Heterocyclic Polyfluoro-compounds. Part 40.[1] Preparation of Polyfluoroazepines

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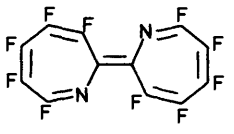
The hexafluoro-Dewar-benzene adduct of phenyl azide yields hexafluoro-1-phenyl-1*H*-azepine on pyrolysis. Reaction of ethyl azidoformate with hexafluorobenzene yields ethyl hexafluoro-1*H*-azepine-1-carboxylate (21%), with octafluoronaphthalene yields 1,2-(ethoxycarbonylimino)-1,2,3,4,5,6,7,8-octafluoro-1,2-dihydronaphthalene (23%), and with 1,2,3,4-tetrafluoronaphthalene yields 1,2-(ethoxycarbonylimino)-1,2,3,4-tetrafluoro-1-1,2-dihydronaphthalene (18%) and ethyl 5,6,7,8-tetrafluoro-1-naphthylcarbamate (48%). No azepines were obtained from the reaction of cyanogen azide with the two naphthalenes.

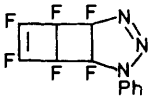
POLYFLUORINATED azepines are a rare class of compound. Hexafluoro-1-cyano-1*H*-azepine has been obtained from the reaction of hexafluorobenzene with cyanonitrene (from cyanogen azide),[2] but other nitrenes appear less reactive towards fluoroaromatic compounds.[3] Unlike phenyl azide, pentafluorophenyl azide did not yield azepines when decomposed in hot anilines,[4] but ring-expansion of pentafluorophenylnitrene is apparently possible since flow pyrolysis of the azide produced perfluorobi-(1-azacyclohepta-3,5,7-trien-2-ylidene) (1) in low yield.[4,5]

Hexafluoro-Dewar-benzene, readily obtained by photochemical isomerization of hexafluorobenzene,[6] is a reactive dipolarophile and forms the adduct (2) with phenyl azide.[7] The adduct (2), when heated in n-decane at 100 °C for 7 days, lost nitrogen and gave the *N*-phenylazepine (3). This is in contrast to the phenyl azide adduct of hexamethyl-Dewar-benzene, which undergoes rearrangement to a triazonine without loss of nitrogen upon heating.[8] It is uncertain whether decomposition of the triazoline portion precedes or follows cleavage of the central C–C bonds,[9] but the route obviates the reluctance of hexafluorobenzene to undergo nitrene addition.

Despite the report of the use of hexafluorobenzene as an inert solvent for the study of ethoxycarbonylnitrene insertions into the C–H bonds of *trans*-1,2-dimethylcyclohexane,[3] we find that thermal decomposition of ethyl azidoformate in an excess of hexafluorobenzene at 90 °C for 72 h yields the *N*-ethoxycarbonylazepine (4) in moderate yield (21%). Photolysis of ethyl azidoformate in hexafluorobenzene also yields the azepine (4). With octafluoronaphthalene in methylene dichloride, the ethoxycarbonylnitrene adduct (5) was obtained in similar yield (23%). The tautomeric benzazepine structure (6) was ruled out, since, in contrast to the azepines (3) and (4), a high-field shift of the fluorine nuclei adjacent to the nitrogen was observed in the ^{19}F n.m.r. spectrum, indicating that they were attached to a saturated carbon atom. This effect of annelation is presumably due to resonance energy differences. Compound (5), when heated at 155 °C in toluene, gave a low yield of an isomeric compound identified spectroscopically as (7). This remarkable rearrangement

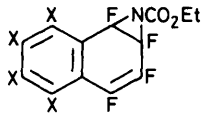


(1)

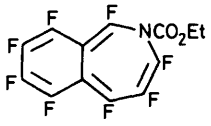


(2)

(3) R = Ph
(4) R = CO_2Et



(5) X = F
(8) X = H



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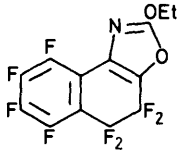

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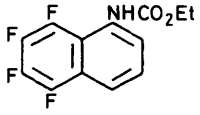

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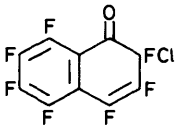

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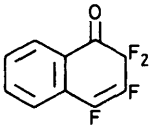

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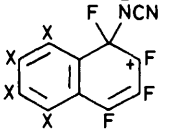


(12) X = H or F

requires an aziridine-to-oxazoline rearrangement,[10] and two sigmatropic fluorine shifts.

1,2,3,4-Tetrafluoronaphthalene has a fluorocarbon and a hydrocarbon ring for comparison. With a deficiency

of ethyl azidoformate in methylene dichloride at 90 °C for 24 h it gave compound (8) by addition to the fluorinated portion, and the urethane (9) by insertion, in the ratio 27 : 73.

No azepines were obtained from the reaction of cyanogen azide (from cyanogen chloride and sodium azide) in acetonitrile with the two naphthalenes. From octafluoronaphthalene, a very low yield of the ketone (10) was obtained, and tetrafluoronaphthalene gave the ketone (11) (10%). A dipolar intermediate of type (12) could lead eventually to these products by chloride ion attack or fluorine shift and hydrolysis of a cyanoimine to a ketone.

Very recently, it has been stated that nitrene insertions into benzene rings with electron-withdrawing substituents to give azepines are unknown, and the thermolysis of 4-(2-azidobenzyl)methoxycarbonylbenzene, which results in an intramolecular insertion, was claimed as a first example.[11] The reaction of cyanogen azide with hexafluorobenzene provides an earlier example,[2] and of ethyl azidoformate another.

EXPERIMENTAL

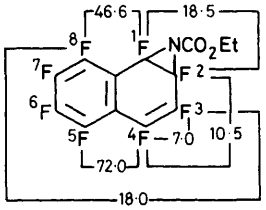
Products were identified by elemental analysis, i.r. spectroscopy (Perkin-Elmer model 257), n.m.r. spectroscopy [Varian HA 100 instrument operating at 100 MHz for ^1H nuclei (internal tetramethylsilane reference) and 94.1 MHz for ^{19}F nuclei (external trifluoroacetic acid reference)], mass spectrometry (A.E.I. MS902 spectrometer), and g.l.c. The appropriate precautions were taken when handling the highly explosive cyanogen azide [12] and the toxic cyanogen chloride.[13]

Pyrolysis of 1,2,3,4,5,6-*Hexafluoro*-9-*phenyl*-7,8,9-*triazatricyclo*[4.3.0.0^{2,5}]*nona*-3,7-*diene* (2).—The title phenyl azide adduct (2) (0.66 g, 2.1 mmol) and n-decane (1.8 g) were sealed in a Pyrex ampoule (10 cm^3) and heated at 110 °C for 7 d. The resulting solution was chromatographed on silica gel to give after elution with chloroform, removal of the solvent *in vacuo*, and sublimation at 40 °C and 0.1 mmHg *hexafluoro*-1-*phenyl*-1H-*azepine* (3) (0.54 g, 1.95 mmol, 93%) (Found: C, 51.9; H, 1.8; F, 40.8. $C_{12}H_5F_6N$ requires C, 52.0; H, 1.8; F, 41.2%), as a pale yellow solid, m.p. 64—65 °C, with $\nu_{max.}$ 1 723m,sh, 1 713s, and 1 702m,sh cm^{-1} (CF=CF str.) and δ_F −8.4 (F-2,7), −66.4, and −76.2 p.p.m. (*cf.*,[2] the *N*-cyano-compound).

Preparation of Ethyl Hexafluoro-1H-*azepine*-1-*carboxylate* (4).—Ethyl azidoformate [14] (3.28 g, 28.5 mmol) and hexafluorobenzene (31.75 g, 170.7 mmol), sealed in a Pyrex ampoule (100 cm^3) and heated *in vacuo* at 90 °C for 72 h, gave nitrogen as a noncondensable gas, material volatile at room temperature, which was fractionated by trap-to-trap distillation *in vacuo* to give a mixture of carbon dioxide and ethylene (10 mg), and recovered hexafluorobenzene (30.10 g, 161.8 mmol, 95%). The residue was distilled, *in vacuo*, to give *ethyl hexafluoro*-1H-*azepine*-1-*carboxylate* (4) (1.63 g, 6.0 mmol, 21%) (Found: C, 39.5; H, 2.3; F, 41.7; N, 5.4. $C_9H_5F_6NO_2$ requires C, 39.5; H, 1.8; F, 41.7; N, 5.1%), b.p. 58 °C at 0.05 mmHg, and tris(ethoxycarbonyl)amine [15] (3.05 g, 13.1 mmol, 46%), b.p. 69 °C at 0.05 mmHg, which was identified spectroscopically and a tarry residue, which t.l.c. indicated to be a complex mixture. The azepine (4) showed $\nu_{max.}$ 1 778s (C=O str.), 1 724s,sh, and 1 718s cm^{-1} (CF=CF str.), $\lambda_{max.}$ (n-hexane) 221 (ε 4 505) and 253 nm (3 280), δ_H (CCl_4) 1.38 (CH_3) and 4.35 (CH_2), and δ_F −13.9 (F-2,7), −66.5, and −76.8 p.p.m.

Hexafluorobenzene (32.3 g, 174 mmol) and ethyl azidoformate (3.1 g, 27 mmol), sealed in a silica tube (300 cm^3) and irradiated with u.v. light (Hanovia S500 lamp at a distance of 15 cm) for 66 h, gave nitrogen, recovered hexafluorobenzene (30.3 g, 163 mmol), the azepine derivative (4) (0.73 g, 2.7 mmol, 10%), tris(ethoxycarbonyl)amine (1.2 g, 5.2 mmol, 57%), and a tarry residue (0.4 g).

Preparation of 1,2-(*Ethoxycarbonylimino*)-1,2,3,4,5,6,7,8-*octafluoro*-1,2-*dihydronaphthalene* (5).—Octafluoronaphthalene (13.15 g, 48.3 mmol) in methylene dichloride (33.6 g) and ethyl azidoformate (2.20 g, 19.1 mmol), sealed in a Pyrex ampoule (300 cm^3) and heated at 90 °C for 48 h, gave as volatile products nitrogen (0.50 g, 17.8 mmol, 93%), traces of carbon dioxide and ethylene, and recovered



SCHEME 1

methylene dichloride (33.1 g, 98%), and an involatile residue (15.0 g). Chromatography of the residue on Florisil (60—100 mesh) gave recovered octafluoronaphthalene (12.0 g, 44.0 mmol, 91%), which was eluted with light petroleum (b.p. 40—60 °C), the *imino-derivative* (5) (1.55 g, 4.3 mmol, 23%) (Found: C, 43.6; H, 1.6; F, 42.2; N, 3.7%; $M^{+\cdot}$, 359. $C_{13}H_5F_8NO_2$ requires C, 43.4; H, 1.4; F, 42.3; N, 3.9%; *M*, 359), as a liquid, b.p. 136 °C at 774 mmHg (Siwoloboff), which was eluted with carbon tetrachloride, and a fraction (0.63 g) eluted with ethanol, which t.l.c. indicated to be a complex mixture.

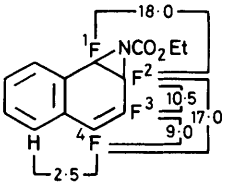
Compound (5) showed $\lambda_{max.}$ (n-hexane) 304 (ε 1 070), 293 (1 120), 256 (2 510), and 220 nm (3 540), $\nu_{max.}$ 1 767vs (C=O str.), 1 709s (CF=CF str.), and 1 642, 1 522, and 1 495s cm^{-1} (ring str.), δ_H (50% w/w in CCl_4) 4.06 (CH_2) and 1.14 (CH_3) and δ_F (see Scheme 1) −60.0 (F-8), −63.9 (F-5), −68.0 (F-1), −69.2 (F-7), −71.9 (F-4), −72.7 (F-3), −74.3 (F-6), and −85.6 p.p.m. (F-2) and the substantial coupling constants (Hz) shown. Similar large four-bond coupling constants of *peri*-fluorines are seen in perfluoro-1,2-dihydronaphthalene [16] ($J_{1,8}$ = 32.2 and $J_{4,5}$ = 62 Hz), but the more rigid system here shows the larger values.

Reaction of Ethyl Azidoformate with 1,2,3,4-*Tetrafluoronaphthalene*.—Ethyl azidoformate (0.92 g, 8.0 mmol) and 1,2,3,4-tetrafluoronaphthalene [17] (4.80 g, 24.0 mmol) in dichloromethane (20.3 g), sealed *in vacuo* in a Pyrex ampoule (300 cm^3) and heated at 90 °C for 24 h, gave as volatile products nitrogen (0.22 g, 7.9 mmol, 98%) and dichloromethane (20.1 g) and a solid residue which was extracted with dichloromethane to give after removal of the solvent a pale yellow solid (5.4 g). This was sublimed at 60 °C *in vacuo* to give a pale yellow sublimate (3.6 g) and a residue. The sublimate was chromatographed on Florisil to give 1,2,3,4-tetrafluoronaphthalene (3.00 g, 15.0 mmol, 63% recovery), which was eluted with light petroleum (b.p. 40—60 °C), 1,2-(*ethoxycarbonylimino*)-1,2,3,4-*tetrafluoro*-1,2-*dihydronaphthalene* (8) (0.40 g, 1.4 mmol, 18%)

(Found: C, 54.4; H, 3.2; F, 26.4; N, 4.7%; $M^{+\bullet}$, 287. $C_{13}H_9F_4NO_2$ requires C, 54.4; H, 3.2; F, 26.5; N, 4.9%; M, 287), as a white solid, m.p. 65—68 °C, eluted with chloroform, a trace of tris(ethoxycarbonyl)amine, eluted with chloroform, and an unidentified red solid, eluted with ethanol.

The non-sublimable residue was similarly chromatographed to yield a trace of tetrafluoronaphthalene, *ethyl* 5,6,7,8-*tetrafluoro*-1-*naphthylcarbamate* (9) (1.10 g, 3.8 mmol, 48%) (Found: C, 54.6; H, 3.5; F, 26.2; N, 4.8%; $M^{+\bullet}$, 287. $C_{13}H_9F_4NO_2$ requires C, 54.4; H, 3.2; F, 26.5; N, 4.9%; M, 287), as a white solid, m.p. 133—135 °C, eluted with carbon tetrachloride, and traces of tris(ethoxycarbonyl)amine, and an unidentified red solid.

Compound (8) showed $\lambda_{max.}$ (ethanol) 252 nm (ε 8 160), $\nu_{max.}$ 1 764s (C=O str.), 1 700m (CF=CF str.), and 1 669m, 1 616m, 1 517s, 1 495vs, and 1 471s cm^{-1} (ring str.), δ_H (10% w/w in CCl_4) 0.89 (CH_3), 3.87 (CH_2), and *ca.* 7.6 (complex, 4H), and δ_H [see Scheme 2, where the F,F and



SCHEME 2

H,F coupling constants (Hz) are shown] −70.6 (F-1), −71.4 (F-4), −75.2 (F-3), and −83.8 p.p.m. (F-2).

The urethane (9) showed $\lambda_{max.}$ (ethanol) 221 (ε 41 390) and 293 nm (6 185), $\nu_{max.}$ 3 322s (N–H str.), 1 740vs (C=O str.), 1 615m, 1 618m, 1 565s, 1 522s, 1 495s, 1 471s (ring str.), and 1 250s cm^{-1} (C–O str.), δ_H (10% w/w in $CDCl_3$) 7.5—8.2 (3 Ar-H), 7.9 (NH), 4.23 (CH_2), and 1.32 (CH_3), and δ_F 69.0 (2F) and 80.2 p.p.m. (2F).

Reaction of Cyanogen Azide with Octafluoronaphthalene.—Sodium azide (3.25 g, 50.0 mmol), activated by treatment with hydrazine hydrate,[14] octafluoronaphthalene (12.90 g, 47.4 mmol), cyanogen chloride (4.90 g, 79.7 mmol), and acetonitrile (27.70 g), were sealed (Fisher Porter valve) *in vacuo* in a Pyrex ampoule (100 cm^3) and rapidly shaken at 20 °C for 5 days. Further acetonitrile (25.70 g) was then added *via* the valve and shaking was continued for a further 5 days at 45 °C. The ampoule was then cooled to −196 °C, nitrogen (1.36 g, 48.6 mmol, 97%) removed *in vacuo*, and then acetonitrile (53.4 g) containing cyanogen chloride (1.00 g, 16.3 mmol) was removed *in vacuo* at room temperature. The residue was continuously extracted with methylene dichloride leaving an insoluble residue (7.94 g), which was not further investigated. The soluble material (10.21 g) was chromatographed on Florisil to give octafluoronaphthalene (5.70 g, 20.9 mmol, 44%), eluted with light petroleum (b.p. 40—60 °C), 2-chloroperfluoronaphthalene-1(2*H*)-one (10) (0.59 g, 1.94 mmol, 4%) (Found: C, 39.7; F, 42.6; Cl, 10.5. Calc. for $C_{10}ClF_7O$: C, 39.4; F, 43.7; Cl, 11.7%), eluted with methylene dichloride and spectroscopically identical to that previously reported,[18] an unidentified brown solid (1.47 g), eluted with ethanol, and a solid that remained on the column and was not investigated further.

Reaction of Cyanogen Azide with 1,2,3,4-*Tetrafluoronaphthalene.*—Activated sodium azide (0.85 g, 13.1 mmol), cyanogen chloride (1.61 g, 26.2 mmol), and acetonitrile (4.70 g) were sealed in a Pyrex ampoule (60 cm^3) and shaken at 20 °C for 4 days, when 1,2,3,4-tetrafluoronaphthalene (2.94 g, 14.10 mmol) in dichloromethane (24.06 g) was added, and the shaking continued at 45 °C for 2 days. Nitrogen (0.35 g, 12.5 mmol, 95%) was then removed at −196 °C, and cyanogen chloride (0.79 g, 12.8 mmol), acetonitrile (4.70 g), and methylene dichloride (24.06 g) were removed at room temperature *in vacuo*. The methylene dichloride soluble portion (2.40 g) of the residue (4.25 g) was sublimed *in vacuo* to give 1,2,3,4-tetrafluoronaphthalene (1.45 g, 7.25 mmol, 49% recovery), which sublimed at 40 °C, 2,2,3,4-tetrafluoronaphthalene-1(2*H*)-one (11) (0.27 g, 1.35 mmol, 10%) (Found: C, 57.6; H, 2.2%; $M^{+\bullet}$, 216. Calc. for $C_{10}H_{14}F_4O$: C, 55.6; H, 1.9%; M, 216), as a yellow solid, m.p. 82—84 °C, which sublimed at 50—75 °C, and an involatile residue which was no longer soluble in methylene dichloride.

2,2,3,4-Tetrafluoronaphthalene-1(2*H*)-one (11) showed $\nu_{max.}$ 1 733m (CF=CF str.) and 1 712s cm^{-1} (C=O str.), *m/e* 216 ($C_{10}H_4F_4C^{+\bullet}$, 100), 188 ($C_9H_4F_4^{+\bullet}$, 49), 187 ($C_9H_3F_4^{+\bullet}$, 50), 168 ($C_9H_9F_3^{+\bullet}$, 79), 137 ($C_8H_3F_2^{+\bullet}$, 20), and 69 ($CF_3^{+\bullet}$, 14%), δ_H (10% w/w in CCl_4) *ca.* 7.6 (3H) and 8.04 (H-4), and δ_F −33.6 (F-2, $|J_{2,3}|$ 21.5, $|J_{2,4}|$ 14.2 Hz), −66.8 (F-4, $|J_{3,4}|$ 8.5 Hz), and −80.9 p.p.m. (F-3).

Thermal Rearrangement of 1,2-(*Ethoxycarbonylimino*)-1,2,-3,4,5,6,7,8-*octafluoro*-1,2-*dihydronaphthalene* (5).—The imino-compound (8) (1.5 g, 4.2 mmol) and toluene (58.1 g), sealed in a Pyrex ampoule (300 cm^3) and heated at 155 °C for 60 h, gave, after removal of the solvent *in vacuo*, a residue (1.3 g) which was distilled at 75 °C and 0.05 mmHg to give a fraction (0.53 g) shown by g.l.c. (2 m SE30 at 180 °C) to be mainly (90%) one component, together with two others. The major component was identified spectroscopically as 2-ethoxyperfluoro-4,5-dihydronaphtho[1,2-*d*]oxazole (7) (Found: $M^{+\bullet}$ 359. Calc. for $C_{13}H_5F_8NO_2$: M, 359), with $\nu_{max.}$ 2 985m, 1 761m, 1 600s, 1 515s, 1 493s, 1 439s, 1 408s, 1 389s, 1 156s, and 1 230s cm^{-1}, *m/e* 359 ($C_{13}H_5F_8NO_2^{+\bullet}$, 23), 331 ($C_{11}HF_8NO_2^{+\bullet}$, 100), 297 ($C_{11}H_5F_6NO_2^{+\bullet}$, 15), 295 ($C_{11}F_7NO^{+\bullet}$, 12), 286 ($C_{10}F_8N^{+\bullet}$, 19), 272 ($C_{10}F_8^{+\bullet}$, 8), 241 ($C_9F_7^{+\bullet}$, 14), 224 ($C_6F_8^{+\bullet}$, 31), and 186 ($C_6F_6^{+\bullet}$, 11%), δ_H (20% w/w in CCl_4) 1.50 (CH_3) and 4.58 (CH_2), and δ_F −32.0 (F-1, $|J_{1,8}|$ 33 Hz), −40.2 (F-2), −58.8 (F-8), −60.8 (F-5), −70.4 (F-6), and −74.2 (F-7).

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