

Effect of Intramolecular Chelation on Configurational Interconversion of Sulphur-stabilized Carbanions

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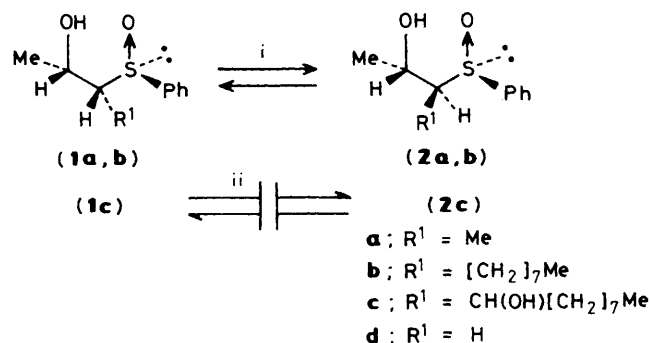
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Sulphur-stabilized carbanions $R^1R^2\bar{C}-SO$ undergo configurational interconversion, which is affected by intramolecular chelation and the bulk of R.

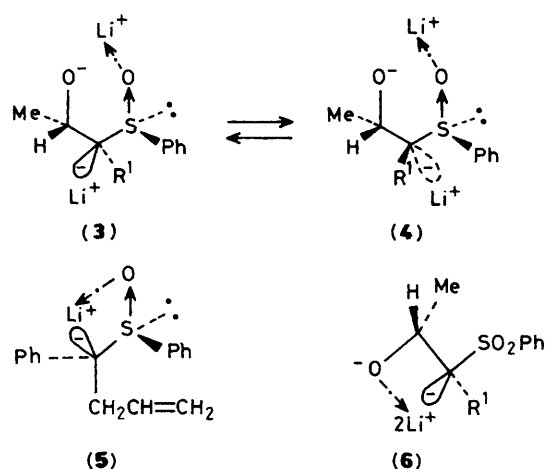
The configuration of the non-enolizable carbanions $R^1\bar{C}H-SO$ and $R^1\bar{C}H-SO_2^{1-3}$ may be determined by trapping with reactive electrophiles such as D_2O , MeI, and acetone, on the assumption that no stereochemical change occurs under the given conditions.^{1,4-6} However it has been reported recently that the configurational assignment of the deuteriated product from $Ph\bar{C}H-SOBut$ is in error.⁷ Therefore a further configurational investigation of the protonation reaction of the sulphur-stabilized carbanion is required. Here we report the preparation of the diastereoisomeric β -hydroxy sulfoxides (**1a**—**c**) and (**2a**—**c**), and the configurational interconversion of the carbanions $R^1R^2\bar{C}-SO$ generated from them.

The racemic β -hydroxy sulfoxide (**1d**) was prepared by reduction [1.2 equiv. of di-isobutylaluminium hydride, tetrahydrofuran (THF), $-78^\circ C$, 1 h] of the corresponding β -oxo

sulfoxide,⁸ followed by recrystallization [hexane-EtOAc (2 : 1)]. Lithiation (2.2 equiv. of BuLi, THF, $-78^\circ C$, 30 min) of (**1d**), and subsequent alkylation (1.5 equiv. of MeI or $Me[CH_2]_7I$, $-78^\circ C$ to room temp., 1 h) gave a diastereoisomeric mixture of (**1a**) and (**2a**) (22 : 78; yield 86%), or (**1b**) and (**2b**) (34 : 66; yield 71%). After similar lithiation of (**1d**), treatment of the resulting dianion with $Me[CH_2]_7CHO$ (1.2 equiv.) (THF, $-10^\circ C$, 30 min) produced a diastereoisomeric mixture of (**1c**) and (**2c**) (81 : 19; yield 63%). The mixtures of (**1a**) and (**2a**), (**1b**) and (**2b**), and (**1c**) and (**2c**) were separated by column chromatography [silica gel; hexane-EtOAc (2 : 1)] and preparative h.p.l.c. [20 mm (int. diam.) \times 250 mm column packed with Cosmosil C₁₈-10, MeOH-H₂O (1 : 2); and 50 mm (int. diam.) \times 250 mm column packed with Shim-pack PREP-SIL(L), hexane-EtOAc (1 : 1)]. The configurations of



Scheme 1. Reagents and conditions: i, BuLi (2.2 equiv.), THF, -78 °C [(1a)] or -78 °C to room temp. [(1b)], then H₂O; ii, BuLi (3.3 equiv.), THF, -78 °C to room temp., then H₂O.



Scheme 2. Configurations of the carbanions (3)–(6).

(1a), (2a), (1b), and (2b) were determined on the basis of ¹H n.m.r. *J*(CHMe, CHR¹) values [2.0 (1a), 8.0 (2a), 1.0 (1b), and 6.0 Hz (2b)].⁹ The configurations of (1c) and (2c) were determined by ¹H n.m.r. as described previously,¹⁰ after conversion into the corresponding sulphones and then acetals.

It has been suggested that the stereochemistry in the reactions of R¹CH–SO is controlled by the ability of the metal cation to form intramolecular chelates.^{1,4} Interestingly, in the alkylation of the dianion of (1d) by BuLi in THF, chelation between the first-formed oxyanion –O–Li⁺ and a polar S→O group plays an important role; hence the Li⁺ cation associated with the carbanion formed later is not stabilized by intramolecular chelation.¹¹ Therefore, the dianions generated from (1a,b and d) and (2a,b and d) might be expected to undergo configurational interconversion readily, although (1a) and (2a) did not interconvert on treatment with 1 equiv. of BuLi.¹¹

Lithiation of racemic (1a) or (2a) with BuLi (2.2 equiv.) (THF, -78 °C, 30 min), quenching with H₂O, and chromatography on silica gel yielded a mixture of (1a) and (2a). The ratios of (1a) to (2a) [h.p.l.c. on 4.6 mm (int. diam.) × 250 mm column packed with PYE,¹² MeOH–H₂O (85:15)] obtained starting from (1a) and (2a) were 24:76 (recovery 82%) and 9:91 (recovery 86%), respectively. This difference suggests that the reactions were quenched before equilibrium was reached. However if equilibration was attempted, (1a) and (2a) would decompose to a considerable extent under the

strongly basic conditions. Although no isomerization of the dianion (3b) derived from (1b) was observed at -78 °C, after warming to room temperature during 1 h a mixture of (1b) and (2b) was isolated in the ratio 38:62 (recovery 71%) [h.p.l.c. on 4.6 mm (int. diam.) × 150 mm column packed with Cosmosil C₁₈, MeOH–H₂O (1:2)]. The interconversion between the two kinds of carbanion is apparently affected by the bulk of R¹. Consequently, we would expect the dianion generated from (1d) to undergo configurational interconversion readily.

When enantiomerically pure (2*S*,3*R*)-[(*R*)-3-phenylsulphiny]undecan-2-ol [(+)-(1b)] was employed, both (+)-(1b) and (2*S*,3*S*)-[(*R*)-3-phenylsulphiny]undecan-2-ol [(-)-(1b)] were isolated in enantiomerically pure form. Thus no combined retro-aldol/aldol reactions took place. Although the ready formation of dianions (3)/(4) was confirmed by quenching with D₂O, the ratio of (1) to (2) was found to vary gradually with reaction time.

These findings may be rationalised on the basis that (i) the combined process of deprotonation and protonation proceeds with retention of configuration; (ii) the configuration of the carbanion (3)/(4) is pyramidal (or planar but strongly Li⁺-paired); and (iii) inversion of the carbanion occurs slowly probably *via* a planar carbanion without loss of chirality at the adjacent atom.

On the other hand, under similar reaction conditions (BuLi, THF, -78 °C to room temp., 1 h) neither the trianion of (1c) nor the monoanions of (4*R*^{*})- and (4*S*^{*})-4-[phenyl-4-(*R*^{*})-phenylsulphiny]but-1-enes underwent configurational interconversion. Furthermore, the dianion (6; R¹ = [CH₂]₇Me), generated from the β-hydroxy sulphone, in which there is no chelation formed between the oxyanion –O–Li⁺ and the SO₂ group,¹¹ was found to be configurationally stable. In all these cases the carbanion is assumed to be stabilized by an Li⁺ cation intramolecularly co-ordinated to an oxyanion [in (3c) and (6)]^{13,14} or an S → O group [in (5)].

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