The Absolute Configuration of Methionine Sulphoxide

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METHIONINE SULPHOXIDE is of widespread natural occurrence and considerable biochemical interest. We now report the absolute configurations of the four stereoisomeric forms of this amino-acid.

Upon oxidation of L-methionine with hydrogen peroxide nearly equal amounts of the diastereoisomeric sulphoxides, (I) and (II), are produced.[1] The dextrorotatory isomer, $[\alpha]_D^{24} + 131°$ (c 1·8; 1N-HCl), liberated from the less soluble picrate,[1] was subjected to decarboxylation by heating in acetophenone[2] (nitrogen atmosphere, 150°, 70 min.) to give the dextrorotatory 3-methylsulphinylpropylamine, m.p. 27°, $[\alpha]_D^{22} + 122°$ (c 0·8; 96% EtOH), the lævorotatory enantiomer of which has previously been described.[3] In a recent communication[4] the (*R*)-configuration (III) was deduced for the latter. Hence, the dextrorotatory sulphoxide, derived from L-methionine, possesses the (*S*)-configuration around the asymmetric sulphur atom and is represented by (I). The diastereoisomeric, lævorotatory sulphoxide[1] [with (*R*)-configuration at the sulphur atom]

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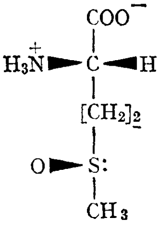
[1] T. F. Lavine, *J. Biol. Chem.*, 1947, **169**, 477.

[2] G. Chatelus, *Compt. rend.*, 1959, **248**, 690.

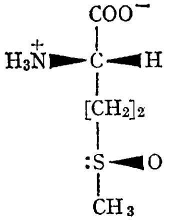
[3] P. Karrer, E. Scheitlin, and H. Siegrist, *Helv. Chim. Acta*, 1950, **33**, 1237.

[4] K. K. Cheung, A. Kjær, and G. A. Sim, *Chem. Comm.*, 1965, 100.

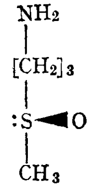
consequently has the structure (II). The enantiomers of (I) and (II), derived from D-methionine, constitute the remaining two of the four possible stereoisomeric methionine sulphoxides. The established absolute configurations support the conclusions reached on basis of o.r.d. measurements.[5]



(I)

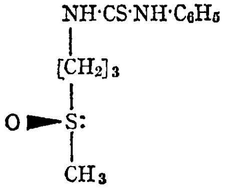


(II)



(−)

(III)



(+)

(IV)

In order to substantiate further the correlations within this series the dextrorotatory 3-methylsulphinylpropylamine was converted into the dextrorotatory 1-(3-methylsulphinylpropyl)-3-phenylthiourea (IV), m.p. 136°, $[\alpha]_D^{22} + 54°$ (c 2·4; 96% EtOH), on reaction with phenyl isothiocyanate. The enantiomeric relationship of (IV) and the lævorotatory phenylthiourea, produced from synthetic[3] or naturally derived[4,6] (−)(*R*)-3-methylsulphinylpropyl isothiocyanate (iberin) and aniline, was confirmed by formation of the corresponding racemic modification, m.p. 122°, on admixture of equal amounts of the two enantiomers. The racemate proved identical with a previously recorded authentic sample of the racemic phenylthiourea, m.p. 122°.[3]

Reconsideration of several biological properties of methionine sulphoxide in the light of the established absolute configuration may now be possible.

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[5] W. Gaffield, F. F. Wong, and J. F. Carson, *J. Org. Chem.*, 1965, **30**, 951.

[6] A. Kjær and R. Gmelin, *Acta Chem. Scand.*, 1956, **10**, 1100.