FLUORINATED ISOCYANATES – REACTIONS WITH FLUORINATED ANHYDRIDES, ACIDS, AND RELATED SUBSTRATES

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SUMMARY

F-Phenylisocyanate reacts with cyclic or linear anhydrides with the aid of catalysts to form F-(N-arylimides) in good yields. Similar reactions with fluorinated acids lead directly to amides. This isocyanate undergoes smooth reaction with various substrates (hexafluoroacetone, trioctylphosphine oxide, and itself). Several reactions between F-aryl and F-alkyl isocyanates are compared. Reaction between the latter and F-anhydrides or acids gives products derived from fluoride ion transfer reactions.

INTRODUCTION

The chemistry of fluorinated isocyanates has received limited attention.[1] Hydrocarbon isocyanates are good electrophiles;[2] substitution of F-alkyl or F-aryl for the hydrocarbon group affords an extremely electrophilic isocyanate. In the course of experimentation we have found that fluorinated isocyanates react with extremely weak nucleophiles under relatively mild conditions. This work deals with the reactions between fluorinated isocyanates and fluorinated anhydrides, acids, and related substrates. Attention is focused on the different types of products obtained from the reactions between a given substrate and an F-alkyl or F-aryl isocyanate.

RESULTS AND DISCUSSION

Reactions of F-phenylisocyanate

Anhydrides

F-Phenylisocyanate[3] cleanly reacts with F-glutaric anhydride to afford F-(N-phenylglutarimide) in good yields. The reaction liberates carbon dioxide and is catalyzed by DMF, triethylamine, and the like.

81%
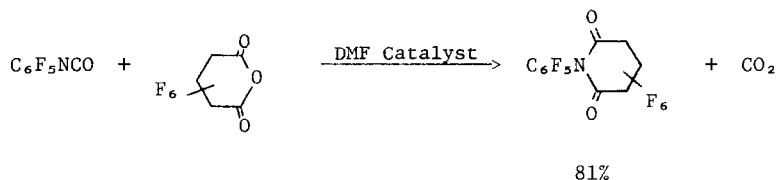
A minor side product, $C_6F_5NHCO(CF_2)_3CON(CH_3)_2$ also was isolated and characterized in this reaction.

The reaction between the isocyanate and a linear F-anhydride[4] proceeds similarly and at a faster rate.

$$C_6F_5NCO + (C_3F_7CO)_2O \xrightarrow{\text{DMF Catalyst}} C_6F_5N(COC_3F_7)_2 + CO_2$$

55%
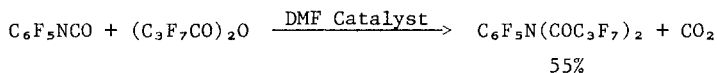
Examination of the crude reaction mixture (GLC) indicates the presence of a minor component, not yet fully characterized, from which the product is easily separated by distillation. The linear imide is unstable to atmospheric moisture; distillation bottoms contain $C_6F_5NHCOC_3F_7$, which apparently results from hydrolysis by adventitious moisture.

These are convenient, one step, preparations of F-(N-arylimides) which appear to be generally applicable. It should be noted that in these sequences no attempt was made to maximize yields.

Scheme A is suggested to account for the observed products.

Scheme A

$$(R_fCO)_2O + B: \longrightarrow R_fCOB^+ \ OCOR_f^- \xrightarrow{\text{ArNCO}} ArNCOOCOR_f + B:$$
$$\underset{COR_f}{|}$$

I

$$I + B: \longrightarrow ArNCO_2^- \ BCOR_f^+ \xrightarrow[-B]{-CO_2} ArN(COR_f)_2 \qquad B = DMF$$
$$\underset{COR_f}{|}$$

II
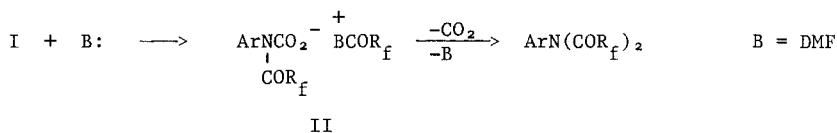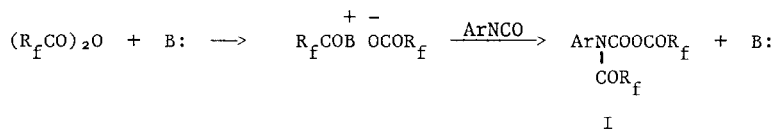
An alternate but similar sequence involves preliminary complex formation between DMF and the isocyanate followed by complex reaction with anhydride to form I. The reaction is insensitive to the order of addition of reagents, so perhaps both sequences are operable. The elimination of carbon dioxide derived from the isocyanate carbonyl via II is preferred over that derived from the anhydride carbonyl due to precedence in related hydrocarbon chemistry[5] as well as the relative ease of carbamic acid over fluorinated acid decarboxylation. In reactions (above) involving cyclic fluorinated anhydrides intermediate I may be cyclic or oligomeric.

In this scheme DMF catalysis is surprising; this reagent is known to react with fluorinated anhydrides[6] to form amides, i.e., $R_fCON(CH_3)_2$. Since such amides are not catalysts in the imide forming reactions, appreciable quantities of DMF must persist throughout the reaction sequence.

Acids and related reactions

F-Phenylisocyanate reacts with F-alkyl carboxylic acids without catalysts at room temperature. As the reaction proceeds carbon dioxide is liberated while amide product precipitates. The following scheme using F-butyric acid is representative.

$$C_6F_5NCO \ + \ C_3F_7CO_2H \ \longrightarrow \ C_6F_5NHCOC_3F_7 \ + \ CO_2$$
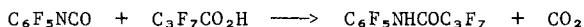
Hexafluoroacetone aniline previously has been prepared by various routes,[7] one of which involves a phosphine imine precursor.

$$\phi_3PO \ + \ C_6H_5NCO \ \xrightarrow{-CO_2} \ \phi_3P{=}NC_6H_5 \ \xrightarrow{(CF_3)_2CO} \ \phi N{=}C(CF_3)_2$$
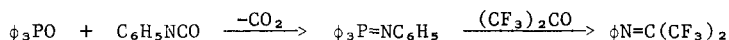
To the best of our knowledge, this partially fluorinated imine has not been prepared by the direct reaction between the isocyanate and ketone. This contrasts the preparation of F-acetoneaniline which now has been prepared by the DMF catalyzed reaction between F-phenylisocyanate and hexafluoroacetone.

$$C_6F_5NCO \ + \ (CF_3)_2CO \ \xrightarrow[150°]{DMF} \ C_6F_5N{=}C(CF_3)_2 \ + \ CO_2$$
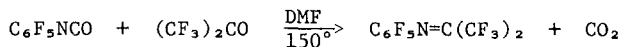
The success of the above reaction further demonstrates the powerful elec-trophilic character that an F-aryl substituent imparts to an isocyanate group. Similar to the hydrocarbon analog, F-phenylisocyanate reacts with trioctylphosphine oxide affording the corresponding phosphine imine. The

imine, a waxy solid, is an effective C_6F_5N transfer agent; prepared in situ, it reacts smoothly with F-glutaric anhydride to give the expected imide.

$$C_6F_5NCO \ + \ (Oct)_3PO \ \xrightarrow{-CO_2} \ C_6F_5N=P(Oct)_3 \ \xrightarrow{\hspace{2cm}} \ C_6F_5N$$

69%
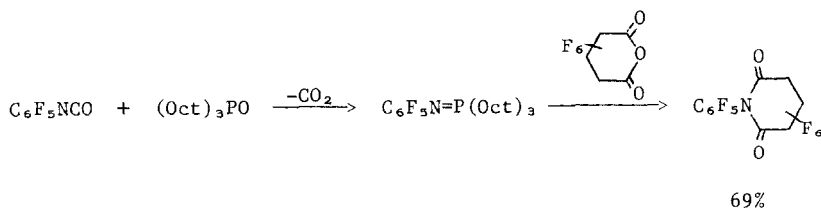
Lastly, F-phenylisocyanate trimerizes to the isocyanurate in the presence of pyridine. Isocyanate dimer was not detected in the crude reaction mixture.

$$C_6F_5NCO \ \xrightarrow[110°]{\text{pyridine}}$$

50%
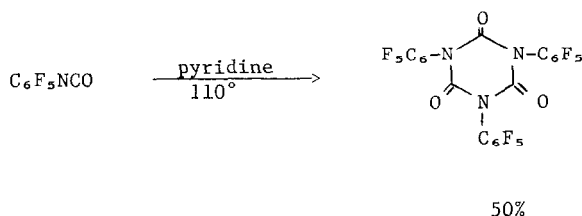
Related reactions of F-heptyl isocyanate
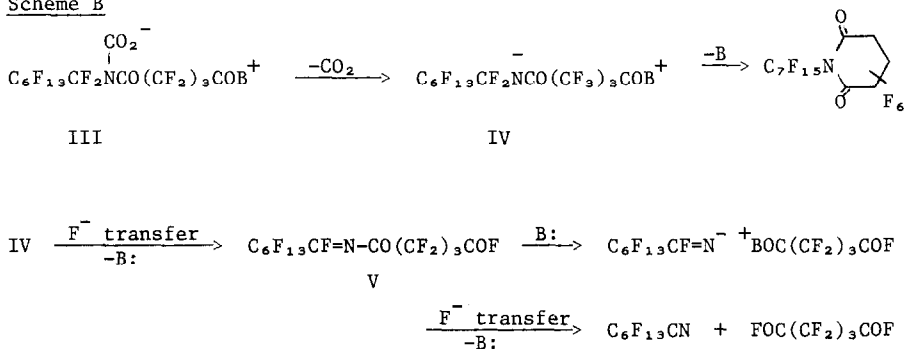
For comparative purposes, F-heptyl isocyanate was prepared and reacted with F-glutaric anhydride and F-octanoic acid. The anhydride reaction proceeded at a rate comparable to the corresponding reaction with F-phenyl-isocyanate, but afforded the imide as a minor product.

Two low-boiling materials, identified as F-heptanonitrile and F-glutaryl fluoride, were the major products.

$$C_7F_{15}NCO \ + \ \xrightarrow{\text{DMF catalysis}} \ C_6F_{13}CN \ + \ FOC(CF_2)_3COF \ + \ \text{} \ + \ CO_2$$
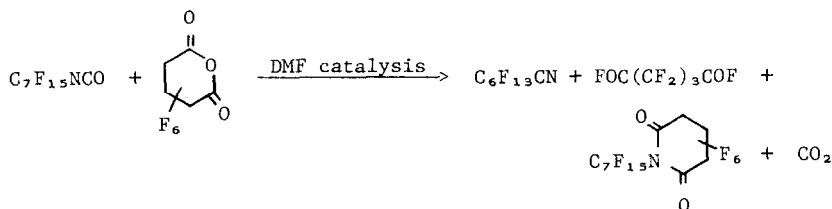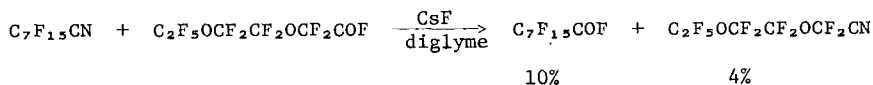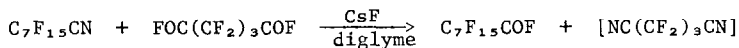
The formation of nitrile and acid fluoride in this reaction is a direct consequence of kinetically labile α-fluorine substituents on the starting isocyanate. Scheme B which should be similar to Scheme A up to the formation of intermediate III accounts for these observations.

Scheme B

$$C_6F_{13}CF_2\overset{\underset{\displaystyle CO_2^-}{|}}{N}CO(CF_2)_3COB^+ \xrightarrow{-CO_2} C_6F_{13}CF_2\overset{-}{N}CO(CF_2)_3COB^+ \xrightarrow{-B} C_7F_{15}N$$

III   IV

$$IV \xrightarrow[-B:]{F^- \text{ transfer}} C_6F_{13}CF=N-CO(CF_2)_3COF \xrightarrow{B:} C_6F_{13}CF=N^- {}^+BOC(CF_2)_3COF$$

V

$$\xrightarrow[-B:]{F^- \text{ transfer}} C_6F_{13}CN + FOC(CF_2)_3COF$$

Intermediate IV apparently undergoes facile fluoride ion transfer[*] eventually leading to the nitrile and diacid fluoride in competition with ring closure which affords imide. The azaamide (V) apparently is unstable to the reaction conditions and dissociates affording nitrile and diacid fluoride. Fluoride ion transfers such as these may be viewed as the fluorocarbon counterparts to proton shifts in hydrocarbon chemistry. In effect the fluorines α to the NCO group are transferred to the anhydride forming nitrile, diacid fluoride, and CO_2.
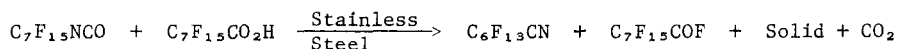
It is notable that in an attempt to prepare an F-(N-alkylglutarimide) or intermediate V by an alternate route, what is believed to be a nitrile-acid fluoride metathasis occurred. The cesium fluoride catalyzed reaction between F-octanonitrile and F-glutaryl fluoride in diglyme affords F-octanoyl fluoride. Similar reaction between the same nitrile and tetrafluoroethylene oxide trimer acid fluoride resulted in CN/COF exchange in a low conversion experiment.

$$C_7F_{15}CN + FOC(CF_2)_3COF \xrightarrow[\text{diglyme}]{CsF} C_7F_{15}COF + [NC(CF_2)_3CN]$$

$$C_7F_{15}CN + C_2F_5OCF_2CF_2OCF_2COF \xrightarrow[\text{diglyme}]{CsF} C_7F_{15}COF + C_2F_5OCF_2CF_2OCF_2CN$$

                                                                    10%   4%

An intermediate such as $R_fCF = NCOR'_f$ may be formed and subsequently exchange N for O atoms in unimolecular or bimolecular, fluoride ion catalyzed processes.[8]

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[*] The data do not distinguish between inter or intra-molecular fluoride ion transfer.

The products obtained from the reaction between F-heptyl isocyanate and a fluorinated acid are predictable based on the anhydride results. A representative reaction is shown below.

$$C_7F_{15}NCO \ + \ C_7F_{15}CO_2H \ \xrightarrow[\text{Steel}]{\text{Stainless}} \ C_6F_{13}CN \ + \ C_7F_{15}COF \ + \ Solid + CO_2$$

The solid is believed to be composed mostly of the azaamide, $C_6F_{13}CF=NCOC_7F_{15}$ which could not be isolated in a pure state. Exposure of the solid to moist air followed by recrystalization from CCl_4 gave the following imide-rich[*] mixture.

$$Solid \ \xrightarrow[\substack{\text{2) recrystali-}\\\text{zation}}]{\text{1) } H_2O} \ C_6F_{13}CONHCOC_7F_{15} \ + \ C_6F_{13}CONH_2 \ + \ C_7F_{15}CONH_2$$

EXPERIMENTAL

The highly fluorinated starting materials used in this work are supplied by PCR, Inc. Vapor phase chromatographic analysis was performed on a Hewlett-Packard Model 700 instrument using an 8 ft x 0.25 in. 15 or 35% PFO-XR on Gas-Chrom R 60-80 mesh column. Infrared spectra were recorded on a Perkin-Elmer Infracord spectrometer. ^{19}F NMR spectra were recorded on a Varian XL-100 spectrometer at 94.1 MHz. The mass spectra were recorded on Model 14-107 Bendix time of flight spectrometer.

Reaction between F-phenylisocyanate and F-glutaric anhydride; Preparation of F-(N-phenylglutarimide)(n.c.)

F-Glutaric anhydride (21.2 g, 0.0955 mole), and F-phenylisocyanate (20.0 g, 0.0955 mole) were stirred together at 25°C. No gas was evolved. The mixture was heated to reflux and stirred for 0.25 hr; still no gas was evolved. Then 2 ml of DMF was added, gas evolved at a slow but steady rate. The reaction was heated (bath temperature 125°) with stirring overnight. In the morning, gas was no longer evolving. The reaction mixture was dark in color and on cooling solidified. The contents were sublimed at 0.1 mm (50° bath temperature)

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*This imide would not have been characterized if it were not for independent experimentation by Dr. K. B. Baucom of PCR, Inc.

affording the corresponding imide (30.0 g, theory 37.0 g, 81%). This material had a m.p. 70–72°. Recrystallization from hexane (25 g imide/100 g hexane) afforded an analytical sample, m.p. 73° (infrared, nujol, C=O. 5.65μ).

> Anal. Calcd $C_{11}F_{11}NO_2$: C, 34.1; N, 3.62
>
>   Found: C, 34.25; N, 3.81

The dark material left in the sublimation apparatus (3.0 g) was recrystallized from toluene to a constant m.p. 161–162°. This material showed CH (3.3–3.5μ), C=O (5.8, 5.9μ), C=C (aromatic 6.6μ, and C–F (8.5–8.8μ) absorptions in the infrared. These data are consistent with the structure $C_6F_5NHCO(CF_2)_3CONMe_2$ (n.c.).

> Anal. Calcd $C_{13}H_7F_{11}N_2O_2$: C, 36.1; H, 1.62; N, 6.5
>
>   Found: C, 35.79; H, 1.25; N, 6.32

Reaction between F-phenylisocyanate and F-butyric anhydride

F-Phenylisocyanate (15.3 g, 0.0732 mole), F-butyric anhydride (30.0 g, 0.0732 mole), and DMF (2 ml) were mixed together in a round bottom flask. The temperature of the reaction rose to 32° while gas was evolved; the reaction mixture was allowed to maintain this temperature without heating for 1 hr, then heated at 60° for 2 hr. GLC showed two products of similar retention time in a 30:59 ratio. The major product, $C_6F_5N(COC_3F_7)_2$ (n.c.), was isolated by distillation (23.2 g), b.p. 64°/1 mm, C=O, 5.65μ. The structure of the minor product is uncertain.

The residue from the distillation solidified on standing (7.8 g) and was recrystallized from Freon-113, m.p. 84–86°, C=O, 5.78μ and NH 3.02μ.

$$\overset{\text{O}}{\overset{||}{}}$$

This is consistent with the structure $C_6F_5NHCC_3F_7$ (n.c.). Since the assigned NH band was absent from the crude reaction mixture, this product is presumably formed by hydrolysis from adventitious moisture during distillation.

> Anal. Calcd for $C_{14}F_{19}NO_2$: C, 29.2; N, 2.44
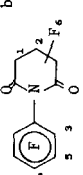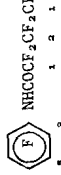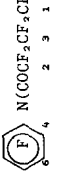>
>   Found: C, 29.0; N, 2.56
>
> Anal. Calcd for $C_{10}HF_{13}NO$: C, 31.8; H, 0.26; N, 3.7
>
>   Found: C, 31.6; H, 0.35; N, 3.8
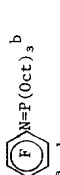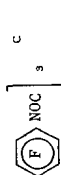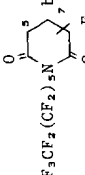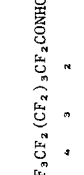
Reaction between F-phenylisocyanate and F-butyric acid

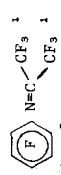F-Phenylisocyanate (6.05 g, 0.029 mole) and F-butyric acid (6.2 g, 0.029 mole) were stirred together in a nitrogen atmosphere at 25°C. A white solid formed slowly as CO_2 was evolved. The reaction was heated to 65°C and maintained at this temperature for 15 hr. At this time the

TABLE I

^{19}F NMR^a and mass spectra data

Structure	1	2	3	4	5	6	7	Mass Spec.
[pentafluorophenyl glutarimide, F_6, N, O, O; ring positions 1,2,3; ring F positions 4,5,3] ^{b}	42.8(T,4)	58.6(P,2)	64.9(D,2)	68.8(T,1)	80.9(T,2)			--
[ring-F]$NHCOCF_2CF_2CF_2CON(CH_3)_2$ ^{a} (positions 1,2,3,1)	40.2(M,4)	47.2(S,2)	67.6(BD,2)	79.4(T,1)	86.6(M,2)	[^{1}H-3.3(D,6), 8.2(BS,1)]		
[ring-F]$N(COCF_2CF_2CF_3)_2$ ^{b} (positions 2,3,1)	4.1(T,6)	36.7(Q,4)	48.3(S,4)	68(D,2)	72(T,1)	84.7(M,2)		
[ring-F]$NHCOCF_2CF_2CF_3$ ^{c} (positions 2,3,1)	3.7(T,3)	42.7(Q,2)	49.8(S,2)	68.4(D,2)	78.6(T,1)	86.4(M,2)	[^{1}H-BS-10.5]	--
[ring-F]$N=P(Oct)_3$ ^{b} (positions 2,3,1)	69.6(M,2)	75.5(M,1)	86.5(M,2)	[^{1}H, typical octyl]				
[ring-F]$N=C(CF_3)_2$ (positions 3,2; subscripts 4,1)	-6.9(BD,6)	76(BD,2)	83(T,1)					M(331), M-F(312), M-CF$_3$(262)
$[$[ring-F]$NOC]_3$ ^{c} (positions 2,3,1)	65.2(M,2)	74(BD,2)	85(M,2)	87(M,2)				--
$CF_3CF_2(CF_2)_5N$ [structure with F$_6$, O, ring positions 5,7, 2-4; subscripts 1,6,2] ^{b}	3.2(T,3)	41(BM,4)	43.6(BM,4)	44.7(B,2)	45.4(T,4)	48.1(B,2)	59.6(P,2)	M-F(570), M-CF$_3$(520), M-C$_5$F$_6$NO$_2$ (369), M-C$_7$F$_{15}$(220)
$CF_3CF_2(CF_2)_3CF_2CONHCOCF_2(CF_2)_4CF_2CF_3$ ^{c} (positions 1,2,3,2,2,4,3,2,1)	3.9(BT,6)	41.7(B,4)	44-45.3(B,14)	48.9(B,4)	[^{1}H,BS-4.8]			--

(a) ^{19}F ppm to high field from external CF$_3$CO$_2$H, ^{1}H ppm from TMS; S=singlet, D=doublet, T=triplet, Q=quintet, B=broad.
(b) CCl$_4$ solution.   (c) Acetone-d$_6$ Solvent

reaction mixture was a solid mass. The mixture was diluted with 10 ml Freon-113, filtered, and washed with 10 ml Freon-113 leaving 7.0 g of $C_6F_5NHCOC_3F_7$, m.p. 84-86°C. Concentration of the Freon-113 afforded another 1.6 g of amide; total 8.6 g (theory 11.0 g, 78% yield).

Reaction between F-phenylisocyanate and hexafluoroacetone

F-Phenylisocyanate (10.0 g, 0.0478 mole) and DMF (0.1 ml) were charged into an 80-ml S.S. autoclave. The autoclave was cooled in a bath of liquid oxygen and evacuated. Hexafluoroacetone (7.94 g, 0.0478 mole) was transferred into the autoclave. The contents were heated to 150° for 18 hr, cooled, and vented. There was recovered 5.8 g of a ketone/CO_2 mixture. The remaining liquid (8.6 g) was distilled to give 3.8 g of $(CF_3)_2C=NC_6F_5$, (n.c.), b.p. 145-148° (infrared C=N, 5.75μ).

In situ preparation of $(Oct)_3P=NC_6F_5$ (n.c.) and its reaction with F-glutaric anhydride

Trioctyl phosphine oxide (10.7 g, 0.0278 mole) was heated to 85°C while F-phenylisocyanate (5.8 g, 0.0278 mole) was added dropwise. As the isocyanate was added CO_2 was evolved. The reaction mixture was maintained at 75° during the isocyanate addition (0.75 hr). On cooling, the reaction mixture solidified to a wax, m.p. 40-41°. Infrared and GLC indicated the disappearance of isocyanate. The intermediate phosphine imine was warmed to 55° while F-glutaric anhydride was added dropwise. At the completion of the addition (0.5 hr) the reaction mixture was heated to 75° and held for 1 hr. The crude mixture was sublimed at 45-50°/0.1 mm; there was obtained 8.1 g of F-(N-phenylglutarimide), m.p. 72-73° (69% yield).

Preparation of tris-(F-phenyl)isocyanurate (n.c.)

F-Phenylisocyanate (5.0 g, 0.024 mole) and pyridine (0.5 ml) were heated at 110°/1 hr. The volatiles were removed from the dark resulting mixture and the residue sublimed at 120°/<1 mm. The crystalline sublimate (2.5 g) was the titled compound, m.p. 169-170°; infrared, nujol, C=O (5.72μ, C=C aromatic (6.6μ).

Anal. Calcd for $C_{21}F_{15}N_3O_3$:   C, 40.0; N, 6.7
            Found: C, 40.0; N, 6.96

Reaction between F-heptylisocyanate and F-glutaric anhydride

F-Heptylisocyanate (7.5 g, 0.0182 mole), F-glutaric anhydride (4.1 g, 0.0182 mole) and Et_3N (0.25 cc) were placed in a flask and heated to 65° in a nitrogen atmosphere. A gas was slowly evolved. The reaction was maintained

at 65° for 16 hr then cooled. GLC showed consumption of starting materials and two low boiling and a high boiling product in the ratio 7:7:5. The low boilers were removed at 5 mm; 5.1 g were collected. The low boilers were identified as $C_6F_{13}CN$ and $FOC(CF_2)_3COF$ from GLC and infrared. The bottoms distilled at 73-78°/1 mm; 3.0 g was collected. The distillate is composed of one major product, tentatively assigned $C_7F_{15}N(COCF_2)_2CF_2$ (n.c.) from spectroscopic data (infrared, CO-5.7µ).

Reaction between F-octanonitrile and F-glutaryl fluoride

F-Octanonitrile (5.0 g, 0.0126 mole), F-glutaryl fluoride (3.1 g, 0.0126 mole CsF (ca. 25 mg), and diglyme (10 ml) were stirred in an 80-ml stainless steel autoclave at 25° overnight. Infrared and GLC showed that no appreciable reaction occurred. The mixture was heated with stirring at 85-95° for 48 hr. GLC of the bottom layer showed that both the nitrile and F-glutaryl fluoride were consumed and replaced by F-octanoyl fluoride. The ratio of $C_7F_{15}CN$ to $C_7F_{15}COF$ was ca. 1:2. Futher heating at 110-120° for 24 hr formed more F-octanoyl fluoride. At this time the ratio of $C_7F_{15}CN:C_7F_{15}COF$ was 1:3. It is possible that $(CF_2)_3(CN)_2$ (b.p. 38°) was formed during the reaction and subsequently lost on sampling.

In a similar manner $C_7F_{15}CN$ (4 g, 0.01 mole) and $C_2F_5OCF_2CF_2OCF_2COF$ (4.1 g, 0.01 mole) were treated with CsF (25 mg) in 10 ml of diglyme with stirring at 100° for 24 hour. GLC showed that ca. 10% of the nitrile was converted to F-octanoyl fluoride. A minor peak was shown to be $C_2F_5OC_2F_4OCF_2CN$ by comparison with an authentic sample.

Reaction between F-heptylisocyanate and F-octanoic acid

An 80-ml S.S. autoclave was charged with F-heptylisocyanate (5.0 g, 0.012 mole) and F-octanoic acid (5.0 g, 0.012 mole). The autoclave was stirred and heated at 75° for 18 hr. The autoclave was vented at 0°C. The contents were diluted with 25 ml of Freon-113 and pressure filtered. The resulting solid was dried at 0.1 mm overnight leaving 3.9 g of a white solid m.p. 96-104°. GLC of the filtrates showed the disappearance of starting isocyanate and a 3:1 ratio of F-octanoyl fluoride:F-heptanonitrile. The solid was exposed to the moist atmosphere then recrystalized from CCl_4 affording a mixture of three compounds (TLC, I_2 developed) which proved to be $C_6F_{13}CONH_2$, $C_7F_{15}CONH_2$ (infrared C=O both 5.85µ) and $C_6F_{13}CONHCOC_7F_{15}$ (n.c.) (infrared bands at 5.55, 5.75, and 6.6µ). A similar reaction using F- butyric acid gave comparable results

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