The Configuration of Glaucarubin

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THE relative configuration depicted in (I) can be assigned to the p-bromobenzoate of glaucarubin on the basis of X-ray analysis.[1,2] The close structural relationship between glaucarubin and simarolide (II),[3,4] both bitter principles from the *Simarubaceae*, suggests a common absolute configuration. The absolute configuration of simarolide has been determined as that shown in (II) by the anomalous-dispersion X-ray method,[3] and its relationship to that of triterpenes of the euphol type has been pointed out.[3–5] Although the anomalous dispersion method has not been applied to glaucarubin, circular-dichroism measurements[2] indicate that its carbocyclic nucleus has, in fact, the same absolute configuration as that of simarolide.

Now, the relative configuration shown in (I) implies a particular absolute configuration, since hydrolysis of glaucarubin gives (+)-2-hydroxy-2-methylbutyric acid,[6] which has been assigned the (S)-configuration (III).[7] However, the formation of (III) from glaucarubin requires that the latter have the opposite absolute configuration to that shown in (I), if this formulation correctly represents the relative configuration.

In order to exclude the possibility that this discrepancy arises from a mistaken assignment of the configuration of (+)-2-hydroxy-2-methylbutyric acid, we have redetermined this by the Prelog method,[8] a method different from that used

earlier.[7] Reaction of (−)-menthyl pyruvate with ethylmagnesium bromide followed by hydrolysis gave 2-hydroxy-2-methylbutyric acid with $[a]_D = +2\cdot2°$ corresponding to a 24% excess of the (+)-acid, and fully corroborating the earlier assignment. The only remaining recourse is revision of the previously assigned relative configuration of the side chain asymmetric carbon atom C(21) in (I).* The resulting expression, (IV), would then depict both the relative and absolute configuration of the compound.

This could be achieved by interchanging any two of the three groups attached to C(21): methyl, ethyl, or hydroxyl. The temperature factors of the atoms in the $CH_3\cdot CH_2 C(OH)CH_3$ moiety are all high ($B > 10$ Å^2) giving rise to large uncertainties in atomic locations and electron density. However, it seems unlikely that the ethyl group has been wrongly located; there are no conflicts with other molecules such as might occur with a wrongly located terminal methyl group.

More doubt exists, however, concerning the methyl and hydroxyl groups C(24) and O(11) for which there is some evidence that their positions should be interchanged. The evidence comes from examination of the location of the neighbouring atoms on adjacent molecules. One would expect the hydroxyl O(11), (0·2483, 0·8500, −0·0417), to be hydrogen-bonded (if this is at all possible) and

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* We have adhered to the arbitrary numbering scheme of Kartha and Haas. (Reference 1).

[1] G. Kartha and D. J. Haas, *J. Amer. Chem. Soc.*, 1964, **86**, 3630.

[2] The structure of glaucarubin has been deduced independently on chemical grounds: J. Polonsky, C. Fouquey, A. Gaudemer, Z. Baskevitch, N. Bourguignon, and F. Prestat-Gaudemer, *Bull. Soc. chim. France*, 1964, 1827; P. Yates and G. L. Walford, unpublished.

[3] W. A. C. Brown and G. A. Sim, *Proc. Chem. Soc.*, 1964, 293.

[4] J. Polonsky, *Proc. Chem. Soc.*, 1964, 292.

[5] *Cf.* J. B. Bredenberg, *Chem. and Ind.*, 1964, 75.

[6] E. A. Ham, H. M. Schafer, R. G. Denkewalter, and N. G. Brink, *J. Amer. Chem. Soc.*, 1954, **76**, 6066.

[7] B. W. Christensen and A. Kjær, *Acta Chem. Scand.*, 1962, **16**, 2466.

[8] E L. Eliel, "Stereochemistry of Carbon Compounds", McGraw-Hill, New York, 1962, p. 114; *cf.* A. McKenzie. *J. Chem. Soc.*, 1906, **89**, 365.

indeed one finds the nearest atom to be O'(4), (0·2746, 0·9700, −0·2561). It is also the nearest atom to C(24), (0·2617, 1·1167, −0·0617). However, the interatomic distances, as they stand, are C(24)–O'(4), 2·95 Å and O(11)–O'(4), 3·26 Å
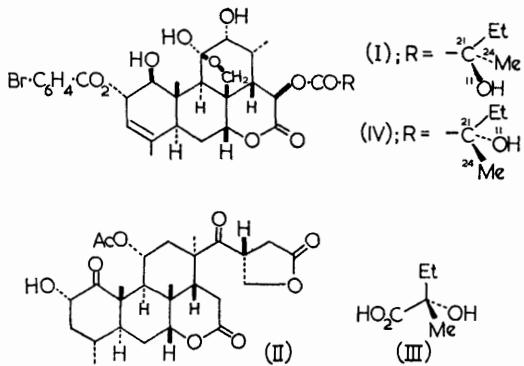
whereas one would expect, if anything, the latter to be the shorter.

If one interchanges C(24) and O'(4), one has to readjust the lengths of the bonds made with C(21). Keeping C(21) fixed (note it has $B = 10·1$ Å²) and the interbond angles unchanged one finds that, making the new bond lengths C–C, 1·54 Å, C–O, 1·36 Å, the new interatomic distances with O'(4) are:

$$C(24) \text{ new–}O'(4) \quad 2·97 \text{ Å}$$

$$O(11) \text{ new–}O'(4) \quad 3·18 \text{ Å}$$
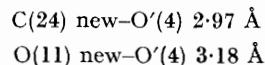
Thus the discrepancy in interatomic distances still persists but is less severe than formerly. Accordingly, in addition to chemical evidence, we consider the X-ray evidence to constitute a *prima facie* case for interchanging C(24) and O(11) and hence inverting the configuration of the side chain asymmetric carbon atom C(21).