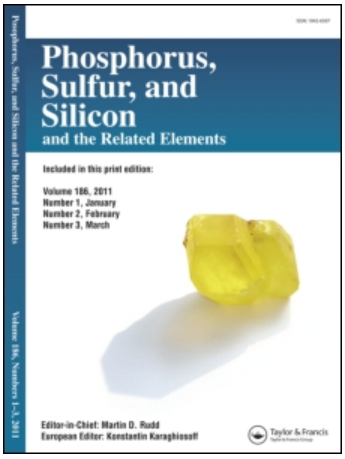

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DIASTEREOSELECTIVE SYNTHESIS AND STEREOCHEMISTRY OF (*Z*)-1-[3-ARYL-2-(PHENYLSULFANYL)-2-OXIRANYL]-1-ETHANONES

E. Karthikeyan[a]; S. Perumal[a]; s. Selvaraj[a]
[a] Department of Organic Chemistry, School of Chemistry, Madurai Kamaraj University, Madurai, India

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DIASTEREOSELECTIVE SYNTHESIS AND STEREOCHEMISTRY OF (*Z*)-1-[3-ARYL-2-(PHENYLSULFANYL)-2-OXIRANYL]-1-ETHANONES

E. Karthikeyan, S. Perumal, and S. Selvaraj
Department of Organic Chemistry, School of Chemistry, Madurai Kamaraj University, Madurai, India

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*Diastereoselective synthesis of a series of (*Z*)-1-[3-aryl-2-(phenylsulfanyl)-2-oxiranyl]-1-ethanones was effected from the reaction of (*Z*)-4-aryl-3-(phenylsulfanyl)-3-buten-2-ones with alkaline hydrogen peroxide in tetrahydrofuran. The stereochemistry of the oxiranes has been deduced from two-dimensional NOESY spectrum.*

Keywords: 1-[3-aryl-2-(phenylsulfanyl)-2-oxiranyl]-1-ethanones; hydrogen peroxide; NMR; synthesis; stereochemistry; (*Z*)-4-aryl-3-(phenylsulfanyl)-3-buten-2-ones

INTRODUCTION

Epoxidation of alkenes is a synthetically important reaction because epoxides can be transformed into a range of diverse compounds.[1] Upon reaction with alkaline hydrogen peroxide or hydroperoxides, electron-deficient alkenes such as α, β-unsaturated carbonyl compounds usually afford a mixture of (*E*)- and (*Z*)-oxiranes,[2] the yield and the (*E*)/(*Z*)-ratio depending on the nature of substrate, oxidant, and reaction conditions. For instance, in the epoxidation of (*E*)-cinnamaldehyde and its derivatives by ROOH (R = H, Et, cumyl, and *t*-butyl), the (*E*)/(*Z*) ratio is found to vary with the nature of the oxidant.[3]

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Address correspondence to S. Perumal, Department of Organic Chemistry, School of Chemistry, Madurai Kamaraj University, Madurai 625 021, India. E-mail: subbu_perum@rediffmail.com

In our recent study, the epoxidation of a series of *E*,*E*-2,2′-sulfonylbis1,3-diarylprop-2-en-1-ones with alkaline hydrogen peroxide afforded a single diastereomeric *bis* oxirane, while (*E*,*E*)-2,2′-thiobis(1,3-diarylprop-2-en-1-ones) afforded (*E*)- and (*Z*)-oxiranes in unequal amounts, the steric interactions in the intermediate enolates being held responsible for the stereochemistry of the major sulfonylbis and thiobis oxiranes.[4]

The present work describes the diastereoselective synthesis of 1-[3-aryl-2-(phenylsulfanyl)-2-oxiranyl]-1-ethanones **2** from the reaction of (*Z*)-4-aryl-3-(phenylsulfanyl)-3-buten-2-ones **1** with alkaline hydrogen peroxide. These oxiranes and their derivatives such as their β-hydroxy oxiranes could serve as valuable synthons for the construction of novel heterocycles. It is also of interest to examine the influence of the relative sizes and interaction between the functionalities of the trisubstituted alkenes, viz. (*Z*)-4-aryl-3-(phenylsulfanyl)-3-buten-2-ones **1** on the stereochemical outcome of this reaction.

RESULTS AND DISCUSSION

In the present investigation, the (*Z*)-4-aryl-3-(phenylsulfanyl)-3-buten-2-ones **1** employed in the epoxidation were prepared by the condensation of 1-(phenylsulfanyl)acetone with the appropriate aromatic aldehydes in presence of piperidinium acetate in ethanol. The yields of **1** obtained in the present method (Table I) are higher than those reported earlier by refluxing the starting materials with piperidine in toluene,[5]

TABLE I Synthesis of 4-Aryl-3-(phenylsulfanyl)-3-buten-2-ones[a] **1**

					% Analyses calc. (found)	
1	X	Time (Lit. time) (h)	Yield (Lit. yield) (%)	Mol. formula	C	H
a	H[b]	4 (144)	85 (75)[7]	—	—	
b	4-Cl	6	84	$C_{16}H_{13}ClOS$	66.54 (66.49)	4.54 (4.50)
c	4-Me[b]	5 (144)	83 (71)[7]	—	—	
d	4-F	6	77	$C_{16}H_{13}FOS$	70.56 (70.61)	4.81 (4.73)
e	4-NO_2[b]	3 (15)	89 (85)[7]	—	—	
f	2-Cl	7	84	$C_{16}H_{13}ClOS$	66.54 (66.49)	4.54 (4.56)
g	2-Me	8	83	$C_{17}H_{16}OS$	76.08 (76.01)	6.01 (5.94)
h	2-MeO	9	80	$C_{17}H_{16}O_2S$	71.80 (71.78)	5.67 (5.63)
i	4-MeO[b]	6	81[5]	—	—	

[a]Melting points not reported because all the compounds are semisolids except for (**e**) m.p. 58°C (lit.[7] 56–60°C).

[b]Known compounds.

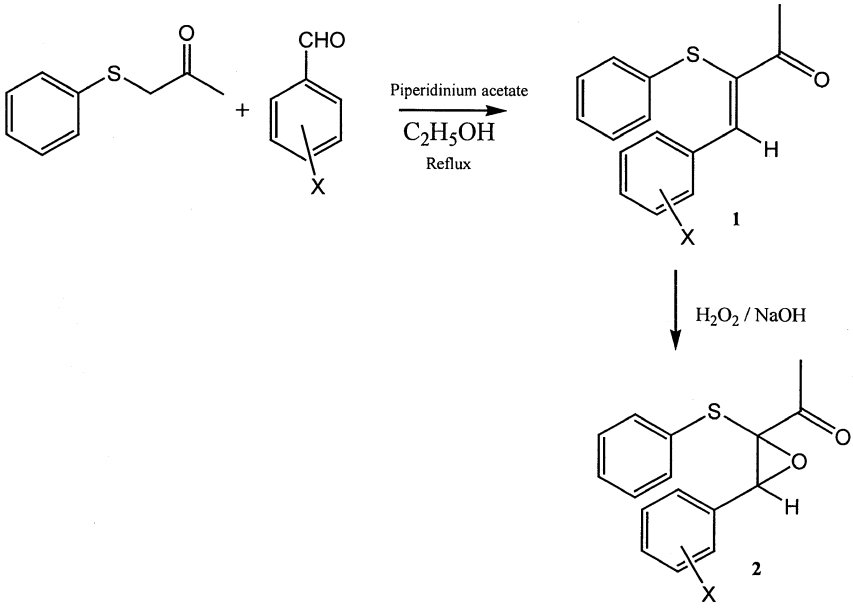
TABLE II ^{1}H and ^{13}C NMR Data of 4-Aryl-3-(phenylsulfanyl)-3-buten-2-ones **1**

1	^{1}H-NMR [$CDCl_3$/TMS, δ (ppm)]	^{13}C-NMR [$CDCl_3$/TMS, δ (ppm)]
a	2.33 (s, 3H), 7.14–7.85 (m, 10H), 7.94 (s, 1H)	27.6, 126.3, 127.7, 128.3, 129.3, 130.1, 130.8, 132.2, 134.1, 135.2, 144.2, 198.9
b	2.16 (s, 3H), 6.93–7.59 (m, 9H), 7.62 (s, 1H)	27.3, 126.3, 127.5, 128.3, 129.2, 131.8, 132.4, 132.6, 134.6, 135.7, 42.3, 198.2
c	2.20 (s, 6H), 6.83–7.68 (m, 9H), 7.84 (s, 1H)	21.5, 27.6, 126.2, 127.5, 128.7, 129.1, 129.3, 131.1, 131.4, 135.5, 140.8, 144.9, 199.1
d	2.34 (s, 3H), 6.87–7.90 (m, 9H), 7.91 (s, 1H)	27.6, 115.4, 115.7, 126.5, 127.5, 127.6, 129.0, 129.5, 133.0, 133.2, 135.0, 137.2, 143.2, 198.9
e	2.24 (s, 3H), 7.15–8.18 (m, 9H), 7.72 (s, 1H)	27.8, 123.3, 126.9, 127.2, 128.4, 128.9, 129.5, 130.9, 136.7, 139.3, 147.5, 198.4
f	2.28 (s, 3H), 7.04–7.86 (m, 9H), 7.98 (s, 1H)	27.6, 126.3, 126.6, 127.4, 128.1, 129.4, 129.4, 130.6, 130.7, 132.9, 134.8, 135.9, 140.5, 198.2
g	2.27 (s, 3H), 2.30 (s, 3H), 7.02–7.74 (m, 9H), 7.98 (s, 1H)	20.1, 27.7, 125.5, 126.3, 127.8, 129.1, 129.3, 129.5, 130.1, 131.6, 133.6, 134.3, 135.5, 143.0, 203.6
h	2.35 (s, 3H), 3.85 (s, 3H), 6.84–8.02 (m, 9H), 8.27 (s, 1H)	27.5, 55.5, 110.4, 119.9, 126.0, 127.5, 129.2, 130.2, 131.5, 132.5, 135.8, 137.1, 140.4, 158.3, 190.4
i	2.29 (s, 3H), 3.83 (s, 3H), 6.93–7.79 (m, 9H), 7.94 (s, 1H)	27.6, 55.4, 113.9, 126.1, 127.2, 127.4, 129.0, 129.3, 129.9, 133.3, 145.4, 164.6, 199.2

or in benzene with azeotropic removal of water,[6] or in chloroform.[7] The shorter reaction time and the enhanced yield of **1** in the present study could probably arise from the role of piperidinium acetate functioning in concert as (1) a base (OAc^-) leading to the formation of enolate ion from the 1-(phenylsulfanyl)acetone, or (2) as an acid (piperidinium ion) enhancing the electrophilicity of the aldehyde. The NMR spectroscopic data of the butenones **1** are presented in Table II.

The 1-(phenylsulfanyl)acetone required for the present study, in turn, was obtained by the reaction of chloroacetone with benzenethiol in methanol in the absence of any added base in an excellent yield of 95%, while the literature yields in presence of sodium hydroxide or pyridine were much lower, 53 and 64%, respectively.[8]

Epoxidation was affected by reacting **1** with hydrogen peroxide in a 1:1 molar ratio in tetrahydrofuran (THF) in presence of sodium hydroxide at room temperature (Scheme 1). Monitoring the reaction by thin layer chromatography (TLC) helped in optimizing the reaction time (Table III). Reactions performed for longer durations led to a mixture of products, suggesting further reactions of the oxiranes.



1 and **2**	X
a	H
b	4-Cl
c	4-Me
d	4-F
e	4-NO_2
f	2-Cl
g	2-Me
h[a]	2-MeO
i[a]	4-MeO

[a]For **1** only

SCHEME 1

TABLE III Synthesis of 1-[3-Aryl-2-(phenylsulfanyl)-2-oxiranyl]-1-ethanones[a] **2**

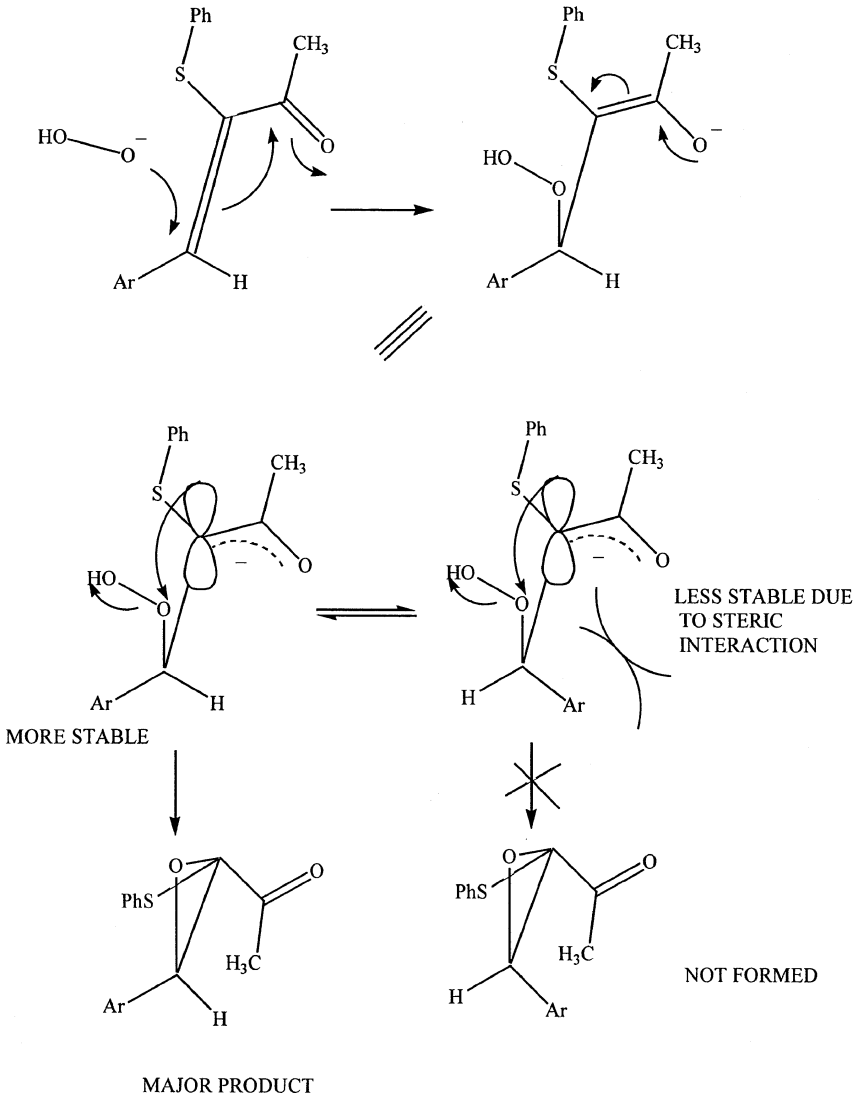
2	X	Time (h)	Yield (%)	Mol. formula	% Analyses calc. (found) C	H
a	H	39	67	$C_{16}H_{14}O_2S$	71.08 (71.13)	5.22 (5.13)
b	4-Cl	36	85	$C_{16}H_{13}ClO_2S$	63.05 (62.93)	4.30 (4.25)
c	4-Me	23	86	$C_{17}H_{16}O_2S$	71.80 (70.91)	5.67 (5.57)
d	4-F	19	79	$C_{16}H_{13}FO_2S$	66.65 (66.71)	4.54 (4.50)
e	4-NO_2	17	84	$C_{16}H_{13}NO_4S$	60.94 (60.87)	4.16 (4.27)
f	2-Cl	34	86	$C_{16}H_{13}ClO_2S$	63.05 (63.13)	4.30 (4.24)
g	2-Me	25	87	$C_{17}H_{16}O_2S$	71.80 (71.92)	5.67 (5.60)
h	2-MeO	23	—[b]	—	—	—
i	4-MeO	21	—[b]	—	—	—

[a]Melting points not reported as all the products are semisolids.
[b]In these cases, retro-aldol condensation took place affording the corresponding benzaldehydes and 1-(phenylsulfanyl)acetone.

All the oxiranes of the present work are hitherto unreported. The analytical data and the ^1H and ^{13}C NMR data are in accordance with the structure of the oxiranes (Table IV). The ^1H NMR spectrum for a representative example **2a** is discussed here. The acetyl methyl and the methine protons give singlets at 2.23 and 4.28 ppm, respectively. The aromatic protons of the phenyl rings give a multiplet integrating for 10 protons in the region of 7.27–7.49 ppm. The other oxiranes also showed similar spectroscopic data supporting their structure.

That the acetyl group and the methine hydrogen in the oxirane **2a** are in a *cis* relationship is revealed by the presence of a contour correlating the chemical shifts of these protons in the NOESY spectrum of **2a**. This shows that this oxirane has (*Z*)-configuration. The predominant formation of the diastereomer **2a** may presumably be rationalized on the basis that the steric interaction between the 2-phenylsulfanyl group and the 3-aryl group is likely to be less than that between the acetyl and the 3-aryl group both in the oxiranes and the corresponding transition states (Scheme 2).

In the case of 4-(2-methoxyphenyl)-3-(phenylsulfanyl)-3-buten-2-one **1h** and 4-(4-methoxyphenyl)-3-(phenylsulfanyl)-3-buten-2-one **1i**, the reaction with alkaline hydrogen peroxide afforded the corresponding aldehydes (2-methoxy- and 4-methoxy-benzaldehydes, respectively) and 1-(phenylsulfanyl)acetone, presumably via retro-aldol condensation triggered by the attack of hydroxide ion. In the case of **1h** and **1i**, the stronger conjugative interaction between the methoxy groups with the α,β-unsaturated carbonyl moiety could probably



SCHEME 2 Mechanism of epoxidation.

raise the energy of activation for the attack of $^{-}$OOH ion relative to the attack by $^{-}$OH, as in $^{-}$OOH two oxygens with their lone pairs could be repelled strongly by the electron-rich conjugated system.

TABLE IV The ^{1}H and ^{13}C NMR Data of 1-[3-Aryl-2-(phenylsulfanyl)-2-oxirany1]-1-ethanones **2**

2	^{1}H-NMR [$CDCl_3$/TMS, δ (ppm)]	^{13}C-NMR [$CDCl_3$/TMS, δ (ppm)]
a	2.23 (s, 3H), 4.28 (s, 1H), 7.27–7.49 (m, 10H).	26.9, 62.5, 76.3, 127.3, 127.9, 128.0, 129.1, 129.4, 131.2, 131.3, 132.0, 201.3
b	2.15 (s, 3H), 4.18 (s, 1H), 7.19–7.41 (m, 9H).	26.8, 61.9, 76.2, 128.3, 128.7, 129.0, 129.4, 130.5, 130.8, 131.3, 135.07, 200.9
c	2.14 (s, 3H), 2.31 (s, 3H), 4.17 (s, 1H), 7.12–7.42 (m, 9H).	21.3, 26.9, 62.6, 76.4, 127.3, 127.8, 128.8, 128.9, 129.3, 131.2, 131.4, 139.1, 201.4
d	2.15 (s, 3H), 4.18 (s, 1H), 7.02–7.41 (m, 9H).	26.9, 62.0, 76.3, 115.0, 115.3, 127.1, 127.4, 127.9, 129.0, 129.2, 129.3, 129.4, 130.9, 131.3, 201.1
e	2.16 (s, 3H), 4.30 (s, 1H), 7.19–8.20 (m, 9H).	26.8, 61.5, 76.0, 123.3, 127.5, 128.3, 129.0, 129.3, 129.5, 131.7, 139.3, 200.4
f	2.33 (s, 3H), 4.42 (s, 1H), 7.27–7.56 (m, 9H).	27.0, 60.8, 75.6, 126.6, 127.9, 128.8, 128.9, 129.4, 130.1, 130.8, 130.9, 131.0, 132.9, 200.5
g	2.25 (s, 3H), 2.36 (s, 3H), 4.29 (s, 1H), 7.21–7.51 (m, 9H).	18.8, 26.9, 61.3, 76.0, 125.7, 126.8, 127.4, 127.9, 128.8, 129.0, 129.3, 129.8, 131.0, 131.4, 201.3

EXPERIMENTAL

THF was purified and distilled. Aldehydes were freshly distilled before use. The ^{1}H and ^{13}C NMR spectra were measured using $CDCl_3$ as solvent in a Bruker (Avance) instrument at 300 and 75 MHz, respectively, and their chemical shifts referenced to TMS.

Preparation of 1-(Phenylsulfanyl)acetone

To a solution of benzenethiol (10.2 ml, 0.1 mol) in methanol (15 ml) cooled in an ice bath, a solution of chloroacetone (7.96 ml, 0.1 mol) in methanol (25 ml) was added dropwise with stirring. After completion of the addition, the temperature was allowed to rise to 15–20°C and the stirring continued overnight at 15–20°C. Then the reaction mixture was poured into crushed ice, extracted with ether, organic layer was washed thoroughly with water, dried over anhydrous sodium sulfate, and the solvent removed. 1-(Phenylsulfanyl)acetone was obtained as a colorless crystalline solid (15.8 g, 95%), m.p. 27–28°C (lit.[8] m.p. 25–30°C).

Synthesis of (*Z*)-4-Aryl-3-(phenylsulfanyl)-3-buten-2-ones (1a–i): General Procedure

Benzaldehyde (0.30 ml, 0.003 mol) was added to a solution of 1-(phenylsulfanyl)acetone (0.5 g, 0.003 mol) in ethanol (5 ml), followed

by 3 drops of piperidine and 2 drops of acetic acid. Then the reaction mixture was refluxed for 6 h. After the completion of the reaction as indicated by TLC, the reaction mixture was poured into ice water, extracted with ether, and the organic layer was washed successively with sodium bisulfite to remove the unreacted aldehyde. Then the organic layer was dried over anhydrous sodium sulfate and the solvent removed. The residue obtained was purified by column chromotography using silica gel with petroleum ether:ethyl acetate (97:3 v/v) as eluent to give the pure semisolid product, yield 0.66 g (85%).

Synthesis of (*Z*)-1-[3-Aryl-2-(phenylsulfanyl)-2-oxiranyl]-1-ethanones (2a–g): General Procedure

To a solution of (*Z*)-4-phenyl-3-(phenylsulfanyl)-3-buten-2-one (0.26 g, 0.001 mol) in tetrahydrofuran (10 ml), hydrogen peroxide (1.2 ml, 15%) was added in one batch followed by a dropwise addition of sodium hydroxide solution (1 ml, 10%) with stirring. Stirring was continued for 39 h, and the reaction progress was monitored by TLC. After completion of the reaction, the reaction mixture was dissolved in ether, washed with water repeatedly, the organic layer dried over anhydrous sodium sulfate, and the solvent removed. The product was purified using column chromatography over silica gel with petroleum ether:ethyl acetate (98:2 v/v) as eluent, yield 0.19 g (67%).

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