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Note

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Syntheses of 7-substituted anthra[2,3-*b*]thiophene derivatives and naphtho[2,3-*b*:6,7-*b′*]dithiophene

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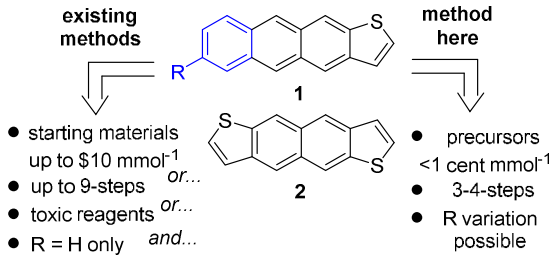
Supporting Information

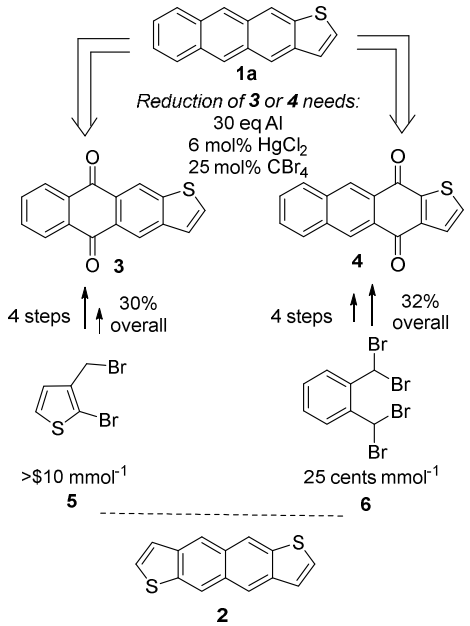


ABSTRACT: **7**-R-anthra[2,3-*b*]thiophene derivatives (**1**, R = H, Me, *i*-Pr, MeO) are prepared in three steps (in average overall yield >50%) starting from (*E*)-4-$RC_6H_4CH_2(HOCH_2)C{=}CI(CH_2OH)$. The latter are commercial or readily prepared from 2-butyne-1,4-diol and $ArCH_2Cl$ (both costing <1 cent/mmol) at 10 g scales. These allow selective formation of (otherwise unattainable) higher solubility 7-derivatives. Similar methods allow preparation of naphtho[2,3-*b*:6,7-*b′*]dithiophene **2** using equally low cost starting materials.

Acene-cores terminating at one or both ends with thiophene units are attractive motifs for the formation of organic electronic semiconductor devices.[1-6] For example, anthra[2,3-*b*]thiophene **1a** (Scheme 1) has been used to derive organic field effect transistors (OFETs) showing carrier mobilities of 0.13 - 0.15 $cm^2\ V^{-1}\ s^{-1}$.[7,8] Similarly, derivatives of **2** have also been used in OFET devices with even higher carrier mobilities of 0.5 - 1.5 $cm^2\ V^{-1}\ s^{-1}$.[9]

The parent anthra[2,3-*b*]thiophene **1a** has been known since 1981.[10-15] Various methodologies have been employed for its preparation. Multi-step syntheses using expensive (in either cost or time) or higher toxicity or environmentally less than desirable reagents are the norm.[10,11] The current best synthetic methods for **1a** use compounds **3** or **4** as key intermediates (Scheme 1), but these are not without issues. Several steps are needed to prepare **3** in 30% overall yield from lachrymatory and expensive 2-bromo-3-(bromomethyl)thiophene **5** ($210 for 5 g[16]). Similarly, **4** has to be synthesized from **6**, which although more modest in cost ($64 per 100 g[16]) still requires four steps from this significantly carcinogenic material. Finally, the environmental metrics of the reduction of **3** or **4** to **1a** could be improved: 30 equivalents of aluminum, 6 mol% of toxic $HgCl_2$ and 25 mol% of CBr_4 are required.[7]

Scheme 1. Conventional syntheses of compound 1a using dihydroanthra[2,3-*b*]thiophenediones and related 2.



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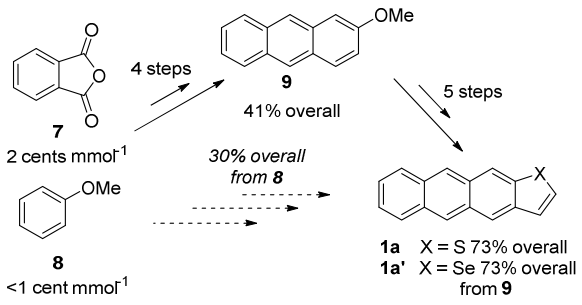
Another recent synthesis of anthra [2,3-*b*]thiophene **1a** uses non-commercial 2-methoxyanthracene **9** as the key intermediate.[17] The latter requires 4 steps resulting in an overall yield of 41% to **9**.[17,18] Thus, the total step count to **1a** by this route is rather high (Scheme 2).

Scheme 2. Synthesis of compound 1a from 2-methylanthracene 9

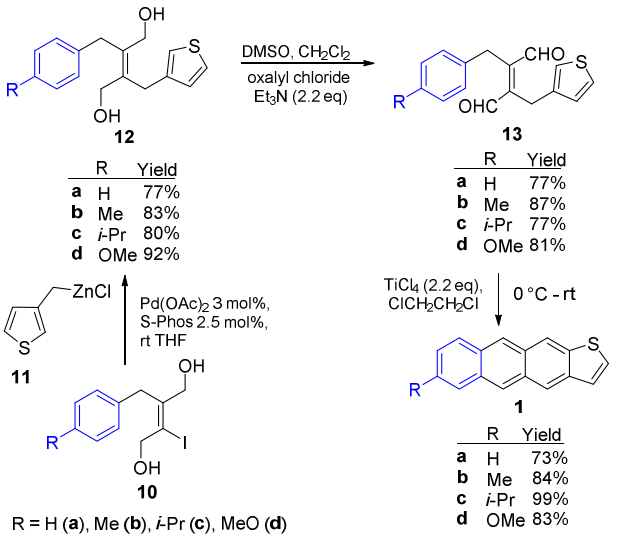


Although, this latter approach uses cheap starting materials **7** and **8**, and allows access to selenophene **1a'**, it still requires a total of nine steps including a boron tribromide peomoted MeO-deprotection and a Sonogashira coupling to complete the synthesis.[17]

In conclusion, the starting materials for all reported routes to anthra[2,3-*b*]thiophene **1a** require multi-step synthesis, using commercially expensive precursors which often have significant toxicity issues. Finally, while existing routes to anthra[2,3-*b*]thiophenes **1** can allow subsequent preparation of 2-substituted derivatives, they cannot be easily be used for regiospecific mono-substitution of the terminal phenylene. Dissymmetric reagents would result in regio-isomeric products. However, employment of a two-directional[19] Bradsher[20] disconnection should be an effective alternative. It was anticipated that 7-alkyl substitution would also increase the solubility of the resultant anthra[2,3-*b*]thiophenes **1**.

Our approach to **1a-d** (Scheme 3) begins with the crystalline iodides **10a-d**, a number of which are commercially available.[21] Alternatively, **10a-d** are easily prepared from 2-butyne-1,4-diol and benzylic chlorides, both of which are typically available at low cost (<1 cent mmol^{-1}). Copper-catalyzed Grignard carbocupration allows **10a-d** to be prepared at 10 g scales without recourse to chromatography (see Experimental Section). Use of $Pd(OAc)_2$ (3 mol%) and a deficiency of S-Phos (2.5 mol%) allows direct Negishi-coupling of with (thien-3-ylmethyl)zinc(II) chloride (**11**) affording **12** without protection of the free alcohols. Swern oxidation of **12** to the yellow dialdehydes **13** proceeds in good yield, provided a small additional amount of DMSO was used in the reaction to facilitate complete dissolution of **12** at low temperature. Purification of intermediates **12-13** is facilitated by their highly crystalline nature. Finally, double[19] Bradsher closure[22] of **13** is effected cleanly in the presence of $TiCl_4$.[23] Isolation of **1a-d** is simplified by use of a 1:1 quench mixture of acetone/methanol. The titanium by-products generated in the closure are soluble in this mixture and **1** may be isolated by simple filtration (use of Whatman glass microfiber GF/A filter paper makes this very straight forward, see Experimental Section). The average overall yield for the derivatives **1** over the three steps of Scheme 4 ranges 43-61% (average 57%).

Scheme 3. Consise methodology for synthesis of anthra[2,3-*b*]thiophenes (1a-d)



One of the advantages of Scheme 4 is the greater solubility of the 7-alkyl derivatives **1b-d**, allowing routine acquisition of fully assigned ^{13}C NMR spectra, while **1b-d** are also easier to process in subsequent further functionalization or device preparations. Soluble diols **12a-d** can be purified either using column chromatography to yield (70-90%) or can be attained as analytically pure colorless needles by recrystallization with hot acetonitrile and cooling to 4 °C.

Optimization of Scheme 4 revealed interesting observations relevant to the scope and limitations of each of its steps (Schemes 4-6). Attempts to use the regio-isomeric Negishi reagent **14** with iodide **10b** provided only low yields of **15** (32%) (Scheme 4). Extensive catalyst deactivation is observed in these reactions (see Experimental Section and Scheme 4).

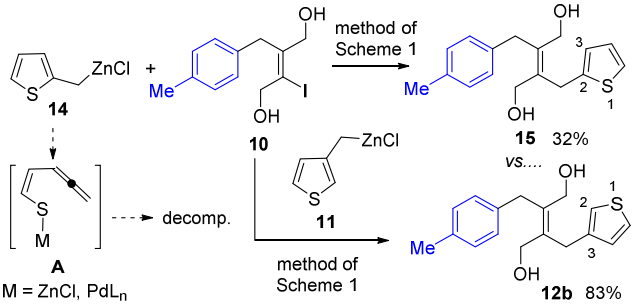
Relatively few examples of 2-thienylmethyl organometallics are present in the primary literature;[24,25] with these sometimes being implicated as thermo-labile species. The appearance of multiple 1:1 signals in the range δ_H 5.0 - 6.4 in the crude spectra of **15** (assigned to $=CH_2$ units) is in accord with *anti*-elimination of **14** and subsequent decomposition of the potentially derived reactive putative allene intermediate **A**. Compound **11**, however, behaves cleanly. Interestingly regio-isomeric alcohols **12b** and **15** also show different behavior upon their oxidation.

While **15** cleanly provides **16** under our preferred aerobic oxidation conditions[19] (Scheme 5) initial tests of **12b** led to complex mixtures under Stahl-catalysis.[26] Similar issues were seen on attempted use of MnO_2 and PCC oxidants. From these complicated mixtures the only isolable product is **17** based on spectroscopic data (Scheme 5), indicating that chemoselective oxidation is not attained. Fortunately, this issue could be over-

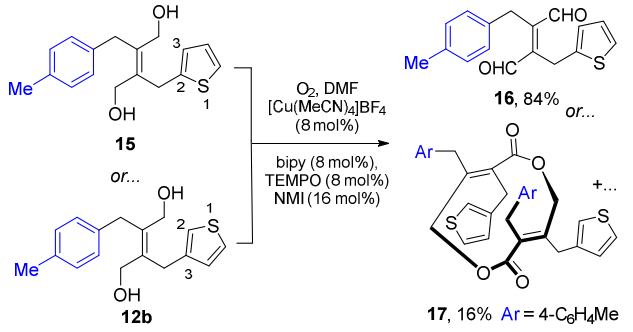
B

come by simply increasing the DMSO content of Swern-based oxidations used in general conversions of **12** to **13**.

Scheme 4. Lower stability of (thien-2-ylmethyl)zinc(II) chloride (14)



Scheme 5. Comparative oxidation of diols 15 and 1b

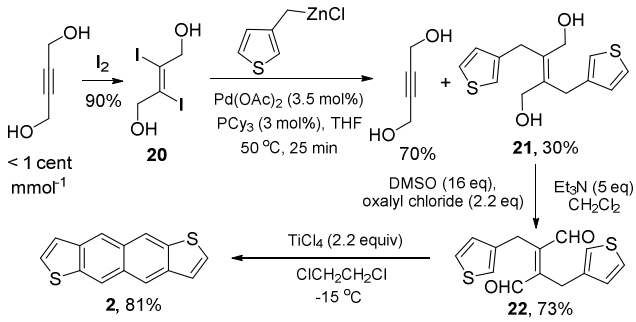


The final Bradsher closure[19,20] of step of Scheme 4 easily affords **1a-d** in good yields (73-99%) as bright yellow powders. These reactions show typical Friedel-Crafts behavior: at shorter reactions times mono closure onto just the electron-rich thiophene unit is observed. Thus, the scope of the final step in Scheme 4 is limited to the preparation of electron-rich anthra[2,3-*b*]thiophenes **1**. In support of this idea closure of **13** to **1** where R = F was not achieved. The other steps of Scheme 4 are tolerant of alkyl, aryl, OR, F and Br substituents.[19]

In contrast to anthra[2,3-*b*]thiophenes **1**, previous literature syntheses of naphtho[2,3-b:6,7-*b′*]dithiophene **2**, are limited to a single route.[9,27] Commercial 2,6-dihydroxynaphthalene ($80 for 5 g[16]) **18**, is brominated to afford 1,3,5,7-tetrabromonaphthalene-2,6-diol **19** by known procedures.[28,29] Unfortunately, the literature yields for this process are reported to be highly variable (4-51%), additionally, a further four steps are required to convert **19** to **2**.

We considered alternative preparation of **2** based on Negishi coupling of the diiodide **20**[19] (derived from low cost 2-butyne-1,4-diol, Scheme 6). Although the yield of **21** was modest (30%), due to competing transmetallation-elimination, the butyne diol by-product produced is insoluble and very simply and easily separated. The remaining steps of the sequence all give good yields and involve chromatography-free work-up procedures. Alternative procedures via the 3-thienyl analogue of **10** were investigated but were not as successful due to lower yields (see Experimental Section).

Scheme 6. Straightforward synthesis of naphtho[2,3-*b*:6,7-*b′*]dithiophene (2)



Preparation of **2** was confirmed by HRMS together with ^{1}H, ^{13}C, IR and UV-vis spectroscopy. Using the latter the optical bandgaps (E_g) of **1a-d** and **2** were measured using standard Tauc plots (Table 1). Hall effect studies suggested the carrier mobilities of our samples of **1-2** were less than 0.1 $m^2 V^{-1} s^{-1}$.

Table 1. The optical bandgaps for compounds 1a-d and compound 2

compound	λ_{max} (nm) [a]	E_g (eV) [b]
1a	435	2.75
1b	437	2.73
1c	436	2.72
1d	443	2.69
2	402	2.98

[a] In argon saturated CH_2Cl_2; longest wavelength absorption band. [b] Determined by Tauc plot of UV-Vis data.

In conclusion, we have established new approaches for the efficient synthesis of 7-substituted anthra[2,3-*b*]thiophenes **1a-d** and the unsubstituted naphtho[2,3-*b*:6,7-*b′*]dithiophene **2**. The methods employed are simple, use low cost starting materials, and which are scalable, avoiding chromatography in many cases. These methods also offer simple flexible approaches to the inclusion of 7-substituted thiophene-acenes **1** that cannot be prepared by existing approaches. Finally, in our approach compounds **1a-d** are prepared in three steps in average overall yields of >50%. Existing reported methods require four steps to attain key intermediates **3** and **4**, both in ca. 30% overall yield. Final reduction of **3** is high yielding but requires toxic $HgCl_2$. Conversely $Al(O\text{-}c\text{-}C_6H_{11})_3$ reduction of **4**, although environmentally benign, proceeds in modest 59% yield. The approaches herein constitute useful cleaner and sustainable alternatives to these important classes of organic electronic fragments. The formation of bulk thermoelectric devices based on derivatives of **1-2** is the subject of our own future work.

EXPERIMENTAL SECTION

General Information. Reactions involving air-sensitive reagents were carried out under argon atmospheres in

flame-dried glassware. All solvents were commercial (Sigma-Aldrich and Fisher Scientific UK Ltd) and were used as supplied unless otherwise stated. Dichloromethane (DCM), dimethyl sulfoxide (DMSO), triethylamine, diisopropylethylamine and 1,2-dichloroethane were dried with molecular sieve (4 Å). Tetrahydrofuran (anaerobic, <10 ppm water) was from an anhydrous solvent unit (Inert Technologies PureSolv). The compounds 2-butyne-1,4-diol, iodine, PCy_3 (Cy = *cyclo*-C_6H_{11}) S-Phos (2-dicyclohexylphosphino-2,6-dimethoxybiphenyl), $Pd(OAc)_2$, 2,2,6,6-tetramethylpiperidine-1-oxyl (TEMPO), CuCN, $CuBr{\cdot}SMe_2$ were commercial from Alfa-Aesar, Fisher, Merck or Sigma-Aldrich and used as recieved. Lithium chloride (Aldrich, anhydrous, >99%) and $TiCl_4$ (Fluka, >98%) were stored under argon. Benzyl chlorides were commercial (Sigma-Aldrich): BnCl, 4-$RC_6H_4CH_2Cl$ (R = Me, MeO, F), or prepared by literature routes (R = *i*-Pr).[30] Diols (**10a-e**) were commercial (**10d**, Key Organics) or prepared according to a literature procedure.[19] Zinc dust (<10 μm, Sigma-Aldrich: 209988-1KG) was activated by trimethylsilyl chloride. All temperatures refer to those of the cooling and heating baths used. Thin layer chromatography was performed on Merck silica gel 60 F_{254}. Nuclear magnetic resonance spectra were recorded on Bruker DPX-400 (400.1 MHz), AV400 (400.1 MHz), AV(III)400 (400.1 MHz) or a Bruker Ascend 500 (500.1 MHz) spectrometers at ambient temperature. Proton spectra were referenced to $CDCl_3$ (δ = 7.27 ppm). All ^{13}C NMR samples were proton-decoupled and referenced to $CDCl_3$ (δ = 77.0 ppm). Coupling constants (*J*) are quoted in Hertz. Melting points were determined with a Gallenkamp MFB-600-010F apparatus. Infrared spectra (IR) were recorded with a Varian FTS-7000 FT-IR spectrometer using (ATR) at room temperature. UV-Vis spectra were recorded by Cary UV VIS NIR spectrometer using ca. 10^{-4} M dichloromethane solutions. Semi-quantitative log(ε) values are given as a guide to relative peak height. Mass spectrometry was performed using a Bruker MicroTOF or VG Micromass AutoSpec spectrometers using electrospray (ESI), electron impact (EI) ionization modes. Elemental CH analyses were conducted on a CE-440 instrument.

Preparation of starting materials, 2-(Chloromethyl)thiophene: To a solution of thien-2-ylmethanol (10.0 g, 87.6 mmol) in dry dichloromethane (350 mL) at 0 °C, thionyl chloride ($SOCl_2$, 12.8 mL, 45.2 mmol) was slowly added over ca. 6 min at 0 °C. The mixture was stirred for 10 minutes at 0 °C and then stirring was continued over 20 hours at room temperature. The mixture was poured on to ice, the dichloromethane was separated, and the remaining aqueous layer re-extracted with dichloromethane (3 × 70 mL). The combined organics were dried ($MgSO_4$) and The solvent was removed under reduced pressure to give the crude 2-(chloromethyl)thiophene as a brown oil (10.4 g, 90% yield). For zinc subsequent reagent formation, the compound was distilled at 45 °C and 4 mbar to give a colorless oil. **^{1}H NMR** (400.1 MHz, $CDCl_3$) δ 7.32 (dd, *J* = 5.1, 1.2 Hz, 1H), 7.13 – 7.07 (m, 1H), 6.96 (dd, *J* = 5.1, 3.5 Hz, 1H). **^{13}C{^{1}H}NMR** (100.6 MHz, $CDCl_3$) δ 140.2, 127.8, 127.0, 127.0, 40.5. These data were consistent with literature values.[31]

*(Thien-2-ylmethyl)zinc(II) chloride (**14**):* Zinc dust (<10 μm, 0.23 g, 3.57 mmol) was dried under vacuum at (0.5 mbar) at >200 °C (3-5 min), then cooled to room temperature under an atmosphere of argon. Dry tetrahydrofuran (3.0 mL) was then added, forming a grey suspension. The reaction mixture was cooled to 0 °C and trimethylsilyl chloride (12 μL, 95 μmol, 0.04 equiv) was added in one portion and the mixture stirred (30 min). Freshly distilled 2-(chloromethyl)thiophene (316 mg, 2.38 mmol) was added over 10 min. After addition the mixture was stirred at 0 ºC (5 h). A turbid white suspension (which normally titrated at >0.54 M, >74% yield) resulted over the remaining residual zinc powder. The supernatant solution could be stored for up to one week at 4 °C (resulting in clear or pale yellow supernatants), but typically the organometallic was used within 24 has attained.

3-(Chloromethyl)thiophene: To a solution of 3-thienylmethanol (4.57 g, 40.0 mmol) in dry dichloromethane (160 mL) at 0 °C, thionyl chloride ($SOCl_2$, 5.85 mL, 80.1 mmol) was added slowly. The mixture was stirred for 10 minutes at 0 ºC and the mixture allowed to warm to room temperature over 16 hours. The mixture was poured on to ice and the dichloromethane separated and the remaining aqueous layer re-extracted with dichloromethane (3 × 70) mL and dried ($MgSO_4$). The solvent was removed under reduced pressure to give crude 3-(chloromethyl)thiophene as a brown oil. The crude compound was distilled at 70-75 °C and 16-18 mbar to give a colorless liquid (3.95 g, 67%); **IR** (diamond-ATR): ν_{max}/cm^{-1} 3103, 2957, 2866, 1760, 1441, 1415, 1263, 1239, 1162, 1080, 908, 857, 829, 784, 691, 671, 612, 551; **^{1}H NMR** (400.1 MHz, $CDCl_3$) δ 7.33 (dd, *J* = 5.0, 3.0 Hz, 1H), 7.30 (m, 1H), 7.14 (dd, *J* = 5.0, 1.4 Hz, 1H), 4.64 (s, 3H); **^{13}C{^{1}H}NMR** (100.6 MHz, $CDCl_3$) δ 138.2, 127.7, 126.8, 124.1, 40.8. These data were consistent with literature values.[32]

*(Thienyl-3-ylmethyl)zinc(II) chloride (**11**):* A dry, argon-flushed Schlenk flask equipped with a magnetic stirrer and a septum was charged with zinc dust <10 μm, (2.50 g, 38.7 mmol, 2.0 equiv). The flask was heated for 5 min under high vacuum (<0.5 mbar) using a heat gun. After cooling to 25 °C, the flask was flushed again with argon and dry THF (21.5 mL) was added and forming a grey suspension. The mixture was cooled to 0 °C and trimethylsilyl chloride (98.6 μL, 0.77 mmol, 0.04 equiv) added in one portion. The mixture allowed to stir for (35 min) at 25 °C. Freshly distilled 3-(chloromethyl)thiophene (2.57 g, 19.4 mmol) was added slowly (over 5 min) at 25 °C. (Note: equivalent results were attained using crude 3-(chloromethyl)thiophene dried overnight at rt with calcium hydride instead of distillation). After addition of the 3-(chloromethyl)thiophene was complete the mixture was warmed to 40 °C and stirred (4 h). When titrated with iodine the reaction assayed at

80%, 0.64 M. This solution could be stored at 4 °C for at least five days but was usually used as attained.

(Thienyl-3-ylmethyl)magnesium chloride: Magnesium metal (3.66 g, 150 mmol) was activated by stirring at rt overnight under argon. Anhydrous THF (50 mL) was added followed by 3-(chloromethyl)thiophene (9.24 g, 69.7 mmol), added dropwise over (16 h) using a syringe pump. The black solution when titrated with iodine indicated the desired Grignard reagent (1.77 M, 88%). The solution was used immediately to the next step. This reagent has only been described in passing in the literature.[33]

Isopropylbenzyl chloride: Neat 4-isopropylbenzyl alcohol (20.4 mL, 20.0 g, 133 mmol) was added dropwise to $SOCl_2$ (29.1 mL, 47.5 g, 399 mmol) under argon at 25 °C. The reaction mixture was warm to refluxed (1 h), and afterward distilled under reduced pressure (118 °C at 22 mbar) to yield (17.35 g, 77%) as a colorless oil. **^{1}H NMR** (500.1 MHz, $CDCl_3$) δ 7.32 (d, *J* = 8.2 Hz, 2H), 7.23 (d, *J* = 8.2 Hz, 2H), 4.58 (s, 2H), 2.92 (hept, *J* = 6.9 Hz, 1H), 1.25 (d, *J* = 6.9 Hz, 6H); **^{13}C{^{1}H}NMR** (125.8 MHz, $CDCl_3$) δ 149.4, 135.0, 128.8, 127.0, 46.4, 34.0, 24.1. These experimental data match the published values.[30]

Grignard reagent preparation, representative example: (4-methylbenzyl)magnesium chloride: Magnesium metal (10.0 g, 156 mmol) was activated by mechanistic stirring (7 h) under argon in the presence of iodine crystals (ca. 3.0 mg) at (22 °C) until its color became black. Anhydrous tetrahydrofuran (156 mL) was then added at 20 °C giving a suspension of black activated magnesium. Distilled neat 4-methylbenzyl chloride (20.7 mL, 156 mmol) was then added dropwise to the reaction mixture over (15 h) using a syringe pump. After completion of the addition the reaction mixture was which typically titrated against the iodine to give 0.85 M equivalent to a 96% yield. The reagent was used as attained.

*Preparation of starting diols (**10a-e**), representative example: (Z)-2-iodo-3-(4-isopropylbenzyl)but-2-ene-1,4-diol (**10c**):* A solution of (4-isopropylbenzyl)magnesium chloride (39 mL, 1.1 M tetrahydrofuran solution, 42.9 mmol) was added to a stirred solution of 2-butyne-1,4-diol (1.10 g, 12.9 mmol) in dry tetrahydrofuran (23 mL) at 0 °C to form a colorless precipitate within a grey solution. The reaction mixture was allowed to warm to room temperature and stirred for 5 mins. Solid cuprous bromide dimethyl sulfide (52.9 mg, 0.26 mmol, 2 mol% based on diol) was added subsequently, against an argon flow, and the reaction mixture quickly transferred to pre-equilibrated oil bath at 60-65 °C. After 1 h at 60-65 °C the solid had dissolved forming a dark solution which was cooled first to 25 °C and then to -60 °C in a lightly lagged bath (that would allow warming from -60 to 0 °C over ca. 2 h). Solid I_2 (4.35 g, 17.2 mmol) was added, against an argon flow, and the brown mixture stirred as it came to 0 °C over (2 h). The reaction mixture was extracted with EtOAc (3 × 70 mL) and washed with sodium metabisulfite (2 × 70 mL of 5% w/w aqueous solution) and water (1 × 50 mL). The resulting pale yellow solution was dried over $MgSO_4$, filtered and the solvent evaporated. To the crude oily mixture, that contained traces of EtOAc, was added a mixture of Et_2O and pentane (1:1, ca. 75 mL) and the mixture cooled to (5 °C) overnight to afforded colorless microneedles. A combined yield was attained over three crops (2.35 g, 6.79 mmol, 53%). TLC: **R*f*** (ethyl acetate) 0.53; **m.p.** 74-75 °C; **IR** (diamond-ATR): ν_{max}/cm^{-1} 3213, 2954, 2927, 2864, 1625, 1510, 1454, 1434, 1419, 1383, 1361, 1238, 1169, 1067, 1013, 997, 918, 830, 799, 742, 705, 609, 565, 543; **^{1}H NMR** (500.1 MHz, $CDCl_3$) δ 7.17 (d, *J* = 8.2 Hz, 2H), 7.10 (d, *J* = 8.2 Hz, 2H), 4.50 (d, *J* = 6.6 Hz, 2H), 4.24 (d, *J* = 6.6 Hz, 2H), 3.77 (s, 2H), 2.88 (hept, *J* = 6.9 Hz, 1H), 2.02 (t, *J* = 6.6 Hz, 1H), 1.67 (t, *J* = 6.6 Hz, 1H), 1.23 (d, *J* = 6.9 Hz, 6H); **^{13}C{^{1}H}NMR** (125.8 MHz, $CDCl_3$) δ 147.5, 144.8, 135.18, 128.4, 127.0, 106, 5, 71.3, 67.8, 35.7, 33.8, 24.1; HRMS (ESI-TOF) *m/z*: $[M + Na]^+$ Calcd for $C_{14}H_{19}IO_2Na$ 369.0322; Found 369.0311; **Anal:** Calcd for $C_{14}H_{19}IO_2$ C, 48.57; H, 5.53; Found C, 48.56; H, 5.41%.

*(Z)-2-Benzyl-3-iodobut-2-ene-1,4-diol (**10a**):* Attained in a similar manner to compound (**10c**) using freshly prepared benzyl magnesium chloride (175 mL, 0.8 M THF solution, 140 mmol) 2-butyne-1,4-diol (3.61 g, 42.0 mmol) in THF (23 mL), $CuBr{\cdot}SMe_2$ (0.17 mg, 0.84 mmol, 2 mol%) and I_2 (14.2 g, 56 mmol), yielding (**10a**) as colorless microneedles (7.40 g, 24.3 mmol, 59%) after crystallization with Et_2O/pentane (three crops). TLC: **R*f*** (ethyl acetate) 0.68; **m.p.** 94-95 °C; **^{1}H NMR** (500.1 MHz, $CDCl_3$) δ 7.32 – 7.29 (m, 2H), 7.25 – 7.18 (m, 3H), 4.50 (d, *J* = 6.6 Hz, 2H), 4.24 (d, *J* = 6.6 Hz, 2H), 3.81 (s, 2H); 1.97 (t, *J* = 6.6 Hz, 1H), 1.61 (t, *J* = 6.6 Hz, 1H); **^{13}C{^{1}H}NMR** (125.8 MHz, $CDCl_3$) δ 144.6, 138.0, 129.0, 129.0, 128.5, 127.0, 71.2, 68.0, 36.1; **IR** (diamond-ATR): ν_{max}/cm^{-1} 3192, 3058, 2918, 2866, 1618, 1601, 1492, 1449, 1429, 1361, 1237, 1063, 1022, 996, 933, 888, 838, 724, 693, 656, 601, 492, 457, 423; HRMS (ESI-TOF) *m/z*: M^+ Calcd for $C_{11}H_{13}IO_2$ 303.9960, Found 303.9941. The experimental data were consistent with published values.[19]

*(Z)-2-Iodo-3-(4-methylbenzyl)but-2-ene-1,4-diol (**10b**):* Prepared by similar procedure to compound (**10c**) using 4-methylbenzylmagnesium chloride (176 mL, 0.85 M THF solution, 150 mmol), 2-butyne-1,4-diol (3.88 g, 45.05 mmol) in THF (25 mL), $CuBr{\cdot}SMe_2$ (185 mg, 0.9 mmol, 2 mol%) and I_2 (15.3 g, 60.0 mmol) to yield (**10b**) as a colorless powder 9.91 g, 31.2 mmol (69%) on trituration with Et_2O:pentane. TLC: **R*f*** (1:1 EtOAc:pentane) 0.56; **m.p.** 115- 116 °C; **IR** (diamond-ATR): ν_{max}/cm^{-1} 3242, 3045, 3019, 2920, 2874, 1510, 1476, 1493, 1440, 1414, 1316, 1237, 1169, 1072, 1036, 1017, 990, 961, 921, 831, 800, 751, 658, 553, 480, 436; **^{1}H NMR** (500.1 MHz, $CDCl_3$) δ 7.11 (d, *J* = 8.0 Hz, 2H), 7.07 (d, *J* = 8.0 Hz, 2H), 4.49 (d, *J* = 6.5 Hz, 2H), 4.23 (d, *J* = 6.5 Hz, 2H), 3.76 (s, 2H), 2.32 (s, 3H) 2.01 (t, *J* = 6.5 Hz, 1H,), 1.66 (t, *J* = 6.5 Hz, 1H); **^{13}C{^{1}H}NMR** (125.8 MHz, $CDCl_3$) δ 144.8, 136.5, 134.8, 129.7 (2 C), 128.4 (2 C), 106.5, 71.09, 67.67, 35.6, 21.0; HRMS (ESI-TOF) *m/z*: $[M + Na]^+$ Calcd for $C_{12}H_{15}IO_2Na$

341.0009; Found 340.9998. The data of the compound match publish values.[19]

*(Z)-2-Iodo-3-(thien-3-ylmethyl)but-2-ene-1,4-diol (**10e**):* Prepared by a similar procedure to compound (**10c**) using (thien-3-ylmethyl)magnesium chloride (55 mL, 1.07 M THF solution, 59.2 mmol), 2-butyne-1,4-diol (1.53 g, 17.8 mmol) in THF (14 mL) and I_2 (6.01 g, 23.7 mmol) to yield **(10e)** (2.00 g, 6.45 mmol, 36%) after column chromatography (2:1 dichloromethane/EtOAc). TLC: $\mathbf{R}_f$ (2:1 dichloromethane/EtOAc) 0.43; **m.p.** 93-94 °C ; **IR** (diamond-ATR): ν_{max}/cm^{-1} 3196, 3095, 2922, 2866, 1626, 1488, 1456, 1434, 1407, 1381, 1356, 1294, 1238, 1167, 1143, 1070, 1017, 997, 935, 921, 868, 833, 773, 737, 712, 699, 685, 589, 570, 501, 413; **^{1}H NMR** (500.1 MHz, $CDCl_3$) δ 7.29 (dd, *J* = 4.9, 3.0 Hz, 1H), 7.00 (m, 1H), 6.94 (d, *J* = 4.9 Hz, 1H), 4.48 (d, *J* = 6.6 Hz, 2H), 4.28 (d, *J* = 6.6 Hz, 2H), 3.78 (s, 2H), 1.95 (t, *J* = 6.6 Hz, 1H), 1.63 (t, *J* = 6.6 Hz, 1H); **^{13}C{^{1}H}NMR** (125.8 MHz, $CDCl_3$) δ 144.5, 138.4, 128.0, 126.5, 121.7, 106.4, 71.4, 67.8, 31.1; HRMS (ESI-TOF) *m/z*: [M+] Calcd for $C_9H_{11}IO_2S$ 309.9518; Found 309.9534.

*Preparation of (E)-2-(4-methylbenzyl)-3-(thien-2-ylmethyl)but-2-ene-1,4-diol (**15**) by heterocoupling of (Z)-2-iod o-3-(4-methylbenzyl)but-2-ene-1,4-diol (**10b**) with (thien-2-ylmethyl)zinc(II) chloride:* Lithium chloride (16.1 mg, 0.38 mmol, 1.0 equiv) was dried under vacuum (ca. 1 mbar) at >200 °C until free flowing (ca. 6 min), then cooled under an atmosphere of argon. Solid **10b** (0.12 g, 0.38 mmol) and THF (0.9 mL) were added. To the stirred solution solid S-Phos (4.8 mg, 11 μmol, 3.8 mol%) and $Pd(OAc)_2$ (2.8 mg, 12 μmol, 4 mol%) were added forming a dark brown reaction mixture. Promptly, (thien-2-ylmethyl)zinc(II) chloride (0.7 mL of 0.7 M THF solution, 0.5 mmol, 1.5 equiv) was added slowly at rt over (ca. 5 min). Once the zinc reagent was added the reaction color became bright orange. Monitored by TLC, indicated poorer conversion and chemoselectivity than for **12a-d** (even after addition of additional $Pd(OAc)_2$/S-Phos, 2 mol%). After (3 h) the reaction was stopped and quenched with saturated aqueous ammonium chloride solution (10 mL). The mixture was extracted with ethyl acetate (4 × 5 mL), dried ($MgSO_4$), filtered, and evaporated giving a yellow solid. Column chromatography (3:2 EtOAc:pentane) gave a colorless solid (**15**) (28.0 mg, 0.10 mmol, 32%). **R*f*** (3:2 EtOAc:pentane) 0.48; **m.p.** 126-128 °C; **IR** (diamond-ATR): ν_{max}/cm^{-1} 3383, 3317, 2950, 2920, 2853, 1510. 1482, 1433, 1332, 1292, 1252, 1213, 1119, 1076, 1064, 1033, 1014, 995, 927, 879, 848, 837, 805, 762, 748, 687, 607, 527, 497, 478, 450.); **^{1}H NMR** (400.1 MHz, $CDCl_3$) δ 7.15 (dd, *J* = 5.1, 1.2 Hz, 1H), 7.11 (s, 4H), 6.93 (dd, *J* = 5.1, 3.4 Hz, 1H), 6.86 – 6.82 (m, 1H), 4.29 (s, 2H), 4.22 (s, 2H), 3.87 (s, 2H), 3.66 (s, 2H), 2.32 (s, 3H) 1.26 (broad, 2H); **^{13}C{^{1}H}NMR** (100.6 MHz, $CDCl_3$) δ 143.4, 137.4, 136.5, 136.4, 136.0, 129.5 (2C), 128.6 (2C), 127.2, 125.2, 124.0, 61.9 (2C) , 35.3, 30.2, 21.1; HRMS (ESI-TOF) *m/z*: [M + Na]$^+$ Calcd for $C_{17}H_{20}O_2SNa$ 311.1081; Found 311.1076.

*(3E,8E)-4,9-bis(4-methylbenzyl)-3,8-bis(thien-3-ylmethyl)-1,6-dioxecine-2,7(5H,10H)-dione (**17**):* Prepared serendipitously (but reproducibly) using a modified[2] procedure of Stahl,[26] in initial attempts to prepare (**13b**). Diol (**12b**) (0.57 g, 1.97 mmol) was dissolved in DMF (11.5 mL) without any O_2 flowing. The following were promptly added to the reaction mixture sequentially: $Cu(MeCN)_4BF_4$ (49.7 mg, 0.16 mmol, 8 mol%), TEMPO (24.6 mg, 0.16 mmol, 8 mol%), and finally *N*-methylimidazole (NMI, 25.2 μL, 25.9 mg, 0.31 mmol, 16 mol%) giving a dark orange/brown solution. The oxygen flow (~5 bubbles per sec) was immediately started. After (30 min) the reaction mixture a deep green and TLC analysis (1:1 EtOAc/pentane) showed consumption of diol (**12b**, **R*f*** 0.35) and the formation of new species. The O_2 was stopped and the reaction extracted with EtOAc (3 × 30 mL). The organic layer was washed with 2 M HCl (3 × 10 mL) and water (3 × 10 mL). The organic extracts were dried ($MgSO_4$) and evaporated to yield oily crude materials. These were separated using column chromatography (12:1 pentane:EtOAc) to yield (**17**) (180 mg, 0.32 mmol, 16%) with uncharacterized products. TLC: **R*f*** (12:1 pentane:EtOAc) 0.63; **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.29 – 7.23 (m, 2H), 7.16 (d, *J* = 8.0 Hz, 2H), 7.11 (d, *J* = 7.6 Hz, 4H), 7.04 (m, 1H), 7.01 (dd, *J* = 4.9, 1.3 Hz, 2H), 6.93 – 6.89 (m, 2H), 6.76 (dd, *J* = 4.9, 1.3 Hz, 1H), 4.55 (d, *J* = 7.7 Hz, 4H), 3.82 – 3.59 (m, 8H), 2.33 (broad, 6H). **^{13}C{^{1}H}NMR** (125.8 MHz, $CDCl_3$) δ 174.7, 174.6, 160.2, 159.3, 137.9, 137.0, 136.2, 135.6, 134.9, 132.8, 129.7, 129.4, 128.5, 128.4, 128.2, 127.7, 126.9, 126.8, 126.1, 126.0, 122.4, 121.6, 71.3, 33.1, 29.2, 28.1, 24.3, 21.0. HRMS (ESI-TOF) *m/z*: [M + Na]$^+$ Calcd for $C_{34}H_{32}NaO_4S_2$ 591.1639 Found 591.1657.

*Heterocoupling of (**10a-d**) with (thien-3-ylmethyl)zinc(II) chloride (**11**) for non-symmetric diols (**12a-d**), representative example: (E)-2-benzyl-3-(thien-3-ylmethyl)but-2-ene-1,4-diol (**12a**):* Lithium chloride LiCl (57.2 mg, 1.35 mmol, 1.2 equiv) was dried under vacuum using heat gun at >200 °C for (5 min) then allow to cool to r.t. under an atmosphere of argon. Diol (**10a**) (0.34 g, 1.13 mmol) and solid S-Phos (12.5 mg, 0.03 mmol, 2.7 mol% equiv) were added and the solid mixture left under high vacuum for few min. Thereafter, under an atmosphere of argon, tetrahydrofuran (3.3 mL) was added followed promptly by solid $Pd(OAc)_2$ (7.6 mg, 33 μmol, 3 mol%) forming a dark brown colored solution. (If this color was not formed, active catalyst formation was ensued by re-charging with the same amount of ligand and palladium). Immediately after formation of the active catalyst, a solution of (thien-3-ylmethyl)zinc(II) chloride (**11**) (4.0 mL of 0.45 M THF solution, 1.8 mmol, 1.6 equiv) was added in one portion. After addition of the zinc reagent the color of the reaction mixture changed to clear yellow. The reaction was monitored via TLC. Within 1 h this showed conversion to **12a**. The reaction was quenched with saturated aqueous ammonium chloride solution (3 mL) and extracted with ethyl acetate (4 × 10 mL). The organic layer was washed with saturated aqueous sodium hydrogen carbonate (4 × 5 mL) and the organic extracts were dried with Na_2SO_4 or $MgSO_4$. The organic layer concentrated to yield tan solid. Column chromatography (3:2 EtOAc:pentane) gave a colorless solid (0.24 g, 0.87 mmol,

77%). TLC, **R*f*** 0.45 (3:2 EtOAc: pentane); **m.p.** 128-129 °C; **IR** (diamond-ATR): ν_{max}/cm^{-1} 3386, 3328, 3099, 2949, 2916, 2853, 1731, 1601, 1493, 1481, 1452, 1431, 1327, 1127, 1057, 1028, 1011, 992, 942, 855, 828, 786, 757, 729, 700, 632, 583, 493, 434; **^{1}H NMR** (500.1 MHz, $CDCl_3$) δ 7.32 – 7.27 (m, 3H), 7.24 – 7.19 (m, 3H), 6.98 – 6.95 (m, 2H), 4.28 (d, *J* = 5.3 Hz, 2H), 4.22 (d, *J* = 5.3 Hz, 2H), 3.71 (s, 2H), 3.70 (s, 2H), 1.25 (t, *J* = 5.3 Hz, 1H), 1.20 (t, *J* = 5.3 Hz, 1H); **^{13}C{^{1}H}NMR** (125.6 MHz, $CDCl_3$) δ 140.5, 139.9, 136.7, 128.9 (2C), 128.7 (2C), 128.3, 126.5, 126.2, 121.2, 62.2, 61.9, 35.8, 30.8; HRMS (ESI-TOF) *m/z*: $[M + Na]^+$ Calcd for $C_{16}H_{18}NaO_2S$ 297.0920, Found 297.0918.

*(E)-2-(4-methylbenzyl)-3-(thien-3-ylmethyl)but-2-ene-1,4-diol (**12b**):* Prepared by a method analogous to (**12a**) using (*Z*)-2-iodo-3-(4-methylbenzyl)but-2-ene-1,4-diol (**10a**) (1.00 g, 3.71 mmol) and (thien-3-ylmethyl)zinc(II) chloride (**11**) (7.71 mL, 0.64 M THF solution, 4.71 mmol) to yield (**12b**) as a colorless powder (0.75 g, 2.60 mmol, 83%) after column chromatography (3:2 EtOAc:pentane). TLC: **R*f*** (ethyl acetate) 0.66. Colorless thin needles from hot acetonitrile on cooling to ambient, then 4 °C with **m.p.** 127-129 °C; **IR** (diamond-ATR): ν_{max}/cm^{-1} 3381, 3310, 3101, 2950, 2917, 1509, 1482, 1433, 1383, 1331, 1298, 1205, 1128, 1065, 1011, 992, 942, 926, 880, 855, 829, 806, 783, 760, 722, 699, 627, 523, 491; **^{1}H NMR** (500.1 MHz, $CDCl_3$) δ 7.28 – 7.26 (m, 1H), δ 7.12 – 7.08 (m, 4H), 7.97 – 6.94 (m, 2H), 4.27 (s, 2H), 4.21 (s, 2H), 3.68 (s, 2H), 3.66 (s, 2H), 2.32 (s, 3H), 1.43 (broad, 2H); **^{13}C{^{1}H}NMR** (125.8 MHz $CDCl_3$) δ 140.5, 136.9, 136.6, 136.4, 136.0, 129.5, 128.5, 128.3, 126.2, 121.2, 62.2, 61.9, 35.4, 30.8, 21.1. HRMS (ESI-TOF) *m/z*: $[M + Na]^+$ Calcd for $C_{17}H_{19}NaO_2S$ 311.1076, Found 311.1075. **Anal:** calcd for $C_{17}H_{20}O_2S$ C, 70.80; H, 6.99; Found C, 70.61; H, 6.94%.

*(E)-2-(4-isopropylbenzyl)-3-(thien-3-ylmethyl)but-2-ene-1,4-diol (**12c**):* Prepared by a method analogous to (**12a**) using (*Z*)-2-iodo-3-(4-isopropylbenzyl)but-2-ene-1,4-diol (**10c**) (1.50 g, 4.33 mmol) and (thien-3-ylmethyl)zinc(II) chloride (10.0 mL 6.70 mmol, 0.67 M THF solution). To yield (**12c**) as a colorless powder (1.10 g, 4.48 mmol, 80%) after column chromatography (3:2 EtOAc:pentane). TLC; **R*f*** (3:2 EtOAc:pentane) 0.41; **IR** (diamond-ATR): ν_{max}/cm^{-1} 3389, 3334, 3103, 2956, 2889, 2869, 1511, 1481, 1467, 1432, 1415, 1382, 1333, 1296, 1128, 1064, 1009, 990, 942, 928, 880, 856, 837, 784, 719, 700, 623, 550; **^{1}H NMR** (500.1 MHz, $CDCl_3$) δ 7.28 (dd, *J* = 4.8, 3.0 Hz, 1H), 7.17 (d, *J* = 8.0 Hz, 2H), 7.13 (d, *J* = 8.0 Hz, 2H), 6.97 (m, 2H), 4.27 (d, *J* = 5.4 Hz, 2H), 4.22 (d, *J* = 5.4 Hz, 2H), 3.69 (s, 2H), 3.67 (s, 2H), 2.88 (hept, *J* = 7.0 Hz, 1H), 1.32 (t, *J* = 5.4 Hz, 1H), 1.29 (t, *J* = 5.4 Hz, 1H), 1.24 (d, *J* = 7.0 Hz, 6H); **^{13}C{^{1}H}NMR** (125.8 MHz $CDCl_3$) δ 147.1, 140.5, 137.0, 136.8, 136.5, 128.5 (2C), 128.4, 126.9 (2C), 126.1, 121.2, 62.2, 62.0, 35.4, 33.8, 30.8, 24.2 (2C); HRMS (ESI-TOF) *m/z*: $[M + Na]^+$ Calcd for $C_{19}H_{24}NaO_2S$ 339.1389, Found 339.1384.

*(E)-2-(4-methoxybenzyl)-3-(thien-3-ylmethyl)but-2-ene-1,4-diol (**12d**):* Prepared by a method analogous to (**12a**) using (*Z*)-2-iodo-3-(4-methoxybenzyl)but-2-ene-1,4-diol (**10d**) (0.34 g, 1.00 mmol) and (thien-3-ylmethyl)zinc(II) chloride (**11**) (2.30 mL, 0.64 M THF solution 1.50 mmol) to yield (**12d**) as colorless plates (0.28 g, 0.92 mmol, 92%) after column chromatography (3:2 EtOAc:pentane). **R*f*** (3:2 EtOAc: pentane) 0.46; **m.p.** 109-111 °C; **IR** (diamond-ATR): ν_{max}/cm^{-1} 3387, 3324, 3100, 2928, 2834, 1609, 1580, 1508, 1481, 1461, 1432, 1327, 1301, 1247, 1174, 1127, 1062, 1033, 1010, 990, 942, 879, 829, 783, 763, 722, 691, 625, 513; **^{1}H NMR** (500.1 MHz, $CDCl_3$) δ 7.30 – 7.24 (m, 1H), 7.11 (d, *J* = 8.6 Hz, 2H), 6.94 (m, 2H), 6.84 (d, *J* = 8.6 Hz, 2H), 4.27 (s, 2H), 4.19 (s, 2H), 3.78 (s, 3H), 3.68 (s, 2H), 3.63 (s, 2H), overlapped by 1.76 (m, 2H); **^{13}C{^{1}H}NMR** (125.8 MHz $CDCl_3$) δ 158.3, 140.4, 137.1, 136.3, 131.6, 129.6 (2 C), 128.3, 126.2, 121.2, 114.3 (2 C), 62.1, 61.8, 55.4, 35.0, 30.9; HRMS (ESI-TOF) *m/z*: $[M + Na]^+$ Calcd for $C_{17}H_{20}NaO_3S$ 327.1025; Found 327.1024.

*Homocoupling of (E)-2,3-diiodobut-2-ene-1,4-diol (**20**) to the symmetrical diol (E)-2,3-bis(thien-3-ylmethyl)but-2-ene-1,4-diol (**21**):* In dry Schlenk tube LiCl (0.12 g, 2.94 mmol, 2.4 equiv) was heated using heat gun for (5 min.) under high vacuum at >200 °C until free flowing, and then cooled under a argon atmosphere to 25 °C. The diol (**20**) (0.50 g, 1.47 mmol) was added followed by tricyclohexylphosphine (12.3 mg, 44 μmol, 3 mol%) and the solid mixture held under high vacuum for 30 min. Under an atmosphere of argon THF (5.6 mL) was added and the colorless solution was heated to 50 °C. Solid $Pd(OAc)_2$ (11.6 mg, 55 μmol, 3.5 mol%) was added to the heated mixture to form a dark chocolate colored mixture. Promptly (thien-2-ylmethyl)zinc(II) chloride (**11**) (0.42 M in THF, 8.8 mL, 3.7 mmol, 2.5 equiv) was added in one portion forming a clear yellow mixture. After 25 min the reaction became dark black and TLC analysis (3:2 EtOAc:pentane) showed the starting material was >90% consumed and new spots appeared due to (**21**) and $HOCH_2C{\equiv}CCH_2OH$. The mixture cooled to room temperature, quenched with saturated ammonium chloride solution (4 mL) and extracted with EtOAc (3 × 10 ml). The organic layer was washed with immediately with saturated $NaHCO_3$ (3 × 4 mL), dried (Na_2SO_4), filtered and concentrated giving a crude yellow solid. Purification by column chromatography (3:2 EtOAc: pentane) gave (**21**) as a colorless solid (0.13 g, 0.46 mmol, 31%). [Important note: in our experience (**21**) is rather acid sensitive. Concentration of EtOAc its solutions containing even traces of residual NH_4OAc (pKa 4.8) led to decomposition; washing with hydrogen carbonate avoids this]. TLC (3:2 EtOAc: pentane) **R*f*** 0.35; **m.p.** 117-118 °C; **IR** (diamond-ATR): ν_{max}/cm^{-1} 3373, 3312, 3099, 2943, 2901, 2850, 1533, 1481, 1433, 1411, 1383, 1337, 1246, 1202, 1127, 1069, 992, 945, 878, 856, 829, 777, 709, 686, 636, 572; **^{1}H NMR** (500.1 MHz, $CDCl_3$) δ 7.28 (dd, *J* = 4.8, 3.0 Hz, 2H), 7.01 – 6.92 (m, 4H), 4.26 (d, *J* = 5.5 Hz, 4H), 3.68 (s, 4H), 1.24 (t, *J* = 5.5 Hz, 2H); **^{13}C{^{1}H}NMR** (125.6 MHz $CDCl_3$) δ 140.4, 136.5, 128.3, 126.3, 121.2, 62.1, 30.8. HRMS (ESI-TOF) *m/z*: $[M + Na]^+$ Calcd. for $C_{14}H_{16}O_2S_2$ 303.0484; Found 303.0476.

*2-(4-Methylbenzyl)-3-(thien-2-ylmethyl)fumaraldehyde (**16**):* Diol (**15**) was oxidized by aerobic oxidation using a modified procedure of Stahl.[26] Diol (**15**) (40.0 mg, 0.138 mmol) was dissolved in DMF (0.8 mL) without any O_2 flowing. The following reagents were promptly added to the mixture sequentially: $Cu(MeCN)_4BF_4$ (3.5 mg, 0.01 mmol, 8 mol%), TEMPO (1.7 mg, 0.01 mmol, 8 mol%), and finally *N*-methylimidazole (NMI, 1.76 μL, 1.81 mg, 0.02 mmol, 16 mol%) giving a dark orange/brown solution. Oxygen flow (~5 bubbles per sec) immediately was started. Over 30 min the reaction became a deep green and TLC analysis (1:2 EtOAc/pentane) showed consumption of diol (**15**) (**R*f*** 0.13) and complete formation of (**16**) (**R*f*** 0.85, yellow, visible to the eye). The O_2 flow was stopped and the mixture extracted with EtOAc (3 × 5 mL). The organic layer was washed with 2 M HCl (3 × 5 mL) and water (2 × 5 mL). The organic extracts were dried ($MgSO_4$) and evaporated to a yellow solid (33.0 mg, 0.15 mmol, 84%); **m.p.** 94-96 °C; **IR** (diamond-ATR): ν_{max}/cm^{-1} 3094, 2910, 2872, 2856, 1665 (C=O), 1512 1446, 1398, 1249, 1130, 1075, 1045, 967, 899, 874, 849, 810, 753, 686, 577, 513, 491, 473; **^{1}H NMR** (400.1 MHz, $CDCl_3$) δ 10.47 – 10.46 (m, overlapped, 2H), 7.15 (d, *J* = 4.4 Hz, 1H), 7.09 (d, *J* = 7.9 Hz, 2H), 7.03 (d, *J* = 7.9 Hz, 2H), 6.93 – 6.86 (m, 1H), 6.78 (m, 1H), 4.29 (s, 2H), 4.09 (s, 2H), 2.30 (s, 3H); **^{13}C{^{1}H}NMR** (100.6 MHz, $CDCl_3$) δ 193.2, 193.0, 147.7, 146.2, 140.8, 136.6, 134.9, 129.7, 128.3 , 127.3, 125.7, 124.7, 28.9, 23.9, 21.1; HRMS (ESI-TOF) *m/z*: M^+ Calcd for $C_{17}H_{16}O_2S$ 284.0866; Found 284.0871.

*Preparation of dialdehydes (**13a-d**) by modified Swern oxidation method, representative example: 2-benzyl-3-(thien-3-ylmethyl)fumaraldehyde (**13a**):* A mixture of dry DMSO (0.25 mL) and CH_2Cl_2 (1.0 mL) was added slowly to oxalyl chloride (0.15 g, 1.20 mmol, 2.5 equiv) in dry CH_2Cl_2 (2.0 mL) at -78 ºC, and the mixture stirred for 30 min at the same temperature. Diol (**12a**) (132 mg, 0.48 mmol) in dry CH_2Cl_2 (1.2 mL) and DMSO (0.26 mL) was added dropwise over 5 mins. The milky mixture was stirred for another 1.5 h. Dry Et_3N (0.37 mL, 2.41 mmol, 5 equiv) was added at (-78 ºC) and the mixture allow to warm to r.t. (over 30 min) causing the color to change from milky to yellow. The reaction mixture was concentrated under reduced pressure to provide the crude product. The solid was dissolved in the EtOAc and filtrated to remove trace insoluble compounds. The resultant organic layer was washed with water (10 × 5 mL) and dried (Na_2SO_4). Concentration at reduced pressure yielded a yellow solid (100 mg, 0.37 mmol, 77%). **m.p.** 100-102 °C; **IR** (diamond-ATR): ν_{max}/cm^{-1} 3329, 3090, 3025, 2940, 2909, 2873, 1755, 1666, 1598, 1495, 1452, 1396, 1231, 1202, 1127, 1075, 1031, 976, 939, 904, 870, 830, 774, 739, 697, 685, 623, 603, 574, 525, 484; **^{1}H NMR** (500.1 MHz, $CDCl_3$) δ 10.49 (s, 1H), 10.46 (s, 1H), 7.33 – 7.20 (m, 4H), 7.13 (m, 2H), 6.89 (m, 2H), 4.13 (s, 2H), 4.12 (s, 2H); **^{13}C{^{1}H}NMR** (125.8 MHz, $CDCl_3$) δ 193.4, 193.3, 147.3, 147.0, 138.4, 138.2, 129.1, 128.4, 127.8, 126.9, 126.6, 121.9, 29.3, 24.4; HRMS (ESI-TOF) *m/z*: $[M + Na]^+$ Calcd for $C_{16}H_{14}NaO_2S$ 293.0607; Found 293.0597.

*2-(4-Methylbenzyl)-3-(thien-3-ylmethyl)fumaraldehyde (**13b**):* A mixture of dry DMSO (0.38 mL) and CH_2Cl_2 (1.3 mL) was added slowly to a solution of oxalyl chloride (147 μL, 219 mg, 1.73 mmol, 2.5 equiv) in CH_2Cl_2 (2.5 mL) at (-78 ºC), and the mixture stirred for 30 min at the same temperature. The diol (**12b**) (200 mg, 0.69 mmol) in CH_2Cl_2 (1.7 mL) and DMSO (0.4 mL) was added dropwise, and the mixture was stirred for another (1.5 h) before dropwise addition of Et_3N (0.50 mL, 3.46 mmol). The reaction was left to warm to 20 ºC during (30 min). The reaction mixture was concentrated under reduced pressure and the product purified by flash column chromatography (100% CH_2Cl_2) to yield (**13b**) (170 mg, 0.60 mmol, 87%) as yellow solid. TLC: **R*f*** (CH_2Cl_2 100%) 0.75 yellow spot; **m.p.** 104-105 °C; **IR** (diamond-ATR): ν_{max}/cm^{-1} 3330, 3093, 2939, 2911, 2875, 2855, 2361, 2091, 1804, 1665, 1511, 1447, 1397, 1202, 1126, 1022, 938, 874, 832, 773, 750, 680, 625, 584, 490, 454, 417; **^{1}H NMR** (400.1 MHz, $CDCl_3$) δ 10.49 (s, 1H), 10.45 (s, 1H), 7.29 – 7.24 (m, 1H), 7.09 (d, *J* = 8.1 Hz, 2H), 7.02 (d, *J* = 8.1 Hz, 2H), 6.91 – 6.86 (m, 2H), 4.09 (d, *J* = 8.4 Hz, 4H), 2.30 (s, 3H, CH_3); **^{13}C{^{1}H}NMR** (101.6 MHz, $CDCl_3$) δ 193.5, 193.4, 147.5, 146.8, 138.5, 136.6, 135.1, 129.7, 128.3, 127.8, 126.6, 121.8, 28.9, 24.4, 21.1; HRMS (ESI-TOF) *m/z*: $[M + Na]^+$ Calcd for $C_{17}H_{16}NaO_2S$ 307.0763; Found 307.0780.

*2-(4-Isopropylbenzyl)-3-(thien-3-ylmethyl)succinaldehyde (**13c**):* Prepared by a method analogous to (**13a**) from (*E*)-2-(4-isopropylbenzyl)-3-(thien-3-ylmethyl)but-2-ene-1,4-diol (**12c**) (0.25 g, 0.79 mmol), to yield (**13c**) as a bright yellow solid (0.19 g, 0.61 mmol, 77%), TLC: **R*f*** (100% DCM) 0.73 yellow spot (easily visible to the eye); **IR** (diamond-ATR): ν_{max}/cm^{-1} 3331, 3091, 2957, 2907, 2767, 1667, 1513, 1465, 1447, 1397, 1192, 1128, 1020, 980, 938, 877, 830, 773, 681, 626, 582, 549, 506; **^{1}H NMR** (500.1 MHz, $CDCl_3$) δ 10.49 (s, 1H), 10.45 (s, 1H), 7.28 – 7.26 (m, 1H), 7.14 (d, *J* = 7.9 Hz, 2H), 7.05 (d, *J* = 7.9 Hz, 2H), 6.90 – 6.88 (m, 2H), 4.11 (s, 2H), 4.09 (s, 2H), 2.86 (hept, *J* = 6.9 Hz, 1H), 1.22 (d, *J* = 6.9 Hz, 6H); **^{13}C{^{1}H}NMR** (125.8 MHz, $CDCl_3$) δ 193.5, 193.4, 147.6, 147.5, 146.8, 138.5, 135.4, 128.3, 127.8, 127.1, 126.6, 121.9, 33.8, 28.9, 24.4, 24.1; HRMS (ESI-TOF) *m/z*: $[M + Na]^+$ Calcd for $C_{19}H_{20}O_2S$ 312.1178; Found 312.11918.

*2-(4-Methoxybenzyl)-3-(thien-3-ylmethyl)fumaraldehyde (**13d**):* Prepared by a method analogous to (**13a**) from diol (**12d**) (50 mg, 0.16 mmol) to provide compound (**13d**) as a yellow solid (needles on recrystallization from hot isopropanol) (39 mg, 0.13 mmol, 81%). TLC: **R*f*** (EtOAc:pentane, 3:2) 0.84; **m.p.** 120-121 °C; **IR** (diamond-ATR): ν_{max}/cm^{-1} 3332, 3091, 2938, 2911, 1751, 1667, 1608, 1582, 1512, 1445, 1397, 1306, 1244, 1179, 1129, 1025, 938, 877, 830, 774, 752, 704, 679, 625, 582, 528, 512, 480, 459; **^{1}H NMR** (500.1 MHz, $CDCl_3$) δ 10.49 (s, 1H), 10.44 (s, 1H), 7.29 – 7.24 (m, 1H), 7.05 (d, *J* = 8.7 Hz, 2H), 6.90 – 6.87 (m, 2H), 6.81 (d, *J* = 8.7 Hz, 2H), 4.10 (s, 2H), 4.06 (s, 2H), 3.77 (s, 3H); **^{13}C{^{1}H}NMR** (125.8 MHz, $CDCl_3$) δ 193.6, 193.4, 158.6, 147.6, 146.6, 138.5, 130.1, 129.5, 127.7, 126.6, 121.8, 114.5, 55.4, 28.5, 24.4;

MS (ESI+): *m/z* 323; HRMS (ESI-TOF) *m/z*: $[M + Na]^+$ Calcd for $C_{17}H_{16}NaO_3S$ 323.0712; Found 323.0721.

*2,3-Bis(thien-3-ylmethyl)fumaraldehyde (**22**):* Prepared by a method similar to (**13a**) from (*E*)-2,3-bis(thien-3-ylmethyl)but-2-ene-1,4-diol (**21**) (50 mg, 0.17 mmol), to yield (**19**) as a yellow solid (35 mg, 0.13 mmol, 73%). TLC: **R*f*** (2:1 DCM:pentane) 0.51, crystallized from hot *i*-PrOH on cooling to ambient. **IR** (diamond-ATR): ν_{max}/cm^{-1} 3090, 2976, 2941, 2910, 2873, 1665, 1529, 1446, 1395, 1240, 1194, 1159, 1125, 977, 941, 862, 829, 774, 675, 620, 569, 464, 425; **^{1}H NMR** (500.1 MHz, $CDCl_3$) δ 10.46 (s, 2H), 7.28 – 7.26 (m, 2H), 6.89 – 6.88 (m, 4H), 4.11 (s, 4H); **^{13}C{^{1}H}NMR** (125.8 MHz, $CDCl_3$) δ 193.2, 146.8, 138.4, 127.7, 126.7, 121.9, 24.4; HRMS (ESI-TOF) *m/z*: $[M + H]^+$ Calcd for $C_{14}H_{13}O_2S_2$ 277.0351; Found 277.0354.

*Cyclisation to anthra[2,3-b]thiophene using $TiCl_4$; representative example Anthra[2,3-b]thiophene (**1a**):* Dialdehyde (**13a**) (219 mg, 0.18 mmol) was dissolved in dry dichloroethane (5.4 mL) to form a yellow solution. The solution was cooled to 0 °C and $TiCl_4$ (**CAUTION!** Corrosive, toxic) (0.2 mL, 1.8 mmol, 2.1 equiv) added over 1 min at 0 °C forming a brown suspension of the $TiCl_4$-aldehyde adduct. The reaction mixture was stirred for 30 min at 0 °C and at rt for (4 h). During this time the reaction mixture became dark brown and viscous. TLC (9:1:1 pentane:EtOAc:CH_2Cl_2) shown consuming of the starting material (**13a**) while forming a shiny yellow precipitate. The reaction was cooled to 0 °C and 1:1 acetone:MeOH (5 mL) was slowly added forming immediate yellow precipitation of (**1a**). The crude mixture was filtered off onto Whatman glass microfiber GF/A on a 47 mm 3-piece (Hartley) filter, washed with 1:1 acetone:MeOH (3 × 5 mL) and sucked dry under a cushion of argon to provide yellow powder (138 mg, 0.59 mmol, 73%). The crude material could be further purified by vacuum sublimation (230-240 °C, 0.02 mbar) (Figure S1) to give shining bright yellow powders. **m.p.** >250 °C; **IR** (diamond-ATR): ν_{max}/cm^{-1} 3440, 2918, 2849, 1400, 1284, 1018, 955, 899, 825, 739, 727, 661, 470, 457; **^{1}H NMR** (500.1 MHz, $CDCl_3$) δ 8.61 (s, 1H), 8.55 (s, 1H), 8.53 (s, 1H), 8.51 (s, 1H), 8.04 – 8.00 (m, 2H), δ 7.50 – 7.40 (m, 4H); **^{13}C{^{1}H}NMR** (125.8 MHz, $CDCl_3$) δ 139.3, 138.1, 131.5, 131.3, 129.8, 129.7, 128.9, 128.3, 128.2, 126.7, 125.3, 125.1, 123.6, 121.9, 120.7; HRMS (ESI-TOF) *m/z*: [M +]Calcd for $C_{16}H_{10}S$ *m/z* 234.0503; Found 234.0500; **UV/Vis** (CH_2Cl_2, 10^{-4} M): λ_{max}/nm 435 (log ε 4.1), 410 (log ε 4.1), 389 (log ε 3.8), 368 (log ε 3.5). The data of this compound matches publish literatures values.[7,17,11]

*7-Methylanthra[2,3-b]thiophene (**1b**):* Prepared by a method equivalent to (**1a**) using: 2-(4-methylbenzyl)-3-(thien-3-ylmethyl)fumaraldehyde (**13b**) (200 mg, 0.7 mmol), $TiCl_4$ (0.15 mL, 1.46 mmol, 2.1 equiv) in 1,2-dichloroethane (4.5 mL) at 0 °C for 1 h then warmed to rt and stirred over (4 h) to yield (**1b**) as a brilliant yellow powder (145 mg, 0.58 mmol, 84%). Sublimation (200-210 °C, 0.05 mbar) afforded a brilliant yellow powder. **m.p.** >250 °C; **IR** (diamond-ATR): ν_{max}/cm^{-1} 3065, 3010, 2910, 2851, 1704, 1632, 1469, 1402, 1375, 1287, 1270, 1128, 1080, 1005, 961, 901, 827, 809, 792, 745, 723, 674, 658, 568, 469, 457; **^{1}H NMR** (500.1 MHz, $CDCl_3$) δ 8.59 – 8.46 (m, 4H), 7.93 (d, *J* = 8.7 Hz, 1H), 7.76 (s, 1H), 7.47 (d, *J* = 5.6 Hz, 1H), 7.40 (d, *J* = 5.6 Hz, 1H), 7.30 – 7.27 (m, 1H), 2.55 (s, 3H); **^{13}C{^{1}H}NMR** (125.8 MHz, $CDCl_3$) δ 139.2, 137.7, 134.7, 131.6, 130.3, 129.9, 129.4, 128.8, 128.3, 128.1, 126.3, 125.5, 125.0, 123.6, 121.8, 120.7, 22.2; **UV/Vis** (CH_2Cl_2, 10^{-4} M): λ_{max}/nm 437 (log ε 3.6), 412 (log ε 3.7), 390 (log ε 3.4), 360 (log ε 3.1), 343 (log ε 3.0); HRMS (ESI-TOF) *m/z*: M^+ Calcd for $C_{17}H_{12}S$ 248.0654; Found 248.0650; **Anal:** Calcd for $C_{17}H_{12}S$ C, 82.22; H, 4.87; Found C, 82.30; H, 4.90%.

*7-Isopropylanthra[2,3-b]thiophene (**1c**):* Prepared by a method analogous to (**1a**) using: 2-(4-isopropylbenzyl)-3-(thien-3-ylmethyl)succinaldehyde (**13c**) (150 mg, 0.48 mmol), $TiCl_4$ (0.1 mL, 1.0 mmol. 2.1 equiv) in 1,2-dichloroethane (3.1 mL) at 0 °C for 1.5 h and then warmed to 22 °C for 10 min to yield (**1c**) as shiny yellow powder (130 mg, 0.47 mmol, >99%). Sublimation (210-220 °C, 0.01 mbar) afforded a brilliant yellow powder. **m.p.** >250 °C; **IR** (diamond-ATR): ν_{max}/cm^{-1} 3070, 3015, 2955, 2926, 2900, 2863, 2100, 1631, 1510, 1470, 1380, 1309, 1284, 1182, 1128, 1081, 1039, 1016, 948, 904, 826, 803, 747, 726, 661, 620, 548, 470, 459; **^{1}H NMR** (500.1 MHz, $CDCl_3$) δ 8.53 (s, 1H), 8.52 (1H), 8.49 – 8.47 (m, 2H), 7.96 (d, *J* = 8.9 Hz, 1H), 7.78 (s, 1H), 7.47 (d, *J* = 5.7 Hz, 1H), 7.40 (d, *J* = 5.7 Hz, 1H), 7.37 (dd, *J* = 8.8, 1.7 Hz, 1H), 3.10 (hept, *J* = 7.0 Hz, 1H), 1.39 (d, *J* = 7.0 Hz, 6H); **^{13}C{^{1}H}NMR** (125.8 MHz, $CDCl_3$) δ 145.3, 139.2, 137.7, 131.6, 130.7, 129.9, 129.5, 128.7 128.3, 126.1, 126.0, 125.0, 123.6, 123.4, 121.8, 120.7, 34.5, 23.7; **UV/Vis** (CH_2Cl_2, 10^{-4} M): λ_{max}/nm 436 (log ε 3.5), 410 (log ε 3.7), 390 (log ε 3.6), 362 (log ε 3.4), 343 (log ε 3.4); HRMS (ESI-TOF) *m/z*: M^+ Calcd. for $C_{19}H_{16}S$ 276.0967; Found 276.0976; **Anal:** Calcd for $C_{19}H_{16}S$ C, 82.57; H, 5.84; Found C, 82.26; H, 5.96%.

*7-Methoxyanthra[2,3-b]thiophene (**1d**):* Prepared by a method analogous to (**1a**) using: 2-(4-methoxybenzyl)-3-(thien-3-ylmethyl)succinaldehyde (**13d**) (143 mg, 0.48 mmol), $TiCl_4$ (0.1 mL, 1.05 mmol. 2.2 equiv) in 1,2-dichloroethane (4.2 mL) at 0 °C for 2 h and then warmed to 22 °C for (1 h) to yield (**1d**) as a shiny yellow powder (104 mg, 0.39 mmol, 83%). Sublimation (210-220 °C, 0.02 mbar) afforded a brilliant yellow powder. **m.p.** >250 °C; **IR** (diamond-ATR): ν_{max}/cm^{-1} 3094, 3062, 3005, 2965, 2937, 2836, 1800, 1630, 1585, 1473, 1417, 1346, 1285, 1230, 1218, 1172, 1026, 951, 897, 816, 803, 744, 723, 675, 663, 539, 470, 456; **^{1}H NMR** (500.1 MHz, $CDCl_3$) δ 8.50 (s, 1H), 8.44 (m, 3H), 7.91 (d, *J* = 9.2 Hz, 1H), 7.48 (d, *J* = 5.6 Hz, 1H), 7.40 (d, *J* = 5.6 Hz, 1H), 7.19 (m, 1H), 7.14 (dd, *J* = 9.2, 2.5 Hz, 1H), 3.98 (s, 3H); **^{13}C{^{1}H}NMR** (125.8 MHz, $CDCl_3$) δ 157.0, 139.4, 137.1132.1, 130.2, 130, 128.9, 128.6, 128.4, 125.4, 124.3, 123.6, 121.2, 120.9, 120.8, 103.2, 55.4; **UV/Vis** (CH_2Cl_2, 10^{-4} M): λ_{max}/nm 443 (log ε 3.4), 418 (log ε 3.4), 395 (log ε 3.2), 378 (log ε 3.2), 358 (log ε 3.1), 340 (log ε 2.9); HRMS (ESI-TOF) *m/z*: M^+

Calcd for $C_{17}H_{12}OS$ 264.0603; Found 264.0611; **Anal:** Calcd for $C_{17}H_{12}OS$ C, 77.24; H, 4.58; Found C, 77.27; H, 4.49%.

Cyclisation using TiCl4; representative example of by-product formation, 6-(4-methylbenzyl)benzo[b]thiophene-5-carbaldehyde: To a solution of 2-(4-methylbenzyl)-3-(thien-3-ylmethyl)fumaraldehyde (**13b**) (100 mg, 0.35 mmol) in dry dichloroethane (2.3 mL) under argon, titanium tetrachloride (81 µL, 0.74 mmol, 2.1 equiv) was added slowly at (0 oC). The mixture was stirred at 0 °C for 45 mins, during which time it became dark brown-dark and vicious. TLC (10:1:1 pentane:EtOAc:DCM) indicated complete consumption of the starting material (**13b**) (**R*f*** 0.41). The reaction was stopped, and at 0 °C 1:1 acetone:MeOH (5 mL) was slowly added causing immediate yellow precipitation. The mixture was filtered off onto Whatman glass microfiber GF/A on a 47-mm 3-piece (Hartley) filter and washed with 1:1 acetone:MeOH, the half closure product is eluted with the (1:1 acetone:MeOH) wash. The filtered yellow powder precipitate was 7-methylanthra[2,3-*b*]thiophene (**1b**) which accounted for 57% of the mass balance. The organic wash solution was concentrated by high vacuum and purified by preparative TLC (8:1:1 pentane:EtOAc:DCM) to yield (6-(4-methylbenzyl)benzo[*b*]thiophene-5-carbaldehyde) (30.0 mg, 0.11 mmol, 32%) as yellow oil; **R*f*** (9:1:1 pentane:DCM:EtOAc) 0.80; **IR** (diamond-ATR): ν_{max}/cm^{-1} 3099, 3018, 2917, 2854, 2724, 2093, 1760, 1683, 1594, 1539, 1512, 1492, 1450, 1404, 1386, 1314, 1227, 1183, 1155, 1125, 1077, 1006, 902, 878, 833, 794, 761, 748, 725, 699, 645, 620, 577, 535, 490, 469, 429; **^{1}H NMR** (500.1 MHz, $CDCl_3$) δ 10.29 (s, 1H), 8.31 (s, 1H), 7.70 (s, 1H), 7.48 (d, J = 5.5 Hz, 1H), 7.43 (d, *J* = 5.5 Hz, 1H), δ 7.10 (d, *J* = 8.0 Hz, 2H), 7.07 (d, *J* = 8.0 Hz, 2H), 4.52 (s, 2H), 2.32 (s, 3H); **^{13}C{^{1}H}NMR** (125.8 MHz, $CDCl_3$) δ 192.4, 145.4, 138.3, 138.2, 137.4, 135.9, 131.3, 129.4, 128.9, 128.8, 127.6, 125.0, 124.5, 38.2, 21.1; HRMS (ESI-TOF) *m/z*: $[M + Na]^+$ Calcd for $C_{17}H_{14}NaOS$ 289.0658; Found 289.0662.

Naphtho[2,3-b:6,7-b']dithiophene (2): The yellow solution of dialdehyde (**18**) (200 mg, 0.72 mmol) in anhydrous dichloroethane (4.5 mL) was cooled to -15 °C and treated under argon with neat $TiCl_4$ (0.15 mL, 1.6 mmol, 2.2 equiv) over ca. 1 min at -15 °C (**CARE!** $TiCl_4$ is a corrosive reactive Lewis acid; quicker additions may cause uncontrolled reaction). The dark brown thick suspension was allowed to stir at -15 °C (1 h). After this time TLC (10:1:1 pentane:EtOAc:DCM) shown that the starting material was consumed. The reaction was stopped and 1:1 acetone:MeOH (2 mL) was slowly added at -15 °C (**CARE!** vigorous reaction) leading to a pale yellow precipitate of the target product (**2**). This was filtered off onto Whatman glass microfiber GF/A using a 47mm 3-piece (Hartley) filter, washed with 1:1 acetone:MeOH (1 × 3 mL) and sucked dry under a cushion of argon to provide (**2**) as a pale yellow powder (140 mg, 0.85 mmol, 81%). This material was pure enough to use directly in further chemistry, but could be further purified by vacuum sublimation (245-250 °C, 0.01 mbar, Figure S2, supporting infomation). **m.p.** >250 °C; **IR** (diamond-ATR): ν_{max}/cm^{-1} 3094, 3065, 1705, 1505, 1439, 1382, 1311, 1258, 1139, 1078, 1014, 897, 826, 743, 675, 550, 501, 470, 457; **^{1}H NMR** (500.1 MHz, $CDCl_3$) δ 8.51 (s, 2H), 8.40 (s, 2H), 7.50 (d, *J* = 5.6 Hz, 2H), 7.43 (d, *J* = 5.6 Hz, 2H); **^{13}C{^{1}H}NMR** (125.8 MHz, $CDCl_3$) δ 138.9, 137.6, 129.0, 128.5, 123.6, 121.0, 120.9; **UV/Vis** (CH_2Cl_2, 10^{-4} M): λ_{max}/nm 402 (log ε 3.8), 380 (log ε 3.7), 360 (log ε 3.3), 431 (log ε 3.2); HRMS (ESI-TOF) *m/z*: M^+ Calcd for $C_{14}H_8S_2$ 240.0061; Found 240.0054. The data of this compound matches publish literatures values.[9]

▪ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI:
Sublimation set-up, ^{1}H, ^{13}C{^{1}H} NMR and UV-vis spectra (pdf).

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