OLIVOMYCIN AND RELATED ANTIBIOTICS

XXI. Periodate Oxidation of Olivin*

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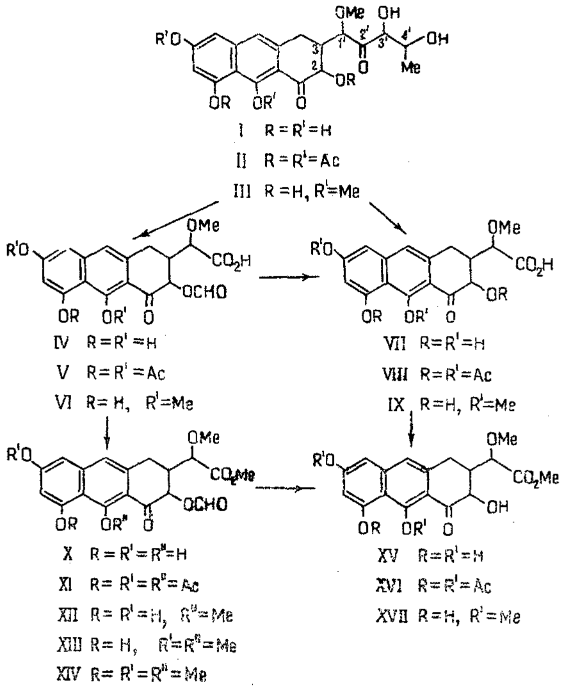
In one of the preceding communications [3], we described the periodate oxidation of olivin tetraacetate (II) to tetraacetylolivinic acid (VIII), the study of which has played an important role in determining the structure of the aglycone of the olivomycin antibiotics. Continuing this work, we undertook the analogous degradation of olivin (I) itself, with the aim of obtaining unacetylated olivinic acid (VII) as a suitable substance for the determination of the configurations of the three vicinal asymmetric centers at C_2, C_3, and $C_{1'}$ of olivin.

It was found that the oxidation of olivin (I) with sodium periodate under mild conditions (0° C, 5 min) consumes slightly more than 2 moles of IO_4^- and forms, in addition to acetaldehyde (0.9 mole) and formic acid (0.3 mole) the required olivinic acid (VII). The structure of the latter was shown by esterification with diazomethane in methanol (XV) with subsequent acetylation to give the previously-described [1] tetraacetate XVI. However, it was found that the yield of olivinic acid in this reaction did not exceed 20% and the main product of the oxidation of olivin was another acid (yield about 60%) with the structure IV. The presence in this compound of a O-formyl group was confirmed by alkaline hydrolysis with the formation of formic acid and olivinic acid (VII), and the position of the formate group was elucidated by the methylation with diazomethane of all the hydroxyls present in the molecule. Depending on the methylation conditions, a mono- (X), di- (XII), tri- (XIII), and tetramethyl (XIV) ether were obtained, their structures being established from their analytical and spectral characteristics.



Neither olivinic acid (VII) nor formyldivin (IV) is converted into the other under the conditions of their formation from olivin, as was established by special experiment. This shows that they are obtained as the result of independent routes of degradation of the initial molecule. Furthermore, it is obvious that in the periodate oxidation of olivin (I),

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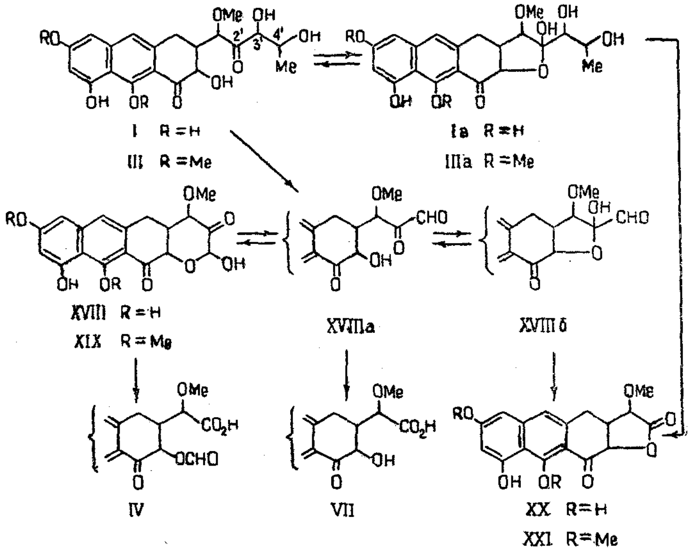
*For parts XIX and XX, see [1,2].

the only possible source of formic acid (both free and combined as the formate IV) is the $C_{3'}$ atom of the side chain. Consequently, the formation of the formate group in position 2 shows the intermediate attachment of the side chain through $C_{3'}$ to the hydroxyl at C_2.

It follows from this that the periodate oxidation of olivin (I) takes place in two stages, the first of which is the cleavage of the 3',4'-diol grouping with the formation of acetaldehyde and the hydroxyketoaldehyde XVIIIa. This hydroxyketoaldehyde, olivinal, then undergoes oxidation by a second mole of periodate to olivinic acid (VII) or cyclizes to form the semiacetal XVIII. The latter is oxidized to formylolivinic acid IV. It may also be assumed that a certain amount of olivinic acid is obtained as a result of the cleavage of olivin (I) at the $C_{2'}$—$C_{3'}$ bond; the lactaldehyde formed in this process is then oxidized to acetaldehyde and formic acid. As the ratio of the end-products of reaction shows, the over-all rate of the prototropic transformation XVIIIa → XVIII and the oxidative cleavage of the ketol grouping of the pyran ring, XVIII → IV, is substantially higher than the rate of oxidation of the α-ketoaldehyde XVIIIa. Thus, the course of the periodate oxidation of olivin is corrected by the participation in an intermediate stage of a "foreign" hydroxyl group, and because of C → O trans-formylation (see [4]) the formal correspondence between the consumption of periodate and the amount of volatile oxidation products formed is disturbed.

A direct proof of the correctness of the ideas put forward concerning the routes of the periodate oxidation of olivin (I) was the isolation from the reaction mixture of the primary product of oxidation, olivinal, which, under the further action of periodate, formed, in addition to a small amount of olivinic acid VII, formylolivinic acid (IV). This conversion, and also the spectral properties of olivinal, shows that olivinal consists mainly of a mixture of the 3'-epimeric semiacetals XVIII, the ketonic carbonyl in them begin hydrated to a considerable extent. In addition to this, it appeared likely that in protonic solvents olivinal exists not only in the pyranose and open forms XVIII$\rightleftarrows$XVIIIa but also in the furanose form XVIIIb, the oxidation of which (and also the direct oxidative cleavage of the C_2—C_3 bond in the semiketal form Ia of the initial olivin) must lead to the formation of the lactone of olivinic acid, olivinolide (XX). In actual fact, a careful chromatographic study of the products of the periodate oxidation of olivin and olivinal has shown the presence of a small amount of a γ-lactone ($\nu_{C=O}$ 1790 cm^{-1}), the structure of which as XX follows unambiguously from its conversion into olivinic acid on mild alkaline hydrolysis. Since the reverse reaction, the cyclization of olivinic acid VII into the lactone XX, takes place slowly even under severe conditions of acid catalysis (for example, on heating with p-toluenesulfonic acid in benzene–acetic acid solution) and is practically impossible under conditions of periodate oxidation, the formation of olivinolide (XX) confirms the existence of yet another route of the oxidative degradation of olivin (I): through the semiketal Ia and (or) XVIIIb.



Finally, it must be mentioned that the periodate oxidation of the 6,9-dimethyl ether of olivin (III) takes place in a manner completely analogous to that described above [3]. In this case dimethylolivinic acid (IX), its 2-formate (VI), its lactone (XXI), and dimethylolivinal (XIX) are formed, and under the further action of $NaIO_4$ compound XIX gives the formyloxy acid VI together with the hydroxy acid IX and its lactone XXI.

EXPERIMENTAL

Chromatography was carried out in a thin nonfixed layer of silica gel of the "vodnaya kremnevaya kislota" ["aqueous silicic acid"] type (activity grade III–IV). Where not specified otherwise, the molecular weights were determined mass-spectrometrically, the IR spectra were taken of the substances in the form of mulls in paraffin oil, the UV spectra were taken of solutions in 96% ethanol, and the NMR spectra of solutions in $CDCl_3$ at 60 MHz with Me_4Si as internal standard (s) singlet; d) doublet; t) triplet; m) multiplet).

The NMR spectra were measured by G. Yu. Pek, the mass spectrometric determinations of the molecular weights were performed by V. G. Zaikin, and the IR spectra were recorded by V. A. Krasnova.

1. **Periodate oxidation of olivin.** A) A solution of 1 g of olivin (I) in 30 ml of methanol at 0° C was treated with 230 ml of a 0.032 M solution of $NaIO_4$. The mixture was kept in the dark with cooling for 5 min and was then extracted with ethyl acetate, and the extract was washed with saturated NaCl solution, dried, and evaporated. The residue was chromatographed in the benzene–acetone (5 : 1) system.

The zone with R_f 0.15–0.27 yielded 540 mg of 2-formylolivinic acid (IV). After crystallization from tetrahydrofuran, the yield was 490 mg (53%), mp 218–220° C, $[\alpha]_D^{20}$ −108° (c 1; ethanol), R_f 0.65 (benzene–acetone–acetic acid (14 : 5 : 1)) system; λ_{max}, mμ: 230, 276, 325, 405 (log ε 4.32, 4.63, 3.67, 4.09); ν_{max}, cm^{-1}: 1512, 1590, 1633, 1736, 3370.

Found, %: C 57.2; H 4.8; mol. wt. 376. Calculated for $C_{18}H_{16}O_9$, %: C 57.5; H 4.3; mol. wt. 376.

The zone with R_f 0.35–0.55 yielded 44 mg (5%) of olivinolide (XX) with mp 227–234° C (decomp., from acetone); $[\alpha]_D^{20}$ −196° (c 0.3; methylcellosolve); λ_{max}, mμ: 230, 278, 326, 415, log ε 4.14, 4.51, 3.51, 4.06; ν_{max} 1520, 1593, 1647, 1790, 3400.

Found, %: C 60.5; H 4.4. Calculated for $C_{17}H_{14}O_7 \cdot 0.5\ H_2O$, %: C 60.3; H 4.4.

The substances present in the zone adjacent to the start were eluted with methanol and were rechromatographed in the benzene-acetone-methanol (15 : 5 : 2) system. The zone with R_f 0.43–0.54 yielded 34 mg (4%) of formylolivinic acid (IV), and the zone with R_f 0.36–0.40 yielded 124 mg (14%) of olivinic acid (VII) with mp 150–153° C (from acetonitrile); $[\alpha]_D^{20}$ +15° (c 1; ethanol); R_f 0.59 [benzene–acetone–acetic acid (14 : 5 : 1) system], λ_{max}, mμ: 231, 277, 326, 405 (log ε 4.28, 4.57, 3.55, 4.01); ν_{max}, cm^{-1} 1595, 1627, 1650, 1715, 3420.

Found, %: C 55.7; H 4.9; mol. wt. 348. Calculated for $C_{17}H_{16}O_8 \cdot H_2O$, %: C 55.7; H 5.0; mol. wt. (anhydrous) 348.

The zone with R_f 0.18–0.33 yielded 114 mg (13%) of olivinal (XVIII). After crystallization from acetone, decomp. p. 215° C; $[\alpha]_D^{25}$ −14° (c 0.7; ethanol); R_f 0.32 [benzene–acetone–ethanol (15 : 5 : 2) system]; λ_{max}, mμ 228, 277, 326, 407 (log ε 4.24, 4.53, 3.58, 4.01); ν_{max}, cm^{-1}: 1464, 1632, 1645, 3400; $\delta^{(CD_3)_2SO}$ 3.45 (3H, s, OMe), 4.4 (1H, d, J 10, $H_{1'}$), 5.10 (1H, s, $H_{3'}$), 5.20 (1H, d, J 12, H_2), 6.30 (1H, d, J 3, H_7), 6.45 (1H, d, J 3, H_5), 6.85 (1H, s, H_{10}).

Found, %: C 58.5; H 5.1. Calculated for $C_{18}H_{16}O_8 \cdot 0.5\ H_2O$, %: C 58.5; H 4.6.

B) Determination of the volatile oxidation products. A solution of 50 mg of olivin (I) in 3 ml of methanol was oxidized with sodium periodate under the conditions of Experiment 1A, and then 0.8 ml of a 0.05 M solution of Na_3AsO_3 and 5 ml of methanol were added, after which the volatile substances were distilled off at 10° C/40 mm into 15 ml of a 0.25% solution of 2,4-dinitrophenylhydrazine in 2 N H_2SO_4. This gave 20.3 mg (75%) of acetaldehyde dinitrophenylhydrazone with mp 147° C (in a control experiment, the yield of dinitrophenylhydrazone was 87%). The determination (calomel method) of the formic acid in the distillate after the periodate oxidation of olivin gave a figure of 0.25 mole/mole (in a control experiment 0.9 mole was found).

2. **Methylation of formylolivinic acid** (IV). A) A solution of 50 mg of the acid IV in 0.5 ml of tetrahydrofuran cooled to −50° C was treated with 4.5 ml of a 0.3 M solution of CH_2N_2 in ether–tetrahydrofuran. The reaction mixture was slowly evaporated, the residue was chromatographed in the benzene–acetone (10 : 1) system, and the substance isolated from the yellow zone was crystallized from chloroform. The yield of methyl formylolivinate (X) was 39 mg (72%); mp 107–109° C; $[\alpha]_D^{23}$ −121° (c 1; acetone); λ_{max}, mμ 231, 276, 324, 405 (log ε 4.10, 4.56, 3.44, 4.04); ν_{max}, cm^{-1}: 1539, 1488, 1645, 1731, 1753, 3295; $\nu_{C=O}^{THF}$, cm^{-1}: 1741, 1760.

Found, %: C 54.6; H 5.1; mol. wt. 390. Calculated for $C_{19}H_{18}O_9 \cdot 1.5\ H_2O$, %: C 54.7; H 5.0; mol. wt. (anhydrous) 390.

B) A solution of 80 mg of the acid IV in 2 ml of methanol was treated successively with two 1.6-ml portions of a 0.45 M ethereal solution of CH_2N_2, the reaction mixture being stirred at 20° C for 30 min each time. Then the solvent was distilled off and the residue was chromatographed as in Experiment 2A. This gave 9 mg of the ester X, R_f 0.60 [benzene–acetone (5 : 1) system] and 55 mg of methyl 2-formyl-9-methylolivinate (XII), R_f 0.54 (in the same system). After crystallization from ethanol, the yield of the ester-ether XII was 38 mg (44%); mp 226–228° C (decomp.); $[\alpha]_D^{23}$ −63° (c 1; acetone; λ_{max}, mμ: 226, 277, 332, 388 (log ε 4.40, 4.64, 3.64, 3.93); ν_{max}, cm^{-1}: 1570, 1628, 1677, 1752, 3375.

Found, %: C 59.2; H 5.0; mol. wt. 404. Calculated for $C_{20}H_{20}O_9$, %: C 59.4; H 5.0; mol. wt. 404.

C) 50 mg of the acid IV was methylated with 0.9 ml of a 0.84 M ethereal solution of CH_2N_2 and was then chromatographed as in Experiment 2B. This yielded 3 mg of the monoester X, 5 mg of the ester-ether XII and 39 mg of methyl 2-formyl-6,9-dimethylolivinate (XIII). After crystallization from ethanol, the yield of the ester-diether XIII was 18 mg (33%), mp 162° C; $[\alpha]_D^{23}$ −48° (c 1; chloroform); R_f 0.70 [benzene–acetone (5 : 1) system]; λ_{max}, mμ: 225, 275, 325, 382 (log ε 4.39, 4.68, 3.68, 3.85); ν_{max}^{KBr} cm^{-1}: 1570, 1607, 1638, 1686, 1756, 3260; $\nu_{C=O}^{THF}$, cm^{-1}: 1698, 1740, 1760; $\delta^{(CH_3)_2SO}$ 3.57 (3H, s, OMe), 3.77 (3H, s, arom. OMe), 3.85 (6H, s, arom. OMe + CO_2Me), 4.10 (1H, d, J 3, $H_{1'}$), 5.05 (1H, d, J 10.5, H_2), 6.50 (1H, d, J 2, $H_{7[5]}$), 6.75 (1H, d, J 2, $H_{[5(7)]}$), 7.40 (1H, s, CHO), 9.70 (1H, s, 8-OH).

Found, %: C 60.4; H 5.3; H_{act} 0.28; mol. wt. 418. Calculated for $C_{21}H_{22}O_9$, %: C 60.3, H 5.3; $1H_{act}$ 0.24; mol. wt. 418.

D) A mixture of the products obtained by the methylation of 50 mg of the acid IV with diazomethane at 20° C for 1.5 hr was chromatographed in the benzene–acetone (5 : 1) system. The zone with a blue fluorescence in UV light (R_f 0.65–0.70) yielded 38 mg of methyl 2-formyl-6,8-9-trimethylolivinate (XIV). After crystallization from ethanol, the yield of the ester XIV was 16 mg (28%); mp 136–138° C; $[\alpha]_D^{23}$ −69° (c 1; chloroform); λ_{max}, mμ: 225, 271, 329, 368 (log ε 4.48, 4.74, 3.87, 3.99); ν_{max}, cm^{-1}: 1568, 1622, 1690, 1733, 1753; $\nu_{C=O}^{THF}$ cm^{-1}: 1702, 1740, 1760; δ 3.47 (3H, s, OMe), 3.85 (3H, s, arom. OMe), 3.90 (6H, s, arom. OMe + CO_2Me), 3.97 (3H, s, arom. OMe), 4.15 (1H, d, J 3, $H_{1'}$), 5.70 (1H, d, J 12, H_2), 6.52 (1H, d, J 2, $H_{[7(5)]}$), 6.65 (1H, d, J 2, $H_{[5(7)]}$), 7.27 (1H, s, H_{10}).

Found, %: C 61.5, H 5.8; mol. wt. 432. Calculated for $C_{22}H_{24}O_9$, %: C 61.1; H 5.6; mol. wt. 432.

3. Periodate oxidation of olivinal (XVIII). With cooling, 3 ml of a 0.065 N solution of $NaIO_4$ was added to a solution of 12 mg of olivinal (XVIII) in 0.5 ml of methanol, and the mixture was kept in the dark at 10° C for 2 hr, the precipitate forming being dissolved by the gradual addition of cooled ethanol (a total of 5 ml). The reaction mixture was diluted twofold with water and was treated as in Experiment 1A. Chromatography in the benzene–acetone (5 : 1) system yielded 7 mg (57%) of formylolivinic acid (IV), identified in the form of the methyl ester (X) (see Experiment 2A), and also olivinic acid (VII) and olivinolide (XX), which were identified chromatographically.

4. Hydrolysis and methanolysis of formylolivinic acid (IV) and its ester (X). A) At 20° C, 10.5 ml of 0.1 N aqueous KOH was added to a solution of 100 mg of the acid IV in 2 ml of ethanol. After 15 min, the reaction solution was acidified with dilute H_2SO_4 to pH 3 and extracted with ethyl acetate, the extract was dried and evaporated, and the residue was crystallized from acetonitrile. This gave 75 mg (81%) of olivinic acid (VII) with mp 152–155° C; $[\alpha]_D^{20}$ +16° (c 1; ethanol). In a parallel experiment, the acidified reaction solution was treated with activated carbon and filtered: on analysis by the calomel method, 89% of formic acid was found.

B) 50 mg of the exter X was dissolved at 20° C in 5 ml of 0.1 N methanolic MeONa. After 15 min, the solution was treated as in Experiment 4A, and the substance obtained was crystallized from ethanol. The yield of methyl olivinate (XV) was 30 mg(66%); mp 215–217° C; $[\alpha]_D^{24}$ −10° (c 1; ethanol); R_f 0.53 [benzene-acetone (5: 1) system]; λ_{max}, mμ: 230, 276, 325, 405 (log ε 4.21, 4.58, 3.69, 4.16); ν_{max}^{KBr}, cm^{-1}: 1588, 1629, 1645, 1727, 1744, 3290, 3420; $\nu_{C=O}^{THC}$, cm^{-1}: 1741, 1760.

Found, %: C 59.5; H 5.1; mol. wt. 362. Calculated for $C_{18}H_{18}O_8$, %: C 59.7; H 5.0; mol. wt. 362.

The same substance was obtained from olivinic acid (VII) and 1 mole of CH_2N_2 at 0° C; after chromatography in the benzene–acetone (10 : 1) system and crystallization from methanol; the yield was 68%.

5. Acetylation of formylolivinic acid (IV), its ester (X), and the ester of olivinic acid (XV). A) 10 mg of the acid IV was dissolved at −20° C in 0.1 ml of pyridine and 0.1 ml of acetic anhydride. The mixture was left at −10° C for 24 hr and was then diluted with 0.5 ml of methanol, kept at 20° C for 1 hr., and evaporated. The residue was dissolved in chloroform and the solution was washed with 1 N H_2SO_4 and with water, and was dried and reevaporated. After crystallization from methanol, 12 mg (90%) of triacetylformylolivinic acid (V) was obtained; mp 127–129° C; $[\alpha]_D^{22}$ − 56° (c 1; chloroform); R_f 0.22; [benzene–acetone (5 : 1) system]; λ_{max}, mμ: 220, 259, 304, 358 (log ε 4.35, 4.73, 3.83, 3.54); ν_{max}, cm^{-1}: 1570, 1630, 1695, 1730, 1760, 1775, 3220, 3530, 3620.

Found, %: C 56.5; H 4.6. Calculated for $C_{24}H_{22}O_{12} \cdot 0.5\ H_2O$, %: C 56.3; H 4.5.

The ester (XI) was obtained by the methylation of the acid V with diazomethane in ether–tetrahydrofuran solution. Yield 84%; mp 172–172.5° C (from ethanol); $[\alpha]_D^{20}$ −71° (c 0.7; chloroform); R_f 0.61 [benzene–acetone (5 : 1) system]; λ_{max}, mμ; 220, 259, 304, 360 (log ε 4.43, 4.80, 3.88, 3.62); ν_{max}, cm^{-1}: 1575, 1630, 1700, 1730, 1755 cm^{-1}; δ 2.37 (3H, s, OAc), 2.45 (3H, s, OAc), 2.55 (3H, s, OAc), 3.52 (3H, s, alip. OMe), 3.90 (3H, s, CO_2Me), 4.17 (1H, d, J 3, $H_{1'}$), 5.80 (1H, d, J 12, H_2), 7.15 (1H, d, J 2, H_7), 7.60 (1H, d, J 2, H_5), 7.70 (1H, s, H_{10}), 8.50 (1H, s, CHO).

Found, %: C 57.9; H 4.8 mol. wt. 516. Calculated for $C_{25}H_{24}O_2$, %: C 58.1; H 4.7; mol. wt. 516.

B) The acetylation of the ester X with Ac_2O + Py (7 hr at 20° C) gave the triacetate XI described in the preceding experiment, with a yield of 69%.

C) Acetylation of the ester XV under the conditions of experiment 5B gave the tetraacetate XVI with a yield of 60%: mp 173–173.5° C (from ethanol); $[\alpha]_D^{22}$ −48.5° (c 1; chloroform); R_f 0.61 [benzene–acetone (5 : 1) system] (see [3]).

6. Periodate oxidation of dimethylolivin (III). A solution of 100 mg of dimethylolivin (III) in 15 ml of methanol was mixed at −15° C with 15 ml of a 0.06 M solution of $NaIO_4$. After 5 min at 0° C, the reaction mixture was diluted with water and extracted with ethyl acetate and the substance extracted was chromatographed in the benzene–acetone–methanol (15 : 5 : 2) system. The zone with R_f 0.76–0.85 yielded 10 mg (12%) of dimethylolivinolide (XXI); mp 169–175° C (from ethanol); $[\alpha]_D^{20}$ −146° (c 0.2; chloroform; λ_{max}, mμ: 226, 275, 326, 378 (log ε 4.32, 4.67, 3.37, 3.87); ν_{max}, cm^{-1}: 1570, 1640, 1708, 1793, 3320. Found: mol. wt. 358. Calculated for $C_{19}H_{18}O_7$: mol. wt. 358.

The zone with R_f 0.64–0.73 yielded 24 mg (25%) of dimethylformylolivinic acid (VI)* with mp 186–190° C (from ethanol); $[\alpha]_D^{20}$ −27° (c 1; ethanol); λ_{max}, mμ: 225, 276, 328, 382 (log ε 4.31, 4.60, 3.63, 3.75); ν_{max}, cm^{-1}: 1568, 1636, 1700, 1730, 3300.

Found, %: C 59.2; H 5.1; mol. wt. 404. Calculated for $C_{20}H_{20}O_9$, %: C 59.5, H 5.0; mol. wt. 404.

The zone with R_f 0.50–0.62 yielded 15 mg (17%) of dimethylolivinic acid (IX); mp 178–185° C (from ethyl acetate); $[\alpha]_D^{23}$ +70° (c 1; ethanol); λ_{max}, mμ: 224, 275, 325, 378 (log ε 4.41, 4.72, 3.76, 3.86); ν_{max}, cm^{-1}: 1573, 1640, 1750, 3330.

Found, %: C 60.2; H 5.5; mol. wt. 376. Calculated for $C_{19}H_{20}O_8$, %: C 60.6; H 5.4; mol. wt. 376.

The action of diazomethane on the acid IX gave methyl dimethylolivinate (XVII), R_f 0.62 [benzene–acetone (5 : 1) system].

The zone with R_f 0.22–0.47 yielded 36 mg (40%) of dimethylolivinal (XIX); mp 144–147° C (from benzene–acetone); $[\alpha]_D^{20}$ − 66° (c 0.75; chloroform); λ_{max}, mμ: 226, 274, 330, 374 (log ε 4.34, 4.58, 3.61, 3.73); ν_{max}, cm^{-1}: 1567, 1617, 1635, 1687, 3400; $\delta^{(CD_3)_2SO}$ 2.88–3.10 (3H, m, H_3 + $2H_4$), 3.50 (3H, s, alip. OMe), 3.87 (3H, s, ar. OMe), 4.02 (3H, s, ar. OMe), 4.20 and 4.45 (1H, 2d, J 10, $H_{1'}$), 4.96 and 5.02 (1H, 2d, J 12.5, H_2), 5.13 and 5.31 (1H, 2s, $H_{3'}$), 6.47 and 6.57 (1H, 2d, J 3, $H_{[7(5)]}$), 6.77 and 6.82 (1H, 2d, J 3, $H_{[5(7)]}$), 7.41 (1H, s, H_{10}), 7.92 (1H, s, 3'-OH), 10.03 (1H, s, 8-OH).**

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*When the oxidation of dimethylolivin was carried out in 10% MeOH, the yield of the acid VI rose to 56%.

**The substance is a mixture of 3'-epimers, in consequence of which some of the protons are represented in its NMR spectrum by two signals with intensities in the ratio 2 : 1.

Found: mol. wt. 358. Calculated for $C_{19}H_{18}O_7$: mol. wt. 358.

When dimethylolivinal was oxidized with periodate under the conditions of Experiment 3, the main product was dimethylformylolivinic acid (VI), together with very small amounts of the acid IX and the lactone XXI.

7. Hydrolysis and esterification of dimethylformylolivinic acid (VI). A) The acid VI (150 mg) was hydrolyzed under the conditions of Experiment 4A. This gave 101 mg (71%) of dimethylolivinic acid (IX), which has been described in Experiment 6.

B) at 20° C, 65 mg of the acid VI was treated with 1 mole of CH_2N_2 in ether–tetrahydrofuran solution. After chromatography in the benzene–acetone (5 : 1) system and crystallization from ethanol, 22 g (33%) of the ester XIII with mp 159–162° C described in Experiment 2C, was obtained.

CONCLUSIONS

The oxidation of olivin (I) by periodate takes place by three alternative routes, two of which include the stage of the intermediate formation of a cyclic semiacetal with the participation of the 2-OH hydroxyl and a 3'-CO or 2'-CO carbonyl group. As a result of this, the oxidative degradation of the dihydroxyketonic grouping of the side chain to form a carboxyl group is accompanied by intramolecular O_2-formylation and lactonization, giving as the main product 2-O-formylolivinic acid (IV), together with olivinic acid (VII), and its lactone (XX).

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