Sesquiterpenes and alkaloids from *Scorodocarpus borneensis*

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Abstract

A new sesquiterpene, scodopin, and a mixture of three tryptamine-type alkaloids, scorodocarpines A–C, were isolated from the fruits of *Scorodocarpus borneensis*, together with a known hemisynthetic sesquiterpene, cadalene-β-carboxylic acid, which was isolated from the bark. The structures of the new compounds were elucidated by interpretation of spectral data, especially tandem mass spectrometry for the alkaloid mixture. © 2001 Elsevier Science Ltd. All rights reserved.

Keywords: *Scorodocarpus borneensis*; Olacaceae; Sesquiterpenes; Tryptamine-type alkaloids; Tandem mass spectrometry

1. Introduction

From the fruits of *Scorodocarpus borneensis* (Baill.) Becc. (Olacaceae) collected in Malaysia, we have isolated a new sesquiterpene scodopin (1) and a mixture of three tryptamine-type alkaloids named scorodocarpines A–C (2–4). In addition, a sesquiterpene (5) of the cadalene group was isolated from the bark. Compound (5) has been synthesized previously, but was not known as a natural product (Parasmeswara Reddy and Khrisna Rao, 1982). The structures of the new compounds were established especially by 2D NMR along with tandem mass spectrometry (LSIMS/MS) for compounds 2–4.

2. Results and discussion

Scodopin (1) gave a MH\(^+\) peak in the HRCIMS at \(m/z\) 233.1545 which matched the molecular formula C\(_{15}\)H\(_{20}\)O\(_2\) (\(\Delta 0.0004\) u). The UV spectrum (\(\lambda_{max}\) 251 and 333 nm) together with the IR spectrum (\(\nu\) 1619 and 1603 cm\(^{-1}\)) suggested a highly conjugated keto derivative. In the \(^{13}\)C NMR spectrum, the carbonyl resonated at \(\delta 174.7\) and a peak at \(\delta 163.5\) could be assigned to a phenolic...
carbon. Only three signals appeared in the aromatic region of the \(^1\)H NMR spectrum, a singlet (1H) at \(\delta 7.23\) and two doublets (1H each; \(J = 11\) Hz) of two vicinal protons at \(\delta 7.12\) and 7.25. The aliphatic region showed the resonances of a methyl group at \(\delta 1.22\) (3H, \(d, J = 6.5\) Hz). The signals of an isopropyl moiety appeared at \(\delta 0.78\) (3H, \(d, J = 6.5\) Hz), 0.87 (3H, \(d, J = 6.5\) Hz) and 1.87 (1H, \(m\)). The spectrum also showed five other signals, which with the aid of the HMQC spectrum were identified as two methine and four methylene protons (Table 1). The connections between the aliphatic carbons were deduced from the spin system H15–H1–H2–H3–H4–H12–Me13–Me14 revealed in the COSY experiment and were confirmed by the HMBC spectrum (Table 1). The latter was used to establish the linkage with the aromatic seven membered A ring (diagnostic cross peaks Me-15/C-10 and H-4/C-10, C-11), as well as the final structure of this ring, which was deduced together with the \(^1\)H and the \(^{13}\)C resonance data from the correlations H-6/C-7, C-8, C-11 and H-9/C-1, C-7, C-8, C-10, C-11. The relative stereochemistry at C-1 and C-4 was determined using the NOESY experiment measured at \(-40^\circ\)C (Table 1). In these conditions, scodopin (1) adopts the usual half chair conformation for ring B. The correlations H-2/\(\alpha\)/Me-13 and H-3/\(\alpha\)/Me-15 indicated H-1\(\beta\) and H-4\(\alpha\) configurations, respectively.

Scorodocarpines A–C (2–4), were isolated as a mixture. The EIMS showed three [M]+ peaks at \(m/z\) 498, 496 and 468 corresponding to the molecular formulas of C\(_{32}\)H\(_{54}\)O\(_2\)N\(_2\), C\(_{32}\)H\(_{52}\)O\(_2\)N\(_2\) and C\(_{30}\)H\(_{48}\)O\(_2\)N\(_2\), respectively. The UV spectrum exhibited maxima at 223, 278 and 304 nm suggesting an indole residue and the IR showed a band at 1636 cm\(^{-1}\) assignable to an amide carbonyl group. These data, along with peaks at \(m/z\) 160 and 146 observed in the mass spectrum (Maeda et al., 1993), were in accordance with the structure of \(\text{N-acyl-5-hydroxytryptamines}\). The acyl residues were saturated (22 carbons) for compound 2, and monounsaturated with 22 and 20 carbons for compounds 3 and 4, respectively. The \(\text{N-acyl-5-hydroxytryptamine}\) type structure was confirmed by the NMR spectra (CDCl\(_3\)–CD\(_3\)OD 9:1, Table 2). The presence of the 5-hydroxyindole moiety

\[\text{Scheme 1.}\]
Table 1

\(^{13}\)C NMR (75 MHz) and \(^1\)H NMR (400 MHz) data for scodopin (1) in CDCl\(_3^a\)

<table>
<thead>
<tr>
<th>Position</th>
<th>(\delta_C) (ppm)</th>
<th>(\delta_H) (J Hz)</th>
<th>HMBC</th>
<th>NOESY(^b)</th>
</tr>
</thead>
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<tr>
<td>1</td>
<td>36.9</td>
<td>2.86 (q) (6)</td>
<td>2,9,10,11,15</td>
<td>2x8,9,15</td>
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<tr>
<td>2</td>
<td>26.9 (\beta) 1.96 (m) (\pm) 1.43 (m)</td>
<td>1,4,15</td>
<td>20,3</td>
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<tr>
<td>3</td>
<td>19.5</td>
<td>1.78 (m)</td>
<td>1,2,4,12</td>
<td>4,15</td>
</tr>
<tr>
<td>4</td>
<td>48.0</td>
<td>2.48 (m)</td>
<td>2,5,10,11,12,13,14</td>
<td>5,12,13,14</td>
</tr>
<tr>
<td>5</td>
<td>142.8</td>
<td>7.25 (d) (11)</td>
<td>4,6,8,10</td>
<td>12,14</td>
</tr>
<tr>
<td>6</td>
<td>126.3</td>
<td>7.12 (d) (11)</td>
<td>5,7,8,11</td>
<td></td>
</tr>
<tr>
<td>7</td>
<td>163.5</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>8</td>
<td>174.7</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>9</td>
<td>122.1</td>
<td>7.23 (s)</td>
<td>1,7,8,10,11</td>
<td>15</td>
</tr>
<tr>
<td>10</td>
<td>152.3</td>
<td></td>
<td></td>
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<tr>
<td>11</td>
<td>141.4</td>
<td></td>
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<tr>
<td>12</td>
<td>33.7</td>
<td>1.87 (m)</td>
<td>4,13</td>
<td>13,14</td>
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<tr>
<td>13</td>
<td>19.8</td>
<td>0.78 (d) (6.5)</td>
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<tr>
<td>15</td>
<td>23.7</td>
<td>1.22 (d) (6.5)</td>
<td>1,2,10</td>
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</tr>
</tbody>
</table>

\(^a\) Assignments based on 2D experiments.

\(^b\) Measured at \(-40^\circ\)C.

was deduced from the coupling pattern of H-7 (\(\delta\) 7.17, \(d, J = 8.5\) Hz), H-6 (\(\delta\) 6.75, \(dd, J = 8.5\) and 2) and H-4 (\(\delta\) 6.99, \(d, J = 2\)), while H-2 gave a singulet at \(\delta\) 6.93, and was further supported by the typical \(^{13}\)C NMR signals of the indole nucleus (Kamano et al., 1999) and the correlations observed in the HMBC experiment (Table 2). The latter also displayed a correlation between C-9 and H-10 of the tryptamine chain (CH\(_3\)-10, \(\delta_H\) 2.85 and \(\delta_C\) 25.7; CH\(_2\)-11, \(\delta_H\) 3.48, \(\delta_C\) 40.0). The signals of the amide NH appeared at \(\delta\) 6.05 (\(t, J = 7\)) and the indole NH at \(\delta\) 8.40 with small intensities due to partial deuterium exchange. The characteristic resonances of the acyl chains are given in Table 2. The geometry of the double bonds (\(\delta_H\) 5.32, \(\delta_C\) 130.1) is Z, which is deduced from the chemical shift of the \(\alpha\)-CH\(_2\) group (\(\delta_C\) 27.4). The chains are linear owing to the presence of an unique signal for a terminal methyl at \(\delta\) 14.3.

The structures of the tryptamine side chains were confirmed by an LSIMS/MS experiment which in addition allowed to determine the position of the double bond inside the chains. The LSIMS spectrum recorded in the presence of lithium iodide showed three peaks at \(m/z\) 505, 503 and 475 corresponding to ions [\(2 + Li\)]\(^+\), [\(3 + Li\)]\(^+\) and [\(4 + Li\)]\(^+\), respectively.

The CID spectra of the precursor ion [\(2 + Li\)]\(^+\) at \(m/z\) 505 displayed a series of peaks separated by 14 mass units in the \(m/z\) range 475-209. These fragments are generated by charge-remote fragmentation processes leading to losses of C\(_{\text{n}}\)H\(_{\text{n}+2}\) neutral species from the precursor ion. They can be attributed to ‘\(C_m\)-type ions \((m = 1, 2, \ldots, 20)\) in agreement with the nomenclature proposed by Griffiths et al. (1996) and completed by Claeyss et al. (1996). The fatty acyl moiety of compound 2 was thus easily identified as a docosanoate chain (Scheme 1).

The CID spectra of the precursor ion [\(3 + Li\)]\(^+\) at \(m/z\) 503 showed fragment ion peaks identical to some of those observed on the corresponding spectrum of [\(2 + Li\)]\(^+\), in particular the signals at \(m/z\) 209/210, 224, 237/238, 251 and 265. Two other ion peaks at \(m/z\) 349 and 403 were characteristic of allylic cleavages on both sides of a double bond located at position C\(_{13}\)C\(_{14}\) (Scheme 1). The fragments at \(m/z\) 335 (\(H_10\)), 417/418 (\(H_{16}/H_{16}\)) corresponded to homodially cleavages and the ions \('V_{12}' and \('V_{14}' (\(m/z\) 363 and 389, respectively) were attributed to the vinyl fragmentations. The 13-docosanoate fatty acyl chain was thus unambiguously recognized by these mass spectrometric data.

The [\(4 + Li\)]\(^+\) ion at \(m/z\) 475 showed a very similar behavior under high-energy collisional activation. The abundant fragment ion at \(m/z\) 321 assigned to the ‘\(A_9\)' ion and the ions at \(m/z\) 375/376 (ions \(A_{13}/A_{13}\)) indicated the presence of a double bond at position C\(_{11}\)-C\(_{12}\). The other signals at \(m/z\) 293 (\(C_7\)), 307 (\(H_8\)), 335 (\(V_{10}\)), 361/362 (\('V_{12}/V_{12}'\) and 389 (\(H_{14}\)) were in agreement with the structure. Thus, compound 4 corresponded to the product of N-acylation of serotonin by 11-eicosanoic acid.

Acyl tryptamines were known to exist in other plants, having various side chains (Maeda et al., 1993; Kamano et al., 1999), but unsaturated side chains were found for the first time in this study. They correspond to known acids isolated from several plants species. However,
these acids have not been found in the Olacaceae family whose chemical study is still scarce.

3. Experimental

3.1. General

Optical rotation at 20° were taken on a Perkin-Elmer 241 polarimeter. Spectra were recorded as follow: UV: MeOH, Varian CARY 100; IR: CHCl₃ or KBr, Perkin-Elmer SPECTRUM BX; NMR: Bruker AM 300 (¹³C NMR spectra) and Bruker AMX 400 (¹H NMR and 2D NMR spectra); EIMS: Thermoquest Automass Multi; HRCIMS: Kratos MS-80 RF, MS/MS: see Section 3.4.

3.2. Plant material

Fruits and bark of Scorodocarpus borneensis (Baill.) Becc. (Olacaceae) were collected from Kuala Kangsar, Perak (Malaysia). The plant was identified by one of us (C.W). Voucher specimens (K1) are deposited at the Chemistry Department, Universiti Pertanian Malaysia.

3.3. Extraction and isolation

Dried fruits (200 g) of S. borneensis were extracted exhaustively with EtOH at room temperature. The extract (5.2 g) was repeatedly chromatographed on silica gel yielding scodopin I (12 mg, 1. CHCl₃–MeOH 99:1, 2. CHCl₃–MeOH 99.5:0.5) and the mixture of scorodocarpines A–C (2–4) (15 mg, 1. CHCl₃–MeOH 99:1, 2. CHCl₃–MeOH 98:2, 3. CHCl₃–MeOH 98:2).

Dried ground bark (300 g) of S. borneensis was extracted in the same way with EtOH. The extract (10.3 g) was again repeatedly chromatographed on silica gel affording compound 5 (20 mg, 1. petroleum ether, 2. petroleum ether–CHCl₃, 99:1).

3.4. Tandem mass spectrometry

The MS/MS spectra were obtained using a ZabSpec-T five sector tandem mass spectrometer (Micromass, Manchester, UK) with E₁B₁E₂-B₂E₃ geometry (E: electrostatic analyzers, B: magnets). The sample was dissolved in a liquid matrix (n-nitrobenzyl alcohol–glycerol–trifluoroacetic acid 50:50:1, saturated with lithium iodide). [M + Li]⁺ precursor ions were generated by cesium ion bombardment at 30 keV. The precursor ions submitted to MS/MS experiments were selected by MSI set at appropriate E and B values and then focused in a collision cell located in the fourth field-free region (between E₂ and B₂). Argon was introduced at a pressure leading to an almost 70% attenuation of the precursor ion beam. The collision cell was floated at 4 kilovolts so as to attain a collision energy of 4 keV. Further experimental details are given elsewhere (Gleye et al., 1999).

3.5. Scodopin (I)

Amorphous gum. [α]D 0° (CHCl₃, c 0.5) UV λ_max nm (log ε) 251 (3.94), 330 (3.75), IR (CHCl₃) ν cm⁻¹ 3388, 1619, 1603. HRCIMS m/z 233.1545 [M + H]⁺ (C₁₃H₂₁O₂, Δ 0.0004 u). ¹H and ¹³C NMR, see Table 1.

3.6. Mixture of scorodocarpines A, B and C (2–4)

Amorphous gum. UV λ_max nm (log ε) 223 (4.55), 278 (4.02), 304 (3.90). IR (KBr) ν cm⁻¹ 3502, 3416, 3405, 1636 1543, 1489, 1470, 800, 730. EIMS m/z 498 [M⁺], m/z 496 [M⁺ ], m/z 468 [M⁺ ], 160, 146. ¹H and ¹³C NMR, see Table 2.

3.7. Cadalene-β-carboxylic acid (5)

¹H NMR (CDCl₃) : 7.46 (1H, d, J = 6.5 Hz, H-2), 7.44 (1H, d, J = 6.5 Hz, H-3), 9.08 (1H, d, J = 2.5 Hz, H-5), 8.18 (1H, dd, J = 8.5, 2.5 Hz, H-7), 8.12 (1H, d, J = 8.5 Hz, H-8), 3.88 (1H, sept, J = 7 Hz, H-11), 1.46 (6H, d, J = 7 Hz, Me-12, Me-13), 2.72 (3H, s, Me-14); ¹³C NMR (CDCl₃): 132.1 (C-1), 129.3 (C-2), 122.4 (C-3), 144.7 (C-4), 128.0 (C-5), 125.8 (C-6), 124.6 (C-7), 125.4 (C-8), 135.7 (C-9), 130.7 (C-10), 28.5 (C-11), 23.8 (C-12, C-13), 19.5 (C-14), 172.7 (C-15).

References


