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# Diels–Alder reaction of optically active (*E*)-γ-keto-α,β-unsaturated *p*-tolylsulfoxides with cyclopentadiene

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**Abstract**—The Diels–Alder reaction of enantiomerically pure (*E*)-γ-keto-α,β-unsaturated *p*-tolylsulphoxides **3** with cyclopentadiene give four easily separable diastereomers. The effect of several Lewis acids on the reaction was studied, finding a high *endo* selectivity with respect to the carbonyl group and moderate π-diastereoselectivity using $BF_3{\cdot}Et_2O$ as catalyst. The reactivity of compounds **3** as well as their *endo* selectivity are both higher than those observed for the corresponding (*E*)-3-sulfinylacrylates.


## 1. Introduction

The combination of Diels–Alder reaction with asymmetric induction exerted by sulphoxides represents a very powerful method for C–C bond formation in a stereocontrolled manner.[1] The sulphinyl group has equally become one of the most interesting chiral inductors in asymmetric Diels–Alder reactions due to the following facts: its ability to differentiate between diastereotopic faces of neighboring double bonds, the ease of chemical transformations into different functional groups including its clean removal under mild conditions, and the existence of several efficient methods that allow the preparation of enantiomerically pure sulphoxides. The poor results obtained in the Diels–Alder reaction using unsubstituted vinylic sulphoxides (low reactivity and only moderate stereoselectivity)[2] were substantially improved by attaching additional groups to the double bond, which increases the reactivity and simultaneously restricts the conformational mobility around the C–S bond, hence improving the stereoselectivity of the dienophile. In this sense, several electron-withdrawing groups have been incorporated to vinylic sulphoxides, such as carbonyl,[3] nitro,[4] sulphonyl,[5] sulphinyl,[6] and cyano.[7] Nevertheless, the most widely studied one is doubtlessly the ester group, the contributions by Koizumi in this field clearly being the most significant.[8]

As part of our studies involving the stereoselective preparation and synthetic application of γ-substituted-α,β-unsaturated sulphoxides, we have recently reported an efficient synthesis of enantiomerically pure (*E*)-γ-hydroxy- and (*E*)-γ-keto-α,β-unsaturated *p*-tolylsulphoxides.[9] We report herein the results obtained in the Diels–Alder reaction between enantiomerically pure (*E*)-γ-keto-α,β-unsaturated *p*-tolylsulphoxides **3** as dienophiles and cyclopentadiene. Both *endo* selectivity of alkylcarbonyl substituent and π-diastereoselectivity are strongly influenced by the nature of Lewis acid present in the reaction.

## 2. Results and discussion

(*E*)-γ-Hydroxy-α,β-unsaturated *p*-tolylsulphoxides **2** were obtained in excellent chemical yield by condensation of enantiomerically pure (*S*,*S*)-bis-*p*-tolylsulfinylmethane **1** with enolizable aldehydes in the presence of piperidine as base and thiophile.[9] The process involves a Knoevenagel condensation between the aldehyde and methylene active bis-sulphoxide **1**, in tandem with an allylic sulphoxide–sulphenate rearrangement and hydrolysis of the sulphenate ester promoted by the thiophilic base. The (*E*)-γ-hydroxysulphoxides **2** were oxidized with PCC and sodium acetate in dichloromethane at room temperature to afford enantiomerically pure (*E*)-γ-keto-α,β-unsaturated *p*-tolylsulphoxides **3** in high chemical yields (Scheme 1).

With the (*E*)-γ-ketosulfphoxides **3a** and **3b** in hand, their

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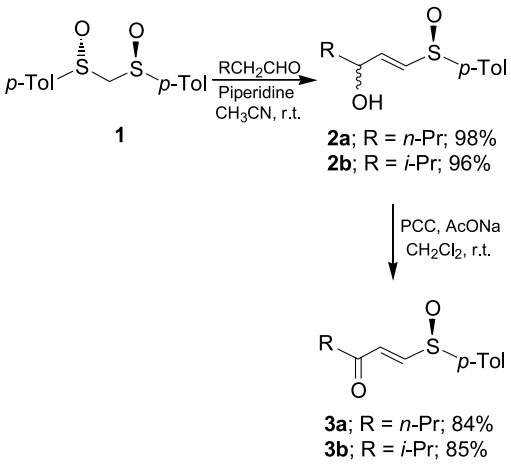


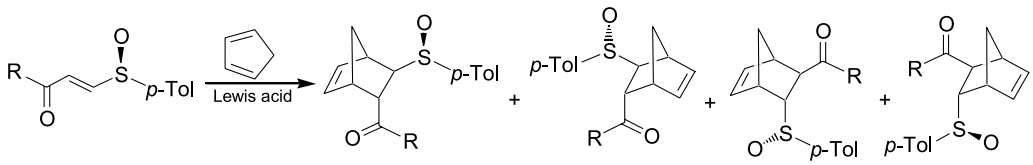

**Scheme 1.**

Diels–Alder reactions with cyclopentadiene under thermal conditions were studied. Initially, we carried out the cycloaddition reaction between enantiopure (*R*)-(*E*)-1-*p*-tolylsulfinyl-1-hexen-3-one **3a** and cyclopentadiene at 25 °C in toluene. After 30 min, analysis of the reaction mixture by TLC showed that the four possible diastereoisomeric norbornenes **4a**, **5a**, **6a** and **7a** were formed, which could be easily separated by flash chromatography affording the four enantiomerically pure cycloadducts (Table 1, entry 1). The *endo*/*exo* ratio (taking the carbonyl group as reference for the *endo* or *exo* designation) and the relative proportions of the four diastereoisomers, were easily determined from the relative intensities of the well-separated vinylic proton signals in the $^1$H NMR (500 MHz) spectrum of the crude. The stereochemistry of the diastereomers **4**–**7** were assigned by irradiation of the proton signals and homonuclear shift correlation in $^1$H and $^{13}$C NMR spectroscopy.

As shown in Table 1, a similar behavior was observed for (*R*)-(*E*)-4-methyl-1-*p*-tolylsulfinyl-1-penten-3-one **3b** in its reaction with cyclopentadiene (entry 2). These results suggest that diastereoselectivity of the Diels–Alder reaction of (*E*)-γ-keto-α,β-unsaturated *p*-tolylsulphoxides **3** is almost independent of the size of the alkyl R group attached to the carbonyl. Additionally, the *endo* preference for carbonyl or sulphinyl group is found to be very similar.

There has been much interest in recent years in the effect of Lewis acids on diastereomeric ratios in the Diels–Alder cycloaddition reaction. Having established the structure and stereochemistry of the four diastereomeric adducts from the thermal Diels–Alder reaction, we turned our attention to the effect of Lewis acid promoters on the process. As expected, the use of Lewis acids increases the reactivity of the dienophile allowing the use of lower reaction temperatures. We carried out the reaction between (*R*)-(*E*)-1-(*p*-tolylsulfinyl)-1-hexen-3-ona **3a** and cyclopentadiene at −78 °C in dichloromethane as solvent in the presence of several Lewis acids, the results are collected in the Table 1. The addition of $SiO_2$ or $LiClO_4$ as promoters (entries 3 and 4), afforded the four adducts **4/5/6/7** in good chemical yield but it had no significant influence on both *endo*/*exo* and π-facial selectivities. The addition of $ZnBr_2$ or $SnCl_4$ (entries 5–8) gave rise to a moderate carbonyl-*endo* selectivity, affording adduct **5** as the predominant stereoisomer. On the other hand, when the Diels–Alder reaction was carried out in the presence of $TiCl_4$, $Et_2AlCl$ or $BF_3{\cdot}Et_2O$ as Lewis acids (entries 9–13), a reversal of the π-facial selectivity was observed, adduct **4** now being the isomer obtained in higher proportion.[10,12] The best promoter for the Diels–Alder reaction of (*R*)-(*E*)-1-(*p*-tolylsulfinyl)-1-hexen-3-ona **3a** with cyclopentadiene resulted to be $BF_3{\cdot}Et_2O$, which increases both *endo*/*exo* and π-facial selectivities from 54:46 (22% d.e. *endo*) in the thermal reaction until 93:7

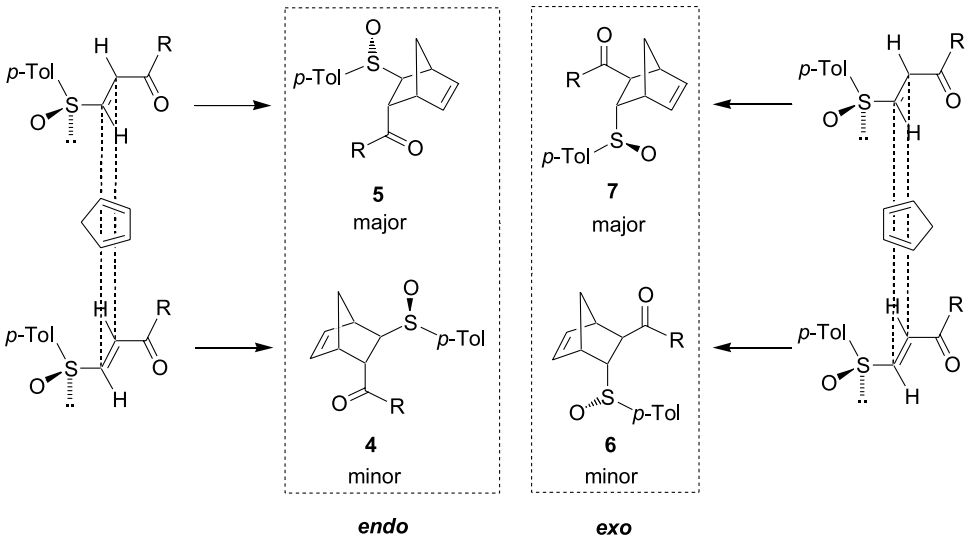
**Table 1**. Diels–Alder reaction of (*E*)-γ-keto-α,β-unsaturated *p*-tolylsulfoxides **3a-b** with cyclopentadiene




**3** **4** **5** **6** **7**

| Entry | R | Lewis acid[a] | *t* (h) | Yield (%) | **4/5/6/7**[b] | *endo*/*exo* | % d.e. *endo* | % d.e. *exo* |
|---|---|---|---|---|---|---|---|---|
| 1 | *n*-Pr | — | 0.5[c] | 90 | 21:33:17:29 | 54:46 | 22 | 26 |
| 2 | *i*-Pr | — | 0.5[c] | 95 | 15:36:17:32 | 51:49 | 41 | 31 |
| 3 | *n*-Pr | $SiO_2$ | 24[d] | 99 | 19:36:16:29 | 55:45 | 31 | 29 |
| 4 | *n*-Pr | $LiClO_4$ | 24[d] | 95 | 20:35:16:29 | 55:45 | 27 | 29 |
| 5 | *n*-Pr | $ZnBr_2$ | 10[d] | 95 | 34:41:12:13 | 75:25 | 9 | 4 |
| 6 | *n*-Pr | $ZnBr_2$[e] | 10[d] | 97 | 32:45:09:14 | 77:23 | 17 | 22 |
| 7 | *n*-Pr | $SnCl_4$ | 2[d] | 80 | 35:54:05:06 | 89:11 | 21 | 9 |
| 8 | *i*-Pr | $SnCl_4$ | 2[d] | 82 | 37:52:06:05 | 89:11 | 17 | 9 |
| 9 | *n*-Pr | $TiCl_4$ | 2[d] | 85 | 53:31:07:09 | 84:16 | 26 | 13 |
| 10 | *n*-Pr | $Et_2AlCl$ | 2[d] | 86 | 60:25:11:04 | 85:15 | 41 | 47 |
| 11 | *n*-Pr | $BF_3{\cdot}Et_2O$ | 2[d] | 98 | 65:26:06:03 | 91:9 | 43 | 33 |
| 12 | *n*-Pr | $BF_3{\cdot}Et_2O$[e] | 2[d] | 97 | 71:22:05:02 | 93:7 | 53 | 43 |
| 13 | *i*-Pr | $BF_3{\cdot}Et_2O$ | 2[d] | 98 | 60:24:10:06 | 86:14 | 42 | 25 |

[a] 1.2 equiv.
[b] Determined by $^1$H NMR integrals of vinylic protons.
[c] Reaction carried out at room temperature.
[d] Reaction carried out at −78 °C.
[e] 2 equiv. of Lewis acid were used.




**Scheme 2.**

(53% d.e. *endo*) in the process carried out in the presence of 2 equiv. of Lewis acid.

The observed π-facial diastereoselectivity in Diels–Alder reactions of (*E*)-γ-keto-α,β-unsaturated *p*-tolyl-sulphoxides **3a** and **3b** with cyclopentadiene may be explained assuming the transition state proposed by Koizumi for the reaction of ethyl *p*-tolylsulfinylmethylenepropionate,[11] in which the α,β-unsaturated sulphoxide adopts the *s-trans* conformation with respect to the S=O and C=C bonds, and the addition of cyclopentadiene takes place where is found the lone pair electrons at sulphur (Scheme 2).

Loss of optical purity for (*E*)-γ-keto-α,β-unsaturated *p*-tolylsulfoxides **3a**-**b** was shown to be minimal in the process by control experiments in which (*E*)-γ-keto-sulfoxides **3a**-**b** were submitted to the reaction conditions in the absence of the cyclopentadiene recovering the corresponding sulphoxide without any loss on its $[\alpha]_D$ value.

## 3. Conclusions

In summary, we can state that the readily obtained (*E*)-γ-keto-α,β-unsaturated *p*-tolylsulphoxides **3** are efficient chiral sulphinyldienophiles exhibiting the following advantages with respect to the corresponding sulfinyl acrilate: higher reactivity, higher degree of stereocontrol when the process is carried out in the presence of $BF_3{\cdot}Et_2O$ as promoter, good chemical yield and easy separation of diastereomeric mixtures affording the four enantiomerically pure cycloadducts.

## 4. Experimental

### 4.1. General

Melting points were determined in open capillary tubes on a Gallenkamp apparatus and are uncorrected. $^1H$ NMR spectra were registered on a Bruker AC-200 (200 MHz) or AMX-500 (500 MHz) and $^{13}C$ NMR on AC-200 (50.3 MHz) or AMX-500 (125.72 MHz). All spectra were obtained using $CDCl_3$ as solvent and TMS as internal standard. Chemical shifts are reported in ppm, and coupling constants in Hz. Optical rotations were taken on a Perkin–Elmer 241-MC polarimeter in an 1 dm tube; concentrations are given in g/100 mL. High resolutions mass measurements were performed on a Kratos MS-80-RFA spectrometer. HPLC analysis was carried out on a Waters, Millipore 600A model using a Chiral OD (Diacel) column or reverse phase column Lichrocart C-18. Routine monitoring of reactions was performed using Merck 60 F 254 silica gel, aluminium supported TLC plates. For the flash chromatography,[13] silica gel 60 (230–400 mesh ASTM, Merck) was used. Flasks, stirrings bars, and hypodermic needles used for the generation of organometallic compounds were dried for ca. 12 h at 120 °C and allowed to cool in a dessicator over anhydrous calcium sulphate. Anhydrous solvents (ethers) were obtained by distillation from benzophenone ketyl.[14]

**4.1.1. (*E*)-γ-Hydroxy-α,β-unsaturated sulfoxides (2a-b).** The general procedure described by Llera et al. was followed.[9]

### 4.2. General procedure for the oxidation of compounds 2a-b

To a solution of (*E*)-γ-hydroxy-α,β-unsaturated sulphoxides **2a**-**b** (1 mol) in dichloromethane was sequentially added sodium acetate (1 equiv.) and pyridinium chlorochromate PCC (3 equiv.). The resulting suspension was vigorously shaken at room temperature and monitored by TLC for the conversion. The reaction mixture was filtered on $SiO_2/CaSO_4$ (9:1) and washed with $CH_2Cl_2$/ether (1:1). After evaporating the solvent, the crude was purified by column chromatography to give (*E*)-γ-ketosulfoxide **3a**-**b**.

**4.2.1. *R*-(*E*)-1-*p*-Tolylsulfinyl-1-hexen-3-one (*R*)-3a.** The general procedure was followed for the oxidation of 1.19 g (4.9 mmol) of **2a**, employing 0.68 g (4.9 mmol) of sodium acetate and 3.21 g (15 mmol) of pyridinium chlorochromate for 5 h. Purification of the reaction mixture by flash

chromatography (hexane/ethyl acetate, 3:1), afforded 0.99 g (84% yield) of (*R*)-**3a** as a white solid. Mp 92.5–93.5 °C. $[\alpha]_D$=+404 (*c*=2, acetone). $^1$H NMR (500 MHz, $CDCl_3$) $\delta$ 0.89 (t, *J*=7.4 Hz, 3H, $CH_3$), 1.61 (m, 2H, $CH_2$), 2.36 (s, 3H, $CH_3Ar$), 2.55 (t, *J*=7.4 Hz, 2H, $CH_2$–C═O), 6.94 (d, $J_{trans}$=15.0 Hz, 1H, CH–S═O), 7.29 (d, $J_{trans}$=15.0 Hz, 1H, CH–C═O), 7.28–7.47 (AA′BB′ system, 4H, aromatics). $^{13}$C NMR (50.29 MHz, $CDCl_3$) $\delta$ 13.5, 17.0, 21.4, 44.3, 124.9, 129.4, 130.4, 138.2, 142.5, 148.6, 197.3. HRMS calcd *m/z* for $C_{13}H_{16}O_2S$: 236.0881. Found: 236.0842. Anal. Calcd for $C_{13}H_{16}O_2S$: C, 66.07; H, 6.83. Found: C, 65.98; H, 6.54.

**4.2.2. (*R*)-(*E*)-4-Methyl-1-*p*-tolylsulfinyl-1-penten-3-one (*R*)-3b.** The general procedure was followed for the oxidation of 1.18 g (4.95 mmol) of **2b**, employing 0.68 g (5.0 mmol) of sodium acetate and 3.20 g (15 mmol) of pyridinium chlorochromate for 2.5 h. Purification of the reaction mixture by flash chromatography (hexane/ethyl acetate, 4:1), afforded 1.0 g (85% yield) of (*R*)-**3b** as a white solid. Mp 76–77 °C. $[\alpha]_D$=+350 (*c*=2, acetone). $^1$H NMR (500 MHz, $CDCl_3$) $\delta$ 1.15 (d, *J*=6.9 Hz, 6H, $(CH_3)_2$), 2.40 (s, 3H, $CH_3Ar$), 2.80 (m, 1H, CH), 7.10 (d, $J_{trans}$=15.0 Hz, 1H, CH–S═O), 7.38 (d, $J_{trans}$=15.0 Hz, 1H, CH–C═O), 7.32–7.50 (AA′BB′ system, 4H, aromatics). $^{13}$C NMR (50.29 MHz, $CDCl_3$) $\delta$ 17.8, 21.5, 40.8, 125.1, 128.1, 130.5, 138.2, 142.6, 149.1, 200.7. HRMS calcd *m/z* for $C_{13}H_{16}O_2S$: 236.0881. Found: 236.0842. Anal. Calcd for $C_{13}H_{16}O_2S$: C, 66.07; H, 6.83. Found: C, 65.91; H, 6.53.

### 4.3. Diels–Alder reaction of (*R*)-(*E*)-1-*p*-tolylsulfinyl-1-hexen-3-one (*R*)-3a

A solution of (*R*)-**3a** (550 mg, 2.3 mmol) and freshly distilled cyclopentadiene (750 mg, 0.94 mL, 11.5 mmol) in toluene (10 mL) was stirred for 30 min at room temperature. The solvent was evaporated under reduced pressure and the crude product was purified by column chromatography eluting with hexane/ether/ethyl acetate (3:2:1) to give the products **4**–**7a** (90% chemical yield).

**4.3.1. Compound 4a.** Yield 19.1%, white solid. Mp 89.5–91 °C. $[\alpha]_D$=0 (*c*=2, acetone). $^1$H NMR (200 MHz, $CDCl_3$) $\delta$ 0.64 (t, *J*=7.1 Hz, 3H, $CH_3$), 1.06 (m, 2H, –$CH_2$–), 1.47 (dd, *J*=8.7, 1.7 Hz, 1H, $H_{7a}$), 1.98 (dt, *J*=16.9, 7.2 Hz, 1H, $H_{1'a}$), 2.09 (m, 1H, $H_{7b}$), 2.18 (dt, *J*=16.9, 7.2 Hz, 1H, $H_{1'b}$), 2.36 (s, 3H, $CH_3Ar$), 3.00 (dd, *J*=4.7, 1.7 Hz, 1H, $H_2$), 3.18 (m, 1H, $H_4$), 3.25 (m, 1H, $H_1$), 3.38 (dd, *J*=4.7, 3.5 Hz, 1H, $H_3$), 5.90 (dd, *J*=5.6, 2.8 Hz, 1H, $H_5$), 6.30 (dd, *J*=5.6, 3.2 Hz, 1H, $H_6$), 7.22–7.37 (AA′BB′ system, 4H, aromatics). $^{13}$C NMR (50.29 MHz, $CDCl_3$) $\delta$ 13.4, 16.8, 21.2, 43.0, 45.8, 46.1, 47.2, 49.0, 64.0, 123.7, 129.6, 135.5, 137.6, 140.1, 140.8, 207.3. Anal. Calcd for $C_{18}H_{22}O_2S$: C, 71.48; H, 7.33. Found: C, 71.14; H, 7.21.

**4.3.2. Compound 5a.** Yield 25.9%, white solid. Mp 94–95 °C. $[\alpha]_D$=0 (*c*=2, acetone). $^1$H NMR (200 MHz, $CDCl_3$) $\delta$ 0.72 (t, *J*=7.0 Hz, 3H, $CH_3$), 1.37 (m, 2H, –$CH_2$–), 1.55 (dd, *J*=8.9, 1.8 Hz, 1H, $H_{7a}$), 1.97 (m, 1H, $H_{7b}$), 2.11 (dt, *J*=16.9, 7.2 Hz, 1H, $H_{1'a}$), 2.22 (dt, *J*=16.9, 7.2 Hz, 1H, $H_{1'b}$), 2.36 (s, 3H, $CH_3Ar$), 3.99 (dd, *J*=4.7, 3.5 Hz, 1H, $H_3$), 3.16 (dd, *J*=4.7, 1.8 Hz, 1H, $H_2$), 3.24 (m, 1H, $H_1$), 3.28 (m, 1H, $H_4$), 5.90 (dd, *J*=5.6, 3.3 Hz, 1H, $H_5$), 6.18 (dd, *J*=5.6, 2.7 Hz, 1H, $H_6$), 7.27–7.53 (AA′BB′ system, 4H, aromatics). $^{13}$C NMR (50.29 MHz, $CDCl_3$) $\delta$ 13.2, 16.9, 21.4, 43.2, 44.1, 46.7, 47.6, 53.4, 65.3, 125.1, 129.9, 134.9, 137.5, 139.6, 141.9, 206.8. Anal. Calcd for $C_{18}H_{22}O_2S$: C, 71.48; H, 7.33. Found: C, 71.13; H, 7.27.

**4.3.3. Compound 6a.** Yield 11.7%, viscous oil. $[\alpha]_D$=+24 (*c*=2, acetone). $^1$H NMR (200 MHz, $CDCl_3$) $\delta$ 0.81 (t, *J*=7.3 Hz, 3H, $CH_3$), 1.40 (m, 1H, $H_{7a}$), 1.45 (m, 2H, –$CH_2$–), 1.61 (m, 1H, $H_{7b}$), 2.33 (dt, *J*=17.3, 7.3 Hz, 1H, $H_{1'a}$), 2.38 (s, 3H, $CH_3Ar$), 2.49 (dt, *J*=17.3, 7.3 Hz, 1H, $H_{1'b}$), 2.84 (m, 1H, $H_1$), 2.88 (dd, *J*=4.6, 1.7 Hz, 1H, $H_3$), 2.97 (m, 1H, $H_4$), 3.65 (dd, *J*=4.6, 3.3 Hz, 1H, $H_2$), 6.25 (dd, *J*=5.6, 2.7 Hz, 1H, $H_6$), 6.35 (dd, *J*=5.6, 3.1 Hz, 1H, $H_5$), 7.37–7.47 (AA′BB′ system, 4H, aromatics). $^{13}$C NMR (50.29 MHz, $CDCl_3$) $\delta$ 13.6, 17.0, 21.4, 44.1, 44.3, 47.0, 47.1, 51.0, 69.5, 124.2, 129.8, 134.9, 137.1, 140.8, 141.5, 209.7. Anal. Calcd for $C_{18}H_{22}O_2S$: C, 71.48; H, 7.33. Found: C, 71.23; H, 7.37.

**4.3.4. Compound 7a.** Yield 29.4%, white solid. Mp 109.5–110 °C. $[\alpha]_D$=+8 (*c*=2, acetone). $^1$H NMR (200 MHz, $CDCl_3$) $\delta$ 0.62 (t, *J*=7.2 Hz, 3H, $CH_3$), 1.22 (m, 2H, –$CH_2$–), 1.51 (dq, *J*=9.1, 1.6 Hz, 1H, $H_{7a}$), 1.60 (dd, *J*=9.1, 1.6 Hz, 1H, $H_{7b}$), 1.66 (dt, *J*=17.2, 7.2 Hz, 1H, $H_{1'a}$), 2.02 (dd, *J*=4.7, 1.4 Hz, 1H, $H_3$), 2.18 (dt, *J*=17.2, 7.2 Hz, 1H, $H_{1'b}$), 2.34 (s, 3H, $CH_3Ar$), 2.89 (m, 1H, $H_4$), 3.45 (m, 1H, $H_1$), 3.91 (dd, *J*=4.7, 3.3 Hz, 1H, $H_2$), 6.34 (dd, *J*=5.6, 3.1 Hz, 1H, $H_5$), 6.50 (dd, *J*=5.6, 2.8 Hz, 1H, $H_6$), 7.22–7.51 (AA′BB′ system, 4H, aromatics). $^{13}$C NMR (50.29 MHz, $CDCl_3$) $\delta$ 13.4, 16.7, 21.4, 44.0, 44.3, 45.9, 47.4, 52.0, 69.5, 125.6, 129.9, 136.1, 137.4, 139.8, 142.3, 207.8. Anal. Calcd for $C_{18}H_{22}O_2S$: C, 71.48; H, 7.33. Found: C, 71.18; H, 7.31.

### 4.4. Diels–Alder reaction of (*R*)-(*E*)-4-methyl-1-(*p*-tolylsulfinyl)-1-penten-3-ona (*R*)-3b

A solution of (*R*)-**3a** (500 mg, 2.1 mmol) and freshly distilled ciclopentadiene (750 mg, 0.94 mL, 11.5 mmol) in toluene (10 mL) was heated under for 30 min at 25 °C. The solvent was evaporated under vacuum and the crude product was purified by column chromatography eluting with hexane/ether/ethyl acetate (2:2:1) to give the products **4b**–**7b** (95% global yield).

**4.4.1. Compound 4b.** Yield 18.3%, white solid. Mp 103–105 °C. $[\alpha]_D$=+68 (*c*=2, acetone). $^1$H NMR (200 MHz, $CDCl_3$) $\delta$ 0.59 (d, *J*=6.9 Hz, 3H, $(CH_3)_2CH$), 0.82 (d, *J*=6.9 Hz, 3H, $(CH_3)_2CH$), 1.47 (dd, *J*=8.6, 1.7 Hz, 1H, $H_{7a}$), 2.14 (d, *J*=8.6 Hz, 1H, $H_{7b}$), 2.31 (s, 3H, $CH_3Ar$), 2.46 (h, *J*=6.9 Hz, 1H, $(CH_3)_2CH$), 3.04 (dd, *J*=4.7, 1.8 Hz, 1H, $H_2$), 3.18 (m, 1H, $H_4$), 3.27 (m, 1H, $H_1$), 3.49 (dd, *J*=4.7, 3.5 Hz, 1H, $H_3$), 5.84 (dd, *J*=5.6, 2.7 Hz, 1H, $H_5$), 6.31 (dd, *J*=5.6, 3.2 Hz, 1H, $H_6$), 7.20–7.35 (AA′BB′ system, 4H, aromatics). $^{13}$C NMR (50.29 MHz, $CDCl_3$) $\delta$ 17.8, 18.8, 21.2, 39.1, 46.0, 47.2, 47.5, 63.4, 123.8, 129.6, 135.5, 137.8, 140.0, 140.7, 211.5. Anal. Calcd for $C_{18}H_{22}O_2S$: C, 71.48; H, 7.33. Found: C, 71.20; H, 7.26.

**4.4.2. Compound 5b.** Yield 33.6%, white solid. Mp 133–134 °C. $[\alpha]_D$=+46 (*c*=2, acetone). $^1$H NMR (200 MHz, $CDCl_3$) $\delta$ 0.75 (d, *J*=7.0 Hz, 3H, $(CH_3)_2CH$), 0.88 (d,

$J$=7.0 Hz, 3H, $(CH_3)_2CH$), 1.56 (dq, $J$=8.9, 1.8 Hz, 1H, $H_{7a}$), 1.96 (d, $J$=8.9 Hz, 1H, $H_{7b}$), 2.34 (s, 3H, $CH_3Ar$), 2.52 (h, $J$=7.0 Hz, 1H, $(CH_3)_2CH$), 3.08 (dd, $J$=4.6, 3.6 Hz, 1H, $H_3$), 3.21 (dd, $J$=4.6, 1.8 Hz, 1H, $H_2$), 3.26 (m, 2H, $H_1$ and $H_4$), 5.83 (dd, $J$=5.6, 2.7 Hz, 1H, $H_5$), 6.18 (dd, $J$=5.6, 3.7 Hz, 1H, $H_6$), 7.24–7.52 (AA′BB′ system, 4H, aromatics). $^{13}$C NMR (50.29 MHz, $CDCl_3$) $\delta$ 17.7, 18.9, 21.4, 39.1, 44.1, 46.9, 47.7, 51.6, 65.1, 125.3, 129.9, 134.7, 137.4, 139.5, 141.9, 210.6. Anal. Calcd for $C_{18}H_{22}O_2S$: C, 71.48; H, 7.33. Found: C, 71.28; H, 7.36.

**4.4.3. Compound 6b.** Yield 13.0%, viscous oil. $[\alpha]_D$=+79.5 ($c$=5.94, acetone). $^1$H NMR (200 MHz, $CDCl_3$) $\delta$ 0.90 (d, $J$=6.9 Hz, 3H, $(CH_3)_2CH$), 1.06 (d, $J$=6.9 Hz, 3H, $(CH_3)_2CH$), 1.41 (ddd, $J$=8.9, 3.4, 1.7 Hz, 1H, $H_{7a}$), 1.67 (d, $J$=8.9 Hz, 1H, $H_{7b}$), 2.38 (s, 3H, $CH_3Ar$), 2.72 (h, $J$=6.9 Hz, 1H, $(CH_3)_2CH$), 2.90 (m, 1H, $H_1$), 2.96 (m, 1H, $H_4$), 3.05 (dd, $J$=4.5, 1.7 Hz, 1H, $H_3$), 3.70 (dd, $J$=4.5, 3.3 Hz, 1H, $H_3$), 6.28 (dd, $J$=5.6, 2.7 Hz, 1H, $H_6$), 6.38 (dd, $J$=5.6, 2.7 Hz, 1H, $H_5$), 7.28–7.47 (AA′BB′ system, 4H, aromatics). $^{13}$C NMR (50.29 MHz, $CDCl_3$) $\delta$ 18.3, 18.4, 21.3, 40.3, 45.2, 46.7, 47.4, 49.4, 69.2, 124.2, 129.8, 134.9, 136.9, 140.7, 141.4, 213.4. Anal. Calcd for $C_{18}H_{22}O_2S$: C, 71.48; H, 7.33. Found: C, 71.30; H, 7.31.

**4.4.4. Compound 7b.** Yield 29.7%, white solid. Mp 154.5–156 °C. $[\alpha]_D$=+16 ($c$=2, acetone). $^1$H NMR (200 MHz, $CDCl_3$) $\delta$ 0.46 (d, $J$=6.9 Hz, 3H, $(CH_3)_2CH$), 0.87 (d, $J$=6.9 Hz, 3H, $(CH_3)_2CH$), 1.49 (ddd, $J$=9.0, 3.2, 1.6 Hz, 1H, $H_{7a}$), 1.58 (d, $J$=9.0 Hz, 1H, $H_{7b}$), 2.12 (dd, $J$=4.6, 1.6 Hz, 1H, $H_3$), 2.21 (h, $J$=6.9 Hz, 1H, $(CH_3)_2CH$), 2.31 (s, 3H, $CH_3Ar$), 2.89 (m, 1H, $H_4$), 3.45 (m, 1H, $H_1$), 3.99 (dd, $J$=4.6, 3.4 Hz, 1H, H2), 6.34 (dd, $J$=5.6, 3.4 Hz, 1H, $H_5$), 6.50 (dd, $J$=5.6, 2.8 Hz, 1H, $H_6$), 7.20–7.50 (AA′BB′ system, 4H, aromatics). $^{13}$C NMR (50.29 MHz, $CDCl_3$) $\delta$ 18.1, 21.3, 40.1, 44.4, 45.6, 47.6, 50.7, 68.7, 126.0, 129.9, 136.2, 137.3, 139.6, 142.5, 211.5. Anal. Calcd for $C_{18}H_{22}O_2S$: C, 71.48; H, 7.33. Found: C, 71.29; H, 7.36.

### 4.5. Diels–Alder reaction of (*R*)-(*E*)-1-(*p*-tolylsulfinyl)-1-hexen-3-ona (*R*)-2a with Lewis acids

The ketosulphoxide (50 mg, 0.2 mmol) was dissolved in anhydrous dichloromethane (5 mL) under a $N_2$ atmosphere and a solution of Lewis acid (0.25 mmol) was added dropwise at −78 °C. The solution was stirred for 20 min and treated at −78 °C with freshly distilled ciclopentadiene (2.3 mmol). After being stirred for (2–24 h) at −78 °C, the reaction was quenched with water (2 mL). The organic phase was separated and washed successively with 10% hydrochloric acid solution, saturated aqueous $NaHCO_3$ solution and saturated aqueous NaCl solution and dried over $Na_2SO_4$. The solvent was removed under reduced pressure and the proportion of cycloadducts was analyzed by $^1$H NMR (500 MHz).

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