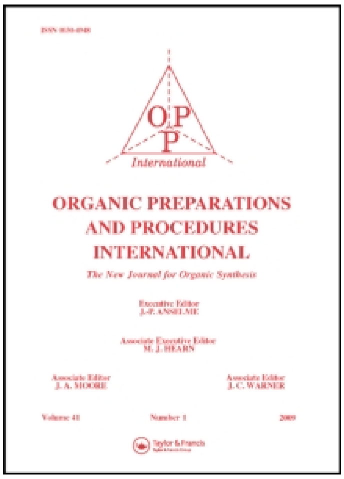

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REACTION OF 3-SULFOLENES WITH CONJUGATED ALDEHYDES AND KETONES

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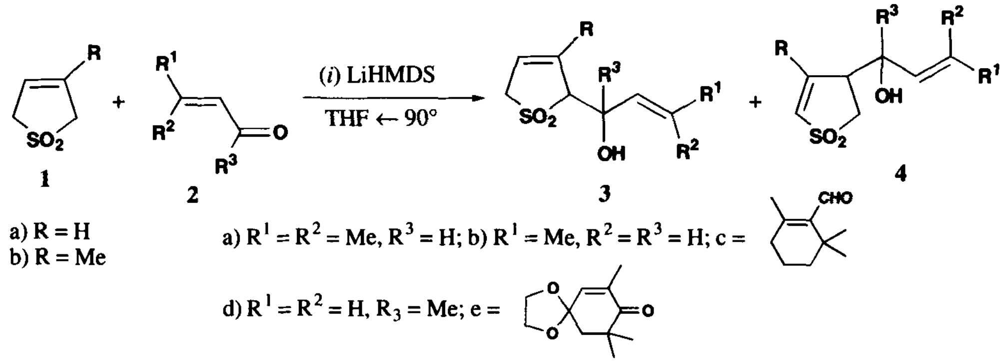
The reaction of 3-sulfolene anion with alkyl iodides followed by thermal extrusion of sulfur dioxide provides a facile stereoselective method for synthesis of (E), (EZ) and (EE) conjugated dienes.[1-7] The extension of this reaction to carbonyl compounds leads to synthesis of 5-hydroxy-1,3-dienes.[8] The 1,3-dienes find further applications in *intra* and *intermolecular* Diels-Alder reactions as well as in the total synthesis of natural products such was pheromones and other perfume chemicals. However, there is only one report[8] for the reaction of sulfolene α-carbanion with methyl vinyl ketone which led predominantly to 1,4-addition with products of 1,2-addition being the minor products. We now report that the alkylation of 3-sulfolene (**1a**) and 3-methyl-3-sulfolene (**1b**) led to predominant 1,2-addition to conjugated aldehydes and ketones **2** at < -90° to yield sulfolenes **3** and **4**.

The reaction of one equiv. of 3-sulfolene (**1a**) or 3-methyl-3-sulfolene (**1b**) with two equiv. of the appropriate aldehyde or ketone in dry THF at < -90° in the presence of two equiv. of 1,1,1,3,3,3-hexamethyldisilazane lithium salt (LiHMDS) yielded predominantly 2-(1-hydroxy-2-alkenyl)-3-sulfolene (**3**) and/or 4-(1-hydroxy-2-alkenyl)-2-sulfolene (**4**) (Table 1). The formation of the sulfolene **4** may be rationalized by attack of the anion delocalized at the γ-position.

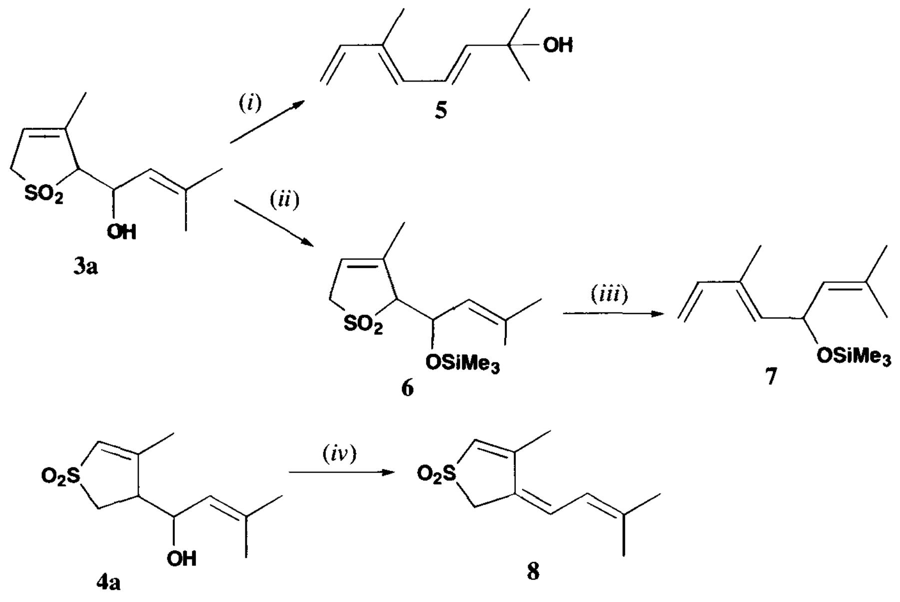


a) R = H
b) R = Me

a) $R^1 = R^2 = Me, R^3 = H$; b) $R^1 = Me, R^2 = R^3 = H$; c =

d) $R^1 = R^2 = H, R_3 = Me$; e =

The desulfonylation of hydroxysulfolenes **3** and **4** was attempted using a variety of conditions. Heating of sulfolene **3a** in the presence of K_2CO_3 in EtOH (sealed tube) yielded the rearranged hydroxytriene **5**. Therefore, the hydroxyl group was converted to trimethylsilyl derivative **6** which underwent smooth desulfonylation in pyridine at reflux to yield the triene **7**. Heating of hydroxysulfolene **4a** in pyridine in the presence of 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU) afforded sulfolene **8**.



i) K_2CO_3 EtOH, Sealed tube *ii*) TMSCl, pyridine, ether *iii*) pyridine, Δ *iv*) DBU, pyridine, Δ

Table 1. Reaction of 3-Sulfolenes with Conjugated Carbonyl Compounds

Sulfolene	Carbonyl Compound	(2)	Products (%)	
1b	3-Methyl-2-butenal	**(2a)**	**3a** (80)	**4a** (20)
1b	Crotonaldehyde	**(2b)**	**3b** (85)	**4b** (15)
1b	β-Cyclocitral	**(2c)**	**3c** (71)	**4c** (0)
1b	Methyl vinyl ketone	**(2d)**	**3d** (60)	**4d** (0)
1b	Ketone	**(2e)**	**3e** (0)	**4e** (49)[a]
1a	Ketone	**(2e)**	**3f** (0)	**4f** (64)[a]

a) Deketalization occurred during workup.

EXPERIMENTAL SECTION

^{1}H NMR spectra were determined on Hitachi R-600 (60 MHz) and Varian (300 MHz) using TMS as internal standard. Mass spectra were recorded with Shimadzu GC MS QP 1000 spectrometer at 70 eV. IR spectra were obtained in a Perkin Elmer 681 spectrometer. The microanalyses were carried out using a Carlo Erba strumentazione 1106 Elemental Analyzer.

TABLE 2. Spectral Data of Compounds **3-8**

Compd	IR (cm^{-1})^a	NMR (δ)^b
3a	3480, 1610, 1480 1320, 1150	5.8 (1H, bs), 4.7 (1H, m), 3.7 (3H, bs), 1.95 (3H, s), 1.85 (3H, s) 1.7 (3H, s)
4a	3510, 1630, 1410 1320, 1150	6.2 (1H, bs), 5.2 (1H, d), 4.8 (1H, m), 3.1-3.4 (3H, m), 2.1 (3H, s) 1.8(6H, s)
3b	3480, 1610, 1310 1280, 1150	5.38 (3H, m), 4.5 (1H, bt), 3.7(3H, bs), 3.5 (1H, s, OH), 1.9 (3H, s), 1.7 (3H, d)
4b	3510, 1630, 1320 1120	6.25 (1H, bs), 5.8 (1H, m), 5.4 (1H, m), 4.5 (1H, bt), 3.25 (2H, m), 2.1-2.2 (4H, m), 1.7 (3H, d)
3c	3510, 1620, 1540 1380, 1280	5.78 (1H, bs), 4.67 (1H, d, J = 10.2Hz), 4.1 (1H, d, J = 10.2Hz), 3.82 (1H, m), 3.7 (1H, m)2.0 (2H, m), 1.92(3H, s), 1.85 (3H, s), 1.5-1.65 (2H, m), 1.45 (2H, m), 1.07 (3H, s), 0.85 (3H, s)
3d	3510, 1620, 1350 1280, 1150	6.0 (1H, m), 5.8 (1H, bs), 5.1-5.4 (2H, m), 3.4 (3H, bs), 1.95 (6H, bs), 1.4 (3H, s)
4e	3510, 1710, 1480 1320, 1290, 1150^c	6.84 (1H, s), 5.96 (1H, s), 5.07 (1H, s, OH), 3.31(1H, m), .3.06 (2H, m), 2.95 (1H, d, J = 17Hz),2.05(1H, d, J = 17Hz), 1.91(3H, s),1.88 (3H, s), 0.96(3H, s), 0.94 (3H, s)^d
4f	3500, 1705, 1610 1380, 1250, 1180^c	7.05 (1H, dd, J = 6.7Hz, 2.3Hz), 6.50 (1H, dd, J = 6.7Hz, 2.9Hz), 5.9 (1H, s), 5.21 (1H, s, 0H),3.8 (1H, m), 3.55 (1H, m), 3.4 (1H, m), 2.7 (1H, d, J = 18.1Hz), 2.1 (1H, d, J = 18.1 Hz), 1.86 (3H, s) 0.95 (3H, s) 0.92 (3H, s)
5	3500, 1630, 1580, 1350, 1180	5.8-6.7 (4H, m) 5.3 (1H, d J = 17.5Hz), 5.1 (1H, d, J = 10.5Hz), 1.9 (3H, s), 1.4 (6H, s)^d
6	1630, 1580, 1350 1210, 1180, 1020	5.8 (1H, bs), 5.3 (1H, bt), 4.8 (1H, dd, J = 11Hz, 4Hz), 3.5 (3H, bs), 1.95 (3H, bs), 1.90 (3H, s),1.7 (3H, s), 0.1 (9H, s)
7	1650, 1620, 1430 1380, 1320	6.3 (1H, dd, J = 18Hz, 12Hz), 5.2 (4H, m), 1.8 (3H, s), 1.7 (6H, s), 0.1 (9H, s)
8	1630, 1610, 1480 1350, 1280	6.6 (1H, d, J = 12Hz), 6.4 (1H, bs), 5.8 (1H, d, J = 12Hz), 3.95 (2H, bs),2.1 (3H, s), 1.9 (6H, s)

a) Neat unless otherwise noted. b) In $CDCl_3$ unless otherwise noted, c) As Nujol mull d) In DMSO-d_6

Preparation of 2-(1-hydroxy-2-alkenyl)-3-sulfolene (3) and 4-(1-hydroxy2-alkenyl)-2-sulfolene (4).- To a mixture of sulfolene **1a** or **1b** (10 mmol) and conjugated aldehyde or ketone **2** (20 mmol) in THF (10 mL) at < -90° (MeOH, liq. N_2) added dropwise a solution of LiHMDS (10 mmol) in THF (5 mL) under an atmosphere of Ar. The resulting mixture was allowed to warm up gradually to 0° and quenched with a saturated solution of ammonium chloride (10 mL). The organic layer was separated and the solvent was removed under reduced pressure. The semi-solid residue was diluted with ethyl acetate (20 mL), washed with brine, dried over $MgSO_4$ and evaporated to dryness. The semi-solid residue was purified by column chromatography over silica gel (100-200 mesh, eluent:petroleum ether and ethylacetate 3:1) to yield sulfolenes **3** and **4** (Table 1).

TABLE 3. Elemental Analyses and MS Data

Cmpd	CH Analysis (Found)		MS(M^+m/z)	Calcd
	C	H		
3a	55.53 (55.35)	7.46 (7.30)	216	216.30
4a	55.53 (55.30)	7.45 (7.31)	216	216.30
3b	53.45 (53.20)	6.98 (6.78)	202	202.27
4b	53.45 (53.28)	6.98 (6.79)	202	202.27
3c	63.35 (63.25)	8.50 (8.28)	284	284.41
3d	53.44 (53.21)	6.99 (6.63)	202	202.27
4e	59.13 (59.08)	7.09 (7.03)	284	284.37
4f	57.76 (57.48)	6.72 (6.60)	270	270.34
5	78.90 (78.74)	10.59 (10.37)	152	152.23
6	54.14 (54.07)	8.39 (8.29)	288	288.48
7	69.59 (65.47)	10.79 (10.60)	224	224.41
8	60.58 (60.39)	7.12 (7.05)	198	198.28

Synthesis of Trimethylsilyl Derivative 6.- To a solution of **3a** (1.08 g, 5 mmol) in pyridine (5 mL) and ether (20 mL) at 0° was added dropwise chlorotrimethylsilane (0.5 g, 5 mmol) under an argon atmosphere. The reaction mixture was stirred for 1 hr and poured into ice cold water and extracted with ether (2 x 50 mL). The organic layer was concentrated and the viscous residue was purified by column chromatography over silica gel to yield compound **6** (1.09 g, 73%).

Thermolysis of Sulfolene 6.- A solution of **6** (1.44 g, 5 mmol) in pyridine (20 mL) was refluxed for 1 hr. Then pyridine was removed under vacuum and the residue was chromatographed over silica gel to yield the triene **7** (0.8 g, 72%).

Thermolysis of Sulfolene 3a.- A solution of **3a** (1.08 g, 5 mmol) in ethanol (5 mL) and K_2CO_3 (0.2 g) was taken in a sealed tube. It was heated at 125° for 30 minutes and the reaction mixture was extracted with ethyl acetate, dried over anhydrous sodium sulfate and evaporated to dryness in vacuum and purified by column chromatography over silica gel to yield the rearranged hydroxytriene **5**.

Attempted Thermolysis of Sulfolene 4a.- A mixture of **4a** (1.08 g, 5 mmol) and DBU (1.12 g, 10 mmol) in pyridine (20 mL) was refluxed vigorously for 23 hrs. Pyridine was removed under vacuum and the residue was chromatographed over silica gel to yield dehydration product **8** (0.7 g, 80%).

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