

PTEROPODINE AND ISOPTEROPODINE, THE ALKALOIDS FROM

UNCARIA PTEROPODA

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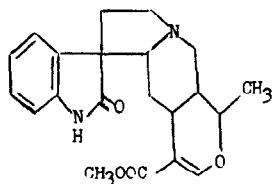
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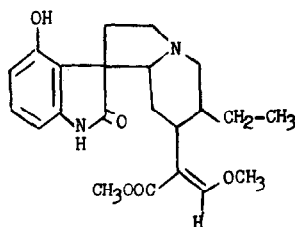
Malaya.

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Mitragyna and Uncaria species of the Rubiaceae family contain a number of oxindole alkaloids. Recent investigations have led to the isolation and elucidation of the structure of mitraphylline as (1) from the bark of Mitragyna rubrostipulacea.<sup>1</sup> Uncarine-A and its stereoisomer, uncarine-B were isolated from the root, bark, and stem of Uncaria Kewakamii Hayata.<sup>2</sup> The same structure (1) has been proposed for these alkaloids.<sup>3</sup>



(1)



(2)

The genus of Uncaria comprises some thirty species of trees found in Malaya. The presence of alkaloids in Uncaria pteropoda collected in Ulu Langat, Selangor, Malaya, has been noted in the course of a continuing screening program for alkaloid-bearing plants.<sup>4</sup> We have now examined the alkaloids of Uncaria pteropoda. Extracting the stem, bark, and root by the conventional procedures afforded a mixture of basic material amounting to 0.4%, 2.8% and 0.94% of the respective dry weights. Paper chromatographic tests showed the presence of two alkaloids. A convenient but not complete separation of the two alkaloids can be achieved by partitioning the mixture between benzene and 0.2N acetic acid. The major alkaloid for which we propose the name pteropodine is obtained from the acid fraction, while the benzene layer yields the other base designated as isopteropodine. Both the bases are not identical with mitraphylline or uncarine-A or -B. However, from the spectral evidence, they are most probably stereoisomeric with these alkaloids.

The properties of these two alkaloids are recorded in Table I.

TABLE I

|                     | pteropodine                          | isopteropodine                       |
|---------------------|--------------------------------------|--------------------------------------|
| m.p.                | 217-219°C                            | 209-211°C                            |
| $[\alpha]_D^{19}$   | -102.5(c, 1.0 in CHCl <sub>3</sub> ) | -111.0(c, 1.0 in CHCl <sub>3</sub> ) |
| pKa                 | 4.8                                  | 4.05                                 |
| M.W.                | -                                    | 380                                  |
| picrate, m.p.       | 143-144°C                            | 147-148°C                            |
| methiodide, m.p.    | 209-211°(softens at 203°)            | 217-219°(softens at 210°)            |
| hydrochloride, m.p. | -                                    | 181-183°C                            |
| hydroiodide, m.p.   | -                                    | 216-218°C                            |

Analyses of pteropodine and isopteropodine show that they each contain one methoxyl group, but no N-methyl group, and have molecular formula, C<sub>21</sub>H<sub>24</sub>O<sub>4</sub>N<sub>2</sub>. Titrations of pteropodine and isopteropodine show them to be monoacidic bases. Clearly, pteropodine and isopteropodine are stereoisomers, and this evidence is confirmed below.

| <u>Analyses</u>  | C     | H    | N    | OMe     | MW  |
|--|-------|------|------|---------|-----|
| pteropodine  | 68.86 | 6.80 | 7.36 | 8.52    | -   |
| isopteropodine   | 68.53 | 6.74 | 7.25 | 8.52    | 380 |
| C <sub>21</sub> H <sub>24</sub> O <sub>4</sub> N <sub>2</sub> requires | 68.46 | 6.57 | 7.48 | 8.29(1) | 368 |

The ultraviolet and infrared spectra of pteropodine and isopteropodine are similar to each other and are closely similar to those of mitraphylline<sup>1</sup> and uncarine-A and -B,<sup>5</sup> [Table II and IIIa and IIIb], indicating that pteropodine and isopteropodine contain an oxindole chromophore and the  $\text{CH}_3\text{OOC} - \text{C}^1 = \text{CHOR}$  grouping. In support of this, the infrared peaks of pteropodine and isopteropodine at  $1627 \text{ cm}^{-1}$  and  $1627 \text{ cm}^{-1}$  respectively confirmed the presence of the carbomethoxyl group as discussed by Marion et al.<sup>1</sup>

TABLE II

Ultraviolet Spectra of Pteropodine, Isopteropodine, Mitraphylline,<sup>1</sup> Uncarine-A and -B<sup>5</sup> in EtOH

|                | $\lambda_{\text{min}}$<br>(m $\mu$ ) | log $\epsilon$ | $\lambda_{\text{max}}$<br>(m $\mu$ ) | log $\epsilon$ | Shoulder<br>(m $\mu$ ) | log $\epsilon$ |
|----------------|--------------------------------------|----------------|--------------------------------------|----------------|------------------------|----------------|
| Pteropodine    | 225                                  | 3.93           | 246                                  | 4.20           | 280                    | 3.25           |
| Isopteropodine | 225                                  | 4.00           | 246                                  | 4.22           | 280                    | 3.27           |
| Mitraphylline  | 224                                  | 4.02           | 243                                  | 4.22           | 280                    | 3.09           |
| Uncarine-A     | 225                                  | 4.06           | 245                                  | 4.24           | 278                    | 3.09           |
| Uncarine-B     | 225                                  | 4.03           | 244                                  | 4.24           | 278                    | 3.09           |

TABLE IIIa

Infrared Spectra of Pteropodine, Isopteropodine, Mitraphylline<sup>1</sup> in Chloroform (cm<sup>-1</sup>)




|   | Pteropodine | Isopteropodine | Mitraphylline |
|---|-------------|----------------|---------------|
| NH  | 3415 (20)   | 3415 (19)      | 3415 (20)     |
| C=O   | 1708 (93)   | 1708 (92)      | 1715 (81)     |
|  | 1627 (76)   | 1627 (74)      | 1625 (68)     |

TABLE IIIb

Infrared Spectra of Pteropodine, Isopteropodine, Mitraphylline,<sup>1</sup> Uncarine-A and -B<sup>5</sup> in Nujol mull (cm<sup>-1</sup>)

|   | Pteropodine | Isopteropodine | Mitraphylline | Uncarine-A | -B   |
|---|-------------|----------------|---------------|------------|------|
|   | 3446        | 3436           | 3260          | 3340       | 3200 |
| Ester C=O   | 1719        | 1712           | 1725          | 1715       | 1730 |
| Oxindole C=O  | 1688        | 1677           | 1704          | 1693       | 1693 |
|    | 1627        | 1627           | 1626          | 1626       | 1626 |
| Cyclic ether  | 1081        | 1077           | 1105          | 1107       | 1107 |
|  | 750         | 755            | 755           | 757        | 757  |

Apart from the similarities in ultraviolet and infrared spectra, the N.M.R. spectra of pteropodine and isopteropodine show many common features, again suggesting that the two are structurally closely related - (Table IV). In the spectra of pteropodine and isopteropodine, the  $\overset{\text{O}}{\text{C}}\text{-OCH}_3$ ,  $\text{-C}=\overset{\text{O}}{\text{C}}\text{-O-}$   
H

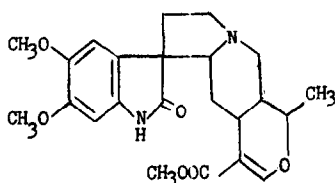
TABLE IV

N.M.R. Spectra of Pteropodine, Isopteropodine, Speciofoline, Stipulatine,<sup>7</sup> Carapaubine  
and Isoreserpilline<sup>8</sup> (in CCl<sub>3</sub> at 60 Mc in P.P.M. from TMS)

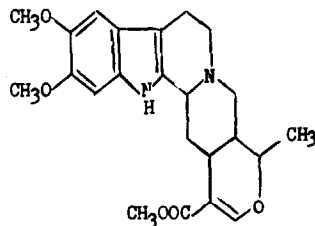
| Functional Groups   | Pteropodine     | Isopteropodine  | Speciofoline  | Stipulatine   | Carapaubine          | Isoreserpilline      |
|---------------------|-----------------|-----------------|---------------|---------------|----------------------|----------------------|
| CH <sub>3</sub> CHO | 1.60(doublet)   | 1.65(doublet)   |               |               | 1.40(doublet)        | 1.37(doublet)        |
| CH <sub>3</sub> COO | 3.80(singlet)   | 3.82(singlet)   | 3.78(singlet) | 3.70(singlet) | 3.61(singlet)        | 3.72(singlet)        |
| Aromatic H          | 7.30(multiplet) | 7.28(multiplet) | 7.08(triplet) | 7.45(triplet) | 6.55, 6.74(singlets) | 6.77, 6.90(singlets) |
| Olefinic H          | 7.70(singlet)   | 7.72(singlet)   | 7.40(singlet) | 7.23(singlet) | 7.44(singlet)        | 7.57(singlet)        |
| - N -               | 9.47(singlet)   | 9.49(singlet)   | 8.48(singlet) | 9.16(singlet) | 8.73(singlet)        | 7.95(singlet)        |

and aliphatic -NH protons give rise to singlets at 3.82 p.p.m., 7.70 p.p.m. and 9.47 p.p.m., respectively, similar to those of stipulatine and speciofoline whose structures (2) have been proposed.<sup>7</sup> The C-Me group of the CH<sub>3</sub>CHO function is indicated by the respective three proton doublet at 1.60 and 1.65 p.p.m. similar to those of caraparaubine and isoreserpiline whose structures (3,4) have recently been reported.<sup>8</sup> The respective multiplet at 7.30 p.p.m. and 7.28 p.p.m. are assigned to the aromatic protons.

Furthermore, when pteropodine is heated with pyridine, it isomerizes into an equilibrium mixture of pteropodine (20%) and isopteropodine (80%). Similarly, isopteropodine can be isomerized with 10% acetic acid into an equilibrium mixture of pteropodine (70%) and isopteropodine (30%). This characteristic parallel behaviour has also been demonstrated in mitraphylline<sup>9</sup> and uncarine-A and -B.<sup>10</sup>



(3)



(4)

Since the ultraviolet and infrared spectra are consistent with those of mitraphylline, it is reasonable to suggest that pteropodine and isopteropodine are stereisomeric with mitraphylline and that they have the same structure as (1). Work on the structural degradations of these two alkaloids is in progress.

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