

## Selective Synthesis of $\alpha$ -Sulphenyl-, $\alpha$ -Sulphinyl-, and $\alpha$ -Sulphonyl- $\alpha,\beta$ -unsaturated Carbonyl Compounds by the Knoevenagel Reaction

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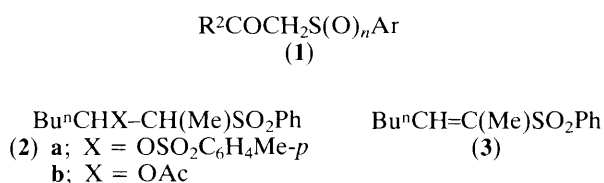
Simple treatment of aldehydes with the carbonyl compounds (**1**) [ $R^2COCH_2S(O)_nAr$ ;  $n = 0, 1, 2$ ] and piperidine stereoselectively produces the condensation products (**7**), the stereochemistry of which is controlled by the steric requirements of two functional groups  $COR^2$  and  $S(O)_nAr$  in a sulphur-stabilized carbanion intermediate.

Carbonyl, sulphenyl, sulphinyl, and sulphonyl groups exert a strong stabilizing effect on carbanions. In aldol condensations the sodium and lithium enolates of methyl phenylsulphenylacetate (**1**;  $R^2 = OMe$ ,  $Ar = Ph$ ,  $n = 0$ ) and ethyl phenylsulphinylacetate (**1**;  $R^2 = OEt$ ,  $Ar = Ph$ ,  $n = 1$ ) are too stable to react with aldehydes (**6**) whereas the use of magnesium and zinc salts drives the equilibrium of the condensations towards products.<sup>1,2</sup> When a leaving group is  $\beta$  to the above functional groups in  $\beta$ -elimination reactions,

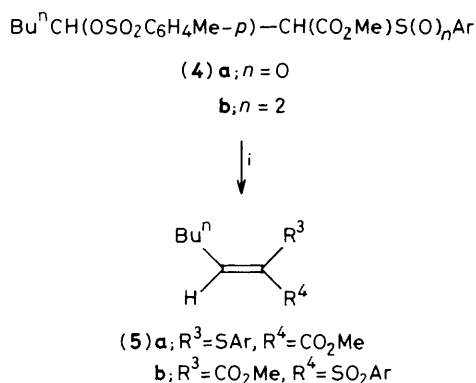
elimination probably proceeds by the *E1cb* mechanism sometimes in a stereoconvergent manner to give the most thermodynamically stable isomer of the olefin.<sup>3,4</sup> Julia *et al.* treated the sulphones (**2a, b**) with a base and found that *threo*- and *erythro*-(**2a**) underwent stereospecific elimination to yield *Z*- and *E*-isomers of the sulphone (**3**), respectively, while both *threo*- and *erythro*- (**2b**) afforded only the *E*-isomer of (**3**).<sup>5</sup> On the other hand, we have found that treatment of a diastereoisomeric mixture (*threo* : *erythro*, 55 : 45)<sup>1</sup> of the sulphide (**4a**)

**Table 1.** Preparation of (7) by the Knoevenagel reaction.

Compound (7)	R <sup>1</sup>	R <sup>2</sup>	Ar	n	Temp./ °C	Time/ h	Yield/ %	Configuration
a	Bu <sup>n</sup>	OMe	C <sub>6</sub> H <sub>4</sub> Cl- <i>p</i>	2	0	24	80	<i>E</i>
b	Bu <sup>n</sup>	OMe	C <sub>6</sub> H <sub>4</sub> Cl- <i>p</i>	1	0	24	70	<i>E</i>
c	Bu <sup>n</sup>	OBu <sup>t</sup>	Ph	1	0	24	67	<i>E</i>
d	Pr <sup>i</sup>	OMe	C <sub>6</sub> H <sub>4</sub> Cl- <i>p</i>	1	20	24	90	<i>E</i>
e	Ph	OMe	Ph	1	60	6	85	<i>E</i>
f	Bu <sup>n</sup>	Ph	Ph	0	60	6	73	<i>Z</i>
g	Bu <sup>n</sup>	Ph	Ph	1	0	10	61	<i>E</i>
h	Bu <sup>n</sup>	Me	Ph	0	60	6	63	<i>Z</i>
i	Bu <sup>n</sup>	Me	Ph	1	0	6	68	<i>Z</i>
j	Bu <sup>n</sup>	Me	Ph	2	0	24	60	<i>E</i>



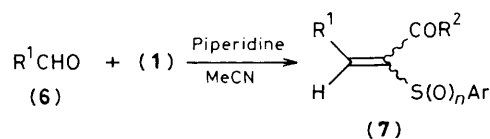
**Scheme 1.** Ar = C<sub>6</sub>H<sub>4</sub>Cl-*p*; i, DBU, CH<sub>2</sub>Cl<sub>2</sub>, room temp.



or the sulphone (4b) with 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU) leads to the *Z*-sulphide (5a) (87% yield) or the *E*-sulphide (5b) (89% yield), respectively (Scheme 1).

These results suggest that the combined stabilizing effect of both a carbonyl group and a sulphur atom on a carbanion should result in stereoconvergent elimination, regardless of the leaving group. Using this assumption α-sulphenyl-, α-sulphinyl-, and α-sulphonyl-α,β-unsaturated carbonyl compounds (7) were prepared stereoselectively from (6) and the carbonyl compounds (1). Dressler and Graham have reported the Knoevenagel condensations of aromatic aldehydes and (1; R<sup>2</sup> = OEt, Ar = Ph, n = 2), but the stereochemistry remained uncertain.<sup>6</sup>

A solution of (6) (1.2 equiv.), (1), and piperidine (0.1 equiv.) in MeCN was kept at 0–60 °C. Chromatography on silica gel gave one isomer of (7). The yields of the other diastereoisomers were lower than 3%, for example, the *E*:*Z* ratio in (7b) was 99:1 in the reaction mixture (by h.p.l.c.). Treatment of the sulphoxides [e.g., (7b)] with NaI and (CF<sub>3</sub>CO)<sub>2</sub>O in acetone<sup>7</sup> gave the corresponding sulphides



[e.g., *E*-isomer of (5a)] in quantitative yields with retention of configuration. The structural assignments were confirmed by the comparison of the olefinic proton signals in <sup>1</sup>H n.m.r. spectra with those of the conjugated sulphides (7; n = 0), in which the signal *cis* to a carbonyl group is shifted markedly downfield. Typical results from reactions of (1) and (6) are shown in Table 1.

Similar treatment of butanal with methyl benzoylacetate gave the condensation product in 77% yield, but with low stereoselectivity (*E*:*Z* 40:60). It may be concluded then that a sulphur atom plays an important role in stabilizing the intermediate carbanion, and the steric requirements of the functional groups decrease in the order SO<sub>2</sub>Ar > COMe > S(O)Ar > COAr > CO<sub>2</sub>Me > SAr.

The present synthetic method has the following advantages: (1) reagents are readily available, (2) the procedure is simple, and (3) the applications of stereospecific oxidation (using *m*-chloroperbenzoic acid) and reduction [NaI-(CF<sub>3</sub>CO)<sub>2</sub>O] make it possible to prepare stereoselectively *E*- and *Z*-isomers of (7), which may be used as Michael acceptors<sup>8,9</sup> and as Diels–Alder dienophiles.

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## References

- 1 T. R. Hoye and M. J. Kurth, *J. Org. Chem.*, 1980, **45**, 3549.
- 2 N. Kunieda, J. Nokami, and M. Kinoshita, *Tetrahedron Lett.*, 1974, 3997.
- 3 P. L. Southwick, A. K. Colter, R. J. Owellen, and Y.-C. Lee, *J. Am. Chem. Soc.*, 1962, **84**, 4299.
- 4 S. J. Cristol and P. Pappas, *J. Org. Chem.*, 1963, **28**, 2066.
- 5 M. Julia, M. Launay, J.-P. Stacino, and J.-N. Verpeaux, *Tetrahedron Lett.*, 1982, 2465.
- 6 H. Dressler and J. E. Graham, *J. Org. Chem.*, 1967, **32**, 985.
- 7 J. Drabowicz and S. Oae, *Synthesis*, 1977, 404.
- 8 H. Hagiwara, K. Nakayama, and H. Uda, *Bull. Chem. Soc. Jpn.*, 1975, **48**, 3769.
- 9 G. H. Posner, J. P. Mallamo, and K. Miura, *J. Am. Chem. Soc.*, 1981, **103**, 2886.