Journal of Fluorine Chemistry, 50 (1990) 319–325

Received: March 2, 1990; accepted: August 23, 1990

SYNTHETIC UTILITY OF 3-(PERFLUORO-1,1-DIMETHYLBUTYL)-1-PROPENE. PART IV.* SYNTHESIS AND PROPERTIES OF 1,1,1,2,2,3,3,8,9,9,9-UNDECAFLUORO-4,4,8-TRIS(TRIFLUOROMETHYL)NONANE - A NEW POTENTIAL OXYGEN CARRIER FOR BIOMEDICAL USE

Wojciech DMOWSKI

Institute of Organic Chemistry, Polish Academy of Sciences,
01-224 Warsaw (Poland)

SUMMARY

The title compound, $CF_3CF_2CF_2(CF_3)_2CCH_2CH_2CH_2CF(CF_3)_2$, was synthesised in high yield by a free radical addition of heptafluoroisopropyl iodide to 3-(perfluoro-1, 1-dimethylbutyl)-1-propene followed by reduction of the adduct. Physical properties and solubilities for oxygen, nitrogen, carbon dioxide and air of the new fluorohydrocarbon have been determined.

INTRODUCTION

Riess and Le Blanc [1] proposed incompletely fluorinated alkenes and alkanes, $R_FCH=CHR_F$ and $R_FCH_2CH_2R_F$, as potential oxygen carrying agents for blood substitutes. Such compounds have shown high chemical inertness and the oxygen and carbon dioxide carrying capacities comparable to that of perfluorocarbons, and even better emulsion stability. A number of 1,2-bis-(perfluoroalkyl)ethenes and ethanes, where R_F = n-C_4F_9, n-C_6F_{13} n-C_8F_{17} and iso-C_3F_7 were synthesised [2,3,4]. While continuing studies on the synthetic utility of readily available

---

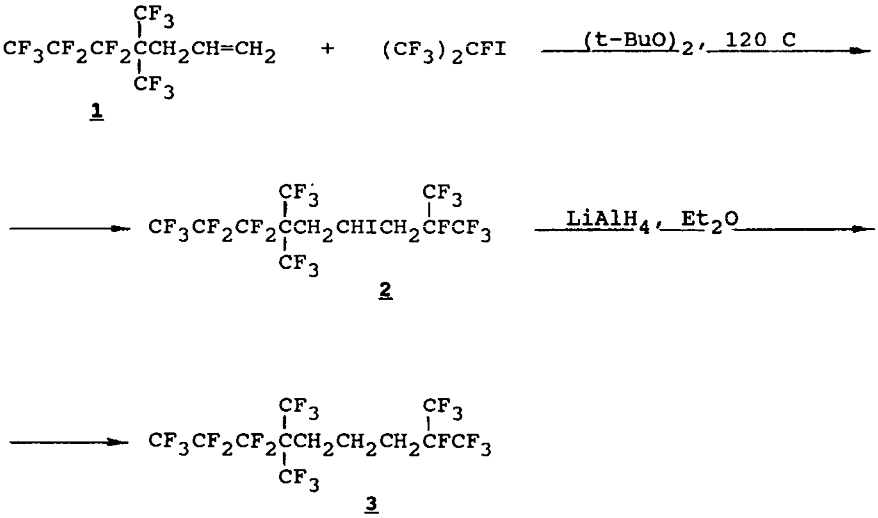
* For part III see J.Fluorine Chem., **48** (1990) 77.

0022-1139/90/$3.50

3-(perfluoro-1,1-dimethylbutyl)-1-propene 1 [5,6], we have found that this compound is a convenient intermediate to highly fluorinated alkanes, $CF_3CF_2CF_2(CF_3)_2CCH_2CH_2CH_2R_F$. The latter compounds differ from the above mentioned fluorohydrocarbons by the presence of, at least one, internally branched perfluoroaliphatic group C_6F_{13}*, and by one carbon atom longer non-fluorinated bridges. The present paper describes conversion of alkene 1 to 1,1,1,2,2,3,3,8,9,9,9-undecafluoro-4,4,8-tris(trifluoromethyl)nonane (3) and reports basic physical properties and solubilities for gases of this new, highly branched fluorohydrocarbon.

RESULTS AND DISCUSSION

The synthesis of 1,1,1,2,2,3,3,8,9,9,9-undecafluoro-4,4,8-tris(trifluoromethyl)nonane (3) involves two stages: a peroxide promoted addition of heptafluoroisopropyl iodide to alkene 1, and reduction of adduct 2 with lithium aluminium hydride.



$$\underset{\mathbf{1}}{CF_3CF_2CF_2\overset{CF_3}{\underset{CF_3}{C}}CH_2CH{=}CH_2} + (CF_3)_2CFI \xrightarrow{(t\text{-}BuO)_2,\ 120\ C}$$

$$\longrightarrow \underset{\mathbf{2}}{CF_3CF_2CF_2\overset{CF_3}{\underset{CF_3}{C}}CH_2CHICH_2\overset{CF_3}{C}FCF_3} \xrightarrow{LiAlH_4,\ Et_2O}$$

$$\longrightarrow \underset{\mathbf{3}}{CF_3CF_2CF_2\overset{CF_3}{\underset{CF_3}{C}}CH_2CH_2CH_2\overset{CF_3}{C}FCF_3}$$

---

* Some compounds reported so far were terminally branched [4].

Di-tert-butyl peroxide has been found to be the best initiator for the iodide addition reaction; its half-life time at the temperature required for the reaction to proceed (120°C) is long enough (ca. 24 hours) to insure a steady generation of free radicals during the course of the reaction. The crude addition product usually consisted of ca. 75% of adduct **2** together with dimeric and oligomeric iodides formed by the consecutive addition of **2** to alkene **1** and so on. The mixture of iodoalkanes was treated as a whole (adduct **2** was isolated for identification purposes, only) with lithium aluminium hydride in diethyl ether to give a mixture of **3** and higher molecular weight alkanes, mostly dimer $C_{21}H_{11}F_{33}$. The attempted catalytic reduction (Pt/C) with gaseous hydrogen gave no satisfactory results. Distillation gave alkane **3** of 98% purity (GLC estimate) in ca. 50% yield with respect to alkene **1**. Careful rectification afforded a product of 99.9% purity, which was used for determination of physical properties and solubilities of gases.

The structure of alkane **3** was confirmed by elemental analysis, mass spectrum, and ^1H and ^{19}F NMR spectra.

TABLE

Physical properties and solubilities of gases for 1,1,1,2,2,-3,3,8,9,9,9-undecafluoro-4,4,8-tris(trifluoromethyl)nonane (**3**).

Molecular weight	530.17 (calculated)
Boiling point	175 - 176°C (760 Torr)
Melting point	below -20°C
Density (at 20°C)	1.7230 g/cm^3
Refraction index (n_D^{25})	1.3117
Vapour pressure (at 20°C)	3 Torr
(at 37°C)	7 Torr
Solubility of gases (vol %, at 37°C and 760 Torr)	
oxygen	45.4
nitrogen	38.7
carbon dioxide	215.0
air	40.1

The oxygen solubility in <u>3</u> is within the range reported for numerous fluorocarbons [7] and the solubility for carbon dioxide is <u>ca.</u> one and half times higher than for fluorocarbons [8]. Other physical properties of fluorohydrocarbon <u>3</u>, e.g. low melting point, high boiling point and a vapour pressure at 37°C between that of perfluoro-tripropylamine and perfluorodecalin, comply with requirements for potential oxygen-carrying agents for biomedical applications [8]. However, the chances of compound <u>3</u> to become a serious candidate blood substitute, in view of its molecular weight which implies an organ half-retention time longer than that of F-tripropylamine [9,10], are rather low. Nevertheless, it seems that 1,1,1,2,2,3,3,8,9,9,9-undecafluoro-4,4,8-tris(trifluoromethyl)nonane (<u>3</u>) may find non-transfusional applications, e.g. in organ preservation or as a contrast agent in diagnosis [10].

EXPERIMENTAL

The NMR spectra were recorded in $CDCl_3$ solutions with a JEOL 100 MHz spectrometer. Chemical shifts are from internal TMS for the ^1H, and from internal CCl_3F for the ^{19}F spectra (positive upfield). Purity of compounds was checked by GLC using a 3.5 m x 4 mm column packed with Chromosorb G coated with 3% Silicon Oil SE-52. Mass spectra were obtained with a Finnigan MAT 8200 instrument at 70 eV. Densities were measured by a picnometric method and vapour pressures by a isoteniscope method. Solubilities of gases were determined volumetrically [11].

Syntheses of 3-(perfluoro-1,1-dimethylbutyl)-1-propene <u>1</u> [5,6] and heptafluoroisopropyl iodide [12] were described previously.

Addition of heptafluoroisopropyl iodide to 3-(perfluoro-1,1-dimethylbutyl)-1-propene (1)

The reaction was performed in a 800 ml capacity Pyrex glass pressure tube (internal diameter <u>ca.</u> 50 mm) fitted with a ROTAFLO valve and a magnetic stirring bar.

The tube was flushed with dry argon then, alkene **1** (270 g, 0.75 mole), heptafluoroisopropyl iodide (240 g, 0.76 mole) and di-t-butyl peroxide (6 ml) were added. The tube was immersed in an oil bath and heated, with stirring, at 118 - 122°C for 24 hours. An evident volume contraction of the reaction mixture occurred. The resultant yellowish liquid (480 g) was shown by GLC to contain, besides the main product (70 - 75%), longer retention time components (20 - 25%) and small amounts of both substrates.

A portion of the reaction mixture was subjected to vacuum distillation. The main component was collected at 98 - 102°C (20 Torr) and identified as adduct **2**. A colourless oily liquid; found: C, 22.1; H, 0.7; I, 19.2; F, 57.8%. $C_{12}H_5IF_{20}$ requires: C, 22.0; H, 0.8; I, 19.3; F, 57.9%; MS: m/z 529(13)M^+-I, 489 (13)M^+-I-2HF, 337(11)$C_6H_5IF_7^+$, 281(11)$C_6F_{11}^+$, 189(12)$C_6H_3F_6^+$, 181(43)$C_4F_7^+$, 169(25)$C_3F_7^+$, 145(25)$C_4H_2F_5^+$, 69(100)CF_3^+, 41(38) $C_3H_5^+$; ^{1}H NMR: 3.05 ppm (4H, CH_2) and 4.62 ppm (1H, CHI) (ABXMN spin system); ^{19}F NMR: 61.3 ppm (CF_3), 63.2 ppm (CF_3), 76.4 ppm (CF_3), 78.4 ppm (CF_3), 80.7 ppm (CF_3), 107.3 ppm (CF_2), 123.8 ppm (CF_2), 189 ppm (CF).

1,1,1,2,2,3,3,8,9,9,9-Undecafluoro-4,4,8-tris(trifluoromethyl)-nonane (3)

The reaction was carried out in a 2000 ml glass reactor fitted with a mechanical stirrer, dropping funnel (250 ml) and an efficient reflux condenser. Before use, the apparatus was swept with dry argon.

Diethyl ether (300 ml, freshly distilled from $LiAlH_4$) and lithium aluminium hydride (20 g) were placed in the reactor and brought to boiling. A solution of the crude product of addition of heptafluoroisopropyl iodide to alkene **1** (262 g) in diethyl ether (300 ml) was added dropwise until vigorous reaction started. Then, the reactor was placed in a cooling bath and the rest of the solution was added at such a rate as to keep boiling spontaneously (1 - 1.5 hour). When the exothermic reaction ceased, heat was applied again to keep boiling for five hours. After cooling to 0°C, 30% sulphuric acid (400 ml) following by water (100 ml) were added, while vigorously stirring. The upper ethereal layer was separated, the water layer was extracted with ether (3 x 300 ml), and the combined ether solutions were washed with aqueous sodium sulphite (removal of free iodine) and dried over anhydrous calcium chloride. The ether was distilled off under atmospheric pressure and the residue was subjected to vacuum distillation. Alkene **3** of ca. 98% purity (100 -110 g) was collected at 70 - 80°C(15 - 17 Torr). Rectification with a 500 mm Fisher column gave a product of 99.9% purity (90 - 95 g, ca. 43% with respect to **1**). A colourless and odourless liquid; found: C, 27.1; H, 1.1; F, 71.6%. $C_{12}H_6F_{20}$ requires: C, 27.2; H, 1.1; F, 71.7%; MS: m/z 511(0.5)M^+-F, 491(1)M^+-F_2, 471(1)M^+-HF_3, 145(16)$C_4H_2F_5^+$, 119(10)$C_2F_5^+$, 69(100)CF_3^+, 47(12)$C_2H_4F^+$, 41(19)$C_3H_5^+$; ^1H NMR: 2.10 ppm (2H), 2.23 ppm (4H); ^{19}F NMR: 64.2 ppm (6F, CF_3), 77.2 ppm (6F, CF_3), 80.8 ppm (CF_3), 107.4 ppm (CF_2), 123.5 ppm (CF_2), 184.4 ppm (CF).

ACKNOWLEDGEMENTS

The author is indebted to Professor S.Petri of the Medical University of Łódź (Poland), for determining physical properties of alkene **1** and the solubilities of gases.

This work has been supported by the Ministry of Health and by the Polish Academy of Sciences (project CPBP-01.13.1.21).

REFERENCES

1 J.G.Riess and M.LeBlanc, Angew.Chemie, **90** (1978) 654.
2 G.Santini, M.LeBlanc and J.G.Riess, Tetrahedron, **29** (1973) 24.
3 F.Jeanneaux, M.LeBlanc, A.Cambon and J.Guion, J.Fluorine Chem., **4** (1974) 261.
4 C.Arlen, Y.Gauffreteau, F.Jeanneaux, M.Le Blanc and J.G.Riess Bull.Soc.Chim., (**1985**) 562.
5 W.Dmowski and R.Woźniacki, Pol.Pat., 145018 (1989).
6 W.Dmowski and J.Porwisiak. Pol.Pat.Appl., P-265914 (1987).

7 E.P.Wesseler, R.Iltis and L.C.Clark,Jr., J.Fluorine Chem., **9** (1977) 137.

8 K.Yokoyama, T.Suyama and R.Naito, in R.Filler and Y.Kobayashi (Ed.), 'Biomedical Aspects of Fluorine Chemistry', Elsevier Biomedical, Amsterdam, New York, Oxford (1982), p. 191-210.

9 J.G.Riess, Artif.Organs, **8** (1984) 44.

10 J.G.Riess, Current Surgery, **45** (1988) 365.

11 A.Kufelnicki, S.Petri and K.Witkowski, Acta Polon.Pharm., **42** (1985) 273 and references therein.

12 W.Dmowski, Pol.Pat.Appl., P-273371 (1988).