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Highly regioselective lithiation of inter-ring carbon of bis(thien-2yl)methane: a general *meso*-elaboration protocol

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ABSTRACT

Bis(thien-2yl)methane is regioselectively lithiated at the inter-ring methylene carbon using dimsyl anion in THF at 0 °C; quenching with appropriate electrophile furnishes *meso*-elaborated derivatives, exclusively with synthetic advantage.

1. Introduction

Lithiation of heterocyclic species such as thiophene is ubiquitous in organic chemistry and has attracted the attention of many chemists.[1] However, methods for regioselective *meso*-elaboration of bis(heterocyclyl)methane derivatives are more scarce. Based upon the rationalisation of the acidity of the ring vs inter-ring (*meso* or C_α) carbon centres, which determines the proclivity of lithiation of either of these positions with proper choice of a base and solvent, we have recently, disclosed pliable routes for the *meso*-elaboration of bis(pyrrole-2yl)methane[2] and bis(furan-2yl)methane,[3] but notice that the *meso*-elaboration of bis(thien-2yl)methane has been controversial. In a programme aimed at the synthesis of functionally decorated cyclic conjugated chemical entities, we required a robust general protocol to append tailor-made substituents at the inter-ring carbon of bis(thienyl-2yl)methane.

Approaches reported in the literature for obtaining bis(thien-2yl)methane derivatives have been limited to the traditional use of carbonyl substrates to create inter-ring carbon unit through acid catalysed[4] condensation reaction with thiophene. Anhydrous zinc chloride assisted condensation[5] of *N*-(α-benzotriazolylalkyl)-carbamate (itself a condensation product of benzotriazole, an aldehyde and an alkyl carbamate) with an excess of thiophene derivative furnishes bis(thien-2yl)methane derivative, bearing *meso*-substituent derived from the carbonyl component. Likewise, tris-2-thienylmethane has been prepared from the condensation of thiophene with thiophene-2-carboxaldehyde in the presence of P_2O_5 as catalyst.[6,7]

Substituted thiophene derivatives are also important building blocks for pharmaceuticals,[8] conducting polymers,[9] liquid crystals,[10] novel porphyrinoids,[11] molecular machines,[12] molecular switches[13] etc. Recently, a $AuCl_3$ catalysed condensation of C-2(5) methyl thiophene and an aryl aldehyde leading to *meso*-aryl bis(thien-2yl)methane derivatives has been reported.[14] However, the applicability of these synthetic routes has been limited to the synthesis of *meso*-unsubstituted or a few *meso*-aryl bis(thien-2yl)methane derivatives, owing to the operational limitations of carbonyl substrates in addition to their side reactions of the aliphatic counterparts. Thus the use of a regioselective lithiation-substitution approach remains an attractive alternative to produce *meso*-substituted bis(thien-2yl)methane derivatives.

2. Results and discussion

Critically dependent upon temperature, the lithiation of bis(thien-2yl)methane **1** using excess of *n*-BuLi in ether at −5 to 0 °C followed by treatment with carbon dioxide has been reported to furnish a mixture of the 5-mono- and 5,5′-dicarboxylic acid.[15] Above 5 °C, complete dimetalation is accomplished, while only mono-lithiation is observed below −10 °C, regardless of the amount of the base used. However, the use of this protocol to accomplish 5,5′-diformylation has been reported to fail.[16] In yet another reaction, lithiation of **1** with *n*-BuLi in ethereal solvents at 0 °C selectively furnished corresponding alcohol,[17] after quenching

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with benzaldehyde. Use of co-additives such as DMSO and TMEDA in combination with THF,[17] in very high unexplained excess (1:1–1:5, v/v) has been suggested, wherein lithiation of **1** with *n*-BuLi in a mixture of THF/TMEDA or DMSO (1:1, v/v)[17] at −60 °C, followed by quenching with benzaldehyde, led to C_α substitution. However, a C-5 substituted product was obtained when the reaction was conducted using only 1.5 equiv of TMEDA. However, this protocol of using a large excess of additional 'high-solvating'[18] solvents has been limited only to a few examples and cannot be purported to be a general protocol.

Using appropriate activating agents, through aggregative activation phenomenon,[19] it is possible to modify the bacisity/nucleophilicity of a metalating agent as well as the regioselectivity of metallation.[3] The correlation of the reported pK_a values[20,21] suggests C-5 position of **1** to be less acidic (pK_a 32.5) in comparison with C_α (pK_a<30.0). Consequently, it is envisaged that dimsyl anion [pK_a (DMSO) 35.0][21] should in principle deprotonate C_α proton in preference to C-5H, and render regioselectivity to the deprotonation and subsequent substitution reaction, through the activation of the *meso*-position as proposed in Figure 1.

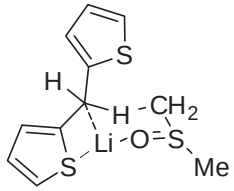
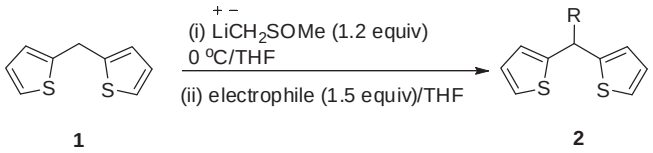


Figure 1. Proposed transition state in deprotonation of the *meso*-position of **1**.

To test this hypothesis, when **1** in anhydrous THF at 0 °C was added to a stirring dimsyl anion (1.2 equiv) [generated from DMSO and *n*-BuLi (1.2 equiv each) in anhydrous THF, 0 °C] solution (Scheme 1), under the blanket of anhydrous nitrogen atmosphere, a turbid red anion was formed, which after stirring for 0.5 h was quenched with an anhydrous solution of iodomethane (1.5 equiv). Upon completion (TLC) the reaction was treated with saturated aqueous solution of ammonium chloride and extracted with ethyl acetate. Removal of solvent and column chromatography of the residue furnished 2,2′-(ethane-1,1-diyl)dithiophene **2a** in 98% yield. Similar reactions of **1** with a number of electrophiles such as alkyl/aralkyl halides, carbon dioxide, chloroacetonitrile, aldehyde and ketone furnished the corresponding *meso*-elaborated bis(thien-2yl)methane derivatives **2** in good to excellent yield (Table 1). Reaction of *meso*-lithiated **1** with acetone, which failed in the reported protocol (using THF/DMSO, 1:1, v/v)[17] was also successful and furnished the required product in 85% isolable yield. As depicted in the entries in Table 1, a number of long aliphatic chains in addition to other functionalities could be conveniently appended at the *meso*-position of **1**.



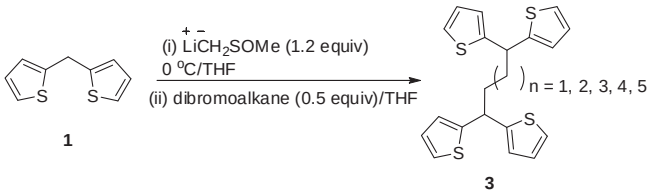
Scheme 1. *meso*-Elaboration of bis(thien-2yl)methane **1**.

Covalently linked multiporphyrinoids have been attracting continuous attention owing to the requirement of interesting properties such as amphiphilicity, required for photodynamic cancer therapy.[22] *meso*–*meso*-Linked bis(thien-2yl)methane **3** derivatives constitute important building blocks for obtaining such architecturally sophisticated porphyrinoid designs of immense practical utility. In this direction, bridged bis(thien-2yl)methane **3** derivatives (Scheme 2) may be visualised as fascinating building blocks for exploring novel connectivities between porphyrinoids. We were intrigued by the prospect of applying this methodology to the synthesis of a number of bridged bis(thien-2yl)methane **3** derivatives.

Table 1
Synthesis of *meso*-functionalized bis(thien-2yl)methane **2**

Entry	Electrophile	R	Product (% yield[a])
1	CH_3I	CH_3	**2a**, 98
2	C_2H_5Br	C_2H_5Br	**2b**, 97
3	*n*-C_3H_7Br	*n*-C_3H_7	**2c**, 93
4	*n*-C_4H_9Br	*n*-C_4H_9	**2d**, 94
5	*n*-$C_5H_{11}Br$	*n*-C_5H_{11}	**2e**, 93
6	*n*-$C_{10}H_{21}Br$	*n*-$C_{10}H_{21}$	**2f**, 95
7	*n*-$C_{11}H_{23}Br$	*n*-$C_{11}H_{23}$	**2g**, 97
8	$C_6H_5CH_2Br$	$C_6H_5CH_2$	**2h**, 84
9	CO_2	COOH	**2i**, 85
10	$ClCH_2CN$	CH_2CN	**2j**, 78
11	CH_3COCH_3	$(CH_3)_2C(OH)$	**2k**, 85
12	3,4-$(CH_3O)_2$–C_6H_3CHO	3,4-$(CH_3O)_2$–$C_6H_3CH(OH)$	**2l**, 82

[a] Isolated yield.



Scheme 2. Synthesis of *meso*-linked bis(thien-2yl)methane **3**.

Treatment of anion of **1** with ethylene dibromide furnished compound **3a** in 86% isolated yield (Table 2, entry 1). Other possible products such as *meso*-spirocyclic bis(thien-2yl)methane derivatives were not detected even upon increasing the amount of the base. Similar reactions with a number of other dihalides with varying chain lengths furnished corresponding *meso*–*meso* bridged compounds **3b**–**e**, in a synthetically useful manner (Table 2). To the best of our knowledge, this is the first report on the synthesis of bridged bis(thein-2yl)methane **3** derivatives. The envisaged alternate carbonyl approach would be limited by the non-availability of the corresponding dialdehydes. It is worth mentioning that none of the aldehydes required for obtaining compounds reported in Table 2 and functionalized aldehydes corresponding to entries **9**–**12** (Table 1), are commercially available[23] and the physical state of the available ones such as acetaldehyde (oligomeric) and glutaraldehyde (aqueous solution) are cumbersome to use especially under anhydrous conditions.

Table 2
Synthesis of *meso*-linked bis(thien-2yl)methane **3**

Entry	Electrophile	*n*	Product (% yield[a])
1	$BrCH_2CH_2Br$	1	**3a**, 98
2	$BrCH_2CH_2CH_2Br$	2	**3b**, 97
3	$BrCH_2CH_2CH_2CH_2Br$	3	**3c**, 93
4	$BrCH_2CH_2CH_2CH_2CH_2Br$	4	**3d**, 94
5	$BrCH_2CH_2CH_2H_2CH_2CH_2Br$	5	**3e**, 93

[a] Isolated yield.

3. Conclusions

In summary, we have developed an efficient, highly regioselective and useful general method for the *meso*-elaboration of bis(thien-2yl)methane using near stoichiometric amount of dimsyl anion. It is reasonable to assume that present work provides better understanding of the lithiation process of **1** and the methodology

avoids the use of vulnerable carbonyl components. We have also demonstrated the first synthesis of *meso*-meso bridged bis(thien-2yl)methane derivatives, in a synthetically useful manner. Currently we are exploring the use of *meso*-elaborated bis(thien-2yl)methane derivatives **2** as well as **3** in the synthesis of cyclic conjugated chemical entities.

4. Experimental

4.1. General

All liquid reagents were dried/purified following recommended drying agents and/or distilled over 4 Å molecular sieves. THF was dried (Na/benzophenone ketyl) under nitrogen and drawn with hypodermic glass syringes. ^{1}H NMR and ^{13}C NMR spectra have been recorded on JEOL-FT NMR-AL at 300 MHz and Bruker Avance at 400 MHz, with TMS as internal standard using $CDCl_3$ as deuterated solvent. Mass spectrum (LCMS) was recorded on Bruker Daltonics esquire 3000 spectrometer. IR spectrum was recorded on FTIR-SHIMADZU 8400 Fourier-transform spectrophotometer in range 400–4000 cm^{-1} using KBr/$CHCl_3$ as medium. The purity of the solid product was checked by elemental analysis performed at Department of Chemistry, GND University, Amritsar on Thermoelectron FLASH EA1112, CHNS analyzer. All reported yields are isolated yields. Freshly prepared *n*-BuLi (2.3 N solution in hexanes) was used and true normality was determined as necessary, according to the titration method outlined by Kofron et al.[24] The commercially available thiophene was distilled before use. Bis(thien-2yl)methane was synthesized from reported protocol.[4b] Melting points were determined in open capillaries and are uncorrected. For column chromatography silica gel (60–120 mesh) was employed and eluents were ethyl acetate/hexane mixtures.

4.2. General procedure for synthesis of compounds 2a–l

To a clear solution of freshly distilled DMSO (0.24 mL, 3.07 mmol) in THF at 0 °C was added a solution of *n*-BuLi (1.45 mL, 3.33 mmol) and the reaction mixture was stirred for 15 min. To this bis(thien-2yl)methane **1** (500 mg, 2.77 mmol) dissolved in THF was added through cannula at same temperature. The reaction mixture was stirred for 30 min whereupon a turbid red coloured anion was generated. The electrophile (4.15 mmol) dissolved in dry THF (10 mL) was then added dropwise, and the reaction mixture was stirred for 30 min, quenched with saturated aqueous solution of NH_4Cl. The reaction mixture was extracted with EtOAC (3×20 mL), the combined organic phases were dried over Na_2SO_4, and the solvent was removed under reduced pressure. The products were purified by flash chromatography using silica gel (60–120 mesh) and mixture of ethyl acetate/hexane as eluents. The yields of the purified products **2a–l** are reported in Table 1.

*4.2.1. 2,2′-(Ethane-1,1-diyl)dithiophene (**2a**).* Colourless oil; [found: C, 61.76; H, 5.31; S, 32.82. $C_{10}H_{10}S_2$ requires C, 61.85; H, 5.15; S, 32.98%]; R_f (hexane) 0.94; ν_{max} ($CHCl_3$) 2875, 1082, 1025, 846, 710 cm^{-1}; δ_H (400 MHz, $CDCl_3$) 7.22–7.24 (2H, m, ArH), 6.86–6.97 (2H, m, ArH), 6.86–6.89 (2H, m, ArH), 4.62 (1H, q, *J* 7.2 Hz, *meso* CH), 1.76 (3H, d, *J* 7.2 Hz, CH_3); δ_C (75 MHz, $CDCl_3$) 150.0, 126.5, 123.7, 123.6, 36.1, 24.5; *m*/*z* 217 (M+23).

*4.2.2. 2,2′-(Propane-1,1-diyl)dithiophene (**2b**).* Colourless oil; [found: C, 63.12; H, 5.56; S, 30.92. $C_{11}H_{12}S_2$ requires C, 63.46; H, 5.76; S, 30.76%]; R_f (hexane) 0.94; ν_{max} ($CHCl_3$) 2870, 1080, 1025, 845, 710 cm^{-1}; δ_H (300 MHz, $CDCl_3$) 7.14–7.17 (2H, m, ArH), 6.89–6.93 (2H, m, ArH), 6.86–6.89 (2H, m, ArH), 4.30 (1H, m, *meso* CH), 2.17 (2H, m, CH_2CH_3), 0.79 (3H, t, *J* 7.2 Hz, CH_2CH_3); δ_C (75 MHz, $CDCl_3$) 148.7, 126.4, 124.0, 123.6, 43.7, 31.9, 12.5; *m*/*z* 231 (M+23).

*4.2.3. 2,2′-(Butane-1,1-diyl)dithiophene (**2c**).* Colourless oil; [found: C, 64.75; H, 6.09; S, 29.02. $C_{12}H_{14}S_2$ requires C, 64.86; H, 6.30; S, 28.82%]; R_f (hexane) 0.94; ν_{max} ($CHCl_3$) 2920, 1450, 1030, 845 cm^{-1}; δ_H (300 MHz, $CDCl_3$) 7.14–7.17 (2H, m, ArH), 6.90–6.93 (2H, m, ArH), 6.86–6.88 (2H, m, ArH), 4.43 (1H, t, *J* 7.5 Hz, *meso* CH), 2.07 (2H, m, $CH_3CH_2CH_2$), 1.34 (2H, m, $CH_2CH_2CH_3$), 0.93 (3H, t, *J* 7.2 Hz, $CH_2CH_2CH_3$); δ_C (75 MHz, $CDCl_3$) 148.9, 126.4, 123.9, 123.5, 41.6, 40.9, 20.9, 13.7; *m*/*z* 245 (M+23).

*4.2.4. 2,2′-(Pentane-1,1-diyl)dithiophene (**2d**).* Colourless oil; [found: C, 65.86; H, 6.73; S, 26.94. $C_{13}H_{16}S_2$ requires C, 66.10; H, 6.77; S, 27.11%]; R_f (hexane) 0.94; ν_{max} ($CHCl_3$) 2925, 1080, 1030, 840, 705 cm^{-1}; δ_H (300 MHz, $CDCl_3$) 7.15–7.17 (2H, m, ArH), 6.89–6.94 (2H, m, ArH), 6.86–6.88 (2H, m, ArH), 4.40 (1H, t, *J* 7.5 Hz, *meso* CH), 2.10 (2H, m, $CH_2(CH_2)_2CH_3$), 1.31 (4H, m, $CH_2(CH_2)_2CH_3$), 0.87 (3H, t, *J* 6.9 Hz, CH_2CH_3); δ_C (75 MHz, $CDCl_3$) 149.0, 126.4, 123.9, 123.5, 41.9, 38.9, 29.9, 22.3, 13.9; *m*/*z* 259 (M+23).

*4.2.5. 2,2′-(Hexane-1,1-diyl)dithiophene (**2e**).* Colourless oil; [found: C, 66.86; H, 6.83; S, 25.94. $C_{14}H_{18}S_2$ requires C, 67.20; H, 7.20; S, 25.60%]; R_f (hexane) 0.95; ν_{max} ($CHCl_3$) 2910, 1460, 1075, 1035, 835 cm^{-1}; δ_H (300 MHz, $CDCl_3$) 7.10–7.25 (2H, m, ArH), 6.88–7.03 (2H, m, ArH), 6.80–6.87 (2H, m, ArH), 4.41 (1H, t, *J* 7.6 Hz, *meso* CH), 2.08 (2H, m, CH_2CH_2), 1.30 (6H, m, $CH_2(CH_2)_3CH_3$), 0.85 (3H, t, *J* 6.9 Hz, CH_2CH_3); δ_C (75 MHz, $CDCl_3$) 149.0, 126.4, 123.9, 123.5, 41.9, 38.8, 31.5, 27.4, 22.4, 14.0; *m*/*z* 273 (M+23).

*4.2.6. 2,2′-(Undecane-1,1-diyl)dithiophene (**2f**).* Colourless oil; [found: C, 71.35; H, 8.72; S, 19.76. $C_{19}H_{28}S_2$ requires C, 71.25; H, 8.75; S, 20.00%]; R_f (hexane) 0.96; ν_{max} ($CHCl_3$) 2920, 1450, 1040, 840, 705 cm^{-1}; δ_H (300 MHz, $CDCl_3$) 7.14–7.16 (2H, m, ArH), 6.90–6.93 (2H, m, ArH), 6.85–6.87 (2H, m, ArH), 4.40 (1H, t, *J* 7.8 Hz, *meso* CH), 2.08 (2H, m, $CH_2(CH_2)_8CH_3$), 1.29 (16H, m, $CH_2(CH_2)_8CH_3$), 0.87 (3H, t, *J* 6.7 Hz, CH_2CH_3); δ_C (75 MHz, $CDCl_3$) 149.0, 126.4, 123.9, 123.5, 41.9, 38.8, 31.8, 29.5, 29.4, 29.3, 27.7, 22.6, 14.1; *m*/*z* 343 (M+23).

*4.2.7. 2,2′-(Dodecane-1,1-diyl)dithiophene (**2g**).* Colourless oil; [found: C, 72.04; H, 9.32; S, 19.01. $C_{20}H_{30}S_2$ requires C, 71.85; H, 8.98; S, 19.16%]; R_f (hexane) 0.96; ν_{max} ($CHCl_3$) 2930, 1450, 1025, 850, 710 cm^{-1}; δ_H (300 MHz, $CDCl_3$) 7.13–7.16 (2H, m, ArH), 6.89–6.94 (2H, m, ArH), 6.85–6.88 (2H, m, ArH), 4.40 (1H, t, *J* 7.5 Hz, *meso* CH), 2.07 (2H, m, $CH_2(CH_2)_9CH_3$), 1.29 (18H, m, $CH_2(CH_2)_9CH_3$), 0.87 (3H, t, *J* 6.7 Hz, CH_3); δ_C (75 MHz, $CDCl_3$) 149.0, 126.4, 123.9, 123.5, 41.9, 38.8, 31.8, 29.6, 29.5, 29.4, 29.3, 29.2, 27.7, 22.6, 14.1; *m*/*z* 357 (M+23).

*4.2.8. 2,2′-(2-Phenylethane-1,1-diyl)dithiophene (**2h**).* Colourless oil; [found: C, 70.89; H, 5.37; S, 24.01. $C_{16}H_{14}S_2$ requires C, 71.11; H, 5.18; S, 23.70%]; R_f (5% EtOAc/hexane) 0.30; ν_{max} ($CHCl_3$) 1520, 1040, 710, 680 cm^{-1}; δ_H (300 MHz, $CDCl_3$) 7.19–7.23 (5H, m, ArH), 7.15–7.18 (2H, m, ArH), 7.04–7.15 (2H, m, ArH), 6.80–6.89 (2H, m, ArH), 4.72 (1H, t, *J* 7.6 Hz, *meso* CH), 3.39 (2H, d, *J* 7.8 Hz, CH_2Ar); δ_C (75 MHz, $CDCl_3$) 147.8, 139.1, 128.9, 128.1, 126.4, 126.2, 124.4, 123.8, 45.1, 44.0; *m*/*z* 293 (M+23).

*4.2.9. 2,2-Di(thiophen-2-yl)acetic acid (**2i**).* White solid; [found: C, 53.36; H, 3.28; S, 28.75. $C_{10}H_8O_2S_2$ requires C, 53.57; H, 3.57; S, 28.57%]; R_f (5% EtOAc/hexane) 0.75; mp: 163–165 °C (DCM/hexane); ν_{max} (KBr) 1700, 1265, 1020, 850, 705 cm^{-1}; δ_H (300 MHz, $CDCl_3$) 7.09–7.19 (2H, m, ArH), 6.78–6.80 (4H, m, ArH), 5.16 (1H, s, *meso* CH); δ_C (75 MHz, $CDCl_3$) 172.2, 145.6, 126.3, 125.7, 124.2, 50.1; *m*/*z* 247 (M+23).

*4.2.10. 3,3-Di(thiophen-2-yl)propanenitrile (**2j**).* Colourless oil; [found: C, 60.05; H, 4.35; S, 29.02; N, 6.24. $C_{11}H_9NS_2$ requires C,

60.27; H, 4.10; S, 29.22; N, 6.39%]; R_f (10% EtOAc/hexane) 0.82; ν_{max} ($CHCl_3$) 1520, 1040, 710, 680 cm^{-1}; δ_H (300 MHz, $CDCl_3$) 7.22–7.31 (2H, m, ArH), 6.99–7.04 (2H, m, ArH), 6.90–6.99 (2H, m, ArH), 4.89 (1H, t, *J* 7.2 Hz, *meso* CH), 3.10 (2H, d, *J* 7.2 Hz, $CNCH_2$); δ_C (75 MHz, $CDCl_3$) 143.9, 126.8, 125.2, 125.0, 117.4, 37.7, 27.1; *m*/*z* 242 (M+23).

*4.2.11. 2-Methyl-1,1-di(thiophen-2-yl)propan-2-ol (**2k**).* Colourless oil; [found: C, 60.21; H, 5.69; S, 27.12. $C_{12}H_{14}OS_2$ requires C, 60.50; H, 5.88; S, 26.89%]; R_f (10% EtOAc/hexane) 0.76; ν_{max} ($CHCl_3$) 3600, 1375, 1080, 1050, 1025, 845, 710 cm^{-1}; δ_H (300 MHz, $CDCl_3$) 7.17–7.19 (2H, m, ArH), 7.02–7.02 (2H, s, ArH), 6.92–6.93 (2H, m, ArH), 4.53 (1H, s, *meso* CH), 1.82 (1H, br s, exchanged with D_2O, OH), 1.27 (6H, s, $C(CH_3)_2$); δ_C (75 MHz, $CDCl_3$) 143.3, 126.5, 126.3, 124.5, 72.7, 53.8, 28.4; *m*/*z* 261 (M+23).

*4.2.12. 1-(3,4-Dimethoxyphenyl)-2,2-di(thiophen-2-yl)ethanol (**2l**).* White solid; [found: C, 62.21; H, 5.49; S, 18.12. $C_{18}H_{18}O_3S_2$ requires C, 62.42; H, 5.20; S, 18.49%]; R_f (15% EtOAc/hexane) 0.75; mp: 60–62 °C (DCM/hexane); ν_{max} (KBr) 3050, 2830, 1340, 1030, 850, 705 cm^{-1}; δ_H (300 MHz, $CDCl_3$) 7.24–7.26 (3H, m, ArH), 6.96–7.11 (1H, m, ArH), 6.69–6.85 (5H, m, ArH), 5.14 (1H, d, *J* 4.8 Hz, CHOH), 4.73 (1H, d, *J* 6.9 Hz, *meso* CH), 3.84 (3H, s, OCH_3), 3.75 (3H, s, OCH_3), 2.35 (1H, d, *J* 2.7 Hz, exchanged with D_2O, OH); δ_C (75 MHz, $CDCl_3$) 148.4, 148.3, 144.1, 142.8, 133.9, 126.4, 126.4, 125.6, 124.9, 124.2, 118.9, 110.4, 109.5, 78.0, 55.7, 55.6, 50.8; *m*/*z* 369 (M+23).

4.3. General procedure for synthesis of compounds 3a–e

To a clear solution of freshly distilled DMSO (0.24 mL, 3.07 mmol) in THF at 0 °C was added a solution of *n*-BuLi (1.45 mL, 3.33 mmol) and the reaction mixture was stirred for 15 min. To this bis(thien-2yl)methane **1** (500 mg, 2.17 mmol) dissolved in THF was added through cannula at same temperature. The reaction mixture was stirred for 30 min, whereupon a turbid red coloured anion was generated. The electrophile (1.08 mmol) dissolved in dry THF (10 mL) was then added dropwise, and the reaction mixture was stirred for 30 min, quenched with saturated aqueous solution of NH_4Cl. The reaction mixture was extracted with ethyl acetate (20 mL×3), the combined organic phases were dried over Na_2SO_4, filtered and solvent was removed under reduced pressure. The product was purified by flash chromatography using silica gel (60–120 mesh) and mixture of ethyl acetate/hexanes as eluents. The yields of the purified products **3a–e** are reported in Table 2.

*4.3.1. 1,1,4,4-Tetra(thiophen-2-yl)butane (**3a**).* White solid; [found: C, 61.88; H, 4.67; S, 33.07. $C_{20}H_{18}S_4$ requires C, 62.17; H, 4.66; S, 33.16%]; R_f (5% EtOAc/hexane) 0.41; mp: 114–115 °C (DCM/hexane); ν_{max} (KBr) 2870, 1080, 1035, 845, 700 cm^{-1}; δ_H (300 MHz, $CDCl_3$) 7.13–7.15 (4H, m, ArH), 6.84–6.91 (4H, m, ArH), 6.77–6.84 (4H, m, ArH), 4.44 (2H, br s, *meso* CH), 2.13 (4H, m, CH_2CH_2); δ_C (75 MHz, $CDCl_3$) 144.0, 126.9, 125.3, 125.0, 38.5, 37.8; *m*/*z* 387 (M+1).

*4.3.2. 1,1,5,5-Tetra(thiophen-2-yl)pentane (**3b**).* White solid; [found: C, 62.86; H, 5.37; S, 32.17. $C_{21}H_{20}S_4$ requires C, 63.00; H, 5.00; S, 32.00%]; R_f (5% EtOAc/hexane) 0.41; mp: 105–106 °C (DCM/hexane); ν_{max} (KBr) 2860, 1080, 1035, 850, 700 cm^{-1}; δ_H (400 MHz, $CDCl_3$) 7.07–7.12 (4H, m, ArH), 6.87–6.92 (4H, m, ArH), 6.77–6.82 (4H, m, ArH), 4.36 (2H, t, *J* 7.6 Hz, *meso* CH), 2.11 (4H, m, $CH_2CH_2CH_2$), 1.37 (2H, m, $CH_2CH_2CH_2$); δ_C (100 MHz, $CDCl_3$) 148.5, 126.4, 124.0, 123.6, 41.6, 38.4, 25.7; *m*/*z* 401 (M+1).

*4.3.3. 1,1,6,6-Tetra(thiophen-2-yl)hexane (**3c**).* White solid; [found: C, 63.95; H, 5.49; S, 30.72. $C_{22}H_{22}S_4$ requires C, 63.76; H, 5.31; S, 30.91%]; R_f (5% EtOAc/hexane) 0.44; mp: 90–92 °C (DCM/hexane); ν_{max} (KBr) 2860, 1080, 1036, 845, 710 cm^{-1}; δ_H (300 MHz, $CDCl_3$) 7.11–7.22 (4H, m, ArH), 6.77–6.99 (8H, m, ArH), 4.37 (2H, t, *J* 7.5 Hz, *meso* CH), 2.08 (4H, m, $CH_2(CH_2)_2CH_2$), 1.36 (4H, m, $CH_2(CH_2)_2CH_2$); δ_C (100 MHz, $CDCl_3$) 148.7, 126.4, 124.0, 123.6, 41.8, 38.6, 27.3; *m*/*z* 415 (M+1).

*4.3.4. 1,1,7,7-Tetra(thiophen-2-yl)heptane (**3d**).* White solid; [found: C, 64.21; H, 5.83; S, 29.74. $C_{23}H_{24}S_4$ requires C, 64.48; H, 5.60; S, 29.90%]; R_f (5% EtOAc/hexane) 0.44; mp: 75–76 °C (DCM/hexane); ν_{max} (KBr) 2865, 1080, 1035, 840, 710 cm^{-1}; δ_H (300 MHz, $CDCl_3$) 7.13–7.15 (4H, m, ArH), 6.84–6.94 (8H, m, ArH), 4.38 (2H, t, *J* 7.5 Hz, *meso* CH), 2.05 (4H, m, $CH_2(CH_2)_3CH_2$), 1.29 (6H, m, $CH_2(CH_2)_3CH_2$); δ_C (75 MHz, $CDCl_3$) 148.8, 126.4, 123.9, 123.5, 41.9, 38.7, 28.9, 27.5; *m*/*z* 429 (M+1).

*4.3.5. 1,1,8,8-Tetra(thiophen-2-yl)octane (**3e**).* White solid; [found: C, 65.10; H, 6.21; S, 29.29. $C_{24}H_{26}S_4$ requires C, 65.15; H, 5.88; S, 28.95%]; R_f (5% EtOAc/hexane) 0.44; mp: 59–60 °C (DCM/hexane); ν_{max} (KBr) 2870, 1035, 840, 710 cm^{-1}; δ_H (300 MHz, $CDCl_3$) 7.11–7.15 (4H, m, ArH), 6.83–6.91 (8H, m, ArH), 4.38 (2H, t, *J* 7.5 Hz, *meso* CH), 2.05 (4H, m, $CH_2(CH_2)_4CH_2$), 1.29 (8H, m, $CH_2(CH_2)_4CH_2$); δ_C (75 MHz, $CDCl_3$) 148.9, 126.4, 123.9, 123.5, 41.9, 38.8, 29.0, 27.6; *m*/*z* 443 (M+1).

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References and notes

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