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THE STEREOCHEMICAL COURSE OF ANIONIC DECARBOXYLATION OF α-SULFONYL CARBOXYLIC ACIDS

E. J. Corey and Thomas H. Lowry
Department of Chemistry, Harvard University, Cambridge, Mass. 02138

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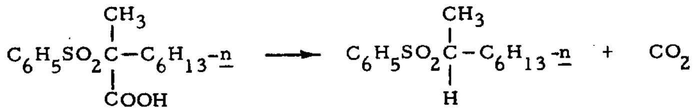
α-Sulfonyl carbanions of structure $R-SO_2-\bar{C}(R_1)(R_2)$ can be generated from optically active precursors $R-SO_2-C(R_1)(R_2)(Y)$ in hydroxylic media and protonated to give optically active products, $R-SO_2-CH(R_1)(R_2)$, with high stereospecificity. This remarkable phenomenon has been observed, for example, in the anionic decarboxylation of optically active I to form II of 97 ± 3% optical purity (1-3).



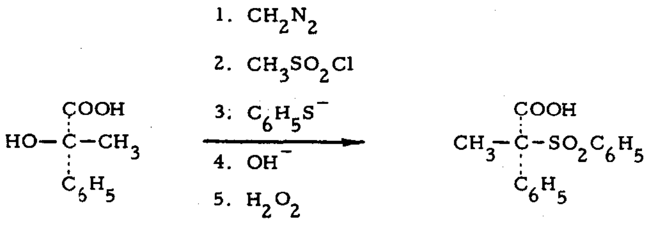
$$C_6H_5SO_2\underset{\underset{COOH}{|}}{\overset{\overset{CH_3}{|}}{C}}-C_6H_{13}\text{-}\underline{n} \longrightarrow C_6H_5SO_2\underset{\underset{H}{|}}{\overset{\overset{CH_3}{|}}{C}}-C_6H_{13}\text{-}\underline{n} + CO_2$$

I II

This note presents direct stereochemical evidence that the stereospecific replacement of carboxyl by hydrogen occurs with retention of configuration.

The particular substrate for these studies was R(−) 2-benzenesulfonyl-2-phenylpropionic acid $[\alpha]_D^{30}$ −36.8° (c= 1.5 in methanol), IV.

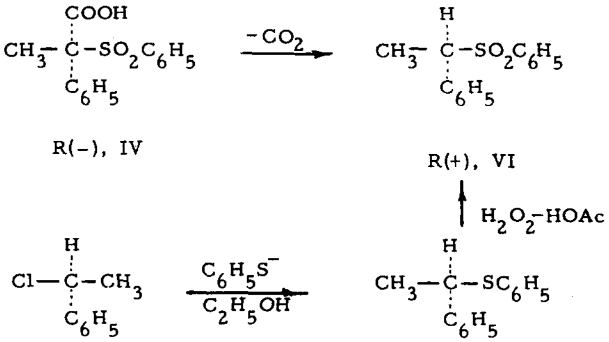
This antipode was synthesized from optically active S(+) atrolactic acid (4) $[\alpha]_D^{22}$ + 48.4° (c= 1.4 in water) (III)as indicated below; the



S(+), III R(–), IV

absolute configuration follows from the known absolute configuration of the starting acid III and the method of synthesis. The displacement of methanesulfonate by thiophenoxide was carried out using a concentrated solution of the nucleophile in methanol, conditions which have been shown in numerous instances to lead to S_N2 reaction, and it is assumed that inversion occurs at this stage and at no other. The key step in the synthesis of IV, the conversion of methyl atrolactate to the methanesulfonate derivative, was carried out by the slow addition of anhydrous pyridine (3.5 equivalents) to a cold (-20°) mixture of the hydroxy ester (1 equivalent) and methanesulfonyl chloride (3.5 equivalents) and then allowing the reaction to proceed at 0° for 62 hr. The methanesulfonate was obtained as an oil by careful work-up and was used without purification (yield 60-70%).

The decarboxylation of the acid IV was carried out using 0.01 equivalent of sodium hydroxide in 4:3 dioxane-water and was conducted only to 65% of completion so that excess acid was present to preclude hydroxide-ion catalyzed racemization of the decarboxylated sulfone. This reaction required about 80 min. at 65°; in contrast the acid I was recovered quantitatively after similar treatment for 150 hr., indicating marked acceleration by phenyl. The neutral product was R(+) 1-phenylethyl phenyl sulfone, $[\alpha]_D^{30}$ +94.0° (c= 1.5 in methanol). The absolute configuration of dextrorotatory 1-phenylethyl phenyl sulfone was demonstrated as R (expressed by VI) by synthesis from S(−) 1-phenylethyl chloride V using a displacement reaction with thiophenoxide in ethanol and subsequent oxidation of sulfide to sulfone by hydrogen peroxide. Thus it is demonstrated that the replacement of carboxyl



R(−), IV

R(+), VI

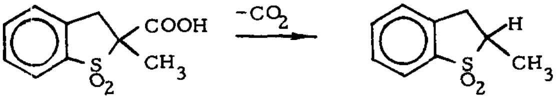
S(−), V

in IV by hydrogen through anionic decarboxylation must proceed with retention of configuration. Further, the decarboxylation is highly stereospecific. Using 1-phenylethyl chloride α_D -52.9° (neat, 10 cm.) which was 42.3% optically pure (for optically pure chloride, $\alpha_D = \pm$ 125°

(6)) the sulfone VI obtained by displacement and oxidation had $[\alpha]_D$ + 39.8° (c= 2.6 in methanol) which gives $[\alpha]_D$ + 94° for optically pure sulfone VI assuming stereospecific inversion in the displacement step. Therefore, the sulfone VI obtained by decarboxylation of levorotatory IV appears to be optically pure within experimental error.

This is the first experimental demonstration of the stereochemical course of the anionic decarboxylation of an α-sulfonyl carboxylic acid of type $R-SO_2-C(R_1)(R_2)(COOH)$ (7). The high degree of stereospecificity which has been observed in the decarboxylation of acids I and IV and other data which demonstrate quite similar behavior of the intermediate α-sulfonyl carbanions lead to the view that retention of configuration should also be the course of the reaction I $\longrightarrow$ II. In addition there seems to be no clear reason why the same stereochemical pathway should not be general for the series $R-SO_2-C(R_1)(R_2)(COOH)$ as R, R_1 and R_2 are varied.

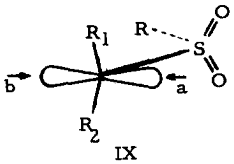
At this point it is important to recall the contrasting case of the decarboxylation of optically active VII to give racemic VIII (again under conditions such that the free acid VII was always present in addition to the carboxylate ion so that subsequent racemization of the primary product VIII was avoided) (1,8). In this instance rotation about the C_α-S bond is prevented by the ring system and further the intermediate carbanion must be optically inactive if the carbanion is



VII, optically active VIII, racemic

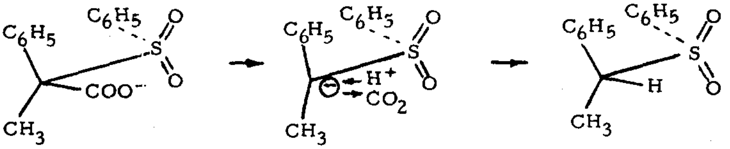
flat or rapidly inverting (plane of symmetry). As pointed out previously this result is inconsistent with the view that α-sulfonyl carbanions are asymmetric because the α-carbon is pyramidal with a barrier to inversion but not to C_α–S rotation; it is in accord with predictions for a flat or a rapidly inverting and "effectively" planar carbanion.

Several other lines of evidence indicate that the essential factor for maintenance of configuration of α-sulfonyl carbanions is the barrier to rotation and not a barrier to inversion (1, 9). Of special relevance here are the kinetic data for base-catalyzed racemization and α-hydrogen-deuterium exchange in deuterated medium for the sulfones II and VI. At 72.0° in 2:1 ethanol-water the ratio $k_{exc.}/k_{rac.}$ for II is 41 and that for VI is 44; however, $k_{exc.}$ for VI exceeds that for II by almost 10^4 (10). Thus it is clear that replacement of n-hexyl by phenyl at C_α gives rise to powerful additional stabilization of the carbanion, but it does not facilitate racemization of the carbanion once formed. If the racemization process involved inversion of a pyramidal carbanion, the rate of racemization of the carbanion should be greatly increased by substituents such as phenyl which stabilize the planar form by π-conjugation. Earlier (1) we have reported that $k_{exc.}/k_{rac.}$ for the sulfone $C_6H_5-SO_2-CH(CH_3)(t\text{-}Bu)$ at 72° in 2:1 ethanol-water is 58, which together with the figure for II also indicates a planar carbanion structure, and a species (IX) having molecular asymmetry with restricted rotation about C_α–S (and essentially planar C_α) has been advanced (11).



IX

In the accompanying note it is shown that the asymmetric α-sulfonyl carbanions are protonated stereospecifically as shown by path a in IX rather than by path b (9); i.e. the attachment of a proton at C_α occurs syn to the two sulfonyl oxygens rather than anti relative to the C_α-S bond. This finding allows the further conclusion that the departure of carbon dioxide from the carboxylate anion of IV must also occur syn to the oxygens of the sulfonyl group and leads to a stereochemical course for the conversion of IV to VI as follows:



Cram and Wingrove (2) have shown that base-catalyzed reverse-aldol cleavage and anionic decarboxylation proceed to give asymmetric α-sulfonyl carbanions by the same stereochemical pathway. The above representation, therefore, can be extended to other carbon leaving groups, departure being syn to the sulfonyl oxygens.

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References

1. E. J. Corey, H. König and T. H. Lowry, Tetrahedron Letters, No. 12, 515 (1962); this example of stereospecific anionic decarboxylation was initially described by us at the I. U. P. A. C. Symposium on Dynamic Stereochemistry, Montreal, Aug. 1961.

2. The stereospecific decarboxylation of I to form II has also been

reported by D. J. Cram and A. S. Wingrove, *J. Am. Chem. Soc.*, **85**, 1100 (1963); *ibid.*, **84**, 1496 (1962).

3. The first report of optical activity in the product from anionic decarboxylation of an optically active α-sulfonyl carboxylic acid was made by J. E. Taylor and F. H. Verhoek, *ibid.*, **81**, 4537 (1959). The degree of stereoselectivity was not determined for this case, however.

4. For absolute configuration see D. J. Cram, K. R. Kopecky, F. Hauck, and A. Langemann, *ibid.*, **81**, 5754 (1959).

5. For absolute configuration see E. D. Hughes, C. K. Ingold and A. D. Scott, *J. Chem. Soc.*, 1201 (1937).

6. H. M. R. Hoffmann and E. D. Hughes, *ibid.*, 1244 (1964).

7. It has been assumed by Cram and Wingrove (ref. 2) that anionic decarboxylation in such systems proceeds with retention of configuration. The basis for their assumption is not clear; in principle either inversion or retention is possible for reaction proceeding via an α-sulfonyl carbanion which maintains asymmetry because of restricted rotation about the C_α–S bond (see ref. 1).

8. The mechanism for base-catalyzed racemization of VIII suggested by C. Y. Meyers, Meeting of the American Chemical Society, April, 1963, Abstracts p. 4M., as an explanation for the formation of racemic VIII in the decarboxylation is untenable because of the acidic reaction conditions used.

9. See E. J. Corey and T. H. Lowry, accompanying paper.

10. T. H. Lowry, Ph.D. Thesis, Harvard University, October, 1964.

11. See also E. J. Corey and E. T. Kaiser, *J. Am. Chem. Soc.*, **83**, 490 (1961).