



### 3 EXPERIMENTAL

#### 3.1 Preparation of thailandine

A mixture of 6-methyl-2-aminopyridine, 10.8 g. (0.10mole), benzaldehyde, 10.6 g. (0.10mole) and resorcinol, 11.0 g. (0.10mole) in 150 ml. of ethanol was refluxed for 2.5 hours. The mixture was allowed to cool and then poured into 2000 ml. of distilled water. The resulting brick precipitate was filtered to give an air-dried product, 23.23 g.. The latter was hydrolyzed in 100 ml. of 6 N. sodium hydroxide over a water bath for 1 hour. The deep-red solution was filtered and acidified with 6 M. hydrochloric acid to precipitate a reddish-brown solid, which was washed free of acid and air-dried to give thailandine, 10.5 g.. The compound was purified by dissolving it in 30 ml. of ethanol over a water bath for ten minutes, then filtered and the filtrate was poured into an excess of distilled water (ca. 200 ml.) to precipitate the purer product. Repetition of the purification process yielded purer thailandine, 3.9 g..

The evidence that 6-methyl-2-aminopyridine acts as a catalyst in the reaction leading to thailandine was demonstrated by repeating the above experiment without the addition of 6-methyl-2-aminopyridine. No precipitate was isolated after refluxing the mixture for 2.5 hours followed by pouring it into an excess of distilled water.

#### 3.2 Methylation of thailandine (4)

A solution of 6 M. sodium hydroxide, 50 ml., and

thailandine 1.0 g. (0.0007 mole) was placed in a 500 ml. three-necked flask equipped with a separatory funnel, a magnetic stirrer, and a reflux condenser. To the stirred solution were added 15 ml. of dimethylsulfate dropwise through the separatory funnel over the period of 15 minutes whilst stirring the mixture vigorously. The mixture was then refluxed with stirring for 30 minutes to complete the methylation. A red precipitate was formed. It was allowed to cool, filtered and washed once with distilled water, twice with 20 ml. dilute  $H_2SO_4$  and then with distilled water until the washing was neutral to litmus paper. The product was air-dried to give 870 mg. of the methyl derivative. Purification was by repeatedly dissolving the precipitate in a small amount of ethanol, followed by filtration and addition of an excess of distilled water to precipitate the purer product, 420 mg., m.p.  $160-162^\circ C$ . Elemental analyses correspond to the formation of trideca methyl thailandine. Anal. Calcd. found C = 77.01% H = 5.69% O = 17.30%.  $C_{108}H_{96}O_{19}$ , requires C = 76.42% H = 5.66% O = 17.92%.

The I.R. spectrum of the methylated product still reveals the presence of hydrogen-bonded hydroxyls at  $3550\text{ cm.}^{-1}$ . This indicates the presence of hydrogen-bonded hydroxyls in the parent thailandine, which resist methylation. They are postulated to be the two hydroxyl groups shown by asterisks in the proposed formula on page 8. The I.R. spectrum as shown in Figure 4.

### 3.3 Acetylation of thailandine

Thailandine, 1.0 g. (0.0007mole), was dissolved in 35 ml.

of 6 M. NaOH solution in 100 ml. round-bottomed flask. Acetic anhydride, 20 ml., was added. The flask was shaken vigorously for about 15 minutes, after which the red-orange precipitate of thailandine acetate separated. It was filtered and washed with distilled water until the washing was neutral to litmus paper. The product was air-dried to give an acetyl derivative, 880 mg. The compound was purified by dissolving it in a small amount of ethanol (ca. 10 ml.) over a water bath for 10 minutes, filtered and the filtrate poured into an excess of distilled water (ca. 25 ml.) to precipitate the product. Repetition of the purification process yielded pure acetyl derivative, 250 mg., b.p. 169-171 c.

The compound gave unidentified analytical results which may be due to the formation of a mixture of acetyl derivative. Anal. found : C = 72.30 %, H = 5.22 %, O = 20.6 %. The I.R. spectrum indicates incomplete acetylation as shown in Figure 6.

#### 3.4 Benzoylation of thailandine

Thailandine, 1.0 g. (0.0007 mole), was mixed with 35 ml. of 6 M. NaOH solution in 250 ml. round-bottomed flask. Benzoyl-chloride, 20 ml., was added. The bottle was corked and shaken vigorously, then left in a refrigerator overnight. The precipitate was filtered and washed with hot water until all benzoic acid dissolved. The product was air-dried to give 790 mg. of benzoyl derivative. The compound was purified in the same way as mentioned in the acetylation to yield benzoyl derivative, 220 mg.. The compound gave unidentified analytical results which may be due to formation of a mixture of benzoyl

derivatives. Anal. found : C = 76.66 %, H = 4.46 %, O = 17.9 %.  
The I.R. spectrum indicates incomplete benzylation as shown  
in Figure 7.

### 3.5 Oxidation of thailandine with bleaching powder

Thailandine, 1.0 g. (0.0007 mole), was dissolved in 35 ml. of 6 M. NaOH solution in a 250 ml. beaker. The solution was heated over a water bath and 25 ml. of saturated calcium hypochlorite solution were added with stirring. The red color disappeared immediately. The solution was filtered and acidified with 6 M. HCl to precipitate a yellow solid. It was filtered and washed with distilled water until the washing was neutral to litmus paper. The air-dried oxidation product, 560 mg., was obtained. The compound was purified in the same way as mentioned in the acetylation to yield an oxidation product, 175 mg.. The product gave unidentified elemental analyses.

Repetition of the above procedure with 95 %  $H_2O_2$  in place of bleaching powder afforded the same oxidation product with identical I.R. spectra, as shown in Figure 5.

### 3.6 Degradation of thailandine with concentrated nitric acid

Thailandine, 2.0 g. (0.0014 mole), was mixed with 100 ml. of conc.  $HNO_3$  in a 500 ml. beaker and heated on a hot plate until no trace of red-brown vapor of nitrogen dioxide was given off, and a yellow solution was obtained. The solution was then heated to dryness. The residue was dissolved in distilled water (ca. 50 ml.) and the solution was warmed on the water bath.

The clear solution was separated by filtration. The pale-yellow oxidation product precipitated on cooling. The pure compound was obtained by fractional crystallization in a hot distilled water. The yield was 252 mg., 12.6 %, m.p. 135-137° c. Anal. Calcd. for  $C_7H_5NO_4$  : C = 50.24 %, H = 3.08 %, N = 7.97 %, O = 38.71 %. Molecular weight (mass spectrometry) 167 (found: C = 50.3 %, H = 3.0 %, N = 8.38 %, O = 38.32 %). The I.R. spectrum is shown in Figure 8.