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Carbanions α to sulfoxide.
Ion-pairing and stereoselectivity.

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Highly stereoselective ^1H-^2H exchange has been observed in a number of sulfoxides (1-7). The removal of the diastereoisotopic protons by a strong base and the reactions of the thus generated carbanion α to the sulfoxide are known to be stereoselective (7-9). Such a preference may be caused by the "gauche effect" (10), although this theory is derived from ab initio calculations assuming the carbanion to be present as a free ion. Published data suggest that factors other than electronic may play an important role (11). We propose to demonstrate the importance of ion-pairing phenomena in the stereoselectivity of the intermediate α lithio sulfoxide.

The reaction of α lithio benzyl methyl sulfoxide (BMSO) with deuterium oxide and methyl iodide at -78°C in tetrahydrofuran (THF) is stereoselective, two diastereoisomers being obtained in 15:1 and 18:1 ratio respectively. Deuteration and methylation follow opposite stereochemical courses (12) (8).

The lithium derivative ($BMSO^-$ Li^+) was generated according to the published procedure at -78°C by action of n-butyllithium on BMSO in THF (12), and quenched after 3, 15 and 30 min. with methyl iodide. The methylated products (Figure 1) obtained in quantitative yield are in a ratio of R = 19:1.

Medium effect - This ratio (14) is not altered by the addition of cation complexing agents such as N,N,N',N'-tetramethylethylene diamine (TMEDA, 10 eq.), dimethoxy ethane (DME, 2 eq.), triglyme (TG, 1 to 5 eq.) or a dissociated common salt ($LiBPh_4$, large excess).

In presence of hexamethylphosphotriamide (HMPT, large excess) the ratio changes to R = 9:1.

On the addition of the macrobicyclic diamino polyether (2,2,2) (1,2 eq.) (15) and quenching with methyl iodide after 60 min., R is found to be 9:1. After 120 min., the ratio decreases to 5:1. However if in this case deuterium oxide is added instead of methyl iodide, the ratio of the deuterated diastereoisomers is 1:1 (14).

When preparing the α lithio derivative in THF/TMEDA, the variation of R after the addition of (2,2,2) is more rapid. R = 19:1 after 10 min. ; R = 9:1 after 20 min. ; R = 7:1 after 45 min. and 4:1 after 60 min.

Temperature effect - The α sulfinyl anion prepared at 0°C cooled to -78°C and quenched with methyl iodide affords the ratio R = 19:1, but when the reaction is quenched at 0°C, the ratio becomes 5:1 (8).

In summary, R is not affected by the addition of a common salt and solvating species such as > TMEDA, DME, TG. The strong solvating agent HMPT decreases R. The change in R in the presence of (2,2,2) is time dependent and its limiting value is low, depending on the nature of the reagent.

Preliminary conductimetric experiments performed at -78°C show that the species present in the solution of BMSO$^-$Li$^+$ where R is not solvent affected eg: THF, THF-TMEDA, THF-DME, THF-TG, are not conductive. In contrast under the same conditions a solution of the carbanion derived from benzyl phenyl thioether (BPT$^-$)is conductive, indicating that the thioether lithio compound is more dissociated than BMSO$^-$Li$^+$. After the addition of (2,2,2) to a BMSO$^-$Li$^+$ the solution becomes conducting and the conductivity increases with time in the same manner as the variation of R and constant conductivity is reached after 30-40 min. For the BPT$^-$Li$^+$ solution the conductivity reaches its limiting value in 3 min. The final conductivity of both carbanions corresponds to a small degree of dissociation to the free ions or multiple ions. These results are interpreted in the following manner: in THF solutions, BMSO$^-$Li$^+$ exists as intimate or solvated ion-pairs and/or aggregates. In the presence of (2,2,2), an equilibrium between cryptate separated ion pairs and a low percentage of free ions may be assumed. The slow variation of R and of the conductivity with time is not due to a slow conformational change of (2,2,2) during the complexation : under these conditions the conductivity of a solution of BPT$^-$Li$^+$ in the presence of (2,2,2) changes rapidly. The slow cryptation of BMSO$^-$Li$^+$ must therefore be due to another factor present in these intimate or solvated ion pairs : this is possibly caused by an intramolecular (or inter-) chelation between the cation and the oxygen of BMSO$^-$ (see Figure 2)*.

The reaction of the intimate or solvated ion pair BMSO$^-$Li$^+$ is stereoselective. This behaviour may be due to a conformational preference for one of the two diastereoisotopic carbanions : $\underline{a} \rightleftarrows \underline{b}$ (see Figure 3) whose reaction with methyl iodide proceeds with inversion at the carbanionic centre and with deuterium oxide proceeds with retention of configuration or a very strong preference from carbanion whose reactions are only partially stereoselective.

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* A chelation between lithium and free electron pairs in the carbanion derived from dithiane has recently been proposed on the basis of their highly stereoselective reactions (16).

In the cryptate separated ion pair and in the free ion the carbanion is either sp^2 hybridised and one has a 1,2 asymmetric induction (18) or is sp^3. In this latter case, the interconversion* of both species should be as rapid as their reaction with methyliodide or deuterium oxide. A competition between the 1,2 asymmetric induction and the gauche effect which would be effective in these species could explain these results.

Such a cation-oxygen chelation in carbanions α to sulfoxides and by extention to sulfones may play an important role in their chemistry. Other of their stereoselective reactions may be caused by this interaction.

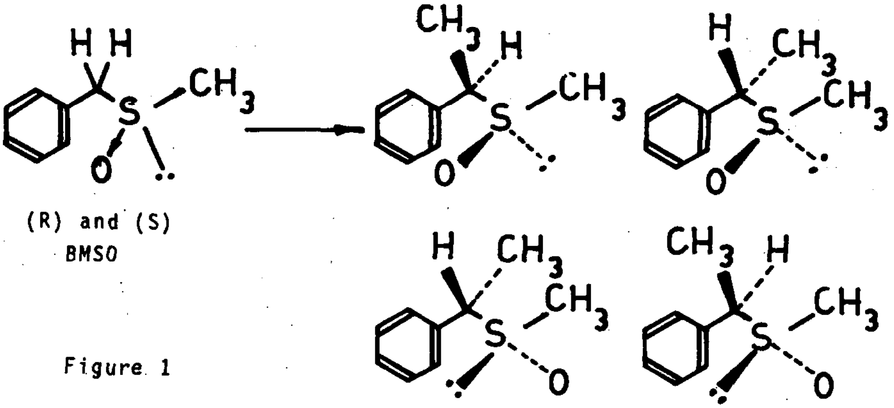

Figure 1

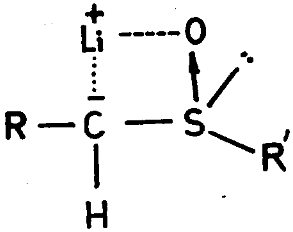

Figure 2

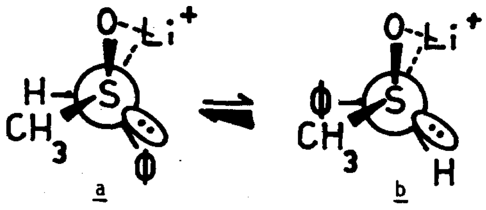

Figure 3

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* The presence of a phenyl group possibly reduces the interconversion barrier of the carbanion.

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