reaction in greater detail. The procedure being employed was the usual treatment of a benzene solution of an alcohol (codeine) with an acetylglycosyl bromide in the presence of silver carbonate. As the reaction proceeded, there was a pronounced frothing and the silver carbonate became black. Analysis of the benzene-insoluble material at the conclusion of the reaction established the presence of considerable free silver, indicating that an unexpected oxidation had occurred. That it was the codeine being oxidized was demonstrated by an experiment in which the acetylglycosyl bromide was omitted and from which codeinone was isolated in fair yield.

A study was then made of various factors in this reaction and their effect on the yield of codeinone. The quantity of silver carbonate, the mode of addition of silver carbonate and codeine, and the time of reflux were all varied, and conditions were found which resulted in a 75% yield of codeinone. These consisted of simply heating under reflux a solution of codeine in benzene with 500 mole per cent of silver carbonate. Although the chromic acid oxidation of codeine to codeinone has been much improved recently[2] and an excellent Oppenauer oxidation procedure is now available,[3] the simplicity and very good yield of the present silver carbonate method make it an attractive alternative for preparing codeinone.

A search of the literature revealed no such previous application of silver carbonate, although silver oxide in anhydrous ether has been used in the preparation of quinones[4,5] and silver salts (and silver hydroxide) have served for various oxidations.[5] In seeking possible extensions and limitations of this silver carbonate oxidation procedure, the reactions with dihydrocodeine and neopine were tried. No reaction took place with dihydrocodeine and it was recovered quantitatively. With neopine definite blackening of the silver carbonate occurred but the only isolable product was neopine in an 18% recovery.

Experimental

Preparation of Silver Carbonate.—The yellow precipitate of silver carbonate formed when 300 ml. of an aqueous solution containing 25.6 g. of sodium bicarbonate was added to 480 ml. of 10% aqueous silver nitrate was washed by decantation six times with 1.5-l. portions of distilled water and four times with 700 ml. portions of methanol. It was then transferred to and washed on a suction filter funnel using a total of 2 l. of absolute ether. After being sucked dry on the funnel for about 20 min., the product was stored *in vacuo* over magnesium perchlorate in the dark. When first prepared, the silver carbonate is yellow, but on storage the color gradually changes to yellow-green and finally brown. This seems to have no adverse effect on its ability to oxidize codeine, and preparations over a month old have been used successfully.

Anal. Calcd. for Ag_2CO_3: Ag, 78.2; C, 4.4. Found: Ag, 78.1; C, 4.4.

Codeinone.—After 25 ml. was distilled from a solution of 6 g. (0.02 mole) of codeine in 125 ml. of benzene, 27.6 g. (0.1 mole) of silver carbonate was added and the mixture was heated under reflux with rapid stirring in a nitrogen atmosphere for one hour during which an additional 10 ml. of solvent was removed by distillation. The hot mixture was then filtered, the insoluble portion was digested with two 50-ml. portions of benzene, and the combined filtrate and digests were concentrated at the water-pump until crystals began to appear. These were removed by filtration after cooling, and the filtrate was further concentrated. In this manner, two crops were obtained, for a total of 4.5 g. (75% yield), melting at 179–182° to a characteristic red melt. On recrystallization from benzene using decolorizing carbon, 4.0 g. of practically colorless codeinone resulted, m.p. 181–182°, $[\alpha]^{21}D$ −208° (*c* 1.0, 95% ethanol) [reported[2] m.p. 181.5–182.5°, $[\alpha]^{20}D$ −205° (*c* 0.8, 99% alcohol)].

Codeinone oxime hydrochloride was prepared and melted at 257–260° dec. (reported[2] m.p. 258°). On reduction with sodium borohydride, codeinone was converted to codeine,[6] m.p. 156–157°.

(2) S. P. Findlay and L. F. Small, THIS JOURNAL, **72**, 3247 (1950).

(3) A. H. Homeyer and G. B. DeLaMater, U. S. Patent 2,654,756 (Oct. 6, 1953). Using this process we have obtained repeated yields of 40–60% of codeinone.

(4) R. Willstätter and A. Pfannstiel, *Ber.*, **37**, 4744 (1904).

(5) *E.g.*, J. Houben, "Die Methoden der Organischen Chemie," Third Edition, Vol. 2, Verlag Georg Thieme, Leipzig, 1925.

(6) M. Gates. THIS JOURNAL, **75**, 4340 (1953).

DEPARTMENT OF CHEMISTRY AND RADIATION LABORATORY
UNIVERSITY OF CALIFORNIA
BERKELEY, CALIFORNIA

On the Role of Polyphenoloxidase in Lignin Biosynthesis

BY H. S. MASON AND M. CRONYN

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It has been proposed that lignin is formed from coniferyl alcohol[1] under the influence of polyphenoloxidase and oxygen.[2–7] However, in the experiments upon which this hypothesis is based, the enzyme preparations which were employed were crude and presumably heterogeneous[8]; and conditions were utilized in which the growth of microorganisms[9] as well as the denaturation of enzymes is favored.[10]

Our interest in this matter derives from the possibility that polyphenoloxidases have continuity of biochemical function throughout the plant and animal worlds and that the lignins correspond to some pigments of higher organisms in being the products of the action of polyphenoloxidases upon *o*-diphenols (*cf.* reference 13).

Accordingly, we have re-examined the action of mushroom polyphenoloxidase, prepared by following the directions of Freudenberg,[2] upon coniferyl alcohol, and have compared it with the corresponding action of a purified mushroom polyphenoloxidase. Typical results are depicted in the Fig. 1. Oxygen consumption by coniferyl alcohol in the presence of Freudenberg crude oxidase was equivalent to about $^1/_2$ atom per molecule, an observa-

(1) P. Klason, *Svensk. Kem. Tidsk*, **9**, 135 (1897); cited by G. de Stevens and F. F. Nord, *Proc. Nat. Acad. Sci.*, **39**, 80 (1953).

(2) K. Freudenberg and H. Richtzenhain, *Ber.*, **76**, 997 (1943).

(3) K. Freudenberg, H. Reznik, H. Beosenberg and D. Rasenack, *ibid.*, **85**, 641 (1952).

(4) K. Freudenberg and W. Heimberger, *ibid.*, **83**, 519 (1950).

(5) K. Freudenberg and H. Dietrich, *ibid.*, **86**, 1157 (1953).

(6) K. Freudenberg and F. Bittner, *ibid.*, **86**, 155 (1953).

(7) L. Freudenberg, R. Kraft and W. Heimberger, *ibid.*, **84**, 473 (1951).

(8) The enzyme was variously described by Freudenberg as catecholoxidase, phenoldehydrogenase, mushroom dehydrogenase and redoxase.

(9) These conditions involved incubations of 3–28 days in the presence of crude mushroom proteins.

(10) Oxygen was continuously bubbled through the reaction mixtures. This has been shown to inactivate mushroom polyphenoloxidase.[11,12]

(11) M. H. Adams and J. M. Nelson, THIS JOURNAL, **60**, 2474 (1938).

(12) I. Asimov and C. R. Dawson, *ibid.*, **70**, 1184 (1948).

(13) G. Johnson and L. A. Schaal, *Science*, **115**, 627 (1952).

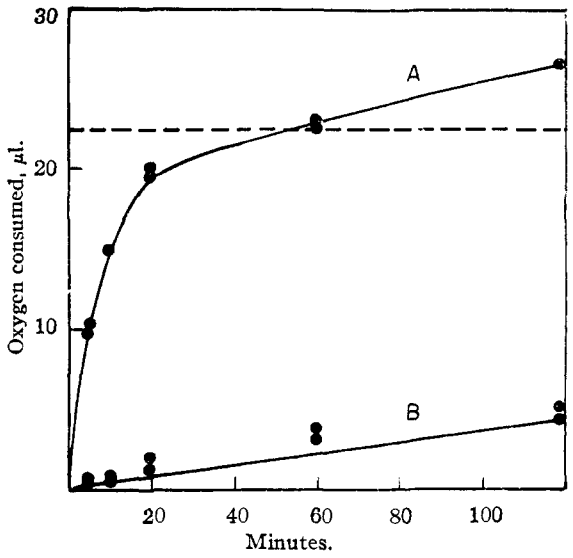


Fig. 1.—Oxygen consumption by coniferyl alcohol in the presence of mushroom extracts. Each Warburg vessel contained 4 μmoles of coniferyl alcohol dissolved in 2.8 ml. of 0.1 *M* phosphate buffer, *p*H 6.8, in addition to, (A) 4 mg. of Freudenberg oxidase (160 catecholase units), (B) 4 mg. of Freudenberg oxidase heated to 100° for 3 minutes, or 160 catecholase units of purified mushroom polyphenoloxidase, or 3 μmoles of cupric ion. The dotted line indicates an amount of oxygen equivalent to $^1/_2$ atom per molecule of coniferyl alcohol. KOH was present in the central well.

tion in accord with the earlier work. However, in the presence of the same number of catecholase units[14] of purified mushroom polyphenoloxidase[15] the oxygen consumption was negligible, as was the case in the presence of boiled Freudenberg oxidase, or cupric ion.

We conclude that there is present in crude mushroom extracts a heat-labile system which catalyzes the consumption of some oxygen by coniferyl alcohol, but it is not polyphenoloxidase which does this. The present experiments do not rule out a biosynthetic relationship between the lignins and melanins but they do show that the particular process proposed by Freudenberg is not pertinent to the concept.

Experimental

Coniferyl Alcohol.—The coniferyl alcohol was prepared by the lithium aluminum hydride reduction of ethyl acetoferulate using a modification of the method of Allen and Byers.[16] The ester (0.025 mole) was added in one portion to a solution of lithium aluminum hydride (0.100 mole) in 800 ml. of ether at −60°. The temperature was allowed to rise to 0° over a period of 1.5 hours and the solution was then filtered and the salt was hydrolysed and crystallized as described.[16] This method gave a product which crystallized immediately and without difficulty from the petroleum ether–ether mixture.

DEPARTMENT OF BIOCHEMISTRY
UNIVERSITY OF OREGON MEDICAL SCHOOL
AND THE DEPARTMENT OF CHEMISTRY
REED COLLEGE
PORTLAND, OREGON

(14) W. H. Miller, M. F. Mallette, L. J. Roth and C. R. Dawson, THIS JOURNAL, **66**, 514 (1944).

(15) The Treemond Company, New York, supplied our preparation, which contained 6200 catecholase units per ml., or 1510 units per mg.

(16) C. F. H. Allen and J. R. Byers, Jr., THIS JOURNAL, **71**, 2683 (1949).

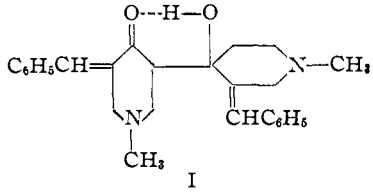
Piperidine Derivatives. XXVI. 1-Methyl-3-benzal-4-piperidone Dimer

BY S. M. MCELVAIN AND P. HAROLD PARKER, JR.[1]

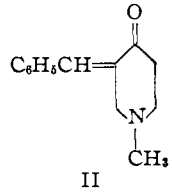
RECEIVED AUGUST 18, 1954

The dimeric structure I is now assigned to the compound described as 1-methyl-3-benzal-4-piperidone (II) in paper XVIII of this series.[2] This compound was obtained in the earlier work from 1-methyl-4-piperidone and benzaldehyde as well as from 1-methyl-3,5-dibenzal-4-piperidone (III) when the reaction was carried out in a solvent (4% solution of potassium hydroxide in 60% ethanol) from which III did not precipitate. The structure II was assigned on the basis of the elemental analyses and the methods by which it had been prepared, although some concern was expressed over the much lower solubility of the monobenzal derivative II as compared to that of the dibenzal derivative III; also the melting point of the former compound (224°) is considerably higher than that of the latter (117°).[3]

In the present work doubt was cast on the structure II when it was found that (a) the compound could not be converted to the dibenzal derivative III, although the reverse transformation is possible[2] and (b) the hydrogenation of the compound did not yield the expected 1-methyl-3-benzyl-4-piperidone,[4] but a compound with a wide melting range (85–95°) that showed a molecular weight of *ca.* 390. The structure I accounts for these results as well as for the following observations: the compound (a) shows a molecular weight of 408 (calcd. for I, 402), (b) has a broad associated hydroxyl band joining the C–H band at 3.3 μ and also a hydrogen bonded, conjugated carbonyl band at 6.1 μ in the infrared spectrum,[5] (c) shows a maximum absorption at 290 mμ (log ε 4.43) in the ultraviolet spectrum[6] and (d) yields an acetate in whose infrared spectrum there is no hydroxy band and in which the α,β-unsaturated carbonyl band, which is apparent in the ultraviolet spectrum, is masked by the ester carbonyl band at 5.75 μ.



I



II

It is possible that the high melting point of I and its insolubility in non-polar solvents may be due to a salt-like character resulting from the interaction of the carbonyl group which is posi-

(1) Wisconsin Alumni Research Foundation Research Assistant (1953).

(2) S. M. McElvain and K. Rorig, THIS JOURNAL, **70**, 1820 (1948).

(3) It may also be noted that the analog of II, 2-benzalcyclohexanone, is reported, (D. Vorländer and K. Kunze, *Ber.*, **59**, 2078 (1926), to melt at 54° and can be converted quantitatively to 2,6-dibenzalcyclohexanone, m.p. 118°.

(4) This compound, a liquid, b.p. 104–105° (0.1 mm.), has been prepared in this Laboratory by Martin D. Barnett by the decarbethoxylation of 1-methyl-3-benzyl-3-carbethoxy-4-piperidone, which was obtained by the benzylation of 1-methyl-3-carbethoxy-4-piperidone.

(5) *Cf.* R. S. Rasmussen, D. D. Tunnicliff and R. R. Brattain, THIS JOURNAL, **71**, 1068 (1949).

(6) *Cf.* L. Dorfman, *Chem. Revs.*, **53**, 47 (1953)