The Absolute Configuration of Sulphoxide Mustard Oils

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WE now report the absolute configuration of the asymmetric sulphur atoms in the laevorotatory ω-methylsulphinylalkyl isothiocyanates (I; n = 3–6, 8–10) as well as in (−)-sulphoraphene(II), all derived from glucosidic progenitors in cruciferous plants.[1,2]

Iberin (I; n = 3), produced by enzymic hydrolysis of glucoiberin from seeds of *Iberis amara* L.,[3] was converted, upon reaction with (+)-(R)-1-phenylethylamine in chloroform solution, into a

$$CH_3{\cdot}SO{\cdot}[CH_2]_n{\cdot}NCS$$

(I)

$$CH_3{\cdot}SO{\cdot}CH{=}CH{\cdot}[CH_2]_2{\cdot}NCS$$

(II)

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[1] A. Kjær, *Fortsch. Chem. Org. Naturstoffe*, 1960, **18**, 122.

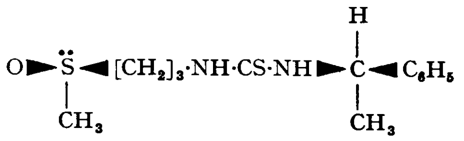
[2] B. W. Christensen and A. Kjær, *Acta Chem. Scand.*, 1963, **17**, 846.

[3] O.-E. Schultz and R. Gmelin, *Arch. Pharm.*, 1954, **287/59**, 404.

crystalline thiourea, $C_{13}H_{20}ON_2S_2$, m.p. 148° (from EtOAc), $[\alpha]_D^{21}$ − 56° (*c* 1·2; MeOH), which was subjected to a three-dimensional *X*-ray analysis.

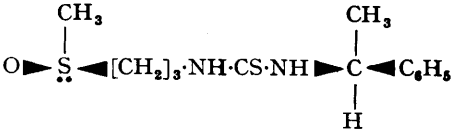
The disubstituted thiourea crystallizes in the orthorhombic system, space group $P2_12_12_1$, with four molecules in a unit cell of dimensions $a = 16{\cdot}48$, $b = 11{\cdot}02$, $c = 8{\cdot}54$ Å. Three-dimensional *X*-ray intensity data were recorded on equi-inclination Weissenberg photographs and estimated visually; in all, we evaluated 1524 independent structure amplitudes. The atoms other than hydrogen were located by calculating three-dimensional Patterson and Fourier syntheses. Subsequent refinement of the atomic co-ordinates by the least-squares method has reduced the *R* factor to 11·8%. No allowance has yet been made for the hydrogen atoms.

The results of the crystal-structure determination define the stereochemistry of the substituted thiourea to be either (III) or (IV); since the asymmetric carbon atom is known to possess the (*R*)-configuration, as indicated in (III), it follows that (III), with the (*R*)-configuration around the sulphoxide grouping, represents the correct absolute stereochemistry of the molecule.



$$\mathrm{O}\blacktriangleright\underset{\mathrm{CH_3}}{\overset{\bullet\bullet}{\mathrm{S}}}\blacktriangleleft[\mathrm{CH_2}]_3\cdot\mathrm{NH\cdot CS\cdot NH}\blacktriangleright\underset{\mathrm{CH_3}}{\overset{\mathrm{H}}{\mathrm{C}}}\blacktriangleleft\mathrm{C_6H_5}$$

(III)



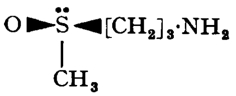
$$\mathrm{O}\blacktriangleright\underset{\bullet\bullet}{\overset{\mathrm{CH_3}}{\mathrm{S}}}\blacktriangleleft[\mathrm{CH_2}]_3\cdot\mathrm{NH\cdot CS\cdot NH}\blacktriangleright\underset{\mathrm{H}}{\overset{\mathrm{CH_3}}{\mathrm{C}}}\blacktriangleleft\mathrm{C_6H_5}$$

(IV)

The atomic co-ordinates suggest that the alkyl chain in (III) is not fully saturated but contains a carbon-carbon double bond (1·29 Å) immediately adjacent to the thiourea residue. However, the central atom of the three-carbon alkyl chain occurred in the electron-density distributions markedly elongated perpendicular to the chain direction and, correspondingly, the least-squares refinement assigned a very anisotropic temperature factor to the atom. It is clear that there is some disorder associated with the position of this atom. It is likely that the disorder is purely a packing effect of a fully saturated alkyl chain, for a mass-spectrometric examination of the compound revealed no significant peak at $m/e = 282$ and the analytical results are in accord with a saturated chain [Found: C 54·85, 54·8; H 7·1, 7·2; N 9·6, 9·75. Calculated for $C_{13}H_{20}ON_2S_2$: C 54·9; H 7·1; N 9·85. For $C_{13}H_{18}ON_2S_2$: C 55·3; H 6·4; N 9·9%]. The anomalous bond length is caused by the assignment of the carbon atom to the centre of the ellipsoidal electron-density peak rather than to a number of alternative sites throughout the peak.

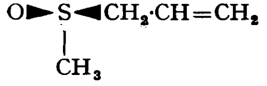
This disorder in the crystal structure does not, of course, affect our conclusion concerning the stereochemistry of the sulphoxide group.

On the basis of optical rotatory dispersion studies,[4] the (*R*)-configuration can now be assigned to all naturally derived sulphoxide mustard oils (I, *n* = 3—6, 8—10; II), as well as to the glucosides whence they are derived.[1] Similar conclusions have recently been reached by o.r.d. comparisons with configurationally known sulphoxides.[5,6] (−)-Iberin has previously been synthesized from (−)-3-methylsulphinylpropylamine[7] and the latter transformed into (−)-allyl methyl sulphoxide.[8] Consequently, these sulphoxides are of the (*R*)-series, and possess the structures (V) and (VI).



$$\mathrm{O}\blacktriangleright\underset{\mathrm{CH_3}}{\overset{\bullet\bullet}{\mathrm{S}}}\blacktriangleleft[\mathrm{CH_2}]_3\cdot\mathrm{NH_2}$$

(V)



$$\mathrm{O}\blacktriangleright\underset{\mathrm{CH_3}}{\overset{\bullet\bullet}{\mathrm{S}}}\blacktriangleleft\mathrm{CH_2\cdot CH{=}CH_2}$$

(VI)

It is noteworthy that (+)-S-methyl-L-cysteine sulphoxide, isolated from related crucifers, belongs to the opposite stereochemical series.[9]

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[4] W. Klyne, J. Day, and A. Kjær, *Acta Chem. Scand.*, 1960, **14**, 215.

[5] K. K. Andersen, *J. Org. Chem.*, 1964, **29**, 1953.

[6] K. Mislow, M. M. Green, P. Laur, and D. R. Chisholm, *J. Amer. Chem. Soc.*, 1965, **87**, 665.

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

[8] P. Karrer, N. J. Antia, and R. Schwyzer, *Helv. Chim. Acta*, 1951, **34**, 1392.

[9] R. Hine and D. Rogers, *Chem. and Ind.*, 1956, 1428.

The acquired knowledge of the absolute configuration of simple sulphoxides affords possibilities for further chemical correlations which are presently being explored.

The calculations were performed on the DEUCE computer at Glasgow University and the IBM 7094 computer at the University of Illinois.

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