The Isolation of 2,4-Dihydroxy-3,6-dimethylbenzoic Acid (3-Methylorsellinic Acid) from a Culture of *Aspergillus terreus*

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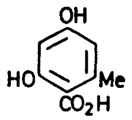
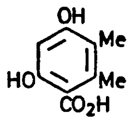
Summary 3-Methylorsellinic acid (**3**) was isolated from a culture of *Aspergillus terreus*; feeding experiment of radioactive precursors showed that formate was incorporated into (**3**), but not into orsellinic acid (**1**), suggesting that the methyl carbon at C-3 position was derived from formate.

Orsellinic acid (**1**) has been known as the simplest phenolic compound derived from a ketomethylene chain and isolated from the culture of various organisms.[1] 5-Methylorsellinic acid (**2**) was isolated from the culture of *Aspergillus terreus*,[2] and recently its direct incorporation into mycophenolic acid by *Penicillium brevi-compactum* was reported.[3] Scott *et al.*[4] have observed that (**3**) was incorporated into stipitatic and stipitatonic acids by *Penicillium stipitatum*, indicating the intermediary formation of (**3**). However, as far as we are aware, no report on the isolation of (**3**) from other organisms has been made. Now we report the isolation of (**3**) from a strain of *Aspergillus terreus*.

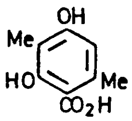
Our strain was grown on a surface for 30 days at 27° in a chloride-ion free Czapeck-Dox medium. Two kinds of phenolic compounds were obtained by fractionation of the ether extract of the filtered medium through a silica gel column. The first compound was identified as (**1**) by comparison with an authentic specimen. The second compound, m.p. 183—185° (decomp.), $C_9H_{10}O_4$, showed n.m.r. (CD_3OD) δ 2·01 (3H, s, CH_3), 2·47 (3H, s, CH_3), 6·21 p.p.m. (1H, s, ring proton); u.v. λ_{max} (methanol) (log ϵ) 217 (4·41), 266 (4·14), 303 nm (3·56); i.r. ν_{max} (KBr disc) 3400, 1635, 1612, 1596, 1490, 1266, 1190, 1097 cm^{-1} and was deduced to be (**3**) from these data. This was unequivocally proved by comparison with a synthesized specimen.[5]



(1)



(2)



(3)

[1-^{14}C]Acetate was incorporated into (**3**) (total incorporation 5·26%) and (**1**) (3·58%). Decarboxylation of (**3**) (3·29 × 10^7 d.p.m./mmol) by heating in conc. hydrochloric acid gave carbon dioxide (0·85 × 10^7 d.p.m./mmol) which had a quarter of the radioactivity of (**3**). [^{14}C]Formate was incorporated into (**3**) (3·36%), but incorporation into (**1**) was negligible. Decarboxylation of (**3**) (1·92 × 10^7 d.p.m./mmol) obtained on feeding with [^{14}C]formate gave non-radioactive carbon dioxide. It is apparent that the methyl carbon at C-3 is derived from formate, similarly to the case of the methyl carbon at C-5 of (**2**).[2] The biogenetic pathway of (**2**) and (**3**) may involve a methylation step at a different position of the polyketide chain. Our strain produced neither (**2**), nor any tropolone derivative, but some new polycyclic compounds which are supposed to be derived from shikimic acid.

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