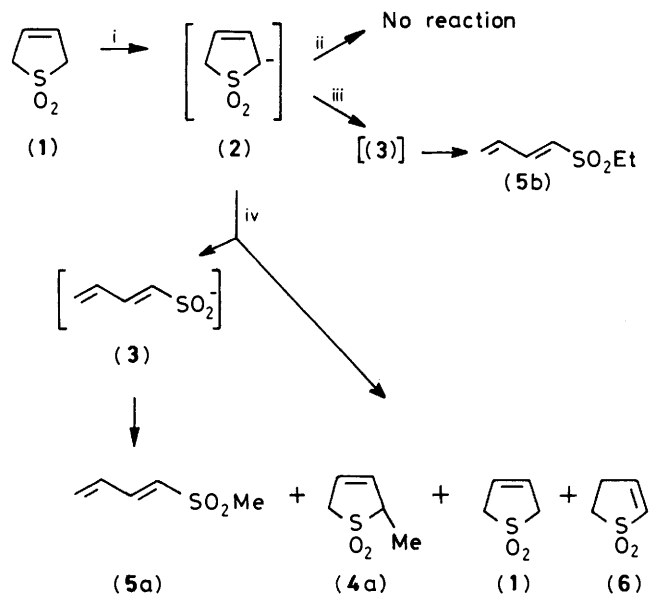
Study of the Alkylation Reactions of Sulphol-3-enes

Ta-shue Chou,* Hsi-Hua Tso, and Lee-Jean Chang
Institute of Chemistry, Academia Sinica, Nankang, Taipei, Taiwan, Republic of China

Sulphol-3-ene can be deprotonated with sodium hydride in DMF to form the α-anion which reacts with various alkyl halides to give the 2-alkylsulpholenes. This approach provides a regiospecific preparation of disubstituted sulphol-3-enes and sulphol-2-enes.

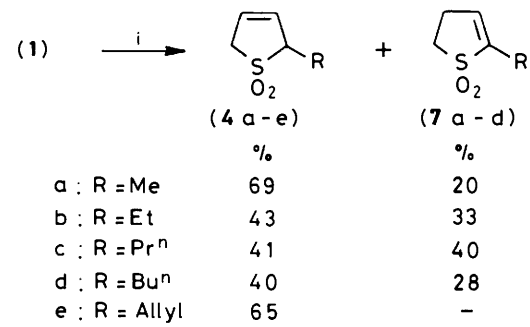
Substituted 2,5-dihydrothiophene 1,1-dioxides (sulphol-3-enes)[1] are ideal precursors of conjugated dienes, the transformation being achieved by thermal or photochemical extrusion of SO_2.[2] Until recently, attempted deprotonation of sulphol-3-ene with strong base followed by direct alkylation to produce the 2-substituted sulphol-3-enes failed, generally because of instantaneous ring-opening reactions of the α-carbanion intermediate.[3] Such ring-opening problems do not, apparently, exist in benzosulpholene systems.[4] The methodology of multistep, indirect alkylation which skillfully avoided ring-opening by masking the sulphol-3-ene as its cyclopentadiene cycloadduct was developed recently.[5] Conversely, currently, direct deprotonation of sulphol-3-ene with hindered lithium amide bases followed by alkylation gave 2-substituted and 2,5-disubstituted sulphol-3-enes for use in the synthesis of pheromones and vitamin D derivatives.[6] There has been no mention of the expected base-induced double-bond migration of sulphol-3-enes to sulphol-2-enes.[7] These reports prompt us to describe the results of our independent work on the direct alkylation of sulpholenes with NaH and alkyl iodides.[8]

At an early stage, we found that the reaction of sulphol-3-ene with NaH in several solvent systems including tetrahydrofuran (THF) dimethoxyethane (DME), and diglyme at relatively low temperatures proceeded smoothly to give the desired α-carbanion (**2**). Attempted deprotonation with BuLi, LDA, with or without co-solvents such as hexamethylphosphoric triamide (HMPA) and tetramethylethylenediamine (TMEDA), caused ring-opening almost instantaneously even at temperatures as low as −78 °C. When the NaH-deprotonated sulphol-3-ene (**2**) was treated with MeI in DME, 2-methylsulphol-3-ene (**4a**) and methylbutadienyl sulphone (**5a**) were produced along with sulphol-2-ene (**6**) and the recovered sulphol-3-ene (**1**). Product (**5a**) was the result of methylation of the ring-opened intermediate (**3**). Reaction with MeOTs under similar conditions gave a comparable result. Since the sulpholenes (**1**), (**6**), and (**4a**) were all partially decomposed upon elution through a silica gel or alumina column, purification by h.p.l.c. was preferred (Scheme 1).



Scheme 1. *Reagents:* i, NaH–DME; ii, EtI; iii, EtI–$AgNO_3$; iv, MeI

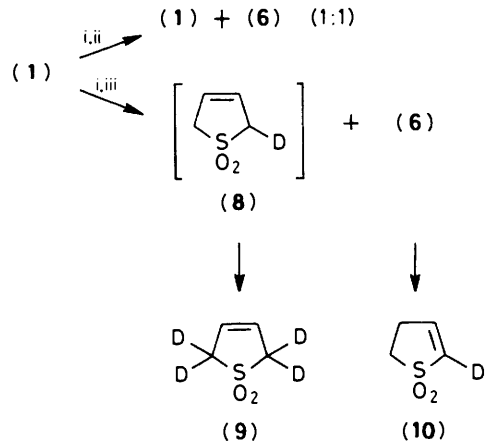
Although compound (**1**) was methylated quite smoothly, other attempted aklylations were unsuccessful. For example, when EtI or EtOTs was treated with (**2**) in DME at room temperature, no reaction took place even with a prolonged period of stirring. However, attempted alkylation at elevated temperature or with EtI–$AgNO_3$ at −30 °C gave only butadienyl ethyl sulphone (**5b**). An attempted direct alkylation with allyl iodide under similar conditions also failed. Alkylation reactions changed dramatically upon varying the solvent systems. It was found that the deprotonation and alkylation reactions proceeded very well in DMF for various alkyl halides. No ring-opening products could be detected, but double-bond isomerization was unavoidable (Scheme 2).



	(4) %	(7) %
a : R = Me	69	20
b : R = Et	43	33
c : R = Pr^n	41	40
d : R = Bu^n	40	28
e : R = Allyl	65	–

Scheme 2. *Reagents:* i, NaH–DMF, RI (2 equiv.)

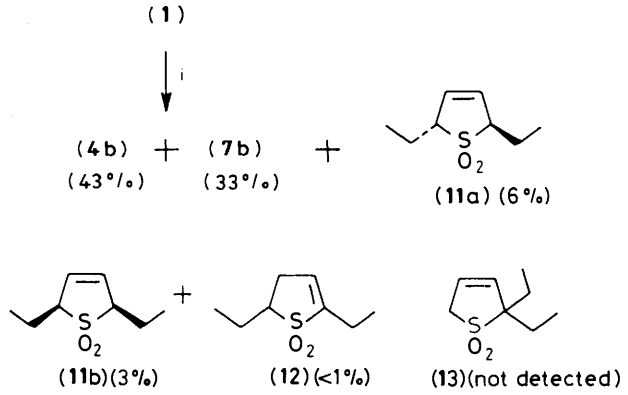
For this type of reaction, alkyl halides must be added to sulphol-3-ene (**1**) before deprotonation, otherwise, polymerization gradually takes place and the solution becomes black. Polymerization could be detected by n.m.r. spectroscopy, the vinyl proton signal decreasing with time. Temperature control was essential to the reaction since high temperatures accelerated polymerization and low temperatures retarded deprotonation. Protonation of (**2**) resulted in the formation of a mixture of sulphol-3-ene (**1**) and sulphol-2-ene (**6**) in a 1:1 ratio. This result was consistent with the known base-induced double-bond isomerization of sulphol-3-enes.[7] Protonation with D_2O resulted in the formation of 2,2,5,5-tetradeuteriosulphol-3-ene (**9**) and 2-deuteriosulphol-2-ene (**10**) in a 1:1 ratio, no other compound being detected. Compounds (**9**) and (**10**) were thought to be generated *via* the known, rapid deuterium exchange of 2-deuteriosulphol-3-ene (**8**) and sulphol-2-ene (**6**), respectively. No deuterium was found at the 3- or 4-positions suggesting that the basicity of the α-position was higher than that of the γ-position (Scheme 3).



Scheme 3. *Reagents:* i, NaH–DMF; ii, H_2O; iii, D_2O

Although alkylation of the deprotonated sulphol-3-ene with alkyl bromides also gave the desired products, the yields were lower and the products less pure. Alkylation with MeOTs or EtOTs unexpectedly resulted in no reaction and complete recovery of the tosylates.

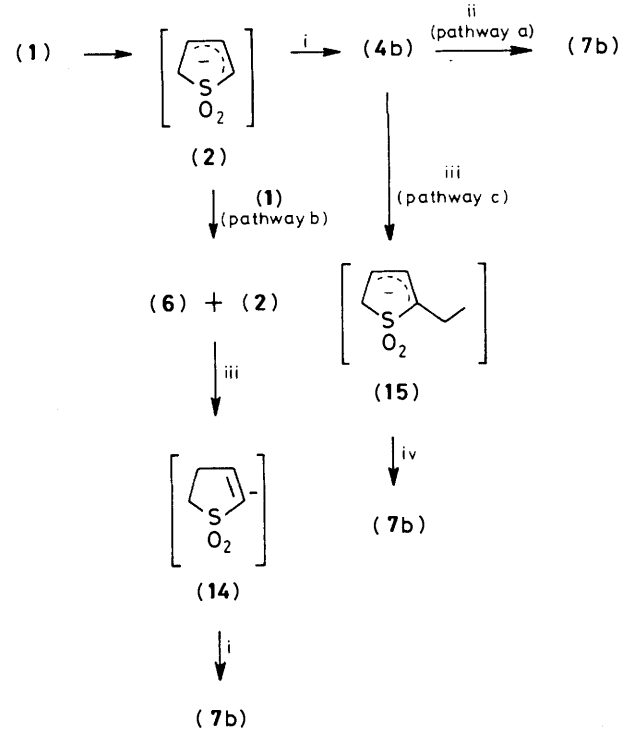
In order to understand this type of reaction better, we carefully analysed the minor products from the reaction of EtI with deprotonated sulphol-3-ene. Products of bisalkylation were detected and isolated (Scheme 4). In fact, 2,5-diethyl-



Scheme 4. *Reagents:* i, NaH–DMF, EtI

sulpholenes (**11a**), (**11b**), and (**12**) constituted *ca.* 10% of the total yield, but the other bisalkylation product, 2,2-diethylsulpholene (**13**) could not be detected. The stereochemistry of the *trans*-product (**11a**) and the *cis*-product (**11b**) was determined by comparison with the ^{13}C and ^{1}H n.m.r. spectra of (**11b**) kindly provided by Professor McIntosh. The formation of the diethylsulpholenes indicated that (**4b**) could be deprotonated further by NaH and then alkylated. The product distribution suggested that deprotonation of (**4b**) occurred at the less hindered position. No γ-alkylation products could be detected indicating that the γ-position if nucleophilic at all was less so than the α-position. Combining this result with that from the deuteriation experiment, it was concluded that the charge density of sulphol-3-ene carbanion (**2**) was localized on the α-carbon; this agreed with the results for the allylic anion of α,β-unsaturated sulphones which are discussed elsewhere.[9]

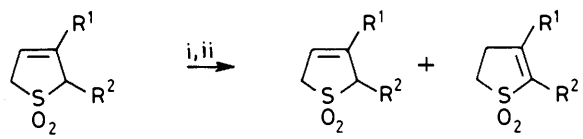
There are several possible pathways for the formation of 2-alkylsulphol-2-enes (Scheme 5). That aqueous NaOH-induced isomerization of (**4b**) occurred during work-up (pathway *a*) could be disregarded since there was no isomerization when



Scheme 5. *Reagents:* i, EtI; ii, NaOH; iii, NaH; iv, H_2O

pure 2-ethylsulphol-3-ene (**4b**) was treated either with 5% NaOH–H_2O or with 5% NaOH–DMF. Pathway *b* could also be eliminated on the basis of the indirect evidence that when (**6**) was treated with EtI under similar ethylation conditions as those for (**1**), the same products in an identical ratio were obtained. The vinyl anion (**14**) cannot, therefore, have been present, otherwise (**7b**) would have been produced in higher yield for the reaction of (**6**) than for the reaction of (**1**). As mentioned above, NaH, EtI, and the sulpholene were ordinarily mixed together in DMF for the reaction to proceed. However, if NaH and sulpholene were mixed first for deprotonation, and excess of solid NaH was removed from the dark solution before the addition of EtI, only (**4b**) was obtained in low yield, (**7b**) not being detected. This suggested that, under ordinary conditions, the excess of NaH solid was responsible for the isomerization of the double bond in the sulpholene system (pathway *c*). Indeed, deprotonated sulphol-3-ene (**2**) in the absence of solid NaH, was found to be incapable of isomerizing (**4b**) to (**7b**). Therefore, it seemed reasonable to assume that 2-alkylsulphol-2-enes were found *via* pathway *c*.

NaH-Induced double-bond isomerization of several substituted sulphol-3-enes were studied (Scheme 6). It was found that,



(**1**) $R^1=R^2=H$	(**1**) (50%)	(**6**) (50%)
(**4a**) $R^1=H$, $R^2=Me$	(**4a**) (0%)	(**7a**) (100%)
(**4b**) $R^1=H$, $R^2=Et$	(**4b**) (0%)	(**7b**) (100%)
(**16**) $R^1=Me$, $R^2=H$	(**16**) (17%)	(**17**) (83%)
(**18**) $R^1=R^2=Me$	(**18**) (0%)	(**19**) (100%)

Scheme 6. *Reagents:* i, NaH–DMF; ii, H_2O

except for sulphol-3-ene, (**1**), itself, the base treatment favoured the double bond to migrate to the 2 position, in this way being conjugated with sulphone functionality as well as becoming a more substituted double bond. The sulphol-2-enes were thermodynamically so favoured and the isomerization so rapid that an excess of NaH was unavoidable during the alkylation reaction; this led to isomerization of the 2-alkylsulphol-3-enes. In fact, when the ethylation of (**1**) was carried out in the presence of a three-fold excess of NaH, the only product obtained was (**7b**). If less (1.2 equiv.) of NaH was used during the ethylation, an increase in the reaction time increased the ratio of (**7b**) to (**4b**). That Yamada *et al.*[6] failed to report the problem of double-bond isomerization was probably because the base systems used in their procedures gave more rapid deprotonation than NaH, with a consequent shift of the rate-determining step to alkylation; this minimized the double-bond migration.

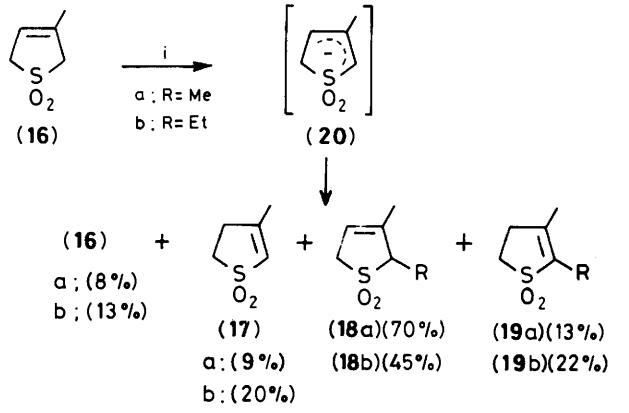
Direct alkylation of substituted sulphol-3-enes was examined in order to study the regioselectivity of the second substituent. When (**4b**) was deprotonated and alkylated with EtI, (**11**) and (**12**) were produced in 63% total yield; (**13**) was not detected and 37% of (**4b**) and (**7b**) were recovered (Scheme 7). The

$$\text{(4b)} \xrightarrow[\text{EtI}]{\text{NaH–DMF}} \text{(4b)}\ (12\%) + \text{(7b)}\ (25\%) + \text{(11)}\ (37\%) + \text{(12)}\ (26\%)$$

Scheme 7.

alkylation was highly regioselective and favoured the less substituted site. The *trans*- and *cis*-products (**11a**) and (**11b**) were obtained in a *ca.* 2:1 ratio, an indication of the low stereoselectivity of the reaction. Compound (**12**) was assumed to be formed from NaH-induced isomerization of (**11a**) and (**11b**). Treatment of (**7b**) with NaH and EtI in DMF resulted in complete recovery of starting material indicating that (**7b**) was probably not deprotonated.

The 3-substituted sulphone (**16**) was deprotonated and alkylated with RI with a high degree of regioselectivity (Scheme 8). The substitution took place only at the 2-position. Structures



Scheme 8. *Reagents:* i, NaH–DMF, RI

of (**18a**) and (**18b**) were confirmed by NaH-induced isomerization to (**19a**) and (**19b**), respectively. Although the reason for the deprotonation occurring solely at the more hindered 2 position is not fully understood, it may be due to the double bond of the allylic C-2 anion (**20**) being more substituted than that of the C-5 anion.

In summary, we have described a direct, highly regioselective alkylation procedure to produce substituted sulpholenes accompanied by no ring-opened products. A possible path for the isomerization of the double bond is proposed.

Experimental

General.—^{1}H N.m.r. spectra were determined on a Jeol C-60HL n.m.r. spectrometer as solutions in $CDCl_3$ unless otherwise noted. ^{13}C N.m.r. spectra were determined on a Jeol FX-100 n.m.r. spectrometer. I.r. spectra were determined on a Perkin-Elmer 297 i.r. spectrophotometer. Mass spectra were recorded on a Hitachi EMS-4 mass spectrometer or a Jeol JMS-D-100 mass spectrometer. Elemental analyses were performed at the National Taiwan University, Taipei. All reactions were carried out under an atmosphere of dry nitrogen. All anhydrous solvents were freshly distilled before use.

Methylation of 2,5-*Dihydrothiophene* 1,1-*Dioxide* (**1**) *in DME.*—To a suspension of sodium hydride (0.36 g, 8.3 mmol) and compound (**1**) (0.86 g, 7.3 mmol) in anhydrous DME (10 ml) cooled at −2 °C was added MeI (5.2 g, 36.5 mmol) and the resulting mixture was stirred at room temperature for 24 h. After removal of excess of solvent under reduced pressure, water (5 ml) was added and the whole extracted with $CHCl_3$ (20 ml × 3). The combined organic layers were dried ($MgSO_4$) and evaporated under reduced pressure to give the crude product mixtures. Separation by column chromatography (silica gel) and h.p.l.c. (LiChrosorb, Merck) with EtOAc–hexane gave (**1**) (88.0 mg, 11%), (**6**) (88.0 mg, 11%), (**4a**) (0.55 g, 56%), and 1-methylsulphonylbuta-1,3-diene (**5a**) (0.12 g, 12%); for (**5a**) δ 2.95 (3 H, s), 5.53—5.70 (2 H, m), and 6.18—7.60 (3 H, m). The n.m.r. and i.r. data of (**5a**) are identical with those reported earlier.[3a,3c]

1-*Ethylsulphonylbuta*-1,3-*diene* (**5b**).—To a suspension of sodium hydride (0.36 g, 8.3 mmol) and (**1**) (0.86 g, 7.3 mmol) in anhydrous DME (10 ml) cooled at −2 °C was added $AgNO_3$–EtI [prepared by mixing $AgNO_3$ (6.20 g, 36.5 mmol) and EtI (5.32 g, 36.5 mmol) in DME (10 ml) at −10 °C]. The resulting mixture was stirred at room temperature for 24 h. After removal of excess of solvent, water (5 ml) was added and the whole extracted with $CHCl_3$ (20 ml × 3). The organic layers were dried ($MgSO_4$) and evaporated under reduced pressure. The crude product was purified by column chromatography (silica gel, EtOAc–hexane, 1:1) to give (**5b**) as a colourless oil (0.45 g, 42%); δ 1.37 (3 H, t, *J* 8.0 Hz), 3.04 (2 H, q, *J* 8.0 Hz), 5.53—5.75 (2 H, m), and 6.12—7.68 (3 H, m). The n.m.r. data are identical with those reported.[3c]

Alkylation of 2,5-*Dihydrothiophene* 1,1-*Dioxide* (**1**) *in DMF.*—To a suspension of sodium hydride (2.2 mmol) in anhydrous DMF (6 ml) cooled at −4 °C were added freshly distilled alkyl iodide (4.0 mmol) and then compound (**1**) (2.4 mmol) in DMF. The resulting mixture was quenched with water (1 ml) at 0 °C and then ether (90 ml) was added. The organic layer was dried ($MgSO_4$), the excess of solvent was removed under reduced pressure, and the residue purified by column chromatography (silica gel, EtOAc–hexane 1:4) and h.p.l.c. (LiChrosorb column, Merck, EtOAc–hexane 1:1) to give the pure products.

2-*Methyl*-2,5-*dihydrothiophene* 1,1-*dioxide* (**4a**). A colourless oil (69%), ν_{max} (liquid) 1 620, 1 440, 1 400, 1 380, 1 348, and 1 300 cm^{-1}; δ 1.36 (3 H, d, *J* 8.0 Hz), 3.75 (1 H, q, *J* 8.0 Hz), 3.70 (2 H, s), and 5.98 (2 H, s); *m/z* 132 (M^+) and 68 (100%), 53; i.r. data identical with those reported.[3a]

2-*Ethyl*-2,5-*dihydrothiophene* 1,1-*dioxide* (**4b**). A colourless oil (43%), ν_{max} (liquid) 1 620, 1 300, and 1 120 cm^{-1}; δ 1.05 (3 H, t, *J* 7.5 Hz), 1.51—2.10 (2 H, m), 3.67 (1 H, t, *J* 7.5 Hz), 3.70 (2 H, s), and 5.91 (2 H, s); *m/z* 146 (M^+), 82 (100%), 67, and 53

(Found: C, 49.65; H, 7.05. $C_6H_{10}O_2S$ requires C, 49.29; H, 6.89%).

2-*Propyl*-2,5-*dihydrothiophene* 1,1-*dioxide* (**4c**). A pale yellow *oil* (41%), ν_{max} (liquid) 1 620, 1 300, and 1 130 cm^{-1}; δ 1.10 (3 H, t, *J* 7.5 Hz), 1.50—2.00 (4 H, m), 3.75 (1 H, t, *J* 7.5 Hz), 3.70 (2 H, s), and 6.09 (2 H, s); *m/z* 160 (M^+), 96, 67 (100%), and 53 (Found: C, 52.7; H, 7.75%; M, 160.0552. $C_7H_{12}O_2S$ requires C, 52.47; H, 7.55%; *M*, 160.0555).

2-*Butyl*-2,5-*dihydrothiophene* 1,1-*dioxide* (**4d**). A pale yellow oil (40%), ν_{max} (liquid) 1 640, 1 300, and 1 130 cm^{-1}; δ 1.06 (3 H, t, *J* 8.0 Hz), 1.20—1.80 (6 H, m), 3.75 (1 H, t, *J* 8.0 Hz), and 6.05 (2 H, s); *m/z* 174 (M^+), 110, 81, 67 (100%), and 53 (Found: C, 54.75; H, 8.05. $C_8H_{14}O_2S$ requires C, 55.14; H, 8.10%).

2-*Allyl*-2,5-*dihydrothiophene* 1,1-*dioxide* (**4e**). A colourless oil (65%), ν_{max} (liquid) 1 640, 1 620, 1 305, and 1 130 cm^{-1}; δ 2.23—3.00 (2 H, m), 3.77 (1 H, t, *J* 8.0 Hz), 3.70 (2 H, s), 5.09—5.32 (2 H, m), 5.60—6.01 (1 H, m), and 6.09 (2 H, s); *m/z* 158 (M^+), 94, 79 (100%), 64, and 53 (Found: C, 52.85; H, 6.6. $C_7H_{10}O_2S$ requires C, 53.14; H, 6.37).

2-*Methyl*-4,5-*dihydrothiophene* 1,1-*dioxide* (**7a**).[7c] A white solid (20%), m.p. 53—55 °C; ν_{max} (KBr) 1 460, 1 440, 1 280, and 1 140 cm^{-1}; δ 1.22 (3 H, t, *J* 7.0 Hz), 2.36 (2 H, q, *J* 7.0 Hz), 2.60—2.90 (2 H, m), 3.26 (2 H, t, *J* 7.0 Hz), and 6.24 (1 H, br s); *m/z* 132 (M^+), 89, 67 (100%), and 53. The n.m.r. data are identical with those reported.[7c]

2-*Ethyl*-4,5-*dihydrothiophene* 1,1-*dioxide* (**7b**). A white solid (33%), m.p. 53.5—55.5 °C; ν_{max} (KBr) 1 460, 1 440, 1 280, and 1 140 cm^{-1}; δ 1.22 (3 H, t, *J* 7.0 Hz), 2.36 (2 H, q, *J* 7.0 Hz), 2.60—2.88 (2 H, m), 3.12 (2 H, t, *J* 7.0 Hz), and 6.19 (1 H, br s); δ_C 145.9, 129.7, 47.9, 23.8, 17.0, and 11.9; *m/z* 146 (M^+), 129, 81, 79, 67, and 57 (100%) (Found: C, 49.0; H, 6.85. $C_6H_{10}O_2S$ requires C, 49.29; H, 6.89).

2-*Propyl*-4,5-*dihydrothiophene* 1,1-*dioxide* (**7c**). A colourless oil (40%), ν_{max} (liquid) 1 605, 1 470, 1 440, 1 410, 1 140, and 1 110 cm^{-1}; δ 0.92 (3 H, t, *J* 7.0 Hz), 1.30—1.80 (2 H, m), 2.36 (2 H, t, *J* 7.0 Hz), 2.60—2.88 (2 H, m), 3.22 (2 H, t, *J* 7.0 Hz), and 6.18 (1 H, br s); *m/z* 160 (M^+), 95, 81, and 67 (100%) (Found: C, 52.75; H, 7.6%; *M*, 160.0548 $C_7H_{12}O_2S$ requires C, 52.47; H, 7.55%; *M*, 160.0555).

2-*Butyl*-4,5-*dihydrothiophene* 1,1-*dioxide* (**7d**). A colourless oil (28%), ν_{max} (liquid) 1 610, 1 470, 1 410, 1 295, and 1 140 cm^{-1}; δ 0.92 (3 H, t, *J* 7.0 Hz), 1.11—1.80 (4 H, m), 2.38 (2 H, t, *J* 7.0 Hz), 2.64—2.88 (2 H, m), 3.22 (2 H, t, *J* 7.0 Hz), and 6.18 (1 H,br s); *m/z* 174 (M^+), 132, 109, and 67 (100%) (Found: C, 54.75; H, 8.0%; *M*, 174.069 9. $C_8H_{14}O_2S$ requires C, 55.14; H, 8.10%; *M*, 174.071 5).

Analysis of Products from the Reaction of 2,5-*Dihydrothiophene* 1,1-*Dioxide* (**1**) *with Ethyl Iodide*.—To a suspension of NaH (0.81 g, 16.9 mmol) cooled at −8 °C were added freshly distilled EtI (2.37 g, 17.5 mmol) and then compound (**1**) (2.39 g, 20.5 mmol) in DMF (6 ml). The resulting mixture was stirred at −8 °C for 22 h after which time water (3 ml) and then $CHCl_3$ were added and the layers separated. The organic layer was dried ($MgSO_4$) the excess of solvent was removed under reduced pressure, and crude product mixture was purified by column chromatography and h.p.l.c. The yields of the products are indicated in Scheme 4.

trans-2,5-*Diethyl*-2,5-*dihydrothiophene* 1,1-*dioxide* (**11a**). A colourless oil, ν_{max} (liquid) 1 460, 1 295, 1 260, 1 225, and 1 115 cm^{-1}; δ 1.12 (6 H, t, *J* 7.0 Hz), 1.72 (2 H, q, *J* 7.0 Hz), 1.98 (2 H, dq, $J_1 = J_2 = 7.0$ Hz), 3.54 (2 H, t, *J* 7.0 Hz), 5.96 (2 H, s); δ_C 128.6, 65.9, 22.4, and 11.6; *m/z* 174 (M^+), 110. 81 (100%), and 68.

cis-2,5-*Diethyl*-2,5-*dihydrothiophene* 1,1-*dioxide* (**11b**). A colourless oil, ν_{max} (liquid) 1 460, 1 295, 1 240, 1 125, and 1 045 cm^{-1}; δ 1.12 (6 H, t, *J* 7.0 Hz), 1.62 (2 H, q, *J* 7.0 Hz), 1.96 (2 H, dq, $J_1 = J_2 = 7.0$ Hz), 3.59 (2 H, t, *J* 7.0 Hz), and 5.92 (2 H, s); δ_C 128.3, 66.6, 23.1, and 12.7; *m/z* 174 (M^+), 110, 81 (100%), and 68. The n.m.r. data are identical with those provided by Professor J. M. McIntosh.[10]

2,5-*Diethyl*-4,5-*dihydrothiophene* 1,1-*dioxide* (**12**). A colourless oil, ν_{max} (liquid) 1 465, 1 440, 1 285, 1 265, and 1 140 cm^{-1}; δ 1.12 (3 H, t, *J* 7.0 Hz), 1.21 (3 H, t, *J* 7.0 Hz), 1.68 (1 H, dq, $J_1 = J_2 = 7.0$ Hz), 2.04 (1 H, dq, $J_1 = J_2 = 7.0$ Hz), 2.44 (2 H, q, *J* = 7.0 Hz), 2.60—3.20 (3 H, m), and 6.16 (1 H, br s); δ_C 145.5, 128.7, 60.2, 31.4, 22.5, 17.9, 12.4, and 12.1; *m/z* 174 (M^+), 157, 81, 67 (100%), 57, and 55 (Found: C, 55.4; H, 8.0%; *M*, 174.0719 $C_8H_{14}O_2S$ requires C, 55.14; H, 8.10%; *M*, 174.0715).

Base-induced Isomerization of (**1**), (**4a**), (**4b**), (**16**), *and* (**18a**) *to* (**6**), (**7a**), (**7b**), (**17**), *and* (**19a**), *respectively*.—To a suspension of NaH (4.0 mmol) in anhydrous DMF (6 ml) at room temperature was added the sulpholene (2.0 mmol) in DMF. The resulting mixture was stirred at room temperature for 2 h after which water or [$^2H_2$]water (0.5 ml) were added and the mixture worked up. The product ratios were determined by n.m.r. analysis and the yields are indicated in Scheme 6.

2-*Deuteriated*-4,5-*dihydrothiophene* 1,1-*dioxide* (**10**). A white solid; δ 2.56—3.10 (2 H, complex), 3.23 (2 H, t, *J* 7.0 Hz), and 6.80 (1 H, br s).

2,2,5,5-*Tetradeuteriated*-2,5-*dihydrothiophene* 1,1-*dioxide* (**9**). A colourless oil; δ 6.07 (s).

Reaction of 2-*Ethyl*-2,5-*dihydrothiophene* 1,1-*Dioxide* (**4b**) *with Ethyl Iodide*.—To a suspension of NaH (11.0 mg, 0.23 mmol) in anhydrous DMF (0.3 ml) cooled at −3 °C were added freshly distilled EtI (146 mg, 0.94 mmol) and then (**4b**) (18 mg, 0.15 mmol) in DMF. The resulting mixture was stirred at −3 °C for 22 h after which time water (0.2 ml) then ether (25 ml) were added and the layers separated. The organic layer was dried ($MgSO_4$) and the excess of solvent was removed under reduced pressure. The crude product was purified by column chromatography and the ratio of the products was determined by h.p.l.c. analysis. The yields of the products are indicated in Scheme 7.

Alkylation of 3-*Methyl*-2,5-*dihydrothiophene* 1,1-*Dioxide* (**16**).—To a suspension of NaH (3 mmol) in anhydrous DMF (6 ml) cooled at −4 °C were added freshly distilled alkyl iodide (3.6 mmol) and then (**16**) (6 mmol) in DMF. The resulting mixture was stirred at −4 °C for 24 h after which time water (2 ml) was added. $CHCl_3$ (60 ml) was then added and the layers separated. The organic layer was dried ($MgSO_4$), the excess of solvent was removed under reduced pressure, and the residue purified by column chromatography and h.p.l.c. The yields are indicated in Scheme 8.

2,3-*Dimethyl*-2,5-*dihydrothiophene* 1,1-*dioxide* (**18a**). A colourless oil, ν_{max} (liquid) 1 450, 1 310, 1 250, 1 230, and 1 120 cm^{-1}; δ 1.40 (3 H, d, *J* 7.0 Hz), 1.82 (3 H, s), 3.54 (1 H, q, *J* 7.0 Hz), 3.68 (2 H, s), and 5.62 (1 H, br s); δ_C 116.0, 62.0, 55.1, 17.3, and 12.0; *m/z* 146 (M^+), 82, and 67 (100%). The n.m.r. data are identical with those reported.[11]

2-*Ethyl*-3-*methyl*-2,5-*dihydrothiophene* 1,1-*dioxide* (**18b**). A colourless oil, ν_{max} (liquid) 1 450, 1 305, 1 250, 1 220, and 1 120 cm^{-1}; δ 1.08 (3 H, t, *J* 7.0 Hz), 1.68—2.04 (2 H, m), 1.80 (3 H, s), 3.40 (1 H, t, *J* 7.0 Hz), 3.62 (2 H, s), and 5.62 (1 H, br s); *m/z* 160 (M^+), 96, and 81 (100%) (Found: C, 52.3; H, 7.5%; *M*, 160.0559. $C_7H_{12}O_2S$ requires C, 52.47; H, 7.55%; *M*, 160.0555).

2,3-*Dimethyl*-4,5-*dihydrothiophene* 1,1-*dioxide* (**19a**). A white solid, m.p. 72—73 °C; ν_{max} (KBr) 1 440, 1 380, 1 270, 1 150, and 1 110 cm^{-1}; δ 1.86 (3 H, s), 1.92 (3 H, s), 2.70 (2 H, t, *J* 7.0 Hz), and 3.23 (2 H, t, *J* 7.0 Hz); *m/z* 146 (M^+), 103 (100%), 67, and 54 (Found: C, 49.2; H, 6.8%; *M*, 146.0402. $C_6H_{10}O_2S$ requires C, 49.29; H, 6.89%; *M*, 146.0401).

2-*Ethyl*-3-*methyl*-4,5-*dihydrothiophene* 1,1-*dioxide* (**19b**). A

white solid, m.p. 73.5—74.5 °C; ν_{max} (KBr) 1 440, 1 410, 1 285, 1 245, 1 150, and 1 105 cm^{-1}; δ 1.20 (3 H, t, *J* 7.0 Hz), 1.84 (3 H, s), 2.44 (2 H, q, *J* 7.0 Hz), 2.70 (2 H, t, *J* 7.0 Hz), and 3.22 (2 H, t, *J* 7.0 Hz); *m/z* 160 (M^+), 103, 81 (100%), and 67 (Found: C, 52.35; H, 7.7. $C_7H_{12}O_2S$ requires C, 52.47; H, 7.55%).

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