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A FACILE METHOD FOR THE PERFLUOROALKYLATION OF PYRIDINE AND ITS DERIVATIVES

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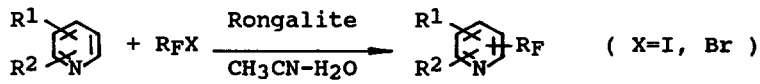
Summary: Perfluoroalkylation of pyridine and its derivatives was achieved by reacting with perfluoroalkyl iodides or bromides in the presence of rongalite under mild conditions.

Although a considerable number of works have been done with electron-rich aromatic compounds, works dealing with the perfluoroalkylation of pyridine were rarely reported. Pyridine is very stable to many alkylating reagents and can be used as a solvent in some perfluoroalkylation reactions[1]. Trifluoromethylpyridine could be prepared through Diels-Alder cyclization reactions[2] or by means of $(CF_3)_2Te$[3] and SF_4[4]. Cowell[5] found that the perfluoroalkylation of pyridine with perfluoroalkyl iodides took place through thermolysis reaction, but a high temperature and long time (200°C over 20h) were needed. Yoshida et al.[6] have recently reported the perfluoroalkylation of nitrogen-containing heteroaromatics with bis(perfluoroalkanoyl) peroxides, in which only some specially substituted pyridines gave alkylation products, and perfluoroalkylation of pyridine itself was not achieved. In this paper we wish to present a facile method for the perfluoroalkylation of pyridines with R_FI in the presence of rongalite.

Rongalite is a useful reducing agent in industry. As a new sulfinatodehalogenation reagent, it can convert perfluoroalkyl iodides or bromides to the corresponding sodium sulfinates[7]. The conversion was thought to be a free radical process, and expected addition products were obtained when olefins were added to trap the fluoroalkyl radicals generated from the R_FI-rongalite system[8]. It prompted us to examine whether the R_F radical thus formed could react with other substrates. It was found that the perfluoroalkylation of pyridine occurred predominantly and no or very small amount of sulfinates was detected when pyridine was added into the reaction system. The reaction proceeded readily at 70-75°C, and cosolvent such as acetonitrile and DMF was used to improve the mutual solubility of the reactants. On prolonged reaction time, the reaction could also be applied to quinoline and R_FBr.



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1a: R^1=R^2=H; **1b**: R^1=4-CH_3, R^2=H; **1c**: R^1=3-CH_3, R^2=H; **1d**: R^1=3-CH_3, R^2=5-CH_3; **1e**: R^1=4-NH_2, R^2=H; **1f**: quinoline; **1g**: iso-quinoline.

In a typical experiment, a mixture of 8.92 g (20 mmol) $C_6F_{13}I$, 3.1 g (40 mmol) pyridine, 5 g rongalite, 3.3 g $NaHCO_3$, 12 mL MeCN and 24 mL water was stirred at 70-75°C for 6h. The product was extracted with ether (3 X 25 mL),

washed with water and dried over anhydrous Na_2SO_4. Distillation under reduced pressure gave 4.5 g (57% yield) of colorless liquid, b.p. 66-68°C/5 mmHg. Ortho and meta tridecafluorohexyl pyridine were isolated by column chromatography on silica gel with petroleum ether-benzene (1:1) as eluant. The existence of the para isomer was indicated by ^{19}F NMR.

Table 1. Perfluoroalkylation of pyridine and its derivatives[a].

R_FX	Aromatics	Reaction time (hr)	Isolated yield (%)	Isomer comp.(%)[b]		
				o	m	p
$C_6F_{13}I$	**1a**	5	57	46	47	7
$C_7F_{15}I$	**1a**	5	62	46	45	9
$C_8F_{17}I$	**1a**	6	68	47	45	8
$ClC_8F_{16}I$	**1a**	5	63	48	44	8
ClC_4F_8I	**1a**	6	58	47	44	9
$C_7F_{15}Br$	**1a**	24	52	48	43	9
$ClC_6F_{12}Br$	**1a**	25	48	45	45	10
$C_6F_{13}I$	**1b**	8	52	48	52	
$ClC_6F_{12}I$	**1b**	8	42	44	56	
$ClC_6F_{12}I$	**1c**	6	46	61	26	13
ClC_4F_8I	**1c**	6	42	60	27	13
$C_6F_{13}I$	**1d**	6	28	100		
$ClC_6F_{12}I$	**1e**	10	20[b]			
ClC_4F_8I	**1f**	10	44			
ClC_4F_8I	**1g**	8	57			

[a] The structure of products was characterized by elemental analysis, MS, IR, ^1H NMR and ^{19}F NMR; [b] Determined by ^{19}F NMR.

As illustrated in Table 1 which summarized the results obtained from several compounds examined, the distribution of isomers was consistent with a radical reaction mechanism. It is noteworthy that the yield decreased when pyridine was substituted by methyl. Furthermore, in the case of 4-aminopyridine (**1e**), the reduction of R_FI predominated over alkylation. The detailed mechanism is now under further investigation. On the basis of this finding, a new method for the preparation of perfluoroalkylpyridines has been developed.

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