Nucleophilic Substitution at Sulphur with Retention of Configuration

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Summary The conversion methionine sulphoxide → methionine sulphimine seems to proceed predominantly with *retention* of configuration, contrary to observations made under similar conditions in other sulphoxide series.

THE stereochemical course of the conversion sulphoxide → sulphimine has attracted much recent interest.[1-5] Cram *et al.*[1,2] concluded that the reaction, in the case of methyl *p*-tolyl sulphoxide, proceeded with inversion; a similar stereochemical course was noted for cyclic sulphoxides by others.[3-5] The oxidation of sulphimines to sulphoximines is generally believed to proceed with retention.[2,3,5]

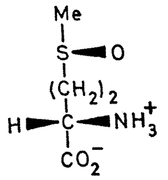
We report on a similar sequence of reactions, starting from 2(*S*),S(*S*)-methionine sulphoxide[6] (I) which, on treatment with *N*-ethoxycarbonylphthalimide,[7] afforded the *N*-phthaloyl-derivative† m.p. 215—217° (dec.); $[\alpha]_D^{24}$ + 13° (*c* 0·35, EtOH).

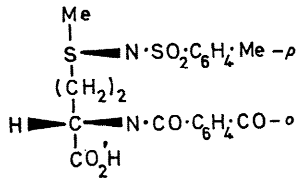
On reaction of the latter with *N*-sulphinyl-*p*-toluenesulphonamide in pyridine,[8] the sulphimine (II) was obtained.‡ This, in turn, was oxidized with potassium permanganate in pyridine to the sulphoximine (III)‡ which was subjected to hydrazinolysis to give (IV).‡

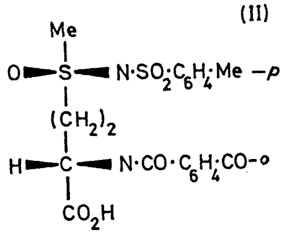
Finally, treatment of (IV) with concentrated sulphuric acid gave the free sulphoximine. Quantitative amino-acid analysis,[9] as well as comparison of the i.r. spectrum (KBr disc) with those of authentic specimens of the *S*-diastereomers,[10] demonstrated its identity as a *ca.* 85:15 mixture of 2(*S*),S(*R*)- (V) and 2(*S*),S(*S*)-methionine sulphoximine.

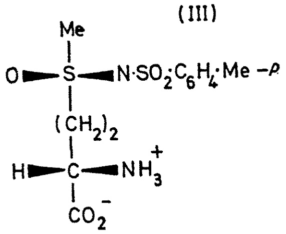
The observed predominant formation of (V) logically requires that the conversions sulphoxide → sulphimine and sulphimine → sulphoximine, *both* proceed predominantly with inversion, or, alternatively, retention. Since oxidation most probably takes place with retention,[2,3,5] we conclude that methionine sulphoxide is converted into the corresponding sulphimine predominantly *with retention* of configuration. To our knowledge this stereochemical course of nucleophilic substitution at sulphur has no documented precedent.[11]

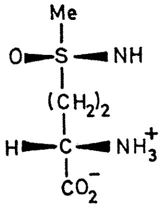
The observed reactions can be rationalized in terms of the topology of the bipyramidal transition state or intermediate most probably involved.[12]


(I)


(II)


(III)


(IV)


(V)

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† Combustion analyses were within 0·2% of theory.

‡ Non-analysed specimen; the product, including possible stereoisomers, was isolated quantitatively by chromatography on silica gel columns.

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[5] C. R. Johnson and J. J. Rigau, *J. Org. Chem.*, 1968, **33**, 4340.
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[7] G. H. L. Nefkens, G. I. Tesser, and R. J. F. Nivard, *Rec. Trav. chim.*, 1960, **79**, 688.
[8] G. Schultz and G. Kresze, *Angew. Chem.*, 1963, **75**, 1022.
[9] A procedure similar to that described by J. M. Manning, S. Moore, W. B. Rowe, and A. Meister, *Biochemistry*, 1969, **8**, 268, was employed.
[10] B. W. Christensen, A. Kjær, S. Neidle, and D. Rogers, *Chem. Comm.*, 1969, 169.
[11] After the present communication was submitted our attention was drawn to a similar course of reaction: S. Oae, M. Yokoyama, M. Kise, and N. Furukawa, *Tetrahedron Letters*, 1968, 4131.
[12] For a recent discussion, see B. M. Trost, R. LaRochelle, and R. C. Atkins, *J. Amer. Chem. Soc.*, 1969, **91**, 2175, and references cited therein.