UNSATURATED ACIDS AND MACROCYCLIC LACTONES

COMMUNICATION 14.* CONFIGURATION OF meso-2,4-DIMETHYL-1,3,5-PENTANETRIOL AND OT THE ASYMMETRIC CENTER AT C_3 IN ERYTHROMYCIN AND OLEANDOMYCIN†

(UDC 547.9+541.632)

S. G. Batrakov and L. D. Bergel'son

Institute for the Chemistry of Natural Products, Academy of Sciences, USSR
Translated from Izvestiya Akademii Nauk SSSR, Seriya Khimicheskaya, No. 9, pp. 1640-1648, September, 1964
Original article submitted February 26, 1964

In connection with the work being carried out in our laboratory on the absolute configuration of macrolidic antibiotics it was necessary to establish the configuration of meso-2,4-dimethyl-1,3,5-pentanetriol (IV). This triol, which was isolated in the cleavage of the macrolidic antibiotic erythromycin (I) [2] (see scheme 1), was formed from $C_{(1)}$–$C_{(5)}$ section of the carbon chain of the corresponding aglycon – erythronolide (Ia). The authors, who studied the structure of erythromycin, proved that this triol has one of two possible meso configurations ("ribo" or "xylo"). However, their decision in favor of the "xylo" configuration on the sole grounds that the precursor of the triol (IV) – the β-hydroxy δ-lactone (III) – is stable under dehydration conditions cannot be regarded as sufficiently convincing. The same authors carried out an independent synthesis of the meso triol (IV) by the lithium aluminum hydride reduction of the crystalline meso isomer of 3-hydroxy-2,4-dimethylglutaric acid (VII), which was prepared earlier by Reformatskii [3]. Recently, the same acid was isolated as a product of the oxidative cleavage of the macrolidic antiobiotic oleandomycin (II) [4], and in this case also it was formed from the $C_{(1)}$–$C_{(5)}$ fragment of the carbon chain of the corresponding aglycon. Hence, the establishment of the configuration of meso-2,4-dimethyl-1,3,5-pentanedione (IV), and therefore also of the corresponding meso-3-hydroxy-2,4-dimethylglutaric acid (VII), would enable us to prove the absolute configuration at C_3 in the erythromycin molecule and the relative configurations of the asymmetric centers at C_2, C_3, and C_4 in the oleandomycin molecule.

To prove the configurations of the compounds (IV) and (VII) we decided to convert the triol (IV) into a simpler compound with two asymmetric centers and establish its configuration by independent stereospecific synthesis. With this object the triol (IV)‡ (see scheme 1) was converted into the 1,3-O-isopropylidene derivative (V), the tosylate of which (VIII), as a result of lithium aluminum hydride hydrogenolysis and subsequent acid hydrolysis, gave one of the isomeric 2,4-dimethyl-1,3-pentanediols (IXa). To determine the configuration of this diol we carried out the stereospecific synthesis of the two possible diastereoisomeric 2,4-dimethyl-1,3-pentanediols from cis- and trans-2,4-dimethyl-2-pentenoic acids** (Xa) and (Xb) (see scheme 2).

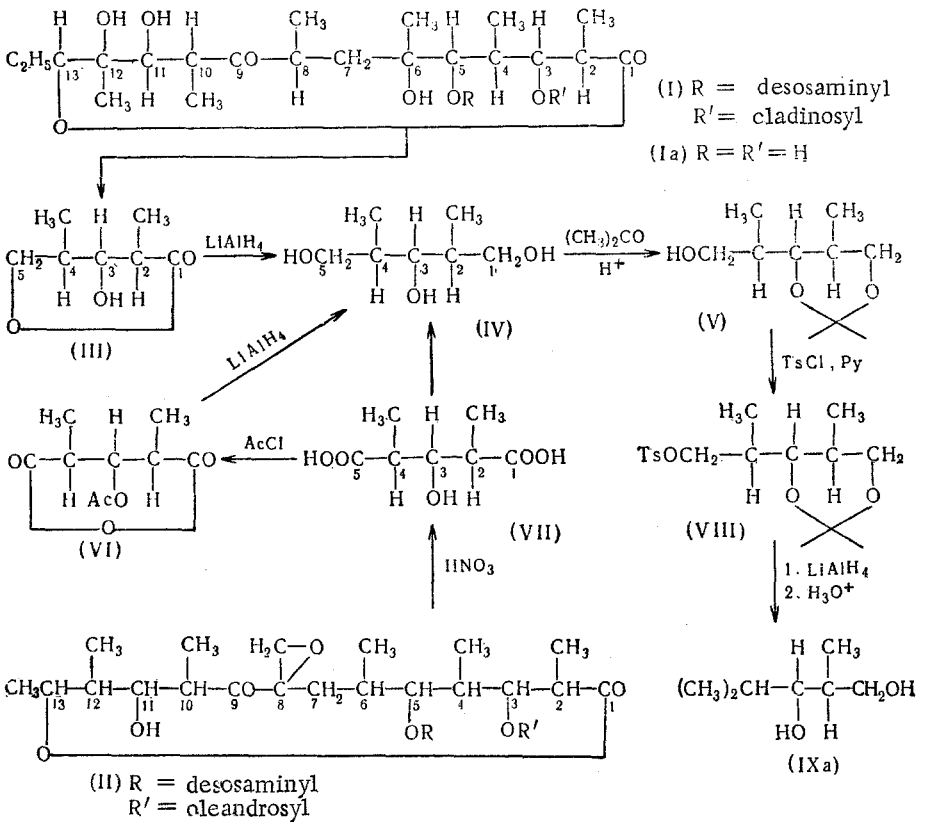
We prepared the "trans" acid (Xb) by the Reformatskii condensation of isobutyraldehyde with ethyl 2-bromopropionate with hydrolysis and dehydration of the condensation product obtained. According to gas-liquid chromatography there is then formed a mixture of "trans" and "cis" acids containing not less than 90% of the "trans" isomer. By the fractional distillation of this mixture we isolated the pure "trans" isomer, m. p. 29-30°. The methyl

*For Communication 13 see [1].

† This article is published in accordance with a resolution of the Conference of Chief Editors of Journals of the Academy of Sciences of the USSR, July 12, 1962, as a dissertation paper by S. G. Batrakov.

‡ At first we prepared the triol (IV) by a previously described method [2], i.e., by the lithium aluminum hydride reduction of the solid isomer of 3-hydroxy-2,4-dimethylglutaric acid (VII), but it was later found that the same triol is obtained in a purer form and in higher yield by the reduction of 3-acetoxy-2,4-dimethylglutaraldehyde [3] with lithium aluminum hydride.

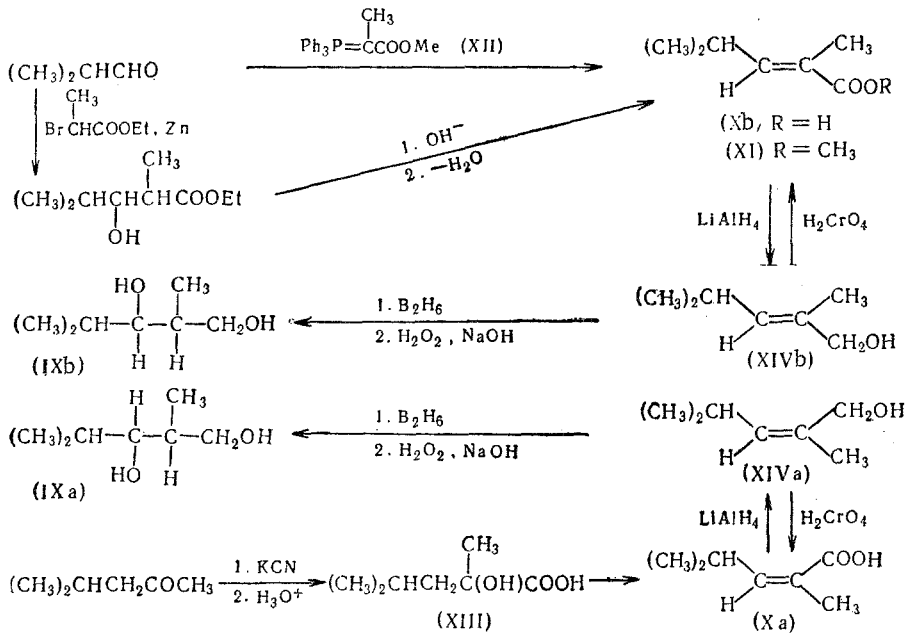
** The denotations "cis" and "trans" are applied to α-methyl α,β-unsaturated acids in accordance with the principle generally adopted for tiglic ("tran") and angelic ("cis") acids.



ester (XI) of this "trans" isomer was prepared also by Wittig reaction between isobutyraldehyde and methyl 2-(triphenylphosphoranylidene)propionate (XII). It was shown previously that the phosphorylid (XII) reacts with aldehydes stereospecifically with selective formation of "trans" isomers [5]. We prepared "cis"-2,4-dimethyl-2-pentenoic acid (Xa) by the pyrolytic dehydration of 2-hydroxy-2,4-dimethylpentanoic acid (XIII) (cf. [6]). The configurations of the two isomers (Xa) and (Xb) were finally established by a comparison of their ultraviolet spectra and dissociation constants. It is known that "trans" acids of the tiglic type are characterized by more intense absorption in the ultraviolet and higher dissociation constants than their "cis" isomers [7-11]. Comparison of the extinction coefficients and pK_a values of the acids (Xa) and (Xb) with the corresponding constants of analogous stereoisomeric acids of known configuration (see table) proves that the first is the "cis" and the second the "trans" isomer.

For the synthesis of the diol (IXa) and its stereoisomer (IXb) the isomeric acids (Xa) and (Xb) were reduced with lithium aluminum hydride to the corresponding allyl alcohols (XIVa) and (XIVb). The structures of the latter were proved by their oxidation into the above acids (Xa) and (Xb) with chromic acid in acetone [12]. Both alcohols (XIVa) and (XIVb) were then subjected to hydroboration by Brown's method [13] with subsequent oxidation of the borate complexes with alkaline hydrogen peroxide. It is known that Brown hydration goes in the direction opposite to that required by Markovnikov's rule [13]. In good accord with these data the α-glycol content of the products of the hydration of "cis"- and "trans"-2,4-dimethyl-2-penten-1-ols (XIVa) and (XIVb),* judging from the results of periodate oxidation, did not exceed 15-18%. It has been shown on a number of occasions that in the reaction of diborane with olefins the "cis" addition of the elements of the boron hydride occurs and the subsequent oxidation goes with preservation of configuration [14-17]. From this it follows that the hydration of the "trans" alcohol (XIVb) should lead to "erythro"-2,4-dimethyl-1,3-pentanediol,and, correspondingly, the hydration of the "cis" alcohol (XIVa) – to the "threo" isomer. By the Brown hydration of these alcohols we obtained the following results. The "trans" alcohol (XIVb) gave liquid 2,4-dimethyl-1,3-pentanediol (IXb), the bis-3,5-dinitrobenzoate and bis-p-nitrobenzoate of which differed from the corresponding derivatives of the diol (IXa) prepared from meso-2,4-dimethyl-1,3,5-pentanetriol (IV); on the other hand, by the hydration of the "cis" alcohol (XIVa) we obtained the solid "threo" diol, identical to the diol (IXa).

*We freed the mixture of diols from admixture of α-diols by treatment with periodic acid.



Ultraviolet Spectral Data for α-Methyl α,β-Unsaturated Acids and Their Methyl Esters (in alcohol) and the pK_a Values of the Acids (in water)

Acid	For acid		For ester		pH_a of acid
	λ_{max}, mμ	ε	λ_{max}, mμ	ε	
Tiglic	212	13500 [8]	–	–	5.05 [9]
Angelic	216	9500 [8]	–	–	4.30 [9]
trans-2-Methyl-2-pentenoic	216	10092 [9]	220	12700 [11]	5.00 [9]
cis-2-Methyl-2-pentenoic	216	6770 [9]	216	7500 [11]	4.35 [9]
trans-2-Methyl-2-hexenoic	–	–	214	12380 [11]	5.13 [7]
cis-2-Methyl-2-hexenoic	–	–	212	7600 [11]	4.44 [7]
trans-2,4-Dimethyl-2-] pentenoic (Xb)	215	12400	217	11500	5.00
cis-2,4-Dimethyl-2-pentenoic (Xa)	215	9100	216	7420	4.33

Since epimerization in the course of the conversion of the triol (IV) into the diol (IXa) is excluded, the relative configuration of the asymmetric centers at C_3 and C_2 (or C_4) in the triol (IV) must correspond to the relative configuration of the asymmetric centers in the diol (IXa), from which it follows that meso-2,4-dimethyl-1,3,5-pentanetriol (IV) obtained in the degradation of erythromycin (I) and the solid isomer of 3-hydroxy-2,4-dimethylglutaric acid (VII) correspond to the "xylo" configuration represented in scheme 1. In the degradation of erythromycin (I) the triol (IV) is formed from the $C_{(1)}-C_{(5)}$ section of the carbon chain of erythronolide (Ia) [2], and as it is known that the asymmetric center at C_2 of the latter has the S configuration [2], the adjacent asymmetric center at C_3 must have the R configuration, assumed tentatively on the basis of indirect data. As regards the configuration of the asymmetric centers at C_2, C_3, and C_4 in oleandomycin (II), it must correspond to the relative configuration of the same centers in meso-3-hydroxy-2,4-dimethylglutaric acid (VII), for the latter is formed from the $C_{(1)}-C_{(5)}$ section of the carbon chain of the aglycon of oleandomycin. It was thus proved that the $C_{(1)}-C_{(5)}$ section of the oleandomycin molecule has a "xylo" configuration.

EXPERIMENTAL

Melting points were determined in capillaries and are not corrected. Ultraviolet spectra were determined on an SF-4 spectrophotometer (solvent 95% alcohol). Potentiometric titrations were carried out with an SBR-2c "Radiometer" titrograph; for titration we used 0.01 M aqueous solutions of the acids investigated.

meso-2,4-Dimethyl-1,3,5-pentanetriol (IV). By a continuous-extraction method, 20.0 g of meso-3-acetoxy-2,4-dimethylglutaric anhydride (VII) was added in the course of four hours to a solution of 250 mmoles of $LiAlH_4$ in 2000 ml of ether [2, 3]. The mixture was then boiled with stirring for 12 h more, after which it was cooled to 5°, excess of $LiAlH_4$ was decomposed with water, and 25% sodium hydroxide solution was added until a crystalline precipitate formed. The latter was filtered off and washed on the filter with 500 ml of ether; the combined filtrates were dried with $MgSO_4$. Ether was driven off, and we obtained 5.33 g (36%) of the meso triol (IV), m. p. 78-80°. The literature [2] gives m. p. 78-80°.

3,5-(Isopropyldienedioxy)-2,4-dimethyl-1-pentanol (V). 20 g of anhydrous $MgSO_4$ powder was added to a solution of 5.1 g of the meso triol (IV) in 250 ml of dry acetone containing 200 mg of p-toluenesulfonic acid, and the mixture was shaken for 48 h at 20°; for neutralization it was then shaken with $PbCO_3$. The precipitate was filtered off and washed with acetone; the combined filtrates were evaporated, and the liquid residue remaining after the removal of acetone was vacuum-distilled. We obtained 5.6 g (87%) of (V); b. p. 110-112° (10 mm); n_D^{25} 1.4528, d_4^{25} 1.0053. Found: C 63.58; H 10.75%. $C_{10}H_{20}O_3$ Calculated: C 63.79; H 10.71%.

3,5-Dinitrobenzoate: m. p. 83-84° (from absolute alcohol). Found: N 7.47%. $C_{17}H_{22}N_2O_8$. Calculated: N 7.33%.

3,5-(Isopropylidenedioxy)-2,4-dimethyl-1-pentanol tosylate (VIII). 5.43 g of p-toluenesulfonyl chloride was added to a solution of 5.1 g of the isopropylidene derivative (V) in 20 ml of dry pyridine at 10°. The mixture was shaken until the p-toluenesulfonyl chloride had dissolved completely and then left for one day at 20°, after which it was poured into 25 ml of water and acidified with cooling to 0-5° with 5% hydrochloric acid to pH 1. The crystalline precipitate formed was filtered off and dissolved in 50 ml of ether. The ethereal solution was washed with 5% sodium carbonate solution and water, and was dried with $MgSO_4$. Ether was driven off, and we obtained 8.2 g (88%) of the tosylate (VIII), m. p. 90.5-91° (from hexane). Found: C 59.62; H 7.78; S 9.33%. $C_{17}H_{26}O_5S$. Calculated: C 59.63; H 7.65; S 9.35%.

threo-2,4-Dimethyl-1,3-pentanediol (IXa). A solution of 10 mmoles of $LiAlH_4$ in 10 ml of dry tetrahydrofuran was added to a solution of 1.0 g of the tosylate (VIII) in 5 ml of tetrahydrofuran. The mixture was boiled for five hours; it was cooled, excess of $LiAlH_4$ was decomposed with acetone, and saturated ammonium chloride solution and anhydrous $MgSO_4$ were added. The precipitate was filtered off and washed with ether, and the combined filtrates were washed with water and dried with $MgSO_4$. Solvents were driven off, and the liquid residue was dissolved in a mixture of 5 ml of methanol and 1 ml of concentrated hydrochloric acid. The mixture was left for 12 h at 20°, after which it was evaporated down to 1.5 ml, diluted with 10 ml of water, and extracted with four 10 ml portions of ether. The combined ether extracts were washed with 10% KOH solution and water, and were dried with $MgSO_4$. Ether was driven off, and we obtained 220 mg of oily threo diol (IXa), which crystallized on standing at 0°; m. p. 53.5-54.5° (from a mixture of hexane and dipropyl ether). Found: C 63.79; H 12.22%. $C_7H_{16}O_2$. Calculated: C 63.59; H 12.20%.

Bis-p-nitrobenzoate: m. p. 114-115° (from a mixture of absolute alcohol and butanone). Found: C 58.72; H 5.05; N 6.83%. $C_{21}H_{22}N_2O_8$. Calculated: C 58.60; H 5.15; N 6.51%. Bis-3,5-dinitrobenzoate: m. p. 137-138° (from a mixture of absolute alcohol and butanone). Found: C 48.64; H 3.88; N 10.96%. $C_{21}H_{20}N_4O_{12}$. Calculated: C 48.46; H 3.85; N 10.77%.

2-Hydroxy-2,4-dimethylpentanoic acid (XIII). 180 ml of 40% H_2SO_4 was added with vigorous stirring at 10-15° in the course of 2.5 h to a mixture of 108 g of 4-methyl-2-pentanone, 51.3 g of KCN, and 125 ml of water, after which stirring was continued further for 40 min. The organic layer was then separated, 200 ml of concentrated hydrochloric acid was added, and the mixture was boiled for ten hours with stirring; it was then cooled, diluted with 100 ml of water, and extracted with three 200 ml portions of methylene chloride. The combined extracts were washed with saturated NaCl solution, methylene chloride was driven off, and the crystalline residue was recrystsllized from benzene. We obtained 71 g (55%) of the hydroxy acid (XIII), m. p. 89.5-90°. Found: C 57.68; H 9.56%. $C_7H_{14}O_3$. Calculated: C 57.51; H 9.65%.

cis-2,4-Dimethyl-2-pentenoic acid (Xa). 67 g of the acid (XIII) was distilled at atmospheric pressure at a bath temperature of 245-260°, the distillate was dissolved in 200 ml of ether, water was separated, and the ethereal

solution was dried with $MgSO_4$. The liquid residue remaining after the removal of ether was vacuum-distilled with collection of a fraction (27.6 g) that came over in the range 96-102° (9 mm); n_D^{20} 1.4492. To separate the α,β-unsaturated acid (Xa) from the β,γ isomer we used the idolactonization method [18]. For this purpose the distillate was dissolved in 400 ml of saturated $NaHCO_3$ solution, and to this solution we added a solution of 91 g of iodine and 147 g of potassium iodide in 450 ml of water. The mixture was shaken for 15 min and then decolorized by the addition of sodium thiosulfate; it was washed with two 200 ml portions of ether, acidified to pH 1 with 50γ H_2SO_4, and extracted with three 300 ml portions of ether. The combined ether extracts were washed with saturated NaCl solution and dried with $MgSO_4$. The liquid residue remaining after the removal of ether was vacuum-distilled. We obtained 24.0 g (41%) of the cis acid (Xa); b. p. 97-98° (9 mm); n_D^{20} 1.4492. Ultraviolet spectrum – see table. Found: C 73.88; H 12.55%. $C_7H_{12}O_2$. Calculated: C 73.63; H 12.36%. p-Phenylphenacyl ester: m. p. 72-73° (from alcohol). Found: C 78.37; H 7.02%. $C_{21}H_{22}O_3$. Calculated: C 78.23; H 6.88%.

Treatment of an ethereal solution of the acid (Xa) with ethereal diazomethane at 0° gave its methyl ester; b. p. 58-59° (23 mm); n_D^{20} 1.4328. Ultraviolet spectrum – see table. Found: C 67.52; H 9.97%. $C_8H_{14}O_2$. Calculated: C 67.57; H 9.93%.

trans-2,4-Dimethyl-2-pentenoic acid (Xb). A mixture of 913.7 g of ethyl 2-bromopropionate and 50.4 g of isobutyraldehyde was added with stirring to 70 g of zinc turnings in 300 ml of boiling benzene at such a rate that a gentle boil was maintained. The mixture was boiled further with stirring for two hours, and it was then cooled to 10° and 10% H_2SO_4 was added until the precipitate formed initially had dissolved completely. The organic layer was separated, the aqueous layer was extracted with two 200 ml portions of ether, and the combined extracts were washed with water, 5% sodium carbonate solution, and again water, and were dried with $MgSO_4$. The liquid residue remaining after the removal of solvents was vacuum-distilled. A solution of 55 g of KOH in 600 ml of water was added to the fraction of b. p. 87-107° (10 mm). The mixture was stirred for four hours at 20° and then for 20 h at 65°; when cool, it was washed with two 200 ml portions of ether, acidified to pH 1 with 50% H_2SO_4, and extracted with four 200 ml portions of ether. The combined ether extracts were washed with saturated NaCl solution and dried with $MgSO_4$. The oily residue remaining after the removal of ether was distilled at atmospheric pressure at a bath temperature of 240-260°. The distillate was dissolved in 250 ml of ether, water was separated, and the ethereal solution was dried with $MgSO_4$. The oily residue remaining after the removal of ether was vacuum-distilled with collection of the fraction (38.4 g) of b. p. 106-114° (11 mm); n_D^{20} 1.4630. The latter was dissolved in saturated $NaHCO_3$ solution, a solution of 101.7 g of iodine and 164.7 g of potassium iodide in 480 ml of water was added, and the mixture was shaken for 15 min; sodium thiosulfate was added to decolorize the mixture, which was then washed with two 200 ml portions of ethers, acidified to pH 1 with 50% H_2SO_4, and extracted with three 300 ml portions of ether. The combined ether extracts were washed with saturated sodium chloride solution and dried with $MgSO_4$. The liquid residue remaining after the removal of ether was vacuum-distilled. The fraction of b. p. 108-109° (10 mm) and n_D^{20} 1.4532 (32.6 g) was dissolved in hexane at 20°, and the solution was left for ten hours at −50°. By filtration we isolated 28.1 g of the trans acid (Xb), m. p. 29-30°. Ultraviolet spectrum – see table. Found: C 65.83; H 9.32%. $C_7H_{12}O_2$. Calculated: C 65.59; H 9.44%. The p-phenylphenacyl ester of the acid (Xb) had a double melting point: 40-50° and 61-62° (from alcohol). Found: C 78.52; H 6.90%. $C_{21}H_{22}O_3$. Calculated: C 78.23; H 6.88%.

By treating the acid (Xb) with the equivalent amount of ethereal diazomethane at 0° we obtained its methyl ester (XI); b. p. 49-50° (10 mm); n_D^{20} 1.4384. Ultraviolet spectrum – see table. Found: C 67.38; H 9.95%. $C_8H_{14}O_2$. Calculated: C 67.57; H 9.93%.

A solution of 6.04 g of isobutyraldehyde and 29.2 g of the phosphorane (XII) [19] in 100 ml of dry benzene was boiled for six hours in an atmosphere of nitrogen, after which benzene was driven off and the partially crystallized residue was extracted with petroleum ether. The liquid residue remaining after the removal of petroleum ether was vacuum-distilled. We obtained 9.54 g (80%) of the methyl ester (XI); b. p. 58-60° (13 mm); n_D^{20} 1.4382.

cis-2,4-Dimethyl-2-penten-1-ol (XIVa). A solution of 66 mmoles of $LiAlH_4$ in 70 ml of ether was added in the course of one hour with vigorous stirring at between −10 and −5° to a solution of 10.25 g of the cis acid (Xa) in 100 ml of dry ether. The mixture was stirred further for two hours at the same temperature and for three hours at 20°, after which excess of $LiAlH_4$ was decomposed with water and 25% NaOH solution was added until a readily filterable precipitate had formed; this was filtered off and washed with ether. The combined filtrates were washed with saturated NaCl solution and dried with K_2CO_3. The liquid residue that remained after the removal of ether was vacuum-distilled. We obtained 6.65 g (73%) of cis-2,4-dimethyl-2-penten-1-ol (XIVa), b. p. 74-75° (23 mm); n_D^{20} 1.4422, d_4^{20} 0.8349. Found: C 73.77; H 2.31%. $C_7H_{14}O$. Calculated: C 73.63; H 12.36%. 3,5-Dinitrobenzoate: m. p. 43.5-44.5° (from hexane). Found: C 54.62; H 5.08; N 9.27%. $C_{14}H_{16}N_2O_6$. Calculated: C 54.54; H 5.23; N 9.09%.

trans-2,4-Dimethyl-2-penten-1-ol (XIVb). By procedure analogous to that for the alcohol (XIVa), by the reduction of 10.25 g of the trans acid (Xb) with 66 mmoles of $LiAlH_4$ we obtained 6.18 g (68%) of trans-2,4-dimethyl-2-penten-1-ol (XIVb); b. p. 79-80° (22 mm); n_D^{20} 1.4430. Found: C 73.84; H 12.42%. $C_7H_{14}O$. Calculated: C 73.63; H 12.36%.

Oxidation of cis- and trans-2,4-dimethyl-2-penten-1-ols (XIVa) and (SIVb). 15 ml of a 2 M solution of chromic acid in acetone was added at 5° with stirring to a solution of 2.24 g of cis-2,4-dimethyl-2-penten-1-ol (XIVa) in 10 ml of acetone (see [12]). The mixture was stirred for 30 min at 20° and then vacuum-evaporated down to 10 ml; 50 ml of water was added, and the mixture was extracted with five 20 ml portions of ether. The combined ether extracts were washed with 5% sodium carbonate solution, and the washings were treated with 20 ml of ether and then acidified to pH 1 with hydrochloric acid; the solution was extracted with four 15 ml portions of ether. The combined ether extracts were washed with saturated NaCl solution and dried with $MgSO_4$. The liquid residue remaining after the removal of ether was vacuum-distilled. We obtained 1.87 g (73%) of the cis acid (Xa); b. p. 98-99° (9 mm); n_D^{20} 1.4494. The p-phenylphenacyl ether had m. p. 72-73° (from alcohol), undepressed by admixture of a known sample.

By the analogous oxidation of 2.24 g of trans-2,4-dimethyl-2-penten-1-ol (XIVb) we obtained 2.0 g (78%) of the trans acid (Xb), m. p. 29-30° (from hexane), undepressed by admixture of the above-described sample.

Hydroboration of cis- and trans-2,4-dimethyl-2-penten-1-ols (XIVa) and (XIVb). Diborane prepared by the action of a solution of 50 mmoles of $LiAlH_4$ in 50 ml of dry tetrahydrofuran on a solution of 7.1 g of BF_3 etherate in 20 ml of tetrahydrofuran was passed in a stream of nitrogen over a period of one hour into a stirred solution of 2.85 g of cis-2,4-dimethyl-2-penten-1-ol (XIVa) in 20 ml of tetrahydrofuran at between −2 and 0°. Stirring of the mixture in an atmosphere of nitrogen was continued for one hour at 20°, and then excess of diborane was decomposed with water with cooling to 0°. At this temperature 20 ml of 3 N NaOH was added, and then the mixture was cooled to −10° and 10 ml of 30% hydrogen peroxide was added dropwise. The mixture was then stirred for one hour at 50°, cooled, and extracted with four 25 ml portions of ether. The combined ether extracts were washed with sodium thiosulfate solution, KOH solution, and saturated NaCl solution; they were dried with $MgSO_4$. The liquid residue remaining after the removal of solvents was vacuum-distilled with collection of the fraction (2.68 g) of b. p. 110-112° (9 mm); n_D^{20} 1.4512. This was dissolved in 25 ml of methanol, a solution of 20 mmoles of periodic acid in 10 ml of water was added, and the mixture was left for 12 h at 20°; it was then neutralized with anhydrous sodium carbonate. The precipitate was filtered off, the filtrate was evaporated down to a volume of 15 ml, 25 ml of water was added, and the mixture was extracted with four 20 ml portions of ether. The combined ether extracts were washed with 5% sodium carbonate solution and with saturated NaCl solution; they were dried with $MgSO_4$. The oily residue remaining after the removal of ether crystallized on standing at 0°. The crystalline product was recrystallized from a mixture of dipropyl ether and hexane, and we obtained 2.28 g (69%) of the threo diol (IXa), m. p. 53-54°, undepressed by admixture with the sample prepared from the triol (IV).

Similarly, from 2.85 g of trans-2,4-dimethyl-2-penten-1-ol (XIVb) we obtained 1.91 g (58%) of the erythro diol (IXb); b. p. 109-112° (9 mm); n_D^{20} 1.4508. Found: C 63.81; H 12.15%. $C_7H_{16}O_2$. Calculated: C 63.59; H 12.20%.

Bis-2,5-dinitrobenzoate: m. p. 117.5-118.5° (from a mixture of absolute alcohol and butanone). Found: C 58.43; H 4.98; N 6.65%. $C_{21}H_{22}N_2O_8$. Calculated: C 58.60; H 5.15; N 6.51%.

Both derivatives melted with depression in admixture with the corresponding derivatives of 2,4-dimethyl-1,3-pentanediol (IXa) prepared from the triol (IV).

SUMMARY

1. meso-2,4-Dimethyl-1,3,5-pentanetriol formed by the cleavage of the macrolidic antibiotic erythromycin has a "xylo" configuration.

2. The asymmetric center at C_3 in the erythromycin molecule has the R configuration.

3. The asymmetric centers at C_2, C_3, and C_4 in the macrolidic antibiotic oleandomycin correspond to the "xylo" configuration.

LITERATURE CITED

1. L. D. Bergel'son, V. A. Vaver, A. A. Bezzubov, and M. M. Shemyakin, Izv. AN SSSR, Ser. Khim., 1964, 1453.
2. K. Gerzon, E. H. Flyn, M. V. Sigal, P. F. Wiley, R. Monahan, and U. C Quarn, J. Amer. Chem. Soc., 78, 6396 (1956).
3. S. Refromatskii, Zh. russk. fix.-khim. obshch., 30, 456 (1898).
4. F. A. Hochstein, H. Els, W D. Celmer, B. L. Shapiro, and R. B. Woodward, J. Amer. Chem. Soc., 82, 3225 (1960).
5. H. O. House and G H. Rasmusson, J. Organ. Chem., 26, 4278 (1961).
6. H. J. Lucas and A N. Prater, J. Amer. Chem. Soc., 59 1682 (1937).
7. J. Cason and M. J. Kalm, J. Organ. Chem., 19, 1947 (1954).
8. R. Adams and B. L. van Duuren, J. Amer. Chem. Soc., 75, 4631 (1953).
9. L. D. Bergel'son, É. V. Dyatlovitskaya, M. Tikhi, and V V. Voronkova, Izv. AN SSSR, Otd. Khim. N., 1962, 1612.
10. D H. Hey, J. Chem. Soc., 1928, 2321.
11. L. D. Bergel'son, É. V. Dyatlovitskaya, and M. M. Shemyakin, Izv. AN SSSR, Otd. Khim. N., 1963, 506.
12. S. J. Heilbron, E. R. H. Jones, and F. Sondheimer, J. Chem. Soc., 1949, 604.
13. H. C. Brown and B C. Subba Rao, J. Organ. Chem., 22, 1135 (1957).
14. H. C. Brown and G. Zweifel, J. Amer. Chem. Soc., 83, 2544 (1961).
15. G. Sweifel, R. Ayyangar Nagarai, and H. C. Brown, J. Amer. Chem. Soc., 84, 4342 (1962).
16. E. L. Allred, J. Sonnenberg, and S. Winstein, J. Organ. Chem., 25, 26 (1960).
17. J. Canceill, J. J. Basselier, and J. Jacques, Bull. Soc. chim. France, 1963, 1906.
18. R. P. Linstead and C. J May, J. Chem. Soc., 1927, 2565.
19. O. Isler, H. Gutmann, M. Montavon, R. Rüegg, G. Ryser, and P. Zeller, Helv. chim. acta, 40, 1242 (1957).

All abbreviations of periodicals in the above bibliography are letter-by-letter transliterations of the abbreviations as given in the original Russian journal. *Some or all of this periodical literature may well be available in English translation.* A complete list of the cover-to-cover English translations appears at the back of this issue.
