

Supporting Information

Oxygenated solanapyrone analogs from *Nigrospora* sp. IQ-064, a mangrove associated fungus

Carlos A. Fajardo-Hernández^a, Ángel Sahid Aguilar-Colorado^a, Leslie Maribel Corona-Cabello^a, Ingrid Yadira Martínez-Aldino^a, and José Rivera-Chávez^{a,*}

^a Instituto de Química, Departamento de Productos Naturales, Universidad Nacional Autónoma de México, Mexico City, Mexico.

, e-mail jrivera@iquimica.unam.mx.

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T: FTMS - c ESI Full ms [135.0000-2000.0000]

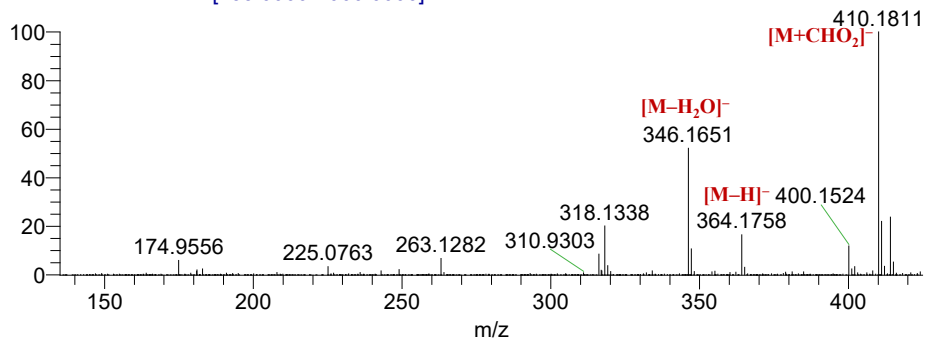


Figure S1. HR-ESI-MS spectrum of nigrosporapyrone E (1) m/z : 364.1758 $[M-H]^-$ calculated for $C_{19}H_{26}NO_6$ 364.1755, $\Delta+0.9$ ppm.

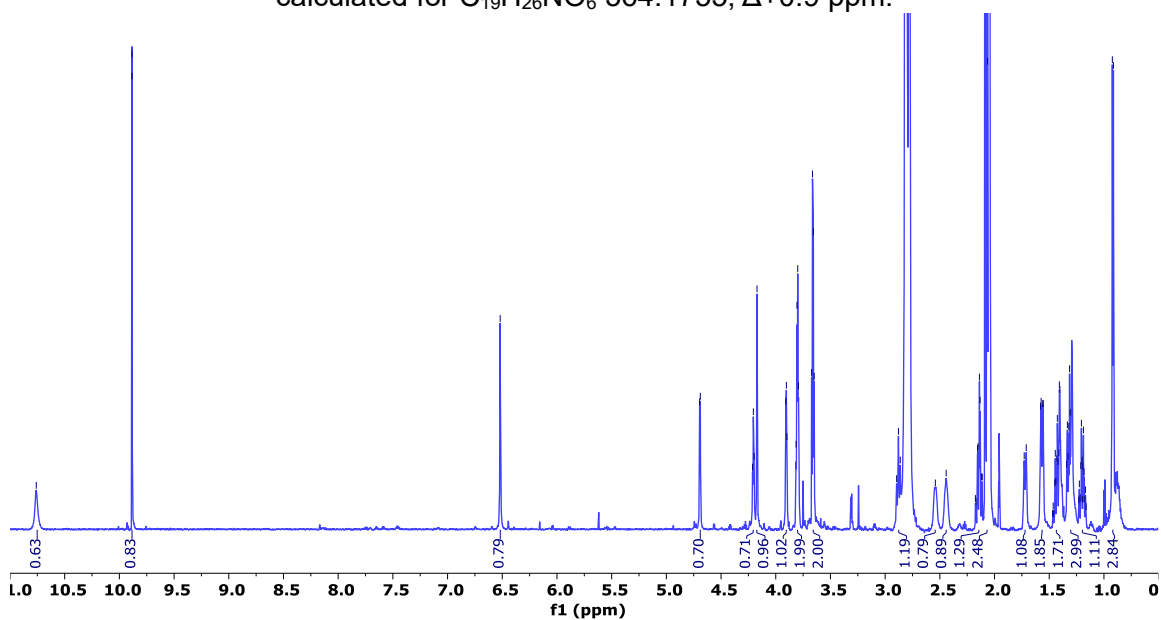


Figure S2. 1H -NMR spectrum of nigrosporapyrone E (1) (Acetone- d_6 , 700 MHz).

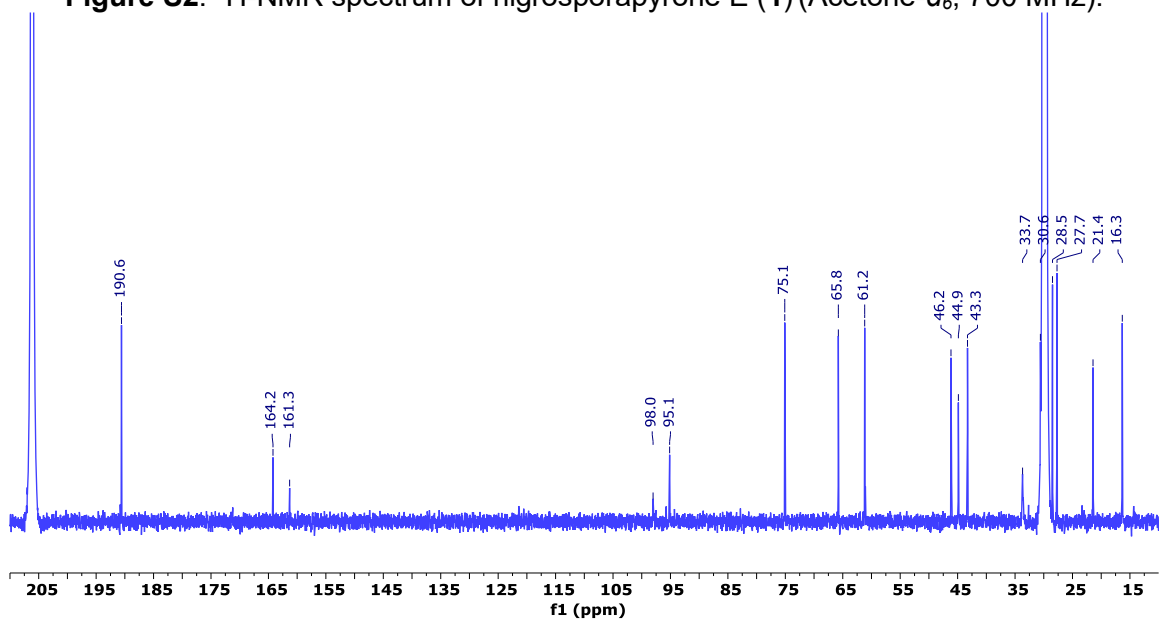


Figure S3. ^{13}C -NMR spectrum of nigrosporapyrone E (1) (Acetone- d_6 , 175 MHz).

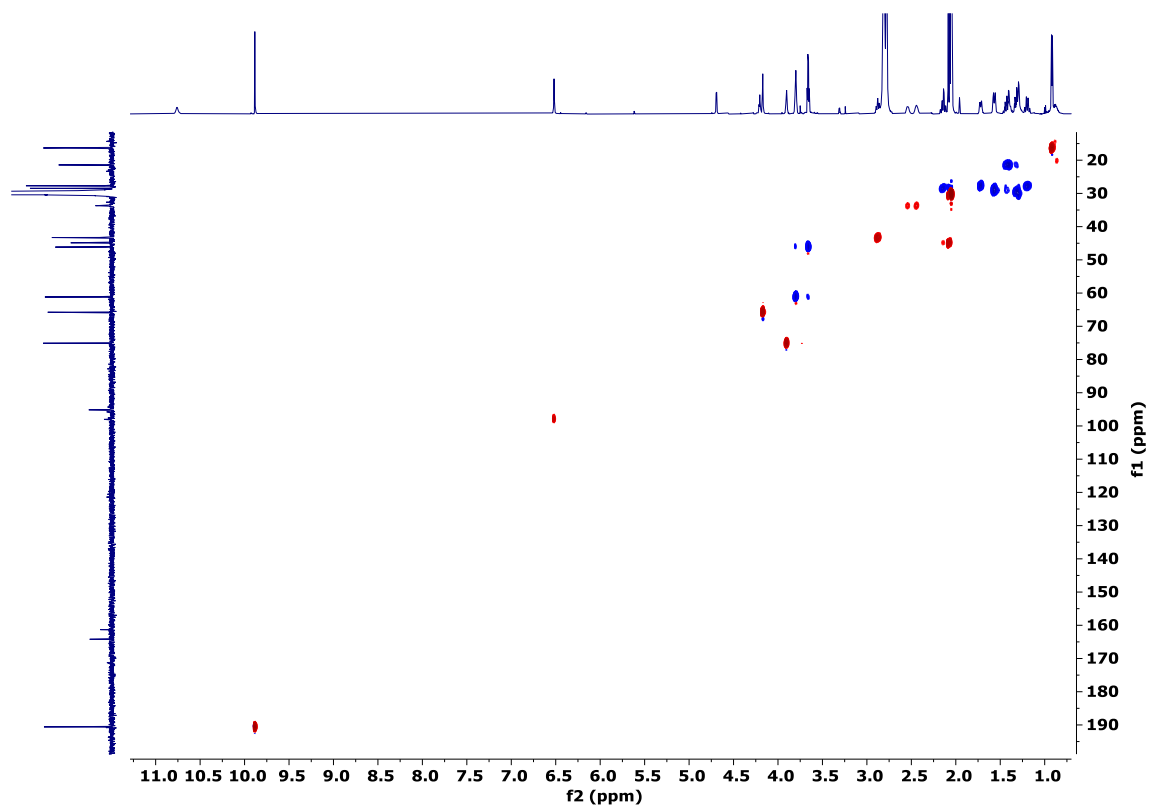


Figure S4. HSQC-NMR spectrum of nigrosporapyrone E (**1**) (Acetone- d_6 700 MHz).

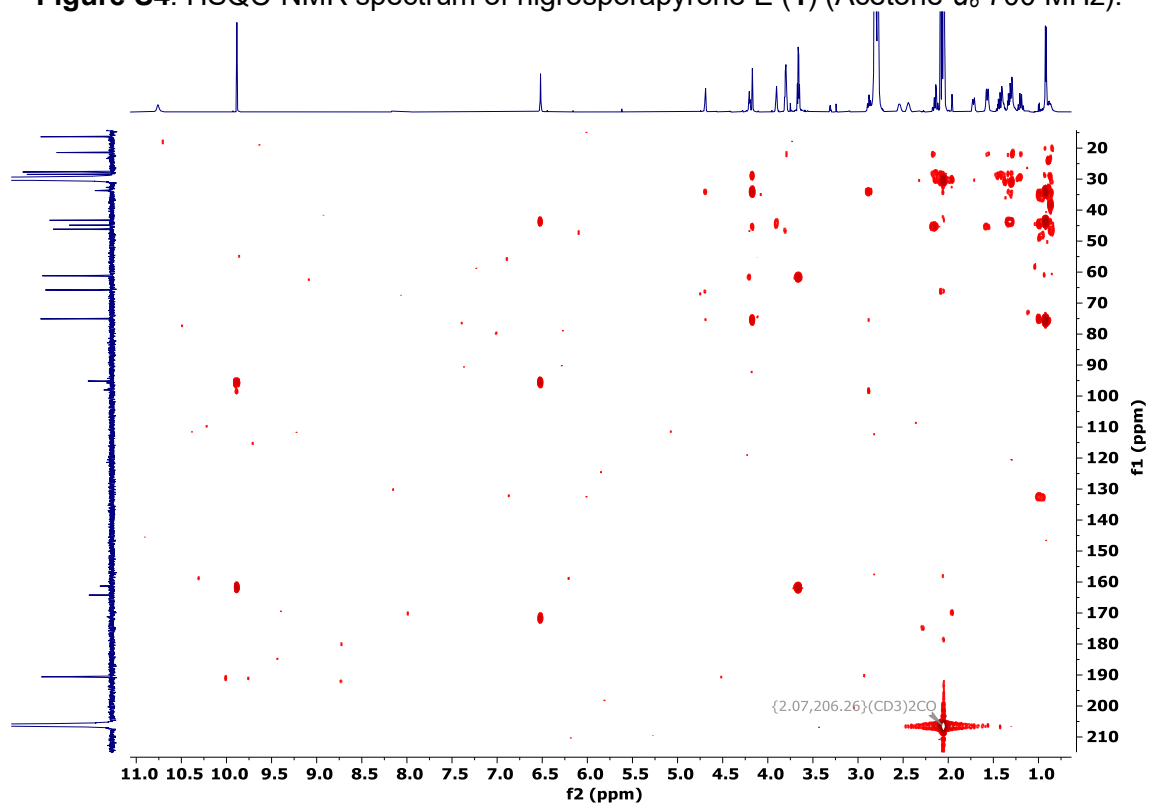


Figure S5. HMBC-NMR spectrum of nigrosporapyrone E (**1**) (Acetone- d_6 700 MHz).

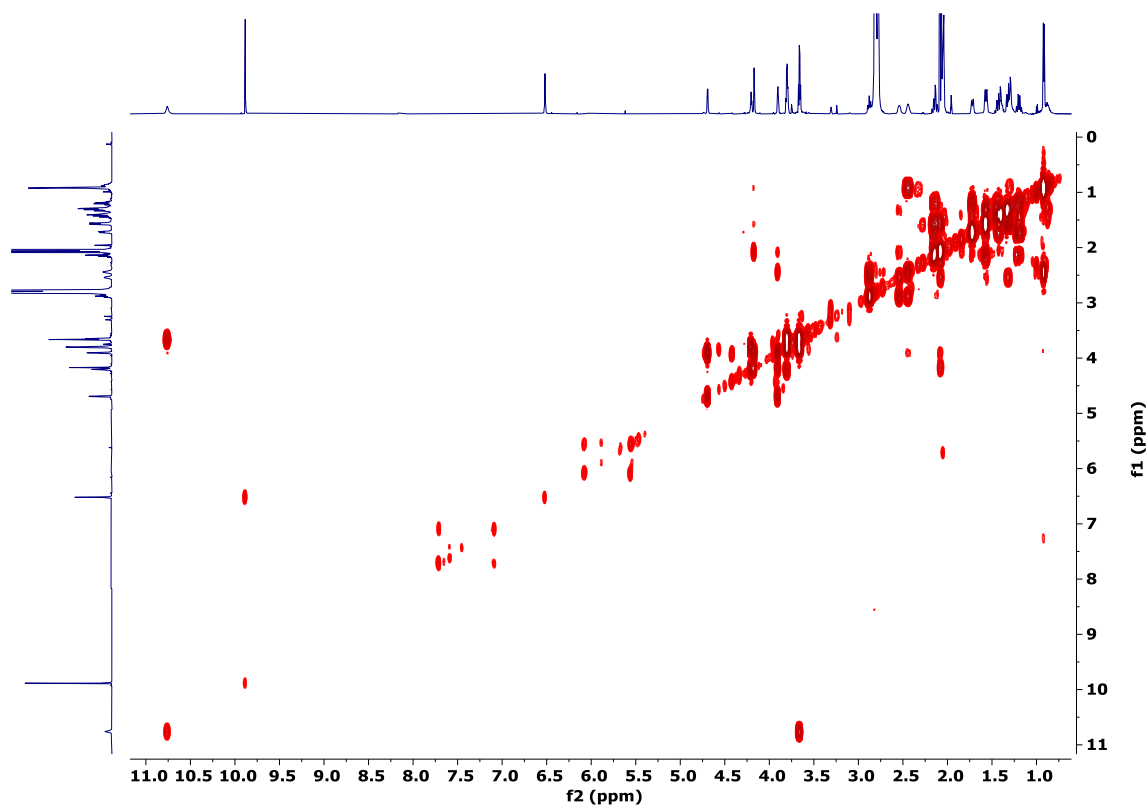


Figure S6. COSY-NMR spectrum of nigrosporapyrone E (**1**) (Acetone- d_6 700 MHz).

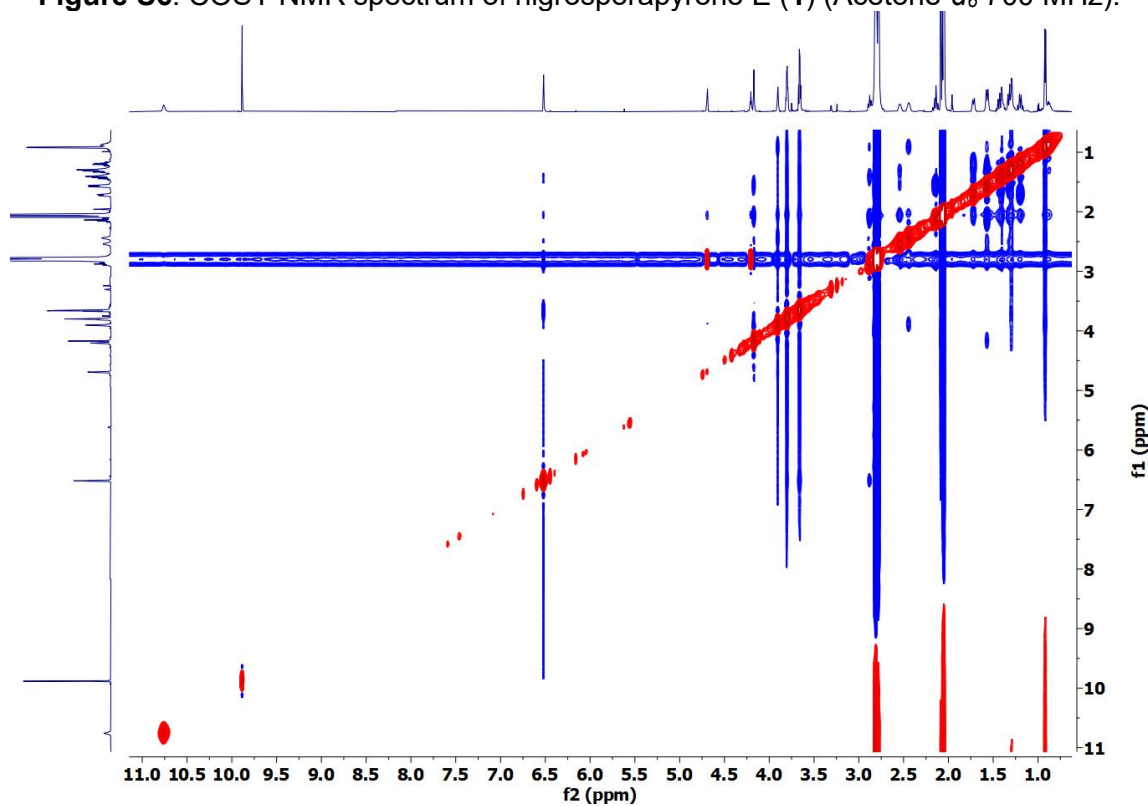


Figure S7. NOESY-NMR spectrum of nigrosporapyrone E (**1**) (Acetone- d_6 700 MHz).

T: FTMS - c ESI Full ms [135.0000-2000.0000]

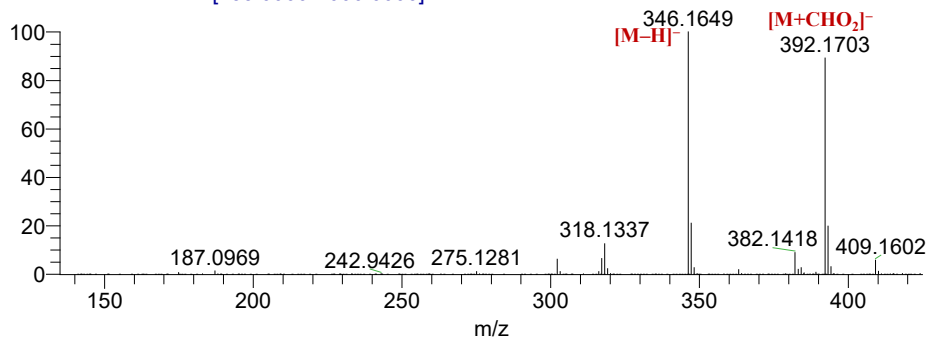


Figure S8. HR-ESI-MS spectrum of nigrosporapyrone F (**2**) m/z : 346.1649 [M-H]⁻ calculated for C₁₉H₂₄NO₅ 346.1649, Δ 0.0 ppm.

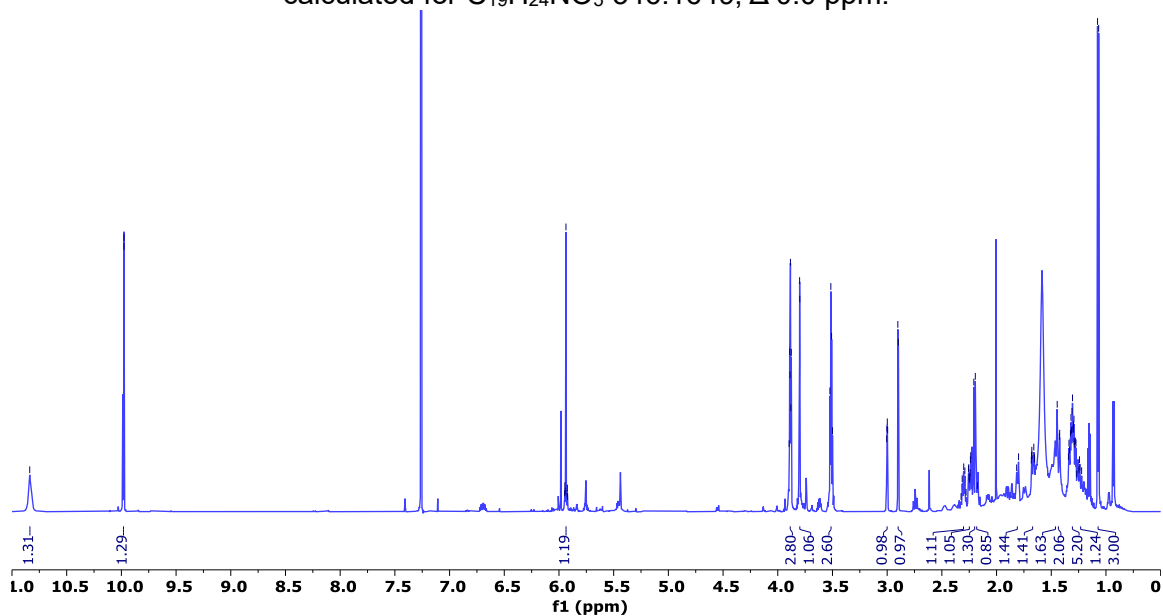


Figure S9. ¹H-NMR spectrum of nigrosporapyrone F (**2**) (CDCl₃, 700 MHz).

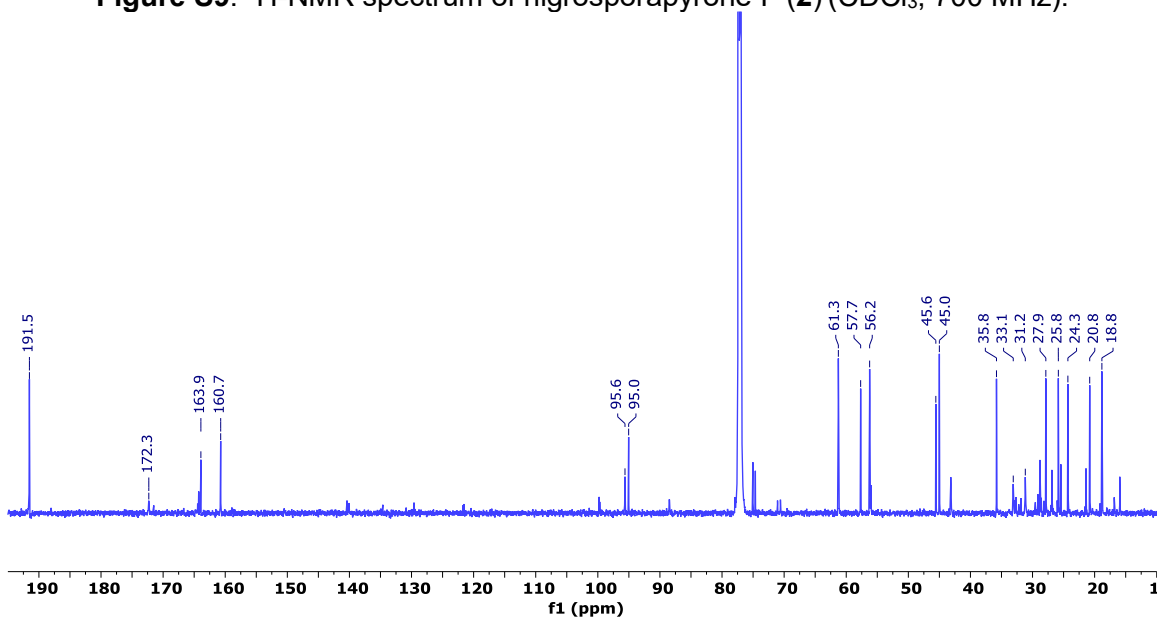


Figure S10. ¹³C-NMR spectrum of nigrosporapyrone F (**2**) (CDCl₃, 175 MHz).

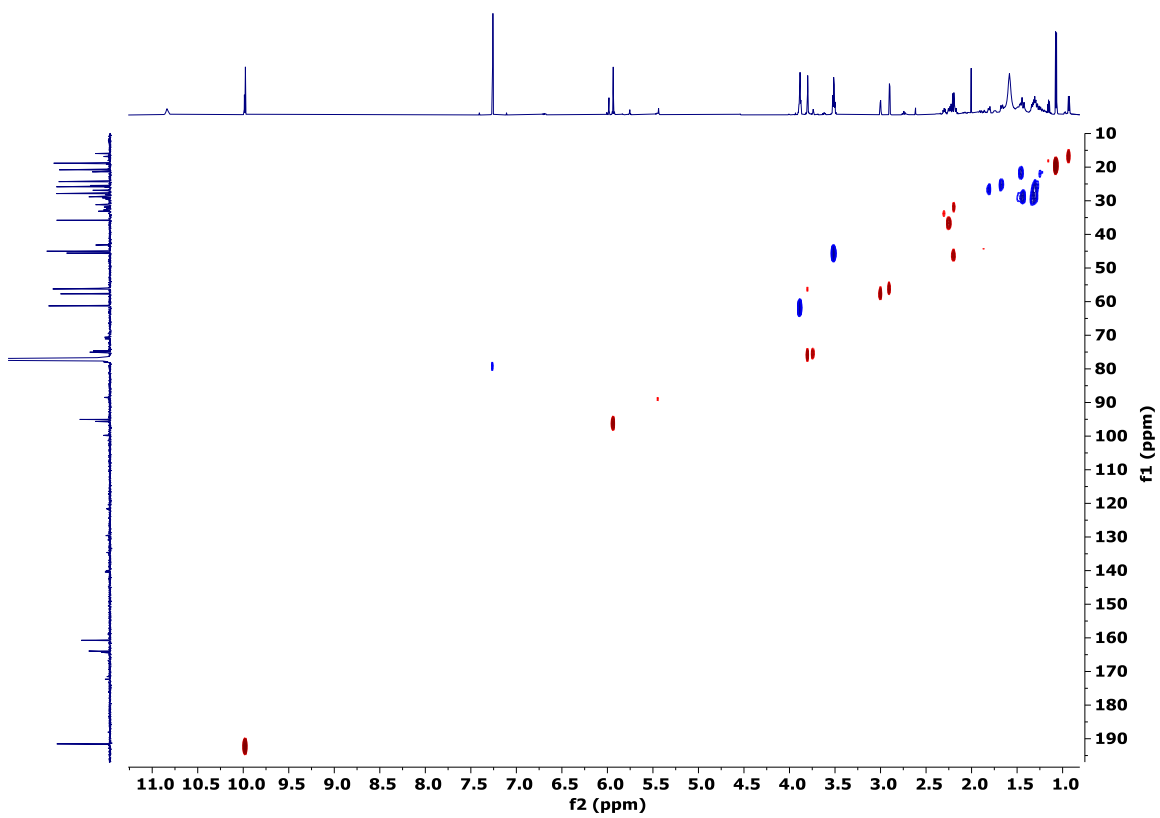


Figure S11. HSQC-NMR spectrum of nigrosporapyrone F (**2**) (CDCl₃, 700 MHz).

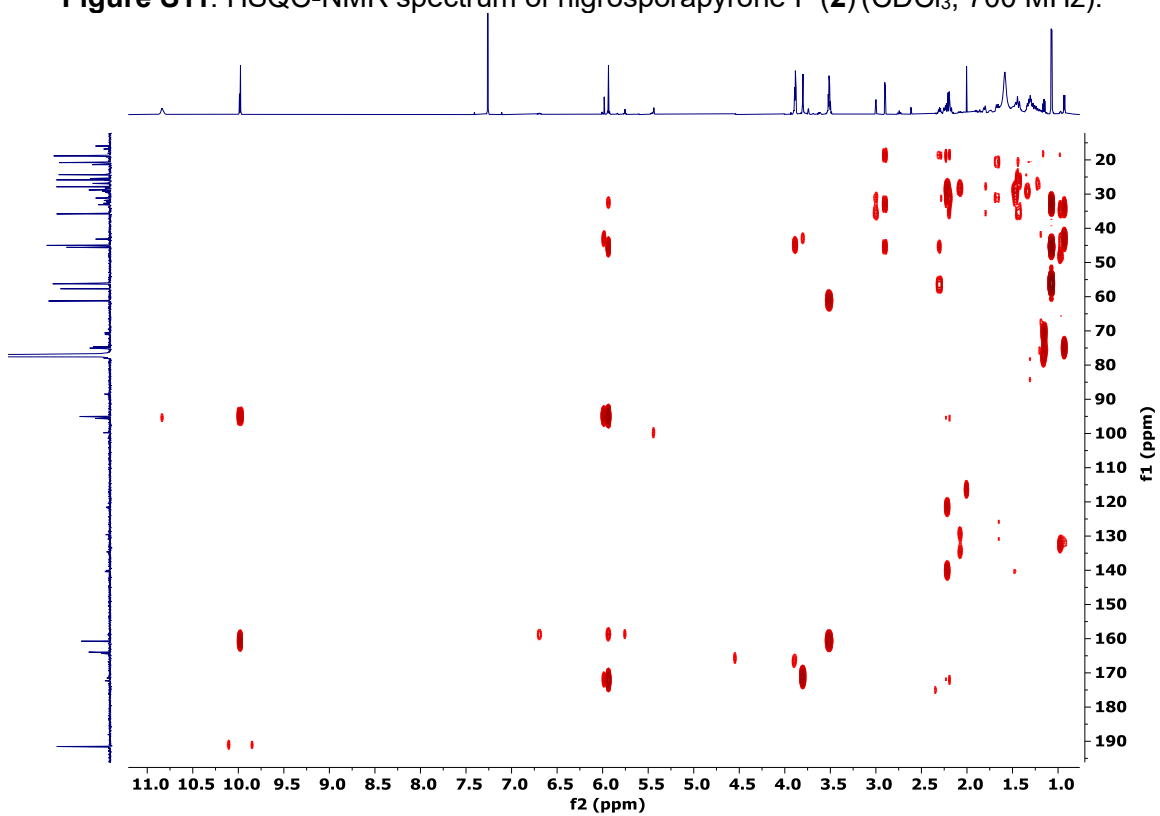


Figure S12. HMBC-NMR spectrum of nigrosporapyrone F (**2**) (CDCl₃, 700 MHz).

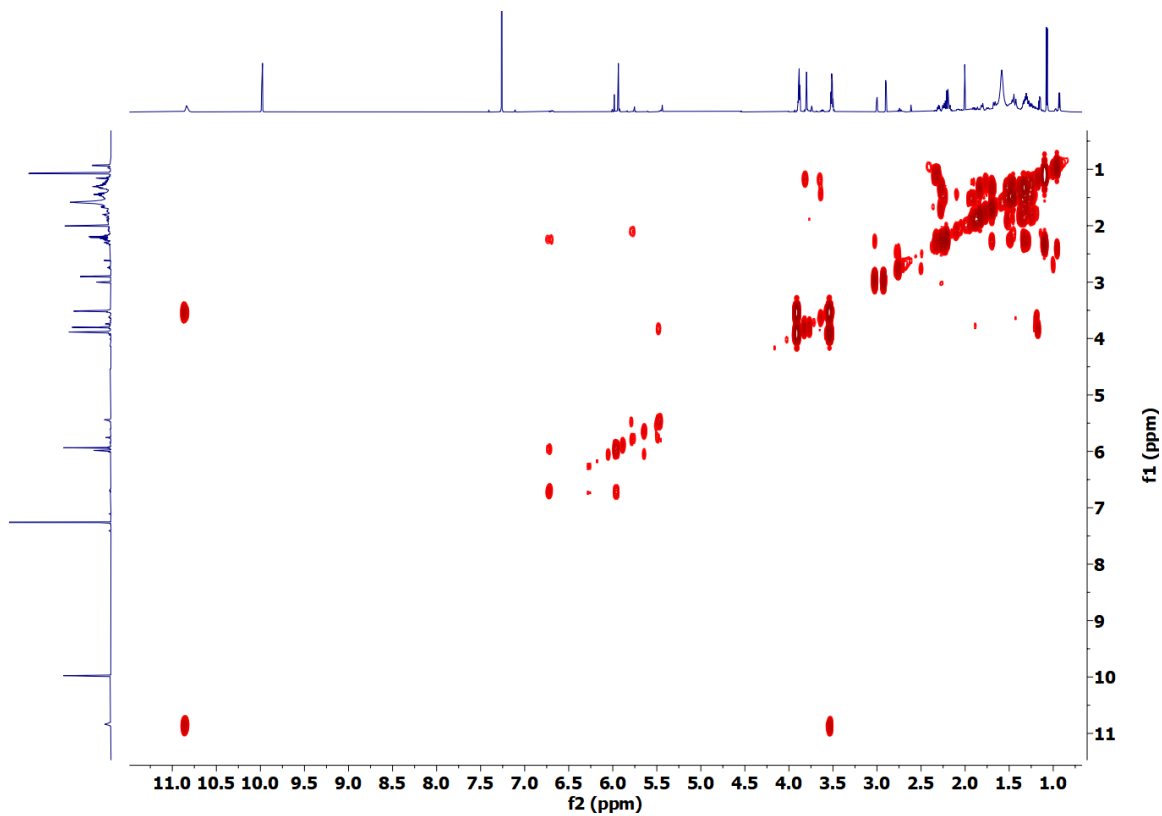


Figure S13. COSY-NMR spectrum of nigrosporapyrone F (**2**) (CDCl₃, 700 MHz).

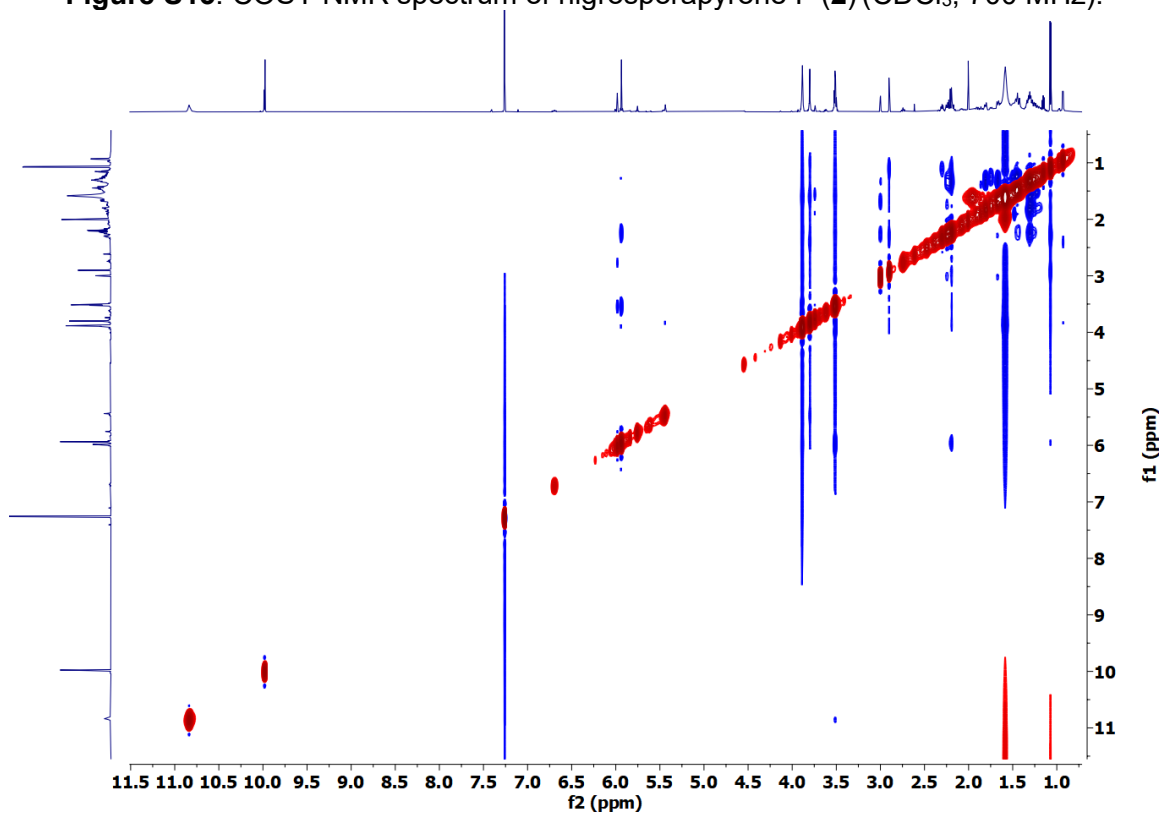


Figure S14. NOESY-NMR spectrum of nigrosporapyrone F (**2**) (CDCl₃, 700 MHz).

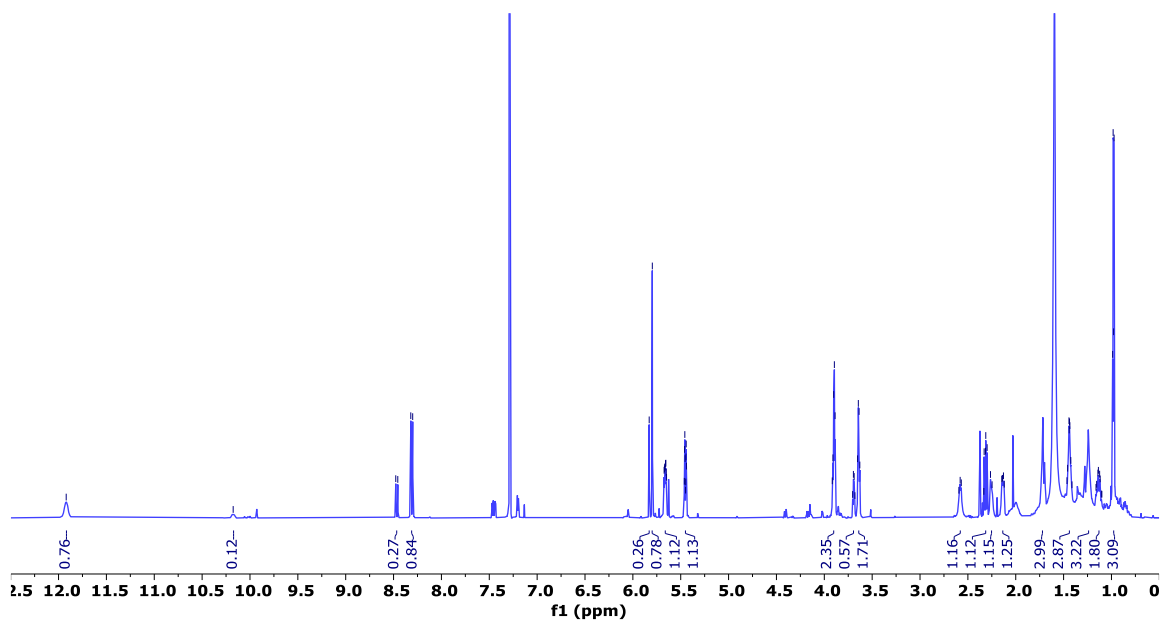


Figure S15. ¹H-NMR spectrum of sphasolanapyrone F (3) (CDCl₃, 700 MHz).

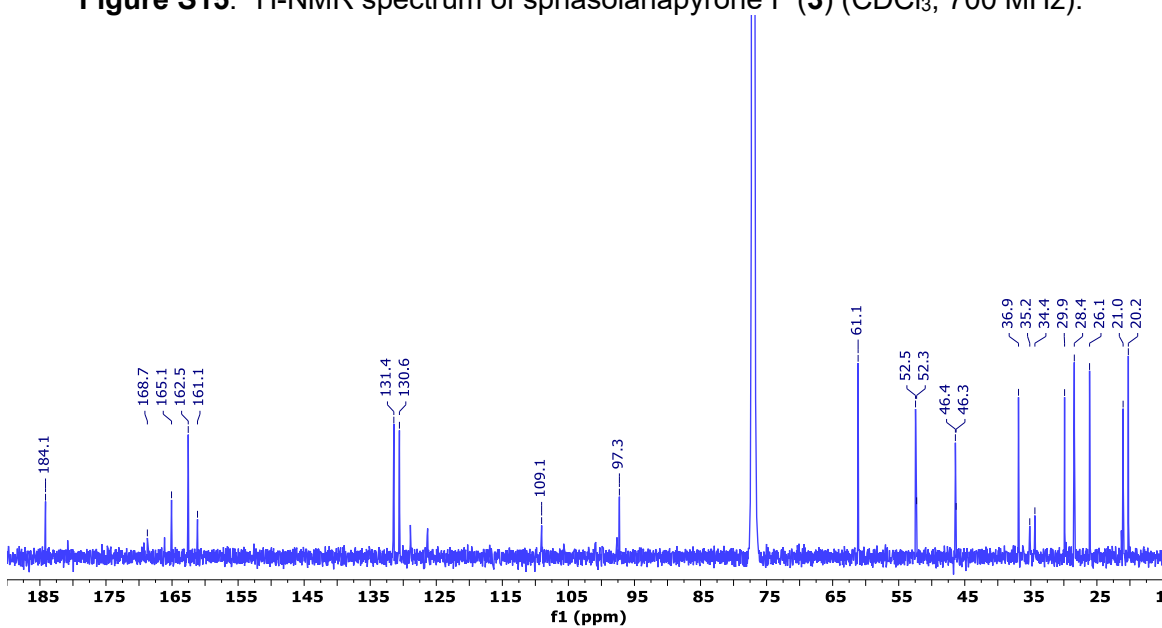
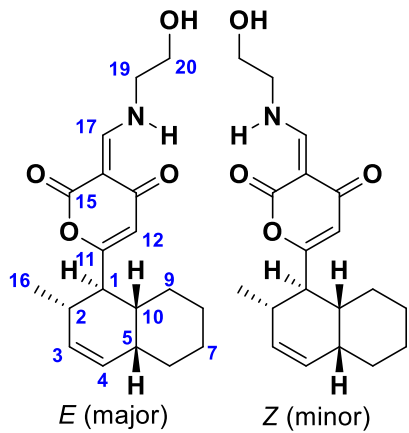


Figure S16. ¹³C-NMR spectrum of sphasolanapyrone F (3) (CDCl₃, 175 MHz).

sphasolanapyrone F (**3**): HR-DART⁺ m/z 332.1846 [M+H]⁺ calculated for C₁₉H₂₆NO₄ 332.1856, Δ-3.1 ppm.

¹H NMR (700 MHz, CDCl₃): 2(E) δ_H 11.92 (s-broad, 1H, NH-18), 8.31 (d, J = 13.8 Hz, 1H, H-17), 5.80 (s, 1H, H-12), 5.66 (ddd, J = 9.9, 5.0, 2.6 Hz, 1H, H-4), 5.45 (dq, J = 9.9, 1.8 Hz, 1H, H-3), 3.90 (dt, J = 10.1, 5.0 Hz, 2H, H₂-20), 3.64 (q, J = 5.6 Hz, 2H, H₂-19), 2.57 (m, 1H, H-2), 2.31 (dd, J = 11.9, 9.8 Hz, 1H, H-1), 2.26 (d-broad, J = 11.7 Hz, 1H, H-10), 2.13 (dd, J = 12.5, 5.7 Hz, 1H, H-5), 1.70 (m overlapped, 2H, H-6a, H-7a), 1.60 (m, 1H, H-9b), 1.44 (m overlapped, 2H, H-8a, H-9a), 1.24 (m overlapped, 2H, H-7b, H-8b), 1.13 (m, 1H, H-6b), 0.98 (d, J = 7.0 Hz, 3H, H₃-16).

2(Z) δ_H 10.18 (s-broad, 1H, NH-18), 8.47 (d, J = 13.8 Hz, 1H, H-17), 5.83 (s, 1H, H-12), 5.66 (ddd, J = 9.9, 5.0, 2.6 Hz, 1H, H-4), 5.45 (dq, J = 9.9, 1.8 Hz, 1H, H-3), 3.90 (dt, J = 10.1, 5.0 Hz, 2H, H₂-20), 3.69 (q, J = 5.5 Hz, 2H, H₂-19), 2.57 (m, 1H, H-2), 2.31 (dd, J = 11.9, 9.8 Hz, 1H, H-1), 2.26 (d-broad, J = 11.7 Hz, 1H, H-10), 2.13 (dd, J = 12.5, 5.7 Hz, 1H, H-5), 1.70 (m overlapped, 2H, H-6a, H-7a), 1.60 (m, 1H, H-9b), 1.44 (m overlapped, 2H, H-8a, H-9a), 1.24 (m overlapped, 2H, H-7b, H-8b), 1.13 (m, 1H, H-6b), 0.99 (d, J = 7.0 Hz, 3H, H₃-16).



¹³C NMR (175 MHz, CDCl₃): 2(E) δ_C 184.1 (C-13), 169.4 (C-11), 165.1 (C-15), 162.5 (C-17), 131.4 (C-4), 130.6 (C-3), 109.1 (C-12), 97.3 (C-14), 61.1 (C-20), 52.5 (C-19), 46.4 (C-1), 36.9 (C-5), 35.2 (C-10), 34.4 (C-2), 29.9 (C-6), 28.4 (C-9), 26.1 (C-7), 21.0 (C-8), 20.2 (C-16).

2(Z) δ_C 180.7 (C-13), 169.4 (C-11), 166.1 (C-15), 161.1 (C-17), 131.4 (C-4), 130.6 (C-3), 109.1 (C-12), 97.3 (C-14), 61.1 (C-20), 52.3 (C-19), 46.3 (C-1), 36.9 (C-5), 35.2 (C-10), 34.4 (C-2), 29.9 (C-6), 28.4 (C-9), 26.1 (C-7), 21.0 (C-8), 20.2 (C-16).

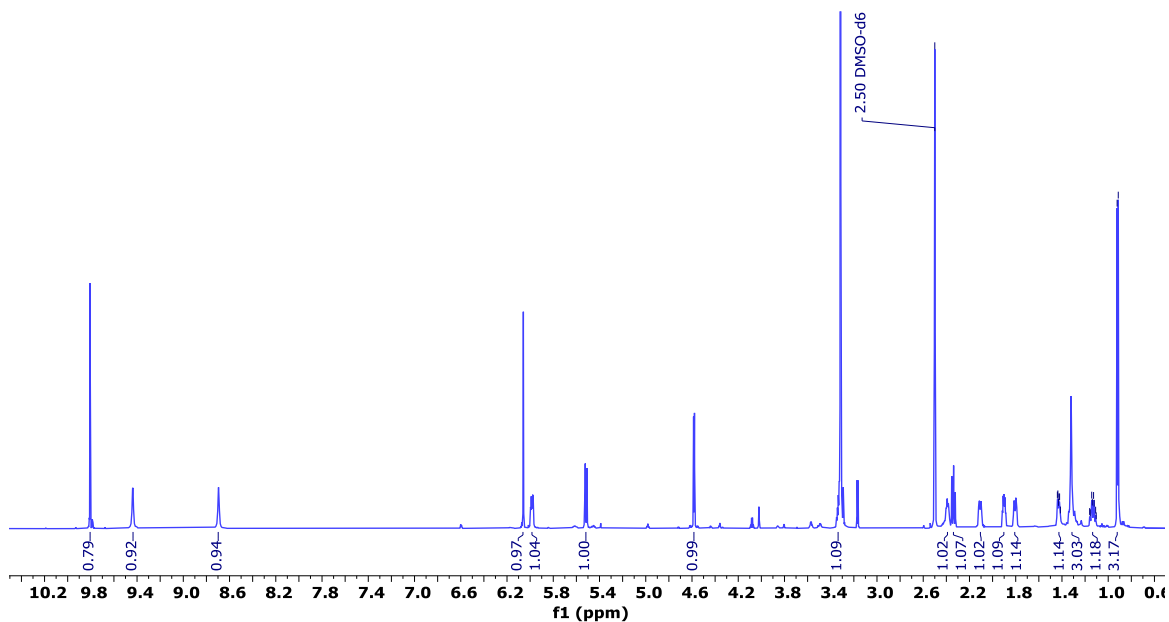


Figure S17. ^1H -NMR spectrum of solanapyrone W (**4**) (CDCl_3 , 700 MHz).

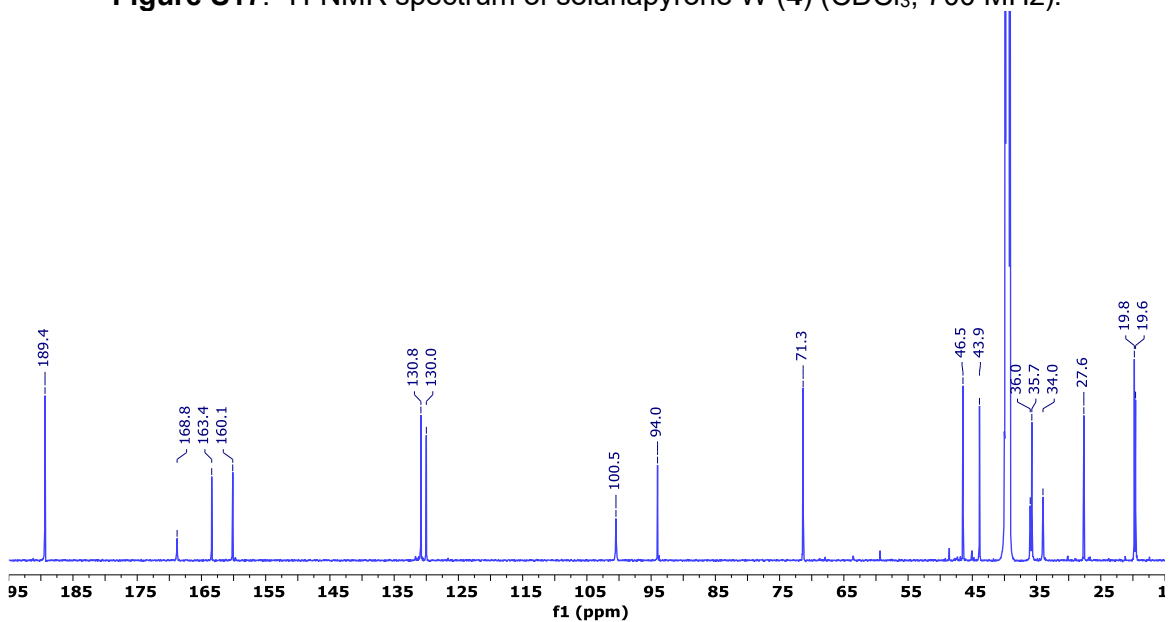
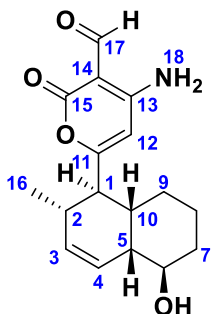


Figure S18. ^{13}C -NMR spectrum of solanapyrone W (**4**) (CDCl_3 , 175 MHz).

solanapyrone W (**4**): HR-DART⁺ m/z 304.1558 [$\text{M}+\text{H}$]⁺ calculated for $\text{C}_{17}\text{H}_{22}\text{NO}_4$ 304.1543, Δ +4.8 ppm.

^1H NMR (700 MHz, $\text{DMSO}-d_6$): δ_{H} 9.81 (d, J = 0.6 Hz, 1H, H-17), 9.44 (d, J = 3.7 Hz, 1H, NH-18), 8.69 (d, J = 3.7 Hz, 1H, NH-18), 6.06 (d, J = 0.7 Hz, 1H, H-12), 5.98 (ddd, J = 10.1, 5.0, 2.6 Hz, 1H, H-4), 5.52 (dt, J = 10.1, 1.7 Hz, 1H, H-3), 4.58 (d, J = 5.5 Hz, 1H, 6-OH), 3.33 (overlapped, 1H, H-6), 2.39 (ddt, J = 9.2, 4.4, 2.2 Hz, 1H, H-2), 2.34 (dd, J = 11.7, 10.0 Hz, 1H, H-1), 2.11 (dt, J = 11.6, 3.9 Hz, 1H, H-10), 1.90 (dtt, J = 10.0, 5.0, 1.5 Hz, 1H, H-5), 1.80 (dt, J = 13.0, 3.9 Hz, 1H, H-7a), 1.43 (m, 1H, H-8a), 1.32 (m overlapped, 3H, H-8b, H₂-9), 1.13 (qd, J = 12.3, 3.6 Hz, H-7b), 0.92 (d, J = 6.9 Hz, 3H, H₃-16).

^{13}C NMR ($\text{DMSO}-d_6$, 175 MHz): δ_{C} 189.4 (C-17), 168.8 (C-15), 163.4 (C-11), 160.1 (C-13), 130.8 (C-3), 130.0 (C-4), 100.5 (C-12), 94.0 (C-14), 71.3 (C-6), 46.5 (C-1), 43.9 (C-5), 36.0 (C-10), 35.7 (C-7), 34.0 (C-2), 27.6 (C-8), 19.8 (C-16), 19.6 (C-9).



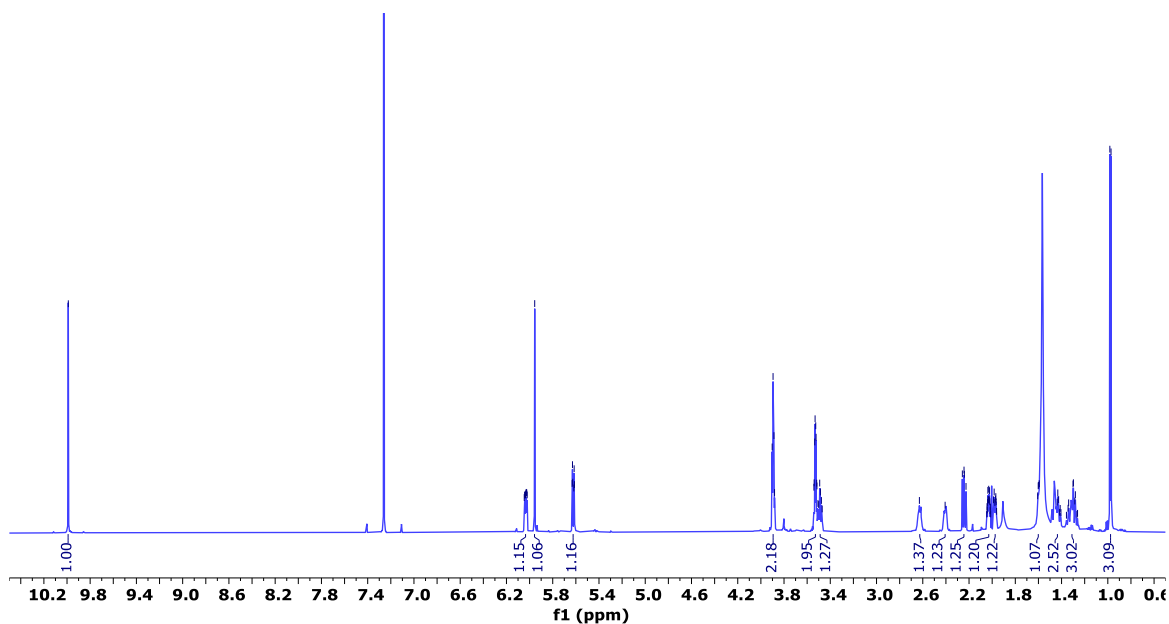


Figure S19. ^1H -NMR spectrum of nigrosporapyrone B (**5**) (CDCl_3 , 700 MHz).

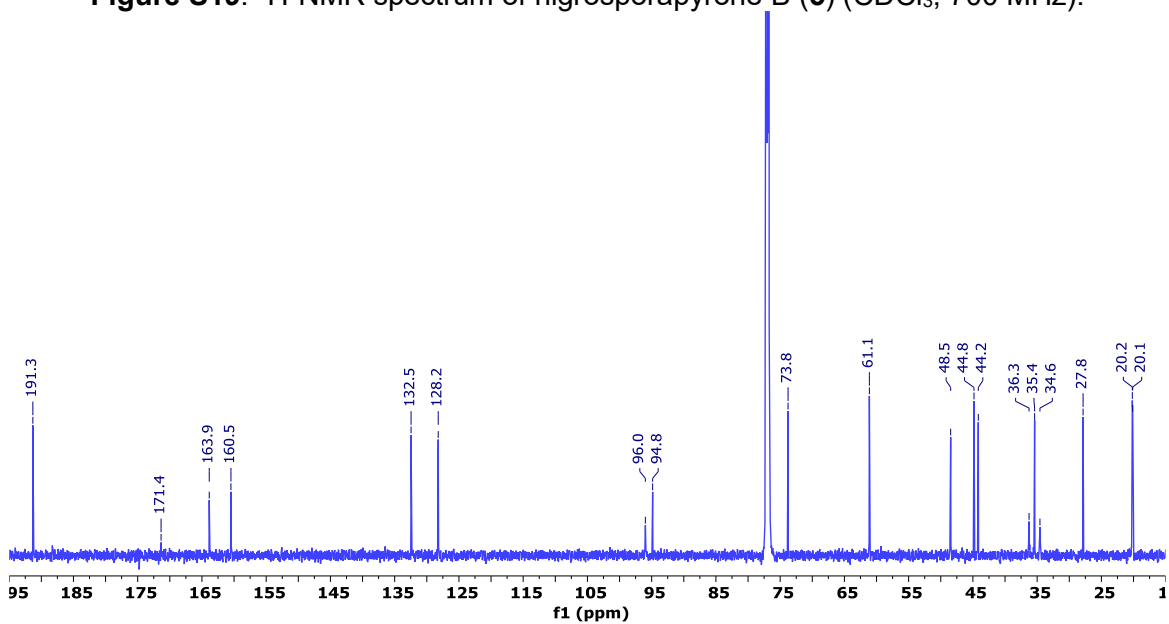
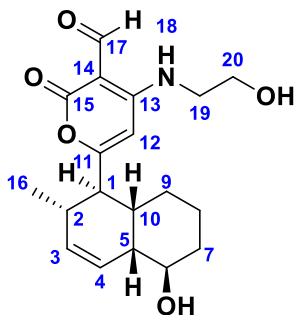


Figure S20. ^{13}C -NMR spectrum of nigrosporapyrone B (**5**) (CDCl_3 , 175 MHz).

nigrosporapyrone B (**5**): HR-DART⁺ m/z 348.1815 [$\text{M}+\text{H}$]⁺ calculated for $\text{C}_{19}\text{H}_{26}\text{NO}_5$ 348.1811, Δ +2.7 ppm.

^1H NMR (700 MHz, CDCl_3): δ_{H} 10.86 (s-broad, 1H, NH-18), 9.98 (s, 1H, H-17), 6.03 (ddd, $J = 10.1, 5.1, 2.5$ Hz, 1H, H-4), 5.96 (s, 1H, H-12), 5.62 (dd, $J = 10.1, 1.8$ Hz, 1H, H-3), 3.89 (q, $J = 4.6$ Hz, 2H, H₂-20), 3.53 (qd, $J = 5.2, 1.6$ Hz, 2H, H₂-19), 3.49 (td, $J = 10.5, 4.5$ Hz, 1H, H-6), 2.63 (m, 1H, H-2), 2.41 (m, 1H, H-10), 2.24 (dd, $J = 12.0, 10.0$ Hz, 1H, H-1), 2.03 (ddd, $J = 10.1, 5.1, 1.6$ Hz, 1H, H-5), 1.98 (m, 1H, H-7a), 1.60 (m, 1H, H-9a), 1.44 (m, 2H, H₂-8), 1.30 (m overlapped, 2H, H-7b, H-9b), 0.98 (d, $J = 7.0$ Hz, 3H, H₃-16).

^{13}C NMR (175 MHz, CDCl_3): δ_{C} 191.3 (C-17), 171.4 (C-11), 163.9 (C-15), 160.5 (C-13), 132.5 (C-3), 128.2 (C-4), 96.0 (C-12), 94.8 (C-14), 73.8 (C-6), 61.1 (C-20), 48.5 (C-1), 44.8 (C-19), 44.2 (C-5), 36.3 (C-10), 35.4 (C-7), 34.6 (C-2), 27.8 (C-8), 20.2 (C-16), 20.1 (C-9).



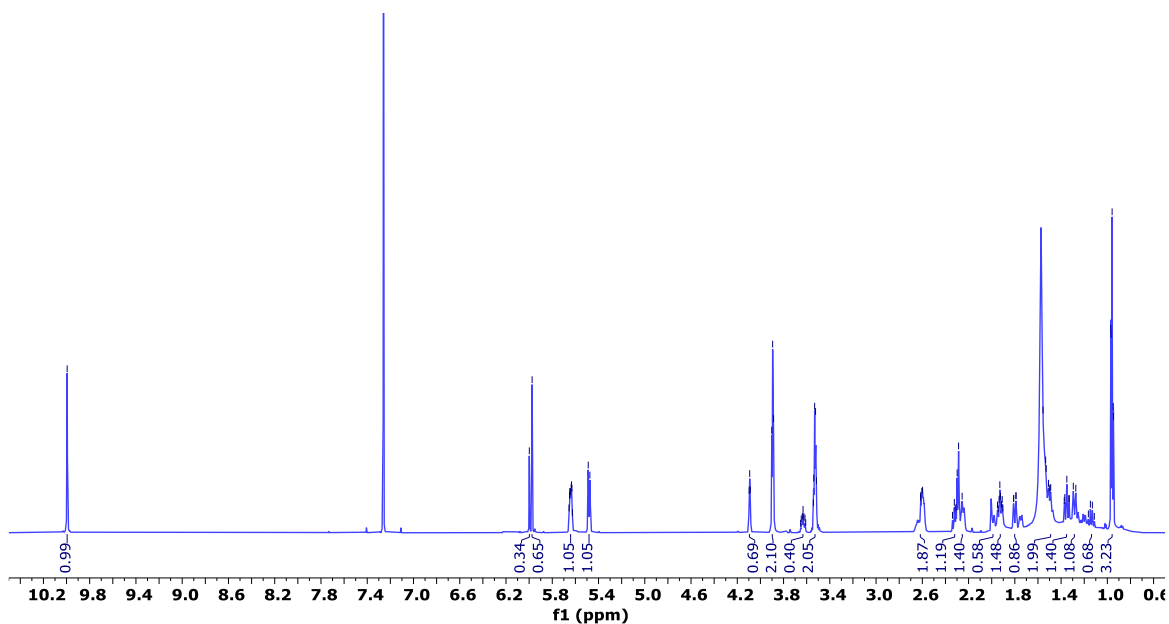


Figure S21. ^1H -NMR spectrum of nigrosporapyrone C (**6**) (CDCl_3 , 700 MHz).

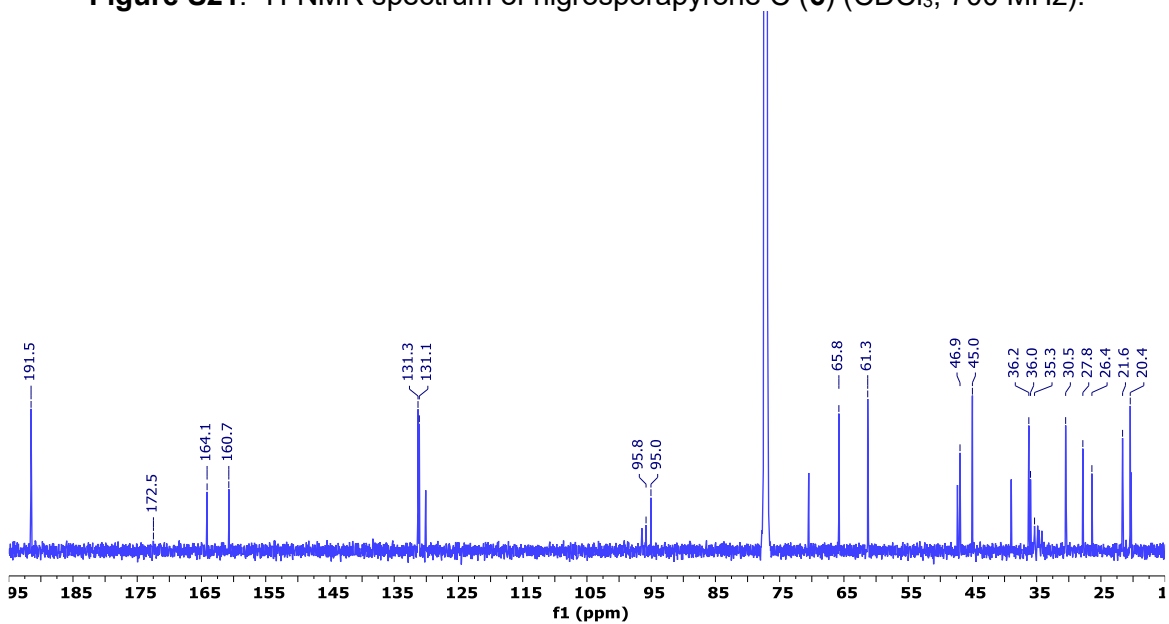
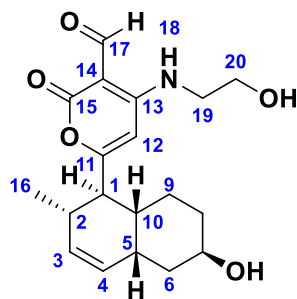


Figure S22. ^{13}C -NMR spectrum of nigrosporapyrone C (**6**) (CDCl_3 , 175 MHz).



nigrosporapyrone C (**6**): HR-DART⁺ m/z 348.1816 [$\text{M}+\text{H}$]⁺ calculated for $\text{C}_{19}\text{H}_{26}\text{NO}_5$ 348.1805, $\Delta +3.2$ ppm.

^1H NMR (700 MHz, CDCl_3): δ_{H} 10.86 (s-broad, 1H, NH-18), 9.99 (s, 1H, H-17), 5.99 (s, 1H), 5.64 (ddd, $J = 11.3, 5.7, 3.0$ Hz, 1H, H-4), 5.48 (d-broad, $J = 10.0$ Hz, 1H, H-3), 4.09 (t, $J = 3.2$ Hz, 1H, H-7), 3.89 (t, $J = 5.3$ Hz, 2H, H₂-20), 3.53 (q, $J = 5.5$ Hz, 2H, H₂-19), 2.61 (m overlapped, 2H, H-2, H-5), 2.30 (m, 1H, H-1), 2.25 (m, 1H, H-10), 1.93 (ddt, $J = 14.1, 8.4, 4.2$ Hz, 1H, H-9a), 1.80 (d, $J = 14.2$ Hz, 1H, H-6a), 1.50 (m overlapped, 2H, H-8a, H-8b), 1.35 (td, $J = 14.0, 2.7$ Hz, 1H, H-6b), 1.28 (d-broad, $J = 15.2$ Hz, 1H, H-9b), 0.96 (t, $J = 7.3$ Hz, 3H, H₃-16).

^{13}C NMR (175 MHz, CDCl_3): δ_{C} 191.5 (C-17), 172.5 (C-11), 164.1 (C-15), 160.7 (C-13), 131.3 (C-4), 131.1 (C-3), 95.8 (C-12), 95.0 (C-14), 65.8 (C-7), 61.3 (C-20), 46.9 (C-1), 45.0 (C-19), 39.0, 36.2 (C-6), 36.0 (C-10), 35.3 (C-2), 34.8, 34.6, 34.2, 30.5 (C-5), 30.4, 27.8 (C-8), 21.6 (C-9), 20.4 (C-16).

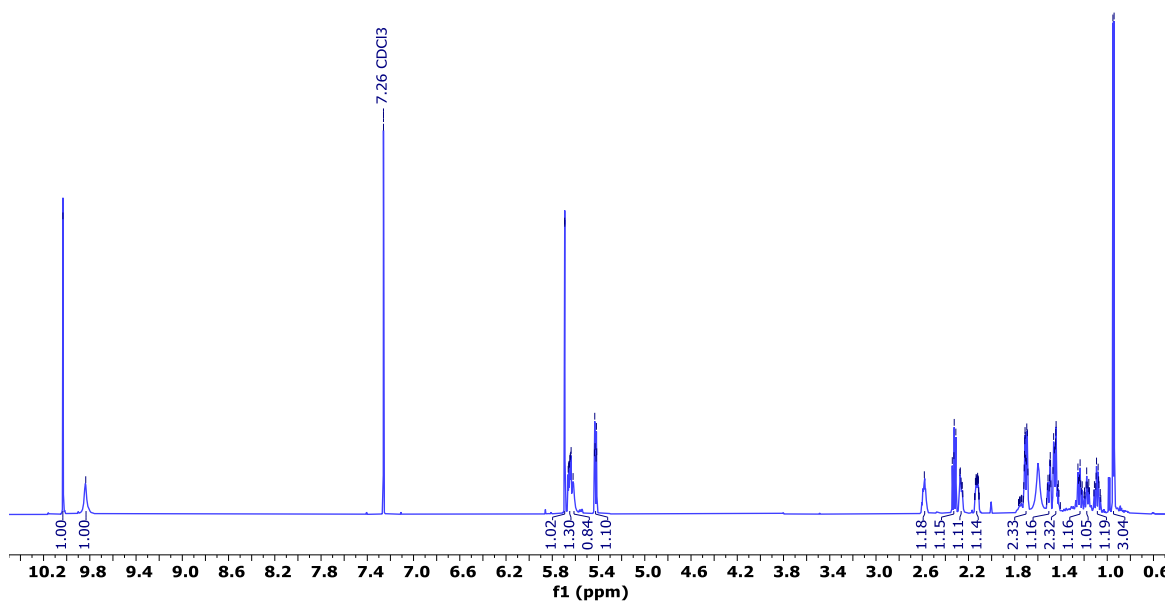


Figure S23. $^1\text{H-NMR}$ spectrum of solanapyrone G (**7**) (CDCl_3 , 500 MHz).

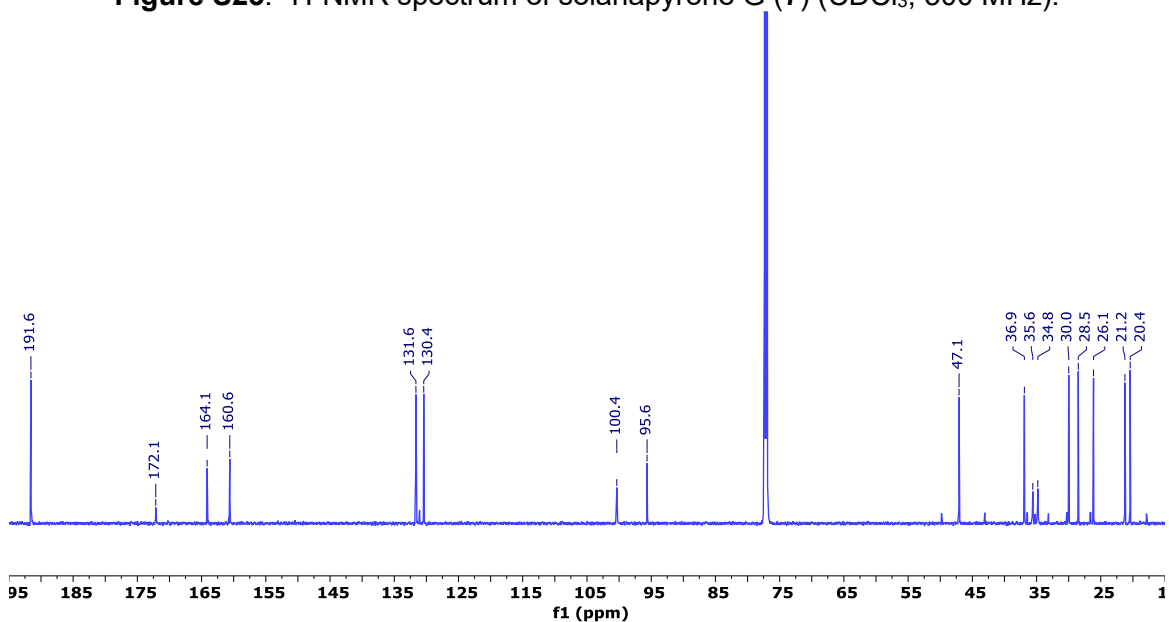
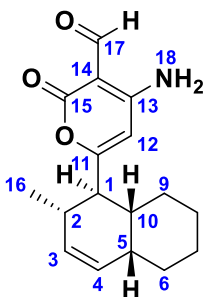


Figure S24. $^{13}\text{C-NMR}$ spectrum of solanapyrone G (**7**) (CDCl_3 , 125 MHz).

solanapyrone G (**9**): HR-ESI $^+$ m/z 288.1583 [$\text{M}+\text{H}$] $^+$ calculated for $\text{C}_{17}\text{H}_{22}\text{NO}_3$ 288.1594, Δ -3.9 ppm.

$^1\text{H NMR}$ (700 MHz, CDCl_3): δ_{H} 10.03 (s, 1H, H-17), 9.84 (s-broad, 2H, NH-18), 5.69 (d, J = 0.6 Hz, 1H, H-12), 5.65 (ddd, J = 10.1, 5.1, 2.6 Hz, 1H, H-4), 5.43 (dt, J = 9.9, 1.8 Hz, 1H, H-3), 2.58 (m, 1H, H-2), 2.32 (dd, J = 11.8, 9.8 Hz, 1H, H-1), 2.26 (m, 1H, H-10), 2.13 (m, 1H, H-5), 1.72 (m overlapped, 2H, H-6b, H-7b), 1.50 (m, 1H, H-9a), 1.45 (m overlapped, 2H, H-8b, H-9b), 1.23 (ddd, J = 12.5, 9.4, 3.3 Hz, 1H, H-7a), 1.18 (dd, J = 13.3, 3.2 Hz, 1H, H-8a), 1.08 (ddd, J = 12.6, 9.9, 2.9 Hz, 1H, H-6a), 0.95 (d, J = 7.1 Hz, 3H, H₃-16).

$^{13}\text{C NMR}$ (175 MHz, CDCl_3): δ_{C} 191.6 (C-17), 172.1 (C-13), 164.1 (C-11), 160.6 (C-15), 131.6 (C-4), 130.4 (C-3), 100.4 (C-12), 95.6 (C-14), 47.1 (C-1), 36.9 (C-5), 35.6 (C-10), 34.8 (C-2), 30.0 (C-6), 28.5 (C-9), 26.1 (C-7), 21.2 (C-8), 20.4 (C-16).



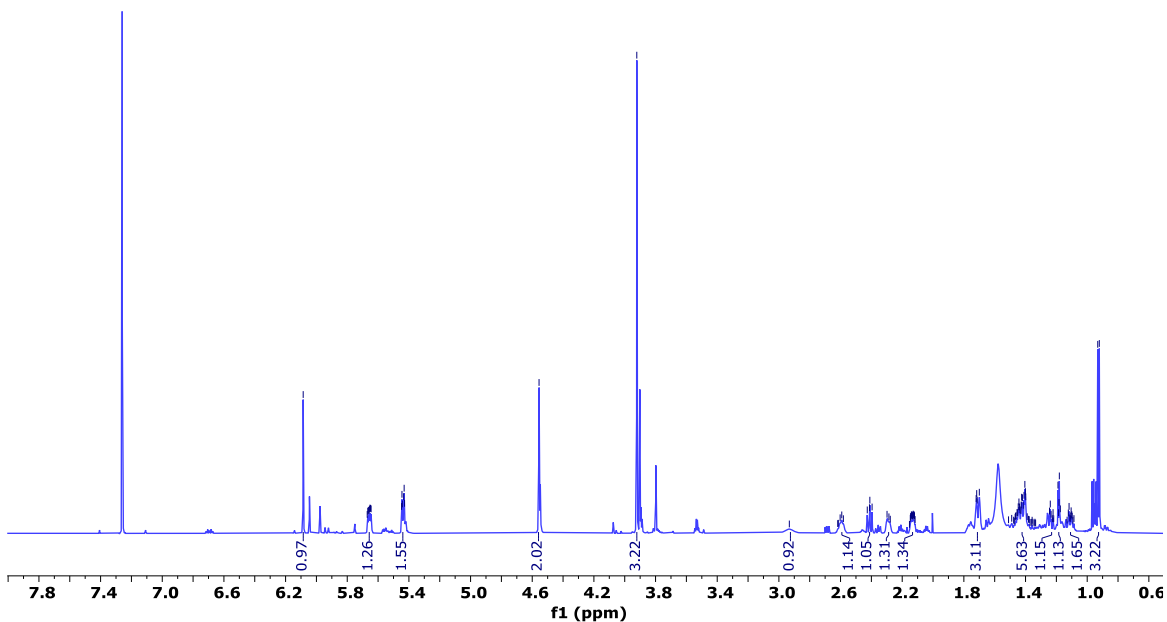


Figure S25. ^1H -NMR spectrum of solanapyrone B (**8**) (CDCl_3 , 700 MHz).

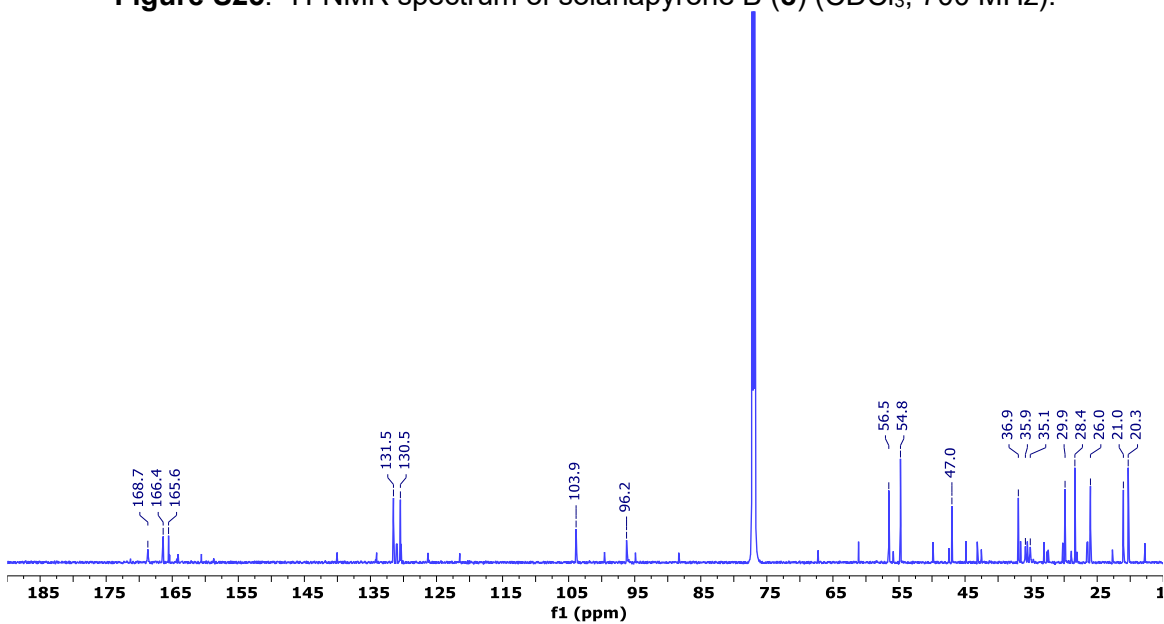
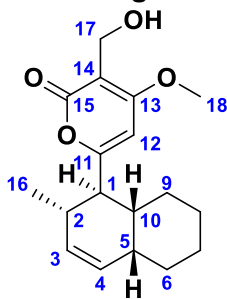


Figure S26. ^{13}C -NMR spectrum of solanapyrone B (**8**) (CDCl_3 , 175 MHz).



solanapyrone B (**8**): HR-ESI $^+$ m/z 305.1735 $[\text{M}+\text{H}]^+$ calculated for $\text{C}_{18}\text{H}_{25}\text{O}_4$ 305.1747, Δ -4.0 ppm and m/z 287.1631 $[\text{M}-\text{H}_2\text{O}]^+$ calculated for $\text{C}_{18}\text{H}_{23}\text{O}_3$ 287.1642, Δ -3.7 ppm.

^1H NMR (700 MHz, CDCl_3): δ_{H} 6.09 (s, 1H, H-12), 5.66 (ddd, J = 10.0, 5.1, 2.6 Hz, 1H, H-4), 5.44 (dt, J = 9.9, 1.8 Hz, 1H, H-3), 4.52 (s, 1H, H-17), 3.92 (s, 3H, H₃-18), 2.59 (m, 1H, H-2), 2.41 (dd, J = 11.8, 10.1 Hz, 1H, H-1), 2.29 (m, 1H, H-5), 2.13 (m, 1H, H-10), 1.71 (m overlapped, 2H, H-6b, H-7b), 1.42 (m overlapped, 3H, H-8b, H₂-9), 1.23 (dt, J = 12.1, 3.2 Hz, 1H, H-7a), 1.18 (dd, J = 6.2, 4.5 Hz, 1H, H-8a), 1.10 (m, 1H, H-6a), 0.93 (d, J = 7.0 Hz, 3H, H₃-16).

^{13}C NMR (175 MHz, CDCl_3): δ_{C} 168.7 (C-11), 166.4 (C-13), 165.6 (C-15), 131.5 (C-4), 130.5 (C-3), 103.9 (C-14), 96.2 (C-12), 56.5 (C-18), 54.8 (C-17), 47.0 (C-1), 36.9 (C-10), 35.9 (C-5), 35.1 (C-2), 29.9 (C-6), 28.4 (C-9), 26.0 (C-7), 21.0 (C-8), 20.3 (C-16).

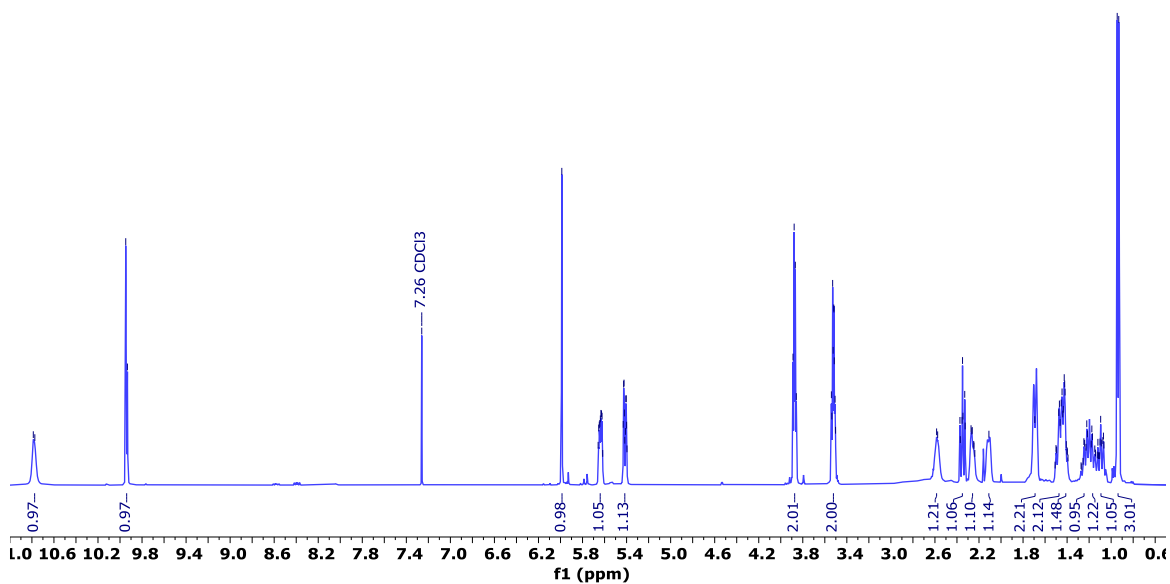


Figure S27. $^1\text{H-NMR}$ spectrum of solanapyrone C (**9**) (CDCl_3 , 500 MHz).

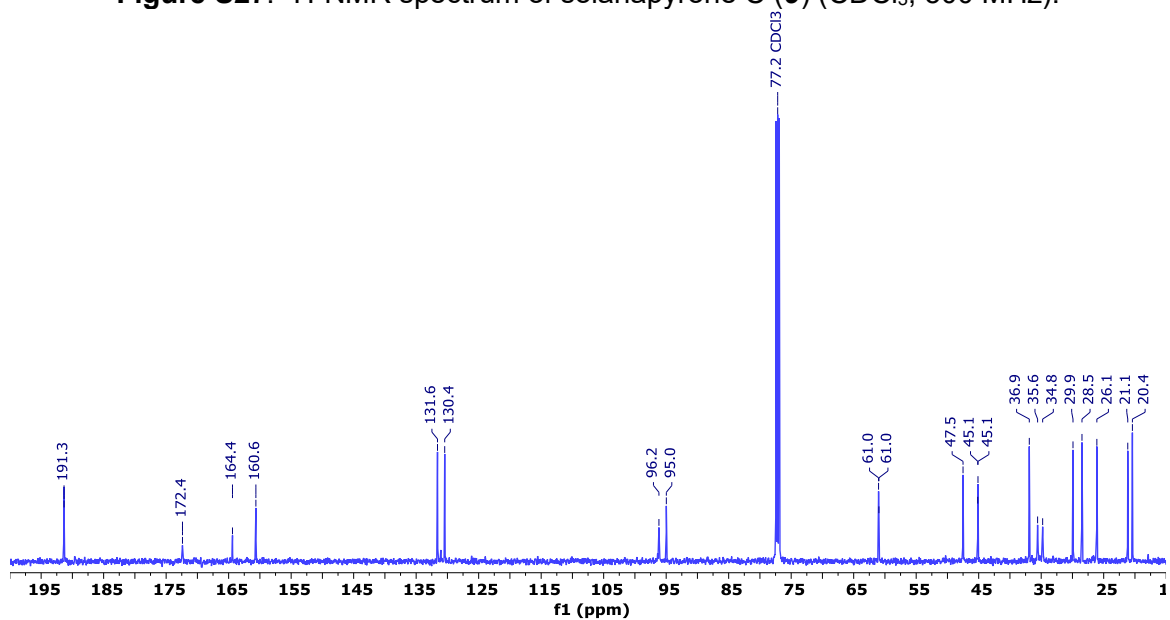
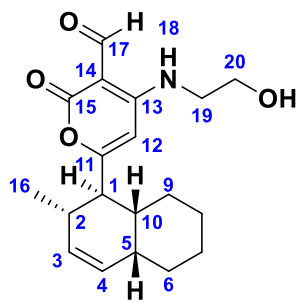


Figure S28. $^{13}\text{C-NMR}$ spectrum of solanapyrone C (**9**) (CDCl_3 , 125 MHz).



solanapyrone C (**9**): HR-ESI⁺ m/z 332.1842 [$\text{M}+\text{H}$]⁺ calculated for $\text{C}_{19}\text{H}_{26}\text{NO}_4$ 332.1856, Δ -4.3 ppm.

$^1\text{H NMR}$ (500 MHz, CDCl_3): δ_{H} 10.78 (s-broad, 1H, NH-18), 9.94 (s, 1H, H-17), 5.99 (s, 1H, H-12), 5.64 (ddt, J = 10.5, 5.5, 2.8 Hz, 1H, H-4), 5.41 (ddt, J = 9.9, 3.4, 1.8 Hz, 1H, H-3), 3.87 (q, J = 4.8 Hz, 2H, H₂-20), 3.52 (qd, J = 5.4, 2.8 Hz, 2H, H₂-19), 2.58 (m, 1H, H-2), 2.35 (ddd, J = 11.7, 9.8, 1.8 Hz, 1H, H-1), 2.26 (m, 1H, H-10), 2.11 (m, 1H, H-5), 1.69 (m overlapped, 2H, H-6b, H-7b), 1.47 (td, J = 15.0, 2.8 Hz, 2H, H-9a, H-9b), 1.42 (m, 1H, H-8b), 1.24 (dt, J = 12.9, 3.3 Hz, 1H, H-7a), 1.16 (dd, J = 13.5, 2.8 Hz, 1H, H-8b), 1.10 (tt, J = 11.8, 2.4 Hz, 1H, H-6a), 0.94 (d, J = 7.0 Hz, 3H, H₃-16).

$^{13}\text{C NMR}$ (125 MHz, CDCl_3): δ_{C} 191.3 (C-17), 172.4 (C-13), 164.4 (C-11), 160.6 (C-15), 131.6 (C-4), 130.4 (C-5), 96.2 (C-12), 95.0 (C-14), 61.0 (C-20), 47.5 (C-1), 45.1 (C-19), 36.9 (C-5), 35.6 (C-10), 34.8 (C-2), 29.9 (C-6), 28.5 (C-9), 26.1 (C-7), 21.1 (C-8), 20.4 (C-16).

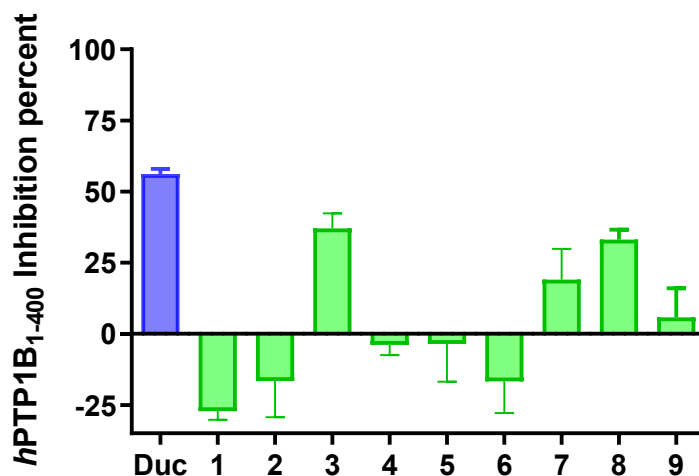


Figure S29. *hPTP1B₁₋₄₀₀* inhibition percentage for compounds 1–9. Duclauxin (Duc) was employed as a positive control at 20 μ M, compounds were tested at 100 μ M.

Table S1. Inhibitory activity against *Acinetobacter baumannii* strain A564 by some compounds of *Nigrospora* sp. IQ-064.

Compound	Growth inhibition (%)
Solanapyrone G (7)	15.98 \pm 5.12
Solanapyrone C (9)	31.61 \pm 1.71
Positive control Colistin in water at 20 ppm	99.95 \pm 0.22
Positive control Gentamicin in water at 64 ppm	29.80 \pm 2.79
Negative control	0

Compounds were evaluated at a concentration of 100 ppm in dimethyl sulfoxide. The average and standard deviation of at least 3 replicates are reported.

Table S2. ADME properties predicted for compounds **1-9**.

Compound	1	2	3	4	5	6	7	8	9
Physicochemical Properties									
Formula	C ₁₉ H ₂₇ NO ₆	C ₁₉ H ₂₅ NO ₅	C ₁₉ H ₂₅ NO ₄	C ₁₇ H ₂₁ NO ₄	C ₁₉ H ₂₅ NO ₅	C ₁₉ H ₂₅ NO ₅	C ₁₇ H ₂₁ NO ₃	C ₁₈ H ₂₄ O ₄	C ₁₉ H ₂₅ NO ₄
MW	365.42	347.41	331.41	303.35	347.41	347.41	287.35	304.38	331.41
#Heavy atoms	26	25	24	22	25	25	21	22	24
#Aromatic heavy atoms	6	6	0	6	6	6	6	6	6
Fraction Csp3	0.68	0.68	0.58	0.53	0.58	0.58	0.53	0.61	0.58
#Rotatable bonds	5	5	4	2	5	5	2	3	5
#H-bond acceptors	6	5	4	4	5	5	3	4	4
#H-bond donors	4	2	2	2	3	3	1	1	2
MR	96.77	93.42	91.13	84.27	95.14	95.14	83.1	85.93	93.97
TPSA	120	92.07	75.63	93.53	99.77	99.77	73.3	59.67	79.54
Lipophilicity									
iLOGP	1.86	2.29	3.03	1.5	2.15	1.93	1.89	3.09	2.33
XLOGP3	1.69	2.68	3.6	2.05	2.03	1.85	3.58	3.68	3.56
WLOGP	0.93	1.97	2.09	2.11	1.73	1.73	3.14	3.08	2.76
MLOGP	0.23	1.03	1.57	1.29	0.95	0.95	2.12	2.44	1.76
Silicos-IT Log P	1.57	2.81	2.2	1.83	2.06	2.06	2.74	3.19	2.95
Consensus Log P	1.26	2.16	2.5	1.76	1.78	1.7	2.69	3.1	2.67
Water Solubility									
ESOL Log S	-3.01	-3.53	-3.9	-3.08	-3.12	-3.01	-3.96	-4.05	-3.99
ESOL Solubility (mg/ml)	3.56e-01	1.03e-01	4.18e-02	2.51e-01	2.63e-01	3.42e-01	3.18e-02	2.72e-02	3.37e-02
ESOL Solubility (mol/l)	9.75e-04	2.95e-04	1.26e-04	8.28e-04	7.58e-04	9.84e-04	1.11e-04	8.93e-05	1.02e-04
ESOL Class	Soluble	Soluble	Soluble	Soluble	Soluble	Soluble	Soluble	Moderately soluble	Soluble
Ali Log S	-3.82	-4.27	-4.88	-3.64	-3.75	-3.57	-4.81	-4.62	-4.92
Ali Solubility (mg/ml)	5.47e-02	1.88e-02	4.42e-03	6.91e-02	6.14e-02	9.43e-02	4.50e-03	7.25e-03	4.02e-03
Ali Solubility (mol/l)	1.50e-04	5.42e-05	1.33e-05	2.28e-04	1.77e-04	2.72e-04	1.57e-05	2.38e-05	1.21e-05
Ali Class	Soluble	Moderately soluble	Moderately soluble	Soluble	Soluble	Soluble	Moderately soluble	Moderately soluble	Moderately soluble
Silicos-IT LogSw	-2.75	-3.65	-2.6	-2.48	-3.1	-3.1	-3.29	-3.65	-3.92
Silicos-IT Solubility (mg/ml)	6.48e-01	7.85e-02	8.34e-01	1.00e+00	2.76e-01	2.76e-01	1.46e-01	6.77e-02	4.02e-02

Compound	1	2	3	4	5	6	7	8	9
Water Solubility									
Silicos-IT Solubility (mol/l)	1.77e-03	2.26e-04	2.52e-03	3.30e-03	7.94e-04	7.94e-04	5.09e-04	2.22e-04	1.21e-04
Silicos-IT class	Soluble	Soluble	Soluble	Soluble	Soluble	Soluble	Soluble	Soluble	Soluble
Pharmacokinetics									
GI absorption	High	High	High	High	High	High	High	High	High
BBB permeant	No	No	Yes	No	No	No	Yes	Yes	No
Pgp substrate	Yes	Yes	No	Yes	Yes	Yes	No	No	Yes
CYP1A2 inhibitor	No	No	No	No	No	No	No	No	No
CYP2C19 inhibitor	No	No	No	No	No	No	No	No	No
CYP2C9 inhibitor	No	No	Yes	No	No	No	No	No	No
CYP2D6 inhibitor	No	Yes	No	No	No	No	No	Yes	No
CYP3A4 inhibitor	No	No	No	No	No	No	No	No	Yes
log Kp (cm/s)	-7.33	-6.52	-5.77	-6.69	-6.98	-7.11	-5.51	-5.54	-5.79
Druglikeness									
Lipinski #violations	0	0	0	0	0	0	0	0	0
Ghose #violations	0	0	0	0	0	0	0	0	0
Veber #violations	0	0	0	0	0	0	0	0	0
Egan #violations	0	0	0	0	0	0	0	0	0
Muegge #violations	0	0	0	0	0	0	0	0	0
Bioavailability Score	0.55	0.55	0.56	0.55	0.55	0.55	0.55	0.55	0.55
Medicinal Chemistry									
PAINS #alerts	0	0	0	0	0	0	0	0	0
Brenk #alerts	1	2	3	2	2	2	2	1	2
Leadlikeness #violations	1	0	1	0	0	0	1	1	1
Synthetic Accessibility	5.09	4.96	5.21	4.75	4.99	4.96	4.63	4.79	4.83

Table S3. PASS analysis for compounds **1–9**. The predicted probabilities of activity (Pa) and inactivity (Pi) are shown for each compound. Only activities with Pa values $\geq 0,700$ were considered for this analysis.

Compound	CDP-glycerol glycerophosphotransferase inhibitor		Phosphatase inhibitor		CYP3A1 substrate		CYP2C11 substrate		Caspase 3 stimulant		Antiparasitic		Respiratory analeptic		Antieczematic	
	Pa	Pi	Pa	Pi	Pa	Pi	Pa	Pi	Pa	Pi	Pa	Pi	Pa	Pi	Pa	Pi
1	0,779	0,035	0,703	0,012												
2	0,739	0,007	0,719	0,049												
3																
4	0,800	0,030	0,728	0,008	0,701	0,009	0,701	0,007	0,769	0,007			0,736	0,012		
5	0,763	0,038	0,706	0,012												
6	0,763	0,038	0,700	0,013	0,717	0,023					0,708	0,005				
7	0,771	0,036	0,713	0,010			0,737	0,006								
8					0,703	0,009			0,744	0,009					0,703	0,045
9	0,729	0,046									0,725	0,005				