SUPPLEMENTARY MATERIAL

New monoterpenoid alkaloids from the aerial parts of *Uncaria hirsuta*

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New monoterpenoid alkaloids from the aerial parts of *Uncaria hirsuta*

To investigate the chemical constituents of medicinal plant *Uncaria hirsuta*, three new monoterpenoid alkaloids, named hirsutanines A-C (**1-3**), were isolated. Their structures with absolute configurations were elucidated by means of NMR, X-ray diffraction, and CD analysis. Compound **3** was the first dimeric monoterpenoid alkaloid obtained from genus *Uncaria*.

Keywords: Rubiaceae; *Uncaria hirsuta*; alkaloids

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Figure S1. ¹H NMR spectrum of compound **1** in DMSO-*d*₆ (300 MHz).

Figure S2. ¹³C spectrum of compound **1** in DMSO-*d*₆ (75 MHz).

Figure S3. DEPT-135 spectrum of compound **1** in DMSO- d_6 (75 MHz).

Figure S4. ^1H - ^1H COSY spectrum of compound **1** in DMSO- d_6 .

Figure S5. HSQC spectrum of compound **1** in DMSO- d_6 .

Figure S6. HMBC spectrum of compound **1** in DMSO- d_6 .

Figure S7. NOESY spectrum of compound **1** in DMSO- d_6 .

Figure S8. HR-ESI-MS spectrum of **1**.

Figure S9. UV spectrum of **1** in CH₃OH.

Figure S10. IR (KBr disc) spectrum of **1**.

Figure S11. Single crystal X-ray data and structures of **1**.

Crystal data of compound **1** was deposited in the Cambridge Crystallographic Data Centre (CCDC 980271).

Table S1. Crystal data and structure refinement for **1**.

Identification code	1
Empirical formula	C ₁₁ H ₁₅ N O ₃
Formula weight	209.24
Temperature	173.02(18) K
Wavelength	1.5418 Å
Crystal system, space group	Orthorhombic, P 2 ₁ 2 ₁ 2 ₁
Unit cell dimensions	a = 8.2646(2) Å alpha = 90 deg. b = 11.2177(3) Å beta = 90 deg. c = 11.7920(3) Å gamma = 90 deg.
Volume	1093.23(5) Å ³
Z, Calculated density	4, 1.198 Mg/m ³
Absorption coefficient	0.730 mm ⁻¹
F(000)	424
Crystal size	0.32 x 0.28 x 0.24 mm
Theta range for data collection	5.44 to 62.83 deg.
Limiting indices	-9 ≤ h ≤ 9, -12 ≤ k ≤ 12, -13 ≤ l ≤ 13
Reflections collected / unique	8820 / 1742 [R(int) = 0.0294]
Completeness to theta = 62.83	99.1 %
Absorption correction	Semi-empirical from equivalents

Max. and min. transmission	1.00000 and 0.70217
Refinement method	Full-matrix least-squares on F ²
Data / restraints / parameters	1742 / 0 / 137
Goodness-of-fit on F ²	1.083
Final R indices [I>2sigma(I)]	R1 = 0.0264, wR2 = 0.0693
R indices (all data)	R1 = 0.0271, wR2 = 0.0698
Absolute structure parameter	-0.2(2)
Largest diff. peak and hole	0.103 and -0.153 e.A ⁻³

Table S2. Atomic coordinates ($\times 10^4$) and equivalent isotropic displacement parameters ($\text{\AA}^2 \times 10^3$) for **1**. U(eq) is defined as one third of the trace of the orthogonalized U_{ij} tensor.

U(eq)		x	y	z
N(2)	8090(2)	8450(1)	3338(1)	32(1)
O(1)	8101(1)	6363(1)	3015(1)	34(1)
O(2)	9294(1)	9434(1)	-522(1)	39(1)
O(3)	7702(2)	10573(1)	490(1)	44(1)
C(1)	9044(2)	7366(1)	3342(1)	29(1)
C(3)	7940(2)	9103(1)	2392(1)	27(1)
C(4)	8661(2)	8826(1)	1392(1)	26(1)
C(5)	9719(2)	7733(1)	1318(1)	26(1)
C(6)	10990(2)	7923(1)	402(1)	34(1)
C(7)	10186(2)	8330(2)	-676(1)	38(1)
C(8)	11637(2)	8394(1)	2866(1)	34(1)
C(9)	10435(2)	7467(1)	2497(1)	29(1)
C(10)	13113(2)	8162(2)	3207(1)	42(1)
C(11)	8502(2)	9652(1)	467(1)	32(1)
C(12)	6890(2)	6053(2)	3819(1)	44(1)

Table S3. Bond lengths [$\text{\AA}$] and angles [deg] for **1**.

N(2)-C(3)	1.3400(17)
N(2)-C(1)	1.4494(17)
N(2)-H(2)	0.8600

O(1)-C(1)	1.4214(17)
O(1)-C(12)	1.4219(18)
O(2)-C(11)	1.3598(17)
O(2)-C(7)	1.4527(19)
O(3)-C(11)	1.2264(18)
C(1)-C(9)	1.525(2)
C(1)-H(1)	0.9800
C(3)-C(4)	1.3566(19)
C(3)-H(3)	0.9300
C(4)-C(11)	1.4374(19)
C(4)-C(5)	1.5092(18)
C(5)-C(6)	1.5217(19)
C(5)-C(9)	1.5403(19)
C(5)-H(5)	0.9800
C(6)-C(7)	1.505(2)
C(6)-H(6A)	0.9700
C(6)-H(6B)	0.9700
C(7)-H(7A)	0.9700
C(7)-H(7B)	0.9700
C(8)-C(10)	1.310(2)
C(8)-C(9)	1.503(2)
C(8)-H(8)	0.9300
C(9)-H(9)	0.9800
C(10)-H(10A)	0.9300
C(10)-H(10B)	0.9300
C(12)-H(12A)	0.9600
C(12)-H(12B)	0.9600
C(12)-H(12C)	0.9600
C(3)-N(2)-C(1)	120.77(11)
C(3)-N(2)-H(2)	119.6
C(1)-N(2)-H(2)	119.6
C(1)-O(1)-C(12)	113.52(11)
C(11)-O(2)-C(7)	120.31(11)
O(1)-C(1)-N(2)	111.37(11)
O(1)-C(1)-C(9)	107.16(10)
N(2)-C(1)-C(9)	110.21(11)
O(1)-C(1)-H(1)	109.4
N(2)-C(1)-H(1)	109.4
C(9)-C(1)-H(1)	109.4
N(2)-C(3)-C(4)	123.89(12)
N(2)-C(3)-H(3)	118.1
C(4)-C(3)-H(3)	118.1
C(3)-C(4)-C(11)	118.14(12)

C(3)-C(4)-C(5)	119.41(12)
C(11)-C(4)-C(5)	122.20(12)
C(4)-C(5)-C(6)	109.10(11)
C(4)-C(5)-C(9)	109.08(10)
C(6)-C(5)-C(9)	113.77(11)
C(4)-C(5)-H(5)	108.3
C(6)-C(5)-H(5)	108.3
C(9)-C(5)-H(5)	108.3
C(7)-C(6)-C(5)	109.70(12)
C(7)-C(6)-H(6A)	109.7
C(5)-C(6)-H(6A)	109.7
C(7)-C(6)-H(6B)	109.7
C(5)-C(6)-H(6B)	109.7
H(6A)-C(6)-H(6B)	108.2
O(2)-C(7)-C(6)	112.18(12)
O(2)-C(7)-H(7A)	109.2
C(6)-C(7)-H(7A)	109.2
O(2)-C(7)-H(7B)	109.2
C(6)-C(7)-H(7B)	109.2
H(7A)-C(7)-H(7B)	107.9
C(10)-C(8)-C(9)	124.57(14)
C(10)-C(8)-H(8)	117.7
C(9)-C(8)-H(8)	117.7
C(8)-C(9)-C(1)	111.14(11)
C(8)-C(9)-C(5)	112.45(11)
C(1)-C(9)-C(5)	108.35(11)
C(8)-C(9)-H(9)	108.3
C(1)-C(9)-H(9)	108.3
C(5)-C(9)-H(9)	108.3
C(8)-C(10)-H(10A)	120.0
C(8)-C(10)-H(10B)	120.0
H(10A)-C(10)-H(10B)	120.0
O(3)-C(11)-O(2)	115.42(12)
O(3)-C(11)-C(4)	125.17(13)
O(2)-C(11)-C(4)	119.41(12)
O(1)-C(12)-H(12A)	109.5
O(1)-C(12)-H(12B)	109.5
H(12A)-C(12)-H(12B)	109.5
O(1)-C(12)-H(12C)	109.5
H(12A)-C(12)-H(12C)	109.5
H(12B)-C(12)-H(12C)	109.5

Symmetry transformations used to generate equivalent atoms:

Table S4. Anisotropic displacement parameters ($\text{\AA}^2 \times 10^3$) for **1**. The anisotropic displacement factor exponent takes the form: $-2 \pi^2 [h^2 a^{*2} U_{11} + \dots + 2 h k a^* b^* U_{12}]$

	U11	U22	U33	U23	U13	U12
N(2)	44(1)	29(1)	24(1)	-2(1)	4(1)	9(1)
O(1)	42(1)	28(1)	31(1)	-1(1)	3(1)	0(1)
O(2)	48(1)	43(1)	26(1)	6(1)	1(1)	1(1)
O(3)	66(1)	33(1)	34(1)	4(1)	-8(1)	14(1)
C(1)	39(1)	25(1)	24(1)	0(1)	-5(1)	4(1)
C(3)	31(1)	23(1)	28(1)	-4(1)	-3(1)	5(1)
C(4)	28(1)	24(1)	25(1)	-1(1)	-4(1)	2(1)
C(5)	27(1)	25(1)	26(1)	-5(1)	-1(1)	3(1)
C(6)	32(1)	42(1)	30(1)	-6(1)	3(1)	3(1)
C(7)	37(1)	50(1)	27(1)	-4(1)	6(1)	-1(1)
C(8)	40(1)	32(1)	31(1)	-1(1)	-5(1)	2(1)
C(9)	33(1)	24(1)	29(1)	-2(1)	-4(1)	7(1)
C(10)	40(1)	49(1)	39(1)	2(1)	-8(1)	-3(1)
C(11)	38(1)	32(1)	26(1)	-1(1)	-7(1)	-2(1)
C(12)	49(1)	42(1)	42(1)	5(1)	7(1)	0(1)

Table S5. Hydrogen coordinates ($\times 10^4$) and isotropic displacement parameters ($\text{\AA}^2 \times 10^3$) for **1**.

	x	y	z	U(eq)
H(2)	7613	8676	3949	38
H(1)	9483	7234	4104	35
H(3)	7305	9787	2423	33
H(5)	9040	7056	1094	31
H(6A)	11764	8518	650	41
H(6B)	11569	7185	266	41
H(7A)	11003	8445	-1256	46
H(7B)	9450	7715	-936	46
H(8)	11311	9187	2852	41
H(9)	10989	6696	2463	34
H(10A)	13479	7379	3232	51
H(10B)	13794	8781	3424	51

H(12A)	7393	5843	4525	66
H(12B)	6279	5387	3541	66
H(12C)	6180	6720	3934	66

Table S6. Torsion angles [deg] for **1**.

C(12)-O(1)-C(1)-N(2)	-67.92(14)
C(12)-O(1)-C(1)-C(9)	171.47(11)
C(3)-N(2)-C(1)-O(1)	-87.87(15)
C(3)-N(2)-C(1)-C(9)	30.93(17)
C(1)-N(2)-C(3)-C(4)	-0.8(2)
N(2)-C(3)-C(4)-C(11)	-175.30(13)
N(2)-C(3)-C(4)-C(5)	-0.9(2)
C(3)-C(4)-C(5)-C(6)	-152.01(13)
C(11)-C(4)-C(5)-C(6)	22.18(17)
C(3)-C(4)-C(5)-C(9)	-27.19(17)
C(11)-C(4)-C(5)-C(9)	147.00(13)
C(4)-C(5)-C(6)-C(7)	-50.68(15)
C(9)-C(5)-C(6)-C(7)	-172.72(12)
C(11)-O(2)-C(7)-C(6)	-35.89(18)
C(5)-C(6)-C(7)-O(2)	59.20(16)
C(10)-C(8)-C(9)-C(1)	111.52(16)
C(10)-C(8)-C(9)-C(5)	-126.81(16)
O(1)-C(1)-C(9)-C(8)	-171.80(10)
N(2)-C(1)-C(9)-C(8)	66.86(14)
O(1)-C(1)-C(9)-C(5)	64.17(12)
N(2)-C(1)-C(9)-C(5)	-57.17(14)
C(4)-C(5)-C(9)-C(8)	-68.45(14)
C(6)-C(5)-C(9)-C(8)	53.60(15)
C(4)-C(5)-C(9)-C(1)	54.80(14)
C(6)-C(5)-C(9)-C(1)	176.84(11)
C(7)-O(2)-C(11)-O(3)	-175.65(13)
C(7)-O(2)-C(11)-C(4)	4.98(19)
C(3)-C(4)-C(11)-O(3)	-3.4(2)
C(5)-C(4)-C(11)-O(3)	-177.63(14)
C(3)-C(4)-C(11)-O(2)	175.94(13)
C(5)-C(4)-C(11)-O(2)	1.7(2)

Symmetry transformations used to generate equivalent atoms:

Table S 7. Hydrogen bonds for **1** [Å and deg.].

D-H...A	d(D-H)	d(H...A)	d(D...A)	<(DHA)

Figure S12. ^1H NMR spectrum of compound **2** in $\text{DMSO-}d_6$ (300 MHz).

Figure S13. ^{13}C spectrum of compound **2** in $\text{DMSO-}d_6$ (75 MHz).

Figure S14. DEPT-135 spectrum of compound **2** in DMSO- d_6 (75 MHz).

Figure S15. ^1H - ^1H COSY spectrum of compound **2** in DMSO- d_6 .

Figure S16. HSQC spectrum of compound **2** in DMSO- d_6 .

Figure S17. HMBC spectrum of compound **2** in DMSO- d_6 .

Figure S18. NOESY spectrum of compound **2** in DMSO- d_6 .

Figure S19. HR-ESI-MS spectrum of **2**.

Figure S20. UV spectrum of **2** in CH₃OH.

Figure S21. IR spectrum of **2** in CH₃OH.

Figure S22. ¹H NMR spectrum of compound **3** in DMSO-*d*₆ (300 MHz).

Figure S23. ¹³C NMR spectrum of compound **3** in DMSO-*d*₆ (75 MHz).

Figure S24. DEPT-135 spectrum of compound **3** in DMSO- d_6 (75 MHz).

Figure S25. ^1H - ^1H COSY spectrum of compound **3** in DMSO- d_6 .

Figure S26. HSQC spectrum of compound **3** in DMSO- d_6 .

Figure S27. HMBC spectrum of compound **3** in DMSO- d_6 .

Figure S28. NOESY spectrum of compound **3** in DMSO- d_6 .

a

b

Figure S29. HR-ESI-MS (a) and MS/MS (b) of compound **3** (negative mode) and the proposed fragmentation pathway (c).

Figure S30. Key ^1H - ^1H COSY and HMBC correlations of **1** and **2**.

Figure S31. Key NOESY correlations of **1**.

Figure S32. Key HMBC correlations of **3**.