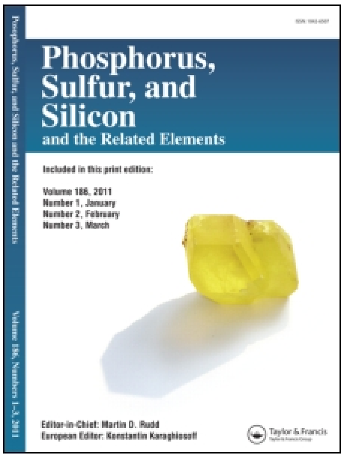

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CLAY-CATALYZED THIOALKYLATION OF THIOPHENES AND BENZO[*b*]THIOPHENES

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A method for the direct thioalkylation of thiophene (**1**) and benzo[*b*]thiophene (**7**) by reaction of either heterocycle with an alkyldisulfide using a $ZnCl_2$-modified montmorillonite clay catalyst is described. The clay-catalyzed reaction of **1** with excess dimethyl disulfide (DMDS) over 24 hours in refluxing chlorobenzene yielded a mixture of *bis*-, *tris*-, and *tetrakis*(methylthio)thiophenes (**2–5**) from which 2,3,5-*tris*(methylthio)thiophene (**4a**) and *tetrakis*(methylthio)thiophene (**5**) could be isolated in modest yield. Prolonging the reaction time gave (**4a**) and **5** in isolated yields of 21 and 16% respectively. Carrying out the same reaction in a sealed autoclave at 150°C with an air overpressure resulted in a clean and rapid (5 h) conversion of thiophene to the tetramethylthio-derivative **5** in moderate isolated yield (50%). In a similar manner **7** could be converted to 2,3-*bis*(methylthio)benzo[*b*]thiophene (**8a**) or 2,3,6-*tris*- and 2,3,6,7-*tetrakis*(methylthio) derivatives **9** and **10a** by clay catalyzed reactions with DMDS in halogenated solvents. **7** was also found to react smoothly with diethyl- and di-*n*-propyl disulfides yielding 2,3-*bis*(alkylthio)benzo[*b*]thiophenes (**8b–c**) in good isolated yields (73 and 64%).

Key words: Thiophene, benzo[*b*]thiophene, clayzic, K10, thioalkylation.

INTRODUCTION

Sulfur-substituted thiophenes and (methylthio)thiophenes **2–5** have been the subject of recent interest[1–5] in connection with general synthesis and in the preparation of electrically conducting thiophene derivatives. A recent paper by Gronowitz and coworkers[6] reported the synthesis of several *bis*- and *tris*(methylthio)thiophenes by lithiation of bromothiophenes and subsequent reaction of the thienyl-lithium derivatives with dimethyl disulfide (DMDS). This method is quite useful but requires preparation of appropriately substituted bromothiophenes and the use of expensive solvents and reagents. Other methods for the synthesis of (methylthio)thiophene derivatives have utilized alkylation of the sodium salts of thiophene thiols,[7] thioalkylation of thienyl lithiums[8–11] or multi-step ring closure reaction.[12–16] In all cases, several steps are required to prepare the necessary reagents and intermediates.

Only 2- and 3-(methylthio)benzo[*b*]thiophenes have been reported,[17] each compound having been prepared by reaction of lithio-derivatives of benzo[*b*]thiophene (**7**) with DMDS. In the case of the 3-derivative, the 3-lithio compound was prepared from 3-bromobenzo[*b*]thiophene. The 2-lithio derivative was prepared by direct metalation of **7**.

Recent work in our laboratories has shown that benzylation of thiophene using a $ZnCl_2$-modified montmorillonite clay (K10, ex-Fluka Chemical Company) catalyst proceeds efficiently giving a high yield of the kinetically-controlled 2-benzyl iso-

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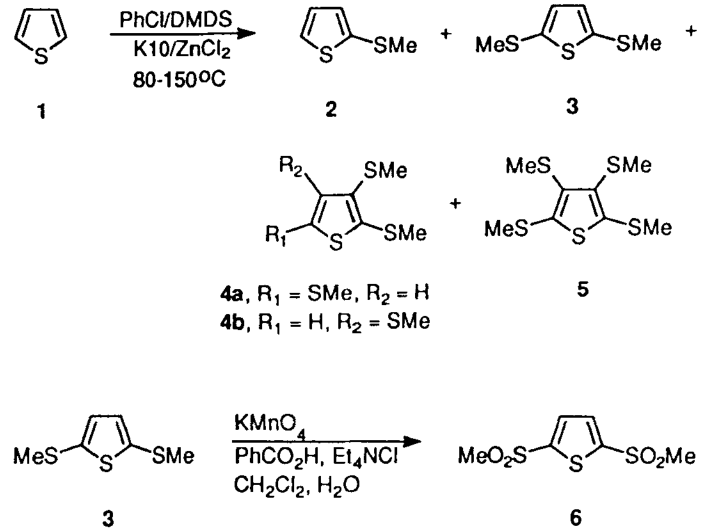
mer.[18] In part, the success of this reaction stems from the limited free space available in the mesopores of the clay which prevents polymerization of **1**. In contrast, benzylation of **1** using either $AlCl_3$ or $ZnCl_2$ in free solution results in considerable polymerization and poor yields of a mixture of 2- and 3-benzylthiophene and polybenzylated products. Under these conditions, it is thought that polymerization occurs via protonation of **1** at either the 2- or 3-positions and reaction of the resultant carbocation with another molecule of **1**.[19] Repeat of these steps leads to formation of polymeric products. Clearly, such reactions would be limited within the pore structure of the clay. Other studies have shown that modified clay catalysts are useful for a variety of transformations on benzothiophene[20,21] and benzene derivatives.[22-27]

We reasoned that $ZnCl_2$-modified K10 montmorillonite, commonly referred to as clayzic, should facilitate thioalkylation of aromatic and heteroaromatic compounds by coordination of one sulfur atom of an alkyldisulfide to a zinc cation on the clay surface rendering the adjacent S-atom electrophilic in nature (see Scheme III). Moreover, as in the case of the benzylation reaction described previously, it was envisaged that the mesoporous structure of the clay would inhibit polymerization of **1** or the methylthio-products. In this paper, we describe the successful synthesis of a variety of (methylthio)thiophene and (alkylthio)benzo[*b*]thiophene derivatives using clayzic and other modified K10 montmorillonite clays. In the case of **1**, it was possible to prepare the *tetrakis*(methylthio) derivative **5** in good yield in a one-step synthesis. These syntheses are believed to be the only method reported so far for direct introduction of alkylthio groups into **1** and **7**.

RESULTS AND DISCUSSION

Thiomethylation of **1**. Reaction of **1** with 1 equivalent of DMDS and clayzic in chlorobenzene solution at 80°C was slow such that only low yields of methylthio-products **2–5** were obtained (Scheme I). GC-MS analysis of the crude product showed that *di*- and *tri*-substituted products, **3** and **4a**, were the major products. However, only very low isolated yields of **3** and **4a** were obtained since only 1 equivalent of DMDS was used. By increasing the quantity of DMDS to 10 equivalents, extending the heating period to 48 h and placing a balloon on the reflux condenser to reduce thiophene loss by evaporation, the *tri*- and *tetra*(thiomethyl)-products **4a** and **5** were formed as major products. The structures of **2–5** were confirmed by comparison of spectra to published information.[6] In addition, **3** was characterized as its di-sulfone **6** to confirm that it was the 2,5-disubstituted derivative.

It was noticed that better yields of products were obtained if the reactions were conducted in an air atmosphere as opposed to in an argon atmosphere. Thus, when **1** was heated at 150°C for 5 h with 8 equivalents of DMDS and the clayzic in an autoclave overpressured with air (1060 psi, 1 equivalent of O_2 with respect to DMDS), a clean product mixture containing 81% **5**, 11% **4a** and 8% **3** was obtained. From this mixture, **5** was obtained in 50% isolated yield. Use of lower amounts of DMDS under the same conditions gave mixtures in low isolated yields containing **2**, **3**, **4a** and **5** although **4a** was found as a major product when 0.5–2.0 equivalents of DMDS was used (see Table I for a summary of these experiments). It proved very difficult to isolate **4a** in an analytically pure state since it appears to undergo



SCHEME I. Reaction of 1 with dimethyl disulfide in the presence of K10-$ZnCl_2$.

TABLE I

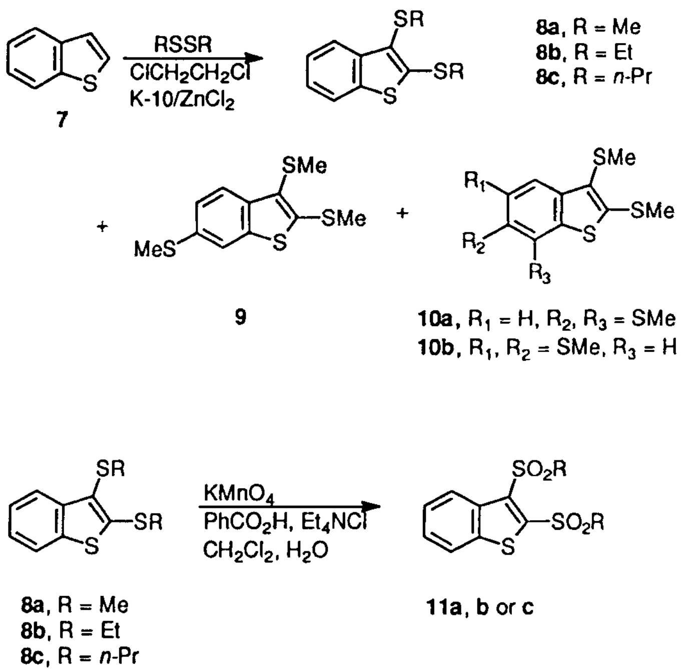
Autoclave reaction of thiophene[a] at 150°C for 5 h in the presence of air[b] and clayzic (20 g)

	Concentration of DMDS[c]		
Products	0.5 (eq.)	2 (eq.)	8 (eq.)
3	33%	6.6%	9%
4a	50%	15%	12%
5	18%	78%	88%
Crude yield	1.37 g	5.99 g	8.18 g

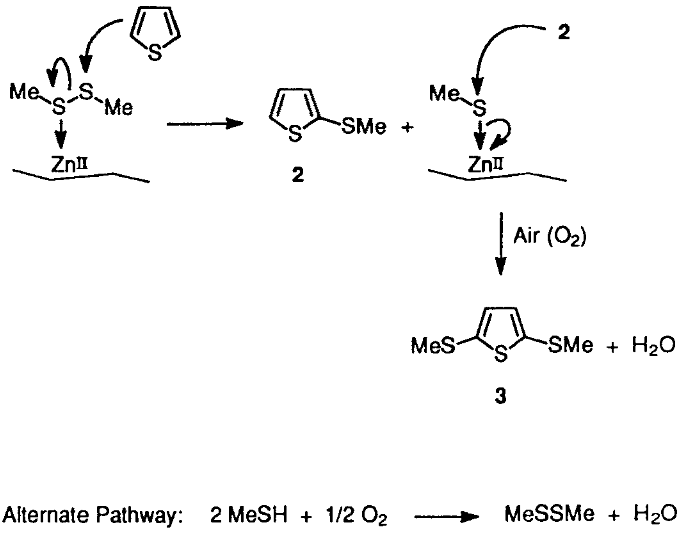
[a] (5.25 g, 62.5 mmol).
[b] 1.1 equivalents of air was added with respect to the amount of DMDS used.
[c] With respect to thiophene.

rearrangement to the 2,3,4-*tris*(methylthio) derivative **4b** when subjected to either distillation or standard chromatographic separation procedures. The rearrangement of **4a** to **4b** is not unexpected as it has been shown previously[28,29] that 2,3,5-*tris*(alkylthio)-derivatives undergo rearrangement to 2,3,4-*tris*-compounds under acidic conditions. In this work, it is suspected that clay fines not removed during product isolation facilitated rearrangement during the attempted distillation of **4a** and that chromatographic absorbents possess enough acid sites to promote rearrangement.

Thioalkylation of **7**. As was the case for the thiomethylation of **1**, it was not possible to isolate mono-methylthio products by treating **7** with stoichiometric quantities of DMDS and excess clayzic. However, with excess DMDS, the 2,3-*bis*(dimethylthio)-derivative **8a** was obtained in good yield (see Scheme II and Table II). It was noticed that the reaction proceeded quickly in the initial stages but required prolonged reflux to obtain complete reaction. Similarly, reaction of **7** with diethyl- and di-*n*-propyl disulfides in the presence of clayzic gave 2,3-*bis*(alkylthio)benzothiophenes **8b** and **8c** in isolated yields of 73 and 64% respectively. No trace of other disubstituted products were observed in the crude reaction product mixtures. Previous work[30,31] has shown that **7** undergoes electrophilic disubstitution either at



SCHEME II. Reaction of **7** with alkyl disulfides in the presence of K-10/ZnCl$_2$.



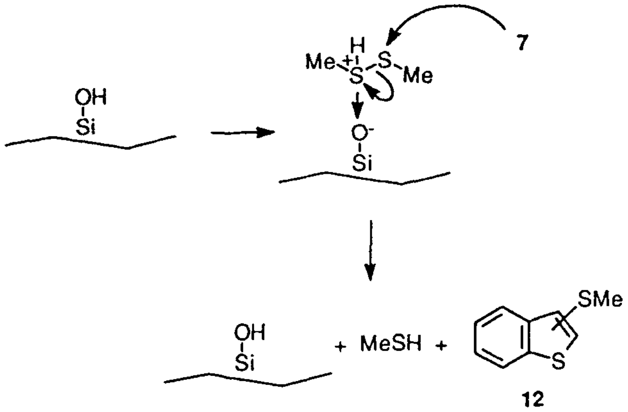
SCHEME III. Proposed mechanism of thioalkylation at Lewis sites.

the 2,3- or 2,6-positions depending on the steric bulk of the incoming electrophile. NMR spectra of (**8a–c**) did not allow conclusive structural assignment. Consequently in order to confirm the structures of **8a–c** which were isolated as oils, these compounds were oxidized to sulfone derivatives **11a–c** using KMnO$_4$ under phase transfer conditions.[32] The X-ray structure of the sulfone **8b** showed that disubstitution had occurred at the 2,3-positions.[33] Based on the X-ray structure determination of **8b** and

TABLE II

Reaction of benzo[*b*]thiophene with *n*-alkyldisulfides (10 eq.) in clayzic

Disulfide	Solvent	Time (hr)	Temp (°C)	O_2 Pressure	Yield (%)	Product
Methyl	1,2-$EtCl_2$	20	83	no	66	**8a**
Methyl	PhCl	6	150	yes	74	**8a**
Ethyl	1,2-$EtCl_2$	40	83	no	73	**8b**
n-propyl	1,2-$EtCl_2$	48	83	no	64	**8c**



SCHEME IV. Proposed mechanism of thioalkylation at Brönsted sites.

the similarity of the NMR spectra of **8a–c** and **11a–c**, we conclude that disubstitution had occurred in the 2,3-positions in each case.

Since no trace of other disubstituted products were observed in the crude product mixtures it is possible that both thiomethyl groups were introduced into **7** in a concerted manner from the same DMDS molecule. This possibility was examined by reacting **7** with a mixture of excess DMDS and diethyl disulfide (DEDS) in the presence of clayzic with the expectation that a mixture of the 2,3-diethyl and 2,3-dimethyl derivatives would be obtained if the reaction occurred by a concerted mechanism. GC-MS analysis of the crude product showed that a 25:50:25 mixture of *bis*(methylthio), methylethylthio- and *bis*(diethylthio)-benzothiophenes was produced. In addition, the crude reaction mixture contained DMDS, DEDS and methylethyl disulfide suggesting that scrambling of the reagent disulfides was probably occurring at the catalyst surface. This suggestion was confirmed by isolation of the mixed disulfide when the reaction was carried out in the absence of **7**. Furthermore, reaction of di-*t*-butyl disulfide and DMDS with clayzic in refluxing dichloroethane over 1 h resulted in formation of *t*-butylmethyl disulfide as 50% of the reaction mixture (GC-MS analysis). Thus, it can be concluded that clayzic is an efficient catalyst for synthesis of mixed disulfides but that this reaction precludes determination of whether thiomethylation of **7** occurs by a concerted process.

The activity of the clayzic is thought[24] to be due, in the main, to Lewis acid sites created by addition of $ZnCl_2$ to the clay. However, we reasoned that Bronsted acid sites might also promote thioalkylation (see Scheme IV). To test this hypothesis, sulfuric acid was added to K10 to produce Bronsted sites. This modified catalyst proved to be exceptionally reactive as the *bis*(thiomethyl)-product **8a** was obtained in a shorter reaction time in comparison to the standard clayzic catalyst along with significant quantities of 2,3,6-*tris*(methylthio)benzothiophene (**9**) and traces of two tetrathiomethyl derivatives (Scheme II). Prolonged reaction in refluxing dichloroethane and addition of further sulfuric acid and DMDS resulted in 2,3,6,7-*tetrakis*(thiomethyl)benzothiophene (**10a**) being produced as a significant product along with lesser amounts of 2,3,5,6-*tetrakis*(methylthio)benzothiophene (**10b**) and the *tris*(thiomethyl) derivative **9**. The two isomers of **10** were produced from **7** in 13% yield when 20 equivalents of DMDS and H_2SO_4 was used in the presence of K10. Separation of two isomers **10a** and **10b** was achieved using preparative HPLC chromatography. The substitution pattern of **10a** was confirmed by X-ray analysis[34] as NMR spectra did not allow a conclusive structural determination. This structure and the observation that **10a** is the major tetra-substituted product infers that the third methylthio-substituent entered position 6. This conclusion is in accord with the observation that benzothiophenes containing electron donating substituents in the 2 and 3 positions undergoes substitution at position 6. NMR data (see experimental section) shows conclusively that the minor tetra-substituted product **10b** has the 2,3,5,6-substitution pattern.

Reaction of **7** with DMDS and the clayzic catalyst in the presence of air and excess DMDS in chlorobenzene solution lead to **8a** in high yield (74%) (see Table II). As was the case in reactions with **1**, the presence of air resulted in cleaner reactions and higher isolated yields of product. However, prolonged reaction of **7** in the presence of air did not lead to polysubstituted products **9**, **10a**, and **10b**. These products were formed only with K10 doped with H_2SO_4.

To test the efficiency of clayzic in comparison to $ZnCl_2$, H_2SO_4 and K10, the thiomethylation of **1** and **7** was carried out with K10, $ZnCl_2$ and H_2SO_4 as separate catalysts. K10 and H_2SO_4 showed no reaction under the standard conditions in the presence of **1** and **7**. $ZnCl_2$ resulted in only poor conversion of **1** and **7** to thiomethylated products.

Comments on the Mechanism of Thiomethylation

The general mechanism outlined in Scheme III shows interaction of DMDS with a Lewis site (Zn II) at the clay surface and subsequent reaction with **1**. The proton released by the substitution reaction will likely be picked up by methylthiolate anion to form methanethiol bound at the surface. Further reaction of bound methanethiol with thiophene or a (methylthio)thiophene product is unlikely because it would require loss of a hydride ion from the reaction intermediate. If hydride loss did occur, hydrogen might have been observed as a reaction product. However, hydrogen has not been detected. Consequently, methanethiol would build up in the system and compete with DMDS for Lewis sites on the catalyst surface. It was noted earlier that in the presence of air, reactions proceeded more rapidly and gave poly-substituted derivatives in the case of **1** if sufficient disulfide was used. The presence of O_2 in the system could facilitate thiomethylation reactions in two ways. Firstly, it could offer an alternate pathway, presumable radical in nature, for removal of hydrogen during reaction of a heteroaromatic species with methanethiol coordinated to a Lewis site. Secondly, it could simply oxidize two methanethiol molecules to DMDS and water and free-up catalyst sites for reactions with the disulfide. It is expected that the water formed in either process would interact with the clay to form Bronsted sites.

In addition to acceleration of the reactions by air, it was shown that the rate and degree of thiomethylation of **7** was increased when K10 was doped with H_2SO_4. The doping procedure probably increases the concentration of Bronsted sites on the clay surface adding to the Lewis sites provided by Zn(II). Reaction could occur at Bronsted sites by protonation of the disulfide and subsequent reaction as shown in Scheme IV. This sequence results in the re-formation of the bronsted site but, as previously, the associated production of methanethiol could still decrease the rate of reaction by occupying the active sites.

Thiomethylation of **1** with H_2SO_4 and K10 resulted in only very poor yields of **2–5** presumably as a result of acid catalyzed polymerization of **1**, a well known[19] and troublesome reaction encountered during standard Friedel-Crafts alkylation of thiophene. This observation stresses the importance of employing clay catalysts with predominantly Lewis sites for reactions with thiophene.

CONCLUSIONS

A one-step method for the thiomethylation and thioalkylation of **1** and **7** using clayzic and acid modified clayzic catalysts has been established. In the case of **1**, thiomethylation is enhanced by the presence of O_2 (air). Thiomethylation of **7** is enhanced either by the presence of air or by doping the clay catalyst with H_2SO_4. These reactions constitute the only direct synthetic method for the preparation of thiomethyl-thiophenes and offer a new method for the formation of C—S bonds in thiophenic substrates. Future reports will describe the application of these methods to benzene derivatives and other aromatic systems.

EXPERIMENTAL

General. Organic chemicals were obtained from commercial suppliers and were used without purification. Solvents were dried and purified according to standard procedures. NMR spectra were recorded on a Bruker AC200 or AM400 spectrometer in $CDCl_3$. Chemical shifts are reported in parts per million (ppm) internally referred to TMS. IR spectra were obtained on a Mattson 4030 galaxy series FTIR spectrometer. Mass spectra were obtained on a Hewlett Packard HP5890. Melting points were taken on a Fisher-Johns melting point apparatus and are uncorrected. Elemental analyses were obtained by D. Fox on a Control Equipment Corporation 440 EA, in the Analytical Service Laboratories of the Department of Chemistry at The University of Calgary. Preparative HPLC were done on a Varian 5000 Liquid Chromatograph using a Whatman Partisil M20 10/50 column and hexane as eluent.

K10/ZnCl$_2$ (Clayzic) Catalyst Preparation. K10 montmorillonite (Fluka Chemical Company, used as received) was modified by addition of $ZnCl_2$ (2 mmol per gram of clay) using procedures described previously. The modified catalyst was activated by heating at 150°C for 24 h and was stored in a desiccator. In some experiments, K10, heated to 150°C for 24 h was activated by addition of 98% sulfuric acid directly to the reaction mixture.

General Procedure for the Thiomethylation of **1** *at Standard Pressure in an Argon Atmosphere.* A mixture of **1** (5 mL, 62.5 mmol), DMDS (45 mL, 0.5 mol) and clayzic (20 g) in chlorobenzene (100 mL) was heated under reflux in an argon atmosphere for 48 h. The reaction mixture was cooled and filtered and excess DMDS and solvent were removed by rotary evaporation of the filtrate. The crude product was dissolved in dichloromethane and the solution was decolorized by treatment with activated charcoal. Filtration through an alumina plug and evaporation of the solvent left a pale yellow oil which was distilled under vacuum to yield a pale yellow oil (2.86 g, 21%) consisting of 85% 2,3,5-*tris*-(methylthio)-thiophene (**4a**) and 15% of the 2,3,4-isomer, b.p. 90°C at 0.01 mmHg, δ_H (200 MHz) 6.90 (1H, s), 2.47 (3H, s), 2.45 (3H, s) and 2.43 (3H, s) and 2,3,4,5-*tetrakis*(methylthio)thiophene **5** (2.68 g, 16%) as a pale yellow oil, b.p. 105°C at 0.01 mmHg. (Found: C, 35.48; H, 4.53; $C_8H_{12}S_3$ requires C, 35.79; H, 4.51%); ν_{max} (neat) 2984, 2917, 1431, 1420, 1372, 1308, 970, and 882 cm^{-1}, δ_c (50 MHz) 140.8 (2q), 138.4 (2q), 19.6 ($2CH_3$) and 19.2 ($2CH_3$); m/z 268 (M^+, 100%).

General Procedure for the Thiomethylation of **1** *to Prepare* **3**, **4a**, **5**, *and Thiomethylation of* **7** *to Prepare* **8a** *Under Air Pressure.* Reagents, in the proportions detailed in Table I, were placed in a 300 mL capacity, Magnedrive stirred (1000 rpm) autoclave fitted with an internal cooling coil and thermocouple. The system was sealed and was pressure tested with air to 1000 psi. If no leaks were observed, the pressure was adjusted to attain an equimolar quantity of oxygen with respect to the quantity of DMDS used in the experiment. Details of reagents used, reaction conditions and products obtained are reported in Table I. After the autoclave had been heated at the desired conditions, the system was cooled by passing water through the internal coil. The reaction mixtures were recovered from the autoclave and were filtered to remove the catalyst. Evaporation of the filtrates afforded dark brown oils which were re-dissolved in hexane:toluene (85:15). Filtration of these solutions through alumina plugs and evaporation of the solvent yielded the crude products as pale yellow oils. The individual products were isolated as follows.

Isolation of 2,5-bis(methylthio)thiophene (**3**) *and 2,3,5-tris(methylthio)thiophene* (**4a**). Kugelrohr distillation of the product from the reaction of thiophene (5 mL, 62.5 mmol) with DMDS (0.5 eq.) under air pressure gave **3** (0.41 g, 3.7%), b.p. 60°C at 0.01 mmHg, as a pale yellow oil with spectral characteristics identical to those published previously[6] and **4a** (0.68 g, 4.9%), b.p. 90°C at 0.01 mmHg, with spectroscopic properties identical to those described earlier.

Isolation of 2,3,4,5-tetrakis(methylthio)thiophene (**5**). Distillation of the crude product obtained from the reaction of thiophene (5 mL, 62.5 mmol) with DMDS (8 eq.) under air pressure yielded **5** (8.4 g, 50%), b.p. 105°C at 0.01 mmHg, displaying spectroscopic properties identical to those recorded earlier.

2,5-bis(methylsulfonyl)thiophene (**6**). A solution of potassium permanganate (1.74 g, 10.96 mmol) in water (50 mL) was added to a solution of **3** (0.484 g, 2.7 mmol), benzoic acid (0.33 g, 2.74 mmol), tetraethylammonium chloride (0.07 g, 0.43 mmol) in dichloromethane (25 mL) and the reaction mixture was stirred vigorously for 4 h. Aqueous concentrated sodium metabisulfite solution was added until the mixture attained a beige colour. The resultant mixture was filtered through a celite pad and the organic layer was washed with 1 M aqueous hydrazine hydrochloride solution (20 mL), saturated sodium carbonate solution (20 mL) and with saturated brine (20 mL). Evaporation of the dried ($MgSO_4$) organic solution left a white solid, which was recrystallized from ethanol to yield **6** (0.56 g, 85%), mp 168–171° (lit.[35] 174–175°C); (Found: C, 29.57; H, 3.73. $C_6H_8O_4S_3$ requires C, 29.99; H, 3.36%); ν_{max} (KBr) 3018, 2929, 2365, 1314, 1136, 1041, 958, and 762 cm^{-1}; δ_H (200 MHz) 7.86 (2H, s) and 3.38 (6H, s); δ_c (50 MHz) 148.9 (2q), 134.0 (2CH), and 45.9 ($2CH_3$); m/z 240 (M^+, 100%).

2,3-bis(methylthio)benzo[b]thiophene (**8a**). A suspension of clayzic (10 g) and **7** (1 g, 7.5 mmol), DMDS (7.05 g, 75 mmol) and 1,2-dichloroethane (50 mL) was stirred under reflux for 20 h. The cooled reaction mixture was filtered through an alumina plug (30 g) and the filtrate was evaporated yielding a yellow oil. Kuglerohr distillation at reduced pressure afforded **8a** as a pale yellow oil (1.12 g, 66%), b.p. 110°C at 0.25 mmHg. (Found: C, 53.57; H, 4.46; m/z 225.9947. $C_{10}H_{10}S_3$ requires C, 53.06; H, 4.45%; m/z 225.9945); ν_{max} (neat) 2918, 1465, 1450, 1417, 1248, 906, 754 and 731 cm^{-1}; δ_H (400 MHz) 7.88 (1H, dd, $J_o = 8.0$, $J_m = 1.7$, $J_p = 0.6$ Hz), 7.75 (1H, dd, $J_o = 8.0$, $J_m = 1.5$, $J_p = 0.8$ Hz), 7.41 (1H, m), 7.32 (1H, m), 2.66 (3H, s) and 2.37 (3H, s); δ_c (100 MHz) 145.1 (q), 140.7 (q), 138.6 (q), 124.9 (CH), 124.7 (q), 124.0 (CH), 122.1 (CH), 121.9 (CH), 18.4 (CH_3) and 18.1 (CH_3); m/z 226 (M^+, 100%).

2,3-bis(ethylthio)benzo[b]thiophene (**8b**). In a similar fashion **8b** was prepared using diethyl disulfide (9.16 g, 7.5 mmol) and a heating period of 40 h. The crude product was obtained as yellow oil which on Kuglerohr distillation at reduced pressure afforded **8b** as a pale yellow oil (1.39 g, 73%), b.p. 100°C at 0.025 mmHg. (Found: C, 56.51; H, 5.61. $C_{12}H_{14}S_3$ requires C, 56.65; H, 5.55%); ν_{max} (neat) 2970, 2924, 1448, 1413, 1260, 1245, 752 and 729 cm^{-1}; δ_H (400 MHz) 7.91 (1H, dd, $J_o = 8.0$, $J_m = 1.3$, $J_p = 0.65$ Hz), 7.74 (1H, dd, $J_o = 8.0$, $J_m = 1.8$, $J_p = 0.89$ Hz), 7.75 (1H, m), 7.33 (1H, m), 3.13 (2H, q), 2.85 (2H, q), 1.42 (3H, t) and 1.20 (3H, t); δ_c (100 MHz) 144 (q), 141.3 (q), 139.0 (q), 125.4 (q), 124.8 (CH), 124.2 (CH), 122.6 (CH), 121.8 (CH), 30.2 (CH_2), 29.5 (CH_2), 15.2 (CH_3) and 14.8 (CH_3); m/z 254 (M^+, 100%).

2,3-bis(n-propylthio)benzo[b]thiophene (**8c**). **8c** was prepared using the procedure described for **8a** but with di-*n*-propyl disulfide (11.27 g, 7.5 mmol) and a heating period of 48 h. Kuglerohr distillation of the crude product at reduced pressure gave **8c** as a yellow oil (1.34 g, 64%), b.p. 117°C at 0.025 mmHg. (Found: C, 58.97; H, 6.37; m/z 282.0579. $C_{14}H_{18}S_3$ requires C, 59.53; H, 6.42%; m/z 282.0570); ν_{max} (neat) 2962, 2929, 2867, 1458, 1450, 1413, 1375, 1290, 1234, 1014, 754 and 729 cm^{-1}; δ_H 7.90 (1H, dd, $J_o = 7.2$, $J_m = 1.3$, $J_p = 0.8$ Hz), 7.73 (1H, dd, $J_o = 7.0$, $J_m = 1.6$, $J_p = 0.97$ Hz), 7.4 (1H, m), 7.32 (1H, m), 3.06 (2H, t), 2.80 (2H, t), 1.77 (2H, m), 1.56 (2H, m), 1.07 (3H, t) and 0.99 (3H, t); δ_c (100 MHz) 144 (q), 141.2 (q), 138.9 (q), 125.4 (q), 124.7 (CH), 124.2 (CH), 122.5 (CH), 121.8 (CH), 38.0 (CH_2), 37.4 (CH_2), 23.4 (CH_2), 23.0 (CH_2) and 13.3 ($2CH_3$); m/z 282 (M^+, 100%).

Preparation of 2,3-bis(alkylsulfonyl)benzo[b]thiophenes (**11a–c**). These compounds were oxidized using the procedure described for the preparation of **6** and were obtained as white solid after the isolation procedure.

2,3-bis(methylsulfonyl)benzo[b]thiophene (**11a**). The crude product was recrystallized from ethanol to afford white platelets **11a** (0.46 g, 87%), m.p. 222–223°C. (Found: C, 41.13; H, 3.34. $C_{10}H_{10}O_4S_3$ requires C, 41.37; H, 3.47%); ν_{max} (nujol) 1582, 1459, 1366, 1311, 1205, 1138, 1019 and 965 cm^{-1}; δ_H (400 MHz) 8.69 (1H, m), 7.95 (1H, m), 7.62 (2H, m), 3.65 (3H, s); δ_c (100 MHz) 150 (q), 139.6 (q), 136.4 (q), 135 (q), 128.4 (CH), 127.2 (CH), 125.9 (CH), 122.6 (CH), 45.9 (CH_3) and 45.5 (CH_3); m/z 290 (M^+, 100%).

2,3-bis(ethylsulfonyl)benzo[b]thiophene (**11b**). Recrystallized from ethanol to afforded white platelets **11b** (0.8 g, 80%), m.p. 136–137°C. (Found: C, 45.38; H, 4.14. $C_{12}H_{14}O_4S_3$ requires C, 45.27; H, 4.43%); ν_{max} (nujol) 1374, 1324, 1136, 1011, 962 and 725 cm^{-1}; δ_H (400 MHz) 8.68 (1H, m), 7.95 (1H, m), 7.60 (2H, m), 3.84 (2H, q), 3.56 (2H, q) and 1.45–1.23 (6H, 2t); δ_c (100 MHz) 148.7 (q), 139.8 (q), 137.4 (q), 134 (q), 128.1 (CH), 127 (CH), 126.1 (CH), 122.3 (CH), 52.1 (CH_2), 52.0 (CH_2), 7.4 (CH_3) and 6.7 (CH_3); m/z 318 (M^+, 100%).

2,3-bis(n-propylsulfonyl)benzo[b]thiophene (**11c**). The crude product was recrystallized from *iso*-propanol to afford white platelets **11c** (0.6 g, 69%), m.p. 138–139°C. (Found: C, 48.75; H, 5.30. $C_{14}H_{18}O_4S_3$ requires C, 48.53; H, 5.24%); ν_{max} (nujol) 1581, 1456, 1407, 1396, 1308, 1244, 1200, 1133, 1009, 916, 852, 765 and 729 cm^{-1}; δ_H (400 MHz) 8.69 (1H, m), 7.95 (1H, m), 7.62 (2H, m) 3.80 (2H, m), 3.52 (2H, m), 1.87 (4H, m) and 1.07 (6H, m); δ_c (100 MHz) 149.3 (q), 139.8 (q), 137.2 (q), 134.5 (q), 128.1 (CH), 127.0 (CH), 126.0 (CH), 122.3 (CH), 59.2 ($2CH_2$), 16.6 (CH_2), 15.9 (CH_2), 12.9 (CH_3) and 12.8 (CH_3); m/z 346 (M^+, 70%).

2,3,6-tri(methylthio)benzo[b]thiophene (**9**). Concentrated sulfuric acid (4.2 mL, 75 mmol) was added dropwise to a stirred, refluxing mixture of K10 (10 g), **7** (1 g, 7.5 mmol) and DMDS (7.05 g, 75 mmol) in 1,2-dichloroethane (40 mL). After 1 h, the reaction mixture was filtered through an alumina plug (10 g) and the solvent was evaporated. Kuglerohr distillation of residual brown oil gave **9** as an orange oil (0.68 g, 33%), b.p. 135°C at 0.025 mmHg which solidified (m.p. 76–78°C) on standing (3 months). (Found: C, 48.43; H, 4.27. $C_{11}H_{12}S_4$ requires, C, 48.49; H, 4.44); ν_{max} (neat) 2983, 2916, 1582, 1418, 1375, 1355, 1312, 969, 955, 810 and 757 cm^{-1}; δ_H (400 MHz) 7.74 (1H, d, $J = 8.5$ Hz), 7.6 (1H, d, $J = 1.7$ Hz), 7.32 (1H, dd, $J = 8.3$, 1.7 Hz), 2.62 (3H, s), 2.53 (3H, s) and 2.35 (3H, s); δ_c (100 MHz); 143.8 (q), 139.3 (q), 138.4 (q), 134.4 (q), 124.8 (q), 124.7 (CH), 122.1 (CH), 119.6 (CH), 18.4 (CH_3), 18.1 (CH_3) and 16.6 (CH_3); m/z 272 (M^+, 100%).

2,3,6,7- and 2,3,5,6-tetrakis(methylthio)benzo[b]thiophene (**10a** *and* **10b**). A suspension of K10 (40 g), **7** (4 g, 30 mmol), DMDS (56.4 g, 0.6 mol) and 1,2-dichloroethane (200 mL) was stirred under reflux. H_2SO_4 (conc.) (34 mL, 0.6 mol) was added slowly and after stirring the reaction mixture for 6 h, solids were recovered by filtration through an alumina plug (30 g). The filtrate was evaporated yielding a brown oil. The oil was Kuglerohr distilled up to 135°C at 0.01 mmHg, redissolved in dichloromethane and stirred with activated charcoal to remove colored impurities. The mixture was filtered through a celite pad and the organic solvent evaporated under reduced pressure to yield a yellow oil (2.49 g).

Preparative HPLC (95% hexane: 5% THF) affords **10a** as bright yellow crystals (0.69 g, 7.4%), m.p. 105–106°C. (Found: C, 45.67; H, 4.36. $C_{12}H_{14}S_5$ requires C, 45.25; H, 4.43%); ν_{max} (nujol) 2919, 2853, 1563, 1528, 1454, 1411, 1353, 1308, 1279, 971, and 946 cm^{-1}; δ_H (400 MHz) 7.77 (1H, d, $J = 8.4$ Hz), 7.24 (1H, d, $J = 8.4$ Hz), 2.67 (3H, s), 2.54 (3H, s), 2.45 (3H, s) and 2.35 (3H, s); δ_c (100 MHz) 146.6 (q), 145.3 (q), 140.3 (q), 138.0 (q), 125.1 (q), 124.9 (q), 122.7 (CH), 122.2 (CH), 18.23 (CH_3), 18.20 (CH_3), 17.6 (CH_3), and 16.0 (CH_3); m/z 318 (M^+, 100%).

Preparative HPLC (95% hexane; 5% THF) affords **10b** as a white powder (0.48 g, 5.1%) m.p. 95–96°C. (Found C: 45.39; H, 4.57. $C_{12}H_{14}S_5$ requires C, 45.25; 4.43%); ν_{max} (nujol) 2922, 2853, 2360, 1569, 1459, 1373, 1084, 967, 846, 836, 752, 720, and 666 cm^{-1}; δ_H (400 MHz) 7.69 (1H, s), 7.58 (1H, s), 2.64 (3H, s), 2.57 (3H, s), 2.52 (3H, s), and 2.35 (3H, s); δ_c (100 MHz) 145.0 (q), 139.3 (q), 136.5 (q), 135.6 (q), 134.1

(q), 124.2 (q), 120.3 (CH), 120.1 (CH), 18.4 (CH_3), 18.1 (CH_3), 17.0 (CH_3), and 16.8 (CH_3); m/z 318 (M^+, 100%).

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