

Supplementary Information

Novel soraphens from precursor directed biosynthesis

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3'-Fluoro soraphen A 2: ¹H NMR (360 MHz, CDCl₃) δ 1.03 (3H, d, *J* 6.8 Hz, 21-H₃), 1.06 (3H, d, *J* 7.5 Hz, 20-H₃), 1.13 (3H, d, *J* 7.2 Hz, 18-H₃), 1.20 (1H, m, 14a-H), 1.31 (1H, m, 13a-H), 1.34 (1H, m, 15a-H), 1.46 (1H, m, 15b-H), 1.48 (1H, m, 14b-H), 1.66 (1H, m, 16a-H), 1.73 (1H, m, 13b-H), 1.93 (1H, m, 6-H), 2.11 (1H, m, 16b-H), 2.50 (1H, m, 8-H), 3.14 (1H, d, *J* 7.1 Hz, 2-H), 3.18 (1H, d, *J* 1.5 Hz, 4-H), 3.28 (3H, s, 22-H₃), 3.38 (3H, s, 19-H₃), 3.42 (1H, m, 12-H), 3.44 (3H, s, 23-H₃), 3.59 (1H, s, 5-OH), 3.66 (1H, dd, *J* 9.5, 2.2 Hz, 11-H), 3.82 (1H, dd, *J* 10.5, 2.8 Hz, 7-H), 4.03 (1H, d, *J* 9.0, 5-H), 4.24 (1H, s, 3-OH), 5.48 (1H, ddd, *J* 16.2, 9.5, 1.9 Hz, 10-H), 5.82 (1H, dd, *J* 11.0, 4.1 Hz, 17-H), 6.16 (1H, dd, *J* 16.2, 3.8 Hz, 9-H), 6.97 (1H, dd, *J* 3.2 Hz, *J*_{HF} 8.2 Hz, 2'-H), 7.02 (dm, *J*_{HF} 8.4 Hz, 4'-H), 7.11 (1H, d, *J* 7.8 Hz, 6'-H), 7.31 (1H, dt, *J* 7.9 Hz, *J*_{HF} 5.8 Hz, 5'-H). ¹³C NMR (100 MHz, CDCl₃) δ 10.3 (C-20), 11.7 (C-18), 12.5 (C-21), 23.1 (C-14), 25.7 (C-15), 30.2 (C-13), 35.3 (C-8), 35.6 (C-6), 35.7 (C-16), 46.3 (C-2), 56.2 (C-22), 57.4 (C-19), 58.0 (C-23), 68.8 (C-5), 72.5 (C-7), 73.7 (C-17), 76.1 (C-4), 82.6 (C-12), 84.7 (C-11), 99.5 (C-3), 113.1 (d, *J*_{CF} 22 Hz, C-2'), 115.1 (d, *J*_{CF} 21 Hz, C-4'), 121.8 (C-6'), 122.8 (C-10), 130.2 (C-5'), 139.6 (C-9), 143.6 (C-1'), 162.9 (d, *J*_{CF} 247 Hz, C-3'), 170.7 (C-1). ¹⁹F

NMR (338 MHz, CDCl₃) δ -113.45. HRMS-FAB: C₂₉H₄₃FO₈Na (M+Na)_{calcd} 561.2840, (M+Na)_{obs} 561.2870.

4'-Fluoro soraphen A 3: ¹H NMR (360 MHz, CDCl₃) δ 1.02 (3H, d, *J* 6.8 Hz, 21-H₃), 1.06 (3H, d, *J* 7.9 Hz, 20-H₃), 1.08 (3H, d, *J* 7.4 Hz, 18-H₃), 1.20 (1H, m, 14a-H), 1.23 (1H, m, 13a-H), 1.25 (1H, m, 15a-H), 1.47 (1H, m, 15b-H), 1.68 (1H, m, 14b-H), 1.92 (1H, m, 16a-H), 2.06 (1H, m, 13b-H), 2.10 (1H, m, 6-H), 2.13 (1H, m, 16b-H), 2.49 (1H, m, 8-H), 3.14 (1H, d, *J* 7.1 Hz, 2-H), 3.18 (1H, d, *J* 2.5 Hz, 4-H), 3.28 (3H, s, 22-H₃), 3.38 (3H, s, 19-H₃), 3.42 (1H, m, 12-H), 3.44 (3H, s, 23-H₃), 3.54 (1H, d, *J* 9.8 Hz, 5-OH), 3.67 (1H, dd, *J* 9.5, 2.2 Hz, 11-H), 3.83 (1H, dd, *J* 10.5, 2.8 Hz, 7-H), 4.03 (1H, d, *J* 9.8, 5-H), 4.28 (1H, s, 5-OH), 5.48 (1H, ddd, *J* 16.1, 9.5, 1.9 Hz, 10-H), 5.82 (1H, dd, *J* 11.0, 4.1 Hz, 17-H), 6.16 (1H, dd, *J* 16.1, 3.8 Hz, 9-H), 7.03 (2H, dd, *J* 8.7 Hz, *J*_{HF} 8.7 Hz, 3'/5'-H), 7.31 (dd, *J* 8.7 Hz, *J*_{HF} 5.2 Hz, 2'/6'-H). ¹³C NMR (100 MHz, CDCl₃) δ 10.3 (C-20), 11.7 (C-18), 12.5 (C-21), 23.1 (C-14), 25.7 (C-15), 30.2 (C-13), 35.3 (C-8), 35.5 (C-6), 35.6 (C-16), 46.3 (C-2), 56.2 (C-22), 57.4 (C-19), 58.0 (C-23), 68.8 (C-5), 72.5 (C-7), 73.8 (C-17), 76.1 (C-4), 82.7 (C-12), 84.7 (C-11), 99.5 (C-3), 115.5 (d, *J*_{CF} 22 Hz, C-3'/5'), 122.8 (C-10), 128.1 (d, *J*_{CF} 22 Hz, C-2'/6'), 136.8 (C-1'), 139.6 (C-9), 162.5 (d, *J*_{CF} 246 Hz, C-4'), 170.8 (C-1). ¹⁹F NMR (338 MHz, CDCl₃) δ -114.25. HRMS-FAB: C₂₉H₄₃FO₈Na (M+Na)_{calcd} 561.2840, (M+Na)_{obs} 561.2870.

3',4'-Difluoro soraphen A 4: ¹H NMR (500 MHz, CDCl₃) δ 1.03 (3H, d, *J* 6.8 Hz, 21-H₃), 1.05 (3H, d, *J* 7.5 Hz, 20-H₃), 1.10 (3H, d, *J* 7.1 Hz, 18-H₃), 1.21 (1H, m, 14a-H), 1.30 (1H, m, 13a-H), 1.35 (1H, m, 15a-H), 1.46 (1H, m, 15b-H), 1.48 (1H, m, 14b-H), 1.66 (1H, m, 16a-H), 1.71 (1H, m, 13b-H), 1.93 (1H, m, 6-H), 2.05 (1H, m, 16b-H), 2.50 (1H, m, 8-H), 3.14 (1H, d, *J* 7.1

Hz, 2-H), 3.17 (1H, d, J 2.8 Hz, 4-H), 3.28 (3H, s, 22-H₃), 3.38 (3H, s, 19-H₃), 3.42 (1H, m, 12-H), 3.44 (3H, s, 23-H₃), 3.49 (1H, d, J 5.3 Hz, 5-OH), 3.65 (1H, dd, J 9.5, 2.4 Hz, 11-H), 3.81 (1H, dd, J 10.5, 2.8 Hz, 7-H), 4.03 (1H, d, J 9.6, 5-H), 4.20 (1H, s, 3-OH), 5.48 (1H, ddd, J 16.2, 9.5, 1.8 Hz, 10-H), 5.79 (1H, dd, J 11.0, 4.0 Hz, 17-H), 6.15 (1H, dd, J 16.1, 3.8 Hz, 9-H), 7.05-7.19 (3H, m, 2'/5'/6'-H). ¹³C NMR (100 MHz, CDCl₃) δ 10.3 (C-20), 11.6 (C-18), 12.5 (C-21), 23.1 (C-14), 25.6 (C-15), 30.2 (C-13), 35.2 (C-8), 35.4 (C-6), 35.6 (C-16), 46.2 (C-2), 56.2 (C-22), 57.4 (C-19), 58.0 (C-23), 68.8 (C-5), 72.5 (C-7), 73.1 (C-17), 76.1 (C-4), 82.6 (C-12), 84.7 (C-11), 99.4 (C-3), 115.3 (d, J_{CF} 18 Hz, C-2'), 117.5 (d, J_{CF} 18 Hz, C-5'), 122.8 (C-10), 138.0 (C-1'), 139.6 (C-9), 150.1 (dd, J_{CF} 248, 12 Hz, C-4'), 150.4 (dd, J_{CF} 248, 13 Hz, C-3'), 170.8 (C-1). ¹⁹F NMR (376 MHz, CDCl₃) δ -137.25 (3'-F), -138.55 (4'-F). HRMS-FAB: C₂₉H₄₂F₂O₈Cs (M+Cs)_{calcd} 689.1902, (M+Cs)_{obs} 689.1897.

Table S1: LC-MS and ¹⁹F NMR data for soraphen analogues.

Soraphen	R _t (min)	Observed M ^c	δ ¹⁹ F (ppm) ^d
1	19 ^a , 8 ^b	543	
2	22.4 ^a	561	-113.45
3	22.4 ^a	561	-114.25
4	9.0 ^b	579	-137.25, -138.55
5	10.3 ^b	579	-109.65, -110.79
6	12.0 ^b	577 (75%) 579 (25%)	
7	13.0 ^b	621 (50%) 623 (50%)	

^a LC-MS analysis was carried out on a Finnigan LCQ using a reverse-phase Hichrom 5 μ m C18 column of 4.6 mm internal diameter x 250 mm kept at 40°C in 70% MeOH, 30% H₂O and a flow rate of 1 mL/min; ^b LC-MS analysis carried out using 80% MeOH, 20% H₂O; ^c observed as sodium adducts; ^d referenced to CFCl₃.