LETTERS TO THE EDITOR

CRYSTAL AND MOLECULAR STRUCTURE OF PYRIDOXAL*

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THE classical studies of Rabinowitz and Snell[1] in 1948 demonstrated that Vitamin B_6 exists in three forms in the tissues of animals and plants, namely, pyridoxine (PN), pyridoxal (PL) and pyridoxamine (PM) (I). It was shown that PL is catalytically involved in several decarboxylation, deamination, racemization and nonenzymatic transamination reactions[2-6]. Involvement of pyridoxal 5′-phosphate (PLP) in several enzymatic transamination reactions has also been reported[7,9]. Detailed IR and NMR studies have been done on PL and its analogues[10-13]. From these studies it was shown that PL exists as hemiacetal in neutral and acidic medium and also in the solid state. Crystal structures of different forms of Vitamin B_6 and related compounds, namely, PN.HCl[14], pyridoxamine phosphate hydrochloride (PMP.HCl)[15], PLP oxime[16], PLP.H_2O[17], PLP methylhemiacetal[17] and PM.HCl[18] have been solved. We report here the molecular structure of pyridoxal free base.

Trigonal prism-shaped crystals of PL were grown from aqueous solution of PL. HCl neutralised to a pH of about 7 by addition of sodium hydroxide solution. The intensities of 972 reflections upto a Bragg angle θ of 28° were collected on a CAD-4 diffractometer using graphite monochromated MoKα radiation. The crystal data are: molecular formula $C_8H_9NO_3$, a = 12·086(2), b = 9·108(1), c = 7·309(1) Å, β = 113·90(1)°, V = 735·54 Å^3, Z = 4, D_m = 1·51 g cm^{-3}, D_c = 1·507 g cm^{-3}, space group Cc or C2/c. Considerations of space group requirements and molecular geometry require the space group to be Cc.

The structure was solved by direct methods[19]. All hydrogen positions were determined from a difference electron density map. The structure was refined by block diagonal least squares to a final R value of 0·046 with anisotropic temperature factors for nonhydrogen atoms.*

The interesting feature of the structure is the interaction of aldehyde group with the 5-hydroxymethyl group to form hemiacetal, resulting in the formation of a five membered ring involving C(3), C(4), C(7), C(8) and O(3) atoms (figure 1). The molecule is virtually planar. However, a small deviation (0·14 Å) of O(3) gives the 5-membered ring

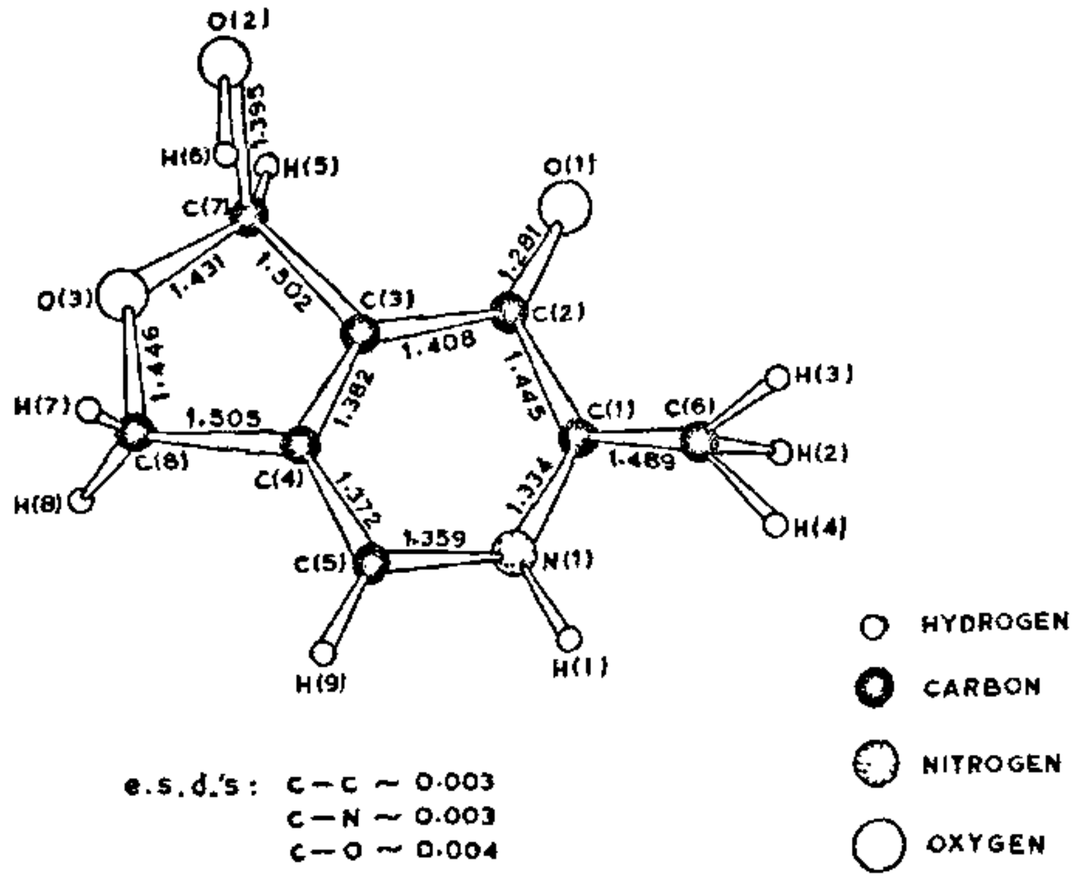
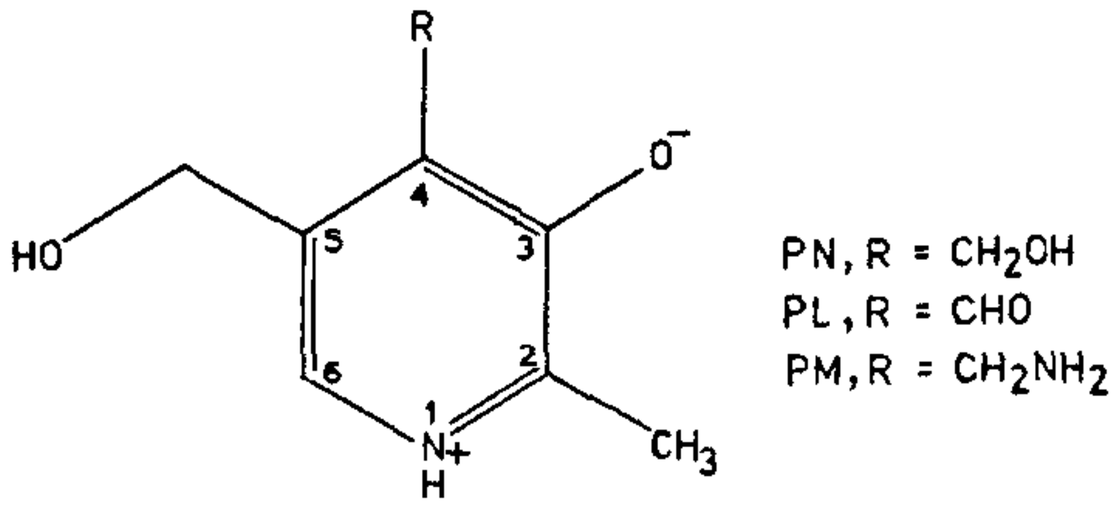


Figure 1. Molecular structure of pyridoxal.

an envelope conformation. The bond lengths and valence angles of the pyridine ring are comparable with the corresponding values in similar structures[14,17,18]. The considerably short C(2)-O(1) bond (1·28 Å) indicates that it has partial double bond character and that PL exists in tautomeric form (I) wherein pyridine nitrogen is protonated. Phenolic oxygen O(1) is involved in two intermolecular hydrogen bonds, one with pyridine nitrogen N(1)



I

*3-hydroxy-5-hydroxymethyl-2- methyl-4-pyridinecarboxaldehyde.

*Final atomic coordinates will be made available by the authors on request.

(N . . . .O=2·68 Å) and the other with oxygen of the aliphatic hydroxyl group of the hemiacetal ring, O(2), (O. . . . O=2·74 Å) of different molecules. The short N . . . . O distance is due not only to hydrogen bond interaction but also to the effect of electrostatic interaction between the positively charged N(1) and negatively charged O(1) atoms. No intramolecular hydrogen bonding between O(1) and O(2) is found as suggested by Heinert and Martell[10]. A 'trans-stacking' is found between glide-related molecules which are separated by an average distance of 3·65 Å with an angle of 2° between their mean planes. The stacking is different from that observed in $PLP.H_2O$[17] or PM.HCl[18] where almost eclipsed overlap of the pyridine rings is observed.

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CONVERSION OF *o*-ALLYLPHENOL TO COUMARIN USING SINGLET OXYGEN

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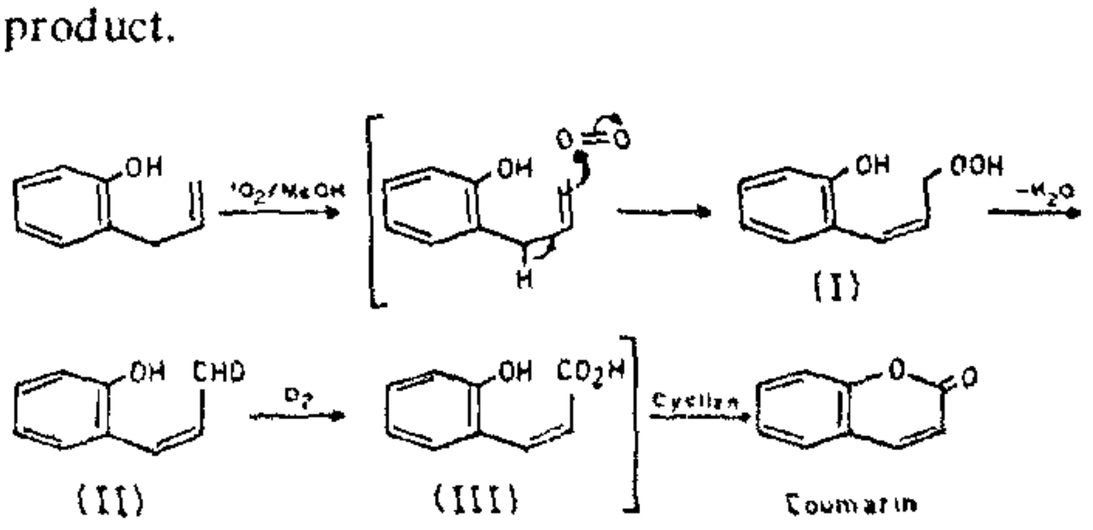
THE sensitized photooxygenations of variously substituted 2'-hydroxychalcones give ring closed products due to the participation of 2'-hydroxyl function[1-3]. In the light of the above effect of *ortho*-hydroxyl in assisting ring closure, it was thought worthwhile to investigate the sensitized photooxygenation of *o*-allyl phenols.

In a typical photooxygenation procedure, a solution of the substrate in MeOH or CCl_4 containing a catalytic amount of methylene blue or Rose Bengal as sensitizer was irradiated with a 100 W tungsten filament lamp while air was slowly and continuously passed through the solution. The progress of photooxygenation was monitored by TLC and the reaction worked up by removing excess solvent under reduced pressure, extracting the crude photolysate with ether, chloroform and ethyl acetate respectively, and finally subjecting the combined extracts to column chromatography over silica gel. Participation of singlet oxygen was proved by running the reactions in presence of DABCO ($^1O_2$ quencher)[4]. Blank runs were also carried out in the presence of sensitizer and in absence of air.

Of the five substrates studied, only 2-allylphenol reacted within 30 hr giving two products, one of which has been identified as coumarin (yield 20%) on the basis of spectral data and comparison with an authentic sample. a plausible mechanism (scheme I) for the formation of coumarin involves the initial formation of an allylic hydroperoxide (I) which dehydrates to the α, β-unsaturated aldehyde (II). Molecular oxygen brings about the oxidation of (II) to *o*-hydroxycinnamic acid (III), which undergoes spontaneous cyclization to afford the observed product.



Scheme–I

Of the other substrates, 6-allyl-2-methylphenol and 2-allyl-4-methylphenol failed to react even after 60 hr of irradiation, 1-allyl-2-naphthol showed some reactivity but the reaction was very sluggish with 8-