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One-Pot Desulfurative−Fluorination−Bromination. Synthesis of 2,5-Dibromo-3-(1,1-difluoroalkyl)thiophenes

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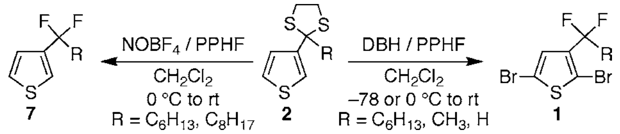
ABSTRACT



A unique one-pot, high-yield desulfurative−fluorination−bromination reaction which leads to the synthesis of 2,5-dibromo-3-(1,1-difluoroalkyl)thiophenes is reported. A single dithiolane reactant can be used to produce both 2,5-dibromo-3-(1,1-difluoroalkyl)thiophene and 3-(1,1-difluoroalkyl)thiophene with longer alkyl chains.

There is great interest in fluorinated conductive polymers due to the anticipated improvement in chemical and thermal stabilities relative to the alkyl analogues.[1−3] Such materials, with sufficient fluorine atoms, might be potential candidates for *n*-type semiconductors.[4−6] Fluorine-substituted conjugated polymers could thus have a variety of practical uses such as in organic field-effect transistors (OFET) and photovoltaic and sensor devices.[7−10] The introduction of a fluorine atom to replace a hydrogen atom significantly changes the physical and the chemical properties of an organic molecule. The fluorinated organic materials have remarkable features such as greater thermal and oxidative stability which lead to a longer lifetime of the devices and a relatively higher hydrophobicity and lipophobicity.[11,12] The introduction of electron-withdrawing groups such as fluoro or fluoroalkyl into the π-conjugated system would stabilize the LUMO energy level and might, if the effect is large enough, facilitate electron injection.[5,12,14−18] Further, the introduction of such groups also often lowers the HOMO energy level which helps stabilize the system particularly toward oxidative degradation.[12]

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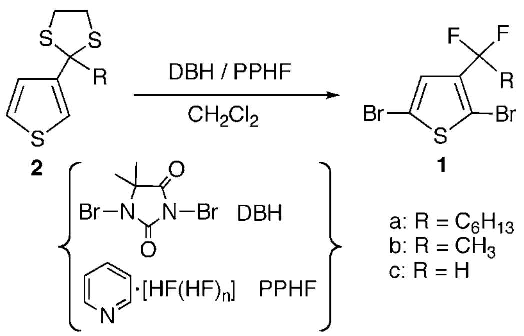
2,5-Dibromo-3-(1,1-difluoroalkyl)thiophene (**1**) is a class of interesting monomers that could, upon polymerization, lead to interesting polymers. In addition, 3-(1,1-difluoroalkyl)thiophene is a class of monomers which could also lead to similar polymers. These polymers would have significant advantages over perfluorinated polymers since the alkyl chain is known to render the polymer soluble in most organic solvents,[19] while the reported poly(perfluoroalkylthiophenes) are soluble only in supercritical carbon dioxide.[13,20,21]

Here we demonstrate the synthesis of 2,5-dibromo-3-(1,1-difluoroalkyl)thiophene and of 1,1-difluoroalkyl)thiophene. 2,5-Dibromo-3-(1,1-difluoroheptyl)thiophene (**1a**) was prepared in an unprecedented one-pot reaction in 90% yield (Scheme 1) from 2-hexyl-2-(thiophene-3-yl)-1,3-dithiolane (**2a**) which was desulfurated, fluorinated, and brominated in the single reaction flask. The synthesis was accomplished from commercially available aldehyde **3** in five steps and 48% overall yield. It is worth noting that in an earlier report the fluorodesulfuration reaction of thiophene dithiolanes using DBH/PPHF (1,3-dibromo-5,5-dimethylhydantoin/pyridinium polyhydrogen fluoride) at low temperatures led to the formation of the desired difluorinated products with small amounts of ring and/or side chain brominated byproducts.[22] The use of R = methyl and R = H also provided the corresponding dibromo−difluoro thiophenes in quite reasonable yields (Scheme 1).

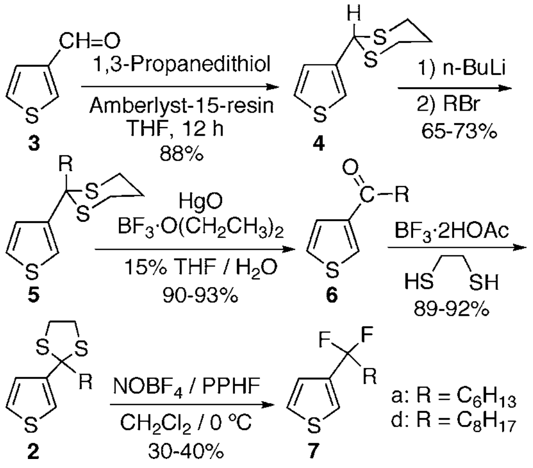
Scheme 1. Desufurative−Fluorination−Bromination Reaction



product	R	reaction temp (°C)	product yield (%)
1a	C_6H_{13}	−78	90
1b	CH_3	−78	60
1c	H	0	65

When the fluorodesulfuration of **2a** was performed using $NOBF_4$/PPHF at 0 °C, the reaction led cleanly to the formation of the desired difluorinated product **7** in moderate yield (40%) as shown in Scheme 2. It should be noted that the hexyl derivative **2a** must be prepared by the reaction sequence shown in Scheme 2 (via the dithiane, **4**→**5**) since it is well-known that alkylation of dithiolanes such as **2c** leads to cleavage of the dithiolane ring.[23] Our attempts to replace the hexyl group with methyl or hydrogen (**2b** and **2c**) did not give the corresponding difluoroalkyl compounds. However, the octyl dithiolane (**2d**: R = C_8H_{17}, Scheme 2) did indeed produce 3-(1,1-difluorononyl)thiophene again in moderate yield (30%). Sampson reported that this fluorodesulfuration reaction provides a "... convenient synthetic entry to 2-(1,1-difluoroalkyl)thiophenes (alkyl ≠ methyl)," suggesting he too had problems with the methyl substitution.[22] The reason for the difference between the longer and shorter side chains is not presently clear.

Scheme 2. Synthesis of 3-(1,1-Difluoroalkyl)thiophenes (**7a**, **7d**)



2-Hexyl- and 2-octyl-(2-thiophen-3-yl)-1,3-dithiolane (**2a** and **2d**) are readily prepared (Scheme 2) in four steps from thiophene-3-carbaldehyde (**3**). As mentioned above, 2-hexyl- and 2-octyl-(2-thiophen-3-yl)-1,3-dithiane (**5a** and **d**) must be pepared first and used for the alkylation to prevent ring cleavage.[23] Thiophene-3-carbaldehyde (**3**) was treated with 2 equiv of 1,3-propanedithiol in the presence of Amberlyst-15 resin to generate 2-(thiophene-3-yl)-1,3-dithiane (**4**) in 88% yield. Metalation of the dithiane **4** with *n*-butyllithium followed by electrophilic quenching with 1-bromohexane or 1-bromooctane led to the formation of 2-hexyl- and 2-octyl-2-(thiophene-3-yl)-1,3-dithiane (**5a** and **5d**) in 73 and 65% yield, respectively. The hydrolysis of **5a** and **5d** with red mercuric oxide and boron trifluoride etherate in THF led to the formation of 3-heptanoyl- and 3-nonanoylthiophene (**6a** and **6d**) in 93% and 90% yield, respectively.

3-Heptanoyl- and 3-nonanoylthiophene (**6a** and **6d**)[24] were converted to the 2-alkyl-2-(thiophen-3-yl)-1,3-dithiolanes (**2a** and **2d**), in 89% and 92% yield, respectively, using the method of Sondej and Katzenellenbogen.[25] This involved

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the addition of 1 equiv of the BF_3•2HOAc complex and 2 equiv of 1,2-ethanedithiol to the 3-alkanoylthiophenes **6a** and **6d**. Treatment of **2a** and **2d** with PPHF/$NOBF_4$ at 0 °C led to the formation of 3-(1,1-difluoroheptyl)- and of 3-(1,1-difluorononyl)thiophene (**7a** and **7b**) as colorless liquids in 40% and 30% yield, respectively.

To summarize, this one-pot desulfurative−fluorination−bromination is clearly an excellent and efficient way to prepare a variety of 2,5-dibromo-3-(1,1-difluoroalkyl)thiophenes (**1**) which would be a ready entry into the corresponding poly[3-(1,1-difluoroalkyl)thiophenes]. In addition, the 3-(1,1-difluoroalkyl)thiophenes (**7**) with the longer side chains, such as heptyl and nonyl, should also be useful entries into these same polymeric systems. Both systems can be prepared, in appropriate cases, from a single reactant, namely, the dithiolane **2**.

Finally, it is worth noting that the attempted desulfurative−fluorination−bromination of the dithiane **5a** led to an inseparable mixture of products, while reaction of **5a** with $NOBF_4$/PPHF gave the difluoro compound **7a**. Why we see this difference in the chemistry of the two cyclic dithioacetals is currently unclear.

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Supporting Information Available: Experimental procedures and spectroscopic data. This material is available free of charge via the Internet at http://pubs.acs.org.

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