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DETERMINATION OF ABSOLUTE CONFIGURATIONS BY NMR.

STEREOCHEMISTRY OF THE BASE-CATALYZED DECARBOXYLATION OF 2-METHYL-2,3-DIHYDROBENZOTHIOPHENE-2-CARBOXYLIC ACID 1-DIOXIDE

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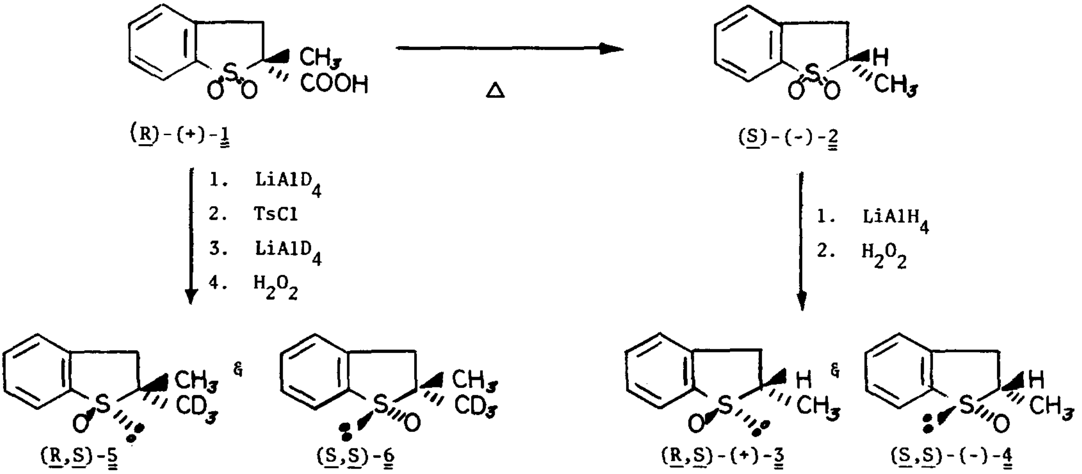
Study of the base-catalyzed decarboxylation of (-)-1 shows that (+)-2 forms in 20-64% optical yield in ethylene glycol, water, and acetic acid while, in DMSO, 100% racemization occurs. However, use of *tert*-butyl alcohol gives (-)-2 in low (*ca*. 3%) optical yield. When optically pure (+)-2-*h* and (-)-2-*d* were subjected to base-catalyzed hydrogen-deuterium exchange and racemization experiments,[1] the stereochemical course of this electrophilic substitution reaction was found to proceed with net inversion in all solvents studied. This suggests that the stereochemistry of the decarboxylation of 1 also proceeds with inversion (except in *tert*-butyl alcohol). Several analogies also exist which tentatively suggest assignment of an inversion mechanism to the decarboxylation of 1[1,2]. However, as neither the absolute nor relative configurations of (-)-1 and (+)-2 were determined, an unequivocal assignment of the stereochemical course of decarboxylation was not possible.

We wish to report the determination of the absolute configurations of (+)-1 and (-)-2 using the chiral nmr solvent method reported in the accompanying paper.[3]



Partially resolved samples of sulfones 1 and 2 have been converted, as shown, to sulfoxides 3, 4, and 5, 6. The reaction sequence does not disturb the configuration at the chiral carbon so each diastereomer is partially resolved. Diastereomers 3 and 4, separable by preparative tlc, have the same configuration at carbon as does 2 but differ in configuration about sulfur. Relative configurations (at carbon and sulfur) are assigned via nmr chemical shifts and R_f values. In benzene, the highest R_f diastereomer (minor) has its methyl resonance at lower field (δ 1.20) than does the major diastereomer (δ 0.85) and its methine resonance at higher field (δ 2.94 *vs.* *ca.* 3.20). Accordingly, it is assigned the *cis* structure 4 on the basis of the known deshielding effect of a proximate sulfinyl oxygen. Examined in (*R*)-(-)-1-phenyl-2,2,2-trifluoroethanol (7), the enantiomers of 4 have nonequivalent 220 MHz nmr spectra. In particular, the chemical shifts of the methyl and one of the methylene protons[4] of the major enantiomer occur at higher field than the corresponding signals of the minor enantiomer[5] (high field sense). This establishes[3] the (*S*) configuration at sulfur and the (*S*) configuration at carbon. Similarly, diastereomer 3 shows a low field sense of nonequivalence[5] for the methyl, methylene, and methine protons, establishing the (*R*) configuration at sulfur and the (*S*) configuration at carbon. These assignments agree with the conclusions reached by Anet *et al.*[6] on the basis of ORD data.

Using the route shown, (+)-enriched sulfone 1 was converted to a 1:1 mixture of sulfoxides 5 and 6, diastereotopic by virtue of deuterium substitution. The diastereomer having the high field methyl resonance (δ 1.31) was assigned structure 6, that having the low field methyl resonance (δ 1.42) was assigned structure 5. In (-) alcohol 7, the enantiomers of sulfoxide 6 show a high field sense of methyl nonequivalence whereas the enantiomers of 5 show a low field sense of nonequivalence.[5] Accordingly, 6 has the (*S*) configuration at sulfur and the (*S*) configuration at carbon whereas 5 has the (*R*)[3] and (*S*) configurations, respectively. Keeping in mind the correct priorities, it is seen that (+)-sulfone 1 has the (*R*) configuration and, on decarboxylation, must invert since (-)-sulfone 2 has the (*S*) configuration.

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4. The overlapping of the resonances of the remaining methylene and methine protons precludes determination of nonequivalence sense.
5. Each of the diastereomeric sulfoxides corresponds in enantiomeric purity to that of its sulfone precursor.
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