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STEREOCHEMISTRY IN THE CARBONATION OF BENZYL METHYL SULPHOXIDE

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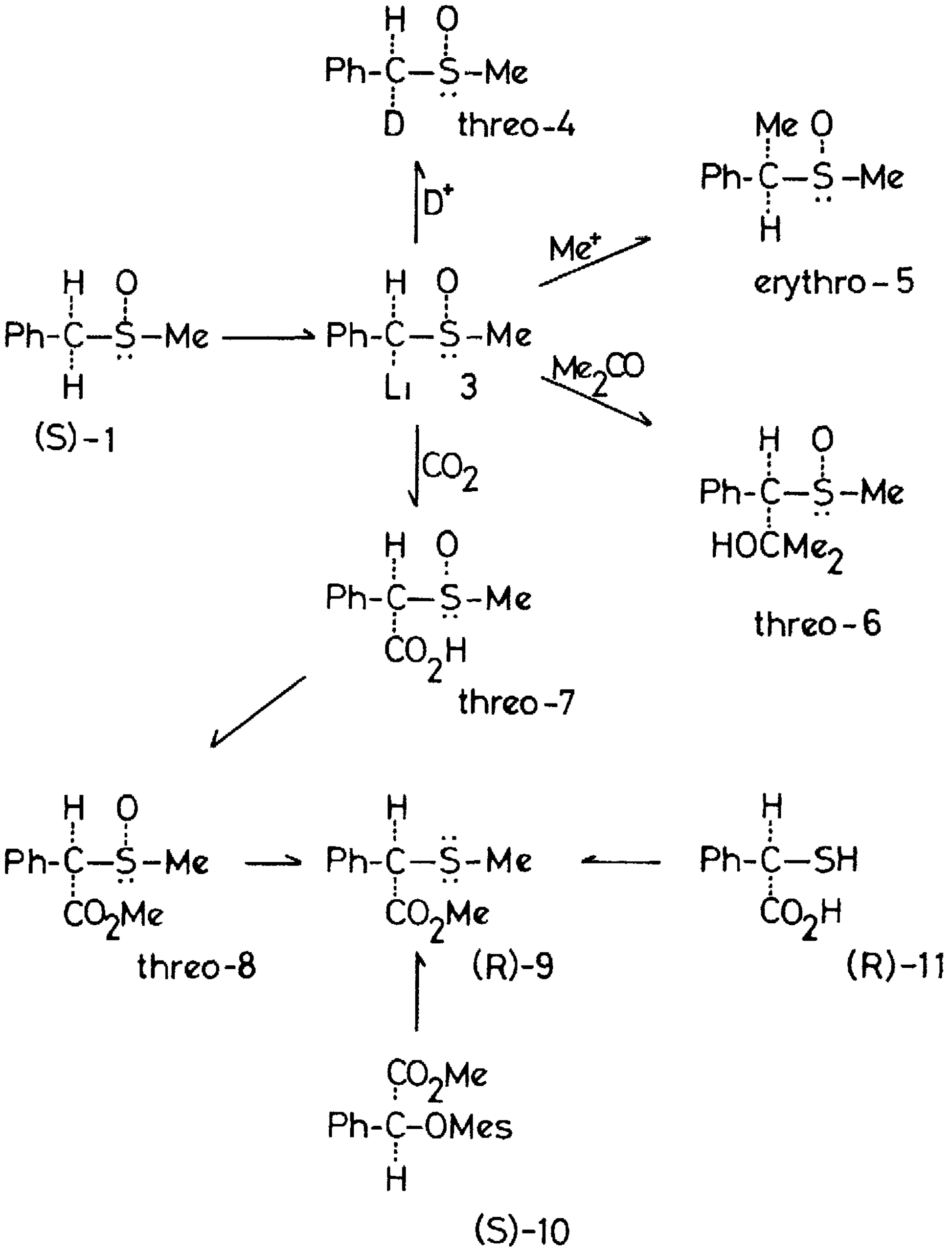
It has been shown that protonation (or deuteriation) and methylation of lithio derivative of benzyl methyl (1) and benzyl t-butyl sulphoxide (2) proceed with inverse stereochemistry[1] In these reactions, although there is still room to debate, it has been suggested that the protonation occurs with retention whereas the methylation proceeds with configurational inversion at carbon[1b-d] Thus quenchings of α-lithiobenzyl methyl sulphoxide (3) with deuterium and methyl cation give predominantly (ca. 19 : 1, in THF at -70°) (CS,SS)-α-deuteriobenzyl methyl sulphoxide (4) and (CR,SS)-1-phenylethyl methyl sulphoxide (5), respectively. Durst reported later that quenching of the lithio derivative of (S)-1 with acetone gives predominantly (15 1) the corresponding β-hydroxyalkyl sulphoxide (6) of (CR,SS)-configuration[2] The stereochemistry of this reaction therefore coincides with that of the protonation reaction.[3] We here report that the configuration at carbon of α-methylsulphinyl phenyl acetic acid (7), produced preferentially by carbonation of (S)-1, is also (R)

A tetrahydofuran solution of (S)-1 (6.2 g, 40 mmol), (α)D +71° (EtOH, 71 % optically pure[4]) was treated with 1.1 equiv. of n-BuLi under nitrogen at -70° and this was quenched with carbon dioxide (dry ice) An oily product[5] which precipitated (4 g) was crystallized on treatment with ether. Recrystallization from chloroform gave pure α-methylsulphinyl phenyl acetic acid (7), 2.4 g, mp 105° (dec)[6], (α)D +182° (acetone). This was methylated


threo-4
D⁺
Me⁺
erythro-5
(S)-1
3
Me₂CO
CO₂
threo-6
threo-7
threo-8
(R)-9
(R)-11
(S)-10

with CH_2N_2 to give methyl α-methylsulphinyl phenyl acetate (8), 84 %, mp 129°, (α)D -130° (acetone).[6] A solution of 8 (0.64 g) in methylene chloride was treated at room temperature with 1.5 g of 0,0-diethyl dithiophosphoric acid[7] for 4 h. Work-up on the reaction mixture and purification by preparative layer chromatography (benzene : n-hexane = 4 : 1) gave oily sulphide, methyl α-methylthio phenyl acetate (9)[6], 0.5 g, 85 %, (α)D -36° ($CHCl_3$).

Optically active (R)-methyl α-methylthio phenyl acetate (9), (α)D -68°, has been obtained by Durst et al. by treating (S)-methyl O-methanesulphonyl mandelate (10) with sodium methyl mercaptide.[2] *The assignment of (-)-9 as (R) was based on a reasonable assumption* that the reaction of the mandelate with thiolate anion occurs with the configurational inversion. To confirm this we prepared (R)-9 from *α-mercapto phenyl acetic acid (11) of established configuration. Thus* (R)-(-)-11, (α)D -96° (EtOH, 95 % optically pure[8]), prepared by an optical resolution via cinconidine salt,[8] was methylated with CH_2N_2 to give (R)-methyl α-methylthio phenyl acetate (9), (α)D -63° ($CHCl_3$).

The above sequence of reactions establishes that the configuration of 7 is (CR,SS) *and therefore* the carbonation of 1 must have proceeded in the same stereochemical sense as the deuteriation or hydroxyalkylation.

Evidence has been accumulated that the isotopic exchange occurs with retention of configuration at the carbanion centre[9]. Therefore it is likely that the protonation (deuteriation), the hydroxyalkylation and the carbonation of 1 proceeded with retention of the carbanion configuration. The methylation, however, must have occurred via a completely different stereochemical pathway since this results in a predominant *formation of the diastereoisomer of different configuration* (erythro). It is not clear why a change in the electrophile causes such an effect on the stereochemical course of the substitution. It may be that the effective crowdedness of the methyl cation and the accompanying anion is an important factor. It is not certain, however, whether this implies an attack of Me$^+$ on the same carbanion conformer with inversion, or the methyl cation prefers a less populated carbanion conformer.

We thank Professor T Taguchi (Kyushu Univ.) for his advice.

REFERENCES AND FOOTNOTES

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3 Threo-erythro notations were used in the Scheme to avoid confusion According to the Sequence Rule, (C*R*,S*S*)-6 and 7 correspond configurationally to (C*S*,S*S*)-3, 4, and 5. A change in the notation (at sulphur configuration) also occurs if Me is replaced by Bu^t or Ph

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5 N m r analysis of the total crude material revealed that the product is almost diastereomerically pure

6 Elemental analyses gave correct results N m.r δ ppm 4.83 (1H, s, CH), 2.37 (3H, s, SOMe), 8 5 - 12 (1H, broad s, COOH) for 7 (DMSO-d_6), 4.67 (1H, s, CH), 3 83 (3H, s, COOMe), 2.10 (3H, s, SOMe), for 8 (CDCl$_3$), 4 51 (1H, s, CH), 3 70 (3H, s, COOMe), 2.05 (3H, s, SMe) for 9 (CDCl$_3$) M s. m/e 196 (M$^+$), 149, 137, 121, 105 for 9.

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