
Stereochemistry in Electrophilic Reactions to Carbanions not Stabilized by Intramolecular Chelation

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Methylation of an α -sulphinyl carbanion, not stabilized by intramolecular chelation, leads to inversion of configuration, whereas reaction with water or formaldehyde proceeds with retention of configuration.

Although α -sulphinyl carbanions are useful synthetic intermediates, there is some controversy over the stereochemistry of the products which result from their reactions with electrophiles.¹⁻⁷ From a mechanistic viewpoint it is essential to elucidate the following factors: (i) the stereochemistry of the carbanion initially formed, (ii) the configurational interconversion of the carbanion during reaction, and (iii) the mode in which an electrophile attacks the carbanion. Previously we suggested that intramolecular chelation affects the configurational interconversion of α -sulphinyl carbanions:⁸ here we report the stereochemistry of an electrophilic reaction in which the α -sulphinyl carbanion is not stabilized by intramolecular chelation.

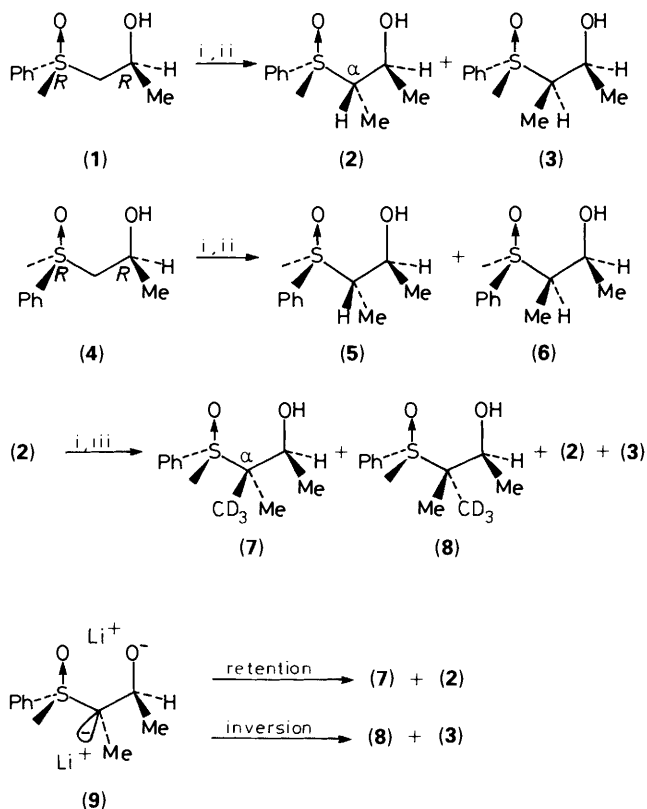
Lithiation (2.2 equiv. of BuLi, THF, -78°C , 15 min) of the

racemic β -hydroxy sulphoxide (1) or (4), and subsequent methylation (1.5 equiv. of MeI, -78°C to room temp., 1 h) of the resulting dianion gave a diastereoisomeric mixture of (2) and (3) (78:22; yield 86%) or (5)/(6) (96:4; yield 70%). Isomers (2), (3), and (5) were isolated by preparative h.p.l.c. [50 mm (int. diam.) \times 250 mm column packed with Cosmosil C₁₈-10; MeOH-H₂O (45:55)]. The ¹H n.m.r. spectra of (2) and (3) revealed Me-C₂ doublets at δ 0.93 and 1.39. After a similar lithiation of (2), deuteriomethylation (1.5 equiv. of CD₃I, -78°C to room temp., 1 h) of the dianion, and subsequent quenching with water afforded a mixture of (7)/(8) (23:77; yield 57%) and (2)/(3) (93:7; recovery 29%). The configuration and the ratio of (7)/(8) were determined on the basis of ¹H n.m.r. $\delta(\text{Me-C}_2)$ values [0.89 (7) and 1.41 (8)].

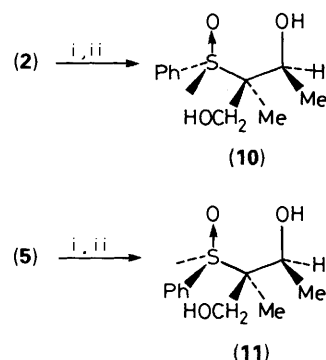
Table. Stereochemistry in deuterio-methylation of the dianions of (2), (3), and (5)

Substrate	Electrophile	Retention:Inversion ^a	
		Deuterio-methylated product	Recovered substrate ^b
(2)	CD ₃ I	23:77	93:7
(2)	(CD ₃ O) ₂ SO ₂	19:81	88:12
(3)	CD ₃ I	19:81	87:13
(5)	CD ₃ I	2:98	99:1

^a Determined by ¹H n.m.r. ^b Obtained by quenching with H₂O after deuterio-methylation.

**Scheme 1.** Reagents: i, BuLi (2.2 equiv.); ii, MeI (1.5 equiv.), H⁺; iii, CD₃I (1.5 equiv.), H⁺

Since the first formed oxyanion $\text{O}^- \text{Li}^+$ in the dianion of (1) is assumed to form a chelated structure with a polar $\text{S} \rightarrow \text{O}$ group,^{5,6,9} the dianion generated from (2) may be represented by structure (9), in which the Li^+ cation associated with the carbanion is not affected by a $\text{S} \rightarrow \text{O}$ group, and therefore the common behaviour of carbanion can be predicted. Evidently CD₃I might approach the carbanion mainly from the side opposite the Li^+ cation to yield (8) with inversion of configuration as a major product. Immediately after lithiation, quenching of the dianion with water did not lead to formation of (3). This finding suggests that water, on the contrary, approaches the carbanion with retention of configuration, and during the deuteriomethylation the configurational interconversion of the carbanion occurs to a certain extent. Upon similar treatment of (3) or (5) with CD₃I or (CD₃O)₂SO₂ deuterio-

**Scheme 2.** Reagents: i, BuLi (2.2 equiv.); ii, (CH₂O)_n (1.5 equiv.)

methylation was also found to proceed with inversion. These results are shown in the Table.

Lithiation of (2) or (5), and subsequent treatment of the resulting dianion with paraformaldehyde (1.5 equiv. of CH₂O, -78°C to room temp., 1 h) produced (10) or (11), but no other diastereoisomer was obtained. The configuration of the product was determined by the observation of the nuclear Overhauser effect in ¹H n.m.r. spectra. The reaction proceeded with retention of configuration probably with the aid of coordination of a $\text{C}=\text{O}$ group to the Li^+ cation associated with the carbanion. The striking aspect of the present results is that the extreme bulkiness of (5) which much influenced the approach of CD₃I, but did not prevent the attack of CH₂O. In conclusion, steric factors play an important role in alkylation, whereas coordination is predominant in the reaction with an aldehyde.

The present results regarding to the reactivities of diastereoisomeric carbanions may provide much information on carbanion chemistry.

Experimental

To a stirred solution of (2), (3), or (5) (1 mmol) in dry THF (10 ml) at -78°C was added dropwise BuLi in hexane (1.6M; 1.4 ml). The mixture was stirred for 15 min, after which CD₃I, (CD₃O)₂SO₂, or paraformaldehyde (1.5 mmol) was added, and the resulting solution stirred for 1 h at -78°C , and then warmed to room temperature, and quenched with water. The organic layer was washed with water, dried (MgSO₄), and evaporated. Chromatography of the residue on silica-gel column with EtOAc gave (7)/(8), (12)/(13), (10), or (11) [(12)/(13); deuterio-methylated products with retention/inversion from (5)]: (7)/(8); ν_{max} 3 300 and 1 030 cm^{-1} ; δ_{H} (400 MHz, CDCl₃) 0.89 [(7)-Me, (0.68 H, s)], 1.16 (3 H, d, J 6.41 Hz), 1.41 [(8)-Me, (2.32 H, s)], 4.06 (1 H, q, J 6.41 Hz), 4.23 (1 H, br s), and 7.53—7.67 (5 H, m); (10); ν_{max} 3 400 and 1 030 cm^{-1} ; δ_{H} (400 MHz, CDCl₃) 0.99 (3 H, s), 1.44 (3 H, d, J 6.41 Hz), 1.93 (1 H, br s), 3.43 (1 H, d, J 12.51 Hz), 3.95 (1 H, br s), 4.00 (1 H, d, J 12.51 Hz), 4.75 (1 H, q, J 6.41 Hz), and 7.55—7.79 (5 H, m); (11); ν_{max} 3 400 and 1 030 cm^{-1} ; δ_{H} (400 MHz, CDCl₃) 1.14 (3 H, s), 1.33 (3 H, d, J 6.41 Hz), 3.44 (1 H, d, J 12.21 Hz), 3.73 (1 H, d, J 12.21 Hz), 3.75 (2 H, br s), 4.29 (1 H, q, J 6.41 Hz), and 7.51—7.77 (5 H, m); (12)/(13); ν_{max} 3 300 and 1 030 cm^{-1} ; δ_{H} (400 MHz, CDCl₃) 0.94 [(12)-Me, (0.06 H, s)], 1.11 [(13)-Me, (2.94 H, s)], 1.22 (3 H, d, J 6.41 Hz), 3.95 (1 H, br s), 4.21 (1 H, q, J 6.41 Hz), and 7.48—7.68 (5 H, m).

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