Cimifrigines A-G, Cytotoxic Triterpenes with an Oxime Group from the Flowers of *Cimicifuga frigida*

Yin Nian, Hui Yan, Xiao-Nian Li, Lin Zhou, Ming-Hua Qiu

State Key Laboratory of Phytochemistry and Plant Resources in West China,

Kunming Institute of Botany, Chinese Academy of Sciences, Kunming 650201,

People's Republic of China

Supporting Information List

Characterization Data of New Compounds

Page 2-8, ¹H, ¹³C, HSQC, HMBC, COSY and ROESY NMR spectra and HREIMS experiment of compound **1**.

Page 9-15, ¹H, ¹³C, HSQC, HMBC, COSY and ROESY NMR spectra and HREIMS experiment of compound **2**.

Page 16-22, ¹H, ¹³C, HSQC, HMBC, COSY and ROESY NMR spectra and HREIMS experiment of compound **3**.

Page 23-29, ¹H, ¹³C, HSQC, HMBC, COSY and ROESY NMR spectra and HREIMS experiment of compound **4**.

Page 30-36, ¹H, ¹³C, HSQC, HMBC, COSY and ROESY NMR spectra and HREIMS experiment of compound **5**.

Page 37-43, ¹H, ¹³C, HSQC, HMBC, COSY and ROESY NMR spectra and HREIMS experiment of compound **6**.

Page 44-50, ¹H, ¹³C, HSQC, HMBC, COSY and ROESY NMR spectra and HREIMS experiment of compound **7**.

Page 51, Table S1: Cytotoxicity of compounds isolated from the flowers of C. frigida

Figure S1. ¹H (500 Hz) NMR Spectrum of cimifrigine A (1) in Pyridine- d_5



Figure S2. ¹³C (150 Hz) NMR Spectrum of cimifrigine A (1) in Pyridine- d_5



Figure S3. HSQC (600 Hz) Spectrum of cimifrigine A(1) in Pyridine- d_5



Figure S4. HMBC (600 Hz) Spectrum of cimifrigine A (1) in Pyridine-d₅









Figure S6. ROESY (600 Hz) Spectrum of cimifrigine A (1) in Pyridine- d_5

Figure S7. HREIMS of cimifrigine A (1)



Figure S8. ¹H (500 Hz) NMR Spectrum of cimifrigine **B** (2) in Pyridine- d_5



Figure S9. ¹³C (150 Hz) NMR Spectrum of cimifrigine **B** (2) in Pyridine- d_5





Figure S10. HSQC (600 Hz) Spectrum of cimifrigine B (2) in Pyridine-d₅

Figure S11. HMBC (600 Hz) Spectrum of cimifrigine **B** (2) in Pyridine- d_5



Figure S12. ¹H-¹H COSY (600 Hz) Spectrum of cimifrigine **B** (2) in Pyridine- d_5







Figure S14. HREIMS of cimifrigine B (2)



Figure S15. ¹H (500 Hz) NMR Spectrum of cimifrigine C (3) in Pyridine- d_5



Figure S16. ¹³C (150 Hz) NMR Spectrum of cimifrigine C (3) in Pyridine- d_5



Figure S17. HSQC (600 Hz) Spectrum of cimifrigine C (3) in Pyridine-*d*₅



Figure S18. HMBC (600 Hz) Spectrum of cimifrigine C (3) in Pyridine-*d*₅





Figure S19. ${}^{1}\text{H}{}^{-1}\text{H}$ COSY (600 Hz) Spectrum of cimifrigine **C** (3) in Pyridine- d_5

f1 (ppm)



Figure S21. HREIMS of cimifrigine C (3)



Figure S22. ¹H (500 Hz) NMR Spectrum of cimifrigine **D** (4) in Pyridine- d_5



Figure S23. ¹³C (150 Hz) NMR Spectrum of cimifrigine **D** (4) in Pyridine- d_5



Figure S24. HSQC (600 Hz) Spectrum of cimifrigine D (4) in Pyridine-d₅



Figure S25. HMBC (600 Hz) Spectrum of cimifrigine **D** (4) in Pyridine- d_5



khx29 khx29 cosy -0 CH₃ 0= 0 -1 `OH -2 0 3 Ē١ Н 198 m N-OH 1 -3 Η, 4 он /10-/ -4 HO 00 ÓН -5 6 -6 . -7 --8 -9 12 10 6 f2 (ppm) 11 9 5 3 2 0 8 7 4 1

Figure S26. ¹H-¹H COSY (600 Hz) Spectrum of cimifrigine **D** (4) in Pyridine- d_5





Figure S28. HREIMS of cimifrigine D (4)



Figure S29. ¹H (500 Hz) NMR Spectrum of cimifrigine E (5) in Pyridine- d_5



Figure S30. ¹³C (150 Hz) NMR Spectrum of cimifrigine E (5) in Pyridine- d_5



Figure S31. HSQC (600 Hz) Spectrum of cimifrigine E (5) in Pyridine-*d*₅



Figure S32. HMBC (600 Hz) Spectrum of cimifrigine E (5) in Pyridine-d₅





Figure S33. ¹H-¹H COSY (600 Hz) Spectrum of cimifrigine **E** (**5**) in Pyridine- d_5



Figure S35. HREIMS of cimifrigine E (5)



Figure S36. ¹H (500 Hz) NMR Spectrum of cimifrigine \mathbf{F} (6) in Pyridine- d_5





Figure S37. ¹³C (150 Hz) NMR Spectrum of cimifrigine \mathbf{F} (6) in Pyridine- d_5

Figure S38 HSQC (600 Hz) Spectrum of cimifrigine \mathbf{F} (6) in Pyridine- d_5



Figure S39 HMBC (600 Hz) Spectrum of cimifrigine F (6) in Pyridine- d_5









Figure S41 ROESY (600 Hz) Spectrum of cimifrigine \mathbf{F} (6) in Pyridine- d_5

Figure S42. HREIMS of cimifrigine F (6)



43

Figure S43. ¹H (500 Hz) NMR Spectrum of cimifrigine G (7) in Pyridine- d_5



Figure S44. ¹³C (150 Hz) NMR Spectrum of cimifrigine G (7) in Pyridine- d_5



οн khx30 chsqcPyrav600 H -10 -20 Ĥ 1 н N-OH 0 -30 Η.,, -0 7 0 --40 HO OH 68 (0) -50 Ò. .0 0.00 f1 (ppm) -60 ĊH₃ 80 . -70 0 -80 0 -90 -100 0 -110 0 -120 6.0 5.5 5.0 3.5 3.0 f2 (ppm) 2.5 2.0 1.5 1.0 0.5 0.0 4.5 4.0

Figure S45 HSQC (600 Hz) Spectrum of cimifrigine G (7) in Pyridine-d₅

н khx30 hmbc_pr Pyr av600 -10 5.0 -20 Ó -30 Ĥ H 40 N-OH 1 -50 7 -60 HO OH -70 -80 0 -90 ĊH₃ -100 -110 -120 -130 -140 --150 -160 -170 -180 11 12 10 ò 9 3 1 8 7 6 f2 (ppm) 5 4 2

Figure S46 HMBC (600 Hz) Spectrum of cimifrigine G (7) in Pyridine- d_5





Figure S48 ROESY (600 Hz) Spectrum of cimifrigine G (7) in Pyridine- d_5

Figure S49. HREIMS of cimifrigine G (7)



Compounds	HL-60	SMMC-7721	A549	MCF-7	SW480
1	19.3 ± 1.3	25.7 ± 0.7	24.1 ± 1.4	> 30	> 30
2	18.4 ± 0.7	23.8 ± 1.2	25.3 ± 2.0	> 30	> 30
3	25.9 ± 1.1	> 30	> 30	> 30	> 30
4	10.4 ± 0.8	11.2 ± 1.0	9.3 ± 0.6	12.7 ± 0.7	13.2 ± 0.8
5	1.2 ± 0.1	4.5 ± 0.2	4.0 ± 0.3	5.8 ± 0.6	6.3 ± 0.3
6	12.5 ± 1.3	14.3 ± 1.2	9.8 ± 1.0	11.4 ± 0.8	8.9 ± 0.9
7	0.8 ± 0.09	2.6 ± 0.1	1.4 ± 0.08	3.7 ± 0.07	4.3 ± 0.4
Cisplatin ^c	0.5 ± 0.03	3.3 ± 0.2	2.3 ± 0.1	5.4 ± 0.3	4.4 ± 0.2

Table S1 Cytotoxicity of compounds isolated from the flowers of *C*. $frigida^{a,b}$

^{*a*}Results are expressed as the average (n = 3) of IC₅₀ values (μ M). ^{*b*}0.1% DMSO as the solvent control and did not show any cytotoxicity to those cell lines. ^{*c*}Used as a positive control substance for the cytotoxicity assay.