The fungal natural product class of the sorbicillinoids: structures, bioactivities, biosynthesis, and synthesis

Tobias M. Milzarek,*[a] and Tobias A. M. Gulder*[ab]

[a] Helmholtz Institute for Pharmaceutical Research Saarland (HIPS), Department of Natural Product Biotechnology, Helmholtz Centre for Infection Research (HZI) and Department of Pharmacy at Saarland University, 66123 Saarbrücken, Germany.
E-Mail: tobias.milzarek@helmholtz-hips.de
[b] Chair of Technical Biochemistry, Technische Universität Dresden, Bergstraße 66, 01069 Dresden, Germany.
E-mail: tobias.gulder@tu-dresden.de

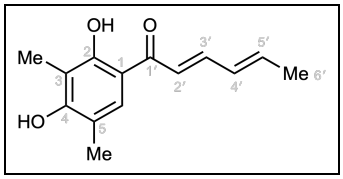
Supporting Information

1 Fact sheets

1.1 Monomeric sorbicillinoids

1.1.1 Sorbicillin(ol) analogues

Sorbicillin (1a) [(2*E*,4*E*)-1-(2,4-Dihydroxy-3,5-dimethylphenyl)hexa-2,4-dien-1-one, CAS: 79950-85-9]



SMILES: OC1=C(C(/C=C/C=C/C)=O)C=C(C)C(O)=C1C

Fungus of origin: *Acremonium* sp. AN-13[1], *Clonostachys rosea* YRS-06[2], *Emericella* sp. IFM57991[3], *Hypocrea jecorina* H8[4], *Penicillium allii-sativi* MCCC 3A00580[5], *Penicillium chrysogenum* E01-10/3[6,7], *Penicillium chrysogenum* sp.[8], *Penicillium notatum*[9,10], *Penicillium* sp. P-1[11], *Trichoderma citrinoviride* A12[12], *Trichoderma longibrachiatum* UAMH 4159[13], *Trichoderma reesei* Z56-8[14], *Trichoderma* sp.[15], *Trichoderma* sp. f-13[16], *Trichoderma* sp. PR-35[17], *Trichoderma* sp. USF-2690[18], *Trichothecium* sp.[19], *Verticillium intertextum*[20,21].

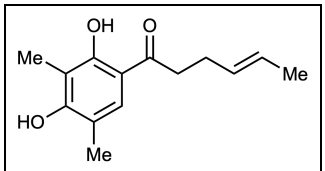
Bioactivity: Cytotoxicity against leukemic HL-60 cell line (IC_{50} = 11.0-12.7 µM)[16,19], cervical cancer cells HeLa (IC_{50} = 1.60 µM)[11], human liver cancer cells HepG2 (IC_{50} = 27.2 µM)[11], lymphomic U937 cells (IC_{50} = 11.4 µM)[19], human breast cancer cell line T47D IC_{50} = 28.6 µM)[19]. DPPH-radical scavenging activity (ED_{50} = 152 µM).[18] Antibacterial against *Staphylococcus aureus* ATCC 6538 (MIC= 128 µg/mL).[1]

Biosynthesis: See figure S1A,B.[7,20–23]

Total synthesis: See Fig. S8A-D. Sorbicillin (**1a**) can be synthesized in three steps (*ortho*-formylation, reduction, Friedel-Crafts acylation with sorbyl chloride) starting from 2-methylresorcinol [CAS: 608-25-3].[24–26]

Analytics: Yellow crystals. **MP**: 123–125 °C .[1]**H-NMR** ($CDCl_3$): δ = 13.61 (s, 1H, O*H*), 7.46 (ddd, *J* = 15.4, 11.0, 2.0 Hz, 1H, CH_{sorbyl}), 7.45 (s, 1H, Ar*H*), 6.94 (d, *J* = 15.4 Hz, 1H, CH_{sorbyl}), 6.43 (ddd, *J* = 15.4, 11.0, 1.0 Hz, 1H, CH_{sorbyl}), 6.26 (qdd, *J* = 15.4, 6.5, 2.0 Hz, 1H, CH_{sorbyl}), 5.45 (s, 1H, O*H*), 2.23 (s, 3H, ArCH_3), 2.16 (s, 3H, ArCH_3), 1.90 (d, *J* = 6.5 Hz, 3H, CH_3). [13]**C-NMR** (DMSO-d_6): δ = 191.5, 166.6, 161.9, 143.6, 140.5, 130.4, 128.7, 122.2, 115.8, 112.2, 110.5, 18.6, 16.2, 8.2.[24]

2′,3′-Dihydrosorbicillin (1b) [(*E*)-1-(2,4-Dihydroxy-3,5-dimethylphenyl)hex-4-en-1-one, CAS: 79950-82-6]



2′,3′-Dihydrosorbicillin (**1b**)

SMILES: OC1=C(C(CC/C=C/C)=O)C=C(C)C(O)=C1C

Fungus of origin: *Hypocrea jecorina* H8[4], *Penicillium allii-sativi* MCCC 3A00580[5], *Penicillium chrysogenum* E01-10/3[7], *Penicillium chrysogenum* R03-8/4[27], *Penicillium notatum*[28], *Penicillium* sp. DM815[29], *Penicillium* sp. P-1[11], *Trichoderma citrinoviride* A12[12], *Trichoderma reesei* Z56-8[14], *Trichoderma* sp.[15], *Trichoderma* sp. f-13[16], *Verticillium intertextum*[20,21].

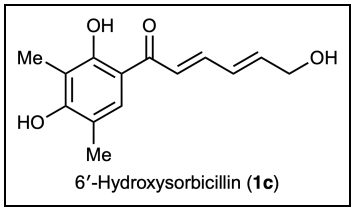
Bioactivity: Cytotoxicity against leukemic HL-60 cell line (IC_{50} > 50.0 µM)[16], cervical cancer cells HeLa (IC_{50} = 7.4 µM)[11], human liver cancer cells HepG2 (IC_{50} = 44.4 µM)[11], human breast cancer cell line MCF-7 (IC_{50} = 21.9 µg/mL)[15], human colon cancer cell line Lovo (IC_{50} = 11.1 µg/mL)[15], human hepatic cancer cell line Bel-7402 (IC_{50} = 9.2 µg/mL)[15], human lung cancer cell line A549 (IC_{50} = 13.1 µg/mL)[15], human nasopharyngeal carcinoma cell line CNE1 (IC_{50} = 18.9 µg/mL)[15], human nasopharyngeal carcinoma cell line CNE2 (IC_{50} = 13.4 µg/mL)[15], human nasopharyngeal carcinoma cell line KB (IC_{50} = 12.0 µg/mL)[15], human nasopharyngeal carcinoma cell line SUNE1 (IC_{50} = 10.2 µg/mL)[15]. Antibacterial against *Staphylococcus aureus* and *Bacillus subtilis* (weak).[28]

Biosynthesis: See figure S1A,B.

Total synthesis: 2′,3′-Dihydrosorbicillin (**1b**) can be synthesized similar to sorbicillin (**1a**) by using the reduced sorbyl chloride for the Friedel-Crafts acylation.

Analytics: Colorless needles. **MP**: 68–70 °C. [1]**H-NMR** (200 MHz, $CDCl_3$): δ = 12.97 (s, 1H, O*H*), 7.40 (s, 1H, Ar*H*), 5.70-5.40 (m, 2H, C*H*), 5.24 (s, 1H, O*H*), 2.97 (t, 2H, CH_2), 2.50-2.30 (m, 2H, CH_2), 2.21 (s, 3H, ArCH_3), 2.14 (s, 3H, ArCH_3), 1.66 (d, *J* = 7.5 Hz, 3H, CH_3). [13]**C-NMR** (25.1 MHz, $CDCl_3$): δ = 204.3, 161.5, 158.6, 129.2, 128.8, 125.9, 114.5, 112.5, 110.1, 37.5, 27.2, 18.7, 15.5, 7.2.[21]

6′-Hydroxysorbicillin (1c) [((2*E*,4*E*)-1-(2,4-Dihydroxy-3,5-dimethylphenyl)-6-hydroxyhexa-2,4-dien-1-one, CAS: 2351133-37-2]



6′-Hydroxysorbicillin (**1c**)

SMILES: OC1=C(C(/C=C/C=C/CO)=O)C=C(C)C(O)=C1C

Fungus of origin: *Hypocrea jecorina* H8[4], *Trichoderma reesei 4670*[30].

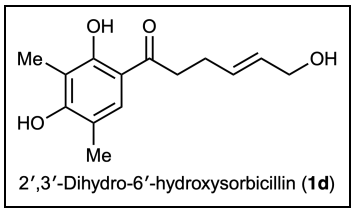
Bioactivity: Anti-inflammatory activity due to inhibition of nitric oxide formation in LPS-induced RAW264.7 cells ($IC_{50} > 6.8$ µM).[30]

Biosynthesis: See figure S1A,B.

Total synthesis: Hydroxysorbicillin (**1c**) can be synthesized from sorbicillin (**1a**) using olefin metathesis. A combination of allyl alcohol and Hoveyda-Grubbs catalyst (2nd generation) or Grubbs catalyst (2nd generation) allows the formation up to 40%.[31]

Analytics: Yellow powder. ^{1}**H-NMR** (400 MHz, CD_3OD): δ = 7.56 (s, 1H, Ar*H*), 7.45 (dd, *J* = 14.8, 11.2 Hz, 1H, C*H*$_{sorbyl}$), 7.22 (d, *J* = 14.8 Hz, 1H, C*H*$_{sorbyl}$), 6.62 (m, 1H, C*H*$_{sorbyl}$), 6.35 (dt, *J* = 15.2, 4.8 Hz, 1H, C*H*$_{sorbyl}$), 4.23 (d, *J* = 4.4 Hz, 2H, C*H*$_2$OH), 2.17 (s, 3H, ArC*H*$_3$), 2.06 (s, 3H, ArC*H*$_3$). ^{13}**C-NMR** (100 MHz, CD_3OD): δ = 193.7, 163.7, 162.3, 144.3 (2C), 130.1, 129.3, 125.2, 117.3, 113.9, 112.0, 62.9, 16.4, 8.0. **IR**: *ν* 3375, 2921, 2857, 1706, 1618, 1561, 1483, 1420, 1368, 1286, 1221, 1145, 1074, 992, 860, 765 cm^{-1}. **HRMS** (ESI/LTQ) *m/z*: $[M-H]^-$ calcd for $C_{14}H_{15}O_4$ 247.0976, found 247.0977.[30]

2′,3′-Dihydro-6′-hydroxysorbicillin (1d) [(*E*)-1-(2,4-Dihydroxy-3,5-dimethylphenyl)-6-hydroxyhex-4-en-1-one, CAS: 2365301-46-6]



2′,3′-Dihydro-6′-hydroxysorbicillin (**1d**)

SMILES: OC1=C(C(CC/C=C/CO)=O)C=C(C)C(O)=C1C

Fungus of origin: *Trichoderma reesei 4670*[30].

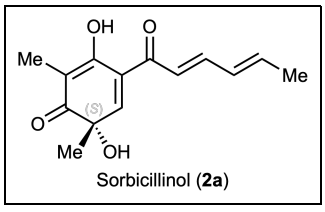
Bioactivity: Anti-inflammatory activity due to inhibition of nitric oxide formation in LPS-induced RAW264.7 cells ($IC_{50} > 2.9$ µM).[30]

Biosynthesis: See figure S1A,B.

Total synthesis: A possible total synthesis would be based on the formation of 6′-hydroxysorbicillin (**1c**) using dehydrosorbicillin (**1b**) instead of sorbicillin (**1a**) in the Grubbs metathesis.[31]

Analytics: White powder. ^{1}**H-NMR** (400 MHz, CD_3OD): δ = 7.39 (s, 1H, Ar*H*), 5.78 (m, 1H, C*H*), 5.68 (m, 1H, C*H*), 4.02 (d, *J* = 5.6 Hz, 2H, C*H*$_2$OH), 3.04 (t, *J* = 7.2 Hz, 2H, C*H*$_2$), 2.45 (dd, *J* = 13.6, 6.8 Hz, 2H, C*H*$_2$), 2.19 (s, 3H, ArC*H*$_3$), 2.08 (s, 3H, ArC*H*$_3$). ^{13}**C-NMR** (100 MHz, CD_3OD): δ = 205.5, 162.5, 162.0, 131.7, 131.3, 130.3, 117.2, 113.4, 111.9, 63.6, 38.2, 28.4, 16.4, 8.0. **IR**: *ν* 3421, 3153, 2947, 1593, 1506, 1352, 1265, 1149, 1028, 962, 845, 762 cm^{-1}. **HRMS** (ESI/LTQ) *m/z*: $[M-H]^-$ calcd for $C_{14}H_{17}O_4$ 249.1132, found 249.1136.[30]

Sorbicillinol (2a) [(*S*)-4-((2*E*,4*E*)-Hexa-2,4-dienoyl)-3,6-dihydroxy-2,6-dimethylcyclohexa-2,4-dien-1-one, CAS: 251091-31-3]



Sorbicillinol (**2a**)

SMILES: OC1=C(C)C([C@](O)(C)C=C1C(/C=C/C=C/C)=O)=O

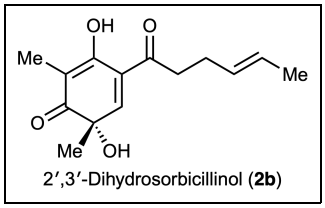
Fungus of origin: *Penicillium chrysogenum* E01-10/3[6], *Penicillium chrysogenum* sp.[8], *Penicillium notatum*[28], *Trichoderma longibrachiatum* UAMH 4159[32], *Trichoderma* sp. USF-2690[33].

Biosynthesis: See figure S1A,B.[7,23]

Total synthesis: The racemic version of sorbicillinol (*O*-acetyl protected) can be obtained by treating sorbicillin (**1a**) with lead tetraacetate.[25,33–35] The first enantioselective routes were described by the research groups of Pettus[36] using and chiral tether combined with hypervalent iodine chemistry (51% *ee*) and Deng[37] using an enantioselective cyanosilylation (92% *ee*). Both approaches deliver protected sorbicillinol synthons.[26] The first chemo-enzymatic approach using the monooxygenase SorbC was reported by Cox and co-workers.[7]

Analytics: Due to the high reactivity of sorbicillinol (**2a**) towards dimerization ([4+2], Michael addition) it can only be isolated with an *O*-protecting group (preferably *O*-acetyl).[7,25,34] In the following, the analytical data of *O*-acetyl sorbicillinol displayed. **MP**: 149-150 °C. **TLC**: R_f = 0.41 (DCM/acetone = 9:1). **ORD**: $[\alpha]_D^{20} = -80.0$ (c = 0.1, MeOH). ^{1}**H-NMR** (500 MHz, $CDCl_3$): δ = 11.90 (s, 1H, O*H*), 7.46 (dd, *J* = 14.8, 10.8 Hz, 1H, C*H*$_{sorbyl}$), 7.25 (s, 1H, C*H*), 6.66 (d, *J* = 14.8 Hz, 1H, C*H*$_{sorbyl}$), 6.38 (m, 1H, C*H*$_{sorbyl}$), 6.31 (m, 1H, C*H*$_{sorbyl}$), 2.15 (s, 3H, C*H*$_3$), 1.93 (d, *J* = 6.6 Hz, 3H, C*H*$_3$), 1.86 (s, 3H, C*H*$_3$), 1.49 (s, 3H, C*H*$_3$). ^{13}**C-NMR** (125 MHz, $CDCl_3$): δ = 195.4, 193.7, 170.4, 162.9, 152.3, 148.7, 145.3, 130.5, 125.9, 120.6, 112.1, 78.6, 24.5, 21.0, 19.6, 7.6. **HRMS** (MALDI) *m/z*: $[M+Na]^+$ calcd for $C_{16}H_{18}O_5Na$ 313.1052, found 313.1055.[33,34]

2′,3′-Dihydrosorbicillinol (2b) [(*S*,*E*)-4-(Hex-4-enoyl)-3,6-dihydroxy-2,6-dimethylcyclohexa-2,4-dien-1-one, CAS: 2414589-70-9]



2′,3′-Dihydrosorbicillinol (**2b**)

SMILES: OC1=C(C)C([C@](O)(C)C=C1C(CC/C=C/C)=O)=O

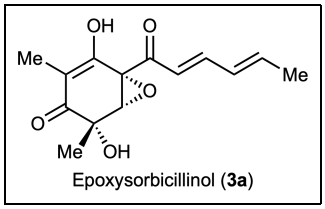
Fungus of origin: *Penicillium chrysogenum* E01-10/3[7], *Penicillium chrysogenum* sp.[8].

Biosynthesis: See figure S1A,B.[7]

Total synthesis: 2′,3′-Dihydrosorbicillinol (**2b**) can be synthesized similar to sorbicillinol (**2a**) by starting with the more saturated sorbyl side chain. The first chemo-enzymatic formation was described by Cox and co-workers.[7]

Analytics: Due to the high reactivity of 2′,3′-dihydrossorbicillinol (**2b**) towards dimerization ([4+2], Michael addition) it can only be isolated with an *O*-protecting group (preferably *O*-acetyl).[7,38,39]

Epoxysorbicillinol (3a) [(1*R*,2*S*,6*R*)-6-((2*E*,4*E*)-Hexa-2,4-dienoyl)-2,5-dihydroxy-2,4-dimethyl-7-oxabicyclo[4.1.0]hept-4-en-3-one, CAS: 219954-66-2, 331961-51-4]



Epoxysorbicillinol (**3a**)

SMILES: OC1=C(C)C([C@](O)(C)[C@@H](O2)[C@]12C(/C=C/C=C/C)=O)=O

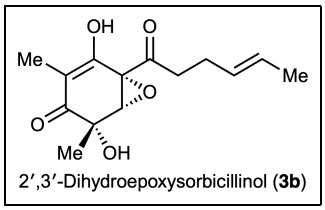
Fungus of origin: *Trichoderma longibrachiatum*[40], *Trichoderma* sp.[41].

Biosynthesis: See figure S1A,B.[40]

Total synthesis: See figure S9. Epoxysorbicillinol (**3a**) can be synthesized from sorbicillinol (**2a**) using *tert*-butyl hydroperoxide [CAS: 75-91-2] in aqueous solution (25% yield).[42] The racemic analogue was synthesized previously by Wood and co-workers.[43] Based on commercially available diethyl methylmalonate [CAS: 609-08-5], *rac*-epoxysorbicillinol (**3a**) was synthesized in 13 steps having a novel 1,3-dipolar cycloaddition between α-diazo ketone and a propiolate ester as a key reaction.

Analytics: Yellow amorphous powder. **TLC**: R_f = 0.16 (DCM/MeOH = 7:1). ^{1}**H-NMR** (400 MHz, $CDCl_3$): δ = 10.16 (s, 1H, O*H*), 7.58 (m, 1H, CH_{sorbyl}), 6.45 (m, 1H, CH_{sorbyl}), 6.30 (m, 2H, CH_{sorbyl}), 3.98 (s, 1H, O*H*), 1.95 (d, *J* = 6.8 Hz, 3H, CH_3), 1.83 (s, 3H, CH_3), 1.35 (s, 3H, CH_3). ^{1}**H-NMR** (400 MHz, CD_3OD): δ = 7.29 (m, 1H, C*H*), 6.66-6.27 (m, 3H, C*H*), 3.56 (s, 1H, C*H*), 1.86 (d, *J* = 5.9 Hz, 3H, CH_3), 1.64 (s, 3H, CH_3), 1.46 (s, 3H, CH_3). ^{13}**C-NMR** (101 MHz, CD_3OD): δ = 194.7, 189.0, 173.0, 147.4, 144.5, 131.7, 124.7, 107.8, 70.6, 64.0, 62.9, 26.3, 19.2, 8.1. **IR**: *ν* 3420, 3009, 1675, 1390, 800 cm^{-1}. **HRMS** (CI) *m/z*: $[M+H]^+$ calcd for $C_{14}H_{16}O_5$ 265.0998, found 265.1007.[36,40]

2′,3′-Dihydroepoxysorbicillinol (3b) [(1*R*,2*S*,6*R*)-6-((*E*)-Hex-4-enoyl)-2,5-dihydroxy-2,4-dimethyl-7-oxabicyclo[4.1.0]hept-4-en-3-one]



2′,3′-Dihydroepoxysorbicillinol (**3b**)

SMILES: OC1=C(C)C([C@](O)(C)[C@@H](O2)[C@]12C(CC/C=C/C)=O)=O

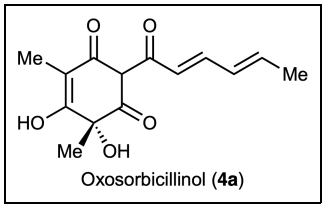
Fungus of origin: *Trichoderma longibrachiatum* SFC100166[44].

Bioactivity: Antifungal activity against *Phytophthora infestans* (IC_{50} = 400 μg/mL)[44].

Biosynthesis: See figure S1A,B.

Analytics: Viscous yellow oil. ^{1}**H-NMR** (400 MHz, CD_3OD): δ = 5.48 (p, *J* = 6.0 Hz, 2H, C*H*), 2.67 (m, 2H, CH_2), 2.28 (m, 2H, CH_2), 1.69 (s, 3H, CH_3), 1.65 (d, *J* = 5.4 Hz, 3H, CH_3), 1.48 (s, 3H, CH_3).[44]

Oxosorbicillinol (4a) [(6*R*)-2-((2*E*,4*E*)-Hexa-2,4-dienoyl)-5,6-dihydroxy-4,6-dimethylcyclohex-4-ene-1,3-dione, CAS: 271795-00-7]



Oxosorbicillinol (**4a**)

SMILES: O=C(C(C)=C(O)[C@]1(O)C)C(C(/C=C/C=C/C)=O)C1=O

Fungus of origin: *Penicillium chrysogenum* E01-10/3[6], *Penicillium chrysogenum* sp.[8], *Penicillium notatum*[28], *Penicillium* sp. 06T121[45], *Penicillium* sp. NX-S-6[46], *Trichoderma* sp. USF-2690[33,47].

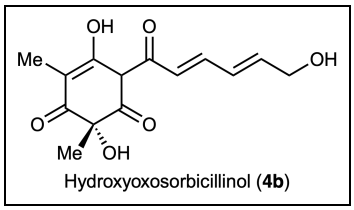
Bioactivity: Antibacterial against *Staphylococcus aureus* and *Bacillus subtilis* (weak).[28] Inhibitory effect on soybean lipoxygenase ($IC_{50} > 150$ µM).[45] DPPH-radical scavenging activity ($ED_{50} = 87.7$ µM).[47]

Biosynthesis: See figure S1A,B.[48]

Total synthesis: Oxosorbicillinol (**4a**) can be synthesized chemo-enzymatically using the monooxygenase SorbC and 6-hydroxysorbicillin (21% yield).[42]

Analytics: Yellowish, amorphous powder. **MP**: 126–132 °C. **ORD**: $[\alpha]_D^{20} = -40.7$ (c = 1.0, MeOH). ^{1}**H-NMR** (400 MHz, acetone-d_6): δ = 18.90 (s, 1H, O*H*), 7.50 (dd, *J* = 15.4, 9.5 Hz, 1H, CH_{sorbyl}), 7.38 (d, *J* = 14.7 Hz, 1H, CH_{sorbyl}), 6.42 (dd, *J* = 15.4, 5.9 Hz, 1H, CH_{sorbyl}), 6.35 (dd, *J* = 15.4, 9.5 Hz, 1H, CH_{sorbyl}), 1.90 (d, *J* = 5.8 Hz, 3H, CH_3), 1.82 (s, 3H, CH_3), 1.53 (s, 3H, CH_3). ^{1}**H-NMR** (400 MHz, $CDCl_3$): δ = 18.55 (s, 1H, O*H*), 7.54 (dd, *J* = 15.2, 10.6 Hz, 1H, CH_{sorbyl}), 7.29 (d, *J* = 15.2 Hz, 1H, CH_{sorbyl}), 6.36 (dd, *J* = 15.6, 10.6 Hz, 1H, CH_{sorbyl}), 6.27 (dq, *J* = 15.6, 6.4 Hz, 1H, CH_{sorbyl}), 1.91 (d, *J* = 6.4 Hz, 3H, CH_3), 1.86 (s, 3H, CH_3), 1.58 (s, 3H, CH_3). ^{13}**C-NMR** (100 MHz, acetone-d_6): δ = 196.8, 192.8, 185.2, 171.5, 145.4, 141.8, 132.0, 124.2, 105.7, 105.4, 76.0, 30.0, 18.9, 7.3. ^{13}**C-NMR** (100 MHz, $CDCl_3$): δ = 196.3, 192.2, 184.5, 167.4, 145.8, 141.7, 131.2, 122.5, 106.3, 104.5, 75.3, 30.4, 18.9, 7.1. **IR**: *ν* 3501, 3171, 1740, 1606 cm^{-1}. **HRMS** (FAB) *m/z*: $[M+H]^+$ calcd for $C_{14}H_{17}O_5$ 265.1076, found 265.1073.[45,47]

Hydroxyoxosorbicillinol (4b) [(6*R*)-5,6-Dihydroxy-2-((2*E*,4*E*)-6-hydroxyhexa-2,4-dienoyl)-4,6-dimethylcyclohex-4-ene-1,3-dione, CAS: 1426818-05-4]



Hydroxyoxosorbicillinol (**4b**)

SMILES: OC1=C(C)C([C@](O)(C)C(C1C(/C=C/C=C/CO)=O)=O)=O

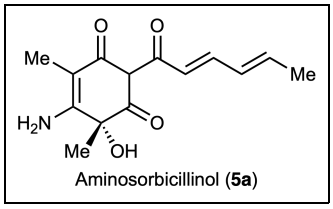
Fungus of origin: *Penicillium* sp. 06T121[45].

Bioactivity: Inhibitory effect on soybean lipoxygenase ($IC_{50} > 16$ µM). Release suppression activity of rostaglandin D_2 ($IC_{50} > 10$ µM) and leucotriene B_4 ($IC_{50} > 100$ µM).[45]

Biosynthesis: See figure S1A,B.

Analytics: Yellowish, amorphous powder. **MP**: 116–120 °C. **ORD**: $[\alpha]_D^{20} = -5.5$ (c = 1.0, MeOH). ^{1}**H-NMR** (400 MHz, acetone-d_6): δ = 18.93 (s, 1H, O*H*), 7.55 (dt, *J* = 15.4, 4.4 Hz, 1H, CH_{sorbyl}), 7.46 (d, *J* = 15.4 Hz, 1H, CH_{sorbyl}), 6.62 (ddt, *J* = 15.4, 11.0, 2.2 Hz, 1H, CH_{sorbyl}), 6.44 (dd, *J* = 15.4, 11.0 Hz, 1H, CH_{sorbyl}), 4.28 (dd, *J* = 4.4, 2.2 Hz, 1H, CH_2OH), 1.82 (s, 3H, CH_3), 1.54 (s, 3H, CH_3). ^{13}**C-NMR** (100 MHz, acetone-d_6): δ = 196.0, 191.9, 184.2, 171.0, 145.0, 143.8, 127.7, 124.6, 104.9, 103.7, 75.2, 61.7, 28.7, 6.4. **IR**: *ν* 3474, 3164, 1670, 1609, 1523 cm^{-1}. **HRMS** (FAB) *m/z*: $[M+H]^+$ calcd for $C_{14}H_{17}O_6$ 281.1025, found 281.1024.[45]

Aminosorbicillinol (5a) [(6*R*)-A-amino-2-((2*E*,4*E*)-hexa-2,4-dienoyl)-6-hydroxy-4,6-dimethylcyclohex-4-ene-1,3-dione]



Aminosorbicillinol (**5a**)

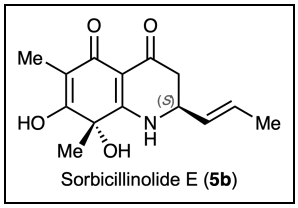
SMILES: O=C(C(C)=C(N)[C@]1(O)C)C(C(/C=C/C=C/C)=O)C1=O

Fungus of origin: *Penicillium* sp. NX-S-6[46].

Biosynthesis: See figure S1A,B.

Analytics: Yellowish powder. **ORD**: $[\alpha]_D^{25} = +8.0$ (c = 0.1, MeOH). ^{1}**H-NMR** (500 MHz, DMSO-d_6): δ = 7.48 (dd, *J* = 15.1, 11.0 Hz, 1H, CH_{sorbyl}), 7.34 (d, *J* = 15.1 Hz, 1H, CH_{sorbyl}), 6.35 (dd, *J* = 15.1, 11.0 Hz, 1H, CH_{sorbyl}), 6.21 (dq, *J* = 14.6, 6.7 Hz, 1H, CH_{sorbyl}), 1.89 (d, *J* = 6.7 Hz, 3H, CH_3), 1.80 (s, 3H, CH_3), 1.58 (s, 3H, CH_3). ^{13}**C-NMR** (125 MHz, DMSO-d_6): δ = 196.5, 187.9, 185.1, 163.5, 144.1, 140.4, 131.2, 123.8, 103.4, 97.3, 75.0, 32.8, 18.9, 7.6. **IR**: *ν* 3338, 3193, 2930, 1697, 1642, 1526, 1435 cm^{-1}. **HRMS** (ESI) *m/z*: $[M+H]^+$ calcd for $C_{14}H_{18}NO_4$ 264.1236, found 264.1231.[46]

Sorbicillinolide E (5b)



Sorbicillinolide E (**5b**)

SMILES: O=C1C(C2=O)=C(N[C@H](/C=C/C)C2)[C@@](O)(C)C(O)=C1C

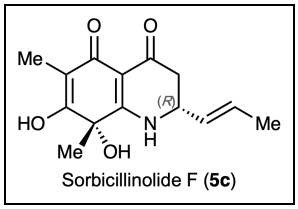
Fungus of origin: *Penicillium rubens* F54.[49]

Bioactivity: Anti-inflammatory activity due to inhibition of nitric oxide (41.9%) and prostaglandin E2 (PGE2, 54.1%) formation.[49]

Biosynthesis: See figure S1C.

Analytics: Yellow oil. **ORD**: $[\alpha]_D$ = +128.0 (c = 0.1, MeOH). ^{1}**H-NMR** (400 MHz, DMSO-d_6): δ = 13.46 (s, 1H, O*H*), 9.41 (s, 1H, N*H*), 5.72 (qd, *J* = 15.3, 6.3 Hz, 1H, C*H*), 5.62 (dd, *J* = 15.3, 6.5 Hz, 1H, C*H*), 4.50 (s, 1H, O*H*), 4.32 (ddd, *J* = 6.5, 4.6, 2.0 Hz, 1H, C*H*), 2.59 (dd, *J* = 14.0, 4.6 Hz, 1H, CH_2), 2.56 (dd, *J* = 14.0, 2.0 Hz, 1H, CH_2), 1.68 (d, *J* = 6.3 Hz, 3H, CH_3), 1.60 (s, 3H, CH_3), 1.40 (s, 3H, CH_3). ^{13}**C-NMR** (100 MHz, DMSO-d_6): δ = 194.5, 192.2, 173.8, 168.7, 128.9, 128.4, 97.6, 94.5, 74.3, 53.0, 39.4, 32.2, 18.0, 7.1. **IR**: *ν* 3421, 1613, 1576, 1520, 1440 cm^{-1}. **HRMS** (ESI) *m/z*: $[M-H]^-$ calcd for $C_{14}H_{16}NO_4$ 262.1079, found 262.1077.[49]

Sorbicillinolide F (5c)



Sorbicillinolide F (**5c**)

SMILES: O=C1C(C2=O)=C(N[C@@H](/C=C/C)C2)[C@@](O)(C)C(O)=C1C

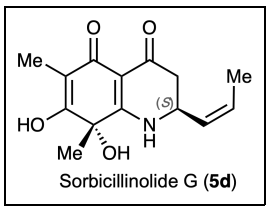
Fungus of origin: *Penicillium rubens* F54.[49]

Bioactivity: Anti-inflammatory activity due to inhibition of nitric oxide (44.5%) and prostaglandin E2 (PGE2, 59.2%) formation.[49]

Biosynthesis: See figure S1C.

Analytics: Yellow oil. **ORD**: $[\alpha]_D$ = +132.5 (c = 0.1, MeOH). ^{1}**H-NMR** (400 MHz, DMSO-d_6): δ = 13.46 (s, 1H, O*H*), 9.83 (s, 1H, N*H*), 6.40 (s, 1H, O*H*), 5.56 (qd, *J* = 15.5, 6.3 Hz, 1H, C*H*), 5.43 (dd, *J* = 15.5, 5.3 Hz, 1H, C*H*), 4.31 (ddd, *J* = 8.0, 5.3, 1.5 Hz, 1H, C*H*), 3.03 (dd, *J* = 16.0, 8.0 Hz, 1H, CH_2), 2.33 (dd, *J* = 16.0, 1.5 Hz, 1H, CH_2), 1.62 (d, *J* = 6.3 Hz, 3H, CH_3), 1.59 (s, 3H, CH_3), 1.40 (s, 3H, CH_3). ^{13}**C-NMR** (100 MHz, DMSO-d_6): δ = 194.5, 191.0, 173.8, 169.0, 128.0, 127.2, 97.0, 93.9, 74.6, 50.8, 38.4, 32.4, 17.8, 7.2. **IR**: *ν* 3247, 2922, 1610, 1574, 1519, 1428 cm^{-1}. **HRMS** (ESI) *m/z*: $[M-H]^-$ calcd for $C_{14}H_{16}NO_4$ 262.1079, found 262.1078.[49]

Sorbicillinolide G (5d)



Sorbicillinolide G (**5d**)

SMILES: O=C1C(C2=O)=C(N[C@H](/C=C\C)C2)[C@@](O)(C)C(O)=C1C

Fungus of origin: *Penicillium rubens* F54.[49]

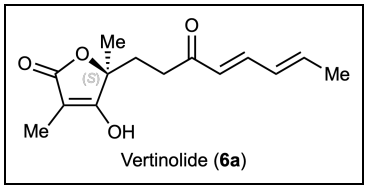
Bioactivity: Anti-inflammatory activity due to inhibition of nitric oxide (54.9%) and prostaglandin E2 (PGE2, 60.2%) formation.[49]

Biosynthesis: See figure S1C.

Analytics: Yellow oil. **ORD**: $[\alpha]_D$ = +104.6 (c = 0.1, MeOH). ^{1}**H-NMR** (400 MHz, DMSO-d_6): δ = 13.45 (s, 1H, O*H*), 9.41 (s, 1H, N*H*), 5.67 (dd, *J* = 10.5, 7.1 Hz, 1H, C*H*), 5.57 (dq, *J* = 10.5, 6.8 Hz, 1H, C*H*), 4.70 (dt, *J* = 10.5, 7.1 Hz, 1H, C*H*), 2.55 (dd, *J* = 16.0, 10.5 Hz, 1H, CH_2), 2.45 (dd, *J* = 16.0, 7.1 Hz, 1H, CH_2), 1.66 (d, *J* = 6.8 Hz, 3H, CH_3), 1.60 (s, 3H, CH_3), 1.41 (s, 3H, CH_3). ^{13}**C-NMR** (100 MHz, DMSO-d_6): δ = 194.6, 192.1, 174.4, 168.7, 128.7, 127.6, 97.5, 94.5, 74.5, 48.8, 40.0, 32.2, 13.4, 7.2. **IR**: *ν* 3247, 2921, 1606, 1573, 1522, 1429, 1378 cm^{-1}. **HRMS** (ESI) *m/z*: $[M-H]^-$ calcd for $C_{14}H_{16}NO_4$ 262.1079, found 262.1081.[49]

1.1.2 Vertinolides

Vertinolide (6a) [(*S*)-4-Hydroxy-3,5-dimethyl-5-((4*E*,6*E*)-3-oxoocta-4,6-dien-1-yl)furan-2(5*H*)-one, CAS: 79950-84-8]



Vertinolide (**6a**)

SMILES: O=C1C(C)=C(O)[C@@](CCC(/C=C/C=C/C)=O)(C)O1

Fungus of origin: *Clonostachys rosea* B5-2[50], *Penicillium* sp. SCSIO06871[51], *Trichoderma* sp.[41,52], *Trichoderma* sp. FM652[53], *Trichoderma viride*[41], *Verticillium intertextum*[20,21,54].

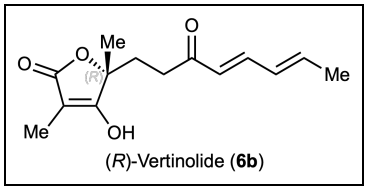
Bioactivity: No phytotoxicity against lettuce seedlings (*Lactuca sativa* L.).[50]

Biosynthesis: See figure S1D.[38]

Total synthesis: See figures S10 and S11. Chiral 2,2-disubstituted 4,5-dihydrofuran-3-one as precursor leads to vertinolide (**6a**) in 12 steps with an overall yield of 12%.[55] Eight steps from (2*S*,3*S*)-geranyl oxide (selective epoxide opening with NaCN, lactonization, dehydration, alkylation, ozonolysis, Grignard addition, protiodesilylation).[56] Numerous other syntheses have been developed since the 1980s.[57–59]

Analytics: Colourless prisms. **MP**: 149–152 °C. **TLC**: R_f = 0.25 ($CHCl_3$/EtOH = 94:6). **ORD**: $[\alpha]_D^{20} = -25.0$ (c = 0.1, $CHCl_3$). ^{1}**H-NMR** (200 MHz, CD_3COCD_3): δ = 9.80 (bs, 1H, O*H*), 7.19 (dd, *J* = 15.4, 9.6 Hz, 1H, C*H*$_{sorbyl}$), 6.25 (m, 2H, C*H*$_{sorbyl}$), 6.06 (d, *J* = 15.4 Hz, 1H, C*H*$_{sorbyl}$), 2.60 (m, 2H, CH_2), 2.25 (m, 2H, CH_2), 1.89 (d, *J* = 5.4 Hz, 3H, CH_3), 1.68 (s, 3H, CH_3), 1.48 (s, 3H, CH_3). ^{13}**C-NMR** (25.1 MHz, CD_3COCD_3): δ = 199.1, 176.6, 173.9, 143.5, 140.7, 131.4, 128.6, 97.2, 82.6, 34.8, 31.7, 23.6, 18.7, 6.2. **IR**: *ν* 1740, 1690, 1671, 1638, 1594 cm^{-1}.[20,54]

(*R*)-Vertinolide (6b) [(*R*)-4-Hydroxy-3,5-dimethyl-5-((4*E*,6*E*)-3-oxoocta-4,6-dien-1-yl)furan-2(5*H*)-one]



(*R*)-Vertinolide (**6b**)

SMILES: O=C1C(C)=C(O)[C@](CCC(/C=C/C=C/C)=O)(C)O1

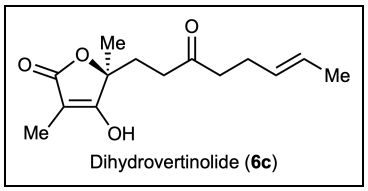
Fungus of origin: *Verticillium citrinoviride*[60].

Biosynthesis: See figure S1D.

Total synthesis: In theory, the total synthesis of (*R*)-vertinolide (**5b**) could follow the same strategies as for vertinolide (**6a**) by simple inverting the stereo information.

Analytics: NMR, IR and MS data are the same as for vertinolide (**5a**). **ORD**: $[\alpha]_D^{20} = +25.0$.[60] *R*)-Vertinolide (**6b**) has only been isolated once in this configuration.

Dihydrovertinolide (6c) [((*S*,*E*)-4-Hydroxy-3,5-dimethyl-5-(3-oxooct-6-en-1-yl)furan-2(5*H*)-one, CAS: 2408047-25-4]



Dihydrovertinolide (**6c**)

SMILES: O=C1C(C)=C(O)[C@@](CCC(CC/C=C/C)=O)(C)O1

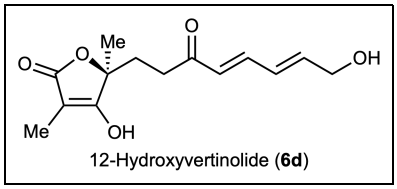
Fungus of origin: *Clonostachys rosea* B5-2[50,61].

Bioactivity: Phytotoxic activity against lettuce seedlings (IC_{50} = 50 µg/mL)[50].

Biosynthesis: See figure S1D.

Analytics: White amorphous powder. ^{1}**H-NMR** (600 MHz, $CDCl_3$): δ = 5.41 (m, 1H, C*H*), 5.37 (m, 1H, C*H*), 2.44 (t, *J* = 7.8 Hz, 2H, CH_2), 2.34 (m, 1H, CH_2), 2.26 (m, 1H, CH_2), 2.15 (m, 2H, CH_2) 2.00 (m, 1H, CH_2), 1.96 (m, 1H, CH_2), 1.64 (s, 3H, CH_3), 1.58 (d, *J* = 6.6 Hz, 3H, CH_3), 1.40 (s, 3H, CH_3). ^{13}**C-NMR** (150 MHz, $CDCl_3$): δ = 209.9, 177.5, 175.6, 129.5, 125.4, 95.2, 82.6, 42.0, 35.9, 29.9, 26.5, 22.2, 16.7, 4.6. **IR**: *ν* 3300, 2935, 1720, 1666, 1180, 1064 cm^{-1}. **HRMS** (ESI/TOF) *m/z*: $[M+H]^+$ calcd for $C_{14}H_{21}O_4$ 253.1442, found 253.1444.[50]

12-Hydroxyvertinolide (6d) [(*S*)-4-Hydroxy-5-((4*E*,6*E*)-8-hydroxy-3-oxoocta-4,6-dien-1-yl)-3,5-dimethylfuran-2(5*H*)-one]



12-Hydroxyvertinolide (**6d**)

SMILES: O=C1C(C)=C(O)[C@@](CCC(/C=C/C=C/CO)=O)(C)O1

Fungus of origin: *Trichoderma saturnisporum* DI-IA[62].

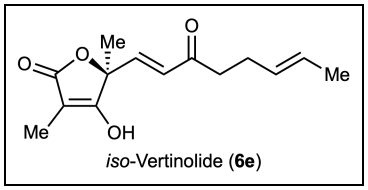
Bioactivity: Antimicrobial activity against *Staphylococcus aureus* ATCC 29213 (IC_{50} = 3.3 µg/mL), vancomycin-resistant *Enterococci faecalis* A4 (VRE, IC_{50} = 1.6 µg/mL),*Bacillus subtilis* ATCC 6051 (IC_{50} > 64 µg/mL), *Pseudomonas aeruginosa* 14 (IC_{50} = 6.7 µg/mL), and *Klebsiella pneumoniae* WNX-1 (IC_{50} = 6.7 µg/mL).[62]

Biosynthesis: See figure S1D.[62]

Analytics: Light yellow oil. **ORD**: $[\alpha]_D^{20} = -15.0$ (c = 1.0, $CHCl_3$). ^{1}**H-NMR** (400 MHz, CD_3OD): δ = 7.25 (dd, *J* = 16.0, 10.6 Hz, 1H, C*H*$_{sorbyl}$), 6.47 (dd, *J* = 16.0, 10.6 Hz, 1H, C*H*$_{sorbyl}$), 6.36 (dt, *J* = 16.0, 4.6 Hz, 1H, C*H*$_{sorbyl}$), 6.18 (d, *J* = 16.0 Hz, 1H, C*H*$_{sorbyl}$), 4.22 (d, *J* = 4.6 Hz, 2H, CH_2OH), 2.50 (t, *J* = 7.6 Hz, 2H, CH_2), 2.07 (t, *J* = 7.6 Hz, 2H, CH_2), 1.66 (s, 3H, CH_3), 1.44 (s, 3H, CH_3).

^{13}**C-NMR** (100 MHz, CD_3OD): δ = 200.6, 180.8, 176.8, 143.6, 142.9, 128.5, 127.4, 93.6, 83.0, 61.4, 33.7, 30.6, 22.2, 4.6. **IR**: *ν* 3422, 2924, 2853, 1737, 1655, 1640, 1366 cm^{-1}. **HRMS** (ESI) *m/z*: $[M-H]^-$ calcd for $C_{14}H_{17}O_5$ 265.1076, found 265.1073.[62]

***iso*-Vertinolide (6e)** [5,6-Dehydrovertinolide, (*S*)-4-Hydroxy-3,5-dimethyl-5-((1*E*,6*E*)-3-oxoocta-1,6-dien-1-yl)furan-2(5*H*)-one]



iso-Vertinolide (**6e**)

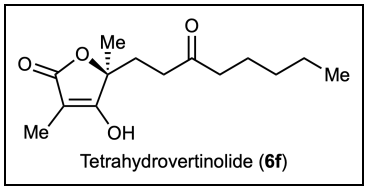
SMILES: O=C1C(C)=C(O)[C@@](/C=C/C(CC/C=C/C)=O)(C)O1

Fungus of origin: *Penicillium* sp. SCSIO06871[51].

Biosynthesis: See figure S1D.[51]

Analytics: Yellow oil. **ORD**: $[\alpha]_D^{20}$ = +3.5 (c = 0.1, MeOH). ^{1}**H-NMR** (700 MHz, CD_3OD): δ =6.83 (d, *J* = 16.1 Hz, 1H, C*H*), 6.38 (d, *J* = 16.1 Hz, 1H, C*H*), 5.47 (m, 1H, C*H*), 5.42 (m, 1H, C*H*), 2.67 (t, *J* =7.7 Hz, 2H, CH_2), 2.25 (brq, *J* =7.0 Hz, 2H, CH_2), 1.67 (s, 3H, CH_3), 1.62 (dd, *J* =5.6, 1.4 Hz, 3H, CH_3), 1.59 (s, 3H, CH_3). ^{13}**C-NMR** (175 MHz, CD_3OD): δ = 201.6, 177.9, 176.4, 143.8, 130.7, 129.7, 126.9, 95.4, 83.3, 41.6, 28.0, 23.0, 18.0, 6.1. **HRMS** (ESI) *m/z*: $[M-Na]^-$ calcd for $C_{14}H_{17}O_4$ 249.1132, found 249.1126.[51]

Tetrahydrovertinolide (6f) [(*S*)-4-Hydroxy-3,5-dimethyl-5-(3-oxooctyl)furan-2(5*H*)-one, CAS: 82224-93-9]



Tetrahydrovertinolide (**6f**)

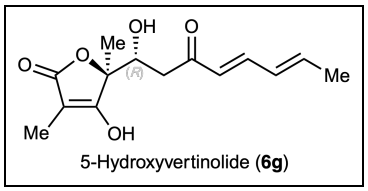
SMILES: O=C1C(C)=C(O)[C@@](CCC(CCCCC)=O)(C)O1

Fungus of origin / Biosynthesis: This compound was never isolated from nature. It has been synthesized to characterize the stereo information in vertinolide (**6a**).[63]

Total synthesis: Tetrahydrovertinolide (**6f**) can be obtained upon reduction of vertinolides (**5a**,**c**,**f**).[50,54]

Analytics: **MP**: 61–62 °C. **ORD**: $[\alpha]_D^{20}$ = +16.8 (c = 4.5, $CHCl_3$). ^{1}**H-NMR** (400 MHz, $CDCl_3$): δ = 2.41 (t, 2H, COCH_2), 2.09 (t, 2H, COCH_2), 1.70 (s, 3H, CH_3), 1.49 (s, 3H, CH_3), 1.50 (m, 2H, CH_2), 1.30 (m, 4H, CH_2), 1.28 (m, 2H, CH_2), 0.88 (s, 3H, CH_3). ^{13}**C-NMR** (125 MHz, acetone-d_6): δ = 209.3, 177.3, 174.2, 96.2, 82.5, 42.9, 36.8, 32.0, 31.1, 24.0, 23.6, 23.1, 14.2, 6.3. ^{13}**C-NMR** (125 MHz, $CDCl_3$): δ = 211.3, 177.7, 176.0, 96.2, 83.2, 41.9, 36.4, 31.3, 30.1, 23.7, 23.5, 23.1, 13.9, 5.9. **IR**: *ν* 1740, 1700, 1655 cm^{-1}.[63]

5-Hydroxyvertinolide (6g) [((*S*)-4-Hydroxy-5-((*R*,4*E*,6*E*)-1-hydroxy-3-oxoocta-4,6-dien-1-yl)-3,5-dimethylfuran-2(5*H*)-one]



5-Hydroxyvertinolide (**6g**)

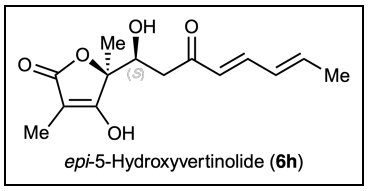
SMILES: O=C1C(C)=C(O)[C@@]([C@H](O)CC(/C=C/C=C/C)=O)(C)O1

Fungus of origin: *Trichoderma longibrachiatum* Rifai aggr.[64], *Trichoderma longibrachiatum* UAMH 4159[13], *Trichoderma* sp. USF-2690[65].

Biosynthesis: See figure S1D.[65]

Analytics: Colourless amorphous solid. **ORD**: $[\alpha]_D^{20}$ = −64.0 (c = 0.1, MeOH). ^{1}**H-NMR** (360 MHz, acetone-d_6): δ = 10.0 (bs, 1H, O*H*), 7.21 (dd, *J* =16.0, 10.0 Hz, 1H, CH_{sorbyl}), 6.25 (m, 2H, CH_{sorbyl}), 6.08 (d, *J* =15.0 Hz, 1H, CH_{sorbyl}), 4.14 (dd, *J* =10.0, 2.0 Hz, 1H, C*H*), 3.49 (bs, 1H, O*H*), 3.15 (dd, *J* =16.0, 2.0 Hz, 1H, CH_2), 2.77 (dd, *J* =16.0, 10.0 Hz, 1H, CH_2), 1.90 (d, *J* =6.5 Hz, 3H, CH_3), 1.74 (s, 3H, CH_3), 1.49 (s, 3H, CH_3). ^{13}**C-NMR** (100 MHz, acetone-d_6): δ = 189.5, 175.4, 173.4, 143.5, 140.6, 129.7, 127.2, 96.4, 82.8, 70.3, 40.5, 18.1, 5.3. **IR**: *ν* 3360, 3025, 2987, 2965, 2936, 1749, 1729, 1666, 1638, 1593, 1447, 1402, 1306, 1064, 1020, 762 cm^{-1}.[64]

***epi*-5-Hydroxyvertinolide (6h)** [((*S*)-4-Hydroxy-5-((*S*,4*E*,6*E*)-1-hydroxy-3-oxoocta-4,6-dien-1-yl)-3,5-dimethylfuran-2(5*H*)-one]



epi-5-Hydroxyvertinolide (**6h**)

SMILES: O=C1C(C)=C(O)[C@@]([C@@H](O)CC(/C=C/C=C/C)=O)(C)O1

Fungus of origin: *Trichoderma* sp. USF-2690[65].

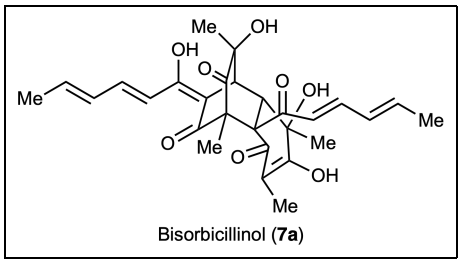
Biosynthesis: See figure S1D.[65]

Analytics: Colorless amorphous powder. **ORD**: $[\alpha]_D^{23}$ = −18.3 (c = 0.2, MeOH). ^{1}**H-NMR** (400 MHz, acetone-d_6): δ = 7.19 (m, 1H, CH_{sorbyl}), 6.25 (m, 2H, CH_{sorbyl}), 6.12 (d, *J* =15.4 Hz, 1H, CH_{sorbyl}), 4.30 (dd, *J* =9.8, 2.4 Hz, 1H, C*H*), 2.84 (dd, *J* =16.1, 9.8 Hz, 1H, CH_2), 2.54 (dd, *J* =16.1, 2.4 Hz, 1H, CH_2), 1.85 (dd, *J* =4.9, 2.4 Hz, 3H, CH_3), 1.63 (s, 3H, CH_3), 1.49 (s, 3H, CH_3). ^{13}**C-NMR** (100 MHz, acetone-d_6): δ = 198.7, 176.3, 173.9, 143.9, 141.1, 131.3, 129.1, 97.1, 84.7, 71.3, 42.3, 19.8, 18.8, 6.4. **IR**: *ν* 3409, 2925, 2855, 1726, 1660, 1631, 1592, 1301, 1063, 1023 cm^{-1}. **HRMS** (FAB) *m/z*: $[M+H]^+$ calcd for $C_{14}H_{19}O_5$ 267.1232, found 267.1224.[65]

1.2 Oligomeric sorbicillinoids

1.2.1 Dimeric Diels-Alder-type sorbicillinoids

Bisorbicillinol (7a) [CAS: 209167-87-3]



Bisorbicillinol (**7a**)

SMILES: O[C@@]1(C)[C@@H]2/C(C([C@@](C1=O)(C)[C@]3(C(/C=C/C=C/C)=O)[C@H]2[C@@](O)(C)C(O)=C(C)C3=O)=O)=C(/C=C/C=C/C)O

Fungus of origin: *Penicillium chrysogenum* sp.[8],*Penicillium notatum*[28], *Trichoderma* sp. f-13[16], *Trichoderma* sp. USF-2690[18,33,66], *Villosiclava virens* albino strain LN02[67].

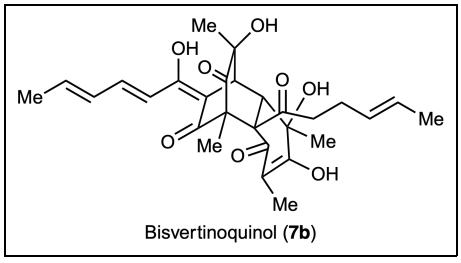
Bioactivity: Antibacterial against *Staphylococcus aureus* and *Bacillus subtilis* (weak).[28] DPPH radical scavenging activity ($ED_{50} = 31.4$ µM).[66] Inhibition of Lyn tyrosine kinase for allergic response on RBL-2H3 cells.[68]

Biosynthesis: See figure S2E.[23,66,69]

Total synthesis: The first racemic total synthesis was described by Nicolaou and co-workers by using the *O*-acetyl protected sorbicillinol.[34,35] Enantiomeric enriched strategies were developed by Deng and Pettus using their previous described formation of sorbicillinol (**2a**).[36,37]

Analytics: Yellowish amorphous powder. **ORD**: $[\alpha]_D^{28} = +195.2$ (c = 0.5, MeOH). ^{1}**H-NMR** (400 MHz, C_6D_6/CD_3OD = 9:1): δ = 14.30 (bs, 1H, O*H*), 7.39 (dd, *J* =15.2, 11.0 Hz, 1H, CH_{sorbyl}), 7.38 (dd, *J* =14.8, 10.4 Hz, 1H, CH_{sorbyl}), 6.74 (d, *J* =14.8 Hz, 1H, CH_{sorbyl}), 6.47 (d, *J* =15.2 Hz, 1H, CH_{sorbyl}), 6.15 (dd, *J* =14.6, 11.0 Hz, 1H, CH_{sorbyl}), 5.93 (m, 1H, CH_{sorbyl}), 5.89 (m, 1H, CH_{sorbyl}), 5.76 (dq, *J* =14.6, 6.4 Hz, 1H, CH_{sorbyl}), 3.99 (d, *J* =2.0 Hz, 1H, C*H*), 3.77 (d, *J* =2.0 Hz, 1H, C*H*), 1.99 (s, 3H, CH_3), 1.73 (s, 3H, CH_3), 1.56 (d, *J* =6.4 Hz, 3H, CH_3), 1.52 (s, 3H, CH_3), 1.50 (d, *J* =5.2 Hz, 3H, CH_3), 1.33 (s, 3H, CH_3). ^{13}**C-NMR** (100 MHz, C_6D_6/CD_3OD = 9:1): δ = 208.6, 199.8, 196.8, 185.0-175.0 (2C), 169.5, 147.0, 143.5, 142.7, 139.3, 131.6, 130.9, 124.9, 119.4, 111.7, 109.6, 75.3, 70.4, 68.9, 67.7, 48.3, 42.2, 33.2, 25.0, 18.7, 18.6, 10.7, 8.9. **IR**: *ν* 3425, 1740, 1630, 1390, 1330, 1245, 1210, 1010 cm^{-1}. **HRMS** (FAB) *m/z*: $[M+H]^+$ calcd for $C_{28}H_{33}O_8$ 497.2176, found 497.2180.[66]

Bisvertinoquinol (7b) [CAS: 79950-83-7]



Bisvertinoquinol (**7b**)

SMILES: O[C@@]1(C)[C@@H]2/C(C([C@@](C1=O)(C)[C@]3(C(CC/C=C/C)=O)[C@H]2[C@@](O)(C)C(O)=C(C)C3=O)=O)=C(/C=C/C=C/C)O

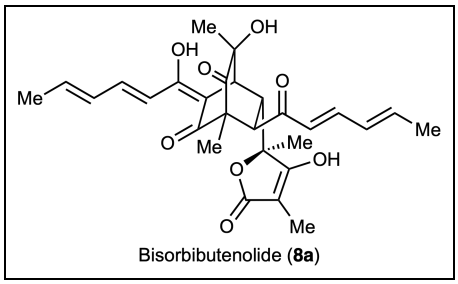
Fungus of origin: *Penicillium chrysogenum* sp.[8],*Penicillium notatum*[28], *Trichoderma* sp. f-13[16], *Verticillium intertextum*[20,21].

Bioactivity: Antibacterial against *Staphylococcus aureus* and *Bacillus subtilis*.[28]

Biosynthesis: See figure S2E.[21]

Analytics: Yellow solid. **MP**: 160-163 °C. **ORD**: $[\alpha]_D^{20} = +329$ (c = 0.2, $CHCl_3$). ^{1}**H-NMR** (360 MHz, CD_3OD): δ = 7.22 (ddd, *J* =15.0, 0.5, 2.0 Hz, 1H, CH_{sorbyl}), 6.30 (m, 1H, CH_{sorbyl}), 6.27 (d, *J* =15.0 Hz, 1H, CH_{sorbyl}), 6.19 (dq, *J* =15.0, 6.5 Hz, 1H, CH_{sorbyl}), 5.35 (m, 2H, C*H*), 3.62 (d, 1H, *J* =2.5 Hz, C*H*), 3.38 (d, *J* =2.5 Hz, 1H, C*H*), 2.65 (m, 1H, CH_2), 2.45 (m, 1H, CH_2), 2.20 (m, 2H, CH_2), 1.87 (d, *J* =6.5 Hz, 3H, CH_3), 1.60 (d, *J* =5.0 Hz, 3H, CH_3), 1.57 (s, 3H, CH_3), 1.45 (s, 3H, CH_3), 1.18 (s, 3H, CH_3), 1.13 (s, 3H, CH_3). **IR**: *ν* 3550, 3250, 2980, 2920, 2850, 1732, 1700, 1660, 1628, 1605, 1560 cm^{-1}.[21]

Bisorbibutenolide (8a) [Bislongiquinolide, Trichotetronine]



Bisorbibutenolide (**8a**)

SMILES: O[C@@]1(C)[C@@H]2/C(C([C@@](C1=O)(C)[C@H](C(/C=C/C=C/C)=O)[C@H]2[C@]3(C)OC(C(C)=C3O)=O)=O)=C(/C=C/C=C/C)O

Fungus of origin: *Acremonium citrinum* SS-g13[70], *Paecilomyces* sp. KMU21009[71], *Penicillium chrysogenum* sp.[8], *Penicillium citrinum* SpI080624G1f01[72], *Penicillium citrinum* XIA-16[73], *Penicillium* sp. NX-S-6[46], *Stagonospora* sp. SYSU-MS7888[74], *Trichoderma citrinoviride* ITEM 4484[75,76], *Trichoderma longibrachiatum*[40], *Trichoderma longibrachiatum* Rifai aggr.[64], *Trichoderma longibrachiatum* UAMH 4159[13], *Trichoderma viride*[41], *Trichoderma* sp.[41,52,77], *Trichoderma* sp. f-13[16], *Trichoderma* sp. USF-2690[18,33], *Villosiclava virens* albino strain LN02[67].

Bioactivity: Cytotoxity against human glioblastoma U373 cells ($IC_{50} = 4.0$ µM), adenocarcinomic human alveolar basal epithelial A549 cells ($IC_{50} = 11.0$ µM), malignant melanoma SKMEL-28 cells ($IC_{50} = 8.0$ µM), human esophageal squamous cell carcinoma OE21

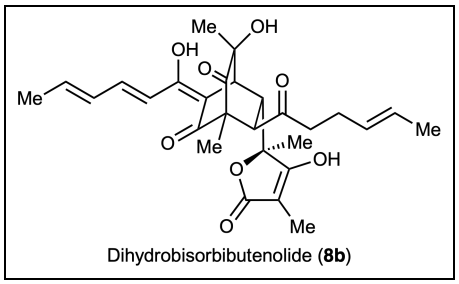
cells (IC_{50} = 9.0 μM), glioma Hs683 cells (IC_{50} = 22.0 μM), and mouse melanoma B16F10 cell line (IC_{50} = 3.0 μM).[76] Cytotoxicity against leukemic HL-60 cell line (IC_{50} > 50 μM).[16] Effect on feeding preference of the aphid.[75] DPPH-radical scavenging activity (ED_{50} = 80.8 μM).[18]

Biosynthesis: See figure S2E.[18,69]

Total synthesis: The transformation from bisorbicillinol (**7a**) to bisorbibutenolide (**8a**) can be performed with a base (KHMDS) followed by an acidic workup (one step: 80% yield).[34,35]

Analytics: Yellow amorphous powder. **ORD**: $[\alpha]_D^{27}$ = +124.4 (c = 0.5, MeOH). ^{1}**H-NMR** (400 MHz, $CDCl_3$): δ = 13.99 (bs, 1H, O*H*), 7.33 (dd, *J* =15.0, 10.6 Hz, 1H, CH_{sorbyl}), 7.22 (dd, *J* =15.0, 10.4 Hz, 1H, CH_{sorbyl}), 6.38 (dq, *J* =15.2, 7.2 Hz, 1H, CH_{sorbyl}), 6.28 (dd, *J* =14.4, 10.6 Hz, 1H, CH_{sorbyl}), 6.24 (dq, *J* =14.4, 6.8 Hz, 1H, CH_{sorbyl}), 6.21 (dd, *J* =15.2, 10.4 Hz, 1H, CH_{sorbyl}), 6.13 (d, *J* =15.0 Hz, 1H, CH_{sorbyl}), 6.12 (d, *J* =15.0 Hz, 1H, CH_{sorbyl}), 3.43 (d, *J* =4.8 Hz, 1H, C*H*), 3.36 (s, 1H, C*H*), 3.21 (dd, *J* =4.8, 1.2 Hz, 1H, C*H*), 1.90 (d, *J* =7.2 Hz, 3H, CH_3), 1.88 (d, *J* =6.8 Hz, 3H, CH_3), 1.58 (s, 3H, CH_3), 1.51 (s, 3H, CH_3), 1.29 (s, 3H, CH_3), 1.12 (s, 3H, CH_3). ^{13}**C-NMR** (125 MHz, $CDCl_3$): δ = 208.3, 202.7, 194.9, 176.5, 174.9, 169.8, 148.0, 145.5, 143.9, 140.9, 131.0, 130.3, 127.0, 117.6, 108.5, 98.2, 83.2, 75.0, 62.6, 51.3, 43.6, 42.4, 23.5, 23.1, 19.1, 18.9, 11.0, 6.3. **IR**: *ν* 3445, 2980, 2940, 1740, 1665, 1630, 1565, 1380, 1200, 1000 cm^{-1}. **HRMS** (FAB) *m/z*: $[M+H]^+$ calcd for $C_{28}H_{33}O_8$ 497.2176, found 497.2222.[18]

Dihydrobisorbibutenolide (8b)



Dihydrobisorbibutenolide (**8b**)

SMILES: O[C@@]1(C)[C@@H]2/C(C([C@@](C1=O)(C)[C@H](C(CC/C=C/C)=O)[C@H]2[C@]3(C)OC(C(C)=C3O)=O)=O)=C(/C=C/C=C/C)O

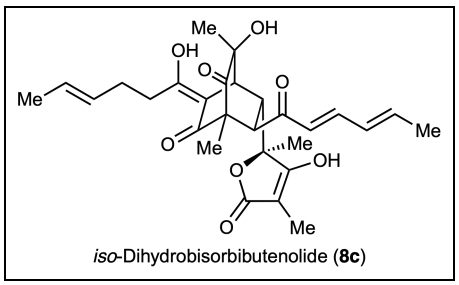
Fungus of origin: *Acremonium citrinum* SS-g13[70], *Penicillium dipodomyis* YJ-11[78], *Penicillium* sp. SCSIO06871[51], *Trichoderma citrinoviride* ITEM 4484[75,76], *Trichoderma* sp.[77].

Bioactivity: Weak siderophore activity and DPPH-radical scavenging activity (ED_{50} = 89.6 μM).[78]

Biosynthesis: See figure S2E.

Analytics: Pale yellow amorphous powder. **ORD**: $[\alpha]_D^{20}$ = +354.0 (c = 0.1, MeOH). ^{1}**H-NMR** (400 MHz, $CDCl_3$): δ = 7.34 (dd, *J* =14.8, 10.7 Hz, 1H, CH_{sorbyl}), 6.32 (ddd, *J* =14.9, 10.7, 1.1 Hz, 1H, CH_{sorbyl}), 6.23 (ddd, *J* =14.9, 12.8, 6.4 Hz, 1H, CH_{sorbyl}), 6.16 (d, *J* =14.9 Hz, 1H, CH_{sorbyl}), 5.47 (tddd, *J* =15.2, 12.3, 6.2, 1.2 Hz, 1H, C*H*), 5.36 (dddd, *J* =15.2, 13.5, 6.6, 1.5 Hz, 1H, C*H*), 3.41 (s, 1H, C*H*), 3.10 (s, 2H, C*H*), 2.63 (dd, *J* =14.7, 7.2 Hz, 2H, CH_2), 2.22 (dd, *J* =14.3, 7.0 Hz, 2H, CH_2), 1.90 (d, *J* =6.4 Hz, 3H, CH_3), 1.62 (dd, *J* =6.2, 1.3 Hz, 3H, CH_3), 1.60 (s, 3H, CH_3), 1.48 (s, 3H, CH_3), 1.26 (s, 3H, CH_3), 1.15 (s, 3H, CH_3). ^{13}**C-NMR** (100 MHz, $CDCl_3$): δ = 213.8, 208.1, 194.8, 176.1, 173.9, 169.8, 143.9, 140.9, 131.0, 128.7, 126.8, 117.6, 108.3, 98.0, 83.0, 75.1, 62.1, 54.2, 45.8, 43.7, 42.1, 25.9, 23.7, 22.4, 19.0, 17.8, 11.0 , 6.1. **IR**: *ν* 3434, 2930, 1734, 1632, 1605, 1561, 1447, 1383, 1314, 1256, 1138, 1055, 997 cm^{-1}. **HRMS** (FAB) *m/z*: $[M+Na]^+$ calcd for $C_{28}H_{34}O_8Na$ 521.2152, found 521.2131.[77]

***iso*-Dihydrobisorbibutenolide (8c)**



iso-Dihydrobisorbibutenolide (**8c**)

SMILES: O[C@@]1(C)[C@@H]2/C(C([C@@](C1=O)(C)[C@H](C(/C=C/C=C/C)=O)[C@H]2[C@]3(C)OC(C(C)=C3O)=O)=O)=C(CC/C=C/C)\O

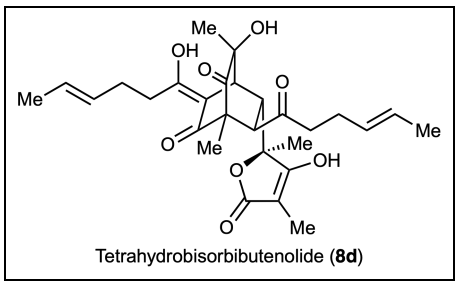
Fungus of origin: *Acremonium citrinum* SS-g13[70], *Penicillium dipodomyis* YJ-11[78], *Penicillium* sp. SCSIO06871[51].

Bioactivity: Siderophore activity (ED_{50} = 400 μM).[78]

Biosynthesis: See figure S2E.

Analytics: **ORD**: $[\alpha]_D^{20}$ = +35.6 (c = 0.1, MeOH). ^{1}**H-NMR** (600 MHz, $CDCl_3$): δ = 14.45 (bs, 1H, O*H*), 7.16 (dd, *J* =15.0, 10.6 Hz, 1H, CH_{sorbyl}), 6.42 (m, 1H, CH_{sorbyl}), 6.24 (dd, *J* =15.0, 10.6 Hz, 1H, CH_{sorbyl}), 6.02 (d, *J* =15.0 Hz, 1H, CH_{sorbyl}), 5.52 (dq, *J* =15.3, 6.0 Hz, 1H, C*H*), 5.44 (dt, *J* =15.3, 6.7 Hz, 1H, C*H*), 3.36 (s, 1H, C*H*), 3.20 (d, *J* =7.0 Hz, 1H, C*H*), 2.95 (d, *J* =7.0 Hz, 1H, C*H*), 2.51 (t, *J* =7.4 Hz, 2H, CH_2), 2.42 (m, 2H, CH_2), 1.93 (d, *J* =6.7 Hz, 3H, CH_3), 1.64 (d, *J* =6.0 Hz, 3H, CH_3), 1.61 (s, 3H, CH_3), 1.57 (s, 3H, CH_3), 1.34 (s, 3H, CH_3), 1.05 (s, 3H, CH_3). ^{13}**C-NMR** (150 MHz, $CDCl_3$): δ = 209.9, 202.1, 193.0, 181.3, 175.8, 174.4, 148.3, 146.0, 130.1, 129.1, 127.2, 126.9, 108.4, 98.8, 83.1, 75.3, 61.7, 50.7, 42.8, 42.0, 32.5, 28.4, 19.2, 17.8, 24.1, 21.8, 10.5, 6.1. **HRMS** (ESII) *m/z*: $[M-H]^-$ calcd for $C_{28}H_{34}O_8$ 497.2170), found 497.2185.[78]

Tetrahydrobisorbibutenolide (8d)



Tetrahydrobisorbibutenolide (**8d**)

SMILES: O[C@@]1(C)[C@@H]2/C(C([C@@](C1=O)(C)[C@H](C(CC/C=C/C)=O)[C@H]2[C@]3(C)OC(C(C)=C3O)=O)=O)=C(CC/C=C/C)\O

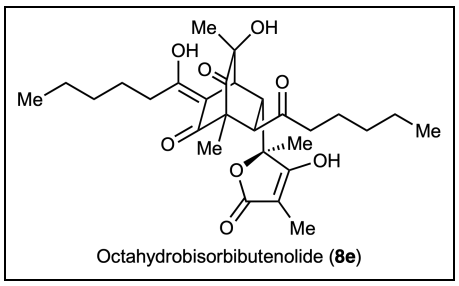
Fungus of origin: *Acremonium citrinum* SS-g13[70], *Penicillium chrysogenum* DM815[29], *Penicillium dipodomyis* YJ-11[78], *Penicillium* sp. SCSIO06871[51].

Bioactivity: Siderophore activity ($ED_{50} = 400$ μM), DPPH-radical scavenging activity ($ED_{50} = 167$ μM).[78]

Biosynthesis: See figure S2E.

Analytics: **ORD**: $[\alpha]_D^{20} = +71.8$ (c = 0.5, MeOH). ^{1}**H-NMR** (600 MHz, $CDCl_3$): δ = 14.45 (bs, 1H, O*H*), 5.50 (m, 3H, C*H*), 5.34 (m, 1H, C*H*), 3.42 (s, 1H, C*H*), 3.15 (d, *J* =6.6 Hz, 1H, C*H*), 2.65 (d, *J* =6.6 Hz, 1H, C*H*), 2.53 (m, 4H, CH_2), 2.39 (m, 2H, CH_2), 2.15 (m, 2H, CH_2), 1.71 (s, 3H, CH_3), 1.63 (m, 6H, CH_3), 1.55 (s, 3H, CH_3), 1.31 (s, 3H, CH_3), 1.13 (s, 3H, CH_3). ^{13}**C-NMR** (150 MHz, $CDCl_3$): δ = 213.2, 209.1, 192.9, 181.2, 177.3, 175.4, 129.0, 128.5, 126.9, 126.8, 108.4, 97.8, 84.0, 75.2, 61.4, 54.0, 45.9, 42.7, 42.6, 32.4, 28.4, 25.9, 24.0, 21.3, 17.8 (2C), 10.6, 5.9. **HRMS** (ESII) *m/z*: $[M-H]^-$ calcd for $C_{28}H_{36}O_8$ 499.2326, found 499.2343.[78]

Octaahydrobisorbibutenolide (8e)



Octahydrobisorbibutenolide (**8e**)

SMILES: O[C@@]1(C)[C@@H]2/C(C([C@@](C1=O)(C)[C@H](C(CCCCC)=O)[C@H]2[C@]3(C)OC(C(C)=C3O)=O)=O)=C(CCCCC)\O

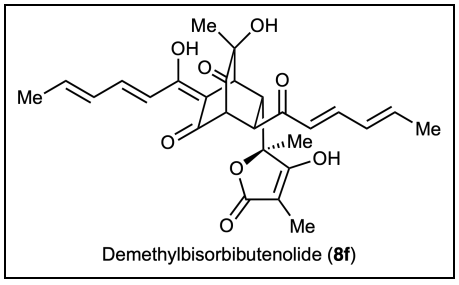
Fungus of origin: *Penicillium dipodomyis* YJ-11[78].

Biosynthesis: See figure S2E.

Total synthesis: Bisorbibutenolides **8a**-**d** in methanol were hydrogenated over palladium on carbon at room temperature overnight to give this saturated derivative.[78]

Analytics: **ORD**: $[\alpha]_D^{20} = +78.4$ (c = 0.1, MeOH) . ^{1}**H-NMR** (600 MHz, $CDCl_3$): δ = 14.46 (bs, 1H, O*H*), 3.39 (s, 1H, C*H*), 3.08 (d, *J* =7.3 Hz, 1H, C*H*), 2.75 (d, *J* =7.3 Hz, 1H, C*H*), 2.45 (m, 4H, CH_2), 1.70 (m, 2H, CH_2), 1.67 (s, 3H, CH_3), 1.50 (s, 3H, CH_3), 1.48 (m, 2H, CH_2), 1.35 (m, 4H, CH_2), 1.30 (s, 3H, CH_3), 1.25 (m, 4H, CH_2), 1.11 (s, 3H, CH_3), 0.89 (t, *J* =6.5 Hz, 3H, CH_3), 0.87 (t, *J* =7.3 Hz, 3H, CH_3). ^{13}**C-NMR** (150 MHz, $CDCl_3$): δ = 214.3, 209.2, 192.9, 182.4, 176.0, 173.6, 106.3, 98.2, 83.1, 75.3, 61.4, 54.3, 46.0, 42.9, 42.7, 32.4, 31.9, 31.0, 29.8, 25.2, 24.2, 22.5 (2C), 21.5, 14.0 (2C), 10.7, 6.1. **HRMS** (ESI) *m/z*: $[M+Na]^+$ calcd for $C_{28}H_{40}O_8Na$ 527.2615, found 527.2608.[78]

Demethylbisorbibutenolide (8f)



Demethylbisorbibutenolide (**8f**)

SMILES: O[C@@]1(C)[C@@H]2/C(C([C@H](C1=O)[C@H](C(/C=C/C=C/C)=O)[C@H]2[C@]3(C)OC(C(C)=C3O)=O)=O)=C(/C=C/C=C/C)O

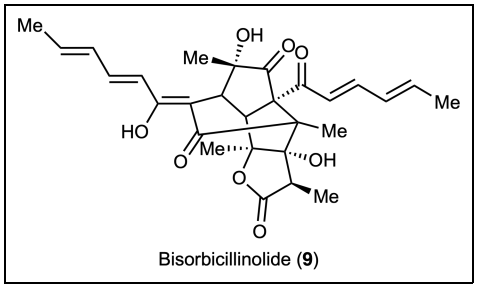
Fungus of origin: *Trichoderma* sp. USF-4860[79].

Bioactivity: DPPH-radical scavenging activity ($ED_{50} > 149$ μM, time-dependent).[79]

Biosynthesis: See figure S2E.

Analytics: Yellowish amorphous powder. **ORD**: $[\alpha]_D^{23} = -143.7$ (c = 0.1, MeOH). ^{1}**H-NMR** (400 MHz, CD_3COCD_3): δ = 13.78 (bs, 1H, O*H*), 7.27 (dd, *J* =15.2, 9.4 Hz, 1H, CH_{sorbyl}), 7.26 (dd, *J* = 14.8, 11.0 Hz, 1H, CH_{sorbyl}), 6.60 (d, *J* =15.2 Hz, 1H, CH_{sorbyl}), 6.57 (d, *J* = 14.8 Hz, 1H, CH_{sorbyl}), 6.40 (m, 1H, CH_{sorbyl}), 6.35 (m, 1H, CH_{sorbyl}), 6.34 (m, 1H, CH_{sorbyl}), 6.28 (m, 1H, CH_{sorbyl}), 3.71 (d, *J* =2.0 Hz, 1H, C*H*), 3.38 (dd, *J* = 8.0, 2.0 Hz, 1H, C*H*), 3.35 (d, *J* = 2.0 Hz, 1H, C*H*), 3.25 (dd, *J* = 8.0, 2.0 Hz, 1H, C*H*), 1.90 (d, *J* =6.7 Hz, 3H, CH_3), 1.88 (d, *J* =6.6 Hz, 3H, CH_3), 1.57 (s, 3H, CH_3), 1.39 (s, 3H, CH_3), 1.15 (s, 3H, CH_3). ^{13}**C-NMR** (100 MHz, CD_3COCD_3): δ = 206.7, 197.8, 196.5, 175.4, 172.9, 166.4, 144.9, 142.3, 141.7, 139.1, 132.1, 131.2, 126.7, 120.4, 113.3, 98.4, 82.7, 74.2, 63.2, 50.5, 46.3, 40.0, 23.3, 21.7, 18.9 (2C), 6.3. **IR**: *ν* 3440, 2920, 1740, 1640, 1380, 1000 cm^{-1}. **HRMS** (FAB) *m/z*: $[M+H]^+$ calcd for $C_{27}H_{32}O_8$ 483.2019, found 483.2002.[79]

Bisorbicillinolide (9)



Bisorbicillinolide (**9**)

SMILES: O=C1[C@H](C)[C@@](C2(C)[C@@]3(C(/C=C/C=C/C)=O)C4C(/C(C2=O)=C(\C=C\C=C\C)O)[C@@](O)(C)C3=O)(O)[C@@]4(C)O1

Fungus of origin: *Trichoderma citrinoviride*[80], *Trichoderma reesei* BGRg-3[81], *Trichoderma* sp. USF-2690[18,33].

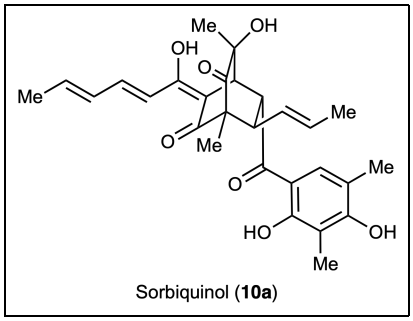
Bioactivity: DPPH-radical scavenging activity ($ED_{50} = 88.8$ µM).[18]

Biosynthesis: See figure S2E.[18,23,69]

Total synthesis: The total synthesis of bisorbicillinolide (**9**) was first described by Deng and co-workers.[37] The treatment of bisorbicillinol (**7a**) with methanol at room temperature for 48 h enables the formation of bisorbicillinolide (**9**) in 64% yield with the byproduct formation of bisorbibutenolide (**8a**) in 10% yield.

Analytics: Yellowish amorphous powder. **ORD**: $[\alpha]_D^{27} = +318.0$ (c = 0.1, MeOH). ^{1}**H-NMR** (400 MHz, $CDCl_3$): δ = 16.01 (bs, 1H, O*H*), 7.42 (dd, *J* = 14.8, 11.2 Hz, 1H, CH_{sorbyl}), 7.39 (dd, *J* = 14.8, 10.4 Hz, 1H, CH_{sorbyl}), 6.46 (d, *J* = 14.8 Hz, 1H, CH_{sorbyl}), 6.36 (dq, *J* = 15.2, 7.6 Hz, 1H, CH_{sorbyl}), 6.30 (m, 2H, CH_{sorbyl}), 6.25 (bs, 1H, O*H*), 6.21 (dd, *J* = 15.2, 11.2 Hz, 1H, CH_{sorbyl}), 6.14 (d, *J* = 14.8 Hz, 1H, CH_{sorbyl}), 5.80 (bs, 1H, O*H*), 3.73 (d, *J* = 5.4 Hz, 1H, C*H*), 3.38 (d, *J* = 5.4 Hz, 1H, C*H*), 2.66 (q, *J* = 8.0 Hz, 1H, C*H*), 1.90 (d, *J* =5.2 Hz, 3H, CH_3), 1.89 (d, *J* =7.6 Hz, 3H, CH_3), 1.39 (s, 3H, CH_3), 1.15 (s, 3H, CH_3), 1.36 (s, 3H, CH_3), 1.21 (d, *J* =8.0 Hz, 3H, CH_3). ^{13}**C-NMR** (100 MHz, $CDCl_3$): δ = 210.3, 199.4, 194.5, 177.9, 177.3, 147.9, 145.0, 144.6, 141.5, 131.0, 130.3, 123.8, 119.0, 107.3, 93.8, 88.3, 84.1, 73.5, 68.0, 56.9, 44.4, 41.1, 24.3, 19.0, 18.9, 18.1, 13.7, 10.3. **IR**: *ν* 3450, 3000, 2995, 1760, 1620, 1580, 1450, 1380, 1250, 1130, 1090, 1000 cm^{-1}. **HRMS** (FAB) *m/z*: $[M+H]^+$ calcd for $C_{28}H_{33}O_8$ 497.2176, found 497.2202.[18]

Sorbiquinol (10a)



Sorbiquinol (**10a**)

SMILES: O[C@@]1(C)[C@@H]2/C(C([C@@](C1=O)(C)[C@H](/C=C/C)[C@H]2C(C3=C(O)C(C)=C(O)C(C)=C3)=O)=O)=C(/C=C/C=C/C)O

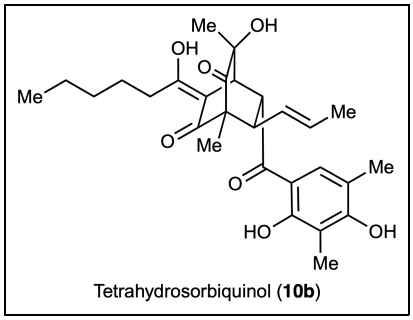
Fungus of origin: *Acremonium* sp. AN-13[1], *Trichoderma* sp. FM652[53], *Trichoderma longibrachiatum* UAMH 4159[13,32].

Bioactivity: Anti-proliferative activity against ovarian cancer cell line A2780.[53]

Biosynthesis: See figure S2F.

Analytics: Pale yellow amorphous solid. **TLC**: R_f = 0.28 (2% EtOH in $CHCl_3$).**ORD**: $[\alpha]_D^{20} = +234.0$ (c = 0.4, MeOH). ^{1}**H-NMR** (300 MHz, actone-d_6): δ = 8.05 (bs, 1H, O*H*), 7.69 (s, 1H, Ar*H*), 7.12 (dd, *J* = 15.0, 10.0 Hz, 1H, CH_{sorbyl}), 6.13 (dq, *J* = 15.0, 7.0 Hz, 1H, CH_{sorbyl}), 5.95 (ddq, *J* = 15.0, 10.0, 1.5 Hz, 1H, C*H*), 5.82 (d, *J* = 15.0 Hz 1H, CH_{sorbyl}), 5.45 (dq, *J* = 15.0, 7.0 Hz, 1H, CH_{sorbyl}), 5.16 (ddq, *J* = 15.0, 10.0, 1.5 Hz, 1H, C*H*), 4.48 (dd, *J* = 6.5, 1.5 Hz, 1H, C*H*), 3.79 (bs, 1H, O*H*), 3.50 (d, *J* = 1.5 Hz, 1H, C*H*), 3.19 (dd, *J* = 10.0, 6.5 Hz, 1H, C*H*), 2.24 (s, 3H, CH_3), 1.58 (dd, *J* = 7.0, 1.5 Hz, 1H, C*H*), 1.20 (s, 3H, CH_3), 1.07 (s, 3H, CH_3). ^{1}**H-NMR** (300 MHz, $CDCl_3$): δ = 13.98 (bs, 1H, O*H*), 12.58 (bs, 1H, O*H*), 7.59 (s, 1H, Ar*H*), 7.17 (dd, *J* = 15.0, 10.5 Hz, 1H, CH_{sorbyl}), 6.08 (dq, *J* = 15.0, 7.0 Hz, 1H, CH_{sorbyl}), 5.93 (ddq, *J* = 15.0, 10.0, 1.5 Hz, 1H, C*H*), 5.53 (d, *J* = 15.0 Hz, 1H, CH_{sorbyl}), 5.45 (dq, *J* = 15.0, 6.5 Hz, 1H, CH_{sorbyl}), 5.02 (ddq, *J* = 15.0, 10.0, 1.5 Hz, 1H, C*H*), 4.28 (dd, *J* = 6.5, 1.5 Hz, 1H, C*H*), 3.32 (dd, *J* = 1.5 Hz, 1H, C*H*), 3.26 (dd, *J* = 10.0, 6.5 Hz, 1H, C*H*), 2.26 (s, 3H, CH_3), 2.12 (s, 3H, CH_3), 1.82 (dd, *J* = 7.0, 1.5 Hz, 3H, CH_3), 1.60 (dd, *J* = 6.5, 1.5 Hz, 3H, CH_3), 1.20 (s, 3H, CH_3), 1.16 (s, 3H, CH_3). ^{13}**C-NMR** (76 MHz, $CDCl_3$): δ = 211.5, 202.1, 198.0, 168.8, 161.9, 159.0, 142.4, 139.4, 130.8, 130.6, 129.0, 128.6, 117.2, 115.0, 112.0, 110.7, 106.8, 75.7, 63.2, 47.0, 46.7, 46.5, 24.3, 18.9, 17.8, 16.0, 10.0, 7.5. **IR**: *ν* 3450, 3020, 2960, 2920, 2850, 1730, 1627, 1606, 1562, 1380, 1166, 995 cm^{-1}. **HRMS** (EI) *m/z*: $[M]^+$ calcd for $C_{28}H_{32}O_7$ 480.2149, found 480.2132.[32]

Tetrahydrosorbiquinol (10b)



Tetrahydrosorbiquinol (**10b**)

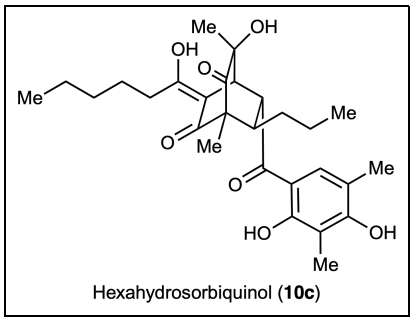
SMILES: O[C@@]1(C)[C@@H]2/C(C([C@@](C1=O)(C)[C@H](/C=C/C)[C@H]2C(C3=C(O)C(C)=C(O)C(C)=C3)=O)=O)=C(CCCCC)\O

Fungus of origin: This compound was never isolated from nature. It has been synthesized from sorbiquinol (**9a**).[32]

Total synthesis: Hydrogenation of sorbiquinol (**10a**) with excess 5% palladium on carbon in ethyl acetate at room temperature and pressure for 1 h.[32]

Analytics: **TLC**: R_f = 0.26 (2% EtOH in $CHCl_3$). **ORD**: $[\alpha]_D^{20}$ = +86.0 (c = 0.2, MeOH). **^{1}H-NMR** (300 MHz, $CDCl_3$): δ = 14.37 (bs, 1H, O*H*), 12.79 (bs, 1H, O*H*), 7.60 (s, 1H, Ar*H*), 5.44 (dq, *J* = 15.0, 7.0 Hz, 1H, C*H*), 4.99 (ddq, *J* = 15.0, 10.0, 1.5 Hz, 1H, C*H*), 4.27 (dd, *J* = 7.0, 1.5 Hz, 1H, C*H*), 3.247 (d, *J* = 1.5 Hz, 1H, C*H*), 3.245 (dd, *J* = 10.0, 6.5 Hz, 1H, C*H*), 2.87 (bs, 1H, O*H*), 2.26 (s, 3H, CH_3), 2.13 (s, 3H, CH_3), 1.96 (t, *J* = 8.0 Hz, 2H, CH_2), 1.60 (dd, *J* = 7.0, 1.5 Hz, 3H, CH_3), 1.45 (m, 2H, CH_2), 1.23 (s, 3H, CH_3), 1.16 (s, 3H, CH_3), 1.00 (m, 4H, CH_2), 0.78 (t, *J* = 7.5 Hz, 3H, CH_3). **^{13}C-NMR** (76 MHz, $CDCl_3$): δ = 211.4, 202.2, 196.9, 180.7, 162.0, 159.0, 130.5, 129.0, 127.2, 115.0, 111.9, 110.6, 106.3, 75.4, 62.6, 47.0 (2C), 46.5, 31.7, 31.5, 26.1, 24.3, 22.1, 17.8, 15.7, 13.9, 9.7, 7.5. **IR**: *ν* 3450, 2960, 2870, 2850, 1730, 1625, 1490, 1380, 1292, 1165, 1145 cm^{-1}. **HRMS** (EI) *m/z*: $[M]^+$ calcd for $C_{28}H_{36}O_7$ 484.2462, found 484.2460.[32]

Hexahydrosorbiquinol (10c)



Hexahydrosorbiquinol (**10c**)

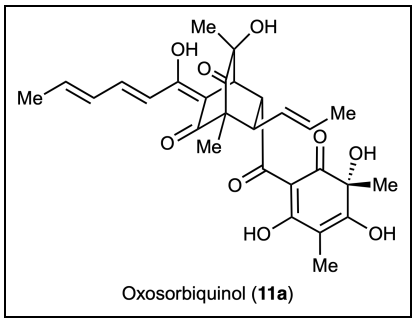
SMILES: O[C@@]1(C)[C@@H]2/C(C([C@@](C1=O)(C)[C@H](CCC)[C@H]2C(C3=C(O)C(C)=C(O)C(C)=C3)=O)=O)=C(CCCCC)\O

Fungus of origin: This compound was never isolated from nature. It has been synthesized from sorbiquinol (**10a**).[32]

Total synthesis: Hydrogenation of sorbiquinol (**9a**) with excess 5% palladium on carbon in ethyl acetate at room temperature and pressure for 48 h.[32]

Analytics: **TLC**: R_f = 0.25 (2% EtOH in $CHCl_3$). **ORD**: $[\alpha]_D^{20}$ = +117.0 (c = 0.4, MeOH). **^{1}H-NMR** (300 MHz, $CDCl_3$): δ = 14.38 (bs, 1H, O*H*), 12.84 (bs, 1H, O*H*), 7.64 (s, 1H, Ar*H*), 5.36 (bs, 1H, O*H*), 4.18 (dd, *J* = 7.0, 1.5 Hz, 1H, C*H*), 3.22 (d, *J* = 1.5 Hz, 1H, C*H*), 2.81 (bs, 1H, O*H*), 2.72 (m, 1H, C*H*), 2.27 (s, 3H, CH_3), 2.14 (s, 3H, CH_3), 1.94 (t, *J* = 7.0 Hz, 2H, CH_2), 1.47 (m, 2H, CH_2), 1.29 (s, 3H, CH_3), 1.21 (s, 3H, CH_3), 1.10 (m, 8H, CH_2), 0.79 (m, 6H, CH_3). **^{13}C-NMR** (76 MHz, $CDCl_3$): δ = 211.6, 202.9, 197.5, 180.4, 162.3, 159.0, 128.7, 115.2, 111.3, 110.8, 106.4, 75.4, 63.1, 46.9, 46.4, 42.7, 33.3, 32.7, 31.6, 26.1, 24.4, 21.1, 20.7, 16.0, 14.0, 13.8, 9.7, 7.5. **IR**: *ν* 3480, 2955, 2865, 1732, 1627, 1482, 1450, 1382, 1188, 757 cm^{-1}. **HRMS** (EI) *m/z*: $[M]^+$ calcd for $C_{28}H_{38}O_7$ 486.2618, found 486.2616.[32]

Oxosorbiquinol (11a)



Oxosorbiquinol (**11a**)

SMILES: O[C@@]1(C)[C@@H]2/C(C([C@@](C1=O)(C)[C@H](/C=C/C)[C@H]2C(C3=C(O)C(C)=C(O)[C@](O)(C)C3=O)=O)=O)=C(/C=C/C=C/C)O

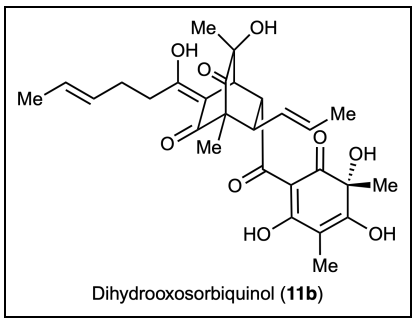
Fungus of origin: *Phialocephala* sp. FL30r[82].

Bioactivity: Cytotoxicity against leukemic P388 cells (IC_{50} = 29.9 μM), human lung cancer cell line A549 (IC_{50} = 104μM), leukemia cell line HL60 (IC_{50} = 8.90 μM), hepatocellular carcinoma cells BEL7402 (IC_{50} = 12.7 μM), lymphoblast cells K562 (IC_{50} = 56.3 μM).[82]

Biosynthesis: See figure S2F.

Analytics: Brown syrup. **ORD**: $[\alpha]_D^{20}$ = +255.0 (c = 0.1, MeOH). **^{1}H-NMR** (600 MHz, $CDCl_3$): δ = 18.50 (bs, 1H, O*H*), 14.00 (bs, 1H, O*H*), 7.22 (dd, *J* = 14.8, 10.3 Hz, 1H, CH_{sorbyl}), 6.14 (m, 1H, CH_{sorbyl}), 6.08 (m, 1H, CH_{sorbyl}), 5.81 (d, *J* = 14.8 Hz, 1H, CH_{sorbyl}), 5.41 (m, 1H, C*H*), 5.04 (dd, *J* = 14.8, 11.6 Hz, 1H, C*H*), 4.37 (d, *J* = 3.8 Hz, 1H, C*H*), 3.48 (s, 1H, C*H*), 3.19 (dd, *J* = 10.3, 5.8 Hz, 1H, C*H*), 1.85 (d, *J* =6.4 Hz, 3H, CH_3), 1.82 (s, 3H, CH_3), 1.60 (d, *J* =4.5 Hz, 3H, CH_3, 1.60 (s, 3H, CH_3), 1.26 (s, 3H, CH_3), 1.15 (s, 3H, CH_3). **^{13}C-NMR** (150 MHz, $CDCl_3$): δ = 210.6, 200.5, 198.1, 195.9, 190.0, 170.1, 168.6, 142.4, 140.0, 130.7, 130.1, 128.6, 117.2, 107.1, 104.4, 103.8, 75.8, 75.5, 63.3, 18.0, 47.2, 45.3, 30.5, 24.4, 18.8, 17.8, 10.1, 6.9. **IR**: *ν* 3421, 2929, 1730, 1670, 1631, 1605, 1560, 1454, 1382, 1247, 997 cm^{-1}. **HRMS** (ESI) *m/z*: $[M+H]^+$ calcd for $C_{28}H_{32}O_9$ 511.1968, found 511.1950.[82]

Dihydrooxosorbiquinol (11b)



Dihydrooxosorbiquinol (**11b**)

SMILES: O[C@@]1(C)[C@@H]2/C(C([C@@](C1=O)(C)[C@H](/C=C/C)[C@H]2C(C3=C(O)C(C)=C(O)[C@](O)(C)C3=O)=O)=O)=C(CC/C=C/C)\O

Fungus of origin: *Phialocephala* sp. FL30r[82].

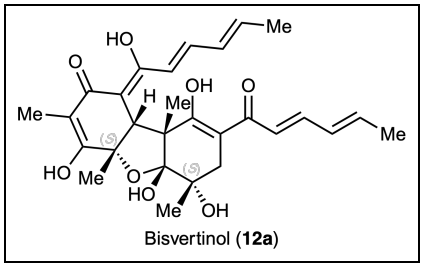
Bioactivity: Cytotoxicity against leukemic P388 cells ($IC_{50} = 40.3$ μM), human lung cancer cell line A549 ($IC_{50} = 97.6$ μM), leukemia cell line HL60 ($IC_{50} = 10.5$ μM), hepatocellular carcinoma cells BEL7402 ($IC_{50} = 31.8$ μM), lymphoblast cells K562 ($IC_{50} = 68.2$ μM).[82]

Biosynthesis: See figure S2F.

Analytics: Brown syrup. **ORD**: $[\alpha]_D^{20} = +94.0$ (c = 0.1, MeOH). ^{1}**H-NMR** (600 MHz, $CDCl_3$): δ = 18.80 (bs, 1H, O*H*), 14.50 (bs, 1H, O*H*), 5.35 (m, 1H, C*H*), 5.26 (m, 2H, C*H*), 5.02 (dd, *J* = 14.8, 10.8 Hz, 1H, C*H*), 4.32 (d, *J* = 3.2 Hz, 1H, C*H*), 3.43 (s, 1H, C*H*), 3.15 (dd, *J* = 10.8, 5.9 Hz, 1H, C*H*), 2.24 (m, 1H, CH_2), 2.15 (m, 2H, CH_2), 2.02 (m, 1H, CH_2), 1.86 (s, 3H, CH_3), 1.59 (d, *J* =6.0 Hz, 3H, CH_3), 1.58 (d, *J* =6.6 Hz, 3H, CH_3, 1.58 (s, 3H, CH_3), 1.28 (s, 3H, CH_3), 1.14 (s, 3H, CH_3). ^{13}**C-NMR** (150 MHz, $CDCl_3$): δ = 214.1, 200.5, 197.0, 196.0, 190.8, 180.0, 170.3, 130.1, 128.8, 128.4, 126.6, 106.9, 104.3, 99.9, 76.3, 75.5, 62.7, 47.8, 47.4, 45.8, 31.8, 30.7, 29.0, 24.6, 17.8, 17.7, 10.0, 6.9. **IR**: *ν* 3419, 2936, 1728, 1639, 1631, 1601, 1537, 1449, 1247, 968 cm^{-1}. **HRMS** (ESI) *m/z*: $[M+Na]^+$ calcd for $C_{28}H_{34}O_9Na$ 537.2101, found 537.2110.[82]

1.2.2 Dimeric Michael-type sorbicillinoids

Bisvertinol (12a) [CAS: 103804-06-4]



Bisvertinol (**12a**)

SMILES: OC1=C(C(/C=C/C=C/C)=O)C[C@@](O)(C)[C@@]2(O)[C@]1(C)[C@](/C(C(C(C)=C3O)=O)=C(\C=C\C=C\C)O)([H])[C@]3(C)O2

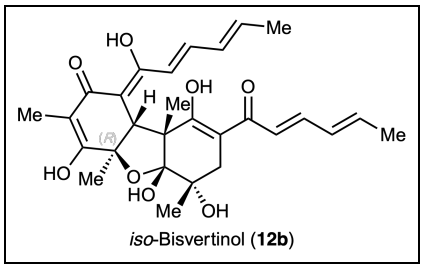
Fungus of origin: *Aspergillus* sp. FKI-1746[83], *Hypocrea jecorina* H[4], *Paecilomyces* sp. KMU21009[71], *Penicillium chrysogenum* sp.[8], *Trichoderma citrinoviride* DAOM 242931[60], *Trichoderma longibrachiatum* UAMH 4159[13], *Trichoderma reesei* HN-2016-018[84], *Trichoderma viride*[41], *Trichoderma* sp.[41,52], *Trichoderma* sp. FM652[53], *Trichoderma yunnanense* Ty10[85], *Verticillium intertextum*[22].

Bioactivity: Anti-inflammatory activity due to inhibition of nitric oxide formation in LPS-induced RAW264.7 cells ($IC_{50} = 9.9$ µM).[30]

Biosynthesis: See figure S3G.[22]

Analytics: Yellow-orange amorphous solid. **MP**: 139–141 °C. **TLC**: $R_f = 0.34$ ($CHCl_3$/EtOH = 94:16). **ORD**: $[\alpha]_D^{20} = -1467.0$. ^{1}**H-NMR** (360 MHz, CD_3OD): δ = 7.27 (dd, *J* = 15.0, 11.0 Hz, 1H, C*H*$_{sorbyl}$), 7.23 (dd, *J* = 15.0, 11.0 Hz, 1H, C*H*$_{sorbyl}$), 6.48 (d, *J* = 15.0 Hz, 1H, C*H*$_{sorbyl}$), 6.40 (m, 4H, C*H*$_{sorbyl}$), 6.30 (d, *J* = 15.0 Hz, 1H, C*H*$_{sorbyl}$), 3.63 (s, 1H, C*H*), 2.72 (d, *J* = 14.5 Hz, 1H, C*H*$_2$), 2.43 (d, *J* = 14.5 Hz, 1H, C*H*$_2$), 1.85 (m, 6H, C*H*$_3$), 1.44 (s, 3H, C*H*$_3$), 1.41 (s, 3H, C*H*$_3$), 1.27 (s, 3H, C*H*$_3$), 1.20 (s, 3H, C*H*$_3$). ^{13}**C-NMR** (25.2 MHz, CD_3OD): δ = 194.4, 193.0, 178.6, 168.9, 168.0, 143.0, 140.4, 139.1, 137.2, 132.2, 132.0, 121.4 (2C), 110.2, 107.0, 105.8, 102.3, 80.2, 74.0, 60.2, 54.6, 36.2, 25.8, 22.7, 20.0, 19.1, 18.9, 7.2.[22]

***iso*-Bisvertinol (12b)**



iso-Bisvertinol (**12b**)

SMILES: OC1=C(C(/C=C/C=C/C)=O)C[C@@](O)(C)[C@@]2(O)[C@]1(C)[C@](/C(C(C(C)=C3O)=O)=C(\C=C\C=C\C)O)([H])[C@@]3(C)O2

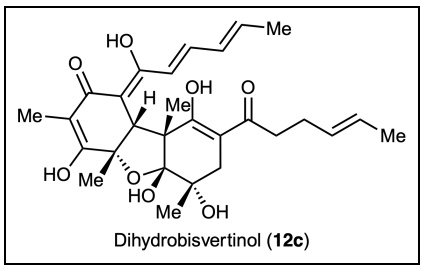
Fungus of origin: *Aspergillus* sp. FKI-1746[83],

Bioactivity: Inhibitory effect on lipid droplet accumulation in mouse macrophages.[83]

Biosynthesis: See figure S2G.

Analytics: Yellow amorphous solid. **ORD**: $[\alpha]_D^{26} = -400.8$ (c = 0.01, MeOH). ^{1}**H-NMR** (300 MHz, CD_3OD): δ = 7.24 (dd, 1H, C*H*$_{sorbyl}$), 7.05 (dd, 1H, C*H*$_{sorbyl}$), 6.40 (m, 2H, C*H*$_{sorbyl}$), 6.16 (m, 1H, C*H*$_{sorbyl}$), 6.05 (m, 2H, C*H*$_{sorbyl}$), 5.78 (d, 1H, C*H*$_{sorbyl}$), 3.19 (s, 1H, C*H*), 2.86 (d, 1H, C*H*$_2$), 2.63 (d, 1H, C*H*$_2$), 1.89 (d, 3H, C*H*$_3$), 1.82 (d, 3H, C*H*$_3$), 1.72 (s, 3H, C*H*$_3$), 1.42 (s, 3H, C*H*$_3$), 1.39 (s, 3H, C*H*$_3$), 1.06 (s, 3H, C*H*$_3$). ^{13}**C-NMR** (75 MHz, CD_3OD): δ = 206.3, 193.0, 170.8, 170.3, 170.1, 140.7, 139.2, 138.5, 137.0, 132.9, 132.5, 122.0, 121.3, 110.6, 109.6, 104.6, 102.0, 81.6, 73.7, 62.8, 55.8, 33.8, 25.4, 22.8, 18.9, 18.8, 14.7, 7.5. **IR**: *ν* 3415, 2981, 2937, 2837, 2873, 1675, 1621, 1554 cm^{-1}. **HRMS** (FAB) *m/z*: $[M+H]^+$ calcd for $C_{28}H_{34}O_8$ 499.2332, found 499.2331.[83]

Dihydrobisvertinol (12c) [Trichobisvertinol A, CAS: 2450413-08-6]



Dihydrobisvertinol (**12c**)

SMILES: OC1=C(C(CC/C=C/C)=O)C[C@@](O)(C)[C@@]2(O)[C@]1(C)[C@](/C(C(C(C)=C3O)=O)=C(\C=C\C=C\C)O)([H])[C@]3(C)O2

Fungus of origin: *Aspergillus* sp. FKI-1746[83], *Penicillium chrysogenum* DM815[29], *Verticillium intertextum*[22].

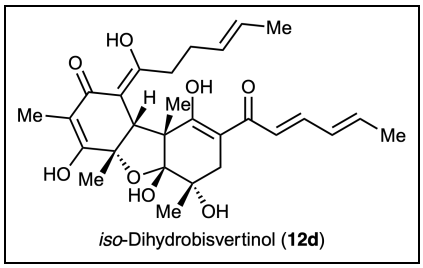
Bioactivity: Evaluation of inhibition of lipid droplet accumulation in macrophages displayed no activity.[83]

Biosynthesis: See figure S3G.[22]

Analytics: Yellow amorphous solid. **MP**: 104–107 °C. **TLC**: $R_f = 0.35$ ($CHCl_3$/EtOH = 94:16). **ORD**: $[\alpha]_D^{20} = -652.0$. ^{1}**H-NMR** (200 MHz, $CDCl_3$): δ = 16.27 (bs, 1H, O*H*), 16.05 (bs, 1H, O*H*), 7.50 (bs, 1H, O*H*), 7.29 (dd, *J* = 15.0, 11.0 Hz, 1H, C*H*$_{sorbyl}$), 6.42 (d, *J* = 15.0 Hz, 1H, C*H*$_{sorbyl}$), 6.31 (dd, *J* = 15.0, 11.0 Hz, 1H, C*H*$_{sorbyl}$), 6.10 (dq, *J* = 15.0, 6.0 Hz, 1H, C*H*$_{sorbyl}$), 5.50 (m, 2H, C*H*), 4.18 (bs, 1H, O*H*), 3.67 (s, 1H, C*H*), 3.20 (bs, 1H, O*H*), 2.50 (m, 2H, C*H*$_2$), 2.71 (d, *J* = 14.5 Hz, 1H, C*H*$_2$), 2.50 (m, 1H, C*H*$_2$), 2.30 (m, 2H, C*H*$_2$), 1.88 (d, *J* = 6.0 Hz, 3H, C*H*$_3$), 1.64 (d, *J* = 4.7 Hz, 3H, C*H*$_3$), 1.56 (s, 3H, C*H*$_3$), 1.49 (s, 3H, C*H*$_3$), 1.35 (s, 3H, C*H*$_3$), 1.29 (s, 3H, C*H*$_3$), ^{13}**C-NMR** (25.2 MHz, $CDCl_3$): δ = 199.3, 191.8, 181.0, 167.8, 166.8, 138.7, 137.2, 130.8, 129.0, 126.0, 120.0, 108.8, 105.5, 103.5, 100.8, 79.2, 73.8, 56.3, 52.8, 36.9,

35.7, 27.4, 25.2, 22.1, 18.9, 18.5, 18.0, 7.0. **IR**: *v* 3540, 3450-3100, 2980, 2920, 2850, 1710, 1670, 1615, 1555 cm^{-1}.[22]

iso-Dihydrobisvertinol (12d)


iso-Dihydrobisvertinol (**12d**)

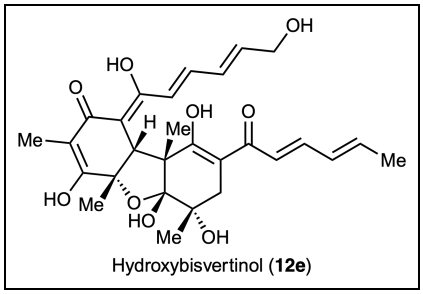
SMILES: OC1=C(C(/C=C/C=C/C)=O)C[C@@](O)(C)[C@@]2(O)[C@]1(C)[C@](/C(C(C(C)=C3O)=O)=C(CC/C=C/C)/O)([H])[C@]3(C)O2

Fungus of origin: *Verticillium intertextum*[22].

Biosynthesis: See figure S3G.[22]

Analytics: Yellow amorphous solid. **MP**: 106-109 °C. **TLC**: R_f = 0.38 ($CHCl_3$/EtOH = 94:16). **ORD**: $[\alpha]_D^{20} = -543.0$. ^{1}**H-NMR** (200 MHz, $CDCl_3$): δ = 16.83 (bs, 1H, O*H*), 16.28 (bs, 1H, O*H*), 8.46 (bs, 1H, O*H*), 7.30 (m, 1H, CH_{sorbyl}), 6.25 (m, 3H, CH_{sorbyl}), 5.45 (m, 2H, C*H*), 4.50 (bs, 1H, O*H*), 3.84 (bs, 1H, O*H*), 3.58 (s, 1H, C*H*), 2.83 (d, *J* = 14.0 Hz, 1H, CH_2), 2.62 (d, *J* = 14.0 Hz, 1H, CH_2), 2.55 (m, 4H, CH_2), 1.85 (m, 3H, CH_3), 1.62 (d, *J* = 4.4 Hz, 3H, CH_3), 1.52 (s, 3H, CH_3), 1.48 (s, 3H, CH_3), 1.37 (s, 3H, CH_3), 1.32 (s, 3H, CH_3). ^{13}**C-NMR** (25.2 MHz, $CDCl_3$): δ = 192.5, 191.5, 178.9, 177.6, 166.2, 142.7, 140.2, 130.8, 129.3, 126.2, 120.2, 109.2, 105.9, 104.1, 99.9, 79.7, 73.8, 58.3, 54.2, 35.5, 32.7, 29.9, 25.3, 22.4, 19.3, 19.0, 18.1, 6.9. **IR**: *v* 3550, 3450-3100, 2980, 2930, 2880, 2860, 1713, 1600, 1640, 1606, 1570, 1540 cm^{-1}.[22]

Hydroxybisvertinol (12e) [Saturnispol B]


Hydroxybisvertinol (**12e**)

SMILES: OC1=C(C(/C=C/C=C/C)=O)C[C@@](O)(C)[C@@]2(O)[C@]1(C)[C@](/C(C(C(C)=C3O)=O)=C(\C=C\C=C\CO)O)([H])[C@]3(C)O2

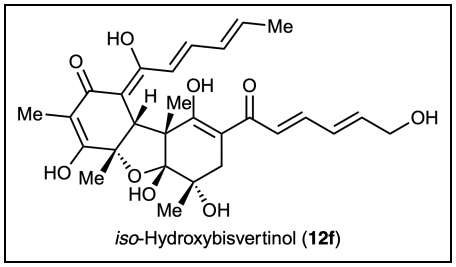
Fungus of origin: *Trichoderma reesei* 4670[30,84], *Trichoderma saturnisporum* DI-IA[62].

Bioactivity: Anti-inflammatory activity due to inhibition of nitric oxide formation in LPS-induced RAW264.7 cells (IC_{50} = 6.1 μM).[30] Weak antimicrobial activities against *Staphylococcus aureus*, vancomycin-resistant *enterococci* (VRE), *Bacillus subtilis*, *Pseudomonas aeruginosa*, and *Klebsiella pneumoniae*.[62]

Biosynthesis: See figure S3G.

Analytics: **ORD**: $[\alpha]_D^{20} = -377.0$ (c = 0.1, MeOH). ^{1}**H-NMR** (400 MHz, CD_3OD): δ = 7.27 (dd, *J* = 14.7, 11.2 Hz, 1H, CH_{sorbyl}), 7.19 (dd, *J* = 14.7, 11.2 Hz, 1H, CH_{sorbyl}), 6.54 (m, 1H, CH_{sorbyl}), 6.49 (d, *J* = 14.7 Hz, 1H, CH_{sorbyl}), 6.42 (d, *J* = 14.7 Hz, 1H, CH_{sorbyl}), 6.35 (m, 1H, CH_{sorbyl}), 6.26 (dd, *J* = 14.7, 4.3 Hz, 1H, CH_{sorbyl}), 6.11 (dq, *J* = 14.7, 6.6 Hz, 1H, CH_{sorbyl}), 4.22 (d, *J* = 4.3 Hz, 2H, CH_2OH), 3.65 (s, 1H, C*H*), 2.74 (d, *J* = 14.5 Hz, 1H, CH_2), 2.46 (d, *J* = 14.5 Hz, 1H, CH_2), 1.87 (d, *J* = 6.6 Hz, 3H, CH_3), 1.43 (s, 3H, CH_3), 1.41 (s, 3H, CH_3), 1.28 (s, 3H, CH_3), 1.21 (s, 3H, CH_3). ^{13}**C-NMR** (100 MHz, CD_3OD): δ = 195.3, 193.5, 178.7, 169.1, 168.6, 143.2, 142.3, 139.4, 137.3, 132.5, 129.7, 123.6, 121.8, 110.7, 107.3, 106.5, 102.6, 80.6, 74.3, 62.9, 60.6, 55.1, 36.5, 25.8, 22.8, 20.1, 18.7, 7.1. **IR**: *v* 3739, 3390, 3265, 2933, 1711, 1612, 1556, 1361, 1027 cm^{-1}. **HRMS** (ESI) *m/z*: $[M-H]^-$ calcd for $C_{28}H_{33}O_9$ 513.2130, found 513.2136.[84]

***iso*-Hydroxybisvertinol (12f)**


iso-Hydroxybisvertinol (**12f**)

SMILES: OC1=C(C(/C=C/C=C/CO)=O)C[C@@](O)(C)[C@@]2(O)[C@]1(C)[C@](/C(C(C(C)=C3O)=O)=C(\C=C\C=C\C)O)([H])[C@]3(C)O2

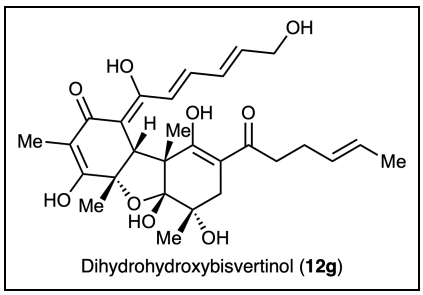
Fungus of origin: *Trichoderma reesei* 4670[84].

Bioactivity: Cytotoxicity was analysed in five different cancer cell lins: A549, HepG2, HCT 116, HeLa, MCF-7.[84]

Biosynthesis: See figure S3G.

Analytics: Yellow, amorphous powder. **ORD**: $[\alpha]_D^{20} = -380.0$ (c = 0.03, MeOH). ^{1}**H-NMR** (400 MHz, CD_3OD): δ = 7.24 (m, 2H, CH_{sorbyl}), 6.62 (d, *J* = 14.8 Hz, 1H, CH_{sorbyl}), 6.53 (m, 1H, CH_{sorbyl}), 6.44 (m, 1H, CH_{sorbyl}), 6.31 (m, 1H, CH_{sorbyl}), 6.20 (m, 2H, CH_{sorbyl}), 4.22 (d, *J* = 4.0 Hz, 2H, CH_2OH), 3.66 (t, *J* = 3.2 Hz, 1H, C*H*), 2.73 (dd, *J* = 14.4, 6.8 Hz, 1H, CH_2), 2.46 (dd, *J* = 14.4, 6.0 Hz, 1H, CH_2), 1.89 (d, *J* = 6.4 Hz, 3H, CH_3), 1.44 (s, 3H, CH_3), 1.42 (s, 3H, CH_3), 1.28 (s, 3H, CH_3), 1.21 (s, 3H, CH_3). ^{13}**C-NMR** (100 MHz, CD_3OD): δ = 194.1, 193.5, 179.8, 169.4, 167.8, 143.5, 140.6, 140.0, 138.3, 132.2, 130.3, 123.8, 121.8, 110.7, 107.3, 106.1, 103.1, 80.5, 74.2, 63.0, 60.4, 54.9, 36.5, 25.8, 22.7, 20.0, 18.9, 7.1. **IR**: *v* 3741, 3383, 3261, 2927, 1701, 1616, 1549, 1348, 1014 cm^{-1}. **HRMS** (ESI) *m/z*: $[M-H]^-$ calcd for $C_{28}H_{33}O_9$ 513.2130, found 513.2132.[30]

Dihydrohydroxybisvertinol (12g) [Trichobisvertinol B]



Dihydrohydroxybisvertinol (**12g**)

SMILES: OC1=C(C(CC/C=C/C)=O)C[C@@](O)(C)[C@@]2(O)[C@]1(C)[C@](/C(C(C(C)=C3O)=O)=C(\C=C\C=C\CO)O)([H])[C@]3(C)O2

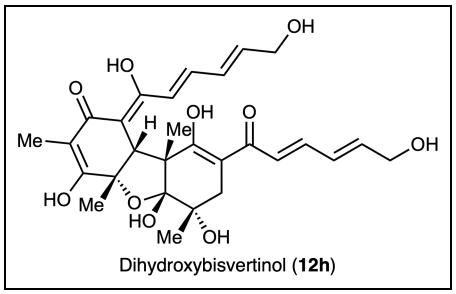
Fungus of origin: *Trichoderma reesei* 4670[30].

Bioactivity: Anti-inflammatory activity due to inhibition of nitric oxide formation in LPS-induced RAW264.7 cells ($IC_{50} = 22.0$ μM).[30]

Biosynthesis: See figure S3G.

Analytics: Yellow, amorphous powder. **ORD**: $[\alpha]_D^{20} = -470.0$ (c = 0.4, MeOH). **^{1}H-NMR** (400 MHz, CD_3OD): δ = 7.22 (dd, *J* = 14.8, 10.8 Hz, 1H, C*H*$_{sorbyl}$), 6.61 (d, *J* = 14.8 Hz, 1H, C*H*$_{sorbyl}$), 6.53 (m, 1H, C*H*$_{sorbyl}$), 6.17 (dt, *J* = 15.2, 5.2 Hz, 1H, C*H*$_{sorbyl}$), 5.50 (m, 2H, C*H*), 4.21 (d, *J* = 4.3 Hz, 2H, C*H*$_2$OH), 3.67 (s, 1H, C*H*), 2.67 (d, *J* = 14.4 Hz, 1H, C*H*$_2$), 2.46 (m, 2H, C*H*$_2$), 2.38 (d, *J* = 14.4 Hz, 1H, C*H*$_2$), 2.24 (m, 2H, C*H*$_2$), 1.65 (d, *J* = 4.8 Hz, 3H, C*H*$_3$), 1.46 (s, 3H, C*H*$_3$), 1.45 (s, 3H, C*H*$_3$), 1.30 (s, 3H, C*H*$_3$), 1.21 (s, 3H, C*H*$_3$). **^{13}C-NMR** (100 MHz, CD_3OD): δ = 201.2, 193.6, 182.0, 167.4 (2C), 139.9, 138.2, 130.9, 130.4, 126.9, 123.9, 109.8, 107.1, 105.6, 103.1, 80.3, 74.1, 63.0, 58.1, 54.3, 38.3, 37.0, 28.6, 26.0, 22.6, 19.2, 18.1, 7.3. **IR**: *ν* 3359, 2926, 1616, 1564, 1346, 1213, 1082, 1022 cm^{-1}. **HRMS** (ESI) *m/z*: $[M-H]^-$ calcd for $C_{28}H_{35}O_9$ 515.2287, found 515.2284.[30]

Dihydroxybisvertinol (12h) [Saturnispol A]



Dihydroxybisvertinol (**12h**)

SMILES: OC1=C(C(/C=C/C=C/CO)=O)C[C@@](O)(C)[C@@]2(O)[C@]1(C)[C@](/C(C(C(C)=C3O)=O)=C(\C=C\C=C\CO)O)([H])[C@]3(C)O2

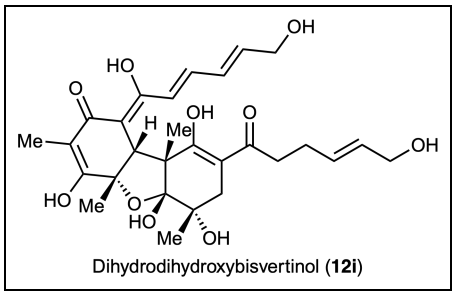
Fungus of origin: *Trichoderma reesei* 4670[30].

Bioactivity: Anti-inflammatory activity due to inhibition of nitric oxide formation in LPS-induced RAW264.7 cells ($IC_{50} > 50.0$ μM).[30]

Biosynthesis: See figure S3G.

Analytics: Yellow, amorphous powder. **ORD**: $[\alpha]_D^{20} = -310.0$ (c = 0.1, MeOH). **^{1}H-NMR** (400 MHz, CD_3OD): δ = 7.26 (m, 1H, C*H*$_{sorbyl}$), 7.19 (m, 1H, C*H*$_{sorbyl}$), 6.59 (d, *J* = 14.8 Hz, 1H, C*H*$_{sorbyl}$), 6.50 (m, 2H, C*H*$_{sorbyl}$), 6.39 (d, *J* = 14.8 Hz, 1H, C*H*$_{sorbyl}$), 6.24 (dt, *J* = 15.2, 4.8 Hz, 1H, C*H*$_{sorbyl}$), 6.15 (dt, *J* = 15.2, 4.8 Hz, 1H, C*H*$_{sorbyl}$), 4.19 (m, 4H, C*H*$_2$OH), 3.63 (s, 1H, C*H*), 2.71 (d, *J* = 14.4 Hz, 1H, C*H*$_2$), 2.43 (d, *J* = 14.4 Hz, 1H, C*H*$_2$), 1.41 (s, 3H, C*H*$_3$), 1.39 (s, 3H, C*H*$_3$), 1.25 (s, 3H, C*H*$_3$), 1.17 (s, 3H, C*H*$_3$). **^{13}C-NMR** (100 MHz, CD_3OD): δ = 195.1, 193.3, 178.7, 169.8, 167.8, 143.1, 142.3, 140.0, 138.3, 130.3, 129.6, 123.7, 123.6, 110.7, 107.3, 106.4, 103.1, 80.6, 74.2, 63.0 (2C), 60.5, 55.0, 36.4, 25.8, 22.7, 20.1, 7.1. **IR**: *ν* 3439, 2926, 1626, 1444, 1084, 881, 575, 478 cm^{-1}. **HRMS** (ESI) *m/z*: $[M-H]^-$ calcd for $C_{28}H_{33}O_{10}$ 529.2068, found 529.2085.[30]

Dihydrodihydroxybisvertinol (12i) [Trichobisvertinol C]



Dihydrodihydroxybisvertinol (**12i**)

SMILES: OC1=C(C(CC/C=C/CO)=O)C[C@@](O)(C)[C@@]2(O)[C@]1(C)[C@](/C(C(C(C)=C3O)=O)=C(\C=C\C=C\CO)O)([H])[C@]3(C)O2

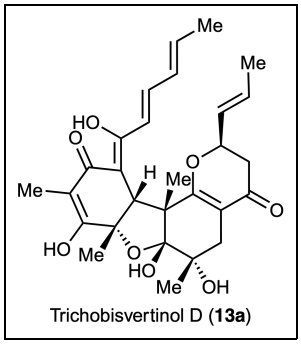
Fungus of origin: *Trichoderma reesei* 4670[30].

Bioactivity: Anti-inflammatory activity due to inhibition of nitric oxide formation in LPS-induced RAW264.7 cells ($IC_{50} = 24.0$ μM).[30]

Biosynthesis: See figure S3G.

Analytics: Yellow, amorphous powder. **ORD**: $[\alpha]_D^{20} = -380.0$ (c = 0.2, MeOH). **^{1}H-NMR** (400 MHz, CD_3OD): δ = 7.24 (dd, *J* = 14.8, 10.8 Hz, 1H, C*H*$_{sorbyl}$), 6.62 (d, *J* = 14.8 Hz, 1H, C*H*$_{sorbyl}$), 6.54 (m, 1H, C*H*$_{sorbyl}$), 6.18 (dt, *J* = 15.2, 5.2 Hz, 1H, C*H*$_{sorbyl}$), 5.70 (m, 2H, C*H*), 4.22 (d, *J* = 4.4 Hz, 2H, C*H*$_2$OH), 4.02 (d, *J* = 5.2 Hz, 2H, C*H*$_2$OH), 3.69 (s, 1H, C*H*), 2.68 (d, *J* = 14.4 Hz, 1H, C*H*$_2$), 2.52 (m, 2H, C*H*$_2$), 2.40 (d, *J* = 14.4 Hz, 1H, C*H*$_2$), 2.31 (m, 2H, C*H*$_2$), 1.47 (s, 3H, C*H*$_3$), 1.46 (s, 3H, C*H*$_3$), 1.30 (s, 3H, C*H*$_3$), 1.22 (s, 3H, C*H*$_3$). **^{13}C-NMR** (100 MHz, CD_3OD): δ = 201.1, 193.5, 181.7, 170.1, 167.4, 139.9, 138.2, 131.6, 131.3, 130.3, 123.9, 109.7, 107.0, 105.6, 103.1, 80.3, 74.1, 63.5, 63.0, 58.0, 54.3, 37.9, 37.0, 28.1, 26.0, 22.6, 19.2, 7.3. **IR**: *ν* 3430, 2922, 1695, 1622, 1456, 1365, 1070, 884, 701, 484 cm^{-1}. **HRMS** (ESI) *m/z*: $[M+H]^+$ calcd for $C_{28}H_{37}O_{10}$ 533.2381, found 533.2380.[30]

Trichobisvertinol D (13a) [Ustisorbicillinol A]



Trichobisvertinol D (**13a**)

<u>*SMILES*</u>: O[C@]1(C)[C@@]2(O)[C@@]([C@](/C(C(C(C)=C3O)=O)=C(O)\C=C\C=C\C)([H])[C@]3(C)O2)(C)C(O[C@@H](/C=C/C)CC4=O)=C4C1

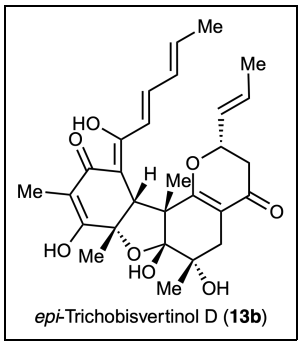
<u>*Fungus of origin*</u>: *Trichoderma reesei* 4670[30], *Ustilaginoidea virens*[86].

<u>*Bioactivity*</u>: Anti-inflammatory activity due to inhibition of nitric oxide formation in LPS-induced RAW264.7 cells ($IC_{50} = 22.0$ μM).[30]

<u>*Biosynthesis*</u>: See figure S3G.

<u>*Analytics*</u>: Yellow, amorphous powder. **ORD**: $[\alpha]_D^{20} = -150.0$ (c = 0.3, MeOH), $[\alpha]_D^{25} = -356.0$ (c = 0.1, MeOH). ^{1}**H-NMR** (400 MHz, CD_3OD): δ = 7.14 (dd, *J* = 14.8, 10.8 Hz, 1H, C*H*$_{sorbyl}$), 6.45 (d, *J* = 14.8 Hz, 1H, C*H*$_{sorbyl}$), 6.32 (m, 1H, C*H*$_{sorbyl}$), 6.07 (m, 1H, C*H*$_{sorbyl}$), 5.79 (m, 1H, C*H*), 5.47 (ddd, *J* = 15.6, 6.1, 1.6 Hz, 1H, C*H*), 4.26 (m, 1H, C*H*), 3.67 (s, 1H, C*H*), 2.54 (d, *J* = 15.2 Hz, 1H, CH_2), 2.44 (dd, *J* = 16.8, 13.2 Hz, 1H, CH_2), 2.32 (dd, *J* = 16.8, 4.0 Hz, 1H, CH_2), 2.26 (d, *J* = 15.2 Hz, 1H, CH_2), 1.85 (d, *J* = 6.7 Hz, 3H, CH_3), 1.72 (d, *J* = 6.4 Hz, 3H, CH_3), 1.61 (s, 3H, CH_3), 1.45 (s, 3H, CH_3), 1.31 (s, 3H, CH_3), 1.10 (s, 3H, CH_3). ^{13}**C-NMR** (100 MHz, CD_3OD): δ = 193.7 (2C), 172.1 (2C), 168.0, 139.1, 137.2, 132.5, 131.7, 128.6, 122.0, 110.1, 108.6, 107.5, 102.8, 80.3, 79.2, 74.4, 57.7, 53.9, 41.1, 33.1, 26.6, 22.2, 19.7, 18.7, 18.0, 7.8. **IR**: *ν* 3406, 2929, 1724, 1599, 1450, 1406, 1379, 1346 cm^{-1}. **HRMS** (ESI) *m/z*: $[M-H]^-$ calcd for $C_{28}H_{33}O_8$ 497.2181, found 497.2182.[30,86]

***epi*-Trichobisvertinol D (13b)** [Ustisorbicillinol B]



epi-Trichobisvertinol D (**13b**)

<u>*SMILES*</u>: O[C@]1(C)[C@@]2(O)[C@@]([C@](/C(C(C(C)=C3O)=O)=C(O)\C=C\C=C\C)([H])[C@]3(C)O2)(C)C(O[C@@H](/C=C/C)CC4=O)=C4C1

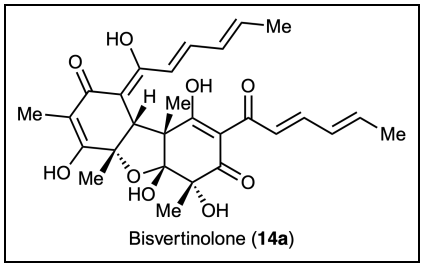
<u>*Fungus of origin*</u>: *Trichoderma reesei* 4670[30], *Ustilaginoidea virens*[86].

<u>*Bioactivity*</u>: Anti-inflammatory activity due to inhibition of nitric oxide formation in LPS-induced RAW264.7 cells ($IC_{50} = 32.0$ μM).[30]

<u>*Biosynthesis*</u>: See figure S3G.

<u>*Analytics*</u>: Yellow, amorphous powder. **ORD**: $[\alpha]_D^{20} = -130.0$ (c = 0.2, MeOH), $[\alpha]_D^{25} = -188.0$ (c = 0.1, MeOH). ^{1}**H-NMR** (400 MHz, CD_3OD): δ = 7.18 (dd, *J* = 14.8, 10.8 Hz, 1H, C*H*$_{sorbyl}$), 6.47 (d, *J* = 14.8 Hz, 1H, C*H*$_{sorbyl}$), 6.34 (m, 1H, C*H*$_{sorbyl}$), 6.10 (m, 1H, C*H*$_{sorbyl}$), 5.79 (m, 1H, C*H*), 5.47 (ddd, *J* = 15.6, 6.4, 2.0 Hz, 1H, C*H*), 4.58 (m, 1H, C*H*), 3.70 (s, 1H, C*H*), 2.49 (d, *J* = 16.0 Hz, 1H, CH_2), 2.31 (d, *J* = 16.0 Hz, 1H, CH_2), 2.24 (dd, *J* = 16.8, 3.6 Hz, 1H, CH_2), 2.14 (dd, *J* = 16.8, 14.8 Hz, 1H, CH_2), 1.88 (d, *J* = 6.8 Hz, 3H, CH_3), 1.75 (d, *J* = 6.4 Hz, 3H, CH_3), 1.60 (s, 3H, CH_3), 1.47 (s, 3H, CH_3), 1.31 (s, 3H, CH_3), 1.19 (s, 3H, CH_3). ^{13}**C-NMR** (100 MHz, CD_3OD): δ = 194.3 (2C), 171.6 (2C), 168.2, 139.3, 137.3, 132.5, 130.7, 129.2, 121.9, 110.2, 108.7, 107.7, 102.7, 80.6, 80.2, 74.1, 57.8, 53.9, 42.3, 34.2, 26.6, 22.6, 19.0, 18.7, 17.9, 7.8. **IR**: *ν* 3406, 2929,1724, 1599, 1450, 1406, 1379, 1346 cm^{-1}. **HRMS** (ESI) *m/z*: $[M-H]^-$ calcd for $C_{28}H_{33}O_8$ 497.2181, found 497.2185.[30,86]

Bisvertinolone (14a)



Bisvertinolone (**14a**)

<u>*SMILES*</u>: OC([C@]([C@](/C(C(C(C)=C1O)=O)=C(\C=C\C=C\C)O)([H])[C@]1(C)O2)(C)[C@]2(O)[C@]3(O)C)=C(C(/C=C/C=C/C)=O)C3=O

<u>*Fungus of origin*</u>: *Acremonium citrinum* SS-g13[70], *Acremonium strictum*[87], *Penicillium chrysogenum* E01-10/3[6], *Penicillium chrysogenum* sp.[8], *Penicillium citrinum* SpI080624G1f01[72], *Penicillium notatum*[28], *Trichoderma longibrachiatum* UAMH 4159[13], *Trichoderma* sp. f-13[16], *Trichoderma* sp. JH8[88], *Trichoderma* sp. USF-2690[33,66], *Verticillium intertextum*[22].

<u>*Bioactivity*</u>: Cytotoxicity against leukemic HL-60 cell line (IC_{50} =5.3 μM).[16] Inhibitory effect on β-1,6-glucan biosynthesis.[72]

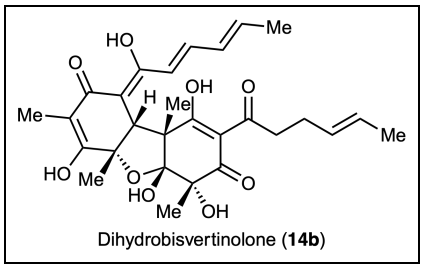
<u>*Biosynthesis*</u>: See figure S3H.

<u>*Total synthesis*</u>: Bisvertinolone (**14a**) has been synthesized chemo-enzymatically using the heterologous expressed monooxygenase SorbC together with sorbicillin (**1a**) and oxosorbicillinol (**4a**) (20% yield).[42] space0.5ex

<u>*Analytics*</u>: Yellow rosettes. **MP**: 156–158 °C. **TLC**: R_f = 0.29 ($CHCl_3$/EtOH = 94:16). **ORD**: $[\alpha]_D^{20} = -1046.0$. ^{1}**H-NMR** (200 MHz, $CDCl_3$): δ = 17.71 (bs, 1H, O*H*), 16.35 (bs, 1H, O*H*), 7.58 (dd, *J* = 15.0, 10.0 Hz, 1H, C*H*$_{sorbyl}$), 7.41 (d, *J* = 15.0 Hz, 1H, C*H*$_{sorbyl}$), 7.33 (dd, *J* = 15.0, 11.0 Hz, 1H, C*H*$_{sorbyl}$), 6.40 (d, *J* = 15.0 Hz, 1H, C*H*$_{sorbyl}$), 6.32 (m, 3H, C*H*$_{sorbyl}$), 6.19 (bs, 1H, O*H*), 6.13 (dq,

J = 15.0, 7.0 Hz, 1H, CH_{sorbyl}), 4.51 (bs, 1H, OH), 4.12 (bs, 1H, OH), 3.75 (s, 1H, CH), 1.92 (d, J = 5.0 Hz, 3H, CH_3), 1.88 (dd, J = 7.0, 1.0 Hz, 3H, CH_3), 1.49 (s, 3H, CH_3), 1.47 (s, 3H, CH_3), 1.45 (s, 3H, CH_3), 1.38 (s, 3H, CH_3). ^{13}**C-NMR** (25.2 MHz, $CDCl_3$): δ = 199.6, 196.2, 191.0, 185.5, 169.9, 163.8, 148.1, 143.8, 139.4, 137.3, 131.3, 130.8, 121.8, 119.9, 110.7, 107.1, 103.9, 99.8, 79.8, 79.2, 59.8, 54.4, 25.7, 22.9, 19.1, 18.7, 18.5, 7.0. **IR**: ν 3430, 3030, 2930, 2855, 1738, 1670, 1605, 1565, 1515 cm^{-1}.[22]

Dihydrobisvertinolone (14b) [16,17-Dihydrobisvertinolone]


Dihydrobisvertinolone (**14b**)

SMILES: OC([C@]([C@](/C(C(C(C)=C1O)=O)=C(\C=C\C=C\C)O)([H])[C@]1(C)O2)(C)[C@]2(O)[C@]3(O)C)=C(C(CC/C=C/C)=O)C3=O

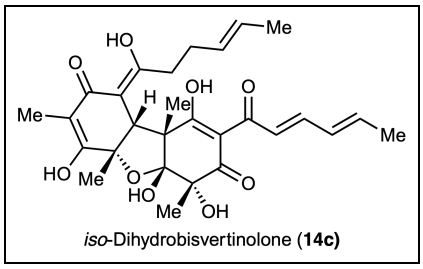
Fungus of origin: *Acremonium citrinum* SS-g13[70], *Penicillium chrysogenum* sp.[8], *Penicillium terrestre*[89].

Bioactivity: Cytotoxicity against leukemic P388 cells (IC_{50} = 1.70 μM), and human lung cancer cell line A549 (IC_{50} = 520 nM).[89]

Biosynthesis: See figure S3H.

Analytics: Yellowish, amorphous powder. **MP**: 115–119 °C. **ORD**: $[\alpha]_D^{20}$ = −668.0 (c = 0.2, MeOH). ^{1}**H-NMR** (600 MHz, $CDCl_3$): δ = 18.21 (bs, 1H, OH), 16.32 (bs, 1H, OH), 7.33 (dd, J = 14.9, 11.1 Hz, 1H, CH_{sorbyl}), 6.98 (bs, 1H, OH), 6.39 (d, J = 14.8 Hz, 1H, CH_{sorbyl}), 6.29 (m, 1H, CH_{sorbyl}), 6.15 (dq, J = 14.8, 6.6 Hz, 1H, CH_{sorbyl}), 5.50 (m, 1H, CH), 5.46 (m, 1H, CH), 4.80 (bs, 1H, OH), 4.64 (bs, 1H, OH), 3.81 (s, 1H, CH), 3.06 (m, 1H, CH_2), 2.89 (m, 1H, CH_2), 2.35 (m, 1H, CH_2), 2.24 (m, 1H, CH_2), 1.88 (d, J = 6.6 Hz, 3H, CH_3), 1.63 (d, J = 5.8 Hz, 3H, CH_3), 1.52 (s, 6H, CH_3), 1.49 (s, 3H, CH_3), 1.41 (s, 3H, CH_3). ^{13}**C-NMR** (150 MHz, $CDCl_3$): δ = 202.8, 197.4, 196.3, 191.1, 170.3, 163.7, 139.8, 137.8, 130.9, 129.0, 126.4, 119.8, 110.6, 108.2, 104.0, 99.5, 79.9, 78.9, 58.7, 54.2, 38.8, 28.0, 25.7, 23.1, 18.8, 18.2, 17.9, 7.0. **IR**: ν 3425, 2986, 2938, 1670, 1616, 1555, 1445, 1412, 1378, 1347, 1205, 1025, 992, 968, 942 cm^{-1}. **HRMS** (ESI) m/z: $[M+H]^+$ calcd for $C_{28}H_{35}O_9$ 515.2281, found 515.2283.[89]

***iso*-Dihydrobisvertinolone (14c)** [10,11-Dihydrobisvertinolone]


iso-Dihydrobisvertinolone (**14c**)

SMILES: OC([C@]([C@](/C(C(C(C)=C1O)=O)=C(CC/C=C/C)/O)([H])[C@]1(C)O2)(C)[C@]2(O)[C@]3(O)C)=C(C(/C=C/C=C/C)=O)C3=O

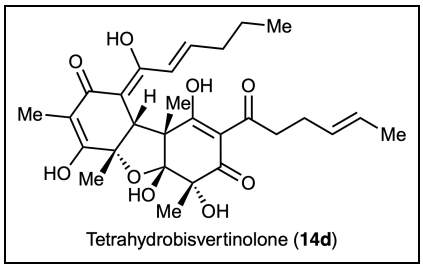
Fungus of origin: *Trichoderma* sp. f-13[16].

Bioactivity: Cytotoxicity against leukemic HL-60 cell line (IC_{50} = 49.0 μM).[16]

Biosynthesis: See figure S3H.

Analytics: **ORD**: $[\alpha]_D^{20}$ = −340.0 (c = 0.3, MeOH). ^{1}**H-NMR** (600 MHz, $CDCl_3$): δ = 17.75 (bs, 1H, OH), 16.66 (bs, 1H, OH), 7.59 (dd, J = 14.8, 9.9 Hz, 1H, CH_{sorbyl}), 7.40 (d, J = 14.8 Hz, 1H, CH_{sorbyl}), 6.35 (m, 2H, CH_{sorbyl}), 5.50 (m, 2H, CH), 3.67 (s, 1H, CH), 2.64 (m, 1H, CH_2), 2.49 (m, 1H, CH_2), 2.40 (m, 2H, CH_2), 1.92 (d, J = 4.9 Hz, 3H, CH_3), 1.63 (d, J = 5.5 Hz, 3H, CH_3), 1.51 (s, 3H, CH_3), 1.49 (s, 3H, CH_3), 1.44 (s, 3H, CH_3), 1.40 (s, 3H, CH_3). ^{13}**C-NMR** (150 MHz, $CDCl_3$): δ = 200.5, 197.1, 191.1, 186.2, 181.0, 164.2, 149.0, 144.8, 131.9, 129.9, 127.1, 122.4, 110.7, 107.7, 104.6, 99.6, 80.5, 79.6, 60.1, 55.5, 33.5, 30.3, 25.9, 23.6, 19.8, 19.2, 18.5, 7.5. **IR**: ν 3420, 2935, 1670, 1601, 1547, 1448, 1379, 1345, 1212, 1100, 1154, 1026 cm^{-1}. **HRMS** (ESI) m/z: $[M+H]^+$ calcd for $C_{28}H_{35}O_9$ 515.2281, found 515.2265.[16]

Tetrahydrobisvertinolone (14d)


Tetrahydrobisvertinolone (**14d**)

SMILES: OC([C@]([C@](/C(C(C(C)=C1O)=O)=C(\C=C\CCC)O)([H])[C@]1(C)O2)(C)[C@]2(O)[C@]3(O)C)=C(C(CC/C=C/C)=O)C3=O

Fungus of origin: *Acremonium citrinum* SS-g13[70], *Penicillium chrysogenum* sp.[8], *Penicillium terrestre*[89].

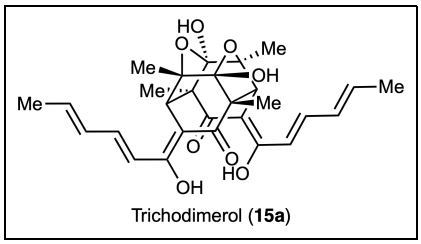
Bioactivity: Cytotoxicity against leukemic P388 cells (IC_{50} > 100 μM), and human lung cancer cell line A549 (IC_{50} = 16.7 μM).[89]

Biosynthesis: See figure S3H.

Analytics: Yellowish, amorphous powder. **MP**: 82–87 °C. **ORD**: $[\alpha]_D^{20}$ = −371.0 (c = 0.4, MeOH). ^{1}**H-NMR** (600 MHz, $CDCl_3$): δ = 18.20 (bs, 1H, OH), 16.64 (bs, 1H, OH), 5.50 (m, 2H, CH), 5.47 (m, 2H, CH), 3.71 (s, 1H, CH), 3.05 (m, 1H, CH_2), 2.89 (m, 1H, CH_2), 2.64 (m, 1H, CH_2), 2.49 (m, 1H, CH_2), 2.41

(m, 2H, CH_2), 2.34 (m, 1H, CH_2), 2.24 (m, 1H, CH_2), 1.64(dd, J = 7.0, 1.6 Hz, 6H, CH_3), 1.50 (s, 6H, CH_3), 1.48 (s, 3H, CH_3), 1.40 (s, 3H, CH_3). ^{13}**C-NMR** (150 MHz, $CDCl_3$): δ = 202.7, 197.5, 196.3, 190.4, 180.4, 163.5, 129.3, 129.1, 126.5, 126.4, 109.8, 108.2, 104.0, 98.8, 79.9, 78.8, 58.4, 54.8, 38.7, 32.9, 29.7, 28.0, 25.4, 23.1, 18.2, 17.9, 17.8, 6.9. **IR**: ν 3417, 2992, 2935, 1670, 1598, 1446, 1378, 1343, 1210, 1025, 966, 933 cm^{-1}. **HRMS** (ESI) m/z: $[M+Na]^+$ calcd for $C_{28}H_{36}O_9Na$ 539.2257, found 539.2214.[89]

Trichodimerol (15a) [CAS: 1027091-95-7]



Trichodimerol (**15a**)

SMILES: O=C1[C@]2(C)[C@](O3)(O)[C@@]4(C)O[C@@]([C@]5(C)C4/C1=C(\C=C\C=C\C)O)(O)[C@]3(C)C2/C(C5=O)=C(O)\C=C\C=C\C

Fungus of origin: *Acremonium* sp. AN-13[1], *Clonostachys rosea* YRS-06[2], *Paecilomyces* sp. KMU21009[71], *Penicillium chrysogenum* DM815[29], *Penicillium chrysogenum* V39673[90,91], *Penicillium chrysogenum* sp.[8], *Penicillium citrinum* SpI080624G1f01[72], *Penicillium terrestre*[92], *Trichoderma citrinoviride* ITEM 4484[75], *Trichoderma longibrachiatum* UAMH 4159[13], *Trichoderma* sp.[41,52,77], *Trichoderma* sp. f-13[16], *Trichoderma* sp. JH8[88], *Trichoderma* sp. USF-2690[33,66], *Trichoderma viride*[41], *Trichothecium* sp.[19], unidentified fungus B00853[93].

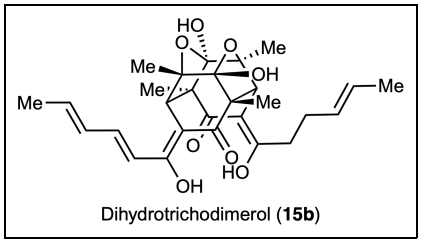
Bioactivity: Cytotoxicity against leukemic P388 cells (IC_{50} = 0.33 μM), and human lung cancer cell line A549 (IC_{50} = 4.70 μM).[92] Inhibition of bacterial endotoxin-induced production of tumor necrosis factor (TNF-α) in murine macrophages and human peripheral blood monocytes.[91]

Biosynthesis: See figure S3I.[33]

Total synthesis: The racemic version can be synthesized by using acetyl-protected sorbicillin and lead(IV) acetate [CAS: 546-67-8] leading to *rac*-sorbicillinol (**2a**) which spontaneously dimerizes to trichodimerol (**14aa**).[25] Trichodimerol (**15a**) has been synthesized chemo-enzymatically using the heterologous expressed monooxygenase SorbC together with sorbicillin (**1a**) (27% yield).[26]

Analytics: Yellowish crystals. **MP**: 235–238 °C. **TLC**: R_f = 0.73 ($CHCl_3$/acetone = 3:1). **ORD**: $[\alpha]_D^{20}$ = −410.5 (c = 0.4, MeOH), $[\alpha]_D$ = −376.0 (c = 0.3, MeOH). ^{1}**H-NMR** (600 MHz, acetone-d_6): δ = 16.60 (bs, 2H, OH), 7.26 (dd, J = 14.7, 11.4 Hz, 2H, CH_{sorbyl}), 6.45 (d, J = 14.7 Hz, 2H, CH_{sorbyl}), 6.40 (m, 2H, CH_{sorbyl}), 6.24 (dq, J = 15.0, 6.6 Hz, 2H, CH_{sorbyl}), 5.66 (bs, 2H, OH), 3.14 (s, 2H, CH), 1.86 (d, J = 6.6 Hz, 6H, CH_3), 1.41 (s, 6H, CH_3), 1.34 (s, 6H, CH_3). ^{1}**H-NMR** (360 MHz, $CDCl_3$): δ = 16.33 (bs, 2H, OH), 7.32 (dd, J = 15.5, 10.0 Hz, 2H, CH), 6.23 (m, 6H, CH), 3.20 (bs, 2H, OH), 3.00 (s, 2H, CH), 1.89 (d, J = 6.5 Hz, 6H, CH_3), 1.46 (s, 6H, CH_3), 1.43 (s, 6H, CH_3). ^{1}**H-NMR** (360 MHz, C_6D_6): δ = 17.14 (bs, 2H, OH), 7.38 (dd, J = 14.5, 11.0 Hz, 2H, CH_{sorbyl}), 6.25 (d, J = 15.0 Hz, 2H, CH_{sorbyl}), 5.88 (ddq, J = 15.0, 11.0, 1.5 Hz, 2H, CH_{sorbyl}), 5.55 (dq, J = 15.0, 7.0 Hz, 2H, CH_{sorbyl}), 3.35 (s, 2H, OH), 3.12 (s, 2H, CH), 1.54 (s, 6H, CH_3), 1.46 (s, 6H, CH_3), 1.42 (dd, J = 7.0, 1.6 Hz, 6H, CH_3). ^{13}**C-NMR** (150 MHz, acetone-d_6): δ = 201.0 (2C), 176.1 (2C), 143.3 (2C), 140.2 (2C), 131.9 (2C), 120.3 (2C), 105.2 (2C), 104.5 (2C), 79.6 (2C), 60.4 (2C), 58.1 (2C), 21.8 (2C), 19.7 (2C), 18.8 (2C). ^{13}**C-NMR** (75.5 MHz, $CDCl_3$): δ = 197.9 (2C), 176.0 (2C), 143.6 (2C), 140.3 (2C), 131.0 (2C), 118.6 (2C), 104.1 (2C), 102.8 (2C), 78.9 (2C), 58.9 (2C), 57.6 (2C), 21.3 (2C), 18.9 (2C), 18.7 (2C). **IR**: ν 3441, 2983, 2939, 1613, 1547, 1414, 1300, 1264, 1160, 1126, 940 cm^{-1}. **HRMS** (EI) m/z: $[M]^+$ calcd for $C_{28}H_{32}O_8$ 496.2098, found 496.2090.[13,92]

Dihydrotrichodimerol (15b)



Dihydrotrichodimerol (**15b**)

SMILES: O=C1[C@]2(C)[C@](O3)(O)[C@@]4(C)O[C@@]([C@]5(C)C4/C1=C(\C=C\C=C\C)O)(O)[C@]3(C)C2/C(C5=O)=C(O)\CC/C=C/C

Fungus of origin: *Acremonium* sp. AN-13[1], *Clonostachys rosea* YRS-06[2], *Penicillium chrysogenum* DM815[29], *Penicillium terrestre*[92], *Trichoderma citrinoviride* ITEM 4484[75,76], *Trichoderma* sp. f-13[16], unidentified fungus B00853[93].

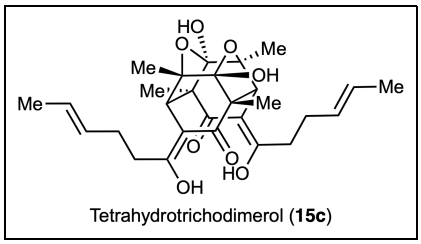
Bioactivity: Cytotoxicity against leukemic P388 cells (IC_{50} = 2.80 μM), and human lung cancer cell line A549 (IC_{50} = 2.10μM).[92] **Cytotoxity** against human glioblastoma U373 cells (IC_{50} = 25.0 μM), adenocarcinomic human alveolar basal epithelial A549 cells (IC_{50} = 33.0 μM), malignant melanoma SKMEL-28 cells (IC_{50} = 33.0 μM), human esophageal squamous cell carcinoma OE21 cells (IC_{50} = 28.0 μM), glioma Hs683 cells (IC_{50} = 34.0 μM), and mouse melanoma B16F10 cell line (IC_{50} = 3.00 μM).[76]

Biosynthesis: See figure S3I.

Analytics: Yellowish powder. **MP**: 112–117 °C. **ORD**: $[\alpha]_D^{20}$ = +60.0 (c = 0.2, MeOH). ^{1}**H-NMR** (600 MHz, acetone-d_6): δ = 16.80 (bs, 1H, OH), 16.60 (bs, 1H, OH), 7.28 (dd, J = 15.1, 11.0 Hz, 1H, CH_{sorbyl}), 6.46 (d, J = 14.7 Hz, 1H, CH_{sorbyl}), 6.40 (m, 1H, CH_{sorbyl}), 6.23 (dq, J = 15.1, 6.9 Hz, 1H, CH_{sorbyl}), 5.49 (m, 1H, CH), 5.46 (m, 1H, CH), 3.14 (s, 1H, CH), 3.03 (s, 1H, CH), 2.56 (dt, J = 15.1, 7.8 Hz, 1H, CH_2), 2.40 (dt, J = 15.1, 6.9 Hz, 1H, CH_2), 2.25 (m, 1H, CH), 1.85 (dd, J = 6.9, 1.4 Hz, 3H, CH_3), 1.61 (d, J = 4.4 Hz, 3H,

CH_3), 1.41 (s, 3H, CH_3), 1.39 (s, 3H, CH_3), 1.36 (s, 3H, CH_3), 1.34 (s, 3H, CH_3). ^{13}**C-NMR** (150 MHz, acetone-d_6): δ = 201.9, 193.1, 192.7, 174.5, 143.2, 140.1, 131.9, 130.5, 126.5, 120.1, 105.1, 105.0, 104.7, 104.5, 79.6, 79.5, 60.4, 58.9, 58.6, 58.3, 35.2, 29.0, 21.9 (2C), 20.1, 19.6, 18.8, 18.0. **IR**: *ν* 3441, 2984, 2940, 1612, 1261, 1127, 992 cm^{-1}. **HRMS** (ESI) *m/z*: $[M+Na]^+$ calcd for $C_{28}H_{34}O_8Na$ 521.2151, found 521.2122.[92]

Tetrahydrotrichodimerol (15c)



Tetrahydrotrichodimerol (**15c**)

SMILES: O=C1[C@]2(C)[C@](O3)(O)[C@@]4(C)O[C@@]([C@]5(C)C4/C1=C(CC/C=C/C)/O)(O)[C@]3(C)C2/C(C5=O)=C(O)\CC/C=C/C

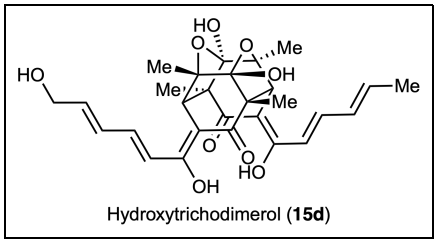
Fungus of origin: *Acremonium* sp. AN-13[1], *Clonostachys rosea* YRS-06[2], *Penicillium chrysogenum* DM815[29], *Penicillium* sp. SCSIO06871[51], *Penicillium terrestre*[92].

Bioactivity: Cytotoxicity against leukemic P388 cells (IC_{50} = 8.80 μM), and human lung cancer cell line A549 (IC_{50} = 4.30 μM).[92] Antibacterial against *Staphylococcus aureus* ATCC 6538 (MIC= 128 μg/mL).[1]

Biosynthesis: See figure S3I.

Analytics: Yellowish powder. **MP**: 40–50 °C. **ORD**: $[\alpha]_D^{20}$ = +190.3 (c = 0.2, MeOH). ^{1}**H-NMR** (600 MHz, acetone-d_6): δ = 16.61 (bs, 1H, O*H*), 5.49 (m, 2H, C*H*), 5.45 (m, 2H, C*H*), 3.02 (s, 2H, C*H*), 2.57 (dt, *J* = 15.4, 7.7 Hz, 2H, CH_2), 2.41 (dt, *J* = 14.9, 7.4 Hz, 2H, CH_2), 2.25 (m, 4H, CH_2), 1.61 (d, *J* = 5.0 Hz, 6H, CH_3), 1.38 (s, 6H, CH_3), 1.35 (s, 6H, CH_3). ^{13}**C-NMR** (150 MHz, acetone-d_6): δ = 193.8 (2C), 192.3 (2C), 130.4 (2C), 126.5 (2C), 105.0 (2C), 104.8 (2C), 79.5 (2C), 58.7 (4C), 35.1 (2C), 29.0 (2C), 21.9 (2C), 19.9 (2C), 18.0 (2C). **IR**: *ν* 3428, 2984, 2940, 1595, 1451, 1378, 1261, 1127, 1011, 965, 874 cm^{-1}. **HRMS** (ESI) *m/z*: $[M+Na]^+$ calcd for $C_{28}H_{36}O_8Na$ 523.2308, found 523.2292.[92]

Hydroxytrichodimerol (15d) [24-Hydroxytrichodimerol]



Hydroxytrichodimerol (**15d**)

SMILES: O=C1[C@]2(C)[C@](O3)(O)[C@@]4(C)O[C@@]([C@]5(C)C4/C1=C(\C=C\C=C\CO)O)(O)[C@]3(C)C2/C(C5=O)=C(O)\C=C\C=C\C

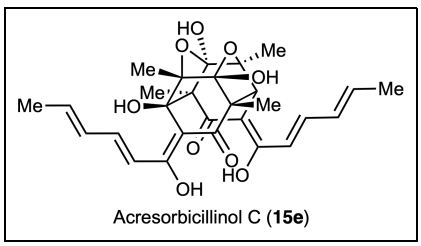
Fungus of origin: *Trichoderma reesei* HN-2016-018[84].

Bioactivity: Cytotoxic activity against human lung cancer cell line A549 (IC_{50} = 5.10 μM), human breast cancer cell line MCF-7 (IC_{50} = 9.50 μM), colon cancer HCT 116 cell lines (IC_{50} = 13.7 μM), and human umbilical vein endothelial cells (HUVEC, IC_{50} > 40.0 μM).[84]

Biosynthesis: See figure S3I.

Analytics: Yellow, amorphous powder. **ORD**: $[\alpha]_D^{25}$ = −405.6 (c = 0.1, MeOH). ^{1}**H-NMR** (600 MHz, CD_3OD): δ = 7.33 (dd, *J* = 14.7, 11.3 Hz, 1H, CH_{sorbyl}), 7.28 (dd, *J* = 14.7, 11.1 Hz, 1H, CH_{sorbyl}), 6.56 (dd, *J* = 14.7, 11.3 Hz, 1H, CH_{sorbyl}), 6.43 (d, *J* = 14.7 Hz, 1H, CH_{sorbyl}), 6.37 (m, 1H, CH_{sorbyl}), 6.31 (d, *J* = 14.7 Hz, 1H, CH_{sorbyl}), 6.27 (dt, *J* = 14.7, 4.4 Hz, 1H, CH_{sorbyl}), 6.21 (dd, *J* = 14.7, 6.6 Hz, 1H, CH_{sorbyl}), 4.22 (d, *J* = 4.4 Hz, 2H, CH_2OH), 3.09 (s, 1H, C*H*), 3.08 (s, 1H, C*H*), 1.89 (d, *J* = 6.6 Hz, 3H, CH_3), 1.37 (s, 6H, CH_3), 1.35 (s, 6H, CH_3). ^{13}**C-NMR** (150 MHz, CD_3OD): δ = 201.9, 201.3, 175.9, 175.2, 144.2, 143.4, 143.1, 140.8, 132.3, 129.7, 122.1, 120.2, 105.8 (2C), 105.0, 104.6, 80.4 (2C), 62.9, 61.1, 61.0, 58.7 (2C), 21.8 (2C), 19.8 (2C), 18.9. **IR**: *ν* 3435, 2979, 2933, 1615, 1297, 1178, 1121 cm^{-1}. **HRMS** (ESI) *m/z*: $[M+H]^+$ calcd for $C_{28}H_{33}O_9$ 513.2130, found 513.2129.[84]

Acresorbicillinol C (15e)



Acresorbicillinol C (**15e**)

SMILES: O=C1[C@]2(C)[C@](O3)(O)[C@@]4(C)O[C@@]([C@]5(C)[C@]4(O)/C1=C(\C=C\C=C\C)O)(O)[C@]3(C)C2/C(C5=O)=C(O)\C=C\C=C\C

Fungus of origin: *Acremonium chrysogenum* C10[48,94].

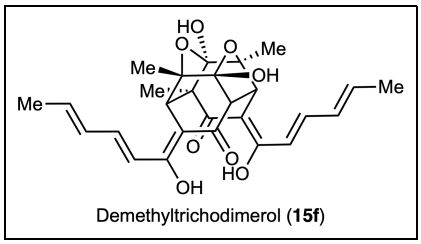
Bioactivity: Strong DPPH-radical scavenging activity (IC_{50} = 11.5 − 60.3 μM). **Antifungal** against *Cryptococcus neoformans* (IC_{50} = 69.1 μM).[94]

Biosynthesis: MSee figure S3I.[48]

Analytics: Bright yellow solid. **ORD**: $[\alpha]_D^{25}$ = −1048.0 (c = 0.1, MeOH). ^{1}**H-NMR** (500 MHz, $CDCl_3$/DMSO-d_6 = 3:1): δ = 7.48 (dd, *J* = 14.6, 10.9 Hz, 1H, CH_{sorbyl}), 7.38 (d, *J* = 14.6 Hz, 1H, CH_{sorbyl}), 7.12 (dd, *J* = 14.6, 10.9 Hz, 1H, CH_{sorbyl}), 6.49 (d, *J* = 14.6 Hz, 1H, CH_{sorbyl}), 6.42 (overlapping, 1H, CH_{sorbyl}), 6.38 (dd, *J* = 14.6, 10.9 Hz, 1H, CH_{sorbyl}), 6.38 (dd, *J* = 14.6, 10.9 Hz, 1H, CH_{sorbyl}), 6.10 (dd, *J* = 14.6, 6.8 Hz, 1H, CH_{sorbyl}), 3.69 (s,

1H, C*H*), 1.89 (d, *J* = 6.8 Hz, 3H, CH_3), 1.83 (d, *J* = 6.8 Hz, 3H, CH_3), 1.31 (s, 3H, CH_3), 1.30 (s, 3H, CH_3), 1.29 (s, 3H, CH_3), 1.19 (s, 3H, CH_3). ^{13}**C-NMR** (125 MHz, $CDCl_3$/DMSO-d_6 = 3:1): δ = 199.3, 190.9, 185.2, 167.9, 146.5, 143.4, 137.8, 136.2, 131.1 (2C), 122.4, 120.6, 108.0, 107.8, 103.5, 100.6, 78.7, 78.3, 78.2, 59.2, 59.2, 53.9, 25.2, 22.2, 18.8 (2C), 18.4, 18.3. **IR**: *ν* 3420, 1664, 1606, 1556, 1412, 1347, 1209 cm^{-1}. **HRMS** (ESI) *m/z*: $[M+H]^+$ calcd for $C_{28}H_{33}O_9$ 513.2119, found 513.2119.[48,94]

Demethyltrichodimerol (15f)



Demethyltrichodimerol (**15f**)

SMILES: O=C1C2[C@](O3)(O)[C@@]4(C)O[C@@]([C@]5(C)C4/C1=C(\C=C\C=C\C)O)(O)[C@]3(C)C2/C(C5=O)=C(O)\C=C\C=C\C

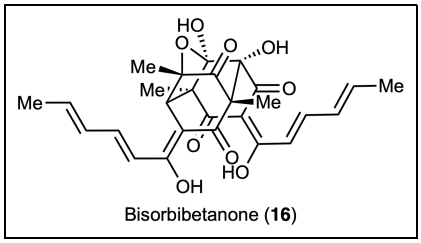
Fungus of origin: *Trichoderma* sp. USF-2690[66], *Villosiclava virens* albino strain LN02[67].

Bioactivity: DPPH-radical scavenging activity (IC_{50} = 42.4 μM).[66]

Biosynthesis: See figure S3I.

Analytics: Yellowish,amorphous powder. **ORD**: $[\alpha]_D^{28}$ = −278.5 (c = 2.0, MeOH). ^{1}**H-NMR** (400 MHz, C_6D_6/CD_3OD = 9:1): δ = 16.93 (bs, 1H, O*H*), 16.51 (bs, 1H, O*H*), 7.38 (dd, *J* = 14.4, 11.2 Hz, 1H, CH_{sorbyl}), 7.37 (dd, *J* = 14.4, 11.2 Hz, 1H, CH_{sorbyl}), 6.40 (d, *J* = 14.4 Hz, 1H, CH_{sorbyl}), 6.31 (d, *J* = 14.4 Hz, 1H, CH_{sorbyl}), 6.09 (dd, *J* = 14.8, 11.2 Hz, 1H, CH_{sorbyl}), 5.98 (dd, *J* = 13.6, 11.2 Hz, 1H, CH_{sorbyl}), 5.70 (m, 2H, CH_{sorbyl}), 3.81 (d, *J* = 12.6 Hz, 1H, C*H*), 3.55 (d, *J* = 12.6 Hz, 1H, C*H*), 3.19 (s, 1H, C*H*), 1.77 (s, 3H, CH_3), 1.60 (s, 6H, CH_3), 1.54 (d, *J* = 6.2 Hz, 3H, CH_3), 1.50 (d, *J* = 6.8 Hz, 3H, CH_3). ^{13}**C-NMR** (100 MHz, C_6D_6/CD_3OD = 9:1): δ = 200.1, 198.5, 175.8, 175.1, 144.3, 143.6, 140.3, 139.6, 131.6, 131.3, 119.5, 119.1, 105.3, 104.6 (2C), 103.6, 81.5, 79.7, 61.6, 60.3, 59.4, 48.2, 21.0 (2C), 20.2, 18.6 (2C). **IR**: *ν* 3420, 1620, 1580, 1420, 1310, 1130, 1000 cm^{-1}. **HRMS** (FAB) *m/z*: $[M+H]^+$ calcd for $C_{27}H_{32}O_8$ 483.2019, found 483.2033.[66].

Bisorbibetanone (16)



Bisorbibetanone (**16**)

SMILES: O=C([C@@]1(C)O2)[C@@]([C@]([C@@]2(O)[C@]3(C)C1/C4=C(\C=C\C=C\C)O)(O)C(/C(C3=O)=C(O)\C=C\C=C\C)=O)(C)C4=O

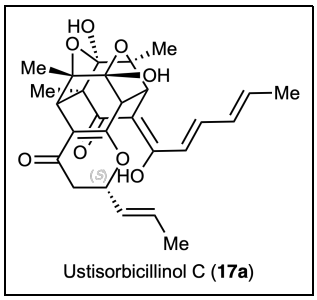
Fungus of origin: *Trichoderma* sp. USF-2690[33,95].

Bioactivity: DPPH-radical scavenging activity (ED_{50} = 62.5 μM).[95]

Biosynthesis: See figure S3J.

Analytics: Yellowish, amorphous powder. **ORD**: $[\alpha]_D^{26}$ = −561.0 (c = 0.1, MeOH). ^{1}**H-NMR** (400 MHz, $CDCl_3$): δ = 18.51 (bs, 1H, O*H*), 14.88 (bs, 1H, O*H*), 7.65 (dd, *J* = 16.0, 10.4 Hz, 1H, CH_{sorbyl}), 7.38 (dd, *J* = 14.8, 11.2 Hz, 1H, CH_{sorbyl}), 7.27 (d, *J* = 16.0 Hz, 1H, CH_{sorbyl}), 6.40 (dd, *J* = 15.2, 11.2 Hz, 1H, CH_{sorbyl}), 6.27 (dq, *J* = 15.2, 6.4 Hz, 1H, CH_{sorbyl}), 6.11 (d, *J* = 14.8 Hz, 1H, CH_{sorbyl}), 6.30 (m, 2H, CH_{sorbyl}), 4.88 (bs, 1H, O*H*), 4.47 (bs, 1H, O*H*), 3.34 (s, 1H, C*H*), 1.98 (d, *J* = 5.2 Hz, 3H, CH_3), 1.97 (d, *J* = 6.4 Hz, 3H, CH_3), 1.71 (s, 3H, CH_3), 1.58 (s, 3H, CH_3), 1.29 (s, 3H, CH_3). ^{13}**C-NMR** (100 MHz, $CDCl_3$): δ = 200.4, 197.3, 195.2, 189.9, 188.0, 173.0, 149.8, 145.0, 144.6, 141.4, 131.4, 130.9, 121.9, 117.9, 108.9, 106.2, 103.4, 84.8, 79.2, 67.1, 57.5, 53.1, 19.1, 19.0, 18.9, 18.1, 8.6. **IR**: *ν* 3430, 1750, 1605, 1550, 1395, 1245, 1000 cm^{-1}. **HRMS** (FAB) *m/z*: $[M+H]^+$ calcd for $C_{27}H_{29}O_9$ 497.1812, found 497.1890.[95]

Ustisorbicillinol C (17a)



Ustisorbicillinol C (**17a**)

SMILES: OC(/C=C/C=C/C)=C(C1[C@@]2(C)[C@@]3(O)[C@]4(C)C5C6=C(O[C@H](/C=C/C)CC6=O)C1[C@](O2)(O)[C@@]5(C)O3)\C4=O

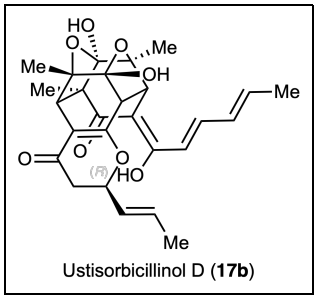
Fungus of origin: *Ustilaginoidea virens*[86].

Biosynthesis: See figure S3J.

Analytics: Yellow amorphous powder. **ORD**: $[\alpha]_D^{25}$ = +28.0 (c = 0.1, MeOH). ^{1}**H-NMR** (600 MHz, CD_3COCD_3): δ = 7.28 (dd, *J* = 14.8, 10.9 Hz, 1H, CH_{sorbyl}), 6.56 (d, *J* = 14.8 Hz, 1H, CH_{sorbyl}), 6.38 (m, 1H, CH_{sorbyl}), 6.25 (dq, *J* = 15.1, 6.8 Hz, 1H, CH_{sorbyl}), 5.76 (dqd, *J* = 15.2, 6.6, 1.0 Hz, 1H, C*H*), 5.43 (ddq, *J* = 15.2, 7.3, 1.7 Hz, 1H, C*H*), 4.93 (m, 1H, C*H*), 3.67 (d, *J* = 12.0 Hz, 1H, C*H*), 3.12 (s, 1H, C*H*), 3.00 (d, *J* = 12.0 Hz, 1H, C*H*), 2.58 (dd, *J* = 16.7, 4.8 Hz, 1H, CH_2), 2.18 (dd, *J* = 16.7, 8.7 Hz, 1H, CH_2), 1.87 (dd, *J* = 6.8, 1.6 Hz, 3H, CH_3), 1.65 (ddd, *J* = 6.6, 1.7, 0.7 Hz, 3H, CH_3), 1.35 (s, 3H, CH_3), 1.31 (s, 3H, CH_3), 1.27 (s, 3H, CH_3). ^{13}**C-NMR** (150 MHz, CD_3COCD_3): δ = 202.2, 188.3, 174.2, 170.8, 142.6, 139.5, 132.0, 131.4, 128.3, 120.7, 109.1, 105.3, 105.1, 104.9, 81.3, 80.2, 79.0, 60.4, 55.7, 55.4, 48.6, 41.1, 21.5, 20.9, 20.1, 18.8, 17.9. **IR**: *ν*

3726, 3421, 2922, 2852, 1734, 1717, 1695, 1653, 1617, 1576, 1455, 1442, 1384, 1306, 1199, 1131, 1019, 913, 840, 667, 579 cm^{-1}. **HRMS** (ESI) *m/z*: $[M+H]^+$ calcd for $C_{27}H_{31}O_8$ 483.2013, found 483.2006.[86]

Ustisorbicillinol D (17b)



Ustisorbicillinol D (**17b**)

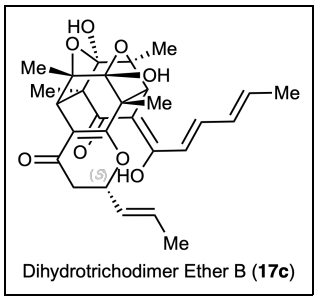
SMILES: OC(/C=C/C=C/C)=C(C1[C@@]2(C)[C@@]3(O)[C@]4(C)C5C6=C(O[C@@H](/C=C/C)CC6=O)C1[C@](O2)(O)[C@@]5(C)O3)\C4=O

Fungus of origin: *Ustilaginoidea virens*[86].

Biosynthesis: See figure S3J.

Analytics: Yellow amorphous powder. **ORD**: $[\alpha]_D^{25} = -32.0$ (c = 0.1, MeOH). ^{1}**H-NMR** (600 MHz, CD_3COCD_3): δ = 7.29 (dd, *J* = 14.8, 10.9Hz, 1H, C*H*$_{sorbyl}$), 6.53 (d, *J* = 14.8 Hz, 1H, C*H*$_{sorbyl}$), 6.36 (m, 1H, C*H*$_{sorbyl}$), 6.26 (dq, *J* = 15.0, 6.8 Hz, 1H, C*H*$_{sorbyl}$), 5.73 (dqd, *J* = 15.0, 6.6, 1.0 Hz, 1H, C*H*), 5.57 (ddq, *J* = 15.0, 7.0, 1.7 Hz, 1H, C*H*), 4.38 (ddd, *J* = 13.4, 7.0, 3.5 Hz, 1H, C*H*), 3.67 (d, *J* = 12.2 Hz, 1H, C*H*), 3.12 (s, 1H, C*H*), 3.00 (d, *J* = 12.2 Hz, 1H, C*H*), 2.56 (dd, *J* = 16.8, 13.4 Hz, 1H, CH_2), 2.29 (dd, *J* = 16.8, 3.5 Hz, 1H, CH_2), 1.87 (dd, *J* = 6.8, 1.6 Hz, 3H, CH_3), 1.66 (ddd, *J* = 6.6, 1.7, 0.7 Hz, 3H, CH_3), 1.36 (s, 3H, CH_3), 1.31 (s, 3H, CH_3), 1.25 (s, 3H, CH_3). ^{13}**C-NMR** (150 MHz, CD_3COCD_3): δ = 202.2, 188.7, 174.0, 172.3, 142.6, 139.6, 132.0 (2C), 128.7, 120.6, 109.8, 105.3 (2C), 104.3, 81.5, 81.1, 79.2, 60.7, 56,0, 54.9, 48.5, 41.7, 21.5, 20.9, 19.9, 18.8, 17.8. **IR**: *v* 3727, 3385, 2936, 1654, 1616, 1439, 1383, 1305, 1256, 1192, 1128, 1050, 1006, 913, 862, 843, 580 cm^{-1}. **HRMS** (ESI) *m/z*: $[M+H]^+$ calcd for $C_{27}H_{31}O_8$ 483.2013, found 483.2006.[86]

Dihydrotrichodimer Ether B (17c)



Dihydrotrichodimer Ether B (**17c**)

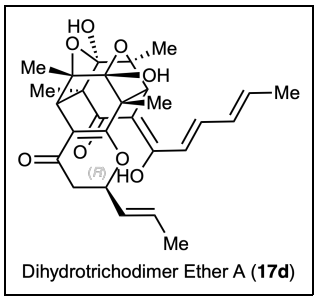
SMILES: OC(/C=C/C=C/C)=C(C1[C@@]2(C)[C@@]3(O)[C@]4(C)C5C6=C(O[C@H](/C=C/C)CC6=O)[C@]1(C)[C@](O2)(O)[C@@]5(C)O3)\C4=O

Fungus of origin: *Clonostachys rosea* YRS-06[2], *Penicillium chrysogenum* DM815[29].

Biosynthesis: See figure S3J.

Analytics: Light yellow powder. **ORD**: $[\alpha]_D^{15} = +100.0$ (c = 0.1, MeOH). ^{1}**H-NMR** (400 MHz, acetone-d_6): δ = 7.31 (dd, *J* = 14.8, 11.2 Hz, 1H, C*H*$_{sorbyl}$), 6.51 (d, *J* = 15.2 Hz, 1H, C*H*$_{sorbyl}$), 6.42 (ddd, *J* = 14.8, 10.8, 1.2 Hz, 1H, C*H*$_{sorbyl}$), 6.25 (dq, *J* = 14.8, 6.8 Hz, 1H, C*H*$_{sorbyl}$), 5.76 (ddq, *J* = 15.2, 6.8, 1.2 Hz, 1H, C*H*), 5.67 (bs, 1H, O*H*), 5.57 (bs, 1H, O*H*), 5.44 (ddd, *J* = 15.2, 10.8, 1.6 Hz, 1H, C*H*), 4.90 (m, 1H, C*H*), 3.18 (s, 1H, C*H*), 3.11 (s, 1H, C*H*), 2.54 (dd, *J* = 16.8, 4.4 Hz, 1H, CH_2), 2.15 (dd, *J* = 16.8, 8.4 Hz, 1H, CH_2), 1.87 (d, *J* = 6.0 Hz, 3H, CH_3), 1.66 (dd, *J* = 6.4, 0.8 Hz, 3H, CH_3), 1.39 (s, 3H, CH_3), 1.33 (s, 3H, CH_3), 1.31 (s, 3H, CH_3), 1.26 (s, 3H, CH_3). ^{13}**C-NMR** (100 MHz, acetone-d_6): δ = 202.0, 188.7, 175.8, 172.2, 143.0, 139.8, 132.1, 131.1, 128.4, 120.7, 108.9, 105.7, 105.5, 105.4, 80.0, 79.7, 79.2, 60.2, 59.2, 56.0, 54.7, 41.0, 22.2, 21.8, 19.8 (2C), 18.9, 18.0. **IR**: *v* 3396, 2923, 2854, 1720, 1610, 1459, 1416, 1379, 1263, 1126, 1016, 871, 735 cm^{-1}. **HRMS** (ESI) *m/z*: $[M+Na]^+$ calcd for $C_{28}H_{32}O_8Na$ 519.1989, found 519.1970.[2]

Dihydrotrichodimer Ether A (17d)



Dihydrotrichodimer Ether A (**17d**)

SMILES: OC(/C=C/C=C/C)=C(C1[C@@]2(C)[C@@]3(O)[C@]4(C)C5C6=C(O[C@@H](/C=C/C)CC6=O)[C@]1(C)[C@](O2)(O)[C@@]5(C)O3)\C4=O

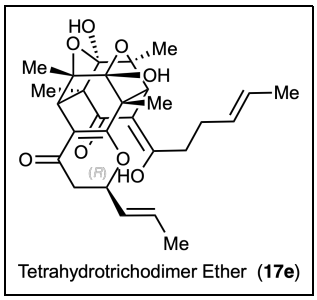
Fungus of origin: *Clonostachys rosea* YRS-06[2], *Penicillium chrysogenum* DM815[29], *Villosiclava virens* albino strain LN02[67].

Biosynthesis: See figure S3J.

Analytics: Light yellow powder. **ORD**: $[\alpha]_D^{15} = +30.0$ (c = 0.1, MeOH). ^{1}**H-NMR** (400 MHz, acetone-d_6): δ = 7.32 (dd, *J* = 14.8, 10.8 Hz, 1H, C*H*$_{sorbyl}$), 6.50 (d, *J* = 14.8 Hz, 1H, C*H*$_{sorbyl}$), 6.41 (ddd, *J* = 14.8, 10.8, 1.2 Hz, 1H, C*H*$_{sorbyl}$), 6.26 (dq, *J* = 15.2, 7.2 Hz, 1H, C*H*$_{sorbyl}$), 5.75 (ddq, *J* = 15.2, 6.4, 1.2 Hz, 1H, C*H*), 5.62 (bs, 1H, O*H*), 5.57 (ddd, *J* = 15.2, 6.8, 1.6 Hz, 1H, C*H*), 5.56 (bs, 1H, O*H*), 4.32 (ddd, *J* = 13.2, 6.8, 3.2 Hz, 1H, C*H*), 3.19 (s, 1H, C*H*), 3.11 (s, 1H, C*H*), 2.52 (dd, *J* = 16.8, 13.2 Hz, 1H, CH_2), 2.28 (dd, *J* = 16.8, 3.6 Hz, 1H, CH_2), 1.87 (d, *J* = 6.0 Hz, 3H, CH_3), 1.66 (dd, *J* = 6.4, 0.8 Hz, 3H, CH_3), 1.41 (s, 3H, CH_3), 1.34 (s, 3H, CH_3), 1.31 (s, 3H, CH_3), 1.24 (s, 3H, CH_3). ^{13}**C-NMR** (100 MHz, acetone-d_6): δ = 202.0, 189.1, 175.7, 173.6, 143, 139.9, 132.1, 131.6, 128.9, 120.7, 109.6, 105.7, 105.4, 105.0, 81.4, 79.5, 79.3, 60.6, 59.0, 56.5, 54.1, 41.7, 22.3, 21.7, 19.7, 19.4, 18.9, 17.9. **IR**: *v* 3410, 2930, 2855, 1720, 1611, 1546, 1416, 1296, 1262, 1164, 1128, 1035, 963, 870, 736 cm^{-1}. **HRMS** (ESI)

m/z: $[M+Na]^+$ calcd for $C_{28}H_{32}O_8Na$ 519.1989, found 519.1973.[2]

Tetrahydrotrichodimer Ether (17e)


Tetrahydrotrichodimer Ether (**17e**)

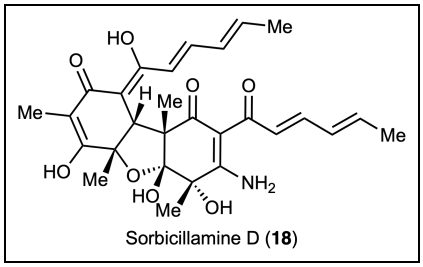
SMILES: O/C(CC/C=C/C)=C(C1[C@@]2(C)[C@@]3(O)[C@]4(C)C5C6=C(O[C@@H](/C=C/C)CC6=O)[C@]1(C)[C@](O2)(O)[C@@]5(C)O3)\C4=O

Fungus of origin: *Clonostachys rosea* YRS-06[2].

Biosynthesis: See figure S3J.

Analytics: Light yellow block crystals. **ORD**: $[\alpha]_D^{15} = +70.0$ (c = 0.1, MeOH). ^{1}**H-NMR** (400 MHz, acetone-d_6): δ = 5.85 (dq, *J* = 15.6, 6.8 Hz, 1H, C*H*), 5.66 (ddd, *J* = 15.6, 6.4, 1.2 Hz, 1H, C*H*), 5.63 (bs, 1H, O*H*), 5.57 (bs, 1H, O*H*), 5.51 (m, 1H, C*H*), 5.50 (m, 1H, C*H*), 4.46 (m, 1H, C*H*), 3.17 (s, 1H, C*H*), 2.98 (s, 1H, C*H*), 2.60 (dd, *J* = 14.8, 8.0 Hz, 1H, CH_2), 2.54 (dd, *J* = 16.8, 13.2 Hz, 1H, CH_2), 2.46 (dd, *J* = 14.8, 6.4 Hz, 1H, CH_2), 2.33 (dd, *J* = 16.8, 3.2 Hz, 1H, CH_2), 2.26 (m, 2H, CH_2), 1.73 (d, *J* = 6.4 Hz, 3H, CH_3), 1.63 (d, *J* = 4.0 Hz, 3H, CH_3), 1.39 (s, 3H, CH_3), 1.35 (s, 3H, CH_3), 1.31 (s, 3H, CH_3), 1.24 (s, 3H, CH_3). ^{13}**C-NMR** (100 MHz, acetone-d_6): δ = 195.5, 192.6, 189.0, 173.4, 131.0, 130.6, 129.0, 126.7, 109.8, 105.6, 105.3, 105.1, 81.2, 79.6, 79.3, 59.4, 59.1, 56.3, 54.0, 41.6, 35.2, 29.6, 22.2, 21.8, 19.9, 19.6, 18.1, 18.0. **IR**: *ν* 3404, 2918, 2850, 1721, 1656, 1639, 1611, 1511, 1459, 1421, 1265, 1165, 1127, 1017, 966, 739, 704 cm^{-1}. **HRMS** (ESI) *m/z*: $[M+Na]^+$ calcd for $C_{28}H_{34}O_8Na$ 521.2146, found 521.2131.[2]

Sorbicillamine D (18)


Sorbicillamine D (**18**)

SMILES: [H][C@@]1([C@@](C(C(C(/C=C/C=C/C)=O)=C(N)[C@]2(C)O)=O)(C)[C@@]2(O)O3)[C@@]3(C)C(O)=C(C)C(/C1=C(/C=C/C=C/C)O)=O

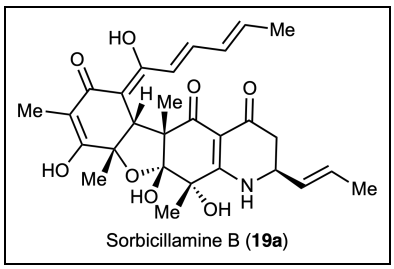
Fungus of origin: *Penicillium* sp. F232[96].

Bioactivity: Cytotoxicity screening against cervical cancer cells (HeLa), human hepatic cancer cell line (BEL-7402), HEK-293 cells, and human colon cancer HCT116 cell lines showed inactivity ($IC_{50} > 10.0$ μM).[96]

Biosynthesis: See figure S3K.

Analytics: Yellow, amorphous powder. **ORD**: $[\alpha]_D^{20} = -177.0$ (c = 0.1, MeOH). ^{1}**H-NMR** (600 MHz, DMSO-d_6): δ = 16.50 (bs, 1H, O*H*), 11.26 (d, *J* = 5.5 Hz, 1H, N*H*), 9.85 (bs, 1H, O*H*), 8.51 (d, *J* = 5.0 Hz, 1H, N*H*), 7.11 (dd, *J* = 14.9, 14.8 Hz, 1H, CH_{sorbyl}), 6.92 (dd, *J* = 15.4, 15.4 Hz, 1H, CH_{sorbyl}), 6.62 (d, *J* = 15.4 Hz, 1H, CH_{sorbyl}), 6.52 (d, *J* = 14.9 Hz, 1H, CH_{sorbyl}), 6.37 (dd, *J* = 14.2, 13.8 Hz, 1H, CH_{sorbyl}), 6.13 (dq, *J* = 14.8, 7.4 Hz, 1H, CH_{sorbyl}), 6.10 (dd, *J* = 15.4, 14.8 Hz, 1H, CH_{sorbyl}), 6.09 (m, 1H, CH_{sorbyl}), 3.62 (s, 1H, C*H*), 1.82 (d, *J* = 7.4 Hz, 3H, CH_3), 1.81 (d, *J* = 6.6 Hz, 3H, CH_3), 1.33 (s, 3H, CH_3), 1.29 (s, 3H, CH_3), 1.25 (s, 3H, CH_3), 1.14 (s, 3H, CH_3). ^{13}**C-NMR** (150 MHz, DMSO-d_6): δ = 190.8, 190.5, 188.7, 175.4, 168.8, 167.0, 137.9, 136.8, 136.4, 130.9, 130.5, 129.8, 121.0 (2C), 107.3, 104.6, 103.7, 101.4, 78.3, 74.1, 60.2, 53.1, 26.2, 24.7, 19.4, 18.1, 18.0, 7.4. **IR**: *ν* 3363, 3212, 2931, 1690, 1638, 1554, 1410, 1207, 1008, 982 cm^{-1}. **HRMS** (ESI) *m/z*: $[M+H]^+$ calcd for $C_{28}H_{34}NO_8$ 512.2279, found 512.2280.[96]

Sorbicillamine B (19a)


Sorbicillamine B (**19a**)

SMILES: [H][C@@]1([C@@](C(C(C(C[C@@H](/C=C/C)N2)=O)=C2[C@]3(C)O)=O)(C)[C@@]3(O)O4)[C@@]4(C)C(O)=C(C)C(/C1=C(/C=C/C=C/C)O)=O

Fungus of origin: *Penicillium* sp. F232[96].

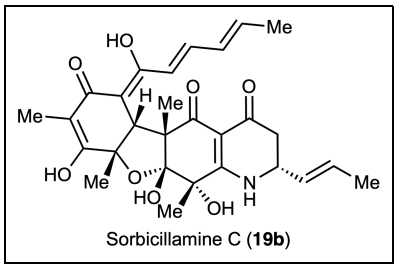
Bioactivity: Cytotoxicity screening against cervical cancer cells (HeLa), human hepatic cancer cell line (BEL-7402), HEK-293 cells, and human colon cancer HCT116 cell lines showed inactivity ($IC_{50} > 10.0$ μM).[96]

Biosynthesis: See figure S3K.

Analytics: Yellow, amorphous solid. **ORD**: $[\alpha]_D^{20} = -108.0$ (c = 0.1, MeOH). ^{1}**H-NMR** (600 MHz, DMSO-d_6): δ = 16.40 (bs, 1H, O*H*), 9.90 (bs, 1H, O*H*), 8.46 (bs, 1H, N*H*), 7.07 (dd, *J* = 14.8, 13.5 Hz, 1H, CH_{sorbyl}), 6.49 (d, *J* = 14.8 Hz, 1H, CH_{sorbyl}), 6.35 (dd, *J* = 14.0, 13.5 Hz, 1H, CH_{sorbyl}), 6.12 (dq, *J* = 14.8, 6.6 Hz, 1H, CH_{sorbyl}), 5.59 (dq, *J* = 14.8, 6.6 Hz, 1H, C*H*), 5.44 (dd, *J* = 14.8, 5.5 Hz, 1H, C*H*), 4.22 (m, 1H, C*H*), 3.52 (s, 1H, C*H*), 2.52 (m, 1H, CH_2), 2.13 (m, 1H, CH_2), 1.82 (d, *J* = 6.6 Hz, 3H, CH_3), 1.64 (d, *J* = 6.6 Hz, 3H, CH_3), 1.31 (s, 3H, CH_3), 1.30 (s, 3H,

CH_3), 1.29 (s, 3H, CH_3), 1.08 (s, 3H, CH_3). ^{13}**C-NMR** (150 MHz, DMSO-d_6): δ = 191.6, 186.2, 185.6, 171.9, 168.1, 167.7, 137.6, 136.5, 131.8, 129.2, 127.4, 121.8, 109.0, 105.1, 104.2, 102.4, 79.3, 74.5, 60.6, 53.7, 52.2, 41.9, 26.6, 25.3, 19.9, 19.0, 18.1, 8.0. **IR**: *v* 3363, 3212, 2931, 1690, 1608, 1558, 1433, 1208, 1108, 966 cm^{-1}. **HRMS** (ESI) *m/z*: $[M+H]^+$ calcd for $C_{28}H_{34}NO_8$ 512.2279, found 512.2278.

Sorbicillamine C (19b)



Sorbicillamine C (**19b**)

SMILES: [H][C@@]1([C@@](C(C(C(C[C@H](/C=C/C)N2)=O)=C2[C@]3(C)O)=O)(C)[C@@]3(O)O4)[C@@]4(C)C(O)=C(C)C(/C1=C(/C=C/C=C/C)O)=O

Fungus of origin: *Penicillium* sp. F232[96].

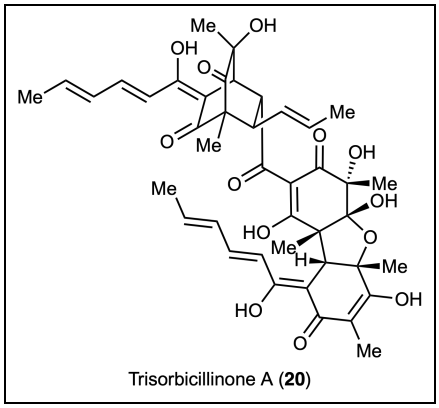
Bioactivity: Cytotoxicity screening against cervical cancer cells (HeLa), human hepatic cancer cell line (BEL-7402), HEK-293 cells, and human colon cancer HCT116 cell lines showed inactivity ($IC_{50} > 10.0$ μM).[96]

Biosynthesis: See figure S3K.

Analytics: Yellow, amorphous solid. **ORD**: $[\alpha]_D^{20} = -213.0$ (c = 0.1, MeOH). ^{1}**H-NMR** (600 MHz, DMSO-d_6): δ = 16.41 (bs, 1H, O*H*), 9.72 (bs, 1H, O*H*), 8.47 (bs, 1H, N*H*), 7.06 (dd, *J* = 14.9, 14.2 Hz, 1H, CH_{sorbyl}), 6.49 (d, *J* = 14.9 Hz, 1H, CH_{sorbyl}), 6.35 (dd, *J* = 14.2, 13.7 Hz, 1H, CH_{sorbyl}), 6.12 (dq, *J* = 13.7, 6.6 Hz, 1H, CH_{sorbyl}), 5.74 (dd, *J* = 15.4, 6.1 Hz, 1H, C*H*), 5.66 (dq, *J* = 15.4, 6.1 Hz, 1H, C*H*), 4.14 (m, 1H, C*H*), 3.52 (s, 1H, C*H*), 2.41 (m, 1H, CH_2), 2.08 (m, 1H, CH_2), 1.82 (d, *J* = 6.6 Hz, 3H, CH_3), 1.67 (d, *J* = 6.1 Hz, 3H, CH_3), 1.35 (s, 3H, CH_3), 1.30 (s, 6H, CH_3), 1.07 (s, 3H, CH_3). ^{13}**C-NMR** (150 MHz, DMSO-d_6): δ = 190.9, 185.5, 185.5, 170.8, 166.8, 166.5, 136.5, 135.3, 130.9, 129.1, 126.9, 121.0, 108.2, 104.1, 103.0, 101.7, 78.1, 73.6, 59.2, 52.9, 51.8, 41.5, 25.5, 24.4, 19.2, 18.1, 17.2, 7.1. **IR**: *v* 3363, 3212, 2931, 1690, 1608, 1558, 1433, 1208, 1108, 966 cm^{-1}. **HRMS** (ESI) *m/z*: $[M+H]^+$ calcd for $C_{28}H_{34}NO_8$ 512.2279, found 512.2277.[96]

1.2.3 Trimeric sorbicillinoids

Trisorbicillinone A (20)



Trisorbicillinone A (**20**)

SMILES: O[C@@]1(C)[C@@H]2/C(C([C@@](C1=O)(C)[C@H](/C=C/C)[C@H]2C(C3=C(O)[C@]([C@](/C(C(C(C)=C4O)=O)=C(\C=C\C=C\C)O)([H])[C@]4(C)O5)(C)[C@]5(O)[C@](O)(C)C3=O)=O)=O)=C(/C=C/C=C/C)O

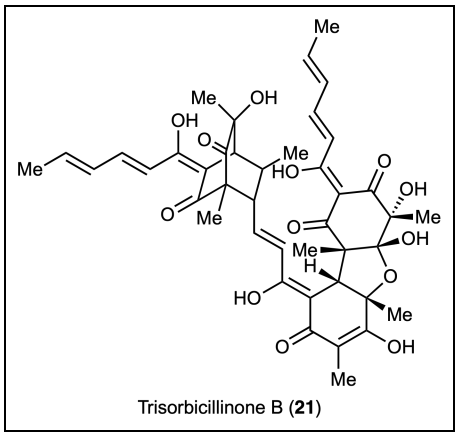
Fungus of origin: *Phialocephala* sp. FL30r[97].

Bioactivity: Cytotoxicity against leukemic P388 cells ($IC_{50} = 9.10$ µM), and human leukemia cell line HL60 ($IC_{50} = 3.14$ µM).[97]

Biosynthesis: See figure S4L.[97]

Analytics: ^{1}**H-NMR** (600 MHz, $CDCl_3$): δ = 17.89 (bs, 1H, O*H*), 16.35 (bs, 1H, O*H*), 14.15 (bs, 1H, O*H*), 7.32 (m, 1H, CH_{sorbyl}), 7.30 (m, 1H, CH_{sorbyl}), 6.38 (d, J = 14.9 Hz, 1H, CH_{sorbyl}), 6.30 (dd, J = 14.3, 12.1 Hz, 1H, CH_{sorbyl}), 6.21 (m, 1H, CH_{sorbyl}), 6.18 (m, 1H, CH_{sorbyl}), 6.15 (m, 1H, CH_{sorbyl}), 6.11 (d, J = 14.9 Hz, 1H, CH_{sorbyl}), 5.30 (m, 1H, C*H*), 4.96 (dd, J = 14.3, 10.9 Hz, 1H, C*H*), 4.42 (d, J = 7.2 Hz, 1H, C*H*), 3.81 (s, 1H, C*H*), 3.55 (s, 1H, C*H*), 2.73 (dd, J = 9.4, 7.6 Hz, 1H, C*H*), 1.88 (d, J = 6.6 Hz, 3H, CH_3), 1.87 (d, J = 6.6 Hz, 3H, CH_3), 1.55 (d, J = 3.7 Hz, 3H, CH_3), 1.47 (s, 3H, CH_3), 1.45 (s, 6H, CH_3), 1.32 (s, 3H, CH_3), 1.28 (s, 3H, CH_3), 1.09 (s, 3H, CH_3). ^{13}**C-NMR** (125 MHz, $CDCl_3$): δ = 210.8, 202.6, 197.4, 197.4, 195.8, 191.1, 170.6, 169.3, 163.4, 142.8, 140.1, 140.0, 138.0, 131.0, 130.9, 129.8, 128.3, 119.7, 118.1, 110.8, 110.0, 107.4, 103.8, 99.3, 79.6, 79.0, 76.2, 62.9, 57.9, 53.7, 51.3, 45.2, 44.4, 25.5, 24.3, 22.5, 19.0, 18.8, 18.5, 17.6, 10.0, 7.5. **IR**: ν 3439, 1729, 1620 cm^{-1}. **HRMS** (ESI) m/z: $[M-H]^-$ calcd for $C_{42}H_{48}O_{13}$ 759.3017, found 759.3043.[97]

Trisorbicillinone B (21)



Trisorbicillinone B (**21**)

SMILES: O[C@@]1(C)[C@@H]2/C(C([C@@](C1=O)(C)[C@@H](/C=C/C(O)=C3C(C(C)=C(O)[C@]4(C)[C@@]/3([H])[C@@]5(C)[C@@]([C@](O)(C)C(/C(C5=O)=C(O)\C=C\C=C\C)=O)(O)O4)=O)C2C)=O)=C(/C=C/C=C/C)O

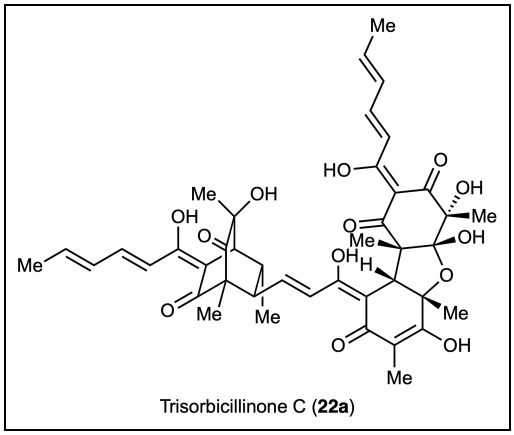
Fungus of origin: *Phialocephala* sp. FL30r[98].

Bioactivity: Cytotoxicity against leukemic P388 cells ($IC_{50} = 77.1$ µM), and lymphoblast cells K562 ($IC_{50} = 88.2$ µM).[98]

Biosynthesis: See figure S4L.[98]

Analytics: Yellow powder. **ORD**: $[\alpha]_D^{25} = -46.9$ (c = 0.2, MeOH). ^{1}**H-NMR** (600 MHz, $CDCl_3$): δ = 17.71 (bs, 1H, O*H*), 16.20 (bs, 1H, O*H*), 14.01 (bs, 1H, O*H*), 7.59 (m, 1H, CH_{sorbyl}), 7.37 (m, 1H, CH_{sorbyl}), 7.34 (dd, J = 14.8, 10.4 Hz, 1H, CH_{sorbyl}), 6.47 (dd, J = 14.7, 10.2 Hz, 1H, CH_{sorbyl}), 6.38 (m, 2H, CH_{sorbyl}), 6.34 (m, 1H, CH_{sorbyl}), 6.31 (m, 1H, CH_{sorbyl}), 6.23 (m, 1H, CH_{sorbyl}), 6.17 (d, J = 14.8 Hz, 1H, CH_{sorbyl}), 3.67 (s, 1H, C*H*), 2.96 (d, J = 1.9 Hz, 1H, C*H*), 2.66 (m, 1H, C*H*), 2.14 (dd, J = 10.2, 6.4 Hz, 1H, C*H*), 1.93 (d, J = 5.2 Hz, 3H, CH_3), 1.91 (d, J = 7.2 Hz, 3H, CH_3), 1.49 (s, 3H, CH_3), 1.45 (s, 3H, CH_3), 1.42 (s, 3H, CH_3), 1.37 (s, 3H, CH_3), 1.22 (s, 3H, CH_3), 1.09 (s, 3H, CH_3), 1.04 (d, J = 6.4 Hz, 3H, CH_3). ^{13}**C-NMR** (150 MHz, $CDCl_3$): δ = 211.4, 199.8, 198.4, 196.3, 191.7, 185.5, 169.1, 168.2, 163.9, 148.7, 144.5, 142.6, 139.9, 139.1, 131.3, 130.9, 124.8, 121.6, 117.7, 110.0, 108.0, 107.1, 104.3, 100.1, 79.5, 78.6, 75.7, 63.3, 59.6, 55.9, 54.2, 47.2, 32.9, 25.8, 24.7, 23.0, 19.4, 19.3, 18.9, 18.6, 10.4, 6.9. **IR**: ν 3439, 2927, 1728, 1633, 1604, 1563, 1514, 1445, 1414, 1380, 1348, 1204 cm^{-1}. **HRMS** (ESI) m/z: $[M+Na]^+$ calcd for $C_{42}H_{48}O_{13}Na$ 783.2993, found 783.2969.[98]

Trisorbicillinone C (22a)


Trisorbicillinone C (**22a**)

SMILES: O[C@@]1(C)[C@@H]2/C(C([C@@](C1=O)(C)[C@H](/C=C/C(O)=C3C(C(C)=C(O)[C@]4(C)[C@@]\3([H])[C@@]5(C)[C@@]([C@](O)(C)C(/C(C5=O)=C(O)\C=C\C=C\C)=O)(O)O4)=O)[C@H]2C)=O)=C(/C=C/C=C/C)O

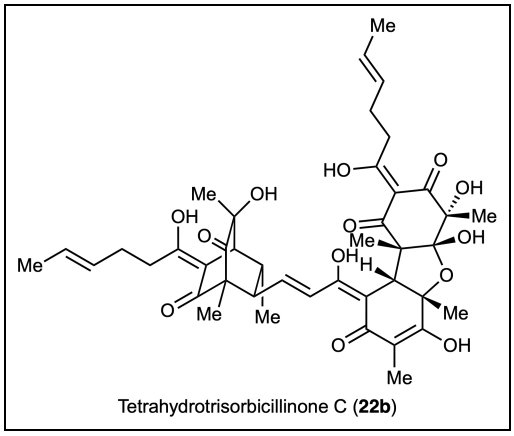
Fungus of origin: *Phialocephala* sp. FL30r[98].

Bioactivity: Cytotoxicity against leukemic P388 cells ($IC_{50} = 78.3$ μM), and lymphoblast cells K562 ($IC_{50} = 54.3$ μM).[98]

Biosynthesis: See figure S4L.[98]

Analytics: Yellow powder. **ORD**: $[\alpha]_D^{25} = -46.9$ (c = 0.2, MeOH). ^{1}**H-NMR** (600 MHz, $CDCl_3$): δ = 17.70 (bs, 1H, O*H*), 16.11 (bs, 1H, O*H*), 14.25 (bs, 1H, O*H*), 7.58 (m, 1H, CH_{sorbyl}), 7.40 (dd, *J* = 15.0, 7.8 Hz, 1H, CH_{sorbyl}), 7.37 (m, 1H, CH_{sorbyl}), 6.36 (m, 4H, CH_{sorbyl}), 6.29 (m, 1H, CH_{sorbyl}), 6.21 (m, 1H, CH_{sorbyl}), 6.18 (d, *J* = 15.4 Hz, 1H, CH_{sorbyl}), 3.68 (s, 1H, C*H*), 3.07 (dqd, *J* = 10.2, 7.4, 1.9 Hz, 1H, C*H*), 2.95 (d, *J* = 1.9 Hz, 1H, C*H*), 2.88 (ddd, *J* = 10.2, 7.4, 2.5 Hz, 1H, C*H*), 1.92 (d, *J* = 5.1 Hz, 3H, CH_3), 1.91 (d, *J* = 7.2 Hz, 3H, CH_3), 1.48 (s, 3H, CH_3), 1.47 (s, 3H, CH_3), 1.42 (s, 3H, CH_3), 1.37 (s, 3H, CH_3), 1.23 (s, 3H, CH_3), 1.14 (s, 3H, CH_3), 0.92 (d, *J* = 7.2 Hz, 3H, CH_3). ^{13}**C-NMR** (150 MHz, $CDCl_3$): δ = 212.3, 199.8, 197.4, 196.3, 191.7, 185.7, 169.2, 167.9, 164.1, 148.6, 144.4, 142.8, 140.0, 138.3, 131.3, 130.9, 125.5, 121.7, 117.7, 111.1, 108.5, 107.2, 104.1, 99.9, 79.7, 78.9, 75.7, 63.0, 59.7, 54.4, 51.2, 48.0, 30.4, 25.7, 24.6, 23.0, 19.2, 18.9, 18.6, 16.8, 10.9, 6.9. **IR**: *ν* 3433, 1730, 1632, 1603, 1564, 1446, 1410, 1380, 1348, 1205, 996, 942 cm^{-1}. **HRMS** (ESI) *m/z*: $[M+Na]^+$ calcd for $C_{42}H_{48}O_{13}Na$ 783.2993, found 783.2975.[98]

Tetrahydrotrisorbicillinone C (22b)


Tetrahydrotrisorbicillinone C (**22b**)

SMILES: O[C@@]1(C)[C@@H]2/C(C([C@@](C1=O)(C)[C@H](/C=C/C(O)=C3C(C(C)=C(O)[C@]4(C)[C@@]\3([H])[C@@]5(C)[C@@]([C@](O)(C)C(/C(C5=O)=C(O)\CC/C=C/C)=O)(O)O4)=O)[C@H]2C)=O)=C(CC/C=C/C)\O

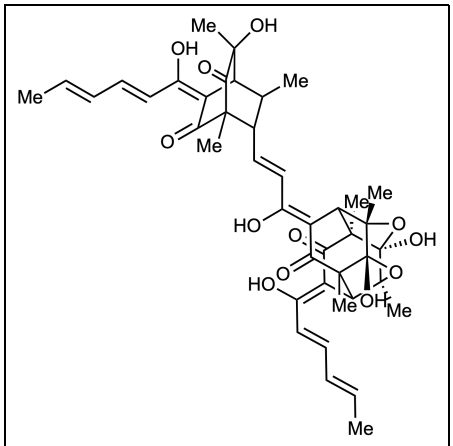
Fungus of origin: *Penicillium chrysogenum* 581F1[99].

Bioactivity: Biomolecular interactions to target proteins GLP-1R and eEF2K with K_d values of 0.0162 μM for GLP-1R and 0.0746 μM for eEF2K.[99]

Biosynthesis: See figure S4L.

Analytics: Yellow powder. **ORD**: $[\alpha]_D^{25} = -203.3$ (c = 0.2, MeOH). ^{1}**H-NMR** (600 MHz, $CDCl_3$): δ = 18.17 (bs, 1H, O*H*), 16.12 (bs, 1H, O*H*), 14.64 (bs, 1H, O*H*), 6.33 (m, 2H, C*H*), 5.50 (m, 2H, C*H*), 5.45 (m, 2H, C*H*), 3.70 (s, 1H, C*H*), 3.05 (m, 2H, C*H*), 2.90 (m, 1H, CH_2), 2.88 (d, *J* = 2.0 Hz, 1H, C*H*), 2.84 (m, 1H, C*H*), 2.45 (m, 2H, CH_2), 2.38 (dd, *J* = 14.1, 6.9 Hz, 2H, CH_2), 2.34 (m, 1H, CH_2), 2.24 (m, 1H, CH_2), 1.65 (dd, *J* = 6.4, 1.4 Hz, 3H, CH_3), 1.63 (dd, *J* = 6.1, 1.2 Hz, 3H, CH_3), 1.50 (s, 3H, CH_3), 1.47 (s, 3H, CH_3), 1.43 (s, 3H, CH_3), 1.36 (s, 3H, CH_3), 1.23 (s, 3H, CH_3), 1.12 (s, 3H, CH_3), 0.92 (d, *J* = 7.4 Hz, 3H, CH_3). ^{13}**C-NMR** (150 MHz, $CDCl_3$): δ = 212.3, 203.0, 197.4, 196.2, 195.9, 191.7, 180.8, 168.2, 164.1, 138.5, 129.2, 129.1, 127.0, 126.6 (2C), 125.6, 110.8, 108.6, 108.4, 104.2, 99.8, 79.7, 78.8, 75.7, 62.6, 58.7, 54.2, 51.3, 48.5, 38.8, 32.4, 30.5, 29.2, 28.1, 25.9, 24.9, 23.2, 18.4, 18.0 (2C), 17.1, 11.0, 7.1. **IR**: *ν* 3434, 2930, 2857, 1730, 1636, 1573, 1448, 1412, 1378, 1349, 1310, 1260, 1208, 1125, 1087, 1026, 995, 970, 941, 904, 833, 584, 529 cm^{-1}. **HRMS** (ESI) *m/z*: $[M+H]^+$ calcd for $C_{42}H_{51}O_{13}$ 763.3330, found 763.3326.[99]

Trisorbicillinone D (23)


Trisorbicillinone D (**23**)

SMILES: O[C@@]1(C)[C@@H]2/C(C([C@@](C1=O)(C)[C@@H](/C=C/C(O)=C(C(C3(C)[C@](O4)(O)[C@@]5(C)O6)=O)\C5[C@@]7(C)[C@]6(O)[C@]4(C)C3/C(C7=O)=C(O)\C=C\C=C\C)C2C)=O)=C(/C=C/C=C/C)O

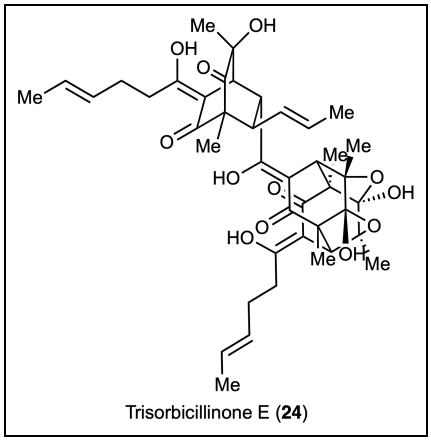
Fungus of origin: *Phialocephala* sp. FL30r[98].

Bioactivity: Cytotoxicity against leukemic P388 cells ($IC_{50} = 65.7$ μM), and lymphoblast cells K562 ($IC_{50} = 51.2$ μM).[98]

Biosynthesis: See figure S4L.[98]

Analytics: Yellow powder. **ORD**: $[\alpha]_D^{25} = +5.2$ (c = 0.2, MeOH). ^{1}**H-NMR** (600 MHz, $CDCl_3$): δ = 16.38 (bs, 1H, O*H*), 16.10 (bs, 1H, O*H*), 14.20 (bs, 1H, O*H*), 7.37 (dd, *J* = 14.7, 10.8 Hz, 1H, CH_{sorbyl}), 7.29 (dd, *J* = 14.4, 10.8 Hz, 1H, CH_{sorbyl}), 6.38 (dd, *J* = 14.7, 11.0 Hz, 1H, CH_{sorbyl}), 6.30 (m, 1H, CH_{sorbyl}), 6.26 (m, 1H, CH_{sorbyl}), 6.25 (m, 1H, CH_{sorbyl}), 6.24 (m, 1H, CH_{sorbyl}), 6.17 (d, *J* = 14.7 Hz, 1H, CH_{sorbyl}), 6.13 (d, *J* = 14.8 Hz, 2H, CH_{sorbyl}), 3.10 (dqd, *J* = 10.2, 7.2, 1.9 Hz, 1H, C*H*), 2.98 (s, 1H, C*H*), 2.95 (d, *J* = 1.9 Hz, 1H, C*H*), 2.84 (s, 1H, C*H*), 2.83 (dd, *J* = 11.0, 10.2 Hz, 1H, C*H*), 1.93 (d, *J* = 6.7 Hz, 3H, CH_3), 1.90 (d, *J* = 6.0 Hz, 3H, CH_3), 1.45 (s, 6H, CH_3), 1.42 (s, 6H, CH_3), 1.09 (s, 3H, CH_3), 1.08 (s, 3H, CH_3), 0.92 (d, *J* = 7.2 Hz, 3H, CH_3). ^{13}**C-NMR** (150 MHz, $CDCl_3$): δ = 212.0, 199.0, 197.3, 197.2, 176.2, 173.7, 169.3, 143.3, 142.9, 142.7, 140.7, 140.1, 130.9, 130.8, 124.5, 118.3, 117.6, 108.4, 104.0, 102.8 (2C), 102.6, 78.7, 78.6, 75.7, 62.7, 58.9, 58.6, 57.5, 57.4, 51.1, 47.9, 30.4, 24.6, 21.2, 21.1, 18.9, 18.7, 18.5 (2C), 16.6, 10.9. **IR**: *ν* 3447, 2980, 2937, 1730, 1617, 1557, 1449, 1381, 1298, 1127, 994, 940 cm^{-1}. **HRMS** (ESI) *m/z*: $[M+H]^+$ calcd for $C_{42}H_{49}O_{13}$ 745.3224, found 745.3222.[98]

Trisorbicillinone E (24)


Trisorbicillinone E (**24**)

SMILES: O[C@@]1(C)[C@@H]2/C(C([C@@](C1=O)(C)[C@H](/C=C/C)[C@H]2/C(O)=C(C(C3(C)[C@](O4)(O)[C@@]5(C)O6)=O)\C5[C@@]7(C)[C@]6(O)[C@]4(C)C3/C(C7=O)=C(O)\CC/C=C/C)=O)=C(CC/C=C/C)\O

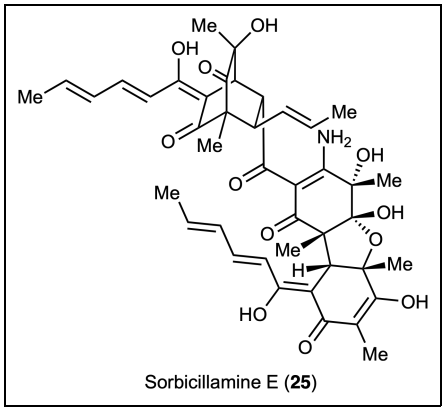
Fungus of origin: *Acremonium citrinum* SS-g13[70].

Bioactivity: Did not exhibit cytotoxic effects against ve human tumor cell lines and HBE cell line, as well as antimicrobial, antifungal, and QS inhibitory activities.[70]

Biosynthesis: See figure S4L.[70]

Analytics: Yellow oil. **ORD**: $[\alpha]_D^{20} = +151.1$ (c = 0.1, MeOH). ^{1}**H-NMR** (500 MHz, $CDCl_3$): δ = 5.50 (m, 1H, C*H*), 5.49 (m, 1H, C*H*), 5.41 (m, 2H, C*H*), 5.35 (m, 1H, C*H*), 4.98 (dd, *J* = 14.6, 9.6 Hz, 1H, C*H*), 3.61 (d, *J* = 6.9 Hz, 1H, C*H*), 3.04 (s, 1H, C*H*), 3.00 (s, 1H, C*H*), 2.92 (s, 1H, C*H*), 2.75 (m, 1H, C*H*), 2.43 (m, 2H, CH_2), 2.28 (m, 4H, CH_2), 2.16 (m, 2H, CH_2), 1.66 (d, *J* = 9.2 Hz, 3H, CH_3), 1.64 (d, *J* = 9.1 Hz, 3H, CH_3), 1.59 (d, *J* = 6.3 Hz, 3H, CH_3), 1.52 (s, 3H, CH_3), 1.44 (s, 3H, CH_3), 1.42 (s, 3H, CH_3), 1.30 (s, 3H, CH_3), 1.26 (s, 3H, CH_3), 1.11 (s, 3H, CH_3). ^{13}**C-NMR** (125 MHz, $CDCl_3$): δ = 211.4, 195.7, 195.1, 193.1, 192.5, 190.6, 181.8, 130.4, 129.3, 129.1, 127.8, 126.8, 126.7, 107.8, 104.3, 104.0, 103.9, 103.7, 78.8, 78.7, 75.8, 62.3, 57.9 (2C), 57.8, 57.6, 50.6, 45.6, 41.9, 34.7, 31.9, 28.5 (2C), 24.9, 21.3, 21.1, 19.0, 18.2, 18.0 (2C), 17.7, 9.9. **IR**: *ν* 3500, 2922, 2856, 1732, 1593, 1448, 1376, 1264, 1135, 1007, 970 cm^{-1}. **HRMS** (ESI) *m/z*: $[M+H]^+$ calcd for $C_{42}H_{53}O_{12}$ 749.3532, found 749.3521.[70]

Sorbicillamine E (25)



Sorbicillamine E (**25**)

SMILES: [H][C@@]1([C@@](C(C(C([C@H]2[C@H]([C@]3(C)O)/C(C([C@@](C3=O)(C)[C@@H]2/C=C/C)=O)=C(/C=C/C=C/C)O)=O)=C(N)[C@]4(C)O)=O)(C)[C@@]4(O)O5)[C@@]5(C)C(O)=C(C)C(/C1=C(/C=C/C=C/C)O)=O

Fungus of origin: *Penicillium* sp. F232[96].

Bioactivity: Cytotoxicity screening against cervical cancer cells (HeLa), human hepatic cancer cell line (BEL-7402), HEK-293 cells, and human colon cancer HCT116 cell lines showed inactivity ($IC_{50} > 10.0\ \mu M$).[96]

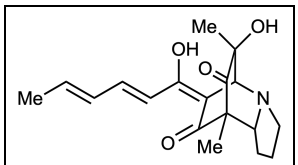
Biosynthesis: See figure S4L.

Analytics: Yellow, amorphous powder. **ORD**: $[\alpha]_D^{20} = +10.3$ (c = 0.1, MeOH). ^{1}**H-NMR** (600 MHz, DMSO-d_6): δ = 16.29 (bs, 1H, O*H*), 13.94 (bs, 1H, O*H*), 10.67 (d, *J* = 5.5 Hz, 1H, N*H*), 9.60 (bs, 1H, O*H*), 8.29 (d, *J* = 5.5 Hz, 1H, N*H*), 7.11 (dd, *J* = 14.9, 11.0 Hz, 1H, CH_{sorbyl}), 7.07 (dd, *J* = 15.4, 14.8 Hz, 1H, CH_{sorbyl}), 6.54 (d, *J* = 14.9 Hz, 1H, CH_{sorbyl}), 6.47 (bs, 1H, O*H*), 6.39 (dd, *J* = 13.7, 11.0 Hz, 1H, CH_{sorbyl}), 6.14 (m, 2H, CH_{sorbyl}), 5.88 (d, *J* = 15.4 Hz, 1H, CH_{sorbyl}), 5.79 (bs, 1H, O*H*), 5.28 (dq, *J* = 14.8, 6.6 Hz, 1H, CH_{sorbyl}), 5.11 (dd, *J* = 14.8, 9.9 Hz, 1H, C*H*), 5.06 (bs, 1H, O*H*), 4.48 (dd, *J* = 3.8, 3.3 Hz, 1H, C*H*), 3.53 (s, 1H, C*H*), 3.22 (dd, *J* = 9.9, 3.8 Hz, 1H, C*H*), 3.15 (d, *J* = 3.3 Hz, 1H, C*H*), 1.83 (d, *J* = 6.6 Hz, 3H, CH_3), 1.78 (d, *J* = 4.9 Hz, 3H, CH_3), 1.58 (d, *J* = 6.6 Hz, 3H, CH_3), 1.27 (s, 6H, CH_3), 1.19 (s, 3H, CH_3), 1.18 (s, 3H, CH_3), 1.02 (s, 3H, CH_3), 0.94 (s, 3H, CH_3). ^{13}**C-NMR** (150 MHz, DMSO-d_6): δ = 210.4, 200.1, 199.4, 191.6, 189.5, 177.0, 168.6, 167.1, 166.6, 141.2, 139.2, 137.4, 136.3, 131.9, 131.5, 131.0, 128.7, 121.7, 118.5, 109.6, 108.2, 104.4, 104.2, 102.4, 79.2, 75.4, 73.9, 64.0, 60.8, 54.1, 50.5, 45.9, 45.8, 26.3, 26.2, 24.2, 20.8, 19.1, 19.0, 18.2, 11.0, 7.3. **IR**: *v* 3425, 3370, 3368, 1711, 1650, 1633, 1509, 1330, 980, 965 cm^{-1}. **HRMS** (ESI) *m/z*: $[M+H]^+$ calcd for $C_{42}H_{50}NO_{12}$ 760.3328, found 760.3343.[96]

1.3 Hybrid sorbicillinoids

1.3.1 Diels-Alder-type hybrid sorbicillinoids

Sorbicillamine A (26)



Sorbicillamine A (**26**)

SMILES: O[C@@]1(C)[C@@H]2/C(C([C@@](C1=O)(C)C3N2CCC3)=O)=C(/C=C/C=C/C)O

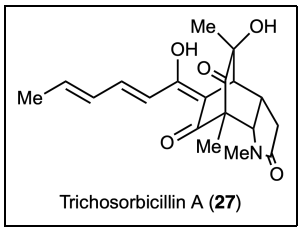
Fungus of origin: *Penicillium* sp. F232[96].

Bioactivity: Evaluation of cytotoxicity against HeLa, BEL-7402, HEK-293, P338, and HCT116 cell lines revealed no effects ($IC_{50} > 10.0$ μM).[96]

Biosynthesis: See figure S5M.

Analytics: Yellow, amorphous powder. **ORD**: $[\alpha]_D^{20} = +13.2$ (c = 0.1, MeOH). ^{1}**H-NMR** (600 MHz, DMSO-d_6): δ = 9.60 (bs, 1H, O*H*), 7.55 (d, *J* = 15.4 Hz, 1H, CH_{sorbyl}), 6.92 (dd, *J* = 15.4, 11.3 Hz, 1H, CH_{sorbyl}), 6.75 (bs, 1H, O*H*), 6.17 (dd, *J* = 14.4, 11.3 Hz, 1H, CH_{sorbyl}), 5.95 (dq, *J* = 14.4, 6.6 Hz, 1H, CH_{sorbyl}), 4.89 (s, 1H, C*H*), 3.73 (dd, *J* = 9.9, 7.1 Hz, 1H, C*H*), 3.47 (dd, *J* = 9.9, 7.1 Hz, 1H, CH_2), 2.76 (m, 1H, CH_2), 2.03 (m, 1H, CH_2), 1.95 (m, 1H, CH_2), 1.78 (d, *J* = 6.6 Hz, 3H, CH_3), 1.69 (m, 1H, CH_2), 1.37 (m, 1H, CH_2), 1.14 (s, 3H, CH_3), 0.96 (s, 3H, CH_3). ^{13}**C-NMR** (150 MHz, DMSO-d_6): δ = 206.1, 180.6, 175.6, 136.9, 134.9, 131.9, 131.0, 100.8, 71.7, 64.7, 64.1, 61.2, 52.4, 28.8, 24.7, 21.8, 18.9, 10.6. ^{19}**N-NMR** (50 MHz, DMSO-d_6): δ = 313.3. **IR**: *ν* 3375, 2935, 1735, 1720, 1449, 1205 cm^{-1}. **HRMS** (ESI) *m/z*: $[M+H]^+$ calcd for $C_{18}H_{24}NO_4$ 318.1700, found 318.1708.[96]

Trichosorbicillin A (27)



Trichosorbicillin A (**27**)

SMILES: O[C@@]1(C)[C@@H]2/C(C([C@@](C1=O)(C)C(N3C)[C@H]2CC3=O)=O)=C(/C=C/C=C/C)O

Fungus of origin: *Trichoderma reesei 4670*[30].

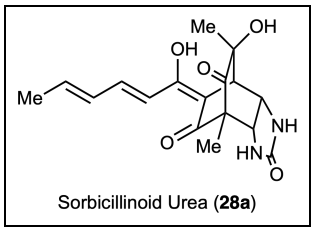
Bioactivity: No cytotoxicity against three human cancer cell lines, MCF-7 (breast cancer), HeLa (cervical cancer), and HepG2. No inhibition of nitric oxide production in RAW264.7 cells.[30]

Biosynthesis: See figure S5M.[30]

Total synthesis: Trichosorbicillin A (**28**) has been synthesized chemo-enzymatically using the heterologous expressed monooxygenase SorbC together with sorbicillin (**1a**) and 1-methyl-1,3-dihydro-2*H*-pyrrol-2-one (14% yield). Compared to the other chemo-enzymatic procedures, this reaction was performed at 80 °C in DMSO. Demethyl-trichosorbicillin A can be accessed in the same manner (10% yield).[31]

Analytics: White powder. **MP**: 150–151 °C. **ORD**: $[\alpha]_D^{20} = +11.5$ (c = 0.2, MeOH). ^{1}**H-NMR** (400 MHz, CD_3OD): δ = 7.37 (dd, *J* = 14.8, 10.8 Hz, 1H, CH_{sorbyl}), 6.45 (m, 2H, CH_{sorbyl}), 6.26 (m, 1H, CH_{sorbyl}), 3.88 (d, *J* = 8.8 Hz, 1H, C*H*), 3.52 (m, 1H, C*H*), 3.19 (d, *J* = 2.4 Hz, 1H, C*H*), 2.83 (s, 3H, CH_3), 2.70 (dd, *J* = 17.6, 11.2 Hz, 1H, CH_2), 2.07 (dd, *J* = 17.6, 3.6 Hz, 1H, CH_2), 1.91 (d, *J* = 6.8 Hz, 3H, CH_3), 1.44 (s, 3H, CH_3), 1.19 (s, 3H, CH_3). ^{13}**C-NMR** (100 MHz, CD_3OD): δ = 210.1, 198.1, 177.8, 170.9, 144.5, 141.1, 132.2, 119.0, 108.2, 75.2, 69.8, 67,0 47.3, 35.2, 32.1, 30.1, 24.2, 18.9, 11.7. **IR**: *ν* 3362, 2914, 1734, 1664, 1603, 1528, 1371, 1312,1155, 1107, 1050, 1000 cm^{-1}. **HRMS** (ESI) *m/z*: $[M-H]^-$ calcd for $C_{19}H_{22}NO_5$ 344.1504, found 344.1506.[30]

Sorbicillinoid Urea (28a)



Sorbicillinoid Urea (**28a**)

SMILES: O[C@@]1(C)[C@@H]2/C(C([C@@](C1=O)(C)C(N3)[C@H]2NC3=O)=O)=C(/C=C/C=C/C)O

Fungus of origin: *Paecilomyces marquandii* (Massee) Hughes isolate BAFC 486[100], *Paecilomyces* sp. KMU21009[71].

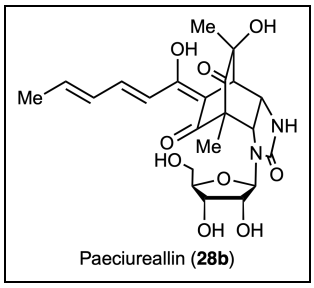
Biosynthesis: See figure S5M.

Total synthesis: Sorbicillinoid urea (**29**) has been synthesized chemo-enzymatically using the heterologous expressed monooxygenase SorbC together with sorbicillin (**1a**) and 1,3-diacetyl-2-imidazolidinone, followed by acetyl deprotection with lithium hydroxide (21% yield over 3 steps).[101]

Analytics: Yellow oil. **ORD**: $[\alpha]_D^{25} = +50.0$ (c = 0.1, MeOH). ^{1}**H-NMR** (500 MHz, $CDCl_3/CD_3OD$ = 9:1): δ = 7.33 (dd, *J* = 14.8, 10.5 Hz, 1H, CH_{sorbyl}), 6.27 (m, 1H, CH_{sorbyl}), 6.24 (m, 1H, CH_{sorbyl}), 6.20 (d, *J* = 14.8 Hz, 1H, CH_{sorbyl}), 4.76 (dd, *J* = 10.0, 3.2 Hz, 1H, C*H*), 4.00 (d, *J* = 10.0 Hz, 1H, C*H*), 3.28 (d, *J* = 3.2 Hz, 1H, C*H*), 1.91 (d, *J* = 6.8 Hz, 3H, CH_3), 1.24 (s, 3H, CH_3), 1.23 (s, 3H, CH_3). ^{1}**H-NMR** (500 MHz, DMSO-d_6): δ = 14.20 (bs, 1H, O*H*), 7.23 (dd, *J* = 14.8, 10.4 Hz, 1H, CH_{sorbyl}), 6.80 (s, 1H, N*H*), 6.57 (s, 1H, N*H*), 6.44 (d, *J* = 14.8 Hz, 1H, CH_{sorbyl}), 6.36 (m, 1H, CH_{sorbyl}), 6.28 (m, 1H, CH_{sorbyl}), 6.09 (bs, 1H, O*H*), 4.50 (m, 1H, C*H*),

3.87 (m, 1H, C*H*), 3.23 (d, J) 2.8 Hz, H-4), 1.86 (d, J = 6.4 Hz, 3H, CH_3), 1.07 (s, 3H, CH_3), 1.06 (s, 3H, CH_3). ^{13}**C-NMR** (125 MHz, $CDCl_3/CD_3OD$ = 9:1): δ = 208.3, 195.3, 169.8, 163.1, 142.9, 139.9, 130.5, 117.4, 106.2, 73.8, 64.8, 59.1, 50.2, 46.4, 23.6, 18.4, 8.9. **IR**: ν 3420, 3401, 3256, 2927, 2861, 1722, 1679, 1637, 1604, 1564, 1466, 1387 cm^{-1}. **HRMS** (ESI) m/z: $[M-H]^-$ calcd for $C_{17}H_{20}N_2O_5$ 331.1293, found 331.1306.[100]

Paeciureallin (28b)



Paeciureallin (**28b**)

SMILES: O[C@@]1(C)[C@@H]2/C(C([C@@](C1=O)(C)C(N3[C@@H]4O[C@H](CO)[C@@H](O)[C@H]4O)[C@H]2NC3=O)=O)=C(/C=C/C=C/C)O

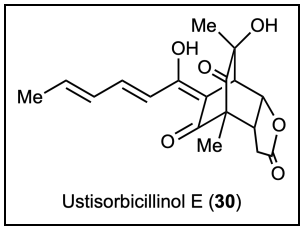
Fungus of origin: *Paecilomyces* sp. KMU21009[71].

Bioactivity: Paeciureallin (**29b**) exhibits cytotoxicity against SW480 (IC_{50} = 32.0 μM) and A549 (IC_{50} = 34.4 μM) cell lines.[71]

Biosynthesis: See figure S5M.[71]

Analytics: Brown and yellow solid. **ORD**: $[\alpha]_D^{20}$ = −26.7 (c = 0.2, MeOH). ^{1}**H-NMR** (600 MHz, CD_3OD): δ = 7.28 (dd, J = 14.9, 11.0 Hz, 1H, CH_{sorbyl}), 6.34 (dd, J = 14.8, 11.0 Hz, 1H, CH_{sorbyl}), 6.30 (d, J = 15.5 Hz, 1H, CH_{sorbyl}), 6.18 (dt, J = 14.3, 7.1 Hz, 1H, CH_{sorbyl}), 4.75 (d, J = 5.4 Hz, 1H, C*H*), 4.71 (d, J = 9.9, 3.3 Hz, 1H, C*H*), 4.60 (t, J = 5.5 Hz, 1H, C*H*), 4.08 (dd, J = 12.6, 5.6 Hz, 1H, C*H*), 4.06 (d, J = 9.9 Hz, 1H, C*H*), 3.75 (dt, J = 5.2 Hz, 1H, C*H*), 3.68 (dd, J = 12.1, 3.1 Hz, 1H, CH_2), 3.56 (dd, J = 12.0, 5.1 Hz, 1H, CH_2), 3.37 (d, J = 3.4 Hz, 1H, C*H*), 1.84 (d, J = 6.9 Hz, 3H, CH_3), 1.31 (s, 3H, CH_3), 1.18 (s, 3H, CH_3). ^{13}**C-NMR** (150 MHz, CD_3OD): δ = 209.2, 196.8, 171.0, 163.4, 144.1, 141.0, 132.1, 119.2, 108.1, 95.0, 84.8, 74.7, 73.1, 71.4, 67.0, 64.8, 63.9, 50.5, 47.0, 24.2, 19.0, 10.7. **IR**: ν 3386, 2937, 1698, 1600, 1556, 1451, 1393, 1204, 1123, 999, 955 cm^{-1}. **HRMS** (ESI) m/z: $[M+H]^+$ calcd for $C_{22}H_{29}N_2O_9$ 465.1868, found 465.1877.

Ustisorbicillinol E (29)



Ustisorbicillinol E (**30**)

SMILES: O[C@@]1(C)[C@@H]2/C(C([C@@](C1=O)(C)C(C3)[C@H]2OC3=O)=O)=C(/C=C/C=C/C)O

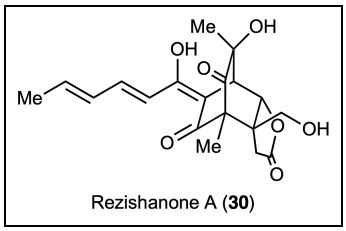
Fungus of origin: *Ustilaginoidea virens* UV8b[86].

Bioactivity: Did not display any significant phytotoxic, cytotoxic, antibacterial, or antifungal activity.[86]

Biosynthesis: See figure S5M.[86]

Analytics: Yellow, amorphous powder. **ORD**: $[\alpha]_D^{25}$ = +116.0 (c = 0.1, MeOH). ^{1}**H-NMR** (600 MHz, $CDCl_3$): δ = 14.32 (bs, 1H, O*H*), 7.38 (dd, J = 14.8, 10.2 Hz, 1H, CH_{sorbyl}), 6.29 (dd, J = 15.3, 10.2 Hz, 1H, CH_{sorbyl}), 6.24 (m, 1H, CH_{sorbyl}), 6.12 (d, J = 14.9 Hz, 1H, CH_{sorbyl}), 5.44 (dd, J = 8.9, 3.5 Hz, 1H, C*H*), 3.60 (d, J = 3.5 Hz, 1H, C*H*), 2.89 (ddd, J = 11.5, 8.9, 5.5 Hz, 1H, C*H*), 2.70 (dd, J = 19.2, 11.6 Hz, 1H, CH_2), 2.24 (dd, J = 19.2, 5.4 Hz, 1H, CH_2), 1.91 (d, J = 6.0 Hz, 3H, CH_3), 1.28 (s, 3H, CH_3), 1.23 (s, 3H, CH_3). ^{13}**C-NMR** (150 MHz, $CDCl_3$): δ = 209.2, 194.9, 174.8, 172.3, 144.6, 141.4, 130.8, 117.2, 104.7, 76.3, 74.2, 62.5, 45.5, 41.4, 30.2, 24.4, 19.0, 10.4. **IR**: ν 3726, 3625, 3599, 3421, 2921, 2851, 1774, 1735, 1652, 1616, 1576, 1454, 1384, 1201, 1025, 912, 876, 580 cm^{-1}. **HRMS** (ESI) m/z: $[M-H]^-$ calcd for $C_{18}H_{19}O_6$ 331.1187, found 331.1201.[86]

Rezishanone A (30)



Rezishanone A (**30**)

SMILES: O[C@@]1(C)[C@@H]2/C(C([C@@](C1=O)(C)[C@](C3)(CO)[C@H]2OC3=O)=O)=C(/C=C/C=C/C)O

Fungus of origin: *Paecilomyces marquandii* (Massee) Hughes isolate BAFC 486[100], *Penicillium notatum*[28], *Trichoderma citrinoviride*[12].

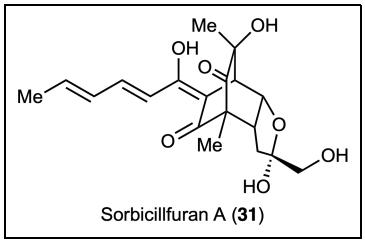
Bioactivity: Antibacterial against *Staphylococcus aureus* and *Bacillus subtilis* (weak).[28]

Biosynthesis: See figure S5M.[102]

Analytics: Colorless solid. **TLC**: R_f = 0.49 (DCM/MeOH = 10:1). ^{1}**H-NMR** (300 MHz, acetone-d_6): δ = 14.32 (bs, 1H, O*H*), 7.32 (dd, J = 15.0, 10.5 Hz, 1H, CH_{sorbyl}), 6.52 (d, J = 15.0 Hz, 1H, CH_{sorbyl}), 6.40 (dd, J = 14.8, 10.6 Hz, 1H, CH_{sorbyl}), 6.30 (dq, J = 14.8, 6.4 Hz, 1H, CH_{sorbyl}), 5.42 (d, J = 3.6 Hz, 1H, C*H*), 5.34 (bs, 1H, O*H*), 4.94 (bs, 1H, O*H*), 3.71 (d, J = 3.6 Hz, 1H, C*H*), 3.65 (m, 2H, CH_2OH), 2.57 (d, J = 19.0 Hz, 1H, CH_2), 2.17 (d, J = 19.0 Hz, 1H, CH_2), 1.88 (d, J = 6.4 Hz, 3H, CH_3), 1.25 (s, 3H, CH_3), 1.12 (s, 3H, CH_3). ^{13}**C-NMR** (75.5 MHz, acetone-d_6): δ = 208.1, 197.4, 174.9, 172.4, 144.2, 141.1, 131.8, 119.2, 106.8, 80.2, 74.0, 66.4, 64.9, 51.1, 46.3, 34.7, 24.9, 18.9, 8.4. **IR**: ν 3425, 2980, 2934, 1780,

1735, 1632, 1603, 1558, 1445, 1386, 1331, 1204, 1115, 1041, 998, 940, 908, 874, 749 cm^{-1}. **HRMS** (ESI) *m/z*: $[M+H]^+$ calcd for $C_{19}H_{23}O_7$ 363.1438, found 363.1438.[28]

Sorbicillfuran A (31)


Sorbicillfuran A (**31**)

SMILES: O[C@@]1(C)[C@@H]2/C(C([C@@](C1=O)(C)C3[C@H]2O[C@@](O)(CO)C3)=O)=C(/C=C/C=C/C)O

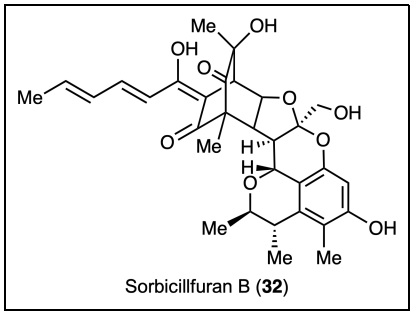
Fungus of origin: *Penicillium citrinum* SCSIO41402[103].

Bioactivity: Evaluation of cytotoxicities against three human renal cancer cell lines (ACHN, OSRC2, 786-O) and three human leukemia cell lines (HL-60, K562, MOLT-4) displayed inactivity.[103]

Biosynthesis: See figure S5M.[103]

Analytics: Yellowish oil. **ORD**: $[\alpha]_D^{25} = +184.0$ (c = 0.1, MeOH). ^{1}**H-NMR** (700 MHz, CD_3OD): $\delta = 7.29$ (dd, J = 15.0, 11.0 Hz, 1H, CH_{sorbyl}), 6.39 (dd, J = 14.8, 11.0 Hz, 1H, CH_{sorbyl}), 6.33 (d, J = 15.0 Hz, 1H, CH_{sorbyl}), 6.20 (dq, J = 14.8, 6.8 Hz, 1H, CH_{sorbyl}), 5.08 (dd, J = 8.8, 3.5 Hz, 1H, C*H*), 3.43 (d, J = 3.5 Hz, 1H, C*H*), 3.40 (d, J = 11.5 Hz, 1H, CH_2), 3.36 (d, J = 11.5 Hz, 1H, CH_2), 2.84 (q, J = 8.8 Hz, 1H, C*H*), 1.99 (dd, J = 13.1, 9.3 Hz, 1H, CH_2), 1.88 (d, J = 6.8 Hz, 3H, CH_3), 1.44 dd, J = 13.1, 8.8 Hz, 1H, CH_2), 1.18 (s, 3H, CH_3), 1.11 (s, 3H, CH_3). ^{13}**C-NMR** (175 MHz, CD_3OD): δ = 210.9, 199.1, 170.7, 143.3, 140.1, 132.3, 119.8, 109.2, 107.4, 76.7, 74.3, 66.8, 64.8, 47.0, 46.5, 38.3, 24.5, 18.9, 11.1. **IR**: *v* 3387, 2939, 1732, 1626, 1556, 1446, 1386, 1230, 1201, 1136, 1047, 997 cm^{-1}. **HRMS** (ESI) *m/z*: $[M-H]^-$ calcd for $C_{19}H_{23}O_7$ 363.1449, found 363.1457.

Sorbicillfuran B (32)


Sorbicillfuran B (**32**)

SMILES: O[C@]1(C)C2/C(C(C(C1=O)(C)[C@H]3[C@@H]2O[C@](O4)(CO)C([H])3[C@@]5([H])O[C@H](C)[C@@H](C)C6=C(C)C(O)=C(C(O)=O)C4=C65)=O)=C(/C=C/C=C/C)O

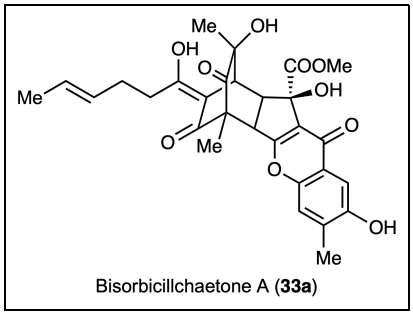
Fungus of origin: *Penicillium citrinum* SCSIO41402[103].

Bioactivity: Cytotoxicity against human leukemia cell line, HL-60 (IC_{50} = 9.60 μM). It is revealed that the citrinin moiety might contribute more to the cytotoxic activity against HL-60.[103]

Biosynthesis: See figure S5M.[103]

Analytics: Yellow, amorphous powder. **ORD**: $[\alpha]_D^{25} = +50.0$ (c = 0.2, MeOH). ^{1}**H-NMR** (700 MHz, acetone-d_6): $\delta = 7.30$ (dd, J = 15.0, 11.0 Hz, 1H, CH_{sorbyl}), 6.54 (d, J = 15.0 Hz, 1H, CH_{sorbyl}), 6.45 (dd, J = 15.0, 11.0 Hz, 1H, CH_{sorbyl}), 6.27 (dq, J = 15.0, 6.8 Hz, 1H, CH_{sorbyl}), 5.51 (dd, J = 7.9, 4.2 Hz, 1H, C*H*), 4.55 (d, J = 7.7 Hz, 1H, C*H*), 4.18 (q, J = 6.8 Hz, 1H, C*H*), 3.75 (d, J = 4.2 Hz, 1H, C*H*), 3.36 (d, J = 11.9 Hz, 1H, CH_2), 3.17 (d, J = 11.9 Hz, 1H, CH_2), 3.02 (dd, J = 7.9, 3.8 Hz, 1H, C*H*), 2.79 (q, J = 7.0 Hz, 1H, C*H*), 2.14 (dd, J = 7.7, 3.8 Hz, 1H, C*H*), 2.11 (s, 3H, CH_3), 1.88 (d, J = 6.8 Hz, 3H, CH_3), 1.28 (s, 3H, CH_3), 1.27 (s, 3H, CH_3), 1.25 (d, J = 7.0 Hz, 3H, CH_3), 1.24 (d, J = 6.8 Hz, 3H, CH_3). ^{13}**C-NMR** (175 MHz, acetone-d_6): δ = 208.5, 197.8, 171.4, 170.6, 160.5, 149.1, 144.6, 143.1, 140.1, 132.1, 119.7, 119.4, 116.2, 113.5, 108.8, 101.6, 80.6, 75.3, 73.5, 68.4, 65.0, 63.9, 54.2, 53.4, 46.4, 35.3, 24.2, 21.5, 18.9, 18.3, 10.6, 9.9. **IR**: *v* 3367, 2926, 1732, 1622, 1591, 1456, 1375, 1159, 1095, 1018, 964 cm^{-1}. **HRMS** (ESI) *m/z*: $[M-H]^-$ calcd for $C_{32}H_{35}O_{11}$ 595.2185, found 595.2177.

Bisorbicillchaetone A (33a)


Bisorbicillchaetone A (**33a**)

SMILES: O[C@]1(C)C2/C(C(C(C1=O)(C)[C@H]3[C@@H]2C(O)(C(OC)=O)C(C4=O)=C3OC5=C4C=C(O)C(C)=C5)=O)=C(CC/C=C/C)\O

Fungus of origin: *Penicillium* sp. NX-S-6[46], *Penicillium* sp. SCSIO06868[104].

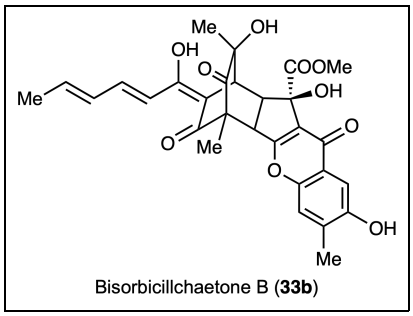
Bioactivity: Inhibitory effect in nitrogen oxide production (IC_{50} = 80.3 μM) induced by LPS (lipopolysaccharide) in RAW264.7 cells.[104]

Biosynthesis: See figure S5M. Bisorbicillchaetone C (**34c**) can be reduced and methylated to produce bisorbicillchaetone A (**34a**).[104]

Analytics: Yellow oil. **ORD**: $[\alpha]_D^{20} = +16.5$ (c = 0.1, MeOH). ^{1}**H-NMR** (700 MHz, $CDCl_3$): $\delta = 14.77$ (bs, 1H, O*H*), 11.80 (bs, 1H, O*H*), 6.77 (s, 1H, Ar*H*), 6.64 (s, 1H, Ar*H*), 5.47 (dq,

J = 15.4, 6.3 Hz, 1H, C*H*), 5.40 (dtd, J = 14.7, 7.0, 1.4 Hz, 1H, C*H*), 4.07 (bs, 1H, O*H*), 3.78 (s, 3H, CH_3), 3.72 (dd, J = 9.1, 2.8 Hz, 1H, C*H*), 3.53 (d, J = 8.4 Hz, 1H, C*H*), 3.49 (d, J = 2.8 Hz, 1H, C*H*), 2.79 (bs, 1H, O*H*), 2.60 (m, 2H, CH_2), 2.40 (s, 3H, CH_3), 2.29 (m, 2H, CH_2), 1.66 (s, 3H, CH_3), 1.62 (dd, J = 6.3, 1.4 Hz, 3H, CH_3), 1.26 (s, 3H, CH_3). ^{13}**C-NMR** (175 MHz, $CDCl_3$): δ = 210.9, 191.1, 186.2, 179.9, 174.5, 167.8, 160.8, 157.3, 148.0, 129.6, 126.5, 121.8, 113.4, 108.9, 108.4, 108.3, 79.7, 74.7, 61.0, 54.0, 51.2, 42.3, 42.1, 33.2, 28.1, 25.1, 22.5, 18.0, 10.7. **HRMS** (ESI) *m/z*: $[M+H]^+$ calcd for $C_{29}H_{31}O_{10}$ 539.1912, found 539.1917.[104]

Bisorbicillchaetone B (33b)



Bisorbicillchaetone B (**33b**)

SMILES: O[C@]1(C)C2/C(C(C(C1=O)(C)[C@H]3[C@@H]2C(O)(C(OC)=O)C(C4=O)=C3OC5=C4C=C(O)C(C)=C5)=O)=C(/C=C/C=C/C)O

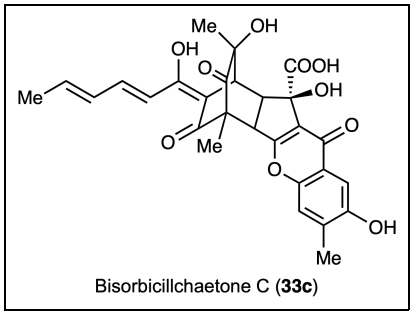
Fungus of origin: *Penicillium* sp. NX-S-6[46], *Penicillium* sp. SCSIO06868[104].

Bioactivity: Inhibitory effect in nitrogen oxide production (IC_{50} = 38.4 μM) induced by LPS (lipopolysaccharide) in RAW264.7 cells.[104]

Biosynthesis: See figure S5M. Bisorbicillchaetone C (**34c**) can be methylated to produce bisorbicillchaetone B (**34b**).[104]

Analytics: Yellow oil. **ORD**: $[\alpha]_D^{20}$ = +11.2 (c = 0.1, MeOH). ^{1}**H-NMR** (700 MHz, $CDCl_3$): δ = 14.23 (bs, 1H, O*H*), 12.06 (bs, 1H, O*H*), 7.13 (dd, J = 15.4, 11.2 Hz, 1H, CH_{sorbyl}), 6.99 (s, 1H, Ar*H*), 6.70 (s, 1H, Ar*H*), 6.63 (d, J = 14.7 Hz, 1H, CH_{sorbyl}), 6.36 (ddd, J = 14.7, 10.5, 0.7 Hz, 1H, CH_{sorbyl}), 6.25 (bs, 1H, O*H*), 6.24 (dq, J = 14.0, 7.0 Hz, 1H, CH_{sorbyl}), 5.94 (bs, 1H, O*H*), 3.86 (d, J = 9.1 Hz, 1H, C*H*), 3.66 (s, 3H, CH_3), 3.53 (dd, J = 9.1, 2.8 Hz, 1H, C*H*), 3.46 (d, J = 2.8 Hz, 1H, C*H*), 2.38 (s, 3H, CH_3), 1.86 (d, J = 6.3 Hz, 3H, CH_3), 1.50 (s, 3H, CH_3), 1.05 (s, 3H, CH_3). ^{13}**C-NMR** (175 MHz, $CDCl_3$): δ = 209.2, 195.1, 179.1, 173.9, 170.6, 168.6, 159.8, 156.4, 147.9, 141.3, 139.2, 131.2, 121.9, 120.6, 112.7, 109.0, 108.2, 108.0, 79.5, 73.4, 62.0, 52.9, 49.5, 42.4, 42.1, 23.9, 21.7, 18.7, 10.7. **HRMS** (ESI) *m/z*: $[M+H]^+$ calcd for $C_{29}H_{29}O_{10}$ 537.1755, found 537.1746.[104]

Bisorbicillchaetone C (33c)



Bisorbicillchaetone C (**33c**)

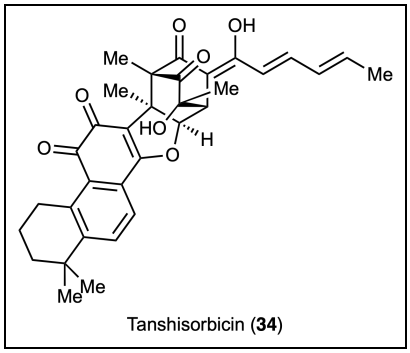
SMILES: O[C@]1(C)C2/C(C(C(C1=O)(C)[C@H]3[C@@H]2C(O)(C(O)=O)C(C4=O)=C3OC5=C4C=C(O)C(C)=C5)=O)=C(/C=C/C=C/C)O

Fungus of origin: *Penicillium* sp. SCSIO06868[104].

Biosynthesis: See figure S5M.[104]

Analytics: Yellow oil. **MP**: °C. **ORD**: $[\alpha]_D^{20}$ = +12.1 (c = 0.1, MeOH). ^{1}**H-NMR** (700 MHz, DMSO-d_6): δ = 14.23 (bs, 1H, O*H*), 12.14 (bs, 1H, O*H*), 7.12 (dd, J = 14.7, 3.5 Hz, 1H, CH_{sorbyl}), 6.98 (s, 1H, Ar*H*), 6.69 (s, 1H, Ar*H*), 6.64 (d, J = 14.7 Hz, 1H, CH_{sorbyl}), 6.36 (ddd, J = 14.7, 11.2, 0.7 Hz, 1H, CH_{sorbyl}), 6.24 (bs, 1H, O*H*), 6.23 (dq, J = 14.7, 7.0 Hz, 1H, CH_{sorbyl}), 3.82 (d, J = 8.4 Hz, 1H, C*H*), 3.55 (dd, J = 9.1, 2.1 Hz, 1H, C*H*), 3.44 (d, J = 2.1 Hz, 1H, C*H*), 2.38 (s, 3H, CH_3), 1.86 (d, J = 6.3 Hz, 3H, CH_3), 1.50 (s, 3H, CH_3), 1.07 (s, 3H, CH_3). ^{13}**C-NMR** (175 MHz, DMSO-d_6): δ = 209.3, 195.2, 179.3, 175.1, 170.5, 168.5, 159.9, 156.5, 147.8, 141.2, 139.0, 131.2, 122.2, 120.7, 112.6, 109.1, 108.1 (2C), 79.1, 73.4, 62.1, 49.5, 42.5, 42.1, 23.9, 21.7, 18.7, 10.7. **HRMS** (ESI) *m/z*: $[M-H]^-$ calcd for $C_{28}H_{25}O_{10}$ 521.1453, found 521.1455.[104]

Tanshisorbicin (34)



Tanshisorbicin (**34**)

SMILES: O=C([C@@]1(C)[C@@](C(C(C(C2=C3C=CC4=C2CCCC4(C)C)=O)=O)=C3O5)(C)[C@@]5([H])[C@@H]/6[C@@](O)(C)C1=O)C6=C(\C=C\C=C\C)O

Fungus of origin: *Hypocrea* sp. AS 3.17108[105].

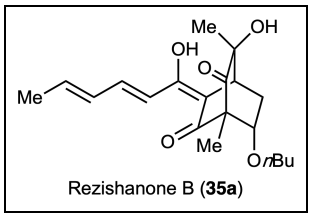
Bioactivity: Antibacterial activities against *Bacillus* Calmette-Guérin Pasteur 1173P2 (IC_{50} = 16.0 μM), *Staphylococcus aureus* ATCC 6538 (IC_{50} = 125 μM), methicillin-resistant *Staphylococcus aureus* (IC_{50} = 31.2 μM), *Bacillus subtilis* ATCC 6633 (IC_{50} = 16.0 μM).[105]

Biosynthesis: See figure S5M.[105]

Analytics: **ORD**: $[\alpha]_D^{20}$ = −72.5 (c = 0.3, $CHCl_3$). ^{1}**H-NMR** (600 MHz, DMSO-d_6): δ = 7.82 (d, J = 8.2 Hz, 1H, Ar*H*), 7.38 (d, J = 8.2 Hz, 1H, Ar*H*), 7.17 (dd J = 14.8, 11.0 Hz, 1H,

CH_{sorbyl}), 6.66 (d, J = 14.9 Hz, 1H, CH_{sorbyl}), 6.44 (m, 1H, CH_{sorbyl}), 6.26 (td, J = 14.8, 6.7 Hz, 1H, CH_{sorbyl}), 5.50 (d, J = 3.7 Hz, 1H, CH), 3.90 (d, J = 3.7 Hz, 1H, CH), 3.04 (m, 2H, CH_2), 1.87 (d, J = 6.7 Hz, 3H, CH_3), 1.70 (m, 2H, CH_2), 1.59 (m, 2H, CH_2), 1.44 (s, 3H, CH_3), 1.28 (s, 3H, CH_3), 1.27 (s, 3H, CH_3), 1.24 (s, 3H, CH_3), 1.17 (s, 3H, CH_3). **^{13}C-NMR** (150 MHz, DMSO-d_6): δ = 209.1, 197.5, 183.6, 175.4, 171.0, 170.6, 152.9, 143.2, 143.0, 140.8, 133.7, 131.6, 128.7, 125.6, 123.0, 119.1, 116.5, 105.7, 91.1, 73.4, 68.5, 54.6, 45.6, 37.8, 35.2, 32.1, 31.9, 29.8, 24.2, 21.5, 19.3, 19.2, 9.3. **HRMS** (ESI) *m/z*: [M+H]$^+$ calcd for $C_{33}H_{35}O_7$ 543.2379, found 543.2394.[105]

Rezishanone B (35a)



Rezishanone B (**35a**)

<u>*SMILES*</u>: O[C@@]1(C)[C@@H]2/C(C([C@@](C1=O)(C)[C@@H](OCCCC)C2)=O)=C(/C=C/C=C/C)O

<u>*Fungus of origin*</u>: *Penicillium chrysogenum*[106], *Penicillium notatum*[28].

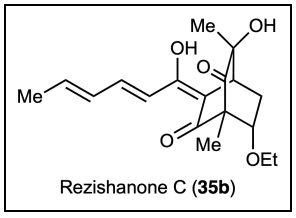
<u>*Bioactivity*</u>: Antibacterial against *Staphylococcus aureus* and *Bacillus subtilis* (weak).[28]

<u>*Biosynthesis*</u>: See figure S5N. In theory, the biosynthesis is based on sorbicillinol (**2a**) and *N*-butyl vinyl ether. However, the vinyl ether has never been isolated as a natural product so far. Therefore an unnatural origin can not be excluded.[28]

<u>*Total synthesis*</u>: Rezishanone B (**22a**) has been synthesized chemo-enzymatically using the heterologous expressed monooxygenase SorbC together with sorbicillin (**1a**) and *N*-butyl vinyl ether (32% yield).[42,107]

<u>*Analytics*</u>: Colorless solid. **TLC**: R_f = 0.46 (DCM/MeOH = 10:1). **ORD**: $[\alpha]_D$ = +253.4 (c = 0.7, MeOH). **^{1}H-NMR** (300 MHz, C_6D_6): δ = 14.71 (bs, 1H, OH), 7.33 (dd, J = 14.9, 11.0 Hz, 1H, CH_{sorbyl}), 5.99 (d, J = 14.9 Hz, 1H, CH_{sorbyl}), 5.93 (ddd, J = 14.9, 11.0, 1.2 Hz, 1H, CH_{sorbyl}), 5.57 (dq, J = 14.8, 6.9 Hz, 1H, CH_{sorbyl}), 3.36 (dd, J = 8.4, 2.3 Hz, 1H, CH), 3.15 (m, 1H, CH_2), 3.04 (d, J = 2.9 Hz, 1H, CH), 2.98 (m, 1H, CH_2), 2.91 (m, 1H, CH_2), 1.67 (s, 3H, CH_3), 1.61 (m, 1H, CH_2), 1.43 (d, J = 6.4 Hz, 3H, CH_3), 1.25 (m, 2H, CH_2), 1.19 (m, 1H, CH_2), 1.12 (s, 3H, CH_3), 0.75 (m, 1H, CH_2), 0.70 (s, 3H, CH_3). **^{13}C-NMR** (75 MHz, C_6D_6): δ = 210.5, 197.0, 166.4, 141.7, 138.4, 131.2, 118.6, 111.0, 79.5, 74.6, 69.8, 67.7, 40.3, 32.0, 30.8, 24.1, 19.6, 18.6, 13.9, 9.7. **IR**: ν 3427, 2982, 2932, 1627, 1603, 1558, 1446, 1386, 1335, 1204, 1105, 1047, 998, 943, 908, 874, 750 cm^{-1}. **HRMS** (ESI) *m/z*: [M+H]$^+$ calcd for $C_{20}H_{29}O_5$ 349.2010, found 349.2009.[28,42]

Rezishanone C (35b) [Sorbivinetone]



Rezishanone C (**35b**)

<u>*SMILES*</u>: O[C@@]1(C)[C@@H]2/C(C([C@@](C1=O)(C)[C@@H](OCC)C2)=O)=C(/C=C/C=C/C)O

<u>*Fungus of origin*</u>: *Penicillium chrysogenum* E01-10/3[6], *Penicillium notatum*[28], *Trichoderma viride*[41], *Trichoderma* sp.[52], unidentified fungus B00853[93].

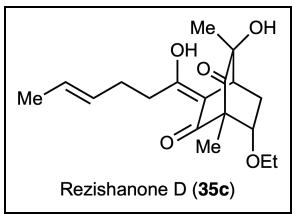
<u>*Bioactivity*</u>: Antibacterial against *Staphylococcus aureus* and *Bacillus subtilis* (weak).[28] Cytotoxicity against murine leukemic lymphoblasts L5178y (IC_{50} > 10.0 mg/mL).[6]

<u>*Biosynthesis*</u>: See figure S5N. In theory, the biosynthesis is based on sorbicillinol (**2a**) and ethyl vinyl ether. However, the vinyl ether has never been isolated as a natural product so far. Therefore an unnatural origin can not be excluded.[28]

<u>*Total synthesis*</u>: Rezishanone C (**22b**) has been synthesized chemo-enzymatically using the heterologous expressed monooxygenase SorbC together with sorbicillin (**1a**) and ethyl vinyl ether (29% yield).[42,107] Willis and co-workers also reported the total synthesis of the enantiomer of rezishanone C (*ent*-**22b**), proving the correct stereo information in the natural product **22b**.[108]

<u>*Analytics*</u>: Colorless solid or light-brown amorphous solid. **MP**: 100–118 °C. **TLC**: R_f = 0.51 (DCM/MeOH = 10:1). **ORD**: $[\alpha]_D$ = 285.7 (c = 0.7, MeOH), $[\alpha]_D^{20}$ = +219.0 (c = 0.1, MeOH). **^{1}H-NMR** (400 MHz, CD_3OD): δ = 7.27 (dd, 1H, CH_{sorbyl}), 6.38 (m, 2H, CH_{sorbyl}), 6.20 (m, 1H, CH_{sorbyl}), 3.62 (m, 1H, CH), 3.58 (dq, 1H, CH_2), 3.35 (m, 1H, CH_2), 3.17 (t, 1H, CH), 2.85 (ddd, 1H, CH_2), 1.88 (dd, J = 6.8 Hz, 3H, CH_3), 1.63 (m, 1H, CH_2), 1.22 (s, 3H, CH_3), 1.15 (s, 3H, CH_3), 1.11 (t, 3H, CH_3). **^{1}H-NMR** (300 MHz, C_6D_6): δ = 14.64 (bs, 1H, OH), 7.33 (dd, J = 15.1, 11.3 Hz, 1H, CH_{sorbyl}), 5.95 (m, 2H, CH_{sorbyl}), 5.58 (dq, J = 13.6, 6.8 Hz, 1H, CH_{sorbyl}), 3.37 (m, 1H, CH), 3.15 (m, 1H, CH_2), 3.06 (m, 1H, CH), 2.92 (m, 1H, CH_2), 2.81 (m, 1H, CH_2), 1.64 (s, 3H, CH_3), 1.46 (d, J = 6.8 Hz, 3H, CH_3), 1.42 (m, 1H, CH_2), 1.01 (s, 3H, CH_3), 0.84 (t, J = 7.2 Hz, 3H, CH_3). **^{13}C-NMR** (100 MHz, CD_3OD): δ = 210.4, 198.3, 167.3, 142.9, 139.7, 132.3, 119.5, 112.3, 79.9, 74.9, 68.7, 66.3, 41.7, 31.8, 24.0, 18.8, 15.4, 9.6. **^{13}C-NMR** (75 MHz, C_6D_6): δ = 210.5, 197.0, 166.4, 141.7, 138.2, 131.2, 118.6, 111.0, 79.3, 74.3, 67.6, 65.5, 40.2, 30.9, 24.1, 18.6, 15.2, 9.6. **IR**: ν 3423, 2977, 2934, 1636, 1600, 1558, 1438, 1386, 1327, 1204, 1109, 1046, 998, 938, 905, 876, 746 cm^{-1}. **HRMS** (ESI) *m/z*: [M+Na]$^+$ calcd for $C_{18}H_{24}O_5Na$ 343.1516, found 343.1516.[6,28,42]

Rezishanone D (35d)



Rezishanone D (**35c**)

SMILES: O[C@@]1(C)[C@@H]2/C(C([C@@](C1=O)(C)[C@@H](OCC)C2)=O)=C(CC/C=C/C)\O

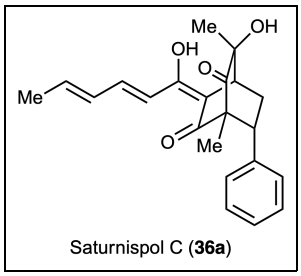
Fungus of origin: *Penicillium notatum*[28], unidentified fungus B00853[93].

Bioactivity: Antibacterial against *Staphylococcus aureus* and *Bacillus subtilis* (weak).[28]

Biosynthesis: See figure S5N. In theory, the biosynthesis is based on dehydrosorbicillinol (**2b**) and ethyl vinyl ether. However, the vinyl ether has never been isolated as a natural product so far. Therefore an unnatural origin can not be excluded.[28]

Analytics: Colorless solid. **TLC**: R_f = 0.51 (DCM/MeOH = 10:1). ^{1}**H-NMR** (300 MHz, C_6D_6): δ = 14.93 (bs, 1H, O*H*), 5.25 (m, 2H, C*H*), 3.37 (m, 1H, C*H*), 3.15 (m, 1H, CH_2), 2.92 (m, 1H, CH_2), 2.81 (m, 1H, C*H*), 3.73 (m, 1H, CH_2), 2.15 (m, 2H, CH_2), 2.05 (m, 2H, CH_2), 1.61 (s, 3H, CH_3), 1.56 (m, 1H, CH_2), 1.49 (d, J = 6.8 Hz, 3H, CH_3), 0.98 (s, 3H, CH_3), 0.84 (t, J = 7.2 Hz, 3H, CH_3). ^{13}**C-NMR** (75 MHz, C_6D_6): δ = 210.4, 195.4, 177.3, 129.6, 126.5, 110.7, 79.3, 74.3, 67.1, 65.4, 40.6, 32.0, 31.2, 29.4, 24.1, 17.9, 15.2, 9.5. **IR**: ν 3423, 2977, 2934, 1636, 1600, 1558, 1438, 1386, 1327, 1204, 1109, 1046, 998, 938, 905, 876, 746 cm^{-1}. **HRMS** (ESI) *m/z*: $[M+Na]^+$ calcd for $C_{18}H_{26}O_5Na$ 345.1672, found 345.1672.[28]

Saturnispol C (36a)



Saturnispol C (**36a**)

SMILES: O[C@@]1(C)[C@@H]2/C(C([C@@](C1=O)(C)[C@@H](C3=CC=CC=C3)C2)=O)=C(/C=C/C=C/C)O

Fungus of origin: *Trichoderma saturnisporum* DI-IA[62].

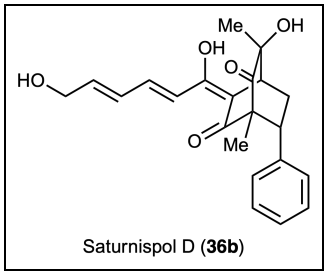
Bioactivity: Weak antimicrobial activities against *Staphylococcus aureus*, vancomycin-resistant *enterococci* (VRE), *Bacillus subtilis*, *Pseudomonas aeruginosa*, and *Klebsiella pneumoniae*.[62]

Biosynthesis: See figure S5N. The biosynthesis is based on the [4+2] Diels-Alder reaction between sorbicillinol (**2a**) and styrene.[62]

Total synthesis: Saturnispol C (**23a**) has been synthesized chemo-enzymatically using the heterologous expressed monooxygenase SorbC together with sorbicillin (**1a**) and styrene.[31]

Analytics: Yellow oil. **ORD**: $[\alpha]_D$ = +20.0 (c = 0.1, MeOH). ^{1}**H-NMR** (400 MHz, $CDCl_3$): δ = 14.34 (bs, 1H, O*H*), 7.41 (dd, J = 14.8, 10.8 Hz, 1H, CH_{sorbyl}), 7.26 (t, J = 7.6 Hz, 3H, Ar*H*), 6.98 (d, J = 7.6 Hz, 2H, Ar*H*), 6.33 (dd, J = 14.8, 10.8 Hz, 1H, CH_{sorbyl}), 6.30 (d, J = 14.8 Hz, 1H, CH_{sorbyl}), 6.25 (dq, J = 14.8, 6.8 Hz, 1H, CH_{sorbyl}), 3.32 (t, J = 2.8 Hz, 1H, C*H*), 3.15 (dd, J = 10.8, 5.6 Hz, 1H, C*H*), 3.05 (ddd, J = 13.5, 10.8, 2.8 Hz, 1H, CH_2), 2.69 (bs, 1H, O*H*), 1.94 (d, J = 6.8 Hz, 3H, CH_3), 1.90 (ddd, J = 13.5, 5.6, 2.8 Hz, 1H, CH_2), 1.29 (s, 3H, CH_3), 0.93 (s, 3H, CH_3). ^{13}**C-NMR** (100 MHz, $CDCl_3$): δ = 211.7, 197.7, 167.1, 142.4, 141.4, 139.7, 130.9, 128.6 (2C), 128.4 (2C), 127.4, 118.1, 112.0, 74.8, 64.6, 47.7, 40.5, 31.4, 24.4, 18.9, 10.5. **IR**: ν 3429, 2925, 2853, 1730, 1712, 1601, 1453, 1377, 1230 cm^{-1}. **HRMS** (ESI) *m/z*: $[M-H]^-$ calcd for $C_{22}H_{23}O_4$ 351.1596, found 351.1600.[62]

Saturnispol D (36b)



Saturnispol D (**36b**)

SMILES: O[C@@]1(C)[C@@H]2/C(C([C@@](C1=O)(C)[C@@H](C3=CC=CC=C3)C2)=O)=C(/C=C/C=C/CO)O

Fungus of origin: *Trichoderma saturnisporum* DI-IA[62].

Bioactivity: Weak antimicrobial activities against *Staphylococcus aureus*, vancomycin-resistant *enterococci* (VRE), *Bacillus subtilis*, *Pseudomonas aeruginosa*, and *Klebsiella pneumoniae*.[62]

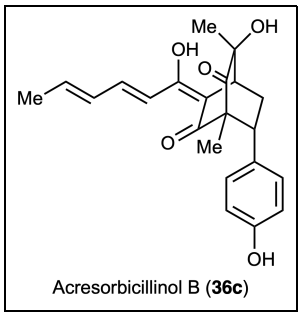
Biosynthesis: See figure S5N. The biosynthesis is based on the [4+2] Diels-Alder reaction between sorbicillinol (**2a**) and styrene, followed by a hydroxylation.[62] However, we have previously shown that the monooxygenase SorbC also tolerates hydroxysorbicillin (**1c**) as a substrate.[31] Therefore, it is unclear if the hydroxylation takes place in the beginning or in the end of the biosynthesis.

Total synthesis: Saturnispol D (**23b**) has been synthesized chemo-enzymatically using the heterologous expressed monooxygenase SorbC together with hydroxysorbicillin (**1c**) and styrene.[31]

Analytics: Yellow oil. **TLC**: R_f = (DCM/acetone = 9:1). **ORD**: $[\alpha]_D$ = +26.0 (c = 0.1, MeOH). ^{1}**H-NMR** (400 MHz, acetone-d_6): δ = 14.40 (bs, 1H, O*H*), 7.43 (dd, J = 15.2, 10.8 Hz, 1H, CH_{sorbyl}), 7.29 (t, J = 7.6 Hz, 2H, Ar*H*), 7.26 (t, J = 7.6 Hz, 1H, Ar*H*), 7.07 (d, J = 7.6 Hz, 2H, Ar*H*), 6.75 (d, J = 15.2 Hz, 1H, CH_{sorbyl}), 6.68 (dd, J = 15.2, 10.8 Hz, 1H, CH_{sorbyl}), 6.39 (dt, J = 15.2, 4.4 Hz, 1H, CH_{sorbyl}), 5.05 (bs, 1H, O*H*), 4.28 (t, J = 4.4 Hz, 2H, CH_2), 4.104 (t, J = 4.4 Hz, 1H, O*H*), 3.46 (t, J = 2.8 Hz, 1H, C*H*), 3.24 (dd,

J = 10.8, 6.0 Hz, 1H, C*H*), 3.09 (ddd, J = 13.5, 10.8, 2.8 Hz, 1H, CH_2), 1.87 (ddd, J = 13.5, 6.0, 2.8 Hz, 1H, CH_2), 1.26 (s, 3H, CH_3), 0.80 (s, 3H, CH_3). ^{13}**C-NMR** (100 MHz, acetone-d_6): δ = 209.2, 198.4, 166.8, 142.9, 142.1, 141.0, 128.4 (4C), 127.7, 127.0, 120.3, 112.9, 73.7, 64.8, 61.7, 46.4, 40.7, 31.5, 23.2, 10.4. **IR**: ν 439, 2926, 2854, 1771, 1732, 1617, 1440, 1390 cm^{-1}. **HRMS** (ESI) m/z: $[M-H]^-$ calcd for $C_{22}H_{23}O_5$ 367.1545, found 367.1544.[62]

Acresorbicillinol B (36c)



Acresorbicillinol B (**36c**)

SMILES: O[C@@]1(C)[C@@H]2/C(C([C@@](C1=O)(C)[C@@H](C3=CC=C(O)C=C3)C2)=O)=C(/C=C/C=C/C)O

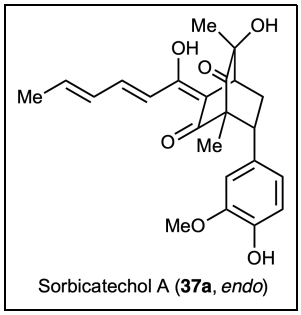
Fungus of origin: *Acremonium chrysogenum* C10[94].

Bioactivity: Antibacterial against *Staphylococcus aureus* (IC_{50} = 86.9 μM).[94]

Biosynthesis: See figure S5N. *endo*-Selective [4+2] Diels-Alder reaction between sorbicillinol (**2a**) and vinylphenol [CAS: 2628-17-3].

Analytics: Pale yellow solid. **ORD**: $[\alpha]_D^{25}$ = +5.0 (c = 0.1, MeOH). ^{1}**H-NMR** (500 MHz, CD_3OD): δ = 7.37 (dd, J = 14.6, 11.0 Hz, 1H, CH_{sorbyl}), 6.80 (d, J = 8.4 Hz, 2H, Ar*H*), 6.67 (d, J = 8.4 Hz, 2H, Ar*H*), 6.48 (d, J = 14.6 Hz, 1H, CH_{sorbyl}), 6.41 (dd, J = 14.6, 11.0 Hz, 1H, CH_{sorbyl}), 6.23 (dq, J = 14.6, 7.0 Hz, 1H, CH_{sorbyl}), 3.30 (t, J = 2.7 Hz, 1H, C*H*), 3.09 (dd, J = 10.6 6.1 Hz, 1H, C*H*), 3.00 (ddd, J = 13.6, 10.6, 2.7 Hz, 1H, CH_2), 1.90 (d, J = 7.0 Hz, 3H, CH_3), 1.80 (ddd, J = 13.6, 6.1, 2.7 Hz, 1H, CH_2), 1.21 (s, 3H, CH_3), 0.80 (s, 3H, CH_3). ^{13}**C-NMR** (125 MHz, CD_3OD): δ = 211.4, 199.7, 167.7, 157.7, 143.3, 140.1, 133.9, 132.3, 130.5 (2C), 119.6, 116.2 (2C), 113.8, 75.2, 66.7, 47.5, 42.3, 32.7, 24.0, 18.9, 11.4. **IR**: ν 3413, 1724, 1624, 1440, 1378, 1243 cm^{-1}. **HRMS** (ESI) m/z: $[M+H]^+$ calcd for $C_{22}H_{25}O_5$ 369.1697, found 369.1696.[94]

Sorbicatechol A (37a) [CAS: 1558039-41-0]



Sorbicatechol A (**37a**, *endo*)

SMILES: O[C@@]1(C)[C@@H]2/C(C([C@@](C1=O)(C)[C@@H](C3=CC(OC)=C(O)C=C3)C2)=O)=C(/C=C/C=C/C)O

Fungus of origin: *Penicillium chrysogenum* PJX-17[109].

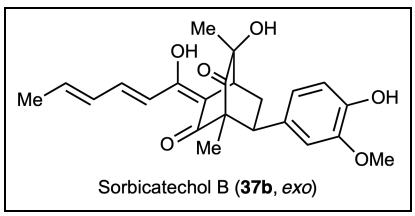
Bioactivity: Antiviral activity against influenza A virus (H1N1, IC_{50} = 85.0 μM).[109] Further evaluation of the activity against IAV has revealed cytotoxicity against the host cell system, rather than a true antiviral effect.[107]

Biosynthesis: See figure S5N. The biosynthesis is based on the *endo*-selective [4+2] Diels-Alder reaction between sorbicillinol (**2a**) and 2-methoxy-4-vinylphenol.[109]

Total synthesis: Sorbicatechol A (**24a**) has been synthesized chemo-enzymatically using heterologous expressed SorbC together with sorbicillin (**1a**) and 2-methoxy-4-vinylphenol.[42,107]

Analytics: Yellow oil. **ORD**: $[\alpha]_D^{20}$ = +19.0 (c = 0.1, MeOH). ^{1}**H-NMR** (600 MHz, $CDCl_3$): δ = 14.32 (bs, 1H, O*H*), 7.38 (dd, J = 14.8, 12.9 Hz, 1H, CH_{sorbyl}), 6.79 (d, J = 8.2 Hz, 1H, Ar*H*), 6.49 (dd, J = 8.2, 1.7 Hz, 1H, Ar*H*), 6.45 (d, J = 1.7 Hz, 1H, Ar*H*), 6.33 (dd, J = 14.8, 12.9 Hz, 1H, CH_{sorbyl}), 6.29 (d, J = 14.8 Hz, 1H, CH_{sorbyl}), 6.23 (m, 1H, CH_{sorbyl}), 3.79 (s, 3H, ArOCH_3), 3.29 (dd, J = 2.8, 2.8 Hz, 1H, C*H*), 3.05 (m, 1H, CH_2), 3.01 (m, 1H, C*H*), 1.91 (d, J = 6.6 Hz, 3H, CH_3), 1.84 (m, 1H, CH_2), 1.26 (s, 3H, CH_3), 0.93 (s, 3H, CH_3). ^{13}**C-NMR** (150 MHz, $CDCl_3$): δ = 211.9, 197.9, 167.1, 146.5, 144.9, 142.5, 139.9, 133.2, 130.9, 121.5, 118.0, 114.3, 112.0, 110.2, 74.6, 65.1, 55.7, 47.8, 40.5, 31.4, 24.3, 18.9, 10.5. **IR**: ν 3408, 2925, 1720, 1629, 1519, 1247, 998 cm^{-1}. **HRMS** (ESI) m/z: $[M+H]^+$ calcd for $C_{23}H_{26}O_6$ 399.1808, found 399.1801.

Sorbicatechol B (37b) [CAS: 1558039-42-1]



Sorbicatechol B (**37b**, *exo*)

SMILES: O[C@@]1(C)[C@@H]2/C(C([C@@](C1=O)(C)[C@H](C3=CC(OC)=C(O)C=C3)C2)=O)=C(/C=C/C=C/C)O

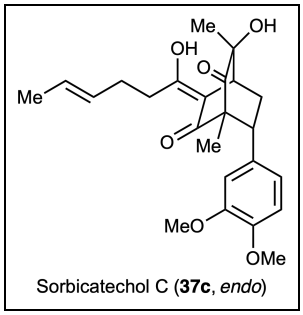
Fungus of origin: *Penicillium chrysogenum* PJX-17[109].

Bioactivity: Antiviral activity against influenza A virus (H1N1, IC_{50} = 113 μM).[109] Further evaluation of the activity against IAV has revealed cytotoxicity against the host cell system, rather than a true antiviral effect.[107]

Biosynthesis: See figure S5N. The biosynthesis is based on the *exo*-selective [4+2] Diels-Alder reaction between sorbicillinol (**2a**) and 2-methoxy-4-vinylphenol.[109]

Analytics: Yellow oil. **ORD**: $[\alpha]_D^{20} = +120.0$ (c = 0.1, MeOH). ^{1}**H-NMR** (600 MHz, $CDCl_3$): δ = 13.93 (bs, 1H, O*H*), 7.33 (dd, *J* = 14.8, 11.0 Hz, 1H, CH_{sorbyl}), 6.80 (d, *J* = 8.2 Hz, 1H, Ar*H*), 6.71 (s, 1H, Ar*H*), 6.60 (d, *J* = 8.2 Hz, 1H, Ar*H*), 6.30 (dd, *J* = 14.8, 11.0 Hz, 1H, CH_{sorbyl}), 6.25 (d, *J* = 14.8 Hz, 1H, CH_{sorbyl}), 6.21 (m, 1H, CH_{sorbyl}), 5.30 (bs, 1H, O*H*), 3.82 (s, 3H, ArOCH_3), 3.23 (s, 1H, C*H*), 3.03 (dd, *J* = 10.9, 7.7 Hz, 1H, C*H*), 2.57 (dd, *J* = 12.7, 7.7 Hz, 1H, CH_2), 2.25 (dt, *J* = 10.9, 3.3 Hz, 1H, CH_2), 1.91 (d, *J* = 6.6 Hz, 3H, CH_3), 1.28 (s, 3H, CH_3), 0.84 (s, 3H, CH_3). ^{13}**C-NMR** (150 MHz, $CDCl_3$): δ = 212.1, 199.7, 167.3, 146.4, 144.9, 142.2, 139.7, 132.0, 131.0, 122.4, 118.1, 114.1, 111.2, 110.5, 75.9, 65.0, 55.9, 49.9, 40.6, 30.2, 25.2, 19.0, 10.3. **IR**: *ν* 3400, 2925, 1720, 1629, 1519, 1247, 998 cm^{-1}. **HRMS** (ESI) *m/z*: $[M+H]^+$ calcd for $C_{23}H_{26}O_6$ 399.1808, found 399.1803.

Sorbicatechol C (37c)



Sorbicatechol C (**37c**, *endo*)

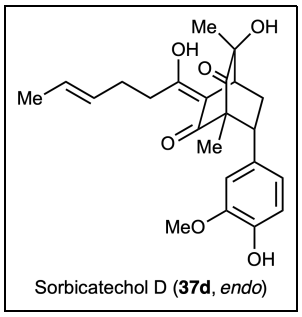
SMILES: O[C@@]1(C)[C@@H]2/C(C([C@@](C1=O)(C)[C@@H](C3=CC(OC)=C(OC)C=C3)C2)=O)=C(CC/C=C/C)\O

Fungus of origin: *Penicillium allii-sativi* MCCC 3A00580[5].

Biosynthesis: See figure S5N.

Analytics: Yellow oil. **ORD**: $[\alpha]_D^{20} = -14.6$ (c = 0.5, MeOH), $[\alpha]_D^{20} = -7.2$ (c = 0.5, $CHCl_3$). ^{1}**H-NMR** (400 MHz, DMSO-d_6): δ = 14.68 (bs, 1H, O*H*), 6.83 (d, *J* = 8.2 Hz, 1H, Ar*H*), 6.53 (d, *J* = 1.5 Hz, 1H, Ar*H*), 6.51 (dd, *J* = 8.2, 1.5 Hz, 1H, Ar*H*), 5.98 (bs, 1H, O*H*), 5.49 (m, 2H, C*H*), 3.70 (s, 3H, ArOCH_3), 3.64 (s, 3H, ArOCH_3), 3.15 (t, *J* = 2.8 Hz, 1H, C*H*), 3.11 (dd, *J* = 10.6, 5.8 Hz, 1H, C*H*), 2.90 (ddd, *J* = 13.2, 10.6, 2.8 Hz, 1H, CH_2), 2.67 (dt, *J* = 14.0, 7.5 Hz, 1H, CH_2), 2.48 (dt, *J* = 14.0, 6.7 Hz, 1H, CH_2), 2.32 (m, 2H, CH_2), 1.70 (ddd, *J* = 13.2, 5.8, 2.8 Hz, 1H, CH_2), 1.56 (d, *J* = 4.7 Hz, 3H, CH_3), 1.13 (s, 3H, CH_3), 0.71 (s, 3H, CH_3). ^{13}**C-NMR** (100 MHz, DMSO-d_6): δ = 209.6, 196.0, 178.7, 148.3, 147.8, 134.3, 129.6, 125.9, 120.2, 112.5, 111.6 (2C), 72.9, 64.1, 55.4, 55.1, 45.3, 41.1, 31.5, 31.3, 28.9, 23.6, 17.7, 10.7. **HRMS** (ESI) *m/z*: $[M+Na]^+$ calcd for $C_{24}H_{30}O_6Na$ 437.1940, found 437.1951.[5]

Sorbicatechol D (37d) [Dehydrosorbicatechol A]



Sorbicatechol D (**37d**, *endo*)

SMILES: O[C@@]1(C)[C@@H]2/C(C([C@@](C1=O)(C)[C@@H](C3=CC(OC)=C(O)C=C3)C2)=O)=C(CC/C=C/C)\O

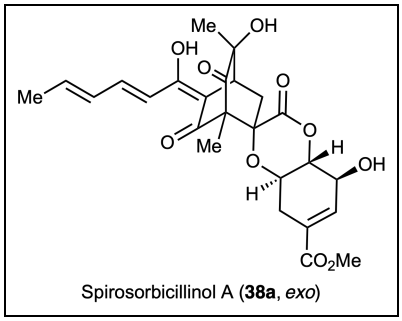
Fungus of origin: *Penicillium allii-sativi* MCCC 3A00580[5].

Bioactivity: Cytotoxicity against HT-29 tumor cells. Inducing cell cycle G2-M phase arresting by increasing the protein levels of p-H3 and cyclin B1.[5]

Biosynthesis: See figure S5N.

Analytics: Yellow oil. **ORD**: $[\alpha]_D^{20} = -19.1$ (c = 0.4, MeOH). ^{1}**H-NMR** (400 MHz, DMSO-d_6): δ = 14.69 (bs, 1H, O*H*), 8.92 (bs, 1H, O*H*), 6.63 (d, *J* = 8.1 Hz, 1H, Ar*H*), 6.49 (d, *J* = 1.8 Hz, 1H, Ar*H*), 6.37 (dd, *J* = 8.1, 1.8 Hz, 1H, Ar*H*), 5.96 (bs, 1H, O*H*), 5.49 (m, 1H, C*H*), 5.47 (m, 1H, C*H*), 3.65 (s, 3H, ArOCH_3), 3.12 (t, *J* = 2.6 Hz, 1H, C*H*), 3.05 (dd, *J* = 10.6, 5.8 Hz, 1H, C*H*), 2.88 (ddd, *J* = 13.4, 10.6, 2.8 Hz, 1H, CH_2), 2.65 (dt, *J* = 14.0, 7.0 Hz, 1H, CH_2), 2.45 (dt, *J* = 14.0, 6.6 Hz, 1H, CH_2), 2.33 (m, 2H, CH_2), 1.68 (ddd, *J* = 13.4, 5.8, 2.8 Hz, 1H, CH_2), 1.57 (d, *J* = 4.7 Hz, 3H, CH_3), 1.14 (s, 3H, CH_3), 0.70 (s, 3H, CH_3). ^{13}**C-NMR** (100 MHz, DMSO-d_6): δ = 209.6, 196.0, 178.6, 147.2, 145.5, 132.8, 129.6, 125.9, 120.6, 115.2, 112.5, 112.1, 72.9, 64.2, 55.3, 45.4, 41.1, 31.5, 31.4, 28.9, 23.6, 17.7, 10.7. **HRMS** (ESI) *m/z*: $[M-H]^-$ calcd for $C_{23}H_{27}O_6$ 399.1808, found 399.1790.[5]

Spirosorbicillinol A (38a)



Spirosorbicillinol A (**38a**, *exo*)

SMILES: O[C@@]1(C)[C@@H]2/C(C([C@@](C1=O)(C)[C@@]3(O[C@@](CC(C(OC)=O)=C[C@@H]4O)([H])[C@]4([H])OC3=O)C2)=O)=C(/C=C/C=C/C)O

Fungus of origin: *Trichoderma citrinoviride*[12], *Trichoderma longibrachiatumm* SFC1001[44], *Trichoderma* sp. USF-4860[79].

Bioactivity: Antifungal activity against *Phytophthora infestans* ($IC_{50} = 400$ μg/mL).[44]

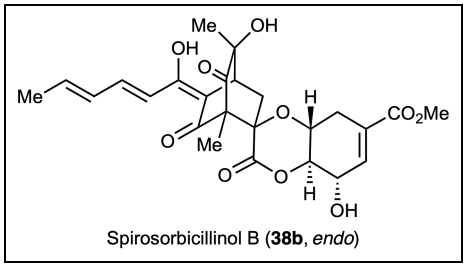
Biosynthesis: See figure S5N. *exo*-Diels-Alder reaction between sorbicillinol (**2a**) and scytolide.[79]

Total synthesis: Spirosorbicillinol A (**25a**) has been synthesized chemo-enzymatically using heterologous expressed SorbC together with sorbicillin (**1a**) and scytolide. The complexity of

this synthesis is based on the formation of the dienophile (9 steps, 35% yield).[110]

Analytics: Yellowish, amorphous powder. **ORD**: $[\alpha]_D^{19} = +165.9$ (c = 0.2, MeOH). ^{1}**H-NMR** (400 MHz, CD_3OD): δ = 7.33 (dd, *J* = 14.4, 10.8 Hz, 1H, C*H*$_{sorbyl}$), 6.65 (dd, *J* = 3.2, 1.6 Hz, 1H, C*H*$_{sorbyl}$), 6.41 (d, *J* = 14.4 Hz, 1H, C*H*$_{sorbyl}$), 6.40 (m, 1H, C*H*$_{sorbyl}$), 6.23 (m, 1H, C*H*$_{sorbyl}$), 4.45 (m, 1H, C*H*), 4.27 (dd, *J* = 10.0, 8.4 Hz, 1H, C*H*), 4.07 (dt, *J* = 10.0, 6.0 Hz, 1H, C*H*), 3.74 (s, 3H, COOC*H*$_3$), 3.31 (overlapping with MeOH signal, 1H, C*H*), 3.05 (dd, *J* = 14.8, 3.0 Hz, 1H, C*H*$_2$), 2.80 (dd, *J* = 17.6, 6.0 Hz, 1H, C*H*), 2.25 (m, 1H, C*H*), 2.18 (dd, *J* = 14.8, 3.0 Hz, 1H, C*H*$_2$), 1.89 (d, *J* = 6.8 Hz, 3H, C*H*$_3$), 1.23 (s, 3H, C*H*$_3$), 1.20 (s, 3H, C*H*$_3$). ^{13}**C-NMR** (100 MHz, CD_3OD): δ = 206.8, 195.6, 172.1, 168.4, 167.5, 143.8, 140.6, 139.6, 132.3, 129.0, 119.3, 111.2, 86.0, 84.4, 74.7, 70.7, 69.4, 67.2, 52.7, 41.5, 37.3, 30.6, 24.9, 18.9, 8.1. **IR**: *ν* 3460, 2920, 1740, 1720, 1610, 1560, 1380 cm^{-1}. **HRMS** (FAB) *m/z*: $[M+Na]^+$ calcd for $C_{25}H_{28}O_{10}Na$ 511.1580, found 511.1593.[79]

Spirosorbicillinol B (38b)



Spirosorbicillinol B (**38b**, *endo*)

SMILES: O[C@@]1(C)[C@@H]2/C(C([C@@](C1=O)(C)[C@@]3(C(O[C@@]([C@@H](O)C=C(C(OC)=O)C4)([H])[C@]4([H])O3)=O)C2)=O)=C(/C=C/C=C/C)O

Fungus of origin: *Trichoderma longibrachiatumm* SFC1001[44], *Trichoderma* sp. USF-4860[79].

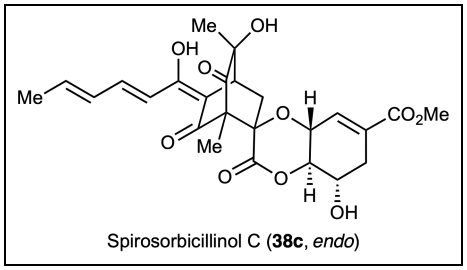
Bioactivity: Antifungal activity against *Phytophthora infestans* ($IC_{50} = 400$ µg/mL).[44]

Biosynthesis: See figure S5N. *endo*-Diels-Alder reaction between sorbicillinol (**2a**) and scytolide.[79]

Total synthesis: Spirosorbicillinol B (**25b**) has been synthesized chemo-enzymatically using heterologous expressed SorbC together with sorbicillin (**1a**) and scytolide. The complexity of this synthesis is based on the formation of the dienophile (9 steps, 35% yield).[110]

Analytics: Yellowish, amorphous powder. **ORD**: $[\alpha]_D^{19} = +316.7$ (c = 0.4, MeOH). ^{1}**H-NMR** (400 MHz, CD_3OD): δ = 7.29 (dd, *J* = 15.2, 10.8 Hz, 1H, C*H*$_{sorbyl}$), 6.64 (dd, *J* = 3.2, 2.0 Hz, 1H, C*H*$_{sorbyl}$), 6.38 (m, 1H, C*H*$_{sorbyl}$), 6.36 (d, *J* = 15.2 Hz, 1H, C*H*), 6.20 (m, 1H, C*H*$_{sorbyl}$), 4.45 (m, 1H, C*H*), 4.36 (dd, *J* = 10.0, 7.6 Hz, 1H, C*H*), 4.01 (dt, *J* = 10.0, 6.8 Hz, 1H, C*H*), 3.75 (s, 3H, COOC*H*$_3$), 3.30 (overlapping with MeOH signal, 1H, C*H*), 2.98 (dd, *J* = 14.0, 2.8 Hz, 1H, C*H*$_2$), 2.90 (dd, *J* = 17.6, 6.8 Hz, 1H, C*H*), 2.29 (m, 1H, C*H*), 2.33 (dd, *J* = 14.0, 2.8 Hz, 1H, C*H*$_2$), 1.88 (d, *J* = 6.8 Hz, 3H, C*H*$_3$), 1.25 (s, 3H, C*H*$_3$), 1.19 (s, 3H, C*H*$_3$). ^{13}**C-NMR** (100 MHz, CD_3OD): δ = 207.2, 196.3, 171.1, 168.0, 167.5, 143.3, 140.1, 139.3, 132.4, 128.1, 119.6, 111.5, 83.8, 82.7, 75.0, 71.4, 71.0, 70.7, 52.7, 41.3, 40.5, 31.5, 24.9, 18.9, 8.8. **IR**: *ν* 3460, 2920, 1740, 1720, 1610, 1560, 1440, 1380, 1260 cm^{-1}. **HRMS** (FAB) *m/z*: $[M+H]^+$ calcd for $C_{25}H_{29}O_{10}$ 489.1761, found 489.1748.[79]

Spirosorbicillinol C (38c)



Spirosorbicillinol C (**38c**, *endo*)

SMILES: O[C@@]1(C)[C@@H]2/C(C([C@@](C1=O)(C)[C@@]3(C(O[C@@]([C@@H](O)CC(C(OC)=O)=C4)([H])[C@]4([H])O3)=O)C2)=O)=C(/C=C/C=C/C)O

Fungus of origin: *Trichoderma longibrachiatumm* SFC1001[44], *Trichoderma* sp. USF-4860[79].

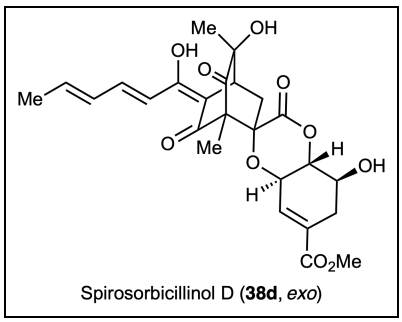
Bioactivity: Antifungal activity against *Phytophthora infestans* ($IC_{50} = 400$ µg/mL).[44]

Biosynthesis: See figure S5N. *endo*-Diels-Alder reaction between sorbicillinol (**2a**) and scytolide isomer.[79]

Total synthesis: Spirosorbicillinol C (**25c**) has been synthesized chemo-enzymatically using heterologous expressed SorbC together with sorbicillin (**1a**) and *epi*-scytolide. The complexity of this synthesis is based on the formation of the dienophile (11 steps, 2% yield).[110]

Analytics: Yellowish, amorphous powder. **ORD**: $[\alpha]_D^{19} = +484.2$ (c = 0.3, MeOH). ^{1}**H-NMR** (400 MHz, CD_3OD): δ = 7.29 (dd, *J* = 14.8, 10.8 Hz, 1H, C*H*$_{sorbyl}$), 6.63 (s, 1H, C*H*), 6.37 (m, 1H, C*H*$_{sorbyl}$), 6.36 (d, *J* = 14.8 Hz, 1H, C*H*$_{sorbyl}$), 6.20 (m, 1H, C*H*$_{sorbyl}$), 4.47 (m, 1H, C*H*), 4.31 (dd, *J* = 10.8, 9.6 Hz, 1H, C*H*), 4.03 (dt, *J* = 9.6, 6.8 Hz, 1H, C*H*), 3.75 (s, 3H, COOC*H*$_3$), 3.31 (overlapping with MeOH signal, 1H, C*H*), 2.99 (dd, *J* = 14.8, 3.2 Hz, 1H, C*H*$_2$), 2.90 (dd, *J* = 17.6, 6.8 Hz, 1H, C*H*), 2.34 (dd, *J* = 14.8, 3.2 Hz, 1H, C*H*$_2$), 2.27 (m, 1H, C*H*), 1.88 (d, *J* = 6.8 Hz, 3H, C*H*$_3$), 1.26 (s, 3H, C*H*$_3$), 1.20 (s, 3H, C*H*$_3$). ^{13}**C-NMR** (100 MHz, CD_3OD): δ = 207.2, 196.2, 171.4, 168.1, 167.5, 143.4, 140.2, 134.3, 132.4, 131.0, 119.5, 111.4, 83.9, 83.0, 75.1 (2C), 71.0, 67.3, 52.7, 41.4, 40.4, 34.2, 24.9, 18.9, 8.6. **IR**: *ν* 3460, 2920, 1740, 1720, 1610, 1560, 1440, 1380, 1260 cm^{-1}. **HRMS** (FAB) *m/z*: $[M+H]^+$ calcd for $C_{25}H_{29}O_{10}$ 489.1761, found 489.1751.[79]

Spirosorbicillinol D (38d)



Spirosorbicillinol D (**38d**, *exo*)

SMILES: O[C@@]1(C)[C@@H]2/C(C([C@@](C1=O)(C)[C@@]3(O[C@@](C=C(C(OC)=O)C[C@@H]4O)([H])[C@]4([H])OC3=O)C2)=O)=C(/C=C/C=C/C)O

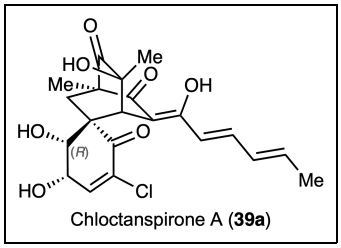
Fungus of origin: *Trichoderma longibrachiatumm* SFC1001[44].

Bioactivity: Antifungal activity against *Phytophthora infestans* ($IC_{50} = 400$ µg/mL).[44]

Biosynthesis: See figure S5N. *exo*-Diels-Alder reaction between sorbicillinol (**2a**) and scytolide isomer.[44]

Analytics: Yellowish, amorphous powder. **ORD**: $[\alpha]_D^{25} = +142.0$ (c = 0.1, MeOH). ^{1}**H-NMR** (400 MHz, CD_3OD): δ = 7.36 (dd, *J* = 14.9, 10.9 Hz, 1H, C*H*$_{sorbyl}$), 6.57 (s, 1H, C*H*), 6.46 (d, *J* = 14.9, 6.8 Hz, 1H, C*H*$_{sorbyl}$), 6.44 (m, 1H, C*H*$_{sorbyl}$), 6.26 (dd, *J* = 14.6, 7.0 Hz, 1H, C*H*$_{sorbyl}$), 4.66 (m, 1H, C*H*), 4.24 (dd, *J* = 10.4, 6.8 Hz, 1H, C*H*), 4.09 (td, *J* = 9.7, 6.8 Hz, 1H, C*H*), 3.77 (s, 3H, COOC*H*$_3$), 3.38 (overlapping with MeOH signal, 1H, C*H*), 3.13 (dd, *J* = 14.2, 2.3 Hz, 1H, C*H*$_2$), 2.95 (dd, *J* = 28.3, 6.9 Hz, 1H, C*H*), 2.32 (m, 1H, C*H*), 2.24 (dd, *J* = 14.2, 3.7 Hz, 1H, C*H*$_2$), 1.92 (d, *J* = 6.8 Hz, 3H, C*H*$_3$), 1.25 (s, 3H, C*H*$_3$), 1.23 (s, 3H, C*H*$_3$). ^{13}**C-NMR** (100 MHz, CD_3OD): δ = 206.8, 195.4, 172.2, 168.3, 167.2, 143.8, 140.6, 134.2, 132.3, 131.7, 119.3, 111.1, 85.8, 84.1, 74.6, 70.3, 69.2, 67.1, 52.7, 41.4, 38.0, 34.4, 24.9, 18.9, 8.3. **HRMS** (ESI) *m/z*: $[M+Na]^+$ calcd for $C_{25}H_{28}O_{10}Na$ 511.1580, found 511.1580.[44]

Chloctanspirone A (39a)



Chloctanspirone A (**39a**)

SMILES: O=C1[C@@]2(C)C[C@]3([C@@H](O)[C@@H](O)C=C(Cl)C3=O)[C@H]([C@@](O)(C)C2=O)/C1=C(\C=C\C=C\C)O.C

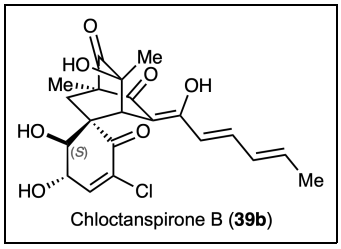
Fungus of origin: *Penicillium terrestre*[111].

Bioactivity: Cytotoxicity against leukemic HL-60 cell line ($IC_{50} = 9.20$ µM) and human lung cancer cell line A549 ($IC_{50} = 39.7$ µM).[111]

Biosynthesis: See figure S5N. The biosynthesis is based on the [4+2] Diels-Alder reaction between sorbicillinol (**2a**) and terrestrol K.[111]

Analytics: Yellow powder. **ORD**: $[\alpha]_D^{25} = +304.0$ (c = 0.1, MeOH). ^{1}**H-NMR** (600 MHz, DMSO-d_6): δ = 13.77 (bs, 1H, O*H*), 7.12 (dd, *J* = 14.6, 10.7 Hz, 1H, C*H*$_{sorbyl}$), 6.83 (dd, *J* = 2.3, 2.2 Hz, 1H, C*H*), 6.41 (d, *J* = 14.6 Hz, 1H, C*H*$_{sorbyl}$), 6.37 (bs, 1H, O*H*), 6.32 (dd, *J* = 15.1, 10.7 Hz, 1H, C*H*$_{sorbyl}$), 6.21 (dq, *J* = 15.1, 6.4 Hz, 1H, C*H*$_{sorbyl}$), 5.43 (d, *J* = 8.3 Hz, 1H, O*H*), 5.34 (d, *J* = 5.5 Hz, 1H, O*H*), 5.03 (ddd, *J* = 8.3, 3.2, 2.3 Hz, 1H, C*H*), 4.66 (dd, *J* = 5.5, 3.2 Hz, 1H, C*H*), 3.49 (s, 1H, C*H*), 2.57 (d, *J* = 14.0 Hz, 1H, C*H*$_2$), 1.84 (d, *J* = 6.4 Hz, 3H, C*H*$_3$), 1.75 (d, *J* = 14.0 Hz, 1H, C*H*$_2$), 1.10 (s, 3H, C*H*$_3$), 1.07 (s, 3H, C*H*$_3$). ^{13}**C-NMR** (150 MHz, DMSO-d_6): δ = 210.2, 198.3, 193.5, 166.6, 145.8, 141.8, 139.1, 130.9, 128.3, 118.5, 109.3, 76.6, 74.8, 66.7, 59.4, 57.6, 45.2, 38.0, 24.7, 18.7, 12.1. **IR**: *ν* 3419, 1735, 1701, 1612 cm^{-1}. **HRMS** (ESI) *m/z*: $[M-H]^-$ calcd for $C_{21}H_{22}O_7Cl$ 421.1054, found 421.1068.[111]

Chloctanspirone B (39b)



Chloctanspirone B (**39b**)

SMILES: O=C1[C@@]2(C)C[C@]3([C@H](O)[C@@H](O)C=C(Cl)C3=O)[C@H]([C@@](O)(C)C2=O)/C1=C(\C=C\C=C\C)O

Fungus of origin: *Penicillium terrestre*[111].

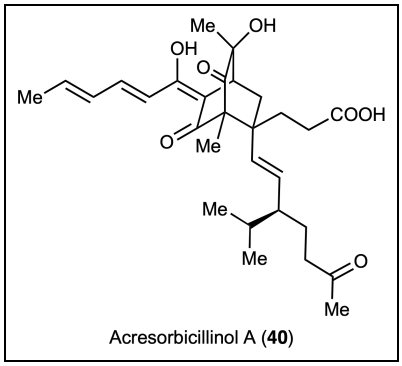
Bioactivity: Cytotoxicity against leukemic HL-60 cell line ($IC_{50} = 37.8$ µM) and human lung cancer cell line A549 ($IC_{50} > 100$ µM).[111]

Biosynthesis: See figure S5N. The biosynthesis is based on the [4+2] Diels-Alder reaction between sorbicillinol (**2a**) and terrestrol L.[111]

Analytics: Yellow powder. **ORD**: $[\alpha]_D^{25} = +110.0$ (c = 0.1, MeOH). ^{1}**H-NMR** (600 MHz, CD_3OD): δ = 7.21 (dd, *J* = 14.6, 11.4 Hz, 1H, C*H*$_{sorbyl}$), 7.08 (d, *J* = 2.2 Hz, 1H, C*H*), 6.33 (dd, *J* = 14.6, 11.4 Hz, 1H, C*H*$_{sorbyl}$), 6.20 (d, *J* = 14.6 Hz, 1H, C*H*$_{sorbyl}$), 6.16 (dq, *J* = 14.6, 6.6 Hz, 1H, C*H*$_{sorbyl}$), 4.87 (m, 1H, C*H*), 3.53 (s, 1H, C*H*), 3.47 (d, *J* = 8.4 Hz, 1H, C*H*), 2.61 (d, *J* = 13.7 Hz, 1H, C*H*$_2$), 2.14 (d, *J* = 13.7 Hz, 1H, C*H*$_2$), 1.88 (d, *J* = 6.6 Hz, 3H, C*H*$_3$), 1.21 (s, 3H, C*H*$_3$), 1.13 (s, 3H, C*H*$_3$). ^{1}**H-NMR** (600 MHz, DMSO-d_6): δ = 13.68 (bs, 1H, O*H*), 7.52 (d, *J* = 6.9 Hz, 1H, O*H*), 7.29 (bs, 1H, O*H*), 7.11 (dd, *J* = 14.9, 11.0 Hz, 1H, C*H*), 7.09 (d, *J* = 2.3 Hz, 1H, C*H*), 6.42 (d, *J* = 14.9 Hz, 1H, C*H*), 6.30 (dd, *J* = 15.1, 11.0 Hz, 1H, C*H*), 6.21 (dq, *J* = 15.1,

6.4 Hz, 1H, C*H*), 6.01 (d, *J* = 5.9 Hz, 1H, O*H*), 4.78 (dd, *J* = 5.9, 5.4 Hz, 1H, C*H*), 3.55 (s, 1H, C*H*), 3.44 (dd, *J* = 6.9, 5.4 Hz, 1H, C*H*), 2.44 (d, *J* = 14.0 Hz, 1H, CH_2), 2.04 (d, *J* = 14.0 Hz, 1H, CH_2), 1.84 (d, *J* = 6.4 Hz, 3H, CH_3), 1.10 (s, 3H, CH_3), 1.01 (s, 3H, CH_3). ^{13}**C-NMR** (150 MHz, DMSO-d_6): δ = 209.8, 198.7, 192.8, 166.1, 147.8, 141.7, 139.1, 130.9, 128.5, 118.5, 109.9, 74.3, 74.1, 69.5, 59.6, 57.0, 45.8, 33.8, 25.0, 18.7, 12.2. **IR**: *ν* 3459, 1735, 1700, 1607 cm^{-1}. **HRMS** (ESI) *m/z*: [M−H]$^-$ calcd for $C_{21}H_{22}O_7Cl$ 421.1054, found 421.1062.[111]

Acresorbicillinol A (40)



Acresorbicillinol A (**40**)

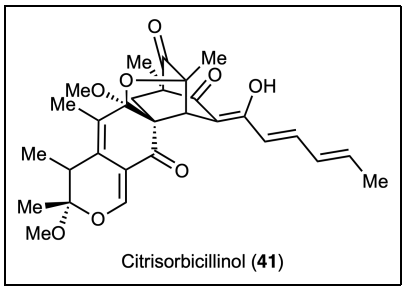
<u>*SMILES*</u>: O[C@@]1(C)[C@@H]2/C(C([C@@](C1=O)(C)[C@](/C=C/[C@@H](CCC(C)=O)C(C)C)(CCC(O)=O)C2)=O)=C(/C=C/C=C/C)O

<u>*Fungus of origin*</u>: *Acremonium chrysogenum* C10[94].

<u>*Biosynthesis*</u>: See figure S5N.

<u>*Analytics*</u>: Pale yellow solid. **ORD**: $[\alpha]_D^{25}$ = +81.0 (c = 0.1, MeOH). ^{1}**H-NMR** (500 MHz, CD_3OD): δ = 7.26 (dd, *J* = 14.6, 10.9 Hz, 1H, CH_{sorbyl}), 6.42 (d, *J* = 14.6 Hz, 1H, CH_{sorbyl}), 6.39 (dd, *J* = 14.6, 10.9 Hz, 1H, CH_{sorbyl}), 6.20 (dq, *J* = 14.6, 7.0 Hz, 1H, CH_{sorbyl}), 5.18 (dd, *J* = 15.6 Hz, 1H, C*H*), 5.13 (dd, *J* = 15.6, 9.0 Hz, 1H, C*H*), 3.18 (t, *J* = 2.8 Hz, 1H, C*H*), 2.42 (m, 1H, CH_2), 2.38 (m, 1H, CH_2), 2.30 (m, 1H, CH_2), 2.16 (m, 2H, CH_2), 2.16 (s, 3H, CH_3), 1.97 (dd, *J* = 13.3, 2.8 Hz, 1H, CH_2), 1.89 (d, *J* = 7.0 Hz, 3H, CH_3), 1.81 (td, *J* = 13.2, 4.8 Hz, 1H, CH_2), 1.68 (m, 1H, C*H*), 1.64 (m, 1H, CH_2), 1.54 (m, 1H, C*H*), 1.50 (m, 1H, CH_2), 1.23 (m, 1H, CH_2), 1.16 (s, 3H, CH_3), 1.12 (s, 3H, CH_3), 0.86 (d, *J* = 7.0 Hz, 3H, CH_3), 0.81 (d, *J* = 7.0 Hz, 3H, CH_3). ^{13}**C-NMR** (125 MHz, CD_3OD): δ = 212.4, 212.3, 200.3, 178.3, 167.6, 142.9, 140.0, 135.9, 135.4, 132.3, 119.5, 112.3, 75.4, 70.3, 50.6, 47.8, 42.4, 41.5, 34.1, 33.4, 31.4, 30.6, 30.0, 27.2, 24.5, 21.2, 19.7, 18.9, 7.4. **IR**: *ν* 3399, 2956, 2872, 1722, 1601, 1446, 1381, 1258 cm^{-1}. **HRMS** (ESI) *m/z*: [M+H]$^+$ calcd for $C_{29}H_{41}O_7$ 501.2847, found 501.2850.[94]

Citrisorbicillinol (41)



Citrisorbicillinol (**41**)

<u>*SMILES*</u>: O=C1[C@@]2(C)C[C@@]3(C4=O)C(C(O[C@]3(OC)C(C)=C5C4=CO[C@](C)(OC)C5C)(C)C2=O)/C1=C(\C=C\C=C\C)O

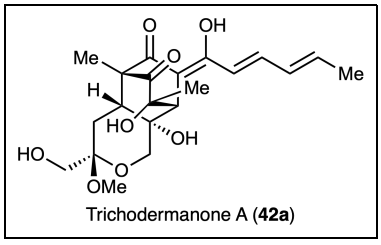
<u>*Fungus of origin*</u>: *Penicillium citrinum* ZY-2[112].

<u>*Bioactivity*</u>: Moderate cytotoxicity against Caco-2, H1299, H23, and A375 cells.[112]

<u>*Biosynthesis*</u>: See figure S5N.

<u>*Analytics*</u>: Pale yellow solid. **ORD**: $[\alpha]_D^{25}$ = +244.4 (c = 0.1, MeOH). ^{1}**H-NMR** (500 MHz, $CDCl_3$): δ = 14.14 (bs, 1H, O*H*), 7.42 (s, 1H, C*H*), 7.26 (dd, *J* = 14.8, 11.0 Hz, 1H, CH_{sorbyl}), 6.19 (dq, *J* = 13.7, 6.8 Hz, 1H, CH_{sorbyl}), 6.06 (dd, *J* = 13.7, 11.0 Hz, 1H, CH_{sorbyl}), 5.74 (d, *J* = 14.8 Hz, 1H, CH_{sorbyl}), 3.55 (s, 1H, C*H*), 3.22 (s, 3H, OCH_3), 3.00 (q, *J* = 7.1 Hz, 1H, C*H*), 2.94 (s, 3H, OCH_3), 2.79 (d, *J* = 13.9 Hz, 1H, CH_2), 2.25 (d, *J* = 13.9 Hz, 1H, CH_2), 1.93 (s, 3H, CH_3), 1.89 (d, *J* = 6.8 Hz, 3H, CH_3), 1.58 (s, 3H, CH_3), 1.35 (s, 3H, CH_3), 1.28 (s, 3H, CH_3), 1.18 (d, *J* = 7.1 Hz, 3H, CH_3). ^{13}**C-NMR** (125 MHz, $CDCl_3$): δ = 202.5, 197.7, 193.2, 170.3, 150.1, 143.3, 140.6, 130.7, 129.4, 124.2, 116.7, 109.8, 109.5, 104.3, 102.2, 80.4, 59.0, 57.3, 52.0, 51.3, 49.9, 37.8, 27.5, 19.1, 18.9, 17.9, 15.0, 11.7, 11.0. **IR**: *ν* 2982, 2940, 1739, 1687 cm^{-1}. **HRMS** (ESI) *m/z*: [M+H]$^+$ calcd for $C_{29}H_{35}O_8$ 511.2326, found 511.2324.[112]

Trichodermanone A (42a)



Trichodermanone A (**42a**)

<u>*SMILES*</u>: O=C([C@@]1(C)[C@](C[C@](CO)(OC)OC2)([H])[C@@]2(O)[C@@H]/3[C@@](O)(C)C1=O)C3=C(\C=C\C=C\C)O

<u>*Fungus of origin*</u>: *Trichoderma* sp.[41,52].

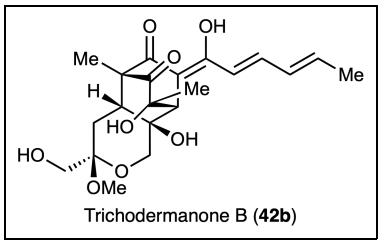
<u>*Bioactivity*</u>: Low DPPH-radical scavenging activity.[52]

<u>*Biosynthesis*</u>: See figure S5O. Diels-Alder reaction between sorbicillinol (**2a**) and another triketide, like 5-oxohex-2-enoic acid, followed by reduction to an aldehyde, ketalization, and hydroxylation.[52]

<u>*Analytics*</u>: Yellowish viscous oil. **ORD**: $[\alpha]_D^{22}$ = +203.0 (c = 0.2, MeOH). ^{1}**H-NMR** (500 MHz, acetone-d_6): δ = 14.20 (bs, 1H, O*H*), 7.22 (dd *J* = 15.0, 10.9 Hz, 1H, CH_{sorbyl}), 6.57 (d *J* = 15.0 Hz, 1H, CH_{sorbyl}), 6.38 (dd *J* = 15.0,

10.9 Hz, 1H, CH_{sorbyl}), 6.18 (dq J = 15.0, 6.8 Hz, 1H, CH_{sorbyl}), 4.35 (d, J = 11.8 Hz, 1H, CH_2OH), 3.82 (d, J = 10.9 Hz, 1H, CH_2), 3.71 (d, J = 11.8 Hz, 1H, CH_2), 3.40 (d, J = 10.9 Hz, 1H, CH_2), 3.38 (s, 1H, CH), 2.98 (s, 3H, CH_3), 2.64 (dd, J = 13.6, 10.7 Hz, 1H, CH_2), 2.56 (d J = 10.7 Hz, 1H, CH), 1.80 (d, J = 6.8 Hz, 3H, CH_3), 1.75 (d, J = 13.6 Hz, 1H, CH_2), 1.14 (s, 3H, CH_3), 1.10 (s, 3H, CH_3). ^{13}**C-NMR** (125 MHz, acetone-d_6): δ = 210.9, 199.0, 167.8, 141.4, 138.7, 132.1, 120.4, 112.3, 110.6, 92.7, 74.7, 69.7, 64.1, 62.7, 50.2, 49.1, 48.8, 38.1, 27.0, 18.8, 10.9. **IR**: ν 3315, 2920, 2851, 1732, 1630, 1602, 1565, 1455, 1381 cm^{-1}. **HRMS** (ESI) m/z: [M−CH_2OH]$^+$ calcd for $C_{20}H_{24}O_7$ 376.1522, found 376.1519.[52]

Trichodermanone B (42b)



Trichodermanone B (**42b**)

SMILES: O=C([C@@]1(C)[C@](C[C@](CO)(OC)OC2)([H])[C@]2(O)[C@@H]/3[C@@](O)(C)C1=O)C3=C(\C=C\C=C\C)O

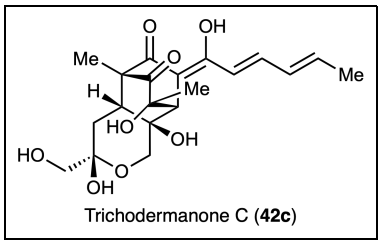
Fungus of origin: *Trichoderma* sp.[41,52].

Bioactivity: Low DPPH-radical scavenging activity.[52]

Biosynthesis: See figure S5O. Diels-Alder reaction between sorbicillinol (**2a**) and another triketide, like 5-oxohex-2-enoic acid, followed by reduction to an aldehyde, ketalization, and hydroxylation.[52]

Analytics: Yellowish viscous oil. **ORD**: $[\alpha]_D^{22}$ = +251.0 (c = 0.2, MeOH). ^{1}**H-NMR** (500 MHz, acetone-d_6): δ = 7.25 (dd J = 15.0, 11.0 Hz, 1H, CH_{sorbyl}), 6.44 (d J = 15.0, 1H, CH_{sorbyl}), 6.39 (dd J = 15.0, 11.0 Hz, 1H, CH_{sorbyl}), 6.23 (dq J = 15.0, 7.0 Hz, 1H, CH_{sorbyl}), 3.91 (m, 2H, CH_2OH), 3.85 (d, J = 11.0 Hz, 1H, CH_2), 3.51 (s, 1H, CH), 3.20 (s, 3H, CH_3), 3.01 (d, J = 11.0 Hz, 1H, CH_2), 2.56 (dd J = 9.9, 7.3 Hz, 1H, CH), 2.17 (dd, J = 13.9, 9.9 Hz, 1H, CH_2), 1.86 (d, J = 7.0 Hz, 3H, CH_3), 1.69 (dd, J = 13.9, 7.3 Hz, 1H, CH_2), 1.14 (s, 3H, CH_3), 1.08 (s, 3H, CH_3). ^{13}**C-NMR** (125 MHz, acetone-d_6): δ = 210.9, 200.2, 168.9, 142.1, 139.5, 132.0, 120.0, 111.5, 111.0, 90.3, 74.7, 68.4, 64.5, 62.2, 49.7, 49.1, 48.9, 40.9, 26.5, 18.8, 11.8. **IR**: ν 3393, 2938, 1733, 1630, 1600, 1561, 1383 cm^{-1}. **HRMS** (ESI) m/z: [M]$^+$ calcd for $C_{21}H_{28}O_8$ 408.1783, found 408.1780.[52]

Trichodermanone C (42c)



Trichodermanone C (**42c**)

SMILES: O=C([C@@]1(C)[C@](C[C@@](O)(CO)OC2)([H])[C@]2(O)[C@@H]/3[C@@](O)(C)C1=O)C3=C(\CC=C\CC=C\CC)O

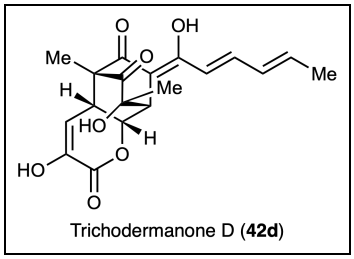
Fungus of origin: *Trichoderma citrinoviride*[12], *Trichoderma* sp.[41,52].

Bioactivity: Low DPPH-radical scavenging activity.[52] Anti-inflammatory activity in lipopolysaccharide-stimulated J774A.1 cells.[12]

Biosynthesis: See figure S5O. Diels-Alder reaction between sorbicillinol (**2a**) and another triketide, like 5-oxohex-2-enoic acid, followed by reduction to an aldehyde, ketalization, and hydroxylation.[52]

Analytics: Yellowish viscous oil. **ORD**: $[\alpha]_D^{22}$ = +265.7 (c = 0.5, MeOH). ^{1}**H-NMR** (500 MHz, acetone-d_6): δ = 7.24 (dd J = 15.0, 10.6 Hz, 1H, CH_{sorbyl}), 6.45 (d J = 15.0 Hz, 1H, CH_{sorbyl}), 6.36 (dd J = 15.0, 10.6 Hz, 1H, CH_{sorbyl}), 6.25 (dq J = 15.0, 6.5 Hz, 1H, CH_{sorbyl}), 4.28 (d, J = 11.7 Hz, 1H, CH_2OH), 3.76 (d, J = 11.7 Hz, 1H, CH_2), 3.37 (s, 1H, CH), 3.29 (s, 3H, CH_2), 2.71 (dd J = 9.9, 7.0 Hz, 1H, CH), 2.17 (dd, J = 14.1, 9.9 Hz, 1H, CH_2), 1.85 (d, J = 6.5 Hz, 3H, CH_3), 1.74 (dd, J = 14.1, 7.0 Hz, 1H, CH_2), 1.14 (s, 3H, CH_3), 1.09 (s, 3H, CH_3). ^{13}**C-NMR** (125 MHz, acetone-d_6): δ = 211.0, 200.0, 168.8, 142.1, 139.3, 132.0, 120.1, 111.6, 107.5, 90.3, 74.7, 68.2, 67.4, 64.4, 49.9, 49.6, 40.3, 26.9, 18.8, 11.0. **IR**: ν 3330, 2937, 1731, 1627, 1597, 1556, 1380 cm^{-1}. **HRMS** (ESI) m/z: [M]$^+$ calcd for $C_{20}H_{26}O_8$ 394.1628, found 394.1625.[52]

Trichodermanone D (42d)



Trichodermanone D (**42d**)

SMILES: O=C([C@@]1(C)[C@](C=C(C(O2)=O)O)([H])[C@]2([H])[C@@H]/3[C@@](O)(C)C1=O)C3=C(\C=C\C=C\C)O

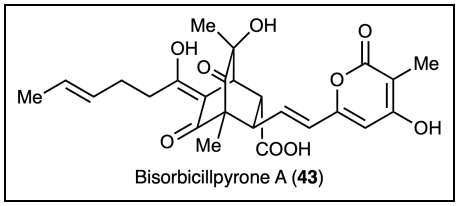
Fungus of origin: *Trichoderma* sp.[41,52].

Biosynthesis: See figure S5O. Diels-Alder reaction between sorbicillinol (**2a**) and another triketide, like 5-oxohex-2-enoic acid, followed by decarboxylation, hydroxylation, oxidation and lactone formation.[52]

Analytics: Yellowish viscous oil. **ORD**: $[\alpha]_D^{22}$ = +51.5 (c = 0.1, MeOH). ^{1}**H-NMR** (500 MHz, acetone-d_6): δ = 7.29 (dd, J = 15.0, 11.0 Hz, 1H, CH_{sorbyl}), 6.55 (d, J = 15.0 Hz, 1H, CH_{sorbyl}),

6.44 (dd, J = 15.0, 11.0 Hz, 1H, CH_{sorbyl}), 6.26 (dq, J = 15.0, 7.0 Hz, 1H, CH_{sorbyl}), 5.75 (d, J = 2.9 Hz, 1H, CH), 5.57 (dd, J = 10.6, 3.7 Hz, 1H, CH), 3.74 (d, J = 3.7 Hz, 1H, CH), 3.58 (dd, J = 10.6, 2.9 Hz, 1H, CH), 1.88 (d, J = 7.0 Hz, 3H, CH_3), 1.25 (s, 3H, CH_3), 1.19 (s, 3H, CH_3). ^{13}**C-NMR** (125 MHz, acetone-d_6): δ = 202.3, 198.9, 170.9, 161.0, 151.7, 143.4, 140.1, 132.6, 120.2, 109.6, 107.8, 80.9, 74.5, 64.7, 53.0, 47.6, 23.9, 19.2, 10.6. **IR**: ν 3383, 2923, 2359, 1729, 1599, 1404 cm^{-1}. **HRMS** (ESI) m/z: $[M-H]^-$ calcd for $C_{19}H_{20}O_7$ 360.1209, found 360.1209.[52]

Bisorbicillpyrone A (43)



Bisorbicillpyrone A (**43**)

SMILES: O[C@@]1(C)[C@@H]2/C(C([C@@](C1=O)(C)[C@H](/C=C/C3=CC(O)=C(C)C(O3)=O)[C@H]2C(O)=O)=O)=C(/C=C/C=C/C)O

Fungus of origin: *Penicillium* sp. SCSIO06868[104], *Penicillium* sp. SCSIO06871[51] .

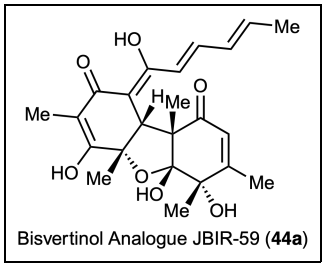
Bioactivity: α-Glycosidase inhibition (IC_{50} = 156.3 μM).[51]

Biosynthesis: See figure S5P. Diels-Alder reaction between sorbicillinol (**2a**) and methylated trichopyrone.[51]

Analytics: Pale yellow powder. **ORD**: $[\alpha]_D^{20}$ = +159.1 (c = 0.1, MeOH). ^{1}**H-NMR** (700 MHz, CD_3OD): δ = 6.17 (dd, J = 15.4, 9.8 Hz, 1H, CH), 6.10 (d, J = 15.4 Hz, 1H, CH), 6.02 (s, 1H, CH), 5.49 (m, 1H, CH), 5.43 (m, 1H, CH), 3.46 (d, J = 2.8 Hz, 1H, CH), 3.37 (dd, J = 5.6, 2.8 Hz, 1H, CH), 3.09 (dd, J = 9.8, 5.6 Hz, 1H, CH), 2.45 (m, 2H, CH_2), 2.27 (m, 2H, CH_2), 1.83 (s, 3H, CH_3), 1.59 (dd, J = 6.3, 0.7 Hz, 3H, CH_3), 1.19 (s, 3H, CH_3), 1.02 (s, 3H, CH_3). ^{13}**C-NMR** (175 MHz, CD_3OD): δ = 210.3, 197.6, 181.6, 176.2, 167.7, 167.2, 156.6, 135.8, 130.7, 127.4, 126.2, 109.1, 102.6, 101.3, 74.7, 63.7, 49.0, 46.7, 45.8, 33.1, 30.1, 24.1, 18.0, 10.9, 8.6. **HRMS** (ESI) m/z: $[M+H]^+$ calcd for $C_{25}H_{29}O_9$ 473.1806, found 473.1806.[51]

1.3.2 Michael-type hybrid sorbicillinoids

Bisvertinol Analogue JBIR-59 (44a)



Bisvertinol Analogue JBIR-59 (**44a**)

SMILES: O=C1C=C(C)[C@@](O)(C)[C@@]2(O)[C@]1(C)[C@](/C(C(C(C)=C3O)=O)=C(\C=C\C=C\C)O)([H])[C@]3(C)O2

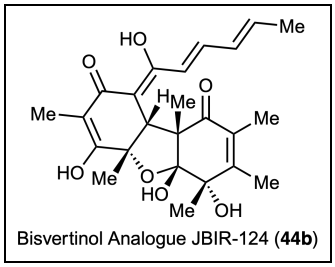
Fungus of origin: *Penicillium citrinum* SpI080624G1f01[72].

Bioactivity: L-glutamate toxicity in N18-RE-105 cells ($EC_{50} = 71.0$ μM).[72]

Biosynthesis: See figure S6Q. Michael reaction between sorbicillinol (**2a**) and dimethylorcin [CAS: 20427-81-0] followed by a ketalization.[102]

Analytics: Yellow, amorphous solid. **ORD**: $[\alpha]_D^{27} = -3501.0$ (c = 0.1, MeOH). ^{1}**H-NMR** (500 MHz, $CDCl_3$): δ = 16.43 (bs, 1H, O*H*), 7.30 (dd, *J* = 15.0, 11.0 Hz, 1H, CH_{sorbyl}), 6.38 (d, *J* = 15.0 Hz, 1H, CH_{sorbyl}), 6.28 (ddd, *J* = 15.0, 11.0, 1.0 Hz, 1H, CH_{sorbyl}), 6.11 (dq, *J* = 15.0, 7.0 Hz, 1H, CH_{sorbyl}), 5.64 (s, 1H, C*H*), 3.65 (s, 1H, C*H*), 2.01 (d, *J* = 1.0 Hz, 3H, CH_3), 1.87 (dd, *J* = 7.0, 1.0 Hz, 3H, CH_3), 1.63 (s, 3H, CH_3), 1.45 (s, 3H, CH_3), 1.36 (s, 3H, CH_3), 1.28 (s, 3H, CH_3). ^{13}**C-NMR** (125 MHz, $CDCl_3$): δ = 194.9, 190.9, 170.8, 162.5, 161.6, 139.6, 137.4, 131.1, 125.6, 120.2, 111.9, 106.7, 100.4, 80.3, 76.9, 59.6, 54.1, 25.8, 24.4, 18.80, 18.78, 18.2, 6.8. **IR**: *ν* 1658 cm^{-1}. **HRMS** (ESI) *m/z*: $[M+H]^+$ calcd for $C_{23}H_{29}O_7$ 417.1913, found 417.1910.[72]

Bisvertinol Analogue JBIR-124 (44b)



Bisvertinol Analogue JBIR-124 (**44b**)

SMILES: O=C1C(C)=C(C)[C@@](O)(C)[C@@]2(O)[C@]1(C)[C@](/C(C(C(C)=C3O)=O)=C(\C=C\C=C\C)O)([H])[C@]3(C)O2

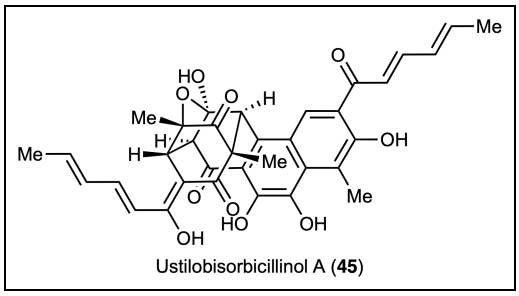
Fungus of origin: *Penicillium citrinum* SpI080624G1f01[113].

Bioactivity: DPPH-radical scavenging activity ($IC_{50} = 30.0$ μM).[113]

Biosynthesis: See figure S6Q. Michael reaction between sorbicillinol (**2a**) and duro-*p*-hydroquinone [CAS: 527-18-4] followed by a ketalization.

Analytics: Yellow, amorphous solid. **ORD**: $[\alpha]_D^{22} = -282.0$ (c = 0.2, MeOH). ^{1}**H-NMR** (600 MHz, $CDCl_3/CD_3OD$ = 1:1): δ = 7.23 (dd, *J* = 15.0, 11.4 Hz, 1H, CH_{sorbyl}), 6.43 (d, *J* = 15.0 Hz, 1H, CH_{sorbyl}), 6.29 (dd, *J* = 15.0, 11.4 Hz, 1H, CH_{sorbyl}), 6.10 (dq, *J* = 15.0, 6.6 Hz, 1H, CH_{sorbyl}), 3.63 (s, 1H, C*H*), 1.97 (s, 3H, CH_3), 1.88 (d, *J* = 6.6 Hz, 3H, CH_3), 1.59 (s, 3H, CH_3), 1.55 (s, 3H, CH_3), 1.42 (s, 3H, CH_3), 1.28 (s, 3H, CH_3), 1.26 (s) (s, 3H, CH_3). ^{13}**C-NMR** (150 MHz, $CDCl_3/CD_3OD$ = 1:1): δ = 196.4, 192.2, 169.5, 167.6, 156.6, 139.3, 137.3, 131.6, 131.0, 120.9, 114.6, 110.7, 106.1, 101.6, 80.0, 76.6, 59.8, 55.1, 26.3, 24.6, 19.5, 18.8, 12.3, 7.9. **IR**: *ν* 1656 cm^{-1}. **HRMS** (ESI) *m/z*: $[M+H]^+$ calcd for $C_{24}H_{31}O_7$ 431.2070, found 431.2086.[113]

Ustilobisorbicillinol A (45)



Ustilobisorbicillinol A (**45**)

SMILES: O=C([C@@]1(C)O2)[C@@]([C@]([C@@]2(O)[C@]3([H])[C@]1([H])/C4=C(\C=C\C=C\C)O)([H])C5=C(C(O)=C(O)C6=C5C=C(C(/C=C/C=C/C)=O)C(O)=C6C)C3=O)(C)C4=O

Fungus of origin: *Ustilaginoidea virens*[114].

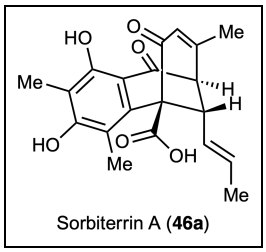
Bioactivity: Influence on the cell-cycle progression with the gastric cancer cell line BGC823 (induction of G0/G1, and G2/M-phase cell-cycle arrest). Cytotoxicity against human colon cancer HCT116 cells ($IC_{50} = 11.5$ μM), human lung cancer NCI-H460 cells ($IC_{50} = 6.34$ μM), human gastric cancer BGC823 cells ($IC_{50} = 4.48$ μM), desmoplastic cerebellar medulloblastoma Daoy cells ($IC_{50} = 9.02$ μM), human hepatoma HepG2 cells ($IC_{50} = 18.6$ μM).[114]

Biosynthesis: See figure S6R. The heterodimer **39** was proposed to be biosynthesized from the phenanthrenedione and sorbicillinol (**2a**) through two rounds of Michael addition and one ketalization.[114]

Analytics: Yellow, amorphous powder. **ORD**: $[\alpha]_D^{25} = -400.0$ (c = 0.1, MeOH). ^{1}**H-NMR** (600 MHz, $CDCl_3$): δ = 14.98 (bs, 1H, O*H*), 13.03 (bs, 1H, O*H*), 12.22 (bs, 1H, O*H*), 8.99, s (s, 1H, Ar*H*), 7.76 (d, *J* = 14.6 Hz, 1H, CH_{sorbyl}), 7.61 (dd, *J* = 14.6, 10.9 Hz, 1H, CH_{sorbyl}, 7.31 (dd, *J* = 14.9, 10.8 Hz, 1H, CH_{sorbyl}), 6.59 (ddd, *J* = 15.0, 10.9, 1.5 Hz, 1H, CH_{sorbyl}), 6.56 (d, *J* = 14.9 Hz, 1H, CH_{sorbyl}), 6.49 (dq, *J* = 15.0, 6.8 Hz, 1H, CH_{sorbyl}), 6.42 (ddd, *J* = 15.1, 10.8, 1.8 Hz, 1H, CH_{sorbyl}), 6.33 (dq, *J* = 15.1, 6.7 Hz, 1H, CH_{sorbyl}), 4.96 (d, *J* = 2.0 Hz, 1H, C*H*), 4.32 (d, *J* = 11.3 Hz, 1H, C*H*), 3.63 (dd, *J* = 11.3, 2.0 Hz, 1H, C*H*), 2.82 (s, 3H, CH_3), 1.93

(d, J = 6.8 Hz, 3H, CH_3), 1.90 (d, J = 6.7 Hz, 3H, CH_3), 1.55 (s, 3H, CH_3), 1.31 (s, 3H, CH_3). ^{13}**C-NMR** (150 MHz, acetone-d_6): δ = 204.1, 198.9, 198.3, 195.3, 173.3, 158.3, 147.7, 145.0, 144.5, 143.7, 141.7, 140.1, 136.4, 132.7, 131.9, 131.7, 131.6, 122.6, 121.6, 120.4, 120.1, 118.4, 116.5, 106.9, 105.9, 81.0, 65.0, 58.0, 54.7, 44.4, 19.1, 19.0, 18.5, 15.7, 13.6. **IR**: ν 3727, 3452, 1737, 1722, 1654, 1618, 1577, 1561 cm^{-1}. **HRMS** (ESI) m/z: [M+H]$^+$ calcd for $C_{35}H_{33}O_{10}$ 613.2068, found 613.2060.[114]

Sorbiterrin A (46a)



Sorbiterrin A (**46a**)

SMILES: O=C(O)[C@]1(C2=O)C3=C(C(O)=C(C)C(O)=C3C)C([C@](C(C)=C2)([H])[C@]1([H])/C=C/C)=O

Fungus of origin: *Penicillium* sp. SCSIO06871[51], *Penicillium terrestre*[115].

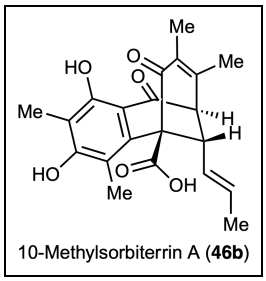
Bioactivity: Inhibition of cholinesterase enzyme (IC_{50} = 25.0 μg/mL).[115]

Biosynthesis: See figure S6S. Michael reaction between sorbicillinol (**2a**) and 3,5-dioxohexanoic acid, followed by dehydration, intramolecular Michael reaction, Aldol condensation and rearrangement.[115]

Total synthesis: See figure S13. Biomimetic approach to sorbiterrin A (**40a**) has been developed employing consecutive Michael additions of 3,5-dioxohexanoic acid to sorbicillinol (**2a**) and bridged aldol/dehydration to construct the [3.3.1] ring system.[116]

Analytics: Yellow oil. **ORD**: $[\alpha]_D^{25}$ = +392.0 (c = 1.0, MeOH). ^{1}**H-NMR** (600 MHz, DMSO-d_6): δ = 13.00 (bs, 1H, O*H*), 5.71 (d, J = 0.9 Hz, 1H, C*H*), 5.70 (m, 1H, C*H*), 5.37 (dd, J = 14.2, 9.1 Hz, 1H, C*H*), 3.57 (dd, J = 9.1, 2.8 Hz, 1H, C*H*), 3.21 (d, J = 2.8 Hz, 1H, C*H*), 2.01 (s, 3H, CH_3), 1.99 (s, 3H, CH_3), 1.94 (d, J = 0.9 Hz, 3H, CH_3), 1.55 (d, J = 5.5 Hz, 3H, CH_3). ^{13}**C-NMR** (150 MHz, DMSO-d_6): δ = 197.0, 190.5, 170.0, 162.6, 161.6, 158.4, 131.9, 130.1, 127.7, 123.0, 120.0, 110.9, 106.6, 60.7, 55.5, 49.9, 22.2, 17.8, 15.0, 8.2. **IR**: ν 3300, 1718, 1676, 1617, 1422, 1355, 1212 cm^{-1}. **HRMS** (ESI) m/z: [M−H]$^-$ calcd for $C_{20}H_{19}O_6$ 355.1182, found 355.1170.[115]

10-Methylsorbiterrin A (46b)



10-Methylsorbiterrin A (**46b**)

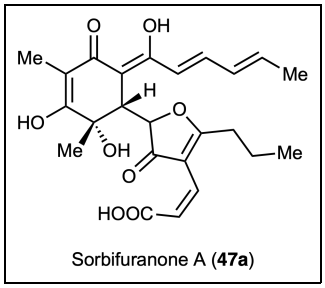
SMILES: O=C(O)[C@]1(C2=O)C3=C(C(O)=C(C)C(O)=C3C)C([C@](C(C)=C2C)([H])[C@]1([H])/C=C/C)=O

Fungus of origin: *Penicillium* sp. SCSIO06871[51].

Biosynthesis: See figure S6S. Identical with sorbiterrin A (**40a**) using 4-methyl-3,5-dioxohexanoic acid instead of 3,5-dioxohexanoic acid.

Analytics: Colorless needles. **MP**: 153–154 °C. **ORD**: $[\alpha]_D^{20}$ = +309.4 (c = 0.1, MeOH). ^{1}**H-NMR** (700 MHz, CD_3OD): δ = 5.77 (dq, J = 14.7, 6.3 Hz, 1H, C*H*), 5.47 (ddd, J = 14.7, 9.8, 2.1 Hz, 1H, C*H*), 3.61 (dd, J = 9.8, 2.8 Hz, 1H, C*H*), 3.19 (d, J = 1.4 Hz, 1H, C*H*), 2.10 (s, 3H, CH_3), 2.08 (s, 3H, CH_3), 2.02 (d, J = 0.7 Hz, 3H, CH_3), 1.74 (s, 3H, CH_3), 1.63 (dd, J = 6.3, 1.4 Hz, 3H, CH_3). ^{13}**C-NMR** (175 MHz, CD_3OD): δ = 199.1, 192.3, 173.0, 163.7, 163.3, 152.8, 133.0, 131.7, 129.6, 128.9, 120.8, 112.5, 108.1, 62.8, 58.2, 51.9, 20.1, 18.1, 15.2, 11.5, 7.9. **HRMS** (ESI) m/z: [M+H]$^+$ calcd for $C_{21}H_{23}O_6$ 371.1489, found 371.1496.[51].

Sorbifuranone A (47a)



Sorbifuranone A (**47a**)

SMILES: O=C(C(C)=C(O)[C@](O)(C)[C@@]/1([H])C2C(C(/C=C/C(O)=O)=C(CCC)O2)=O)C1=C(O)\C=C\C=C\C

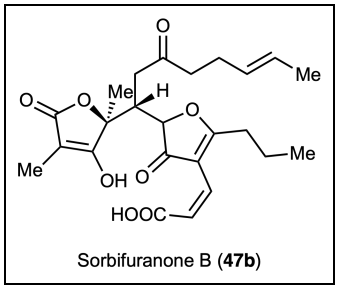
Fungus of origin: *Penicillium* sp.[27].

Biosynthesis: See figure S6T. Michael reaction between sorbicillinol (**2a**) and a special furane ((*E*)-3-(4-oxo-2-propyl-4,5-dihydrofuran-3-yl)acrylic acid). The furane could be based on pentaketidic butyrophenone, with subsequent reduction of the resulting aldehyde and ring closure by enol ether formation of the primary alcohol.[27].

Analytics: Yellow, amorphous solid. **MP**: 107-110 °C. **ORD**: $[\alpha]_D^{20}$ = −10.0 (c = 0.1, MeOH). ^{1}**H-NMR** (600 MHz, CD_3OD): δ = 7.00 (dd, J = 14.7, 10.9 Hz, 1H, CH_{sorbyl}), 6.30 (d, J = 11.9 Hz, 1H, CH_{sorbyl}), 6.24 (m, 1H, CH_{sorbyl}), 6.16 (d, J = 14.7 Hz, 1H, CH_{sorbyl}), 6.02 (m, 1H, C*H*), 5.92 (d, J = 11.9 Hz, 1H, C*H*), 5.27 (d, J = 1.5 Hz, 1H, C*H*), 3.38 (d, J = 1.5 Hz, 1H, C*H*), 2.42 (t, J = 7.8 Hz, 2H, CH_2), 1.84 (dd, J = 6.8, 1.4 Hz, 3H, CH_3), 1.73 (s, 3H, CH_3), 1.50 (m, 2H, CH_2), 1.47 (s, 3H, CH_3), 0.88 (t, J = 7.3 Hz, 3H, CH_3). ^{13}**C-NMR** (150 MHz, CD_3OD): δ = 203.8, 194.0, 193.6, 172.0, 169.4, 169.1, 139.9, 137.4, 132.7, 130.6, 124.4, 121.9, 115.6,

109.2, 102.5, 84.7, 71.9, 50.6, 33.6, 28.4, 20.3, 18.8, 14.3, 7.9. **IR**: ν 3407, 2967, 2937, 2876, 1708, 1635, 1443, 1382, 1342, 1195, 1078 cm^{-1}. **HRMS** (ESI) m/z: $[M+H]^+$ calcd for $C_{24}H_{29}O_8$ 445.1862, found 445.1859.[27]

Sorbifuranone B (47b)



Sorbifuranone B (**47b**)

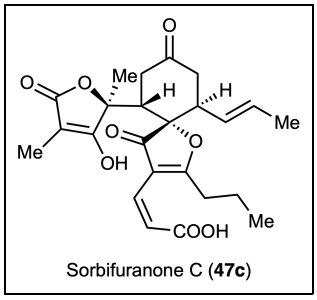
SMILES: O=C(CC/C=C/C)C[C@@](C1C(C(/C=C/C(O)=O)=C(CCC)O1)=O)([H])[C@]2(C)OC(C(C)=C2O)=O

Fungus of origin: *Penicillium* sp.[27].

Biosynthesis: See figure S6T. Sorbifuranone B (**41b**) can be considered as the rearrangement product of a hypothetical dihydrosorbifuranone A , resulting from a nucleophilic attack of the hydroxy group to the carbonyl with cleavage oft a C-C bond.[27]

Analytics: Yellow, amorphous solid. **MP**: 78-83 °C. **ORD**: $[\alpha]_D^{20} = +19.3$ (c = 0.1, MeCN). ^{1}**H-NMR** (600 MHz, acetone-d_6): δ = 6.49 (d, J = 11.7 Hz, 1H, C*H*), 5.97 (d, J = 11.7 Hz, 1H, C*H*), 5.43 (m, 1H, C*H*), 5.38 (m, 1H, C*H*), 4.68 (m, 1H, C*H*), 3.25 (dd, J = 7.6, 3.2 Hz, 1H, C*H*), 2.71 (dd, J = 18.3, 7.6 Hz, 1H, CH_2), 2.60 (m, 2H, CH_2), 2.39 (t, J = 7.6 Hz, 2H, CH_2), 2.28 (dd, J = 18.3, 3.2 Hz, 1H, CH_2), 2.12 (m, 2H, CH_2), 1.75 (m, 2H, CH_2), 1.65 (s, 3H, CH_3), 1.58 (m, 3H, CH_3), 1.50 (s, 3H, CH_3), 1.00 (t, J = 7.3 Hz, 3H, CH_3). ^{13}**C-NMR** (150 MHz, acetone-d_6): δ = 207.0, 198.9, 190.7, 178.0, 173.3, 167.1, 131.0, 130.2, 126.0, 123.8, 115.0, 97.1, 83.9, 82.9, 42.7, 42.0, 36.8, 32.4, 27.4, 22.0, 20.1, 18.1, 14.1, 6.4. **IR**: ν 3405, 2967, 2942, 1715, 1659, 1579, 1441, 1385, 1316, 1252, 1166, 1061, 823 cm^{-1}. **HRMS** (ESI) m/z: $[M-H]^-$ calcd for $C_{24}H_{29}O_8$ 445.1862, found 445.1856.[27]

Sorbifuranone C (47c)



Sorbifuranone C (**47c**)

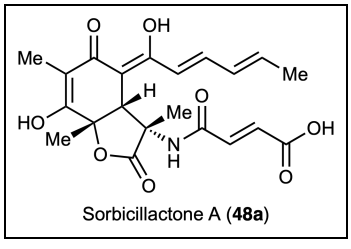
SMILES: O=C1C[C@](/C=C/C)([H])[C@@]2(C(C(/C=C/C(O)=O)=C(CCC)O2)=O)[C@@]([C@]3(C)OC(C(C)=C3O)=O)([H])C1

Fungus of origin: *Penicillium* sp.[27].

Biosynthesis: See figure S6T. Similiar to sorbifuranone B (**41b**) with intramolecular Michael reaction to the sorbyl chain, thus leading to the cyclohexanone moiety.[27]

Analytics: Yellow, amorphous solid. **MP**: 100–101 °C. **ORD**: $[\alpha]_D^{20} = 4-4$ (c = 0.1, MeCN). ^{1}**H-NMR** (600 MHz, acetone-d_6): δ = 6.54 (d, J = 11.7 Hz, 1H, C*H*), 6.00 (d, J = 11.7 Hz, 1H, C*H*), 5.60 (m, 1H, C*H*), 5.28 (ddd, J = 15.1, 8.4, 1.7 Hz, 1H, C*H*), 3.35 (m, 1H, C*H*), 2.94 (dd, J = 16.1, 5.5 Hz, 1H, CH_2), 2.72 (m, 1H, CH_2), 2.71 (dd, J = 6.0, 5.5 Hz, 1H, C*H*), 2.67 (dd, J = 16.1, 5.8 Hz, 1H, CH_2), 2.61 (m, 1H, CH_2), 2.39 (dd, J = 16.1, 5.8 Hz, 1H, CH_2), 2.23 (dd, J = 16.1, 6.0 Hz, 1H, CH_2), 1.76 (m, 2H, CH_2), 1.65 (s, 3H, CH_3), 1.60 (dd, J = 6.5, 1.7 Hz, 3H, CH_3), 1.58 (s, 3H, CH_3), 1.01 (t, J = 7.4 Hz, 3H, CH_3). ^{13}**C-NMR** (150 MHz, acetone-d_6): δ = 205.8, 200.3, 188.5, 176.5, 173.0, 167.2, 130.3, 129.5, 128.2, 123.7, 114.3, 97.0, 90.0, 84.8, 44.6, 43.8, 41.9, 37.6, 32.2, 24.5, 20.3, 18.2, 14.1, 6.4. **IR**: ν 3373, 3175, 2967, 2939, 1699, 1654, 1440, 1384, 1260, 1176, 1047 cm^{-1}. **HRMS** (ESI) m/z: $[M-H]^-$ calcd for $C_{24}H_{27}O_8$ 443.1706, found 443.1715.[27]

Sorbicillactone A (48a)



Sorbicillactone A (**48a**)

SMILES: O=C(C(C)=C(O)[C@](O1)(C)[C@@]/2([H])[C@@](NC(/C=C/C(O)=O)=O)(C)C1=O)C2=C(\C=C\C=C\C)O

Fungus of origin: *Penicillium chrysogenum* E01-10/3[6], *Penicillium chrysogenum* sp.[8].

Bioactivity: Cytotoxicity against murine leukemic lymphoblasts L5178y cells (IC_{50} = 2.20 µg/mL). Sorbicillactone A (**45a**) also showed a high anti-HIV activity. In the concentration range between 0.3 and 3.0 mg/mL, sorbicillactone A (**45a**) protected human T lymphocytes (H9 cells) against the cytopathic effect of HIV-1 and inhibited the expression of viral proteins. Effect on $[Ca^{2+}]_i$ in primary neurons allows consideration as a promising neuroprotective compound also for *in vivo* models.[6]

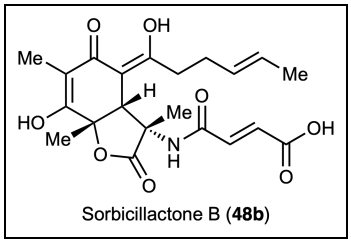
Biosynthesis: See figure S6U. The biosynthesis of sorbicillactone A (**45a**) is based on the reaction between sorbicillinol (**2a**) and alanine (possibly activated by Schiff base formation with pyridoxal phosphate). The first reaction is either the esterification or a Michael addition followed by the respective other reaction. The corresponding lactone attacks a fumaryl-related C_4 unit via the free amine group.[6]

Total synthesis: Sorbicillactone A (**45a**) has been synthesized chemo-enzymatically using the heterologous expressed monooxygenase

SorbC together with sorbicillin (**1a**) and a fumarylazlactone (29% yield).[117]

Analytics: Yellow crystalline needles. **MP**: 205 °C. **ORD**: $[\alpha]_D^{20} = -939.0$ (c = 0.2, MeOH). ^{1}**H-NMR** (600 MHz, THF-d_8): δ = 16.60 (bs, 1H, O*H*), 7.60 (bs, 1H, N*H*), 7.19 (dd, *J* = 14.7, 11.0 Hz, 1H, CH_{sorbyl}), 6.67 (d, *J* = 15.4 Hz, 1H, CH_{sorbyl}), 6.49 (d, *J* = 14.4 Hz, 1H, CH_{sorbyl}), 6.38 (d, *J* = 14.7 Hz, 1H, CH_{sorbyl}), 6.28 (ddd, *J* = 14.5, 11.0, 1.3Hz, 1H, C*H*), 6.08 (m, 1H, C*H*), 3.43 (s, 1H, C*H*), 1.83 (dd, *J* = 6.2, 1.3 Hz, 3H, CH_3), 1.55 (s, 3H, CH_3), 1.54 (s, 3H, CH_3), 1.42 (s, 3H, CH_3). ^{13}**C-NMR** (150 MHz, THF-d_8): δ = 192.1, 173.0, 169.7, 166.5, 166.3, 162.5, 139.1, 136.9, 136.0, 132.0, 131.2, 121.7, 110.9, 99.6, 81.0, 60.0, 53.0, 26.0, 25.0, 18.5, 7.3. **IR**: *ν* 3257, 3089, 2980, 2937, 1771, 1616, 1555, 1446, 1410, 1348, 1264, 1204, 1067, 993, 944 cm^{-1}. **HRMS** (ESI) *m/z*: $[M+H]^+$ calcd for $C_{21}H_{24}ON_8$ 418.1502, found 418.1515.[6]

Sorbicillactone B (48b)



Sorbicillactone B (**48b**)

SMILES: O=C(C(C)=C(O)[C@](O1)(C)[C@@]/2([H])[C@@](NC(/C=C/C(O)=O)=O)(C)C1=O)C2=C(CC/C=C/C)/O

Fungus of origin: *Penicillium chrysogenum* E01-10/3[6], *Penicillium chrysogenum* sp.[8].

Bioactivity: Low cytotoxicity against L5178y, PC12, and HeLa cells ($IC_{50} > 10.0$ µg/mL).

Biosynthesis: See figure S6U. Exactly the same as for sorbicillactone A (**45a**) using dehydrosorbicillinol (**2b**) instead of sorbicillinol (**2a**).[6]

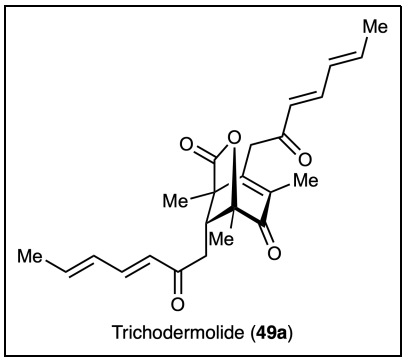
Total synthesis: Sorbicillactone B (**45b**) could be synthesized in the same fashion as sorbicillactone A (**45a**) using dehydrosorbicillin (**1b**) instead of sorbicillin (**1b**).[117]

Analytics: Light-brown amorphous solid. **MP**: 109–115 °C. **ORD**: $[\alpha]_D^{20} = -327.0$ (c = 0.2, MeOH). ^{1}**H-NMR** (600 MHz, THF-d_8): δ = 16.98 (bs, 1H, O*H*), 7.61 (bs, 1H, N*H*), 6.64 (d, *J* = 15.5 Hz, 1H, C*H*), 6.49 (d, *J* = 15.5 Hz, 1H, C*H*), 5.48 (m, 2H, C*H*), 3.31 (s, 1H, C*H*), 2.53 (m, 1H, CH_2), 2.37 (m, 2H, CH_2), 2.32 (m, 1H, CH_2), 1.61 (dd, *J* = 6.2, 1.3 Hz, 3H, CH_3), 1.54 (s, 3H, CH_3), 1.53 (s, 3H, CH_3), 1.44 (s, 3H, CH_3). ^{13}**C-NMR** (150 MHz, THF-d_8): δ = 191.7, 180.2, 172.0, 166.7, 166.6, 162.9, 136.4, 131.6, 130.9, 126.8, 110.2, 98.6, 81.6, 60.1, 53.9, 33.7, 30.6, 25.9, 25.1, 18.2, 7.6. **IR**: *ν* 3291, 3065, 2982, 2931, 1772, 1717, 1672, 1557, 1450, 1384, 1347, 1223, 1108, 1065, 969 cm^{-1}. **HRMS** (ESI) *m/z*: $[M+H]^+$ calcd for $C_{21}H_{26}ON_8$ 420.1658, found 420.1646.[6]

1.4 Other related structures

1.4.1 Pseudo-dimeric Sorbicillinoids

Trichodermolide (49a)



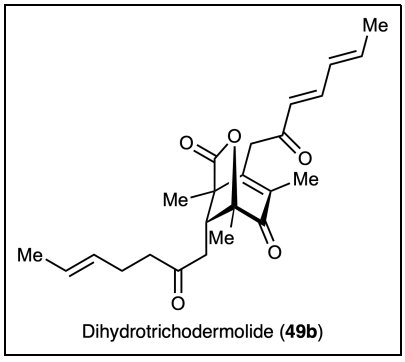
Trichodermolide (**49a**)

SMILES: O=C1[C@@]2(C)[C@H](CC(/C=C/C=C/C)=O)[C@](C(O2)=O)(C)C(CC(/C=C/C=C/C)=O)=C1C

Fungus of origin: *Trichoderma longibrachiatum* Rifai aggr[32].

Analytics: **TLC**: R_f = 0.45 (petroleum ether/EtOAc = 5:2). **ORD**: $[\alpha]_D$ = +97.0 (c = 1.0, EtOH). ^{1}**H-NMR** (300 MHz, $CDCl_3$): δ = 7.24 (dd, *J* = 15.5, 9.5 Hz, 1H, C*H*), 7.20 (dd, *J* = 15.5, 9.5 Hz, 1H, CH_{sorbyl}), 6.23 (m, 4H, CH_{sorbyl}), 6.15 (d, *J* = 15.5 Hz, 1H, CH_{sorbyl}), 6.10 (d, *J* = 15.5 Hz, 1H, CH_{sorbyl}), 3.66 (m, 2H, CH_2), 3.34 (d, *J* = 6.4 Hz, 1H, C*H*), 3.26 (dd, *J* = 18.5, 6.0 Hz, 1H, CH_2), 2.45 (dd, *J* = 18.5, 4.0 Hz, 1H, CH_2), 1.89 (d, *J* = 6.0 Hz, 3H, CH_3), 1.87 (d, *J* = 6.0 Hz, 3H, CH_3), 1.78 (s, 3H, CH_3), 1.45 (s, 3H, CH_3), 1.24 (s, 3H, CH_3). ^{13}**C-NMR** (75.5 MHz, $CDCl_3$): δ = 196.6, 195.5, 191.2, 176.1, 148.6, 144.8, 144.1, 142.4, 141.5, 134.2, 130.2, 129.9, 126.9, 124.4, 87.2, 56.0, 51.8, 42.0, 35.1, 18.9 (2C), 16.2 (2C), 11.6. **IR**: *v* 3015, 2920, 1781, 1687, 1637, 1595, 1375, 1320, 1188, 997 cm^{-1}.[32]

Dihydrotrichodermolide (49b)



Dihydrotrichodermolide (**49b**)

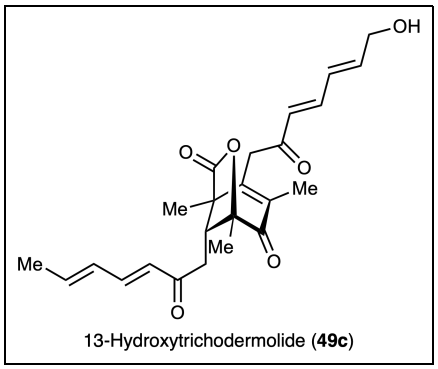
SMILES: O=C1[C@@]2(C)[C@H](CC(CC/C=C/C)=O)[C@](C(O2)=O)(C)C(CC(/C=C/C=C/C)=O)=C1C

Fungus of origin: *Phialocephala* sp. FL30r[118].

Bioactivity: Cytotoxic against P388 (IC_{50} = 11.5 μM) and K562 cells (IC_{50} = 22.9 μM).[118]

Analytics: Deep yellow syrup. **ORD**: $[\alpha]_D^{20}$ = +31.5 (c = 0.1, MeOH). ^{1}**H-NMR** (600 MHz, $CDCl_3$): δ = 7.21 (dd, *J* = 15.6, 10.5 Hz, 1H, CH_{sorbyl}), 6.30 (m, 1H, CH_{sorbyl}), 6.25 (dd, *J* = 15.1, 11.0 Hz, 1H, CH_{sorbyl}), 6.09 (d, *J* = 15.6 Hz, 1H, CH_{sorbyl}), 5.44 (m, 1H, C*H*), 5.38 (dt, *J* = 14.6, 7.2 Hz, 1H, C*H*), 3.68 (d, *J* = 18.0 Hz, 1H, CH_2), 3.63 (d, *J* = 18.0 Hz, 1H, CH_2), 3.27 (dd, *J* = 7.3, 3.6 Hz, 1H, C*H*), 3.17 (dd, *J* = 18.8, 7.3 Hz, 1H, CH_2), 2.61 (dd, *J* = 16.8, 7.3 Hz, 1H, CH_2), 2.51 (dd, *J* = 17.0, 7.3 Hz, 1H, CH_2), 2.30 (dd, *J* = 18.8, 3.6 Hz, 1H, CH_2), 2.25 (dd, *J* = 14.4, 7.4 Hz, 2H, CH_2), 1.91 (d, *J* = 6.9 Hz, 3H, CH_3), 1.75 (s, 3H, CH_3), 1.62 (d, *J* = 6.3 Hz, 3H, CH_3), 1.45 (s, 3H, CH_3), 1.21 (s, 3H, CH_3). ^{13}**C-NMR** (150 MHz, $CDCl_3$): δ = 207.0, 195.8, 191.1, 176.1, 150.0, 145.0, 142.7, 134.1, 129.8, 129.2, 126.3, 126.2, 87.0, 55.5, 51.6, 42.7, 41.9, 37.2, 26.7, 18.9, 17.9, 16.3, 16.1, 11.5. **IR**: *v* 2937, 1783, 1720, 1689, 1636, 1597, 1453, 1381, 1187 cm^{-1}. **HRMS** (ESI) *m/z*: $[M+Na]^+$ calcd for $C_{24}H_{30}O_5Na$ 421.1991, found 421.1993.[118]

13-Hydroxytrichodermolide (49c)



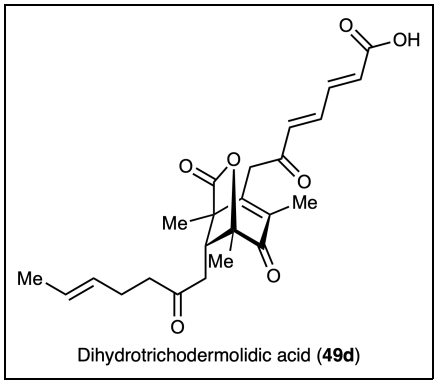
13-Hydroxytrichodermolide (**49c**)

SMILES: O=C1[C@@]2(C)[C@H](CC(/C=C/C=C/C)=O)[C@](C(O2)=O)(C)C(CC(/C=C/C=C/CO)=O)=C1C

Fungus of origin: *Trichoderma reesei* HN-2016-018[84].

Analytics: Yellow amorphous powder. **ORD**: $[\alpha]_D^{25}$ = +27.6 (c = 0.1, MeOH). ^{1}**H-NMR** (600 MHz, $CDCl_3$): δ = 7.24 (dd, *J* = 15.5, 10.9 Hz, 1H, CH_{sorbyl}), 7.20 (dd, *J* = 15.5, 10.7 Hz, 1H, CH_{sorbyl}), 6.46 (m, 1H, CH_{sorbyl}), 6.35 (dt, *J* = 15.5, 4.6 Hz, 1H, CH_{sorbyl}), 6.28 (m, 1H, CH_{sorbyl}), 6.20 (m, 2H, CH_{sorbyl}), 6.11 (d, *J* = 15.5 Hz, 1H, CH_{sorbyl}), 4.34 (d, *J* = 4.6 Hz, 2H, CH_2OH), 3.67 (d, *J* = 5.4 Hz, 2H, CH_2), 3.33 (dd, *J* = 6.4, 4.3 Hz, 1H, C*H*), 3.23 (dd, *J* = 18.4, 6.4 Hz, 1H, CH_2), 2.46 (dd, *J* = 18.4, 4.3 Hz, 1H, CH_2), 1.88 (d, *J* = 6.6 Hz, 3H, CH_3), 1.78 (s, 3H, CH_3), 1.46 (s, 3H, CH_3), 1.23 (s, 3H, CH_3). ^{13}**C-NMR** (150 MHz, $CDCl_3$): δ = 196.6, 195.4, 191.2, 176.1, 149.3, 144.2, 143.9, 143.6, 141.7, 134.3, 130.2, 128.3, 127.5, 126.8, 87.2, 62.6, 55.9, 51.7, 42.1, 35.1, 18.9, 16.2, 16.1, 11.6. **IR**: *v* 3023, 2934, 1785, 1721, 1683, 1634, 1597, 1436, 1381, 1186, 979 cm^{-1}. **HRMS** (ESI) *m/z*: $[M+Na]^+$ calcd for $C_{24}H_{29}O_6$ 413.1959, found 413.1959.[84]

Dihydrotrichodermolidic acid (49d)



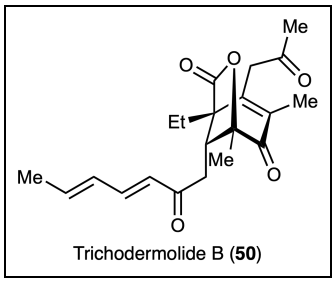
Dihydrotrichodermolidic acid (**49d**)

SMILES: O=C1[C@@]2(C)[C@H](CC(CC/C=C/C)=O)[C@](C(O2)=O)(C)C(CC(/C=C/C=C/C(O)=O)=O)=C1C

Fungus of origin: *Penicillium* sp. SCSIO06871[51].

Analytics: Yellow oil. **ORD**: $[\alpha]_D^{20} = +81.0$ (c = 0.1, MeOH). ^{1}**H-NMR** (700 MHz, CD_3OD): δ = 7.45 (dd, *J* = 15.4, 11.2 Hz, 1H, C*H*), 7.38 (dd, *J* = 15.4, 11.2 Hz, 1H, C*H*), 6.61 (d, *J* = 15.4 Hz, 1H, C*H*), 6.36 (d, *J* = 15.4 Hz, 1H, C*H*), 5.44 (m, 1H, C*H*), 5.42 (m, 1H, C*H*), 3.96 (d, *J* = 18.2 Hz, 1H, CH_2), 3.84 (d, *J* = 18.2 Hz, 1H, CH_2), 3.26 (dd, *J* = 7.0, 3.5 Hz, 1H, C*H*), 3.15 (dd, *J* = 18.2, 7.7 Hz, 1H, CH_2), 2.44 (dd, *J* = 18.9, 3.5 Hz, 1H, CH_2), 2.22 (m, 2H, CH_2), 1.75 (s, 3H, CH_3), 1.61 (dd, *J* = 5.6, 0.7 Hz, 3H, CH_3), 1.42 (s, 3H, CH_3), 1.19 (s, 3H, CH_3). ^{13}**C-NMR** (175 MHz, CD_3OD): δ = 208.8, 197.8, 192.2, 177.6, 168.9, 151.0, 142.6, 141.9, 135.6, 135.4, 131.5, 130.8, 126.9, 88.0, 56.7, 53.0, 43.4, 43.4, 38.1, 27.7, 18.1, 16.9, 16.3, 11.5. **HRMS** (ESI) *m/z*: $[M-H]^-$ calcd for $C_{24}H_{27}O_7$ 427.1762, found 427.1768.[51]

Trichodermolide B (50)



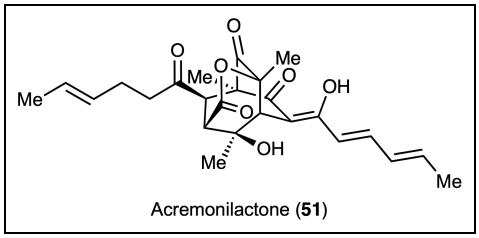
Trichodermolide B (**50**)

SMILES: O=C1[C@@]2(C)[C@H](CC(/C=C/C=C/C)=O)[C@@](C(O2)=O)(CC)C(CC(C)=O)=C1C

Fungus of origin: *Trichoderma reesei* HN-2016-018[84].

Analytics: Yellow oil. **ORD**: $[\alpha]_D^{25} = +64.2$ (c = 0.1, MeOH). ^{1}**H-NMR** (600 MHz, DMSO-d_6): δ = 7.17 (dd, *J* = 15.5, 10.1 Hz, 1H, CH_{sorbyl}), 6.32 (m, 1H, CH_{sorbyl}), 6.27 (m, 1H, CH_{sorbyl}), 6.14 (d, *J* = 15.5 Hz, 1H, CH_{sorbyl}), 3.73 (s, 2H, CH_2), 3.37 (m, 1H, C*H*), 2.99 (dd, *J* = 18.1, 6.2 Hz, 1H, CH_2), 2.54 (dd, *J* = 18.1, 6.2 Hz, 1H, CH_2), 2.20 (s, 3H, CH_3), 2.03 (dd, *J* = 14.1, 7.2 Hz, 1H, CH_2), 1.83 (d, *J* = 6.1 Hz, 3H, CH_3), 1.70 (s, 3H, CH_3), 1.37 (s, 3H, CH_3), 1.25 (dd, *J* = 14.1, 7.2 Hz, 1H, CH_2), 0.82 (t, *J* = 7.2 Hz, 3H, CH_3). ^{13}**C-NMR** (150 MHz, DMSO-d_6): δ = 205.0, 197.2, 191.2, 174.7, 150.9, 143.9, 141.9, 133.9, 130.6, 127.6, 86.5, 55.9, 50.0, 44.7, 35.0, 30.5, 20.5, 19.1, 16.5, 11.9, 8.6. **IR**: *ν* 3023, 2934, 1785, 1721, 1683, 1634, 1597, 1436, 1381, 1186, 979 cm^{-1}. **HRMS** (ESI) *m/z*: $[M+H]^+$ calcd for $C_{21}H_{27}O_5$ 359.1853, found 359.1861.[84]

Acremonilactone (51)



Acremonilactone (**51**)

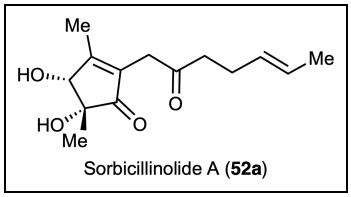
SMILES: O=C(/C(C([C@](O)(C)[C@H]12)C(OC2=O)(C)C3=O)=C(/C=C/C=C/C)O)[C@@]3(C)[C@@H]1C(CC/C=C/C)=O

Fungus of origin: *Acremonium* sp. AN-13[1].

Analytics: White amorphous powder. **ORD**: $[\alpha]_D^{25} = +47.0$ (c = 0.1, MeOH). ^{1}**H-NMR** (500 MHz, $CDCl_3$): δ = 14.04 (bs, 1H, O*H*), 7.36 (dd, *J* = 15.5, 10.5 Hz, 1H, CH_{sorbyl}), 6.30 (dd, *J* = 15.6, 10.5 Hz, 1H, CH_{sorbyl}), 6.25 (dd, *J* = 15.6, 6.2 Hz, 1H, CH_{sorbyl}), 6.14 (d, *J* = 15.5 Hz, 1H, CH_{sorbyl}), 5.45 (m, 1H, C*H*), 5.37 (m, 1H, C*H*), 3.45 (d, *J* = 4.1 Hz, 1H, C*H*), 3.41 (s, 1H, C*H*), 3.11 (d, *J* = 4.1 Hz, 1H, C*H*), 3.01 (dd, *J* = 17.9, 7.7 Hz, 1H, CH_2), 2.69 (dd, *J* = 17.9, 7.2 Hz, 1H, CH_2), 2.28 (m, 2H, CH_2), 1.91 (d, *J* = 6.2 Hz, 3H, CH_3), 1.77 (s, 3H, CH_3), 1.63 (d, *J* = 6.2 Hz, 3H, CH_3), 1.26 (s, 3H, CH_3), 1.11 (s, 3H, CH_3). ^{13}**C-NMR** (125 MHz, $CDCl_3$): δ = 210.0, 200.2, 195.6, 171.0, 169.4, 144.5, 141.4, 131.0, 128.7, 126.9, 117.4, 108.2, 86.6, 75.1, 61.8, 57.8, 50.4, 50.3, 41.6, 27.5, 27.1, 26.7, 19.2, 18.0, 9.9. **IR**: *ν* 3443, 2931, 1687, 1728, 1623, 1449, 1383, 1210, 1126 cm^{-1}. **HRMS** (ESI) *m/z*: $[M+Na]^+$ calcd for $C_{25}H_{30}O_7Na$ 465.1884, found 465.1894.[1]

1.4.2 Vertinolide analogues

Sorbicillinolide A (52a)



Sorbicillinolide A (**52a**)

SMILES: O=C(CC/C=C/C)CC1=C(C)[C@@H](O)[C@](O)(C)C1=O

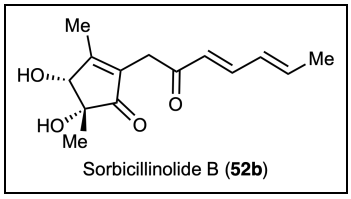
Fungus of origin: *Penicillium rubens* F54[49].

Bioactivity: Sorbicillinolide A (**52a**) exhibits anti-neuroinflammation in LPS- stimulated BV-2 macrophages.[49]

Biosynthesis: See figure S7V.[49]

Analytics: Yellow oil. **ORD**: $[\alpha]_D$ = +64.6 (c = 0.1, MeOH). ^{1}**H-NMR** (400 MHz, DMSO-d_6): δ = 5.39 (d, *J* = 6.0 Hz, 1H, O*H*), 5.38 (dq, *J* = 16.0, 4.7 Hz, 1H, C*H*), 5.37 (dd, *J* = 16.0, 6.0 Hz, 1H, C*H*), 4.87 (s, 1H, O*H*), 4.10 (d, *J* = 6.0 Hz, 1H, C*H*), 3.28 (s, 2H, CH_2), 2.47 (t, *J* = 7.0 Hz, 2H, CH_2), 2.12 (dt, *J* = 7.0, 6.0 Hz, 2H, CH_2), 1.96 (s, 3H, CH_3), 1.58 (d, *J* = 4.7 Hz, 3H, CH_3), 1.12 (s, 3H, CH_3). ^{13}**C-NMR** (100 MHz, DMSO-d_6): δ = 206.2, 206.0, 170.4, 132.5, 130.4, 125.5, 77.5, 73.1, 41.8, 37.0, 26.6, 23.0, 18.2, 14.8. **IR**: *ν* 3406, 2969, 1711, 1651, 1383 cm^{-1}. **HRMS** (ESI) *m/z*: $[M-H]^-$ calcd for $C_{14}H_{19}O_4$ 251.1280, found 251.1283.[49]

Sorbicillinolide B (52b)



Sorbicillinolide B (**52b**)

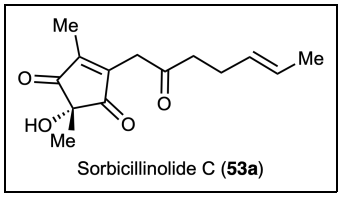
SMILES: O=C(/C=C/C=C/C)CC1=C(C)[C@@H](O)[C@](O)(C)C1=O

Fungus of origin: *Penicillium rubens* F54[49].

Biosynthesis: See figure S7V.[49]

Analytics: Yellow oil. **ORD**: $[\alpha]_D$ = +75.1 (c = 0.1, MeOH). ^{1}**H-NMR** (400 MHz, DMSO-d_6): δ = 7.24 (dd, *J* = 15.5, 9.3 Hz, 1H, CH_{sorbyl}), 6.28 (dq, *J* = 16.0, 5.2 Hz, 1H, CH_{sorbyl}), 6.27 (dd, *J* = 16.0, 9.3 Hz, 1H, CH_{sorbyl}), 6.09 (d, *J* = 15.5 Hz, 1H, CH_{sorbyl}), 5.38 (d, *J* = 6.7 Hz, 1H, O*H*), 4.86 (s, 1H, O*H*), 4.10 (d, *J* = 6.7 Hz, 1H, C*H*), 3.44 (s, 2H, CH_2), 1.97 (s, 3H, CH_3), 1.84 (d, *J* = 5.2 Hz, 3H, CH_3), 1.12 (s, 3H, CH_3). ^{13}**C-NMR** (100 MHz, DMSO-d_6): δ = 206.2, 195.9, 170.4, 143.9, 141.4, 132.8, 130.7, 127.5, 77.5, 73.1, 34.8, 23.1, 19.1, 14.9. **IR**: *ν* 3398, 2973, 1711, 1651, 1382 cm^{-1}. **HRMS** (ESI) *m/z*: $[M-H]^-$ calcd for $C_{14}H_{17}O_4$ 249.1127, found 249.1122.[49]

Sorbicillinolide C (53a))



Sorbicillinolide C (**53a**)

SMILES: O=C(CC/C=C/C)CC1=C(C)C([C@](O)(C)C1=O)=O

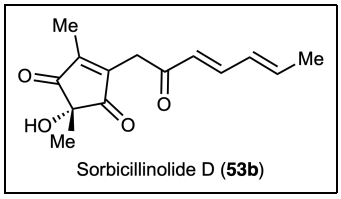
Fungus of origin: *Penicillium rubens* F54[49].

Bioactivity: Sorbicillinolide A (**52a**) exhibits anti-neuroinflammation in LPS- stimulated BV-2 macrophages.[49]

Biosynthesis: See figure S7V.[49]

Analytics: Yellow oil. **ORD**: $[\alpha]_D$ = +82.4 (c = 0.1, MeOH). ^{1}**H-NMR** (400 MHz, DMSO-d_6): δ = 6.07 (s, 1H, O*H*), 5.41 (dd, *J* = 16.0, 5.6 Hz, 1H, C*H*), 5.41 (qd, *J* = 16.0, 4.8 Hz, 1H, C*H*), 3.75 (d, *J* = 14.0 Hz, 1H, CH_2), 3.72 (d, *J* = 14.0 Hz, 1H, CH_2), 2.62 (t, *J* = 7.3 Hz, 2H, CH_2), 2.17 (td, *J* = 7.3, 5.6 Hz, 2H, CH_2), 1.92 (s, 3H, CH_3), 1.60 (d, *J* = 4.8 Hz, 3H, CH_3), 1.17 (s, 3H, CH_3). ^{13}**C-NMR** (100 MHz, DMSO-d_6): δ = 204.7, 204.3, 203.5, 155.2, 150.4, 130.2, 125.7, 70.7, 42.4, 37.8, 26.6, 20.7, 18.1, 9.9. **IR**: *ν* 3200, 2983, 1751, 1704, 1454, 1200 cm^{-1}. **HRMS** (ESI) *m/z*: $[M-H]^-$ calcd for $C_{14}H_{17}O_4$ 249.1127, found 249.1124.[49]

Sorbicillinolide D (53b)



Sorbicillinolide D (**53b**)

SMILES: O=C(/C=C/C=C/C)CC1=C(C)C([C@](O)(C)C1=O)=O

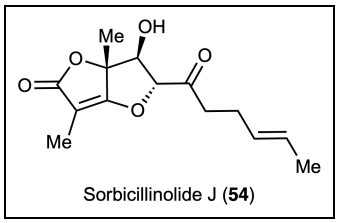
Fungus of origin: *Penicillium rubens* F54[49].

Biosynthesis: See figure S7V.[49]

Analytics: Yellow oil. **ORD**: $[\alpha]_D$ = +93.3 (c = 0.1, MeOH). ^{1}**H-NMR** (400 MHz, DMSO-d_6): δ = 7.32 (dd, *J* = 15.6, 9.7 Hz, 1H, CH_{sorbyl}), 6.35 (dq, *J* = 16.0, 5.7 Hz, 1H, CH_{sorbyl}), 6.33 (dd, *J* = 16.0, 9.7 Hz, 1H, CH_{sorbyl}), 6.18 (d, *J* = 15.6 Hz, 1H, CH_{sorbyl}), 3.90 (d, *J* = 14.0 Hz, 1H, CH_2), 3.88 (d, *J* = 14.0 Hz, 1H, CH_2), 1.94 (s, 3H, CH_3), 1.87 (d, *J* = 5.7 Hz, 3H, CH_3), 1.19 (s, 3H, CH_3). ^{13}**C-NMR** (100 MHz, DMSO-d_6): δ = 204.3, 203.4, 194.5, 155.2, 150.4, 144.9, 142.0, 130.6, 127.4, 70.8, 35.6, 20.8, 19.1,

9.9. **IR**: *v* 3437, 2978, 1751, 1704, 1633, 1381 cm^{-1}. **HRMS** (ESI) *m/z*: $[M-H]^-$ calcd for $C_{14}H_{15}O_4$ 247.0970, found 247.0968.[49]

Sorbicillinolide J (54)



Sorbicillinolide J (**54**)

SMILES: O=C1C(C)=C(O[C@@H](C(CC/C=C/C)=O)[C@@H]2O)[C@]2(C)O1

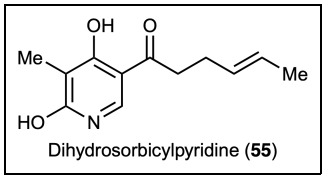
Fungus of origin: *Penicillium rubens* F54[49].

Biosynthesis: See figure S7W.[49]

Analytics: Yellow oil. **ORD**: $[\alpha]_D = +60.0$ (c = 0.1, MeOH). ^{1}**H-NMR** (400 MHz, CD_3OD): δ = 5.54 (d, *J* = 3.1 Hz, 1H, C*H*), 5.48 (td, *J* = 16.0, 6.9 Hz, 1H, C*H*), 5.46 (qd, *J* = 16.0, 4.8 Hz, 1H, C*H*), 4.52 (d, *J* = 3.1 Hz, 1H, C*H*), 2.69 (m, 1H, CH_2), 2.60 (m, 1H, CH_2), 2.26 (m, 2H, CH_2), 1.78 (s, 3H, CH_3), 1.64 (d, *J* = 4.8 Hz, 3H, CH_3), 1.52 (s, 3H, CH_3). ^{13}**C-NMR** (100 MHz, CD_3O): δ = 204.2, 181.1, 176.4, 129.4, 125.4, 96.0, 95.3, 84.4, 73.7, 39.4, 25.2, 20.0, 16.6, 5.0. **IR**: *v* 2933, 1714, 1655, 1402, 1303 cm^{-1}. **HRMS** (ESI) *m/z*: $[M-H]^-$ calcd for $C_{14}H_{17}O_5$ 265.1076, found 265.1080.[49]

1.4.3 Nitrogen-containing analogues

Dihydrosorbicylpyridine (55) [(*E*)-1-(4,6-Dihydroxy-5-methylpyridin-3-yl)hex-4-en-1-one]



Dihydrosorbicylpyridine (**55**)

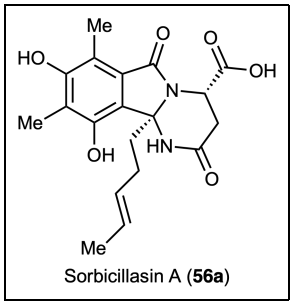
SMILES: OC1=C(C(CC/C=C/C)=O)C=NC(O)=C1C

Fungus of origin: *Penicillium* sp. DM815[29].

Bioactivity: Anti-inflammatory activity due to inhibition of nitric oxide formation in LPS-induced RAW264.7 cells.[29]

Analytics: White amorphous powder. ^{1}**H-NMR** (600 MHz, DMSO-d_6): δ = 12.37 (bs, 1H, O*H*), 12.08 (bs, 1H, O*H*), 8.36 (s, 1H, Ar*H*), 5.48 (dq, *J* = 14.8, 4.9 Hz, 1H, C*H*), 5.43 (dt, *J* = 14.8, 5.2 Hz, 1H, C*H*), 2.97 (t, *J* = 7.3 Hz, 2H, CH_2), 2.26 (m, 2H, CH_2), 1.79 (s, 3H, CH_3), 1.60 (d, *J* = 4.9 Hz, 3H, CH_3). ^{13}**C-NMR** (150 MHz, DMSO-d_6): δ = 203.6, 163.5, 162.9, 142.2, 129.7, 125.3, 106.5, 105.8, 36.2, 26.8, 17.7, 7.6. **IR**: *ν* 3535, 1719, 1651 cm^{-1}. **HRMS** (ESI) *m/z*: $[M+H]^+$ calcd for $C_{12}H_{16}NO_3$ 222.1130, found 222.1137.[29]

Sorbicillasin A (56a)



Sorbicillasin A (**56a**)

SMILES: OC1=C(C)C(O)=C([C@@](NC(C[C@H]2C(O)=O)=O)(CC/C=C/C)N2C3=O)C3=C1C

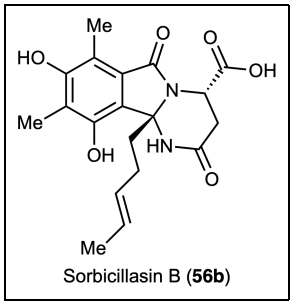
Fungus of origin: *Phialocephala* sp. FL30r[119].

Bioactivity: Screening for cytotoxicity against K562 and MGC-803 cell lines showed inactivity. The compound did not show any DPPH-radical scavenging activity.[119]

Biosynthesis: See figure S7X. The biosynthetic pathway could be based on dehydrosorbicillin (**1a**), which gets carboxylated on the free aromatic position. L-asparagine acts as an external nucleophile, which first performs an amide formation followed by two nucleophilic attacks of the nitrogen functionalities to dehydrosorbyl carbonyl.[119]

Analytics: Pale yellow oil. **ORD**: $[\alpha]_D^{25}$ = −15.5 (c = 0.2, MeOH). ^{1}**H-NMR** (500 MHz, DMSO-d_6): δ = 13.12 (bs, 1H, O*H*), 8.77 (bs, 1H, O*H*), 8.62 (bs, 1H, O*H*), 8.04 (bs, 1H, N*H*), 5.19 (m, 1H, C*H*), 5.17 (m, 1H, C*H*), 4.94 (t, *J* = 7.6 Hz, 1H, C*H*), 2.82 (dd, *J* = 17.1, 6.0 Hz, 1H, CH_2), 2.48 (dd, *J* = 17.1, 6.0 Hz, 1H, CH_2), 2.41 (dt, *J* = 11.8, 4.0 Hz, 1H, CH_2), 2.38 (s, 3H, CH_3), 2.11 (s, 3H, CH_3), 1.90 (dt, *J* = 11.8, 4.0 Hz, 1H, CH_2), 1.80 (dt, *J* = 11.8, 5.8 Hz, 1H, CH_2), 1.48 (d, *J* = 4.2 Hz, 3H, CH_3), 1.12 (dt, *J* = 11.8, 5.8 Hz, 1H, CH_2). ^{13}**C-NMR** (125 MHz, DMSO-d_6): δ = 172.6, 169.0, 167.1, 155.7, 148.4, 130.4, 125.6, 124.8, 118.9, 115.6, 75.2, 48.2, 36.9, 31.0, 27.1, 18.2 (2C), 10.7, 10.1. **IR**: *ν* 3292, 2906, 1670, 1457, 1362, 1207, 1146, 899 cm^{-1}. **HRMS** (ESI) *m/z*: $[M+H]^+$ calcd for $C_{19}H_{23}N_2O_6$ 375.1551, found 375.1550.[119]

Sorbicillasin B (56b)



Sorbicillasin B (**56b**)

SMILES: OC1=C(C)C(O)=C([C@](NC(C[C@H]2C(O)=O)=O)(CC/C=C/C)N2C3=O)C3=C1C

Fungus of origin: *Phialocephala* sp. FL30r[119].

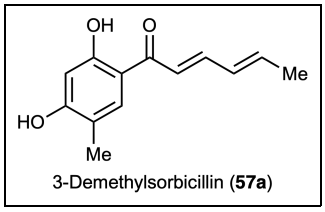
Bioactivity: Screening for cytotoxicity against K562 and MGC-803 cell lines showed inactivity. The compound did not show any DPPH-radical scavenging activity.[119]

Biosynthesis: See figure S7X. The biosynthetic pathway could be based on dehydrosorbicillin (**1a**), which gets carboxylated on the free aromatic position. L-asparagine acts as an external nucleophile, which first performs an amide formation followed by two nucleophilic attacks of the nitrogen functionalities to dehydrosorbyl carbonyl.[119]

Analytics: Pale yellow oil. **ORD**: $[\alpha]_D^{25}$ = +10.4 (c = 0.2, MeOH). ^{1}**H-NMR** (500 MHz, DMSO-d_6): δ = 12.74 (bs, 1H, O*H*), 8.76 (bs, 1H, O*H*), 8.60 (bs, 1H, O*H*), 8.03 (bs, 1H, N*H*), 5.24 (m, 1H, C*H*), 5.19 (m, 1H, C*H*), 4.31 s (s, 1H, C*H*), 2.61 (m, 1H, CH_2), 2.45 (m, 1H, CH_2), 2.35 (m, 1H, CH_2), 2.33 (s, 3H, CH_3), 2.13 (m, 1H, CH_2), 2.10 (s, 3H, CH_3), 1.66 (m, 1H, CH_2), 1.48 (d, *J* = 5.7 Hz, 3H, CH_3), 1.32 (m, 1H, CH_2). ^{13}**C-NMR** (125 MHz, DMSO-d_6): δ = 171.4, 169.5, 168.0, 155.8, 148.4, 130.7, 130.5, 125.6, 125.1, 119.2, 115.8, 75.2, 50.2, 35.9, 34.0, 27.3, 18.3 (2C), 10.7, 10.2. **IR**: *ν* 3329, 2926, 1683, 1558, 1384, 1208, 1143, 838 cm^{-1}. **HRMS** (ESI) *m/z*: $[M+Na]^+$ calcd for $C_{19}H_{22}N_2O_6Na$ 397.1370, found 397.1376.[119]

1.4.4 Phenols

3-Demethylsorbicillin (57a) [(2*E*,4*E*)-1-(2,4-Dihydroxy-5-methylphenyl)hexa-2,4-dien-1-one, CAS: 1173701-55-7]



3-Demethylsorbicillin (**57a**)

SMILES: OC1=C(C(/C=C/C=C/C)=O)C=C(C)C(O)=C1

Fungus of origin: *Hypocrea jecorina* H8[4], *Trichoderma reesei* Z56-8[14], Trichoderma sp. f-13[16], *Trichoderma* sp. USF-2690[47].

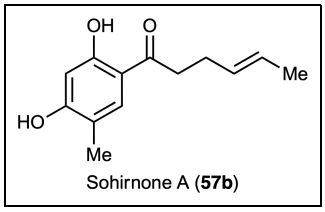
Bioactivity: Evaluation of DPPH-radical scavenging activity showed no effectivity.[47]

Biosynthesis: Follows the same polyketide machinery as sorbicillin (**1a**) without one methylation step through *S*-adenosylmethionine.

Total synthesis: Friedel-Craft reaction between 4-methyl resorcinol [CAS: 496-73-1] and sorbic acid [CAS: 110-44-1] using boron trifluoride etherate [CAS: 109-63-7]. The obtained boron complex can be hydrolyzed with water in THF.[35]

Analytics: Yellowish, amorphous powder. ^{1}**H-NMR** (400 MHz, $CDCl_3$): δ = 13.68 (bs, 1H, O*H*), 7.57 (d, *J* = 8.8 Hz, 1H, Ar*H*), 7.46 (dd, *J* = 15.2, 10.1 Hz, 1H, CH_{sorbyl}), 6.91 (d, *J* = 15.2 Hz, 1H, CH_{sorbyl}), 6.37 (d, *J* = 8.8 Hz, 1H, Ar*H*), 6.34 (dd, *J* = 15.6, 10.1 Hz, 1H, CH_{sorbyl}), 6.28 (dq, *J* = 15.6, 6.0 Hz, 1H, CH_{sorbyl}), 2.14 (s, 3H, CH_3), 1.90 (d, *J* = 6.0 Hz, 3H, CH_3). ^{13}**C-NMR** (100 MHz, $CDCl_3$): δ = 192.7, 164.3, 160.2, 144.8, 141.3, 130.6, 128.6, 121.8, 114.1, 111.3, 106.8, 18.9, 7.3. **IR**: *ν* 3200, 1620, 1370, 1335, 1265, 1115 cm^{-1}. **HRMS** (EI) *m/z*: $[M]^+$ calcd for $C_{13}H_{14}O_3$ 218.0943, found 218.0946.[47]

Sohirnone A (57b) [Dehydro-3-demethylsorbicillin, (*E*)-1-(2,4-Dihydroxy-5-methylphenyl)hex-4-en-1-one, CAS: 859155-90-1]



Sohirnone A (**57b**)

SMILES: OC1=C(C(CC/C=C/C)=O)C=C(C)C(O)=C1

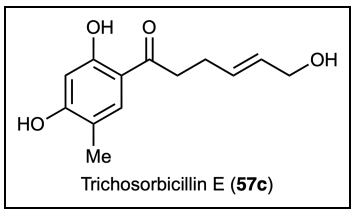
Fungus of origin: *Penicillium allii-sativi* MCCC 3A00580[5], *Penicillium chrysogenum* V11[120], *Penicillium dipodomyis* YJ-11[78], *Penicillium notatum*[28], *Penicillium* sp. SCSIO06871[51], *Trichoderma citrinoviride*[80], *Trichoderma reesei* 4670[30], *Trichoderma* sp. f-13[16], *Trichoderma yunnanense* Ty10[85].

Bioactivity: Antibacterial against *Staphylococcus aureus* and *Bacillus subtilis* (weak).[28]

Biosynthesis: Similar to 3-demethylsorbicillin (**47a**) with one further reduction step within the sorbyl side chain.

Analytics: Pale yellow solid. **TLC**: R_f = 0.12 (DCM/MeOH = 10:1). ^{1}**H-NMR** (300 MHz, CD_3OD): δ = 7.67 (s, 1H, Ar*H*), 7.09 (s, 1H, Ar*H*), 5.49 (m, 2H, C*H*), 3.03 (t, *J* = 7.2 Hz, 2H, CH_2), 2.35 (m, 2H, CH_2), 2.23 (s, 3H, CH_3), 1.62 (m, 3H, CH_3). ^{13}**C-NMR** (75.5 MHz, CD_3OD): δ = 206.7, 163.0, 158.4, 133.0, 130.8, 127.0, 122.4, 117.2, 109.0, 39.2, 28.5, 18.1, 16.0. **IR**: *ν* 3487, 2923, 1647, 1491, 1264, 1244, 1127, 1061, 961, 886, 847, 802, 718, 693, 637, 615 cm^{-1}. **HRMS** (ESI) *m/z*: $[M+Na]^+$ calcd for $C_{13}H_{16}O_3Na$ 243.0992, found 243.0994.[28]

Trichosorbicillin E (57c) [(*E*)-1-(2,4-Dihydroxy-5-methylphenyl)-6-hydroxyhex-4-en-1-one, CAS: 2351107-77-0]



Trichosorbicillin E (**57c**)

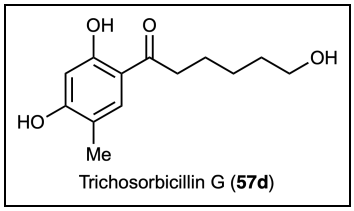
SMILES: OC1=C(C(CC/C=C/CO)=O)C=C(C)C(O)=C1

Fungus of origin: *Trichoderma reesei* 4670[30].

Bioactivity: Evaluation of cytotoxicity against three human cancer cell lines, MCF-7 (breast cancer), HeLa (cervical cancer), and HepG2 showed no effectivity. Anti-inflammatory activity due to inhibition of nitric oxide production in RAW264.7 cells ($IC_{50} > 10.0$ μM).[30]

Analytics: White powder. ^{1}**H-NMR** (400 MHz, CD_3OD): δ = 7.55 (s, 1H, Ar*H*), 6.23 (s, 1H, Ar*H*), 5.74 (m, 2H, CH_2), 5.65 (m, 2H, CH_2), 3.98 (d, *J* = 5.6 Hz, 2H, CH_2), 3.00 (t, *J* = 7.2 Hz, 2H, CH_2), 2.42 (dd, *J* = 14.0, 6.8 Hz, 1H, C*H*), 2.10 (s, 3H, CH_3). ^{13}**C-NMR** (100 MHz, CD_3OD): δ = 205.3, 164.7, 164.6, 133.3, 131.7, 131.3, 118.2, 113.6, 102.9, 63.6, 38.2, 28.2, 15.5. **IR**: *ν* 3400, 2951, 2837, 1649, 1452, 1417, 1028, 665 cm^{-1}. **HRMS** (ESI) *m/z*: $[M-H]^-$ calcd for $C_{13}H_{15}O_4$ 235.0976, found 235.0977.[30]

Trichosorbicillin G (57d) [1-(2,4-Dihydroxy-5-methylphenyl)-6-hydroxyhexan-1-one, CAS: 2351104-22-6]



Trichosorbicillin G (**57d**)

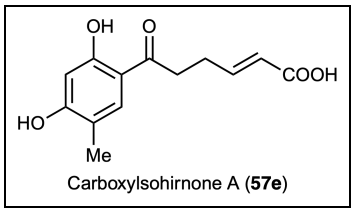
SMILES: OC1=C(C(CCCCCO)=O)C=C(C)C(O)=C1

Fungus of origin: *Trichoderma reesei* 4670[30].

Bioactivity: Evaluation of cytotoxicity against three human cancer cell lines, MCF-7 (breast cancer), HeLa (cervical cancer), and HepG2 showed no effectivity. Anti-inflammatory activity due to inhibition of nitric oxide production in RAW264.7 cells was not observed.[30]

Analytics: White powder. ^{1}**H-NMR** (400 MHz, CD_3OD): δ = 7.54 (s, 1H, Ar*H*), 6.22 (s, 1H, Ar*H*), 3.54 (t, *J* = 6.4 Hz, 2H, CH_2), 2.90 (t, *J* = 7.2 Hz, 2H, CH_2), 2.10 (s, 3H, CH_3), 1.69 (m, 2H, CH_2), 1.56 (m, 2H, CH_2), 1.42 (m, 2H, CH_2). ^{13}**C-NMR** (100 MHz, CD_3OD): δ = 206.3, 164.7, 164.6, 133.4, 118.1, 113.6, 102.9, 62.8, 38.6, 33.5, 26.7, 25.9, 15.5. **IR**: *ν* 3412, 3157, 2939, 1624, 1512, 1390, 1259, 1147, 1032, 968, 845, 756 cm^{-1}. **HRMS** (ESI) *m/z*: $[M-H]^-$ calcd for $C_{13}H_{17}O_4$ 237.1132, found 237.1134.[30]

Carboxylsohirnone A (57e) [(*E*)-6-(2,4-Dihydroxy-5-methylphenyl)-6-oxohex-2-enoic acid, CAS: 1344146-35-5]



Carboxylsohirnone A (**57e**)

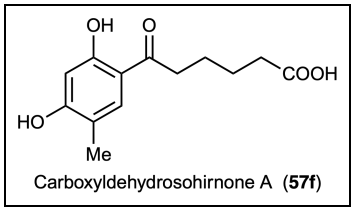
SMILES: OC1=C(C(CC/C=C/C(O)=O)=O)C=C(C)C(O)=C1

Fungus of origin: *Trichoderma* sp.[88].

Bioactivity: Cytotoxicity against leukemic P388 (IC_{50} = 72.8 μM) and HL-60 cell lines (IC_{50} = 52.4 μM). DPPH-radical scavenging activity (IC_{50} = 175 μM).[88]

Analytics: Colorless needles. **MP**: 220–222 °C. ^{1}**H-NMR** (400 MHz, CD_3OD): δ = 7.57 (s, 1H, Ar*H*), 6.98 (m, 1H, C*H*), 6.25 (s, 1H, Ar*H*), 5.88 (d, *J* = 14.9 Hz, 1H, C*H*), 3.10 (t, *J* = 6.9 Hz, 2H, CH_2), 2.58 (q, *J* = 6.9 Hz, 2H, CH_2), 2.11 (s, 3H, CH_3). ^{13}**C-NMR** (100 MHz, CD_3OD): δ = 204.2, 170.7, 164.6 (2C), 148.9, 133.2, 123.9, 118.3, 113.5, 102.9, 36.9, 27.7, 15.5. **IR**: *ν* 3500-2800, 1668, 1628, 1604, 1539, 1512, 1464, 1381, 1267, 1227, 1183, 1142, 1003, 966, 882, 858, 842, 794, 767, 747, 711 cm^{-1}. **HRMS** (ESI) *m/z*: $[M-H]^-$ calcd for $C_{13}H_{13}O_5$ 249.0763, found 249.0767.[88]

Carboxyldehydrosohirnone A (57f) [6-(2,4-Dihydroxyl-5-methylphenyl)-6-oxohexanoic acid, CAS: 1344146-37-7]



Carboxyldehydrosohirnone A (**57f**)

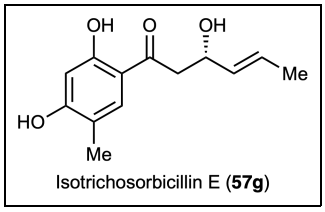
SMILES: OC1=C(C(CCCCC(O)=O)=O)C=C(C)C(O)=C1

Fungus of origin: *Trichoderma* sp.[88].

Bioactivity: Cytotoxicity against leukemic P388 (IC_{50} = 44.5 μM) and HL-60 cell lines (IC_{50} = 81.2 μM). DPPH-radical scavenging activity (IC_{50} = 142 μM).[88]

Analytics: Colorless needles. **MP**: 210–212 °C. ^{1}**H-NMR** (400 MHz, CD_3OD): δ = 7.58 (s, 1H, Ar*H*), 6.24 (s, 1H, Ar*H*), 2.94 (t, *J* = 6.9 Hz, 2H, CH_2), 2.34 (t, *J* = 6.5 Hz, 2H, CH_2), 2.12 (s, 3H, CH_3), 1.72 (m, 4H, CH_2). ^{13}**C-NMR** (100 MHz, CD_3OD): δ = 206.0, 177.8, 164.7, 164.5, 133.4, 118.2, 113.6, 102.9, 38.3, 35.1, 25.9, 25.5, 15.5. **IR**: *ν* 3390-2800, 1633, 1591, 1513, 1462, 1416, 1378, 1316, 1278, 1204, 1183, 1151, 1004, 973, 931, 919, 887, 844, 813, 744, 690 cm^{-1}. **HRMS** (ESI) *m/z*: $[M-H]^-$ calcd for $C_{13}H_{15}O_5$ 251.0919, found 251.0908.[88]

Isotrichosorbicillin E (57g) [(*S*,*E*)-1-(2,4-Dihydroxy-5-methylphenyl)-3-hydroxyhex-4-en-1-one, CAS: 2365301-48-8]



Isotrichosorbicillin E (**57g**)

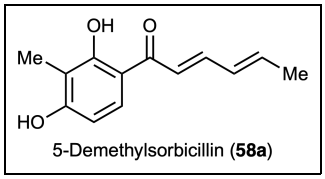
SMILES: OC1=C(C(C[C@H](O)/C=C/C)=O)C=C(C)C(O)=C1

Fungus of origin: *Trichoderma reesei* 4670[30].

Bioactivity: Evaluation of cytotoxicity against three human cancer cell lines, MCF-7 (breast cancer), HeLa (cervical cancer), and HepG2 showed no effectivity. Anti-inflammatory activity due to inhibition of nitric oxide production in RAW264.7 cells (IC_{50} = 12.0 μM).[30]

Analytics: Yellow powder. **ORD**: $[\alpha]_D^{20}$ = +8.1 (c = 0.2, MeOH). ^{1}**H-NMR** (400 MHz, CD_3OD): δ = 7.56 (s, 1H, Ar*H*), 6.23 (s, 1H, Ar*H*), 5.69 (m, 1H, C*H*), 5.57 (m, 1H, C*H*), 4.59 (dd, *J* = 12.8, 6.8 Hz, 1H, C*H*), 3.15 (t, *J* = 15.2, 8.0 Hz, 1H, CH_2), 2.95 (dd, *J* = 15.2, 8.0 Hz, 1H, CH_2), 2.11 (s, 3H, CH_3), 1.67 (d, *J* = 6.4 Hz, 3H, CH_3). ^{13}**C-NMR** (100 MHz, CD_3OD): δ = 203.8, 164.9 (2C), 134.4, 133.8, 127.3, 118.2, 114.2, 102.9, 70.3, 46.3, 17.8, 15.5. **IR**: *ν* 3356, 3201, 2922, 1616, 1367, 1255, 1140, 976, 841 cm^{-1}. **HRMS** (ESI) *m/z*: $[M-H]^-$ calcd for $C_{13}H_{15}O_4$ 235.0976, found 235.0977.[30]

5-Demethylsorbicillin (58a) [(2*E*,4*E*)-1-(2,4-Dihydroxy-3-methylphenyl)hexa-2,4-dien-1-one, CAS: 267001-68-3]



5-Demethylsorbicillin (**58a**)

SMILES: OC1=C(C(/C=C/C=C/C)=O)C=CC(O)=C1C

Fungus of origin: *Trichoderma* sp. USF-2690[47].

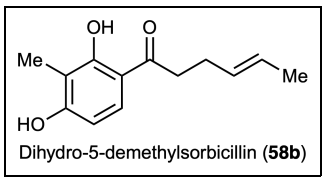
Bioactivity: No DPPH-radical scavenging activity.[47]

Biosynthesis: Follows the same polyketide machinery as sorbicillin (**1a**) without one methylation step through *S*-adenosylmethionine.

Total synthesis: Friedel-Craft reaction between 2-methyl resorcinol [CAS: 608-25-3] and sorbic acid [CAS: 110-44-1] using boron trifluoride etherate [CAS: 109-63-7]. The obtained boron complex can be hydrolyzed with water in THF.[35] Instead of boron trifluoride etherate and sorbic acid, aluminium(III) chloride [CAS: 7446-70-0] and sorbyl chloride [CAS: 2614-88-2] can also be used.[42]

Analytics: Yellowish, amorphous powder. ^{1}**H-NMR** (400 MHz, $CDCl_3$): δ = 13.68 (bs, 1H, O*H*), 7.57 (d, *J* = 8.8 Hz, 1H, Ar*H*), 7.46 (dd, *J* = 15.2, 10.1 Hz, 1H, CH_{sorbyl}), 6.91 (d, *J* = 15.2 Hz, 1H, CH_{sorbyl}), 6.37 (d, *J* = 8.8 Hz, 1H, ArH_{sorbyl}), 6.34 (dd, *J* = 15.6, 10.1 Hz, 1H, CH_{sorbyl}), 6.28 (dq, *J* = 15.6, 6.0 Hz, 1H, C*H*), 2.14 (s, 3H, CH_3), 1.90 (d, *J* = 6.0 Hz, 3H, CH_3). ^{13}**C-NMR** (100 MHz, $CDCl_3$): δ = 192.7, 164.3, 160.2, 144.8, 141.3, 130.6, 128.6, 121.8, 114.1, 111.3, 106.8, 18.9, 7.3. **IR**: *ν* 3200, 1620, 1370, 1335, 1310, 1265, 1115 cm^{-1}. **HRMS** (EI) *m/z*: $[M]^+$ calcd for $C_{13}H_{14}O_3$ 218.0943, found 218.0946.[47]

Dihydro-5-demethylsorbicillin (58b) [(*E*)-1-(2,4-Dihydroxy-3-methylphenyl)hex-4-en-1-one, CAS: 1311204-68-8]



Dihydro-5-demethylsorbicillin (**58b**)

SMILES: OC1=C(C(CC/C=C/C)=O)C=CC(O)=C1C

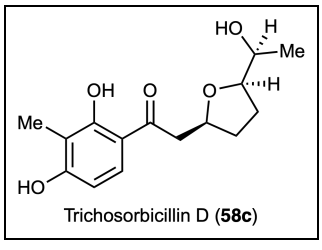
Fungus of origin: *Penicillium* sp. SCSIO06871[51], *Phialocephala* sp. strain FL30r[118].

Bioactivity: Cytotoxicity against leukemic P388 cells ($IC_{50} = 0.10$ µM) and lymphoblast cells (IC_{50} = 4.80 µM).[118]

Biosynthesis: Follows the same polyketide machinery as sorbicillin (**1a**) without one methylation step through *S*-adenosylmethionine and with a further reduction step in the sorbyl side chain.

Analytics: Pale yellow powder. ^{1}**H-NMR** (600 MHz, $CDCl_3$): δ = 13.11 (bs, 1H, O*H*), 7.55 (d, *J* = 8.7 Hz, 1H, Ar*H*), 6.37 (d, *J* = 8.7 Hz, 1H, Ar*H*), 5.51 (m, 1H, C*H*), 5.48 (dt, *J* = 14.1, 5.1 Hz, 1H, C*H*), 2.96 (t, *J* = 7.5 Hz, 2H, CH_2), 2.41 (m, 2H, CH_2), 2.13 (s, 3H, CH_3), 1.65 (d, *J* = 5.1 Hz, 3H, CH_3). ^{13}**C-NMR** (150 MHz, $CDCl_3$): δ = 204.5, 163.2, 159.9, 137.0, 129.4, 129.0, 126.2, 113.5, 106.8, 37.9, 27.6, 17.9, 7.3. **IR**: *ν* 3444, 3421, 2924, 1621, 1501, 1429, 1309, 1099 cm^{-1}. **HRMS** (ESI) *m/z*: $[M-H]^-$ calcd for $C_{13}H_{15}O_3$ 219.1021, found 219.1025.[118].

Trichosorbicillin D (58c) [1-(2,4-Dihydroxy-3-methylphenyl)-2-((2*S*,5*R*)-5-((*S*)-1-hydroxyethyl)tetrahydrofuran-2-yl)ethan-1-one, CAS: 2365301-44-4]



Trichosorbicillin D (**58c**)

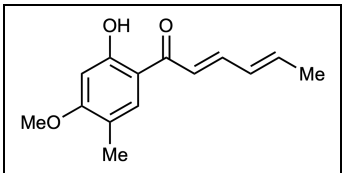
SMILES: OC1=C(C(C[C@@H]2CC[C@@]([C@]([H])(C)O)([H])O2)=O)C=CC(O)=C1C

Fungus of origin: *Trichoderma reesei* 4670[30].

Bioactivity: Evaluation of cytotoxicity against three human cancer cell lines, MCF-7 (breast cancer), HeLa (cervical cancer), and HepG2 showed no effectivity. Anti-inflammatory activity due to inhibition of nitric oxide production in RAW264.7 cells was not observed.[30]

Analytics: White powder **MP**: 149-150 °C. **ORD**: $[\alpha]_D^{20}$ = +8.8 (c = 0.1, MeOH). ^{1}**H-NMR** (400 MHz, CD_3OD): δ = 7.60 (d, *J* = 8.8 Hz, 1H, Ar*H*), 6.36 (d, *J* = 8.8 Hz, 1H, Ar*H*), 4.37 (m, 1H, C*H*), 3.70 (m, 2H, C*H*), 3.18 (dd, *J* = 15.2, 7.2 Hz, 1H, CH_2), 3.06 (dd, *J* = 15.2, 5.6 Hz, 1H, CH_2), 2.07 (m, 1H, CH_2), 2.01 (s, 3H, CH_3), 1.89 (dd, *J* = 14.4, 6.8 Hz, 2H, CH_2), 1.66 (m, 1H, CH_2), 1.09 (d, *J* = 6.0 Hz, 3H, CH_3). ^{13}**C-NMR** (100 MHz, CD_3OD): δ = 204.3, 164.5 (2C), 131.0, 113.8, 112.3, 108.3, 85.1, 77.8, 69.9, 44.9, 32.3, 26.6, 19.5, 7.6. **IR**: *ν* 3118, 2931, 1618, 1503, 1431, 1331, 1093, 798 cm^{-1}. **HRMS** (ESI) *m/z*: $[M-H]^-$ calcd for $C_{15}H_{19}O_5$ 279.1238, found 279.1236.[30]

4-Methoxy-3-demethylsorbicillin (59a) [(2*E*,4*E*)-1-(2-Hydroxy-4-methoxy-5-methylphenyl)hexa-2,4-dien-1-one, CAS: 877377-81-6]



4-Methoxy-3-demethylsorbicillin (**59a**)

SMILES: OC1=C(C(/C=C/C=C/C)=O)C=C(C)C(OC)=C1

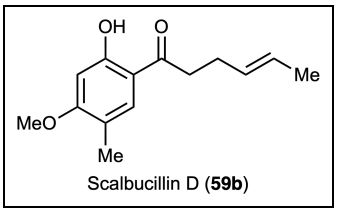
Fungus of origin: *Phaeoacremonium* sp. NRRL 32148[121], *Scytalidium album* MSX51631[122].

Bioactivity: No antifungal activity against *Aspergillus flavus* and *Fusarium verticillioides*.[121]

Biosynthesis: 4-Methoxy-3-demethylsorbicillin (**49a**) is presumably of polyketide origin, with extra methyl groups derived from *S*-adenosylmethionine.

Analytics: Yellow powder. **MP**: 68–70 °C. ^{1}**H-NMR** (400 MHz, $CDCl_3$): δ = 13.40 (bs, 1H, O*H*), 7.49 (s, 1H, Ar*H*), 7.45 (dd, *J* = 15.0, 10.0 Hz, 1H, CH_{sorbyl}), 6.92 (d, *J* = 15.0 Hz, 1H, CH_{sorbyl}), 6.39 (s, 1H, Ar*H*), 6.31 (m, 1H, CH_{sorbyl}), 6.28 (dq, *J* = 15.0, 6.1 Hz, 1H, CH_{sorbyl}), 3.84 (s, 3H, OCH_3), 2.13 (d, *J* = 0.5 Hz, 3H, CH_3), 1.90 (d, *J* = 6.1 Hz, 3H, CH_3). ^{13}**C-NMR** (100 MHz, $CDCl_3$): δ = 192.2, 165.2, 161.2, 144.5, 141.2, 130.6, 130.5, 121.8, 113.0, 99.1, 55.7, 18.9, 15.7. **IR**: *ν* 1618, 1567, 1382,1365, 1261, 1148 cm^{-1}.[121]

Scalbucillin D (59b) [(*E*)-1-(2-Hydroxy-4-(hydroxymethyl)-5-methylphenyl)hex-4-en-1-one]



Scalbucillin D (**59b**)

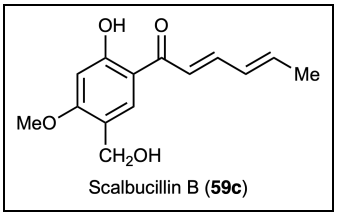
SMILES: OC1=C(C(CC/C=C/C)=O)C=C(C)C(OC)=C1

Fungus of origin: *Scytalidium album* MSX51631[122].

Bioactivity: No cytotoxicity against human cancer lines MDA-MB-435 and SW-620.[122]

Analytics: White solid. ^{1}**H-NMR** (500 MHz, $CDCl_3$): δ = 12.79 (bs, 1H, O*H*), 7.44 (s, 1H, Ar*H*), 6.37 (s, 1H, Ar*H*), 5.50 (dq, *J* = 15.5, 5.2 Hz, 1H, C*H*), 5.49 (dtq, *J* = 15.5, 5.2, 0.6 Hz, 1H, C*H*), 3.84 (s, 3H, OCH_3), 2.95 (dd, *J* = 8.0, 7.5 Hz, 2H, CH_2), 2.40 (ddd, *J* = 8.0, 7.5, 5.2 Hz, 2H, CH_2), 1.65 (dd, *J* = 5.2, 0.6 Hz, 3H, CH_3). ^{13}**C-NMR** (125 MHz, $CDCl_3$): δ = 204.2, 164.3, 164.0, 131.1, 129.6, 126.2, 118.1, 112.7, 99.0, 55.8, 38.0, 27.5, 18.0, 15.8. **HRMS** (ESI) *m/z*: $[M+H]^+$ calcd for $C_{14}H_{18}O_3$ 235.1329, found 235.1323.[122]

Scalbucillin B (59c) [(2*E*,4*E*)-1-(2-Hydroxy-5-(hydroxymethyl)-4-methoxyphenyl)hexa-2,4-dien-1-one, CAS: 1703754-80-6]



Scalbucillin B (**59c**)

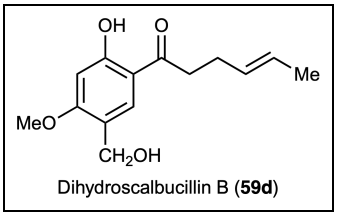
SMILES: OC1=C(C(/C=C/C=C/C)=O)C=C(CO)C(OC)=C1

Fungus of origin: *Scytalidium album* MSX51631[122].

Bioactivity: Cytotoxicity against human cancer lines MDA-MB-435 (IC_{50} = 67.9 μM) and SW-620 (IC_{50} = 16.0 μM). Antifungal activity against *Candida albicans* (IC_{50} > 38.0 μg/mL), *Cryptococcus neoformans* (IC_{50} > 38.0 μg/mL), and *Aspergillus niger* (IC_{50} = 0.60 μg/mL).[122]

Analytics: Yellow solid. ^{1}**H-NMR** (700 MHz, $CDCl_3$): δ = 13.58 (bs, 1H, O*H*), 7.71 (s, 1H, Ar*H*), 7.49 (dd, *J* = 15.0, 10.6 Hz, 1H, CH_{sorbyl}), 6.95 (d, *J* = 15.0 Hz, 1H, CH_{sorbyl}), 6.46 (s, 1H, Ar*H*), 6.34 (m, 1H, CH_{sorbyl}), 6.31 (dq, *J* = 15.0, 6.4 Hz, 1H, CH_{sorbyl}), 4.64 (d, *J* = 6.1 Hz, 2H, CH_2OH), 3.90 (s, 3H, OCH_3), 2.02 (t, *J* = 6.1 Hz, 1H, O*H*), 1.92 (dd, *J* = 6.4, 0.6 Hz, 3H, CH_3). ^{13}**C-NMR** (175 MHz, $CDCl_3$): δ = 192.4, 166.5, 163.8, 145.1, 141.8, 130.4, 129.9, 121.4, 120.7, 113.3, 99.7, 61.2, 55.8, 19.0. **HRMS** (ESI) *m/z*: $[M+H]^+$ calcd for $C_{14}H_{17}O_4$ 249.1121, found 249.1115.[122]

Dihydroscalbucillin B (59d) [(*E*)-1-(2-Hydroxy-5-(hydroxymethyl)-4-methoxyphenyl)hex-4-en-1-one, CAS: 877377-82-7]



Dihydroscalbucillin B (**59d**)

SMILES: OC1=C(C(CC/C=C/C)=O)C=C(CO)C(OC)=C1

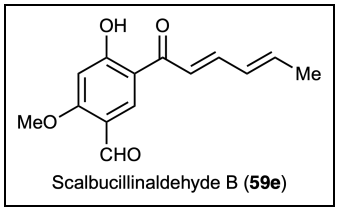
Fungus of origin: *Phaeoacremonium* sp. NRRL 32148[121], *Scytalidium album* MSX51631[122].

Bioactivity: Weak antifungal activity against *Aspergillus flavus* and *Fusarium verticillioides*.[121]

Biosynthesis: Dihydroscalbucillin B (**49c**) is presumably of polyketide origin, with extra methyl groups derived from *S*-adenosylmethionine and a further oxidation to obtain the phenylmethanol functionality.[121]

Analytics: White powder. **MP**: 59–61 °C. ^{1}**H-NMR** (400 MHz, $CDCl_3$): δ = 12.91 (bs, 1H, O*H*), 7.64 (s, 1H, Ar*H*), 6.42 (s, 1H, Ar*H*), 5.49 (dtq, *J* = 15.0, 5.4, 1.1 Hz, 1H, C*H*), 5.47 (dqt, *J* = 15.0, 5.9, 1.1 Hz, 1H, C*H*), 4.61 (bs, 2H, CH_2), 3.87 (s, 3H, OCH_3), 2.96 (t, *J* = 7.4 Hz, 2H, CH_2), 2.39 (m, 2H, CH_2), 2.02 (bs, 1H, O*H*), 1.64 (ddt, *J* = 5.9, 1.1, 1.1 Hz, 3H, CH_3). ^{13}**C-NMR** (100 MHz, $CDCl_3$): δ = 204.3, 165.3, 163.7, 130.3, 129.3, 126.2, 120.8, 99.6, 61.1, 55.8, 37.9, 27.3, 17.9. **IR**: *ν* 1635, 1498, 1446, 1378, 1273, 1209, 1141, 1029 cm^{-1}.[121]

Scalbucillinaldehyde B (59e) [5-((2*E*,4*E*)-Hexa-2,4-dienoyl)-4-hydroxy-2-methoxybenzaldehyde, CAS: 51167-44-3]



Scalbucillinaldehyde B (**59e**)

SMILES: OC1=C(C(/C=C/C=C/C)=O)C=C(C=O)C(OC)=C1

Fungus of origin: *Phaeoacremonium* sp. NRRL 32148[121], *Scytalidium album* MSX51631[122], *Scytalidium* sp. FY[123].

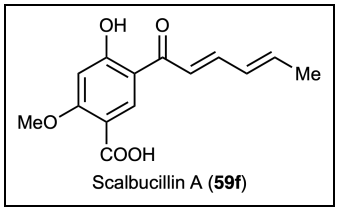
Bioactivity: Antifungal activity against *Aspergillus flavus* and *Fusarium verticillioides*.[121]

Biosynthesis: Dihydroscalbucillinaldehyde B (**49d**) is presumably of polyketide origin, with extra methyl groups derived from *S*-adenosylmethionine and a further oxidation to obtain the benzaldheyde functionality.[121]

Total synthesis: 2,4-Dimethoxybenzaldehyde [CAS: 613-45-6] was treated with aluminium(III) chloride [CAS: 7446-70-0] and chloroacetyl chloride [CAS: 79-04-9] to give 2-chloro-5′-formyl-2′-hydroxy-4′-methoxyacetophenone (22% yield). The latter was combined with zinc and croton aldehyde [CAS: 4170-30-3] leading to scalbucillinaldehyde B (**49d**) in 10% yield.[124]

Analytics: Yellow solid. **MP**: 154–157 °C. ^{1}**H-NMR** (220 MHz, $CDCl_3$): δ = 10.27 (s, 1H, C*H*O), 8.39 (s, 1H, Ar*H*), 7.51 (m, 1H, CH_{sorbyl}), 7.02 (d, *J* = 15.0 Hz, 1H, CH_{sorbyl}), 6.50 (s, 1H, Ar*H*), 6.39 (m, 2H, CH_{sorbyl}), 3.96 (s, 3H, OCH_3), 1.94 (d, *J* = 5.0 Hz, 3H, CH_3). **IR**: *ν* 1680, 1643, 1616, 1582, 1569, 1133 cm^{-1}.[123]

Scalbucillin A (59f) [5-((2*E*,4*E*)-Hexa-2,4-dienoyl)-4-hydroxy-2-methoxybenzoic acid, CAS: 1703754-79-3]



Scalbucillin A (**59f**)

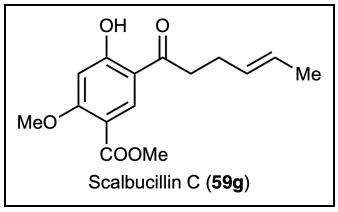
SMILES: OC1=C(C(/C=C/C=C/C)=O)C=C(C(O)=O)C(OC)=C1

Fungus of origin: *Scytalidium album* MSX51631[122].

Bioactivity: No cytotoxicity against human cancer lines MDA-MB-435 and SW-620.[122]

Analytics: Yellow solid. ^{1}**H-NMR** (700 MHz, $CDCl_3$): δ = 13.87 (bs, 1H, O*H*), 10.05 (bs, 1H, O*H*), 8.74 (s, 1H, Ar*H*), 7.54 (dd, *J* = 14.6, 9.9 Hz, 1H, CH_{sorbyl}), 7.05 (d, *J* = 14.6 Hz, 1H, CH_{sorbyl}), 6.58 (s, 1H, Ar*H*), 6.39 (m, 1H, CH_{sorbyl}), 6.38 (dq, *J* = 14.6, 5.1 Hz, 1H, CH_{sorbyl}), 4.12 (s, 3H, OCH_3), 1.94 (d, *J* = 5.1 Hz, 3H, CH_3). ^{13}**C-NMR** (175 MHz, $CDCl_3$): δ = 192.8, 169.6, 164.3, 163.1, 146.9, 143.5, 137.2, 130.4, 120.6, 115.1, 109.2, 100.5, 57.2, 19.1. **HRMS** (ESI) *m/z*: $[M+H]^+$ calcd for $C_{14}H_{15}O_5$ 263.0914, found 263.0910.[122]

Scalbucillin C (59g) [Methyl (*E*)-5-(hex-4-enoyl)-4-hydroxy-2-(hydroxymethyl)benzoate]



Scalbucillin C (**59g**)

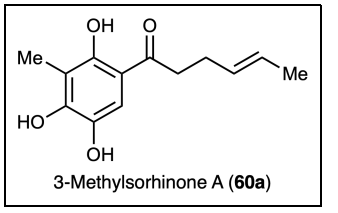
SMILES: OC1=C(C(CC/C=C/C)=O)C=C(C(OC)=O)C(OC)=C1

Fungus of origin: No cytotoxicity against human cancer lines MDA-MB-435 and SW-620.[122] *Scytalidium album* MSX51631[122].

Bioactivity: No cytotoxicity against human cancer lines MDA-MB-435 and SW-620.[122]

Analytics: White solid. ^{1}**H-NMR** (500 MHz, $CDCl_3$): δ = 13.05 (bs, 1H, O*H*), 8.37 (s, 1H, Ar*H*), 6.47 (s, 1H, Ar*H*), 5.50 (dq, *J* = 15.5, 6.3 Hz, 1H, C*H*), 5.49 (dtq, *J* = 15.5, 6.3, 1.2 Hz, 1H, C*H*), 3.93 (s, 3H, OCH_3), 3.88 (s, 3H, OCH_3), 3.02 (dd, *J* = 7.5, 6.9 Hz, 2H, CH_2), 2.41 (ddd, *J* = 7.5, 6.9, 6.3 Hz, 2H, CH_2), 1.65 (dd, *J* = 6.3, 1.2 Hz, 3H, CH_3). ^{13}**C-NMR** (125 MHz, $CDCl_3$): δ = 204.7, 167.9, 165.5, 165.4, 135.9, 129.2, 126.6, 112.9, 111.6, 100.5, 56.5, 52.2, 38.0, 27.2, 18.0. **HRMS** (ESI) *m/z*: $[M+H]^+$ calcd for $C_{15}H_{19}O_5$ 279.1227, found 279.1221.[122]

3-Methylsorhinone A (60a) [5-Hydroxy-dihydrodemethylsorbicillin, (*E*)-1-(2,4,5-Trihydroxy-3-methylphenyl)hex-4-en-1-one, CAS: 2760198-19-2]



3-Methylsorhinone A (**60a**)

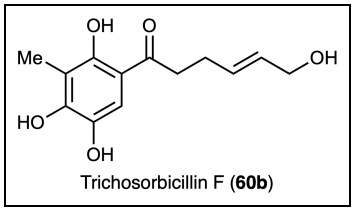
SMILES: OC1=C(C(CC/C=C/C)=O)C=C(O)C(O)=C1C

Fungus of origin: *Penicillium* sp. SCSIO06871[51].

Bioactivity: Antibacterial against *Staphylococcus aureus* and methicillin-resistant *Staphylococcus aureus* (each IC_{50} = 80.0 μg/mL). α-Glycosidase inhibition of IC_{50} = 36.0 μM[51].

Analytics: Colorless block crystal. **MP**: 115 °C. ^{1}**H-NMR** (700 MHz, CD_3OD): δ = 7.06 (s, 1H, Ar*H*), 5.40 (m, 2H, C*H*), 2.89 (t, *J* = 7.0 Hz, 2H, CH_2), 2.66 (m, 2H, CH_2), 2.05 (s, 3H, CH_3), 1.63 (dd, *J* = 9.8, 7.0 Hz, 3H, CH_3). ^{13}**C-NMR** (175 MHz, CD_3OD): δ = 205.5, 158.5, 153.8, 138.5, 131.0, 126.8, 112.7, 112.4, 111.7, 38.9, 29.1, 18.1, 8.0. **HRMS** (ESI) *m/z*: $[M-H]^-$ calcd for $C_{13}H_{15}O_4$ 235.0976, found 235.0967.[51]

Trichosorbicillin F (60b) [(*E*)-6-Hydroxy-1-(2,4,5-trihydroxy-3-methylphenyl)hex-4-en-1-one]



Trichosorbicillin F (**60b**)

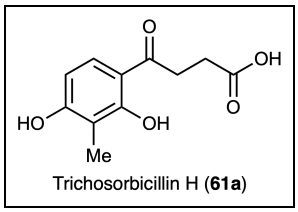
SMILES: OC1=C(C(CC/C=C/CO)=O)C=C(O)C(O)=C1C

Fungus of origin: *Trichoderma reesei* 4670.[30]

Bioactivity: Anti-inflammatory activity due to inhibition of nitric oxide formation in LPS-induced RAW264.7 cells ($IC_{50} > 6.10$ μM).[30]

Analytics: Yellow powder. **MP**: 154-156 °C. ^{1}**H-NMR** (400 MHz, CD_3OD): δ = 7.08 (s, 1H, Ar*H*), 4.01 (dd, *J* = 5.6, 0.8 Hz, 2H, CH_2), 2.97 (t, *J* = 7.6 Hz, 2H, CH_2), 2.44 (q, *J* = 6.8 Hz, 2H, CH_2), 2.07 (s, 3H, CH_3). ^{13}**C-NMR** (100 MHz, CD_3OD): δ = 205.1, 158.5, 153.8, 138.5, 131.7, 131.3, 112.8, 112.6, 111.7, 63.5, 38.4, 28.4, 7.9. **IR**: *ν* 3737, 3489, 3296, 2926, 1572, 1514, 1414, 1333, 1240, 1182, 1024, 750 cm^{-1}. **HRMS** (ESI) *m/z*: $[M-H]^-$ calcd for $C_{13}H_{15}O_5$ 251.0925, found 251.0932.[30]

Trichosorbicillin H (61a) [4-(2,4-Dihydroxy-3-methylphenyl)-4-oxobutanoic acid]



Trichosorbicillin H (**61a**)

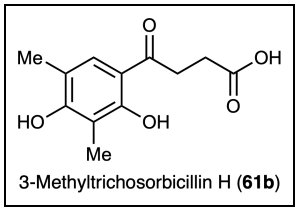
SMILES: O=C(CCC(O)=O)C1=CC=C(O)C(C)=C1O

Fungus of origin: *Trichoderma reesei* 4670.[30]

Bioactivity: Anti-inflammatory activity due to inhibition of nitric oxide formation in LPS-induced RAW264.7 cells ($IC_{50} > 50.0$ μM).[30]

Analytics: White powder. ^{1}**H-NMR** (400 MHz, CD_3OD): δ = 7.59 (s, 1H, Ar*H*), 6.22 (s, 1H, Ar*H*), 3.22 (t, *J* = 6.4 Hz, 2H, CH_2), 2.63 (t, *J* = 6.4 Hz, 2H, CH_2), 2.10 (s, 3H, CH_3). ^{13}**C-NMR** (100 MHz, CD_3OD): δ = 204.0, 177.9, 164.5, 164.4, 133.1, 118.2, 113.6, 102.8, 33.8, 29.4, 15.5. **IR**: *ν* 367, 2926, 1713, 1633, 1508, 1419, 1373, 1267, 1147 cm^{-1}. **HRMS** (ESI) *m/z*: $[M-H]^-$ calcd for $C_{11}H_{11}O_5$ 223.0612, found 223.0613.[30]

3-Methyltrichosorbicillin H (61b) [4-(2,4-Dihydroxy-3,5-dimethylphenyl)-4-oxobutanoic acid]



3-Methyltrichosorbicillin H (**61b**)

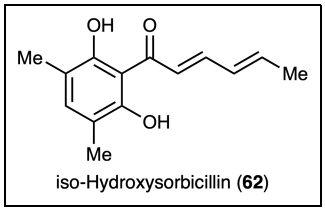
SMILES: O=C(CCC(O)=O)C1=CC(C)=C(O)C(C)=C1O

Fungus of origin: *Trichoderma reesei* 4670.[30]

Bioactivity: Anti-inflammatory activity due to inhibition of nitric oxide formation in LPS-induced RAW264.7 cells ($IC_{50} > 50.0$ μM).[30]

Analytics: White powder. ^{1}**H-NMR** (400 MHz, CD_3OD): δ = 7.49 (s, 1H, Ar*H*), 3.23 (t, *J* = 6.4 Hz, 2H, CH_2), 2.63 (t, *J* = 6.4 Hz, 2H, CH_2), 2.15 (s, 3H, CH_3), 2.03 (s, 3H, CH_3). ^{13}**C-NMR** (100 MHz, CD_3OD): δ = 204.3, 177.4, 162.2, 161.9, 130.1, 117.2, 113.4, 111.9, 33.7, 29.3, 16.3, 8.0. **IR**: *ν* 3180, 2914, 2843, 1624, 1367, 1213, 1147 cm^{-1}. **HRMS** (ESI) *m/z*: $[M-H]^-$ calcd for $C_{12}H_{13}O_5$ 237.0769, found 237.0770.[30]

***iso*-Hydroxysorbicillin (62)** [(2*E*,4*E*)-1-(2,6-Dihydroxy-3,5-dimethylphenyl)hexa-2,4-dien-1-one, CAS: 1062236-42-3]



iso-Hydroxysorbicillin (**62**)

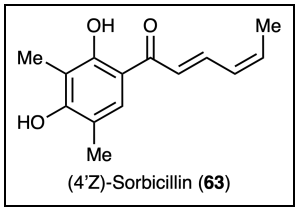
SMILES: OC1=C(C(/C=C/C=C/C)=O)C(O)=C(C)C=C1C

Fungus of origin: *Acremonium* sp. AN-13[1], *Diaporthe* sp. SCSIO 41011[125], *Penicillium* sp. M207142[126].

Bioactivity: Cytotoxicity against cervical cancer cells HeLa (IC_{50} = 11.2 μM) and colorectal cancer SW620 cell lines.[126] Antibacterial activity against *Staphylococcus aureus* ATCC 6538 (IC_{50} = 128 μg/mL).[1]

Analytics: Yellow needle-like crystals. ^{1}**H-NMR** (500 MHz, CD_3OD): δ = 7.56 (s, 1H, Ar*H*), 7.42 (dd, *J* = 14.7, 11.1 Hz, 1H, CH_{sorbyl}), 7.12 (d, *J* = 14.7 Hz, 1H, CH_{sorbyl}), 6.46 (dd, *J* = 14.7, 11.1 Hz, 1H, CH_{sorbyl}), 6.32 m, 1H, CH_{sorbyl}), 2.17 (s, 3H, CH_3), 2.06 (s, 3H, CH_3), 1.90 (d, *J* = 6.7 Hz, 3H, CH_3),. ^{13}**C-NMR** (125 MHz, CD_3OD): δ = 193.9, 163.7, 162.2, 145.3, 141.7, 132.0, 130.1, 123.5, 117.2, 114.0, 112.0, 18.9, 16.4, 8.0. **IR**: *ν* 3343, 2926, 1642, 1626, 1483, 1383, 1365, 1282, 1180, 1154, 1028, 993, 860, 806, 756 cm^{-1}.[126]

(4′Z)-Sorbicillin (63) [(2*E*,4*Z*)-1-(2,4-Dihydroxy-3,5-dimethylphenyl)hexa-2,4-dien-1-one, CAS: 1448337-74-3]



(4'Z)-Sorbicillin (**63**)

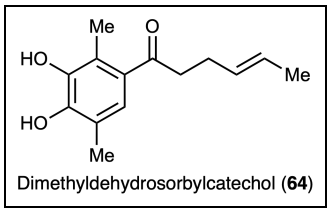
SMILES: OC1=C(C(/C=C/C=C\C)=O)C=C(C)C(O)=C1C

Fungus of origin: *Trichoderma* sp.[15].

Total synthesis: In theory, (4′*Z*)-sorbicillin (**53**) could be synthesized analogously to sorbicillin (**1a**) using a Friedel-Craft reaction with (2′*E*,4′*Z*)-sorbic acid [CAS: 30361-30-9].

Analytics: Yellowish, amorphous solid. ^{1}**H-NMR** (6400 MHz, $CDCl_3$): δ = 13.55 (bs, 1H, O*H*), 7.86 (ddd, *J* = 14.8, 12.0, 1.2 Hz, 1H, CH_{sorbyl}), 7.47 (s, 1H, Ar*H*), 7.04 (d, *J* = 14.8 Hz, 1H, CH_{sorbyl}), 6.32 (ddq, *J* = 12.0, 10.8, 1.6 Hz, 1H, CH_{sorbyl}), 6.05 (ddd, *J* = 10.8, 7.2, 1.2 Hz, 1H, CH_{sorbyl}), 5.26 (bs, 1H, O*H*), 2.23 (s, 3H, CH_3), 2.16 (s, 3H, CH_3), 1.96 (dd, *J* = 7.2, 1.6 Hz, 3H, CH_3). ^{13}**C-NMR** (100 MHz, $CDCl_3$): δ = 192.5, 162.6, 158.8, 138.6, 137.3, 128.8, 128.1, 123.9, 114.4, 113.7, 110.4, 15.6, 14.2, 7.5. **HRMS** (ESI) *m/z*: $[M-H]^-$ calcd for $C_{14}H_{15}O_3$ 231.1027, found 231.1023.[15]

Dimethyldehydrosorbylcatechol (64) [2-Deoxysohirnone C, (*E*)-1-(3,4-Dihydroxy-2,5-dimethylphenyl)hex-4-en-1-one]



Dimethyldehydrosorbylcatechol (**64**)

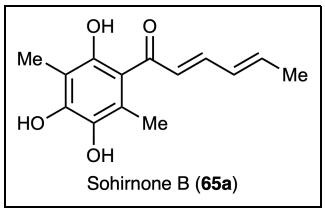
SMILES: O=C(CC/C=C/C)C1=C(C)C(O)=C(O)C(C)=C1

Fungus of origin: *Penicillium* sp. GD6[127], *Penicillium*sp. SCSIO06871[51].

Bioactivity: Antibacterial activity against methicillin-resistant *Staphylococcus aureus* (IC_{50} = 80 μg/mL).[127]

Analytics: Colorless gum. ^{1}**H-NMR** (500 MHz, CD_3OD): δ = 7.44 (s, 1H, Ar*H*), 5.49 (m, 2H, C*H*), 2.94 (t, *J* = 7.5 Hz, 2H, CH_2), 2.34 (m, 2H, CH_2), 2.15 (s, 3H, CH_3), 2.05 (s, 3H, CH_3), 1.62 (m, 3H, CH_3). ^{13}**C-NMR** (125 MHz, CD_3OD): δ = 205.9, 162.5, 161.9, 131.0, 130.4, 126.8, 117.1, 113.4, 111.9, 38.7, 29.0, 18.0, 16.3, 8.0. **IR**: *ν* 3426, 1630, 1252, 1236, 1164, 1045, 1008 cm^{-1}. **HRMS** (ESI) *m/z*: $[M+Na]^+$ calcd for $C_{14}H_{18}O_3Na$ 257.1154, found 257.1159.[127]

Sohirnone B (65a) [(2*E*,4*E*)-1-(2,4,5-Trihydroxy-3,6-dimethylphenyl)hexa-2,4-dien-1-one, CAS: 859155-91-2]



Sohirnone B (**65a**)

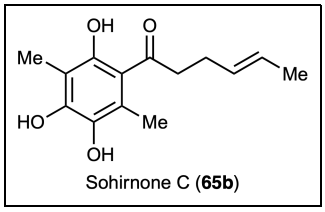
SMILES: OC1=C(C(/C=C/C=C/C)=O)C(C)=C(O)C(O)=C1C

Fungus of origin: *Penicillium notatum*[28].

Bioactivity: Antibacterial against *Staphylococcus aureus* and *Bacillus subtilis* (weak).[28]

Analytics: Yellow solid. **TLC**: R_f = 0.07 (DCM/MeOH = 10:1). ^{1}**H-NMR** (300 MHz, CD_3OD): δ = 6.98 (dd, *J* = 15.6, 10.5 Hz, 1H, CH_{sorbyl}), 6.34 (m, 1H, CH_{sorbyl}), 6.32 (d, *J* = 15.6 Hz, 1H, CH_{sorbyl}), 6.21 (m, 1H, CH_{sorbyl}), 2.19 (s, 3H, CH_3), 2.03 (s, 3H, CH_3), 1.84 (m, 3H, CH_3). ^{13}**C-NMR** (75.5 MHz, CD_3OD): δ = 200.8, 148.6, 147.1, 143.1, 142.8, 141.4, 131.7, 130.7, 127.3, 122.0, 120.6, 19.0, 11.3, 10.3. **IR**: *ν* 3283, 1643, 1609, 1558, 1290, 1243, 1051, 998, 786, 726, 640, 616 cm^{-1}. **HRMS** (ESI) *m/z*: $[M+Na]^+$ calcd for $C_{14}H_{16}O_4Na$ 271.0941, found 271.0940.[28]

Sohirnone C (65b) [Dihydrosohirnone B, (*E*)-1-(2,4,5-Trihydroxy-3,6-dimethylphenyl)hex-4-en-1-one, CAS: 859155-92-3]



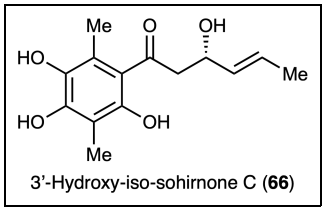
Sohirnone C (**65b**)

SMILES:

Fungus of origin: *Penicillium notatum*[28].

Analytics: Pale yellow solid. **TLC**: R_f = 0.08 (DCM/MeOH = 10:1). ^{1}**H-NMR** (300 MHz, CD_3OD): δ = 5.43 (m, 2H, C*H*), 2.87 (t, *J* = 7.1 Hz, 2H, CH_2), 2.52 (m, 2H, CH_2), 2.19 (s, 3H, CH_3), 2.06 (s, 3H, CH_3), 1.81 (m, 3H, CH_3). ^{13}**C-NMR** (75.5 MHz, CD_3OD): δ = 210.4, 146.7, 143.2, 126.7, 141.3, 131.0, 129.5, 121.4, 120.6, 45.5, 28.1, 18.1, 12.9, 10.3. **IR**: *ν* 3422, 1693,1458, 1376, 1284, 1243, 1141, 1057, 965, 771, 745, 639, 610 cm^{-1}. **HRMS** (ESI) *m/z*: $[M+Na]^+$ calcd for $C_{14}H_{18}O_4Na$ 273.1097, found 273.1095.[28]

3′-Hydroxy-iso-sohirnone C (66) [(*S*,*E*)-3-Hydroxy-1-(2,4,5-trihydroxy-3,6-dimethylphenyl)hex-4-en-1-one]



3'-Hydroxy-iso-sohirnone C (**66**)

SMILES: OC1=C(C(CC/C=C/C)=O)C(C)=C(O)C(O)=C1C

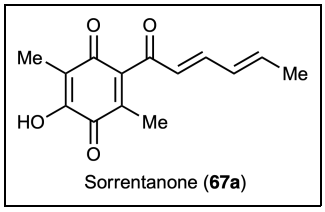
Fungus of origin: *Acremonium* sp.[1].

Bioactivity: DPPH-radical scavenging activity.[1]

Analytics: White amorphous power. **ORD**: $[\alpha]_D^{25} = +7.0$ (c = 0.2, MeOH). ^{1}**H-NMR** (500 MHz, CD_3OD): δ = 5.88 (dq, *J* = 15.6, 6.4 Hz, 1H, C*H*), 5.69 (dd, *J* = 15.6, 6.3 Hz, 1H, C*H*), 4.73 (m, 1H, C*H*), 2.64 (dd, *J* = 16.5, 12.3 Hz, 1H, CH_2), 2.55 (dd, *J* = 16.5, 3.3 Hz, 1H, CH_2), 2.46 (s, 3H, CH_3), 2.06 (s, 3H, CH_3), 1.74 (d, *J* = 6.4 Hz, 3H, CH_3). ^{13}**C-NMR** (125 MHz, CD_3OD): δ = 195.7, 158.4, 153.6, 138.5, 130.6, 130.2, 125.9, 113.1, 110.5, 78.6, 45.4, 17.9, 14.2, 8.6. **IR**: *ν* 3391, 2928, 1652, 1593, 1458, 1290, 1187^{-1}. **HRMS** (ESI) *m/z*: $[M+Na]^+$ calcd for $C_{14}H_{18}O_5Na$ 289.1046, found 289.1059.[1]

1.4.5 Quinones

Sorrentanone (67a) [2-((2*E*,4*E*)-Hexa-2,4-dienoyl)-5-hydroxy-3,6-dimethylcyclohexa-2,5-diene-1,4-dione, CAS: 165337-76-8]



Sorrentanone (**67a**)

SMILES: O=C(C(C)=C1O)C(C(/C=C/C=C/C)=O)=C(C)C1=O

Fungus of origin: *Penicillium chrysogenum* SC 13887[128], *Penicillium* sp. NX-S-6[46].

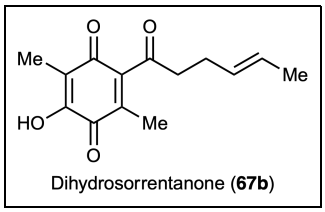
Bioactivity: Antibacterial against *Streptococcus pneumoniae* A9585 (IC_{50} = 32.0 µg/mL), *Streptococcus pyogenes* A9604 (IC_{50} = 16.0 µg/mL), *Enterococcus faecalis* A20688 (IC_{50} = 128 µg/mL), *Staphylococcus aureus* Hetero MR A27218 (IC_{50} = 32.0 µg/mL), *Staphylococcus epidermidis* A24548 (IC_{50} = 32.0 µg/mL), *Staphylococcus haemolyticus* A21638 (IC_{50} = 64.0 µg/mL), and *Bacillus subtilis* (IC_{50} = 32.0 µg/mL).[46,128]

Biosynthesis: Oxidation of (2*E*,4*E*)-1-(2,4,6-trihydroxy-3-methylphenyl)hexa-2,4-dien-1-one using the monoxygenase SorbC.[42]

Total synthesis: Sorrentanone (**67a**) has been synthesized chemo-enzymatically using the heterologous expressed monooxygenase SorbC together with 2,5-dimethylsorbicillin (29% yield).[42]

Analytics: Light orange solid. **TLC**: R_f = 0.44 (5% MeOH in DCM). ^{1}**H-NMR** (500 MHz, CD_3OD): δ = 7.11 (dd, *J* = 15.7, 9.9 Hz, 1H, C*H*$_{sorbyl}$), 6.36 (m, 2H, C*H*$_{sorbyl}$), 6.19 (d, *J* = 15.7 Hz, 1H, C*H*$_{sorbyl}$), 1.87 (m, 9H, C*H*$_3$). ^{13}**C-NMR**: δ = 193.3, 186.1, 183.4, 151.9, 147.5, 142.8, 140.3, 136.8, 130.1, 127.9, 117.1, 18.8, 11.9, 7.7. ^{13}**C-NMR** (75 MHz, CD_3OD): δ = 196.3, 188.0, 184.3, 155.1, 150.2, 144.4, 143.5, 138.6, 131.6, 129.3, 117.7, 19.1, 12.3, 7.7. **IR**: *v* 3376, 2856, 1654, 1632, 1596, 1436, 1392, 1382, 1362, 1318, 1236, 1220, 1144, 1070, 1006, 884, 824 cm^{-1}. **HRMS** (FAB) *m/z*: $[M]^+$ calcd for $C_{14}H_{14}O_4$ 247.0970, found 247.0958.[42,128]

Dihydrosorrentanone (67b) [(*E*)-2-(Hex-4-enoyl)-5-hydroxy-3,6-dimethylcyclohexa-2,5-diene-1,4-dione, CAS: 873443-79-9]



Dihydrosorrentanone (**67b**)

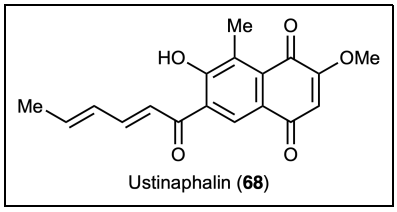
SMILES: O=C(C(C)=C1O)C(C(CC/C=C/C)=O)=C(C)C1=O

Fungus of origin: *Aspergillus* sp. TA01-14[129], *Penicillium terrestre*[89].

Bioactivity: Cytotoxicity against leukemic P388 (IC_{50} = 15.7 µM) and human lung cancer A549 cell lines (IC_{50} = 5.30 µM).[89]

Analytics: Orange needles. **MP**: 127–129 °C. ^{1}**H-NMR** (600 MHz, $CDCl_3$): δ = 6.97 (bs, 1H, O*H*), 5.48 (m, 1H, C*H*), 5.43 (dt, *J* = 15.1, 7.3 Hz, 1H, C*H*), 2.72 (t, *J* = 7.3 Hz, 2H, C*H*$_2$), 2.35 (q, *J* = 7.3 Hz, 2H, C*H*$_2$), 1.96 (s, 3H, C*H*$_3$), 1.94 (s, 3H, C*H*$_3$), 1.64 (dd, *J* = 5.9, 1.4 Hz, 3H, C*H*$_3$). ^{13}**C-NMR** (150 MHz, $CDCl_3$): δ = 203.0, 186.2, 183.6, 151.1, 144.5, 136.1, 128.9, 126.4, 116.9, 44.1, 26.0, 17.8, 11.8, 7.8. **IR**: *v* 3286, 2955, 2919, 1715, 1655, 1639, 1623, 1390, 1378, 1354, 1316, 1288, 1177, 1164, 1071, 919, 731 cm^{-1}. **HRMS** (EI) *m/z*: $[M]^+$ calcd for $C_{14}H_{16}O_4$ 248.1048, found 248.1032.[89]

Ustinaphalin (68) [2-Methoxy-6-sorbyl-7-hydroxyl-8-methyl-1,4-naphthoquinone, CAS: 2345714-98-7]



Ustinaphalin (**68**)

SMILES: O=C(C1=C2C=C(C(/C=C/C=C/C)=O)C(O)=C1C)C(OC)=CC2=O

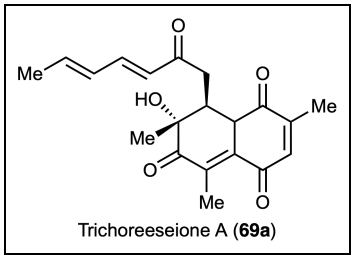
Fungus of origin: *Ustilaginoidea virens*[114].

Bioactivity: Cytotoxicity screening against against human colon cancer HCT116 cells, human lung cancer NCI-H460 cells, human gastric cancer BGC823 cells , desmoplastic cerebellar medulloblastoma Daoy cells, and human hepatoma HepG2 cells showed no activity.[114]

Biosynthesis: Biosynthesis could be based on PKS system combining five malonyl CoA units and a *S*-adenosylmethionine. Cyclization occurs by Aldol and Knoevenagel reaction. The final quinone would be obtained after an oxidation.[114]

Analytics: Yellow amorphous powder. ^{1}**H-NMR** (400 MHz, $CDCl_3$): δ = 14.01 (bs, 1H, O*H*), 8.55 (s, 1H, Ar*H*), 7.61 (dd, *J* = 14.7, 9.9 Hz, 1H, C*H*$_{sorbyl}$), 7.17 (d, *J* = 14.7 Hz, 1H, C*H*$_{sorbyl}$), 6.44 (m, 2H, C*H*$_{sorbyl}$), 6.16 (s, 1H, C*H*), 3.90 (s, 3H, OC*H*$_3$), 2.68 (s, 3H, C*H*$_3$), 1.97 (d, *J* = 4.3 Hz, 3H, C*H*$_3$). ^{13}**C-NMR** (100 MHz, $CDCl_3$): δ = 194.2, 183.7, 181.5, 166.5, 161.3, 148.0, 144.5, 133.0, 132.4, 130.5, 126.7, 123.6, 120.9, 120.8, 109.1, 56.5, 19.2, 12.6. **IR**: *v* 3452, 2917, 2849, 1737, 1722, 1652, 1617, 1570, 1461, 1440, 1382, 1233, 1217, 1029, 852, 721, 674, 580 cm^{-1}. **HRMS** (ESI) *m/z*: $[M-H]^-$ calcd for $C_{18}H_{15}O_5$ 311.0925, found 311.0931.[114]

Trichoreeseione A (69a)



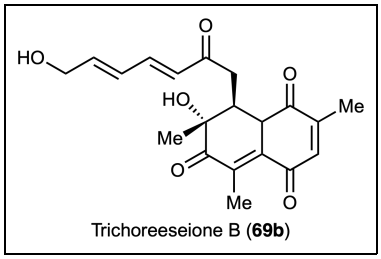
Trichoreeseione A (**69a**)

SMILES: O=C1C(C)=CC(C2=C(C)C([C@@](O)(C)[C@@H](CC(/C=C/C=C/C)=O)C21)=O)=O

Fungus of origin: *Trichoderma reesei* 4670[84].

Analytics: Yellow oil. **ORD**: $[\alpha]_D^{25} = -42.7$ (c = 0.1, MeOH). ^{1}**H-NMR** (600 MHz, $CDCl_3$): δ = 7.30 (dd, *J* = 15.5, 9.7 Hz, 1H, C*H*$_{sorbyl}$), 6.75 (s, 1H, C*H*$_{sorbyl}$), 6.27 (d, *J* = 15.5 Hz, 1H, C*H*$_{sorbyl}$), 6.21 (m, 1H, C*H*$_{sorbyl}$), 6.20 (m, 1H, C*H*$_{sorbyl}$), 3.55 (bs, 1H, O*H*), 3.45 (dd, *J* = 7.5, 3.7 Hz, 1H, C*H*), 2.94 (dd, *J* = 15.5, 7.5 Hz, 1H, C*H*$_2$), 2.84 (dd, *J* = 15.5, 3.7 Hz, 1H, C*H*$_2$), 2.03 (s, 3H, C*H*$_3$), 2.01 (s, 3H, C*H*$_3$), 1.87 (d, *J* = 5.1 Hz, 3H, C*H*$_3$), 1.57 (s, 3H, C*H*$_3$), 1.34 (s, 3H, C*H*$_3$). ^{13}**C-NMR** (150 MHz, $CDCl_3$): δ = 202.5, 199.1, 198.8, 190.5, 148.8, 147.6, 143.0, 140.3, 137.7, 133.6, 130.5, 127.3, 74.9, 54.4, 41.9, 38.4, 22.4, 21.5, 18.9, 17.0, 12.9. **IR**: *ν* 3614, 3566, 3525, 1700, 1683, 1509, 1398, 1026 cm^{-1}. **HRMS** (ESI) *m/z*: $[M+Na]^+$ calcd for $C_{21}H_{24}O_5Na$ 379.1516, found 379.1511.[84]

Trichoreeseione B (69b)



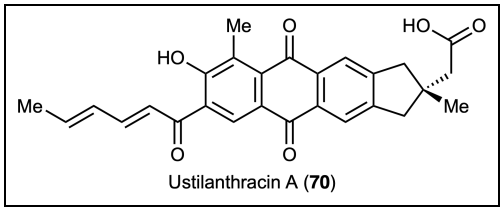
Trichoreeseione B (**69b**)

SMILES: O=C1C(C)=CC(C2=C(C)C([C@@](O)(C)[C@@H](CC(/C=C/C=C/CO)=O)C21)=O)=O

Fungus of origin: *Trichoderma reesei* 4670[84].

Analytics: Yellow oil. **ORD**: $[\alpha]_D^{25} = -39.9$ (c = 0.1, MeOH). ^{1}**H-NMR** (600 MHz, $CDCl_3$): δ = 7.34 (dd, *J* = 15.5, 10.9 Hz, 1H, C*H*$_{sorbyl}$), 6.76 (s, 1H, C*H*), 6.45 (m, 1H, C*H*$_{sorbyl}$), 6.38 (d, *J* = 15.5 Hz, 1H, C*H*$_{sorbyl}$), 6.29 (dt, *J* = 15.5, 4.2 Hz, 1H, C*H*$_{sorbyl}$), 4.31 (d, *J* = 4.2 Hz, 2H, C*H*$_2$), 3.76 (bs, 1H, O*H*), 3.44 (dd, *J* = 7.7, 3.8 Hz, 1H, C*H*), 2.96 (dd, *J* = 15.5, 7.7 Hz, 1H, C*H*$_2$), 2.86 (dd, *J* = 15.5, 3.8 Hz, 1H, C*H*$_2$), 2.04 (s, 3H, C*H*$_3$), 2.02 (s, 3H, C*H*$_3$), 1.57 (s, 3H, C*H*$_3$), 1.34 (s, 3H, C*H*$_3$). ^{13}**C-NMR** (150 MHz, $CDCl_3$): δ = 202.3, 199.0, 198.5, 190.3, 148.7, 147.6, 141.6, 141.4, 137.7, 133.5, 129.4, 128.6, 74.8, 62.9, 54.3, 42.0, 38.6, 22.4, 21.4, 16.9, 12.8. **IR**: *ν* 3629, 3567, 1700, 1683, 1650, 1521, 1457 cm^{-1}. **HRMS** (ESI) *m/z*: $[M+H]^+$ calcd for $C_{21}H_{25}O_6$ 373.1646, found 373.1642.[84]

Ustilanthracin A (70)



Ustilanthracin A (**70**)

SMILES: O=C(C1=C2C=C(C(/C=C/C=C/C)=O)C(O)=C1C)C3=C(C=C(C[C@](CC(O)=O)(C)C4)C4=C3)C2=O

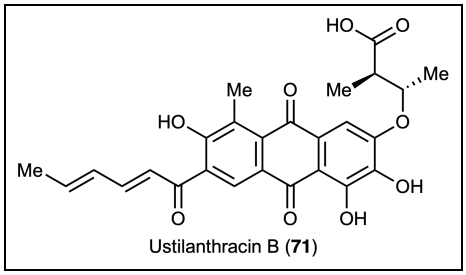
Fungus of origin: *Ustilaginoidea virens*[114].

Bioactivity: Cytotoxicity against human colon cancer HCT116 cells (IC_{50} = 12.3 μM), human lung cancer NCI-H460 cells (IC_{50} > 50.0 μM), human gastric cancer BGC823 cells (IC_{50} = 28.5 μM), desmoplastic cerebellar medulloblastoma Daoy cells (IC_{50} = 25.3 μM), human hepatoma HepG2 cells (IC_{50} = 32.9 μM).[114]

Biosynthesis: Biosynthesis could be based on PKS system combining seven malonyl CoA units and a *S*-adenosylmethionine. Cyclization occurs by Aldol and Knoevenagel reaction. The final quinone would be obtained after an oxidation and 3-oxobutanoic acid is added.[114]

Analytics: Yellow amorphous powder. **ORD**: $[\alpha]_D^{25} = -4.0$ (c = 0.1, acetone). ^{1}**H-NMR** (600 MHz, DMSO-d_6): δ = 14.00 (bs, 1H, O*H*), 12.46 (bs, 1H, O*H*), 8.62 (s, 1H, Ar*H*), 7.58 (dd, *J* = 14.8, 10.6 Hz, 1H, C*H*$_{sorbyl}$), 7.39 (d, *J* = 14.8 Hz, 1H, C*H*$_{sorbyl}$), 7.17 (s, 1H, Ar*H*), 6.63 (dd, *J* = 15.0, 10.6 Hz, 1H, C*H*$_{sorbyl}$), 6.57 (dq, *J* = 15.0, 6.4 Hz, 1H, C*H*$_{sorbyl}$), 3.16 (s, 2H, C*H*$_2$), 2.57 (s, 3H, C*H*$_3$), 1.94 (d, *J* = 6.4 Hz, 3H, C*H*$_3$), 1.85 (s, 3H, C*H*$_3$). ^{13}**C-NMR** (150 MHz, DMSO-d_6): δ = 193.8, 185.8, 182.5, 168.9, 165.9, 153.1, 148.0, 144.8, 144.6, 138.2, 134.8, 131.0, 130.8, 130.7, 127.6, 124.2, 121.6, 121.0, 120.4, 113.5, 101.2, 42.9, 24.6, 19.0, 12.7. **IR**: *ν* 3727, 3626, 3422, 2921, 2851, 1734, 1720, 1699, 1644, 1617, 1576, 1563, 1458, 1383, 1354, 1314, 1218, 1131, 1023, 850, 775, 668, 580 cm^{-1}. **HRMS** (ESI) *m/z*: $[M-H]^-$ calcd for $C_{25}H_{19}O_9$ 463.1035, found 463.1035.[114]

Ustilanthracin B (71)



Ustilanthracin B (**71**)

SMILES: O=C(C1=C2C=C(C(/C=C/C=C/C)=O)C(O)=C1C)C3=C(C(O)=C(O)C(O[C@@H](C)[C@@H](C)C(O)=O)=C3)C2=O

Fungus of origin: *Ustilaginoidea virens*[114].

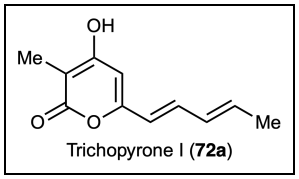
Bioactivity: Cytotoxicity against human colon cancer HCT116 cells ($IC_{50} = 37.4$ μM), human lung cancer NCI-H460 cells ($IC_{50} = 59.8$ μM), human gastric cancer BGC823 cells ($IC_{50} = 65.2$ μM), desmoplastic cerebellar medulloblastoma Daoy cells ($IC_{50} = 34.9$ μM), human hepatoma HepG2 cells ($IC_{50} = 21.8$ μM).[114]

Biosynthesis: Biosynthesis could be based on PKS system combining seven malonyl CoA units and a *S*-adenosylmethionine. Cyclization occurs by Aldol and Knoevenagel reaction. The final quinone would be obtained after an oxidation and 3-hydroxy-2-methylbutanoic acid is added.[114]

Analytics: Yellow amorphous powder. **ORD**: $[\alpha]_D^{25} = -40.0$ (c = 0.1, acetone). ^{1}**H-NMR** (600 MHz, CD_3COCD_3): δ = 8.76 (s, 1H, Ar*H*), 7.65 (dd, *J* = 14.8, 11.0 Hz, 1H, CH_{sorbyl}), 7.47 (s, 1H, Ar*H*), 7.45 (d, *J* = 14.8 Hz, 1H, CH_{sorbyl}), 6.66 (dd, *J* = 15.0, 11.0 Hz, 1H, CH_{sorbyl}), 6.57 (dq, *J* = 15.0, 6.7 Hz, 1H, CH_{sorbyl}), 5.03 (dq, *J* = 7.5, 6.2 Hz, 1H, C*H*), 2.95 (dq, *J* = 7.5, 7.2 Hz, 1H, C*H*), 2.67 (s, 3H, CH_3), 1.97 (d, *J* = 6.7 Hz, 3H, CH_3), 1.42 (d, *J* = 6.1 Hz, 3H, CH_3), 1.28 (d, *J* = 7.2 Hz, 3H, CH_3). ^{13}**C-NMR** (150 MHz, CD_3COCD_3): δ = 195.1, 187.2, 183.7, 175.7, 167.4, 151.42, 151.41, 148.9, 145.2, 142.0, 136.6, 132.1, 131.6, 128.5, 127.7, 126.0, 122.0, 121.5, 112.5, 107.9, 77.7, 45.4, 19.2, 16.8, 12.98, 12.96. **IR**: *ν* 3598, 3566, 3356, 2922, 2851, 1734, 1717, 1696, 1641, 1617, 1577, 1455, 1384, 1367, 1159, 1021, 908, 850, 579 cm^{-1}. **HRMS** (ESI) *m/z*: $[M+H]^+$ calcd for $C_{26}H_{25}O_9$ 481.1493, found 481.1479.[114]

1.4.6 Pyranones

Trichopyrone I (72a) [4-Hydroxy-3-methyl-6-((1*E*,3*E*)-penta-1,3-dien-1-yl)-2*H*-pyran-2-one, CAS: 1000856-86-9]



Trichopyrone I (**72a**)

SMILES: OC1=C(C)C(OC(/C=C/C=C/C)=C1)=O

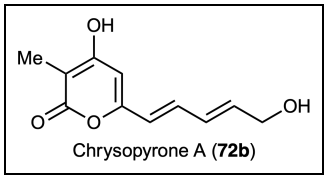
Fungus of origin: *Phialocephala* sp. FL30r[119], *Trichoderma* sp. USF-4860[79].

Bioactivity: Weak DPPH-radical scavenging activity.[79]

Biosynthesis: Trichopyrone I (**72a**) is derived from a pentaketide intermediate obtained by condensation of ve acetate units, and a methylation using methionine.[79]

Analytics: Yellowish amorphous powder. ^{1}**H-NMR** (400 MHz, CD_3OD): $\delta = 6.99$ (dd, $J = 16.0, 10.8$ Hz, 1H, C*H*), 6.23 (ddd, $J = 15.2, 10.8$ Hz, 1H, C*H*), 6.06 (d, $J = 16.0$ Hz, 1H, C*H*), 6.05 (m, 1H, C*H*), 6.03 (s, 1H, C*H*), 1.88 (s, 3H, CH_3), 1.84 (dd, $J = 6.8, 1.2$ Hz, 3H, CH_3). ^{13}**C-NMR** (100 MHz, CD_3OD): $\delta = 166.7, 166.4, 157.1, 135.6, 135.1, 130.5, 119.8, 100.3, 99.0, 17.2, 7.1$. **IR**: ν 3400, 1660, 1650, 1640, 1630, 1585, 1570, 1400 cm^{-1}. **HRMS** (FAB) *m/z*: $[M+H]^+$ calcd for $C_{11}H_{13}O_3$ 193.0865, found 193.0885.[79]

Chrysopyrone A (72b) [Saturnispol H, 4-Hydroxy-6-((1*E*,3*E*)-5-hydroxypenta-1,3-dien-1-yl)-3-methyl-2*H*-pyran-2-one, CAS: 2414922-85-1]



Chrysopyrone A (**72b**)

SMILES: O=C1C(C)=C(O)C=C(/C=C/C=C/CO)O1

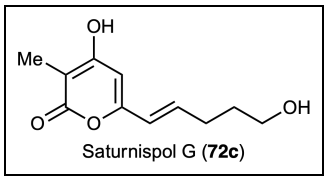
Fungus of origin: *Aspergillus flavipes* DS720[130], *Penicillium chrysogenum* SCSIO 07007[131], *Penicillium decumbens* sp.[132], *Trichoderma reesei* SCNU-F0042[133], *Trichoderma saturnisporum* DI-IA[62].

Bioactivity: Inhibition of human protein tyrosine phosphatase 1B (PTP1B) which is important in type 2 diabetes therapy ($IC_{50} = 9.32$ µg/mL).[131] Antibacterial against vancomycin-resistant *Enterococcus* (VRE) and *Bacillus subtilis* (both $IC_{50} = 12.9$ µg/mL).[62]

Biosynthesis: Meng and co-workers proposed that the biosynthesis of saturnispol H (**72b**) starts from sorbicillinol (**2a**). A redox process delivers an open chain version which forms the six membered ring upon lactonization. Hydroxylation of the sorbyl side chain leads to the desired natural compound.[62]

Analytics: Yellowish amorphous powder. ^{1}**H-NMR** (600 MHz, DMSO-d_6): $\delta = 11.25$ (bs, 1H, O*H*), 6.91 (dd, $J = 15.3, 11.1$ Hz, 1H, C*H*), 6.37 (dd, $J = 15.1, 11.1$ Hz, 1H, C*H*), 6.28 (d, $J = 15.3$ Hz, 1H, C*H*), 6.18 (dt, $J = 15.2, 4.8$ Hz, 1H, C*H*), 6.13 (s, 1H, C*H*), 4.07 (d, $J = 4.8$ Hz, 2H, CH_2), 1.78 (s, 3H, CH_3). ^{1}**H-NMR** (400 MHz, CD_3OD): $\delta = 7.06$ (dd, $J = 15.2, 10.8$ Hz, 1H, C*H*), 6.45 (dd, $J = 15.2, 10.8$ Hz, 1H, C*H*), 6.15 (dt, $J = 15.2, 5.0$ Hz, 1H, C*H*), 6.19 (d, $J = 15.2$ Hz, 1H, C*H*), 6.08 (s, 1H, C*H*), 4.20 (d, $J = 5.0$ Hz, 2H, CH_2OH), 1.90 (s, 3H, CH_3).^{13}**C-NMR** (175 MHz, DMSO-d_6): $\delta = 164.6, 164.1, 155.8, 140.3, 133.5, 127.4, 121.9, 100.9, 98.6, 61.0, 8.7$. ^{13}**C-NMR** (100 MHz, CD_3OD): $\delta = 167.1, 166.7, 156.5, 138.4, 134.0, 128.4, 121.9, 101.4, 99.2, 61.6, 7.2$. **IR**: ν 3366, 1684, 1670, 1558, 1456, 1418, 1204, 1138, 1045, 1024, 999 cm^{-1}. **HRMS** (ESI) *m/z*: $[M+Na]^+$ calcd for $C_{11}H_{12}O_4Na$ 231.0628, found 231.0633.[62,131]

Saturnispol G (72c) [(*E*)-4-Hydroxy-6-(5-hydroxypent-1-en-1-yl)-3-methyl-2*H*-pyran-2-one]



Saturnispol G (**72c**)

SMILES: OC1=C(C)C(OC(/C=C/CCCO)=C1)=O

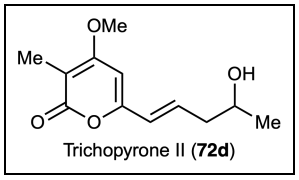
Fungus of origin: *Trichoderma reesei* SCNU-F0042[133], *Trichoderma saturnisporum* DI-IA[62]

Bioactivity: Tested against various microbes (*Staphylococcus aureus*, vancomycin-resistant *Enterococcus*, *Bacillus subtilis*, *Pseudomonas aeruginosa*, *Klebsiella pneumoniae*) without any effect.[62]

Biosynthesis: Following the biosynthesis of chrysopyrone A (**62b**) with a further reduction step in the hydroxylated sorbyl side chain.[62]

Analytics: Yellow oil. ^{1}**H-NMR** (400 MHz, acetone-d_6): $\delta = 6.63$ (dt, $J = 16.0, 7.2$ Hz, 1H, C*H*), 6.11 (d, $J = 16.0$ Hz, 1H, C*H*), 6.01 (s, 1H, C*H*), 3.61 (t, $J = 6.4$ Hz, 2H, CH_2), 2.32 (dt, $J = 7.6, 7.2$ Hz, 2H, CH_2), 1.89 (s, 3H, CH_3), 1.71 (tt, $J = 7.6, 6.4$ Hz, 2H, CH_2). ^{13}**C-NMR** (100 MHz, acetone-d_6): $\delta = 164.8, 164.4, 156.1, 137.1, 122.2, 99.6, 98.9, 60.7, 31.8, 28.8, 8.0$. **IR**: ν 3437, 2923, 1670, 1631, 1570, 1411 cm^{-1}. **HRMS** (ESI) *m/z*: $[M-H]^-$ calcd for $C_{11}H_{13}O_4$ 209.0814, found 209.0811.[62]

Trichopyrone II (72d) [(*E*)-6-(4-Hydroxypent-1-en-1-yl)-4-methoxy-3-methyl-2*H*-pyran-2-one, CAS: 1175065-71-0]



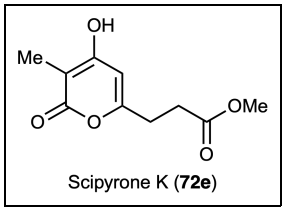
Trichopyrone II (**72d**)

SMILES: O=C1C(C)=C(OC)C=C(/C=C/CC(O)C)O1

Fungus of origin: *Eupenicillium* sp. SCSIO41208[134], *Trichoderma kunmingense* Tk9[85], *Trichoderma viride*[41].

Analytics: Yellowish viscous oil. **ORD**: $[\alpha]_D^{22} = -10.3$ (c = 0.1, MeOH). ^{1}**H-NMR** (300 MHz, acetone-d_6): δ = 6.65 (d, *J* = 15.7 Hz, 1H, C*H*), 6.44 (s, 1H, C*H*), 6.20 (d, *J* = 15.7 Hz, 1H, C*H*), 3.98 (m, 1H, O*H*), 3.95 (s, 3H, OCH_3), 3.91 (dq, *J* = 5.9, 2.9 Hz, 1H, C*H*), 2.35 (dd, *J* = 7.7, 2.9 Hz, 2H, CH_2), 1.84 (s, 3H, CH_3), 1.16 (d, *J* = 5.9 Hz, 3H, CH_3). ^{13}**C-NMR** (75.5 MHz, acetone-d_6): δ = 168.6, 165.1, 158.7, 137.0, 126.1, 103.3, 96.9, 68.2, 57.8, 44.5, 25.2, 10.8. **IR**: *ν* 3384, 2930, 2360, 1676, 1549, 1458, 1258, 1144 cm^{-1}. **HRMS** (EI) *m/z*: $[M]^+$ calcd for $C_{12}H_{16}O_4$ 224.1049, found 224.1046.[41]

Scipyrone K (72e) [Methyl 3-(4-hydroxy-3-methyl-2-oxo-2*H*-pyran-6-yl)propanoate]



Scipyrone K (**72e**)

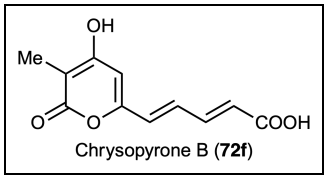
SMILES: O=C1C(C)=C(O)C=C(CCC(OC)=O)O1

Fungus of origin: *Phialocephala* sp. FL30r[119].

Bioactivity: Weak DPPH-radical scavenging activity ($IC_{50} = 27.9$ μM)[119].

Analytics: White amorphous powder. ^{1}**H-NMR** (500 MHz, DMSO-d_6): δ = 11.15 (bs, 1H, O*H*), 5.98 (s, 1H, C*H*), 3.58 (s, 3H, OCH_3), 2.67 (t, *J* = 7.0 Hz, 2H, CH_2), 2.59 (t, *J* = 7.0 Hz, 2H, CH_2), 1.72 (s, 3H, CH_3). ^{13}**C-NMR** (125 MHz, DMSO-d_6): δ = 172.4, 165.3, 165.2, 161.2, 99.9, 97.3, 52.0, 30.2, 28.4, 8.8. **IR**: *ν* 3104, 2954, 2705, 1743, 1407, 1170, 1001, 836 cm^{-1}. **HRMS** (ESI) *m/z*: $[M+H]^+$ calcd for $C_{10}H_{13}O_5$ 213.0757, found 213.0764.[119]

Chrysopyrone B (72f) [(2*E*,4*E*)-5-(4-Hydroxy-3-methyl-2-oxo-2*H*-pyran-6-yl)penta-2,4-dienoic acid]



Chrysopyrone B (**72f**)

SMILES: O=C1C(C)=C(O)C=C(/C=C/C=C/C(O)=O)O1

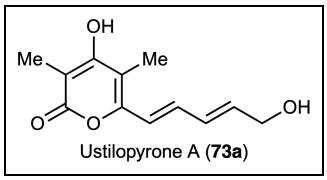
Fungus of origin: *Penicillium chrysogenum* SCSIO 07007[131], *Penicillium* sp. SCSIO06871[51].

Bioactivity: Inhibition of human protein tyrosine phosphatase 1B (PTP1B) which is important in type 2 diabetes therapy ($IC_{50} = 27.8$ μg/mL).[131]

Biosynthesis: Oxidation of trichopyrone I (**62a**).[51]

Analytics: Yellow amorphous solid. ^{1}**H-NMR** (700 MHz, DMSO-d_6): δ = 7.28 (dd, *J* = 15.2, 11.4 Hz, 1H, C*H*), 7.03 (dd, *J* = 15.2, 11.4 Hz, 1H, C*H*), 6.76 (d, *J* = 15.3 Hz, 1H, C*H*), 6.29 (s, 1H, C*H*), 6.21 (d, *J* = 15.3 Hz, 1H, C*H*), 1.81 (s, 3H, CH_3). ^{13}**C-NMR** (175 MHz, DMSO-d_6): δ = 167.6, 164.2, 163.7, 154.4, 142.1, 130.5, 129.9, 126.0, 103.7, 100.3, 8.9. **IR**: *ν* 3167, 1715, 1651, 1607, 1557, 1541, 1418, 1369, 1263, 1175, 1144, 1126, 1022, 995 cm^{-1}. **HRMS** (ESI) *m/z*: $[M-H]^-$ calcd for $C_{11}H_9O_5$ 221.0455, found 221.0462.[131]

Ustilopyrone A (73a) [4-Hydroxy-6-((1*E*,3*E*)-5-hydroxypenta-1,3-dien-1-yl)-3,5-dimethyl-2*H*-pyran-2-one]



Ustilopyrone A (**73a**)

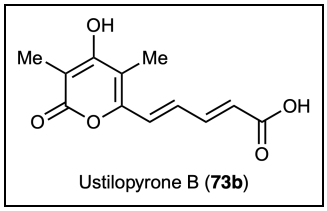
SMILES: O=C1C(C)=C(O)C(C)=C(/C=C/C=C/CO)O1

Fungus of origin: *Penicillium* sp. SCSIO06871[51], *Ustilaginoidea virens*[86].

Biosynthesis: Similar to chrysopyrone B (**62f**) with a further methylation and oxidation.[86]

Analytics: Yellow amorphous powder. ^{1}**H-NMR** (400 MHz, CD_3OD): δ = 7.06 (dd, *J* = 15.1, 11.0 Hz, 1H, C*H*), 6.53 (d, *J* = 15.1 Hz, 1H, C*H*), 6.49 (dd, *J* = 15.1, 11.0 Hz, 1H, C*H*), 6.12 (dt, *J* = 15.0, 5.3 Hz, 1H, C*H*), 4.19 (d, *J* = 5.3 Hz, 2H, CH_2OH), 2.04 (s, 3H, CH_3), 1.94 (s, 3H, CH_3). ^{13}**C-NMR** (100 MHz, CD_3OD): δ = 167.5, 167.4, 153.7, 139.2, 135.4, 130.5, 120.7, 110.5, 100.6, 63.1, 9.6, 9.2. **IR**: *ν* 3647, 3614, 3363, 2933, 1712, 1646, 1623, 1472, 1363, 1239, 1136, 1017, 909, 848, 756, 678, 578, 530 cm^{-1}. **HRMS** (ESI) *m/z*: $[M-H]^-$ calcd for $C_{12}H_{13}O_4$ 221.0819, found 221.0823.[86]

Ustilopyrone B (73b) [(2*E*,4*E*)-5-(4-Hydroxy-3,5-dimethyl-2-oxo-2*H*-pyran-6-yl)penta-2,4-dienoic acid]



Ustilopyrone B (**73b**)

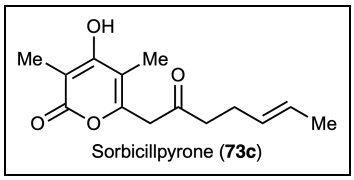
SMILES: O=C1C(C)=C(O)C(C)=C(/C=C/C=C/C(O)=O)O1

Fungus of origin: *Ustilaginoidea virens*[86].

Biosynthesis: Similar to chrysopyrone B (**62f**) with a further methylation and oxidation.[86]

Analytics: Yellow amorphous powder. ^{1}**H-NMR** (400 MHz, CD_3OD): δ = 7.44 (dd, *J* = 15.2, 11.2 Hz, 1H, C*H*), 7.13 (dd, *J* = 15.0, 11.2 Hz, 1H, C*H*), 6.97 (d, *J* = 15.0 Hz, 1H, C*H*), 6.12 (d, *J* = 15.2 Hz, 1H, C*H*), 2.09 (s, 3H, CH_3), 1.96 (s, 3H, CH_3). ^{13}**C-NMR** (100 MHz, CD_3OD): δ = 170.0, 167.03, 166.95, 152.2, 144.6, 132.2, 128.2, 126.0, 113.7, 102.3, 9.9, 9.4. **IR**: *ν* 3732, 3421, 2919, 2850, 1719, 1652, 1617, 1576, 1542, 1455, 1435, 1384, 1270, 1154, 1020, 835, 732, 579 cm^{-1}. **HRMS** (ESI) *m/z*: $[M-H]^-$ calcd for $C_{12}H_{11}O_5$ 235.0612, found 235.0617.[86]

Sorbicillpyrone (73c) [(*E*)-4-Hydroxy-3,5-dimethyl-6-(2-oxohept-5-en-1-yl)-2*H*-pyran-2-one, CAS: 2760198-20-5]



Sorbicillpyrone (**73c**)

SMILES: O=C1C(C)=C(O)C(C)=C(CC(CC/C=C/C)=O)O1

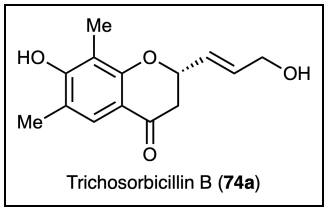
Fungus of origin: *Penicillium* sp. SCSIO06871[51].

Biosynthesis: Formation of **63c** is based on trichopyrone (**62a**).[51]

Analytics: Colorless needles **MP**: 112 °C. ^{1}**H-NMR** (700 MHz, CD_3OD): δ = 5.48 (m, 1H, C*H*), 5.41 (m, 1H, C*H*), 3.77 (s, 2H, CH_2), 2.61 (t, *J* = 7.7 Hz, 2H, CH_2), 2.25 (q, *J* = 7.0 Hz, 2H, CH_2), 1.92 (s, 3H, CH_3), 1.89 (s, 3H, CH_3), 1.62 (dd, *J* = 5.6, 1.4 Hz, 3H, CH_3). ^{13}**C-NMR** (175 MHz, CD_3OD): δ = 206.2, 168.2, 167.5, 153.3, 130.5, 127.1, 112.1, 99.7, 45.9, 43.2, 27.6, 18.0, 10.3, 8.9. **HRMS** (ESI) *m/z*: $[M+H]^+$ calcd for $C_{14}H_{19}O_4$ 251.1278, found 251.1284.[51]

1.4.7 Chromanones

Trichosorbicillin B (74a) [(*S*,*E*)-7-Hydroxy-2-(3-hydroxyprop-1-en-1-yl)-6,8-dimethylchroman-4-one, CAS: 2365301-42-2]



Trichosorbicillin B (**74a**)

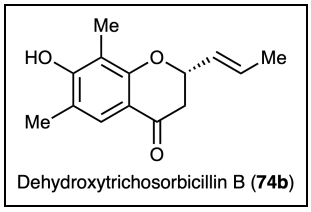
SMILES: OC1=C(C)C=C(C(C[C@@H](/C=C/CO)O2)=O)C2=C1C

Fungus of origin: *Trichoderma reesei* 4670[30].

Bioactivity: Anti-inflammatory activity due to inhibition of NO formation ($IC_{50} < 10.0$ μM).[30]

Analytics: White powder. **ORD**: $[\alpha]_D^{20} = +8.4$ (c = 0.2, MeOH). ^{1}**H-NMR** (400 MHz, CD_3OD): δ = 7.42 (s, 1H, Ar*H*), 6.02 (dt, *J* = 15.6, 4.8 Hz, 1H, C*H*), 5.93 (dd, *J* = 15.6, 5.6 Hz, 1H, C*H*), 4.94 (m, 1H, C*H*), 4.11 (d, *J* = 4.4 Hz, 2H, CH_2OH), 2.66 (m, 2H, CH_2), 2.14 (s, 3H, CH_3), 2.07 (s, 3H, CH_3). ^{13}**C-NMR** (100 MHz, CD_3OD): δ = 193.8, 162.5, 161.1, 134.0, 129.2, 126.4, 120.1, 114.6, 112.5, 78.8, 62.7, 43.4, 16.3, 8.6. **IR**: *ν* 3329, 2922, 1655, 1599, 1458, 1347, 1296, 1182, 1086, 974 cm^{-1}. **HRMS** (ESI) *m/z*: $[M-H]^-$ calcd for $C_{14}H_{15}O_4$ 247.0976, found 247.0977.[30]

Dehydroxytrichosorbicillin B (74b) [(*S*,*E*)-7-Hydroxy-6,8-dimethyl-2-(prop-1-en-1-yl)chroman-4-one, CAS: 1345719-59-6]



Dehydroxytrichosorbicillin B (**74b**)

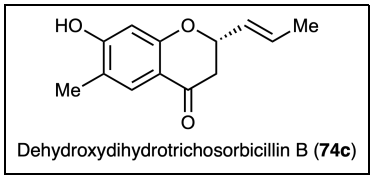
SMILES: OC1=C(C)C=C(C(C[C@@H](/C=C/C)O2)=O)C2=C1C

Fungus of origin: *Aspergillus sydowi* YHll-2[135], *Penicillium citrinum* VM6[136], *Trichoderma* sp.[15].

Bioactivity: Cytotoxicity against P388 cells ($IC_{50} = 0.14$ μM) and human breast cancer cell line MCF-7 ($IC_{50} = 9.51$ μg/mL).[15,135] Antibacterial activity against *E. faecalis* ($IC_{50} = 128$ μg/mL), *S. aureus* ($IC_{50} = 64.0$ μg/mL), and *B. cereus* ($IC_{50} = 64.0$ μg/mL).[136]

Analytics: Yellow needles. **ORD**: $[\alpha]_D^{20} = +44.5$ (c = 0.1, MeOH). ^{1}**H-NMR** (600 MHz, $CDCl_3$): δ = 7.57 (s, 1H, Ar*H*), 5.88 (dqd, *J* = 15.6, 6.4, 1.3 Hz, 1H, C*H*), 5.72 (ddd, *J* = 15.1, 6.0, 1.7 Hz, 1H, C*H*), 5.19 (s, 1H, O*H*), 4.85 (m, 1H, C*H*), 2.71 (m, 2H, CH_2), 2.21 (s, 3H, CH_3), 2.14 (s, 3H, CH_3), 1.78 (dd, *J* = 6.4, 1.0 Hz, 3H, CH_3). ^{13}**C-NMR** (150 MHz, $CDCl_3$): δ = 191.6 , 159.4, 158.6, 129.8, 128.9, 125.8, 117.0, 114.5, 110.5, 78.2, 42.7, 17.9, 15.3, 8.1. **IR**: *ν* 3394, 1659, 1605, 1464, 1361, 1293, 1223, 1195 cm^{-1}. **HRMS** (ESI) *m/z*: $[M-H]^-$ calcd for $C_{14}H_{15}O_3$ 231.1021, found 231.1032.[135]

Dehydroxydihydrotrichosorbicillin B (74c) [(*S*,*E*)-7-Hydroxy-6-methyl-2-(prop-1-en-1-yl)chroman-4-one, CAS: 1448337-75-4]



Dehydroxydihydrotrichosorbicillin B (**74c**)

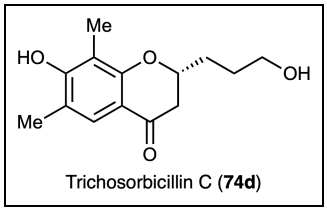
SMILES: OC1=C(C)C=C(C(C[C@@H](/C=C/C)O2)=O)C2=C1

Fungus of origin: *Trichoderma* sp.[15].

Bioactivity: Cytotoxicity against human breast cancer cell line MCF-7 ($IC_{50} = 7.82$ μg/mL).[15]

Analytics: Yellowish amorphous solid. ^{1}**H-NMR** (400 MHz, $CDCl_3$): δ = 7.67 (s, 1H, Ar*H*), 6.36 (s, 1H, Ar*H*), 5.89 (dq, *J* = 16.0, 8.0 Hz, 1H, C*H*), 5.69 (dd, *J* = 16.0, 8.0 Hz, 1H, C*H*), 5.38 (s, 1H, O*H*), 4.85 (m, 1H, C*H*), 2.70 (m, 2H, CH_2), 2.19 (s, 3H, CH_3), 1.77 (d, *J* = 8.0 Hz, 3H, CH_3). ^{13}**C-NMR** (100 MHz, $CDCl_3$): δ = 193.1, 160.6, 158.7, 130.7, 129.3, 128.6, 118.7, 114.1, 103.1, 78.8, 43.0, 17.9, 15.0. **IR**: *ν* 3420, 3040, 2919, 1690, 1650, 1609, 1584, 1465, 1352, 1290, 1216, 1190, 1039, 957 cm^{-1}. **HRMS** (ESI) *m/z*: $[M-H]^-$ calcd for $C_{13}H_{13}O_3$ 217.0880, found 217.0870.[15]

Trichosorbicillin C (74d) [(*R*)-7-Hydroxy-2-(3-hydroxypropyl)-6,8-dimethylchroman-4-one, CAS: 2351129-05-8]



Trichosorbicillin C (**74d**)

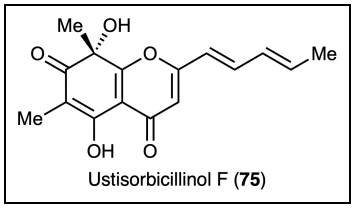
SMILES: OC1=C(C)C=C(C(C[C@@H](CCCO)O2)=O)C2=C1C

Fungus of origin: *Trichoderma reesei* 4670[30].

Bioactivity: Anti-inammatory activity due to inhibition of nitric oxide formation ($IC_{50} = 12.0 - 30.0$ μM).[30].

Analytics: White powder. **ORD**: $[\alpha]_D^{20} = +2.4$ (c = 0.2, MeOH). ^{1}**H-NMR** (400 MHz, CD_3OD): δ = 7.44 (s, 1H, Ar*H*), 4.42 (m, 1H, C*H*), 3.65 (t, *J* = 6.4 Hz, 2H, CH_2OH), 2.60 (m, 2H, CH_2), 2.17 (s, 3H, CH_3), 2.10 (s, 3H, CH_3), 1.89 (m, 2H, CH_2), 1.76 (m, 2H, CH_2). ^{13}**C-NMR** (100 MHz, CD_3OD): δ = 194.5, 162.2, 161.4, 126.4, 119.9, 114.7, 112.5, 79.2, 62.6, 43.6, 32.6, 29.4, 16.3, 8.5. **IR**: *ν* 3298, 2924, 1659, 1605, 1462, 1362, 1306, 1184, 1093, 889, 810 cm^{-1}. **HRMS** (ESI) *m/z*: $[M+H]^+$ calcd for $C_{14}H_{19}O_4$ 251.1278, found 251.1277.[30]

Ustisorbicillinol F (75) [(*R*)-5,8-Dihydroxy-6,8-dimethyl-2-((1*E*,3*E*)-penta-1,3-dien-1-yl)-4*H*-chromene-4,7(8*H*)-dione]



Ustisorbicillinol F (**75**)

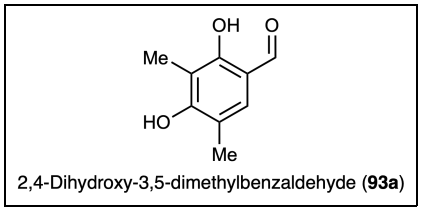
SMILES: O=C1C(C)=C(O)C(C(C=C(/C=C/C=C/C)O2)=O)=C2[C@]1(O)C

Fungus of origin: *Ustilaginoidea virens*[86].

underline*Analytics*: Yellow amorphous powder. **ORD**: $[\alpha]_D^{25} = -24.0$ (c = 0.1, MeOH). ^{1}**H-NMR** (600 MHz, $CDCl_3$): δ = 13.43 (bs, 1H, O*H*), 7.24 (m, 1H, C*H*), 6.31 (s, 1H, C*H*), 6.27 (m, 1H, C*H*), 6.26 (m, 1H, C*H*), 6.12 (d, *J* = 15.4 Hz, 1H, C*H*), 1.92 (d, *J* = 4.9 Hz, 3H, CH_3), 1.88 (s, 3H, CH_3), 1.64 (s, 3H, CH_3). ^{13}**C-NMR** (150 MHz, $CDCl_3$): δ = 196.9, 180.5, 169.2, 165.5, 163.9, 140.6, 140.1, 130.1, 118.6, 111.7, 109.7, 106.1, 73.7, 30.0, 18.9, 6.8. **IR**: *v* 3720, 3648, 3614, 3445, 2918, 2850, 1750, 1717, 1682, 1649, 1566, 1541, 1517, 1488, 1454, 1432, 1384, 1159, 1018, 900, 842, 677, 578 cm^{-1}. **HRMS** (ESI) *m/z*: $[M+Na]^+$ calcd for $C_{16}H_{16}O_5Na$ 311.0890, found 311.0892.[86]

1.5 Artificial sorbicillinoids

2,4-Dihydroxy-3,5-dimethylbenzaldehyde (93a) [CAS: 90536-32-6]



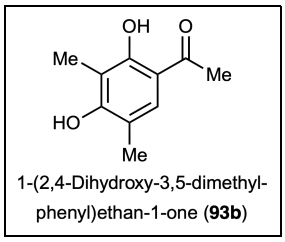
2,4-Dihydroxy-3,5-dimethylbenzaldehyde (**93a**)

SMILES: OC1=C(C=O)C=C(C)C(O)=C1C

Total synthesis: Vilsmeier formylation with 2,4-dimethylbenzene-1,3-diol.[101]

Analytics: White crystalline solid. **MP**: 161-163 °C. ^{1}**H-NMR** (400 MHz, $CDCl_3$): δ = 11.54 (s, 1H, O*H*), 9.66 (s, 1H, C*H*O), 7.14 (s, 1H, Ar*H*), 5.39 (s, 1H, O*H*), 2.23 (s, 3H, CH_3), 2.14 (s, 3H, CH_3). ^{1}**H-NMR** (400 MHz, CD_3OD): δ = 9.59 (s, 1H, C*H*O), 7.17 (s, 1H, Ar*H*), 2.18 (d, *J* = 0.9 Hz, 3H, CH_3), 2.08 (s, 3H, CH_3). ^{13}**C-NMR** (101 MHz, CD_3OD): δ = 196.2, 163.0, 161.5, 134.1, 118.3, 115.4, 111.7, 16.0, 7.7. **IR**: *ν* 3168, 2364, 1628, 1477, 1288, 1252, 1211, 1150, 963, 727 cm^{-1}. **HRMS** (ESI) *m/z*: $[M+H]^+$ calcd for $C_9H_{11}O_3$ 167.0708, found 167.0704.[101,137]

1-(2,4-Dihydroxy-3,5-dimethylphenyl)ethan-1-one (93b) [Clavatol, CAS: 577-45-7]



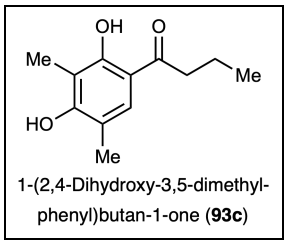
1-(2,4-Dihydroxy-3,5-dimethyl-phenyl)ethan-1-one (**93b**)

SMILES: OC1=C(C(C)=O)C=C(C)C(O)=C1C

Total synthesis: Friedel-Crafts acylation with 2,4-dimethylbenzene-1,3-diol and acetic acid using boron trifluoride etherate.[101]

Analytics: White solid. ^{1}**H-NMR** (600 MHz, $CDCl_3$): δ = 12.87 (s, 1H, O*H*) 7.37 (s, 1H, Ar*H*), 5.28 (s, 1H, O*H*), 2.55 (s, 3H, CH_3), 2.21 (s, 3H, CH_3), 2.13 (s, 3H, CH_3). ^{1}**H-NMR** (600 MHz, DMSO-d_6): δ = 7.52 (s, 1H, Ar*H*), 2.52 (s, 3H, CH_3), 2.13 (s, 3H, CH_3), 2.01 (s, 3H, CH_3). ^{13}**C-NMR** (150 MHz, DMSO-d_6): δ = 201.3, 160.7, 160.5, 130.2, 115.9, 112.1, 110.3, 26.2, 16.2, 8.1.[101,138]

1-(2,4-Dihydroxy-3,5-dimethylphenyl)butan-1-one (93c) [CAS: 2169278-49-1]



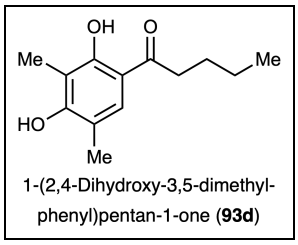
1-(2,4-Dihydroxy-3,5-dimethyl-phenyl)butan-1-one (**93c**)

SMILES: OC1=C(C(CCC)=O)C=C(C)C(O)=C1C

Total synthesis: Friedel-Crafts acylation with 2,4-dimethylbenzene-1,3-diol and butyric acid using boron trifluoride etherate.[101]

Analytics: Pale yellow solid. **MP**: 118–120 °C. ^{1}**H-NMR** (600 MHz, $CDCl_3$): δ = 13.04 (s, 1H, O*H*), 7.40 (s, 1H, Ar*H*), 5.30 (s, 1H, O*H*), 2.88 (t, *J* = 7.4 Hz, 2H, CH_2), 2.21 (s, 3H, CH_3), 2.14 (s, 3H, CH_3), 1.76 (m, 2H, CH_2), 1.01 (t, *J* = 7.4 Hz, 3H, CH_3). ^{13}**C-NMR** (150 MHz, $CDCl_3$): δ = 207.5, 163.7, 158.4, 138.2, 115.7, 111.1, 109.1, 52.8, 25.8, 24.8, 7.6. **IR**: *ν* 3419, 2964, 1633, 1603, 1156 cm^{-1}. **HRMS** (ESI) *m/z*: $[M-H]^-$ calcd for $C_{12}H_{15}O_3$ 207.1027, found 207.1027.[101]

1-(2,4-Dihydroxy-3,5-dimethylphenyl)pentan-1-one (93d)



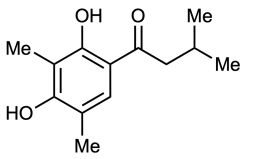
1-(2,4-Dihydroxy-3,5-dimethyl-phenyl)pentan-1-one (**93d**)

SMILES: OC1=C(C(CCCC)=O)C=C(C)C(O)=C1C

Total synthesis: Friedel-Crafts acylation with 2,4-dimethylbenzene-1,3-diol and butanoyl chloride using aluminium(III) chloride.[31]

Analytics: White solid. ^{1}**H-NMR** (300 MHz, $CDCl_3$): δ = 13.05 (bs, 1H, O*H*), 7.39 (s, 1H, Ar*H*), 5.32 (bs, 1H, O*H*), 2.90 (t, *J* = 8.4 Hz, 2H, CH_2), 2.21 (s, 3H, CH_3), 2.13 (s, 3H, CH_3), 1.71 (p, *J* = 7.7 Hz, 2H, CH_2), 1.41 (sx, *J* = 7.5 Hz, 2H, CH_2), 0.96 (t, *J* = 7.3 Hz, 3H, CH_3). ^{13}**C-NMR** (75 MHz, $CDCl_3$): δ = 205.5, 161.6, 158.7, 129.3, 114.5, 113.1, 110.4, 37.8, 27.3, 22.7, 15.9, 14.1, 7.6. **MS** (ESI) *m/z*: 444.7 $[2M+H]^+$, 223.0 $[M+H]^+$.[31]

1-(2,4-Dihydroxy-3,5-dimethylphenyl)-3-methylbutan-1-one (93e)



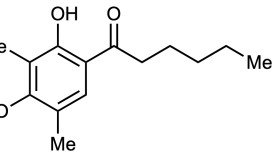
1-(2,4-Dihydroxy-3,5-dimethyl-phenyl)-3-methylbutan-1-one (**93e**)

SMILES: OC1=C(C(CC(C)C)=O)C=C(C)C(O)=C1C

Total synthesis: Friedel-Crafts acylation with 2,4-dimethylbenzene-1,3-diol and *iso*-butanoyl chloride using aluminium(III) chloride.[31]

Analytics: White solid. ^{1}**H-NMR** (300 MHz, DMSO-d_6): δ = 13.12 (s, 1H, O*H*), 9.48 (s, 1H, O*H*), 7.54 (s, 1H, Ar*H*), 2.79 (d, *J* = 7.0 Hz, 2H, CH_2), 2.21–2.08 (m, 4H, CH_2), 2.01 (s, 3H, CH_3), 0.92 (d, *J* = 6.6 Hz, 3H, CH_3). ^{13}**C-NMR** (75 MHz, DMSO-d_6): δ = 205.0, 160.8, 160.6, 129.6, 115.9, 112.1, 110.4, 45.8, 25.4, 22.5, 16.2, 8.2. **HRMS** (ESI) *m/z*: $[M+Na]^+$ calcd for $C_{13}H_{18}O_3Na$ 245.1148, found 245.1145.[31]

1-(2,4-Dihydroxy-3,5-dimethylphenyl)hexan-1-one (93f)



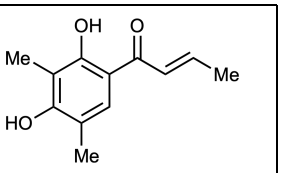
1-(2,4-Dihydroxy-3,5-dimethyl-phenyl)hexan-1-one (**93f**)

SMILES: OC1=C(C(CCCCC)=O)C=C(C)C(O)=C1C

Total synthesis: Friedel-Crafts acylation with 2,4-dimethylbenzene-1,3-diol and hexanoyl chloride using aluminium(III) chloride.[31]

Analytics: White solid. ^{1}**H-NMR** (300 MHz, $CDCl_3$): δ = 13.03 (bs, 1H, O*H*), 7.39 (s, 1H, Ar*H*), 5.28 (bs, 1H, O*H*), 2.89 (t, *J* = 7.4 Hz, 2H, CH_2), 2.21 (s, 3H, CH_3), 2.13 (s, 3H, CH_3), 1.80–1.66 (m, 2, CH_2H), 1.47–1.28 (m, 4H, CH_2), 0.93 (t, *J* = 7.4 Hz, 3H, CH_3). ^{13}**C-NMR** (75 MHz, $CDCl_3$): δ = 205.5, 161.6, 158.7, 129.3, 114.5, 113.1, 110.4, 38.1, 32.7, 24.9, 22.6, 15.8, 14.1, 7.6. **MS** (ESI) *m/z*: 259.0 $[M+Na]^+$, 237.1 $[M+H]^+$.[31]

(*E*)-1-(2,4-Dihydroxy-3,5-dimethylphenyl)but-2-en-1-one (93g)



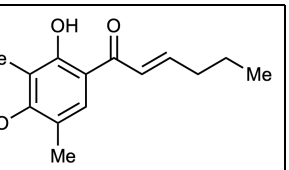
(E)-1-(2,4-Dihydroxy-3,5-dimethyl-phenyl)but-2-en-1-one (**93g**)

SMILES: OC1=C(C(/C=C/C)=O)C=C(C)C(O)=C1C

Total synthesis: Friedel-Crafts acylation with 2,4-dimethylbenzene-1,3-diol and (*E*)-but-2-enoyl chloride using aluminium(III) chloride.[31]

Analytics: Yellow solid. ^{1}**H-NMR** (300 MHz, acetone-d_6): δ = 13.60 (s, 1H, O*H*), 8.91 (s, 1H, O*H*), 7.66 (s, 1H, Ar*H*), 7.27–7.04 (m, 2H, C*H*), 2.21 (d, *J* = 1.0 Hz, 3H, CH_3), 2.11 (s, 3H, CH_3), 1.99 (dd, *J* = 6.6, 1.4 Hz, 3H), CH_3. ^{13}**C-NMR** (75 MHz, acetone-d_6): δ = 192.3, 163.7, 161.3, 144.6, 130.0, 126.6, 116.4, 113.2, 111.6, 18.5, 16.2, 8.1. **HRMS** (ESI) *m/z*: $[M+Na]^+$ calcd for $C_{12}H_{14}O_3Na$ 229.0841, found 229.0836.[31]

(*E*)-1-(2,4-Dihydroxy-3,5-dimethylphenyl)hex-2-en-1-one (93h)



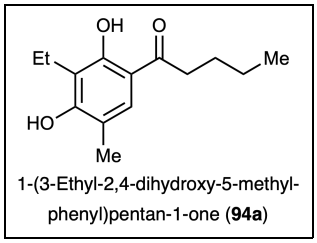
(*E*)-1-(2,4-Dihydroxy-3,5-dimethyl-phenyl)hex-2-en-1-one (**93h**)

SMILES: OC1=C(C(/C=C/CCC)=O)C=C(C)C(O)=C1C

Total synthesis: Friedel-Crafts acylation with 2,4-dimethylbenzene-1,3-diol and (*E*)-hex-2-enoyl chloride using aluminium(III) chloride.[31]

Analytics: Yellow solid. ^{1}**H-NMR** (600 MHz, DMSO-d_6): δ = 13.57 (s, 1H, O*H*), 9.56 (s, 1H, O*H*), 7.70 (s, 1H, Ar*H*), 7.25 (d, *J* = 15,2 Hz, 1H, C*H*), 7.06-6.99 (m, 1H, C*H*), 2.30 (q, *J* = 7.0 Hz, 2H, CH_2), 2.15 (s, 3H, CH_3), 2.03 (s, 3H, CH_3), 1.51 (sx, *J* = 7.4 Hz, 2H, CH_2), 0.92 (t, *J* = 7.4 Hz, 3H, CH_3). ^{13}**C-NMR** (150 MHz, DMSO-d_6): δ = 191.3, 162.1, 160.9, 148.6, 129.3, 124.6, 116.0, 111.7, 110.6, 34.1, 21.1, 16.1, 13.6, 8.2. **MS** (ESI) *m/z*: 509.5 $[2M+Na]^+$, 266.4 $[M+Na]^+$.[31]

1-(3-Ethyl-2,4-dihydroxy-5-methylphenyl)pentan-1-one (94a)



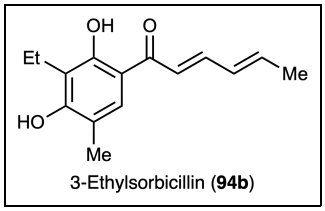
1-(3-Ethyl-2,4-dihydroxy-5-methyl-phenyl)pentan-1-one (**94a**)

SMILES: OC1=C(C(CCCC)=O)C=C(C)C(O)=C1CC

Total synthesis: Friedel-Crafts acylation with 2-ethyl-4-methylbenzene-1,3-diol and valeric acid using boron trifluoride etherate.[101]

Analytics: Pale yellow solid. **MP**: 118-120 °C. ^{1}**H-NMR** (400 MHz, $CDCl_3$): δ = 13.01 (s, 1H, O*H*), 7.39 (s, 1H, Ar*H*), 5.34 (s, 1H, O*H*), 2.89 (t, *J* = 7.5 Hz, 2H, CH_2), 2.67 (q, *J* = 7.5 Hz, 2H, CH_2), 2.21 (s, 3H, CH_3), 1.72 (m, 2H, CH_2), 1.42 (m, 2H, CH_2), 1.15 (t, *J* = 7.5 Hz, 3H, CH_3), 0.96 (t, *J* = 7.3 Hz, 3H, CH_3). ^{13}**C-NMR** (100 MHz, $CDCl_3$): δ = 205.4, 161.3, 158.2, 127.6, 120.7, 113.0, 110.2, 37.7, 27.1, 22.8, 22.5, 14.1, 13.9, 7.4. **IR**: *ν* 3419, 2964, 1633, 1603, 1156 cm^{-1}. **HRMS** (ESI) *m/z*: $[M-H]^-$ calcd for $C_{14}H_{19}O_3$ 235.1340, found 235.1341.[101]

3-Ethylsorbicillin (94b)



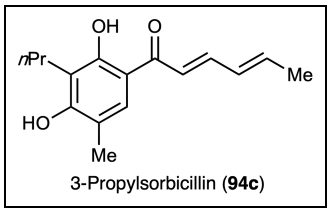
3-Ethylsorbicillin (**94b**)

SMILES: OC1=C(C(/C=C/C=C/C)=O)C=C(C)C(O)=C1CC

Total synthesis: *ortho*-Lithiation of 1,3-dimethoxybenzene with ethyl iodide, followed by deprotection with BBr_3, Vilsmeier formylation, reduction and Friedel-Crafts acylation with sorbyl chloride.[31]

Analytics: Yellow solid. ^{1}**H-NMR** (600 MHz, $CDCl_3$): δ = 13.55 (bs, 1H, O*H*), 7.46 (dd, *J* = 14.8, 10.8 Hz, 1H, CH_{sorbyl}), 7.44 (s, 1H, Ar*H*), 6.94 (d, *J* = 14.9 Hz, 1H, CH_{sorbyl}), 6.39–6.28 (m, 2H, CH_{sorbyl}), 5.28 (bs, 1H, O*H*), 2.69 (q, *J* = 7.6 Hz, 2H, CH_2), 2.22 (s, 3H, CH_3), 1.91 (d, *J* = 5.7 Hz, 3H, CH_3), 1.16 (t, *J* = 7.6 Hz, 3H, CH_3). ^{13}**C-NMR** (150 MHz, $CDCl_3$): δ = 192.7, 162.5, 158.4, 144.6, 141.3, 130.7, 129.1, 122.0, 116.9, 114.6, 113.8, 19.1, 16.1, 15.8, 13.3. **HRMS** (ESI) *m/z*: $[M+Na]^+$ calcd for $C_{15}H_{18}O_3Na$ 269.1148, found 269.1147.[31]

3-Propylsorbicillin (94c)



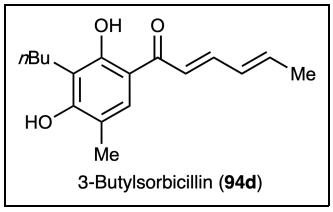
3-Propylsorbicillin (**94c**)

SMILES: OC1=C(C(/C=C/C=C/C)=O)C=C(C)C(O)=C1CCC

Total synthesis: *ortho*-Lithiation of 1,3-dimethoxybenzene with propyl iodide, followed by deprotection with boron tribromide, Vilsmeier formylation, reduction and Friedel-Crafts acylation with sorbyl chloride.[31]

Analytics: Yellow solid. ^{1}**H-NMR** (300 MHz, $CDCl_3$): δ = 13.54 (bs, 1H, O*H*), 7.46 (dd, J = *J* = 14.8, 10.1 Hz, 1H, CH_{sorbyl}), 7.45 (s, 1H, Ar*H*), 6.94 (d, *J* = 14.9 Hz, 1H, CH_{sorbyl}), 6.41–6.20 (m, 2H, CH_{sorbyl}), 5.27 (bs, 1H, O*H*), 2.64 (t, *J* = 6.8 Hz, 2H, CH_2), 2.22 (s, 3H, CH_3), 1.91 (d, *J* = 5.7 Hz, 3H, CH_3), 1.59 (sx, *J* = 7.4 Hz, 2H, CH_2), 0.99 (t,*J* = 7.4 Hz, 3H, CH_3). ^{13}**C-NMR** (75 MHz, $CDCl_3$): δ = 192.7, 162.8, 158.7, 144.6, 141.2, 130.7, 129.1, 122.1, 115.3, 114.6, 113.8, 24.8, 22.0, 19.1, 15.8, 14.3. **HRMS** (ESI) *m/z*: $[M+Na]^+$ calcd for $C_{16}H_{20}O_3Na$ 283.1305, found 283.1303.[31]

3-Butylsorbicillin (94d)



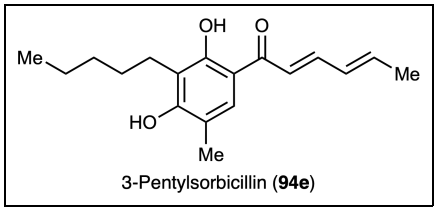
3-Butylsorbicillin (**94d**)

SMILES: OC1=C(C(/C=C/C=C/C)=O)C=C(C)C(O)=C1CCCC

Total synthesis: *ortho*-Lithiation of 1,3-dimethoxybenzene with butyl iodide, followed by deprotection with BBr_3, Vilsmeier formylation, reduction and Friedel-Crafts acylation with sorbyl chloride.[31]

Analytics: Yellow solid. ^{1}**H-NMR** (600 MHz, $CDCl_3$): δ = 13.54 (bs, 1H, O*H*), 7.46 (dd, *J* = 14.8, 10.8 Hz, 1H, CH_{sorbyl}), 7.44 (s, 1H, Ar*H*), 6.94 (d, *J* = 14.9 Hz, 1H, CH_{sorbyl}), 6.38–6.24 (m, 2H, CH_{sorbyl}), 5.27 (bs, 1H, O*H*), 2.67–2.64 (m, 2H, CH_2), 2.22 (d, *J* = 0.9 Hz, 3H, CH_3), 1.91 (d, *J* = 5.6 Hz, 3H, CH_3), 1.56–1.50 (m, 2H, CH_2), 1.41 (sx, *J* = 6.9 Hz, 2H, CH_2), 0.94 (t, *J* = 7.2 Hz, 3H, CH_3). ^{13}**C-NMR** (150 MHz, $CDCl_3$): δ = 192.7, 162.7, 158.6, 144.6, 141.2, 130.7, 129.1, 122.1, 115.6, 114.6, 113.8, 31.0, 23.0, 22.6, 19.1, 15.8, 14.2. **HRMS** (ESI) *m/z*: $[M+Na]^+$ calcd for $C_{17}H_{22}O_3Na$ 297.1467, found 297.1466.[31]

3-Pentylsorbicillin (94e)



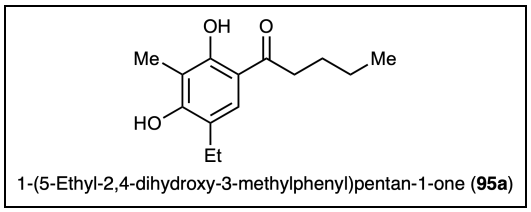
3-Pentylsorbicillin (**94e**)

SMILES: OC1=C(C(/C=C/C=C/C)=O)C=C(C)C(O)=C1CCCCC

Total synthesis: *ortho*-Lithiation of 1,3-dimethoxybenzene with pentyl iodide, followed by deprotection with BBr_3, Vilsmeier formylation, reduction and Friedel-Crafts acylation with sorbyl chloride.[31]

Analytics: yellow solid. ^{1}**H-NMR** (600 MHz, $CDCl_3$): δ = 13.54 (bs, 1H, O*H*), 7.53–7.38 (m, 2H, Ar*H*, CH_{sorbyl}), 6.94 (d, *J* = 14.9 Hz, 1H, CH_{sorbyl}), 6.43–6.17 (m, 2H, CH_{sorbyl}), 5.28 (bs, 1H, O*H*), 2.66–2.63 (m, 2H, CH_2), 2.22 (s, 3H, CH_3), 1.91 (d, *J* = 5.6 Hz, 3H, CH_3), 1.57–1.51 (m, 2H, CH_2), 1.40–1.32 (m, 4H, CH_2), 0.90 (t, *J* = 7.0 Hz, 3H, CH_3). ^{13}**C-NMR** (75 MHz, $CDCl_3$): δ = 192.7, 162.7, 158.6, 144.6, 141.3, 130.7, 129.1, 122.0, 115.6, 114.6, 113.8, 32.1, 28.5, 22.9, 22.8, 19.1, 15.8, 14.2. **HRMS** (ESI) *m/z*: $[M+Na]^+$ calcd for $C_{18}H_{24}O_3Na$ 311.1623, found 311.1622.[31]

1-(5-Ethyl-2,4-dihydroxy-3-methylphenyl)pentan-1-one (95a)



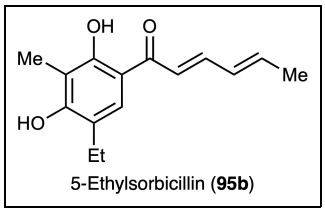
1-(5-Ethyl-2,4-dihydroxy-3-methylphenyl)pentan-1-one (**95a**)

SMILES: OC1=C(C(CCCC)=O)C=C(CC)C(O)=C1C

Total synthesis: Friedel-Crafts acylation with 4-ethyl-4-methylbenzene-1,3-diol and valeric acid using boron trifluoride etherate.[101]

Analytics: White solid. **MP**: 87-89 °C. ^{1}**H-NMR** (400 MHz, $CDCl_3$): δ = 13.06 (s, 1H, O*H*), 7.40 (s, 1H, Ar*H*), 5.29 (s, 1H, O*H*), 2.94 (m, 2H, CH_2), 2.59 (q, *J* = 7.4 Hz, 2H, CH_2), 2.14 (s, 3H, CH_3), 1.70 (m, 2H, CH_2), 1.42 (m, 2H, CH_2), 1.24 (t, *J* = 7.5 Hz, 3H, CH_3), 0.96 (t, *J* = 7.3 Hz, 3H, CH_3). ^{13}**C-NMR** (100 MHz, $CDCl_3$): δ = 205.4, 161.3, 158.2, 127.6, 120.7, 113.0, 110.2, 37.7, 27.1, 22.8, 22.5, 14.1, 13.9, 7.4. **IR**: *ν* 3429, 1962, 1632, 1603, 1110 cm^{-1}. **HRMS** (ESI) *m/z*: $[M-H]^-$ calcd for $C_{14}H_{19}O_3$ 235.1340, found 235.1339.[101]

5-Ethylsorbicillin (95b)



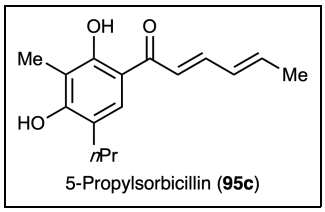
5-Ethylsorbicillin (**95b**)

SMILES: OC1=C(C(/C=C/C=C/C)=O)C=C(CC)C(O)=C1C

Total synthesis: Vilsmeier reaction of methylresorcinol, boron trifluoride etherate and acetic anhydride followed by reduction and Friedel-Crafts acylation with sorbyl chloride.[31]

Analytics: Yellow solid. ^{1}**H-NMR** (600 MHz, $CDCl_3$): δ = 13.62 (bs, 1H, O*H*), 7.47 (dd, *J* = 14.9, 10.9 Hz, 1H, CH_{sorbyl}), 7.44 (s, 1H, Ar*H*), 6.96 (d, *J* = 14.8 Hz, 1H, CH_{sorbyl}), 6.42–6.33 (m, 1H, CH_{sorbyl}), 6.33–6.24 (m, 1H, CH_{sorbyl}), 5.30 (bs, 1H, O*H*), 2.60 (q, *J* = 7.5 Hz, 2H, CH_2), 2.15 (s, 3H, CH_3), 1.90 (d, *J* = 6.0 Hz, 3H, CH_3), 1.24 (t, *J* = 7.5 Hz, 3H, CH_3). ^{13}**C-NMR** (150 MHz, $CDCl_3$): δ = 192.7, 162.6, 158.5, 144.7, 141.3, 130.7, 127.4, 122.0, 120.8, 113.8, 110.4, 23.1, 19.1, 14.3, 7.6. **HRMS** (ESI) *m/z*: $[M+Na]^+$ calcd for $C_{15}H_{18}O_3Na$ 269.1148, found 269.1144.[31]

5-Propylsorbicillin (95c)



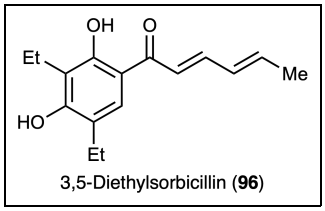
5-Propylsorbicillin (**95c**)

SMILES: OC1=C(C(/C=C/C=C/C)=O)C=C(CCC)C(O)=C1C

Total synthesis: Vilsmeier reaction of methylresorcinol, boron trifluoride etherate and propionic anhydride followed by reduction and Friedel-Crafts acylation with sorbyl chloride.[31]

Analytics: Yellow solid. ^{1}**H-NMR** (600 MHz, $CDCl_3$): δ = 13.60 (bs, 1H, O*H*), 7.47 (dd, *J* = 14.8, 10.9 Hz, 1H, CH_{sorbyl}), 7.42 (s, 1H, Ar*H*), 6.95 (d, *J* = 14.9 Hz, 1H, CH_{sorbyl}), 6.41–6.33 (m, 1H, CH_{sorbyl}), 6.33–6.24 (m, 1H, CH_{sorbyl}), 5.30 (bs, 1H, O*H*), 2.55 (t, *J* = 7.6 Hz, 2H, CH_2), 2.15 (s, 3H, CH_3), 1.91 (d, *J* = 5.9 Hz, 3H, CH_3), 1.63 (sx, *J* = 7.4 Hz, 2H, CH_2), 0.98 (t, *J* = 7.3 Hz, 3H, CH_3). ^{13}**C-NMR** (150 MHz, $CDCl_3$): δ = 192.7, 162.6, 158.6, 144.7, 141.3, 130.7, 128.4, 122.0, 119.3, 113.7, 110.5, 32.1, 23.1, 19.1, 14.1, 7.7. **HRMS** (ESI) *m/z*: $[M+Na]^+$ calcd for $C_{16}H_{20}O_3Na$ 283.1305, found 283.1300.[31]

3,5-Diethylsorbicillin (96)



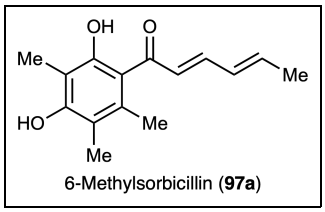
3,5-Diethylsorbicillin (**96**)

SMILES: OC1=C(C(/C=C/C=C/C)=O)C=C(CC)C(O)=C1CC

Total synthesis: Combination of the total synthesis of the 3- and 5-functionalized sorbicillins.[31]

Analytics: Yellow solid. ^{1}**H-NMR** (600 MHz, $CDCl_3$): δ = 13.58 (bs, 1H, O*H*), 7.50–7.45 (m, 1H, CH_{sorbyl}), 7.44 (s, 1H, Ar*H*), 6.96 (d, *J* = 14.9 Hz, 1H, CH_{sorbyl}), 6.42–6.23 (m, 2H, CH_{sorbyl}), 5.42 (bs, 1H, O*H*), 2.69 (q, *J* = 7.6 Hz, 2H, CH_2), 2.60 (q, *J* = 7.6 Hz, 2H, CH_2), 1.91 (d, *J* = 6.6 Hz, 3H, CH_3), 1.25 (t, *J* = 7.6 Hz, 3H, CH_3), 1.17 (t, *J* = 7.6 Hz, 3H, CH_3). ^{13}**C-NMR** (150 MHz, $CDCl_3$): δ = 193.5, 162.4, 158.2, 144.6, 141.2, 130.7, 127.5, 122.0, 121.0, 116.8, 113.9, 23.0, 19.1, 16.1, 14.2, 13.3. **HRMS** (ESI) *m/z*: $[M-H]^-$ calcd for $C_{16}H_{19}O_3$ 259.1340, found 259.1332.[31]

6-Methylsorbicillin (97a)



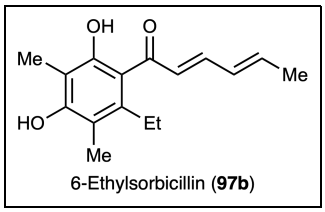
6-Methylsorbicillin (**97a**)

SMILES: OC1=C(C(/C=C/C=C/C)=O)C(C)=C(C)C(O)=C1C

Total synthesis: The alkyl group in position 6 was introduced via the benzaldehyde using the corresponding Grignard reagent.[31]

Analytics: Yellow solid. ^{1}**H-NMR** (300 MHz, $CDCl_3$): δ = 11.55 (bs, 1H, O*H*), 7.35–7.27 (m, 1H, CH_{sorbyl}), 6.49 (d, *J* = 15.0 Hz, 1H, CH_{sorbyl}), 6.32–6.17 (m, 2H, CH_{sorbyl}), 5.25 (bs, 1H, O*H*), 2.36 (s, 3H, CH_3), 2.13 (s, 3H, CH_3), 2.12 (s, 3H, CH_3), 1.89 (d, *J* = 5.2 Hz, 3H, CH_3). ^{13}**C-NMR** (75 MHz, $CDCl_3$): δ = 196.4, 158.5, 156.7, 143.2, 141.1, 135.4, 130.6, 129.3, 117.7, 115.2, 107.5, 20.6, 19.1, 11.7, 8.0. **HRMS** (ESI) *m/z*: $[M+Na]^+$ calcd for $C_{15}H_{18}O_3Na$ 269.1148, found 269.1144.[31]

6-Ethylsorbicillin (97b)



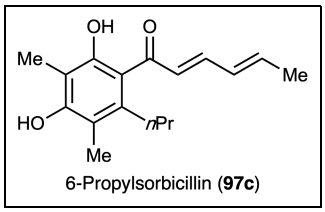
6-Ethylsorbicillin (**97b**)

SMILES: OC1=C(C(/C=C/C=C/C)=O)C(CC)=C(C)C(O)=C1C

Total synthesis: The alkyl group in position 6 was introduced via the benzaldehyde using the corresponding Grignard reagent.[31]

Analytics: Yellow oil. ^{1}**H-NMR** (300 MHz, $CDCl_3$): δ = 7.32–7.23 (m, 1H, CH_{sorbyl}), 6.53 (d, *J* = 14.4 Hz, 1H, C*H*), 6.30–6.21 (m, 2H, CH_{sorbyl}), 2.83 (q, *J* = 7.4 Hz, 2H, CH_2), 2.17 (s, 3H, CH_3), 2.12 (s, 3H, CH_3), 1.89 (d, *J* = 5.0 Hz, 3H, CH_3), 1.15 (t, *J* = 7.4 Hz, 3H, CH_3). ^{13}**C-NMR** (75 MHz, $CDCl_3$): δ = 197.3, 157.4, 156.9, 144.0, 141.4, 141.2, 130.6, 129.1, 117.5, 114.6, 107.9, 25.2, 19.1, 15.2, 11.5, 8.1. **HRMS** (ESI) *m/z*: $[M+Na]^+$ calcd for $C_{16}H_{20}O_3Na$ 283.1305, found 283.1303.[31]

6-Propylsorbicillin (97c)



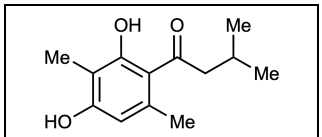
6-Propylsorbicillin (**97c**)

SMILES: OC1=C(C(/C=C/C=C/C)=O)C(CCC)=C(C)C(O)=C1C

Total synthesis: The alkyl group in position 6 was introduced via the benzaldehyde using the corresponding Grignard reagent.[31]

Analytics: Yellow oil. ^{1}**H-NMR** (300 MHz, $CDCl_3$): δ = 10.84 (bs, 1H, O*H*), 7.37–7.23 (m, 1H, CH_{sorbyl}), 6.52 (d, *J* = 15.0 Hz, 1H, CH_{sorbyl}), 6.33–6.19 (m, 2H, CH_{sorbyl}), 5.55 (bs, 1H, O*H*), 2.86–2.74 (m, 2H, CH_2), 2.19 (s, 3H, CH_3), 2.15 (s, 3H, CH_3), 1. 92 (d, *J* = 5.5 Hz, 3H, CH_3), 1.55 (sx, *J* = 7.8 Hz, 2H, CH_2), 0.94 (t, *J* = 7.4 Hz, 3H, CH_3). ^{13}**C-NMR** (75 MHz, $CDCl_3$): δ = 198.3, 157.3, 157.0, 143.7, 141.2, 139.8, 130.5, 129.1, 117.8, 114.8, 108.0, 34.2, 24.1, 19.0, 14.2, 11.6, 8.1. **HRMS** (ESI) *m/z*: $[M+Na]^+$ calcd for $C_{17}H_{22}O_3Na$ 297.1461, found 297.1457.[31]

1-(2,4-Dihydroxy-3,6-dimethylphenyl)-3-methylbutan-1-one (98a)

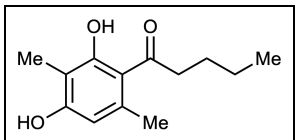

1-(2,4-Dihydroxy-3,6-dimethyl-phenyl)-3-methylbutan-1-one (**98a**)

SMILES: OC1=C(C(CC(C)C)=O)C(C)=CC(O)=C1C

Total synthesis: Friedel-Crafts acylation with 1,3-dimethoxy-2,5-dimethylbenzene and isobutyryl chloride using aluminium(III) chloride followed by methoxy deprotection with BBr_3.[101]

Analytics: White solid. **MP**: 69-71 °C. ^{1}**H-NMR** (400 MHz, $CDCl_3$): δ = 13.34 (s, 1H, O*H*), 6.20 (s, 1H, Ar*H*), 5.10 (s, 1H, O*H*), 2.78 (d, *J* = 6.6 Hz, 1H, C*H*), 2.53 (s, 3H, CH_3), 2.27 (m, 2H, CH_2), 2.09 (s, 3H, CH_3), 0.96 (d, *J* = 6.6 Hz, 6H, CH_3). ^{13}**C-NMR** (100 MHz, $CDCl_3$): δ = 207.6, 163.7, 158.6, 138.3, 115.7, 111.2, 109.3, 52.8, 25.9, 24.7, 22.7, 7.6. **IR**: *ν* 3377, 2959, 1589, 1400, 1110 cm^{-1}. **HRMS** (ESI) *m/z*: $[M-H]^-$ calcd for $C_{13}H_{17}O_3$ 221.1183, found 221.1185.[101]

1-(2,4-Dihydroxy-3,6-dimethylphenyl)pentan-1-one (98b)

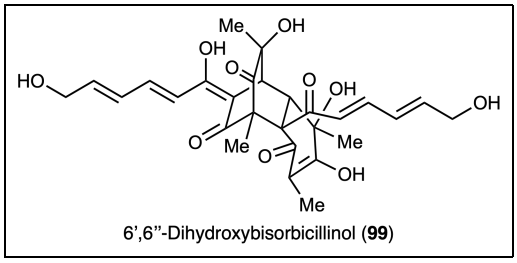

1-(2,4-Dihydroxy-3,6-dimethyl-phenyl)pentan-1-one (**98b**)

SMILES: OC1=C(C(CCCC)=O)C(C)=CC(O)=C1C

Total synthesis: Friedel-Crafts acylation with 1,3-dimethoxy-2,5-dimethylbenzene and propionyl chloride using $AlCl_3$ followed by methoxy deprotection with BBr_3.[101]

Analytics: White solid. ^{1}**H-NMR** (400 MHz, $CDCl_3$): δ = 13.56 (s, 1H, O*H*), 6.21 (s, 1H, Ar*H*), 5.39 (s, 1H, O*H*), 2.88 (t, *J* = 8.0 Hz, 2H, CH_2), 2.53 (s, 3H, CH_3), 2.09 (s, 3H, CH_3), 1.76 (m, 2H, CH_2), 0.98 (t, *J* = 8.0 Hz, 3H, CH_3).[101]

6′,6′′-Dihydroxybisorbicillinol (99)

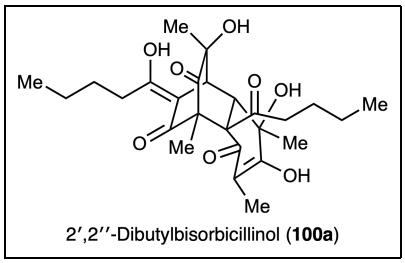

6′,6′′-Dihydroxybisorbicillinol (**99**)

SMILES: O[C@@]1(C)[C@@H]2/C(C([C@@](C1=O)(C)[C@]3(C(/C=C/C=C/CO)=O)[C@H]2[C@@](O)(C)C(O)=C(C)C3=O)=O)=C(/C=C/C=C/CO)O

Total synthesis: Synthesized chemo-enzymatically using the heterologous expressed monooxygenase SorbC together with 6′-hydroxysorbicillin (**1c**).[31]

Analytics: Pale yellow oil. **ORD**: $[\alpha]_D^{25}$ = +109.4 (c = 0.3, MeOH). ^{1}**H-NMR** (600 MHz, CD_3OD): δ = 7.29 (dd, *J* = 15.4, 10.8 Hz, 1H, CH_{sorbyl}), 7.27 (dd, *J* = 15.7, 11.0 Hz, 1H, CH_{sorbyl}), 6.57–6.35 (m, 5H, CH_{sorbyl}), 6.25 (dt, *J* = 15.3, 5.0 Hz, 1H, CH_{sorbyl}), 4.22 (dd, *J* = 5.1, 1.7 Hz, 2H, CH_2OH), 4.20 (dd, *J* = 4.5, 1.9 Hz, 2H, CH_2OH), 3.67 (d, *J* = 2.2 Hz, 1H, C*H*), 3.41 (d, *J* = 2.1 Hz, 1H, C*H*), 1.60 (s, 3H, CH_3), 1.42 (s, 3H, CH_3), 1.20 (s, 3H, CH_3), 1.14 (s, 3H, CH_3). ^{13}**C-NMR** (150 MHz, CD_3OD): δ = 208.6 (2C), 198.3, 197.9, 179.2, 168.7, 146.1, 145.5, 142.5, 141.6, 129.9, 128.5, 127.2, 122.2, 111.6, 110.4, 75.0 (2C), 70.7, 68.7, 62.8, 62.6, 48.0, 42.7, 33.6, 24.9, 10.5, 8.7. **HRMS** (ESI) *m/z*: $[M-H]^-$ calcd for $C_{28}H_{31}O_{10}$ 527.1923, found 527.1920.[31]

2′,2′′-Dibutylbisorbicillinol (100a)

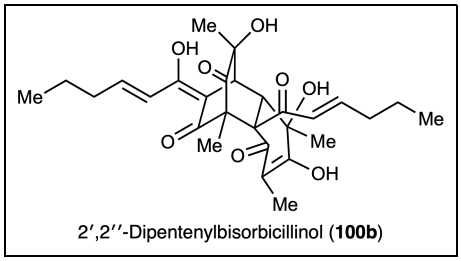

2′,2′′-Dibutylbisorbicillinol (**100a**)

SMILES: O[C@@]1(C)[C@@H]2/C(C([C@@](C1=O)(C)[C@]3(C(CCCC)=O)[C@H]2[C@@](O)(C)C(O)=C(C)C3=O)=O)=C(CCCC)\O

Total synthesis: Synthesized chemo-enzymatically using the heterologous expressed monooxygenase SorbC together with 1-(2,4-dihydroxy-3,5-dimethylphenyl)pentan-1-one (**87d**).[31]

Analytics: Colorless oil. **ORD**: $[\alpha]_D^{25}$ = +99.8 (c = 0.1, MeOH). ^{1}**H-NMR** (600 MHz, CD_3OD): δ = 3.54 (d, *J* = 2.3 Hz, 1H, C*H*), 3.39 (d, *J* = 2.3 Hz, 1H, C*H*), 2.76–2.38 (m, 4H, CH_2), 1.59 (s, 3H, CH_3), 1.58–1.50 (m, 4H, CH_2), 1.48 (s, 3H, CH_3), 1.39 (sx, *J* = 7.3 Hz, 2H, CH_2), 1.31 (sx, *J* = 7.1 Hz, 2H, CH_2), 1.19 (s, 3H, CH_3), 1.16 (s, 3H, CH_3), 0.96 (t, *J* = 7.2 Hz, 3H, CH_3), 0.89 (t, *J* = 7.3 Hz, 3H, CH_3). ^{13}**C-NMR** (150 MHz, CD_3OD): δ = 208.4 (3xC), 195.8, 182.8 (2xC), 111.3, 109.9, 75.3 (2xC), 70.8, 67.7, 47.1, 43.3, 42.0, 33.8, 32.9, 28.9, 27.2, 25.1, 23.8, 23.2, 14.3, 14.2, 10.6, 8.8. **HRMS** (ESI) *m/z*: $[M+Na]^+$ calcd for $C_{26}H_{36}O_8Na$ 499.2308, found 5499.2314.[31]

2′,2′′-Dipentenylbisorbicillinol (100b)



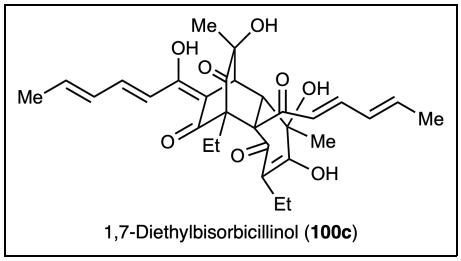
2′,2′′-Dipentenylbisorbicillinol (**100b**)

SMILES: O[C@@]1(C)[C@@H]2/C(C([C@@](C1=O)(C)[C@]3(C(/C=C/CCC)=O)[C@H]2[C@@](O)(C)C(O)=C(C)C3=O)=O)=C(/C=C/CCC)O

Total synthesis: Synthesized chemo-enzymatically using the heterologous expressed monooxygenase SorbC together with (*E*)-1-(2,4-dihydroxy-3,5-dimethylphenyl)hex-2-en-1-one (**87h**).[31]

Analytics: Pale yellow oil. **ORD**: $[\alpha]_D^{25} = +132.0$ (c = 0.1, MeOH). ^{1}**H-NMR** (600 MHz, CD_3OD): δ = 6.99–6.82 (m, 2H, C*H*), 6.44 (d, *J* = 15.3 Hz, 1H, C*H*), 6.31 (d, *J* = 15.5 Hz, 1H, C*H*), 3.65 (d, *J* = 2.2 Hz, 1H, C*H*), 3.39 (d, *J* = 2.1 Hz, 1H, C*H*), 2.39–2.13 (m, 4H, CH_2), 1.60 (s, 3H, CH_3), 1.57–1.46 (m, 4H, CH_2), 1.43 (s, 3H, CH_3), 1.37–1.27 (m, 4H, CH_2), 1.20 (s, 3H, CH_3), 1.13 (s, 3H, CH_3), 0.98 (t, *J* = 7.4 Hz, 3H, CH_3), 0.93 (t, *J* = 7.4 Hz, 3H), CH_3. ^{13}**C-NMR** (150 MHz, CD_3OD): δ = 210.9, 209.8, 198.5, 198.3, 177.3, 169.5, 151.1, 146.9, 128.5, 122.4, 111.8, 109.7, 75.2 (2C), 71.4, 70.4, 36.3, 35.6, 33.8, 25.2, 22.8, 22.4, 14.13, 14.07, 10.8, 8.9. **HRMS** (ESI) *m/z*: $[M+Na]^+$ calcd for $C_{28}H_{36}O_8Na$ 523.2308, found 523.2308.[31]

1,7-Diethylbisorbicillinol (100c)



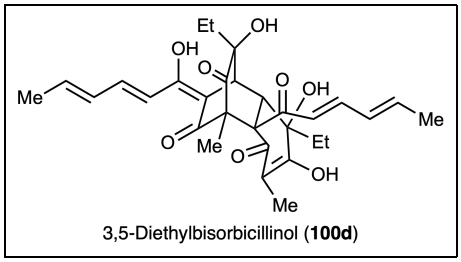
1,7-Diethylbisorbicillinol (**100c**)

SMILES: O[C@@]1(C)[C@@H]2/C(C([C@@](C1=O)(CC)[C@]3(C(/C=C/C=C/C)=O)[C@H]2[C@@](O)(C)C(O)=C(CC)C3=O)=O)=C(/C=C/C=C/C)O

Total synthesis: Synthesized chemo-enzymatically using the heterologous expressed monooxygenase SorbC together with 3-ethylsorbicillin (**88b**).[31]

Analytics: Pale yellow oil. **ORD**: $[\alpha]_D^{25} = +223.1$ (c = 0.9, MeOH). ^{1}**H-NMR** (600 MHz, CD_3OD): δ = 7.23 (dd, *J* = 15.1, 10.6 Hz, 1H, CH_{sorbyl}), 7.19 (dd, *J* = 15.1, 10.6 Hz, 1H, CH_{sorbyl}), 6.54 (d, *J* = 15.0 Hz, 1H, CH_{sorbyl}), 6.40–6.13 (m, 5H, CH_{sorbyl}), 3.63 (d, *J* = 1.5 Hz, 1H, C*H*), 3.51 (d, *J* = 1.5 Hz, 1H, C*H*), 2.39 (dq, *J* = 14.4, 7.2 Hz, 1H, CH_2), 2.26–2.04 (m, 2H, CH_2), 1.87 (d, *J* = 5.5 Hz, 6H, CH_3), 1.7–1.54 (m, 1H, CH_2) 1.30 (s, 3H, CH_3), 1.08 (s, 3H, CH_3), 0.88 (t, *J* = 7.2 Hz, 3H, CH_3), 0.80 (t, *J* = 7.5 Hz, 3H, CH_3). ^{13}**C-NMR** (150 MHz, CD_3OD): δ = 209.5 (2C), 199.1, 198.0, 172.7, 168.4, 146.9, 144.1, 142.5, 139.6, 132.5, 131.7, 125.8, 120.3, 119.1, 111.4, 76.8 (2C), 73.1, 70.1, 50.4, 42.6, 33.2, 24.4, 20.3, 19.0, 18.9, 17.4, 13.6, 10.8. **HRMS** (ESI) *m/z*: $[M+Na]^+$ calcd for $C_{30}H_{36}O_8Na$ 547.2308, found 547.2309.[31]

3,5-Diethylbisorbicillinol (100d)



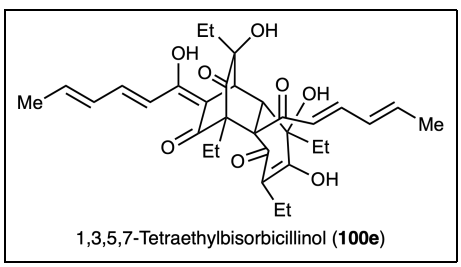
3,5-Diethylbisorbicillinol (**100d**)

SMILES: O[C@@]1(CC)[C@@H]2/C(C([C@@](C1=O)(C)[C@]3(C(/C=C/C=C/C)=O)[C@H]2[C@@](O)(CC)C(O)=C(C)C3=O)=O)=C(/C=C/C=C/C)O

Total synthesis: Synthesized chemo-enzymatically using the heterologous expressed monooxygenase SorbC together with 5-ethylsorbicillin (**89b**).

Analytics: Pale yellow oil. **ORD**: $[\alpha]_D^{25} = +137.8$ (c = 0.5, MeOH). ^{1}**H-NMR** (600 MHz, CD_3OD): δ = 7.31–7.13 (m, 2H, CH_{sorbyl}), 6.50 (d, J*J* = 14.9 Hz, 1H, CH_{sorbyl}), 6.43–6.14 (m, 5H, CH_{sorbyl}), 3.72 (d, *J* = 1.9 Hz, 1H, C*H*), 3.46 (d, *J* = 1.8 Hz, 1H, C*H*), 1.91–1.85 (m, 6H, CH_2), 1.70–1.49 (m, 4H, CH_2), 1.61 (s, 3H, CH_3), 1.21 (s, 3H, CH_3), 0.88 (t, *J* = 7.4 Hz, 3, CH_3H), 0.78 (t, *J* = 7.3 Hz, 3H, CH_3). ^{13}**C-NMR** (150 MHz, CD_3OD): δ = 209.9 (2xC), 199.4, 198.5, 180.5, 169.0, 146.7, 144.0, 142.7, 139.8, 132.6, 131.7, 125.9, 120.8, 113.3, 110.1, 78.4 (2C), 74.5, 69.5, 47.3, 38.8, 30.7 (2C), 19.1, 19.0, 11.0, 8.8, 7.8, 7.1. **HRMS** (ESI) *m/z*: $[M+Na]^+$ calcd for $C_{30}H_{36}O_8Na$ 547.2308, found 547.2306.[31]

1,3,5,7-Tetraethylbisorbicillinol (100e)



1,3,5,7-Tetraethylbisorbicillinol (**100e**)

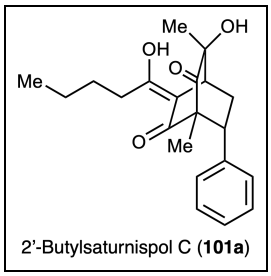
SMILES: O[C@@]1(CC)[C@@H]2/C(C([C@@](C1=O)(CC)[C@]3(C(/C=C/C=C/C)=O)[C@H]2[C@@](O)(CC)C(O)=C(CC)C3=O)=O)=C(/C=C/C=C/C)O

Total synthesis: Synthesized chemo-enzymatically using the heterologous expressed monooxygenase SorbC together with 3,5-diethylsorbicillin (**90**).

Analytics: Pale yellow oil. **ORD**: $[\alpha]_D^{25} = +178.0$ (c = 0.2, MeOH). ^{1}**H-NMR** (600 MHz, CD_3OD): δ = 7.24–7.16 (m, 2H, CH_{sorbyl}), 6.64 (d, *J* = 14.8 Hz, 1H, CH_{sorbyl}), 6.38–6.24 (m, 4H, CH_{sorbyl}), 6.19–6.15 (m, 1H, CH_{sorbyl}), 3.66 (d, *J* = 1.4 Hz, 1H, C*H*), 3.57 (d, *J* = 1.4 Hz, 1H, C*H*), 2.45 (dq, *J* = 14.1, 6.9 Hz, 1 H, CH_2), 2.20 (dq, *J* = 14.1, 7.5 Hz, 1,

CH_2H), 2.08 (dq, J = 14.2, 7.3 Hz, 1H, CH_2), 1.89–1.87 (m, 6H, CH_2), 1.59 (bs, 1H, CH_2), 1.48–1.40 (m, 3H, CH_3), 1.28–1.21 (m, 1H, CH_2), 0.86 (t, J = 7.3 Hz, 6H, CH_3), 0.81 (t, J = 7.4 Hz, 3H, CH_3), 0.76 (bs, 3H, CH_3). ^{13}**C-NMR** (150 MHz, CD_3OD): δ = 209.5 (2C), 198.6, 198.0, 199.6, 171.7, 168.0, 146.6, 144.0, 142.1, 139.3, 132.5, 131.7, 125.9, 120.6, 111.0, 79.2 (2C), 73.3, 71.4, 48.7, 39.0, 30.0, 29.7, 20.1, 19.0, 18.8, 17.4, 13.8, 10.5, 7.7, 6.8. **HRMS** (ESI) *m/z*: $[M+Na]^+$ calcd for $C_{32}H_{40}O_8Na$ 575.2615, found 575.2598.[31]

2′-Butylsaturnispol C (101a)



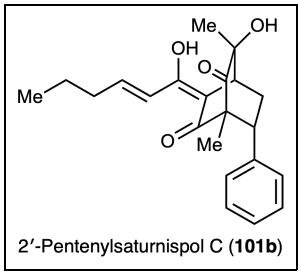
2′-Butylsaturnispol C (**101a**)

SMILES: O[C@@]1(C)[C@@H]2/C(C([C@@](C1=O)(C)[C@@H](C3=CC=CC=C3)C2)=O)=C(CCCC)\O

Total synthesis: Synthesized chemo-enzymatically using the heterologous expressed monooxygenase SorbC together with 1-(2,4-dihydroxy-3,5-dimethylphenyl)pentan-1-one (**87d**) and styrol.[31]

Analytics: Pale yellow oil. **ORD**: $[\alpha]_D^{25}$ = +17.7 (c = 0.3, $CHCl_3$). ^{1}**H-NMR** (300 MHz, $CDCl_3$): δ = 14.71 (bs, 1H, O*H*), 7.30–7.22 (m, 3H, Ar*H*), 6.94 (dd, J = 7.7, 1.9 Hz, 2H, Ar*H*), 3.21 (t, J = 2.8 Hz, 1H, C*H*), 3.11 (dd, J = 10.6, 5.2 Hz, 1H, CH_2), 3.02 (ddd, J = 13.5, 10.6, 2.8 Hz Hz, 1H CH_2), 2.57–2.40 (m, 2H CH_2), 1.84 (ddd, J = 7.4 Hz12.9, 5.3, 2.8, 1H, C*H*), 1.75–1.66 (m, 2H, CH_2), 1.52–1.39 (m, 2H CH_2), 1.29 (s, 3H, CH_3), 0.98 (t, J = 7.3 Hz, 3H, CH_3), 0.90 (s, 3H, CH_3). ^{13}**C-NMR** (75 MHz, $CDCl_3$): δ = 211.6, 195.7, 180.1, 141.5, 128.8 (2C), 128.4 (2C), 127.6, 112.0, 74.7, 64.1, 47.8, 41.0, 32.3, 31.9, 28.7, 24.6, 22.8, 14.0, 10.6. **HRMS** (ESI) *m/z*: $[M+Na]^+$ calcd for $C_{21}H_{26}O_4Na$ 365.1723, found 365.1720.[31]

2′-Pentenylsaturnispol C (101b)



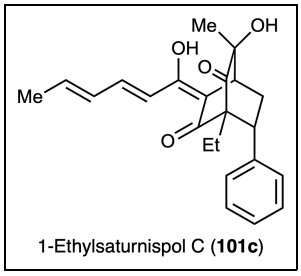
2′-Pentenylsaturnispol C (**101b**)

SMILES: O[C@@]1(C)[C@@H]2/C(C([C@@](C1=O)(C)[C@@H](C3=CC=CC=C3)C2)=O)=C(/C=C/CCC)O

Total synthesis: Synthesized chemo-enzymatically using the heterologous expressed monooxygenase SorbC together with (*E*)-1-(2,4-dihydroxy-3,5-dimethylphenyl)hex-2-en-1-one (**87h**) and styrol.[31]

Analytics: Pale yellow oil. **ORD**: $[\alpha]_D^{25}$ = +14.5 (c = 0.3, $CHCl_3$). ^{1}**H-NMR** (300 MHz, $CDCl_3$): δ = 14.35 (bs, 1H), 7.07 (dt, J = 14.7, 7.1 Hz, 1H, C*H*), 7.29–7.19 (m, 3H, Ar*H*), 6.96 (dd, J = 7.7, 1.9 Hz, 2H, Ar*H*), 6.32 (d, J = 15.3 Hz, 1H, C*H*), 3.31 (t, J = 2.8 Hz, 1H), 3.13 (dd, J = 10.7, 5.5 Hz, 1H, C*H*), 3.02 (ddd, J = 13.5, 10.7, 2.9 Hz, 1H, CH_2), 2.31 (qd, J = 7.2, 1.6 Hz, 2H, CH_2), 1.88 (ddd, J = 13.1, 5.5, 2.8 Hz Hz, 1H, CH_2), 1.57 (sex, J = 7.2 Hz, 2H, CH_2), 1.27 (s, 3H, CH_3), 0.99 (t, J = 7.4 Hz, 3H, CH_3), 0.90 (s, 3H, CH_3). ^{13}**C-NMR** (75 MHz, $CDCl_3$): δ = 211.7, 198.2, 167.0, 147.2, 141.5, 128.8 (2C), 128.5 (2C), 127.5, 120.1, 111.4, 74.5, 64.8, 47.8, 40.5, 35.5, 31.5, 24.5, 21.8, 13.9, 10.7. **HRMS** (ESI) *m/z*: $[M+Na]^+$ calcd for $C_{22}H_{26}O_4Na$ 377.1723, found 377.1717.[31]

1-Ethylsaturnispol C (101c)



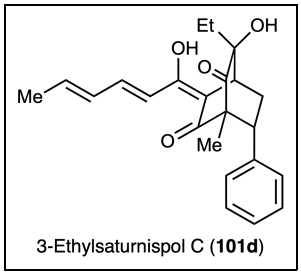
1-Ethylsaturnispol C (**101c**)

SMILES: O[C@@]1(C)[C@@H]2/C(C([C@@](C1=O)(CC)[C@@H](C3=CC=CC=C3)C2)=O)=C(/C=C/C=C/C)O

Total synthesis: Synthesized chemo-enzymatically using the heterologous expressed monooxygenase SorbC together with 3-ethylsorbicillin (**88b**) and styrol.[31]

Analytics: Pale yellow oil. **ORD**: $[\alpha]_D^{25}$ = −29.5 (c = 0.5, $CHCl_3$). ^{1}**H-NMR** (300 MHz, $CDCl_3$): δ = 14.42 (bs, 1H, O*H*), 7.38 (dd, J = 14.9, 10.3 Hz, 1H, CH_{sorbyl}), 7.28–7.18 (m, 3H, Ar*H*), 6.96 (dd, J = 7.7, 1.9 Hz, 2H, Ar*H*), 6.41–6.14 (m, 3H, CH_{sorbyl}), 3.25 (t, J = 2.9 Hz, 1H, C*H*), 3.20 (dd, J = 10.7, 5.5 Hz, 1H, C*H*), 2.99 (ddd, J = 13.5, 10.7, 2.8 Hz, 1H, CH_2), 1.91 (d, J = 6.2 Hz, 3H, CH_3), 1.88 (ddd, J = J = 13.6, 5.5, 2.9 Hz, 1H, CH_2), 1.41 (dq, J = 14.2, 7.1 Hz, 2H), 1.24 (s, 3H, CH_3), 0.91 (t, J = 7.2 Hz, 3H, CH_3). ^{13}**C-NMR** (75 MHz, $CDCl_3$): δ = 212.2, 197.9, 167.2, 142.4, 141.3, 139.7, 131.1, 128.8 (2C), 128.5 (2C), 127.5, 118.3, 112.5, 75.5, 68.0, 48.0, 40.8, 31.9, 24.0, 19.8, 19.0, 9.0. **HRMS** (ESI) *m/z*: $[M+Na]^+$ calcd for $C_{23}H_{26}O_4Na$ 389.1723, found 389.1721.[31]

3-Ethylsaturnispol C (101d)



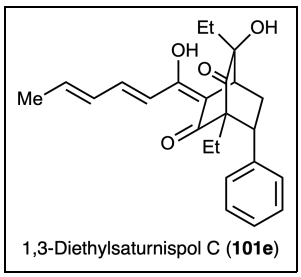
3-Ethylsaturnispol C (**101d**)

SMILES: O[C@@]1(CC)[C@@H]2/C(C([C@@](C1=O)(C)[C@@H](C3=CC=CC=C3)C2)=O)=C(/C=C/C=C/C)O

Total synthesis: Synthesized chemo-enzymatically using the heterologous expressed monooxygenase SorbC together with 5-ethylsorbicillin (**89b**) and styrol.[31]

Analytics: Pale yellow oil. **ORD**: $[\alpha]_D^{25} = -12.6$ (c = 0.8, $CHCl_3$). ^{1}**H-NMR** (300 MHz, $CDCl_3$): δ = 14.30 (bs, 1H, O*H*), 7.39 (dd, *J* = 14.9, 10.4 Hz, 1H, CH_{sorbyl}), 7.39–7.20 (m, 3H, Ar*H*), 6.95 (dd, *J* = 7.6, 1.9 Hz, 2H, Ar*H*), 6.39–6.17 (m, 3H, CH_{sorbyl}), 3.35 (t, *J* = 2.9 Hz, 1H, C*H*), 3.11 (dd, *J* = 10.8, 5.2 Hz, 1H, CH_2), 2.97 (ddd, *J* = 13.5, 10.8, 2.7 Hz, 1H, C*H*), 1.91 (d, *J* = 6.3 Hz, 3H, CH_3), 1.87 (dd, *J* = 5.2, 3.0 Hz, 1H, CH_2), 1.54–1.42 (m, 2H, CH_2), 0.96 (t, *J* = 7.4 Hz, 3H, CH_3), 0.92 (s, 3H, CH_3). ^{13}**C-NMR** (75 MHz, $CDCl_3$): δ = 212.5, 198.1, 166.8, 142.4, 141.4, 139.8, 131.0, 128.8 (2C), 128.5 (2C), 127.6, 118.3, 111.7, 77.3, 64.8, 50.0, 37.7, 32.3, 29.1, 19.1, 10.7, 6.8. **HRMS** (ESI) *m/z*: $[M+Na]^+$ calcd for $C_{23}H_{26}O_4Na$ 389.1723, found 389.1716.[31]

1,3-Diethylsaturnispol C (101e)



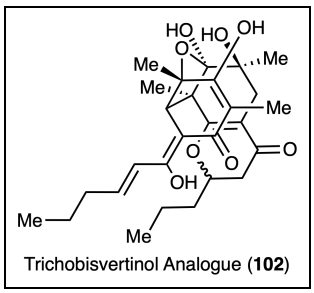
1,3-Diethylsaturnispol C (**101e**)

SMILES: O[C@@]1(CC)[C@@H]2/C(C([C@@](C1=O)(CC)[C@@H](C3=CC=CC=C3)C2)=O)=C(/C=C/C=C/C)O

Total synthesis: Synthesized chemo-enzymatically using the heterologous expressed monooxygenase SorbC together with 3,5-diethylsorbicillin (**90**) and styrol.[31]

Analytics: Pale yellow oil. **ORD**: $[\alpha]_D^{25} = -47.7$ (c = 0.6, $CHCl_3$). ^{1}**H-NMR** (300 MHz, $CDCl_3$): δ = 14.41 (bs, 1H, O*H*), 7.39 (dd, *J* = 14.9, 10.4 Hz, 1H, CH_{sorbyl}), 7.27–7.19 (m, 3H, Ar*H*), 6.94 (dd, *J* = 7.6, 2.0 Hz, 2H, Ar*H*), 6.43–6.15 (m, 3H, CH_{sorbyl}), 3.30 (t, *J* = 2.9 Hz, 1H, C*H*), 3.15 (dd, *J* = 10.8, 4.9 Hz, 1H, C*H*), 2.93 (ddd, *J* = 13.4, 10.8, 2.7 Hz, 1H, CH_2), 1.91 (d, *J* = 6.1 Hz, 3H, CH_3), 1.83 (ddd, *J* = 13.6, 4.9, 3.1 Hz, 1H, CH_2), 1.55–1.25 (m, 4H, CH_2), 0.94 (t, *J* = 7.4 Hz, 3H, CH_3), 0.90 (t, *J* = 7.3 Hz, 3H, CH_3). ^{13}**C-NMR** (75 MHz, $CDCl_3$): δ = 213.0, 198.2, 166.6, 142.1, 141.1, 139.6, 131.1, 128.7 (2C), 128.6 (2C), 127.6, 118.4, 111.9, 78.0, 68.3, 50.0, 38.3, 31.4, 28.5, 20.1, 19.0, 9.3, 6.8. **HRMS** (ESI) *m/z*: $[M-H]^-$ calcd for $C_{24}H_{27}O_4Na$ 379.1915, found 379.1921.[31]

Trichobisvertinol Analogue (102)



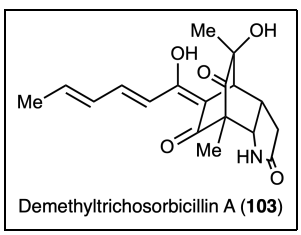
Trichobisvertinol Analogue (**102**)

SMILES: O=C1C(C)=C(O)[C@@]2(C)O[C@@]3(O)[C@](O)(C)CC(C4=O)=C(OC(CCC)C4)[C@@]3(C)[C@@H]2/C1=C(\C=C\CCC)O

Total synthesis: Synthesized chemo-enzymatically using the heterologous expressed monooxygenase SorbC together with (*E*)-1-(2,4-dihydroxy-3,5-dimethylphenyl)hex-2-en-1-one (87h).[31]

Analytics: Pale yellow oil. **ORD**: $[\alpha]_D^{25} = -50.9$ (c = 0.4, MeOH). ^{1}**H-NMR** (600 MHz, CD_3OD): δ = 6.79 (dt, *J* = 14.7, 7.2 Hz, 1H, C*H*), 6.47 (d, *J* = 15.1 Hz, 1H, C*H*), 4.11 (ddt, *J* = 15.3, 9.6, 3.2 Hz, 1H, C*H*), 3.69 (s, 1H, C*H*), 2.48 (d, *J* = 15.8 Hz, 1H, CH_2), 2.31–2.26 (m, 3H, CH_2), 2.23 (dd, *J* = 16.8, 3.1 Hz, 1H, CH_2), 2.09–2.01 (m, 1H, CH_2), 1.62–1.59 (m, 1H, CH_2), 1.59 (s, 3H, CH_3), 1.54 (p, *J* = 7.0 Hz, 2H, CH_2), 1.49–1.47 (m, 2H, CH_2), 1.46 (s, 3H, CH_3), 1.34–1.31 (m, 1H, CH_2), 1.30 (s, 3H, CH_3), 1.17 (s, 3H, CH_3), 0.97 (t, *J* = 7.4 Hz, 3H, CH_3), 0.93 (t, *J* = 7.3 Hz, 3H, CH_3). ^{13}**C-NMR** (150 MHz, CD_3OD): δ = 194.7, 193.8, 178.2, 171.6, 168.2, 142.1, 123.7, 109.8, 108.6, 107.8, 101.7, 80.2, 79.8, 74.1, 57.9, 53.7, 42.2, 38.1, 36.0, 34.2, 26.6, 23.0, 22.2, 19.25, 19.24, 14.02, 14.00, 7.8. **HRMS** (ESI) *m/z*: $[M+Na]^+$ calcd for $C_{28}H_{38}O_8Na$ 525.2464, found 525.2459.[31]

Demethyltrichosorbicillin A (103)



Demethyltrichosorbicillin A (**103**)

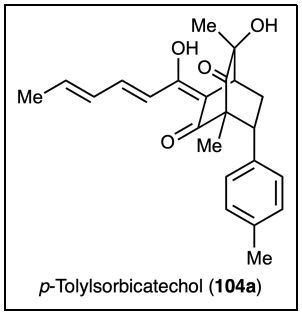
SMILES: O[C@@]1(C)[C@@H]2/C(C([C@@](C1=O)(C)C(N3)[C@H]2CC3=O)=O)=C(/C=C/C=C/C)O

Total synthesis: Synthesized chemo-enzymatically using the heterologous expressed monooxygenase SorbC together with sorbicillin (**1a**) and 1-methyl-1,5-dihydro-2*H*-pyrrol-2-one.[31]

Analytics: Yellow solid. **ORD**: $[\alpha]_D^{25} = +139.8$ (c = 0.2, MeOH). ^{1}**H-NMR** (600 MHz, CD_3OD): δ = 7.36 (dd, *J* = 14.9, 11.0 Hz, 1H, CH_{sorbyl}), 6.45–6.38 (m, 2H, CH_{sorbyl}), 6.28–6.21 (m, 1H, CH_{sorbyl}), 3.89 (d, *J* = 9.5 Hz, 1H, C*H*), 3.61–3.55 (m, 1H, CH_2), 3.19 (d, *J* = 2.9 Hz, 1H, C*H*), 2.67 (dd, *J* = 18.0, 11.0 Hz, 1H, CH_2), 1.99 (dd, *J* = 18.1, 4.2 Hz, 1H, CH_2), 1.90 (d, *J* = 6.9 Hz, 3H, CH_3), 1.21 (s, 3H,

CH_3), 1.19 (s, 3H, CH_3). ^{13}**C-NMR** (150 MHz, CD_3OD): δ = 209.9, 198.4, 180.0, 170.8, 144.4, 141.0, 132.3, 119.1, 108.4, 75.3, 66.8, 63.2, 47.2, 35.4, 31.8, 24.2, 18.9, 10.2. **HRMS** (ESI) *m/z*: $[M+Na]^+$ calcd for $C_{18}H_{21}O_5Na$ 354.1317, found 354.1314.[31]

p-Tolylsorbicatechol (104a)



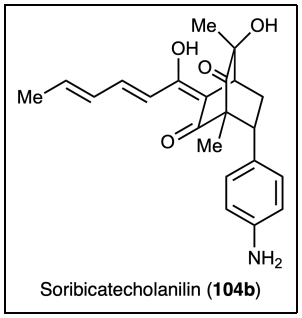
p-Tolylsorbicatechol (**104a**)

SMILES: O[C@@]1(C)[C@@H]2/C(C([C@@]([C@@]1=O)(C)[C@@H](C3=CC=C(C)C=C3)C2)=O)=C(/C=C/C=C/C)O

Total synthesis: Synthesized chemo-enzymatically using the heterologous expressed monooxygenase SorbC together with sorbicillin (1a) and the corresponding vinyl species.[107]

Analytics: Yellow solid. **ORD**: $[\alpha]_D^{25}$ =-35.1 (c = 0.2, MeOH). ^{1}**H-NMR** (500 MHz, $CDCl_3$): δ = 14.31 (bs, 1H, O*H*), 7.38 (dd, *J* = 15.0, 10.9 Hz, 1H, CH_{sorbyl}), 7.06 (d, *J* = 8.0 Hz, 2H, Ar*H*), 6.84 (d, *J* = 8.1 Hz, 2H, Ar*H*), 6.44–6.16 (m, 3H, CH_{sorbyl}), 3.29 (t, *J* = 2.9 Hz, 1H, C*H*), 3.09 (dd, *J* = 10.7, 5.7 Hz, 1H, C*H*), 3.00 (ddd, *J* = 13.6, 10.7, 3.0 Hz, 1H, CH_2), 2.29 (s, 3H), 1.91 (d, *J* = 6.7 Hz, 3H, CH_3), 1.85 (ddd, *J* = 13.4, 5.7, 2.8 Hz, 1H, CH_2), 1.26 (s, 3H, CH_3), 0.90 (s, 3H, CH_3). ^{13}**C-NMR** (125 MHz, $CDCl_3$): δ = 211.9, 197.9, 167.2, 142.5, 139.9, 138.4, 137.2, 131.0, 129.5, 129.5, 128.3, 128.3, 118.2, 112.2, 74.9, 64.9, 47.6, 40.6, 31.4, 24.5, 21.1, 19.1, 10.7. *m/z*: $[M+H]^+$ calcd for $C_{23}H_{27}O_4$ 367.1904, found 367.1905.[107]

Soribicatecholanilin (104b)



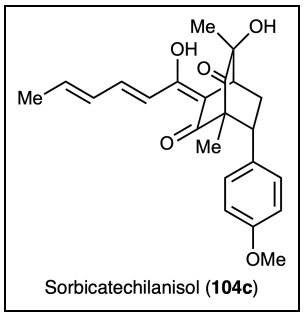
Soribicatecholanilin (**104b**)

SMILES: O[C@@]1(C)[C@@H]2/C(C([C@@]([C@@]1=O)(C)[C@@H](C3=CC=C(N)C=C3)C2)=O)=C(/C=C/C=C/C)O

Total synthesis: Synthesized chemo-enzymatically using the heterologous expressed monooxygenase SorbC together with sorbicillin (1a) and the corresponding vinyl species.[107]

Analytics: Yellow solid. **ORD**: $[\alpha]_D^{25}$ =-9.2 (c = 0.6, MeOH). ^{1}**H-NMR** (500 MHz, CD_3OD): δ = 7.39 (dd, *J* = 14.9, 11.0 Hz, 1H, CH_{sorbyl}), 7.30 (d, *J* = 8.6 Hz, 2H, Ar*H*), 7.17 (d, *J* = 8.6 Hz, 2H, Ar*H*), 6.49 (d, *J* = 15.0 Hz, 1H, CH_{sorbyl}), 6.43 (dd, *J* = 15.0, 11.0 Hz, 1H, CH_{sorbyl}), 6.25 (dd, *J* = 14.8, 7.1 Hz, 1H, CH_{sorbyl}), 3.36–3.33 (m, 1H, C*H*), 3.29 (d, *J* = 6.2 Hz, 1H, C*H*), 3.05 (ddd, *J* = 13.7, 10.6, 3.1 Hz, 1H, CH_2), 1.90 (d, *J* = 6.8 Hz, 3H, CH_3), 1.82 (ddd, *J* = 13.5, 6.1, 2.7 Hz, 1H, CH_2), 1.23 (s, 3H, CH_3), 0.79 (s, 3H, CH_3). ^{13}**C-NMR** (125 MHz, CD_3OD): δ = 210.6, 199.1, 168.4, 161.7, 161.4, 144.7, 143.8, 140.6, 132.3, 131.3, 131.2, 124.2, 119.5, 113.6, 75.1, 65.8, 47.3, 42.2, 32.6, 23.9, 18.9, 11.3. *m/z*: $[M+H]^+$ calcd for $C_{22}H_{25}NO_4$ 368.1856, found 368.1856.[107]

Sorbicatechilanisol (104c)



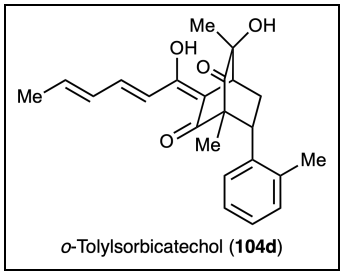
Sorbicatechilanisol (**104c**)

SMILES: O[C@@]1(C)[C@@H]2/C(C([C@@]([C@@]1=O)(C)[C@@H](C3=CC=C(OC)C=C3)C2)=O)=C(/C=C/C=C/C)O

Total synthesis: Synthesized chemo-enzymatically using the heterologous expressed monooxygenase SorbC together with sorbicillin (1a) and the corresponding vinyl species.[107]

Analytics: Yellow solid. **ORD**: $[\alpha]_D^{25}$ =-66.2 (c = 0.3, MeOH). ^{1}**H-NMR** (500 MHz, $CDCl_3$): δ = 14.31 (bs, 1H, O*H*), 7.38 (dd, *J* = 15.0, 10.8 Hz, 1H, CH_{sorbyl}), 6.88 (d, *J* = 8.7 Hz, 2H, Ar*H*), 6.79 (d, *J* = 8.7 Hz, 2H, Ar*H*), 6.39–6.17 (m, 3H, CH_{sorbyl}), 3.76 (s, 3H, OCH_3), 3.28 (t, *J* = 2.9 Hz, 1H, C*H*), 3.09 (dd, *J* = 10.8, 5.5 Hz, 1H, C*H*), 3.00 (ddd, *J* = 13.5, 10.7, 2.9 Hz, 1H, CH_2), 1.91 (d, *J* = 6.7 Hz, 3H), 1.84 (ddd, *J* = 13.3, 5.6, 2.8 Hz, 1H, CH_2), 1.26 (s, 3H, CH_3), 0.90 (s, 3H, CH_3). ^{13}**C-NMR** (125 MHz, $CDCl_3$): δ = 211.9, 197.9, 167.2, 158.9, 142.6, 139.9, 133.4, 131.0, 129.5, 129.5, 118.2, 114.1, 114.1, 112.1, 74.9, 65.1, 55.4, 47.3, 40.6, 31.5, 24.5, 19.1, 10.7. *m/z*: $[M+H]^+$ calcd for $C_{23}H_{27}O_5$ 383.1853, found 383.1854.[107]

o–Tolylsorbicatechol (104d)



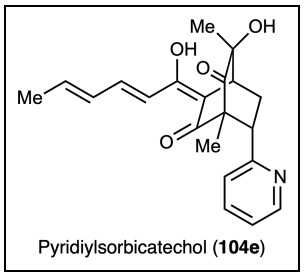
o-Tolylsorbicatechol (**104d**)

SMILES: O[C@@]1(C)[C@@H]2/C(C([C@@](C1=O)(C)[C@@H](C3=CC=CC=C3C)C2)=O)=C(/C=C/C=C/C)O

Total synthesis: Synthesized chemo-enzymatically using the heterologous expressed monooxygenase SorbC together with sorbicillin (1a) and the corresponding vinyl species.[107]

Analytics: Yellow solid. **ORD**: $[\alpha]_D^{25}$ =+84.2 (c = 0.3, MeOH). ^{1}**H-NMR** (600 MHz, $CDCl_3$): δ = 14.39 (bs, 1H, O*H*), 7.38 (dd, *J* = 14.9, 10.8 Hz, 1H, CH_{sorbyl}), 7.15–7.07 (m, 3H, Ar*H*), 6.87 (d, *J* = 7.7 Hz, 1H, CH_{sorbyl}), 6.37–6.19 (m, 3H, Ar*H*, CH_{sorbyl}), 3.56 (dd, *J* = 10.6, 6.5 Hz, 1H, C*H*), 3.29 (t, *J* = 2.6 Hz, 1H, C*H*), 3.01 (ddd, *J* = 13.5, 10.8, 3.0 Hz, 1H, CH_2), 2.29 (s, 3H, CH_3), 1.91 (d, *J* = 7.0 Hz, 3H, CH_3), 1.77 (ddd, *J* = 13.4, 6.6, 2.3 Hz, 1H, CH_2), 1.28 (s, 3H, CH_3), 0.94 (s, 3H, CH_3). ^{13}**C-NMR** (150 MHz, $CDCl_3$): δ = 211.6, 198.0, 167.3, 142.6, 140.4, 139.9, 136.4, 131.0, 130.5, 127.1, 127.0, 127.0, 118.2, 112.2, 74.8, 65.1, 41.2, 40.5, 32.0, 24.5, 20.4, 19.1, 9.7. *m/z*: $[M+H]^+$ calcd for $C_{23}H_{27}O_4$ 367.1904, found 367.1902.[107]

Pyridiylsorbicatechol (104e)



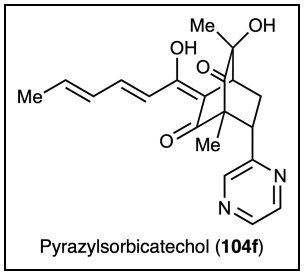
Pyridiylsorbicatechol (**104e**)

SMILES: O[C@@]1(C)[C@@H]2/C(C([C@@](C1=O)(C)[C@@H](C3=CC=CC=N3)C2)=O)=C(/C=C/C=C/C)O

Total synthesis: Synthesized chemo-enzymatically using the heterologous expressed monooxygenase SorbC together with sorbicillin (1a) and the corresponding vinyl species.[107]

Analytics: Yellow solid. **ORD**: $[\alpha]_D^{25}$ =+52.6 (c = 0.5, MeOH). ^{1}**H-NMR** (500 MHz, $CDCl_3$): δ = 14.25 (bs, 1H, O*H*), 8.77 (d, *J* = 4.1 Hz, 1H, Ar*H*), 8.14 (t, *J* = 7.5 Hz, 1H, Ar*H*), 7.67–7.65 (m, 1H, Ar*H*), 7.41 (dd, *J* = 14.8, 10.6 Hz, 1H, CH_{sorbyl}), 7.35 (d, *J* = 7.9 Hz, 1H, CH_{sorbyl}), 6.36–6.23 (m, 3H, Ar*H*, CH_{sorbyl}), 4.00 (dd, *J* = 10.2, 5.3 Hz, 1H, C*H*), 3.39–3.37 (m, 1H, CH_2), 3.23 (t, *J* = 11.6 Hz, 1H, C*H*), 1.92 (d, *J* = 6.4 Hz, 3H, CH_3), 1.87–1.83 (m, 1H, CH_2), 1.31 (s, 3H, CH_3), 0.97 (s, 3H, CH_3). ^{13}**C-NMR** (125 MHz, $CDCl_3$): δ = 208.0, 195.9, 168.8, 158.5, 143.9, 143.7, 143.6, 141.2, 131.0, 124.8, 124.7, 117.7, 111.8, 74.5, 63.2, 44.4, 40.6, 30.8, 24.2, 19.2, 10.4. *m/z*: $[M+H]^+$ calcd for $C_{21}H_{24}NO_4$ 354.1700, found 354.1701.[107]

Pyrazylsorbicatechol (104f)



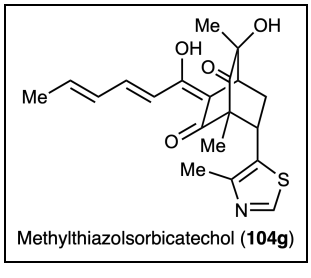
Pyrazylsorbicatechol (**104f**)

SMILES: O[C@@]1(C)[C@@H]2/C(C([C@@](C1=O)(C)[C@@H](C3=CN=CC=N3)C2)=O)=C(/C=C/C=C/C)O

Total synthesis: Synthesized chemo-enzymatically using the heterologous expressed monooxygenase SorbC together with sorbicillin (1a) and the corresponding vinyl species.[107]

Analytics: Yellow solid. **ORD**: $[\alpha]_D^{25}$ =+25.0 (c = 0.5, MeOH). ^{1}**H-NMR** (500 MHz, $CDCl_3$): δ = 14.10 (bs, 1H, O*H*), 8.57 (s, 1H, Ar*H*), 8.43 (d, *J* = 2.5 Hz, 1H, Ar*H*), 8.33 (d, *J* = 1.6 Hz, 1H, Ar*H*), 7.36 (dd, *J* = 14.9, 10.8 Hz, 1H, CH_{sorbyl}), 6.38–6.16 (m, 3H, Ar*H*, CH_{sorbyl}), 3.37 (dd, *J* = 10.5, 6.0 Hz, 1H, C*H*), 3.33 (t, *J* = 3.0 Hz, 1H, C*H*), 2.94 (ddd, *J* = 13.4, 10.5, 3.2 Hz, 1H, CH_2), 2.05 (ddd, *J* = 13.1, 6.1, 2.7 Hz, 1H, CH_2), 1.91 (d, *J* = 6.7 Hz, 3H, CH_3), 1.30 (s, 3H, CH_3), 0.93 (s, 3H, CH_3). ^{13}**C-NMR** (125 MHz, $CDCl_3$): δ = 210.7, 196.4, 167.0, 157.1, 145.4, 143.7, 142.4, 142.3, 139.7, 131.0, 118.2, 111.9, 74.9, 63.5, 45.7, 40.5, 29.4, 24.4, 19.1, 10.7. *m/z*: $[M+H]^+$ calcd for $C_{20}H_{23}N_2O_4$ 355.1652, found 355.1652.[107]

Methylthiazolsorbicatechol (104g)



Methylthiazolsorbicatechol (**104g**)

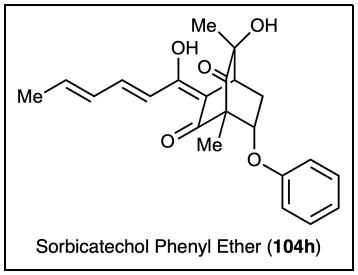
SMILES: O[C@@]1(C)[C@@H]2/C(C([C@@](C1=O)(C)[C@@H](C3=C(C)N=CS3)C2)=O)=C(/C=C/C=C/C)O

Total synthesis: Synthesized chemo-enzymatically using the heterologous expressed monooxygenase SorbC together with sorbicillin (1a) and the corresponding vinyl species.[107]

Analytics: Yellow solid. **ORD**: $[\alpha]_D^{25}$ =+140.1 (c = 0.5, MeOH). ^{1}**H-NMR** (500 MHz, $CDCl_3$): δ = 14.32 (bs, 1H, O*H*), 8.97 (s, 1H, Ar*H*), 7.42 (dd, *J* = 14.8, 10.1 Hz, 1H, CH_{sorbyl}), 6.32–6.22 (m, 3H, CH_{sorbyl}), 3.60 (dd, J = *J* = 10.6, 4.8 Hz, 1H, C*H*), 3.27 (t, *J* = 2.9 Hz, 1H, C*H*), 3.16 (ddd, *J* = 13.4, 10.7, 2.5 Hz, 1H, CH_2), 2,45 (s, 3H, CH_3), 1.92 (d, *J* = 6.0 Hz, 3H, CH_3), 1.71 (ddd, *J* = 13.8, 4.9, 3.1 Hz, 1H, CH_2), 1.27 (s, 3H, CH_3), 1.01 (s, 3H, CH_3). ^{13}**C-NMR** (125 MHz, $CDCl_3$): δ = 210.5, 196.0,

169.0, 152.8, 147.7, 143.9, 141.2, 135.6, 130.9, 117.6, 111.4, 74.8, 64.7, 40.3, 39.8, 33.4, 24.5, 19.2, 14.3, 10.1. *m/z*: $[M+H]^+$ calcd for $C_{20}H_{24}NO_4S$ 374.1421, found 374.1422.[107]

Sorbicatechol Phenyl Ether (104h)



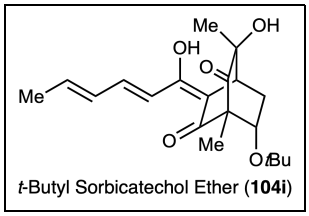
Sorbicatechol Phenyl Ether (**104h**)

SMILES: O[C@@]1(C)[C@@H]2/C(C([C@@](C1=O)(C)[C@@H](OC3=CC=CC=C3)C2)=O)=C(/C=C/C=C/C)O

Total synthesis: Synthesized chemo-enzymatically using the heterologous expressed monooxygenase SorbC together with sorbicillin (**1a**) and the corresponding vinyl species.[107]

Analytics: Yellow solid. **ORD**: $[\alpha]_D^{25}$ =+258.7 (c = 0.6, MeOH). ^{1}**H-NMR** (500 MHz, $CDCl_3$): δ = 14.01 (bs, 1H, O*H*), 7.32 (dd, *J* = 14.9, 10.8 Hz, 1H, CH_{sorbyl}), 7.26–7.22 (m, 2H, Ar*H*), 6.95 (t, *J* = 7.4 Hz, 1H, Ar*H*), 6.80 (d, *J* = 8.6 Hz, 2H, Ar*H*), 6.34-6.14 (m, 3H, CH_{sorbyl}), 4.42 (dd, *J* = 8.2, 2.1 Hz, 1H, C*H*), 3.21 (t, *J* = 2.8 Hz, 1H, C*H*), 3.01 (ddd, *J* = 14.1, 8.2, 2.4 Hz, 1H, CH_2), 1.89 (d, *J* = 6.6 Hz, 3H, CH_3), 1.79 (dt, *J* = 14.1, 3.0 Hz, 1H, CH_2), 1.37 (s, 3H, CH_3), 1.26 (s, 3H, CH_3). ^{13}**C-NMR** (125 MHz, $CDCl_3$): δ = 210.3, 195.9, 167.1, 157.0, 142.5 139.8, 130.9, 129.7, 129.7, 121.6, 117.9, 115.7, 115.7, 110.2, 77.3, 74.7, 66.4, 39.9, 31.0, 24.5, 19.1, 9.2. *m/z*: $[M+H]^+$ calcd for $C_{22}H_{24}O_5$ 369.1697, found 369.1695.[107]

***t*-Butyl Sorbicatechol Ether (104i)**



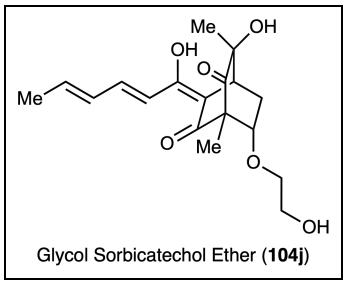
t-Butyl Sorbicatechol Ether (**104i**)

SMILES: O[C@@]1(C)[C@@H]2/C(C([C@@](C1=O)(C)[C@@H](OC(C)(C)C)C2)=O)=C(/C=C/C=C/C)O

Total synthesis: Synthesized chemo-enzymatically using the heterologous expressed monooxygenase SorbC together with sorbicillin (1a) and the corresponding vinyl species.[107]

Analytics: Yellow solid. **ORD**: $[\alpha]_D^{25}$ =+287.9 (c = 0.4, MeOH). ^{1}**H-NMR** (500 MHz, $CDCl_3$): δ = 14.00 (bs, 1H, O*H*), 7.31 (dd, *J* = 14.9, 10.7 Hz, 1H, CH_{sorbyl}), 6.30–6.14 (m, 3H, CH_{sorbyl}), 3.73 (dd, *J* = 8.5, 2.6 Hz, 1H, C*H*), 3.11 (t, *J* = 3.0 Hz, 1H, C*H*), 2.81 (ddd, *J* = 13.7, 8.5, 2.6 Hz, 1H, CH_2), 1.89 (d, *J* = 6.8 Hz, 3H, CH_3), 1.64 (dt, *J* = 13.7, 3.1 Hz, 1H, CH_2), 1.24 (s, 3H, CH_3), 1.19 (s, 3H, CH_3), 1.11 (s, 9H, (CH_3)$_3$). ^{13}**C-NMR** (125 MHz, $CDCl_3$): δ = 211.8, 197.0, 166.2, 141.8, 139.2, 131.0, 118.2, 110.7, 74.7, 72.2, 66.9, 40.0, 34.9, 28.6, 28.6, 28.6, 28.5, 24.4, 19.0, 9.6. *m/z*: $[M+H]^+$ calcd for $C_{20}H_{29}O_5$ 349.2010, found 349.2011.[107]

Glycol Sorbicatechol Ether (104j)



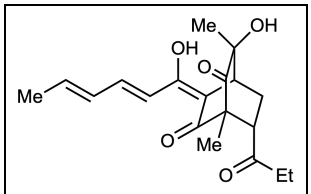
Glycol Sorbicatechol Ether (**104j**)

SMILES: O[C@@]1(C)[C@@H]2/C(C([C@@](C1=O)(C)[C@@H](OCCO)C2)=O)=C(/C=C/C=C/C)O

Total synthesis: Synthesized chemo-enzymatically using the heterologous expressed monooxygenase SorbC together with sorbicillin (1a) and the corresponding vinyl species.[107]

Analytics: Yellow solid. **ORD**: $[\alpha]_D^{25}$ =+342.9 (c = 0.3, MeOH). ^{1}**H-NMR** (500 MHz, $CDCl_3$): δ = 13.93 (bs, 1H, O*H*), 7.31 (dd, *J* = 14.9, 10.8 Hz, 1H, CH_{sorbyl}), 6.32–6.16 (m, 3H, CH_{sorbyl}), 3.69–3.59 (m, 4H, CH_2), 3.43 (ddd, *J* = 9.5, 5.7, 3.4 Hz, 1H, C*H*), 3.17 (t, *J* = 3.2 Hz, 1H, C*H*), 2.82 (ddd, *J* = 13.9, 8.3, 2.6 Hz, 1H, CH_2), 1.89 (d, *J* = 6.5 Hz, 3H, CH_3), 1.70 (dt, *J* = 13.8, 3.0 Hz, 1H, CH_2), 1.34 (s, 3H, CH_3), 1.21 (s, 3H, CH_3). ^{13}**C-NMR** (125 MHz, $CDCl_3$): δ = 210.5, 196.3, 166.9, 142.4, 139.8, 131.0, 117.9, 110.4, 80.0, 74.6, 71.4, 67.1, 61.9, 39.8, 30.5, 24.4, 19.1, 9.2. *m/z*: $[M+H]^+$ calcd for $C_{18}H_{25}O_6$ 337.1646, found 337.1646 .[107]

Propionalsorbicatechol (104k)



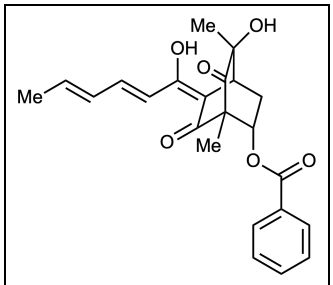
Propionalsorbicatechol (**104k**)

SMILES: O[C@@]1(C)[C@@H]2/C(C([C@@](C1=O)(C)[C@@H](C(CC)=O)C2)=O)=C(/C=C/C=C/C)O

Total synthesis: Synthesized chemo-enzymatically using the heterologous expressed monooxygenase SorbC together with sorbicillin (1a) and the corresponding vinyl species.[107]

Analytics: Yellow solid. **ORD**: $[\alpha]_D^{25}$ =+554.5 (c = 0.1, MeOH). ^{1}**H-NMR** (500 MHz, $CDCl_3$): δ = 14.08 (bs, 1H, O*H*), 7.30 (dd, *J* = 14.9, 10.7 Hz, 1H, CH_{sorbyl}), 6.29–6.13 (m, 3H, CH_{sorbyl}), 3.20 (t, *J* = 2.8 Hz, 1H, C*H*), 3.04 (dd, *J* = 10.9, 5.8 Hz, 1H, C*H*), 2.74 (ddd, *J* = 13.8, 11.0, 3.0 Hz, 1H, CH_2), 2.42 (dd, *J* = 11.4, 7.2 Hz, 2H, CH_2), 1.89 (d, *J* = 6.8 Hz, 3H, CH_3), 1.58 (ddd, *J* = 12.8, 5.8, 2.8 Hz, 1H, CH_2), 1.21 (s, 3H, CH_3), 1.20 (s, 3H, CH_3), 1.01 (t, *J* = 7.2 Hz, 3H, CH_3). ^{13}**C-NMR** (125 MHz, $CDCl_3$): δ = 210.6, 210.0, 196.4, 167.0, 142.3, 139.6, 131.0, 118.0, 110.8, 74.9, 61.7, 50.7, 40.3, 37.6, 26.3, 24.3, 19.0, 10.4, 7.5. *m/z*: $[M+H]^+$ calcd for $C_{19}H_{25}O_5$ 333.1697, found 333.1698 .[107]

Sorbicatechol Benzoate (104l)



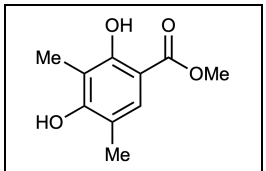
Sorbicatechol Benzoate (**104l**)

SMILES: O[C@@]1(C)[C@@H]2/C(C([C@@](C1=O)(C)[C@@H](OC(C3=CC=CC=C3)=O)C2)=O)=C(/C=C/C=C/C)O

Total synthesis: Synthesized chemo-enzymatically using the heterologous expressed monooxygenase SorbC together with sorbicillin (1a) and the corresponding vinyl species.[107]

Analytics: Yellow solid. **ORD**: $[\alpha]_D^{25}$ =+89.9 (c = 0.1, MeOH). ^{1}**H-NMR** (600 MHz, $CDCl_3$): δ = 14.06 (bs, 1H, O*H*), 7.93 (dd, *J* = 8.3, 1.2 Hz, 2H, Ar*H*), 7.56 (t, *J* = 7.5 Hz, 1H, Ar*H*), 7.47–7.40 (m, 2H, Ar*H*), 7.34 (dd, *J* = 14.8, 10.9 Hz, 1H, CH_{sorbyl}), 6.36–6.18 (m, 3H, CH_{sorbyl}), 5.27 (dd, *J* = 8.7, 2.4 Hz, 1H, C*H*), 3.22 (t, *J* = 2.8 Hz, 1H, C*H*), 3.14 (ddd, *J* = 14.7, 8.7, 2.4 Hz, 1H, CH_2), 1.90 (dd, *J* = 6.8, 1.4 Hz, 3H, CH_3), 1.72 (dt, *J* = 14.6, 3.0 Hz, 1H, CH_2), 1.32 (s, 3H, CH_3), 1.27 (s, 3H, CH_3). ^{13}**C-NMR** (150 MHz, $CDCl_3$): δ = 205.3, 197.0, 190.7, 165.5, 165.2, 148.0, 144.5, 130.3, 130.0, 130.0, 129.9, 129.2, 128.8, 128.8, 121.3, 74.5, 73.0, 67.6, 46.5, 27.2, 24.3, 19.3, 9.8. *m/z*: $[M+H]^+$ calcd for $C_{23}H_{25}O_6$ 397.1646, found 397.1646.[107]

Methyl 2,4-dihydroxy-3,5-dimethylbenzoate (106a)



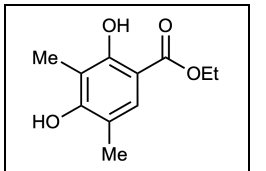
Methyl 2,4-dihydroxy-3,5-dimethylbenzoate (**106a**)

SMILES: OC1=C(C(OC)=O)C=C(C)C(O)=C1C

Total synthesis: Esterification of 2,4-dihydroxy-3,5-dimethylbenzoic acid.[139]

Analytics: White solid. **TLC**: R_f = 0.31 (*n*-pentane/EtOAc = 40:1). ^{1}**H-NMR** (300 MHz, $CDCl_3$): δ = 11.06 (s, 1H, O*H*), 7.49 (bs, 1H, Ar*H*), 3.90 (s, 3H, CH_3), 2.18 (d, *J* = 0.7 Hz, 3H, CH_3), 2.15 (s, 3H, CH_3). ^{13}**C-NMR** (75 MHz, $CDCl_3$): δ = 171.0, 160.0, 158.1, 128.7, 114.7, 110.1, 104.9, 52.1, 15.5, 7.9. *m/z*: $[M+H]^+$ calcd for $C_{10}H_{13}O_4$ 197.0808, found 197.0807.[139]

Ethyl 2,4-dihydroxy-3,5-dimethylbenzoate (106b)



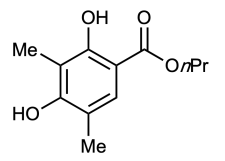
Ethyl 2,4-dihydroxy-3,5-dimethylbenzoate (**106b**)

SMILES: OC1=C(C(OCC)=O)C=C(C)C(O)=C1C

Total synthesis: Esterification of 2,4-dihydroxy-3,5-dimethylbenzoic acid.[139]

Analytics: White solid. **TLC**: R_f = 0.28 (*n*-pentane/EtOAc = 10:1). ^{1}**H-NMR** (300 MHz, $CDCl_3$): δ = 11.16 (bs, 1H, O*H*), 7.50 (bs, 1H, Ar*H*), 4.37 (q, *J* = 7.1 Hz, 2H, CH_2), 2.19 (d, *J* = 0.7 Hz, 3H, CH_3), 2.15 (s, 3H, CH_3), 1.40 (t, *J* = 7.1 Hz, 3H, CH_3). ^{13}**C-NMR** (75 MHz, $CDCl_3$): δ = 170.6, 160.0, 158.0, 128.7, 114.6, 110.1, 105.1, 61.1, 15.5, 14.5, 7.9. *m/z*: $[M+H]^+$ calcd for $C_{11}H_{15}O_4$ 211.0965, found 211.0965.[139]

Propyl 2,4-dihydroxy-3,5-dimethylbenzoate (106c)



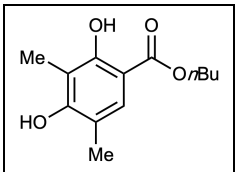
Propyl 2,4-dihydroxy-3,5-dimethylbenzoate (**106c**)

SMILES: OC1=C(C(OCCC)=O)C=C(C)C(O)=C1C

Total synthesis: Esterification of 2,4-dihydroxy-3,5-dimethylbenzoic acid.[139]

Analytics: White solid. **TLC**: R_f = 0.34 (*n*-pentane/EtOAc = 20:1). ^{1}**H-NMR** (300 MHz, $CDCl_3$): δ = 11.17 (s, 1H, O*H*), 7.49 (s, 1H, Ar*H*), 4.27 (t, *J* = 6.7 Hz, 2H, CH_2), 2.19 (d, *J* = 0.7 Hz, 3H, CH_3), 2.15 (s, 3H, CH_3), 1.75–1.84 (m, 2H, CH_2), 1.03 (t, *J* = 7.3 Hz, 3H, CH_3). ^{13}**C-NMR** (75 MHz, $CDCl_3$): δ = 170.7, 160.0, 158.0, 128.6, 114.6, 110.1, 105.1, 66.6, 22.2, 15.5, 10.6, 7.9. *m/z*: $[M+H]^+$ calcd for $C_{12}H_{17}O_4$ 225.1121, found 225.1120.[139]

Butyl 2,4-dihydroxy-3,5-dimethylbenzoate (106d)



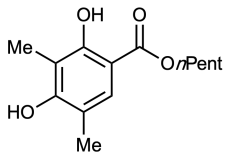
Butyl 2,4-dihydroxy-3,5-dimethylbenzoate (**106d**)

SMILES: OC1=C(C(OCCCC)=O)C=C(C)C(O)=C1C

Total synthesis: Esterification of 2,4-dihydroxy-3,5-dimethylbenzoic acid.[139]

Analytics: White solid. **TLC**: R_f = 0.80 (*n*-pentane/EtOAc = 3:1). ^{1}**H-NMR** (300 MHz, $CDCl_3$): δ = 11.17 (s, 1H, O*H*), 7.48 (bs, 1H, Ar*H*), 4.31 (t, *J* = 6.7 Hz, 2H, CH_2), 2.19 (d, *J* = 0.7 Hz, 3H, CH_3), 2.15 (s, 3H, CH_3), 1.69–1.81 (m, 2H, CH_2), 1.40–1.54 (m, 2H, CH_2), 0.98 (t, *J* = 7.4 Hz, 3H, CH_3). ^{13}**C-NMR** (75 MHz, $CDCl_3$): δ = 170.6, 160.0, 158.0, 128.6, 114.6, 110.1, 105.1, 64.9, 30.9, 19.4, 15.5, 13.9, 7.9. *m/z*: $[M+H]^+$ calcd for $C_{13}H_{19}O_4$ 239.1278, found 239.1278.[139]

Pentyl 2,4-dihydroxy-3,5-dimethylbenzoate (106e)



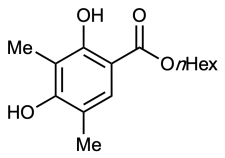
Pentyl 2,4-dihydroxy-3,5-dimethylbenzoate (**106e**)

SMILES: OC1=C(C(OCCCCC)=O)C=C(C)C(O)=C1C

Total synthesis: Esterification of 2,4-dihydroxy-3,5-dimethylbenzoic acid.[139]

Analytics: White solid. **TLC**: R_f = 0.33 (*n*-pentane/EtOAc = 20:1). ^{1}**H-NMR** (300 MHz, $CDCl_3$): δ = 11.17 (s, 1H, O*H*), 7.48 (bs, 1H, Ar*H*), 4.30 (t, *J* = 6.8 Hz, 2H, CH_2), 2.19 (d, *J* = 0.7 Hz, 3H, CH_3), 2.15 (s, 3H, CH_3), 1.71–1.83 (m, 2H, CH_2), 1.35–1.45 (m, 4H, CH_2), 0.90–0.96 (m, 3H, CH_3). ^{13}**C-NMR** (75 MHz, $CDCl_3$): δ = 170.7, 160.0, 158.0, 128.6, 114.6, 110.1, 105.1, 65.2, 28.5, 28.3, 22.5, 15.5, 14.1, 7.9. *m/z*: $[M+H]^+$ calcd for $C_{14}H_{21}O_4$ 253.1434, found 253.1437.[139]

Hexyl 2,4-dihydroxy-3,5-dimethylbenzoate (106f)



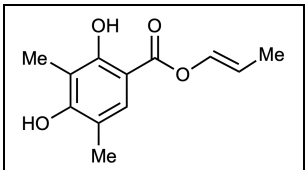
Hexyl 2,4-dihydroxy-3,5-dimethylbenzoate (**106f**)

SMILES: OC1=C(C(OCCCCCC)=O)C=C(C)C(O)=C1C

Total synthesis: Esterification of 2,4-dihydroxy-3,5-dimethylbenzoic acid.[139]

Analytics: White solid. **TLC**: R_f = 0.38 (*n*-pentane/EtOAc = 30:1). ^{1}**H-NMR** (300 MHz, $CDCl_3$): δ = 11.17 (s, 1H, O*H*), 7.48 (bs, 1H, Ar*H*), 4.30 (t, *J* = 6.8 Hz, 2H, CH_2), 2.19 (d, *J* = 0.7 Hz, 3H, CH_3), 2.15 (s, 3H, CH_3), 1.71–1.82 (m, 2H, CH_2), 1.30–1.48 (m, 6H, CH_2), 0.87–0.94 (m, 3H, CH_3). ^{13}**C-NMR** (75 MHz, $CDCl_3$): δ = 170.7, 160.0, 158.0, 128.6, 114.6, 110.1, 105.2, 65.2, 31.6, 28.8, 25.8, 22.7, 15.5, 14.2, 7.9. *m/z*: $[M+H]^+$ calcd for $C_{15}H_{23}O_4$ 267.1591, found 267.1596.[139]

(*E*)-Prop-1-en-1-yl 2,4-dihydroxy3,5-dimethylbenzoate (106g)



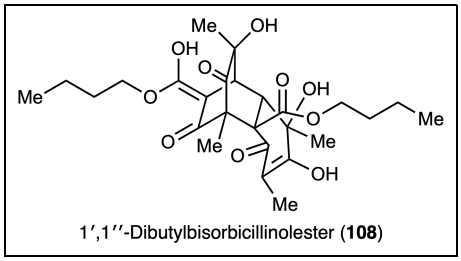
(*E*)-Prop-1-en-1-yl 2,4-dihydroxy-3,5-dimethylbenzoate (**106g**)

SMILES: OC1=C(C(O/C=C/C)=O)C=C(C)C(O)=C1C

Total synthesis: Esterification of 2,4-dihydroxy-3,5-dimethylbenzoic acid.[139]

Analytics: White solid. **TLC**: R_f = 0.29 (*n*-pentane/EtOAc = 20:1). ^{1}**H-NMR** (300 MHz, $CDCl_3$): δ = 11.11 (s, 1H, O*H*), 7.51 (bs, 1H, Ar*H*), 5.81–5.95 (m, 1H, C*H*), 5.63–5.76 (m, 1H, C*H*), 4.74 (dt, *J* = 6.3, 1.2 Hz, 2H, CH_2), 2.18 (d, *J* = 0.7 Hz, 3H, CH_3), 2.14 (s, 3H, CH_3), 1.76 (dq, *J* = 6.4, 1.2 Hz, 3H, CH_3). ^{13}**C-NMR** (75 MHz, $CDCl_3$): δ = 170.4, 160.0, 158.1, 131.9, 128.7, 125.0, 114.6, 110.1, 105.0, 65.7, 18.0, 15.5, 7.9. *m/z*: $[M+H]^+$ calcd for $C_{13}H_{17}O_4$ 237.1121, found 237.1125.[139]

1′,1′′-Dibutylbisorbicillinolester (108)

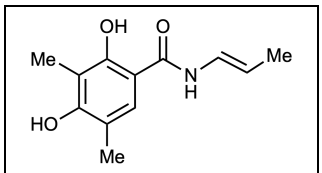

1′,1′′-Dibutylbisorbicillinolester (**108**)

SMILES: O[C@@]1(C)[C@@H]2/C(C([C@@](C1=O)(C)[C@]3(C(OCCCC)=O)[C@H]2[C@@](O)(C)C(O)=C(C)C3=O)=O)=C(OCCCC)\O

Total synthesis: Synthesized chemo-enzymatically using the heterologous expressed monooxygenase SorbC together with **100d**.[139]

Analytics: Yellow solid. **ORD**: $[\alpha]_D^{25} = -56.8$ (MeOH). ^{1}**H-NMR** (600 MHz, CD_3OD): δ = 4.19 (td, *J* = 6.5, 2.5 Hz, 2H, CH_2), 4.14–4.18 (m, 1H, CH_2), 4.03–4.08 (m, 1H, CH_2), 3.68 (d, *J* = 2.9 Hz, 1H, C*H*), 3.40 (d, *J* = 2.9 Hz, 1H, C*H*), 1.67–1.71 (m, 2H, CH_2), 1.67 (s, 3H, CH_3), 1.58–1.64 (m, 2H, CH_2), 1.49 (s, 3H, CH_3), 1.44–1.48 (m, 2H, CH_2), 1.37–1.43 (m, 2H, CH_2), 1.34 (s, 3H, CH_3), 1.22 (s, 3H, CH_3), 0.98 (t, *J* = 7.4 Hz, 3H, CH_3), 0.93 (t, *J* = 7.4 Hz, 3H, CH_3). ^{13}**C-NMR** (150 MHz, CD_3OD): δ = 205.6 (3C), 172.0, 170.2, 169.8, 109.8, 103.5, 72.1, 71.2, 66.5, 65.5, 64.2, 60.3, 48.0, 42.6, 33.0, 31.9, 31.5, 25.3, 20.3, 20.2, 14.0, 13.9, 10.4, 9.3. **HRMS** (ESI) *m/z*: $[M+Na]^+$ calcd for $C_{26}H_{37}O_{10}$ 509.2387, found 509.2380.[139]

(*E*)-2,4-Dihydroxy-3,5-dimethyl-*N*-(prop-1-en-1-yl)benzamide (109)

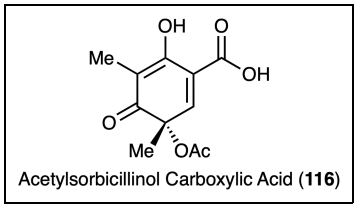

(*E*)-2,4-Dihydroxy-3,5-dimethyl-*N*-(prop-1-en-1-yl)benzamide (**109**)

SMILES: OC1=C(C(N/C=C/C)=O)C=C(C)C(O)=C1C

Total synthesis: Synthesized through peptide coupling between 2,4-dihydroxy-3,5-dimethylbenzoic acid and butyl amine using oxalyl chloride.[140]

Analytics: Colorless oil. ^{1}**H-NMR** (400 MHz, $CDCl_3$): δ = 12.77 (s, 1H, O*H*), 6.95 (s, 1H, N*H*), 6.07 (s, 1H, Ar*H*), 5.02 (s, 1H, O*H*), 3.43 (q, *J* = 6.6 Hz, 2H, CH_2), 2.19 (s, 3H, CH_3), 2.14 (s, 3H, CH_3), 1.60 (m, 2H, CH_2), 1.41 (q, *J* = 7.5 Hz, 2H, CH_2), 0.96 (t, *J* = 7.3 Hz 3H, CH_3). ^{13}**C-NMR** (100 MHz, $CDCl_3$): δ = 170.2, 159.7, 156.5, 123.9, 113.8, 110.8, 106.7, 39.3, 31.6, 20.1, 15.6, 13.7, 7.6. **IR**: *ν* 3390, 2924, 1735, 1635, 1590, 1370 cm^{-1}. **HRMS** (ESI) *m/z*: $[M+H]^+$ calcd for $C_{13}H_{20}NO_3$ 238.1438, found 238.1432.[140]

Acetylsorbicillinol Carboxylic Acid (116)

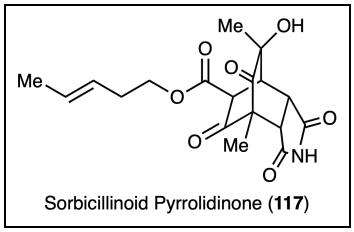

Acetylsorbicillinol Carboxylic Acid (**116**)

SMILES: OC1=C(C)C([C@@](C)(OC(C)=O)C=C1C(O)=O)=O

Total synthesis: Deprotection of **100g** with palladium catalyst and morpholine.[140]

Analytics: Colorless solid. **MP**: 87-90 °C.^{1}**H-NMR** (600 MHz, CD_3OD): δ = 7.55 (s, 1H, Ar*H*), 2.07 (s, 3H, CH_3), 1.78 (s, 3H, CH_3), 1.44 (s, 3H, CH_3). ^{13}**C-NMR** (150 MHz, CD_3OD): δ = 169.3, 169.3,152.5, 119.3, 110.0, 110.0, 77.4, 56.03, 22.9, 18.8, 5.77. **IR**: *ν* 3263, 2945, 1710, 1650, 1614, 1347 cm^{-1}. **HRMS** (ESI) *m/z*: $[M+H]^+$ calcd for $C_{11}H_{13}O_6$ 241.0707, found 241.0706.[140]

Sorbicillinoid Pyrrolidinone (117)


Sorbicillinoid Pyrrolidinone (**117**)

SMILES: O[C@@]1(C)[C@@H]2[C@H](C(OCC/C=C/C)=O)C([C@@](C1=O)(C)C(C3=O)[C@H]2C(N3)=O)=O

Total synthesis: Chemo-enzymatic approach using maleimide as dienophile.[140]

Analytics: Yellow oil. **ORD**: $[\alpha]_D^{25} = +62.0$ (c = 0.1, MeCN). ^{1}**H-NMR** (600 MHz, $CDCl_3$): δ = 11.60 (s, 1H, O*H*), 8.20 (s, 1H, N*H*), 5.83 (dq, *J* = 13.4, 6.5 Hz, 1H, C*H*), 5.59 (dd, *J* = 14.7, 7.4 Hz, 1H, C*H*), 4.67 (dd, *J* = 12.6, 6.4 Hz, 1H, CH_2), 4.60 (m, 1H, CH_2), 3.87 (d, *J* = 3.3 Hz, 1H, C*H*), 3.76 (dd, *J* = 8.5, 3.2 Hz, 1H, C*H*), 2.94 (d, *J* = 8.4 Hz, 1H, C*H*), 1.74 (d, *J* = 6.6 Hz, 3H, CH_3), 1.58 (s, 3H, CH_3), 1.31 (s, 3H, CH_3). ^{13}**C-NMR** (150 MHz, $CDCl_3$): δ = 207.8, 176.6, 173.7, 168.6, 168.5, 132.0, 124.2, 100.0, 71.9, 65.9, 54.2, 47.0, 42.1, 41.3, 24.5, 17.8, 9.5. **IR**: *ν* 2928, 1737, 1705, 1622, 1412, 1378 cm^{-1}. **HRMS** (ESI) *m/z*: $[M+Na]^+$ calcd for $C_{17}H_{19}NO_7Na$ 372.1054, found 372.1048.[140]

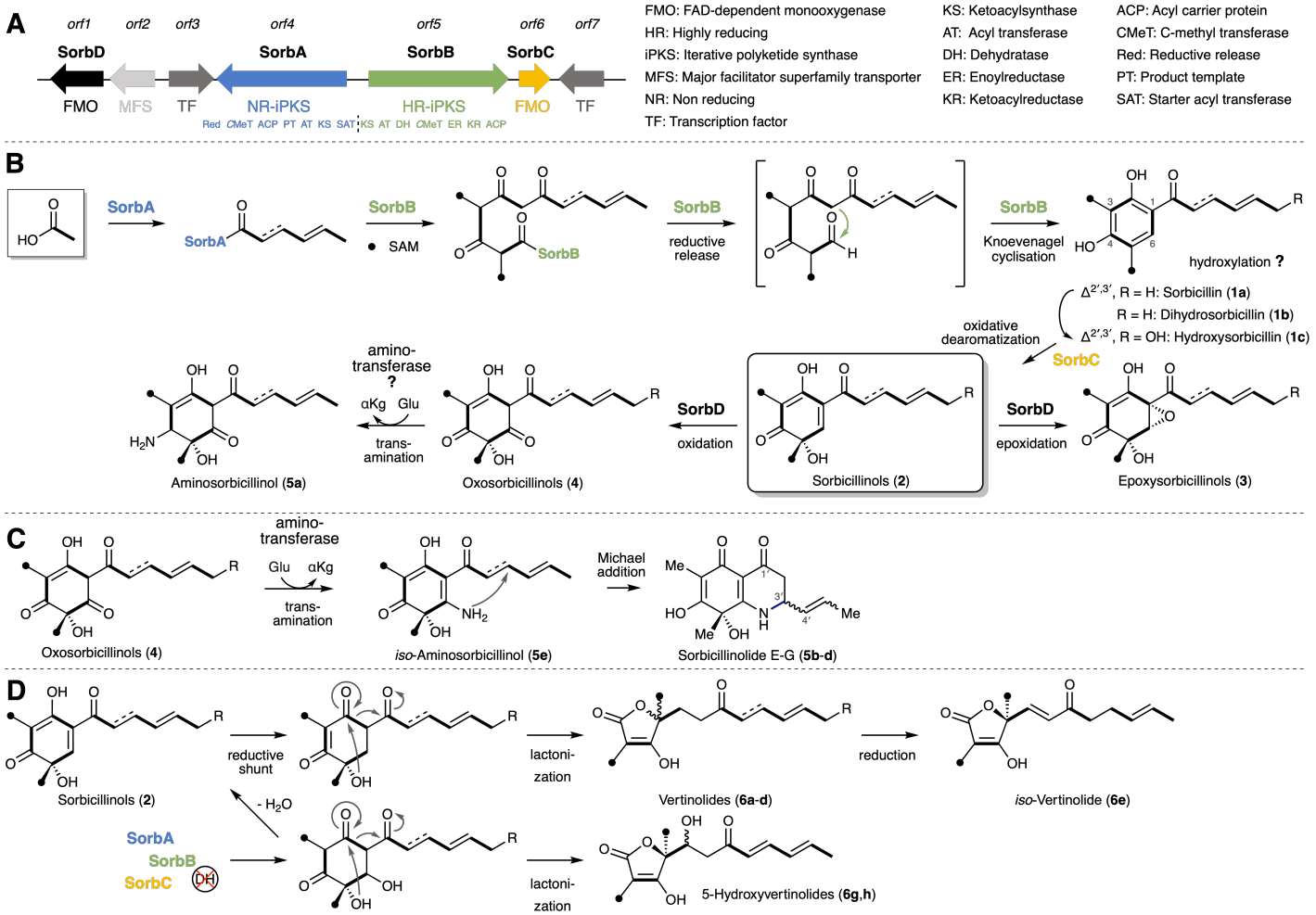


Fig. S1 Detailed biosynthesis of the monomeric sorbicillinoids.

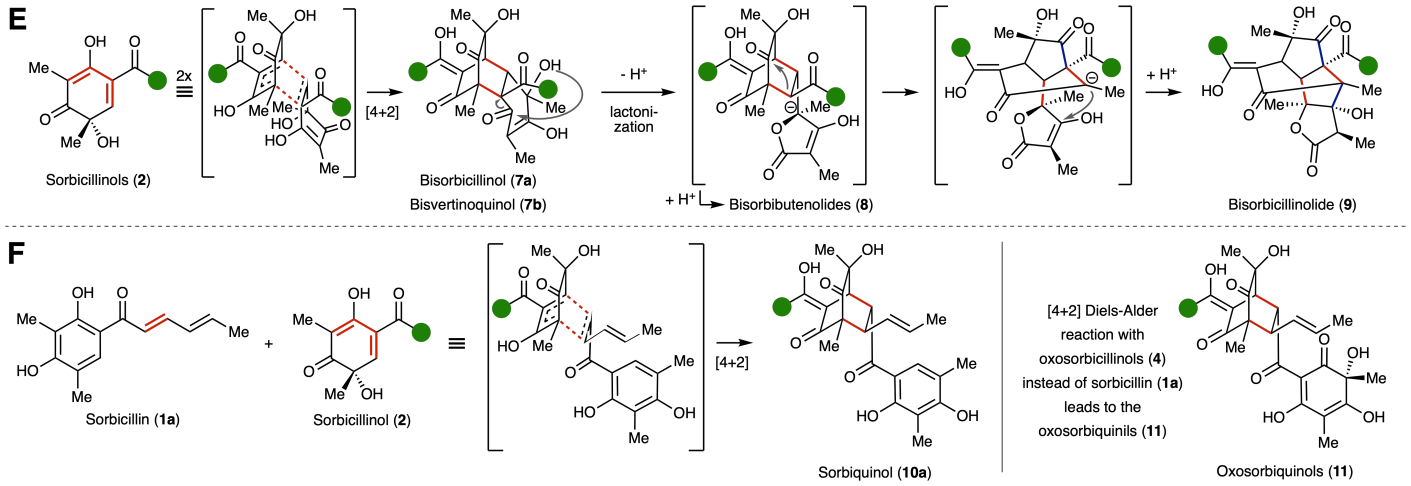


Fig. S2 Detailed biosynthesis of the Diels-Alder-type dimeric sorbicillinoids.

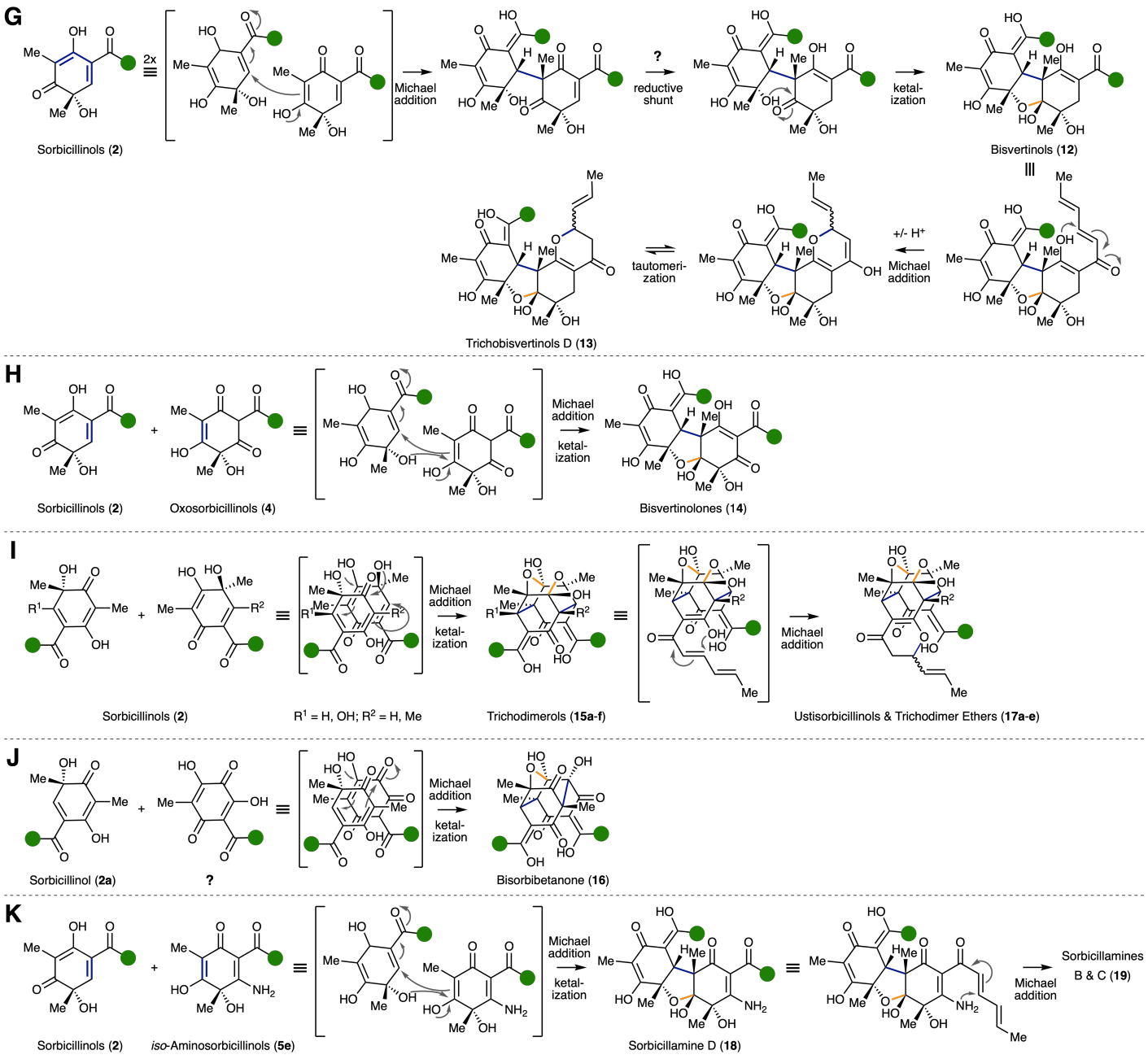


Fig. S3 Detailed biosynthesis of the Michael-type dimeric sorbicillinoids.

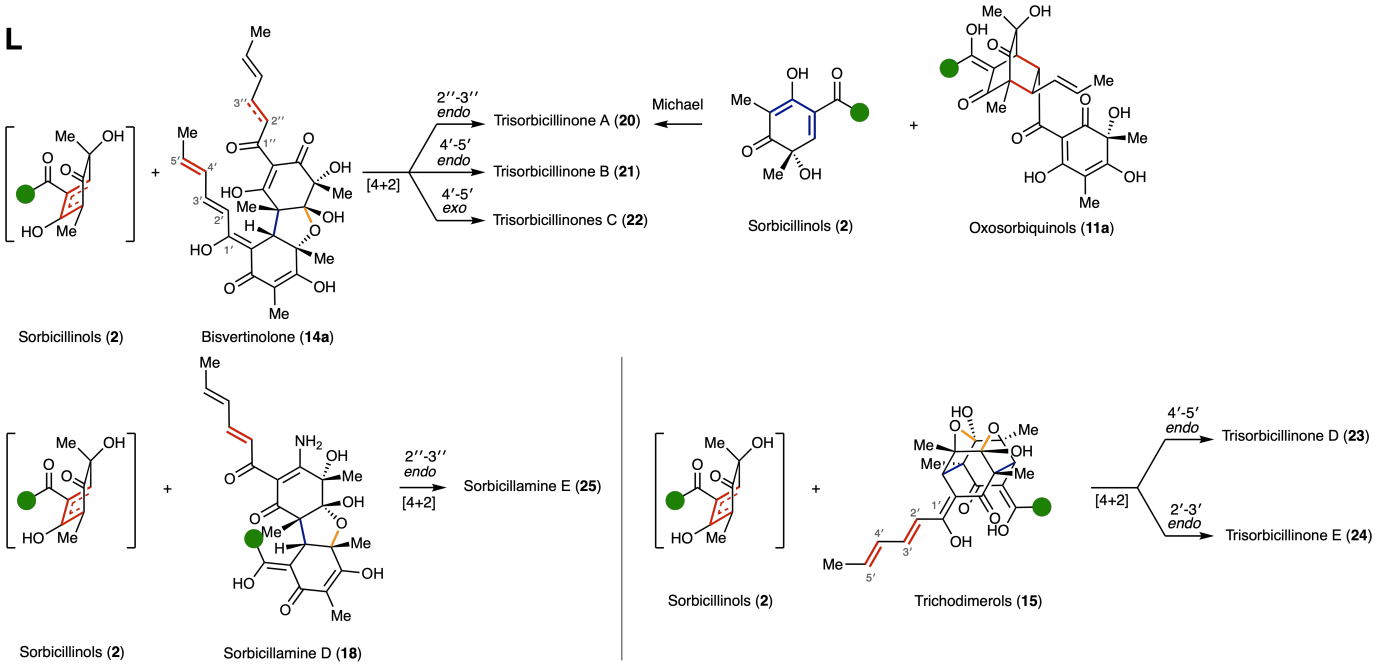


Fig. S4 Detailed biosynthesis oftrimeric sorbicillinoids.

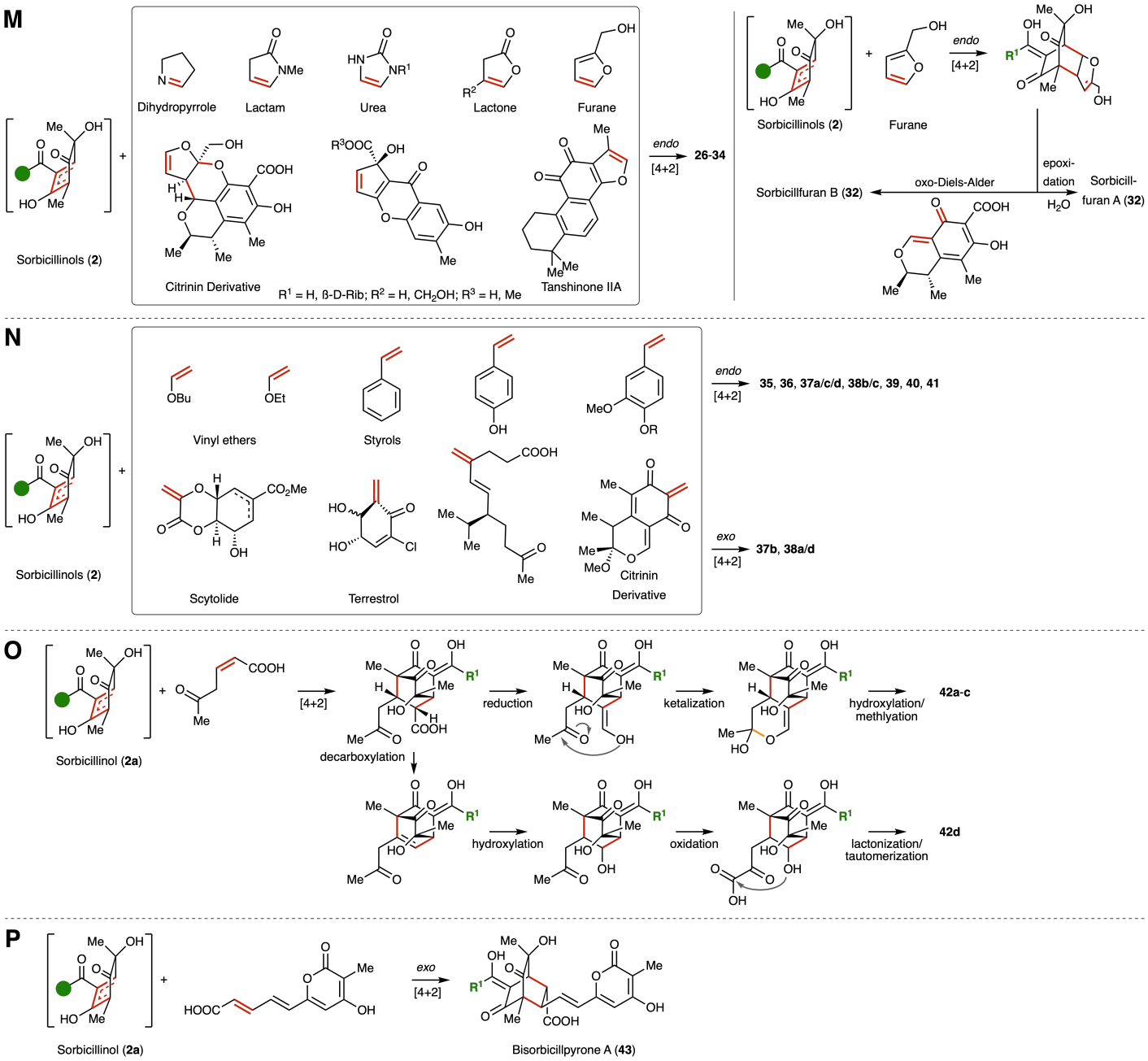


Fig. S5 Detailed biosynthesis of hybrid Diels-Alder-type sorbicillinoids.

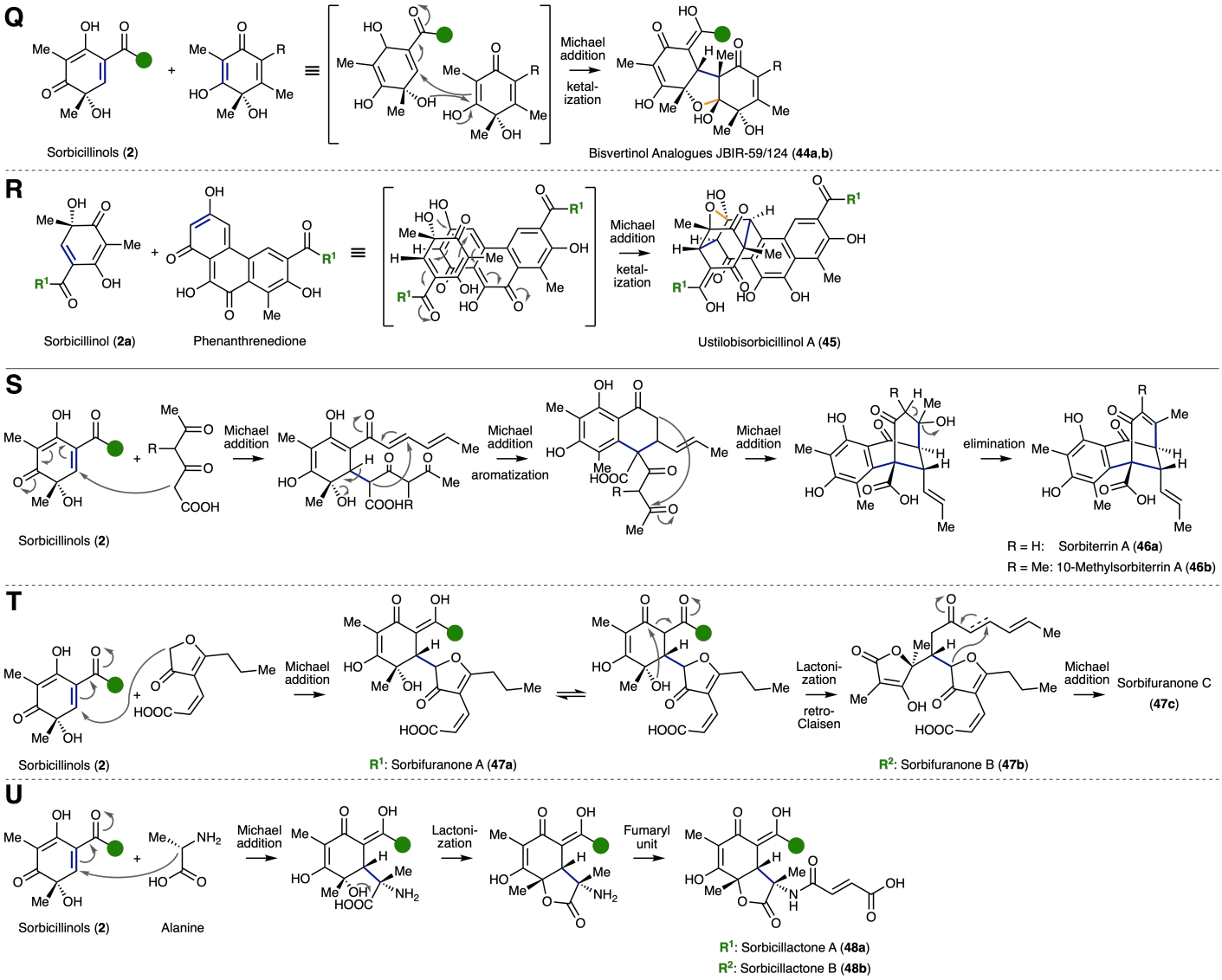


Fig. S6 Detailed biosynthesis of hybrid Michael-type sorbicillinoids.

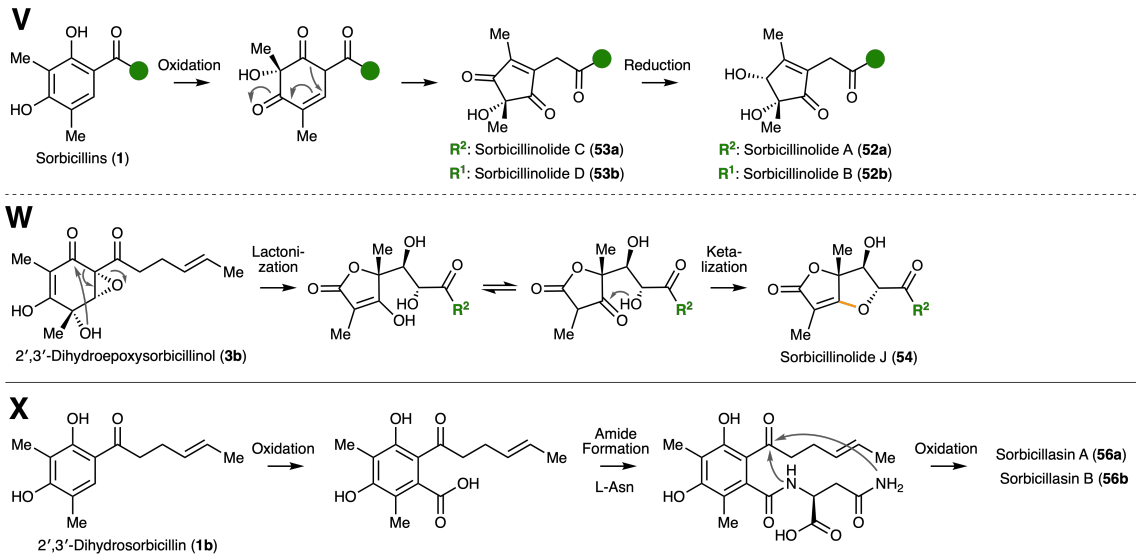


Fig. S7 Detailed biosynthesis of monomeric derivatives related to the sorbicillinoids.

3 Total Synthesis

Sorbicillin (1a)

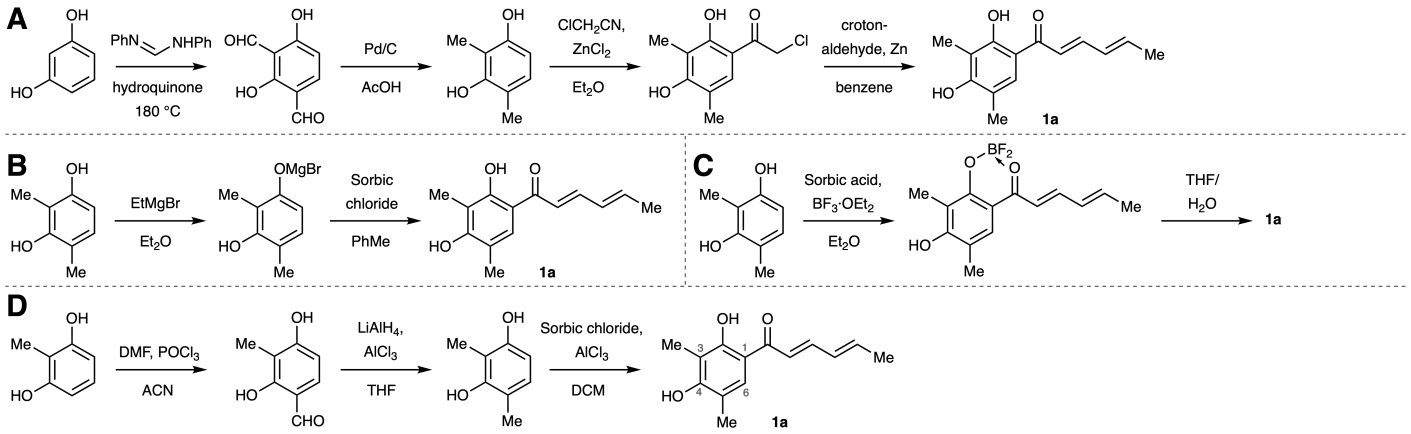


Fig. S8 Overview of different total syntheses of sorbicillin (**1a**). **A**: Kuhn and Staab's synthesis based on a condensation with crotonaldehyde.[141] **B**: Sartori's synthesis using bromomagnesium phenolates.[24] **C**: McOmie's synthesis based on a boron complex.[35] **D**: Our method using a classical Friedel-Crafts acylation.[26]

Epoxysorbicillinol (3a)

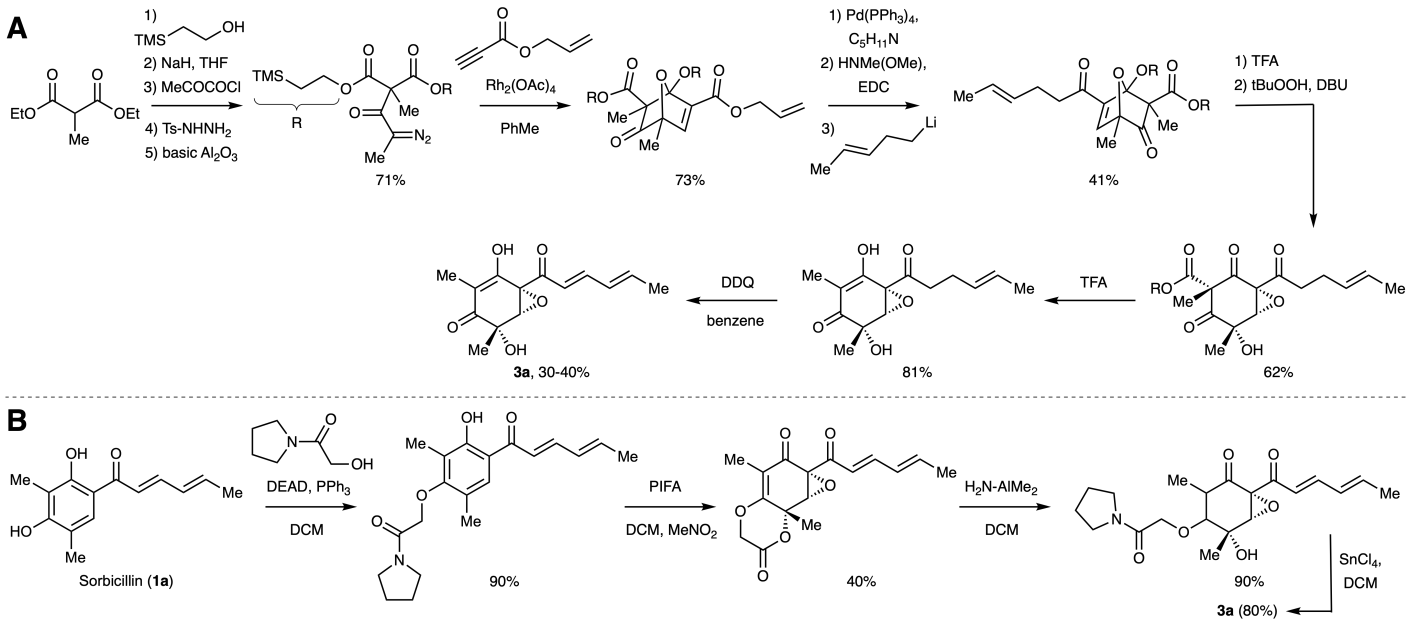


Fig. S9 Overview of different total syntheses of epoxysorbicillinol (**3a**). **A**: Wood's synthesis.[43] **B**: Pettus synthesis.[36]

Vertinolide (6a)

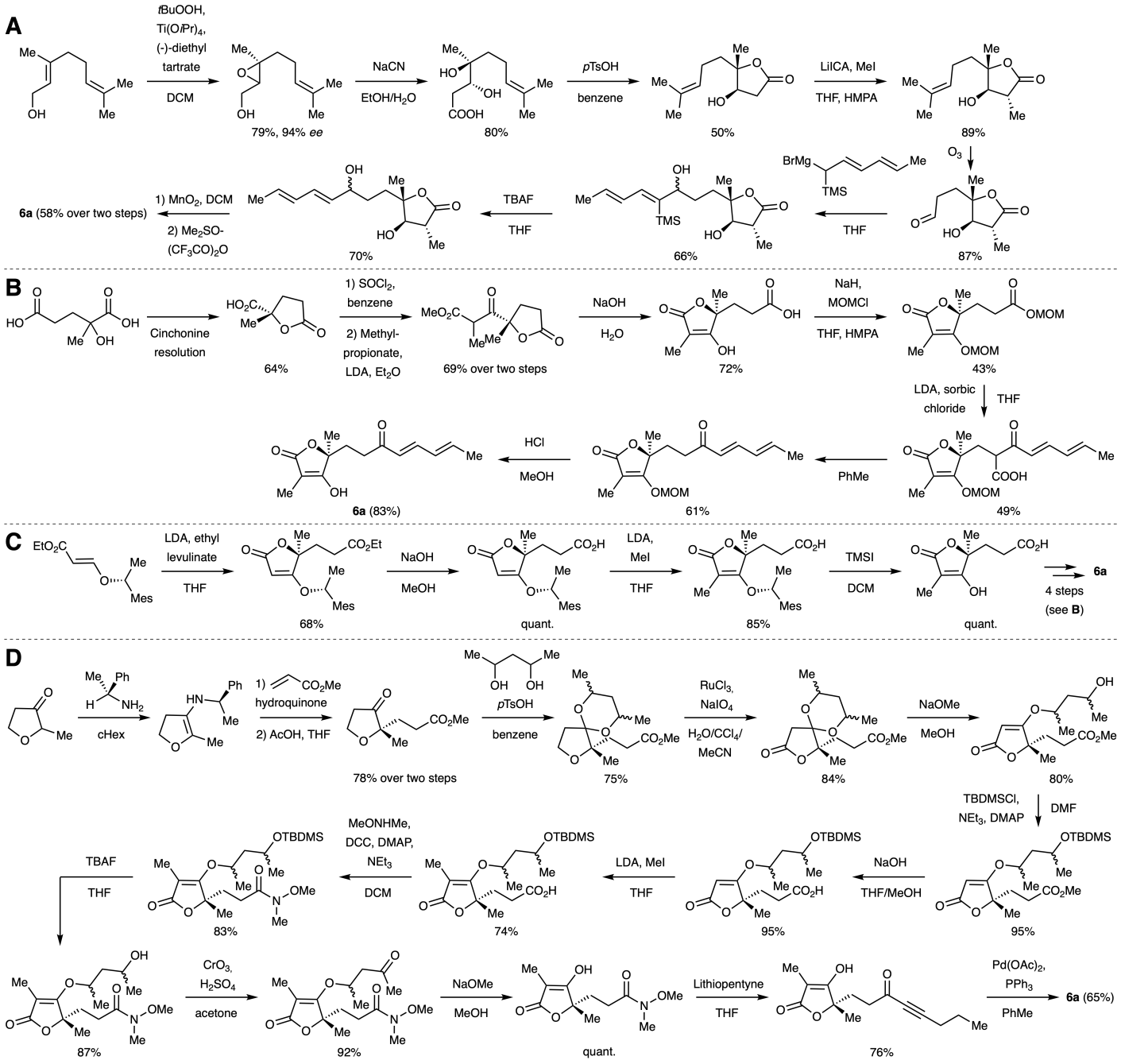


Fig. S10 Overview of different total syntheses of vertinolide (**6a**). **A**: Wrobel and Ganem's synthesis using an asymmetric epoxidation of Sharpless.[56,142] **B**: Synthesis of Takaiwa.[57,143] **C**: Schmidt's synthesis.[144] **D**: Desmaële's strategy.[55]

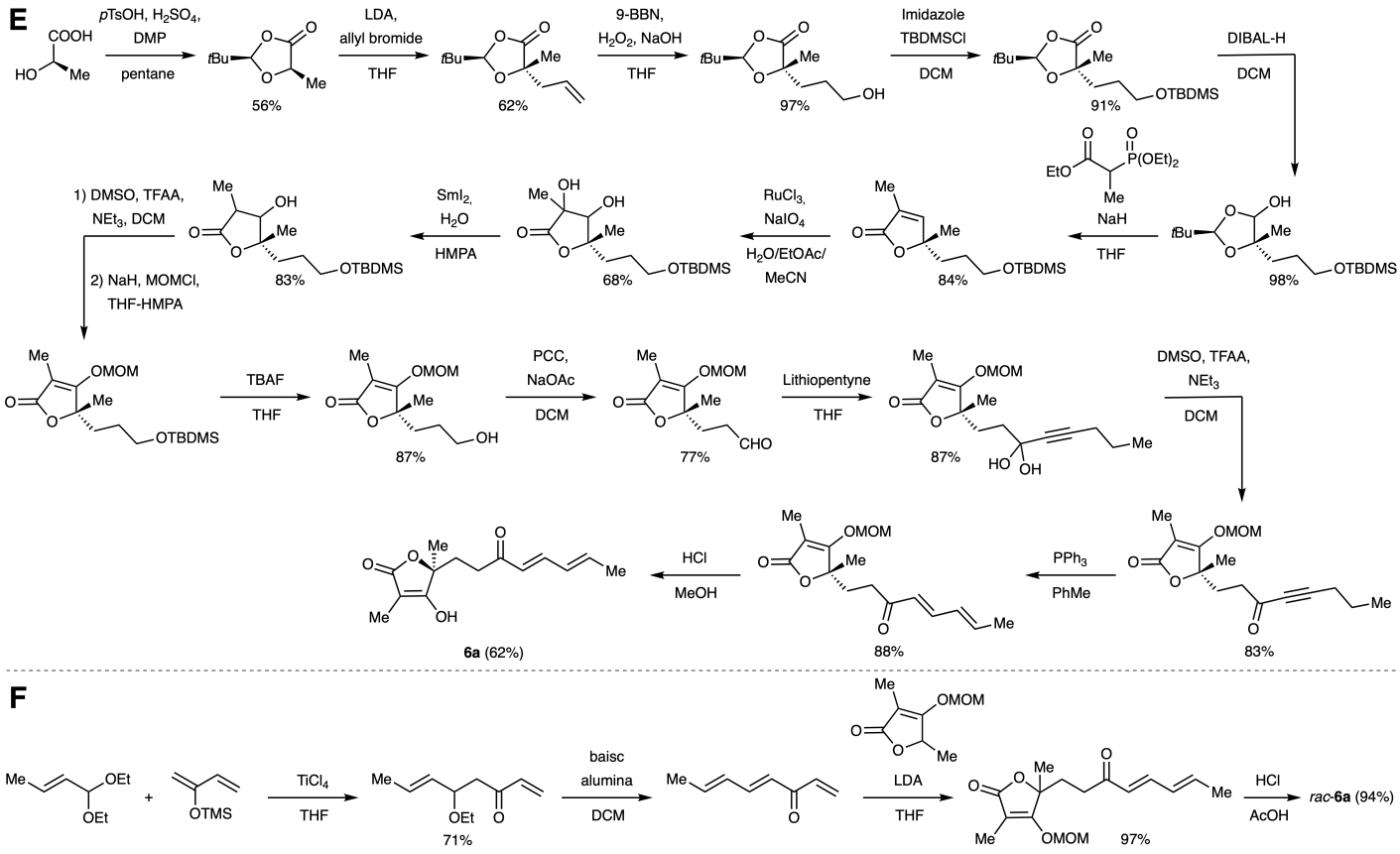


Fig. S11 Overview of different total syntheses of vertinolide (**6a**). **E**: Matsuo's synthesis.[58] **E**: Racemic synthesis by Takabe.[145]

Dimeric Sorbicillinoids

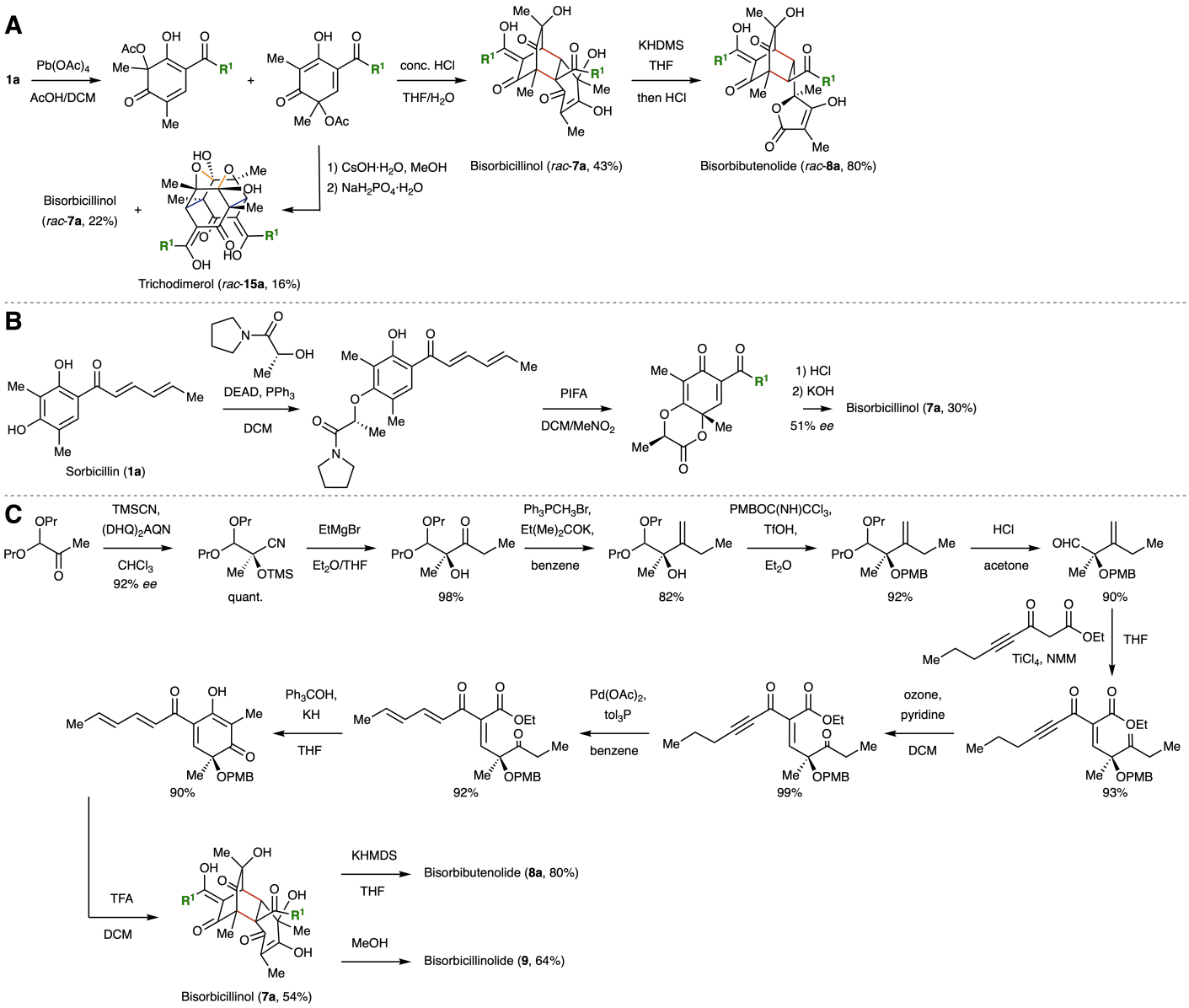


Fig. S12 Overview of different total syntheses of dimeric sorbicillinoids. **A**: Corey's and Nicolaou's racemic synthesis.[25,35] **B**: Enantioselective synthesis by Pettus.[36] **C**: Enantioselective synthesis by Deng.[37]

Sorbiterrin A (46a)

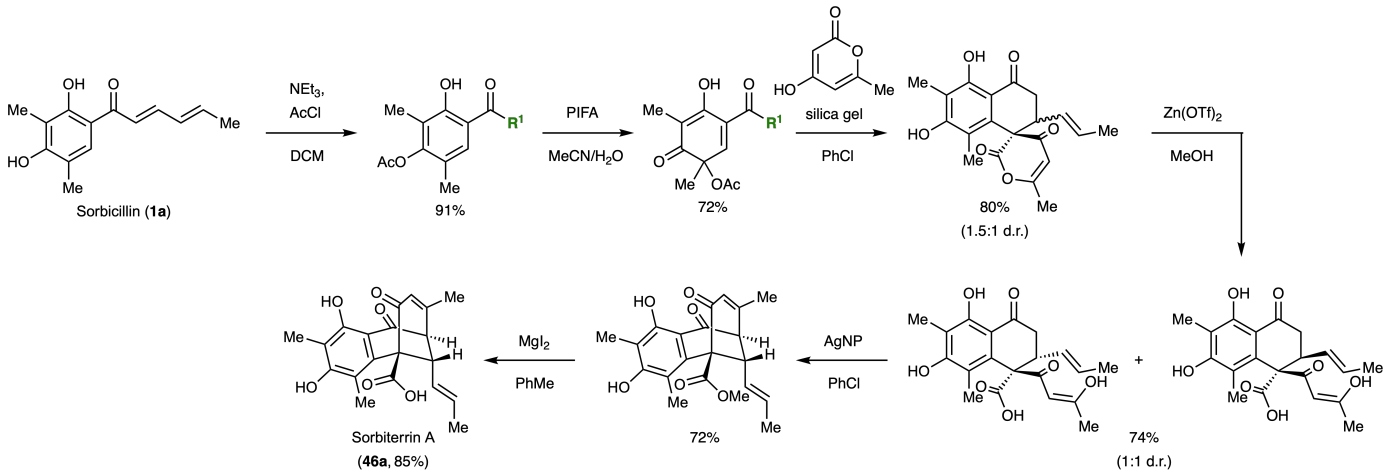


Fig. S13 Total synthesis of sorbiterrin A (**46a**) by Porco.[116]

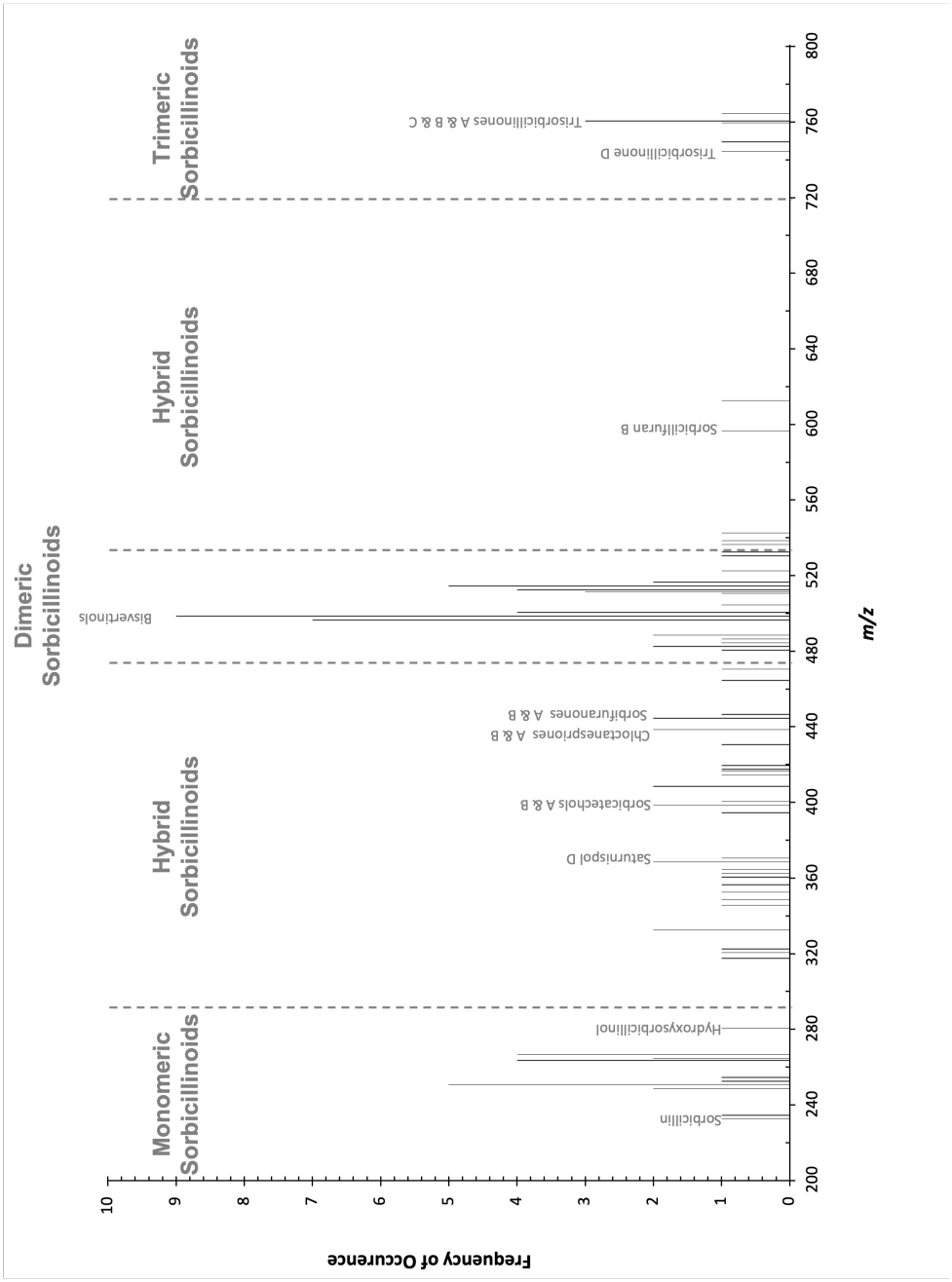


Fig. S14 Overview of the distribution of the exact masses within the sorbicllinoids.

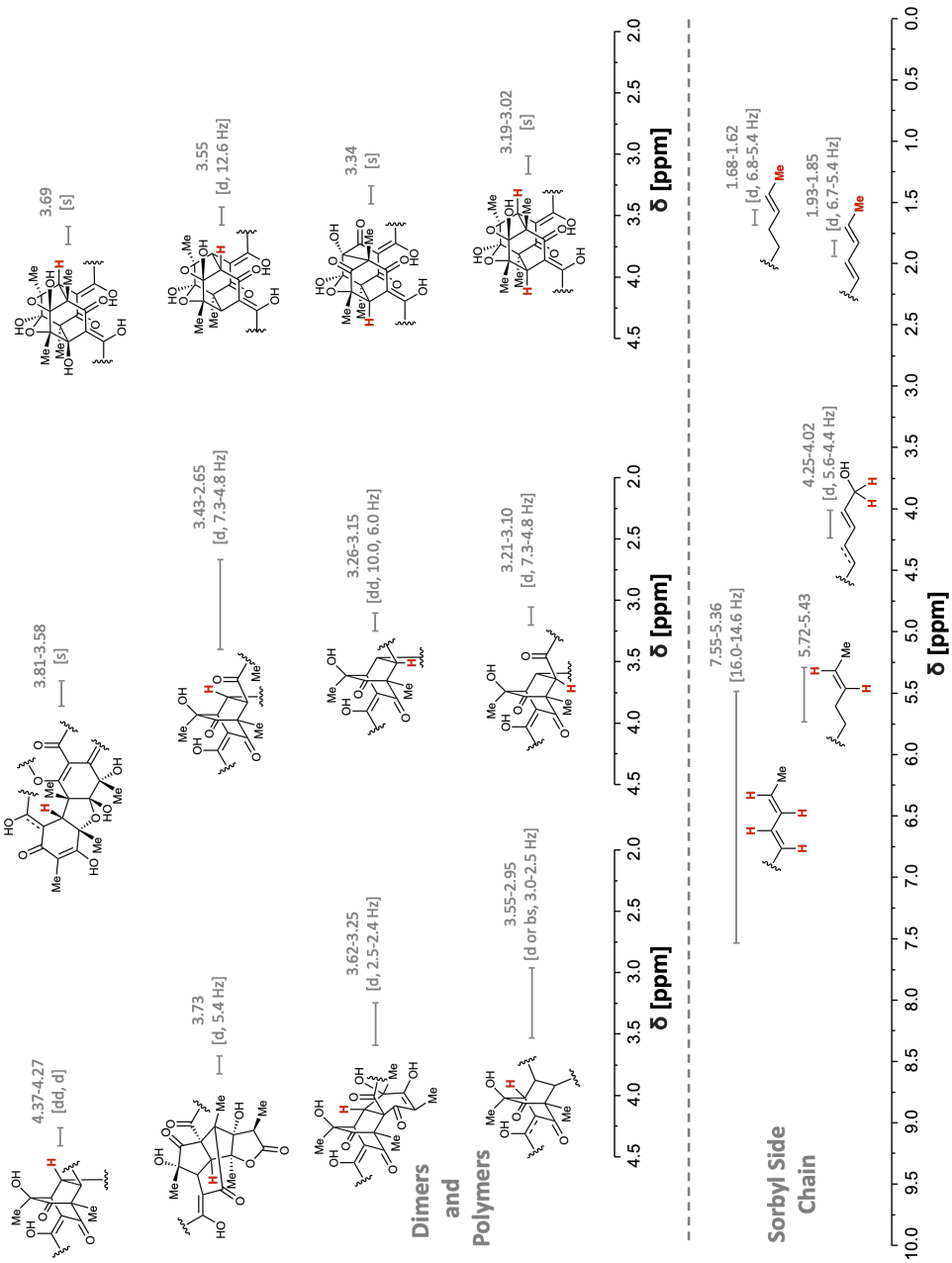


Fig. S15 Overview of the distr ibution of the ^{1}H-NMR fingerprint shifts within monomeric and dimeric sorbicllinoids.

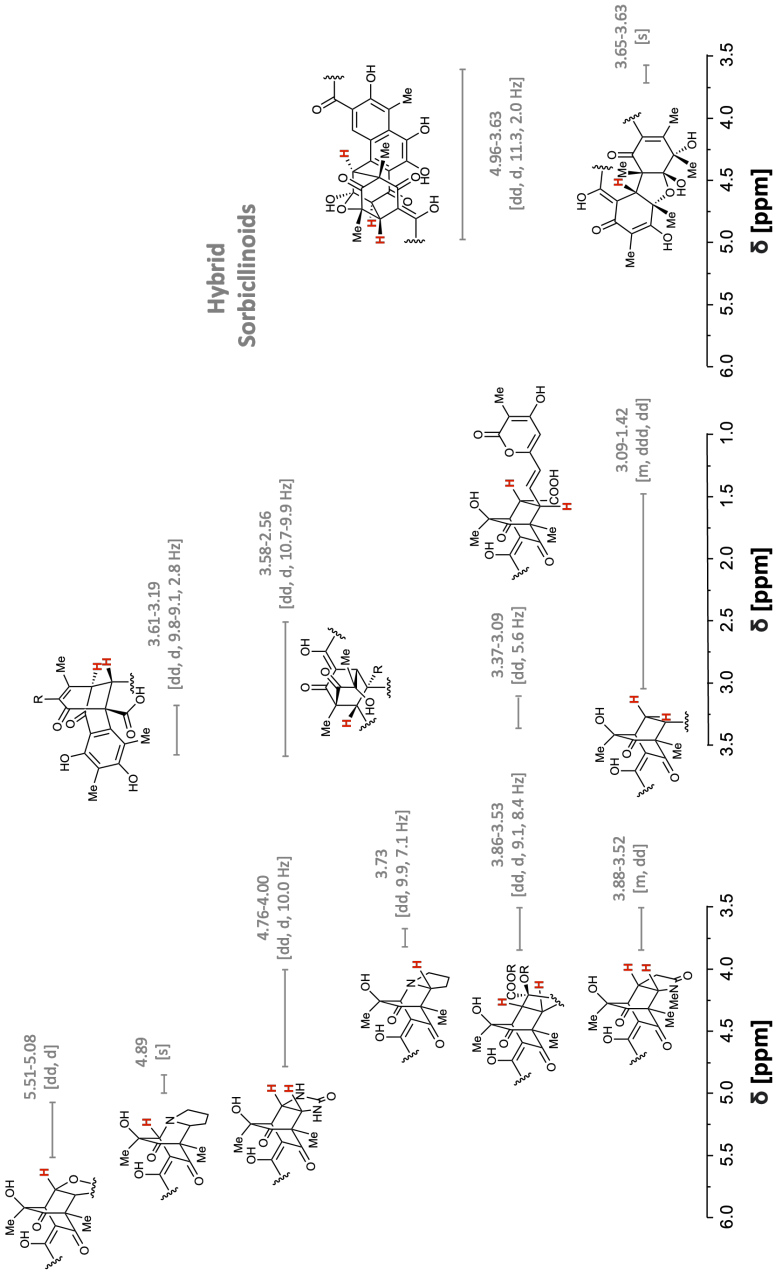


Fig. S16 Overview of the distribution of the ^{1}H-NMR fingerprint shifts within hybrid sorbicllinoids.

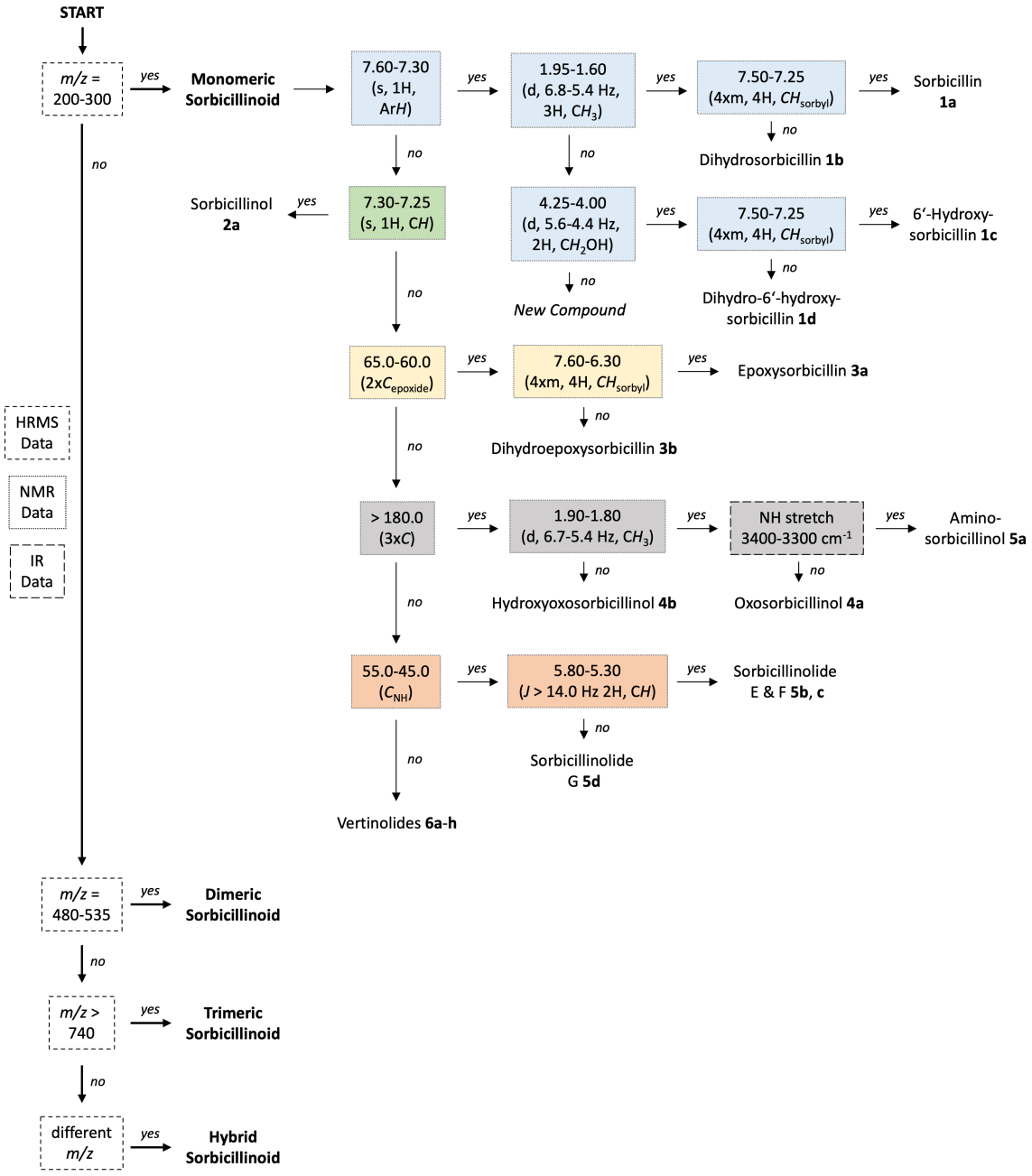


Fig. S17 Sorbicillinoid elucidation guide for the monomers.

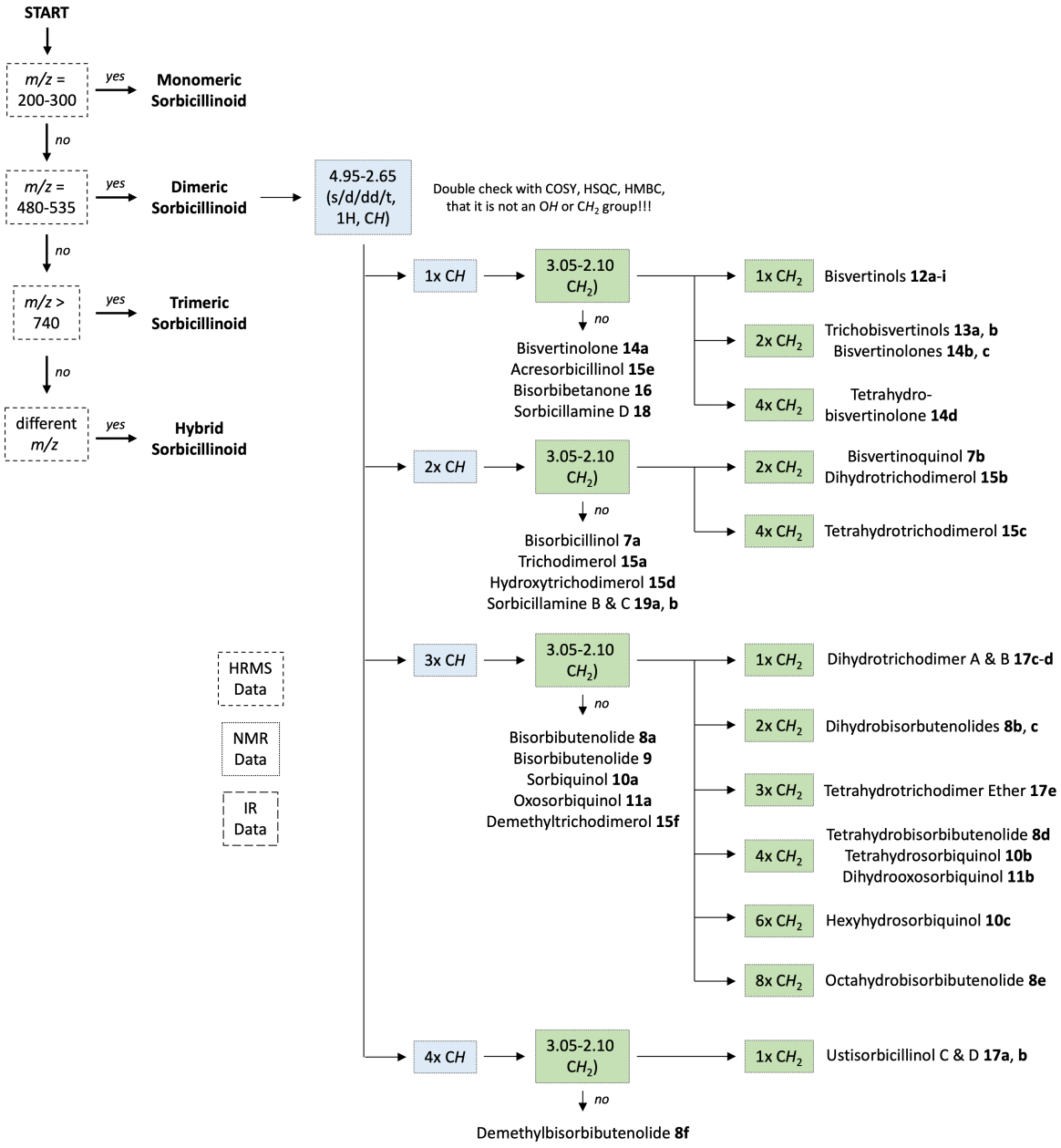


Fig. S18 Sorbicillinoid elucidation guide for the dimers.

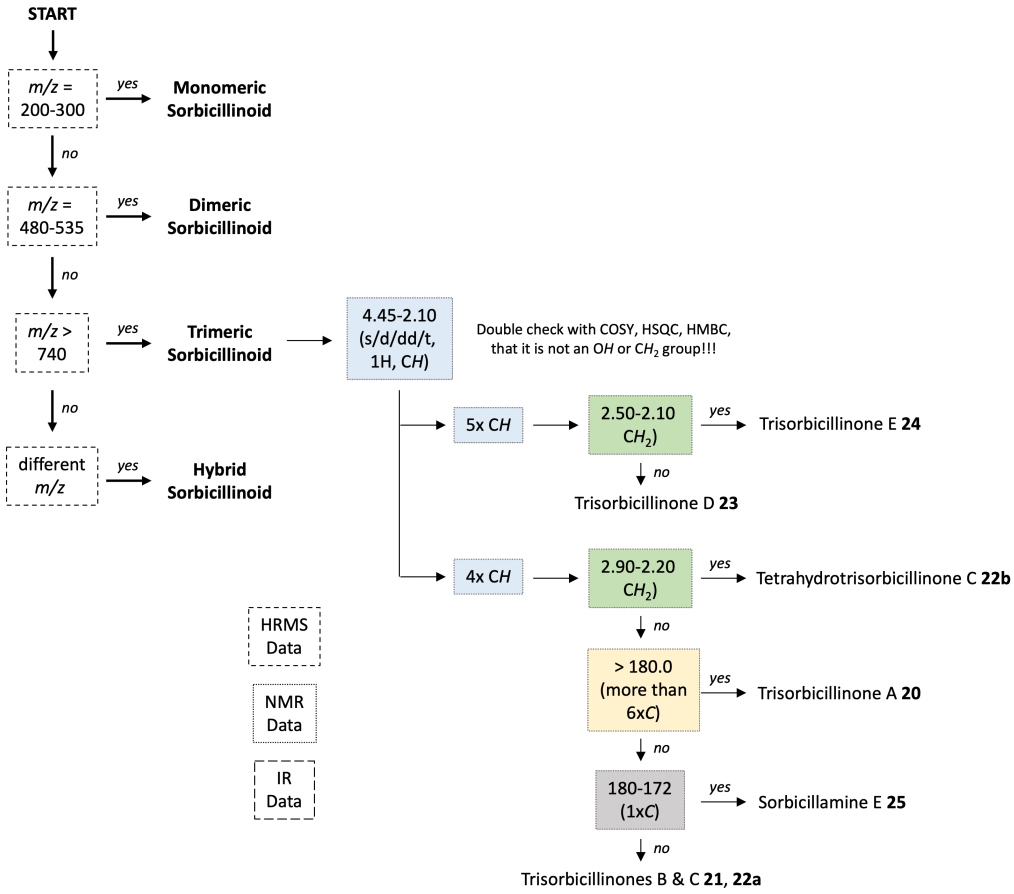


Fig. S19 Sorbicillinoid elucidation guide for the trimers.

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