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Nobumasa Kamigata [a] , Takeshi Ohtsuka [a] , Masato Yoshida [a] & Toshio Shimizu [a]
[a] Department of Chemistry , Faculty of Science, Tokyo Metropolitan University, Minami-ohsawa , Hachioji, Tokyo, 192-03, Japan

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A NOVEL PERFLUOROALKYLATION OF PYRROLES WITH PERFLUOROALKANESULFONYL CHLORIDE CATALYZED BY A RUTHENIUM(II) PHOSPHINE COMPLEX

Nobumasa Kamigata,* Takeshi Ohtsuka, Masato Yoshida, and Toshio Shimizu

Department of Chemistry, Faculty of Science, Tokyo Metropolitan University,
Minami-ohsawa, Hachioji, Tokyo 192-03, Japan

Abstract: Direct perfluoroalkylation of *N*-substituted pyrroles with tridecafluorohexanesulfonyl chloride catalyzed by a ruthenium(II) phosphine complex proceeds regioselectively in high yield.

Recently, much attention has been focused on fluorinated organic compounds due to the characteristic features of the fluorine atom, particularly in the field of medicinal and agricultural chemistry and material science.[1] As a result, considerable efforts have been devoted to the introduction of perfluoroalkyl units in such systems, as exemplified by the reactions using reactive perfluoroalkyl cationic or radical species.[2] However, these processes often require careful preparation of the reactive intermediates[3] and are not amenable to both perfluoroalkylation ($\geq$ C2) and trifluoromethylation. Previously, we reported the chloroperfluoroalkylation of alkenes[4] and perfluoroalkylation of benzene

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*To whom correspondence should be addressed.

derivatives[5] with trifluoromethane- and tridecafluorohexanesulfonyl chlorides catalyzed by a ruthenium(II) complex. We found that the perfluoroalkylating method can be extended to the perfluoroalkylation of pyrroles, and the results are described herein.

When a solution containing tridecafluorohexanesulfonyl chloride, 1-acetylpyrrole (**1a**), and ruthenium(II) complex in pentane was degassed and heated at 120 °C in a sealed tube, the reaction proceeded smoothly with extrusion of sulfur dioxide. Flash column chromatography on Florisil using benzene and followed by gel permeation chromatography using chloroform gave 1-acetyl-2-tridecafluorohexylpyrrole (**2a**) and 1-acetyl-3-tridecafluorohexylpyrrole (**3a**) in 80 and 4% yield, respectively. The reactions of tridecafluorohexanesulfonyl chloride with 1-phenylsulfonyl-, 1-benzoyl-, and 1-carbomethoxypyrroles (**1b**-**1d**) in the presence of the ruthenium(II) catalyst under similar conditions afforded compounds **2**, perfluorohexylated selectively at 2-position, in high yield. However, the reactions of tridecafluorohexanesulfonyl chloride with pyrrole, 2-methylpyrrole, and 2,5-dimethylpyrrole under similar conditions did not give the corresponding perfluorohexylated pyrroles, instead a resinous black tar was formed.

The reaction of tridecafluorohexanesulfonyl chloride with 1-trimethylsilylpyrrole (**1e**) gave 2-tridecafluorohexyl-1-trimethylsilylpyrrole (**2e**, 53%), 2-tridecafluorohexylpyrrole (**2**, R=H; 25%), and 3-tridecafluorohexyl-1-

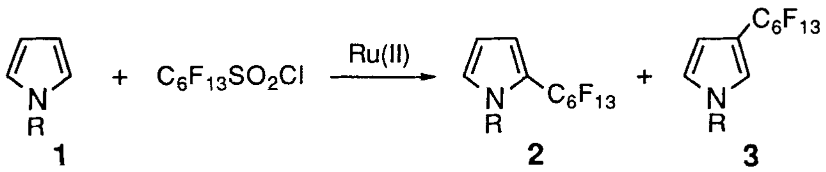

Table Reactions of Tridecafluorohexanesulfonyl Chloride with Pyrroles **1**.

R in **1**		Product / Yield(%)			
1a	COMe	**2a**	80	**3a**	4
1b	SO_2Ph	**2b**	65	**3b**	7
1c	COPh	**2c**	92	**3c**	6
1d	CO_2Me	**2d**	55	**3d**	1
1e	$SiMe_3$	**2e**	53[a]	**3e**	8
1f	$Si(i\text{-}Pr)_3$	**2f**	25	**3f**	59

[a] 2-Tridecafluorohexylpyrrole (**2**, R=H) was also obtained in 25% yield.

trimethylsilylpyrrole (**3e**, 8%). 2-Tridecafluorohexylpyrrole (**2**, R=H) may be formed by the desilylation of 2-tridecafluorohexyl-1-trimethylsilylpyrrole once formed under the reaction conditions, therefore, the total yield of perfluoroalkylation at 2-position is estimated to be 78%. On the other hand, the perfluoroalkylation of 1-triisopropylsilylpyrrole (**1f**) under similar conditions regioselectively occurred at the 3-position and 3-tridecafluorohexyl-1-triisopropylsilylpyrrole (**3f**, 59%) was formed together with 2-tridecafluorohexyl-1-triisopropylsilylpyrrole (**2f**, 25%).

The trialkylsilyl group of the products was replaced by hydrogen in high yield on treatment with tributylammonium fluoride. No product formation was observed in the reaction of tridecafluorohexanesulfonyl chloride with pyrrole catalyzed by ruthenium(II) complex. However, after temporary protection of the N-H function of pyrrole by a trimethylsilyl or triisopropylsilyl group, perfluoroalkylation using perfluoroalkanesulfonyl chloride in the presence of ruthenium(II) complex, followed by desilylation is an excellent method for the regioselective synthesis of 2- and 3-perfluoroalkylpyrroles (**2**, **3**, R=H).

Experimental

Starting materials **1a**,[6] **1b**,[7] **1c**,[6] **1d**,[8] **1e**,[9] and **1f**[10] were prepared by the methods according to the literatures, respectively.

General Procedure for the Reaction of Tridecafluorohexanesulfonyl Chloride with Pyrroles: A solution containing tridecafluorohexanesulfonyl chloride[11] (2.0 mmol), N-substituted pyrrole (10.0 mmol), and dichlorotris(triphenylphosphine)ruthenium(II)[12] (0.02 mmol) in pentane (4.0 ml) was degassed by a freeze-pump-thaw cycle, sealed in an ampoule, and heated at 120 °C for 24 h. The reaction mixture was followed through a Florisil column chromatography using benzene as the eluent to remove the metal complex. The products were separated from the reaction mixture by use of gel permeation chromatography (JAI LC-08) using chloroform as the eluent.

Deprotection of 2-Tridecafluorohexyl-1-trimethylsilylpyrrole (2a): A solution of **2a** and tetrabutylammonium fluoride (2 equiv. amount) in ether was stirred at room temperature for 14 h. The mixture was powered into water and the products were extracted with ether followed by purification using gel permeation chromatography gave 2-tridecafluorohexylpyrrole (**2**, R=H) in 72% yield.

2a: colorless oil; ^{1}H-NMR(CDCl$_3$) δ 2.60 (3H, s), 6.34 (1H, t, J=3.4Hz), 6.82-6.86 (1H, m), 7.31-7.36 (1H, m); *m/z* (EI, 70eV) 427(M$^+$), 408, 386, 366; Found: M$^+$, 427.0272, $C_{12}H_6NOF_{13}$ requires 427.0241. **2b:** colorless oil; ^{1}H-NMR(CDCl$_3$) δ 6.39 (1H, t, J=3.7Hz), 6.78 (1H, bs), 7.50 (2H, t, J=7.8Hz), 7.61

(1H, t, J=7.8Hz), 7.68 (1H, m), 7.82 (2H, d, J=7.8Hz); *m/z* (EI, 70eV) 525(M+), 506, 384; Found: M+, 524.9985, $C_{16}H_8NO_2F_{13}$ requires 525.0068. **2c:** colorless oil; ^{1}H-NMR(CDCl$_3$) δ 6.31 (1H, t, J=3.4Hz), 6.93 (1H, d, J=3.4Hz), 7.03-7.07 (1H, m), 7.52 (2H, t, J=7.8Hz), 7.65 (1H, t, J=7.8Hz), 7.77 (2H, d, J=7.8Hz); *m/z* (EI, 70eV) 489(M+), 470; Found: M+, 489.0453, $C_{17}H_8NOF_{13}$ requires 489.0398. **2d:** colorless oil; ^{1}H-NMR(CDCl$_3$) δ 3.98 (3H, s), 6.28 (1H, t, J=3.7Hz), 6.78-6.85 (1H, m), 7.52-7.58 (1H, m); *m/z* (EI, 70eV) 443(M+), 425, 413; Found: M+, 443.0192, $C_{12}H_6NO_2F_{13}$ requires 443.0191. **2e:** light purple oil; ^{1}H-NMR(CDCl$_3$) δ 0.45 (9H, s), 6.13-6.37 (1H, m), 6.59-6.80 (1H, m), 6.86-7.01 (1H, m); *m/z* (EI, 70eV) 457(M+), 442, 388; Found: M+, 457.0540, $C_{13}H_{12}NF_{13}Si$ requires 457.0531. **2f:** colorless oil; ^{1}H-NMR(CDCl$_3$) δ 1.13 (18H, d, J=7.3Hz), 1.56 (3H, septet, J=7.3Hz), 6.33 (1H, t, J=3.2Hz), 6.80 (1H, bs), 7.09 (1H, bs); *m/z* (EI, 70eV) 541(M+), 522, 498; Found: M+, 541.1471, $C_{19}H_{24}NF_{13}Si$ requires 541.1470. **3a:** colorless oil; ^{1}H-NMR(CDCl$_3$) δ 2.59 (3H, s), 6.46 (1H, bs), 7.35(1H, bs), 7.62 (1H, bs); *m/z* (EI, 70eV) 427(M+), 385, 366; Found: M+, 427.0239, $C_{12}H_6NOF_{13}$ requires 427.0241 **3b:** colorless oil; ^{1}H-NMR(CDCl$_3$) δ 6.45 (1H, bs), 7.22 (1H, bs), 7.50 (1H, bs), 7.56 (2H, t, J=7.8Hz), 7.67 (1H, t, J=7.8Hz), 7.91 (2H, d, J=7.8Hz); *m/z* (EI, 70eV) 525(M+), 506, 456; Found: M+, 525.0128, $C_{16}H_8NO_2F_{13}$ requires 525.0068. **3c:** colorless oil; ^{1}H-NMR(CDCl$_3$) δ 6.51 (1H, bs), 7.37 (1H, bs), 7.56 (2H, t, J=7.8Hz), 7.61 (1H, bs), 7.68 (1H, t, J=7.8Hz), 7.77 (2H, d, J=7.8Hz); *m/z* (EI, 70eV) 489(M+), 470; Found: M+, 489.0372, $C_{17}H_8NOF_{13}$ requires 489.0398. **3d:** colorless oil; ^{1}H-NMR(CDCl$_3$) δ 4.03 (3H, s), 6.42 (1H, bs), 7.34 (1H, bs), 7.61 (1H, bs); *m/z* (EI, 70eV) 443(M+), 424, 412; Found: M++1, 444.0274, $C_{12}H_7NO_2F_{13}$ requires 444.0269. **3e:** pale yellow oil; ^{1}H-NMR(CDCl$_3$) δ 0.45 (9H, s), 6.45 (1H, bs), 6.79 (1H, bs), 7.04 (1H, bs); *m/z* (EI, 70eV) 457(M^+), 442, 388; Found: M^+, 457.0488, $C_{13}H_{12}NF_{13}Si$ requires 457.0531. **3f:** colorless oil; ^{1}H-NMR($CDCl_3$) δ 1.10 (18H, d, J=7.3Hz), 1.46 (3H, septet, J=7.3Hz), 6.45 (1H, bs), 6.78 (1H, bs), 7.03 (1H, bs); *m/z* (EI, 70eV) 541(M^+), 522, 498; Found: M^+, 541.1513, $C_{19}H_{24}NF_{13}Si$ requires 541.1470.

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