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

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In the previous paper ⁽¹⁾, the structure of ambrosic acid, an irritant sesquiterpene isolated from Ambrosia arthemisiifolia, has been fomulated as Ia mainly on the basis of the chemical and spectral data on several derivatives. An ambiguity, remains however, in the configuration of C_{10} - β -methyl group in Ia, which was merely supported by the Cotton effect in O.R.D. spectrum of methyl ambrosiate (Ib). Due to scarsity of the sample for further studies on the complete structural elucidation, we are obliged to decide carring 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	$R=CH_2COC_6H_4Br(p)$

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p-Bromophenacyl ambrosiate was prepared by the usual method as one of the most suitable crystal for our X-ray analysis: $C_{23}H_{25}O_5Br$ (M⁺ 461), mp 119-121°, v^{KRr} (cm⁻¹) 1744 (cyclopentanone), 1725, 1624 ($\Delta^{\alpha,\beta}$ -COOR), 1700, 1586 (COAry1), δ^{CDC1}_3 (TMS) 1.13 s (\exists C-CH₃), 1.28 d 6.5 (>CH-CH₃), 3.02 m (>CH-C(=CH₂)COOR), 4.51 m (>CH-O-C-), 5.64 d 1, 6.42 d 1 (-C(=CH₂)COOR), 5.36 s (-COOCH₂CO-), 7.68 q 8.8 (arom. H). Recrystallization from n-hexane afforded colorless prisms elongated along the c axis. The crystal belongs to the monoclinic system with lattice parameters and space group, a = 19.303 ± 0.02, b = 7.982 ± 0.01, c = 6.781 ± 0.01 Å, β = 89.34 ± 0.1°, V = 1044.7 Å³ and P2₁. The density was calculated to be Dx = 1.46 g cm⁻³ assuming two molecules are contained in the unit cell.

Intensities were measured by a Rigaku Denki four-circle X-ray diffractometer with Ni-filtered CuKa radiation. A total of 1186 independent structure factors were obtained which correspond to about 80% of the theoretically possible ones within 20 of 120°. In order to measure the anomalous dispersion effect of the bromine atom, Zr-filtered MoKa radiation was used and the intensity data for 741 pairs of hkl and hkl reflexions were obtained which constitute the Friedel pairs.

The absolute structure was determined from the phases calculated by the anomalous dispersion method. The electron density map thus obtained showed the location of all the 28 carbon and oxygen atoms. The refinement of the atomic parameters was caried out by the method of least-squares based on the 1186



Fig. 1 and 2 The bond lengths and angles of the molecule of p-bromophenacyl ambrosiate

structure factors measured by CuKa 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: $C_5 - \beta CH_3/C_1 - \alpha OR$ (trans), $C_5 - \beta CH_3/C_{10} - \beta CH_3$ (cis), $C_5 - \beta CH_3/C_7 - \beta C (CH_2) COOR$ (cis), $C_7 - \alpha H/C_8 - \beta H$ (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 C_1 and C_8 . It is of interest to note that the distance between the two $\beta\text{-methyl}$ groups at $C^{}_5$ and $C^{}_{10}$ 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. 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 preceeding communication⁽¹⁾ (Fig. 4).

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