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RENEWED STUDIES ON THE STRUCTURE OF DIDYMIC ACID

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The structure (Ia) of didymic acid proposed on the basis of classical experiments has been reexamined by modern methods. The methyl ester of a controlled oxidation product of methyl O-methyldidymate was studied by X-ray crystallographical analysis to revise the earlier structural formula (III) for this compound to (IV). The allocation of n-C_5H_{11}, COOH and OH on the dibenzofuran ring has been established to confirm the structure (Ia).

KEYWORDS——didymic acid; oxidation product of methyl O-methyldidymate; X-ray analysis

In 1944 one of the authors(S.S.)[1)] proposed a structural formula (Ia) for didymic acid, $C_{22}H_{26}O_5$, mp 171°C(dec.) (micro mp 164°C(dec.)), a metabolite of the lichens,[2)] *Cladonia didyma* Fee, *Cl. pseudodidyma* Asahina, *Cl. floerkeana* (Fr.) Sommerf. var. *suboceanica* Asahina, *Cl. bacillaris* Nyl., and *Cl. incrassata* Flk. The formula was based on classical methods, mostly chemical reactions with UV spectral data measured by Henri's spectroscopic method.[3)]

The structure (Ia) was taken in excluding an alternative formula (II) by the characteristic solubility of sodium didymate as it formed an oily middle layer by shaking ethereal solution of didymic acid with aq. sodium bicarbonate.

The analogous property was shown by some lichen depsides and depsidones having a carboxyl located between a n-heptyl or n-amyl group and a phenolic hydroxyl. This was not the case when a n-propyl was located at the position of the alkyl.

Recently a question was raised by Dr. M.V. Sargent,[4)] who synthesized methyl O-methyldidymate. His synthesized product gave a melting point 96.5°C, 10°C lower than that of Ib recorded in our previous paper.[1)] So he suggested that didymic acid may be represented by the alternative formula (II), even though direct comparison with the sample of methyl O-methyldidymate, which had been lost, was not practical. This urged us to reexamine the structure of didymic acid using the modern physical spectrometric methods now available.

Under the very restricted condition due to the shortage of the original samples of didymic acid and its derivatives which have been kept for a long time, IR, ^1H NMR, and ^{13}C NMR are not so effective in determining the alternative dispositions of n-propyl and n-amyl on the dibenzofuran ring. Since the dibenzofuran ring system is very stable against fragmentation in mass spectrometry, it was not informative in determining the disposition of the alkyl groups.

X-ray crystallographic analysis is an exclusive method for such a purpose, and the methyl ester of controlled oxidation product of methyl O-methyldidymate, which was formulated previously as III, has been recrystallized to form an aggregate of fine crystals, mp 131°C, for the analysis. The observed crystal data of this compound are: Molecular formula, $C_{24}H_{26}O_8$, MW=442, monoclinic, space group $P2_1/n$, Z=4, D_{calc}=1.299 gcm^{-3}, a=19.522(10), b=8.271(4), c=14.153(7)Å, β=97.99(5)°, V=2263Å^3, μ for CuKα=7.74 cm^{-1}.

A small crystal with approximate dimensions 0.02 × 0.08 × 0.3 mm was mounted on a Philips PW 1100 diffractometer and the crystal as well as the intensity data were measured by monochromated CuKα radiation using a graphite plate. A total of 911 out of 2983 reflections were measured above the 2σ(I) level within the 2θ range of 6° through 120° and data were corrected for the Lorentz and polarization factors. The crystal structure was solved by the direct method based on calculations using the MULTAN program.5) Using 125 reflections with $E \geq 1.4$, a set of phase angles generated by 5 reflections besides the origin defining 3 gave a reasonable E-map which indicated the arrangement of atoms in one of the benzene rings. The structure was then subjected to the subsequent calculations. Refinement by the blockdiagonal matrix least-squares method gave the final R value of 0.05 for 911 reflections including anisotropic and isotropic thermal parameters respectively for heavier and hydrogen atoms.6)

A perspective view of the molecular structure is shown in Fig. 1 along with the key to the numbering of the atoms in the molecule. The two methoxyl groups at C3 and C7, methoxy-carbonyl group at C2 and the methylated α-ketonic acid group at C9 are seen to be extended from the dibenzofuran ring nearly in plane, while the *n*-amyl group at C1 turns slightly upwards still taking a trans zigzag conformation with its plane nearly perpendicular to the ring plane.

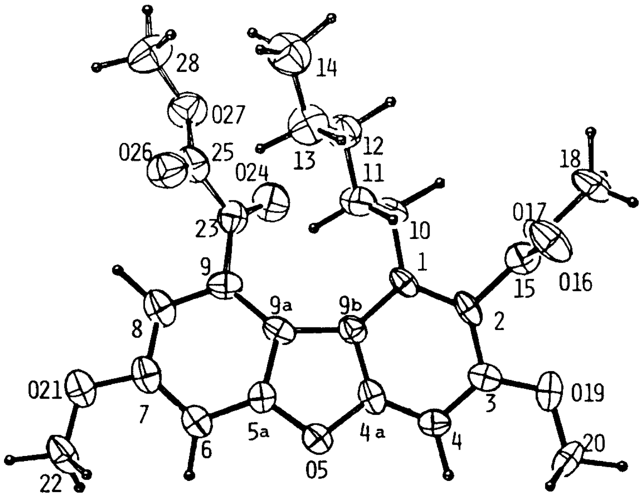

Fig. 1. A Perspective Drawing of the Molecule (IV) by the ORTEP Program7) Viewed Down to the Ring Plane

C and O atoms are drawn by ellipsoids of thermal vibrations enclosing the region in which the center of the atom is found with probabilities of more than 30%.

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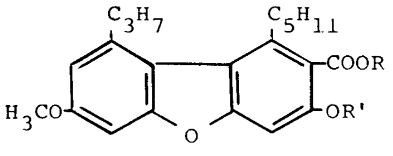
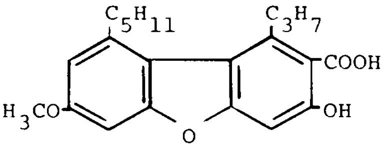
By this X-ray crystallographical experiment, the previously proposed structure (III) for this compound has been revised to IV. The observed data of elementary analysis (Found C, 65.51; H, 6.08) that conform with the previously proposed formula of this compound[1)] (Anal. Calcd for $C_{21}H_{22}O_7$: C, 65.28; H, 5.70) have now been adapted also to the revised formula (Anal. Calcd for $C_{24}H_{26}O_8$: C, 65.15; H, 5.92).

Ib was subjected to controlled permanganate oxidation: 100 mg of Ib was dissolved in 5 ml of pyridine and an aq. solution of $KMnO_4$ (0.8 g in 20 ml) was added dropwise while being heated in a boiling water bath; the reaction was continued for 5 h. and the reaction mixture was treated as usual. In this way *n*-propyl group was partially oxidized into α-ketonic acid which was subsequently methylated with diazomethane to afford a yellow crystalline methyl ester (IV).

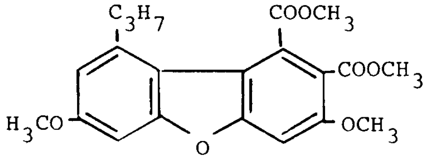
The mass spectrometry of IV gave $[M^+]$ m/z 442.1630, which agreed with the molecular formula, $C_{24}H_{26}O_8$ (mol wt.: 442.1627). The allocation of n-C_5H_{11}, $COOCH_3$ and OCH_3 at the 1, 2 and 3 positions of IV, respectively, revealed the same disposition of n-C_5H_{11}, COOH and OH groups in Ia.



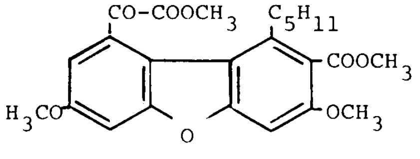
(Ia) R=R'=H (Ib) R=R'=CH_3



(II)



(III)



(IV)

Thus the structural formula (Ia) of didymic acid which was proposed forty years ago has now been confirmed unequivocally.

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