

## COMMUNICATION III

### The Alkaloids of *Lindera pipericarpa* Boerl (Lauraceae)

#### ABSTRAK

*Sebatian alkaloid bagi Lindera pipericarpa diasingkan dan dicirikan sebagai N-metillaurotetanine, isokoridina, dan nor-isokoridina.*

#### ABSTRACT

*The alkaloids of Lindera pipericarpa were isolated and characterized as N-methylaurotetanine, isocorydine, and nor-isocorydine.*

#### INTRODUCTION

*Lindera pipericarpa* Boerl (Lauraceae) is a small tree of lower mountain forests in Peninsular Malaysia. Its seeds and bark are used in Malay traditional medicine and cosmetic preparations. All parts of this plant are aromatic and Burkill (1935) has described the volatile oils of leaves, fruit and bark. The presence of linderone and methyllinderone was reported by Kiang *et al.* (1961), and of laurotetanine and lindcarpine (Kiang and Sim 1967) in the bark. Reinvestigation of the alkaloidal fraction revealed three alkaloids not previously reported for this species.

#### MATERIALS AND METHODS

##### *General*

The bark of *L. pipericarpa* was collected from Bukit Kinta Forest Reserve, Perak, Peninsular Malaysia. The voucher specimen (SA 821) was deposited in the herbarium of Biology Department, Universiti Pertanian Malaysia.

Melting points were determined on a kofler hot stage and are uncorrected. Infra-red and ultraviolet spectra were recorded on Beckmann Acculab-3 and Hitachi 200-20, respectively. <sup>1</sup>H NMR spectra were measured at 300 MHz on Bruker CPX 300 instrument and mass spectra were recorded on a MS 12 instrument at 70 eV. Column and thin-layer chromatography utilized Merck 7734 and 7730 silica gel, respectively. Solvents were distilled before being used.

##### *Extraction of Plant Material*

The bark (800 g) was air dried and ground in a hammer mill to give a powder which was steeped

twice in petroleum ether (b.p. 60-80°C) for 24 h each time. The extracts which were tested for alkaloids (Meyers reagent) gave negative results. The same procedure was repeated using methanol, and each extract was tested for alkaloids until negative results were obtained. The methanol extracts were combined and evaporated under reduced pressure to give a dark brown gum. Acid (1 M, H<sub>2</sub>SO<sub>4</sub>)/chloroform fractionation of the brown gum followed by basification of the aqueous acid with Na<sub>2</sub>CO<sub>3</sub> and extraction with chloroform afforded 1.42 g of crude alkaloids. This was later subjected to gradient elution column chromatography (3.5 cm i.d x 35 cm.) on silica gel. Chloroform/methanol mixture was used as the eluent and 10 per cent increment of methanol concentration was carried out at each addition of 400 ml of solvent. Fractions of 50 ml each were collected and those with similar tlc patterns, were combined to give three combined fractions.

##### *Purification of N-Methylaurotetanine*

The first combined fraction was subjected to preparative thin-layer chromatography on silica gel using CHCl<sub>3</sub>/MeOH (95:5) as eluent to give 103 mg of amorphous solid, m.p. 187-188°C (lit. Base HBr m.p. 220-222°C) (Tewari *et al.* 1972). UV, λ<sub>max</sub> nm (log ε) MeOH: 222(4.58), 281(4.18), 302(4.16); IR, γ<sub>max</sub> cm<sup>-1</sup> (CHCl<sub>3</sub> film); 3250, 3010, 2960, 2860, 1605, 1590, 1525, 1480, 1400, 1345, 1300, 1255, 1120; <sup>1</sup>H NMR δ (300 MHz, CDCl<sub>3</sub>): 8.01 (s, 1H), 6.78 (s, 1H), 6.56 (s, 1H) 3.86 (s, 6H), 3.68(m, 1H), 3.64 (s, 3H), 3.17 (ddd, 6 Hz, 6 Hz, 4 Hz, 1H), 3.06 (dd, 6 Hz, 5 Hz, 1H), 3.03 (dd, 6 Hz, 5 Hz, 1H). 2.95 (dd, 4 Hz, 10 Hz, 1H), 2.66 (dd, 3.5 Hz, 16 Hz, 1H), 2.53 (s, 3H), 2.60-

2.49 (m, 2H); MS  $m/z$  (%): 341 ( $M^+$ , 78), 340 (100), 326 (42), 324 (38), 310 (24), 298 (22), 283 (16), 267 (18)

#### Purification of isocorydine

The second fraction was purified in a similar manner to thaliporphine using silica gel and  $\text{CHCl}_3/\text{MeOH}$  (7:3) mixture as eluent. A brownish amorphous solid (30 mg) was isolated, m.p. 176-180°C (lit. 186°) (Bhakuni *et al.* 1972; Edwards and Handa 1961); UV  $\lambda_{\text{max}}$  nm (log  $\epsilon$ ) MeOH: 220 (4.56), 268 (4.01), 302 (3.8); IR  $\gamma_{\text{max}}$   $\text{cm}^{-1}$  ( $\text{CHCl}_3$ ): 3250, 3010, 2950, 2850, 1605, 1595, 1520, 1470, 1400, 1350, 1300, 1260, 1110,  $^1\text{H NMR}$   $\delta$  (300 MHz,  $\text{CDCl}_3$ ): 8.83 (s, 1H), 6.84 (d, 8 Hz, 1H), 6.82 (d, 8 Hz, 1H), 6.70 (s, 1H), 3.91 (s, 3H), 3.90 (s, 3H), 3.70 (s, 3H), 3.20 (ddd, 6 Hz, 6 Hz, 4 Hz, 1H), 3.06 (dd, 6 Hz, 1H) 3.04 (d, 6 Hz, 1H), 2.92 (dd, 4 Hz, 10 Hz, 1H), 2.70 (dd, 3.5 Hz, 16 Hz, 1H), 2.56 (s, 3H), 2.45-2.54 (m, 2H); MS  $m/z$  (%): 341 ( $M^+$ , 68), 340 (22), 327 (24), 326 (100), 311 (16) 310 (50), 295 (16), 281 (10)

#### Purification of nor-isocorydine

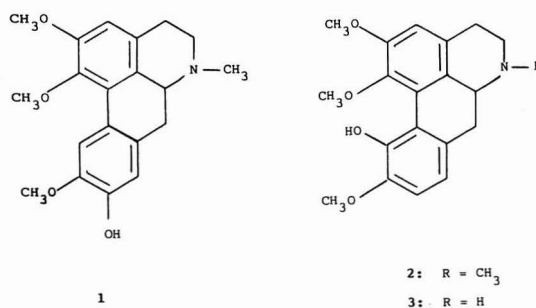
The third fraction was further purified by preparative thin-layer chromatography using silica gel and eluted with  $\text{CHCl}_3/\text{MeOH}$  (9:1) mixture. An amorphous solid (20 mg) was isolated, m.p. 195-200°C, (lit. 203-205°C) (Bhakuni *et al.* 1972; Rueger 1959); UV  $\lambda_{\text{max}}$  nm (log  $\epsilon$ ) MeOH: 220 (4.56), 270 (3.90), 302 (3.60); IR  $\gamma_{\text{max}}$   $\text{cm}^{-1}$  ( $\text{CHCl}_3$ ): 3500, 3320, 3010, 2950, 2860, 1610, 1585, 1530, 1470, 1400, 1350, 1300, 1260, 1220, 1100;  $^1\text{H NMR}$   $\delta$  (500 MHz,  $\text{CDCl}_3$ ): 6.86 (d, 8 Hz, 1H), 6.84 (d, 8 Hz, 1H), 6.71 (s, 1H), 3.94 (m, 1H), 3.91 (s, 6H), 3.70 (s, 3H), 3.37 (dd, 6 Hz, 4 Hz, 1H), 3.04 (m, 1H), 2.95 (dd, 4 Hz, 10 Hz, 1H), 2.80 (dd, 10 Hz, 4 Hz, 1H), 2.70 (d, 10 Hz, 1H), 2.60 (m, 1H); MS  $m/z$  (%): 327 ( $M^+$ , 80), 326 (100), 312 (18), 310 (38), 296 (20), 257 (20)

## RESULTS AND DISCUSSION

The fractionation of the crude methanolic extracts of 800 g of the bark of *L. pipericarpa* yielded 1.42 g of the crude alkaloids. Gradient polarity elution column chromatography of the crude alkaloids on silica using chloroform/methanol as the solvent followed by thin-layer chromatography gave one major and two other minor components. The major alkaloid was isolated as an amorphous solid with the MS having  $M^+$  at 341(78%) and  $M^+ - 1$  at 340(100%), which was consistent with a 1,2,9,10-tetrasubstituted

aporphine (Shamma 1972). The proton NMR spectrum further confirmed the structure as *N*-methylaurotetanine (1) and this was also supported by other spectral data which were consistent with the literature (Tewari *et al.* 1972).

Two other minor alkaloids were isolated as amorphous solids and were characterized as isocorydine (2) and nor-isocorydine (3). The MS of isocorydine has an  $M^+$  at 341 (70%) and  $M^+ - 1$  at 340 (20%) while that of nor-isocorydine has  $M^+$  peak at 327 (80%). Other spectral data of the two compounds were also consistent with the literature (Cordell 1981; Soh *et al.* 1966; Bhakuni *et al.* 1972).



Although the presence of laurotetanine and lindcarpine was previously reported neither alkaloid was isolated during our investigation. Aporphine alkaloids are the common constituents in lauraceous plants and their existence in *L. pipericarpa* is to be expected (Shamma 1972). *N*-methylaurotetanine was previously isolated from *Litsea glutenosa* var. Hook (Tewari *et al.* 1972). Isocorydine coexists with nor-isocorydine in *Annona squamosa* (Annonaceae) (Bhakuni *et al.* 1972) and isocorydine has also been isolated from *Phoebe clemensii*, (Lauraceae) (Johns and Lamberton 1976), *Hernandia ovigera* (Hernandiaceae) (Cava and Beshe 1966) and *Phyllica rogersii* (Rhamnaceae) (Edwards and Handa 1961; Arndt and Baarscher 1964). Aporphine alkaloids display a wide range of pharmacological activities and isocorydine was claimed to be antiadrenergic (Berezhinskaya *et al.* 1968).

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NORDIN HJ. LAJIS, ATAN MOHD SHARIF,  
RUTH KIEW<sup>1</sup>  
MOHAMMAD NIYAZ KHAN and  
ZAINUDIN SAMADI<sup>1</sup>

Department of Chemistry  
Universiti Pertanian Malaysia  
43400 UPM, Serdang  
Selangor Darul Ehsan,  
MALAYSIA

<sup>1</sup>Department of Biology  
Universiti Pertanian Malaysia  
43400 UPM, Serdang  
Selangor Darul Ehsan  
Malaysia

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