

2 METHOD OF PREPARATION OF THAILANDINE

Thailandine was prepared by refluxing equimolecular quantities of 6-methyl-2-aminopyridine, benzaldehyde and resorcinol in ethanol for 2.5 hours. The mixture was poured into an excess of distilled water and the brick precipitate filtered. The latter was hydrolyzed in sodium hydroxide solution and acidified with hydrochloric acid to precipitate the reddish-brown thailandine. The compound was purified by dissolving it in ethanol, filtering and adding an excess of distilled water to precipitate the purer product.

2.1 Properties of thailandine

Thailandine is a reddish-brown amorphous solid which is soluble in dioxane, acetone and ethanol. It dissolves in sodium hydroxide, forming a deep-red solution. In acid the compound precipitates as a yellow amorphous solid. Thailandine is extremely stable in alkaline solution. This is confirmed by refluxing the compound in alkaline sodium hydroxide for 36 hours. Upon acidification the compound subsequently isolated was found unaffected by alkali.

The preliminary investigation of the acid-base property of the compound indicated that it could be used as an indicator in the acid-base titration. The range of the pH change is from 6 to 9 (yellow to red).

Elemental analysis of thailandine gave the following results :-

TABLE 1

Elemental analysis of thailandine

Element	Experimental result
C	75.5 %
H	5.0 %
O	19.6 %
M.W.	1505

Calculation based on the above analyses establishes the molecular formula of thailandine as $C_{95}H_{70}O_{19}$ which requires C = 75.2 %; H = 4.6 % and O = 20.2 %.

2.2 Structural study of thailandine

As shown by elemental analyses, thailandine contains only carbon, hydrogen and oxygen. It was found to contain both phenolic and tertiary alcoholic hydroxyls, as shown by its infra-red and n.m.r. spectra, and by the formation of the methylated product and other phenolic derivatives. Apart from the reaction of hydroxyl functional groups, thailandine shows no characteristic reactions of other functional groups. Osmometric studies of this compound using ethanol or

N,N-dimethylformamide as solvents indicated the molecular weight of approximately 1505. Confirmation of the molecular weight of the compound by mass spectrometric analysis was unsuccessful because the compound decomposed prior to vaporization. Since the analytical results revealed that the compound contains no nitrogen, it is obvious that 6-methyl-2-aminopyridine acts as a catalyst in the condensation reaction leading to thailandine.

The I.R. spectrum of thailandine (KBr pellet) is shown in Figure 1. Its principal absorptions along with the assigned functional groups are listed in Table 2.

TABLE 2
I.R. Absorptions of thailandine (2)

Frequency cm^{-1}	Remarks	Nature of vibration	Assigned functional groups
3240-3440	strong, broad	O-H stretching	polymeric association
3020, 3058	very weak	C-H stretching	aromatic
1610, 1490	strong	C-C multiple bond stretching	aromatic
1200-1220	medium	C-O stretching	triphenyl methyl group (1)
1280-1295	weak		
1075	strong	C-OH stretching	carbinol with six-membered ring
850	medium	C-H stretching	
750	medium		
700	strong		

It can be seen from the above table that thailandine is a poly-phenol; in view of the broad and intense absorption of the OH peaks. This was confirmed by the methylation of thailandine to give a product whose elemental analyses indicated that thirteen methyl groups were introduced into the molecule, giving a trideca methyl derivative. The infra-red spectrum of this methoxy derivative still showed a broad and intense OH stretching band indicative of the presence of hydroxyl groups. This points to incomplete methylation, and the thailandine molecule must comprise some hydrogen-bonded hydroxyl groups which are difficult to methylate.

Thailandine has been found to undergo oxidation readily by alkaline peroxide and by bleaching powder. The oxidation products are identical in both cases as shown by their I.R. spectra. The indicator property is lost in the resulting product.

The spectrum shows a band at 1700 cm^{-1} characteristic of cyclohexanone derivative. This is possibly due to the oxidation of the monohydroxy benzene moiety to the dihydroxy benzene, followed by ketonization to cyclohexanone derivatives.

Thailandine has been found to undergo concentrated nitric acid oxidation to give a pale-yellow oxidation product. The pure compound, whose elemental analyses indicated m-nitro benzoic acid, was obtained by fractional crystallization.

The U.V. spectrum of thailandine shows the maximum absorption at 289 m μ with the molar absorptivity of 3.8×10^4 , as shown in Figure 3.

In order to gain insight into the nature of thailandine with particular emphasis on the number of protons present in the molecule, the compound was investigated by the n.m.r. method. The n.m.r. spectrum of thailandine is in accord with the assigned functional groups detected by I.R. spectrum. The n.m.r. spectrum of thailandine in hexadeuteroacetone with TMS as a reference standard exhibits the following signals as shown in Table 3.

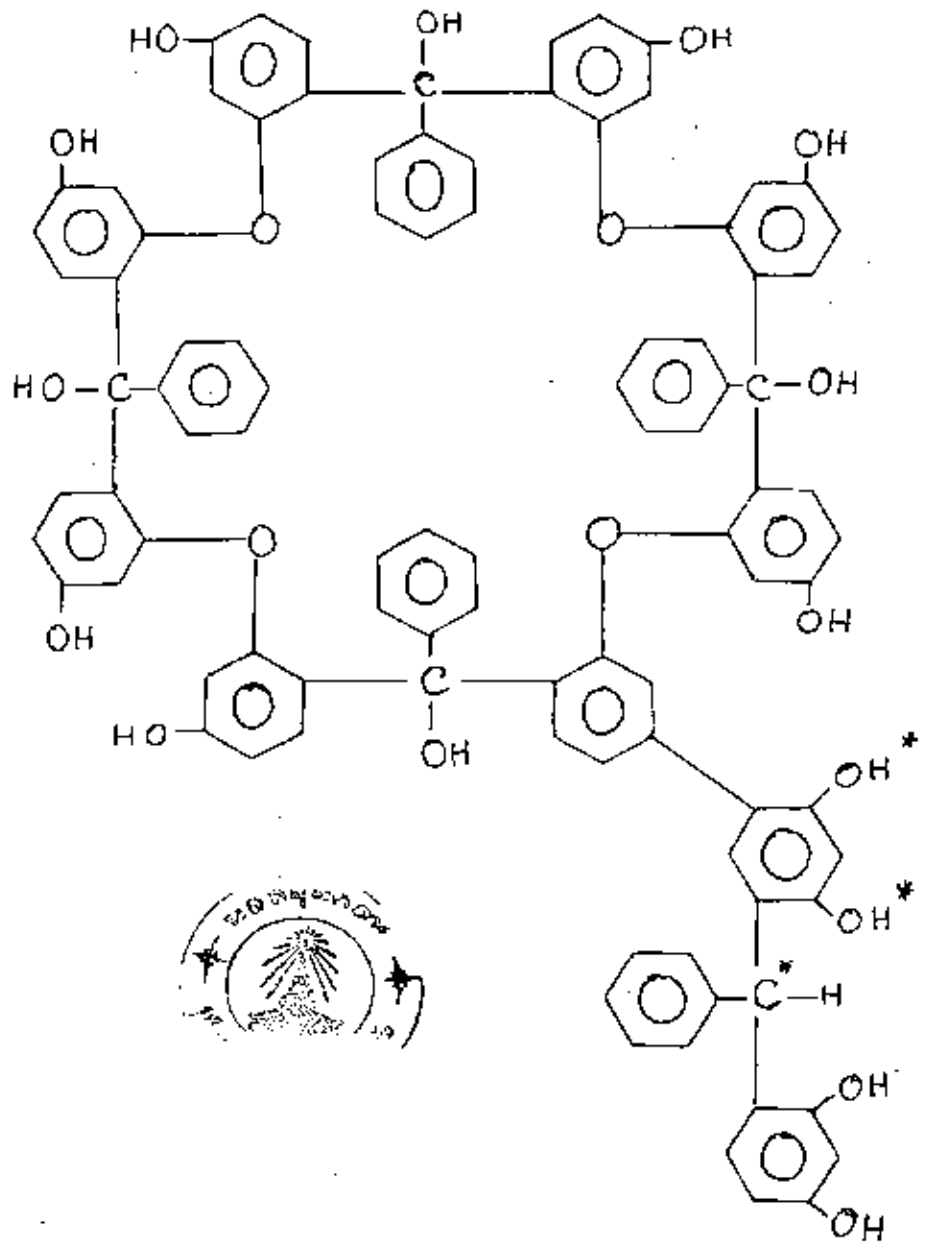
TABLE 3
n.m.r. spectrum of thailandine (6)

Hz	τ	δ	Splitting	Remarks
200-270	5.9	4.1	Broad singlet.	Integral indicates approximately 10 protons. Proper chemical shift for phenol protons. These species occur over a broad range (120-300 Hz)
370-450	3.1	6.9	Broad complex	Integral indicates approximately 55-60 aromatic protons. The pattern is characteristic of mono and trisubstituted benzene.
330-370	4.1	5.9	Broad singlet	Integral indicates 4-8 alcoholic protons. Reasonable chemical shift value.

From the n.m.r. spectrum, the number of hydrogen atoms in benzene nuclei and the number of hydrogen atoms derived from

hydroxyl group can be established. They are in close approximation with the number of hydrogen atoms calculated from elemental analyses. On the basis of n.m.r. evidence, fifteen oxygen atoms can be assigned to fifteen hydroxyl groups. However, four oxygen atoms still remain unassigned in the molecular formula, and it is logical to assume that these extra oxygen atoms are in the form of ether-linkages resulted from the condensation of two hydroxyl groups.

The above evidence coupled with theoretical consideration has led the author to believe that thailandine is a poly-ether formed by polycondensation of five moles of 2,4-dihydroxydiphenyl-phenylcarbinol formed from the condensation between benzaldehyde and resorcinol. The structure of thailandine is therefore proposed as follows :



THAILANDINE