Regiochemical Control of the Diels–Alder Reactions with β-Phenylsulphonylacrylate Esters

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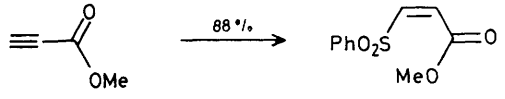
Alkyl β-phenylsulphonylacrylates have been made as geometrically pure isomers; the *Z*-isomer reacts with dienes in Diels–Alder cycloadditions to afford the opposite regiochemistry to that observed with the *E*-isomer and this provides a useful method for reversing normal carbonyl directing effects.

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

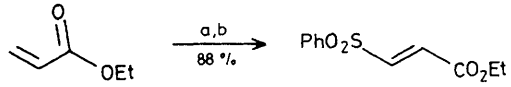
We have found that the boric acid mediated addition of sodium benzenesulphinate to methyl propiolate in the presence of a phase transfer catalyst (Bu_4NHSO_4) gave the *Z*-isomer (**1**) exclusively† (Scheme 1). Thus when a solution (0.05 M) of sodium benzenesulphinate (1 equiv.) in water was added to methyl propiolate (1 equiv.), boric acid (1.2 equiv.), and Bu_4NHSO_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; ^{1}H n.m.r. δ ($CDCl_3$) 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. ν_{max} 1732]. The ethyl ester of the corresponding *E*-isomer (**2**) was made from ethyl acrylate and benzenesulphonyl iodide[5] in two steps (Scheme 2) [88% yield; m.p. 18.5—19.0 °C; ^{1}H n.m.r. δ ($CDCl_3$) 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. ν_{max}, 1725, 1330 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).



(**1**)

Scheme 1. *Reagents:* $PhSO_2^-$ Na^+, $B(OH)_3$, Bu_4NHSO_4, THF: H_2O 1 : 1.



(**2**)

Scheme 2. *Reagents and conditions:* (a) $PhSO_2I/h\nu/C_6H_6$, (b) Et_3N, Et_3OAc, room temp.

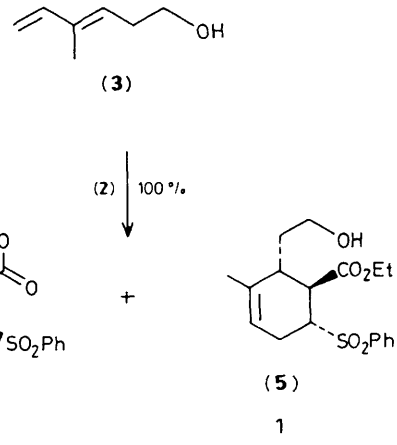
† All new compounds exhibited satisfactory physical data: microanalysis (or accurate mass), i.r., mass spec., ^{13}C and ^{1}H n.m.r.

‡ Compound (**3**) was prepared from (*E*)-2-methylbut-2-enal by the following four-step sequence: (i) $BrCH_2CO_2Et$, Zn, THF, $(MeO)_3B$, room temp., 14 h, 90% yield; (ii) P_2O_5, C_6H_6, reflux, 3 h, 99% yield; (iii) $LiPr^i_2N$, −78 °C, THF/hexamethylphosphoric triamide, 3 h, then AcOH, −78 °C, 1 h (ref. 7); (iv) $LiAlH_4$, Et_2O, 0 °C, 4 h, 95% yield.

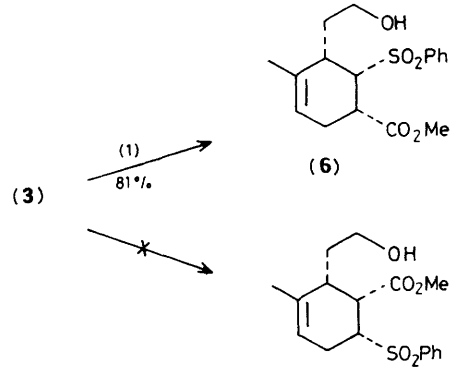
§ All compounds are racemic; only one enantiomer is portrayed.

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).

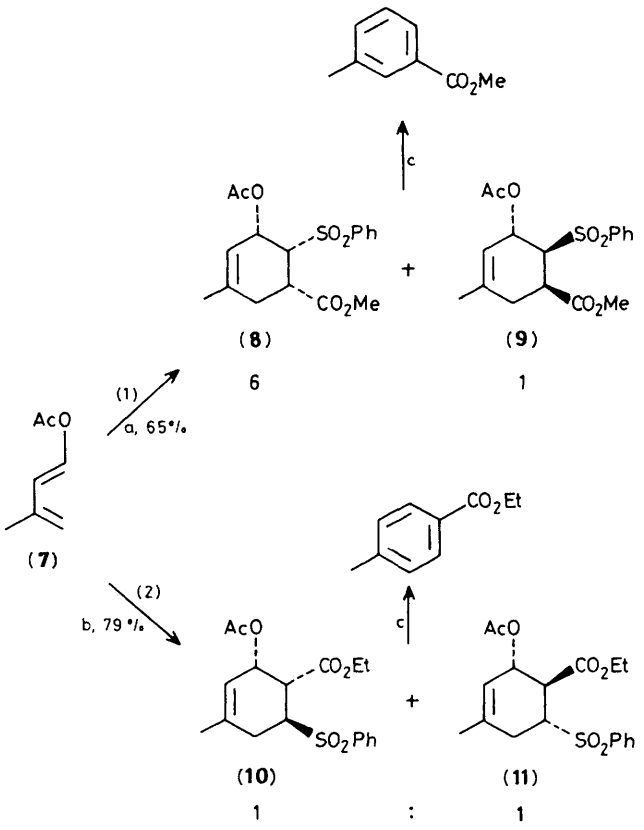
In order to investigate the generality of this reaction, the *Z*- and *E*- acrylates (**1**) and (**2**) were treated with 1-acetoxy-3-methyl-(*E*)-buta-1,3-diene (**7**).[6] The *Z*-isomer (**1**) underwent cycloaddition to yield adducts (**8**) and (**9**) in 65% yield in a ratio of 6 : 1 whereas the 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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