Alkylation of 4*H*,6*H*-Thieno[3,4-*c*]furan 5,5-Dioxide and Its Use as a 3,4-Dimethylenefuran Synthon in Intramolecular Diels–Alder Reaction

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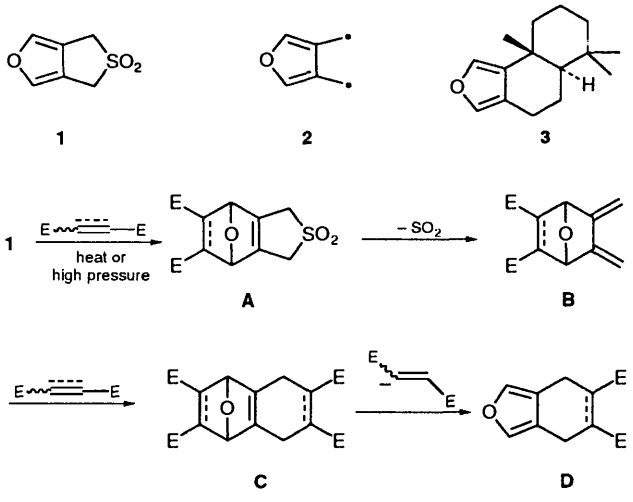
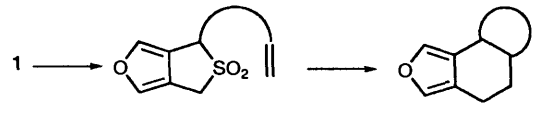
Alkylation of 4*H*,6*H*-thieno[3,4-*c*]furan 5,5-dioxide (furan-annulated sulfolene) **1** readily gave its 4-alkyl, 4,6-dialkyl, or 4,4-dialkyl derivatives, selectively. Attempts were made to use the appropriate derivatives as 3,4-dimethylenefuran synthons in intramolecular Diels–Alder reactions. Thus when they were heated after treatment with methyl vinyl ketone, a Diels–Alder reaction with methyl vinyl ketone on the furan moiety, desulfonylation, intramolecular Diels–Alder reaction of the resulting dienes, and retro Diels–Alder reaction occurred sequentially to afford the tricyclic fused furans **17a–c** in good yields.

4*H*,6*H*-Thieno[3,4-*c*]furan 5,5-dioxide **1** [1] is a useful building block which contains both furan and 3-sulfolene [2] entities. Because the latter can be used as the diene component in Diels–Alder reactions, **1** could sequentially react with two different kinds of dienophiles and offer a rapid elaboration of multicyclic systems. We have already shown that **1** selectively undergoes Diels–Alder reactions on the furan moiety with several dienophiles containing two electron-withdrawing groups to give four kinds of products **A–D** in various ratios depending on the dienophiles and the reaction conditions (Scheme 1).[1c]



Scheme 1

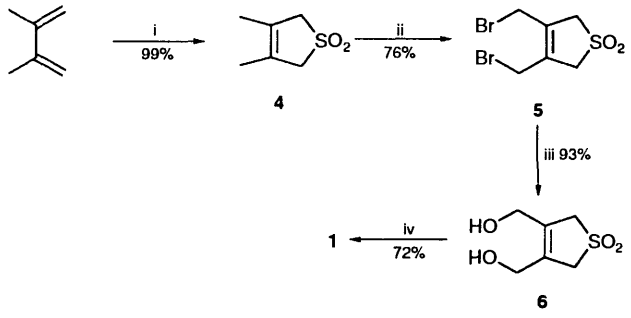
In order to demonstrate the applicability of furan-annulated sulfolene **1** as a building block in synthetic work, we investigated the chemical modifications of **1** at the position α to the SO_2 group. In a preliminary paper,[3] we have reported the preparations of 4-alkyl-4*H*,6*H*-thieno[3,4-*c*]furan 5,5-dioxides, especially those capable of undergoing intramolecular Diels–Alder reactions, and use of the resulting products as 3,4-dimethylenefuran **2** [4] synthons in intramolecular Diels–Alder reactions (Scheme 2). Here we describe the details of this alkylation study of **1** and the intramolecular Diels–Alder reactions of the alkylation products. Scheme 2 illustrates an efficient route to 3,4-fused furan multicyclic systems, which are present in antifungal marine natural products such as euryfuran **3** [5] and spongiadiol.[6]



Scheme 2

Results and Discussion

The preparation of **1** was performed by following the original work [1c] with some modifications (Scheme 3). The cycloadduct of

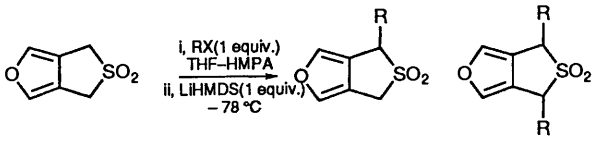


Scheme 3 *Reagents and conditions:* i, SO_2, hydroquinone, MeOH; ii, NBS, CH_2Cl_2, reflux; iii, CF_3CO_2Ag, H_2O; iv, PCC, CF_3CO_2H, acetone–CH_2Cl_2

2,3-dimethylbuta-1,3-diene and sulfur dioxide **4**, was prepared in MeOH in the presence of hydroquinone as a polymerization inhibitor in 99% yield and brominated with *N*-bromosuccinimide (NBS) [7] in 76% yield. The dibromide **5** thus obtained was hydrolysed with silver trifluoroacetate in water to afford the diol **6** (93%). Finally furan-annulated sulfolene **1** was obtained on treatment with pyridinium chlorochromate (PCC) [8] and trifluoroacetic acid in acetone–CH_2Cl_2 (1 : 2).

The alkylation studies are summarized in Table 1. After a solution of **1** in THF–HMPA (4 equiv.) had been treated with $LiN(SiMe_3)_2$ (LiHMDS) (1.0 equiv.) at −78 °C, alkyl halide was added to it (Entry 1, 2), to give **7a** and **7b** in low yields, an indication that the anion from **1** was unexpectedly labile and decomposed to an unidentified complex mixture. By generating the carbanion in the presence of alkyl halides at −78 °C, **1** can be successfully alkylated at the position α to the SO_2 group to afford **7** in good yields along with dialkylated products **8** (Entry 3, 5–12). Attempts to improve the yields of monoalkylation products **7** by lowering the reaction temperature or decreasing the amount of HMPA were unsuccessful. At −105 °C, the yield of **7b** dropped to 36% (Entry 4), probably as a result of the metallation rate being slow compared to the alkylation rate. When the amount of HMPA was decreased to 1 equiv., **7b** was obtained in 57% yield, comparable to the result of Entry 3 (58%). The secondary alkyl halide Pr^iI showed a higher degree of selectivity for monoalkylation (Entry 5), whilst, in contrast,

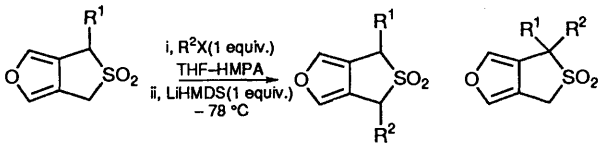
Table 1 Monoalkylation of 4*H*,6*H*-thieno[3,4-*c*]furan 5,5-dioxide **1**



1 **7** **8**[a]

Entry	RX	Method	7 (%)[b]	8 (%)[b]	1 (%)[b]
1	MeI	A	**7a** 26	—	49
2	BuI	A′	**7b** 20	21	7
3	BuI	B	**7b** 58	21	21
4	BuI	C	**7b** 36	36	28
5	Pr^{i}I	B	**7c** 67	10	21
6	CH_2=$CHCH_2Cl$	B	**7d** 44	21	36
7	$PhCH_2Cl$	B	**7e** 40	27	32
8	MeI	B	**7a** 28	44	28
9	CH_2=$CH(CH_2)_3Br$	B	**7f** 59	16	21
10	CH_2=$CH(CH_2)_4Br$	B	**7g** 58	18	24
11	EtO_2CCN	B′	**7h** 89	—	—

Table 2 Preparation of dialkylated compounds **8**



7 **8**[a] **8′**

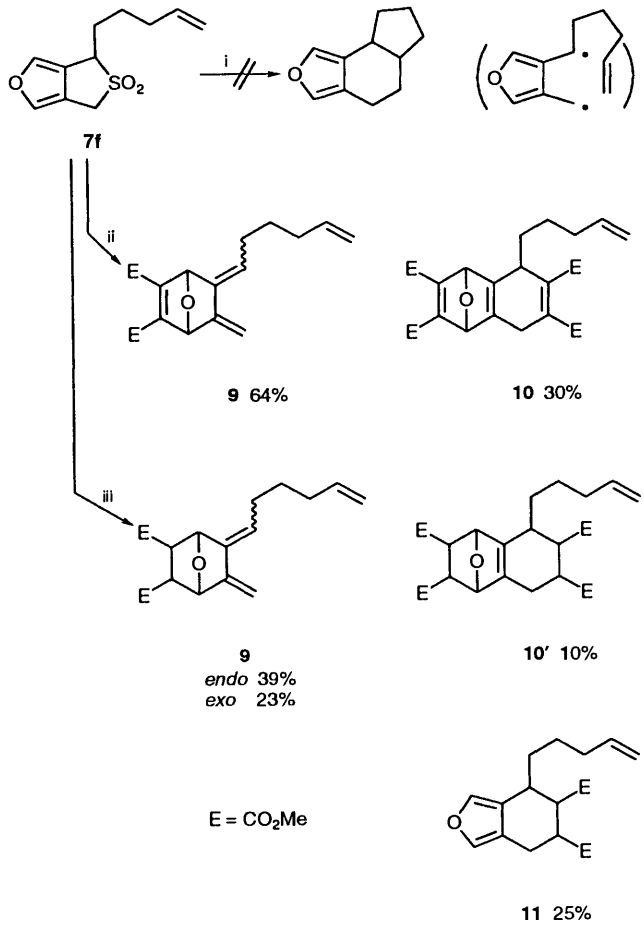
Entry	R^1	R^2X	Method	8 (%)[b]	7 (%)[b]
1	Bu	BuI	D	**8a** 68	18
2	Bu	MeI	B	**8b** 77	23
3	CH_2=$CH(CH_2)_3$	MeI	B	**8c** 97	—
4	CH_2=$CH(CH_2)_3$	$PhCH_2Cl$	B	**8d** 56	22
5	CO_2Et	CH_2=$CH(CH_2)_4Br$	B	**8′a** 86	3

A: RX was added after lithiation (−78 °C, 30 min). A′: (−78 °C, 1 min).
B: The carbanion was generated in the presence of RX at −78 °C.
B′: B except that 2 equiv. of LiHMDS were used.
C: The carbanion was generated in the presence of RX at −105 °C.
D: B except that 1, 2 equiv. of RX, and 2 equiv. of LiHMDS were used.
[a] *cis–trans* Mixture (1 : 1 to 1 : 5). [b] Isolated yield.

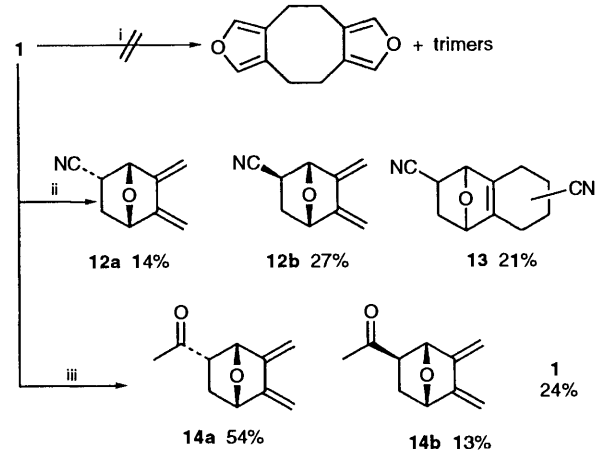
the more reactive allyl, benzyl and methyl halides showed lower selectivities. When ethyl cyanoformate (Mander's reagent)[9] was used as an alkylating reagent, 2 equiv. of LiHMDS were needed to obtain an 89% yield of monoalkylated compound **7h**.

The dialkylation of **1** with BuI (2 equiv.) and LiHMDS (2 equiv.) was performed effectively to give the 4,6-dibutyl derivative **8a** in 68% yield (Table 2, Entry 1). Similarly, the alkylations of **7** with different alkylating reagents by the same method gave 4,6-dialkylated compounds **8** in good to excellent yields (Entries 2–4). All dialkylated compounds **8** were *cis* and *trans* mixture in ratios of 1 : 1 to 1 : 5. Alkylation of **7h** with 6-bromohex-1-ene after treatment with LiHMDS (1 equiv.) gave a 4,4-disubstituted compound **8′a** (86%) (Entry 5), a result which means that regioselective dialkylation of **1** is possible. That is, 4,6-dialkyl derivatives **8** are selectively obtained from **7** (R^1 = alkyl) whilst, on the other hand, 4,4-dialkyl derivatives **8′** are obtained from **7h** since the ethoxycarbonyl group can be easily transformed into several kinds of functional groups, including alkyl.

After establishing the alkylation procedure of **1**, we set about the intramolecular Diels–Alder reactions. Unexpectedly, **7f** decomposed when heated (120–210 °C) rather than generating a 3,4-dimethylenefuran intermediate (Scheme 4). We then investigated the possibility that 3,4-dimethylenefuran **2** was

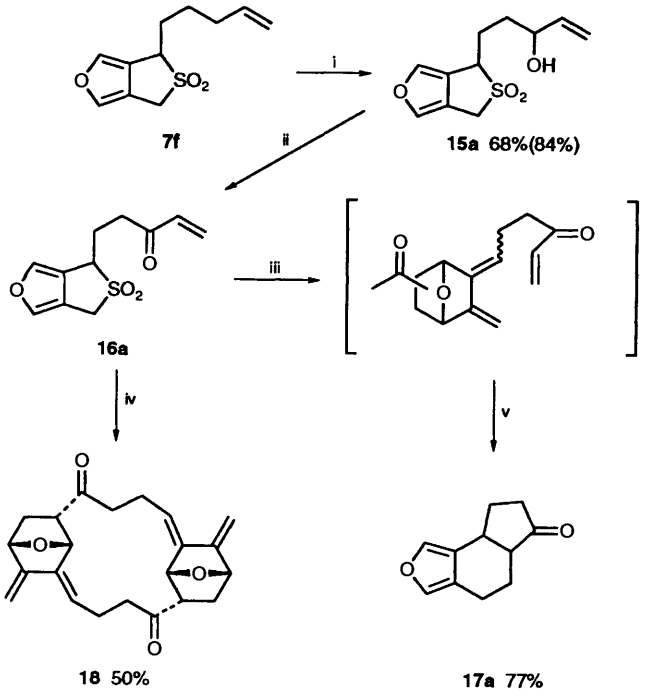


Scheme 4 *Reagents and conditions:* i, 120–210 °C; ii, E—≡—E (2 equiv.), benzene, 150 °C, 2 h; iii, E___/E (3 equiv.), benzene, 120 °C, 12 h

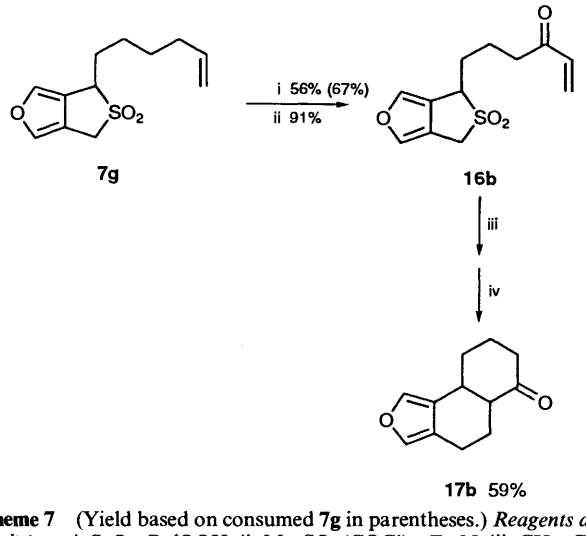


Scheme 5 *Reagents and conditions:* i, 140–200 °C; ii, CH_2=CHCN, benzene, reflux; iii, CH_2=$CHCOCH_3$, benzene, room temp.

formed from **1**.[10] When heated in various solvents, including xylene and dibutyl phthalate (140–200 °C), **1** only gradually decomposed (Scheme 5), but no dimers and trimers were detected,[4] as would be expected if **2** were present. If **7f** was heated in the presence of dimethyl acetylenedicarboxylate, the Diels–Alder reaction occurred first on the furan moiety selectively and the resulting adducts were desulfonylated instantaneously to afford **9** (64%) along with **10**, which was assumed to form from a Diels–Alder reaction of **9** and dimethyl acetylenedicarboxylate. When **9** was thermolysed (200 °C, 2 h) or subjected to high pressure (12 kbar, 80 °C), in the expectation of an intramolecular Diels–Alder reaction occurring, only a



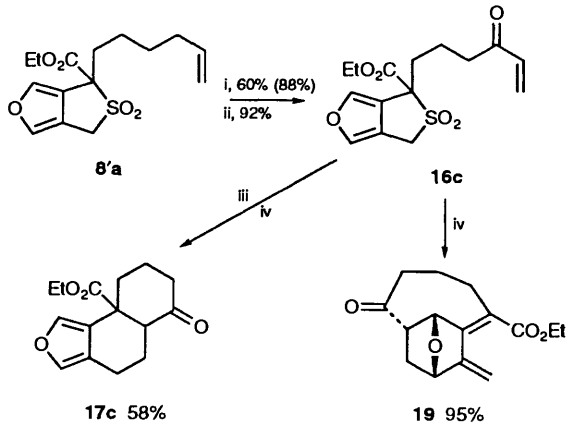
Scheme 6 (Yield based on consumed **7f** in parentheses.) *Reagents and conditions:* i, SeO_2, Bu^tOOH; ii, Me_2SO, $(COCl)_2$, Et_3N, CH_2Cl_2; iii, CH_2=CHCOCH$_3$ (–SO_2); iv, 120 °C, benzene; v, 180 °C, toluene



Scheme 7 (Yield based on consumed **7g** in parentheses.) *Reagents and conditions:* i, SeO_2–Bu^tOOH; ii, Me_2SO–$(COCl)_2$, Et_3N; iii, CH_2=CHCOCH$_3$ (–SO_2); iv, 180 °C

complex mixture was obtained. When dimethyl maleate was used as a dienophile, the fused furan **11** was obtained (25%) along with **9'** (*endo* 39% and *exo* 23%*) and **10'** (10%). Presumably, **11** was formed from **10'** by a retro Diels–Alder reaction. We were interested in this result since, if the furan moiety can be selectively protected, and then the intramolecular Diels–Alder reaction and subsequent deprotection occur, Scheme 2 could be realized.

We looked for a dienophile which reacts only on the furan moiety of **1** to give type **B** compounds predominantly. A previous study[1c] showed that some of the dienophiles containing two electron-withdrawing groups reacted with **1** to give



Scheme 8 (Yield based on consumed **8'a** in parentheses.) *Reagents and conditions:* i, SeO_2–Bu^tOOH; ii, Me_2SO–$(COCl)_2$, Et_3N; iii, CH_2=CHOCH$_3$; iv, toluene, 180 °C

type **B** compounds as main products but not exclusively. We turned our attention to the dienophiles containing one electron-withdrawing group. Acrylonitrile reacted with **1** in benzene at reflux temperature to give type **B** compounds **12a** (*endo* adduct) and **12b** (*exo* adduct) in a combined yield of 41% along with bis-adducts **13** (21%), whereas methyl vinyl ketone reacted with **1** only on the furan moiety at room temperature,[11] to give type **B** compounds **14a** (*endo* adduct) and **14b** (*exo* adduct) (*endo*/*exo*, 4.2) exclusively. It is well known that furan is a poor diene in Diels–Alder reactions due to its aromaticity and that the 7-oxabicyclo[2.2.1]heptene system is thermally unstable, reverting to starting materials. Consequently, intermolecular Diels–Alder reactions of furans usually required very reactive dienophiles (such as arynes[12] and doubly-activated dienophiles[13]), catalysts,[14] or high pressure.[15] It is not clear why **1** reacts with methyl vinyl ketone under such mild conditions (room temperature, 1–2 days), but at least instantaneous desulfonylation prohibits reversal to starting materials.

Treatment of **7f** with methyl vinyl ketone (neat) at room temperature for 1 day gave a crude brown oil whose NMR spectrum showed no furan proton signals. However, thermolysis of this crude oil at 180–200 °C gave no intramolecular Diels–Alder products. Thus, we decided to activate the olefin part. Compound **7f** was oxidized with SeO_2–Bu^tOOH[16] and the resulting allyl alcohols **15a** were submitted to Swern oxidation[17] to afford the enone **16a** † (Scheme 6). The enone **16a** when heated in benzene at 120 °C underwent a bimolecular Diels–Alder reaction followed by desulfonylation to give a dimer, whose structure was tentatively assigned as **18** (^{1}H NMR and MS) in 50% yield from the allyl alcohols **15a**. However, when the enone **16a** was heated for 8 h at 180 °C, after treatment with methyl vinyl ketone at room temperature, an intermolecular Diels–Alder reaction with the methyl vinyl ketone, desulfonylation, and a retro Diels–Alder reaction occurred sequentially to give the tricyclic fused furans **17a** (*cis*–*trans* mixture; ~3.2:1)‡ in 77% isolated yield from the allyl alcohols **15a** after column chromatography on silica gel.

By the same method, **7g** was oxidized to the enone **16b** in a good yield. After treatment with methyl vinyl ketone, the resulting mixture was heated at 180 °C to give the tricyclic

* It has been well established that the expected couplings of bridgehead protons and adjacent *endo* and *exo* protons on substituted 7-oxabicyclo[2.2.1]hept-5-ene systems are 0 and ~4 Hz, respectively (W. L. Nelson and D. R. Allen, *J. Heterocycl. Chem.*, 1972, **9**, 561).

† Although the enones **16a–c** are rather labile especially in a pure state, they can be purified by column chromatography. Since, however, after complete evaporation of the solvent, they sometimes decomposed partially or polymerized, it is desirable that they are used as a crude mixture in the subsequent Diels–Alder reactions. ^{1}H NMR spectra of the crude enones show that Swern oxidation yields are *ca.* 90–98%.

‡ The stereochemistries of **17a–c** were not determined.

furans **17b** (*cis–trans* mixture; ~2.1 : 1) in 59% yield (Scheme 7). In order to prepare a promising synthetic intermediate of euryfuran **3**, **8'a** was oxidized to the enone **16c** by the same procedure (Scheme 8). Although the Diels–Alder reaction of **16c** with methyl vinyl ketone was slow at room temperature, requiring more than 8 days, at 65 °C, it went to completion in 24 h. The resulting adducts were heated at 180 °C to give the tricyclic furan **17c** as a single isomer (58%). The enone **16c** when directly heated at 180 °C underwent an intramolecular Diels–Alder reaction on the furan moiety and, following desulfonylation, gave **19** (95%).

These results show that **1** is easily functionalized and offers facile access to 3,4-fused furan multicyclic systems.[18] In other words, **1** is a very useful functionalizable 3,4-dimethylenefuran synthon. Further studies on the furan-annulated sulfolene **1** are in progress in our laboratory.

Experimental

The melting points are uncorrected. The ^{1}H NMR was recorded in $CDCl_3$ at 400 MHz unless otherwise stated, and the chemical shifts are expressed in ppm relative to tetramethylsilane (TMS). Column chromatography was performed on silica gel (Wakogel C-300). Tetrahydrofuran (THF) was distilled from sodium–benzophenone just before use. CH_2Cl_2 was distilled from CaH_2 under argon. All reactions were conducted under an argon atmosphere.

3,4-*Dimethyl*-2,5-*dihydrothiophene* 1,1-*Dioxide* **4**.—A mixture of 2,3-dimethylbuta-1,3-diene (24.7 g, 0.30 mol), sulfur dioxide (26.3 cm^3, 0.60 mol), hydroquinone (0.6 g, 5.4 mmol) and dry MeOH (30 cm^3) was sealed in a pressure bottle at −78 °C and kept at room temperature for 2 days. After cooling to −78 °C, the bottle was opened and the sulfur dioxide and MeOH were evaporated under reduced pressure. The crude sulfolene was purified by recrystallization from MeOH to give the product as colourless plates (43.4 g, 99%), m.p. 136–137 °C (lit.,[7] 136–137 °C); δ_H 1.79 (6 H, t, *J* 1.2) and 3.73 (4 H, q, *J* 1.2); *m/z* 146 (M^+) and 82.

3,4-*Bis*(*bromomethyl*)-2,5-*dihydrothiophene* 1,1-*Dioxide* **5**.—To a solution of 3,4-dimethyl-2,5-dihydrothiophene 1,1-dioxide (26.9 g, 184 mmol) in CH_2Cl_2 (400 cm^3) was added *N*-bromosuccinimide (NBS) (68.4 g, 384 mmol) and the resulting mixture was heated to reflux for 17 h. It was then washed with water (150 cm^3 × 2) and brine, dried ($MgSO_4$) and evaporated. The residue was recrystallized from 95% EtOH to give the product as colourless plates, (42.2 g, 76%), m.p. 124–125 °C (lit.,[7] 124–125 °C); δ_H 4.02 (4 H, s) and 4.08 (4 H, s); *m/z* 302, 304, 306 (M^+; 3.5, 5.6, 3.1%), 238, 240, 242, 223 and 225.

3,4-*Bis*(*hydroxymethyl*)-2,5-*dihydrothiophene* 1,1-*Dioxide* **6**.—To a solution of silver trifluoroacetate (25.0 g, 113 mmol) in water (200 cm^3) was added 3,4-bis(bromomethyl)-2,5-dihydrothiophene 1,1-dioxide (17.2 g, 56.5 mmol) and the resulting mixture was vigorously stirred at room temperature for 3 days. Filtration of the resulting suspension removed AgBr and the filtrate was subjected to reduced pressure to remove water. The crude solid was recrystallized from AcOEt to give the product as colourless plates (9.4 g, 93%), m.p. 92–94 °C (Found: C, 40.6; H, 5.5. $C_6H_{10}O_4S$ requires C, 40.44; H, 5.66%); δ_H([$^2H_6$]acetone) 3.90 (4 H, s), 4.16 (2 H, t, *J* 5.5) and 4.29 (4 H, d, *J* 5.5); *m/z* 179 (M^+ + 1) and 160.

4H,6H-*Thieno*[3,4-c]*furan* 5,5-*Dioxide* **1**.—To a solution of 3,4-bis(hydroxymethyl)-2,5-dihydrothiophene 1,1-dioxide (1.8 g, 10.0 mmol) in acetone (40 cm^3) were added CH_2Cl_2 (80 cm^3) and pyridinium chlorochromate (PCC) (3.5 g, 15.9 mmol). After 1 min trifluoroacetic acid (4 cm^3) was also added to the mixture and stirring was continued for an additional 30 min. After the addition of sat. aqueous $NaHCO_3$ (45 cm^3), the resulting mixture was extracted with diethyl ether (100 cm^3 × 3) and the combined extracts were washed with brine, dried ($MgSO_4$), and concentrated. Column chromatography (hexane–AcOEt, 4 : 1) and recrystallization from CCl_4 provided **1** as colourless needles (1.14 g, 72%), m.p. 139–140 °C (Found: C, 45.6; H, 3.7. $C_6H_6O_3S$ requires C, 45.56; H, 3.82%); δ_H 4.17 (4 H, d, *J* 0.9) and 7.47 (2 H, t, *J* 0.9); *m/z* 158 (M^+) and 94; $\nu_{max}(CHCl_3)/cm^{-1}$ 1327, 1132, 1033 and 904.

Monoalkylation of **1** *with Alkyl Halides* (Table 1).—To a solution of **1** (32 mg, 0.20 mmol), HMPA (0.14 cm^3, 0.80 mmol), and alkyl halide (0.20 mmol) in THF (2 cm^3) was added 1.0 mol dm^{-3} LiHMDS in THF (0.20 cm^3, 0.20 mmol) in one portion at −78 °C. After 30 min, the reaction was quenched by the addition of aq. NH_4Cl (4 cm^3) and the mixture extracted with AcOEt (10 cm^3 × 3). The combined extracts were washed with brine, dried ($MgSO_4$), and concentrated. Column chromatography (hexane–AcOEt, 6 : 1) of the residue provided the 4,6-dialkylated compounds **8**, the 4-alkylated compound **7** and **1** in this order. The result of each alkylation reaction is shown in Table 1 in the text.

Compound **7a** was obtained as a colourless oil; δ_H 1.62 (3 H, d, *J* 7), 4.14 (2 H, d, *J* 1), 4.16 (1 H, dq, *J* 7, 1) and 7.42 (2 H, t, *J* 1); *m/z* 172 (M^+) and 108 (Found: M^+, 172.0194. $C_7H_8O_3S$ requires *M*, 172.0194).

Compound **7b** was obtained as a colourless oil; δ_H 0.95 (3 H, t, *J* 7.3), 1.39–1.47 (2 H, m), 1.52–1.60 (2 H, m), 1.70–1.80 (1 H, m), 2.09–2.18 (1 H, m), 4.03–4.07 (1 H, m), 4.12 (1 H, d, *J* 1.6) and 7.42–7.44 (2 H, m); *m/z* 214 (M^+) and 150 (Found: M^+, 214.0666. $C_{10}H_{14}O_3S$ requires *M*, 214.0664).

Compound **7c** was obtained as a colourless oil; δ_H 1.00 (3 H, d, *J* 6.7), 1.22 (3 H, d, *J* 6.7), 2.45 (1 H, d septet, *J* 6.1, 6.7), 3.95 (1 H, dd, *J* 6.1, 1.2), 4.03 (1 H, dd, *J* 15, 1.2), 4.14 (1 H, dd, *J* 15, 1.2) and 7.44–7.46 (2 H, m); *m/z* 200 (M^+) and 136 (Found: M^+, 200.0511. $C_9H_{12}O_3S$ requires *M*, 200.0508).

Compound **7d** was obtained as a colourless oil; δ_H 2.43–2.51 (1 H, m), 2.89–2.96 (1 H, m), 4.10–4.17 (3 H, m), 5.23–5.29 (2 H, m), 5.84–5.94 (1 H, m) and 7.42–7.46 (2 H, m); *m/z* 198 (M^+) and 134 (Found: M^+, 198.0362. $C_9H_{10}O_3S$ requires *M*, 198.0351).

Compound **7e** was obtained as colourless needles; m.p. 101.5–102.5 °C (from diethyl ether–hexane) (Found: C, 63.0; H, 5.0. $C_{13}H_{12}O_3S$ requires C, 62.89; H, 4.87%); δ_H 2.87 (1 H, dd, *J* 11, 14), 3.57 (1 H, dd, *J* 5, 14), 4.14 (1 H, dd, *J* 15, 1.5), 4.16 (1 H, dd, *J* 15, 1.5), 4.39 (1 H, ddd, *J* 1.5, 5, 11), 6.77 (1 H, t, *J* 1.5) and 7.24–7.39 (6 H, m); *m/z* 248 (M^+) and 184.

Compound **7f** was obtained as a colourless oil; δ_H 1.64–1.82 (3 H, m), 2.10–2.20 (3 H, m), 4.05–4.08 (1 H, m), 4.12 (2 H, s), 4.99–5.08 (2 H, m), 5.75–5.85 (1 H, m) and 7.42–7.46 (2 H, m); *m/z* 226 (M^+) and 162 (Found: M^+, 226.0665. $C_{11}H_{14}O_3S$ requires *M*, 226.0662).

Compound **7g** was obtained as a colourless oil; δ_H 1.47–1.63 (4 H, m), 1.71–1.80 (1 H, m), 2.07–2.19 (3 H, m), 4.03–4.07 (1 H, m), 4.12 (2 H, s), 4.96–5.05 (2 H, m), 5.75–5.85 (1 H, m), 7.42 (1 H, dd, *J* 1.2, 1.5) and 7.43 (1 H, d, *J* 1.5); *m/z* 240 (M^+) and 176 (Found: M^+, 240.0809. $C_{12}H_{16}O_3S$ requires 240.0819).

Compound **7h** was obtained as a colourless oil; this compound was prepared by using 2.0 equiv. of LiHMDS; δ_H 1.34 (3 H, t, *J* 7.2), 4.21–4.36 (4 H, m), 4.96 (1 H, d, *J* 1.2), 7.49 (1 H, q, *J* 1.2) and 7.58 (1 H, t, *J* 1.2); *m/z* 230 (M^+) and 166 (Found: M^+, 230.0250. $C_9H_{10}O_5S$ requires *M*, 230.0248).

Alkylation of **7** *with Alkyl Halides* (Table 2).—Alkylation of **7** was performed by the above procedure unless otherwise stated. The result of each alkylation reaction is shown in Table 2 in the text.

Compounds **8a** were obtained as a colourless oil (*cis* and *trans* mixture, ~2:1); these compounds were prepared by the treatment of **1** with LiHMDS (2.0 equiv.) and BuI (2.0 equiv.); δ_H 0.92–0.98 (6 H, m), 1.38–1.47 (4 H, m), 1.48–1.63 (4 H, m), 1.63–1.80 (2 H, m), 2.09–2.19 (2 H, m), 3.97–4.05 (2 H, m) and 7.39–7.41 (2 H, m); *m/z* 206 ($M^+ - SO_2$) (Found: $M^+ - SO_2$, 206.1668. $C_{14}H_{22}O$ requires $M - SO_2$, 206.1669).

Compound **8b** (isomer a, 47% yield) was obtained as a colourless oil; δ_H 0.95 (3 H, t, *J* 7.3), 1.34–1.74 (5 H, m), 1.61 (3 H, dd, *J* 7.0, 0.6), 2.10–2.19 (1 H, m), 4.02 (1 H, dd, *J* 6.3, 8.7), 4.10 (1 H, q, *J* 7.0) and 7.40 (2 H, s); *m/z* 228 (M^+) and 164 (Found: M^+, 228.0819. $C_{11}H_{16}O_3S$ requires *M*, 228.0819).

Compound **8b** (isomer b, 30% yield) was obtained as a colourless oil: δ_H 0.97 (3 H, t, *J* 7.3), 1.40–1.66 (4 H, m), 1.62 (3 H, d, *J* 6.9), 1.77–1.86 (1 H, m), 2.10–2.19 (1 H, m), 4.05 (1 H, dt, *J* 1.5, 7.3), 4.15 (1 H, dq, *J* 1.5, 6.9) and 7.38–7.40 (2 H, m); *m/z* 228 (M^+) and 164 (Found: M^+, 228.0817. $C_{11}H_{16}O_3S$ requires *M*, 228.0819).

Compound **8c** (isomer a, 68% yield) was obtained as a colourless oil; δ_H 1.61 (3 H, d, *J* 7.0), 1.59–1.77 (3 H, m), 2.11–2.21 (3 H, m), 4.03 (1 H, t, *J* 7.2), 4.11 (1 H, dq, *J* 0.9, 7.0), 4.98–5.07 (2 H, m), 5.75–5.85 (1 H, m) and 7.40 (2 H, d, *J* 0.9); *m/z* 240 (M^+) and 176 (Found: M^+, 240.0818. $C_{12}H_{16}O_3S$ requires *M*, 240.0819).

Compound **8c** (isomer b, 29% yield) was obtained as a colourless oil; δ_H 1.62 (3 H, d, *J* 7.0), 1.57–1.89 (3 H, m), 2.12–2.22 (3 H, m), 4.07 (1 H, dt, *J* 1.2, 7.2), 4.15 (1 H, dq, *J* 1.2, 7.0), 4.99–5.09 (2 H, m), 5.77–5.87 (1 H, m) and 7.38–7.40 (2 H, m); *m/z* 240 (M^+) and 176 (Found: M^+, 240.0809. $C_{12}H_{16}O_3S$ requires *M*, 240.0819).

Compounds **8d** (*cis* and *trans* mixture, ~1.2:1) were obtained as a colourless oil; δ_H 1.60–1.85 (3 H, m), 2.12–2.22 (3 H, m), 2.82–2.90 (1 H, m), 3.57 (1 H, dd, *J* 5, 14), 4.02 (isomer a; 1 H, ddd, *J* 1.2, 6.7, 7.9), 4.09 (isomer b, 1 H, dt, *J* 1.5, 7.2), 4.31 (isomer a; 1 H, ddd, *J* 1.5, 5, 10.7), 4.39 (isomer b; 1 H, ddd, *J* 1.5, 5, 10.7), 4.98–5.10 (2 H, m), 5.74–5.86 (1 H, m), 6.73 (isomer b; 1 H, t, *J* 1.5), 6.75 (isomer a; 1 H, t, *J* 1.5) and 7.22–7.38 (6 H, m); *m/z* 316 (M^+) and 252 (Found: M^+, 316.1128. $C_{18}H_{20}O_3S$ requires *M*, 316.1132).

Compound **8'a** was obtained as a colourless oil; this reaction was performed overnight at room temperature; δ_H 1.33 (3 H, t, *J* 7.2), 1.34–1.49 (4 H, m), 1.76–1.83 (1 H, m), 2.04–2.09 (2 H, m), 2.44–2.50 (1 H, m), 4.12 (1 H, dd, *J* 1.5, 14.8), 4.27–4.36 (3 H, m), 4.93–5.01 (2 H, m), 5.71–5.81 (1 H, m), 7.46 (1 H, q, *J* 1.5) and 7.60 (1 H, d, *J* 1.5); *m/z* 312 (M^+) and 248 (Found: M^+, 312.1030. $C_{15}H_{20}O_5S$ requires *M*, 312.1031).

Reaction of **1** *with Methyl Vinyl Ketone.*—Compound **1** (19.0 mg, 0.12 mmol) was treated with methyl vinyl ketone (0.1 cm^3) in benzene at room temperature for 2 days. After evaporation of the solvent, the crude oil was purified by column chromatography (hexane–AcOEt 12:1) to provide the *endo* adduct **14a** (10.6 mg, 54%), the *exo* adduct **14b** (2.5 mg, yield 13%), and **1** (4.5 mg, recovery 24%).

Compound **14a** was obtained as a colourless oil; δ_H 1.98 (1 H, ddd, *J* 5.5, 10.7, 12.2), 2.16 (3 H, s), 2.17 (1 H, dd, *J* 4.6, 12.2), 3.32 (1 H, ddd, *J* 4.6, 5.5, 10.7), 4.87 (1 H, d, *J* 5.5), 4.92 (1 H, s), 4.98 (1 H, s), 5.07 (1 H, d, *J* 5.5), 5.21 (1 H, s) and 5.27 (1 H, s); *m/z* 164 (M^+) (Found: M^+, 164.0831. $C_{10}H_{12}O_2$ requires *M*, 164.0837).

Compound **14b** was obtained as a colourless oil; δ_H 1.86 (1 H, dd, *J* 9.2, 12.2), 2.22 (1 H, dt, *J* 12.2, 5.2), 2.24 (3 H, s), 2.83 (1 H, dd, *J* 5.2, 9.2), 4.91 (1 H, d, *J* 5.2), 5.00 (1 H, s), 5.04 (2 H, br s), 5.24 (1 H, s) and 5.26 (1 H, s); *m/z* 164 (M^+) (Found: M^+, 164.0837. $C_{10}H_{12}O_2$ requires *M*, 164.0837).

Allylic Oxidation of **7f**.—To a suspension of SeO_2 (12 mg, 0.11 mmol), salicylic acid (4 mg, 0.03 mmol), and water (0.1 cm^3) in CH_2Cl_2 (2 cm^3) was added 70% Bu^{t}OOH (0.066 cm^3, 0.49 mmol). A solution of **7f** (50 mg, 0.22 mmol) in CH_2Cl_2 (2 cm^3) was then introduced and the resulting mixture was heated to reflux for 21 h. AcOEt (20 cm^3) was added to the mixture which was then washed with 10% aqueous KOH (5 cm^3 × 2), aqueous NH_4Cl and brine, dried ($MgSO_4$) and concentrated. Column chromatography (hexane–AcOEt, 5:1 to 3:1) provided the hydroxy compounds **15a** (36 mg, 68%) as a colourless oil along with **7f** (9.5 mg, recovery 19%). Compounds **15a**: δ_H 1.68–2.03 (4 H, m), 2.14–2.30 (1 H, m), 4.08–4.26 (4 H, m), 5.15–5.31 (2 H, m), 5.84–5.94 (1 H, m) and 7.42–7.46 (2 H, m); *m/z* 224 ($M^+ - H_2O$) and 160 (Found: $M^+ - H_2O$, 224.0480. $C_{11}H_{12}O_3S$ requires $M - H_2O$, 224.0506).

Allylic Oxidation of **7g**.—The above procedure was applied to **7g** (89 mg, 0.37 mmol) to provide **15b** (54 mg, 57%) as a colourless oil along with **7g** (14 mg, recovery 16%). Compounds **15b**: δ_H 1.59–1.84 (6 H, m), 2.13–2.20 (1 H, m), 4.05–4.18 (4 H, m), 5.12–5.27 (2 H, m), 5.84–5.92 (1 H, m) and 7.42–7.46 (2 H, m); *m/z* 238 ($M^+ - H_2O$) and 174 (Found: $M^+ - H_2O$, 238.0670. $C_{12}H_{14}O_3S$ requires $M - H_2O$, 238.0663).

Allylic Oxidation of **8'a**.—The above procedure was applied to **8'a** (378 mg, 1.21 mmol) to provide **15c** (240 mg, 60%) as a colourless oil along with **8'a** (121 mg, recovery 32%). Compounds **15c**: δ_H 1.32 (3 H, t, *J* 7.2), 1.44–1.69 (5 H, m), 1.80–1.88 (1 H, m), 2.46–2.51 (1 H, m), 4.10–4.14 (2 H, m), 4.27–4.36 (3 H, m), 5.09–5.13 (1 H, m), 5.19–5.24 (1 H, m), 5.79–5.88 (1 H, m), 7.46 (1 H, d, *J* 1.2) and 7.61 (1 H, d, *J* 1.2); *m/z* 328 (M^+), 264 and 246 (Found: $M^+ - SO_2$, 246.1253. $C_{15}H_{18}O_3$ requires $M - SO_2$, 246.1256).

Synthesis of **17a**.—To a solution of oxalyl chloride (0.017 cm^3, 0.20 mmol) in CH_2Cl_2 (1 cm^3) was added dimethyl sulfoxide (DMSO) (0.028 cm^3, 0.40 mmol) and then **15a** (21.1 mg, 0.091 mmol) in CH_2Cl_2 (2 cm^3) at −78 °C. The mixture was stirred for 15 min, after which Et_3N (0.12 cm^3, 0.89 mmol) was added to it; it was then allowed to warm to room temperature. The mixture was diluted with cold water (5 cm^3) and AcOEt (15 cm^3) after which the organic layer was separated, washed with water and brine, dried ($MgSO_4$) and concentrated to give crude **16a**. This crude oil was treated with methyl vinyl ketone (0.3 cm^3) at room temperature until the ^1H NMR spectrum showed no furan-H (~24 h). After aqueous work-up, this crude oil was dissolved in toluene (5 cm^3) and the solution heated at 180 °C for 8 h. Column chromatography (hexane–AcOEt, 10:1) of the cooled mixture provided **17a** (12.3 mg, 77% from **15a**) (inseparable *cis* and *trans* mixture; ~3.2:1) as a colourless oil and solid; δ_H 1.35–1.55 (0.24 H, m), 1.74–1.87 (1 H, m), 1.90–2.10 (1.76 H, m), 2.15–2.40 (3 H, m), 2.40–2.75 (3 H, m), 2.84 (0.24 H, dd, *J* 6.5, 16), 3.58 (0.76 H, q, *J* 6.5), 7.14 (0.76 H, q, *J* 1.2), 7.20 (0.24 H, q, *J* 1.2), 7.25 (0.24 H, t, *J* 1.2) and 7.32 (0.76 H, t, *J* 1.2); *m/z* 176 (M^+) (Found: M^+, 176.0830. $C_{11}H_{12}O_2$ requires *M*, 176.0836).

Synthesis of **17b**.—The above procedure was applied to **15b** (14.2 mg, 0.055 mmol) to provide **17b** (5.6 mg, 54% from **15b**) (inseparable *cis* and *trans* mixture; ~2.1:1) as a colourless oil; δ_H 1.45–2.66 (10.32 H, m), 2.74–2.82 (1 H, m), 3.29–3.34 (0.68 H, m), 7.14–7.16 (1 H, m), 7.20 (0.68 H, t, *J* 1.5) and 7.23 (0.32 H, t, *J* 1.5); $\nu_{max}(CHCl_3)/cm^{-1}$ 1707, 1175, 1128 and 1038; *m/z* 190 (M^+) (Found: M^+, 190.0998. $C_{12}H_{14}O_2$ requires *M*, 190.0993).

Synthesis of **17c**.—The above procedure was applied to **15c** (457 mg, 1.39 mmol) to provide **17c** (194 mg, 53% from **15c**) as colourless crystals (recrystallized from hexane–diethyl ether), m.p. 71.8–72.5 °C; δ_H 1.26 (3 H, t, *J* 7.0), 1.72–1.79 (2 H, m), 1.85–1.91 (1 H, m), 2.01–2.38 (5 H, m), 2.45–2.53 (1 H, m), 2.72–2.79 (1 H, m), 3.09 (1 H, dd, *J* 3.1, 8.9), 4.19 (2 H, q, *J* 7.0),

7.15 (1 H, q, *J* 1.5) and 7.45 (1 H, d, *J* 1.5); $\nu_{max}(CHCl_3)/cm^{-1}$ 1747, 1716, 1223, 1184 and 1037; *m/z* 262 (M^+) (Found: M^+, 262.1196. $C_{15}H_{18}O_4$ requires *M*, 262.1205).

Thermal Reaction of **16a**.—A solution of **16a** (12.0 mg, 0.050 mmol) in benzene (1 cm^3) was heated at 120 °C in a sealed tube for 6 h. After evaporation of the solvent, column chromatography (hexane–AcOEt, 3:1) gave **18** (4.6 mg, yield 52%) as a colourless oil; δ_H 1.90 (2 H, dd, *J* 4.2, 12.8), 2.12–2.19 (2 H, m), 2.42–2.52 (4 H, m), 2.71–2.82 (4 H, m), 3.07–3.12 (2 H, m), 4.76 (2 H, d, *J* 5.2), 4.85 (2 H, s), 5.0 (2 H, s), 5.28 (2 H, d, *J* 5.2) and 5.83–5.86 (2 H, m); *m/z* 352 (M^+) and 176; the sample was pure according to ^1H NMR and TLC analysis.

Thermal Reaction of **16c**.—A solution of **16c** (33.8 mg, 0.10 mmol) in toluene (4 cm^3) was heated at 180 °C in a sealed tube for 5 h. After evaporation of the solvent, column chromatography (hexane–AcOEt, 8:1) provided **19** (25.8 mg, 95%) as colourless prisms, m.p. 91–92 °C (recrystallized from hexane–AcOEt) (Found: C, 68.5; H, 6.9. $C_{15}H_{18}O_4$ requires C, 68.69; H, 6.92%); δ_H 1.29 (3 H, t, *J* 7.2), 1.84–2.15 (3 H, m), 2.24 (1 H, dd, *J* 4.3, 12.5), 2.43–2.61 (3 H, m), 2.78 (1 H, dt, *J* 3.4, 12.5), 3.39–3.44 (1 H, m), 4.15–4.24 (2 H, m), 4.84 (1 H, d, *J* 5.2), 5.25 (1 H, s), 5.68 (1 H, d, *J* 5.5) and 5.79 (1 H, s); *m/z* 262 (M^+).

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