Supporting Information

Stereoselective Synthesis of the Published Structure of Feigrisolide A. Structural Revision of Feigrisolides A and B

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General features

NMR spectra were recorded at 500 MHz (^1H NMR) and 125 MHz (^{13}C NMR) in CDCl_3 solution at 25°C . ^{13}C NMR signal multiplicities were determined with the DEPT pulse sequence. Mass spectra were run in the EI (70 eV) or the FAB (*m*-nitrobenzyl alcohol matrix) mode. IR data, which were measured as films on NaCl plates (oils) or as KBr pellets (solids), are given only when relevant functions (C=O, OH) are present. Optical rotations were measured at 25°C . Reactions which required an inert atmosphere (all except those involving water in the reaction medium) were carried out under dry N_2 with flame-dried glassware. Commercial reagents were used as received. THF and Et_2O were freshly distilled from sodium-benzophenone ketyl. Dichloromethane was freshly distilled from CaH_2 . Tertiary amines were freshly distilled from KOH. Unless detailed otherwise, "work-up" means pouring the reaction mixture into brine, followed by extraction with the solvent indicated in parenthesis. If the reaction medium was acidic (basic), an additional washing with 5% aq NaHCO_3 (aq NH_4Cl) was performed. New washing with brine, drying over anhydrous Na_2SO_4 and elimination of the solvent under reduced pressure were followed by chromatography on a silica gel column (60-200 μm) with the indicated eluent. Where solutions were filtered through a Celite pad, the pad was additionally rinsed with the same solvent used, and the washing liquids incorporated to the main organic layer. Column chromatography was performed on silica gel (60-200 μ).

SYNTHETIC SCHEME FOR LACTONE 1

Reagents and conditions: (b) allylBIPc₂ [from (–)-Ipc₂BCl and allylmagnesium bromide], Et₂O, –100 °C, 1 h, (89:11 mixture of diastereomers), 70% of **8** after chromatographic separation. (c) benzyl trichloroacetimidate, TfOH, CH₂Cl₂, RT, 3 h, 83%. (d) 9-BBN, THF, RT, 18 h, 77%. (e) Swern. (f) **17**, Bu₂BOTf, Et₃N, CH₂Cl₂, 0 °C, then addition of the resulting boron enolate to the aldehyde, 0 °C, 18 h, 70% overall. (g) TBSOTf, 2,6-lutidine, CH₂Cl₂, RT, 1 h, 85%. (h) LiOH, H₂O₂, aq THF, RT, 24 h, 76%. (i) Pd/C, H₂, EtOAc, RT, 2 h, 84%. (j) 2,4,6-trichlorobenzoyl chloride, Et₃NiPr₂, DMAP, 1 h, THF, RT, 87%. (k) HF-pyridine, pyridine, THF, 24 h, 55 °C, 70%. (l) Ac₂O, pyridine, RT, 12 h, 80%.

(4S,6S)-6-(tert-Butyldiphenylsilyloxy)-hept-1-en-4-ol (8). Allylmagnesium bromide (commercial 1M solution in Et₂O, 7.5 mL, 7.5 mmol) was added dropwise under N₂ via syringe to a solution of (+)-DIP-Cl (2.89 g, 9 mmol) in dry Et₂O (40 mL) cooled at –78 °C. After replacing the latter by an ice bath, the mixture was stirred for 1 h. The solution was then allowed to stand, which caused precipitation of magnesium chloride. The supernatant solution was then carefully transferred to another flask via canula. After cooling this flask at –100 °C, a solution of freshly prepared (S)-3-(tert-butyl(diphenyl)silyloxy)butanal **7**¹ (1.96 g, 6 mmol) in dry Et₂O (15 mL) was added dropwise via syringe. The resulting solution was further stirred at the same temp. for 1 h. The reaction mixture was then quenched through addition of phosphate pH 7 buffer solution (40 mL), MeOH (40 mL) and 30% H₂O₂ (20 mL). After stirring for 30 min. at room temp., the mixture was poured onto

satd. aq NaHCO₃ and worked up (extraction with EtOAc). This gave **8** as a 89:11 mixture of diastereomers (estimated by means of NMR). Column chromatography of the mixture on silica gel (hexanes-EtOAc, 19:1) afforded pure **8** (1.55 g, 70%): oil, $[\alpha]_D -0.4$ (*c* 1.2, CHCl₃); ¹H NMR (500 MHz) δ 7.75-7.70 (4H, m), 7.50-7.40 (6H, m), 5.82 (1H, m), 5.12-5.05 (2H, m), 4.20 (1H, m), 4.05 (1H, m), 3.00 (br s, 1H, OH), 2.30-2.15 (2H, m), 1.69 (1H, ddd, *J* = 14, 10.2, 4 Hz), 1.55 (1H, ddd, *J* = 14, 5.2, 2.5 Hz), 1.11 (3H, d, *J* = 6 Hz), 1.08 (9H, s); ¹³C NMR (125 MHz) δ 134.0, 133.5, 19.1 (C), 135.9, 135.8, 135.0, 129.8, 129.7, 127.7, 127.6, 68.7, 67.7 (CH), 117.2, 44.0, 42.2 (CH₂), 27.0 (x 3), 22.7 (CH₃); IR $\nu_{\max}$ 3500 (br, OH) cm⁻¹; HR FAB MS *m/z* 369.2247 (M+H⁺). Calcd. for C₂₃H₃₃O₂Si, 369.2250. Anal. Calcd. for C₂₃H₃₂O₂Si: C, 74.95; H, 8.75. Found, C, 74.91; H, 8.89.

¹Claffey, M. M.; Heathcock, C. H. *J. Org. Chem.* **1996**, *61*, 7646-7647.

(4S,6S)-4-Benzyloxy-6-(tert-butyldiphenylsilyloxy)-hept-1-ene (9). An ice-cooled solution of alcohol **8** (1.474 g, 4 mmol) in dry CH₂Cl₂ (10 mL) was treated successively with benzyl trichloroacetimidate (1.12 mL, 6 mmol) and CF₃SO₃H (18 μ L, 0.2 mmol). After stirring for 3 h at room temperature, the mixture was poured onto satd. aq NaHCO₃ and worked up (extraction with CH₂Cl₂). Column chromatography of the oily residue on silica gel (hexanes-Et₂O, 99:1) provided **9** (1.52 g, 83%): oil, $[\alpha]_D +9$ (*c* 1.05, CHCl₃); ¹H NMR (500 MHz) δ 7.80-7.75 (4H, m), 7.50-7.25 (11H, br m), 5.86 (1H, m), 5.15-5.10 (2H, m), 4.54 (1H, d, *J* = 11.3 Hz), 4.27 (1H, d, *J* = 11.3 Hz), 4.20 (1H, m), 3.75 (1H, m), 2.40-2.30 (2H, m), 1.80 (1H, ddd, *J* = 14.2, 8, 3.7 Hz), 1.70 (1H, ddd, *J* = 14.2, 8.6, 4 Hz), 1.13 (3H, d, *J* = 6.2 Hz), 1.12 (9H, s); ¹³C NMR (125 MHz) δ 138.9, 134.9, 134.4, 19.3 (C), 135.9, 135.8, 134.7, 129.5, 129.4, 128.2, 127.6, 127.5, 127.4, 76.0, 67.2 (CH), 117.1, 70.9, 45.0, 38.5 (CH₂), 27.1 (x 3), 24.5 (CH₃); HR FAB MS *m/z* 459.2792 (M+H⁺). Calcd. for C₃₀H₃₉O₂Si, 459.2719. Anal. Calcd. for C₃₀H₃₈O₂Si: C, 78.55; H, 8.35. Found, C, 78.41; H, 8.29.

(4S,6S)-4-Benzyloxy-6-(tert-butyldiphenylsilyloxy)heptan-1-ol (10). A solution of olefin **9** (1.49 g, 3.25 mmol) in dry THF (15 mL) was treated with 9-BBN (13 mL of a 0.5 M solution in THF, 6.5 mmol). After stirring for 18 h at room temperature, the mixture was quenched through addition of MeOH (6 mL), 6M aq NaOH (2 mL) and 30% aq H₂O₂ (7 mL). The mixture was then stirred at 50 °C for 1 h, poured onto brine and worked up (extraction with EtOAc). Column chromatography of the oily residue on silica gel (hexanes-EtOAc, 4:1) furnished **10** (1.19 g, 77%): oil, $[\alpha]_D -4.8$ (*c* 0.65, CHCl₃); ¹H NMR (500 MHz) δ 7.75-7.70 (4H, m), 7.50-7.25 (11H, br m), 4.44 (1H, d, *J* = 11.3 Hz), 4.29 (1H, d, *J* = 11.3 Hz), 4.10 (1H, m), 3.70-3.50 (3H, br m), 1.90 (br s, 1H, OH), 1.80-1.70 (2H, m), 1.60-1.50 (4H, m), 1.13 (3H, d, *J* = 6.1 Hz), 1.12 (9H, s); ¹³C NMR (125 MHz) δ 138.7, 134.8, 134.3, 19.3 (C), 135.9, 135.8, 129.5, 129.4, 128.2, 127.6, 127.5, 127.4, 76.2, 67.3 (CH), 70.8, 63.0, 44.8, 30.4, 28.0 (CH₂), 27.1 (x 3), 24.4 (CH₃); IR $\nu_{\max}$ 3400 (br, OH) cm⁻¹; HR EIMS *m/z* (% rel. int.) 419.2092 (M⁺-*t*Bu, 1), 311 (55), 209 (84), 199 (60), 91 (100). Calcd. for

C₃₀H₄₀O₃Si-*t*Bu, 419.2042. Anal. Calcd. for C₃₀H₄₀O₃Si: C, 75.58; H, 8.46. Found, C, 75.41; H, 8.25.

(3*R*,4*S*,7*S*)-4-Acetoxy-7-[(*S*)-2-acetoxypentyl]-3-methyloxepan-2-one (16). Prepared by acetylation of **1** under the standard conditions (Ac₂O, pyridine, RT): oil; ¹H NMR (500 MHz, CDCl₃) δ 5.13 (1H, m), 4.95 (1H, m), 4.52 (1H, td, J = 10, 2 Hz), 3.30 (1H, dq, J = 6.5, 7.5 Hz), 2.07 (3H, s), 2.04 (3H, s), 2.10-2.00 (3H, m), 1.90 (1H, m), 1.75 (2H, m), 1.36 (3H, d, J = 7.5 Hz), 1.26 (3H, d, J = 6.5 Hz); ¹³C NMR (125 MHz, CDCl₃) δ 173.1, 170.3, 170.1 (C), 75.0, 71.4, 67.9, 46.8 (CH), 43.1, 29.7, 27.4 (CH₂), 21.2, 21.1, 20.7, 12.2 (CH₃).

Table 1. Compared NMR data of synthetic lactone **1** and natural feigrisolide A.

	Compound 1 ¹		Natural feigrisolide A ¹	
Position	H, δ ppm, mult. (J in Hz)	C, δ ppm	H, δ ppm, mult. (J in Hz)	C, δ ppm
1	–	175.0	–	177.5
2	3.20 dq (6, 7.5)	50.4	2.50 dq (8.3, 7.2)	45.3
3	3.90 ddd (6, 5, 2.5)	69.9	3.98 q (8.3)	81.1
4	1.70 dt (15, 5) 2.00-1.90 m	29.1	1.67 m 2.03 m	29.1
5	2.15-2.00 br m	30.0	1.66 m 2.01 m	39.5*
6	4.75 br t (10)	75.7	4.19 m	77.1
7	1.80 ddd (14.5, 10, 2.2) 1.53 ddd (14.5, 10, 2.5)	45.3	1.68 m (2H)	42.9
8	4.11 m	64.0	4.08 m	65.2
9	1.21 d (6.2)	24.3	1.21 d (6.3)	23.1
Me-C ₂	1.39 d (7.5)	13.4	1.16 d (7.2)	13.7

¹At 500 and 125 MHz for ¹H and ¹³C NMR, respectively.

*Feigrisolides A and B should have more or less the same chemical shift values for carbon C-5. However, a value of 39.5 ppm is indicated for feigrisolide A and 30.6 ppm for feigrisolide B. The latter value is also that approximately predicted by an NMR prediction program. In all likelihood, the figure above is a typographical mistake in the original paper and should be 30.5.¹

¹Tang, Y.-Q.; Sattler, I.; Thiericke, R.; Grabley, S.; Feng, X.-Z. *J. Antibiot.* **2000**, 53, 934-943.

Table 2. Compared NMR data of synthetic (-)-nonactic acid and natural feigrisolide A.

Position	(-)-Nonactic acid (300/75 MHz) ¹		Natural feigrisolide A (500/125 MHz) ²	
	H, δ ppm, mult. (J in Hz)	C, δ ppm	H, δ ppm, mult. (J in Hz)	C, δ ppm
1	–	177.9	–	177.5
2	2.51 quint (7.5)	45.3	2.50 dq (8.3, 7.2)	45.3
3	4.10-3.95 m	81.0	3.98 q (8.3)	81.1
4	1.75-1.60 m	29.0	1.67 m 2.03 m	29.1
5	2.10-1.90 m	30.5	1.66 m 2.01 m	39.5*
6	4.19 m	77.2	4.19 m	77.1
7	1.75-1.60 m	42.8	1.68 m (2H)	42.9
8	4.10-3.95 m	65.2	4.08 m	65.2
9	1.21 d (6.3)	23.1	1.21 d (6.3)	23.1
Me-C ₂	1.16 d (7)	13.6	1.16 d (7.2)	13.7

¹NMR data provided by Prof. E. Lee, Seoul National University, Korea.

²Tang, Y.-Q.; Sattler, I.; Thiericke, R.; Grabley, S.; Feng, X.-Z. *J. Antibiot.* **2000**, 53, 934-943.

*See footnote in Table 1.

Table 3. Compared NMR data of synthetic (+)-homomonactric acid and natural feigrisolide B.

	(+)-Homomonactric acid (300/75 MHz)¹		Natural feigrisolide B (500/125 MHz)²	
Position	H, δ ppm, mult. (J in Hz)	C, δ ppm	H, δ ppm, mult. (J in Hz)	C, δ ppm
1	—	178.0	—	177.6
2	2.51 quint (7.5)	45.3	2.50 dq (8.3, 7)	45.3
3	3.99 m	81.0	3.98 br q (8.3)	81.0
4	1.75-1.40 br m	29.0	1.68 m 2.03 m	29.1
5	2.05-2.00 m	30.7	1.65 m 2.01 m	30.6
6	4.20 m	77.3	4.21 m	77.3
7	1.75-1.40 br m	40.8	1.70 m (2H)	40.7
8	3.77 m	70.4	3.78 m	70.4
9	1.75-1.40 br m	29.9	1.51 m (2H)	29.9
10	0.92 t (7.5)	10.0	0.92 t (7.5)	10.0
Me-C ₂	1.15 d (7)	13.6	1.16 d (7)	13.7

¹NMR data provided by Prof. E. Lee, Seoul National University, Korea.

²Tang, Y.-Q.; Sattler, I.; Thiericke, R.; Grabley, S.; Feng, X.-Z. *J. Antibiot.* **2000**, *53*, 934-943.

NMR spectra of selected compounds

10

Current Data Parameters

NAME eun050502
EXPNO 10
PROCNO 1

F2 - Acquisition Parameters

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Time 22.45
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PULPROG zgpg30
TD 65536
SOLVENT CDCl3
VS 160
DS 2
SWH 25455.027 Hz
FIDRES 0.403672 Hz
AQ 1.2386804 sec
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OW 18.900 usec
DE 6.00 usec
TE 300.0 K
D1 2.00000000 sec
d11 0.03000000 sec
DELTA 1.89999998 sec
WOREST 0.00000000 sec
MCWAK 0.01500000 sec

***** CHANNEL f1 *****

NUC1 13C
P1 6.70 usec
PL1 -6.00 dB
SFO1 75.4732993 MHz

***** CHANNEL f2 *****

CPDPRG2 waltz16
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PCPD2 100.00 usec
PL2 -6.00 dB
PL12 13.58 dB
PL13 17.00 dB
SFO2 300.1315007 MHz

F2 - Processing parameters

SF 32768
SF 75.4677501 MHz
WDW EM
SSB 0
LB 1.00 Hz
GB 0
PC 1.40

13 NMR plot parameters

CX 20.00 cm
CY 6.00 cm
FIP 200.000 ppm
F1 15093.55 Hz
F2P -10.000 ppm
F2 -754.68 Hz
PRNOM 10.50000 ppm/cm
H2CM 752.41138 Hz/cm