Supplementary Material

Non-halogenated new sesquiterpenes from Bornean Laurencia snackeyi

Takashi Kamada and Charles Santhanaraju Vairappan*

Laboratory of Natural Products Chemistry, Institute for Tropical Biology and Conservation, Universiti of Malaysia Sabah, 88400 Kota Kinabalu, Sabah, Malaysia

*Author to whom correspondence should be addressed; *E-Mail: csv@ums.edu.my

Tel.: +60-88-320-000 ext. 2397; Fax: +60-88-320-291.

Abstract: Two new non-halogenated sesquiterpenes, snakeol (1) and snakediol (2) were isolated together with 9 known sesquiterpenes such as (R,Z)-33-dimethyl-5-methylene-4-(3-methylpenta-24-dien-1-yl)cyclohex-1-ene (3), palisol (4), pacifigorgiol (5), palisadin D (6), palisadin A (7), palisadin B (8), 5-acetoxypalisadin B (9), debromolaurinterol (10) and α-bromocuparane (11) from the red algae Laurencia snackeyi. The structures of two new metabolites were determined from their spectroscopic data (IR, 1D and 2D NMR and MS). Compounds 1, 2, 10 and 11 showed strong antibacterial activity against selected human clinical bacterial pathogens.

Keywords: Red alga; Rhodomelaceae; Laurencia snackeyi; Sesquiterpene; Chemical race; Antibacterial activity
Supplementary Information

Table S1. $^1$H and $^{13}$C NMR data and HMBC data for snakeol (1) (recorded at 600/150 MHz in CDCl$_3$, $\delta$ in ppm, $J$ in Hz).

Table S2. $^1$H and $^{13}$C NMR data and HMBC data for snakediol (2) (recorded at 600/150 MHz in CDCl$_3$, $\delta$ in ppm, $J$ in Hz).

Table S3. $^1$H and $^{13}$C NMR data and HMBC data for palisadin D (6) (recorded at 600/150 MHz in CDCl$_3$, $\delta$ in ppm, $J$ in Hz).

Table S4. Antibacterial activities of isolated pure compounds.

Figure S2. COSY correlations (bold lines) and selected HMBC correlations (H → C) of 1 and 2.

Figure S3. $^1$H NMR spectrum of snakeol (1) in CDCl$_3$ (600 MHz).

Figure S4. $^{13}$C NMR spectrum of snakeol (1) in CDCl$_3$ (150 MHz).

Figure S5. HSQC spectrum of snakeol (1) in CDCl$_3$.

Figure S6. $^1$H-$^1$H COSY spectrum of snakeol (1) in CDCl$_3$.

Figure S7. HMBC spectrum of snakeol (1) in CDCl$_3$.

Figure S8. NOESY spectrum of snakeol (1) in CDCl$_3$.

Figure S9. $^1$H NMR spectrum of snakediol (2) in CDCl$_3$ (600 MHz).

Figure S10. $^{13}$C NMR spectrum of snakediol (2) in CDCl$_3$ (150 MHz).

Figure S11. HSQC spectrum of snakediol (2) in CDCl$_3$.

Figure S12. $^1$H-$^1$H COSY spectrum of snakediol (2) in CDCl$_3$. 
Figure S13. HMBC spectrum of snakediol (2) in CDCl₃.

Figure S14. NOESY spectrum of snakediol (2) in CDCl₃.

Figure S15. ¹H NMR spectrum of palisadin D (6) in CDCl₃ (600 MHz).

Figure S16. ¹³C NMR spectrum of palisadin D (6) in CDCl₃ (150 MHz).

Figure S17. HSQC spectrum of palisadin D (6) in CDCl₃.

Figure S18. ¹H-¹H COSY spectrum of palisadin D (6) in CDCl₃.

Figure S19. HMBC spectrum of palisadin D (6) in CDCl₃.

Figure S20. NOESY spectrum of palisadin D (6) in CDCl₃.
Table S1. $^1$H and $^{13}$C NMR data and HMBC data for snakeol (1) (recorded at 600/150 MHz in CDCl$_3$, $\delta$ in ppm, $J$ in Hz).

| C  | $^{13}$C (δ) | $^1$H (δ) | multiplicity, $J$ (Hz) | HMBC correlations |
|----|-------------|-----------|------------------------|-------------------|
| 1  | 60.1        | 4.15      | d $J = 7.6$            | C-2, C-3          |
|    |             | 4.15      |            7.6          | C-2, C-3          |
| 2  | 123.7       | 5.40      | t $J = 7.6$            | C-4               |
| 3  | 141.1       |           |                       |                   |
| 4  | 38.6        | 2.01      | m                     | C-2, C-3          |
|    |             | 1.85      | m                     | C-2, C-3, C-5, C-12|
| 5  | 25.5        | 1.60      | m                     |                   |
|    |             | 1.40      | m                     | C-6               |
| 6  | 53.0        | 1.91      | dd $J = 11.7, 3.4$    | C-4, C-7, C-13   |
| 7  | 146.4       |           |                       |                   |
| 8  | 32.9        | 2.65      | br d $J = 17.2$       | C-7, C-9, C-10   |
|    |             | 2.65      | br d $J = 17.2$       | C-7, C-9, C-10   |
| 9  | 123.7       | 5.49      | dt $J = 9.6, 3.4$     | C-7, C-8, C-10, C-11|
| 10 | 137.7       | 5.36      | d $J = 9.6$           | C-6, C-8, C-9, C-11, C-14|
| 11 | 37.9        |           |                       |                   |
| 12 | 17.1        | 1.67      | s                     | C-2, C-3, C-4    |
| 13 | 110.3       | 4.87      | br s                  | C-6, C-8         |
|    |             | 4.68      | br s                  | C-6, C-8         |
| 14 | 26.0        | 0.93      | s                     | C-6, C-9, C-10, C-15|
| 15 | 31.2        | 1.00      | s                     | C-6, C-9, C-10, C-14|
Table S2. \(^1\)H and \(^{13}\)C NMR data and HMBC data for snakediol (2) (recorded at 600/150 MHz in CDCl\(_3\), \(\delta\) in ppm, \(J\) in Hz).

|   | \(^{13}\)C (\(\delta\)) | \(^1\)H (\(\delta\)) | multiplicity, \(J\) (Hz) | HMBC correlations |
|---|-----------------|-----------------|---------------------|------------------|
| 1 | 65.7            | 3.63            | dd \(J = 11.0, 3.4\) | C-2, C-3         |
|   |                 | 3.52            | dd \(J = 11.0, 3.4\) | C-2, C-3         |
| 2 | 71.8            | 4.64            | dd \(J = 11.0, 3.4\) | C-4              |
| 3 | 133.9           |                 |                    |                  |
| 4 | 129.6           | 5.28            | dd \(J = 17.2, 6.9\) | C-2, C-3         |
| 5 | 25.4            | 2.33            | m                   | C-6              |
|   |                 | 1.96            | m                   | C-6              |
| 6 | 53.6            | 1.99            | dd \(J = 11.0, 4.1\) | C-4, C-7, C-13   |
| 7 | 146.2           |                 |                    |                  |
| 8 | 33.1            | 2.65            | br s                | C-7, C-9, C-10   |
|   |                 | 2.65            | br s                | C-7, C-9, C-10   |
| 9 | 123.8           | 5.50            | dt \(J = 10.3, 3.4\) | C-7, C-8, C-10, C-11 |
| 10| 137.6           | 5.36            | d \(J = 10.3\)      | C-6, C-8, C-9, C-11, C-14 |
| 11| 37.8            |                 |                    |                  |
| 12| 19.0            | 1.69            | s                   | C-2, C-3, C-4    |
| 13| 110.6           | 4.88            | br s                | C-6, C-8         |
|   |                 | 4.67            | br s                | C-6, C-8         |
| 14| 31.0            | 1.01            | s                   | C-6, C-9, C-10, C-15 |
| 15| 25.9            | 0.93            | s                   | C-6, C-9, C-10, C-14 |
Table S3. $^1$H and $^{13}$C NMR data and HMBC data for palisadin D (6) (recorded at 600/150 MHz in CDCl$_3$, $\delta$ in ppm, $J$ in Hz).

| C  | $^{13}$C ($\delta$) | $^1$H ($\delta$) | multiplicity, $J$ (Hz) | HMBC correlations |
|----|---------------------|------------------|------------------------|-------------------|
| 1  | 73.1                | 4.08             | t $J = 8.3$             | C-12              |
|    |                     | 3.49             | t $J = 8.3$             |                   |
| 2  | 70.5                | 4.99             | br s                   | C-2               |
| 3  | 142.6               |                  |                        |                   |
| 4  | 121.7               | 5.52             | m                      | C-2               |
| 5  | 27.6                | 2.28             | m                      | C-4, C-7, C-11    |
|    |                     | 2.12             | m                      |                   |
| 6  | 44.5                | 2.33             | m                      | C-4, C-5, C-7, C-11, C-13 |
| 7  | 79.7                |                  |                        |                   |
| 8  | 33.2                | 2.17             | m                      |                   |
|    |                     | 1.34             | m                      |                   |
| 9  | 38.9                | 1.73             | m                      | C-7               |
|    |                     | 1.63             | m                      | C-8               |
| 10 | 71.7                |                  |                        |                   |
| 11 | 42.6                | 1.36             | m                      |                   |
| 12 | 71.9                | 4.40             | d $J = 12.4$            |                   |
|    |                     | 4.32             | d $J = 12.4$            |                   |
| 13 | 20.3                | 1.19             | s                      | C-6, C-7, C-8     |
| 14 | 13.3                | 0.98             | d $J = 6.9$             | C-6, C-10, C-11   |
| 15 | 30.3                | 1.22             | s                      | C-9, C-10, C-11   |
Table S4. Antibacterial activities of isolated pure compounds.

| Compound                | MIC (mM) | MBC (mM) | MBC : MIC  |
|-------------------------|----------|----------|------------|
| Snakeol (1)             |          |          |            |
| *Escherichia coli*      | 0.45     | 1.36     | 3.02 (bactericidal) |
| *Salmonella typhi*      | 0.57     | 1.59     | 2.79 (bactericidal) |
| Snakediol (2)           |          |          |            |
| *Escherichia coli*      | 0.42     | 1.16     | 2.76 (bactericidal) |
| *Salmonella typhi*      | 0.53     | 1.48     | 2.79 (bactericidal) |
| Palisadin D (6)         |          |          |            |
| *Escherichia coli*      | >1.98    | -        | -          |
| *Salmonella typhi*      | -        | -        | -          |
| Palisadin A (7)         |          |          |            |
| *Escherichia coli*      | >1.59    | -        | -          |
| *Salmonella typhi*      | -        | -        | -          |
| Debromolaurinterol (10) |          |          |            |
| *Escherichia coli*      | >2.31    | -        | -          |
| *Salmonella typhi*      | 0.58     | 1.62     | 2.79 (bactericidal) |
| α-Bromocuparane (11)    |          |          |            |
| *Escherichia coli*      | >1.78    | -        | -          |
| *Salmonella typhi*      | 0.36     | 0.98     | 2.72 (bactericidal) |

Note: Kanamycin; MIC-0.15 mM, MBC-0.26 mM, MBC : MIC-1.73 (bactericidal).
Figure S2. COSY correlations (bold lines) and selective HMBC correlations (H → C) for 1 and 2.
Figure S3. $^1$H NMR spectrum of snakeol (1) in CDCl$_3$ (600 MHz).
Figure S4. $^{13}$C NMR spectrum of snakeol (1) in CDCl$_3$ (150 MHz).
Figure S5. HSQC spectrum of snakeol (1) in CDCl$_3$. 
Figure S6. $^1$H-$^1$H COSY spectrum of snakeol (1) in CDCl$_3$. 
Figure S7. HMBC spectrum of snakeol (1) in CDCl$_3$. 
Figure S8. NOESY spectrum of snakeol (1) in CDCl$_3$. 
Figure S9. $^1$H NMR spectrum of snakediol (2) in CDCl$_3$ (600 MHz).
Figure S10. $^{13}$C NMR spectrum of snakediol (2) in CDCl$_3$ (150 MHz).
Figure S11. HSQC spectrum of snakediol (2) in CDCl₃.
Figure S12. $^1$H-$^1$H COSY spectrum of snakediol (2) in CDCl$_3$. 
Figure S13. HMBC spectrum of snakediol (2) in CDCl$_3$. 
Figure S14. NOESY spectrum of snakediol (2) in CDCl₃.
Figure S15. $^1$H NMR spectrum of palisadin D (6) in CDCl$_3$ (600 MHz).
Figure S16. $^{13}$C NMR spectrum of palisadin D (6) in CDCl$_3$ (150 MHz).
Figure S17. HSQC spectrum of palisadin D (6) in CDCl₃.
Figure S18. $^1$H-$^1$H COSY spectrum of palisadin D (6) in CDCl$_3$. 
Figure S19. HMBC spectrum of palisadin D (6) in CDCl₃.
Figure S20. NOESY spectrum of palisadin D (6) in CDCl₃.