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Synthesis and stability of 2-(1,1-difluoroalkyl) thiophenes and related 1,1-difluoroalkyl benzenes: fluorinated building blocks for liquid crystal synthesis

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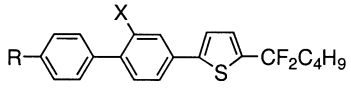
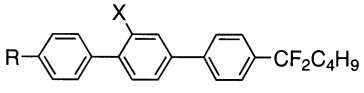
Abstract—The synthesis of a series of 2-(1,1-difluoroalkyl) thiophenes, including some biphenylthienyl liquid crystalline materials, was examined using a variety of fluorination approaches. For comparison purposes, a series of 1,1-difluoroalkyl benzene analogs were also prepared. The direct fluorodeoxygenation of alkyl thienyl ketones and alkyl phenyl ketones using various aminofluorosulfuranes proceeded in only moderate to poor yields. In contrast, fluorodesulfurization of the corresponding 1,3-dithiolanes using $NOBF_4$/PPHF cleanly afforded the desired 2-(1,1-difluoroalkyl) thiophenes (and analogous 1,1-difluoroalkyl benzenes) in high yields. Fluorodesulfurization of 2-alkyl-2-thienyl-1,3-dithiolanes using NBS (or DBH)/PPHF was complicated by competing ring and/or side chain bromination pathways. These problems were avoided when using NIS/PPHF. Although the various 1,1-difluoroalkyl arene products were sensitive to hydrolytic decomposition on prolonged exposure to silica, the purified products proved quite stable and were well suited for use as building blocks for liquid crystal synthesis.

1. Introduction

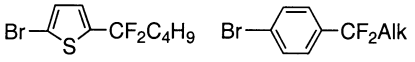
The relatively small size of fluorine and the high dipole moment of the C–F bond have resulted in the increasingly widespread application of fluorine substituents in liquid crystalline materials.[1] As part of a program aimed at the development of novel liquid crystals, we were interested in examining the impact of incorporating a 1,1-difluoroalkyl terminal chain adjacent to a thiophene or a benzene ring as in general structures **1** and **2**.



1 R = $C_{12}H_{25}O$ or $C_{13}H_{27}$
X = H or F
a R = $C_{12}H_{25}O$; X = F
b R = $C_{12}H_{25}O$; X = H



2 R = $C_{12}H_{25}O$ or $C_{13}H_{27}$
X = H or F



3 **4a** Alk = C_4H_9 **4b** Alk = C_7H_{15}

The high transverse molecular dipole imparted by the difluoromethylene unit was expected to afford a high dielectric biaxiality which is necessary for dielectric contrast enhancement of chevron-based surface-stabilized ferroelectric displays,[2] while the relatively small size of the difluoromethylene moiety[3] was anticipated to maintain tilted phase behavior[4] and relatively low material viscosities.[5] Therefore, our attention was directed toward the synthesis of appropriate 1,1-difluoroalkyl arene building blocks **3** and **4**, which we anticipated would prove useful as intermediates in the synthesis of fluorinated mesogens **1** and **2**.

A limited number of methods have been reported previously for the synthesis of simple 1,1-difluoroalkyl *benzenes*; essentially all of this chemistry was directed at the preparation of compounds bearing very short ($\leq C_3$) 1,1-difluoroalkyl chains.[6] The direct fluorodeoxygenation of a limited number of substituted phenyl alkyl ketones has been achieved using [bis(2-methoxyethyl)amino]sulfur trifluoride (DeoxoFluor®)[7] or diethylaminosulfur trifluoride (DAST).[8,9] Other approaches have involved fluorination of an intermediate hydrazone or oxime derivative.[10,11] The fluorodesulfurization of 2-alkyl-2-phenyl-1,3-dithiolanes

Keywords: fluorine and compounds; thiophenes; liquid crystals; halogenation.

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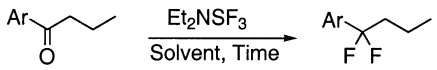
Table 1. Fluorodeoxygenation of alkyl aryl ketones **5** and **6** using DAST



5 Ar = 2-thienyl
6 Ar = phenyl

Entry	Substrate	DAST (equiv.)	*T* (°C)	Solvent	Vessel	Time	Conversion (%)[a]
1	**5**	2	40	CH_2Cl_2	Glass	50 h	0
2	**5**	1	85	Glyme	Glass	23 h	0
3	**5**	1	60	Neat	Glass	50 h	4
4	**5**	0.74	80	Neat	Glass	24 h	5
5	**5**	2	55	Neat	Plastic	102 h	30
6	**5**	2.2	55	Neat	Plastic	6 d	32
7	**6**	1	40	CH_2Cl_2	Glass	45 h	<1
8	**6**	1	85	Glyme	Glass	24 h	3
9	**6**	5	40	Neat	Glass	23 h	18
10	**6**	1.1	60	Neat	Glass	17 h	30
11	**6**	1.1	80	Neat	Glass	24 h	22
12	**6**	1.1	55	Neat	Plastic	27 h	35
13	**6**	2.0	55	Neat	Plastic	6 d	67
14	**6**	1.6	55	Neat	Plastic	14 d	73

[a] % Conversion was determined by GC and was in agreement with NMR ratios of product to starting material.

has previously been reported but with mixed success. Thus, fluorodesulfurization using $Bu_4NH_2F_3$/*N*-iodosuccinimide (NIS) proceeded in good yields in the presence of activated phenyl rings, but complex mixtures of products were formed in the presence of deactivated (nitro-, carbonyl-, or halogen-substituted) phenyl rings.[12] Fluorodesulfurization has also been carried out in low yields using hexafluoropropene-diethylamine in the presence of either 1,3-dibromo-5,5-dimethylhydantoin (DBH) or NIS/water.[13] The use of DBH led to large amounts of dehydrofluorination. Finally, clean fluorodesulfurization of a limited range of ring substituted 2-*methyl*-2-*phenyl*-1,3-dithiolanes was reported using $NOBF_4$/PPHF;[14] however, this method was not applied with other 2-alkyl-2-aryl-1,3-dithiolanes. Interestingly, no applications of this chemistry have appeared since its original communication (see below).

Virtually no attention has been paid in the literature to the synthesis of 1,1-difluoroalkyl thiophenes. There are no examples reported in the literature for the synthesis of 1,1-difluoroalkyl thiophenes that proceed via fluorination of a thiophene-containing ketone precursor or a derivative thereof. Indeed, there is only one literature synthesis of any 2-(1,1-difluoroalkyl) thiophene (where alkyl≠methyl).[15] This chemistry involved de novo construction of the thiophene ring from an acyclic β,β,γ,γ-tetrafluoro ester (rather than fluorination of an α-*oxo* thiophene or a derivative thereof) and it was restricted to the synthesis of 5-(1,1-difluoroalkyl)-3-hydroxythiophene-2-carboxylates.[16,17] As such, it was not useful for the synthesis of the liquid crystalline compounds targeted in the present study.

In a preliminary communication[8d] we reported the synthesis of 1,1-difluoropentyl thiophene **3** in low yield via direct DAST-mediated fluorodeoxygenation of the corresponding 2-pentanoyl thiophene. We now report full details of our exploratory studies aimed at uncovering fluorination methods suitable for the efficient synthesis of 1,1-difluoroalkyl thiophenes **1** and **3**. *This work constitutes the first practical synthetic entry to 1,1-difluoroalkyl thiophenes (where alkyl≠methyl).* For comparative purposes we also report the synthesis of the analogous 1,1-difluoroalkyl benzenes **4** which are, in themselves, useful intermediates en route to the corresponding terphenyl mesogens **2**.[18] The work outlined herein provides the first comparative study of a broad range of potential fluorinating approaches to 2-(1,1-difluoroalkyl) thiophene and 1,1-difluoroalkyl benzene targets and clearly reveals the preferred synthetic methods for the preparation of such targets.[19]

2. Results and discussion

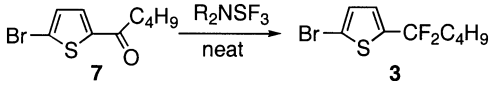
2.1. Synthesis of 1,1-difluoroalkyl aromatic compounds using fluorodeoxygenation approaches

Our initial studies involved the fluorodeoxygenation of alkyl aryl ketones using DAST. Model substrates chosen for initial optimization of the reaction conditions were 2-butanoyl thiophene (**5**) and butanoyl benzene (**6**) (see Table 1). In the presence of solvent, no significant reaction took place even at extended reaction times (entries 1, 2, 7 and 8).

When using neat DAST a slow conversion of the ketone into the difluorinated product was observed (entries 3–6, 9–14). The reaction temperature was found to be an important factor. The use of higher temperatures (80°C) afforded only low conversions to the desired product (entries 4 and 11), perhaps due to DAST decomposition and/or possible hydrolysis of the fluorinated product back to the parent ketone (see later). In contrast, lower temperatures (40°C) led to a very sluggish reaction (entry 9). Optimal conditions employed extended reaction times in the presence of an excess of DAST at 50–60°C (entries 5, 6, 13 and 14). Generally, higher yields were obtained when using plastic rather than glass vessels.

On a preparative scale, application of these optimized conditions to the fluorodeoxygenation of bromothienyl ketone **7** afforded the corresponding 1,1-difluoropentyl

Table 2. Fluorodeoxygenation of thienyl ketone **7** using neat aminofluorosulfuranes



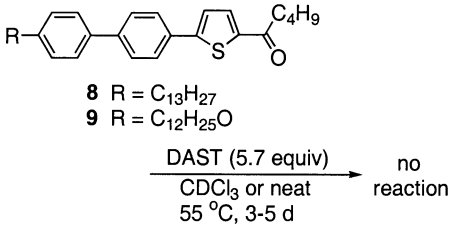
Entry	R_2NSF_3	# equiv.	T (°C)	Time	Yield (%)[a]
1	DAST	3.9	55	60 h	27 (24)
2	DAST	3.8	55	70 h	30 (28)
3	MorphDAST	2.8	75	60 h	31
4	MorphDAST	4.1	65	128 h	36
5	DeoxoFluor	4.3	65	70 h	43
6	DeoxoFluor	4.3	65	6 d	50
7	DeoxoFluor	4.3	80	18 h[b]	25

[a] GC yields, which were in agreement with ^{1}H NMR ratios of product to starting material; isolated yields in parentheses.
[b] No significant change occurred after 18 h.

thiophene **3** in a modest 24–28% isolated yield (Table 2, entries 1 and 2).

Attempts were made to evaluate the utility of other aminofluorosulfuranes for the preparation of **3**. Morph-DAST[20] was employed with no substantial improvement (entries 3 and 4). DeoxoFluor®,[7] led to a somewhat better conversion but only after prolonged reaction times (entries 5 and 6). The use of higher reaction temperatures proved deleterious (entry 7).

Interestingly, employment of DAST with related higher molecular weight thienyl ketones **8** and **9** did not lead to the formation of any fluorinated organic products (Eq. 1).



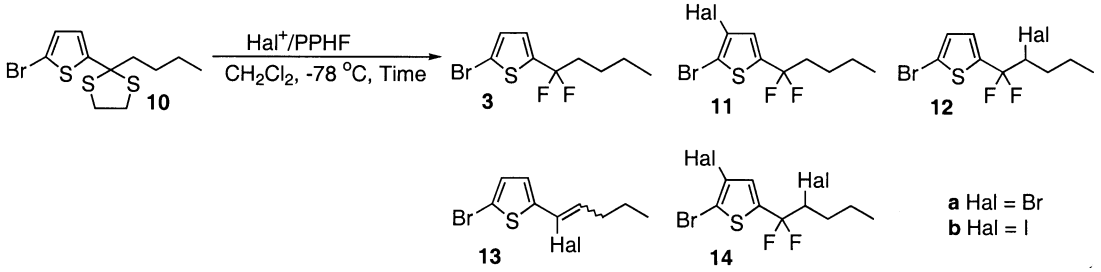
(1)

Instead, the parent ketones were recovered quantitatively in each case after 3–5 days of heating at 55°C in the presence of 5.7 equiv. DAST. This reaction was performed using either neat DAST or using a minimal amount of solvent ($CDCl_3$) to at least partially dissolve the starting ketone. The low solubility of these ketones in DAST may be problematic here, while our earlier studies demonstrated that the presence of solvent can be deleterious to fluorodeoxygenation (see Table 1).

2.2. Synthesis of 1,1-difluoroalkyl aromatic compounds using fluorodesulfurization approaches

The next stage of our investigation focused on the synthesis of 2-(1,1-difluoroalkyl) thiophenes (and the analogous 1,1-difluoroalkyl benzenes) via the fluorodesulfurization of 1,3-dithiolane derivatives of the corresponding alkyl aryl ketones. In preliminary studies, fluorodesulfurization of 2-phenyl-2-propyl-1,3-dithiolane using NBS/PPHF using a protocol analogous to that described by Katzenellenbogen[21] afforded a complex mixture of products from which the desired 1,1-difluorobutyl benzene was isolated by column chromatography in only 17% yield. Attempts to achieve similar fluorodesulfurization of 2-(5-bromothienyl)-2-butyl-1,3-dithiolane (**10**) using DBH/PPHF[21] gave a complex mixture of inseparable products containing the desired 2-bromo-5-(1,1-difluoropentyl)thiophene (**3**) in low (10–20%) yield. The low yield in each of these reactions could be attributed to product decomposition observed during the highly exothermic filtration through a basic alumina plug on workup, along with the instability of the products toward silica gel chromatography. The relatively electron-rich thiophene ring also appeared prone to ring bromination under the reaction and/or workup conditions. These problems could largely be circumvented by dilution of the reaction mixture with petroleum ether–CH_2Cl_2 (7:1) followed by separation of the HF–pyridine layer prior to filtration. Application of this modified workup procedure to the fluorodesulfurization of 2-(2-thienyl)-1,3-dithiolane

Table 3. Fluorodesulfurization of dithiolane **10** using Hal^+/PPHF



Entry	Hal^+ source	Time (min)	Yields (%)[a]					Unidentified products (%)	Combined isolated yield (%)
			3	**11**	**12**	**13**	**14**		
1	DBH	15	58	7	4	1	<1	3	74
2	DBH	45	39	15	2	1	1	2	60
3	NBS	15	58	5	2	3	–	7	75
4	NBS	45	80	<1	1	<1	–	3	84
5[b]	NBS	15	54	<0.2	<0.5	1	–	7	63
6	NIS	15	80	–	–	-	–	<2	80

[a] Yields of each component were determined based on combined isolated yield and GC ratios, which were in accord with ratios obtained by ^{1}H and ^{19}F NMR spectroscopy.
[b] A cooled (−70°C) petroleum ether–CH_2Cl_2 mixture was used during workup.

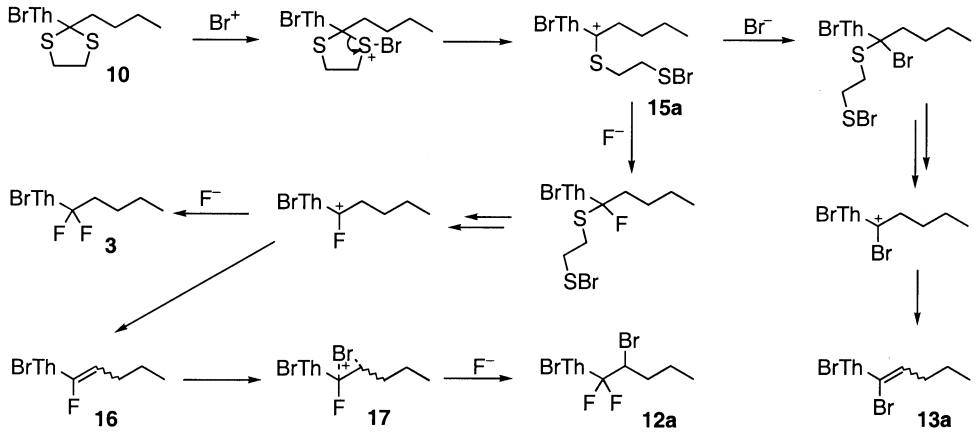
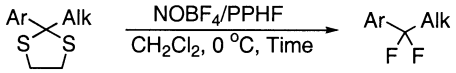
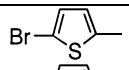
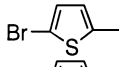
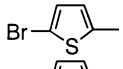
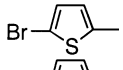
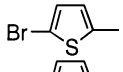
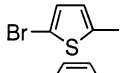
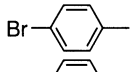
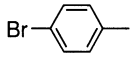
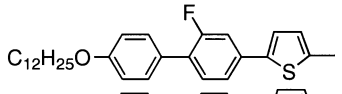
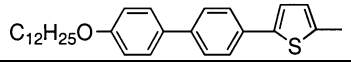


Figure 1. Formation of brominated byproducts during fluorodesulfurization of **10**.

10 with NBS/PPHF or DBH/PPHF allowed us to obtain the desired difluorinated product **3** in moderate to good yield as a mixture with smaller amounts of various ring and/or side chain brominated byproducts (see Table 3). The ratios of products depended on the Hal^+ source and the reaction time. When using DBH, competitive ring bromination was observed even at low reaction temperatures and traces of side-chain brominated byproducts were also obtained (entry 1). Longer reaction times proved deleterious to both the yield and purity of the desired product **3** (entry 2). In contrast, when using NBS, longer reaction times led to a better yield of **3** and a more favorable product distribution (compare entries 3 and 4). One explanation for this observation may be that residual unreacted NBS present after a short reaction time can effect bromination during workup (entry 3). In contrast, longer reaction times lead to the complete consumption of NBS prior to workup, when such side reactions are precluded (entry 4). In any event, these side reactions could be largely (though not completely) suppressed by using precooled (−70°C) petroleum ether–CH_2Cl_2 during workup (entry 5). The somewhat surprising formation of minor byproduct **13a** in all these reactions can be explained by the presence of small amounts of adventitious Br_2 in DBH and NBS (Fig. 1). Reaction of Br_2 with some nucleophilic species in solution would provide a source of bromide ion, which can intercept a carbocation such as **15a**. Subsequent elimination chemistry would then afford **13a**. Formation of **12a** can be envisaged to proceed via electrophilic bromination of the initially formed fluoroalkene **16** with subsequent attack of fluoride ion on the resulting bromonium ion intermediate **17**. Compound **14a** would be formed via an analogous pathway.

Table 4. Fluorodesulfurization of alkyl aryl dithiolanes using $NOBF_4$/PPHF



Entry	Substrate	Ar	Alk	Time (min)	Scale (mmol)	Product	Isolated yield (%)
1	**10**		$-C_4H_9$	60	1.00	**3**	29
2	**10**		$-C_4H_9$	180	1.95	**3**	0
3	**10**		$-C_4H_9$	45	1.97	**3**	38
4	**10**		$-C_4H_9$	6	2.17	**3**	87
5	**10**		$-C_4H_9$	6	4.68	**3**	81
6	**10**		$-C_4H_9$	6	6.25	**3**	75
7	**18**		$-C_4H_9$	6	4.52	**4a**	72
8	**19**		$-C_7H_{15}$	6	4.52	**4b**	81
9	**20**		$-C_4H_9$	6	0.50	**1a**	78
10	**21**		$-C_4H_9$	6	3.00	**1b**	47

All of the byproducts formed in these reactions are close in polarity to the desired product **3** and hence separation was problematic.

In sharp contrast to the results obtained with NBS and DBH, the use of NIS/PPHF provided **3** in 80% yield after 15 min, with no byproduct formation (Table 3, entry 6). Thus, this protocol was the best of the Hal^+/PPHF-based fluorodesulfurization approaches to 2-(1,1-difluoropentyl)-thiophene **3**.

Next we investigated the use of the $NOBF_4$/PPHF-mediated fluorodesulfurization protocol originally developed by Olah and Prakash.[14] It was reported that the HF-containing layer in these reactions could be separated from the reaction mixture during workup after dilution with CH_2Cl_2. The separated product-containing layer could then be filtered through an alumina plug without an exothermic reaction; however, in our hands, separation of the HF-containing layer in these reactions was not observed, which precluded isolation of the reaction product. Therefore, the workup procedure was modified by adding petroleum ether to dilute the reaction mixture, which allowed us to efficiently separate the HF-containing layer. Moreover, the low polarity of this solvent system allowed for a better separation of the product from the various impurities during the filtration process than was possible with a more polar solvent. We found that the reaction time dramatically influenced the outcome of these reactions (see Table 4). In their original work,[14] Olah and Prakash reported the use of 60 min reaction times for the fluorodesulfurization of a range of dithiolanes; however, fluorodesulfurization of our thienyl dithiolane **10** under these conditions gave the desired difluorinated product **3** in only low yield (29%, entry 1). Longer reaction times did not lead to improved yields and, if the reaction was continued for 3 h, no desired product was isolated (entry 2). Apparently, the thiophene-containing product **3** slowly decomposes and/or polymerizes under the reaction conditions. However, the use of a somewhat shorter reaction time (45 min) slightly improved the reaction yield (38%, entry 3), while a very short reaction time (ca.6 min) provided a very good yield of the desired difluorinated product (87%, entry 4). Scaling up the procedure to 4–7 mmol led to a small decrease in yields (75–81%) (compare entries 4–6). No side reactions were observed in any of these experiments.

Several other substrates were then subjected to these optimized conditions. Analogous phenyl-containing dithiolanes **18** and **19** were employed and high yields of the corresponding 1,1-difluoroalkyl benzenes **4a** and **4b** were obtained (entries 7 and 8). In contrast to the results observed during the DAST-mediated fluorodeoxygenation of the corresponding teraryl ketones **8** and **9** (Eq. (1)), even the higher molecular weight biphenylthienyl dithiolanes **20** and **21** could be effectively converted into the corresponding difluorinated liquid crystal derivatives **1a** and **1b** using this procedure, since these substrates have good solubility in CH_2Cl_2 at 0°C. Thus, **20** was fluorinated successfully on a 0.50 mmol scale in 78% yield (entry 9). Larger scale (3.0 mmol) fluorination for **21** led to a more modest 47% yield of the desired product (entry 10). This lower yield is attributed to solubility problems during chromatographic purification (see below). The above results constitute the first application of $NOBF_4$/PPHF-mediated fluorodesulfurization of 1,3-dithiolanes beyond the original literature communication[14] and, under the modified conditions developed herein, provide the first convenient synthetic entry to 2-(1,1-difluoroalkyl) thiophenes (alkyl≠methyl).

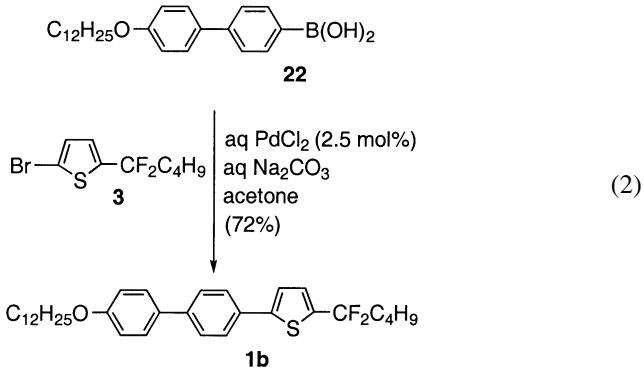
2.3. Stability of 1,1-difluoroalkyl arene products

A priori, we had some concerns as to the likely hydrolytic and thermal stability of the 1,1-difluoroalkyl thiophene and analogous 1,1-difluoroalkyl benzene compounds targeted in this study. Interestingly, however, to our knowledge, the only examples reported in the literature for the hydrolysis of a 1,1-difluoroalkyl arene into the corresponding aryl ketone have involved perfluoroalkyl arene substrates.[22] We found that higher molecular weight (teraryl) 1,1-difluoroalkyl arenes (e.g. **1** or **2**[23]) underwent partial or complete decomposition to the corresponding ketones on prolonged exposure to silica during flash column chromatography or TLC. Therefore, very rapid filtration through a silica plug was required for efficient purification of these substances. Although small amounts of decomposition still occurred, the resulting ketone byproduct was retained by the silica column. Generally, laterally fluorinated teraryls (e.g. biphenylthiophene **1a**) have higher solubility when compared to their non-laterally fluorinated analogs. As a result, the biphenylthiophene **1b** lacking lateral fluorine substitution suffered longer exposure times to silica during filtration and therefore higher levels of decomposition were observed. Such problems were not evident in the case of the lower molecular weight 1,1-difluoroalkyl arenes **3**, **4a** and **4b**, which proved relatively stable to rapid silica gel chromatography. Recrystallization of compounds **1** and **2** from alcohols or any wet solvents also led to a partial decomposition to the corresponding ketone. Pure 1,1-difluoroalkyl thiophene **3** decomposed after 1–5 days in $CDCl_3$ solution in an NMR tube, while the corresponding benzene analogs **4a** and **4b** had somewhat longer lifetimes (1–2 weeks). In each case, the decomposed dark mixtures contained primarily the corresponding ketones. The glass of the NMR tubes was etched after decomposition, suggesting HF formation. Compounds **3**, **4a** and **4b** each had sufficient thermal stability to be reproducibly analyzed by GC (injection port at 290°C). In the purified form, all higher molecular weight (teraryl) difluoroalkyl derivatives (e.g. **1** or **2**) proved to be stable solids (no decomposition over a two-year period), and only high-melting compounds showed decomposition when in the isotropic phase or when approaching the isotropic phase (>180°C).[18] The corresponding liquid 1,1-difluoroalkyl thiophene **3** and 1,1-difluoroalkyl benzenes **4a** and **4b** can be stored for several months in the open air in pyrex glass or plastic vessels without noticeable decomposition. In contrast, some samples decomposed within a few days when stored in borosilicate glass vials. These compounds can also be stored in the presence of Et_3N.

2.4. Application of 1,1-difluoropentyl arene building blocks 3 and 4 in liquid crystal synthesis

The stable 2-(1,1-difluoropentyl)thiophene **3** and its benzene analog **4a** could be prepared on a multigram scale

and proved useful as building blocks in the construction of a series of teraryl liquid crystalline targets bearing the 1,1-difluoropentyl terminal chain. For example, Suzuki cross-coupling of 2-bromo-5-(1,1-difluoropentyl)thiophene (**3**) with dodecyloxy-substituted biphenylboronic acid **22** (0.1 M $PdCl_2$, 2 M aq Na_2CO_3, acetone) afforded mesogenic target **1b** in 72% yield (Eq. 2). In line with other 1,1-difluoropentyl-substituted teraryl mesogenic targets that we have prepared,[8d,18] this compound has a high melting temperature (155.9°C) and supports a disordered smectic A phase below the clearing point (172.4°C); however, in contrast to other related 1,1-difluoropentyl-bearing teraryl mesogens, this particular material also supported a more low lying disordered tilted smectic F phase (160.4°C). In addition, smectic mesophases such as the orthogonal hexatic smectic B phase have been detected in other 1,1-difluoroalkyl-containing teraryl mesogens. A full paper detailing the mesomorphic phase behavior of a series of 1,1-difluoroalkyl-substituted teraryl liquid crystals, as well as various functional group derivatives thereof, will appear separately.[18]



(2)

3. Conclusion

We have described a survey of various methods for the synthesis of 2-(1,1-difluoroalkyl) thiophenes (and related 1,1-difluoroalkyl benzenes). A thorough exploration of various aminofluorosulfurane-mediated fluorodeoxygenation approaches was performed; however, only moderate to low yields of the desired 1,1-difluoroalkyl arene targets could be obtained. A variety of approaches involving fluorodesulfurization of 2-alkyl-2-aryl-1,3-dithiolanes were also explored. The most successful approach to 2-(1,1-difluoropentyl) thiophenes involved use of $NOBF_4$/PPHF employing very short reaction times and a modified workup protocol. Although use of NBS (or DBH)/PPHF also gave reasonable yields of the desired products, competing ring and/or side chain bromination pathways made this approach less attractive. These problems were avoided when using NIS/PPHF. The $NOBF_4$/PPHF fluorodesulfurization conditions also proved useful in the synthesis of analogous 1,1-difluoroalkyl benzenes **4a** and **4b** bearing longer alkyl chains (pentyl and octyl), which had not been previously reported,[6] as well as higher molecular weight biphenylthienyl-based liquid crystalline materials **1a** and **1b**. Although the various 1,1-difluoroalkyl arene products were susceptible to hydrolytic decomposition on prolonged exposure to silica, the purified products proved quite stable. Both 2-bromo-5-(1,1-difluoropentyl) thiophene (**3**) and the 1,1-difluoropentyl benzene analog **4a** were well suited for use as building blocks in the synthesis of liquid crystalline materials via application of Suzuki cross-coupling methodology. The application of this chemistry in the synthesis of a range of 1,1-difluoroalkyl-containing liquid crystalline materials (and variously functionalized analogs thereof), along with full details of their mesomorphic phase behavior, will be reported elsewhere.[18]

4. Experimental

4.1. General

Unless otherwise stated, NMR spectra were recorded in $CDCl_3$ as follows: ^1H NMR (300 MHz), ^{13}C NMR (75 MHz) and ^{19}F NMR (470 MHz). Chemical shifts are reported in ppm downfield from TMS (^1H and ^{13}C NMR) or $CFCl_3$ (^{19}F NMR). Unless otherwise noted, coupling constants refer to ^1H–^1H coupling (J_{H-H}). In some samples containing mixtures of components, overlapping signals precluded the observation of all NMR signals. In these cases, only those selected signals which were readily discernible are reported for each component. Low resolution mass spectra (MS) were recorded using a Hewlett Packard (HP) 5890 Series II GC hooked to an HP 5972 Mass Selective Detector—only selected ions are presented. High resolution mass spectra (HRMS) were recorded in electron impact mode at the Ohio State University Chemistry Mass Spectrometry Facility. Combustion analyses were performed using a LECO Model CHNS-932 elemental analyzer. Transition temperatures for mesogen **1b** were measured upon cooling at a rate of 5°C per minute using a Mettler FP82HT hot-stage and FP90 control unit in conjunction with a Leica Laborlux 12PolS polarizing microscope. The progress of reactions was monitored using either silica TLC or GC using a Shimadzu GC-14A gas chromatograph fitted with a 30 m capillary column. Unless otherwise stated, all chemicals were used as received without additional purification. Anhydrous CH_2Cl_2 was obtained by stirring and distillation from CaH_2. Anhydrous ether and THF were obtained by distillation from benzophenone ketyl. All chromatographic separations were performed using flash column chromatography on silica gel (200–425 mesh) or alumina (activated, basic, 50–200 μm, Acros Organics). The synthesis of ketone **8** will be reported elsewhere.[18] The synthesis of ketone **9** was achieved by deprotection of dithiolane **21** using $Hg(ClO_4)_2{\cdot}3H_2O$.[24]

4.2. Synthesis of ketone precursors

4.2.1. 2-Bromo-5-pentanoylthiophene (7). $FeCl_3$ (9.95 g, 0.0613 mol) was added in one portion to a stirred mixture of 2-bromothiophene (50.0 g, 0.307 mol) and valeric anhydride (65.7 g, 0.353 mol) under nitrogen at rt (a temperature rise to 100°C was noted). The reaction mixture was stirred at rt for a further 2 h (TLC and GC analyses confirmed a complete reaction) and was then poured into water (300 mL). The organic layer was separated and the aqueous layer was washed with ether (2×50 mL). The combined organic extracts were washed with 2 M aq Na_2CO_3 (2×200 mL). The organic layer was dried ($MgSO_4$) and

concentrated in vacuo to give a black liquid. The crude product was distilled in vacuo to give the title compound **7** as a colorless liquid (bp 128–133°C/0.5 mmHg) (62.36 g, 82%). ^{1}H NMR δ 0.94 (t, J=7.2 Hz, 3H), 1.39 (sextet, J=7.5 Hz, 2H), 1.70 (quint, J=7.5 Hz, 2H), 2.82 (t, J=7.2 Hz, 2H), 7.09 (d, J=3.9 Hz, 1H), 7.44 (d, J=3.9 Hz, 1H); ^{13}C NMR δ 13.8, 22.6, 26.6, 38.3, 122.2, 130.5, 132.8, 145.9, 192.3. Anal. Calcd for $C_9H_{11}BrOS$: C, 43.74; H, 4.49; S, 12.97. Found: C, 43.91; H, 4.51; S, 13.06.

4.2.2. 1-Bromo-4-pentanoylbenzene.[25] Valeryl chloride (20.6 g, 0.171 mol) was added dropwise to a stirred, cooled (0°C) mixture of bromobenzene (29.1 g, 0.185 mol) and $AlCl_3$ (49.8 g, 0.373 mol) under argon. The reaction mixture was maintained under these conditions for a further 1 h and was then heated at 70–80°C for 2 h (GC analysis indicated a complete reaction). The cooled mixture was poured into aq HCl (18%, 200 mL). The product was extracted into CH_2Cl_2 (2×100 mL), washed with water (2×100 mL) and dried ($MgSO_4$). Concentration in vacuo followed by vacuum distillation afforded the title compound as a colorless semi-solid (bp 85–87°C/1.1 mmHg) (35.7 g, 85%). ^{1}H NMR δ 0.94 (t, J=7.4 Hz, 3H), 1.39 (sextet, J=7.4 Hz, 2H), 1.70 (quint, J=7.5 Hz, 2H), 2.92 (t, J=7.4 Hz, 2H), 7.59 (d, J=8.7 Hz, 2H), 7.81 (d, J=8.7 Hz, 2H).

4.2.3. 1-Bromo-4-octanoylbenzene.[26] This compound was prepared following the above procedure using octanoyl chloride (35.00 g, 0.2152 mol), bromobenzene (40.00 g, 0.2548 mol) and $AlCl_3$ (57.34 g, 0.4300 mol) under argon. The crude product was distilled in vacuo to give the title compound as a colorless solid (50.61 g, 83%), mp 65–66°C. ^{1}H NMR δ 0.88 (t, J=6.9 Hz, 3H), 1.23–1.42 (m, 8H), 1.72 (quint, J=7.4 Hz, 2H), 2.92 (t, J=7.4 Hz, 2H), 7.59 (d, J=8.5 Hz, 2H), 7.81 (d, J=8.5 Hz, 2H); ^{13}C NMR δ 14.2, 22.7, 24.4, 29.2, 29.4, 31.8, 38.7, 128.1, 129.7, 132.0, 136.0, 199.5.

4.3. General procedure for synthesis of 1,3-dithiolane precursors[27]

4.3.1. 2-(5-Bromothien-2-yl)-2-butyl-1,3-dithiolane (10). BF_3·2HOAc (6.25 mL, 44.9 mmol) was added over a period of 5 min to a mixture of 2-bromo-5-pentanoylthiophene (**7**) (10.04 g, 40.65 mmol) and ethane-1,2-dithiol (7.50 mL, 89.6 mmol) under nitrogen. The resulting solution was stirred vigorously for 20 min. The mixture was diluted with hexanes (100 mL) and washed sequentially with sat. aq $NaHCO_3$, 15% aq NaOH, and brine (3×80 mL in each case). The organic layer was dried (Na_2SO_4) and concentrated in vacuo to afford the title compound **10** as a slightly yellow liquid (12.85 g, 98%) which was sufficiently pure for use in the next step without further purification. ^{1}H NMR δ 0.88 (t, J=7.1 Hz, 3H), 1.23–1.47 (m, 4H), 2.32 (t, J=8.0 Hz, 2H), 3.38 (m, 4H), 6.83 (d, J=3.9 Hz, 1H), 6.86 (d, J=3.9 Hz, 1H); ^{13}C NMR δ 13.8, 22.6, 30.0, 39.5, 44.7, 69.7, 111.3, 125.3, 129.7, 154.6. Anal. Calcd for $C_{11}H_{15}BrS_3$: C, 40.86; H, 4.68; S, 29.75; Found: C, 40.77; H, 4.74; S, 30.11.

4.3.2. 2-(4-Bromophenyl)-2-butyl-1,3-dithiolane (18). This compound was prepared following the procedure described for compound **10** using 1-bromo-4-pentanoylbenzene (9.64 g, 40.0 mmol), ethane-1,2-dithiol (7.37 mL, 88.0 mmol) and BF_3·2HOAc (6.13 mL, 44.0 mmol). The crude dried organic extract was passed through a short silica plug (5 cm long, 4 cm in diameter). The plug was washed with petroleum ether (200 mL). Concentration in vacuo afforded the title compound **18** as a colorless liquid (9.80 g, 77%) which was sufficiently pure for use in the next step without further purification. ^{1}H NMR δ 0.84 (t, J=6.8 Hz, 3H), 1.15–1.30 (m, 4H), 2.32 (t, J=7.9 Hz, 2H), 3.14–3.41 (m, 4H), 7.42 (d, J=8.7 Hz, 2H), 7.59 (d, J=8.7 Hz, 2H). ^{13}C NMR δ 14.1, 22.9, 30.2, 39.3, 45.6, 74.0, 121.0, 129.3, 131.1, 144.8. Anal. Calcd for $C_{13}H_{15}BrS_2$: C, 49.21; H, 5.40; S, 20.21; Found: C, 48.89; H, 5.41; S, 20.60.

4.3.3. 2-(4-Bromophenyl)-2-heptyl-1,3-dithiolane (19). This compound was prepared following the procedure described for compound **10** using 1-bromo-4-octanoylbenzene (5.66 g, 20.0 mmol), ethane-1,2-dithiol (3.7 mL, 44.0 mmol) and BF_3·2HOAc (3.1 mL, 22.0 mmol). The crude dried organic extract was passed through a short silica plug (5 cm long, 4 cm in diameter). The plug was washed with petroleum ether (200 mL). Concentration in vacuo afforded the title compound **19** as a colorless liquid (7.22 g, 100%) which was sufficiently pure for use in the next step without further purification. ^{1}H NMR δ 0.85 (t, J=6.8 Hz, 3H), 1.00–1.40 (m, 10H), 2.30 (t, J=6.6 Hz, 2H), 3.12–3.40 (m, 4H), 7.41 (d, J=8.7 Hz, 2H), 7.58 (d, J=8.7 Hz, 2H). ^{13}C NMR δ 13.9, 22.4, 27.7, 28.8, 29.4, 31.5, 39.0, 45.5, 73.6, 120.6, 128.9, 130.7, 144.4. Anal. Calcd for $C_{16}H_{17}BrS_2$: C, 53.47; H, 6.45; S, 17.84; Found: C, 53.82; H, 6.50; S, 18.22.

4.3.4. 2-Butyl-2-[5-(4′-dodecyloxy-2-fluorobiphenyl-4-yl)-thien-2-yl]-1,3-dithiolane (20). To a stirred biphasic mixture of compound **10** (0.485 g, 1.50 mmol), $(Ph_3P)_4Pd$ (0.085 g, 0.075 mmol) and 2 M aq Na_2CO_3 (1.5 mL, 3.0 mmol) in benzene (3.0 mL), was added 4′-dodecyloxy-2-fluorobiphenyl-4-ylboronic acid[28] (0.752 g, 1.88 mmol) in ethanol (1.5 mL). The reaction mixture was heated under reflux for 3 h. The cooled mixture was diluted with water (20 mL) and extracted with CH_2Cl_2 (4×20 mL). The combined organic extracts were washed with water (3×30 mL), brine (2×30 mL) and dried (Na_2SO_4). Concentration in vacuo gave a dark yellow oil which was purified by gradient column chromatography on silica gel (petroleum ether–$CHCl_3$, 10:1–1:1). The resulting yellow solid was dried in vacuo (P_2O_5, paraffin wax, 1.1 mmHg) to afford the title compound **20** as a yellow solid (0.840 g, 94%). ^{1}H NMR δ 0.89 (t, J=6.9 Hz, 3H), 0.91 (t, J=7.2 Hz, 3H), 1.24–1.51 (m, 22H), 1.81 (quint, J=7.1 Hz, 2H), 2.41 (m, 2H), 3.43 (s, 4H), 4.00 (t, J=6.6 Hz, 2H), 6.97 (d, J=8.8 Hz, 2H), 7.07 (d, J=3.8 Hz, 1H), 7.15 (d, J=3.8 Hz, 1H), 7.29–7.43 (m, 3H), 7.50 (dd, J=8.7 Hz, J_{H-F}=1.5 Hz, 2H); ^{19}F NMR δ −118.4 (br dd, J_{F-H}=7.5, 4.4 Hz). Anal. Calcd for $C_{35}H_{47}FOS_3$: C, 70.19; H, 7.91; S, 16.06; Found: C, 69.79; H, 7.97; S, 16.20.

4.3.5. 2-Butyl-2-[5-(4′-dodecyloxybiphenyl-4-yl)thien-2-yl]-1,3-dithiolane (21). To a stirred, cooled (0°C) solution of $PdCl_2$(dppf) (0.200 g, 0.273 mmol) and dithiolane **10** (7.80 g, 24.1 mmol) in anhydrous THF (20 mL) under argon, was added dropwise, over a period of 30 min, a solution of 4′-dodecyloxybiphenyl-4-yl magnesium bromide

(prepared from magnesium (0.660 g, 0.267 mol) and 4-bromo-4′-dodecyloxybiphenyl[28] (10.43 g, 0.0250 mol) in anhydrous THF (30 mL)). The reaction mixture was allowed to warm to rt and was stirred until completion of the reaction (ca. 1 day, as established by TLC analysis). Methanol (1.0 mL) was added and the reaction mixture was diluted with CH_2Cl_2 (300 mL). The mixture was filtered through a short silica plug and the solvent was evaporated in vacuo. The residue was purified by column chromatography on silica gel (CH_2Cl_2) and dried in vacuo to afford the title compound **21** (5.00 g, 36%) as a yellow solid. ^{1}H NMR δ 0.88 (t, J=6.9 Hz, 3H), 0.90 (t, J=7.2 Hz, 3H), 1.24–1.52 (m, 22H), 1.80 (quint, J=7.2 Hz, 2H), 2.41 (m, 2H), 3.43 (s, 4H), 3.99 (t, J=6.5 Hz, 2H), 6.96 (d, J=8.7 Hz, 2H), 7.05 (d, J=3.6 Hz, 1H), 7.13 (d, J=3.6 Hz, 1H), 7.52 (d, J=8.7 Hz, 2H), 7.53 (d, J=8.4 Hz, 2H), 7.60 (d, J=8.4 Hz, 2H). ^{13}C NMR δ 13.8, 14.0, 22.6, 22.7, 25.9, 29.2 (2), 29.3, 29.5, 30.1, 31.8, 39.6, 45.1, 68.0, 70.0, 114.7, 122.3, 125.7, 126.2, 126.8, 127.7, 132.6, 139.6, 143.1, 152.1, 158.7. Anal. Calcd for $C_{35}H_{48}OS_3$: C, 72.36; H, 8.33; Found: C, 72.34; H, 8.20.

4.4. General procedure for DAST-mediated fluorodeoxygenation of thienyl ketones

4.4.1. 2-Bromo-5-(1,1-difluoropentyl)thiophene (3). 2-Bromo-5-pentanoylthiophene (**7**) (1.00 g, 4.02 mol) was added dropwise to stirred DAST (2.40 g, 14.9 mol) under argon at rt in a 7 mL plastic vial. The reaction mixture was heated at 55°C for 4 days. The cooled reaction mixture was diluted with petroleum ether (40 mL, bp 35–60°C) and washed with saturated aq $NaHCO_3$ until free of acid. The organic layer was filtered through a short silica column (petroleum ether) and the solvent was removed in vacuo to give the title compound **3** as a colorless liquid (0.302 g, 28%); ^{1}H NMR δ 0.91 (t, J=6.9 Hz, 3H), 1.33–1.52 (m, 4H), 2.17 (m, 2H), 6.95 (dt, J=3.6 Hz, J_{H-F}=1.5 Hz, 1H), 6.99 (dt, J=3.6 Hz, J_{H-F}=0.9 Hz, 1H); ^{13}C NMR δ 13.9, 22.4, 24.7, 38.6 (t, J_{C-F}=26.6 Hz), 114.4, 120.8 (t, J_{C-F}=240.3 Hz), 126.4 (t, J_{C-F}=6.0 Hz), 129.8, 141.1 (t, J_{C-F}=32.2 Hz); ^{19}F NMR (282 MHz) δ −85.3 (t, J_{F-H}=16.0 Hz). HRMS found m/z 267.9733 (M^+, ^{79}Br isotope), $C_9H_{11}BrF_2S$ requires 267.9733.

4.5. Fluorodesulfurization of 1,3-dithiolanes using Hal^+/PPHF

4.5.1. (1) NIS/PPHF-Mediated fluorodesulfurization of 2-(5-bromothien-2-yl)-2-butyl-1,3-dithiolane (10) (General procedure). 2-(5-Bromothien-2-yl)-2-butyl-1,3-dithiolane (**10**) (1.29 g, 4.00 mmol) was added dropwise to a stirred, cooled (−78°C) solution of NIS (1.80 g, 8.00 mmol) in CH_2Cl_2 (12 mL) under argon in a 25 mL plastic bottle. After stirring at this temperature for 15 min, the red reaction mixture was poured into a plastic graduated cylinder containing petroleum ether (70 mL). The upper orange organic layer was removed and the bottom dark layer was extracted with petroleum ether–CH_2Cl_2 (7:1, 2×35 mL). The combined organic layers were diluted with petroleum ether (50 mL) and CH_2Cl_2 (5 mL) and passed through a short silica plug followed by short basic alumina plug[29] (7 cm long, 4 cm in diameter). Petroleum ether–CH_2Cl_2 (7:1, 150 mL) was used to wash the plug. The filtrate was concentrated in vacuo to afford 2-bromo-5-(1,1-difluoropentyl)thiophene (**3**) as a clear colorless liquid (0.865 g, 80%). The ^{1}H-, ^{13}C- and ^{19}F NMR spectra of this product were identical to those reported above for this compound.

4.5.2. (2) DBH/PPHF-Mediated fluorodesulfurization of 2-(5-bromothien-2-yl)-2-butyl-1,3-dithiolane (10). 2-(5-Bromothien-2-yl)-2-butyl-1,3-dithiolane (**10**) was subjected to fluorodesulfurization following the general procedure described above except that DBH (1.11 g, 4.00 mmol) was employed as the Hal^+ source and the reaction was allowed to proceed for 45 min. The filtrate was concentrated in vacuo to afford a mixture of several products (0.705 g, 60%). NMR, GC and GC–MS analysis revealed the following components:

2-Bromo-5-(1,1-difluoropentyl)thiophene (3) (39%): the ^{1}H-, ^{13}C- and ^{19}F NMR spectra of this product were identical to those reported above for this compound; MS m/z 270 (20, M^+), 268 (20, M^+), 213 (100, $M^+-C_4H_9$), 211 (98, $M^+-C_4H_9$), 189 (37, M^+−Br), 133 (20, M^+−Br−C_4H_8), 132 (19, M^+−Br−C_4H_9), 57 (8, C_4H_9).

2,3-Dibromo-5-(1,1-difluoropentyl)thiophene (11a) (15%): ^{1}H NMR† (selected signals) δ 7.02 (t, J_{H-F}=1.5 Hz, 0.4H). ^{13}C NMR (selected signals) δ 24.6, 38.5 (t, J_{C-F}=26.3 Hz), 113.9, 120.4 (t, J_{C-F}=241.5 Hz), 128.8 (t, J_{C-F}=6.0 Hz), 140.8 (t, J_{C-F}=32.2 Hz); ^{19}F NMR‡ (282 MHz) δ −86.6 (t, J_{F-H}=16.0 Hz, 0.4F); MS m/z 350 (14, M^+), 348 (28, M^+), 346 (14, M^+), 293 (52, $M^+-C_4H_9$), 291 (100, $M^+-C_4H_9$), 289 (50, $M^+-C_4H_9$), 269 (22, M^+−Br), 267 (17, M^+−Br), 245 (7, $M^+-CF_2C_4H_8$), 244 (8, $M^+-CF_2C_4H_9$), 243 (14, $M^+-CF_2C_4H_8$), 242 (15, $M^+-CF_2C_4H_9$), 241 (8, $M^+-CF_2C_4H_8$), 240 (8, $M^+-CF_2C_4H_9$), 162 (19, $M^+-CF_2C_4H_9$−Br), 160 (14, $M^+-CF_2C_4H_9$−Br), 131 (32, M^+−2Br−C_4H_9), 57 (8, C_4H_9).

2-Bromo-5-(2-bromo-1,1-difluoropentyl)thiophene (12a) (2%): ^{1}H NMR† (selected signals) δ 4.22 (app. ddt, J=2.8, 10.5 Hz, J_{H-F}=10.7 Hz, 0.05H), 7.03 (dt, J=3.9 Hz, J_{H-F}=1.5 Hz, 0.05H); 7.07 (dt, J=3.9 Hz, J_{H-F}=1.1 Hz, 0.05H). ^{13}C NMR (selected signals) δ 54.7 (t, J_{CF}= 26.6 Hz), 128.4 (t, J_{C-F}=6.0 Hz). ^{19}F NMR‡ (282 MHz) δ −89.6 (d, J_{F-H}= 11.0 Hz, 0.05F); MS m/z 350 (3, M^+), 348 (6, M^+), 346 (3, M^+), 269 (2, M^+−Br), 267 (2, M^+−Br), 213 (100, $M^+-C_4H_8Br$), 211 (100, $M^+-C_4H_8Br$), 132 (14, $M^+-C_4H_8Br$−Br), 105 (21, $CF_2C_4H_7$).

2-Bromo-5-(1-bromopent-1-enyl)thiophene (13a) (1%): ^{1}H NMR† (selected signals for major geometrical isomer) δ 6.20 (t, J=7.1 Hz, 0.02H); 7.37 (d, J=3.9 Hz, 0.02H), 7.57 (d, J=3.9 Hz, 0.02H); MS m/z 312 (30, M^+), 310 (57, M^+), 308 (30, M^+), 270 (7, $M^+-C_3H_6$), 268 (13, $M^+-C_3H_6$), 266 (7, $M^+-C_3H_6$), 231 (42, M^+−Br), 229 (41, M^+−Br), 202 (77, M^+−Br-CH_2CH_3), 200 (77, M^+−Br−CH_2CH_3), 189 (35, M^+−Br−C_3H_6), 187 (34, M^+−Br−C_3H_6), 150 (100, M^+−2Br).

2,3-Dibromo-5-(2-bromo-1,1-difluoropentyl)thiophene (14a) (1%): ^{19}F NMR‡ (282 MHz) δ −90.5 (d, J_{F-H}=

† These ^{1}H NMR integrals are relative to 1H/H for the protons in **3**.
‡ These ^{19}F NMR integrals are relative to 1F/F for the fluorine atoms in **3**.

11.0 Hz, 0.02F); MS *m/z* 430 (2, M^+), 428 (6, M^+), 426 (6, M^+), 424 (2, M^+), 349 (0.5, M^+-Br), 347 (1.1, M^+-Br), 345 (0.6, M^+-Br), 293 (51, $M^+-C_4H_8Br$), 291 (100, $M^+-C_4H_8Br$), 289 (52, $M^+-C_4H_8Br$), 212 (5, $M^+-C_4H_8Br-Br$), 210 (5, $M^+-C_4H_8Br-Br$), 162 (8, $M^+-CF_2C_4H_8Br-Br$), 160 (8, $M^+-CF_2C_4H_8Br-Br$), 105 (31, $CF_2C_4H_7$).

4.5.5. (3) NBS/PPHF-Mediated fluorodesulfurization of 2-(5-bromothien-2-yl)-2-butyl-1,3-dithiolane (10). 2-(5-Bromothien-2-yl)-2-butyl-1,3-dithiolane (**10**) was subjected to fluorodesulfurization following the general procedure described above except that NBS (1.42 g, 8.00 mmol) was employed as the Hal^+ source and the reaction was allowed to proceed for 45 min. The filtrate was concentrated in vacuo. NMR, GC and GC–MS analysis revealed a mixture of the following components (based on a comparison with the spectral data for each component listed above): **3** (80%), **11a** (<1%), **12a** (1%), **13a** (<1%).

4.6. General procedure for fluorodesulfurization of 1,3-dithiolanes using $NOBF_4$/PPHF

4.6.1. 2-Bromo-5-(1,1-difluoropentyl)thiophene (3). To a pre-dried 50 mL plastic bottle charged with a magnetic stirrer was added nitrosonium tetrafluoroborate ($NOBF_4$) (0.543 g, 4.64 mmol) under argon. Anhydrous CH_2Cl_2 (10 mL) and pyridinium poly(hydrogen fluoride) (PPHF) (2 mL, 70% HF content) were injected into the bottle and the reaction mixture was cooled to 0°C. A solution of 2(5-bromothien-2-yl)-2-butyl-1,3-dithiolane (**10**) (0.700 g, 2.17 mmol) in anhydrous CH_2Cl_2 (4 mL) was then added dropwise over a period of 3–5 min. The ice bath was removed and the reaction mixture was stirred for a further 2 min before dilution with petroleum ether (80 mL) in a plastic cylinder. The upper organic layer was removed and the dark bottom layer was extracted with a petroleum ether–CH_2Cl_2 mixture (3:1, 40 mL). The organic layers were combined and passed through a short silica plug (5 cm). The colorless filtrate was concentrated in vacuo to afford the title compound **3** as a colorless liquid (0.508 g, 87%). The ^{1}H-, ^{13}C- and ^{19}F NMR spectra of this product were identical to those reported above for this compound.

4.6.2. 1-Bromo-4-(1,1-difluoropentyl)benzene (4a). Compound **4a** was prepared following the above general procedure using $NOBF_4$ (1.27 g, 10.9 mmol) and PPHF (4.5 mL, 70% HF content) in anhydrous CH_2Cl_2 (22 mL), and 2-(4-bromophenyl)-2-butyl-1,3-dithiolane (**18**) (1.43 g, 4.51 mmol) in anhydrous CH_2Cl_2 (9 mL). The title compound **4a** was obtained as a colorless liquid (0.860 g, 72%). ^{1}H NMR δ 0.88 (t, J=7.1 Hz, 3H), 1.25–1.42 (m, 4H), 2.09 (m, 2H), 7.33 (d, J=8.7 Hz, 2H), 7.55 (d, J=8.6 Hz, 2H); ^{13}C NMR δ 13.7, 22.2, 24.4 (t, J_{C-F}=3.5 Hz), 38.6 (t, J_{C-F}=28.0 Hz), 122.7 (t, J_{C-F}=242.5 Hz), 126.7 (t, J_{C-F}=6.2 Hz), 123.8, 131.5, 136.5 (t, J_{C-F}=27.3 Hz); ^{19}F NMR δ −96.0 (t, J_{F-H}=16.0 Hz). HRMS found *m/z* 264.0166 (M^+, ^{81}Br isotope), $C_{11}H_{13}BrF_2$ requires 264.0148.

4.6.3. 1-Bromo-4-(1,1-difluorooctyl)benzene (4b). Compound **4b** was prepared following the above general procedure using $NOBF_4$ (1.270 g, 10.86 mmol) and PPHF (4.5 mL, 70% HF content) in anhydrous CH_2Cl_2 (22 mL), and 2-(4-bromophenyl)-2-heptyl-1,3-dithiolane (**19**) (1.43 g, 4.52 mmol) in anhydrous CH_2Cl_2 (9 mL). The title compound **4b** was obtained as a colorless liquid (1.12 g, 81%). ^{1}H NMR δ 0.87 (t, J=6.8 Hz, 3H), 1.19–1.32 (m, 8H), 1.38 (m, 2H), 2.08 (m, 2H), 7.33 (d, J=8.6 Hz, 2H), 7.54 (d, J=8.7 Hz, 2H); ^{13}C NMR δ 13.9, 22.3, 22.5, 28.9, 29.0, 31.5, 38.9 (t, J_{C-F}=27.3 Hz), 122.7 (t, J_{C-F}=242.3 Hz), 123.8, 126.6 (t, J_{C-F}=6.1 Hz), 131.5, 136.5 (t, J_{C-F}=27.4 Hz); ^{19}F NMR δ −96.0 (t, J_{F-H}=15.7 Hz). HRMS found *m/z* 304.0640 (M^+, ^{81}Br isotope), $C_{14}H_{19}BrF_2$ requires 304.0638.

4.6.4. 2-(4′-Dodecyloxy-2-fluorobiphenyl-4-yl)-5-(1,1-difluoropentyl)thiophene (1a). Compound **1a** was prepared following the above general procedure using $NOBF_4$ (0.156 g, 1.33 mmol) and PPHF (0.5 mL, 70% HF content) in anhydrous CH_2Cl_2 (4 mL) and 2-butyl-2-[5-(4′-dodecyloxy-2-fluorobiphenyl-4-yl)thien-2-yl]-1,3-dithiolane (**20**) (1.43 g, 4.52 mmol) in anhydrous CH_2Cl_2 (2.5 mL). Hexanes–CH_2Cl_2 (3:1) was used as the solvent system for workup and filtration. The resulting solid was dried in vacuo (P_2O_5, paraffin wax, 1.1 mmHg) to afford the title compound **1a** as a white solid (0.213 g, 78%). ^{1}H NMR δ 0.89 (t, J=6.9 Hz, 3H), 0.94 (t, J=7.2 Hz, 3H), 1.24–1.55 (m, 22H), 1.82 (quint, J=7.0 Hz, 2H), 2.25 (m, 2H), 4.01 (t, J=6.6 Hz, 2H), 6.98 (d, J=8.8 Hz, 2H), 7.18 (dt, J=3.8, 1.3 Hz, 1H), 7.23 (dt, J=3.8, 1.2 Hz, 1H), 7.34–7.47 (m, 3H), 7.50 (d, J=8.7 Hz, 1H), 7.51 (d, J=8.7 Hz, 1H). ^{13}C NMR δ 14.0, 14.3, 22.5, 22.9, 24.9, 26.2, 29.4, 29.5, 29.6, 29.8, 32.1, 38.8 (t, J_{C-F}=26.7 Hz), 68.3, 113.6 (d, J_{C-F}=24.8 Hz), 114.7, 121.3 (t, J_{C-F}=239.7 Hz), 122.0 (d, J_{C-F}=2.8 Hz), 123.3, 127.1 (t, J_{C-F}=5.7 Hz), 127.4, 128.5 (d, J_{C-F}=13.4 Hz), 130.1 (d, J_{C-F}=3.2 Hz), 131.0 (d, J_{C-F}=3.8 Hz), 134.1 (d, J_{C-F}=8.3 Hz), 139.2 (t, J_{C-F}=31.8 Hz), 158.2, 159.9 (d, J_{C-F}=247.3 Hz). ^{19}F NMR δ −85.0 (t, J_{F-H}=16.0 Hz, 2F), −117.9 (dd, J_{F-H}=11.0, 7.0 Hz, 1F). Anal. Calcd for $C_{33}H_{43}F_3OS$: C, 72.76; H, 7.96; S, 5.89; found C, 72.94; H, 7.70; S, 6.26.

4.6.5. 2-(4′-Dodecyloxybiphenyl-4-yl)-5-(1,1-difluoropentyl)thiophene (1b). Compound **1b** was prepared following the above general procedure using $NOBF_4$ (0.907 g, 7.75 mmol) and PPHF (3.0 mL, 70% HF content) in anhydrous CH_2Cl_2 (15 mL) and 2-butyl-2-[5-(4′-dodecyloxybiphenyl-4-yl)thien-2-yl]-1,3-dithiolane (**21**) (1.74 g, 3.00 mmol) in anhydrous CH_2Cl_2 (9.0 mL). The combined organic extracts were filtered through a short (7 cm long, 4 cm in diameter) silica plug (hexanes–dichloromethane, 4:1) to obtain pure **1b** after drying in vacuo (P_2O_5, paraffin wax, 1.1 mmHg) (0.472 g, 30%). Product decomposition was observed during filtration (the corresponding ketone produced a bright blue band under UV light as decomposition occurred). The plug was washed with CH_2Cl_2 and the filtrate concentrated in vacuo to afford a mixture of title compound **1b** (0.270 g, 17%: based on ^{1}H NMR ratio; total yield 47%) together with the corresponding 2-(4′-dodecyloxybiphenyl-4-yl)-5-pentanoylthiophene (**9**) (0.203 g, 13%: based on ^{1}H NMR ratio). **1b**: ^{1}H NMR δ 0.88 (t, J=6.9 Hz, 3H), 0.93 (t, J=7.2 Hz, 3H), 1.27–1.56 (m, 22H), 1.81 (quint, J=6.6 Hz, 2H), 2.25 (m, 2H), 4.00 (t, J=6.6 Hz, 2H), 6.98 (d, J=9.0 Hz, 2H), 7.17 (dt, J=3.9 Hz, J_{H-F}=1.5 Hz, 1H), 7.22 (dt, J=3.6 Hz, J_{H-F}=1.2 Hz, 1H), 7.54 (d, J=8.7 Hz, 2H), 7.57 (d, J=9.0 Hz, 2H), 7.63 (d,

J=8.7 Hz, 2H); ^{13}C NMR δ 13.7, 14.0, 22.2, 22.6, 24.6, 26.0, 29.2, 29.3 (2), 29.5, 31.8, 38.6 (t, J_{C-F}=26.5 Hz), 68.0, 114.8, 121.2 (t, J_{C-F}=237.5 Hz), 122.3, 126.2, 126.7 (t, J_{C-F}=4.8 Hz), 127.0, 127.8, 131.8, 132.4, 138.2 (t, J_{C-F}= 31.2 Hz), 140.5, 145.6, 158.9; ^{19}F NMR δ −85.1(t, J_{F-H}= 16.2 Hz). Anal. Calcd for $C_{33}H_{44}F_2OS$: C, 75.24; H, 8.42; S, 6.09; Found: C, 75.54; H, 8.62; S, 5.97. **9**: identified by comparison of its ^{1}H NMR spectrum with an authentic sample prepared by the deprotection of thienyl dithiolane **21** using $Hg(ClO_4)_2 \cdot 3H_2O$:[24] δ 0.88 (t, J=6.8 Hz, 3H), 0.97 (t, J=7.4 Hz, 3H), 1.24–1.51 (m, 22H), 1.78 (quint, J= 7.5 Hz, 2H), 2.90 (t, J=7.5 Hz, 2H), 4.01 (t, J=6.6 Hz, 2H), 6.98 (d, J=8.7 Hz, 2H), 7.34 (d, J=3.6 Hz, 1H), 7.55 (d, J=8.7 Hz, 2H), 7.60 (d, J=8.1 Hz, 2H), 7.69 (d, J= 3.6 Hz, 1H), 7.00 (d, J=8.4 Hz, 2H).

4.7. Synthesis of 2-(4′-dodecyloxybiphenyl-4-yl)-5-(1,1-difluoropentyl)thiophene (1b) via Suzuki cross-coupling approach

Palladium(II) chloride (0.1 M solution in water, 0.2 mL, 0.02 mmol) was added in one portion to a stirred mixture of 4′-dodecyloxybiphenyl-4-ylboronic acid (**22**)[18] (0.500 g, 1.30 mmol), 2-bromo-5-(1,1-difluoropentyl)thiophene (**3**) (0.210 g, 0.78 mmol) and sodium carbonate (2.0 M, 1.68 mL, 3.36 mmol) in acetone (10 mL) under dry argon. The reaction mixture was heated under reflux for 40 h and the cooled reaction mixture was then diluted with aq hydrochloric acid (10%, 10 mL) and extracted with CH_2Cl_2 (3×20 mL). The combined organic extracts were washed with water (100 mL) and dried (Na_2SO_4). The drying agent was filtered off and the extract was filtered through a column of silica gel (petroleum ether–dichloromethane, 3:1) before the solvent was removed in vacuo. The crude product was crystallized from ethyl acetate followed by petroleum ether (bp 35–60°C) to afford the title compound **1b** as a white solid, which was dried in vacuo (P_2O_5, paraffin wax, 24 h) (0.280 g, 72%). The ^{1}H, ^{13}C and ^{19}F NMR spectra of this product were identical to those reported above for this compound. Liquid crystal transitions (°C): Cryst 155.9 S_F 160.4 S_A 172.4 I.

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27. The synthesis of dithiolanes followed the protocol reported by Katzenellenbogen (Ref. 21).
28. The synthesis of this compound will be reported separately (see Ref. 18).
29. The grade of basic alumina employed had a profound impact on the outcome of this filtration step. Use of activated basic alumina (50–200 μm) from Acros Organics as the support for this filtration step worked well; however, when Brockman activity I-grade basic alumina from Fisher Scientific was employed, a substantial amount of HF elimination was observed. Monofluoroalkenyl- and alkynylthiophene products were obtained in varying ratios along with little or none of the desired 1,1-difluoropentylthiophene **3**.