

## Regiochemical Control of the Diels–Alder Reactions with $\beta$ -Phenylsulphonylacrylate Esters

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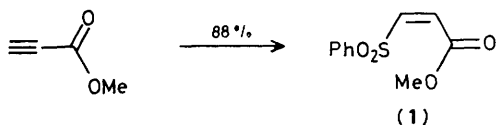
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Alkyl  $\beta$ -phenylsulphonylacrylates have been made as geometrically pure isomers; the *Z*-isomer reacts with dienes in Diels–Alder cycloadditions to afford the opposite regiochemistry to that observed with the *E*-isomer and this provides a useful method for reversing normal carbonyl directing effects.

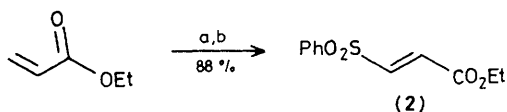
We have been involved in a detailed study of the stereocontrol in Diels–Alder reactions for the construction of important biologically active macrocyclic amides.<sup>1</sup> For this purpose we required an efficient route to the alkyl *Z*- and *E*- $\beta$ -phenylsulphonylacrylates, which, apart from the report of Colonna *et al.*<sup>2</sup> [which details a very long synthesis of the methyl (*E*)-isomer and lacks physical data] are poorly described in the literature.<sup>3</sup> Paquette has recently reported the use of methyl (*Z*)- $\beta$ -phenylsulphonylacrylate in quadricyclane syntheses; however, experimental details are unclear as is the reference to its preparation.<sup>4</sup>

We have found that the boric acid mediated addition of sodium benzenesulphonate to methyl propiolate in the presence of a phase transfer catalyst ( $\text{Bu}_4\text{NHSO}_4$ ) gave the *Z*-isomer (1) exclusively† (Scheme 1). Thus when a solution (0.05 M) of sodium benzenesulphonate (1 equiv.) in water was added to methyl propiolate (1 equiv.), boric acid (1.2 equiv.), and  $\text{Bu}_4\text{NHSO}_4$  (10 mol %) in tetrahydrofuran (THF) (0.05 M) and the mixture stirred at room temperature for 12 h, the *Z*-isomer (1) was isolated from this one-step reaction in 88% yield [m.p. 50.5–51.5 °C; <sup>1</sup>H n.m.r.  $\delta$  ( $\text{CDCl}_3$ ) 3.82 (3H, s), 6.52 (1H, d, *J* 11.5 Hz), 6.57 (1H, d, *J* 1.5 Hz), 7.6–7.9 (5H, c); i.r.  $\nu_{\text{max}}$  1732]. The ethyl ester of the corresponding *E*-isomer (2) was made from ethyl acrylate and benzenesulphonyl iodide<sup>5</sup> in two steps (Scheme 2) [88% yield; m.p. 18.5–19.0 °C; <sup>1</sup>H n.m.r.  $\delta$  ( $\text{CDCl}_3$ ) 1.30 (3H, t), 4.25 (2H, q), 6.83 (1H, d, *J* 15.25 Hz), 7.37 (1H, d, *J* 15.25 Hz), 7.6–7.9 (5H, c); i.r.  $\nu_{\text{max}}$ , 1725, 1330  $\text{cm}^{-1}$ ].

When the *E*-isomer (2) was heated with 4-methyl-(*E*)-hexa-3,5-dien-1-ol (3),‡ the *endo* Diels–Alder adducts (4) and (5)§ were obtained quantitatively in a ratio of 2.3:1 (Scheme 3).



**Scheme 1.** Reagents:  $\text{PhSO}_2^- \text{Na}^+$ ,  $\text{B(OH)}_3$ ,  $\text{Bu}_4\text{NHSO}_4$ , THF:  $\text{H}_2\text{O}$  1:1.



**Scheme 2.** Reagents and conditions: (a)  $\text{PhSO}_2\text{I}/h\nu/\text{C}_6\text{H}_6$ , (b)  $\text{Et}_3\text{N}$ ,  $\text{Et}_3\text{OAc}$ , room temp.

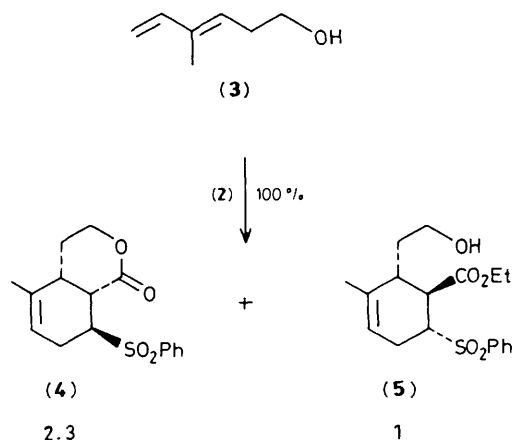
† All new compounds exhibited satisfactory physical data: microanalysis (or accurate mass), i.r., mass spec., <sup>13</sup>C and <sup>1</sup>H n.m.r.

‡ Compound (3) was prepared from (*E*)-2-methylbut-2-enal by the following four-step sequence: (i)  $\text{BrCH}_2\text{CO}_2\text{Et}$ , Zn, THF,  $(\text{MeO})_3\text{B}$ , room temp., 14 h, 90% yield; (ii)  $\text{P}_2\text{O}_5$ ,  $\text{C}_6\text{H}_6$ , reflux, 3 h, 99% yield; (iii)  $\text{LiPr}_2\text{N}$ ,  $-78^\circ\text{C}$ , THF/hexamethylphosphoric triamide, 3 h, then AcOH,  $-78^\circ\text{C}$ , 1 h (ref. 7); (iv)  $\text{LiAlH}_4$ ,  $\text{Et}_2\text{O}$ ,  $0^\circ\text{C}$ , 4 h, 95% yield.

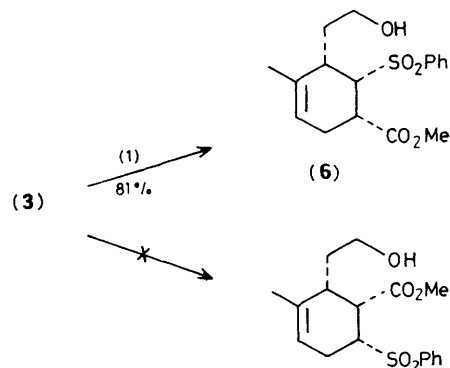
§ All compounds are racemic; only one enantiomer is portrayed.

Heating diene (3) with the *Z*-isomer (1) gave the *endo* adduct (6) in 81% yield. This isomer has the opposite sulphone regiochemistry to (4) and (5) and thus the reaction presents an interesting method for controlling the regiochemistry of the acrylate moiety with *endo* integrity maintained (Scheme 4).

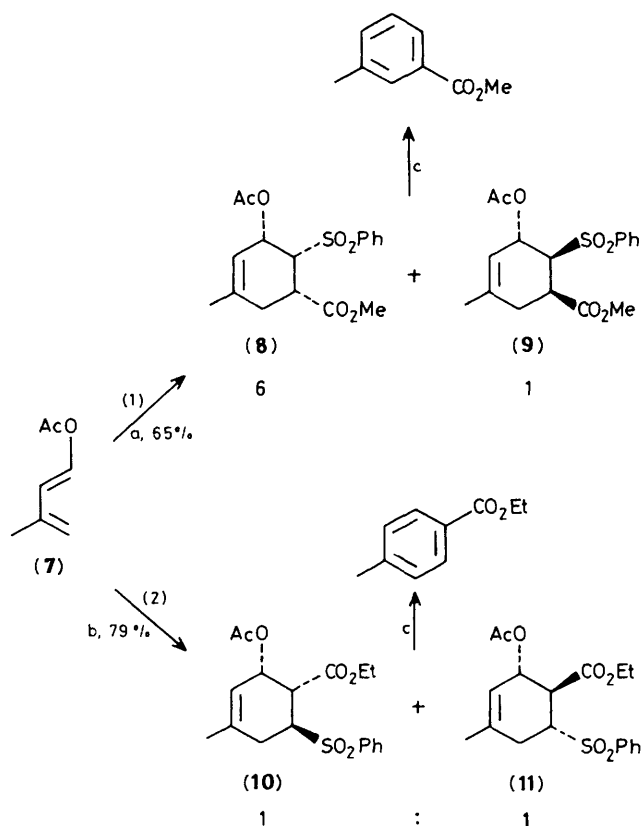
In order to investigate the generality of this reaction, the *Z*- and *E*-acrylates (1) and (2) were treated with 1-acetoxy-3-methyl-(*E*)-buta-1,3-diene (7).<sup>6</sup> The *Z*-isomer (1) underwent cycloaddition to yield adducts (8) and (9) in 65% yield in a ratio of 6:1 whereas the reaction with the *E*-isomer (2) gave rise to the opposite regiochemistry with an equimolar mixture of (10) and (11) in 79% overall yield. Treatment of (8) and (9) with sodium ethoxide in boiling benzene gave ethyl *m*-toluate as the sole product. Analogous reactions of (10) and (11) gave



**Scheme 3.** Reagents and conditions: toluene, Methylene Blue, reflux, 48 h.



**Scheme 4.** Reagents and conditions: toluene, Methylene Blue, reflux, 7 days.



**Scheme 5.** Reagents and conditions: (a) toluene, Methylene Blue, reflux, 6 days; (b) toluene, Methylene Blue, reflux, 5 days; (c) NaOEt, benzene, reflux.

methyl *p*-toluate (Scheme 5). The carbonyl group in (2) appears to be dominant in directing the regiochemistry of addition (*cf.* Scheme 3); presumably the ester carbonyl suffers

no steric interference from the phenylsulphonyl group, and good orbital overlap between the ester carbonyl and the double bond can take place. In the *Z*-isomer (1) the ester carbonyl could be twisted out of the plane of the carbon-carbon double bond resulting in a dominant sulphonyl directing effect.

These reactions provide a facile route to many aromatic compounds; base induced elimination of the phenylsulphonyl moiety would provide a selective entry into both possible regioisomers resulting from alkyl propiolate Diels-Alder reactions whereas reductive removal of the phenylsulphonyl group would represent regiochemical control of the ester group in an acrylate Diels-Alder reaction.

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