Asymmetric Induction in the Reaction of a Chiral Lithiated Sulphoxide and Aldehydes

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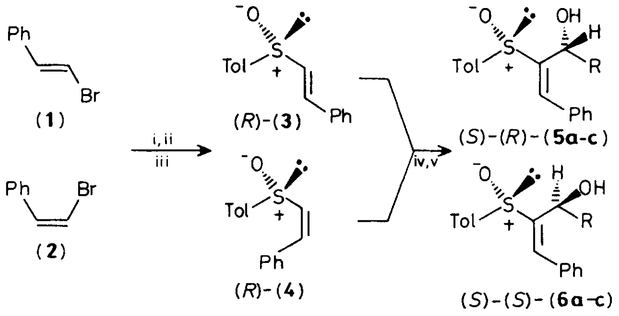
Significant asymmetric induction has been observed in the reaction of 1-lithio-2-phenyl-1-(*R*)-*p*-tolylsulphinylethylene; the sense of this induction has been established by an *X*-ray structure on one of the products.

α-Lithiated sulphoxides react with carbonyl compounds to give poor asymmetric induction.[1] As part of a detailed study on chiral heteroatom stabilised vinyl anions, we have prepared the (*R*)-(*E*) and (*R*)-(*Z*) sulphoxide isomers (**3**) and (**4**) from a mixture of the halides (**1**) and (**2**).[2] The sulphur configuration in (**3**) and (**4**) was assigned as (*R*) by analogy with other cases of Grignard reagents reacting with (−)-menthyl (*S*)-toluene-*p*-sulphinate.[3] The isomers (**3**) and (**4**) were separated by chromatography, and each was lithiated and reacted with the range of aldehydes indicated† (Scheme 1).

Significant asymmetric induction was observed in the case of the highly hindered trimethyl acetaldehyde (compounds **c**). The major isomer was purified and an *X*-ray crystal structure was carried out to determine the configuration of the new chiral centre in (**6**). Figure 1 shows the result of this determination.



a; R = Me
b; R = Me_2CH
c; R = Me_3C
Tol = *p*-MeC_6H_4

Scheme 1. *Reagents:* i, Mg, tetrahydrofuran (THF), gentle reflux, 20 min; ii, menthyl (*S*)-toluene-*p*-sulphinate, benzene, room temp., 1.5 h; iii, separation; iv, lithium di-isopropylamide (LDA), THF, −78°C; v, RCHO.

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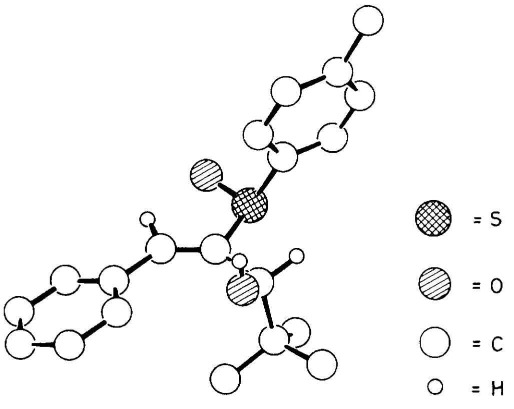
† All new compounds gave satisfactory spectroscopic data; satisfactory microanalyses were obtained for (**5b—c**), (**6b—c**) derived from (**3**) and on (**5c**) and (**6b—c**) derived from (**4**). High resolution mass spectral data were satisfactory for compounds (**5**), (**6a**) derived from (**3**), and (**6a**) derived from (**4**).

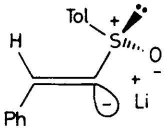
Table 1. Diastereoisomers (**5**) and (**6**) obtained from (**3**) and (**4**).

Isomer		Ratio by h.p.l.c. (**5a**—**c**) : (**6a**—**c**)	% Yield[a] (**5a**—**c**)	% Yield[a] (**6a**—**c**)	$[\alpha]_D$(°), $CHCl_3$ (**5a**—**c**)	$[\alpha]_D$(°), $CHCl_3$ (**6a**—**c**)
	a	45 : 55	18	34	+101	+11.5
(**3**)	**b**	34 : 66	16	44	+35	+24
	c	15 : 85	–	59[b]	−52	+142
	a	47 : 53	18	25	+100	+9
(**4**)	**b**	41 : 59	25	35	+35	+23
	c	14 : 86	–	71[b]	–	–

[a] A small amount of dimer formed by attack of the carbanion on the starting material was also isolated. [b] Total yield of both diastereoisomers.

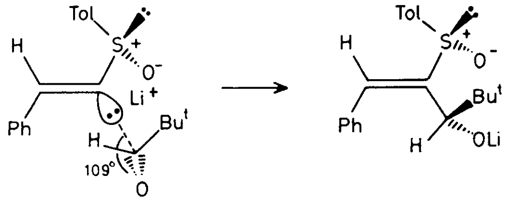


♦ **Figure 1.** *X*-Ray crystal structure of (**6c**).‡



(A)

The same pair of diastereoisomers (**5**) and (**6**) was obtained from both the (*R*)-(*E*)-(**3**) and (*R*)-(*Z*)-(**4**) isomers. In keeping with previous results,[4] the (*E*) isomer remained configurationally stable during the deprotonation but the (*Z*) isomer underwent a *cis–trans* isomerization.[5] Fears of racemization were dismissed when deprotonation followed by reprotonation of (**4**) gave (**3**) of the same optical purity as an original sample. This was reinforced by the fact that isomers (**5a**—**c**) and (**6a**—**c**) obtained from (**4**) had, within estimated experimental error, the same respective optical rotations as those obtained from (**3**) (Table 1).



Scheme 2

Speculation on the nature of the transition state for the reaction of the vinyl anion with aldehydes is complicated by the fact that in the *X*-ray structure the new C–C bond and the sulphoxide bond are *anti*. It would be reasonable to expect the anion to exist mainly in conformation (A), where the lone pair on the sulphur atom can overlap with the double bond and the sulphoxide oxygen is close enough to interact with the lithium atom. Such co-ordination has been proposed in other α-lithiosulphoxides.[6] Bearing in mind the direction of approach of a nucleophile to a carbonyl group, we tentatively propose the transition state shown in Scheme 2 to explain our results. In this model, the plane of the alkene atoms and the plane of the carbonyl atoms approach each other at the tetrahedral angle; the approach of the aldehyde to the anion occurs so that the t-butyl group is on the less hindered side away from the phenyl ring.

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‡ *Crystal data:* (**6c**), $C_{20}H_{24}O_2S$, M = 328.47, orthorhombic, space group $P2_12_12_1$, a = 11.026(30), b = 9.198(10), c = 18.065(13) Å, U = 1832.1 Å^3, Z = 4, μ = 1.45 cm^{-1}, λ (Mo-K_α) = 0.7107 Å, $F(000)$ = 704.0, D_c = 1.191 g cm^{-3}. The intensities of 1699 unique reflections with $2\theta < 50°$ and $(+h+k+l)$ were measured on a Stoe STADI-2 Weissenberg diffractometer. The data were corrected for Lorentz and polarization effects to yield 1117 reflections with $I \geq 3\sigma(I)$. The structure was solved using the TREF option of SHELXS 84.[7] All subsequent calculations were carried out using SHELX.[8] Final cycles of refinement employed a weighting parameter g(0.00051) and gave the final residual indices R = 0.060 and R_w = 0.065. Atomic co-ordinates, bond lengths and angles, and thermal parameters have been deposited at the Cambridge Crystallographic Data Centre. See Notice to Authors, Issue No. 1.