

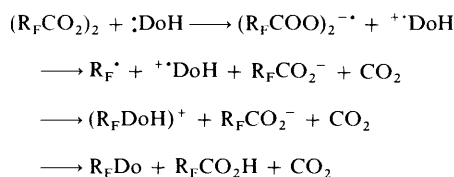
Perfluoroalkylations of Nitrogen-containing Heteroaromatic Compounds with Bis(perfluoroalkanoyl) Peroxides

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Perfluoroalkylations of nitrogen-containing heteroaromatic compounds with bis(perfluoroalkanoyl) peroxides were studied. Bis(trifluoroacetyl) peroxide, bis(heptafluorobutyryl) peroxide, and bis(pentadecafluoro-octanoyl) peroxide were found to be useful and effective reagents for perfluoromethylations, perfluoropropylations, or perfluoroheptylations of pyrrole and its derivatives, while these peroxides could not be applied for the perfluoroalkylations of pyridine or imidazole. For the perfluoroalkylations with the peroxides, electron transfer from the substrate to the peroxide, which affords a perfluoroalkyl radical and a cation radical of the substrate in a solvent cage, is proposed. In pyrroles, since the delocalization of the N lone pair to π -systems lowers the nucleophilicity of the N lone pair and increases the electron density at the π -orbital, the electron transfer readily occurred and perfluoroalkylated pyrroles were obtained in good yield and regioselectively. However, nucleophilic attack of the N lone pair to the O–O bond of the peroxide was superior to the electron transfer in pyridine or imidazole of which the N lone pairs are very nucleophilic.

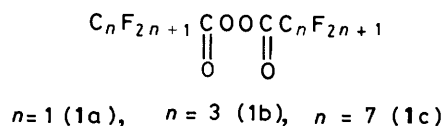
Recently, attention has been focussed on fluoroalkyl-containing compounds due to their unique properties. However, the introduction of perfluoroalkyl groups is not easy since the usual methods for alkylation cannot be applied to perfluoroalkylation. Thus, the introduction of perfluoroalkyl groups has been the subject of much research in organofluorine chemistry. We have been studying perfluoroalkylations with bis(perfluoroalkanoyl) peroxides (**1**), and have succeeded in introducing the perfluoroalkyl groups into electron-rich benzenes, naphthalene, anthracene, thiophenes, furans, and electron-rich olefins.^{1–3} We proposed the electron-transfer mechanism for these perfluoroalkylations. The reaction is initiated by electron transfer from the substrate to the peroxide (**1**) to give a radical cation and a radical anion. The radical anion of the peroxide (**1**) decomposes into perfluoroalkyl radical, perfluoroalkanoate, and carbon dioxide. The perfluoroalkyl radical recombines with the radical cation of the substrate to give perfluoroalkylated compound *via* the cation intermediate as shown in Scheme 1.



Scheme 1. DoH = electron donor, $\text{R}_F = \text{C}_n\text{F}_{2n+1}$

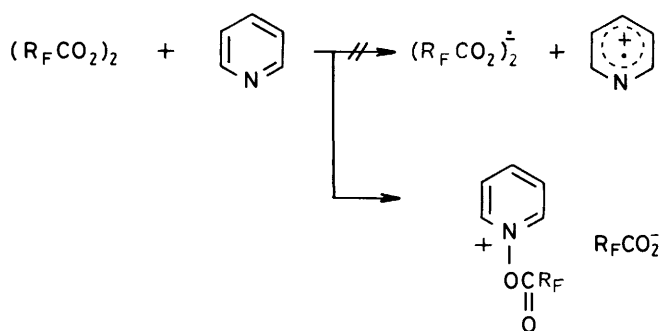
Owing to the high electronegativity of fluorine, perfluoroalkylations of aromatic compounds *via* perfluoroalkyl cation intermediates, such as the Friedel–Crafts reaction, are very limited,⁴ so the introduction of perfluoroalkyl groups using radical intermediates should be an important new route. However, control of chemo- and regio-selectivities in the radical reactions are very difficult due to the high reactivity of perfluoroalkyl radicals. Since in the reactions of peroxides (**1**) and electron donors the perfluoroalkyl radical is produced as a radical pair in close proximity with the radical cation of the substrate in a solvent cage, the perfluoroalkyl radical is introduced into the radical cation selectively to give a perfluoroalkylated cation. As the electron-transfer reaction proceeds *via* a cation intermediate, perfluoroalkylation with the peroxide (**1**) is superficially equivalent to cationic perfluoro-

alkylation. In this paper, we report the perfluoromethylation, perfluoropropylation, and perfluoroheptylation of nitrogen-containing heteroaromatic compounds with bis(trifluoroacetyl) peroxide (**1a**), bis(heptafluorobutyryl) peroxide (**1b**), and bis(pentadecafluoro-octanoyl) peroxide (**1c**).

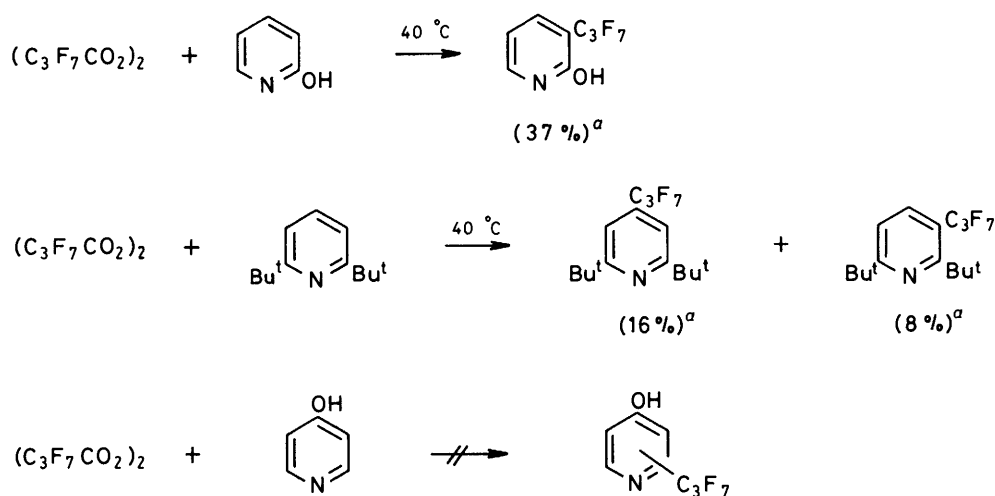


Results and Discussion

As was described in our previous paper, perfluoropropylation of pyridine could not be achieved with peroxide (**1b**).³ In the reactions of peroxides (**1**) and pyridine, the peroxides were decomposed instantly when pyridine was added to a solution of a peroxide in Freon 113 ($\text{CCl}_2\text{F}-\text{CClF}_2$). However, perfluoroalkylpyridines were not produced in these reactions. Usually, two types of reaction are known to occur on treatment of peroxides with nucleophiles;⁵ one is $\text{S}_\text{N}2$ -type nucleophilic reaction and the other is electron-transfer reaction from the nucleophile to the peroxide. Although the electron transfer from the substrate to the peroxide is essential for perfluoroalkylation with peroxides (**1**), the nucleophilic attack of the N lone pair of pyridine on the O–O bond of the peroxide probably occurs in preference to the electron transfer from the π -orbital of pyridine (Scheme 2).



Scheme 2.

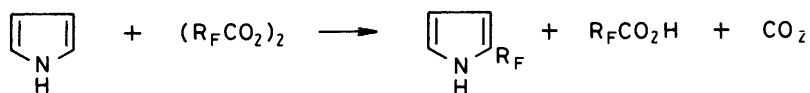


So, two factors, ionization potential and nucleophilicity of the N lone pair, may determine whether or not the perfluoroalkylations with peroxides (**1**) are applicable to nitrogen-containing aromatic compounds.

First we examined the reactions of 2-hydroxypyridine, 4-hydroxypyridine, and 2,6-di-*t*-butylpyridine with peroxide (**1b**). The nucleophilicity of the N lone pair of 2-hydroxypyridine was suppressed by tautomerism between the hydroxy form and the keto (amide) form; the pK_a for proton addition to nitrogen of 2-hydroxypyridine is 0.7, while that of pyridine is 5.23. It is estimated that the ionization potential of 4-hydroxypyridine is lowered by the electron-donating OH group, but the nucleophilicity is not so reduced compared with that of 2-hydroxypyridine considering the pK_a values (pK_a of 4-hydroxypyridine is 3.27). As a measure of nucleophilicity of the N lone pair, we used pK_a values for proton addition to nitrogen. Probably the nucleophilic attack of the N lone pair of 2,6-di-*t*-butylpyridine is also prevented by steric hindrance of 2,6-di-*t*-butyl groups. The results are summarized in Scheme 3.

The perfluoroalkylations of 2-hydroxypyridine and 2,6-di-*t*-butylpyridine, which were not very nucleophilic, occurred at C-3 in 2-hydroxypyridine and at C-3 and C-4 in 2,6-di-*t*-butylpyridine. However, peroxide (**1b**) decomposed immediately without perfluoropropylation in the reaction with 4-hydroxypyridine, as was observed with pyridine.

Pyrrrole, of which the N lone pair is delocalized into the π -system and shows little nucleophilicity, reacted with the peroxides rapidly to give 2-perfluoroalkylpyrrroles in good yield and regioselectively. The results are summarized in Table 1.



The reactions of peroxides (**1**) and pyrrole were very fast at room temperature and proceeded even at -80°C . The best yields could be achieved at -30°C in Freon 113, while the perfluoroalkylations of benzene, thiophene, or furan were performed at 40°C .^{1,3} The high reactivity of pyrrole should be due to its low ionization potential (IP 8.20 eV) compared with those of benzene (9.24 eV), thiophene (8.87 eV), or furan (8.89 eV). Perfluoroalkylated pyrroles were first synthesized by Wakselman and co-workers; the electron-transfer reactions of *N*-methylpyrrrole or *N*-benzylpyrrrole with perfluoroalkyl iodides such as $\text{C}_2\text{F}_5\text{I}$ or $\text{C}_6\text{F}_{13}\text{I}$ gave perfluoroalkylated

Table 1. Perfluoroalkylations of pyrrole with peroxides (**1**)

R_F of (1)	Temp. ($^\circ\text{C}$)	Solvent	Yield ^a / %
CF_3	Room temp.	Freon 113*	56
C_3F_7	Room temp.	Freon 113	87
C_7F_{15}	Room temp.	Freon 113	61
CF_3	-30	Freon 113	72
C_3F_7	-30	Freon 113	100
C_7F_{15}	-30	Freon 113	81
CF_3	-30	Ether ^b	42 ^c
C_3F_7	-30	Ether ^b	95
C_7F_{15}	-30	Ether ^b	61
C_3F_7	-80	Ether ^b	89

* $\text{CCl}_2\text{F}\cdot\text{CClF}_2$



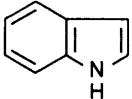
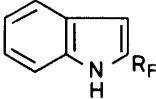
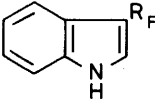
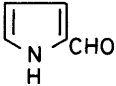
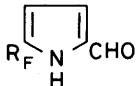
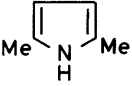
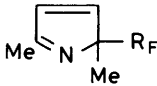
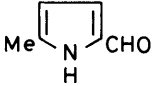
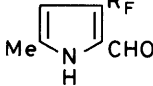
^a Determined by g.l.c. based on starting (**1**). ^b The peroxide in Freon 113 was added to an ethereal solution of pyrrole. ^c A considerable amount of trifluoroacetylated (CF_3CO_2) pyrrole was formed.

pyrrroles, but the method could not be applied to pyrrole itself.⁶ Photochemical trifluoromethylation of pyrrole or *N*-methylpyrrrole was reported by Kobayashi *et al.*, but the yields were poor.⁷ Recently, perfluoroalkyl(phenyl)iodonium trifluoromethanesulphonates (FITS) have been developed as cationic perfluoroalkylating agents; the octyl reagent could be used for the preparation of perfluoro-octylpyrrrole in good yield,⁸ but the

methyl analogue has not been applied to trifluoromethylation.[†] In the present study, various perfluoroalkyl groups such as CF_3 , C_3F_7 , or C_7F_{15} were found to be introduced into pyrrole in good yield and regioselectively with the corresponding peroxides. Thus, the peroxides (**1**) will be useful and effective reagents for the perfluoroalkylations of pyrrole.

[†] Umemoto and Ando have reported the use of *N*-trifluoromethyl-*N*-nitrosotrifluoromethanesulphonamide as a trifluoromethylating agent; T. Umemoto and A. Ando, *Bull. Chem. Soc. Jpn.*, 1986, **59**, 447.

Table 2. Perfluoroalkylations of pyrrole derivatives with peroxides (1)^a

Substrate	R _F	Temp./°C	Products (Yields ^b %)	
	CF ₃	-30		(trace)
	C ₃ F ₇	-30		(76)
	C ₇ F ₁₅	-30		(70)
	CF ₃	-30		(24 ^d)
	C ₃ F ₇	-80 ^c		(63 ^d)
				(11 ^d)
				(13 ^d)
	C ₃ F ₇	Room temp.		(58)
	CF ₃	-80 ^c		(68)
	C ₃ F ₇	-80 ^c		(89)
	CF ₃	60		(trace)
	C ₃ F ₇	Room temp.		(48 ^d)
	C ₃ F ₇	-80 ^c		(none)

^a Substrate/peroxide 1.5. ^b Determined by g.l.c. based on starting (1). ^c Ether was used as solvent. ^d Isolated yield.

The perfluoroalkylations of various pyrrole derivatives were also studied. The results are summarized in Table 2.

In the reaction of peroxide (1a) and *N*-methylpyrrole, the peroxide decomposed at once; however, perfluoromethylation of *N*-methylpyrrole hardly occurred and non-volatile, polymeric compounds were obtained.* On the other hand, perfluoropropylation or perfluoroheptylation of *N*-methylpyrrole with peroxide (1b) or (1c) occurred in good yield. The peroxide (1a) might be decomposed by nucleophilic attack of *N*-methylpyrrole; nucleophilic attack occurs not at nitrogen but at C-2 due to the contribution of the charged canonical form.⁹ Both electron-transfer and nucleophilic reactions were observed in the reactions of peroxide (1b) with carbanions as was reported in our previous paper.¹⁰ The peroxide (1a) may suffer nucleophilic attack more easily than does (1b) or (1c). Electron transfer is known not to be appreciably affected by steric hindrance compared with nucleophilic attack;¹¹ in order for nucleophilic reactions to occur, two reactants have to approach each other more closely than in electron transfer. In peroxide (1b) or (1c), the long fluoroalkyl chains sterically protect the O-O bonds from the approach of *N*-methylpyrrole, so that electron transfer dominates over nucleophilic attack.

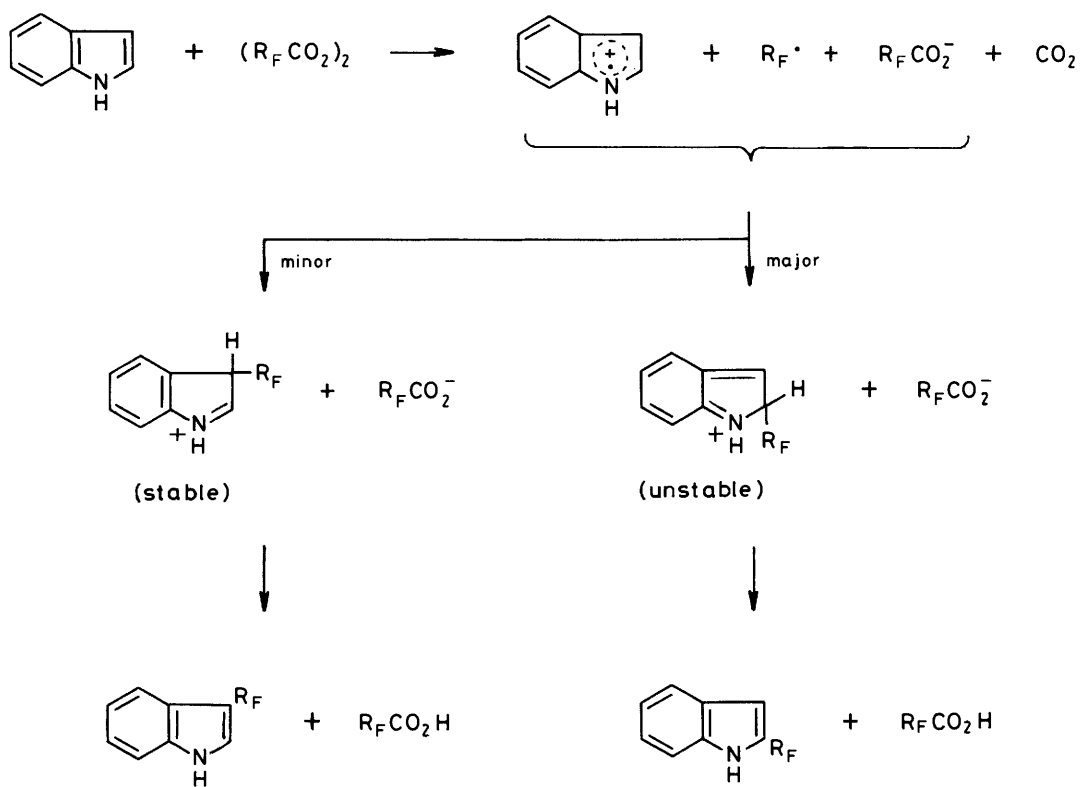
Electron-withdrawing groups deactivate the electron transfer;

however, perfluoroalkylation of 2-formylpyrrole with (1b) proceeded gently at room temperature to give 2-formyl-5-perfluoropropylpyrrole as the sole product. The formyl group is an important functional group due to its extensive utility in synthetic chemistry. Therefore, 2-formyl-5-perfluoroalkylpyrroles may have high potential as synthetic intermediates.

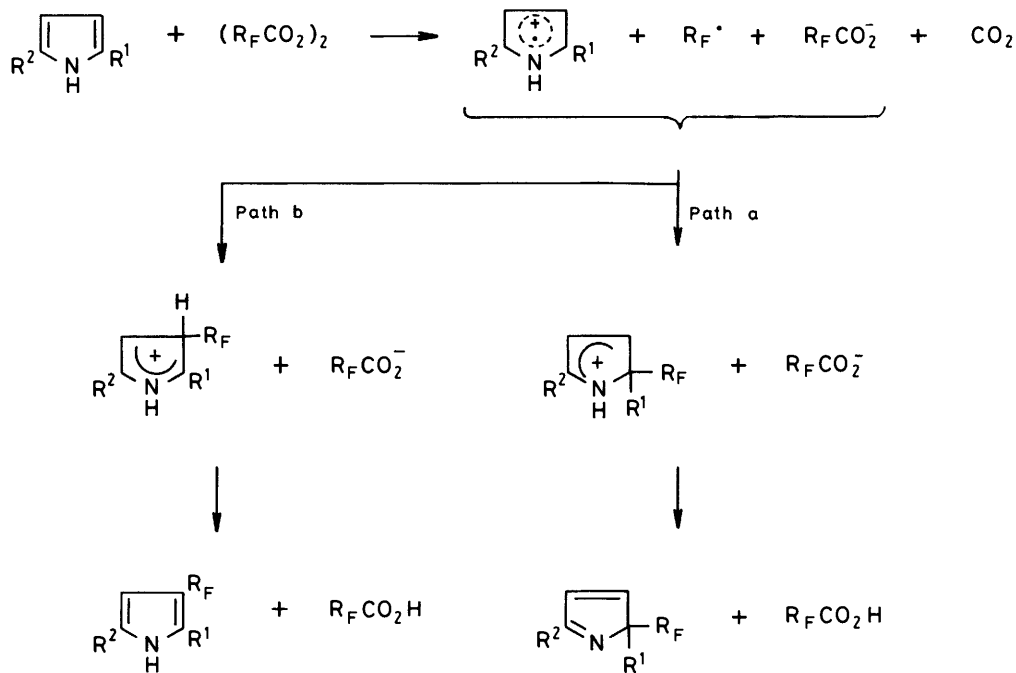
Indole was also perfluoroalkylated with peroxides (1). This is the first example of the direct introduction of perfluoroalkyl groups into indole. Hitherto, trifluoromethylindoles were synthesized from trifluoromethylquinolines in four steps.¹² In the reaction of indole and peroxides (1), perfluoroalkyl groups were introduced at C-2 preferentially. Usually, electrophilic substitutions of indole occur at C-3;¹³ the selectivity should be due to the stability of the Wheland intermediate (Scheme 4). The observed orientation in the perfluoropropylation of indole, therefore, cannot be explained by the stability of the cationic intermediate, but may be attributed to the spin density distribution in a radical cation of indole. Usually the regioselectivities in electron-transfer reactions are identical with those predicted for electrophilic reactions. However, different regioselectivities between electrophilic and electron-transfer reactions have occasionally been observed.^{14,15}

In the reaction of 2,5-dimethylpyrrole and peroxides (1), unprecedented products, 2,5-dimethyl-2-perfluoroalkyl-2H-pyrroles, were obtained in good yields as shown in Table 2. Two types of reaction products are plausible in the reactions of 2,5-disubstituted pyrroles and (1) as shown in Scheme 5; one is a

* No signal for the CF₃ group was detected in the ¹⁹F n.m.r. spectra of these compounds.



Scheme 4.



Scheme 5.

2*H*-pyrrole, which is produced by the coupling of the radical cation of the pyrrole at the α -position with perfluoroalkyl radical (path a in Scheme 5), and the other is the 3-perfluoroalkylated pyrrole (path b in Scheme 5). It is known that the spin density of the radical cation of 2,5-dimethylpyrrole is higher at the α -position than at the β -position.¹⁶ Thus, the couplings of

2,5-dimethylpyrrole with perfluoroalkyl radicals occurred at the α -position, although the resulting product, the 2*H*-pyrrole, should be thermodynamically unstable because the aromaticity of the pyrrole ring is lost. Indeed the 2*H*-pyrroles, especially 2-trifluoromethyl-2*H*-pyrrole, readily dimerized. The best yields of the 2*H*-pyrroles could be obtained at -80°C . On the other

hand, the reaction of 2-formyl-5-methylpyrrole and peroxide (**1b**) did not proceed at -80°C ; the electron transfer from the pyrrole to peroxides (**1**) scarcely occurred at -80°C owing to the effect of the electron-withdrawing formyl group. The reaction, however, proceeded at room temperature to give 2-formyl-5-methyl-3-perfluoropropylpyrrole in 48% yield but not 2*H*-pyrrole-type products, although we cannot explain the selectivity at the present time. This is the first example of the direct introduction of a perfluoroalkyl group into the β -positions of pyrrole or its derivatives as far as we know. 2-Formyl-5-methyl-3-perfluoroalkylpyrroles can be used for further synthesis of new pyrroles substituted by fluoroalkyl groups at the β -position, especially as an important starting material for fluoroalkyl-containing porphyrins.¹⁷

We further examined the reactions of imidazole, thiazole, or oxazole with the peroxide (**1b**). Imidazole, in which the nitrogen is very nucleophilic (pK_a 6.95), decomposed the peroxide at once as was observed in the reaction of pyridine and (**1b**). In the reactions of thiazole (pK_a 2.5, IP 9.50 eV) and oxazole (pK_a 0.8, IP 9.83 eV) with peroxide (**1b**), complex reaction products were detected by g.l.c. analysis. Although thiazole and oxazole do not show high nucleophilicity, their ionization potential is too high to induce the electron transfer to the peroxide. Thus, homolytic cleavage of peroxide (**1b**) probably occurs unimolecularly to generate two perfluoroalkyl radicals, even in the presence of thiazole or oxazole.¹⁸

In conclusion, it is essential in the perfluoroalkylations of *N*-containing heteroaromatic compounds with peroxides (**1**) that electron transfer from substrate to the peroxide be superior to nucleophilic attack of the *N* lone pair to the O–O bond. We found that the peroxides (**1**) were effective and useful reagents for perfluoroalkylations of pyrrole and its derivatives; delocalization of the *N* lone pair to π -systems in pyrroles lowers the nucleophilicity of the *N* lone pair and accelerates the electron transfer from the π -system. The peroxides were synthesized from the commercially available and relatively cheap perfluoroalkanoic acids [for (**1b**) and (**1c**)] or acid anhydride [for (**1a**)]. Thus, the method for perfluoroalkylation described here has high potential as a general and practical electrophilic perfluoroalkylation of pyrroles.

Experimental

¹H N.m.r. spectra were taken with a JEOL JNM PMX 60SI (60 MHz) spectrometer. ¹³C and ¹⁹F n.m.r. spectra were taken with a JEOL JNM FX90Q FT n.m.r. spectrometer. I.r. spectra were recorded on a Hitachi 260-10 spectrometer. Gas chromatography was performed by a Hitachi 163 or 263-30 gas chromatograph with SE-30 (10%), Apiezon-L (10%), or PEG-20M (10%) 1- and 2-m stainless steel columns. Gel-permeation chromatography was performed by means of a JAI Model LC-08 liquid chromatograph equipped with two JAIGEL-1H columns (20 ϕ \times 600 mm) with chloroform as eluant. Mass spectra were obtained with a JEOL JMS DX-300 spectrometer by an electron-impact (EI) ionization technique at 70 eV.

Materials.—Bis(trifluoroacetyl) peroxide (**1a**) was prepared from trifluoroacetic anhydride and hydrogen peroxide in Freon 113–water according to the method described in the literature.¹⁹ Bis(heptafluorobutyl) peroxide (**1b**) and bis(pentadecafluoro-octanoyl) peroxide (**1c**) were prepared from the corresponding acid chlorides and hydrogen peroxide in Freon 113–water according to the literature.¹⁹ The peroxides were not isolated and were used as solutions in Freon 113; the concentrations of the peroxides were determined by iodometry. Pyrrole, *N*-methylpyrrole, and 2,5-dimethylpyrrole were obtained from Tokyo Kasei Co. and distilled prior to

use. 2-Hydroxypyridine (Kanto Chemicals) (from ethanol), 4-hydroxypyridine (Wako Chemicals) (from water), and 2-formylpyrrole (Aldrich Chemicals) (from hexane) were purified by recrystallization. 2-Formyl-5-methylpyrrole was synthesized from 2-methylpyrrole, which was obtained by the reduction of 2-formylpyrrole with LiAlH₄,²⁰ with *N,N*-dimethylformamide and POCl₃; recrystallized from hexane, it had m.p. 68.0–69.5 $^{\circ}\text{C}$ (lit.,²¹ 68–69 $^{\circ}\text{C}$).

General Procedure for Reactions of Peroxides (1) and Pyridines.—A solution of peroxide (**1**) (0.5 mmol) and a pyridine (0.75 mmol) in Freon 113 (5 ml) was degassed by a freeze–pump–thaw cycle, sealed in an ampoule, and kept at 40 $^{\circ}\text{C}$ for 5 h. The reaction mixture was washed three times with water, and the organic layer was separated and dried over MgSO₄. The yields of the products were determined by g.l.c. with bromobenzene for 2-hydroxypyridine and chlorobenzene for 2,6-di-*t*-butylpyridine as internal standards. 3-Heptafluoropropyl-2-hydroxypyridine was purified by recrystallization from pentane–ether (2:1). 4-Heptafluoropropyl-2,6-di-*t*-butylpyridine and 3-heptafluoropropyl-2,6-di-*t*-butylpyridine were isolated by gel-permeation chromatography.

3-Heptafluoropropyl-2-hydroxypyridine had m.p. 101.0–102.5 $^{\circ}\text{C}$; $\delta_{\text{H}}(\text{CDCl}_3)$ 6.42 (1 H, dd), 7.65 (1 H, d, *J* 6.1 Hz), and 7.82 (1 H, d, *J* 7.1 Hz); $\delta_{\text{C}}(\text{CDCl}_3)$ 105.6 (C-5), 139.8 (C-6), 143.3 (t, *J*_{CCCF} 8.4 Hz, C-4), and 161.2 (t, *J*_{CCCF} 2.9 Hz, C-2); ν_{max} 1 670 (C=O), 1 340 (CF₃), and 1 230 cm⁻¹ (CF₂); *m/z* 263 (*M*⁺) (Found: *M*⁺, 263.0152. C₈H₄F₇NO requires *M*, 263.0181).

4-Heptafluoropropyl-2,6-di-*t*-butylpyridine had $\delta_{\text{H}}(\text{CDCl}_3)$ 1.33 (18 H, s) and 7.05 (2 H, s); $\delta_{\text{C}}(\text{CDCl}_3)$ 30.1 (Me), 38.2 (Me₃C), 112.8 (t, *J*_{CCCF} 6.1 Hz, C-3), and 169.3 (C-2); ν_{max} 1 350 (CF₃) and 1 230 cm⁻¹ (CF₂); *m/z* 359 (*M*⁺) (Found: *M*⁺, 359.1496. C₁₆H₂₀F₇N requires *M*, 359.1484).

3-Heptafluoropropyl-2,6-di-*t*-butylpyridine had $\delta_{\text{H}}(\text{CDCl}_3)$ 1.34 (9 H, s), 1.41 (9 H, s), and 7.15 and 7.65 (2 H, ABq, *J* 8.4 Hz); $\delta_{\text{C}}(\text{CDCl}_3)$ 29.9 (6-CMe₃), 31.0 (t, *J*_{CF} 4.9 Hz, 2-CMe₃), 38.2 (Me₃C), 41.4 (Me₃C), 115.5 (C-5), 138.5 (m, C-4), and 165.4 (C-6); ν_{max} 1 340 (CF₃) and 1 230 cm⁻¹ (CF₂); *m/z* 359 (*M*⁺) (Found: 359.1449).

General Procedure for Reactions of Peroxides (1) and Pyrroles.—A pyrrole (0.75 mmol) was dissolved in the appropriate solvent (Freon 113 or ether) (30 ml) in a three-necked flask, and to the resulting solution under nitrogen was added a solution of a peroxide (**1**) (0.50 mmol) in Freon 113 *via* syringe. The solution was allowed to react until the peroxide was consumed. The decay of the peroxide was monitored by iodometry. The reaction mixture was washed with water three times and the organic layer was dried over MgSO₄. The yields of the products were determined by g.l.c. using an internal standard. The products were isolated from the reaction mixture by column chromatography over silica gel (Wakogel C-60 or Florisil 100–200 mesh), preparative layer chromatography (p.l.c.) (Merck Silica Gel 60PF), and/or gel permeation chromatography.

2-Trifluoromethylpyrrole (oil; lit.,⁷ b.p. 100 $^{\circ}\text{C}$), isolated by column chromatography on Florisil with Freon 113 as eluant, had $\delta_{\text{H}}(\text{CDCl}_3)$ 6.2 (1 H, m), 6.5 (1 H, m), 6.7 (1 H, m), and 8.3 (1 H, br); $\delta_{\text{C}}(\text{CDCl}_3)$ 109.4 (C-4), 110.1 (q, *J*_{CCCF} 2.5 Hz, C-3), and 120.6 (C-5); ν_{max} 3 480 (NH) and 1 320 cm⁻¹ (CF₃); *m/z* 135 (*M*⁺) (Found: *M*⁺, 135.0267. C₅H₄F₃N requires *M*, 135.0296).

2-Heptafluoropropyl- and 2-pentadecafluoroheptyl-pyrrole, and 2-heptafluoropropyl- and 2-pentadecafluoroheptyl-*N*-methylpyrrole were isolated by gel-permeation chromatography after the reaction mixture had been subjected to preliminary column chromatography on Wakogel with pentane as eluant.

2-Heptafluoropropylpyrrole had $\delta_{\text{H}}(\text{CDCl}_3)$ 6.3 (1 H, m), 6.6 (1 H, m), and 6.9 (1 H, m); $\delta_{\text{C}}(\text{CDCl}_3)$ 109.9 (C-4), 111.9 (t, *J*_{CCCF}

3.7 Hz, C-3), and 121.5 (C-5); $\phi_F(\text{CDCl}_3)$; p.p.m. from external $\text{CF}_3\text{CO}_2\text{H}$, -4.4, -32.2, and -51.1; ν_{max} . 3 500 (NH), 1 360 (CF_3), and 1 240 cm^{-1} (CF_2); m/z 235 (M^+) (Found: M^+ , 235.0291. $\text{C}_7\text{H}_4\text{F}_7\text{N}$ requires M , 235.0232).

2-Pentadecafluoroheptylpyrrole had $\delta_H(\text{CDCl}_3)$ 6.2 (1 H, m), 6.5 (1 H, m), 6.9 (1 H, m), and 8.4 (1 H, br); $\delta_C(\text{CDCl}_3)$ 110.1 (C-4), 112.4 (t, J_{CCFF} 4.9 Hz, C-3), and 121.7 (C-5); ν_{max} . 3 500 (NH), 1 310 (CF_3), and 1 240 cm^{-1} (CF_2); m/z 435 (M^+) (Found: M^+ , 435.0059. $\text{C}_{11}\text{H}_4\text{F}_{15}\text{N}$ requires M , 435.0105).

2-Heptafluoropropyl-N-methylpyrrole had $\delta_H(\text{CDCl}_3)$ 3.67 (3 H, s), 6.1 (1 H, m), 6.5 (1 H, m), and 6.7 (1 H, m); $\delta_C(\text{CDCl}_3)$ 35.8 (Me), 108.0 (C-4), 114.5 (t, J_{CCFF} 5.5 Hz, C-3), and 128.2 (C-5); $\phi_F(\text{CDCl}_3)$; p.p.m. from external $\text{CF}_3\text{CO}_2\text{H}$ -4.3, -29.1, and -49.5; ν_{max} . 1 350 (CF_3) and 1 230 cm^{-1} (CF_2); m/z 249 (M^+) (Found: M^+ , 249.0394. $\text{C}_8\text{H}_6\text{F}_7\text{N}$ requires M , 249.0388).

N-Methyl-2-pentadecafluoroheptylpyrrole $\delta_H(\text{CDCl}_3)$ 3.64 (3 H, s), 6.1 (1 H, m), 6.5 (1 H, m), and 6.6 (1 H, m); $\delta_C(\text{CDCl}_3)$ 35.7 (Me), 108.0 (C-4), 114.6 (t, J_{CCFF} 4.9 Hz, C-3), and 128.2 (C-2); ν_{max} . 1 320 (CF_3) and 1 240 cm^{-1} (CF_2); m/z 449 (M^+) (Found: M^+ , 449.0286. $\text{C}_{12}\text{H}_6\text{F}_{15}\text{N}$ requires M , 449.0261).

From the reaction mixture of indole with peroxide (1a), a mixture of 2- and 3-trifluoromethylindole was isolated by column chromatography with benzene-hexane (1:1) as eluant. The isomers were separated by gel-permeation chromatography and separately recrystallized from hexane.

2-Trifluoromethylindole had m.p. 107–108 °C (lit.¹² 102 °C); $\delta_H(\text{CDCl}_3)$ 6.79 (1 H, s), 7.0–7.6 (4 H, m), and 8.3 (1 H, br); $\delta_C(\text{CDCl}_3)$ 104.3 (q, J_{CCFF} 3.7 Hz, C-3), 111.7 (C-7), 121.2 (C-6), 122.1 (C-4), 124.8 (C-5), 127.0 (C-3a), and 136.8 (C-7a); ν_{max} . 3 400 (NH) and 1 310 cm^{-1} (CF_3); m/z 185 (M^+).

3-Trifluoromethylindole had m.p. 109–110.5 °C (lit.¹² 110 °C); $\delta_H(\text{CDCl}_3)$ 7.1–7.8 (5 H, m) and 8.3 (1 H, br); $\delta_C(\text{CDCl}_3)$ 111.6 (C-7), 119.5 (C-6), 121.5 (C-4), 123.5 (C-5), 124.3 (q, J_{CCFF} 6.1 Hz, C-3a), and 136.9 (C-7a); ν_{max} . 3 400 (NH) and 1 340 cm^{-1} (CF_3); m/z 185 (M^+).

Heptafluoropropylindoles were obtained in a similar way to the trifluoromethylindoles, although benzene was used as the eluant for column chromatography.

2-Heptafluoropropylindole had m.p. 63–65 °C; $\delta_H(\text{CDCl}_3)$ 6.9–7.7 (5 H, m) and 8.3 (1 H, br); $\delta_C(\text{CDCl}_3)$ 106.5 (t, J_{CCFF} 3.7 Hz, C-3), 111.8 (C-7), 121.2 (C-6), 122.1 (C-4), 125.0 (C-5), 127.0 (C-3a), and 136.8 (C-7a); ν_{max} . 3 400 (NH), 1 340 (CF_3), and 1 230 cm^{-1} (CF_2); m/z 285 (M^+) (Found: M^+ , 285.0384. $\text{C}_{11}\text{H}_6\text{F}_7\text{N}$ requires: M , 285.0388).

3-Heptafluoropropylindole had m.p. 50–52 °C; $\delta_H(\text{CDCl}_3)$ 7.0–7.4 (4 H, m), 7.6–7.8 (1 H, m), and 8.3 (1 H, br); $\delta_C(\text{CDCl}_3)$ 111.7 (C-7), 120.2 (C-6), 121.7 (C-4), 123.5 (C-5), 125.8 (t, J_{CCFF} 8.5 Hz, C-3a), and 136.0 (C-7a); ν_{max} . 3 400 (NH), 1 340 (CF_3), and 1 230 cm^{-1} (CF_2); m/z 285 (M^+) (Found: M^+ , 285.0366).

5-Heptafluoropropylpyrrole-2-carbaldehyde, isolated by preliminary column chromatography with chloroform-ether (1:1) as eluant and then by gel-permeation chromatography, had $\delta_H(\text{CDCl}_3)$ 7.6–7.7 (1 H, m), 7.9–8.0 (1 H, m), 9.53 (1 H, s), and 10.3 (1 H, br); $\delta_C(\text{CDCl}_3)$ 113.1 (t, J_{CCFF} 12.8 Hz, C-4), 120.2 (C-3), 125.7 (t, J_{CCF} 34.2 Hz, C-5), 134.8 (C-2), and 180.5 (CHO); ν_{max} . 3 450 (NH), 1 350 (CF_3), and 1 230 cm^{-1} (CF_2); m/z 263 (M^+) (Found: M^+ , 263.0165. $\text{C}_8\text{H}_4\text{F}_7\text{NO}$ requires M , 263.0180).

2-Heptafluoropropyl-2,5-dimethyl-2H-pyrrole, isolated by distillation and then by gel-permeation chromatography, had $\delta_H(\text{CDCl}_3)$ 1.49 (3 H, s), 2.27 (3 H, s), and 6.33 and 7.20 (2 H, ABq, J 5.1 Hz); $\delta_C(\text{CDCl}_3)$ 16.9 (t, J_{CCFF} 3.7 Hz, 2-Me), 18.5 (5-Me), 83.4 (t, J_{CCF} 20.8 Hz, C-2), 131.4 (C-4), 153.5 (t, J_{CCFF} 2.4

Hz, C-3), and 176.9 (C-5); $\phi_F(\text{CDCl}_3)$; p.p.m. from external $\text{CF}_3\text{CO}_2\text{H}$ -5.0, -38.2, and -41.5; ν_{max} . 1 350 (CF_3) and 1 230 cm^{-1} (CF_2); m/z 263 (M^+) (Found: M^+ , 263.0531. $\text{C}_9\text{H}_8\text{F}_7\text{N}$ requires M , 263.0545).

2,5-Dimethyl-2-trifluoromethyl-2H-pyrrole, isolated by column chromatography with ether as eluant and then gel-permeation chromatography, had $\delta_H(\text{CDCl}_3)$ 1.57 (3 H, s), 2.39 (3 H, s), and 6.45 and 7.21 (2 H, ABq, J 5.1 Hz); $\delta_C(\text{CDCl}_3)$ 16.6 (q, J_{CCFF} 2.4 Hz, 2-Me), 18.9 (5-Me), 83.2 (q, J_{CCF} 26.9, C-2), 132.2 (C-4), 152.6 (C-3), and 176.7 (C-5); ν_{max} . 1 320 cm^{-1} (CF_3); m/z 163 (M^+) (Found: M^+ , 163.0612. $\text{C}_7\text{H}_8\text{F}_3\text{N}$ requires M , 163.0609).

3-Heptafluoro-5-methylpyrrole-2-carbaldehyde, isolated by p.l.c. with dichloromethane as developer, had m.p. 46.5–48.5 °C (from hexane); $\delta_H(\text{CDCl}_3)$ 2.36 (3 H, s), 6.21 (1 H, m), 9.46 (1 H, s), and 10.8 (1 H, br); $\delta_C(\text{CDCl}_3)$ 12.8 (Me), 110.6 (t, J_{CCFF} 6.1 Hz, C-4), 129.7 (C-2), 137.6 (C-5), and 179.0 (t, J_{CF} 3.7 Hz, CHO); ν_{max} . 3 270 (NH), 1 340 (CF_3), and 1 230 cm^{-1} (CF_2); m/z 277 (M^+) (Found: M^+ , 277.0316. $\text{C}_9\text{H}_6\text{F}_7\text{NO}$ requires M , 277.0338).

References

- M. Yoshida, H. Amemiya, M. Kobayashi, H. Sawada, H. Hagii, and K. Aoshima, *J. Chem. Soc., Chem. Commun.*, 1985, 234.
- M. Yoshida, K. Moriya, H. Sawada, and M. Kobayashi, *Chem. Lett.*, 1985, 755.
- H. Sawada, M. Yoshida, H. Hagii, K. Aoshima, and M. Kobayashi, *Bull. Chem. Soc. Jpn.*, 1986, **59**, 215.
- T. Umamoto and Y. Gotoh, *Bull. Chem. Soc. Jpn.*, 1986, **59**, 439 and references cited therein.
- B. Plesnicar, 'The Chemistry of Peroxides,' ed. S. Patai, Wiley, New York, 1983, ch. 17; W. A. Pryor and W. H. Hendrickson, Jr., *J. Am. Chem. Soc.*, 1983, **105**, 7114 and references cited therein.
- D. Cantacuzene, C. Wakselman, and R. Dorme, *J. Chem. Soc., Perkin Trans. 1*, 1977, 1365.
- Y. Kobayashi, I. Kumadaki, A. Ohsawa, S. Murakami, and T. Nakano, *Chem. Pharm. Bull.*, 1978, **26**, 1247.
- T. Umamoto, Y. Kuriu, and H. Shuyama, *Chem. Lett.*, 1981, 1663.
- Y. Chiang and E. B. Whipple, *J. Am. Chem. Soc.*, 1963, **85**, 2763.
- M. Yoshida, K. Shimokoshi, and M. Kobayashi, *Chem. Lett.*, 1987, 433.
- K. Shimada and M. Szwarc, *J. Am. Chem. Soc.*, 1975, **97**, 3313.
- Y. Kobayashi, I. Kumadaki, Y. Hirose, and Y. Hanzawa, *J. Org. Chem.*, 1974, **39**, 1836.
- D. J. Chadwick, 'Comprehensive Heterocyclic Chemistry,' eds. C. W. Bird and G. W. H. Cheesman, Pergamon, New York, 1984, vol. 4, ch. 3.04.
- K. Yoshida, *J. Am. Chem. Soc.*, 1977, **99**, 611; *J. Chem. Soc., Chem. Commun.*, 1978, 1108.
- M. Yoshida, T. Yoshida, N. Kamigata, and M. Kobayashi, *Bull. Chem. Soc. Jpn.*, 1988, **61**, 3549.
- A. G. Davies, L. Julia, and S. N. Yazdi, *J. Chem. Soc., Chem. Commun.*, 1987, 929.
- H. Ogoshi, M. Homma, K. Yokota, H. Toi, and Y. Aoyama, *Tetrahedron Lett.*, 1983, **24**, 929.
- M. Yoshida, M. Kobayashi, H. Sawada, H. Hagii, and K. Aoshima, *Nippon Kagaku Kaishi*, 1985, 1958 (*Chem. Abstr.*, 1986, **105**, 4218g).
- C. Zhao, R. Zhou, H. Pan, X. Jin, Y. Qu, C. Wu, and X. Jiang, *J. Org. Chem.*, 1982, **47**, 2009.
- R. H. Hinman and S. Theodoropoulos, *J. Org. Chem.*, 1963, **28**, 3052.
- D. B. Stierle and D. J. Faulkner, *J. Org. Chem.*, 1980, **45**, 4980.

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