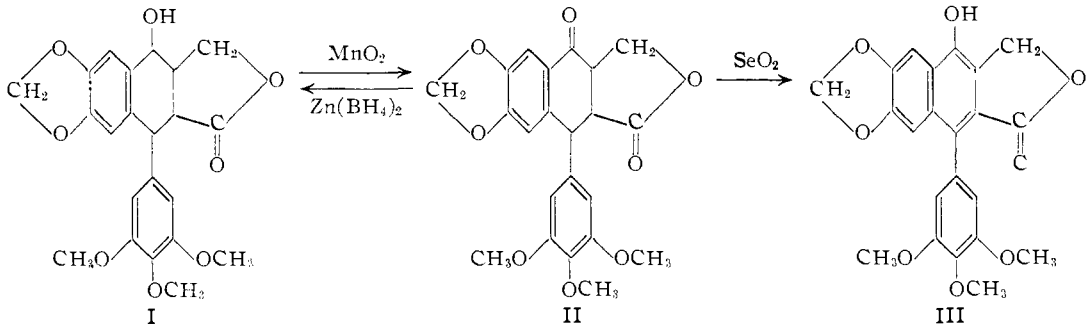
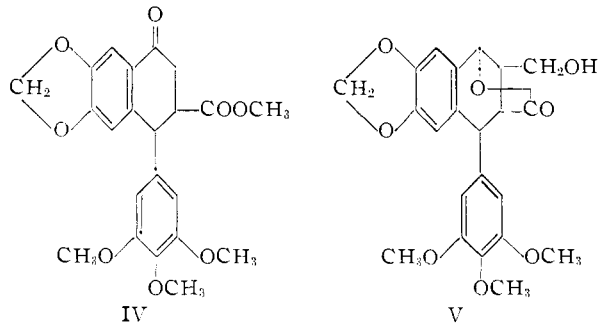



I
a, podophyllotoxin
b, picropodophyllin

II
a, podophyllotoxone
b, picopodophyllone

III
dehydropodophyllotoxin




IV V

very kindly carried out direct comparisons of his dehydropodophyllotoxin with our compound III. He reports that the two materials are the same.

Ketones IIa and IIb should prove of value in elaborating structural and stereochemical derivatives of podophyllotoxin.

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RECEIVED MAY 7, 1955

## POLYTHIOLSTYRENE—A NEW OXIDATION-REDUCTION ION EXCHANGE RESIN

*Sir:*

Oxidation-reduction polymers of the dihydroxybenzene type have been described by Cassidy[1] and Manecke.[2] We wish to report on a new oxidation–reduction resin of the thiophenol type.

Polystyrene (mol. wt. 30,000) was nitrated[3] to form polynitrostyrene, which was reduced by hydrogenation using a palladium catalyst to polyaminostyrene. Calcd. for $C_8H_9N$: N, 11.75. Found: N, 11.25.

Diazotization of polyaminostyrene with nitrous acid to form the diazonium chloride, followed by treatment with potassium ethylxanthate, gave insoluble polystyrene xanthate. Calcd. for $C_{11}H_{12}OS_2$: S, 28.58. Found: S, 26.96. Conversion to the polythiol was by hydrolysis with base, then acidification with acid to give polythiolstyrene. Calcd. for $C_8H_8S$: 23.50. Found: 21.77.

The resin was obtained as large brown granules; these were ground to a powder which was insoluble in all common solvents and swelled about 25% in alkaline solutions. Cross-linking probably occurred during decomposition of the diazo polymer.

(1) H. G. Cassidy, *et al.*, THIS JOURNAL, **75**, 1615 (1953).

(2) G. Manecke, *Z. Elektrochem. Ber. Bunsenges. physik. Chem.*, **58**, 369 (1954).

(3) A. Skogseid, Dissertation, Oslo, 1948.

The reducing capacity of the resin was determined in columns containing 0.1–0.4 g. of resin. Reductions were carried out using excess amounts of 0.5–2 *M* solutions of either sodium hydrosulfite, sodium sulfide or thioglycolic acid (at *p*H 8). The resin was then oxidized with known amounts of standard 0.1 *N* iodine in 0.25 *N* potassium iodide in a phosphate buffer (*p*H 8). The reducing capacity as calculated from back-titrations of the iodine effluent was 6.6 ± 0.4 meq./g. of resin for about ten consecutive cycles each on two columns. The theoretical capacity based on the sulfur analysis is 6.79 meq./g.

This new resin is a very strong reducing agent. In the oxidized state it can be reduced only by very strong reducing agents, not by weaker agents as acid-iodide. It is apparently stable to all but strong oxidizing agents such as permanganate. It is also highly specific toward metals which form mercaptides. Detailed experiments will be reported upon later.

This investigation was supported in part by the Office of Naval Research and by a research grant, RG 2934(C3), from the Division of Research Grants of the National Institutes of Health, Public Health Service. One of us (D.D.) was supported by the Boris Kidric Foundation, to which he wishes to express his thanks.

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## THE SYNTHESIS OF POLY-*p*-THIOLSTYRENE, AN OXIDATION REDUCTION POLYMER

*Sir:*

We wish to report the successful synthesis of pure poly-*p*-thiolstyrene. This polymer and its copolymers are of both practical and theoretical interest because of the reversible oxidation reduction system of a thiol group and a disulfide group which is the basis for the activity of a number of proteolytic enzymes. In this system disulfide formation provides a labile cross-link. These polymers are also of a potential use as prophylactics for ionizing radiation which are not rapidly excreted from the body.

*p*-Aminoacetophenone (I) was converted to the xanthate by diazotization followed by reaction with

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.

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RECEIVED MAY 14, 1955

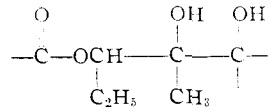
## ERYTHROMYCIN. IV. DEGRADATIVE STUDIES

*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).