

# Synthesis of Furan-, Thiophene- and Pyrrole-fused Sultines and their Application in Diels–Alder Reaction†

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The synthesis of 1,4-dihydrofuran[3,4-*d*]-3,2-oxathiine 2-oxide **8**, 5,7-dimethyl-1,4-dihydrothieno[3,4-*d*]-3,2-oxathiine 2-oxide **9** and 1,4-dihydro-6-tosylpyrrolo[3,4-*d*]-3,2-oxathiine 2-oxide **10**, precursors for nonclassical heteroaromatic *o*-quinodimethanes, and their application in the Diels–Alder reactions are reported.

The chemistry of heterocyclic analogues of *o*-quinodimethane (*o*-QDM, **1**) has attracted a great deal of attention recently, and several reports of the generation of the furan and pyrrole derivatives have appeared.<sup>1</sup> The compounds 3,4-dimethylidene-furan **2**, 3,4-dimethylidenethiophene **3** and 3,4-dimethylidenepyrrole **4** are  $\pi$ -conjugated non-Kekulé molecules that have aroused theoretical and synthetic interest.<sup>1,2</sup> These 3,4-dimethylidene-heteroaromatics **2–4** were generated from the corresponding diazenes<sup>2</sup> and have been detected by EPR, UV and NMR spectroscopy. They have also been shown by Berson and coworkers<sup>2</sup> to react with a series of alkenes to form two types of cycloadducts: fused and bridged. The results are synthetically useful and have been elaborated upon by Takayama and coworkers in syntheses of multicyclic compounds.<sup>1b,c</sup>

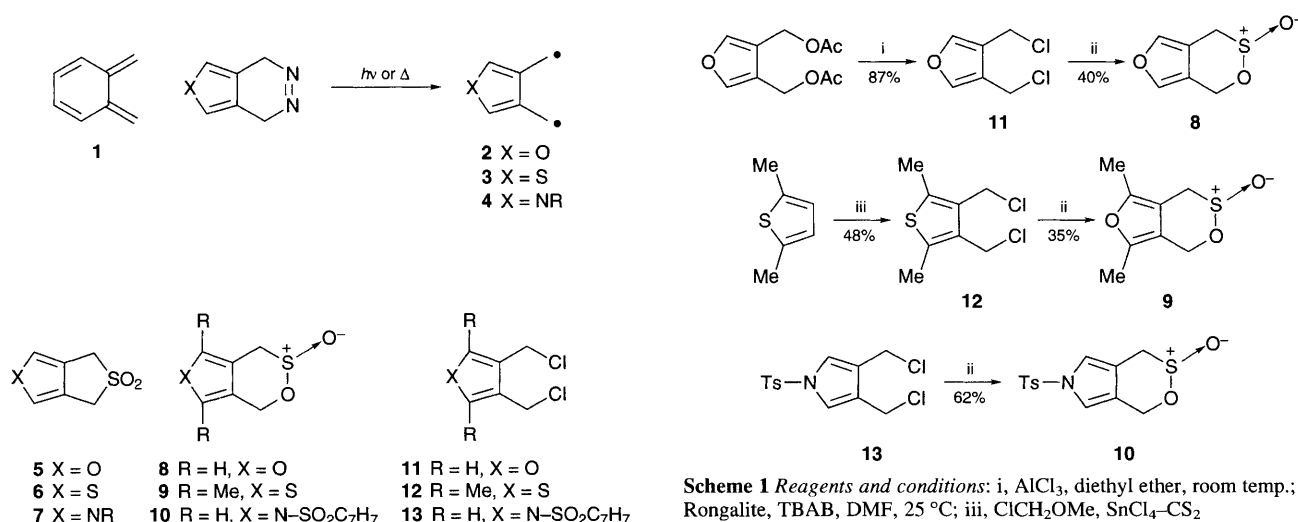
Diazene precursors are usually unstable at room temperature, therefore the search for possible substitutes becomes important. Various methods for generation of these highly reactive dienes have been developed.<sup>3,4</sup> Among the many known methods for their preparation, that involving cheletropic elimination of SO<sub>2</sub> from heteroaromatic-fused 3-sulfolenes **5–7** has drawn the most attention.<sup>1,4</sup> Durst *et al.* were the first to generate *o*-QDM by thermal elimination of SO<sub>2</sub> from a sultine, 1,4-dihydro-2,3-benzoxathiine 3-oxide.<sup>5</sup> A significant advantage of using sultines is that their thermolysis occurs at a much lower temperature than that of corresponding sulfolenes (80 vs. 170–220 °C). Recently other papers on using sultines as *o*-QDM precursors have appeared,<sup>6,7</sup> however, the use of sultines in heteroaromatic analogues is still rare. We report here our work on the synthesis of furanosultine **8**, thienosultine **9** and pyrrolosultine **10** and their applications in Diels–Alder reactions with alkenes and alkynes.

Previously unknown furanosultine **8** and thienosultine **9** are synthesized in two steps with good yield, as shown in Scheme 1. The 3,4-bis(chloromethyl)furan **11** was prepared by the known method.<sup>2b,8</sup> The bis(chloromethyl)thiophene **12** was obtained by chloromethylation of 2,5-dimethylthiophene adapted according to the procedures developed by Wynberg *et al.* in the synthesis of corresponding sulfoxes **6**.<sup>9</sup> The 3,4-bis(chloromethyl)-*N*-tosylpyrrole **13** was synthesized in four steps (41%

overall yield) as described by Berson and co-workers in the syntheses of corresponding diazenes.<sup>2</sup> The key step in the syntheses of sultines **8–10** is the use of Rongalite<sup>6,7a</sup> (sodium formaldehyde sulfoxylate) with the corresponding dichlorides **11–13**.‡

The Diels–Alder reactions of furan-fused sultine **8** with several dienophiles are presented in Table 1 (entries 1–5) and Scheme 2. Heating **8** with 3 equivalents of dimethyl acetylenedicarboxylate (DMAD) in benzene at 120–123 °C in a sealed tube for 1 h produced 5,6-dimethylidene-7-oxanorbornene **14a** in 38% yield plus some polymer by-products (Table 1, entry 1). Essentially the same types of reactions were observed with diethyl fumarate (DEF), dimethyl maleate (DMM) and fumaronitrile (FN) (Table 1, entries 2–4). With *N*-phenylmaleimide (NPM), thermolysis at 134–140 °C gave a new type of product **15e** in 24% yield. The low to medium yields of these reactions of furanosultine **8** with various dienophiles are disappointing, however, as their reaction products are different from those reported by Takayama and co-workers for the reactions of furan-fused sulfolene **5**,<sup>1b,c</sup> where two types of products **14** and **15** were formed. Furthermore, the high yield of intractable polymers in all cases also implies that radical or biradical-initiated polymerization is involved.

Thermal Diels–Alder reaction of 2,5-dimethylthiopheno-sultine **9** with several dienophiles was studied next (Table 1, entries 6–9). In the absence of a dienophile, sultine **9** underwent thermolysis to give the sulfolene **6** in excellent yield (90%, entry 6). Heating **9** with DMAD, DMF or NPM at 180 °C gave both the isomerized sulfolene **6** and fused adducts **16g** and **16h** in 89–97% yields. Unexpectedly, no adducts were formed when the thiophene-fused sulfolene **6** was heated in the presence of DMAD or DMF at the same reaction temperature (Table 1, entries 10–11). About 10% of the fused adduct **16h** was obtained only when a strong dienophile such as NPM was used (entries 9, 12). Wynberg *et al.*<sup>9a</sup> were the first to synthesize thiophene-fused sulfolene **6b** (R = CO<sub>2</sub>Me), however, they did not detail its chemical reactivities other than pyrolysis. Our results show that thiophene-fused sulfolene **6** has very low reactivity compared to the corresponding sultine **9** in the Diels–



Alder reaction. Thus, in the reaction conditions studied here, the fused Diels–Alder adducts **16g–h** can be obtained from the reaction of sultine **9** with dienophiles, but not from sulfolene **6**. It is interesting to observe the great similarity between our results with sultines with those with diazenes reported by Berson *et al.*<sup>2</sup> For example, in the thiophene–biradical **3** trapping experiments, the sole adducts found (85–100% yields) had the fused structure **16** rather than the bridged structure **14**.

Reactions of *N*-tosylpyrrolisultine **10** with a series of dienophiles (3 equiv.) at 150–170 °C run smoothly to give three types of products: sulfolene **7** (20–40%), 1:2 Diels–Alder adducts **15** (0–42%) and fused adducts **16** (5–73%) (Table 1, entries 13–18). Basically the same reaction products are obtained even at 110 °C (Table 1, entry 15), however to our surprise, only **7** and the fused adduct **16i** were obtained when

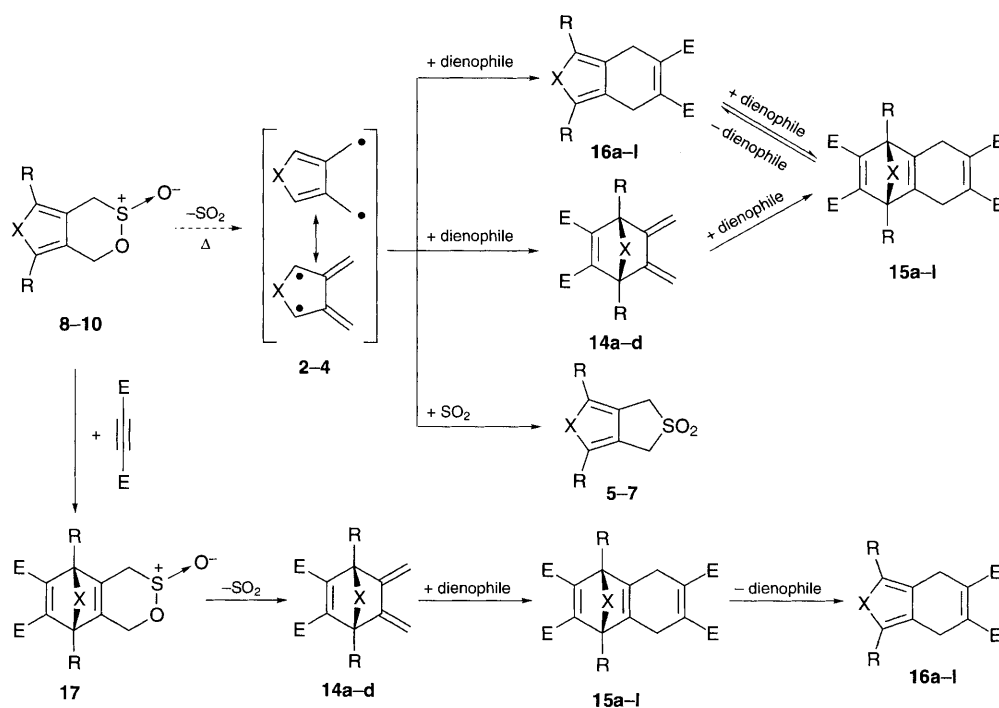
DMAD was reduced to 1 equiv. (entry 14). The *N*-tosylpyrrolisulfolene **7** had been shown to be unreactive<sup>10</sup> with dimethyl fumarate (DMF) even at 240 °C, however the *N*-tosylpyrrolisultine **10** reacted with DMF at 170 °C to give a fused adduct **16j** (63%) and the isomerized **7** (32%) (Table 1, entry 16 vs. 20). It is also of interest to isolate the fused adduct **16i** (5%) in the reaction of sultine **10** with DMAD compared with that of sulfolene **7**,<sup>1b,c</sup> where **15i** was the only product formed (entry 13 vs. 19).

These results can be explained by two mechanisms. The most obvious possibility is the formation of non-Kekulé biradicals (**2–4**), followed by Diels–Alder reaction with a dienophile to form either bridged (**14**) or fused adducts (**16**).<sup>2</sup> Both adducts can add another dienophile to form the 1:2 adducts (**15**). Alternatively, a Diels–Alder reaction may first occur on the aromatic moieties of sultines **8–10** to give **17**, from which SO<sub>2</sub>

Table 1 The Diels–Alder reactions of sultines **8–10** and sulfolenes **6–7** with dienophiles<sup>a</sup>

Entry	Diene	Dienophile	T/°C	t/h	Products (yield %) <sup>c</sup>	Total yield (%)	Ref.
1	<b>8</b>	DMAD	120–123	1	<b>14a</b> (38)	38	
2	<b>8</b>	DEF	140–145	6	<b>14b</b> (46)	46	
3	<b>8</b>	DMM	130–138	12	<b>14c</b> (38)	38	
4	<b>8</b>	FN	135–142	4	<b>14d</b> (53)	53	
5	<b>8</b>	NPM	134–140	3	<b>15e</b> (24)	24	
6	<b>9</b>	—	180	24	<b>6</b> (90)	90	
7	<b>9</b>	DMAD	180	24	<b>6</b> (44) + unknown	>44	
8	<b>9</b>	DMF	180	24	<b>6</b> (49) + <b>16g</b> (40)	89	
9	<b>9</b>	NPM	180	24	<b>6</b> (6) + <b>16h</b> (91)	97	
10	<b>6</b>	DMF	180	24	<b>6</b> (99)	99	
11	<b>6</b>	FN	180	24	<b>6</b> (99)	99	
12	<b>6</b>	NPM	180	24	<b>6</b> (89) + <b>16h</b> (10)	99	
13	<b>10</b>	DMAD	165–170	12	<b>7</b> (40) + <b>15i</b> (42) + <b>16i</b> (5)	87	
14	<b>10</b>	DMAD (1 equiv.)	155	12	<b>7</b> (40) + <b>16i</b> (9)	49	
15	<b>10</b>	DMAD	110	12	<b>7</b> (30) + <b>15i</b> (38) + <b>16i</b> (8)	76	
16	<b>10</b>	DMF	170	14	<b>7</b> (32) + <b>16j</b> (63)	95	
17	<b>10</b>	FN	170	17	<b>7</b> (34) + <b>16k</b> (50)	84	
18	<b>10</b>	NPM (4 equiv.)	156–160	22	<b>7</b> (20) + <b>16l</b> (73)	93	
19	<b>7</b>	DMAD	170	14	<b>15i</b> (97)	97	1b, 1c
20	<b>7</b>	DMF	170–240 <sup>b</sup>	33	<b>7</b> (73)	73	1b, 1c

<sup>a</sup> Reactions were run with 3 equiv. of dienophiles in benzene (sealed tube) unless otherwise specified. <sup>b</sup> Reaction was run in xylene. <sup>c</sup> Isolated yield. For structures of products **14a–16l** see Scheme 2.



Scheme 2 Possible reaction pathways

is eliminated instantaneously to give bridged adducts **14**. Compound **14** further reacts with another dienophile to give the 1:2 adducts **15**, and finally a retro-Diels–Alder reaction of **15** would occur to form **16** (Scheme 2). The latter mechanism was proposed by Takayama to explain results with corresponding sulfolenes **5** and **7**. We conclude that the furano-, thieno- and *N*-tosylpyrrolo-fused sultines **8–10** reacted under milder condition than the corresponding sulfones **5–7** and their reaction products were different in many cases. When generated in the presence of a dienophile, they can provide elegant synthons for the formation of [4 + 2] cycloadducts. If less reactive trapping agents were used, the diene was recaptured by SO<sub>2</sub> to afford the sulfones **5–7** (path 3 in Scheme 2).<sup>11</sup>

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### Footnotes

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‡ Dichlorides **11**,<sup>2</sup> **12<sup>ab</sup>** and **13<sup>2</sup>** have been reported in the literature and our samples correspond in all respects with the reported properties. For all products satisfactory spectral data were obtained. *Selected data for 8*: light yellow oil; <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>) δ 7.40 (1 H, s), 7.36 (1 H, s), 5.28 (1 H, AB, *J* 14.4 Hz), 5.02 (1 H, AB, *J* 14.4 Hz), 3.87 (1 H, A'B', *J* 15.6 Hz) and 3.65 (1 H, A'B', *J* 15.3 Hz); <sup>13</sup>C NMR (75.4 MHz, CDCl<sub>3</sub>) δ 141.01 (CH), 136.38 (CH), 113.92 (C<sub>q</sub>), 108.00 (C<sub>q</sub>), 55.03 (CH<sub>2</sub>) and 46.64 (CH<sub>2</sub>). For **9**: white solid, mp 70–71 °C; <sup>1</sup>H NMR, δ 5.16 (1 H, AB, *J* 14.1 Hz), 4.92 (1 H, AB, *J* 13.5 Hz), 3.88 (1 H, A'B', *J* 15.6 Hz), 3.58 (1 H, A'B', *J* 15.0 Hz) and 2.27 (6 H, s); <sup>13</sup>C NMR, 133.15 (C<sub>q</sub>), 128.72 (C<sub>q</sub>), 125.40 (C<sub>q</sub>), 119.13 (C<sub>q</sub>), 58.73 (CH<sub>2</sub>), 50.92 (CH<sub>2</sub>) and 12.11 (CH<sub>3</sub>); *m/z* 202 (M<sup>+</sup>), 138 (100%), 123 and 91; (Found: M<sup>+</sup> 202.0116 C<sub>8</sub>H<sub>10</sub>O<sub>2</sub>S<sub>2</sub> requires 202.0122). For **10**, white solid, mp 152–153 °C; <sup>1</sup>H NMR, δ 7.76 (2 H, d, *J* 8.8 Hz), 7.31 (2 H, d, *J* 8.1 Hz), 7.07 (1 H, s), 7.01 (1 H, s), 5.20 (1 H, AB, *J* 14.2 Hz), 4.91 (1 H, AB, *J* 14.2 Hz), 3.88 (1 H, A'B', *J* 15.6 Hz), 3.56 (1 H, A'B', *J* 15.6 Hz) and 2.42 (3 H, s); <sup>13</sup>C NMR, 145.50 (C<sub>q</sub>), 135.54 (C<sub>q</sub>), 130.15 (CH), 127.03 (CH), 119.19 (CH), 117.12 (C<sub>q</sub>), 114.44 (CH), 110.97 (C<sub>q</sub>),

55.99 (CH<sub>2</sub>), 48.21 (CH<sub>2</sub>) and 21.64 (CH<sub>3</sub>); *m/z* 311 (M<sup>+</sup>), 247 (100%), 155 and 92.

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