potassium ethyl xanthate. The intermediate xanthate (II) was not isolated but was reduced directly with sodium borohydride in alcohol solution followed by saponification to give *p*-thiol-α-methyl benzyl alcohol (III) ($n^{25.4}$D 1.5880, $d^{25.5}_4$ 1.1408, m.p. 44.8–46.2°; Calcd. for $C_8H_{10}OS$: C, 62.30; H, 6.54; S, 20.79. Found: C, 62.23; H, 6.68; S, 20.90) in 63% yield. III was converted to the diacetate (IV) ($n^{25.5}$D 1.5422, $d^{25.5}_4$ 1.1460; Calcd. for $C_{12}H_{14}O_3S$: C, 60.48; H, 5.92; S, 13.45. Found: C, 60.42; H, 5.81; S, 13.56) in 90% yield which was then successfully deacetylated by passing through a hot tube at 450° to give *p*-vinylphenyl thioacetate (V) ($n^{25.3}$D 1.5992, $d^{25.5}_4$ 1.0953; Calcd. for $C_{10}H_{10}OS$: C, 67.38; H, 5.66; S, 17.99. Found: C, 67.51; H, 5.44; S, 18.28) in 48% yield. V was successfully polymerized with 2,2′-azo-bis-isobutyronitrile as the catalyst to give poly-*p*-vinylphenyl thioacetate, [η], 0.305, in benzene. Calcd. for $(C_{10}H_{10}OS)_x$: C, 67.38; H, 5.66. Found: C, 67.16; H, 5.67.

A polymer sample of lower molecular weight, [η] = 0.124, in benzene, was saponified by dropping its benzene solution into boiling dilute alcoholic base to give poly-*p*-thiolstyrene. (Calcd. for C_8H_8S: C, 70.54; H, 5.92. Found: C, 70.41; H, 6.09.)

This polymer is a white powder soluble in basic solution and partially soluble in organic solvents such as benzene and cyclohexanone. It is precipitated from such a solution by methanol or petroleum ether. An intrinsic viscosity of the soluble portion (96%) in benzene, gave a value [η] = 0.090. The polymer was easily oxidized with characteristic oxidizing agents such as iodine to give an insoluble polymer. The reversible oxidation reduction system and the use of this polymer and some of its copolymers as model proteolytic enzymes will be reported separately.

We wish to thank the Public Health Service, National Institutes of Health for their generous support of this work, Contract US PHG-4154.

INSTITUTE OF POLYMER RESEARCH
DEPARTMENT OF CHEMISTRY C. G. OVERBERGER
POLYTECHNIC INSTITUTE OF BROOKLYN
BROOKLYN, NEW YORK ALEXANDER LEBOVITS

RECEIVED MAY 14, 1955

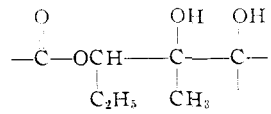
ERYTHROMYCIN. IV. DEGRADATIVE STUDIES

Sir:

Reduction of erythromycin[1] (I) with sodium trimethoxyborohydride gave dihydroerythromycin (II), m.p. 133–135° [Calcd. for $C_{37}H_{69}NO_{13}$: C, 60.38; H, 9.45; N, 1.90; mol. wt., 737. Found: C, 60.34; H, 9.44; N, 1.88; mol. wt., 736 (electrometric titration); pK'_a 8.6 in 66% dimethylformamide]. The infrared spectrum of II has only one carbonyl band at 5.84 μ. The 5.90 μ carbonyl band of erythromycin has disappeared as has the ultraviolet band at 278 mμ. The disappearance of these two bands on borohydride reduction indicates that they result from a ketonic carbonyl in erythromycin and this carbonyl is reduced in the formation of II.

Treatment of II with methanolic hydrogen chloride resulted in degradation to X-O-desosaminyldihydroerythronolide[2] (III), m.p. 212–213° [Calcd. for $C_{29}H_{55}NO_{10}$: C, 60.29; H, 9.59; N, 2.42; C-CH_3 (7), 18.2; mol. wt., 577. Found: C, 60.39; H, 9.67; N, 2.35; C-CH_3, 16.34; mol. wt., 585 (electrometric titration); $[\alpha]^{25}$D −2° (*C*, 1 in methanol); $[\alpha]^{25}$D −5° (*C*, 1 in pyridine); pK'_a 8.0 in 66% dimethylformamide]. The infrared absorption spectrum of III indicated hydroxyl and ester or lactone carbonyl (2.85 μ and 5.86 μ) since there was no evidence of ketonic carbonyl in the ultraviolet spectrum. Consumption of one mole of periodate per mole of III indicated the presence of a pair of adjacent hydroxyl groups. Hydrolysis of III with 2 *N* hydrochloric acid in a two phase system gave, in addition to desosamine,[1,3] products IV, V and VI all containing twenty-one carbon atoms. Dihydroerythronolide (IV) was the principal product, m.p. 185–187° [Calcd. for $C_{21}H_{40}O_8$: C, 59.97; H, 9.59; C-CH_3 (6), 21.4; mol. wt., 420. Found: C, 60.04; H, 9.56; C-CH_3, 20.21; mol. wt., 405; $[\alpha]^{27}$D + 9.5° (*C*, 2 in methanol)]. The infrared spectrum had a broad band at 2.75–2.90 μ and a band at 5.86 μ. The ultraviolet absorption spectrum was transparent in the 220–400 mμ region. This compound consumed two moles of periodate per mole. Compound V melted at 230–231° [Calcd. for $C_{21}H_{38}O_7$: C, 62.66; H, 9.52; O, 27.83; C-CH_3 (6), 22.45; mol. wt., 402.5. Found: C, 62.53; H, 9.53; O, 27.84; C-CH_3, 19.89; mol. wt., 405.9 (X-ray crystallographic analysis)] and Compound VI melted at 192–193° [Calcd. for $C_{21}H_{38}O_7$: C, 62.66; H, 9.52; O, 27.83; C-CH_3 (6), 22.45; mol. wt., 402.5. Found: C, 62.85; H, 9.36; O, 27.95; C-CH_3, 20.36; mol. wt., 401 (X-ray crystallographic analysis)].

Oxidation of erythromycin-N-oxide and compounds III and IV with sodium metaperiodate followed by mild alkaline hydrolysis gave rise to a steam volatile product (VII). This compound reacted slowly with 2,4-dinitrophenylhydrazine to form 2,3-pentanedionebis-(2,4-dinitrophenylhydrazone), melting point and X-ray diffraction pattern identical with those of an authentic sample. Compound VII is not 2,3-pentanedione since it did not form a precipitate in the presence of a nickel salt and hydroxylamine but did form such a precipitate after oxidation with ferric chloride. These data indicate an α-hydroxyketone. Periodate oxidation of base hydrolysed IV resulted in isolation of propionaldehyde and acetic acid which definitely shows that VII is 3-hydroxy-2-pentanone. Since VII survived the periodate oxidation of III and IV it must be present as an ester during the oxidation and be released only on hydrolysis. The lack of ketonic carbonyl in III and IV prior to periodate oxidation is proof that the carbonyl of V arises by an oxidative cleavage. These facts are evidence that IV is an ester or lactone containing the grouping



(1) E. H. Flynn, M. V. Sigal, Jr., P. F. Wiley and K. Gerzon, THIS JOURNAL, **76**, 3121 (1954).

(2) The name erythronolide is proposed for the R(OH)$_2$ (R = $C_{21}H_{36}O_6$) portion of formula XIV in ref. 1.

(3) R. K. Clark, *Antibiotics and Chemotherapy*, **3**, 663 (1953).

The quantitative periodate oxidation experiments on III and IV indicate the presence of a single 1,2-glycol grouping in III and the appearance of a second one in IV as a result of the removal of desosamine. This evidence shows that desosamine is linked to one or the other of the carbon atoms involved in this second group.

LILLY RESEARCH LABORATORIES
INDIANAPOLIS 6, INDIANA

PAUL F. WILEY
KOERT GERZON
EDWIN H. FLYNN
MAX V. SIGAL, JR.
U. CAROL QUARCK

RECEIVED JUNE 4, 1955

ERYTHROMYCIN. V. ISOLATION AND STRUCTURE OF DEGRADATION PRODUCTS

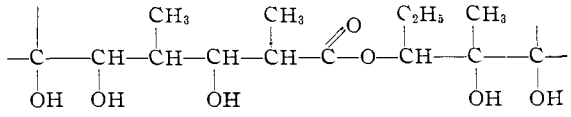
Sir:

Periodate oxidation of dihydroerythronolide (I)[1] followed by alkaline hydrolysis and oxidation gave an acid (II). This acid was identified as α,α'-dimethyl-β-hydroxyglutaric acid by conversion to its bis-(*p*-bromophenacyl) ester, m.p. 138–141° [Calcd. for $C_{23}H_{22}O_7Br_2$: C, 48.44; H, 3.89; Br, 28.03; mol. wt., 570. Found: C, 48.68; H, 4.09; Br, 27.46; mol. wt., 590] identical with the derivative of an authentic sample[2] as shown by the usual physical tests.

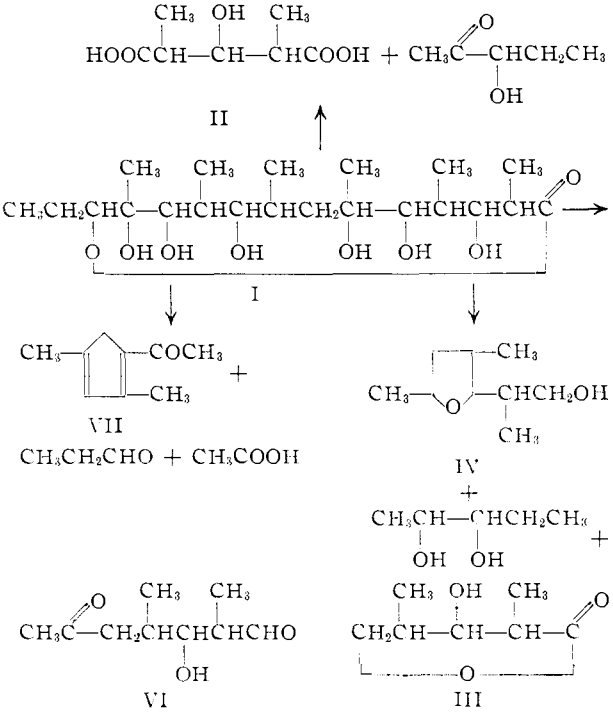
Degradation of I by periodate oxidation followed by catalytic reduction and alkaline hydrolysis formed three products. One of these was a sodium salt which on acidification gave a lactone (III), m.p. 88–88.5° [Calcd. for $C_7H_{12}O_3$: C, 58.33; H, 8.33; C-CH_3 (2), 20.9; mol. wt., 144. Found: C, 58.27; H, 8.27; C-CH_3, 19.9; mol. wt., 144 (saponification equivalent); $[\alpha]^{27}D$ −5° (*C*, 2 in methanol)]. There was infrared absorption in the 2.9 μ region indicative of hydroxyl and a lactone band at 5.82 μ. The second product was a neutral liquid (IV), b.p. 87–88° at 5 mm. [Calcd. for $C_9H_{18}O_2$: C, 68.31; H, 11.47; C-CH_3 (3), 28.5; mol. wt., 158. Found: C, 68.15; H, 11.39; C-CH_3, 23.8; mol. wt., 176; $n^{20}D$ 1.4519; $[\alpha]^{26}D$ +15° (*C*, 1 in methanol)]. Infrared absorption at 2.85 μ indicated hydroxyl. This compound gave a negative iodoform reaction and did not decolorize bromine in carbon tetrachloride. 2,3-Pentanediol (V),[3] b.p. 38° at 0.05 mm. [Calcd. for $C_5H_{12}O_2$: C, 57.69; H, 11.54. Found: C, 57.74; H, 11.78; $n^{25}D$ 1.4402; $[\alpha]^{28}D$ +20° (*C*, 1 in water)] also was isolated and identified by consumption of one mole of periodate per mole and oxidation with bromine to 2,3-pentanedione whose bis-(2,4-dinitrophenylhydrazone) was identical with an authentic sample as shown by the usual physical tests.

Base hydrolysis of dihydroerythronolide followed by periodate oxidation formed propionaldehyde, acetic acid, a neutral product (VI) and another acid presumably an aldehyde acid. Compound VI gave a positive iodoform reaction and formed an incompletely purified bis-(2,4-dinitrophenylhydrazone), m.p. 235–237° [Calcd. for $C_{21}H_{24}N_8O_9$: N, 21.12. Found: N, 21.19]. Treatment of VI with dilute sodium hydroxide gave a product (VII) which formed a 2,4-dinitrophenylhydrazone, m.p. 205–206° dec. [Calcd. for $C_{15}H_{16}N_4O_4$: C, 56.96; H, 5.08; N, 17.71, mol. wt., 316. Found: C, 56.78; H, 5.16; N, 17.48, mol. wt., 321]. The ultraviolet spectrum had a maximum at 402 mμ, ϵ 75,800 consistent with an α,β-γ,δ-unsaturated carbonyl 2,4-dinitrophenylhydrazone.

The first seven carbon atoms of I must be represented by the two seven-carbon compounds isolated since these are the only ones containing the —C(=O)—O— grouping of I. The presence of a second carboxyl in II and the hydroxylactone nature of III are consistent with periodate oxidation of I to an aldehyde-acid followed by oxidation to II or reduction to III. This also establishes the structure of III. In conjunction with the previous evidence[1] regarding the ester or lactone grouping in I, the following partial structure can be written for I.



The remaining nine carbon fragment of I is represented by IV and VII. These must be derived from a common precursor (VI) which would be expected to have two carbonyl and one hydroxyl oxygen atoms. The bis-(2,4-dinitrophenylhydrazone) of VI establishes the presence of two carbonyl groups. The positive iodoform reaction on VI indicates an acetyl or potential acetyl group. The molecular formula for VII is that expected if in VI there is β-hydroxycarbonyl and 1,4-, 1,5- or 1,6-dicarbonyl. The molecular formula for IV coupled with its saturation indicates a tetrahydrofuran or tetrahydropyran. The negative iodoform



(1) P. F. Wiley, K. Gerzon, E. H. Flynn, M. V. Sigal, Jr., and U. C. Quarck, THIS JOURNAL, **77**, 3676 (1955).

(2) S. Reformatski, *Ber.*, **28**, 3263 (1895).

(3) The synthesis of *dl*-erythro-2,3-pentanediol has been reported: see H. J. Lucas, M. J. Schlatter and R. C. Jones, THIS JOURNAL, **63**, 22 (1941).