Photochromic molecular switches

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Chapter 7

A Mild Titanium-Mediated Transformation of *t*-Butyl Thioethers into Thio-Acetates

In this chapter a straightforward method for the rapid conversion of thioethers to thio-acetates using $TiCl_4$, in good to excellent yields is presented. The reaction conditions tolerate a variety of functional groups, including halide, nitro, ether, thiophene and acetylene functionalities. A catalytic variant of this reaction is also described.

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7.1 Introduction

Numerous nanoscale materials and devices[1] are based on self-assembled monolayers (SAMs) of thiols on gold substrates.[2] Thiols have proven to be versatile anchoring groups[3] for immobilising functional units for photoswitching,[4] molecular electronics,[5] control of surface wettability,[6] cell adhesion,[7] to name but a few examples. Although thiol chemistry is often used in SAM formation,[3] the introduction of a thiol group in a compound frequently presents synthetic challenges[8] because the R-S-H group can be deprotonated, is nucleophilic, and is prone to oxidation.[2] Hence, protected thiols such as thio-acetates are frequently used. Indeed, acetyl and trityl protected thiols can be deprotected readily *in situ* during self-assembly on gold surfaces.[2] In particular acetyl protected thiol substituted arenes are convenient in their use as these can typically be cleaved *in situ* without requiring a exogenous base to form stable monolayers equivalent to those formed starting from free thiols.[9,10,11]

However, the thio-acetate group is often not stable under aqueous reaction conditions, while the thio-trityl group is not stable under various other reaction conditions, such as those employed in Suzuki-Miyaura cross-coupling reactions.[12] These drawbacks can be overcome through a method developed by Stuhr-Hansen in which the thiol is initially protected by a *t*-butyl protecting group and later exchanged for the desired acetyl protecting group by treatment with BBr_3.[13] The *t*-butyl thioether has the benefit that it is typically stable under both acidic[14] and basic conditions.[15] Furthermore, *t*-butyl thioethers can be synthesised with relative ease, either from the free thiol using *t*-butyl chloride or *t*-butanol, or from halides (R-X) using *t*-butyl thiol. Once the synthetic steps incompatible with the thio-acetate have been performed, exchange of the protecting groups can be achieved by deprotection of the *t*-butyl thioether by BBr_3 followed by quenching with acetyl chloride at room temperature.[13]

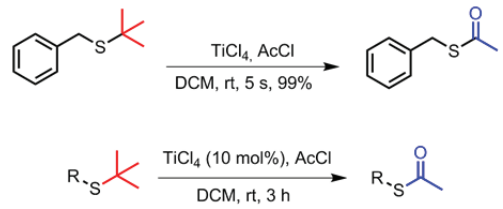


Figure 7.1: Titaniumchloride mediated *t*-butyl thioether to thioacetate exchange.

Although S-*t*-butyl to S-acetyl exchange procedures have been reported (using BBr_3,[13] but also Br_2[8] or $AlCl_3$[16]), several important functionalities do not tolerate these conditions, examples being vinyl, TBDMSO, acetylene, aldehyde, and nitro functionalities.[8,13] This, prompted us to identify another more versatile Lewis acids,

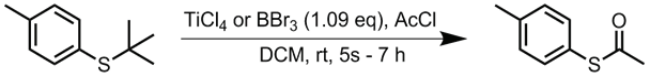
with which the exchange reaction can be performed under mild conditions while tolerating a wider variety of functionalities. One such candidate is $TiCl_4$, as there have been several examples of $TiCl_4$/*n*-Bu_4NI-mediated deprotections of ethers (R-O-R).[17] Furthermore, $TiCl_4$ has been used in the deprotection of silyl ethers to alcohols. The results of Tanabe and co-workers, who successfully deprotected aryl and aliphatic TBDMS-ethers in excellent yields (91-99%) using $TiCl_4$-Lewis base (AcOEt, CH_3NO_2) complexes, are particularly encouraging.[18] Finally, $TiCl_4$ was used with great efficacy as a deprotection reagent in the hydrolysis of *t*-butyl esters in *β*-lactam chemistry, whereas the use of $AlCl_3$, BF_3, and $FeCl_3$ resulted in degradation of the starting material or poor yields.[19]

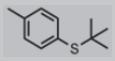
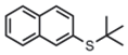
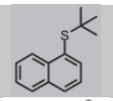
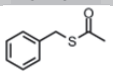
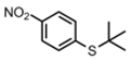
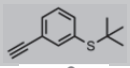
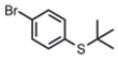
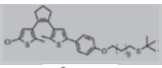
In this chapter, we present a robust method for the conversion of *t*-butyl thioethers to thio-acetates using $TiCl_4$ instead of BBr_3. We have found that $TiCl_4$ is tolerant towards a wider variety of functional groups and performs consistently better than BBr_3, providing the desired thio-acetates in high yields in short reaction times.

7.2 Results and Discussion

In order to investigate the use of $TiCl_4$ for the conversion of thioethers (**a**) to thio-acetates (**b**), 12 substrates were examined (Table 7.1). *t*-Butyl thioethers **1-6a** were converted to the corresponding thio-acetates **1-6b** in good to excellent isolated yields using $TiCl_4$ or BBr_3. However, whereas the reactions using BBr_3 were complete after 2.5 to 7 h, the use of $TiCl_4$ allowed for substantial shorter reaction times, in several cases providing the thio-acetate within seconds (**2a, 4a**, and **6a** as well as **8a** and **10a**). In addition, improvements in yield were observed for several substrates when $TiCl_4$ was used (**1a**, **3a**, and **5a**). Conversion of **7a-10a** using BBr_3 was found to result in decomposition only. In sharp contrast, **7a** and **8a** were converted to their corresponding thio-acetates in high yield when $TiCl_4$ was used. To obtain information on functional group limitations aldehyde and pyridine functionalized thioethers were examined. Treatment of aldehyde **9a** under these reaction conditions still resulted in decomposition. Analysis of the product revealed that under BBr_3 conditions the *t*-butyl group is cleaved while under $TiCl_4$ conditions the *t*-butyl group remains intact. In neither case, however, was thio-acetate **9b** obtained. For thioether **10a**, the $TiCl_4$-mediated reaction also did not provide the desired product as full conversion to an unidentified compound was observed.[20,21]

Table 7.1: Thioether to thio-acetate exchange: comparison of BBr_3 and $TiCl_4$.

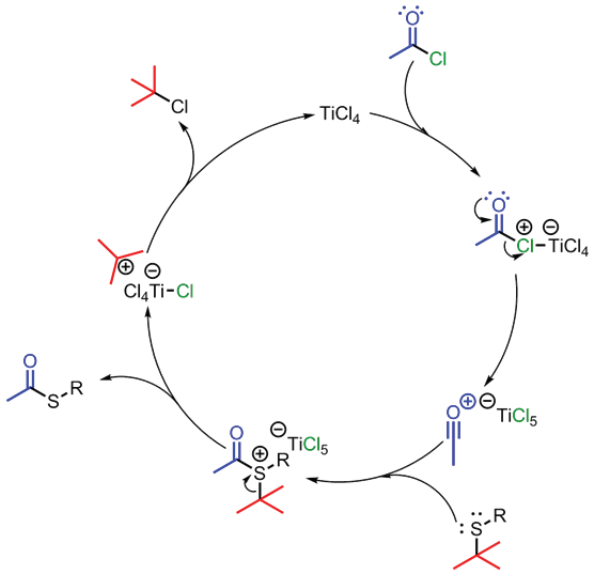


Number	Compound	Reaction time BBr_3	Yield	Reaction time $TiCl_4$	Yield
1a		5 h	81%	<1 h	93%
2a		6 h	96%	5 s	94%
3a		5 h	76%	<1 h	88%
4a		7 h	>99%	5 s	>99%
5a		3 h	92%	1 h	>99%
6a		-	dec.	<1 h	88%
7a		-	-[a]	5 s	83%
8a		-	dec.	-	dec.
9a		7 h	dec.	5 s	-[b]
10a		4 h	65%	5 s	89%
11a		n.a.	n.a.	2 h	87%
12a		7 h	no conv.	3 h	94%[c]

a) Forms multiple products. b) Full conversion to an unidentified product with an R_f = 0.19 on SiO_2. c) The Fiedel-Crafts acylation product *p*-$CH_3(C{=}O)C_6H_4SCH_3$ is isolated in 94 % yield.[22]

It was also attempted to use the above reaction conditions for the conversion of a methyl thioether group to the corresponding thioacetate group. The methyl thioether group of **12a** was found to be stable to both BBr_3 and $TiCl_4$. However, treatment of **12a** with $TiCl_4$ for 3 h resulted in the aromatic Fiedel-Crafts acylation product.

A possible mechanism by which the reaction may proceed is that addition of $TiCl_4$ to acetyl chloride results in the formation of the acylium ion (Scheme 7.1),[23] as is supported by the Friedel-Crafts acylation product obtained with compound **12a**. The acylium ion undergoes nucleophilic attack from the sulfur of the thioether. Expulsion of the 2-methylpropan-2-ylium carbocation subsequently results in product formation. Conversion of the anionic Ti species is achieved by dissociation of a chloride and the subsequent capture of the chloride ion by the carbocation resulting in the formation of 2-chloro-2-methylpropane and $TiCl_4$, thus completing the catalytic cycle for the exchange of the *t*-Bu thioether to the thio-acetate. In d_2-dichloromethane, the formation of *iso*-2-chloro-2-methylpropane was observed, whereas the formation of isobutene was not, which supports the anticipated pathway (Figure 7.3).



Scheme 7.1: Proposed cycle for the conversion of thioethers to thio-acetates using $TiCl_4$ catalyst.

The reaction mechanism proposed furthermore implies that $TiCl_4$ might be used catalytically. Indeed, it was found that treatment of **4a** with a catalytic amount of $TiCl_4$ (10 mol%) resulted in full conversion to the thio-acetate in 3 h (Figure 7.2). These results therefore support the proposed mechanism and further establish the potency of $TiCl_4$ to mediate the S-*t*-Bu to S-acetyl exchange reaction. The conversion from **4a** to **4b** under stoichiometric was conditions is completed in 5 s, whereas under catalytic conditions the reaction was finished in 3 h. It should be noted that under these catalytic

conditions the catalytic reaction still proceeds faster with $TiCl_4$ then when a stoichiometric quantity of BBr_3 is used.

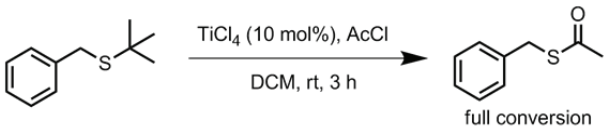


Figure 7.2: Thioether conversion to thio-acetate catalysed by $TiCl_4$.

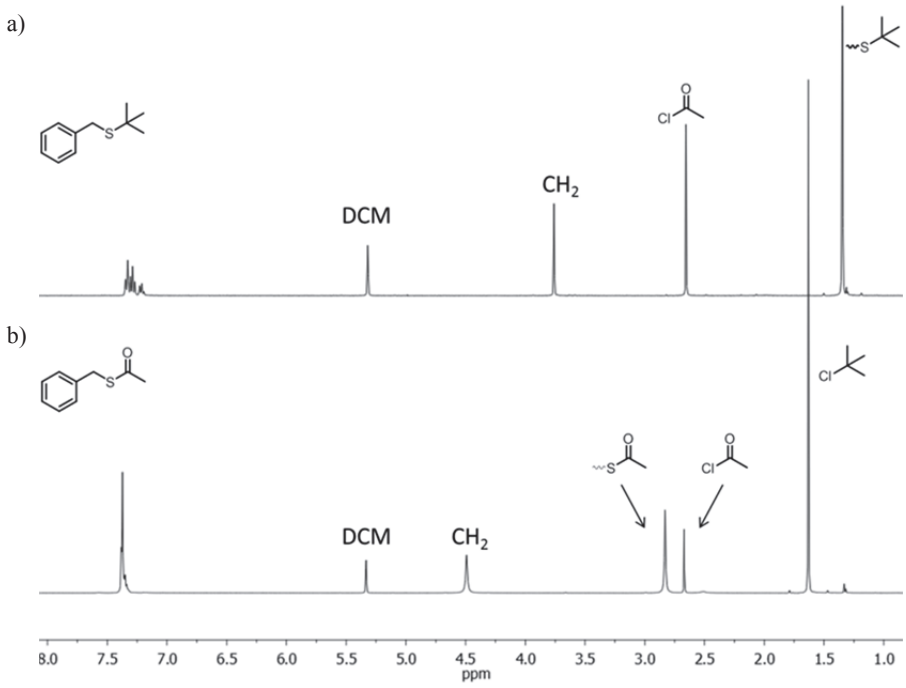


Figure 7.3: ^{1}H-NMR spectra showing conversion of **4a** — (a, at t_0: no $TiCl_4$ added) to b) **4b** — using $TiCl_4$ (after 30 min) in CD_2Cl_2.

7.3 Conclusions

In summary, the methode presented in this chapter provides a versatile, mild and selective method compared to existing thioether to thio-acetate exchange methods. The use of $TiCl_4$ is more economic then the use of BBr_3 given that the former can be employed catalytically. Furthermore, conditions using $TiCl_4$ for the exchange tolerate a wider range of functional groups than BBr_3-mediated methods, including acetylene

groups, which is in contrast to conditions using Br_2 that provide only moderate conversion to the thio-acetate.[8] The exchange of the *t*-butyl protecting group for a thio-acetate group in aliphatic thioether **11a** provides **11b** in high yield (Table 7.1), even though **11a** contains a dithienylethene photochromic switching unit. The high reaction rate at room temperature implies that the exchange reaction is also able to proceed at low temperature. This was confirmed by performing the exchange reaction of **4a** to **4b** at -78 °C, whereby the reaction was found to proceed to full conversion in 30 min. Performing the exchange at low temperature opens opportunities to avoid undesirable side-reactions of sensitive substituents. In conclusion, the conversion from thioether to thio-acetate using $TiCl_4$ represents a highly versatile and fast method for a wide range of applications, not least those involving the synthesis of SAM forming thiols.

7.4 Experimental details

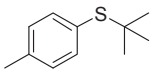
For synthesis all chemicals were obtained from commercial sources and used as received unless stated otherwise. Solvents were reagent grade. For column chromatography, silica gel (Silicycle Siliaflash P60, 40-63m, 230-400 mesh) was used in all cases. Separation was determined on Merck TLC silica gel 60, kieselguhr F254. ^{1}H and ^{13}C NMR spectra were recorded on a Varian Gemini-200 (operating at 200 and 50 MHz), a Varian VXR-300 (operating at 300 and 75 MHz) and a Varian AMX400 (operating at 400 and 100 MHz) spectrometer in $CDCl_3$ and CD_2Cl_2 chemical shifts are reported in values (ppm) relative to $CDCl_3$ (^{1}H = 7.24, ^{13}C = 77.2), CD_2Cl_2 (^{1}H = 5.32, ^{13}C = 54.0), For ^{1}H-NMR the signals were assigned as following: singlet (s), doublet (d), double doublet (dd), triplet (t), quartet (q), and multiplet (m). For ^{13}C-NMR, the signals were designated as: primary carbon (CH_3), secondary carbon (CH_2), tertiary carbon (CH), quaternary carbon (C). MS spectra were obtained on a Hewlett-Packard HP 6890 GC with HP 5973 mass selective detector, containing a Agilent 5% -25(phenyl)methylpolysiloxane column (25 m × 0.25 mm × 0.25 m. HRMS (ESI, APCI) spectra were obtained on a Thermo scientific LTQ Orbitrap XL.

General procedure for the preparation of *t*-butyl-acetyl substrates

General synthetic procedure:[13a] Over the course of 15 min $AlCl_3$ (121 mg, 0.9 mmol) was added in portions to a solution of thiol (18.1 mmol) in DCM (17 mL) at rt. The resulting mixture was stirred at 35°C for 30 min and was subsequently poured onto water (50 mL) and extracted with pentane (3 × 50 mL). The organic layers were combined and washed with brine and dried over Na_2SO_4. The organic solvent was

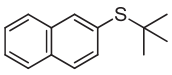
removed in vacuo and the thioether was further purified by flash column chromatography.

tert-butyl(p-tolyl)sulfane (1a) TLC (SiO_2: heptane/ethyl acetate, 4:1, R_f = 0.75) (58%)



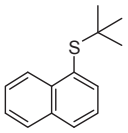
^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.42 (d, *J* = 7.8 Hz, 2H), 7.13 (d, *J* = 7.8 Hz, 2H), 2.35 (s, 3H), 1.28 (s, 9H). ^{13}C NMR (101 MHz, $CDCl_3$) δ: 138.8 (C), 137.6 (CH), 129.4 (C), 129.4 (CH), 45.7 (C), 31.1 (CH_3), 21.4 (CH_3). *m/z* (EI) 180. HRMS (APCI): calcd. for $C_{11}H_{16}OS$: 181.1046, found 181.1043.

tert-butyl(naphthalen-2-yl)sulfane (2a) TLC (SiO_2: heptane/ethyl acetate, 4:1, R_f = 0.70) (85%)



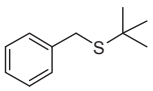
^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.06 (s, 1H), 7.83 (dd, *J* = 9.2, 3.1 Hz, 2H), 7.77 (d, *J* = 8.5 Hz, 1H), 7.58 (d, *J* = 8.4 Hz, 1H), 7.49 (dd, *J* = 6.1, 3.3 Hz, 2H), 1.33 (s, 9H). ^{13}C NMR (101 MHz, $CDCl_3$) δ: 137.3 (CH), 134.5 (CH), 133.6 (C), 133.3 (C), 130.4 (C), 128.1 (CH), 128.0 (CH), 127.8 (CH), 126.9 (CH), 126.5 (CH), 46.5 (C), 31.3 (CH_3). *m/z* (EI) 216. HRMS (APCI): calcd. for $C_{14}H_{16}S$: 217.01046, found 217.1045.

tert-butyl(naphthalen-1-yl)sulfane (3a) Obtained as a white solid TLC (SiO_2: heptane/ethyl acetate, 4:1, R_f = 0.70) (80%)



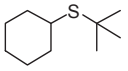
^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.74 (d, *J* = 8.3 Hz, 1H), 7.90-7.78 (m, 3H), 7.58-7.39 (m, 3H), 1.29 (s, 9H). ^{13}C NMR (101 MHz, $CDCl_3$) δ: 137.6 (CH), 137.0 (C), 134.3 (C), 130.9 (C), 130.0 (CH), 128.4 (CH) , 127.6 (CH), 126.6 (CH), 126.2 (CH), 125.4 (CH), 47.7 (C), 31.5 (CH_3). *m/z* (EI) 216. HRMS (APCI): calcd. for $C_{14}H_{16}S$: 217.1046, found 217.1044.

benzyl(tert-butyl)sulfane (4a) TLC (SiO_2: heptane/ethyl acetate, 4:1, R_f = 0.80) (87%)



^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.33 (d, *J* = 7.4 Hz, 2H), 7.27 (t, *J* = 7.5 Hz, 2H), 7.20 (t, *J* = 7.3 Hz, 1H), 3.75 (s, 2H), 1.34 (s, 9H). ^{13}C NMR (101 MHz, $CDCl_3$) δ: 138.8 (C), 129.1 (CH), 128.6 (CH), 126.9 (CH), 43.0 (C), 33.6 (CH_2), 31.1 (CH_3). HRMS (APCI): calcd. for $C_{11}H_{16}S$: 181.046, found 181.1044.

tert-butyl(cyclohexyl)sulfane (5a) TLC (SiO_2: heptane/ethyl acetate, 4:1, R_f = 0.84).



Colorless liquid (70%) ^{1}H NMR (400 MHz, $CDCl_3$) δ: 2.62-2.56 (m, 1H), 1.98-1.91 (m, 2H), 1.74-1.66 (m, 2H), 1.58-1.50 (m, 1H), 1.40-1.32 (m, 4H), 1.31 (s, 9H), 1.25-1.14 (m, 1H).^{13}C NMR (101 MHz, $CDCl_3$) δ: 42.9 (C), 41.2 (CH), 36.2 (CH_2), 31.6 (CH_3), 26.4 (CH_2), 25.5 (CH_2). *m/z* (EI) 172. HRMS (APCI): calcd. for $C_{10}H_{20}S$: 173.1359, found 173.1358.

(4-bromophenyl)(tert-butyl)sulfane (6a) distilled under reduced pressure 1.7×10^{-2} mbar at 90°C colorless liquid (89%). TLC (SiO_2: heptanes/ethyl acetate, 4:1, R_f = 0.85). ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.67 (dd, *J* = 26.1, 7.1 Hz, 4H), 1.53 (s, 9H). ^{13}C NMR (101 MHz, $CDCl_3$) δ: 139.0 (CH), 132.0 (C), 131.8 (CH), 123.6 (C), 46.2 (C), 31.0 (CH_3). *m/z* (EI) 246. HRMS (APCI): calcd. for C_8H_8BrS: 244.9817, found 244.9816.

tert-butyl(4-nitrophenyl)sulfane (7a) TLC (SiO_2: heptane/ethyl acetate, 4:1, R_f = 0.64) (73%) ^{1}H NMR (400 MHz, $CDCl_3$) δ: ^{1}H NMR (300 MHz, $CDCl_3$) δ: 8.13 (d, *J* = 8.7 Hz, 2H), 7.64 (d, *J* = 8.7 Hz, 2H), 1.32 (s, 9H). ^{13}C NMR (101 MHz, $CDCl_3$) δ: 147.9 (C), 142.5 (C), 137.0 (CH), 123.5 (CH), 47.7 (C), 31.3 (CH_3). *m/z* (EI) 211. HRMS (APCI): calcd. for $C_{10}H_{13}NO_2S$: 212.0740, found 212.0739.

tert-butyl(3-ethynylphenyl)sulfane (8a) TLC (SiO_2: heptane/ethyl acetate, 4:1, R_f = 0.81) ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.67 (s, 1H), 7.50 (dd, *J* = 13.5, 7.7 Hz, 2H), 7.28 (t, *J* = 7.8 Hz, 1H), 3.10 (s, 1H), 1.29 (s, 9H). ^{13}C NMR (101 MHz, $CDCl_3$) δ: 140.9 (CH), 138.1 (CH), 133.3 (C), 132.5 (CH), 128.6 (CH), 122.7 (C), 83.2 (C), 78.0 (CH), 46.4 (C), 31.2 (CH_3). *m/z* (EI) 190. HRMS (APCI): calcd. for $C_{12}H_{14}S$: 191.0887, found 191.0887.

2-(tert-butylthio)pyridine (10a) TLC (SiO_2: heptane/ethyl acetate, 4:1, R_f = 0.19) (4%) ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.48 (dd, *J* = 4.8, 0.9 Hz, 1H), 7.47 (td, *J* = 7.7, 1.9 Hz, 1H), 7.29 (d, *J* = 7.9 Hz, 1H), 7.03 (ddd, *J* = 7.2, 4.9, 0.8 Hz, 1H), 1.49 (s, 9H). ^{13}C NMR (101 MHz, $CDCl_3$) δ: 158.7 (C), 149.6 (CH), 136.0 (CH), 127.4 (CH), 120.8 (CH), 47.6 (C), 31.2 (CH_3). *m/z* (EI) 167. HRMS (APCI): calcd. for $C_9H_{13}NS$: 168.0842, found 168.0840.

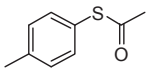
5-(4-((11-(tert-butylthio)undecyl)oxy)phenyl)-3-(2-(5-chloro-2-methylthiophen-3-yl)cyclopent-1-en-1-yl)-2-methylthiophene (11a). To a solution of 1,2-bis(5-chloro-2-methylthiophen-3-yl)cyclopent-1-ene (2.98 g, 9.04 mmol) in THF (40 mL) n-BuLi (1.6 M, 6.8 ml, 10.85 mmol) was added dropwise at 0°C under an atmosphere of argon. The temperature was allowed to reach rt, while stirring was continued for 1 h. Subsequently, the reaction mixture was cooled to 0°C and tributyl borate (2.50 g, 10.85 mmol) was added dropwise. The mixture was allowed to reach rt and was stirred for 1.5 h. The resulting solution of boronic ester was added without further purification to a solution of (11-(4-bromophenoxy)undecyl)(tert-

butyl)sulfane (3.87 g, 9.33 mmol), Na_2CO_3 in H_2O (40 ml, 2M) and ethylene glycol (1 mL) in THF (20 mL) under an argon atmosphere. The reaction mixture was heated to reflux and stirred for 48 h. Upon completion the mixture was allowed to attain room temperature and DCM (200 mL) was added. The organic layer was washed with H_2O (3 × 100 mL) and brine (100 mL), dried over $MgSO_4$ and subsequently concentrated under reduced pressure. **11a** was further purified using flash chromatography and was obtained as a brown oil (4.03 g, 6.41 mmol, 71%). ^{1}H NMR (300 MHz, $CDCl_3$) δ: 7.40 (d, *J* = 8.7 Hz, 2H), 6.86 (t, *J* = 4.3 Hz, 3H), 6.62 (s, 1H), 3.94 (t, *J* = 6.5 Hz, 2H), 2.77 (dt, *J* = 17.1, 7.2 Hz, 4H), 2.52 (t, *J* = 7.4 Hz, 2H), 2.02 (dd, *J* = 13.4, 5.8 Hz, 3H), 1.97 (s, 3H), 1.89 (d, *J* = 6.9 Hz, 3H), 1.81-1.71 (m, 3H), 1.56 (dd, *J* = 14.8, 7.5 Hz, 3H), 1.35 (m, 28H). ^{13}C NMR (101 MHz, $CDCl_3$) δ: 158.5 (C), 140.0 (C), 136.2 (C), 135.5 (C), 135.3 (C), 133.6 (C), 133.3 (C), 133.3 (C), 127.2 (C), 126.9 (CH), 126.6 (CH), 125.0 (C), 122.7 (CH), 114.9 (CH), 68.1 (CH_2), 41.8 (C), 38.6 (CH_2), 38.5 (CH_2), 31.1 (CH_3), 30.0 (CH_2), 29.7 (CH_2), 29.7 (CH_2), 29.6 (CH_2), 29.5 (CH_2), 29.4 (CH_2), 29.4 (CH_2), 29.4 (CH_2), 28.4 (CH_2), 26.2 (CH_2), 23.0 (CH_2), 14.4 (CH_3), 14.3 (CH_3). HRMS (ESI): calcd. for $C_{36}H_{50}ClOS_3$: 629.2707, found: 629.2673.

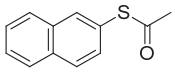
General procedure for S-*t*-butyl to S-acetyl replacement

$TiCl_4$ (0.13 mL, 1.22 mmol) was added in a dropwise fashion to a solution of *t*-butyl thioether (1.11 mmol) and acetyl chloride (0.09 ml, 1.22 mmol) in DCM at 0°C. The resulting mixture was stirred at rt and the conversion was verified by TLC (heptane/ethyl acetate, 4:1). Typically, reaction times with $TiCl_4$ were between 5 s and 1 h, while reactions with BBr_3 took 2.5 to 7 h. Upon completion water (10 ml) was added and the aqueous layer was extracted with DCM (3 × 15 mL). The organic layers were combined and washed with brine (20 mL), dried over $MgSO_4$ and the organic solvent was removed in vacuo. Where necessary the product was further purified by flash column chromatography (heptane/ethyl acetate, 4:1).

S-(*p*-tolyl) ethanethioate (1b) $TiCl_4$: 90%, BBr_3: 96%. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.27 (d, *J* = 8.1 Hz, 2H), 7.20 (d, *J* = 7.9 Hz, 2H), 2.38 (s, 3H), 2.36 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ: 194.7 (C), 139.8 (C), 134.6 (CH), 130.2 (CH), 124.6 (C), 30.3 (CH_3), 21.5 (CH_3). *m/z* (EI) 166. HRMS (ESI): calcd. for $C_9H_{11}OS$: 167.0525, found 167.0522.



S-naphthalen-2-yl ethanethioate (2b) TLC (SiO_2: heptane/ethyl acetate, 4:1, R_f = 0.63). $TiCl_4$: 94%, BBr_3: 96%. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.98 (s, 1H), 7.90-7.82 (m, 3H), 7.56-7.48 (m, 3H), 2.47 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ: 194.3 (C), 134.4 (CH), 133.6 (C), 133.4 (C), 131.0 (CH), 128.9 (CH), 128.1 (CH), 127.9 (CH), 127.3 (CH), 126.7 (CH), 125.4 (C), 31.3 (C), 30.3 (CH_3). HRMS (ESI): calcd. for $C_{12}H_{11}OS$: 203.0525, found 203.0523.



S-naphthalen-1-yl ethanethioate (3b) $TiCl_4$: 88%, BBr_3: 76%. ^1H NMR (500 MHz, $CDCl_3$) δ: 8.23 (d, *J* = 8.3 Hz, 1H), 7.95 (d, *J* = 8.2 Hz, 1H), 7.89 (d, *J* = 7.9 Hz, 1H), 7.72 (d, *J* = 7.0 Hz, 1H), 7.55 (ddd, *J* = 30.3, 15.1, 7.3 Hz, 3H), 2.48 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ: 194.2 (C), 135.1 (CH), 134.3 (2 × C), 131.1 (CH), 128.8 (CH), 127.3 (CH), 126.6 (CH), 125.7 (CH), 125.6 (C), 125.4 (CH), 30.4 (CH_3). *m/z* (EI) 202. HRMS (ESI): calcd. for $C_{12}H_{11}OS$: 203.0525, found 203.0521.

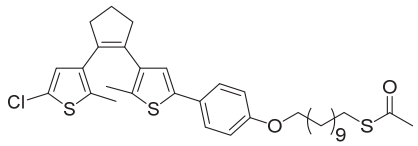
S-benzyl ethanethioate (4b) TLC (SiO_2: heptane/ethyl acetate, 4:1, R_f = 0.66) $TiCl_4$: >99% $TiCl_4$ (10% mol): full conversion, BBr_3: >99%. $CDCl_3$) δ: 7.33-7.26 (m, 4H), 7.90-7.82 (m, 1H), 4.13 (s, 2H), 2.34 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ: 195.1 (C), 137.7 (C), 128.9 (CH), 128.7 (C), 127.4 (CH), 33.5 (C), 30.4 (CH_3). *m/z* (EI) 166. HRMS (ESI): calcd. for $C_9H_{11}OS$: 167.0525, found 167.0521.

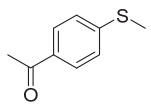
S-cyclohexyl ethanethioate (5b) TLC (SiO_2: heptane/ethyl acetate, 4:1, R_f = 0.57). $TiCl_4$: >99%, BBr_3: 92%. $CDCl_3$) δ: 3.47-3.41 (m, 1H), 2.23 (s, 3H), 1.85-1.81 (m, 2H), 1.60-1.63 (m, 2H), 1.54-1.51 (m, 1H), 1.42-1.29 (m, 4H), 1.25-1.19 (m, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ: 195.8 (C), 42.5 (CH), 33.1 (CH_3), 30.9 (CH_2), 26,0 (CH_2), 25.7 (CH_2). *m/z* (EI) 158. HRMS (ESI): calcd. for $C_8H_{15}OS$: 159.0838, found 159.0836.

S-(4-bromophenyl) ethanethioate (6b) TLC (SiO_2: heptane/ethyl acetate, 4:1, R_f = 0.58) $TiCl_4$ 89%, BBr_3: 65% ^1H NMR (400 MHz, $CDCl_3$) δ: 7.53 (d, *J* = 8.5 Hz, 2H), 7.26 (d, *J* = 8.5 Hz, 2H), 2.41 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ: 193.21 (C), 135.94 (CH), 132.45 (CH), 127.05 (C), 124.14 (C), 30.31 (CH_3). HRMS (ESI): calcd. for $C_9H_{11}OS$: 230.9474, found 230.9470.

S-4-nitrophenyl ethanethioate (7b) $TiCl_4$: 88%. ^1H NMR (400 MHz, $CDCl_3$) δ: ^1H NMR (500 MHz, $CDCL_3$) δ: 8.21 (d, *J* = 8.9 Hz, 2H), 7.57 (d, *J* = 8.9 Hz, 2H), 2.46 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ: 191.7 (C), 148.3 (C), 136.5 (C), 134.8 (CH), 124.1 (CH), 30.7 (CH_3). *m/z* (EI) 197. HRMS (APCI): calcd. for $C_8H_8NO_3S$: 198.0219, found 198.0215.

S-3-ethynylphenyl ethanethioate (8b) TLC (SiO_2: heptanes/ethyl acetate, 4:1, R_f = 0.54) $TiCl_4$: 83%. ^1H NMR (400 MHz, $CDCl_3$) δ: 7.55-7.51 (m, 2H), 7.42-7.35 (m, 2H), 3.11 (s, 1H), 2.43 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ: 193.2 (C), 137.8 (CH), 134.9 (CH), 133.0 (CH), 129.2 (CH), 128.4 (C), 123.4 (C), 82.6 (C), 78.6 (CH), 30.3 (CH_3). *m/z* (EI, %): 176 (M+, 14), 134 (100); HRMS (APPI): calcd. for $C_{10}H_9OS$ ([M + H]+): 177.0369, found 177.0364.

S-(11-(4-(4-(2-(5-chloro-2-methylthiophen-3-yl)cyclopent-1-en-1-yl)-5-methylthiophen-2-yl)phenoxy)undecyl) ethanethioate (11b)  $TiCl_4$: 87 %. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.39 (d, J = 8.6 Hz, 2H), 6.88-6.82 (m, 3H), 6.61 (s, 1H), 3.94 (t, J = 6.5 Hz, 2H), 2.85 (t, J = 7.3 Hz, 2H), 2.76 (dt, J = 25.3, 7.3 Hz, 4H), 2.31 (s, 3H), 2.09-1.99 (m, 2H), 1.97 (s, 3H), 1.87 (s, 3H), 1.82-1.71 (m, 2H), 1.60-1.50 (m, 2H), 1.43 (dd, J = 14.6, 6.9 Hz, 2H), 1.36-1.26 (m, 12H). ^{13}C NMR (101 MHz, $CDCl_3$) δ: 196.1 (C), 158.6 (C), 140.0 (C), 136.3 (C), 135.6 (C), 135.4 (C), 133.7 (C), 133.5 (C),133.4 (C), 127.3 (C), 127.0 (CH), 126.7 (CH), 125.1 (C), 122.8 (CH), 115.0 (CH), 68.3 (CH_2), 38.6 (CH_2) 38.5 (CH_2), 30.8 (CH_3), 29.7 (CH_2), 29.7 (CH_2), 29.7 (CH_2), 29.6 (CH_2), 29.4 (CH_2), 29.3 (CH_2), 29.3 (CH_2), 29.0 (CH_3), 26.2 (CH_3), 23.1 (CH_2), 14.5 (CH_2), 14.4 (CH_2). HRMS (ESI): calcd. for $C_{34}H_{44}ClO_2S_3$: 615.2187, found 615.2159.

1-(4-(methylthio)phenyl)ethan-1-one (12b) TLC (SiO_2: heptane/ethyl acetate, 4:1, R_f = 0.41) $TiCl_4$ 94%  ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.75 (d, J = 8.7 Hz, 2H), 7.14 (d, J = 8.6 Hz, 2H), 2.46 (s, 3H), 2.40 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ: 196.89 (C), 145.77 (C), 133.23 (C), 128.54 (CH), 124.71 (CH), 26.28 (CH_3), 14.54 (CH_3). *m/z* (EI) 166. HRMS (ESI): calcd. for $C_9H_{11}OS$: 167.0525, found 167.0521.

7.5 Acknowledgment

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7.6 References

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