

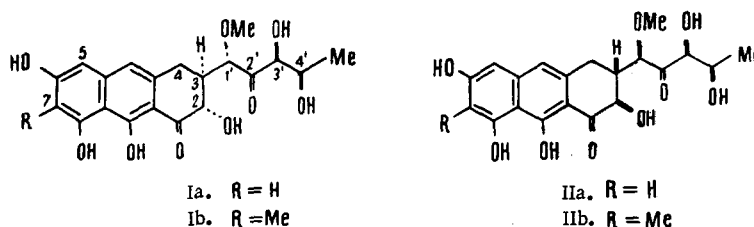
OLIVOMYCIN AND RELATED ANTIBIOTICS

XXVI.* THE ABSOLUTE CONFIGURATIONS OF OLIVIN AND OF CHROMOMYCINONE

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The antitumoral antibiotics, olivomycins and chromomycins, are glycosides of the closely related aglycones, olivin and chromomycinone, for which we and Japanese workers have proposed, respectively, the spatial formulas (Ia) [1] and (IIb) [3]. According to these formulas, olivin and chromomycinone differ both in relation to the substituent at C₇ and in relation to the configuration of the chiral section C₂-C₃-C₄. Nevertheless, the structural similarity of these compounds has permitted the assumption that the routes of their biogenesis are completely analogous, with the exception of the fact that in the case of olivin, at one of the stages of biosynthesis, the process of enzymatic C-methylation is blocked. Consequently, it is likely that olivin and chromomycinone actually differ only homologically; i.e., they have the same relative and absolute configurations.



The results of a spectropolarimetric study of both aglycones has completely confirmed this hypothesis. It was found that the ORD curves of olivin and chromomycinone, and also those of their acetates, practically coincide (Fig. 1). Consequently, the configurations of these compounds are identical. Thus, it was established that one of the formulas (I or II) is erroneous, but it was not known which. The further investigations that we have performed have shown that formula (I) is the correct one.

The previous conclusions on the absolute configuration of the C₂-C₃-C₄ chiral centers in olivin [1] and in chromomycinone [3] were essentially indirect, since they were based on spectropolarimetric data, the interpretation of which was not unambiguous. Consequently, we decided to obtain a direct chemical proof of the absolute configuration of olivin by directed degradation with the splitting out of the fragment containing the C₄ chiral center and its direct identification.

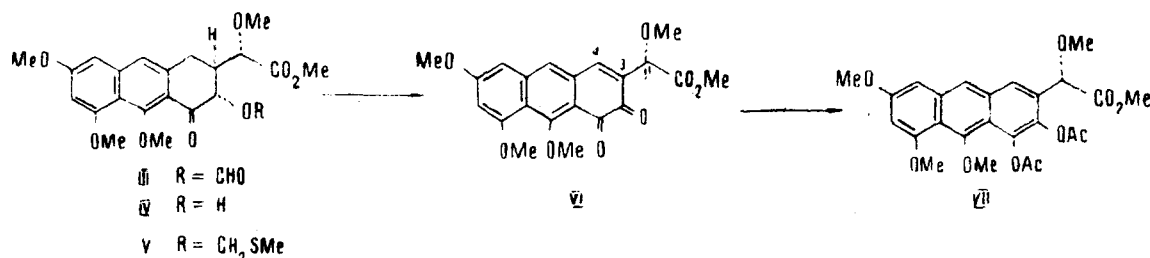
To perform such a degradation it was necessary first to develop a method for introducing a double bond or some functional group into the saturated ring of olefin in order to facilitate the subsequent degradative oxidation of this part of the molecule. Using the trimethylolivinic ester (IV) as a model substance, we found that the required modification of the hydroaromatic ring can easily be achieved by oxidation with dimethyl sulfoxide and acetic anhydride. This forms, in addition to a small amount of the 2-methylthio-methyl ether (V), the orthoquinone (VI) containing the desired double bond in the 3,4 position; its structure being confirmed by conversion into the diacetate (VII) on reductive acetylation.

*For Communication XXV, see [1], and for a preliminary communication see [2].

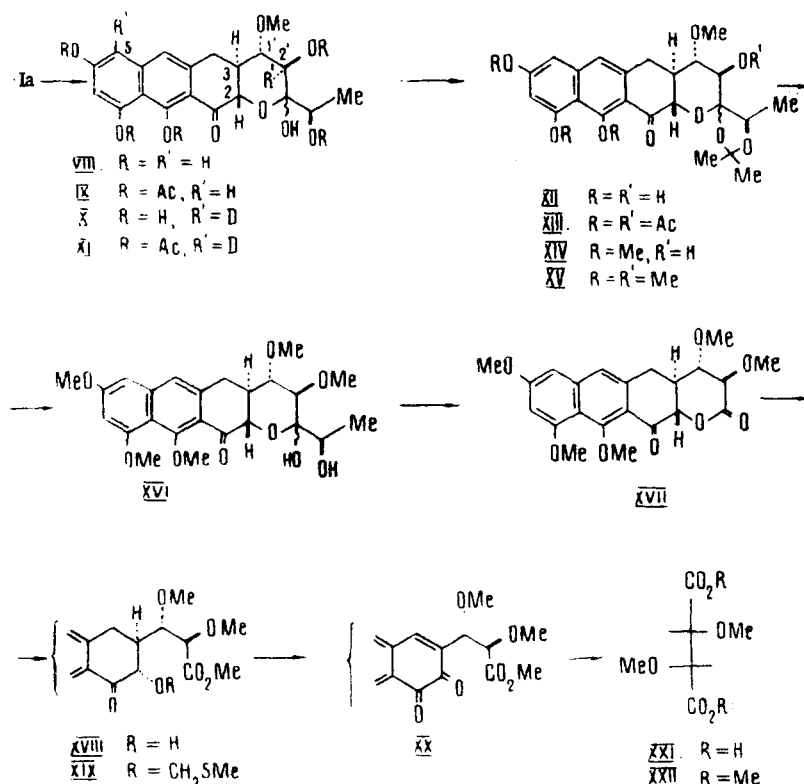
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The oxidative splitting off of the side chain of olivin must lead to the "excision" of the C_3 atom in the form of a carboxy group; when a ketonic carbonyl is present in position 2', a β -oxo acid is formed in which the C_1 center can easily lose its chirality (in consequence of decarboxylation) or change its configuration to the "unnatural" one (as a consequence of inversion through an enol stage). Consequently, in order to avoid a negative result or an artifact, it was necessary first to eliminate the oxo group from the 2' position of the side chain, and we did this by means of a reaction described previously for chromomycinone (Ib) [4].



By the action of 0.1 N KOH, olivin (Ia) was isomerized into the corresponding 2'-hydroxy-3'-oxo compound, isoolivin, which exists in the form of the semiketal (VIII), as is shown by the absence from its IR spectrum of the band of a nonconjugated carbonyl group and the predominant formation of a pentaacetyl derivative (IX) under those conditions in which olivin itself smoothly gives a hexaacetate. When the analogous isomerization was performed in D_2O solution, dideuteroisoolivin (X) was obtained, and this was then converted into the pentaacetate (XI). The NMR spectrum of this substance (Fig. 2) shows that in its formation from olivin, only $\text{H}_{2'}$ and H_3 are replaced by deuterium, while $\text{H}_{1'}$ does not exchange with the solvent and, consequently, the configuration of the C_1 center undergoes no change during the isomerization of olivin. Furthermore, it follows from the NMR spectra of the acetates (IX) and (XI) that all the hydrogen atoms in the tetrahydropyran ring of isoolivin are located axially ($J_{2,3} = 12.5 \text{ Hz}$, $J_{3,1} = 9 \text{ Hz}$, and $J_{1',2'} = 10 \text{ Hz}$). On the one hand, this confirms the previously established relative configuration of the $\text{C}_2-\text{C}_3-\text{C}_1$ fragment [5] and, on the other hand, it shows the threo arrangement of the substituents at C_1 and C_2 , which is necessary to exclude intramolecular optical compensation in the final dehydration product of the tartaric acid type (see below).



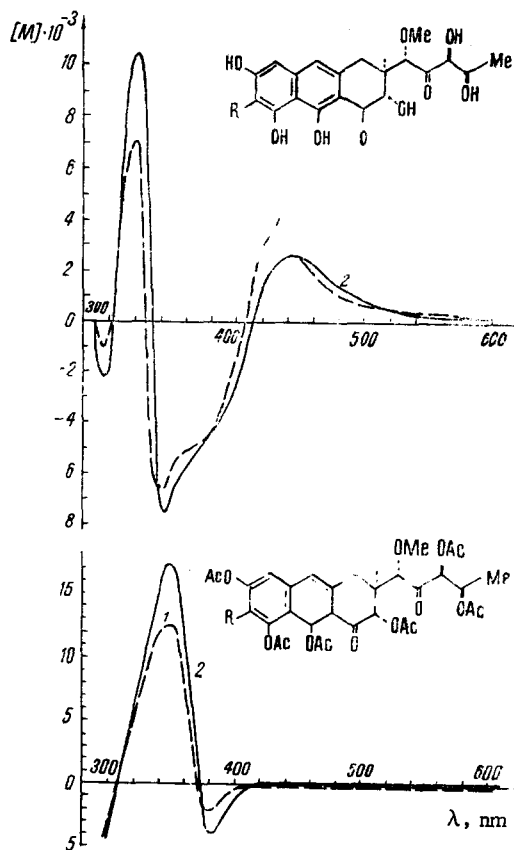


Fig. 1. ORD curves of olivin (Ia) and chromomycinone (Ib) (96% ethanol), and of hexaacetyl-olivinate (Ac-Ia) and hexaacetylchromomycinone (Ac-Ib) (dioxane): 1) R = H; 2) R = Me.

with water. The methanolysis product was extracted with ethyl acetate and chromatographed in the benzene-acetone (5:1) system, the zone with R_f 0.59–0.74 being taken. After crystallization from ethanol, the yield of the hydroxy ester (IV) was 230 mg (57%), mp 123–124°C; $[\alpha]_D^{25} - 28^\circ$ (c 1; chloroform); R_f 0.31 [in the hexane-ethyl acetate (3:1) system]; λ_{\max} 226, 272, 368 nm (log ϵ 4.46; 4.67; 3.94); ν_{\max} 1570, 1620, 1680, 1747, 3440 cm^{-1} .

Found: mol. wt. 404. $\text{C}_{21}\text{H}_{24}\text{O}_8$. Calculated: mol. wt. 404.

B. A solution of 50 mg of methyl formyltrimethylolivate (III) in 1 ml of methanol was mixed at 20°C with 5 ml of 0.1 N NaOH and the mixture was treated as in experiment 1A. The zone with R_f 0.25–0.45 yielded 30 mg (66%) of 6,8,9-trimethylolivinic acid with mp 187–189°C (from ethanol); $[\alpha]_D^{25} - 16^\circ$ (c 0.8; acetone); λ_{\max} 226, 271, 336, 366 nm (log ϵ 4.05; 4.68; 3.82; 3.90); ν_{\max} 1570, 1625, 1680, 1710, 1750, 3480 cm^{-1} .

Found: mol. wt. 390. $\text{C}_{20}\text{H}_{22}\text{O}_8$. Calculated: mol. wt. 390.

The methylation of this acid in tetrahydrofuran with an excess of an ethereal solution of CH_2N_2 gave the ester (IV) described in experiment 1A, with a yield of 50%.

2. Methyl 6,8,9-Trimethyl-3,4-dehydroolivinate 1,2-Quinone (VI) and the Product of Its Reductive Acetylation (VII). A. A solution of 202 mg of the ketol (IV) in 2 ml of Me_2SO and 2 ml of Ac_2O was kept at 20°C for 60 h, poured into water, extracted with ethyl acetate, and chromatographed in the benzene-acetone (5:1) system. The zone with R_f 0.52–0.72 yielded 130 mg (65%) of the quinone (VI) with mp 179–180°C

The subsequent transformations were as follows: by the usual method, isoolivin (VIII) was converted into the acetone (XII); the latter was methylated (first with diazomethane and then with methyl iodide in the presence of NaH in dimethyl sulfoxide) to the tetramethyl derivative (XV). After hydrolysis of the isopropylidene protective group, the hydroxy semiketal (XVI) was obtained, and the oxidation of the latter with lead tetraacetate gave the δ -lactone (XVII). The product of its acid methanolysis, the hydroxy oxo ester (XVIII), was dehydrogenated with dimethyl sulfoxide and acetic acid to form the orthoquinone (XX). The methylthiomethyl ether (XIX) was formed as a byproduct, as in the case of the model hydroxy oxo ester (IV). The oxidation of the quinone (XX) with potassium permanganate yielded (+)-dimethoxysuccinic acid, which was identical with an authentic sample of the dimethyl ether of D-tartaric acid (XXI), thanks to which the S configuration of the C_1 chiral center in the initial molecule was shown unambiguously.

Thus, olivin and chromomycinone possess the spatial structure (I).*

EXPERIMENTAL

For general information on the experiments, see [1].

The elementary analyses of compounds IV, VI, VIII, XII, XIII, XV, XVI, XVII, XVIII, and XX corresponded to the calculated figures.

1. Methyl 6,8,9-Trimethylolivate (IV). A. At 20°C, 1.5 ml of a 1 N solution of MeONa was added to a solution of 430 mg of methyl 2-formyl-6,8,9-trimethylolivinic acid (III) [7] in 20 ml of methanol. After 10 min, the mixture was acidified with 0.5 N H_2SO_4 and was diluted

*After our publication of the absolute configuration of olivin (Ia) [2], the Japanese workers reconsidered their former ideas [3] and adopted for chromomycinone the corrected stereofomula (Ib) [6].

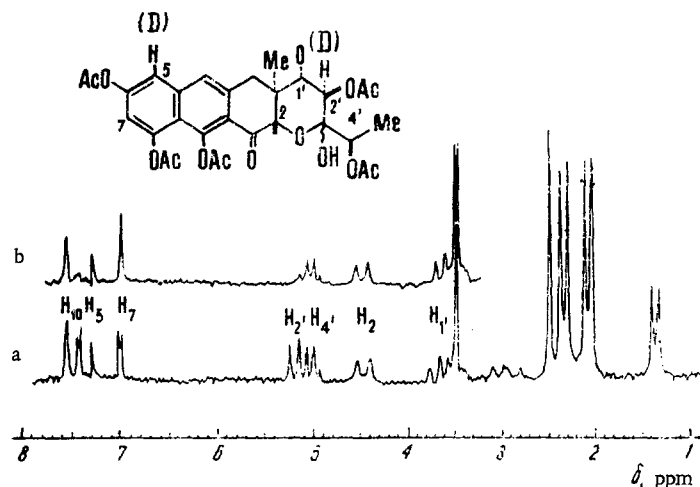


Fig. 2. NMR spectra of pentaacetylisoolivin (IX) (a) and of $[D_2]$ pentaacetylisoolivin (XI) (b) (100 MHz, $CDCl_3$, TMS).

(from ethanol); $[\alpha]_D^{25} - 80^\circ$ (c 0.5; acetone); λ_{\max} 258, 301, 490 nm ($\log \epsilon$ 4.67; 4.61; 4.18); ν_{\max} 1565, 1610, 1630, 1660, 1680, 1738 cm^{-1} , δ_{Me_2SO} 4.82 (1H, s; $H_{1'}$), 6.71 (1H, d, J 1.5; H_7), 7.06 (1H, d, J 1.5; H_5), 7.71 (3H, s; H_{10}), 7.80 (3H, s; H_4).

Found: m/e_{\max} 402 (M + 2, see [8]). $C_{21}H_{20}O_8$. Calculated: mol. wt. 400.

The zone with R_f 0.80-0.90 yielded the methylthiomethyl ether (V). After crystallization from ethanol, yield 27.5 mg (19%); mp 138-140°C; $[\alpha]_D^{23} - 202^\circ$ (c 1; chloroform); λ_{\max} 226, 271, 365 nm ($\log \epsilon$ 4.42; 4.62; 3.88); ν_{\max} 1565, 1615, 1690, 1750 cm^{-1} .

Found, %: S 6.8. $C_{23}H_{28}O_8S$. Calculated, %: S 6.9.

B. A mixture of 80 mg of the quinone (VI), 400 mg of Zn dust, and 5 mg of AcONa in 4 ml of Ac_2O was boiled for 10 min and evaporated, and the residue was chromatographed in the benzene-acetone (5:1) system. The zone with R_f 0.61-0.81 yielded 66 mg (68%) of the diacetate (VII); $[\alpha]_D^{23} + 80^\circ$ (c 1; chloroform); λ_{\max} 237, 273, 344, 362, 405 nm ($\log \epsilon$ 4.53; 5.11; 3.68; 3.76; 3.66); ν_{\max} 1570, 1630, 1710, 1755, 1775 cm^{-1} ; δ 3.44 (3H, s; $O_{1'}$ -Me); 3.74 (3H, s), 3.92 (6H, s), 3.99 (3H, s) (O_6 -Me, O_8 -Me, O_9 -Me and CO_2 Me), 4.98 (1H, s; $H_{1'}$), 6.46 (1H, d, J 1.5; H_7), 6.73 (1H, d, J 1.5; H_5), 7.88 (1H, s, H_{10}), 7.98 (1H, s; H_4).

Found: mol. wt. 486. $C_{25}H_{26}O_{10}$. Calculated: mol. wt. 486.

3. Isoolivins (VIII), 2',5-Dideuteroolivins (X), and Their Pentaacetates (IX) and (XI). A. A solution of 500 mg of olivin (Ia) in 50 ml of 0.1 N KOH was kept at 20°C in an atmosphere of argon for 1 h and was then acidified and extracted with ethyl acetate. The yield of isoolivin (VIII) was 363 mg (73%); mp 207-209°C (decomp., from ethyl acetate); $[\alpha]_D^{25} + 12^\circ$ (c 0.7; ethanol); λ_{\max} 231, 278, 327, 410 nm, ($\log \epsilon$ 4.35; 4.58; 3.71; 4.07); ν_{\max} 1515, 1610, 1640, 3400 cm^{-1} .

Found: mol. wt. 406. $C_{20}H_{22}O_8$. Calculated: mol. wt. 406.

The obtained isoolivin (VIII) was acetylated with a mixture of 2 ml of Ac_2O and 2 ml of Py (72 h at 20°C, and the product was worked up in the usual way and chromatographed in the benzene-acetone (5:1) system. The zone with R_f 0.17-0.28 yielded 221 mg (40%) of pentaacetylisoolivin (IX). After reprecipitation from tetrahydrofuran-ether-hexane, $[\alpha]_D^{25} + 44^\circ$ (c 0.7; benzene); λ_{\max} 222, 258, 301, 354 nm ($\log \epsilon$ 4.44; 4.81; 3.96; 3.64); ν_{\max} 1575, 1630, 1710, 1745, 1778, 3470 cm^{-1} ; δ 1.40 (3H, d, J 6.5; $3H_{5'}$), 2.09 (3H, s; $O_{4'}$ -Ac), 2.13 (3H, s; $O_{2'}$ -Ac), 2.32 (3H, s; O_6 -Ac), 2.39 (3H, s; O_8 -Ac), 2.51 (3H, s; O_9 -Ac), 3.52 (3H, s; $O_{1'}$ -Me), 3.65 (1H, t, J 10; $H_{1'}$), 4.48 (1H, d, J 12.5; H_2), 5.04 (1H' q, J 6.5; $H_{4'}$), 5.20 (1H, d, J 10; $H_{2'}$), 6.99 (1H, d, J 2; H_7), 7.42 (1H, d, J 2; H_5), 7.62 (1H, s; H_{10}).

Found: mol. wt. 616. $C_{30}H_{32}O_{14}$. Calculated: mol. wt. 616.

B. Under the conditions of experiment 3A, 500 mg of olivin (Ia) was isomerized with a solution of 115 mg of sodium in 5 ml of D_2O . The yield of dideuterioisoolivin (X) was 360 mg (72%). The pentaacetate (XI) had δ 1.42 (3H, d, J 6.5; $3H_{5'}$), 2.09 (3H, s; $O_{4'}$ -Ac), 2.15 (3H, s; $O_{2'}$ -Ac), 2.34 (3H, s; O_6 -Ac), 2.41 (3H,

s; O₈-Ac), 2.52 (3H, s; O₉-Ac), 3.54 (3H, s; O₁₁-Me), 3.70 (1H, d, J 10; H₁₁), 4.51 (1H, d, J 12.5; H₂), 5.06 (1H, q, J 6.5; H₄), 7.00 (1H, s; H₇), 7.56 (1H, s; H₁₀).

Found: mol. wt. 618. C₃₀H₃₀D₂O₁₄. Calculated: mol. wt. 618.

4. 3',4'-Isopropylideneisoolivin (XII) and Its Tetraacetate (XIII). A solution of 500 mg of isoolivin (VIII) in 40 ml of acetone containing 50 mg of H₂SO₄ was kept at 20°C for 2 h and was neutralized with dry NaHCO₃ poured into water, and extracted with ethyl acetate. The extract was chromatographed in the benzene-acetone system (5:1). The zone with R_f 0.66-0.86 yielded 324 mg of the acetone (XII). After crystallization from methanol, the yield was 280 mg (51%); mp 214-215°C (decomp.); [α]_D²⁵ + 45° (c 1; ethanol); λ_{max} 231, 278, 327, 410 nm (log ε 4.30; 4.53; 3.64; 4.01); ν_{max} 1520, 1590, 1640, 3400 cm⁻¹.

Found: mol. wt. 446. C₂₃H₂₆O₉·CH₃OH. Calculated: mol. wt. (without MeOH) 446.

The tetraacetate (XIII) was obtained by the action on (XII) of Ac₂O + Py (96 h at 20°C) with subsequent chromatography in the benzene-acetone (10:1) system. R_f 0.63; mp 218-219°C (from ethanol); [α]_D²⁵ + 11° (c 0.9 in benzene); λ_{max} 222, 258, 302, 354 nm (log ε 4.34; 4.76; 3.89; 3.55); ν_{max} 1570, 1630, 1697, 1745, 1770 cm⁻¹; δ 1.26 (3H, d, J 6; 3H₅), 1.52 (6H, s; Me₂C), 2.16 (3H, s; O₂-Ac), 2.33 (3H, s; O₆-Ac), 2.39 (3H, s; O₈-Ac), 2.51 (3H, s; O₉-Ac), 3.51 (3H, s; O₁₁-Me), 3.64 (1H, t, J 10; H₁₁), 4.51 (1H, d, J 12.5; H₂), 4.51 (1H, q, J 6; H₄), 5.04 (1H, d, J 10; H₂), 7.00 (1H, d, J 2; H₇), 7.49 (1H, d, J 2; H₅), 7.58 (1H, s; H₁₀).

Found: mol. wt. 614. C₃₁H₃₄O₁₃. Calculated: mol. wt. 614.

5. 3',4'-Isopropylidene-6,8,9-trimethylisoolivin (XIV) and 3',4'-Isopropylidene-2',6,8,9-tetramethylisoolivin (XV). A mixture of 500 mg of isopropylideneisoolivin (XII) and 5 ml of tetrahydrofuran was treated with 25 ml of a 1 M ethereal solution of CH₂N₂ (2 h at 20°C). Then the solvent was distilled off, and the residue was methylated with 2.5 ml of MeI and 30 mg of NaH in 1 ml of dimethyl sulfoxide (14 h at 20°C). The excess of NaH was decomposed with glacial AcOH, the mixture was diluted with water and extracted with ethyl acetate, and the substance extracted was chromatographed in the benzene-acetone (5:1) system. The zone with R_f 0.47-0.57 yielded 112 mg of the trimethyl ether (XIV). After recrystallization from ethanol, mp 119-120°C; [α]_D²⁵ - 20° (c 0.1; ethanol); λ_{max} 225, 271, 320, 334 and 365 nm (log ε 4.39; 4.64; 3.85; 3.94); ν_{max} 1572, 1622, 1710, 3470 cm⁻¹; δ 1.52 (3H; 3H₅), 1.55 (3H, s) and 1.58 (3H, s) (Me₂C), 3.73 (3H, s; O₁₁-Me), 3.92 (3H, s; O₆-Me), 3.97 (6H, s; O₈-Me and O₉-Me), 4.44 (1H, d, J 12.5; H₂), 4.58 (1H, q; J 7; H₄), 6.46 (1H, d, J 2.5; H₇), 6.59 (1H, d, J 2.5; H₅), 7.24 (1H, s; H₁₀).

Found: mol. wt. 488. C₂₆H₃₂O₉. Calculated: mol. wt. 488.

The zone with R_f 0.60-7.6 yielded 245 mg of the tetramethyl ether (XV). After recrystallization from ethanol, mp 196-197°C; [α]_D²⁵ - 4° (c 0.6; ethyl acetate); λ_{max} 225, 271, 325 and 362 nm (log ε 4.56; 4.77; 3.90; 4.00); ν_{max} 1570, 1620, 1698 cm⁻¹; δ 1.42 (3H, d, J 6.5; 3H₅), 1.50 (6H, s; Me₂C), 3.60 (3H, s; O₂-Me), 3.67 (3H, s; O₁₁-Me), 3.88 (3H, s; O₆-Me), 3.95 (6H, s; O₈-Me and O₉-Me), 4.43 (1H, d, J 13; H₂), 4.51 (1H, q, J 6.5; H₄), 6.43 (1H, d, J 2; H₇), 6.58 (1H, d, J 2; H₅), 7.23 (1H, s; H₁₀).

Found: mol. wt. 502. C₂₇H₃₄O₉·C₂H₅OH. Calculated: mol. wt. (without EtOH) 502.

6. 2',6,8,9-Tetramethylisoolivin (XVI). A solution of 30 mg of the acetone (XV) in 2 ml of methanol and 1.3 ml of 0.5 N HCl was heated at 80°C for 1 h, and after cooling, it was neutralized with dry NaHCO₃ and evaporated. The residue was extracted with ethyl acetate and chromatographed in the benzene-acetone (2:1) system. The zone with R_f 0.52-0.72 yielded 27 mg of tetramethylisoolivin (XVI). After crystallization from benzene, the mp of the substance was 192-193°C; [α]_D²⁵ + 5° (c 0.5; acetone); λ_{max} 225, 271, 335, 366 nm (log ε 4.56; 4.78; 3.92; 4.02); ν_{max} 1568, 1620, 1678, 3430, 3498 cm⁻¹; δ 1.38 (3H, d, J 6.5; 3H₅), 3.65 (3H, s; O₂-Me), 3.69 (3H, s; O₁₁-Me), 3.90 (6H, s; O₆-Me and O₈-Me), 3.94 (3H, s; O₉-Me), 4.50 (1H, d, J 13; H₂), 6.44 (1H, d, J 2.5; H₇), 6.58 (1H, d, J 2.5; H₅), 7.22 (1H, s; H₁₀).

Found: mol. wt. 462. C₂₄H₃₀O₉. Calculated: mol. wt. 462.

7. Lactone of 2'-Methoxy-6,8,9-trimethylhomoolivin Acid (XVII). A solution of 100 mg of tetramethylisoolivin (XVI) and 115 mg of Pb(OAc)₄ in 15 ml of benzene was kept for 30 min, filtered, washed with water, and evaporated. The residue was recrystallized from ethanol. The mother solution, by chromatography in the benzene-acetone (5:1) system, yielded an additional amount of the substance. The yield of the lactone (XVII) was 63 mg (70%); mp 206-207°C (decomp.); [α]_D²⁵ + 29° (c 0.35; benzene); R_f 0.57; λ_{max} 225, 271, 335, 366 nm (log ε 4.47; 4.74; 3.84; 3.97); ν_{max} 1570, 1620, 1710, 1755 cm⁻¹; δ 3.61 (3H, s; O₂-Me), 3.68 (3H, s; O₁₁-Me), 3.82 (1H, d, J 8; H₂), 3.94 (6H, s; O₆-Me and O₈-Me), 3.97 (3H, s; O₉-Me), 4.76 (1H, d, J 12; H₂), 6.47 (1H, d, J 2.5; H₇), 6.59 (1H, d, J 2.5; H₅), 7.23 (1H, s; H₁₀).

Found: mol. wt. 416. $C_{22}H_{24}O_8$. Calculated: mol. wt. 416.

8. Methyl 2'-Methoxy-6,8,9-trimethylhomoolivinate (XVIII). A solution of 1.00 g of the lactone (XVII) in 30 ml of a 1 N methanolic solution of HCl was kept at 20°C for 1 h and was then neutralized with dry $NaHCO_3$, poured into water, and extracted with ethyl acetate. After the evaporation of the extract the residue was chromatographed in the benzene-acetone (10:1) system. The zone with R_f 0.52-0.67 yielded 494 mg of the substance. After recrystallization from benzene-heptane, the yield of the hydroxy ester (XVIII) was 343 mg (33%); mp 127-128°C; $[\alpha]_D^{25} - 87^\circ$ (c 0.5; benzene); R_f 0.74 [benzene-acetone (5:1) system]; λ_{max} 225, 272, 334, 366 nm (log ϵ 4.37; 4.61; 3.79; 3.88); ν_{max} 1570, 1628, 1680, 1730, 3465 cm^{-1} ; δ 3.49 (3H, s; O_2 -Me), 3.63 (3H, s; O_1 -Me), 3.80 (3H, s; CO_2 Me), 3.91 (3H, s; O_6 -Me), 3.93 (3H, s; O_8 -Me), 3.97 (3H, s; O_9 -Me), 6.57 (1H, d, J 2.5; H_7), 6.73 (1H, d, J 2.5; H_5), 7.25 (1H, s; H_{10}).

Found: mol. wt. 448. $C_{23}H_{28}O_9$. Calculated: mol. wt. 448.

9. Methyl 2'-Methoxy-6,8,9-trimethyl-3,4-dehydrohomoolivinate 1,2-Quinone (XX). A solution of 100 mg of the hydroxy ester (XVIII) in 1 ml of MeSO and 1 ml of Ac_2O was kept at 20°C for 65 h and was then worked up as in experiment 2. After chromatography in the benzene-acetone (10:1) system, the substance from the zone with R_f 0.15-0.25 was crystallized from ethanol. The yield of the orthoquinone (XX) was 37 mg (37%); mp 204-205°C; $[\alpha]_D^{25} + 107^\circ$ (c 0.25; acetone); R_f 0.58 [benzene-acetone (5:1) system]; λ_{max} 223, 258, 302, 490 nm (log ϵ 4.35; 4.63; 4.59; 4.17); ν_{max} 1558, 1605, 1632, 1653, 1755 cm^{-1} ; δ [in $(CD_3)_2CO$ at 64°C]: 4.04 (1H, d, J 5; H_{27}), 4.61 (1H, d, J 5; H_{11}), 6.69 (1H, d, J 2.5; H_7), 9.2 (1H, d, J 2.5; H_5), 7.49 (1H, s; H_{10}), 7.67 (1H, s; H_4).

Found: m/e_{max} 446 (M+2). $C_{23}H_{24}O_9$. Calculated: mol. wt. 444.

The zone with R_f 0.46-0.54 yielded 29 mg (26%) of the methylthiomethyl ether (XIX); λ_{max} 226, 272, 332 and 366 nm (log ϵ 4.34; 4.61; 3.74; 3.84); $\nu_{max}^{CCl_4}$ 1576, 1623, 1700, 1745 cm^{-1} .

Found: mol. wt. 508. $C_{25}H_{32}O_9S$. Calculated: mol. wt. 508.

10. 2R,3R-Dimethoxysuccinic Acid (XXI). A. To 50 mg of the orthoquinone (XX) in 5 ml of purified acetone was added 6 ml of a 0.1 M acetone solution of $KMnO_4$, and the mixture was left at 20°C for 20 h. Then it was diluted with water, the acetone was driven off in vacuum, and the aqueous solution was filtered from MnO_2 and evaporated. The residue was heated with 1 ml of 10% KOH (3 h at 95°C), the solution was neutralized with KU-2 resin (H^+ form) and evaporated to dryness, and the residue was chromatographed in the benzene-acetone (1:1) system. The zone with R_f 0.35-0.50 yielded 9.5 mg of the dimethoxysuccinic acid (XXI); $[\alpha]_D^{25} + 69^\circ$ (c 0.2; acetone); R_f 0.55 [on paper in the $n-BuOH-H_2O-AcOH$ (4:5:1) system]. From its R_f values in adsorption and partition chromatography and its ORD curve, the substance was identical with the 2R,3R-dimethoxysuccinic acid described in experiment 10B.

The methylation of this acid with an excess of CH_2N_2 in ether followed by chromatography in the benzene-acetone (10:1) system gave 8.5 mg of the dimethyl ester (XXII); $[\alpha]_D^{25} + 65^\circ$ (c 0.05; benzene); R_f 0.54, V_{ret} 0.63 (relative to methyl stearate, 10% of polyethyleneglycol succinate on Chromosorb W, 150°C; for the meso isomer, V_{ret} 0.50).

B. The dimethyl ester of 2R,3R-dimethoxysuccinic acid (XXII) obtained from D-tartaric acid [9, 10] had $[\alpha]_D^{25} + 111^\circ$ (c 1, benzene); the acid (XXI) [10] had $[\alpha]_D^{25} + 92^\circ$ (c 0.6; acetone).

SUMMARY

The stereochemical correlation of olivin with chromomycinone and the directed degradation of the first of them to di-O-methyl-D-tartaric acid (XXI) has been effected. As a result, it has been shown that olivin and chromomycinone both have the absolute configuration 2S,3R,1'S,3'S,4'R and possess the respective structures (Ia) and (Ib).

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