Tetrahedron Letters No.13, pp. 793-801, 1965. Pergamon Press Ltd.
Printed in Great Britain.

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THE STEREOCHEMICAL COURSE OF PROTONATION OF α-SULFONYL CARBANIONS

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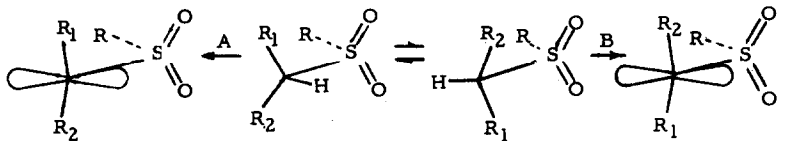
(Received 15 January 1965)

The kinetics of base-catalyzed hydrogen-deuterium exchange and of racemization of sulfones of the type $R-SO_2-CH(R_1)(R_2)$ provided the first indication that α-sulfonyl carbanions can be generated in asymmetric form ($k_{exc.} > k_{rac.}$) (1-3). Asymmetric α-sulfonyl carbanions also result from the anionic decarboxylation of structures of type $R-SO_2-C(R_1)(R_2)(COOH)$ (4-7) and from other processes with carbon as leaving group, e.g. reverse aldol cleavage (6). Evidence has been presented that these carbanions are asymmetric because of restricted rotation about the $C_\alpha-S$ bond and that the hybridization at C_α in the carbanion is either sp^2 or sufficiently close to sp^2 so as not to be the cause of asymmetry (4, 5, 8). This model leads to a geometry for asymmetric α-sulfonyl carbanions which is symbolized by IA or its mirror image IB. The model also necessitates a further condition to satisfy the experimental observation that the asymmetric anions can be formed with high stereospecificity: of the two pathways for deprotonation of an asymmetric sulfone, one of which leads to an

anion of geometry IA and the other to IB (paths A and B, respectively), one must be highly favored (see ref. 4). This note deals with an experimental determination of the mode of proton transfer which

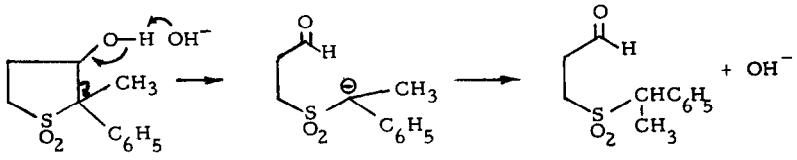


IA IB

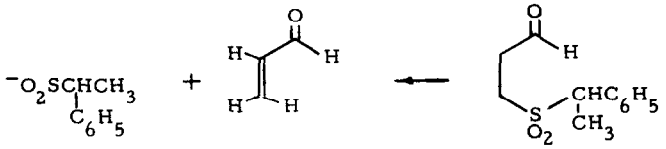
obtains in the generation and neutralization of α-sulfonyl carbanions by proton transfer, i. e. a distinction between paths A and B.

The experimental approach involved the generation of an asymmetric α-sulfonyl carbanion of known absolute configuration and the determination of the absolute configuration of the protonation product of this anion. The unique nature of the asymmetry of a flat α-sulfonyl carbanion such as I implies that the configuration of such an ion can be deduced only if both the configuration of the asymmetric α-carbon and the conformation during carbanion formation are known. Hence, it was necessary to resort to a system so constrained by the presence of a cyclic unit that only one conformation was available for carbanion formation; more specifically the compound II was selected. The synthesis of this substance is described below. As anticipated II underwent rapid base-catalyzed decomposition under mild conditions (1 equivalent of potassium hydroxide in 2:1 ethanol-water at 65-70°) to form potassium 1-phenylethane sulfinate and, presumably, acrolein (and its further transformation products). The sulfinate could be

isolated as the insoluble ferric salt or as benzyl 1-phenylethyl sulfone (using benzyl bromide as reagent), the latter in 54-68% yield. Formation of the 1-phenylethane sulfinic acid anion can be interpreted readily only in terms of the process:



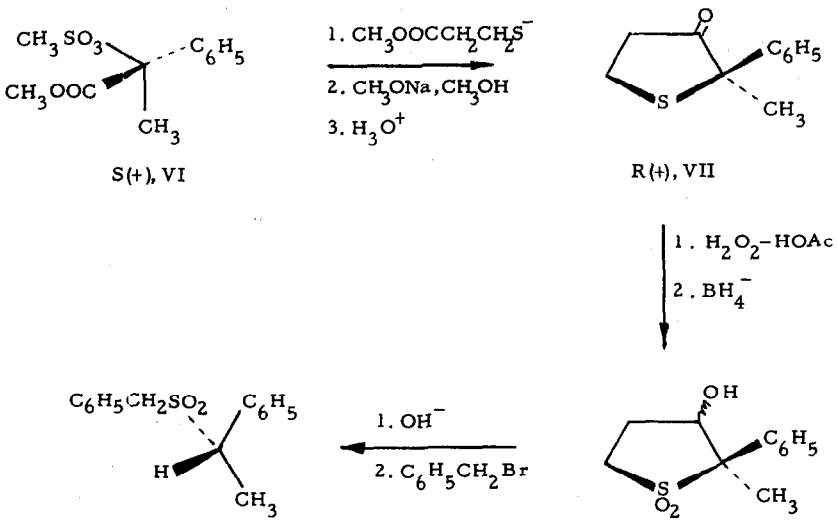
II III IV



V

It is apparent that the intermediate α-sulfonyl carbanion III can be formed initially in only one configuration starting with a given isomer of II and in addition it follows that the mode of protonation of III can be determined from the knowledge of the absolute configuration of the starting material II and the final product V.

Cyclic hydroxy sulfone II was synthesized in optically active form starting with the methanesulfonate of S(+) methylatrolactate (VI) (in turn prepared from S(+) atrolactric acid, see ref. 5) by a sequence involving (1) displacement with the sulfanion of methyl β-mercaptopropionate, (2) Dieckmann cyclization, (3) hydrolysis and decarboxylation to give VII, (4) oxidation to the keto sulfone and (5) reduction to hydroxy sulfone II by sodium borohydride. The hydroxy

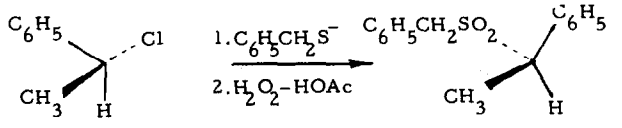


sulfone II was a nicely crystalline substance which was readily recrystallized to constant m. p. 183. 3-184. 3° and rotation, $[\alpha]_D^{25}$ + 56. 8° (c= 2. 9 in acetone), and which appeared to be a single isomer.

Treatment of the R(+) cyclic hydroxy sulfone II (physical constants as indicated above) with one equivalent of base in 2:1 ethanol-water at 65-70° followed by reaction of the product with benzyl bromide afforded S(−) 1-phenylethyl benzyl sulfone, $[\alpha]_D^{25}$ − 57° (VIII). Since this rotation is within experimental error of that for optically pure VIII (see below), the overall reaction must be highly stereospecific (in the range 90-100%). Furthermore, it is apparent

that the protonation of the intermediate asymmetric α-sulfonyl carbanion must have occurred from a direction syn to the oxygens of the sulfonyl group (corresponding to path A above) since in the conversion of R(+) II to S(−) VIII hydrogen has replaced carbon with inversion of configuration.

The absolute configuration of (−) VIII was determined as S by synthesis of the dextrorotatory antipode from S(−) 1-phenylethyl chloride (9, 10) by the sequence:



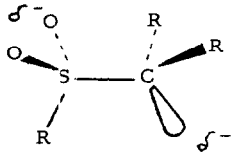
S(−) R(+)

Starting from S(−) chloride of 43.0% optical purity sulfone having $[\alpha]_D^{25}$ + 23° (without recrystallization) was obtained, which leads to $[\alpha]_D^{25}$ approximately + 54° for optically pure R(+) 1-phenylethyl benzyl sulfone.

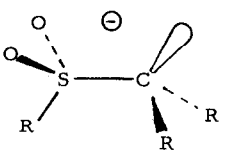
The possibility must be considered that the experiment described above on the protonation of the α-sulfonyl carbanion derived from the cyclic sulfone II is not a valid model for acyclic sulfone systems of type $R-SO_2-CH(R_1)(R_2)$. In particular, it might be argued that the carbon leaving group in II prevents protonation from the direction of its departure (i.e. with retention) because of steric shielding. This objection is untenable because such shielding is insignificant in the decarboxylation of $C_6H_5-SO_2-C(CH_3)(C_6H_5)COOH$ and most probably in the decarboxylation-protonation with $C_6H_5-SO_2-C(CH_3)(C_6H_{13}-\underline{n})COOH$ and in the reverse aldol cleavage-protonation with $C_6H_5-SO_2-C(CH_3)(C_6H_{13}-\underline{n})(CH_3\underset{OH}{C}CH_3)$ (5); these reactions proceed with overall

retention with ~ 97% stereospecificity. It is highly unlikely that steric screening by the leaving carbon group would be completely dominant in the case of II and completely absent in the acyclic compounds.

It is important to note that the above results cannot be reconciled with the proposals (6, 11) that the asymmetry of α-sulfonyl carbanions is due to pyramidal asymmetric α-carbon in which rotation about C_α–S is restricted and which is constrained to hold to the geometry shown in IX because of "electrostatic inhibition of inversion." This



IX

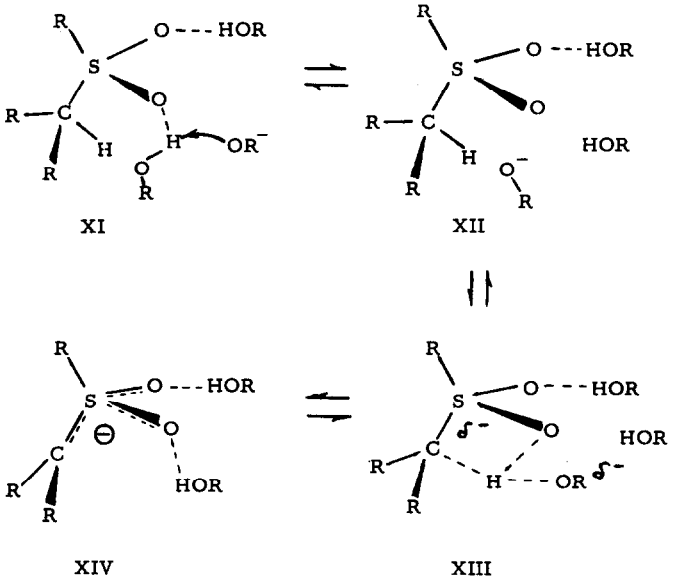


X

hypothesis clearly predicts that the replacement of carbon by hydrogen in the conversion of II to VIII should proceed with retention of configuration. If one wishes to consider the possibility of pyramidal α-sulfonyl carbanions which do not change configuration by inversion, one is now forced to specify a fixed conformation X which is not free to rotate about the C_α–S bond further it must be supposed that the conversion of conformation IX (corresponding to the anion from II) to conformation X is fast and exergonic and that this change proceeds by inversion through a planar carbanion rather than by rotation about C_α–S. Thus, restriction of C_α–S rotation rather than of pyramid inversion can be seen to be the significant factor in maintaining asymmetry of α-sulfonyl carbanions on the basis of the new data as well as from previous results (12).

The reasons for preferential formation of α-sulfonyl carbanions

and their protonation by path A, in which the hydrogen enters or is removed syn to the sulfonyl oxygens about the C_α–S bond, are still unknown. An important factor in producing this effect may be hydrogen bonding between hydroxylic solvent protons and the sulfonyl oxygens, expected to be important both for sulfones and the corresponding conjugate bases. Proton migration from these hydrogen bonds to externally located base would leave behind an RO^- species which is advantageously positioned for attack on the proton at C_α of the sulfone when that proton is syn to the SO_2 oxygens, but not anti. One model for such a process is indicated by the formulae XI-XIV (in which two hydrogen bonded solvent molecules are shown arbitrarily). Clearly this allows for syn-anion formation and proton exchange without racemization.



Obviously the C_α–S rotational barrier does not have to be very large to account for the stereospecific effects now known for anionic reactions of sulfones since protonation of reactive carbanions from hydroxylic media is itself extremely rapid (a rough estimate of 4 kcal./mole has been made for $\Delta F^{\ddagger}$ (6)). There are several arguments which can be devised to explain the existence of a C_α–S rotational barrier in α-sulfonyl carbanions and the relative stability of rotomers IA or IB (see ref. 4, p. 518 and ref. 8). One complication which must be kept in mind is that solvation of the sulfonyl carbanion may have an effect on the relative stability of the C_α–S rotomers. For example, if the hydrogen bonding between solvent and the carbanion oxygens is preferentially oriented either perpendicular to or parallel to the SO_2 plane, a rotational barrier is to be expected in principle on the basis of molecular orbital theory (see ref. 8).

We are indebted to the National Science Foundation and Harvard University for Graduate Fellowships to T. H. L.

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