

THE ABSOLUTE CONFIGURATION OF AMBROSIC ACID
A CRYSTALLOGRAPHIC STUDY OF P-BROMOPHENACYL AMBROSiate*

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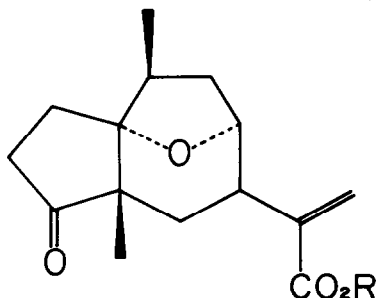
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In the previous paper ⁽¹⁾, the structure of ambrosic acid, an irritant sesquiterpene isolated from *Ambrosia arthemisiifolia*, has been formulated as Ia mainly on the basis of the chemical and spectral data on several derivatives. An ambiguity, remains however, in the configuration of C₁₀-β-methyl group in Ia, which was merely supported by the Cotton effect in O.R.D. spectrum of methyl ambrosiate (Ib). Due to scarcity of the sample for further studies on the complete structural elucidation, we are obliged to decide carrying out a X-ray crystallographic analysis of the p-bromophenacyl ester (Ic) in order to settle the stereochemistry specifically mentioned above and also to establish the absolute configuration of the confirmed structure of ambrosic acid.

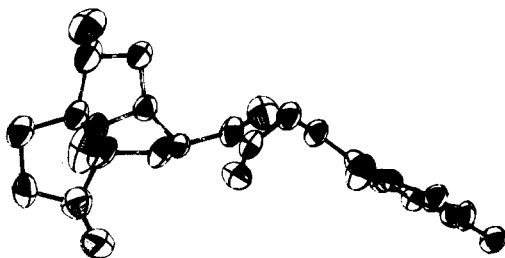


- Ia R=H
Ib R=CH₃
Ic R=CH₂COC₆H₄Br (p)

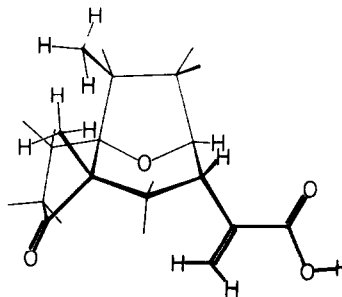
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structure factors measured by CuK α radiation. The R value was reduced to 0.073 allowing for the anisotropic thermal vibrations for each atom. The bond lengths and angles are shown in Figs. 1 and 2, respectively (standard deviations: 0.02Å and 1°).

The absolute stereochemistry of the molecule has now been established as follows: C₅- β CH₃/C₁- α OR (trans), C₅- β CH₃/C₁₀- β CH₃ (cis), C₅- β CH₃/C₇- β C(CH₂)COOR (cis), C₇- α H/C₈- β H (trans). The seven membered ring of the pseudoguaiane skeleton of ambrosic acid is forced to take a boat conformation due to formation of the ether linkage between C₁ and C₈. It is of interest to note that the distance between the two β -methyl groups at C₅ and C₁₀ is 3.23Å, a bit closer than usual, but comparable with those found between the 1, 3 diaxial methyl groups in certain fused cyclohexane ring system^{(2) (3)} (Fig. 3).



(Fig. 3)



(Fig. 4)

The complete stereostructure of p-bromophenacyl ambrosiate thus illustrated by Ic proves directly the absolute structure of ambrosic acid (Ia) proposed by chemical studies in the preceding communication⁽¹⁾ (Fig. 4).

Acknowledgement

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Reference

- (1) S. Inayama, T. Kawamata and M. Yanagita, Chem. Pharm. Bull. in press.
- (2) T. Akiyama, O. Tanaka and Y. Iitaka, Acta Crystallography B26, 163 (1970).
- (3) K. Bjamer, G. Ferguson and R.D. Melville, *ibid.* B24, 855 (1968).