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TETRAHEDRON

Diastereoselective Synthesis of 2,2'-Thio*bis*- and 2,2'-Sulfonyl*bis*- (2-aroyl-3-aryloxiranes)

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Abstract: Epoxidation of 2,2'-thio*bis*(1,3-diarylprop-2-en-1-ones) with H_2O_2/NaOH in THF afforded a mixture of diastereomeric 2,2'-thio*bis*(2-aroyl-3-aryloxiranes) while the same reaction with its sulfonyl counterpart gave a single diastereomer.

Keywords: Epoxidation, sulfones, diastereoselectivity, nmr

INTRODUCTION

2,2'-Thio*bis*(1,3-diarylprop-2-en-1-ones) and their sulfonyl analogues are excellent compounds for the synthesis of six-membered heterocyclic compounds like thiazines and dithianes[1-3] because of the presence of reactive carbonyl, activated double bonds and sulfide/sulfonyl functionalities. In continuation of this work, we were interested in the synthesis of small-ring heterocycles, especially oxiranes (from **1** and **2**) since epoxidation of activated double bonds continues to sustain the interest of chemists.[4-6] As this reaction could afford several diastereomeric epoxides, it is of interest to study whether the epoxidation of the sulfides and sulfones proceeds with significant diastereoselectivity.

RESULTS AND DISCUSSION

Epoxidation of 2,2'-sulfonyl*bis*(1,3-diarylprop-2-en-1-ones) **1** with hydrogen peroxide in the presence of sodium hydroxide in THF afforded diastereoselectively a single *bis* oxirane **3** (Scheme 1) presumably *via* nucleophilic addition of HO_2^- by a Michael-type mechanism.[7] The yields of oxiranes obtained are moderate to good (55-76%). The assignment of signals in the ^1H and ^{13}C NMR spectra was made on the basis of intensity, multiplicity, substitutent induced chemical shift (SCS) considerations and two-dimensional NMR measurements such as H,H- and /or C,H- COSY. The epoxides may exist in two symmetrical configurational isomers (**6** or **7**) wherein the aroyl and aryl groups in both the oxirane rings are either *cis* or *trans* or as the unsymmetrical isomer **8** wherein the aroyl and aryl groups of one oxirane ring are *cis* while those of the other oxirane ring are *trans*.

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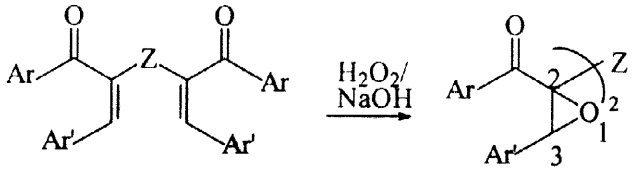
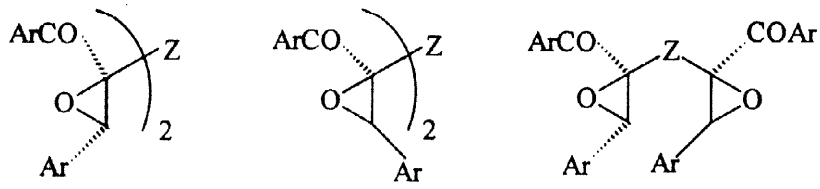


1-4

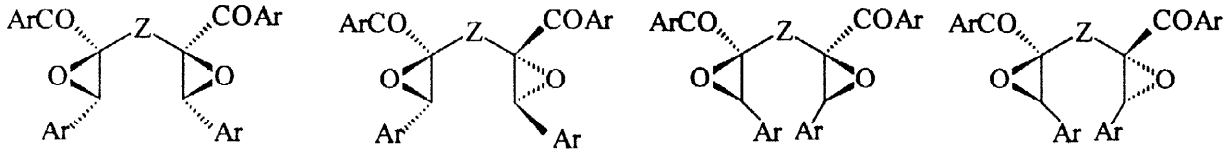
a (Ar=Ar'=C_6H_5)
b (Ar=C_6H_5; Ar'=Cl-C_6H_4)
c (Ar=Cl-C_6H_4; Ar'=Cl-C_6H_4)
d (Ar=Cl-C_6H_4; Ar'=Me-C_6H_4)
e (Ar=Me-C_6H_4; Ar'=C_6H_5)

Scheme 1



6 **7** **8**

The number of ^1H and ^{13}C NMR signals of the compounds (**3a-3e**) are in accord with symmetrical epoxides **6** or **7** each of which could exhibit further diastereoisomerism with respect to oxirane rings as shown in Figure 1.



6a **6b** **7a** **7b**

Figure 1

As available NMR spectroscopic data is not sufficient to firmly distinguish these diastereomers, the stereochemistry of the sulfonyl*bis* oxirane was elucidated completely from an X-ray study.[8] This study of **3a** (Figure 2) has shown that this oxirane exists in configuration **6a** (Z=SO_2). That the other oxiranes, **3b-3e,** also have the same stereochemistry shown in **6a** is evident from NMR spectroscopic data.

Reaction of 2,2'-thio*bis*(1,3-diarylprop-2-en-1-ones) **2** with hydrogen peroxide in the presence of sodium hydroxide in THF afforded a mixture of two *bis* oxiranes **4** in good yields (57-70%) (Z= S, Scheme 1) whose separation by chromatographic techniques was not successful as they have close R_f values under several solvent combinations. The predominant isomers in two cases (**4b** and **4c**) were, however, obtained in a pure state by fractional crystallization.

The ^1H NMR spectrum of the mixture in each case affords the ratio of the two oxiranes as given in Table 1. In cases wherein the signals of the minor isomer have been submerged by that of major isomer, H,H-

COSY spectra helped in locating the signals. The spectroscopic data of the major isomers [**4a-e**(major)] and the minor isomers [**4a-e**(minor)] (assigned as in the case of epoxy sulfones) are consistent with symmetrical structures (**6** or **7**).

Table 1

Compd	Ratio of **4** (major):(minor)	yield [a]
4a	80:20	60
4b	75:25	68
4c	70:30	70
4d	75:25	64
4e	75:25	57

[a] For the mixture of diastereomers

An X-ray study[8] of the major isomer of **4b** reveals that it has the configuration represented by **7b** (Figure 3). The other oxiranes **4a, 4c-4e** also have similar stereochemical arrangement as inferred from their ^{1}H and ^{13}C NMR spectroscopic data.

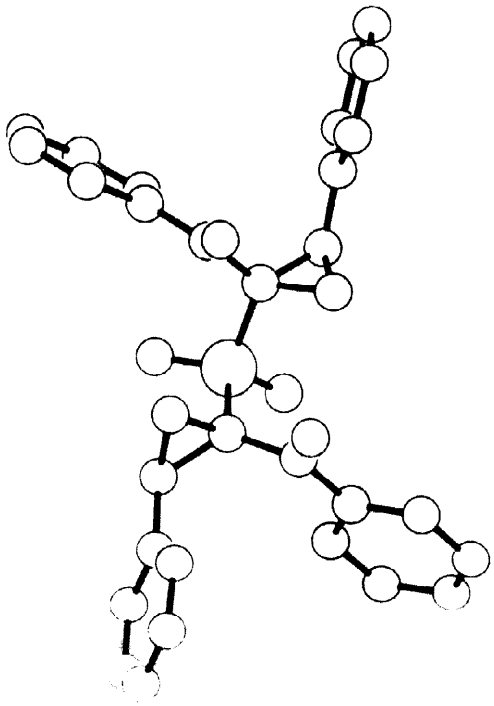


Figure 2 X-ray structure of **3a**

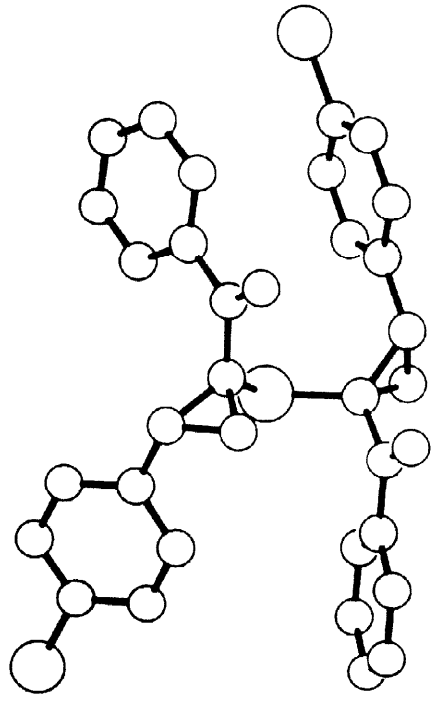


Figure 3 X-ray structure of **4b**

As reasonably good crystals of minor isomers could not be obtained for X-ray studies, their configuration has not been fully established.The abnormal shielding of four *ortho* hydrogens of the aryl groups in the minor isomer, however, indicates that its configuration is unlikely to be **6a** as no such shielding was noticed in **3** whose configuration has been established to be **6a** (*vide supra*). Similar reasoning rules out the configuration to be **6b**. Hence it is tentatively assigned that the minor isomers of **4** may have the configuration given by **7a**. The upfield shift of the *ortho* protons may probably, be attributed to the shielding of these protons by the oxirane ring(s) in one or more preferred conformations of **7a**.

The observed variation in the configuration with respect to the aryl and aroyl groups in the thio*bis* (major isomer) (**7b**) sulfonyl*bis*oxiranes (**6a**), *viz.*, *trans* and *cis* respectively, can probably be explained in terms of the stereochemistry of the carbanion during the formation of oxirane ring.

It is likely that the carbanions arising from both sulfides **2** and sulfones **1** by the addition of HOO^- are fairly long-lived as they are well stabilized leading to an equilibrium between stereoisomers in each case as depicted below. In the case of sulfones both carbanions **B (1)** and **B (2)** may be less stable relative to **A** leading to the *cis* product while in sulfides obviously **C** could be the conformation from which the reaction could occur affording the *trans* product (Figure 4). The above explanation appears plausible as the steric requirements of the groups are likely to be in the order: $-SO_2- > ArCO- > -S-$.

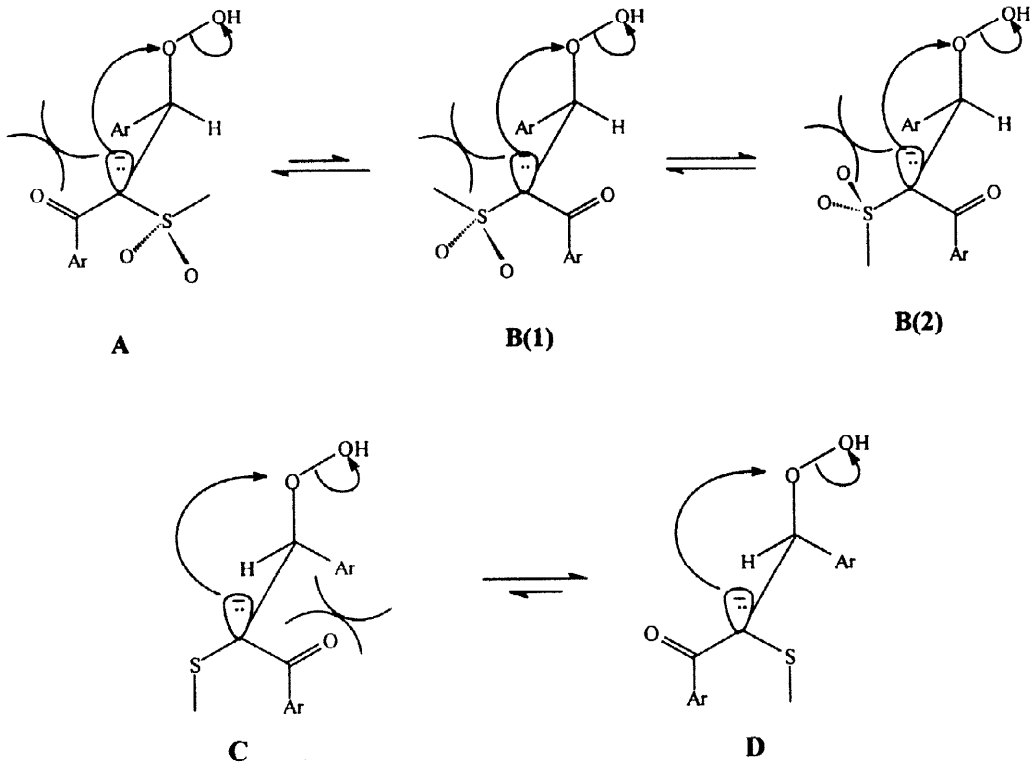


Figure 4

EXPERIMENTAL

The melting points are uncorrected. IR spectra were recorded on a Perkin-Elmer IR-577 instrument with KBr pellets. NMR spectra were recorded at 20 °C on a Bruker AMX 360 instrument operating at 360 MHz for ^1H and at 90 MHz for ^{13}C. Solutions (in $CDCl_3$) were approximately 0.05M and chemical shifts were referenced internally to TMS in all cases. Two-dimensional NMR measurements H,H- and C,H-COSY have also been measured using the above instrument. Standard Bruker software (UXNMR) was used throughout.

General procedure for epoxidation of 2,2'-sulfonyl*bis*(1,3-diarylprop-2-en-1-ones)- Synthesis of 2,2'-sulfonyl*bis*(2-benzoyl-3-phenyloxirane) (3a)

To a solution of 2,2'-sulfonyl*bis*(1,3-diphenylprop-2-en-1-one) (0.48 g, 1 mmol) in THF (10 mL), hydrogen peroxide (0.4 mL, 30%) was added in one lot followed by dropwise addition of sodium hydroxide solution (0.8 mL, 5%). The reaction mixture was allowed to stand for 1 h and the solvent was removed under reduced pressure. The resulting product, after thoroughly washing with water, afforded a colorless solid consisting of a single entity (hplc): 0.33 g (65%) mp 148-53 °C. Crystallization from alcohol-chloroform mixture gave 0.28 g (55%) of colorless crystals, mp 156-58 °C; [Found: C, 70.69; H, 4.32. $C_{30}H_{22}O_6S$ requires C, 70.58; H, 4.34%]; ν_{max} (KBr) 3030, 1668, 1215, 1330, 1140 cm^{-1}; δ_H (360 MHz , $CDCl_3$) 7.96 (4 H, dd, J 7.0, 1.1 Hz, aroyl *ortho*), 7.42 (4 H, t, J 7.0 Hz, aroyl *meta*), 7.55 (2 H, tt, J 7.0, 1.1 Hz, aroyl *para*), 7.16-7.24 (10 H, m, aryl H), 4.83 (2 H, s, C-3H); δ_C (90 MHz , $CDCl_3$) 187.3 (CO), 78.4 (C-2), 61.9 (C-3), 135.2, 129.8, 128.5, 134.6, 126.5, 128.6, 129.6 (Ar-C)

The following compounds were prepared by the same procedure.

2,2'-Sulfonyl*bis*(2-benzoyl-3-(4-chlorophenyl)oxirane) (3b)

The yield was 0.32 g (55 %). Crystallization from alcohol-chloroform mixture gave 0.29 g (50 %) of colorless crystals, mp 168-70 °C; [Found: C, 62.32; H, 3.49. $C_{30}H_{20}Cl_2O_6S$ requires C, 62.18; H, 3.48%]; ν_{max} (KBr) 3024, 1670, 1225, 1320, 1145 cm^{-1}; δ_H (360 MHz , $CDCl_3$) 7.94 (4 H, dd, J 7.0, 1.0 Hz, aroyl *ortho*), 7.43 (4 H, t, J 7.0 Hz, aroyl *meta*), 7.59 (2 H, tt, J 7.0, 1.0 Hz, aroyl *para*), 7.15-7.20 (8 H, m, aryl H), 4.72 (2 H, s, C-3H); δ_C (90 MHz , $CDCl_3$) 187.6 (CO), 78.1 (C-2), 61.8 (C-3), 135.0, 129.7, 128.6, 134.9, 128.3, 127.9, 128.8, 135.7 (Ar-Cs).

2,2'-Sulfonyl*bis*(2-(4-chlorobenzoyl)-3-(4-chlorophenyl)oxirane) (3c)

The yield was 0.37 g (57 %). Crystallization from alcohol-chloroform mixture gave 0.35 g (54 %) of colorless crystals, mp 154-56 °C; [Found: C, 55.48; H, 2.81. $C_{30}H_{18}Cl_4O_6S$ requires C, 55.58; H, 2.80 %]; ν_{max} (KBr) 3032, 1675, 1215, 1332, 1140 cm^{-1}; δ_H (360 MHz , $CDCl_3$) 7.92 (4 H, d, J 7.5 Hz, aroyl *ortho*), 7.45 (4 H, d, J

7.5 Hz, aroyl *meta*), 7.15-7.26 (8 H, m, aryl H), 4.76 (2 H, s, C-3H); δ_C (90 MHz , $CDCl_3$) 186.1 (CO), 78.0 (C-2), 61.7 (C-3), 133.2, 131.1, 129.0, 141.8, 128.0, 127.7, 129.1, 135.9 (Ar-C)

2,2'-Sulfonyl*bis*(2-(4-chlorobenzoyl)-3-(4-methylphenyl)oxirane) (3d)

The yield was 0.37 g (61 %). Crystallization from alcohol-chloroform mixture gave 0.30 g (49 %) of colorless crystals, mp 138-40°C; [Found: C, 63.33; H, 4.00. $C_{32}H_{24}Cl_2O_6S$ requires C, 63.27; H, 3.98 %]; ν_{max} (KBr) 3030, 1675, 1225, 1335, 1135 cm^{-1}; δ_H (360 MHz , $CDCl_3$) 7.92 (4 H, d, J 8.4 Hz, aroyl *ortho*), 7.41 (4 H, d, J 8.4 Hz, aroyl *meta*), 7.01-7.08 (8 H, m, aryl H), 4.82 (2 H, s, C-3H), 2.47 (6 H, s, Me); δ_C (90 MHz , $CDCl_3$) 185.8 (CO), 78.2 (C-2), 62.2 (C-3), 133.4, 131.2, 128.9, 141.2, 126.3, 129.4, 139.9 (Ar-C), 21.2 (Me-C).

2,2'-Sulfonyl*bis*(2-(4-methylbenzoyl)-3-phenyloxirane) (3e)

The yield was 0.41 g (76 %). Crystallization from alcohol-chloroform mixture gave 0.35 g (65 %) of colorless crystals, mp 158-60°C; [Found: C, 71.45; H, 4.86. $C_{32}H_{26}O_6S$ requires C, 71.36; H, 4.87 %]; ν_{max} (KBr) 3025, 1665, 1218, 1324, 1130 cm^{-1}; δ_H (360 MHz , $CDCl_3$)7.89 (4 H, d, J 8.0 Hz, aroyl *ortho*), 7.30 (4 H, d, J 8.0 Hz, aroyl *meta*), 7.15-7.28 (10 H, m, aryl H), 4.89 (2 H, s, C-3H), 2.40 (6 H, s, Me); δ_C (90 MHz , $CDCl_3$) 186.5 (CO), 78.4 (C-2), 62.1 (C-3), 132.8, 130.0, 129.2, 145.8, 126.6, 128.5, 129.5 (Ar-C), 21.9 (Me-C)

General procedure for epoxidation of 2,2'-thio*bis*(1,3-diarylprop-2-en-1-ones) 2- Synthesis of 2,2'-thio*bis*(2-aroyl-3-aryloxiranes) (4)

The method is similar to one that is described above except that 10% NaOH solution was used instead of 5%. However the work up gave a mixture of oxiranes which were not separable by chromatographic methods because of their close R_f values. The major isomer was separated by fractional crystallization in the case of **4b** and **4c.**

2,2'-Thio*bis*(2-benzoyl-3-phenyloxirane) (4a)

It was obtained as colorless crystals in 60 % yield (0.29 g), mp 70-5°C; [Found: C, 75.32; H, 4.65. $C_{30}H_{22}O_4S$ requires C, 75.29; H, 4.63%]; ν_{max} (KBr) 3030, 1650, 1545, 1255 cm^{-1}; δ_H (360 MHz , $CDCl_3$) (major isomer) 7.84 (4 H, d, J 7.0 Hz, aroyl *ortho*), 7.38 (4 H, t, J 7.0 Hz, aroyl meta), 7.55 (2 H, t, J 7.0 Hz, aroyl *para*), 7.25-7.40 (10 H, m, aryl H), 4.26 (2 H, s, C-3H). δ_H (minor isomer) 8.06 (4 H, d, J 7.0 Hz, aroyl *ortho*), 7.55 (4 H, t, J 7.0 Hz, aroyl *meta*), 7.63 (2 H, t, J 7.0 Hz, aroyl *para*), 6.93 (4 H, d, J 7.0 Hz, aryl *ortho*), 7.15 (4 H, t, J 7.0 Hz, aryl *meta*) 7.23 (2 H, t, J 7.0 Hz, aryl *para*), 4.24 (2 H, s, C-3H).

2,2'-Thio*bis*(2-benzoyl-3-(4-chlorophenyl)oxirane) (4b)

It was obtained as colorless crystals in 68 % yield (0.37 g), mp 150-54 °C; [Found: C, 65.72; H, 3.70. $C_{30}H_{20}Cl_2O_4S$ requires C, 65.82; H, 3.68 %];. Mp of the major isomer obtained by fractional crystallization from chloroform- pet ether: 166 °C; ν_{max} (KBr) 3025, 1652, 1555, 1250 cm^{-1}; δ_H (360 MHz , $CDCl_3$) (major

isomer) 7.85 (4 H, d, J 7.5 Hz, aroyl *ortho*), 7.40 (4 H, t, J 7.5 Hz, aroyl *meta*), 7.55 (2 H, t, J 7.5 Hz, aroyl *para*), 7.15-7.25 (8 H, m, aryl H), 4.25 (2 H, s, C-3H). δ_H (minor isomer) 8.01 (4 H, d, J 7.5 Hz, aroyl *ortho*). 7.55 (4 H, t, J 7.5 Hz, aroyl *meta*) , 7.69 (2 H, t, J 7.5 Hz, aroyl *para*), 6.87 (4 H, d, J 8.4 Hz, aryl *ortho*), 7.12 (4 H, d, J 8.4 Hz, aryl *meta*), 4.21 (2 H, s, C-3H).

2,2'-Thio*bis*(2-(4-chlorobenzoyl)-3-(4-chlorophenyl)oxirane) (4c)

It was obtained as colorless crystals in 70 % yield (0.43 g), mp 162-68 °C. [Found: C, 58.55; H, 2.93. $C_{30}H_{18}Cl_4O_4S$ requires C, 58.46; H, 2.94 %]; Mp of the major isomer obtained by fractional crystallization from chloroform-pet ether: 166 °C; ν_{max} (KBr) 3028, 1660, 1545, 1235 cm^{-1}; δ_H (360 MHz , $CDCl_3$) (major isomer) 7.80 (4 H, d, J 8.5 Hz, aroyl *ortho*), 7.40 (4 H, d, J 8.5 Hz, aroyl *meta*), 7.18 (4 H, d, J 8.0 Hz, aryl H). 7.26 (4 H, d, J 8.0 Hz, aryl H), 4.23 (2 H, s, C-3H). δ_H (minor isomer) 7.95 (4 H, d, J 8.5 Hz, aroyl *ortho*), 7.53 (4 H, d, J 8.5 Hz, aroyl *meta*), 6.92 (4 H, d, J 8.0 Hz, aryl *ortho*), 7.18 (4 H, d, J 8.0 Hz, aryl *meta*), 4.19 (2 H. s, C-3H).

2,2'-Thio*bis*(2(4-chlorobenzoyl)-3-(4-methylphenyl)oxirane) (4d)

It was obtained as colorless crystals in 64 % yield (0.37 g), mp 132-40 °C. [Found: C, 66.91; H, 4.21. $C_{32}H_{24}Cl_2O_4S$ requires C, 66.79; H, 4.20 %]; ν_{max} (KBr) 3035, 1663, 1550, 1238 cm^{-1}; δ_H (360 MHz , $CDCl_3$) (major isomer) 7.80 (4 H, d, J 8.5 Hz, aroyl *ortho*), 7.41 (4 H, d, J 8.5 Hz, aroyl *meta*), 7.23 (4 H, d, J 8.0 Hz, aryl H), 7.38 (4 H, d, J 8.0 Hz, aryl H), 4.23 (2 H, s, C-3H), 2.36 (6 H, s, Me). δ_H (minor isomer) 7.98 (4 H, d, J 8.5 Hz, aroyl *ortho*), 7.57 (4 H, d, J 8.5 Hz, aroyl *meta*), 6.95 (4 H, d, J 8.0 Hz, aryl *ortho*), 7.12 (4 H, d, J 8.0 Hz, aryl *meta*), 4.19 (2 H, s, C-3H), 2.45 (6 H, s, Me).

2,2'-Thio*bis*(2-(4-methylbenzoyl)-3-phenyloxirane) (4e)

It was obtained as colorless crystals in 57 % yield (0.29 g), mp 126-31 °C. [Found: C, 75.72; H, 5.15. $C_{32}H_{26}O_4S$ requires C, 75.87; H, 5.17 %]; ν_{max} (KBr) 3030, 1650, 1558, 1245 cm^{-1}; δ_H (360 MHz , $CDCl_3$) (major isomer) 7.75 (4 H, d, J 8.0 Hz, aroyl *ortho*), 7.15 (4 H, d, J 8.0 Hz, aroyl *meta*), 7.30-7.45 (10 H, m. aryl H), 4.23 (2 H, s, C-3H), 2.42 (6 H, s, Me).). δ_H (minor isomer) 7.95 (4H, d, J 8.0 Hz, aroyl *ortho*), 7.35 (4H, d, J 8.0 Hz, aroyl *meta*), 6.96 (4H, d, J 7.5 Hz, aryl *ortho*), 7.15 (4H, d, J 7.5 Hz, aryl *meta*), 7.26 (2H, t, J 7.5 Hz, aryl *para*), 4.20 (2H, s, C-3H), 2.56 (6H, s, Me).

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8. Krishnakumar. V.; Natarajan. S.; Renuga. S.; Selvaraj. S.; Perumal. S. *Acta Cryst.* (submitted); Compound **3a** forms monoclinic crystals, a=13.228(3), b=11.754(6), c=16.835(3), β=104.33(2)°, Z=4, space group $P2_1/n$. The structure was solved from 3365 observed reflections (2ϑ<70°, CuKα radiation) and refined to R=0.093 and R_w = 0.195.

   Compound **4b** forms monoclinic crystals, a=11.768(3), b=16.318(2), c=14.072(2), β=103.66(2)°, Z=4, space group $P2_1/a$. The structure was solved from 3238 observed reflections (2ϑ<50°, MoKα radiation) and refined to R=0.043 and R_w = 0.082.