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SYNTHESIS OF FLUORINATED DIFUNCTIONAL MONOMERS

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SUMMARY

In order to obtain fluorinated difunctional monomers for fluoropolyurethanes, we synthesized novel fluorinated aliphatic diisocyanates [$OCNCH_2(CF_2)_nCH_2NCO$] from corresponding diols [$HOCH_2CH_2(CF_2)_nCH_2CH_2OH$]. Oxidation of the diols with chromium trioxide-sulfuric acid gave α, α, ω, ω-tetrahydroperfluoroalkylene dicarboxylic acids in high yields. Then treating the acids with phosphorus pentachloride afforded corresponding dicarboxyl chlorides, which are easily converted to dicarboxyl azides with hydrazoic acid-pyridine complex. Finally, on Curtius rearrangement of the azides, the end products, α, α, ω, ω-tetrahydroperfluoroalkylene diisocyanates were obtained in 53% (n=4) and 19% (n=6) yields from the starting diols.

INTRODUCTION

Fluorinated polymers are used in various fields because of their characteristic properties such as low surface energy, high chemical resistance and bioinactivity.

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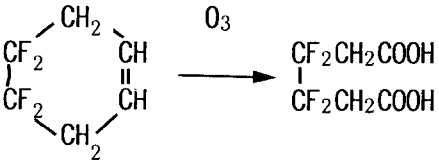
Most of these polymers are currently made by addition polymerization and very few are made by polycondensation, because the fluorinated difunctional monomers are not easily available. Among them, various types of perfluoroalkylene dicarboxylic acids and their derivatives are already known. But polymers derived from them are so unstable in hydrolytic conditions that they cannot be used in practical systems.

We recently reported fluorinated polyurethanes with high mechanical and antithrombus performance [1]. In order to obtain monomers for the polyurethanes we synthesized polyfluoroalkylene dicarboxylic acids and their derivatives, having a methylene group between each functional group and perfluoroalkylene group.

3,3,4,4-Tetrafluorohexanedioic acid is already known as a rare example of this type of dicarboxylic acid [2]. It was prepared by ozonization of 4,4,5,5-tetrafluoro-1-cyclohexene:



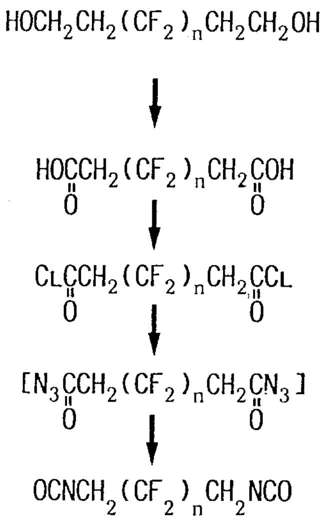
However, this method is not applicable to other carboxylic acids with different carbon numbers, because the starting cycloalkenes other than those with 5- or -6 membered rings are difficult to obtain.

In this article, we would like to report a new synthetic route to α,α,ω,ω-tetrahydroperfluoroalkylene dicarboxylic acids and their derivatives, especially diisocyanates as key monomers of the antithrombus fluorinated polyurethanes.

RESULTS & DISCUSSION

Since one of the key monomers for antithrombogenic fluorinated polyurethanes is a α,α,ω,ω-tetrahydroperfluoroalkylene diisocyanate, our study has focused on introduction of the isocyanate group.

There are several methods for introducing isocyanate, such as phosgenation of amines, Curtius rearrangement of carboxyl azides, Hofmann rearrangement of amides and so on. Although the phosgenation method is commonly used for commercially-based production of various isocyanates, phosgene is very toxic and not always available in laboratories. So we tried the second method, Curtius rearrangement, which seems to be a convenient method on a laboratory scale. Starting from fluorinated diol (**1**) we studied each step to the diisocyanate (**4**) as shown in **Scheme 1**.



$$\begin{aligned}
&HOCH_2CH_2(CF_2)_nCH_2CH_2OH \quad 1 \qquad a : n=4 \quad b : n=6\\
&\downarrow\\
&HO\overset{}{\underset{O}{\overset{\|}{C}}}CH_2(CF_2)_nCH_2\underset{O}{\overset{\|}{C}}OH \quad 2\\
&\downarrow\\
&Cl\underset{O}{\overset{\|}{C}}CH_2(CF_2)_nCH_2\underset{O}{\overset{\|}{C}}Cl \quad 3\\
&\downarrow\\
&[N_3\underset{O}{\overset{\|}{C}}CH_2(CF_2)_nCH_2\underset{O}{\overset{\|}{C}}N_3]\\
&\downarrow\\
&OCNCH_2(CF_2)_nCH_2NCO \quad 4
\end{aligned}$$

SCHEME 1

Oxidation of diol (1)

We tried the oxidation of **1a** to 3,3,4,4,5,5,6,6-octafluorooctanedioic acid (**2a**) by several oxidizing agents ; chromium trioxide, nitric acid and potassium permanganate, which are commonly used for the oxidation of organic compounds. The results of the oxidation are summarized in **Table I.**

Oxidation of **1a** by chromium trioxide-conc.H_2SO_4 in acetone (Jones reagent) [3] gave **2a** in a high yield. And **2a** was also obtained on oxidation with chromium trioxide-acetic acid, but in a low yield (38%) and no starting diol was recovered.

Treatment of 1-bromo-6-hexanol with nitric acid has been reported to give the corresponding carboxylic acid in a high

TABLE I

Oxidation of **1a**

Oxidizing agent	Reaction conditions temperature(°C)/time(hrs)	Yield of **2a** (%)	Other products IR absorption [a] (cm^{-1})
CrO_3-H_2SO_4 aq.	r.t. / 16	95	
CrO_3-CH_3COOH aq.	0-5 / 4	38	1760
HNO_3	90-100/ 2	0	1640-1650
$KMnO_4$-H_2O	60-65 / 5	74 [b]	1780 (shoulder)
$KMnO_4$-KOH aq.	r.t. / 18	0	1740-1780 (brood)
$KMnO_4$-KOH aq.	80 /1.5	0	1780 [c]
$KMnO_4$-H_2SO_4 aq.	r.t. / 1	0	1705

[a] Infrared absorption of carbonyl region.

[b] About 10% of carbonyl group is directly combined to difluoromethylene.

[c] Perfluorohexanedioic acid, $HOOC(CF_2)_4COOH$, was obtained in 53% yield.

yield[4],but under the same conditions,2a was not obtained from **1a**. The strong infrared absorption at 1640-1650cm^{-1} of the resulted oily product suggest the formation of nitrate, and starting diol was also recovered.

Oxidation of **1a** with potassium permanganate in the presence of water, potassium hydroxide or sulfuric acid gave different products respectively. It has been reported that treatment of 1,1,1-trichloro-5-pentanol with potassium permanganate in the presence of water gave the corresponding carboxylic acid in a high yield [5]. According to this procedure, we obtained **2a** from **1a** in 74% yield. But ^{13}C NMR of the obtained dicarboxylic acid revealed that it contained about 10% of carboxyl group combined directly to perfluoroalkylene group. That is, methylene adjacent to perfluoroalkylene group was oxidized, being accompanied with carbon-carbon bond cleavage. Absorption at 1780cm^{-1} in the infrared spectrum of the product also showed the presence of this type of carboxylic acid. Potassium permanganate oxidation in the presence of potassium hydroxide gave only perfluorohexanedioic acid in 53% yield, whilst that in the presence of sulfuric acid gave neither **2a** nor perfluorohexanedioic acid, but only a small amount of unknown powder.

3,3,4,4,5,5,6,6,7,7,8,8-dodecafluorodecanedioic acid (**2b**) was also obtained by the oxidation of **1b** with Jones reagent in 96% yield.

Chlorination of dicarboxylic acid (2)

Chlorination of **2a** was tried with thionyl chloride and phosphorus pentachloride. The results are summarized in **Table II**.

Treatment of **2a** with phosphorus pentachloride [5] gave corresponding dichloride (**3a**) in a high yield, and the product could be isolated and purified easily by distilling directly from the reaction mixture. Acid **2a** with thionyl chloride at a refluxing temperature for 5 hours gave a very small amount of **3a** and about 40% of starting diacid was recovered. Attempted chlorination of **2a** with thionyl chloride in the presence of a catalytic amount of N,N-dimethylformamide or hexamethylphos-

TABLE II

Chlorination of **2a**

Chlorinating agent	Solvent	Mole ratio of agent/-COOH	Reaction conditions	Yield of **3a**(%)	Others
PCl_5	Et_2O	2.1	refluxing, 1hr	78	
$SOCl_2$	none	5.5	refluxing, 5hrs	trace	**2a** was recovered
$SOCl_2$-DMF	none	5.5	refluxing, 3hrs	trace	many products were obtained [a]
$SOCl_2$-HMPA	none	5.5	refluxing, 20min	trace	

[a] analyzed by gas-liquid chromatography

phoric triamide gave virtually no **3a**, but a lot of unidentified products were detected by means of gas- liquid chromatography.

3b was also obtained by treating **2b** with phosphorus pentachloride in 76% yield.

Synthesis of diisocyanates (4)

Reaction of dicarboxyl chlorides (**3**) with hydrazoic acid-pyridine complex gave dicarboxyl azides [7]. This reaction proceeded smoothly even at 5 °C, and infrared spectra of the reaction mixtures showed that no carboxyl chloride remained. Fluorinated carboxyl azides thus obtained were subjected *in situ* to Curtius rearrangement, and 2,2,3,3,4,4,5,5-octafluoro-1,6-diisocyanatohexane (**4a**) and 2,2,3,3,4,4,5,5,6,6,7,7-dodeca-fluoro-1,8-diisocyanatooctane (**4b**) were obtained in 72% and 26% yield respectively. The reason for the low yield of **4b** is not clear, but the diisocyanate once obtained, we think, was converted to some dimeric or trimeric compounds and this reaction lowered the yield of **4b**.

Thus we obtained fluorinated diisocyanates which are key monomers for fluorinated polyurethanes and other polymers. The overall yields of diisocyanates (**4**) from starting diols were 53% for **4a** and 19% for **4b** as shown below.

$$HOCH_2CH_2(CF_2)_nCH_2CH_2OH \dashrightarrow OCNCH_2(CF_2)_nCH_2NCO$$

4

a : n=4, yield 53%

b : n=6, yield 19%

Further the intermediate dicarboxylic acids (**2**) and dicarboxyl chlorides (**3**) are also useful as key monomers for fluorinated polyesters, polyamides and so on.

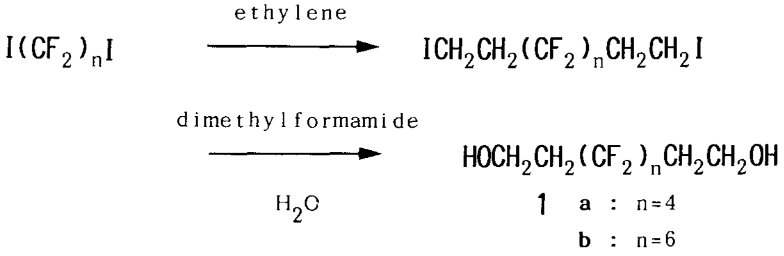
Since various types of fluorinated alkyl iodides and alkylene diiodides are available, this synthetic method can be applied to the synthesis of other fluorocarbon compounds including fluorinated difunctional monomers.

EXPERIMENTAL

Infrared (IR) spectra were measured on a JASCO A-202 spectrophotometer and are expressed in reciprocal centimeters. Proton and fluorine-19 nuclear magnetic resonance (^1H NMR and ^{19}F NMR) spectra were recorded on a Varian EM390 spectrometer operating at 90.0MHz for ^1H and 84.7Hz for ^{19}F. Chemical shifts are reported as values in parts per million (ppm) relative to tetramethylsilane and trichlorofluoromethane respectively. Carbon-13 nuclear magnetic resonance (^{13}C NMR) spectra were obtained with a JEOL JNM-FX100 spectrometer operating at 100MHz. Chemical shifts are reported as values in ppm relative to deuteriochloroform. Mass spectra were obtained on a Hitachi RMU-6MG spectrometer.

Preparation of 3,3,4,4,5,5,6,6-octafluoro-1,8-octanediol (**1a**) and 3,3,4,4,5,5,6,6,7,7,8,8-dodecafluoro-1,10-decanediol (**1b**)

According to the literature [8], **1** were synthesized from corresponding , -diiodoperfluoroalkanes, as show below.



$$I(CF_2)_nI \xrightarrow{\text{ethylene}} ICH_2CH_2(CF_2)_nCH_2CH_2I \xrightarrow[H_2O]{\text{dimethylformamide}} HOCH_2CH_2(CF_2)_nCH_2CH_2OH$$

1 **a** : n=4
b : n=6

1a : yield 68% ; bp 118-119 C/1.0mmHg ; IR (neat) 3350 (OH), 900, 2950 (CH_2), 1160cm^{-1} (CF_2) ; ^1H NMR (acetone-d_6) 3.89 (t, 4H, $CH_2C\underline{H}_2OH$, J_{H-H} = 6.9Hz), 2.37 (tt, 4H, $CF_2C\underline{H}_2CH_2$, J_{H-F} =19.5Hz) ; ^{19}F NMR (acetone-d_6) -113.0 (m, 4F, $CH_2C\underline{F}_2$), -123.4 (m, 4F, $CH_2CF_2C\underline{F}_2$) ; ^{13}C NMR (acetone-d_6, values from acetone-d_6) 89.3 ($CH_2CF_2\underline{C}F_2$), 82.4 ($CH_2\underline{C}F_2$), 24.9 ($CF_2CH_2\underline{C}H_2$), 4.8 ($CF_2\underline{C}H_2$).

1b : yield 63% ; bp 125 C/1.2mmHg ; IR (neat) 3300 (OH), 2880, 2940 (CH_2), 1180cm^{-1} (CF_2) ; ^1H NMR (acetone-d_6) 3.91

(t, $CH_2C\underline{H}_2OH, J_{H-H}$ = 6.7Hz), 2.39 (tt, $CF_2CH_2C\underline{H}_2$, J_{H-F} = 19.7Hz) ; ^{19}F NMR (acetone-d_6) -113.2 (m, 4F) -121.8 (m, 4F), -123.9 (m, 4F).

Synthesis of 3,3,4,4,5,5,6,6-octafluorooctanedioic acid (**2a**)(nc) and 3,3,4,4,5,5,6,6,7,7,8,8-dodecafluorodecanedioic acid (**2b**)(nc)

To a solution of **1a** (125g, 0.43mol) in acetone (1320g) was added Jones reagent, that is a mixture of chromium trioxide (253g, 2.53mol), concentrated sulfuric acid (370g) and deionized water (690g), maintaining the temperature of the reaction mixture at 5-10°C. After an overnight stirring at an ambient temperature, 2-propanol (70ml) was added dropwise to reduce the excess oxidizing reagent, then hydrochloric acid (1mol dm^{-3}, 500ml). Evaporation of acetone and extraction of the residue with ethyl ether gave **2a** (130g, 95% yield) as white powder : mp 195-200°C ; IR (KBr disc) 3050 (OH), 2990, 2950 (CH_2), 1720 (C=O), 1220-1180cm^{-1} (CF_2) ; ^1H NMR (acetone-d_6) 10.53 (s, 2H, -COOH), 3.34 (t, 4H, J_{H-F} = 18.4Hz CH_2) ; ^{19}F NMR (acetone-d_6) -112.1 (m, 4F, $CH_2C\underline{F}_2$), -122.6 (m, 4F, $CH_2CF_2C\underline{F}_2$) ; ^{13}C NMR (acetone-d_6, values from acetone-d_6) 166.0 (COOH), 117.5 ($\underline{C}F_2CF_2CH_2$), 112.4 ($CF_2\underline{C}F_2CH_2$), 37.5 (CH_2).

2b was synthesized by the same procedure as **2a** in 96% yield : mp 180-183°C ; IR (KBr disc) 3000 (OH), 1720 (C=O), 1220 1180 (CF_2) ; ^1H NMR (acetone-d_6) 9.37 (s, 2H, COOH), 3.38 (t, 4H, J_{H-F}= 18.3Hz, CH_2) ; ^{19}F NMR (acetone-d_6) -110.8 (m, 4F), -120.8 (m, 4F), -122.2 (m, 4F).

Synthesis of 3,3,4,4,5,5,6,6-octafluorooctanedioyl chloride (**3a**)(nc) and 3,3,4,4,5,5,6,6,7,7,8,8-dodecafluorodecanedioyl chloride (**3b**)(nc)

To a slurry of **2a** (136g, 410mmol) and anhydrous ethyl ether, was added PCl_5 (183g, 880mmol) in portions at such a rate that ether was refluxed gently. Distillation under reduced pressure gave **3a** (113g, 78% yield) as a slightly yellow liquid : bp 77-78 C at 0.73-0.80mmHg ; IR (neat) 3000,.

2960 (CH_2), 1800 (C=O), 1180 (CF_2) cm^{-1} ; ^1H NMR ($CDCl_3$) 3.72 (t,J_{H-F} = 16.1Hz, CH_2) ; ^{19}F NMR ($CDCl_3$) -112.8 (m, 4F, $CH_2C\underline{F}_2$), -123.0 (m, 4F, $CH_2CF_2C\underline{F}_2$) ; ^{13}C NMR ($CDCl_3$) 86.9 (C=O), 37.4 ($CH_2CF_2\underline{C}F_2$), 33.5 ($CH_2\underline{C}F_2$), -30.1 (CH_2) ; MS m/e(M^+) = 354.

3b was synthesized by the same procedure as **3a** in 76% yield : bp 96 C at 1.2-1.3mmHg, IR (neat) 2970, 2930 (CH_2), 1790 (C=O), 1190 (CF_2) ; ^1H NMR ($CDCl_3$) 3.70 (t, J_{H-F} =17.6Hz, CH_2) ; ^{19}F NMR ($CDCl_3$) -112.7 (m, 4F), -122.3 (m, 4F), 123.4 (m, 4F) ; MS m/e(M^+) = 454.

Synthesis of 2,2,3,3,4,4,5,5-octafluoro-1,6-diisocyanatohexane (**4a**)(nc) and 2,2,3,3,4,4,5,5,6,6,7,7-dodecafluoro-1,8-diisocyanatodecane (**4b**)(nc)

To a solution of **3a** (113g, 320mmol) in dry toluene was added a mixture of pyridine (50.4g, 640mmol) and HN_3 (680mmol) in toluene at 0-5°C. The resultant precipitate was removed by filtration, and the filtrate was subjected to aspirator vacuum for a few minutes to remove the excess HN_3. An IR spectrum of the solution thus obtained showed no carbonyl absorption of dicarboxyl chloride at $1800cm^{-1}$. Two new bands at 2150 and $1700cm^{-1}$ indicated the presence of carboxyl azide.

To dry toluene (150ml) maintained at 95°C, a solution of dicarboxyl azide obtained above was added at such a rate that nitrogen was evolved smoothly. Fractional distillation of the resultant solution under reduced pressure gave **4a** (69.6g, 72% yield) as transparent liquid : bp 65-67°C at 1.0mmHg ; IR (neat) 2250 (NCO), 1180 (CF_2) ; ^1H NMR ($CDCl_3$) 3.90 (t, J_{H-F} = 13.7Hz CH_2) ; ^{19}F NMR ($CDCl_3$) -119.3 (m, 4F, $CH_2C\underline{F}_2$), -124.5 (m, 4F, $CH_2CF_2C\underline{F}_2$) ; ^{13}C NMR ($CDCl_3$) 80.3 (NCO), 37.5 ($\underline{C}F_2CF_2CH_2$), 34.0 ($CF_2\underline{C}F_2CH$), -33.7 (CH_2).

4b was obtained by the same procedure as **4a** in 26% yield : bp 62-65°C at 0.12mmHg ; IR (neat) 2250 (NCO), 1180 (CF_2) ; ^1H NMR ($CDCl_3$) 3.90 (t, J_{H-F} = 13.9Hz, CH_2) ; ^{19}F NMR ($CDCl_3$) -119.2 (m, 4F) , -122.6 (m, 4F), -124.0 (m, 4F).

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