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The determination of absolute configuration by the use of an internal reference asymmetric centre.

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Bijvoet, Peerdeman & van Bommel (1951*a*) have shown how X-ray analysis can determine absolute configuration by using the anomalous scattering of X-rays near an absorption edge. In particular, the absolute configurations of D(+)-tartaric acid (Bijvoet, Peerdeman & van Bommel, 1951*b*; van Bommel, 1953) and of D(−)-*iso*leucine (Trommel & Bijvoet, 1954) have been determined. Hence, all compounds which can be related chemically to tartaric acid or *iso*leucine are determined with respect to their optical behaviour.

For moderately complex organic compounds (20–50 atoms excluding hydrogen) of unknown or only partially known structure (Mathieson, 1955), it may not always be practicable to satisfy the experimental conditions required in respect of X-radiation (Bijvoet *et al.*, 1951*a*) or intensity measurement (Peterson, 1955). With such large molecules, a more direct method of determining the absolute configuration would be to introduce an additional but *known*† asymmetric centre in the form of a derivative. Then X-ray analysis of this diastereoisomer, e.g. $(-)X.\mathrm{L}(-)A^*$, where X is the compound of unknown configuration and A^* is the compound or radical of known configuration, would permit definition of the absolute configurations of the asymmetric centres in the large molecule, X, by reference to the known asymmetric group A^*.

As an indication of the very small amount of additional crystallographic effort involved in the application of this method, we may illustrate by reference to earlier analyses of moderately complex molecules. In the determination of the structure of lanostenol, $C_{30}H_{52}O$ (Fridrichsons & Mathieson, 1953), the iodoacetate derivative was used to provide the 'heavy atom'. As a result, only the *relative* configurations of the asymmetric centres in lanostenol could be deduced from this analysis. If, instead, one lanostenyl iodochloroacetate diastereoisomer,

$$\text{e.g. } (+) \text{ or } (-)\ \mathrm{ICl}\overset{*}{\mathrm{C}}\mathrm{HCOOC_{30}H_{51}},$$

had been analysed, the absolute configuration would have been achieved with only one more atom involved in all calculations. Also, in the X-ray analysis of *iso*cryptopleurine methiodide (Fridrichsons & Mathieson, 1954, 1955) the replacement of the methyl group attached to the nitrogen atom by an asymmetric radical,

$$\text{e.g. D or L } \mathrm{C_2H_5(CH_3)\overset{*}{C}H},$$

would have yielded the absolute configurations of the other asymmetric centres.

This method of introducing a known asymmetric centre as an internal reference has several practical advantages: (1) it does not require special radiations; (2) it has wide application since the reference asymmetric centre can be introduced in the most convenient form either as part of a simple derivative or where possible as solvent of crystallization; (3) only one crystal and one set of crystal data are needed; and (4) the additional computation involved is small.

The proposed method therefore provides an elegant technique whereby not only the structure but also the absolute configuration of a compound of unknown structure can be attained in one step. It is hoped to test this method in the near future.

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† Defined by reference to tartaric acid or *iso*leucine.

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