Novel Building Block, Furan-annelated 3-Sulpholene; Diels–Alder Reactions of 4,6-Dihydrothieno[3,4-*c*]furan *S,S*-Dioxide

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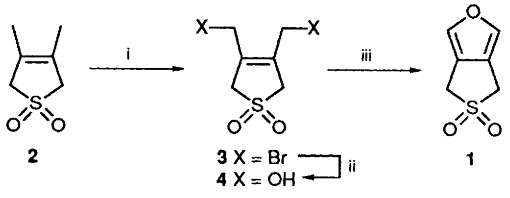
The preparation of the hitherto unknown 4,6-dihydrothieno[3,4-*c*]furan *S,S*-dioxide **1** and its intermolecular Diels–Alder reactions with typical dienophiles are described.

In the course of our studies on the chemistry of 2,5-dihydrothiophene *S,S*-dioxide (3-sulpholene),[1] we synthesized the previously unknown furan-annelated 3-sulpholene **1**, the precursor of the furan analogue of *o*-quinodimethane.[2] This compound **1** contains furan and 3-sulpholene moieties, both of which are readily functionalized, and so it would be expected that it could be used as a bis-diene which can sequentially react with two different kinds of dienophiles (tandem Diels–Alder reaction). Such a sequence is useful in the syntheses of variously substituted multicyclic molecules.

Compound **1** was synthesized as described in Scheme 1. The bromination of 3,4-dimethylsulpholene **2** with *N*-bromosuccinimide (NBS) gave the dibromide **3** (54%),[3] which on hydrolysis with silver trifluoroacetate in water afforded the diol **4** (m.p. 93–95.5 °C; 93%); furan-forming reactions of **4** were attempted under various conditions, but without success.[4] The desired furansulpholene **1** (m.p. 139–140 °C; 72%),† however, was obtained on treatment with pyridinium chlorochromate (PCC) in the presence of trifluoroacetic acid.

The Diels–Alder reaction of **1** with dimethyl acetylenedicarboxylate (DMAD; 3 equiv.) was carried out at 150 °C for 1 h (benzene; sealed tube), affording two types of cycloadducts: the monocycloadduct **5** bearing two methylene groups [(type A), 45%, cycloaddition to furan moiety and then desulphonylation] and the biscycloadduct **7** [(type B), 47%, cycloaddition to both furan and sulpholene, tandem cycloadduct] (Table 1, entry 1). Even at lower temperatures (120 °C; room temperature) the same cycloadducts were obtained (entries 2 and 3). Essentially the same type of reaction was observed with dimethyl fumarate as dienophile (entries 4 and 5). With other ethylenic dienophiles such as dimethyl maleate, cycloaddition proceeded at 150 °C, making it possible to isolate a new type of monocycloadduct **10b** [(type C), 10%, formal cycloaddition to sulpholene moiety, *i.e.* the retroreversion of **8b**] in addition to



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3 X = Br

4 X = OH

1

Scheme 1 *Reagents and conditions:* i, NBS, $CHCl_3$, reflux, 17 h; ii, CF_3CO_2Ag, H_2O, room temp., 72 h; iii, PCC, CF_3CO_2H, CH_2Cl_2, room temp., 30 min

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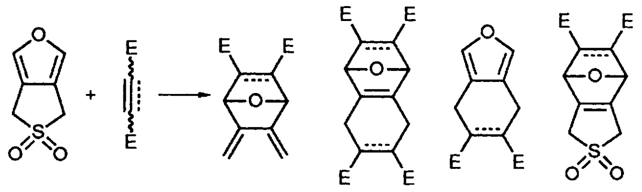
† ^1H NMR ($CDCl_3$; $SiMe_4$) δ 4.16 (4H, d, J 1.5 Hz) and 7.45 (2H, t, J 1.5 Hz); ^{13}C NMR ($CDCl_3$; $SiMe_4$); δ 51.2 (t), 116.5 (s) and 137.4 (d); IR ($CHCl_3$); ν/cm^{-1} 1305, 1115, 1015 and 880 cm^{-1}; m/z 158 (M^+) and 94 ($M^+ - SO_2$).

Table 1 Reactions of furansulpholene **1** with dienophiles



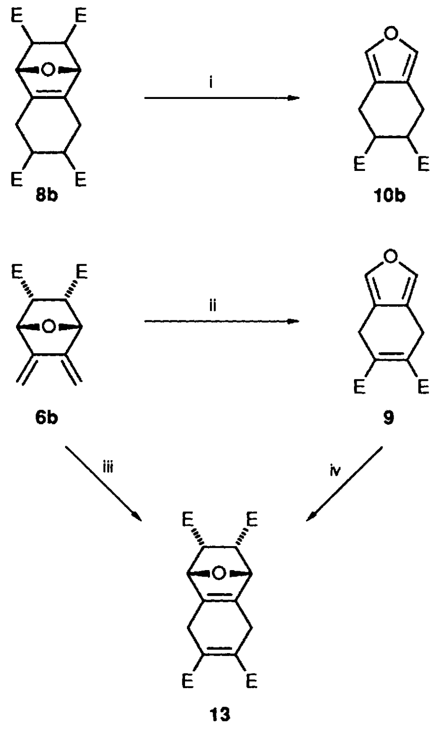
1 Dienophile alkyne alkene — **5** **6** type A — **7** **8** type B — **9** **10** type C — **11** **12** type D

Entry	Dienophile (3 equiv.)	Reaction conditions[a] (sealed tube)	Products (yield, %)[b] Type A	Type B	Type C	Type D	Total yield[c] (%)
1	DMAD	150 °C, 1 h	**5** (45)	**7** (47)			92
2	DMAD	120 °C, 1 h	**5** (62)	**7** (29)			91
3	DMAD	R.t., 168 h	**5** (54)	**7** (39)			93
4	Dimethyl fumarate	150 °C, 2 h	**6a** (61)	**8a** (26)			87
5	Dimethyl fumarate	120 °C, 4 h	**6a** (78)	**8a** (11)			89
6	Dimethyl maleate	150 °C, 3 h	**6b** (*endo* 53) (*exo* 10)		**10b** (10)		73
7	Dimethyl maleate	120 °C, 12 h	**6b** (*endo* 51) (*exo* 10)	**8b** (*endo* 11) (*exo* 18)			90
8	Fumaronitrile	150 °C, 3 h	**6c** (36)		**10c** (38)		74
9	*N*-Phenylmaleimide	150 °C, 3 h	**6d** (*exo* 46)		**10d** (26)		72
10	*N*-Phenylmaleimide	120 °C, 1 h		**8d** (*exo* 72)			72
11	*N*-Phenylmaleimide	150 °C, 4 h	**6e** (*exo* 58)		**10e** (4)		62
12	Maleic anhydride	R.t., 72 h				**12f** (*exo* 62)	62

[a] Each reaction stopped on consumption of the starting material **1**. R.t. = room temperature. [b] Isolated yields. [c] The reaction conditions were not optimized.

the type A monocycloadduct **6b** (entries 6 and 7). With fumaronitrile, the formation of the type C adduct **10c** (38%) predominated over that of type A **6c** (entry 8). Furthermore, **1** added to maleic anhydride at room temperature for 72 h to yield a single product, the fourth type of cycloadduct (**12f**) [(type D), *exo*, 62%, cycloaddition to furan moiety] (entry 12). The structures of all the new compounds thus obtained were confirmed by ^1H and ^{13}C NMR spectral data.

Thus, **1** reacts with various dienophiles to give four types of cycloadduct, A, B, C and D, depending on the dienophile and the reaction conditions, and even reacts with dimethyl maleate and dimethyl furmarate, whose adducts with furan have not been isolated under thermal conditions,[5] to afford Diels–Alder adducts. The formation of type A compounds, **5** and **6**, is the result of spontaneous desulphonylation of initially formed type D adducts, **11** and **12**, respectively. Despite the success in the isolation of **12**, all attempts to detect **11** failed owing to rapid desulphonylation (*e.g.* entry 3), but the isolation of a 1 : 1 adduct **X**‡ of **11** with **1** suggested the



E = CO_2Me

Scheme 2 *Reagent and conditions:* i, benzene, 150 °C, 1 h; ii, DMAD, benzene, 150 °C, 3 h; iii, DMAD, 12 kbar, 28 °C, 48 h; iv, benzene, 150 °C, 1 h

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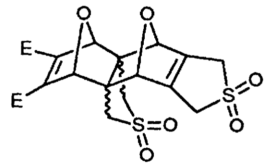
‡ M.p. 160–161 °C (decomp.); ^1H NMR (CD_3SOCD_3; $SiMe_4$) δ 3.60 (6H, s), 3.77 (4H, m), 4.10 (4H, m), 5.09 (2H, s) and 5.38 (2H, s); ^{13}C NMR ($CDSOCD_3$; $SiMe_4$) δ 52.53 (q), 56.15 (t), 56.53 (t), 69.35 (s), 79.06 (d), 82.68 (d), 139.84 (s), 144.78 (s) and 170.56 (s); *m/z*; 330 ($M^+ - 2 \times SO_2$), 299 (330 − OCH_3) and 271 (330 − CO_2CH_3). This adduct has structure **X** (unpublished data).



X

formation of **11**. In this rapid desulphonylation, the extra strain (which is attributed to two '*endo*cyclic alkene–oxa-bridge' repulsions[6]) of the oxanorbornadiene moiety of **11** plays an important role. Furthermore, the formation of the type C adduct at 150 °C can be explained by a retro-Diels–Alder reaction where the 7-oxanorbornene skeleton of the type B adduct **8** releases the unit alkene to afford furan owing to the restoration of aromatic character and the reduction of steric strain.[7] Compound *endo*-**8b**, when kept at 150 °C for 1 h, gave the type C adduct **10b** (36%) and *endo*-**6b** reacted with DMAD at the same temperature for 3 h to afford **9** (84%) which could not be isolated on treatment of **1** with DMAD (Scheme 2). These results suggested the formation of the 7-oxanorbornene system **13**§ by the process shown in Scheme 2. Indeed, **13** underwent retro Diels–Alder reaction to give **9** in quantitative yield.

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§ This compound was prepared from *endo*-**6b** and DMAD under 12 kbar pressure (CH_2Cl_2; 28 °C; 48 h; yield 98%) (unpublished data).

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