

OOSPOLIDE: REVISED STRUCTURE AND ITS CONFIRMATION

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Oospolide (m.p. 111° , $C_8H_{10}O_5$, $pK_a' \sim 3.5$, IR: 2600, 1735, 1660, 1570 cm^{-1} in KBr; 1726, 1692, 1597 cm^{-1} in $CHCl_3$), an acidic metabolite of Oospora astringenes, is an unstable compound both to alkali and hot acid, and the structure (A) has been tentatively suggested (1). However, new observations have now forced us to revise the structure. Here we propose a new structure (Ia) and also present its synthetic evidence.

An enolized β -diketone chromophore, assumed in the previous paper (1), was now found that it is not originally present in oospolide but formed by the action of alkali, since the original UV absorption of oospolide (λ_{max} 264 μ , $\epsilon = 12600$ in H_2O or HCl) was not regenerated even by immediate acidification of its alkaline solution (λ_{max} 296 μ , $\epsilon = 14100$ in $N-NaOH$), instead a new spectrum appeared (λ_{max} 267 μ , $\epsilon = \sim 2000$). The re-acidified solution gave immediate colouration with $FeCl_3$ in contrast to oospolide which gave slowly violet colour. Re-basification of this solution produced the spectrum identical with that of oospolide in $NaOH$ solution. The facts indicate very rapid transformation of oospolide in alkaline condition prior to complete decomposition (1). This was supported by reverse titration of oospolide, the compound being titrated as a dibasic acid ($pK_a' \sim 3.5, 8.3$) though by direct titration it behaves as a monobasic acid ($pK_a' \sim 3.5$).

The second observation is that oospolide can be hydrogenated with $Pd-C$ at 50° to give an oily dihydro-compound (IIa) [IR(liquid film): 2600, 1750 cm^{-1} , NMR: no olefinic proton signal, UV: no absorption above 220 μ], which

still had acidity ($pK_a' \sim 3.6$) comparable to the original compound and smoothly reacted with diazomethane to give an oily methyl ester (IIb), $C_9H_{14}O_5$ (p-bromophenacyl ester (IIc), m.p. 88° , $C_{16}H_{17}O_6Br$). These results show that oospolide is a carboxylic acid. Therefore, in conjunction with the earlier evidence (1) that on permanganate or ozone oxidation oospolide gave β -carboxymethoxypropionic acid (III) ($pK_a' \sim 3.6, 4.7$), we now conclude that oospolide has a partial structure of $R-CH_2-CH_2-O-CH_2-COOH$. The acidity of oospolide and of its dihydro-derivative (IIa) is coincident with that of CH_3-O-CH_2-COOH (pK_a 3.53)(2) rather than $CH_3-O-CH_2-CH_2-COOH$ (pK_a 4.46)(3).

Since the UV absorption of oospolide disappeared by borohydride reduction (1) or by hydrogenation, the chromophoric group, which is corresponding to IR absorptions at 1660 and 1570 cm^{-1} (in KBr), is attributed to a conjugated ketone. In fact, oospolide reacts with 2,4-dinitrophenylhydrazine though the product was difficult to be purified. In contrast, dihydro-oospolide methyl ester (IIb) gave a crystalline 2,4-dinitrophenylhydrazone, $C_{15}H_{18}O_8N_4$, m.p. 115° . Dihydro-oospolide methyl ester (IIb) showed a single carbonyl band at 1750 cm^{-1} , and its 2,4-dinitrophenylhydrazone still exhibited the absorption at 1750 cm^{-1} due to α -oxygenated carbomethoxy group. Therefore, the ketonic group forming dinitrophenylhydrazone must have shown the absorption around 1750 cm^{-1} overlapping with the band of $COOCH_3$. Hence, the ketonic group must be on a five membered ring.


The above and earlier evidences, in association with NMR and NMRD experiments on dihydro-oospolide p-bromophenacyl ester (IIc) (see below), are summarized in the revised structure (Ia).

Dihydro-oospolide p-bromophenacyl ester (IIc) showed signals at δ 7.72, 5.37 (each due to p-bromophenacyl group), 4.28 (singlet, a), 3.78 (triplet, b), 2.05 (quartet, c), 4.50 (multiplet, d), 2.46 (multiplet, e) and 3.94 (AB-quartet, f). The signals a, b, c and f correspond to those at δ 4.15 (2H, s), 3.88 (2H, t), 2.86 (2H, t) and 4.54 (2H, s) of oospolide, respectively. The signal at δ 2.86 of oospolide shows marked high field shift and becomes quartet by hydrogenation. On irradiation of b, the signal c turned to doublet. Irradiation of c changed b to a singlet, and simplified the signal d. When d was

irradiated, c changed to a triplet and e to an AB-quartet.

The confirmation of the structure (Ia) was provided by the synthesis of deoxodihydro-oospolide (IVa) which was obtained as shown in Figure 1 and crystallized as its p-bromophenacyl ester (IVb), $C_{16}H_{19}O_5Br$, m.p. 75° .

The synthesis was achieved as follows. The sodio-derivative of 2-(tetrahydro-2-furyl)-ethanol (V) (4) was treated with ethyl bromoacetate and the product was hydrolysed to the corresponding acid. The p-bromophenacyl ester of this acid was found to be identical (IR, UV, NMR and mixed m.p.) with the specimen (IVb) obtained from the natural product.

We now briefly comment on the chemical shift of carboxyl proton of oospolide, which appeared unusually in high field (66.0--7.0); a fact which in the previous communication (1) misled us to an incorrect structure. We have now supposed that this abnormality is characteristic of the carboxyl proton of alkoxyacetic acid, $R-O-CH_2-COOH$, at least under the condition we used (0.05--0.2M solution in $CDCl_3$ at 20°), as shown by the following examples: IIa, 6.8; IVa, 7.2; - CH_2-O-CH_2-COOH , 6.5; $C_2H_5-O-CH_2-COOH$, 7.4, in δ -value.

Mass spectra of oospolide and of its dihydro-derivative may be reassigned as shown in Figure 2.

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