X-Ray Structure Determination of 4*R*,8*R*-*p*-Menth-1-en-9-ol *p*-Iodobenzoate. Revision of the Absolute Stereochemistry of Natural (+)-Juvabione

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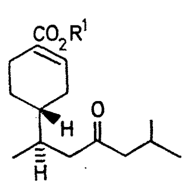
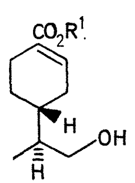
Summary The absolute stereochemistry of (+)-4*R*,8*R*-*p*-menth-1-en-9-ol was determined by single-crystal*X*-ray analysis, and natural (+)-juvabione shown to have the *R*,*S*-configuration.

IN our previous communication,[1] the stereospecific synthesis of natural (+)-juvabione, a compound possessing insect juvenile hormone activity in the linden bug (*Pyrrhocoris apterus*), was reported. Natural (+)-juvabione had been assigned the *R*-configuration at both asymmetric centres, as shown in (Ia), based upon the stereochemistry deduced for the parent (+)-todomatuic acid (Ib)[2]. This synthesis[1] was believed to have confirmed these assignments[3] (4*R*, 8*S*) for the starting (+)-*p*-menth-1-en-9-ol (II).† We subsequently learned[5] of an error in this assignment and have determined the absolute stereochemistry of (II) unambiguously by *X*-ray analysis of its crystalline *p*-iodobenzoate (IIIb), m.p. 45—46°, $[\alpha]_D^{25}$ + 28·2° (*c* 1·01, $CHCl_3$).

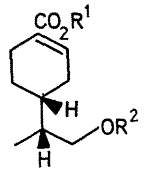


(Ia) R^1=Me

(Ib) R^1=H

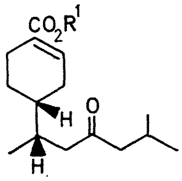


(II)



(IIIa) R^2=H

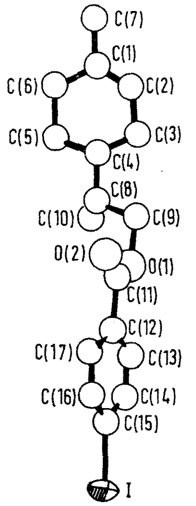
(IIIb) R^2=CO·C_6H_4I-*p*



(IVa) R^1= Me

(IVb) R^1=H

Crystals of (IIIb) are monoclinic, space group $P2_1$, a = 10·508, b = 15·293, c = 10·479 Å, β = 99.73°, D_m = 1·51 g.cm.$^{-3}$, Z = 4, D_c = 1·54 g.cm.$^{-3}$. Intensities of 4779 reflections (2091 unobservedly weak) were measured with a Hilger–Watts four-circle diffractometer, with Cu-K_α radiation. The structure was determined by the usual Patterson and Fourier methods, complicated somewhat by a pseudo-*n*-glide plane relating the iodine atoms and phenyl rings of the two independent molecules in the unit cell. Refinement was carried out by full-matrix least-squares with allowance for the anomalous dispersion of the iodine atoms. Anisotropic thermal parameters were used for the iodine atoms and individual isotropic thermal parameters were used for the lighter atoms. The absolute configuration was established by taking into account the relative intensities of $h\bar{k}l$ and hkl pairs of reflections.[6] The final discrepancy index, *R*, is 0·066 for the observed reflections. The configurations of the two independent molecules differ only by a rotation about the C(9)–O(1) bond. The absolute stereochemistry of one of the two independent molecules in the crystal is shown in the Figure.



FIGURE

Thus, the starting alcohol for the synthesis[1] of natural (+)-juvabione has the 4*R*,8*R*-configuration as shown in (IIIa). Natural (+)-juvabione (IVa) and the parent (+)-todomatuic acid (IVb) therefore have the *R*,*S*-configuration, contrary to the assignment deduced previously[2] and reported to be confirmed in our earlier publication.[1] Accordingly, the diastereoisomeric (+)-epijuvabione and (+)-epitodomatuic acid have the *R*,*R*-configuration shown in (Ia) and (Ib), respectively.

The assistance of Dr. P. Bommer and the Physical Chemistry Department, Hoffmann-La Roche Inc., is gratefully acknowledged.

(*Received, May 5th,* 1969; *Com.* 614.)

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† The alcohol ($[\alpha]_D^{25}$ + 106°) was obtained as described in ref. 1, by hydroboration of *R*-(+)-limonene, fractional crystallization of the 3,5-dinitrobenzoates, and hydrolysis of the less soluble, higher melting fraction.

[1] B. A. Pawson, H.-C. Cheung, S. Gurbaxani, and G. Saucy, *Chem. Comm.*, 1968, 1057.

[2] M. Nakazaki and S. Isoe, *Bull. Chem. Soc. Japan*, 1963, **36**, 1198.

[3] K. H. Schulte-Elte and G. Ohloff, *Helv. Chim. Acta*, 1966, **49**, 2150.

[4] Personal communication from Dr. G. Ohloff. We thank Dr. Ohloff for informing us of this error.

[5] A. F. Peerdeman, A. J. van Brommel, and J. M. Bijvoet, *Proc. k. ned. Akad. Wetenschap.*, 1951, **54**, *B*, 16.