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

Wen-Sheng Chung,* Wen-Ju Lin, Wen-Dar Liu and Liang-Gyi Chen

Department of Applied Chemistry, National Chiao Tung University, Hsinchu, Taiwan 30050, R. O. C.

The synthesis of 1,4-dihydrofurano[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.

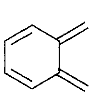
The chemistry of heterocyclic analogues of *o*-quinodimethane (*o*-QDM, **1**) has attracted a great deal of attention recently, and several reports of the generation of the furan and pyrrole derivatives have appeared.[1] The compounds 3,4-dimethylidenefuran **2**, 3,4-dimethylidenethiophene **3** and 3,4-dimethylidenepyrrole **4** are π-conjugated non-Kekulé molecules that have aroused theoretical and synthetic interest.[1,2] These 3,4-dimethylidene-heteroaromatics **2–4** were generated from the corresponding diazenes[2] and have been detected by EPR, UV and NMR spectroscopy. They have also been shown by Berson and coworkers[2] 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.[1b,c]

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.[3,4] Among the many known methods for their preparation, that involving cheletropic elimination of SO_2 from heteroaromatic-fused 3-sulfolenes **5–7** has drawn the most attention.[1,4] Durst *et al.* were the first to generate *o*-QDM by thermal elimination of SO_2 from a sultine, 1,4-dihydro-2,3-benzoxathiine 3-oxide.[5] 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,[6,7] 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.[2b,8] 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 sulfones **6**.[9] 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.[2] The key step in the syntheses of sultines **8–10** is the use of Rongalite[6,7a] (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**,[1b,c] 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-dimethylthiophenosultine **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.*[9a] were the first to synthesize thiophene-fused sulfolene **6b** (R = CO_2Me), 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–



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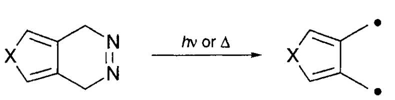
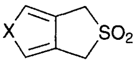
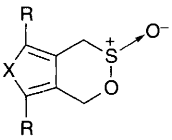


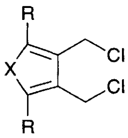
2 X = O
3 X = S
4 X = NR



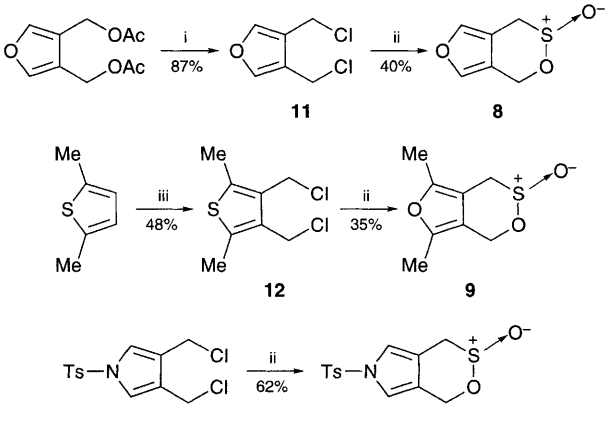
5 X = O
6 X = S
7 X = NR



8 R = H, X = O
9 R = Me, X = S
10 R = H, X = $N{-}SO_2C_7H_7$



11 R = H, X = O
12 R = Me, X = S
13 R = H, X = $N{-}SO_2C_7H_7$



Scheme 1 *Reagents and conditions*: i, $AlCl_3$, diethyl ether, room temp.; ii, Rongalite, TBAB, DMF, 25 °C; iii, $ClCH_2OMe$, $SnCl_4$–CS_2

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.*[2] 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**.

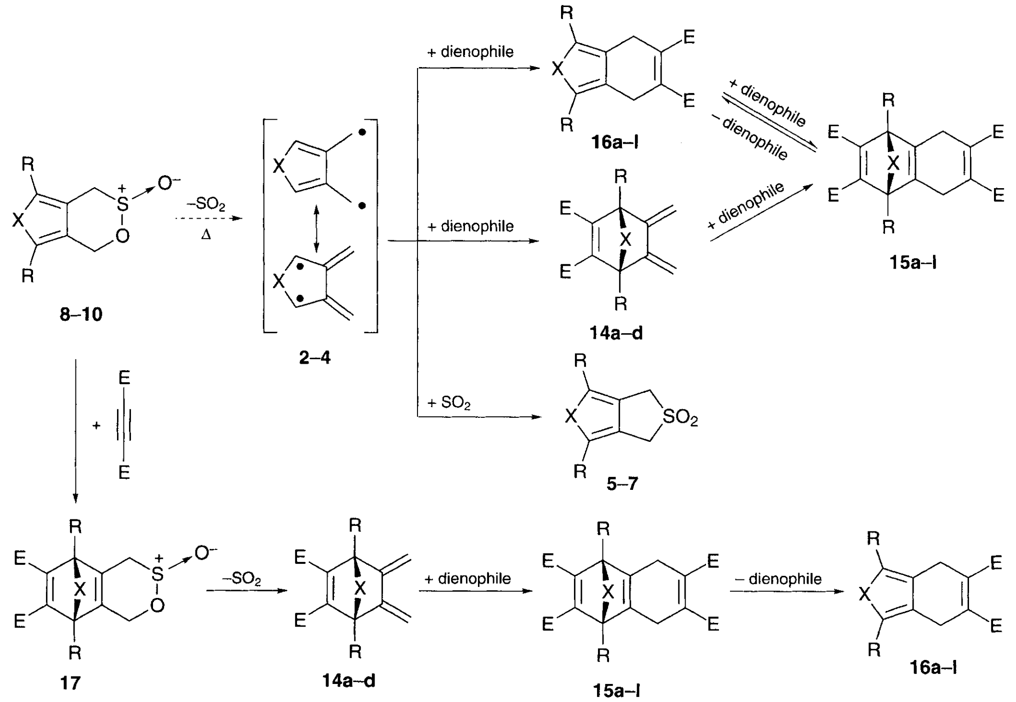
Reactions of *N*-tosylpyrrolosultine **10** with a series of dienophiles (3 equiv.) at 150–170 °C run smoothly to give three types of products: sulfolene **7** (20–40%), 1:2 Diels–Alder adducts **15** (0–42%) and fused adducts **16** (5–73%) (Table 1, entries 13–18). Basically the same reaction products 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*-tosylpyrrolosulfolene **7** had been shown to be unreactive[10] with dimethyl fumarate (DMF) even at 240 °C, however the *N*-tosylpyrrolosultine **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**,[1b,c] 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**).[2] 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_2

Table 1 The Diels–Alder reactions of sultines **8–10** and sulfolenes **6–7** with dienophiles[a]

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

[a] Reactions were run with 3 equiv. of dienophiles in benzene (sealed tube) unless otherwise specified. [b] Reaction was run in xylene. [c] 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_2 to afford the sulfones **5–7** (path 3 in Scheme 2).[11]

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Footnotes

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‡ Dichlorides **11**,[2] **12**[9b] and **13**[2] 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; ^1H NMR (300 MHz, $CDCl_3$) 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); ^{13}C NMR (75.4 MHz, $CDCl_3$) δ 141.01 (CH), 136.38 (CH), 113.92 (C_q), 108.00 (C_q), 55.03 (CH_2) and 46.64 (CH_2). For **9**: white solid, mp 70–71 °C; ^1H 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); ^{13}C NMR, 133.15 (C_q), 128.72 (C_q), 125.40 (C_q), 119.13 (C_q), 58.73 (CH_2), 50.92 (CH_2) and 12.11 (CH_3); *m/z* 202 (M^+), 138 (100%), 123 and 91; (Found: M^+ 202.0116 $C_8H_{10}O_2S_2$ requires 202.0122). For **10**, white solid, mp 152–153 °C; ^1H 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 (1H, 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 (1H, A′B′, *J* 15.6 Hz) and 2.42 (3 H, s); ^{13}C NMR, 145.50 (C_q), 135.54 (C_q), 130.15 (CH), 127.03 (CH), 119.19 (CH), 117.12 (C_q), 114.44 (CH), 110.97 (C_q), 55.99 (CH_2), 48.21 (CH_2) and 21.64 (CH_3); *m/z* 311 (M^+), 247 (100%), 155 and 92.

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