

Short Note

4-(4-(2-Bromoethyl)phenoxy)-2,3,5,6-tetrafluoropyridine

Tiffany H. Li ^{1,†}, Lucas C. Messer ^{2,†}, Nathan J. Weeks ¹, Timothy J. Fuhrer ^{2,*}  and Scott T. Iacono ^{1,*} 

¹ Laboratories for Advanced Materials, Department of Chemistry & Chemistry Research Center, United States Air Force Academy, Colorado Springs, CO 80840, USA; nathan.weeks@afacademy.af.edu (N.J.W.)

² Department of Chemistry, Radford University, Radford, VA 24142, USA

* Correspondence: tfuhrer@radford.edu (T.J.F.); scott.iacono@afacademy.af.edu (S.T.I.)

† These authors contributed equally to this work.

Abstract: The title compound was synthesized in near quantitative yields via initial nucleophilic aromatic substitution of pentafluoropyridine (PFP) with 4-(2-bromoethyl)phenol as a versatile precursor for ionic liquids (ILs). The purity and structure were determined using ¹H, ¹³C, and ¹⁹F NMR and GC-EIMS.

Keywords: organo-fluorine; aryl ether; pentafluoropyridine; ionic liquid; nucleophilic aromatic substitution

1. Introduction

Ionic liquids (IL), often referred to as “liquid salts,” have captivated the scientific community with their unique properties and versatile applications and have been recently reviewed extensively [1]. Unlike traditional liquids, which are primarily composed of molecules, ionic liquids are made up of ions, resulting in their distinct behavior and intriguing characteristics. These remarkable substances exhibit low volatility, high thermal stability, and an exceptional ability to dissolve a wide range of compounds, making them valuable in various fields, such as chemistry, engineering, and materials science. With their tunable properties, including viscosity, conductivity, and solvation ability, ionic liquids have opened up new avenues for innovative research and have the potential to revolutionize numerous cleaner and waste-reducing industrial processes [2]. The preparation of fluorinated ionic liquids has been reported to a lesser extent due to limited synthetic pathways and availability of starting materials but has shown remarkable properties, leaving the pursuit of such novel systems worthwhile [3–5].

Perfluoropyridine (PFP) serves as a remarkably versatile feedstock for nucleophilic aromatic substitution (S_NAr), exhibiting its reactivity towards a wide array of O-, N-, S-, and C-nucleophiles, selectively targeting the 4-position [6,7]. Furthermore, by adding sequentially to the 2,6-positions, the 3,5-fluorines remain unreacted under mild conditions. Notably, PFP showcases its value as a protective agent for phenols [8,9], a reagent for introducing fluorine [10,11], and can also be subjected to site-specific catalytic defluorination [12,13]. Additionally, PFP has been utilized as a derivatization agent for the quantification of phenols in lignin [14]. The impetus behind incorporating PFP into polymer frameworks has resulted in the emergence of an array of novel fluoropolymer architectures, such as solvent processable polyarylethers, fluorosilicones, dendrimers, resins yielding high char, and mechanically milled fluoroelastomers tailored for demanding commercial and defense applications [15,16]. These extraordinary materials have exhibited substantial enhancements in processability, mechanical strength, and compatibility with hybrid composites, all while retaining exceptional resistance to high temperatures. As a potential expansion of the area of fluorinated ionic liquids, we detail the synthesis and structural characterization of a tetrafluoropyridine aryl ether with a halogen alkyl tether as a precursor



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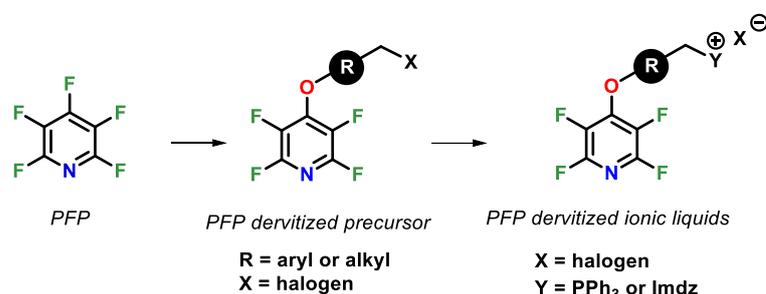
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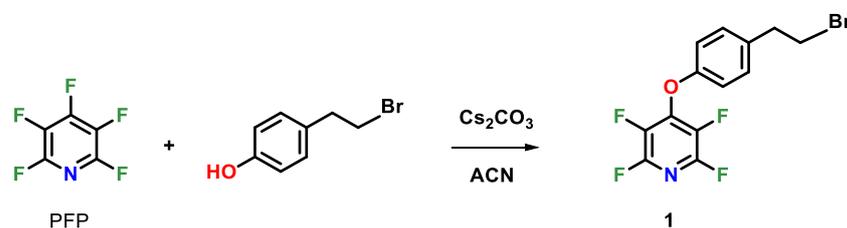
for ionic liquids. As shown in Scheme 1, such a methodology would complement recent reports of ionic liquids using the PFP as a precursor [17,18].



Scheme 1. Perfluoropyridine as a regio-selective electrophile for the synthesis of tetrafluoropyridine IL precursors.

2. Results and Discussion

Nucleophilic aromatic substitution of pentafluoropyridine (PFP) with 4-(2-bromoethyl)phenol using cesium carbonate in acetonitrile at room temperature afforded 4-(4-(2-bromoethyl)phenoxy)-2,3,5,6-tetrafluoropyridine (**1**) in excellent isolated yield (96%) (Scheme 2). Quantitative reaction conversion was observed via ¹⁹F NMR after 16 h and showed the quantitative regio-selective conversion of the 4-substituted F (δ -130 ppm) of PFP to exclusively the set of 2,6- and 3,5-substituted F multiplets at δ -88.525–(-88.535) and δ -153.147–(-153.158) (Figure S2). GC-MS confirmed the purity > 98% with an observed set of molecular ions (due to ⁷⁹Br and ⁸¹Br isotopes) at m/z = 351, 349 [M]⁺ and required no further purification (Figure S4).



Scheme 2. Synthesis of 4-(4-(2-bromoethyl)phenoxy)-2,3,5,6-tetrafluoropyridine **1** from PFP.

3. Materials and Methods

Chemicals and solvents were purchased as reagent grade by commercial suppliers. ¹H, ¹³C{¹H}, and ¹⁹F NMR spectra were recorded on a Jeol 500 MHz spectrometer. Chemical shifts were reported in parts per million (ppm), and the residual solvent peak was used as an internal reference for proton (chloroform δ 7.26) and carbon (chloroform, triplet, δ 77.2 ppm). Data are reported as follows: chemical shift, multiplicity (s = singlet, m = multiplet), coupling constants (Hz), and integration. Gas chromatography–mass spectrometry (GC-MS) analyses were performed on an Agilent 7890 gas chromatograph coupled to an Agilent 5975C electron impact mass spectrometer with initial 2 min temperature hold at 80 °C, then temperature gradient of 80 to 250 °C at 15 °C/min.

4-(4-(2-Bromoethyl)phenoxy)-2,3,5,6-tetrafluoropyridine (**1**)

Cesium carbonate (9.87 g, 30.3 mmol), pentafluoropyridine (5.0 g, 30.3 mmol), and 4-(2-bromoethyl)phenol (5.50 g, 27.3 mmol) were combined in acetonitrile (50 mL) and allowed to stir for 48 h at room temperature. The reaction was monitored via ¹⁹F NMR or GCMS until 100% conversion of the desired product was observed. The solution was vacuum filtered to remove carbonate salts and washed with diethyl ether (100 mL). The filtrate was combined with saturated ammonium chloride (100 mL), and the aqueous layer was extracted with diethyl ether (2 × 50 mL). The combined organic fractions were washed with saturated brine (1 × 100 mL), dried with magnesium sulfate, vacuum filtered, concentrated using

rotary evaporation, and dried under high vacuum, affording a white, waxy crude solid (10.2 g, 96%). Column chromatography (99:1 Hex/EtOAc, *v/v*) of the crude solid afforded the pure titled compound as a light yellow oil (8.0 g, 75%). R_f 0.45 (99:1 Hex:EtOAc). ^1H NMR (CDCl_3 , 500 MHz) δ 7.25–7.21 (m, $J_{AB} = 8.50$ Hz, 2H), 7.01–7.00 (m, $J_{AB} = 8.50$ Hz, 2H), 3.55 (t, $J = 5.0$ Hz, 2H), 3.16 (t, $J = 5.0$ Hz, 2H); $^{13}\text{C}\{^1\text{H}\}$ NMR (126 MHz) δ 154.8, 144.6 (m, C_{ipso}), 144.3 (dm, $J = 244$ Hz), 136.3 (dm, $J = 245$ Hz), 135.9, 130.5, 116.9, 38.5, 32.8; ^{19}F NMR (CDCl_3 , 471 MHz) δ -88.4–(-88.5) (m, 4F), -154.1–(-154.2) (m, 4F); GC–EIMS (70 eV) m/z (% relative intensity) 351, 349 ($[\text{M}]^+$, 40, 38), 270 (35), 256 (100), 138 (25), 91 (30), and 77 (25).

Supplementary Materials: The following supporting information is available online. ^1H , ^{19}F , ^{13}C NMR spectra and GC-MS for **1** (Figures S1–S4).

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