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POLYFLUOROALKYLATION OF BROMOHETEROCYCLIC COMPOUNDS VIA PERFLUOROALKYLCOPPER INTERMEDIATES

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SUMMARY

Reactions between n-$C_6F_{13}I$, Cu, and various bromoheterocyclic compounds in dimethyl sulfoxide provide a convenient method for the perfluoroalkylation of heterocyclic compounds By this method perfluoroalkylated products of pyridine and pyrimidine were synthesized in near quantitative yields Perfluoroalkylation of bromofurans and bromothiophenes also provided good yields of perfluoroalkylated products, however, competing reactions also yielded various by-products indicative of reductive dehalogenation, homocoupling, polysubstitution beyond the number of C-Br bonds in the starting heterocyclic compound and formation of structural isomers

INTRODUCTION

We have previously reported [1] on the perfluoroalkylation of mono and dibromobenzene compounds via perfluoroalkylcopper intermediates Subsequently, this study was extended

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to the perfluoroalkylation of various mono and polybromo-heterocyclic compounds and we are now reporting the results

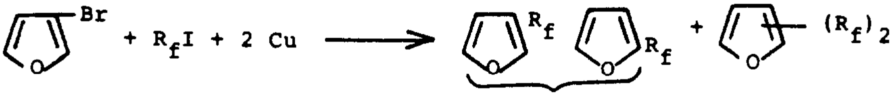
It has generally been accepted that in perfluoroalkylation via organocopper intermediates, the aryl iodides react at a faster rate and provide higher yields of products than their bromo or chloro analogues [1,2,3,4] Solvent effects play an important role in determining the yield of reaction products as well as by-product formation due to competing reactions Numerous aprotic solvents have been examined e g , pyridine, dimethylformamide, dimethyl sulfoxide, dimethylacetamide, hexamethylphosphoramide, sulfolane and 2,6-lutidine Under certain experimental conditions, small yields of by-products were obtained derived from the solvents dimethyl sulfoxide [1,2] and pyridine [3]

Trifluoromethylations of aromatic and heterocyclic compounds have been studied extensively since biological activity due to the CF_3 group has been noted [5] Longer chain perfluoroalkylation of bromoaromatic [2] and bromoheterocyclic [3,4] compounds has attracted only a small interest, perhaps due to the lower yields of perfluoroalkylated products obtained as compared to the iodoaromatics and heterocyclic compounds Our interests are concerned with the effects of longer chain perfluoroalkyl substituents on aromatic [1] and heterocyclic compounds Since there are a greater variety of bromo-substituted heterocyclic compounds than the iodo analogous, we have examined the bromoheterocyclics in more detail in order to determine their efficacy

DISCUSSION

We have found dimethyl sulfoxide to be the solvent of choice in our reactions Good to excellent yields of perfluoroalkylated products were obtained from bromo-substituted heterocycles e g , pyridine, thiophene, furan and pyrimidine (see Table 1) In most instances, the solvent did not react with the starting materials or reaction products In addition to the principal alkylated product, a number of by-products were also obtained indicating competing side reactions These products resulted from a) reductive dehalogenation, b) homocoupling reactions in the case of the polybromo-substituted thiophenes, c) polysubstitution beyond the number of C-Br bonds in thiophenes and furans, d) formation of isomers in the monoalkylated products, and e) decarboxylation Some of these side reactions a, c, d, have been noted previously by other investigators [1-4] in their studies on perfluoroalkylation Trifluoromethylation via copper coupling reactions using CF_3I provides a special case The CF_3Cu intermediate may partially decompose to a CF_2 carbene which reacts with additional CF_3Cu to form C_2F_5Cu In this manner, C_2F_5 alkylated aromatic compounds were produced to some extent from a CF_3I starting material [3] In our studies using longer chain perfluoroalkyl iodides, carbene formation was not likely and therefore, only the perfluoroalkylated products originating from the starting iodides were obtained As mentioned in previous studies [1-3], the type of solvent has an effect on the reaction and product formation It would be interesting to compare the results of our efforts with previous findings However, since the solvent has an influence on the products formed, it would be meaningless to speculate at this time until data generated under comparable experimental conditions of solvent, temperature, and mode of perfluoroalkylcopper formation are obtained

Perfluoroalkylation via copper coupling reactions of the bromo pyridines and pyrimidine with $n\text{-}C_6F_{13}I$ gave excellent yields of perfluoroalkylated products No by-products were indicated by GC/MS analysis of the reaction mixture The bromo pyridines and pyrimidine must be unusually reactive towards the copper coupling reaction as compared to the other bromo heterocyclic compounds examined in our study The 3-perfluoro-n-hexylpyridine (II) and the 5-perfluoro-n-hexylpyrimidine (IV) formed stable CuX complexes whereas the 2,6-di-perfluoro-n-hexylpyridine (III) did not form a stable copper complex These observations may be due to the relative basicity of the various nitrogens or to perhaps steric hindrance of the 2,6-di-substituents on the pyridine The copper complex I gave pure 3-n-perfluorohexylpyridine (II) on thermal decomposition by heating under vacuum or during gas chromatographic analysis Combustion analysis indicated that it was a copper complex containing Cu, Br and I in a Br I ratio of 20 80% The exact structure of the copper complex was not determined Treatment of the copper complexes with aqueous ammonia decomposed them to yield the pure perfluoroalkylated products



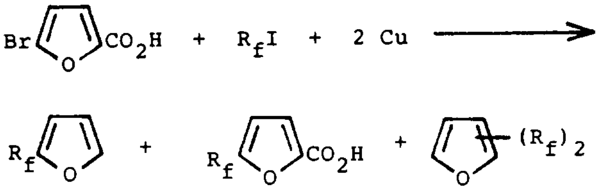
V VI 14%

R_f = n-C_6F_{13} GC area % 76(65%, 3-, 35%, 2-)

The presence of the 2-isomer indicated that some migration of the C_6F_{13} group must have taken place Kobayashi [3] in his studies with 3-bromobenzofuran, CF_3I and Cu (pyridine solvent) also noted some isomerization to produce the 2-substituted CF_3 product It should be pointed out however, that in the course of preparing CF_3Cu, CF_2 carbene formation takes place to some extent and that this may influence somehow 2-substitution or migration of CF_3 In addition to the monosubstituted products V, disubstitution of the 3-bromofuran gave VI in lower yields Since the mixture was inseparable, the exact structures of these two disubstituted isomers were not determined

Perfluoroalkylation of two bromofurans were examined Unlike the pyridines and pyrimidine, the furans did not produce high yields of isomerically pure mono-substituted products as shown in the equation

Perfluoroalkylation of the 5-bromofuroic acid produced a mixture of products indicating the presence of competing reactions



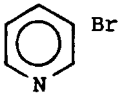
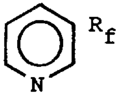
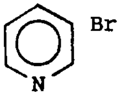
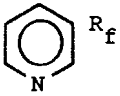
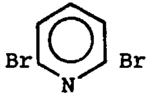
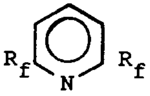
VII VIII VI

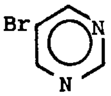
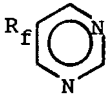
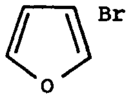
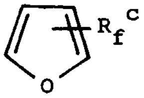
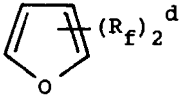
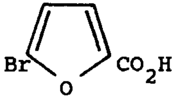
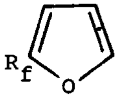
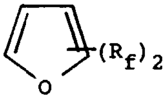
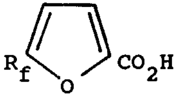
As the data in Table 1 (exp 6,7,8) indicates, Method B, using a preformed R_fCu and a shorter reaction time, favors higher yields of the product VIII It can be seen however, that under nearly the same experimental conditions, longer reaction time (exp 7) yields none of the product VIII It appears that either product VIII or perhaps its copper salt decomposes with time at the elevated reaction temperature In this manner, pure 2-monosubstituted furan VII was obtained in high (GC area %) yield In addition to the decarboxylated product VII, a small quantity of disubstituted products VI were identified by GC/MS analysis

Studies on perfluoroalkylation of halothiophenes have been studied previously by McLoughlin and Thrower [2] using the 1,3-dicopperhexafluoropropane and 2-iodothiophene to give the 1,3-bis(thienyl)hexafluoropropane (25% yield) and with 3-iodopyridine to give the 1,3-bis(3-pyridyl)hexafluoropropane (52% yield) More recently, Wakselman et al [4] reported on the perfluoroalkylation of 2 and 3-bromo and iodothiophenes in dimethylformamide solvent Only a 6% yield of 2-perfluorooctylthiophene was obtained from the copper coupling reaction under the particular experimental conditions used The 3-perfluoroalkylthiophene, however, was prepared in a 30% yield using the 3-bromothiophene and a 50% yield using the 3-iodothiophene In both instances, using the 3-substituted halothiophenes, 2-substituted products were obtained indicating isomerization of the R_f group Under our experimental conditions using DMSO as a reaction solvent, considerably higher yields of products were obtained (see Table 1, exp 9,10,11) The 2-perfluorohexylthiophene IX was obtained isomerically pure, however, the 3-perfluorohexylthiophene XI

TABLE 1

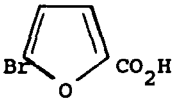
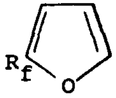
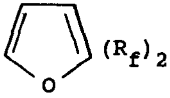
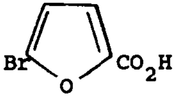
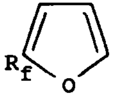
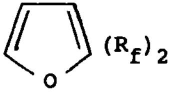
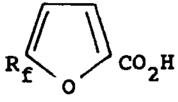
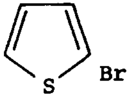
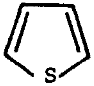
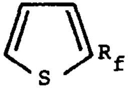
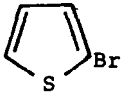
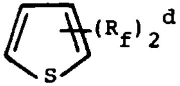
Reactions Between Bromoheterocyclic Compounds, n-$C_6F_{13}I$(R_fI) and Copper

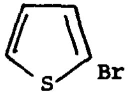
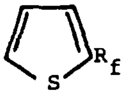
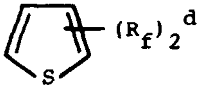
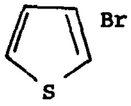
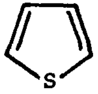
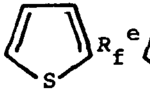
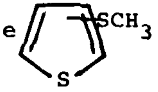
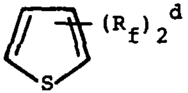
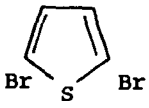
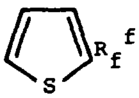
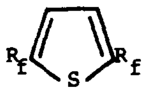
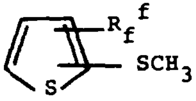
Exp	Method[a]	R_fI, mmol	Heterocyclic Br, (mmol)	Cu, mmol	Reaction Time, h	Products % Yield, (GC Area, Isolated)
1	A	33	 (30)	66	1 5	 CuX[b] (I) (98,71)
2	A	66	 (60)	139	4 0	 (II) (97,82)
3	A	66	 (60)	139	1 5	 (III) (97,89)

4	A	33	 (30)	70	2 0	 (IV) (98,71)
5	B	36	 (30)	82	22 0	 (V) (76,31)  (VI) (14,-)
6	A	36	 (30)	82	4 0	 (VII) (53,-)  (VI) (13,-)^{c}  (VIII) (29,23)

(Continued)

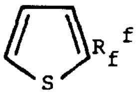
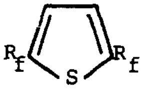
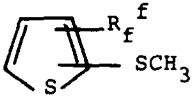
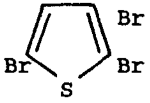
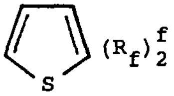
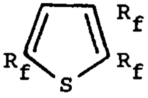
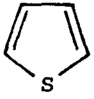
TABLE 1 (cont.)

Exp.	Method[a]	R_fI, mmol	Heterocyclic Br, (mmol)	Cu, mmol	Reaction Time, h	Products % Yield, (GC Area; Isolated)
7	B	36	 (30)	82	21.0	 (VII) (90;51)  (VI) (2;-)[c]
8	B	33	 (30)	69	4.0	 (VII) (28;-)  (VI) (5;-)[c]  (VIII) (57;45)
9	B	33	 (30)	69	17	 (13;-)  (IX) (60;45)  (1;-)  X (14;-) unidentified (12;-)

10	A	33	 (30)	66	1.5	 (8;-)  (64;57) —  (9;-) unidentified (19;-)
11	B	33	 (30)	69	19	 (8;-)  (XI) (68;42)  (1;-)  (20;-) unidentified (3;-)
12	B	48	 (20)	100	3.0	 (10;-)  XII (71;55)  (4;-) $C_8H_5S_2R_f{}^f$ (2;-) $C_8H_4S_2(R_f)_2{}^f$ (10;-)

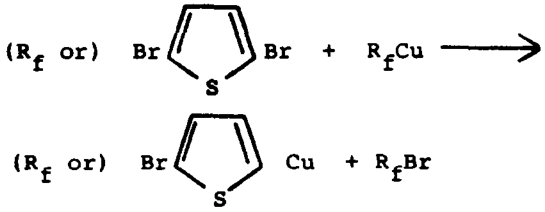
(Continued)

TABLE 1 (cont)

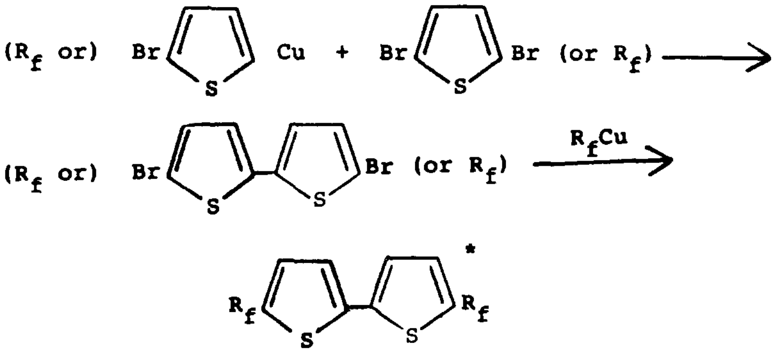
Exp	Method[a]	R_fI, mmol	Heterocyclic Br, (mmol)	Cu, mmol	Reaction Time, h	Products % Yield, (GC Area, Isolated)
13	B at 118 C	48	(20)	100	2 0	 (5,-) XII (89,69) (1,-) $C_8H_5S_2R_f{}^f$ $C_8H_4S_2(R_f)_2{}^f$ (2,-) (2;-)
14	B	72	 (20)	150	22	 (18,-) (XIII) (37,20) (4,-) $C_8H_4S_2(R_f)_4{}^f$ $C_8H_2S_2Br(R_f)_3{}^f$ (26,-) (7,-)

[a] Method A = R_fI added to heterocyclic bromide and Cu in DMSO at 125-130 C, Method B = heterocyclic bromide added to preformed R_fCu in DMSO, b) X = Br I = 20 80%, c) mixture of 2-(35%) and 3-(65%) isomers, d) mixture of two disubstituted products, e) mixture of 2-(11%) and 3-(89%) isomers, f) determined by GC/MS, structures were unidentified

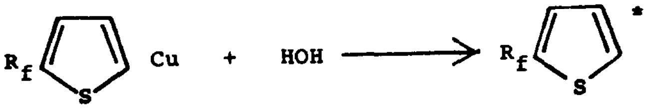
was obtained as a mixture of 2- (11%) and 3- (89%) isomers The copper coupling reactions were extended to the 2,5-dibromothiophene (Table 1, exp 12,13) and the 2,3,5-tribromothiophene (Table 1, exp 14,15) The 2,5-dibromothiophene gave a good yield (71 GC area %) of the disubstituted product XII which was isomerically pure In addition, by-products were obtained indicating other competing reactions Since only a slight excess of copper was used, the Ullmann aryl coupling reaction could not account for the bithiophenes These by-products may have arisen from a copper-bromide exchange reaction e g ,



(1)

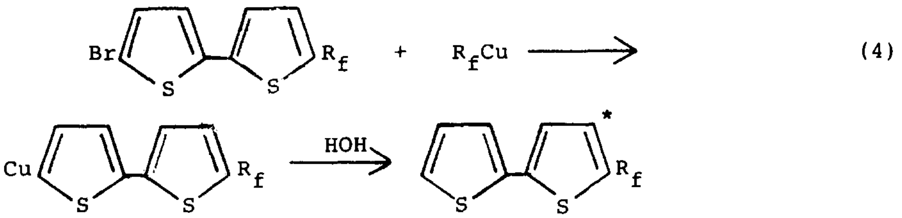


(2)



(3)

*GC/MS identified products



*GC/MS identified products

In addition to the above by-products, a small yield (four GC area %) of a solvent (DMSO) interaction product $C_4H_2S(C_6F_{13})(SCH_3)$ was identified by GC/MS analysis.

Perfluoroalkylation of 2,5-dibromothiophene by Method A produced no perfluoroalkylated product even though the 2,5-dibromothiophene reacted completely. Apparently, the homocoupling reaction of the dibromothiophene with copper, forming a polythiophene, was considerably faster than the reaction of the perfluoroalkyl iodide with copper.

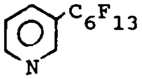
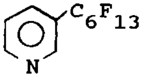
The perfluoroalkylation of the 2,3,5-tribromothiophene (Table 1, exp. 14,15) was studied in a similar manner to the 2,5-dibromothiophene. Triperfluoroalkylated product XIII was obtained in low yield at the expense of the competing reactions. As described above, the formation of these by-products may have occurred by a similar copper-bromine exchange reaction. Attempts to perfluoroalkylate the 2,3,5-tribromothiophene by Method A, as in the case of the 2,5-dibromothiophene, gave no perfluoroalkylated products.

The results of our study have shown that bromobenzenes [1] and a variety of bromoheterocyclic compounds can be readily perfluoroalkylated via organocopper intermediates in dimethylsulfoxide solvent. Yields are generally high and in certain instances approach 95-99%. Competing reactions in certain instances do take place and lower the yields of the desired product. It appears that the cross coupling reaction of bromoarenes with various perfluoroalkyl iodides may provide a general reaction, under appropriate experimental conditions, for the perfluoroalkylation of a variety of compounds.

EXPERIMENTAL

All reactions were carried out in an atmosphere of dry nitrogen with the usual precaution for vigorous exclusion of moisture and air Copper-bronze was purchased from Gallard Schlesinger Chemical Manufacturing Corporation, New York (U S A) and was used directly without activation Dimethylsulfoxide (DMSO), spectrographic grade, was used as purchased from Aldrich Chemical Company, Inc (U S A) Gas chromatographic analyses were performed on a Perkin Elmer Sigma IIB gas chromatograph with a two-foot five percent Dexsil 400 on 100-120 mesh Supelcoport packed column or a Sigma I gas chromatograph with a six-foot, ten percent SE-30 on 80-100 mesh Supelcoport packed column For separation of difficult mixtures of components, a SPB-1, 30 m x 0 25 mm (ID) fused silica capillary column was used The GC/MS analyses were performed on a Finnigan 4021 mass spectrometer using either chemical ionization or electron impact mode Infrared spectra were recorded on a Perkin Elmer 683 spectrometer NMR spectra were performed on an NT-300 spectrometer with TMS and $CFCl_3$ as internal reference for ^1H and ^{19}F, respectively The isomeric purity of 3-bromofuran and 3-bromothiophene is 97 and 98 GC area %, respectively Most compounds were characterized by a combination of analytical techniques e g , IR, GC/MS, NMR and combustion analyses (see Tables 2 and 3) All temperatures are uncorrected Yields of products are reported as isolated yield or GC area % or both (see Table 1) The interactions of perfluorohexyl iodide with various bromoheterocyclic compounds in DMSO were studied by employing two experimental procedures Method A The bromoheterocyclic compounds, copper bronze and DMSO were heated together up to ~ 125°C while the $n-C_6F_{13}I$ was added dropwise at such a rate that the reaction temperature did not rise over 135°C Method B Copper bronze and DMSO were heated to ~ 125 C to which the $n-C_6F_{13}I$ was added dropwise in the similar manner as described above After the reaction was judged to be complete (~ one to 1 5 h), the heterocyclic bromide compound was then added at the reaction temperature of ~ 125 C

Synthesis of 3-perfluoro-n-hexylpyridine CuX (I) and 3-perfluoro-n-hexylpyridine (II) Method A

Perfluoro-n-hexyliodide (14 72 g, 33 mmol) was added dropwise over a period of 30 min to a well-stirred mixture of copper bronze powder (4 19 g, 66 mmol), 3-bromopyridine (4 74 g, 30 mmol) and dimethyl sulfoxide (50 ml) under a nitrogen atmosphere at ~ 125°C An exothermic reaction was noted during the addition and therefore the rate of addition was controlled so that the reaction temperature did not rise over 135°C Aliquot samples were removed periodically, hydrolyzed with water and extracted with diethyl ether and analyzed by GC After stirring at ~ 125 C for 1 5 h, GC analysis showed no 3-bromopyridine and a 98 GC area % of product The reaction mixture was cooled to room temperature, diethyl ether (100 ml) and water (60 ml) were slowly added The mixture was stirred and then centrifuged The aqueous and organic layers were decanted from the solid This solid was extracted with additional diethyl ether (2 x 40 ml) The ether extracts and the previous organic layer were combined, washed with H_2O (2 x 50 ml) and dried over $MgSO_4$ On evaporation of the solvent, a crude product (15 8 g) resulted The crude product was stirred with hexane (20 ml) and filtered The solid was then washed with hexane (2 x 10 ml) to yield white solid product I (12 5 g) The results of elemental analyses suggested that this product was a mixture of  CuI and  CuBr in a four-to-one molar ratio (see Tables 1 and 3) This product I was thermally decomposed (~ 100 C/28 mmHg) to yield 3-perfluoro-n-hexylpyridine (II) (see Table 1)

Another reaction was carried out with double the amounts of starting materials and heating at ~ 125°C for 4 0 h The reaction mixture was worked up in a similar manner to that described above, except the combined ether solution was repeatedly treated with an aqueous ammonium hydroxide solution until no blue color in the aqueous layer was noted The ether layer was separated and then dried ($MgSO_4$) After rotary evaporation of the solvent, the crude liquid residue (22 0 g) was distilled to yield compound II (b p 185-186°C, a colorless liquid, 19 44 g, 82% yield) (see Tables 1, 2, and 3)

2,6-Di-perfluoro-n-hexylpyridine (III) and 5-perfluoro-n-hexylpyrimidine (IV)

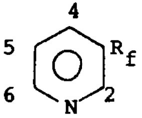
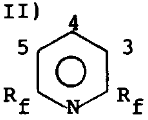
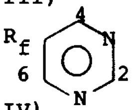
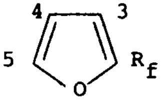
These compounds were synthesized by a similar procedure as described above except the molar ratio of reactants, reaction time and work-up procedure were varied (see Table 1) Compound III was obtained without treatment with aqueous ammonium hydroxide solution Compound IV indicated a copper halide complex formation No attempt was made to isolate the complex since the solubility of the complex in diethyl ether was poor The remaining solid and the organic extracts were combined and treated with an aqueous NH_4OH solution as described above for compound II (see Tables 1, 2, and 3)

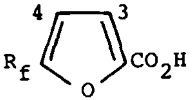
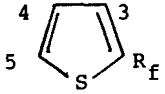
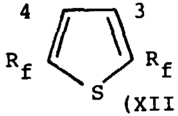
Attempt to prepare 3-perfluoro-n-hexylfuran Method B

Perfluoro-n-hexyliodide (16 1 g, 36 mmol) was added dropwise to a suspension of copper bronze powder (5 21 g, 82 mmol) in DMSO (50 ml) at 125°C After the reaction was judged to be complete (GC analysis showed absence of $C_6F_{13}I$), 3-bromofuran (4 41 g, 30 mmol) was added to the green-brown reaction mixture The mixture was heated for 22 h at ~ 120°C Aliquots were removed from the mixture, hydrolyzed with water, extracted with diethyl ether and analyzed by GC The reaction mixture was hydrolyzed with water and extracted with diethyl ether and the diethyl ether extract dried ($MgSO_4$) After evaporating the diethyl ether solvent, the crude residue (8 8 g) was distilled to yield as a first fraction a mixture of 3- and 2-perfluoro-n-hexylfuran (65 35 ratio) (V) (3 6 g, 31 percent yield, b p 140-146°C)(see Tables 1, 2, and 3) Another distillation fraction (2 3 g) was collected up to 150°C/90 mmHg and GC/MS analysis indicated a mixture of monosubstituted products (two isomers, 62 percent), disubstituted

TABLE 2

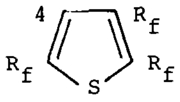
NMR Spectra[a]

Compound[b]	^{1}H-NMR					^{19}F-NMR					
	C_2	C_3	C_4	C_5	C_6	A	B	C	D	E	F
 (II)	8 88 (s)	-	8 80 (d)	7 39 (dd)	7 89 (d)	-81 4 (t)	-111 7 (t)	-121 4 (m)	-121 9 (m)	-122 8 (m)	-126 3 (t)
 (III)	-	7 91 (d)	8 12 (t)	7 91 (d)	-	-81 4 (t)	-114 4 (t)	-122 0 (um)	-122 7 (um)	-123 4 (um)	-126 8 (t)
 (IV)	9 41 (um)	-	8 94 (um)	-	8 94 (um)	-81 4 (t)	-112 9 (t)	-121 6 (um)	-122 6 (um)	-123 1 (um)	-126 6 (t)
 (VII)	-	6 44 (m)	6 81 (d)	7 49 (m)	-	-81 5 (m)	-111 4 (t)	-122 0 (um)	-122 9 (um)	-122 9 (um)	-126 4 (t)

 (VIII)	-	7 47 (m)^{c}	7 43 (m)^{c}	-	-	-80 0 (t)	-110 6 (t)	-121 5 (um)	-122 0 (um)	-122 3 (um)	-125 5 (um)
		3 80 (vb)	$CO_2\underline{H}$								
 (IX)	-	7 40 (d)	7 04 (m)	7 45 (dd)	-	-81 5 (t)	-101 1 (t)	-121 6 (um)	-121 8 (um)	-123 0 (um)	-126 5 (t)
 (XII)	-	7 45 (bs)	7 45 (bbs)	-	-	-83 4 (tt)	-104 3 (t)	-123 6 (um)	-123 6 (um)	-125 0 (um)	-128 5 (um)

(Continued)

TABLE 2 (<u>cont</u>)
NMR Spectra[a]

	^{1}H-NMR					^{19}F-NMR					
Compound[b]	C_2	C_3	C_4	C_5	C_6	A	B	C	D	E	F
 (XIII)	-	-	7 63 (s)	-	-	-81 5 (m)	- 98 1 (um)	-118 8 (um)	-122 0 (um)	-123 2 (um)	-126 6 (um)
							-103 5 (t)	-120 3 (um)			
							-104 8 (um)	-121 8 (um)			

[a] ^{1}H- and ^{19}F-NMR (300 MHz), chemical shifts (ppm/TMS or $CFCl_3$), s (singlet), d (doublet), dd (doublet of doublets), t (triplet), m (multiplet), um (unresolved multiplet), vb (very broad), bs (broad singlet), tt (triplet of triplets)

[b] $R_f = \underset{B}{CF_2}\underset{CDE}{(CF_2)_3}\underset{F}{CF_2}\underset{A}{CF_3}$

[c] either C_3 or C_4

TABLE 3

Analyses of Perfluoro-n-hexyl Substituted Heterocyclic Compounds

Compound	MS	m p (b p) °C/mmHg	Combustion Data (Calculated/Found)						
			%C	%H	%N	%Br	%I	%Cu	%S
I[a]	397(M-CuX)+	-	22 87/ 22 81	0 70/ 0 73	2 42/ 2 57	2 96/ 2 59	17 28/ 17 20	10 81/ 10 82	-
II	397(M)+	(185-186)	33 27/ 33 02	1 02/ 1 06	3 52/ 3 72	-	-	-	-
III	715(M)+	69-70	28 55/ 28 33	0 42/ 0 44	1 96/ 2 20	-	-	-	-
IV	398(M)+	42-43 (125-127/130)	30 17/ 29 63	0 76/ 0 79	7 04/ 6 68	-	-	-	-
V[b]	386(M)+	(140-146)	31 11/ 30 65	0 78/ 0 89	-	-	-	-	-
VII	386(M)+	(157-158)	31 11/ 30 84	0 78 0 82	-	-	-	-	-
VIII	430(M)+	152-154	30 72/ 30 58	0 70/ 0 72	-	-	-	-	-
IX	402(M)+	(92-93/30)	29 87/ 29 60	0 75/ 0 79	-	-	-	-	7 97/ 8 06

(Continued)

TABLE 3 (cont)

Compound	MS	m p (b p) °C/mmHg	Combustion Data (Calculated/Found) %C	%H	%N	%Br	%I	%Cu	%S
XI	402(M)$^+$	(118-122/30)	29 87/ 29 68	0 75/ 0 82	-	-	-	-	7 97/ 7 68
XII	702(M)$^+$	29-30 (69-70/0 15)	26 68/ 26 21	0 28/ 0 35	-	-	-	-	4 45/ 4 47
XIII^c	969(M-CF$_3$)$^+$ 819(M-C$_4$F$_9$)$^+$ 769(M-C$_5$F$_{11}$)	(114-115/0 5)	25 45/ 25 01	0 10/ 0 20	-	-	-	-	3 09/ 3 20

[a] X = Br I = 20 80%, [b] mixture of two isomers [c] molecular ion of compound (1038) was beyond mass limit of spectrometer

products (two isomers, 28 percent) and small quantities of unidentified compounds Structural analysis of the disubstituted compounds was not attempted

Synthesis of 5-perfluoro-n-hexylfuroic acid (VIII) Method A

The reaction was carried out with copper bronze powder (5 21 g, 82 mmol), 5-bromofuroic acid (5 73 g, 30 mmol) DMSO (50 ml) and perfluoro-n-hexyl iodide (16 06 g, 36 mmol) according to Method A After stirring at ~ 125°C for 4 h the reaction mixture was cooled to room temperature, diethyl ether (100 ml) and hydrochloric acid (2 N, 50 ml) were added slowly, and the reaction was worked up in the similar manner as described for compound I (see above) except using hydrochloric acid (2 N) instead of water to wash the combined organic layer A GC/MS analysis of the crude liquid product (8 7 g) showed three major products (GC area %), 2-$R_fC_4H_3O$ (VII) (53%), $(R_f)_2C_4H_2O$ (VI) (13%, two isomers), 5-$R_f(COOH)C_4H_2O$ (VIII) (29%) and some unidentified components (5%) The crude liquid product (8 7 g) from above was added to hexane which caused compound VIII to precipitate (3 8 g, 29%) On sublimation at reduced pressure (~ 160 C/90 mmHg) pure compound VIII was obtained (3 0 g, 23 percent, see Tables 1, 2, and 3) No attempt was made to isolate compounds VI and VII These products were identified only by GC/MS analysis (see Table 1, exp 6) Under slightly different conditions by Method B (see Table 1, exp 8), a higher yield (57%) of compound VIII was obtained

Synthesis of 2-perfluoro-n-hexylfuran (VII) Method B

When experiment 8 was repeated under essentially similar condition except for a longer reaction time (21 h instead of 4 h, see Table 1, exp 7) no 5-perfluoro-n-hexylfuroic acid was obtained Instead of the acid VIII, 2-perfluoro-n-hexylfuran (VII) (90 GC area %) as well as a small yield (2 GC area %) of an isomeric mixture of disubstituted furans were obtained

Distillation of the mixture gave pure compound VII (5 9 g, b p 157-158°, 51% yield)

Synthesis of 2-perfluoro-n-hexylthiophene (IX) Method B

The reaction was performed with copper bronze (4 41 g, 69 mmol), 2-bromothiophene (4 89 g, 30 mmol), perfluoro-n-hexyl iodide (14 72 g, 33 mmol) and DMSO (50 ml) according to Method B After 17 h at 125°C, the reaction mixture was worked up as for compound I The crude residue was distilled to yield compound IX (5 45 g, 45% yield, b p 92-93 C/30 mmHg) (see Tables 1, 2, and 3) The other products were identified only by GC/MS

Attempt to prepare 3-perfluoro-n-hexylthiophene (XI) Method B

The reactions of 3-bromothiophene and n-$C_6F_{13}I$ with copper bronze in DMSO were carried out in the similar manner as described for 2-bromothiophene by Method B (see Table 1, exp 11) The crude residue was distilled to yield a mixture of 3- and 2-perfluoro-n-hexylthiophene XI (5 1 g, b p 118-122°C/ 130 mmHg, 42% yield) (see Table 3) The other products were identified only by GC/MS

Synthesis of 2,5-di-perfluoro-n-hexylthiophene (XII) Method B

The reactions of 2,5-di-bromothiophene and n-$C_6F_{13}I$ with copper bronze in DMSO were carried out in the similar manner as described for 2-bromothiophene by Method B (see Table 1, exp 13) except 2,5-di-bromothiophene was added to the preformed n-$C_6F_{13}Cu$ at 118°C instead of 125°C, and the products were extracted with $CFCl_2CF_2Cl$ instead of diethyl ether (see Tables 1, 2, and 3)

Synthesis of 2,3,5-tri-perfluoro-n-hexylthiophene XIII Method B

The reactions (see Table 1, exp 14) were carried out in the similar manner as described above for compound XII (see Tables 1, 2, and 3)

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