before. The crude product (27.0 g), after being washed with water and dried, was swept in a nitrogen stream (10 l h⁻¹) through a small stirred cobalt fluoride reactor at 80°. This product (27.0 g) was water-washed, dried, and separated by glc (A, 97°, 17; 6.65 g) to give:- (i) dodecafluorocycloheptene(III) (0.6 g): (ii) methoxy-tridecafluorocycloheptane(VIII) nc (2.40 g), b.p. 122° (Found: C, 26.7; H, 0.9. C₈H₃F₁₃O requires C, 26.5; H, 0.8%); ¹H nmr; singlet, 3.52: (iii) fluoromethoxytridecafluorocycloheptane(IX) nc (0.50 g), b.p. 122-123° (Found: C, 25.1; H, 0.5. C₈H₂F₁₄O requires C, 25.3; H, 0.5%); ¹H nmr; doublet, centred at 5.28, J=52: (iv) 1-methoxy-undecafluorocycloheptene(V) (0.65 g), identified by glc and ir.

Dodecafluorocycloheptanone(X) - Methoxytridecafluorocycloheptane(VIII) (1.7 g) sulphuric acid (20 cm³; s.g. 1.84) and water (1.0 cm³) were heated together in a sealed hard-glass tube at 180° for 24 h. The upper layer was separated and distilled to give dodecafluorocycloheptanone(X) nc (1.2 g), b.p. 85-86° (m/e 328 [M], 281 [M-COF], 259 [M-CF₃]), ir 1795 cm⁻¹ (C=O).

Dichlorododecafluorocycloheptane(XI) and (XII). Dodecafluorocycloheptene(III) (3.85 g) and chlorine (2.0g) in a sealed hard-glass tube were irradiated with uv light for 18 h at ca 20°. After being washed with aqueous sodium bisulphite, aqueous sodium bicarbonate, water, and dried, the crude product (3.35 g) was separated by glc (A, 100°, 17) to give: (i) trans-1,2-dichlorododecafluorocycloheptane(XI) (0.15 g): (ii) cis-1,2-dichlorododecafluorocycloheptane(XII) nc (2.90 g), a low-melting solid, b.p. 135° (Found: C, 21.4, Cl, 18.2. $C_7Cl_2F_{12}$ requires C, 21.9, Cl, 18.5%)

1H/2H- and 1H,2H/-Dodecafluorocycloheptane(XIII) and (XIV). Crude dichloride from the previous experiment (6.0 g) in dry diethyl ether (50 cm³) was added during 30 min. to a stirred suspension of lithium aluminium hydride (1.4 g) in ether (150 cm³) at 0°. The mixture was stirred for 2 h at 0° and for 30 min. at 15°. Dilute sulphuric acid (65% by vol.) was added very carefully at 0°, followed by water (100 cm³). The ether layer was separated, dried, the ether evaporated through a 1' distillation column, and the residue separated by glc (A, 103°, 19) to give:- (i) diethyl ether: (ii) 1H/2H-dodecafluorocycloheptane(XIII) nc (0.6 g), b.p. 100° (Found: C, 26.7; H, 0.4. $C_7H_2F_{12}$ requires C, 26.8; H, 0.6%); ir 2985 cm⁻¹ (w) (C-H); identical by glc and ir with fraction 4(ii) from the fluorination of cycloheptane: (iii) unidentified, mixture of two compounds (0.05 g): (iv) 1H,2H/-dodecafluorocycloheptane(XIV) nc (1.90 g) b.p. 120° (Found: C, 27.0; H, 0.5%); ir 3000 cm⁻¹ (w) (C-H): (v) unidentified, (0.9 g) b.p. 112° (Found: C, 28.2; H, 0.6. Calc. for C_7HF_{11} : C, 28.6; H, 0.3%): (vi) unidentified, mixture of two compounds (0.05 g): (vii) unidentified, (0.55 g) (Found: C, 31.7; H, 1.1. Calc. for $C_7H_3F_9$: C, 32.6; H, 1.2%): (viii) unidentified, (0.65 g) (Found: C, 32.9; H, 1.3%).

Reaction of dodecafluorocycloheptene(III) with lithium aluminium hydride. A suspension of lithium aluminium hydride (0.15 g) in dry ether (50 cm³) was added during 20 min. to a stirred solution of the olefin (3.0 g) in ether (70 cm³) at -78°. The mixture was stirred for 20 min. further. Isolation as before gave a mixture, separated by glc (D, 45°, 19.5) to give:- (i) ether; (ii) 1H-undecafluorocycloheptene(XV) nc (0.85 g), b.p. 88° (Found: C, 28.2; H, 0.3. C_7HF_{11} requires C, 28.6; H, 0.3%); ¹H nmr 3.87 dt, Jd=16, Jt=9; ¹⁹F nmr 103.1 (7), 106.8 (2), 116.0 (3), 127.3 (5), 128.7 (4), 129.5 (6) intensity ratio 2:1:2:2:2:2; all complex; ir 1710 cm⁻¹ (C=C): (iii) an unidentified mixture (0.40 g).

Olefin XV was oxidised to give the dianilinium (IVa; 52%) and thence the bis(S-benzylthiuronium)(IVb) salts of decafluoropimelic acid, with correct m.p.s, undepressed on admixture with authentic specimens.

Comparative dehydrofluorinations. Each of 1H,2H/-octafluorocyclopentane [12]; 1H/2H- and 1H,2H/-decafluorocyclohexane [13]; and 1H/2H- (XIII) and 1H,2H/-dodecafluorocycloheptane(XIV) (0.65 g) was treated with aqueous potassium hydroxide (3.0 cm³; 1:1 w/w) at 100° for 45 min. in a sealed tube. In each case the proportions of unchanged dihydro-compounds and of olefinic products (% by glc) were respectively 40, 60; 94, 6; 59, 41; 55, 45; 1, 99.

The olefinic product from the cycloheptanes (XIII and XIV) had a glc retention time corresponding with that of 1H-undecafluorocycloheptene(XV).

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