P_H Optimum of Yeast Hexosephosphatase

P_H	4 Hours P_2O_5, mg.	4 Hours Relative action	8 Hours P_2O_5, mg.	8 Hours Relative action
5.9	0.4	1.7	6.6	25
6.3	6.6	29	19.0	71
6.5	23.0	100	26.8	100
6.7	22.6	98	25.4	95
7.2	10.6	46	18.8	70

The results are given in the table. In each set the maximum amount of phosphorus pentoxide formed was taken as 100, and the others were calculated as percentages of it. It will be seen that the optimum P_H is very close to 6.5. At this P_H in eight hours about 38% of the substrate was hydrolyzed.

Summary

The P_H optimum of the yeast hexosediphosphatase has been determined to be P_H 6.5.

Geneva, New York

[Contribution from the Experimental Research Laboratories, Burroughs Wellcome and Company]

SYNTHESIS OF LODAL AND EPININE

By Johannes S. Buck

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Lodal, 4,5-dimethoxy-2-β-methylamino-ethylbenzaldehyde, was obtained by Pyman[1] by the oxidation of laudanosine. It is also related to papaverine, since N-benzoyltetrahydropapaverine can be degraded to 6,7-dimethoxy-3,4-dihydroisoquinoline,[2] whose methochloride (6,7-dimethoxy-2-methyl-3,4-dihydroisoquinolinium chloride) is identical with the compound obtained from lodal by means of hydrochloric acid.

Epinine, 3,4-dihydroxyphenylethylmethylamine, was obtained by Pyman[1,2] by heating 1-keto-6,7-dimethoxy-2-methyltetrahydroisoquinoline, obtained from laudanosine or papaverine, with hydrochloric acid.

Lodal is a post-partum constrictor for uterine vessels, and a styptic in uterine hemorrhage,[3] while epinine shows hemostatic and pressor properties similar to those of adrenaline,[4] with the advantage of greater stability in solution. Up to the present time no complete syntheses of these compounds have been reported. The author has carried out complete syntheses of lodal and epinine, starting from homoveratrylamine (prepared from vanillin). This amine is monomethylated, via the Schiff base, and

[1] Pyman, *J. Chem. Soc.*, **95**, 1266 (1909).

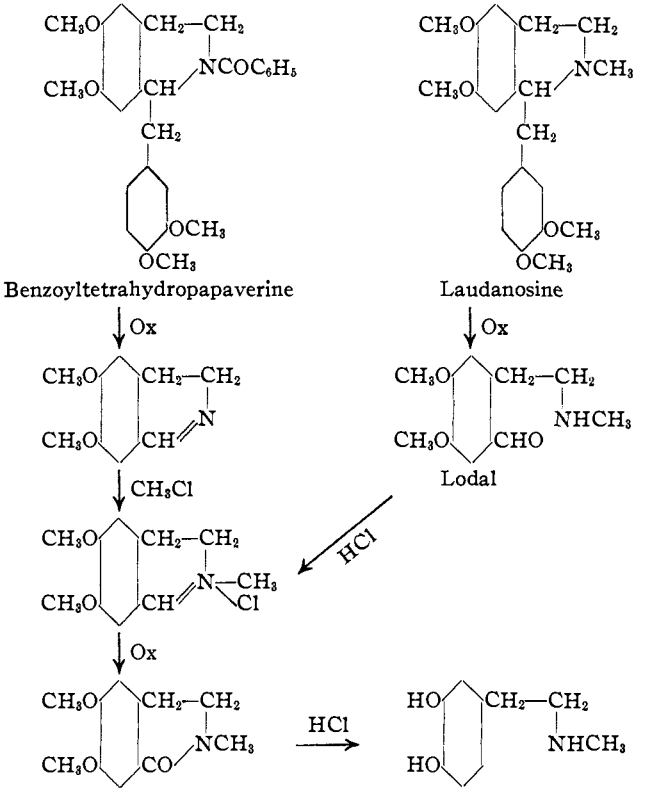
[2] Pyman, *ibid.*, **95**, 1610 (1909).

[3] Laidlaw, *Biochem. J.*, **5**, 243 (1911).

[4] Barger and Dale, *J. Physiol.*, **41**, 19 (1910).

then demethylated to produce epinine hydrochloride. Alternatively, methylhomoveratrylamine is converted into the formyl derivative and this then cyclized by the peculiar reaction of Decker.[5] In both cases the synthetic products were compared with authentic compounds prepared by Pyman's method and found to be identical with these.

The relationships mentioned may be shown thus



Experimental

Homoveratrylamine.[6]—This amine was prepared from dimethoxyphenylpropionamide. Veratric aldehyde was condensed with ethyl acetate and the resulting dimethoxycinnamic ester hydrolyzed and reduced to dimethoxyphenylpropionic acid as described by Perkin and Robinson.[7] By heating the ammonium salt of the acid,[8] dimethoxyphenylpropionamide was obtained. This was then converted into homoveratrylamine by the regular Hofmann method.[5,6]

Methylhomoveratrylamine.—The methylation was carried out by first forming the benzal derivative and then treating this with methyl iodide. The benzal group was then split off, giving methylhomoveratrylamine hydriodide.[5] Molecular amounts of homo-

[5] Decker, *Ann.*, **395**, 390 (1913).

[6] Buck and Perkin, *J. Chem. Soc.*, **125**, 1675 (1924).

[7] Perkin and Robinson, *ibid.*, **91**, 1080 (1907).

veratrylamine and benzaldehyde were mixed. Heat was evolved and the mixture became turbid through the separation of water, which was then removed by heating under reduced pressure. An equivalent amount of methyl iodide was added and the mixture heated, with the careful exclusion of air and moisture for twenty hours at 37°. The resulting solid, yellow, crystalline mass was boiled with 90% alcohol. On cooling and adding ether, the hydriodide of methylhomoveratrylamine separated. The yield was 79% of the theoretical.

The hydriodide after crystallization forms a dull white mass of jagged irregular prisms melting at 131° (uncorr.). It is very soluble in water, readily soluble in alcohol and sparingly soluble in ether.

Anal. Calcd. for $C_{11}H_{18}O_2NI$: C, 40.86; H, 5.57. Found: C, 41.09; H, 5.59.

The base was prepared by adding an excess of strong sodium hydroxide solution to an aqueous solution of the hydriodide and extracting with benzene. It forms an almost colorless and odorless oily liquid, b. p. 159° (11 mm.), n_{15} 1.5362; d_{20}^{20} 1.0597. It is very soluble in water, giving an alkaline solution, and is miscible with the usual organic solvents. Unlike homoveratrylamine, it appears not to form a carbonate in air.

Anal. Calcd. for $C_{11}H_{17}O_2N$: C, 67.69; H, 8.72; N, 7.18. Found: C, 68.09; H, 8.65; N, 6.93.

The picrate, prepared in aqueous solution, forms a yellow crystalline powder, melting at 162–163° (uncorr.).

Anal. Calcd. for $C_{17}H_{20}O_9N_4$: C, 48.11; H, 4.72. Found: C, 47.95; H, 4.75.

The quaternary iodide, formed when the amine is warmed in alcoholic solution with methyl iodide, consists of beautiful pearly masses of plates. It is soluble in water and alcohol and melts at 226° (uncorr.).

Anal. Calcd. for $C_{13}H_{22}O_2NI$: C, 44.44; H, 6.26. Found: C, 44.37; H, 6.39.

The platinichloride forms a pale orange granular precipitate, melting at 190° (uncorr.) with frothing and blackening.

Anal. Calcd. for $(C_{11}H_{17}O_2N)_2 \cdot H_2PtCl_6$: C, 33.0; H, 4.5; Pt, 24.4. Found: C, 34.0; H, 4.5; Pt, 24.6.

The aurichloride forms a bulky orange powder, melting with frothing and blackening at 148° (uncorr.).

Anal. Calcd. for $C_{11}H_{17}O_2N \cdot HAuCl_4$: C, 24.7; H, 3.4; Au, 36.9. Found: C, 25.0; H, 3.5; Au, 37.4.

Epinine.—Methylhomoveratrylamine hydriodide was heated with five times its weight of hydriodic acid (sp. gr. 1.70) for thirty minutes at 120–130°. Surplus acid was then distilled off under reduced pressure. The residual golden oil was dissolved in water and converted into the hydrochloride by means of silver chloride. The yield of hydrochloride was over 65% of the theoretical. The hydrochloride and the base prepared from it were identical in every respect with authentic specimens prepared by Pyman's method. Mixed melting point determinations showed no depression.

Anal. Calcd. for $C_9H_{14}O_2NCl$: N, 6.88; Cl, 17.42. Found: N. 6.90; Cl, 17.54.

Lodal.—Four and nine-tenths grams of methylhomoveratrylamine and 2.3 g. (2 mols) of absolute formic acid were mixed and the whole heated for one hour in an oil-bath at 210°. A clear almost colorless sirup of the formyl compound resulted. This was dissolved in 50 cc. of toluene and boiled with 20 g. of phosphorus pentoxide for thirty minutes. After cooling, the toluene was decanted and the pentoxide added to crushed ice. The solution was then filtered, neutralized with sodium bicarbonate, extracted with benzene, and the aqueous liquor made strongly alkaline with 20% sodium hydroxide solution. On standing, a portion of the product crystallized out and the rest was extracted with benzene; yield, 61% of crude material. The compound was identified by

comparison with an authentic specimen and by mixed melting point determinations on the base, the picrate and the very characteristic cyano derivative.

Summary

Complete syntheses of lodal (4,5-dimethoxy-2-β-methylamino-ethylbenzaldehyde) and epinine (3,4-dihydroxyphenylethylmethylamine), from vanillin, via homoveratrylamine, have been carried out. The products were identical with those prepared by Pyman's[1,2] method from papaverine or laudanosine.

TUCKAHOE, NEW YORK

[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF THE COLLEGE OF LIBERAL ARTS OF NORTHWESTERN UNIVERSITY]

THE ARSONATION OF AROMATIC ALDEHYDES

BY ALBERT B. SCOTT[1] AND CLIFF S. HAMILTON

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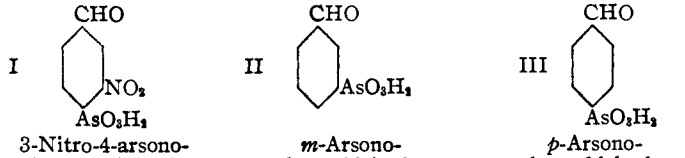
Certain organic arsenical compounds exert a specific curative action in syphilis and the trypanosomiases. Although arsonated aromatic compounds containing the amino group substituted in the nucleus have been widely investigated for many years, little attention has been devoted to arsonated aromatic molecules containing a non-cyclic carbonyl group. The present investigation deals with the preparation and properties of arsonated aromatic aldehydes, molecules which contain a nuclear arsono group (AsO_3H_2) and a non-cyclic carbonyl group. The only reference to this type of substance was found in certain patents. Pfleger and Albert[2] claim derivatives of *p*-arsonobenzaldehyde. Margulies claims 3-nitro-4-arsonobenzaldehyde and *p*-arsonobenzaldehyde.[3]

Kalberlah[4] claims unique effectiveness for a new aromatic arsenical compound containing a non-cyclic carbonyl group.

In the present investigation derivatives of three arsonated aromatic aldehydes have been prepared. The structures of the parent compounds are as follows



3-Nitro-4-arsono-benzaldehyde | *m*-Arsono-benzaldehyde | *p*-Arsono-benzaldehyde

[1] Research Fellow under a grant from Parke, Davis & Co. This article is an abstract of a thesis submitted by Albert B. Scott in partial fulfilment of the requirements for the degree of Doctor of Philosophy at Northwestern University.

[2] Pfleger and Albert, United States Patent 1,472,778 (1923).

[3] Margulies, British Patent 220,688 (1924).

[4] Kalberlah, *Klin. Wochschr.*, **48**, 2185 (1924).