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

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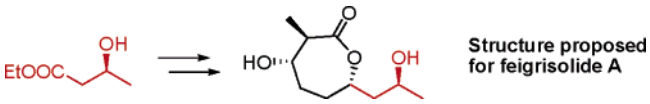

The total synthesis of the proposed structure of feigrisolide A is reported. Ethyl (*S*)-3-hydroxybutyrate was the chiral starting material. A Brown asymmetric allylation and an Evans aldol reaction were key steps of the synthesis. The NMR data of the synthetic product are different from those of the natural product. The published structure of feigrisolide A is therefore erroneous. A subsequent comparison of spectral data strongly suggests that feigrisolides A and B are identical with (−)-nonactic acid and (+)-homononactic acid, respectively.

Introduction

Feigrisolides A−D constitute a group of lactones isolated from the culture broth of strain GT 051022 of *Streptomyces griseus*. They were found to display various degrees of activities in antibacterial, antiviral, cytotoxic, and enzyme inhibition assays.[1] Their structures were assigned to be **1**−**4** (Figure 1), mainly on the basis of spectroscopic analyses. In the case of seven-membered lactones **1** and **2** (feigrisolides A and B), the relative configurations of the three ring stereocenters were established through NOE measurements, supported by molecular mechanics calculations. The absolute configuration at C-8 was established as *S* for **1** and *R* for **2** with the aid of Helmchen's method,[2] but the absolute configurations of the whole molecules

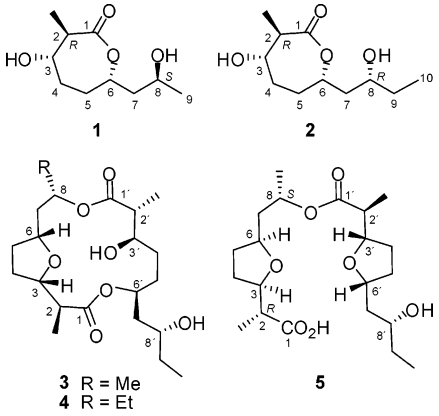

FIGURE 1. Reported structures of feigrisolides A (**1**), B (**2**), C (**3**), and D (**4**) and corrected structure of feigrisolide C (**5**).

were not determined. For their part, macrodiolide structures **3** and **4** were attributed, respectively, to feigrisolides C and D upon comparison of their spectral data with those of **1** and **2**, which were assumed to be their biogenetic precursors.

Very recently, the compound with structure **2** and its triple epimer at the carbon atoms C-2/C-3/C-6 have been prepared.[3] Both products were found to differ from natural feigrisolide B. Hereafter, Lee and co-workers succeeded in synthesizing **3** and its C-3′ epimer, but their physical and spectroscopic features did not match those of natural feigrisolide C. Finally, the latter group was able to establish by means of synthesis that the actual structure of feigrisolide C is **5**.[4]

As shown in Figure 1, the proposed and actual structures of feigrisolide C differ not only in stereochemical features but also in their constitution: in contrast to **3**, structure **5** contains two tetrahydrofurane rings and no lactone moiety. It has been assumed that compounds **1** and **2** are biosynthetic precursors of **5**. Fragments C_1−C_8 (left half) and $C_{1'}$−$C_{10'}$ (right half) of feigrisolide C **5** would then be related to feigrisolide A **1** and feigrisolide B **2**, respectively. In this case, the configurations at C-2 and C-8 in **1** should be *R* and *S*, respectively, as in **5**. Nothing can be predicted, however, in relation to C-3 and C-6, as both stereocenters are part of a tetrahydrofuran ring in **5** but not in **1**. On the basis of NOE studies, Thiericke and co-workers[1] deduced a spatial proximity between H-3 and H-6, which are thus in a syn arrangement. However, these authors did not comment on the existence of NOE correlations between H-3 (or H-6) and H-2. Thus, the relative configuration proposed for C-2 and C-3 relied upon molecular mechanics studies. Obviously, stereochemical ambiguities still persist. For this reason, we have decided to undertake the total synthesis of feigrisolide A to confirm or disregard structure **1**.

Our retrosynthetic concept for the preparation of **1** is shown in Scheme 1. The seven-membered lactone ring is to be created

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

(2) Helmchen, G. *Tetrahedron Lett.* **1974**, *16*, 1527−1530.

(3) Sharma, G. V. M.; Kumar, K. R. *Tetrahedron: Asymmetry* **2004**, *15*, 2323−2326.

(4) (a) Kim, W. H.; Jung, J. H.; Sung, L. T.; Lim, S. M.; Lee, E. *Org. Lett.* **2005**, *7*, 1085−1087. (b) Kim, W. H.; Jung, J. H.; Lee, E. *J. Org. Chem.* **2005**, *70*, 8190−8192. See also the following: Lee, E.; Sung, L. T.; Hong, S. K. *Bull. Kor. Chem. Soc.* **2002**, *23*, 1189−1190.

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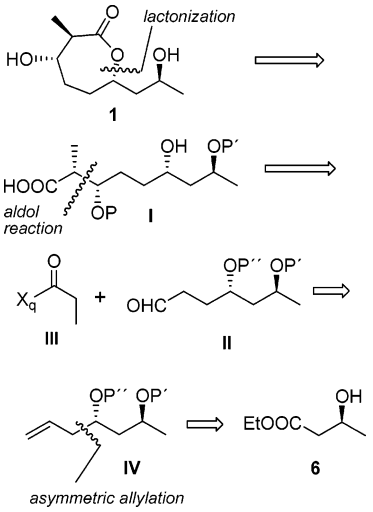
SCHEME 1. Retrosynthetic Analysis of Structure 1

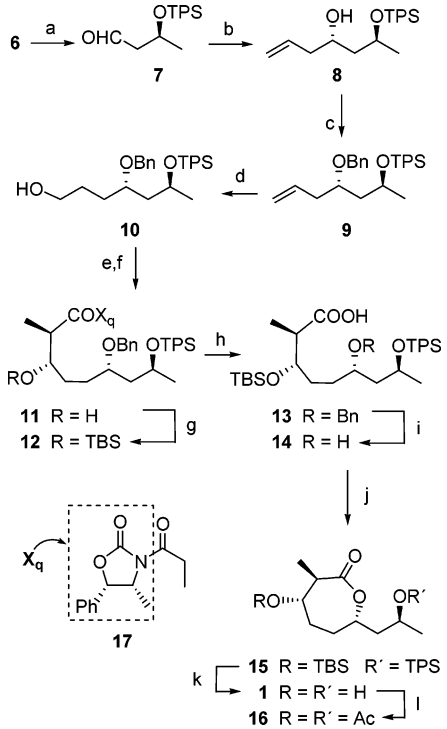


by lactonization of the protected trihydroxy acid **I**. The latter is derived from a syn-selective aldol reaction of aldehyde **II** with a suitable chiral propionate equivalent **III**. Aldehyde **II** in turn should be prepared via **IV** from the commercially available ethyl (*S*)-3-hydroxybutyrate **6** through reduction, asymmetric allylation, and suitable functional manipulation.

Results and Discussion

Scheme 2 depicts the details of the synthesis. The known aldehyde **7** was prepared as reported[5] by protection of the commercially available ethyl (*S*)-3-hydroxybutyrate **6** as its TPS ether followed by reduction with DIBAL. Reaction of **7** with allylBIpc$_2$, prepared as described from (−)-Ipc$_2$BCl and allylmagnesium bromide,[6] gave homoallyl alcohol **8** as a chromatographically separable 89:11 diastereoisomeric mixture. Benzylation of the hydroxyl group was performed with benzyl trichloroacetimidate[7] and yielded **9**, which was then subjected to hydroboration-oxidation to yield primary alcohol **10**. The remaining stereocenters were generated with the aid of the Evans asymmetric aldol methodology.[8] Alcohol **10** was oxidized to the corresponding aldehyde, and the latter was allowed to react with the boron *Z*-enolate of *N*-propionyl oxazolidinone **17**. This gave aldol adduct **11** as a single stereoisomer. Silylation to **12** and hydrolytic cleavage of the chiral auxiliary furnished the protected trihydroxy acid **13**. Selective cleavage of the *O*-benzyl group provided **14**, which was subjected to the Yamaguchi lactonization protocol[9] to afford **15**.[10] Cleavage of the two silyl groups in **15** proved somewhat difficult[11] but was finally achieved by treatment with HF-pyridine in hot THF. This completed the synthesis of dihydroxy lactone **1**.

SCHEME 2. Stereoselective Synthesis of Lactone 1[a]



[a] Reagents and conditions: (a) ref 5; (b) allylBIpc$_2$ [from (−)-Ipc$_2$BCl and allylmagnesium bromide], Et$_2$O, −100 °C, 1 h, (89:11 mixture of diastereoisomers), 70% of **8** after chromatographic separation; (c) benzyl trichloroacetimidate, TfOH, CH$_2$Cl$_2$, room temp, 3 h, 83%; (d) 9-BBN, THF, room temp, 18 h, 77%; (e) Swern; (f) **17**, Bu$_2$BOTf, Et$_3$N, CH$_2$Cl$_2$, 0 °C, then addition of the resulting boron enolate to the aldehyde, 0 °C, 18 h, 70% overall; (g) TBSOTf, 2,6-lutidine, CH$_2$Cl$_2$, room temp, 1 h, 85%; (h) LiOH, H$_2$O$_2$, aq THF, room temp, 24 h, 76%; (i) Pd/C, H$_2$, EtOAc, room temp, 2 h, 84%; (j) 2,4,6-trichlorobenzoyl chloride, Et*N*i*P*r$_2$, DMAP, 1 h, THF, RT, 87%; (k) HF-pyridine, pyridine, THF, 24 h, 55 °C, 70%; (l) Ac$_2$O, pyridine, room temp, 12 h, 80%. Nonstandard abbreviations and acronyms: Ipc, *iso*pinocampheyl; TBS, *tert*-butyldimethylsilyl; TPS, *tert*-butyldiphenylsilyl.

Unexpectedly, the physical and spectral properties of synthetic **1** turned out to be different from those reported for feigrisolide A (see Supporting Information). As commented above, synthetic work has shown that the published structures of feigrisolides B[3] and C[4] are also erroneous.[12] In fact, some additional features also made structure **1** to appear suspicious. For instance, acetylation of synthetic **1** under standard conditions (Ac$_2$O, pyridine, room temperature) provided diacetate **16**, as expected. In contrast, Thiericke et al. reported the formation of a monoacetate from natural feigrisolide A under the same conditions.[1] Furthermore, the structure of feigrisolide C (**5**) contains only tetrahydrofuran hydroxy acid fragments. We thus wondered whether the alleged feigrisolide A might be identical with the known compound (−)-nonactic acid **18** (Figure 2),[13] which contains the tetrahydrofuran moiety corresponding to the left half of **5**. Indeed, structures **1** and **18** have the same molecular

(5) Claffey, M. M.; Heathcock, C. H. *J. Org. Chem.* **1996**, *61*, 7646−7647.

(6) Ramachandran, P. V.; Chen, G.-M.; Brown, H. C. *Tetrahedron Lett.* **1997**, *38*, 2417−2420. For a recent review on asymmetric allylborations, see the following: Ramachandran, P. V. *Aldrichimica Acta* **2002**, *35*, 23−35.

(7) Wessel, H.-P.; Iversen, T.; Bundle, D. R. *J. Chem. Soc., Perkin Trans. 1* **1985**, 2247−2250.

(8) (a) Evans, D. A. *Aldrichimica Acta* **1982**, *15*, 23−32. (b) Kim, B. M.; Williams, S. F.; Masamune, S. In *Comprehensive Organic Synthesis*; Trost, B. M., Fleming, I., Winterfeldt, E., Eds.; Pergamon Press: Oxford, U.K., 1993; Vol. 2, pp 239−276. See also the following: Cowden, C. J.; Paterson, I. *Org. React.* **1997**, *51*, 1−200.

(9) Inanaga, J.; Hirata, K.; Saeki, H.; Katsuki, T.; Yamaguchi, M. *Bull. Chem. Soc. Jpn.* **1979**, *52*, 1989−1993.

(10) The structure of lactone **15** was confirmed by means of an X-ray diffraction study (see Supporting Information).

(11) The TBS group proved reluctant to cleavage.

(12) According to the previous results and those presented here, it seems likely that the structure of feigrisolide D will also need correction.

(13) (a) Gerlach, H.; Prelog, V. *Justus Liebigs Ann. Chem.* **1963**, *669*, 121−135. (b) Gerlach, H.; Wetter, H.-J. *Helv. Chim. Acta* **1974**, *57*, 2306−2321.

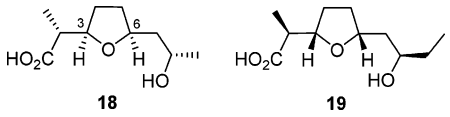


FIGURE 2. The structures of (−)-nonactic acid (**18**) and (+)-homononactic acid (**19**).

weight and C/H atom connectivity. Furthermore, both would show the NOE between H-3 and H-6 reported for feigrisolide A.[1] Structure **18** for feigrisolide A would also explain the formation of a monoacetylated derivative, instead of the expected diacetate. A direct comparison of feigrisolide A and nonactic acid was not possible, because of the nonavailability of authentic samples of the natural compounds. Moreover, accurate, high-resolution ^{1}H and ^{13}C NMR data of *free* nonactic acid have not been reported in the literature.[14] Fortunately, these data were sent to us by Prof. Eun Lee (see acknowledgments).[4] After comparison with the NMR data of feigrisolide A (see the Supporting Information), we have been able to conclude that feigrisolide A is identical with **18**. Structure **1** therefore does not correspond to any natural product reported to date.

Following the same line of reasoning disclosed above, feigrisolide B should correspond to the right half of the structure of feigrisolide C and be thus identical with the known compound (+)-homononactic acid **19** (Figure 2).[15] High-resolution ^{1}H and ^{13}C NMR data of **19** were also sent to us by Prof. E. Lee. Comparison with those of feigrisolide B (see Supporting Information) leads to the conclusion that both compounds are identical. This explains the failure of the previous attempt by Sharma and Kumar[3] at synthesizing feigrisolide B.

Conclusions

We have performed a stereoselective synthesis of the structure published for the natural compound named feigrisolide A. It has been found that the published structure does not correspond to that of the natural product. A revised structure is proposed not only for feigrisolide A but also for the closely related feigrisolide B.

Experimental Section

General Features and Reaction Conditions. Described in the Supporting Information.

Oxazolidinone 11. DMSO (0.42 mL, 6 mmol) was dissolved in dry CH_2Cl_2 (6 mL), cooled to −78 °C and treated with oxalyl chloride (265 μL, ca. 3 mmol). After stirring at this temp for 5 min, a solution of **10** (1.15 g, 2.4 mmol) in dry CH_2Cl_2 (2 mL) was added dropwise, followed by triethylamine (1.7 mL, ca. 12 mmol). The reaction mixture was stirred for 15 min at −78 °C and then for another 60 min at 0 °C. Workup (extraction with CH_2Cl_2) and evaporation in vacuo provided a crude aldehyde which was directly used in the next step.

A solution of oxazolidinone **14** (2.33 g, 10 mmol) in dry CH_2Cl_2 (20 mL) was cooled to 0 °C and treated sequentially with a 1 M solution of Bu_2BOTf in CH_2Cl_2 (11 mL, 11 mmol) and triethylamine (1.8 mL, ca. 13 mmol). The mixture was then stirred for 1 h, followed by the addition of a solution of the crude aldehyde from above in dry CH_2Cl_2 (10 mL). The mixture was then stirred for another 18 h and quenched through the addition of phosphate pH 7 buffer solution (15 mL), MeOH (15 mL), and 30% H_2O_2 (7.5 mL). After stirring for 30 min at room temp, the mixture was poured onto saturated aq $NaHCO_3$ and worked up (extraction with CH_2Cl_2). Column chromatography of the oily residue on silica gel (hexanes−EtOAc, 4:1) yielded **11** (1.19 g, 70% overall from **10**): amorphous solid; $[\alpha]_D$ +3.4 (*c* 2, $CHCl_3$).^{1}H NMR (500 MHz, $CDCl_3$): δ 7.75−7.70 (4H, m), 7.50−7.20 (16H, br m), 5.64 (1H, d, J = 6.9 Hz), 4.77 (1H, quint, J = 6.9 Hz), 4.45 (1H, d, J = 11.3 Hz), 4.27 (1H, d, J = 11.3 Hz), 4.14 (1H, m), 3.92 (1H, m), 3.79 (1H, m), 3.68 (1H, m), 1.75−1.70 (3H, m), 1.60−1.50 (4H, m), 1.25 (3H, d, J = 6.9 Hz), 1.10 (3H, d, J = 6.3 Hz), 1.09 (9H, s), 0.90 (3H, d, J = 6.3 Hz). ^{13}C NMR (125 MHz): δ 177.1, 152.6, 138.8, 134.8, 134.3, 133.2, 19.3 (C), 135.9, 135.8, 129.5, 129.4, 128.7, 128.6, 128.2, 127.6, 127.5, 127.4, 125.6, 78.9, 76.1, 71.7, 67.3, 54.8, 42.5 (CH), 70.7, 44.9, 30.1, 29.2 (CH_2), 27.1 (x 3), 24.4, 14.3, 10.6 (CH_3). IR ν_{max}: 3500 (br, OH), 1782, 1698 (C=O) cm^{-1}. HR FAB MS *m/z:* 708.3755 (M + H$^+$). Calcd for $C_{43}H_{54}NO_6Si$, 708.3720.

Oxazolidinone 12. Oxazolidinone **11** (1.06 g, 1.5 mmol) was dissolved in dry CH_2Cl_2 (20 mL) and treated sequentially with 2,6-lutidine (875 μL, 7.5 mmol) and TBSOTf (1.38 mL, 6 mmol). The reaction mixture was then stirred for 1 h at room temp and worked up (extraction with CH_2Cl_2). Column chromatography on silica gel (hexanes−EtOAc, 19:1) afforded the desired **12** (1.05 g, 85%): oil; $[\alpha]_D$ +6.8 (*c* 1.5, $CHCl_3$). ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.75−7.70 (4H, m), 7.50−7.20 (16H, br m), 5.49 (1H, d, J = 7 Hz), 4.62 (1H, quint, J = 7 Hz), 4.44 (1H, d, J = 11 Hz), 4.24 (1H, d, J = 11 Hz), 4.14 (1H, m), 4.06 (1H, m), 3.89 (1H, m), 3.65 (1H, m), 1.75−1.60 (6H, m), 1.21 (3H, d, J = 6.8 Hz), 1.10 (3H, d, J = 6.3 Hz), 1.09 (9H, s), 0.94 (9H, s), 0.90 (3H, d, J = 6.5 Hz), 0.09 (3H, s), 0.08 (3H, s). ^{13}C NMR (125 MHz): δ 175.1, 152.6, 138.9, 134.8, 134.3, 133.2, 19.2, 18.0 (C), 135.9, 135.8, 129.5, 129.4, 128.6, 128.5, 128.2, 127.6, 127.5, 127.4, 125.6, 78.7, 76.5, 73.3, 67.3, 55.2, 42.8 (CH), 70.7, 45.2, 30.9, 29.2 (CH_2), 27.1 (x 3), 25.9 (x 3), 24.4, 14.1, 12.2, −4.1, −4.8 (CH_3). IR ν_{max}: 1783, 1705 (C=O) cm^{-1}. HR EIMS *m/z* (% relative intensity): 764.3784 (M$^+$-*t*Bu, 1), 656 (2), 199 (56), 91 (100). Calcd for $C_{49}H_{67}NO_6Si_2$-*t*Bu, 764.3802.

(2*R*,3*S*,6*S*,8*S*)-6-Benzyloxy-3-(*tert*-butyldimethylsilyloxy)-8-(*tert*-butyldiphenylsilyloxy)-2-methylnonanoic Acid (13). Compound **12** (1.05 g, 1.27 mmol) from above was dissolved in a 2:1 THF/H_2O mixture (20 mL) and treated with lithium hydroxide monohydrate (105 mg, 2.5 mmol) and 30% aq H_2O_2 (0.8 mL). The mixture was stirred at room temp for 24 h and poured onto 1.6 M Na_2SO_3, followed by workup (extraction with CH_2Cl_2). Column chromatography on silica gel (hexanes−EtOAc, 4:1) afforded acid **13** (644 mg, 76%): oil; $[\alpha]_D$ −3 (*c* 2, $CHCl_3$). ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.70−7.65 (4H, m), 7.50−7.20 (11H, br m), 4.40 (1H, d, J = 11.3 Hz), 4.24 (1H, d, J = 11.3 Hz), 4.12 (1H, sext, J = 6 Hz), 4.00 (1H, dt, J = 4.5, 6 Hz), 3.60 (1H, quint, J = 5.5 Hz), 2.59 (1H, dq, J = 4.5, 7 Hz), 1.68 (2H, m), 1.60−1.50 (4H, m), 1.40 (1H, m), 1.14 (3H, d, J = 7 Hz), 1.10 (3H, d, J = 6 Hz), 1.07 (9H, s), 0.91 (9H, s), 0.09 (3H, s), 0.08 (3H, s). ^{13}C NMR (125 MHz): δ 178.7, 138.8, 134.8, 134.3, 19.3, 18.0 (C), 135.9, 135.8, 129.6, 129.5, 128.3, 127.6, 127.5, 127.4, 76.3, 73.7, 67.3, 44.3 (CH), 70.8, 45.1, 29.9, 29.5 (CH_2), 27.1 (x 3), 25.8 (x 3), 24.5, 10.9, −4.3, −4.8 (CH_3). IR ν_{max}: 3500−2500 (br, COOH), 1708 (C=O) cm^{-1}. HR EIMS *m/z* (% relative intensity): 605.3142 (M$^+$-*t*Bu, 1), 497 (8), 199 (46), 91 (100). Calcd for $C_{39}H_{58}O_5Si_2$-*t*Bu, 605.3118.

(2*R*,3*S*,6*S*,8*S*)-3-(*tert*-Butyldimethylsilyloxy)-8-(*tert*-butyldiphenylsilyloxy)-6-hydroxy-2-methylnonanoic Acid (14). An amount of 10% Pd/C (300 mg) was suspended in EtOAc (5 mL) under an H_2 atmosphere. Acid **13** (630 mg, 0.95 mmol) dissolved in EtOAc (15 mL) was then added via syringe. The mixture was stirred at room temp and ambient pressure for 2 h and then filtered through

(14) We have only found ^{1}H NMR data of (+)-nonactic acid: Fraser, B.; Perlmutter, P. *J. Chem. Soc., Perkin Trans. 1* **2002**, 2896−2899.

(15) (a) Schmidt, U.; Werner, J. *Synthesis* **1986**, 986−992. (b) Kiyota, H.; Abe, M.; Ono, Y.; Oritani, T. *Synlett* **1997**, 1093−1095. See also the following: Stadler, M.; Bauch, F.; Henkel, T.; Mühlbauer, A.; Müller, H.; Spaltmann, F.; Weber, K. *Arch. Pharm.* **2001**, *334*, 143−147.

Celite. Solvent removal in vacuo and column chromatography on silica gel (hexanes−EtOAc, 4:1) gave hydroxy acid **14** (457 mg, 84%): oil; $[\alpha]_D$ −11.5 (*c* 1.45, $CHCl_3$). ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.70−7.65 (4H, m), 7.45−7.35 (6H, m), 4.18 (1H, sext, J = 6 Hz), 4.02 (1H, m), 3.98 (1H, m), 2.60 (1H, dq, J = 4.5, 7 Hz), 1.70−1.30 (8H, br m), 1.15 (3H, d, J = 7 Hz), 1.11 (3H, d, J = 6 Hz), 1.08 (9H, s), 0.90 (9H, s), 0.10 (3H, s), 0.09 (3H, s). ^{13}C NMR (125 MHz): δ 178.7, 133.9, 133.3, 19.1, 18.0 (C), 135.9, 135.8, 129.9, 129.8, 127.7, 127.6, 73.5, 68.7, 68.1, 44.4 (CH), 44.3, 33.2, 29.9 (CH_2), 27.1 (x 3), 25.8 (x 3), 22.6, 11.1, −4.3, −4.8 (CH_3). IR ν_{max}: 3500−2500 (br, COOH), 1709 (C═O) cm^{-1}. HR EIMS *m*/*z* (% relative intensity): 515.2635 (M^+-*t*Bu, 1), 497 (8), 305 (22), 199 (100), 75 (50). Calcd for $C_{32}H_{52}O_5Si_2$-*t*Bu, 515.2649.

Lactone 15. The hydroxy acid **14** from above was dissolved in dry THF (50 mL) and treated sequentially with ethyl diisopropylamine (175 μL, 1 mmol), DMAP (6 mg, 0.05 mmol), and 2,4,6-trichlorobenzoyl chloride (125 μL, 0.8 mmol). The mixture was stirred at room temp for 1 h. Workup (extraction with Et_2O) and column chromatography on silica gel (hexanes−EtOAc, 9:1) afforded lactone **15** (385 mg, 87%): solid; mp 77−78 °C; $[\alpha]_D$ +82 (*c* 0.65, $CHCl_3$). ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.70−7.65 (4H, m), 7.45−7.35 (6H, m), 4.63 (1H, td, J = 10, 2.3 Hz), 4.22 (1H, m), 3.77 (1H, m), 3.10 (1H, dq, J = 6.5, 7.5 Hz), 2.15−2.05 (1H, m), 1.90−1.75 (3H, m), 1.65 (1H, ddd, J = 14.5, 9.5, 2.7 Hz), 1.58 (1H, dt, J = 15, 4 Hz), 1.05 (3H, d, J = 7.5 Hz), 1.04 (9H, s), 1.00 (3H, t, J = 6.2 Hz), 0.87 (9H, s), 0.06 (3H, s), 0.03 (3H, s). ^{13}C NMR (125 MHz, $CDCl_3$): δ 174.4, 134.5, 19.3, 18.0 (C), 135.8, 135.7, 129.6, 127.6, 75.8, 70.1, 66.8, 50.5 (CH), 47.6, 30.4, 29.3 (CH_2), 27.1 (x 3), 25.7 (x 3), 24.3, 12.6, −5.0, −5.1 (CH_3). IR ν_{max}: 1726 (C═O) cm^{-1}. HR EIMS *m*/*z* (% relative intensity): 497.2564 (M^+-*t*Bu, 100), 453 (20), 419 (44), 283 (34), 199 (60). Calcd for $C_{32}H_{50}O_4Si_2$-*t*Bu, 497.2543. Anal. Calcd for $C_{32}H_{50}O_4Si_2$: C, 69.26; H, 9.08. Found: C, 69.37; H, 9.00.

(3*R*,4*S*,7*S*)-4-Hydroxy-7-[(*S*)-2-hydroxypropyl)]-3-methyloxepan-2-one (1). Lactone **15** (360 mg, 0.65 mmol) was dissolved in THF (6 mL) containing pyridine (0.6 mL) and treated with a solution of pyridine (1 mL) and HF-pyridine complex (1.35 mL) in THF (12 mL). The mixture was stirred for 24 h at 55 °C. Workup (extraction with EtOAc) and column chromatography on silica gel (EtOAc) afforded lactone **1** (92 mg, 70%): oil; $[\alpha]_D$ +47.4 (*c* 1.2, $CHCl_3$) (literature values[1] for feigrisolide A, $[\alpha]_D$ +3.4 (*c* 0.3, MeOH)). IR ν_{max}: 3400 (br, OH), 1700 (C═O) cm^{-1}. HR EIMS *m*/*z* (% relative intensity): 203.1287 (M + H^+, 5), 185 (6), 169 (20), 143 (30), 140 (100), 125 (50), 114 (58). Calcd for $C_{10}H_{19}O_4$, 203.1283. Anal. Calcd for $C_{10}H_{18}O_4$: C, 59.39; H, 8.97. Found: C, 59.52; H, 9.02. For NMR data, see Table 1 in Supporting Information.

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Supporting Information Available: Description of general features and experimental procedures; physical and spectral data of compounds **8**−**10** and **16**; graphical ^{1}H and ^{13}C NMR spectra of compounds **1**, **8**−**10**, **13**, **15**, nonactic acid, and homononactic acid; three tables with compared NMR data of **1**, nonactic acid, and homononactic acid with feigrisolide A and feigrisolide B (PDF). A CIF file with crystallographic data of lactone **15**. This material is available free of charge via the Internet at http://pubs.acs.org.

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