Supporting Information

for

Total synthesis of decarboxyaltenusin

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A. Experimental procedures

General

THF and dioxane were distilled from sodium with benzophenone ketyl radical as indicator. All moisture-sensitive reactions were carried out under O\textsubscript{2}-free argon using oven-dried glassware and a vacuum line. Flash column chromatography [1] was carried out using Merck SiO\textsubscript{2} 60 (230–400 mesh) and thin layer chromatography (TLC) was carried out using commercially available Merck F\textsubscript{254} pre-coated sheets. \textsuperscript{1}H and \textsuperscript{13}C NMR spectra were recorded with Bruker Avance 300, 400, or 600 instruments. Chemical shifts are given in ppm and are referenced by using the residual signals of the solvent as internal standard. IR spectra were recorded with a Bruker Alpha spectrometer and mass spectra were recorded with a Finnigan MAT-95 mass spectrometer.

\textit{1,2-Bis(tert-butyldimethyldisiloxy)-4-methylbenzene (3)}

According to a published procedure [2] DMAP (600 mg, 4.91 mmol), imidazole (13.3 g, 196 mmol), and t-BuMe\textsubscript{2}SiCl (16.7 g, 111 mmol) were added to a solution of 4-methylbenzene-1,2-diol (2, 5.17 g, 41.6 mmol) in DMF (150 mL) and the mixture was stirred for 4 h at 50 °C. Then, a saturated aqueous NaHCO\textsubscript{3} solution (200 mL) was added and the mixture was extracted with Et\textsubscript{2}O (4 × 200 mL). The combined organic layers were washed with aqueous HCl solution (1 M, 100 mL), dried (Na\textsubscript{2}SO\textsubscript{4}), and concentrated at reduced pressure to yield 3 as a yellowish oil (14.2 g, 40.3 mmol, 96%). \textsuperscript{1}H NMR (300 MHz, CDCl\textsubscript{3}): δ (ppm) = 0.21 (s, 6 H, SiMe\textsubscript{2}), 0.22, (s, 6 H, SiMe\textsubscript{2}), 1.01 (s, 9 H, SiBu), 1.02 (s, 9 H, SiBu), 2.25 (s, 3 H, ArMe), 6.64 (m, 2 H, 2×Ar\textit{H}), 6.74 (d, \textsuperscript{3}J = 8.0 Hz, 1 H, Ar\textit{H}). These NMR data are in agreement with published data [2].

1. Still, W. C.; Kahn, M.; Mitra, A. J. Org. Chem. 1978, 43, 2923–2925.
2. Berkowitz, D. B.; Smith, M. K. J. Org. Chem. 1995, 60, 1233–1238.
1-Bromo-3,4-bis(tert-butyldimethylsilyloxy)-6-methylbenzene (5a)

In analogy to a published procedure [3] a solution of NBS (4.14 g, 23.3 mmol) in MeCN (60 mL) was added at 0 °C to a solution of protected catechol 3 (7.71 g, 21.9 mmol) in MeCN (75 mL) and stirring was continued for 72 h at room temperature. Then, H2O (200 mL) was added and the mixture was extracted with hexanes (3 × 100 mL). The combined organic layers were dried (Na2SO4) and concentrated at reduced pressure to yield 5a as a red oil (9.09 g, 21.1 mmol, 96%). 1H NMR (400 MHz, CDCl3): δ (ppm) = 0.19 (s, 6 H, SiMe2), 0.20 (s, 6 H, SiMe2), 0.99 (s, 18 H, 2×SiBu), 2.26 (s, 3 H, ArMe), 6.70 (s, 1 H, ArH), 6.95 (s, 1 H, ArH); 13C NMR (100 MHz, CDCl3): δ (ppm) = −4.03 (SiMe), −3.98 (SiMe), 18.6 (C), 22.3 (CH3), 26.1 (CH3), 115.0 (C), 123.1 (CH), 124.6 (CH), 130.5 (C), 145.7 (C), 146.2 (C), signals partly covered; IR (ATR): \(\tilde{\nu}\) (cm\(^{-1}\)) = 2928 (w), 2858 (w), 1495 (m), 1305 (m), 1253 (m), 994 (w), 910 (m), 836 (m), 780 (m); MS (EI, 140 °C): \(m/z\) (%) = 430 (4) [M\(^+\)], 375 (10), 373 (9), 115 (38), 73 (100), 69 (13); HRMS (EI): found 430.1355. C\(_{19}\)H\(_{35}\)O\(_2\)Br\(_2\)Si\(_2\) requires 430.1354.

2-[4,5-Bis(tert-butyldimethylsilyloxy)-2-methylphenyl]-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (6a)

Bromide 5a (5.00 g, 11.6 mmol) was dissolved under an argon atmosphere in THF (150 mL) and the solution was cooled to −78 °C. Then, n-BuLi (2.5M in hexanes, 7.00 mL, 17.5 mmol) was added via a syringe and the mixture was stirred for 45 min at that temperature. 2-Isoproxy-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (4.8 mL, 4.38 g, 23.5 mmol) was added and the temperature was raised to room temperature overnight. H2O (500 mL) and brine (150 mL) were added and the organic layer was dried (Na2SO4), concentrated at reduced pressure, and purified by column chromatography (silica gel, cyclohexane/EtOAc 50:1, with 3% Et3N) to yield 6a as a yellowish, slowly solidifying oil (3.15 g, 6.57 mmol, 57%). \(R_f = 0.66\)

3. Kohler, D.; Podlech, J. Eur. J. Org. Chem. 2019, 1748–1753.
(cyclohexane/EtOAc 10:1); $^1$H NMR (400 MHz, CDCl$_3$): $\delta$ (ppm) = 0.20 (s, 6 H, SiMe$_2$), 0.21 (s, 6 H, SiMe$_2$), 0.99 (s, 9 H, Si$t$Bu), 1.00 (s, 9 H, Si$t$Bu), 1.32 (s, 12 H, Me$_2$CCMe$_2$), 2.42 (s, 3 H, ArMe), 6.64 (s, 1 H, ArH), 7.24 (s, 1 H, ArH); $^{13}$C NMR (100 MHz, CDCl$_3$): $\delta$ (ppm) = –4.0 (SiCH$_3$), –3.9 (SiCH$_3$), 18.6 (C), 18.7 (C), 21.6 (CH$_3$), 25.0 (CH$_3$), 26.1 (CH$_3$), 26.2 (CH$_3$), 83.2 (C), 123.0 (CH), 128.7 (CH), 138.8 (C), 144.0 (C), 149.1 (C); IR (ATR): $\tilde{\nu}$ (cm$^{-1}$) = 2928 (m), 2858 (w), 1504 (m), 1471 (w), 1397 (m), 1334 (m), 1249 (m), 1142 (m), 835 (s), 778 (s); MS (EI, 90 °C): m/z (%) = 479 (12), 478 (38) [M$^+$], 477 (8), 322 (62), 321 (100), 320 (52), 231 (24), 181 (100), 131 (100), 100 (27), 73 (100); HRMS (EI): found 478.3100. C$_{25}$H$_{47}$O$_4^{11}$B$^{28}$Si$_2$ requires 478.3101.

**3-Bromo-5-methoxyphenol (8)**

In slight variation of a published protocol [4] 1-bromo-3,5-dimethoxybenzene (4.23 g, 19.4 mmol) was dissolved under an argon atmosphere in CH$_2$Cl$_2$ (30 mL) and cooled to −78 °C. BBr$_3$ (1 M in CH$_2$Cl$_2$, 17 mL, 17.0 mmol) was added dropwise and the mixture was stirred for 18 h while the temperature raised to room temperature. Then, H$_2$O (40 mL) was added slowly at −78 °C and the mixture was again warmed to room temperature and stirring was continued until clearing of the phases. The aqueous layer was extracted with Et$_2$O (2 × 50 mL) and the combined organic layers were washed with saturated NaHCO$_3$ solution, dried (MgSO$_4$), concentrated at reduced pressure, and purified by column chromatography (silica gel, cyclohexane/EtOAc 3:1 → 1:1) to yield 8 (2.78 g, 13.7 mmol, 71%) and 5-bromoresorcinol (900 mg, 4.76 mmol, 25%) as colorless solids. 8: $R_f = 0.26$ (cyclohexane/EtOAc 3:1); $^1$H NMR (300 MHz, CDCl$_3$): $\delta$ (ppm) = 3.76 (s, 3 H, OMe), 5.01 (s, 1 H, OH), 6.33 (m, 1 H, ArH), 6.61, (m, 1 H, ArH), 6.66 (m, 1 H, ArH). These NMR data are in agreement with published data [4].

4. Lindgren, A. E. G.; Öberg, C. T.; Hillgren, J. M.; Elofsson, M. Eur. J. Org. Chem. 2016, 426–429.
5-Bromoresorcinol: $R_f = 0.08$ (hexanes/EtOAc 3:1); $^1$H NMR (300 MHz, acetone-$d_6$): $\delta$ (ppm) = 6.33 (m, 1 H, 2-H), 6.52 (m, 2 H, 4-H, 6-H), 8.63 (s, 2 H, OH). These NMR data are in agreement with published data [5].

**1-Bromo-3-(tert-butyldimethylsilyloxy)-5-methoxybenzene (9a)**

t-BuMe$_2$SiCl (2.58 g, 17.1 mmol), DMAP (29.0 mg, 0.237 mmol), and imidazole (2.27 g, 33.3 mmol) were added successively to a solution of bromide 8 (2.08 g, 10.2 mmol) in DMF (50 mL). The mixture was stirred for 4 h at 55 °C and cooled to room temperature. Then, H$_2$O (40 mL) and saturated NaHCO$_3$ solution (50 mL) were added and the mixture was extracted with Et$_2$O (3 × 50 mL). The combined organic layers were dried (Na$_2$SO$_4$), concentrated at reduced pressure, and purified by column chromatography (silica gel, cyclohexane with 2.3% Et$_3$N) to yield 9a as a colorless oil (2.37 g, 7.48 mmol, 73%). $R_f = 0.35$ (cyclohexane); $^1$H NMR (400 MHz, CDCl$_3$): $\delta$ (ppm) = 0.20 (s, 6 H, SiMe$_2$), 0.97 (s, 9 H, SirBu), 3.75 (s, 3 H, OMe), 6.32 (t, $^4J = 2.2$ Hz, 1 H, ArH), 6.61 (t, $^4J = 1.9$ Hz, 1 H, ArH), 6.68 (t, $^4J = 1.9$ Hz, 1 H, ArH); $^{13}$C NMR (100 MHz, CDCl$_3$): $\delta$ (ppm) = –4.3 (SiMe$_2$), 18.3 (C), 25.7 (CH$_3$), 55.6 (CH$_3$), 105.7 (CH), 110.5 (CH), 116.3 (CH), 122.7 (C), 157.4 (C), 161.2 (C); IR (ATR): $\tilde{\nu}$ (cm$^{-1}$) = 2929 (w), 2856 (w), 1592 (m), 1441 (m), 1424 (m), 1315 (w), 1288 (w), 1157 (m), 1051 (m), 809 (m), 780 (w); MS (EI, 70 °C): $m/z$ (%) = 318 (26), 316 (25) [M$^+$], 261 (98), 259 (100), 180 (67), 137 (38), 75 (42), 73 (99), 59 (49), 57 (41); HRMS (EI): found 316.0489. C$_{13}$H$_{21}$O$_2$Br$_2$Si requires 316.0488. No spectroscopic data for comparison were given in the literature for this known compound [6].

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5. Wu, X.; Zhou, J.; Snider, B. B. *Angew. Chem.* 2009, 121, 1309–1312; *Angew. Chem. Int. Ed.* 2009, 48, 1283–1286.

6. Wada, Y.; Matsumoto, A.; Asano, K.; Matsubara, S. *RSC Adv.* 2019, 9, 31654–31658.
3’,4,5-Tris(tert-butyldimethylsilyloxy)-5’-methoxy-2-methyl-1,1’-biphenyl (10a)

Borate 6a (2.42 g, 5.05 mmol), bromide 9a (1.99 g, 6.27 mmol), Pd(OAc)$_2$ (40 mg, 0.18 mmol), SPhos (151 mg, 0.366 mmol), and Cs$_2$CO$_3$ (5.92 g, 18.1 mmol) were dissolved in a 500 mL Schlenk flask under an argon atmosphere in degassed dioxane/H$_2$O 7:1 (200 mL). The mixture was heated for 18 h at 70 °C, H$_2$O (300 mL) was added, and the mixture was extracted with EtOAc (4 × 100 mL). The combined organic layers were washed with brine (150 mL), dried (Na$_2$SO$_4$), concentrated at reduced pressure, and purified by column chromatography (silica gel, cyclohexane with 2.5% Et$_3$N) to yield a non-separable mixture of 10a and a non-identified by-product (2.91 g, 4.95 mmol, 98%). $R_f = 0.47$ (cyclohexane); $^1$H NMR (600 MHz, CDCl$_3$): $\delta$ (ppm) = 0.20 (s, 6 H, SiMe$_2$), 0.22 (s, 6 H, SiMe$_2$), 0.23 (s, 6 H, SiMe$_2$), 0.99 (s, 9 H, SitBu), 0.99 (s, 9 H, SitBu), 1.02 (s, 9 H, SitBu), 2.16 (s, 3 H, ArMe), 3.79 (s, 3 H, OMe), 6.36–6.39 (m, 2 H, ArH), 6.44 (s, 1, ArH), 6.69 (s, 1 H, ArH), 6.71 (s, 1 H, ArH); $^{13}$C NMR (150 MHz, CDCl$_3$): $\delta$ (ppm) = –4.2 (2×SiMe$_2$), –3.9 (SiMe$_2$), 18.4 (C), 18.6 (C), 20.0 (CH$_3$), 25.9 (CH$_3$), 26.1 (CH$_3$), 26.1 (CH$_3$), 55.4 (CH$_3$), 104.6 (CH), 108.4 (CH), 114.0 (CH), 122.4 (CH), 122.9 (CH), 128.1 (C), 134.9 (C), 143.8 (C), 144.4 (C), 145.9 (C), 156.4 (C), 160.3 (C); IR (ATR): $\tilde{\nu}$ (cm$^{-1}$) = 2928 (m), 2856 (w), 1590 (m), 1509 (m), 1509 (m), 1290 (m), 1249 (m), 1192 (m), 1158 (m), 1051 (w), 833 (m), 775 (m); MS (EI, 150 °C): m/z (%) = 590 (3), 589 (8), 588 (15) [M$^+$], 401 (16), 115 (13), 73 (100); HRMS (EI) found 588.3481. C$_{32}$H$_{56}$O$_4$Si$_3$ requires 588.3483.

4-Bromo-5-methylbenzene-1,2-diol (4)

In analogy to a published procedure [3] a solution of NBS (6.33 g, 35.6 mmol) in MeCN (85 mL) was added within 30 min to an ice-cooled solution of 4-methylbenzene-1,2-diol (2, 4.10 g, 33.0 mmol) in MeCN (100 mL). The resulting yellow mixture was stirred for 71 h at room temperature while it turned red. It was poured on H$_2$O (200 mL) and the mixture was extracted with EtOAc (3 × 300 mL). The combined organic layers were dried (Na$_2$SO$_4$) and
concentrated at reduced pressure to yield 4 as a brown solid (6.71 g, 33.0 mmol, quant.). Rf = 0.65 (cyclohexane/EtOAc 1:1); 1H NMR (300 MHz, DMSO-d6): δ (ppm) = 2.14 (s, 3 H, CH3), 6.70 (s, 1 H, 3-H or 6-H), 6.88 (s, 1 H, 6-H or 3-H), 9.05 (s, 1 H, OH), 9.14 (s, 1 H, OH); 13C NMR (75 MHz, DMSO-d6): δ (ppm) = 21.5 (CH3), 111.6 (CH), 117.8 (C), 118.6 (CH), 127.1 (C), 144.5 (C), 144.9 (C). The 1H NMR data are in agreement with published data [3,7].

4,5-Dibenzzyloxy-1-bromo-2-methylbenzene (5b)
In analogy to a published procedure [8] a mixture of brominated catechol 4 (2.17 g, 10.6 mmol), KI (136 mg, 0.82 mmol), K2CO3 (5.87 g, 42.5 mmol), and BnBr (2.53 mL, 3.64 g, 21.3 mmol) in DMF/acetone 1:2 (40 mL) under an argon atmosphere was stirred for 30 min at room temperature and for 29 h at 70 °C. Then, H2O (20 mL) was added after cooling and the mixture was extracted with CHCl3 (3 × 70 mL). The combined organic layers were washed with aqueous NaOH solution (5 M, 300 mL) and H2O (2 × 50 mL), dried (MgSO4), concentrated at reduced pressure, and purified by column chromatography (silica gel, hexane/EtOAc 6:1) to yield 5b as a colorless solid (3.50 g, 9.14 mmol, 86%) and benzyloxy-4-bromo-5-methylphenol. 5b: Rf = 0.62 (cyclohexane/EtOAc 6:1); 1H NMR (400 MHz, CDCl3): δ (ppm) = 2.29 (s, 3 H, CH3), 5.10 (s, 2 H, CH2), 5.12 (s, 2 H, CH2), 6.83 (s, 1 H, 3-H or 6-H), 7.12 (s, 1 H, 6-H or 3-H), 7.30–7.43 (m, 10 H, 2 Ph); 13C NMR (100 MHz, CDCl3): δ (ppm) = 22.5 (CH3), 71.7 (CH2), 71.8 (CH2), 115.5 (CH), 117.5 (C), 119.2 (CH), 127.5 (CH), 127.5 (CH), 128.0 (CH), 128.1 (CH), 128.7 (CH), 130.8 (C), 137.0 (C), 137.1 (C), 147.8 (C), 148.3 (C); IR (ATR): v (cm⁻¹) = 3062 (vw), 3034 (vw), 2874 (vw), 1567 (vw), 1499 (w), 1453 (w), 1382 (w), 1369 (w), 1320

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8. da Silva Pinto, A. C.; Silva, L. F. R.; Cavalcanti, B. C.; Melo, M. R. S.; Chaves, F. C. M.; Lotufo, L. V. C.; de Moraes, M. O.; de Andrade-Neto, V. F.; Tadei, W. P.; Pessoa, C. O.; Ribeiro Vieirac, P. P.; Pohlit, A. M. Eur. J. Med. Chem. 2009, 44, 2731–2735.
(w), 1199 (w), 1157 (m), 1008 (w), 914 (w), 848 (w), 747 (w), 719 (w), 696 (m); MS (FAB), m/z (%) = 385 (15), 384 (35) [C_{21}H_{19}^{81}BrO_{2}^+] , 383 (17), 382 (34) [C_{21}H_{19}^{79}BrO_{2}^+], 136 (29), 91 (100) [C_{7}H_{9}^{+}]; HRMS (FAB) found 382.0570. C_{21}H_{19}^{79}BrO_{2}^+ requires 382.0568. 2-Benzylxoy-4-bromo-5-methylphenol: R_{f} = 0.22 (hexanes/EtOAc 19:1); \textsuperscript{1}H NMR (300 MHz, CDCl\textsubscript{3}): \delta (ppm) = 2.29 (s, 3 H, CH\textsubscript{3}), 5.05 (s, 4 H, 2×CH\textsubscript{2}), 5.54 (br s, 1 H, OH), 6.82 (d, J = 10.8 Hz, 1 H, H-3 or H-6), 7.11 (d, J = 9.5 Hz, 1 H, H-6 or H-3), 7.34–7.45 (m, 5 H, Ph).

2-(4,5-Dibenzylxoy-2-methylphenyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (6b)

A solution of bis(benzylether) 5b (100 mg, 0.261 mmol), KOAc (77 mg, 0.78 mmol), Pd(dppf)Cl\textsubscript{2}·CH\textsubscript{2}Cl\textsubscript{2} (21 mg, 0.026 mmol), and bis(pinacolato)diboron (133 mg, 0.524 mmol) in anhydrous and degassed dioxane (1.4 mL) under an argon atmosphere was heated to 80 °C for 17 h. The mixture was filtered through a Celite pad and rinsed with EtOAc, concentrated at reduced pressure, and purified by column chromatography (silica gel, cyclohexane/toluene 1:1 → toluene → cyclohexane/EtOAc 4:1) to yield 6b as a colorless liquid (62 mg, 0.144 mmol, 55%). R_{f} = 0.17 (cyclohexane/toluene 1:1); \textsuperscript{1}H NMR (300 MHz, CDCl\textsubscript{3}): \delta (ppm) = 1.35 (s, 12 H, 4×Me), 2.49 (s, 3 H, 2-Me), 5.16 (s, 2 H, CH\textsubscript{2}) 5.18 (s, 2 H, CH\textsubscript{2}), 6.79 (s, 1 H, 3-H or 6-H), 7.41 (s, 1 H, 6-H or 3-H), 7.27–7.54 (m, 10 H, 2 Ph); \textsuperscript{13}C NMR (100 MHz, CDCl\textsubscript{3}): \delta (ppm) = 21.9 (CH\textsubscript{3}), 25.0 (4×CH\textsubscript{3}), 70.8 (CH\textsubscript{2}), 71.9 (CH\textsubscript{2}), 83.4 (2×C), 116.5 (CH), 122.9 (CH), 127.3 (2×CH) 127.8 (2×CH), 127.8 (CH), 128.5 (2×CH), 128.6 (2× CH), 137.4 (C), 137.8 (C), 140.0 (C), 146.2 (C), 151.3 (C), signal of C-1 could not be detected (due to boron’s quadrupole moment); IR (ATR): ν (cm\textsuperscript{-1}) = 2972 (w), 1592 (m), 1512 (w), 1456 (w), 1407 (m), 1338 (m), 1300 (m), 1248 (m), 1139 (m), 1011 (m), 867 (m), 847 (m), 738 (m), 724 (m), 691 (m); MS (FAB): m/z (%) = 431 (17), 430 (48), 429 (14), 91 (100); HRMS (FAB) found 430.2316. C_{27}H_{31}^{11}BO_{4}^+ requires 430.2315.
1-(Benzyloxy)-3-bromo-5-methoxybenzene (9b)

BnBr (1.17 mL, 9.86 mmol) was added under an argon atmosphere to a solution of bromide 8 (1.61 g, 7.89 mmol) and K₂CO₃ (2.70 g, 19.7 mmol) in DMF/acetone 1:2 (60 mL). The mixture was stirred for 43 h at 80 °C and cooled to room temperature. To the brown suspension were added H₂O (100 mL) and 1 M HCl until pH 8. The aqueous layer was extracted with EtOAc (3 × 100 mL) and the combined organic layers were washed with brine (50 mL) and H₂O (100 mL), dried (MgSO₄), concentrated at reduced pressure, and purified by column chromatography (silica gel, hexanes/EtOAc 2:1) to yield 9b as a colorless oil (2.27 g, 7.74 mmol, 98%). \( R_f = 0.32 \) (cyclohexane/EtOAc 50:1); \(^1\)H NMR (300 MHz, CDCl₃): \( \delta \) (ppm) = 3.77 (s, 3 H, Me), 5.02 (s, 2 H, CH₂), 6.47 (t, \( J = 2.1 \) Hz, 1 H, Ar-H), 6.69 (t, \( J = 1.8 \) Hz, 1 H, Ar-H), 6.77 (t, \( J = 1.9 \) Hz, 1 H, Ar-H), 7.33–7.44 (m, 5 H, Ph); \(^{13}\)C NMR (75 MHz, CDCl₃): \( \delta \) (ppm) = 55.6 (CH₃), 70.4 (CH₂), 100.7 (CH), 110.3 (CH), 110.8 (CH), 123.1 (C), 127.7 (CH), 128.3 (CH), 128.8 (CH), 136.5 (C), 160.5 (C), 161.4 (C); IR (ATR): \( \bar{\nu} \) (cm⁻¹) = 2926 (w), 1595 (m), 1573 (m), 1425 (m), 1378 (m), 1329 (w), 1277 (m), 1192 (m), 1152 (s), 1055 (m), 1024 (m), 812 (m), 735 (m), 696 (m), 675 (m); MS (EI, 20 °C): \( m/z \) (%) = 294 (13) [C₁₄H₁₃⁺BrO₂⁺], 292 (14) [C₁₄H₁₃79BrO₂⁺], 218 (40) [C₈H₈⁺BrO₂⁺], 216 (41) [C₈H₈79BrO₂⁺], 108 (26), 107 (10), 105 (10), 92 (11), 91 (100) [C₇H₇⁺], 79 (13), 77 (18), 69 (21), 65 (10), 58 (19), 57 (14); HRMS (EI) found 292.0098. C₁₄H₁₃O₂⁷⁹Br⁺ requires 292.0099.

3',4,5-Tris(benzyloxy)-5'-methoxy-2-methyl-1,1'-biphenyl (10b)

A solution of boronate 6b (104 mg, 0.242 mmol), bromide 9b (85 mg, 0.290 mmol), Cs₂CO₃ (315 mg, 0.967 mmol), Pd(OAc)₂ (2.7 mg, 12 µmol), and 2-dicyclohexylphosphino-2',6'-dimethoxybiphenyl (SPhos, 8.7 mg, 21 µmol) in degassed dioxane/H₂O 7:1 (9.3 mL) was heated for 18 h at 70 °C under an argon atmosphere. After cooling to room temperature H₂O (15 mL) was added and the aqueous phase was extracted with EtOAc (3 × 40 mL). The combined organic layers were washed with brine (75 mL), dried (Na₂SO₄), concentrated at
reduced pressure, and purified by column chromatography (silica gel, cyclohexane/EtOAc 50:1 → 15:1) to yield 10b as a colorless, highly viscous product (111 mg, 0.215 mmol, 89%). \( R_f = 0.32 \) (cyclohexane/EtOAc 10:1); \(^1\)H NMR (300 MHz, CDCl\(_3\)): \( \delta \) (ppm) = 2.16 (s, 3 H, 2-Me), 3.79 (s, 3 H, OMe), 5.05 (s, 2 H, CH\(_2\)), 5.13 (s, 2 H, CH\(_2\)), 5.18 (s, 2 H, CH\(_2\)), 6.42 (dd, \( J = 2.2, 1.3 \) Hz, 1 H, Ar-H), 6.47 (dd, \( J = 2.2, 1.4 \) Hz, 1 H, Ar-H), 6.52 (t, \( J = 2.3 \) Hz, 1 H, Ar-H), 6.84 (s, 1 H, Ar-H), 6.86 (s, 1 H, Ar-H), 7.29–7.50 (m, 15 H, 3 Ph); \(^13\)C NMR (100 MHz, CDCl\(_3\)) \( \delta \) (ppm) = 20.0 (CH\(_3\)), 55.5 (CH\(_3\)), 70.2 (CH\(_2\)), 71.6 (CH\(_2\)), 71.8 (CH\(_2\)), 99.9 (CH), 108.1 (CH), 108.4 (CH), 117.2 (CH), 117.3 (CH), 127.5 (2×CH), 127.6 (2×CH), 127.6 (2×CH), 127.8 (CH), 127.9 (CH), 128.1 (CH), 128.5 (C), 128.5 (2×CH), 128.6 (2×CH), 128.7 (2×CH), 134.9 (C), 137.1 (C), 137.6 (2×C), 143.8 (C), 146.8 (C), 148.4 (C), 159.7 (C), 160.5 (C); IR (ATR): \( \tilde{\nu} \) (cm\(^{-1}\)) = 3031 (w), 2924 (w), 1590 (m), 1509 (m), 1453 (m), 1427 (w), 1378 (w), 1252 (m), 1190 (m), 1152 (m), 1065 (m), 1025 (m), 839 (m), 735 (m), 696 (m); MS (FAB): \( m/z \) (%) = 517 (11) [M\(^+\)+1], 516 (15) [M\(^+\)], 91 (100) [C\(_7\)H\(_7\)+]; HRMS (FAB) found 516.2293. C\(_{35}\)H\(_{32}\)O\(_4\)+ requires 516.2295.

**5’-Methoxy-6-methyl-[1,1’-biphenyl]-3,3’,4-triol; decarboxyaltenusin (1)**

A mixture of benzyl-protected decarboxyaltenusin 10b (100 mg, 0.194 mmol) and Pd/C (10%, 22 mg, 0.207 mmol) in THF (10 mL) in an autoclave with H\(_2\) pressure (8 bar) was heated at 40 °C for 24 h, cooled, filtered over Celite, dried (Na\(_2\)SO\(_4\)), concentrated at reduced pressure, and purified by column chromatography (silica gel, hexanes/EtOAc 1:1) to yield 1 as a yellow oil (42 mg, 0.171 mmol, 88%). \( R_f = 0.36 \) (hexanes/EtOAc 1:1); \(^1\)H NMR (400 MHz, DMSO-\(d_6\)): \( \delta \) (ppm) = 2.05 (s, 3 H, 6-Me), 3.70 (s, 3 H, OMe), 6.20 (dd, \( J = 2.1, 1.5 \) Hz, 1 H, 6’-H), 6.22 (t, \( J = 1.7 \) Hz, 1 H, 2’-H), 6.25 (t, \( J = 2.2 \) Hz, 1 H, 4’-H), 6.55 (s, 1 H, 2-H), 6.60 (s, 1 H, 5-H), 8.72 (br s, 1 H, 3-OH), 8.78 (br s, 1 H, 4-OH), 9.37 (br s, 1 H, 3’-OH); \(^13\)C NMR (100 MHz, DMSO-\(d_6\)): \( \delta \) (ppm) = 19.4 (CH\(_3\), OMe), 54.9 (CH\(_3\), 6-Me), 99.2 (CH, C-4’), 105.8 (CH, C-6’), 108.8 (CH, C-2’), 116.7 (CH, C-2), 117.5 (CH, C-5), 124.8 (C, C-6), 132.3 (C, C-1),
142.9 (C, C-1’), 143.6 (C, C-4), 144.3 (C, C-3), 158.0 (C, C-3’), 160.0 (C, C-5’); IR (ATR): \(\tilde{\nu}\) (cm\(^{-1}\)) = 3332 (br s), 2919 (m), 2849 (s), 1591 (m), 1519 (s), 1496 (s), 1427 (m); MS (EI, 140 °C): \(m/z\) (%) = 247 (17), 246 (100) [M\(^+\)], 245 (19), 197 (10), 73 (11), 69 (18), 57 (14), 55 (15); HRMS (FAB) found 246.0893. \(\text{C}_{14}\text{H}_{14}\text{O}_{4}^+\) requires 246.0892.

**Cell culture and cytotoxicity studies**

HeLa cells (human cervix carcinoma cell line) cells were cultured in DMEM medium (Gibco) supplemented with 10% fetal bovine serum (FBS, Gibco) and 1% penicillin/streptavidin (Gibco) at 37 °C, 5% CO\(_2\). The cells were trypsinized (0.05% trypsin-EDTA, Gibco) and seeded into 96 well plates (toxicity assay) at 70% confluence for 24 h.

The medium was removed and the cells were treated with the indicated concentrations of decarboxyaltenusin by diluting the DMSO stock solution in 100 µl DMEM supplemented with 10% FBS and penicillin/streptavidin as described above. The cells were incubated for 72 h at 37 °C, 5% CO\(_2\). For the negative control, the cell culture medium was replaced by medium. Eventually, the MTT assay was performed as describe in the manufacturer’s manual (Promega). Prior to MTT assay, the positive control was treated with Triton X-100 (1%). After 3 h of incubation with the 15 µL of the MTT reagent the cells were lysed using the Stop Solution to release the blue-purple formazan. The cell viability was determined by measuring the absorbance of the resulting formazan at 595 nm using a multiwell plate reader (SpectraMax ID3, Molecular Devices, USA). The values were normalized against the positive and negative control. Experiments were performed with \(n = 5\) and standard deviations were calculated using Student’s \(t\)-test.
B. NMR Spectra

1. 1-Bromo-3,4-bis(tert-butyldimethylsilyloxy)-6-methylbenzene (5a)

$^1$H NMR (400 MHz, CDCl$_3$)

$^{13}$C NMR (100 MHz, CDCl$_3$)
2. 2-[4,5-Bis(tetra-tert-butyldimethylsilyloxy)-2-methylphenyl]-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (6a)

$^1$H NMR (400 MHz, CDCl₃)

$^{13}$C NMR (100 MHz, CDCl₃)
3. 1-Bromo-3-(tert-butyldimethylsilyloxy)-5-methoxybenzene (9a)

$^1$H NMR (400 MHz, CDCl$_3$)

$^{13}$C NMR (100 MHz, CDCl$_3$)
4. 3’,4,5-Tris(tert-butyldimethylsilyloxy)-5’-methoxy-2-methyl-1,1’-biphenyl (10a)

$^1$H NMR (400 MHz, CDCl$_3$)

$^{13}$C NMR (400 MHz, CDCl$_3$)
5. 4,5-Dibenzylxyloxy-1-bromo-2-methylbenzene (5b)

$^1$H NMR (400 MHz, CDCl$_3$)

$^{13}$C NMR (100 MHz, CDCl$_3$)
6. 2-(4,5-Dibenzyloxy-2-methylphenyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (6b)

$^1$H NMR (400 MHz, CDCl$_3$)

$^{13}$C NMR (100 MHz, CDCl$_3$)
7. 1-(Benzyloxy)-3-bromo-5-methoxybenzene (9b)

$^1$H NMR (400 MHz, CDCl$_3$)

$^{13}$C NMR (100 MHz, CDCl$_3$)
8. 3',4,5-Tris(benzyloxy)-5'-methoxy-2-methyl-1,1'-biphenyl (10b)

$^1$H NMR (400 MHz, CDCl$_3$)

$^{13}$C NMR (100 MHz, CDCl$_3$)
9. 5’-Methoxy-6-methyl-[1,1’-biphenyl]-3,3’,4-triol; decarboxyaltenusin (1)

$^1$H NMR Spectrum (400 MHz, DMSO-$d_6$)

$^{13}$C NMR (100 MHz, DMSO-$d_6$)
HSQC (100 MHz, DMSO-\textit{d}_6)

COSY (100 MHz, DMSO-\textit{d}_6)
HMBC (100 MHz, DMSO-$d_6$)