

Golden opportunities in natural product synthesis: first total synthesis of (–)-isocyclocapitelline and (–)-isochrysotricine by gold-catalyzed allene cycloisomerization

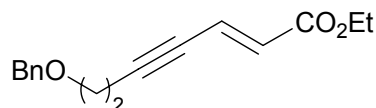
Frank Volz^a and Norbert Krause^{*a}

*Organic Chemistry II, Dortmund University, D-44221 Dortmund, Germany
norbert.krause@uni-dortmund.de*

Supporting Information

General remarks: NMR spectra were recorded with a Bruker DRX 400 or DRX 500 spectrometer in CDCl₃ as solvent and internal standard ($\delta = 7.27$ for ¹H, $\delta = 77.0$ for ¹³C). Carbon atoms were assigned with DEPT experiments [symbols used: (+) for CH₃,CH; (–) for CH₂; (×) for C_{quart.}]. Peaks for the major isomer of a mixture are marked with an asterisk (*).

Ethyl (*E*)-7-Benzyloxyhept-2-en-4-ynoate (**7**)



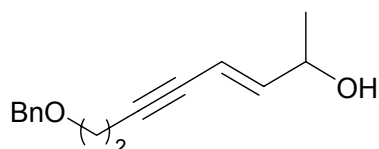
δ H (500 MHz, CDCl₃): 7.38–7.29 (m, 5 H, ArH), 6.76 (dt, $J = 15.9$ Hz, $J = 2.2$ Hz, 1 H, CH=CHC=O), 6.18 (d, $J = 15.9$ Hz, 1 H, CH=CHC=O), 4.57 (s, 2 H, CH₂Ph), 4.22 (q, $J = 7.1$ Hz, 2 H, CH₂CH₃), 3.63 (t, $J = 6.9$ Hz, 2 H, OCH₂), 2.70 (dt, $J = 6.9$ Hz, $J = 1.9$ Hz, 2 H, OCH₂CH₂), 1.30 (t, $J = 7.1$ Hz, 3 H, CH₂CH₃).

δ C (125 MHz, CDCl₃): 166.0 (×, C=O), 137.9 (×, quaternary ArC), 129.8 (+, CH=CHC=O), 128.4 (+, 2 × *m*-ArC), 127.9 (+, 1 × *p*-ArC), 127.6 (+, 2 × *o*-ArC), 125.6 (+, CH=CH-C=O), 97.0 (×, CH₂C≡C), 78.7 (×, CH₂C≡C), 73.0 (–, CH₂Ph), 67.8 (–, OCH₂), 60.6 (–, CH₂CH₃), 21.2 (–, OCH₂CH₂), 14.2 (+, CH₂CH₃).

FAB–MS: m/z (%) = 259 (50, $[M+H]^+$), 257 (7), 92 (100), 78 (18), 66 (8), 42 (7).

FAB–HRMS: $C_{16}H_{18}O_3$ (258.1256), calcd.: 258.1256 ($[M]^+$), found: 258.1252.

(*E*)-8-Benzyloxyoct-3-en-5-yn-2-ol (**8**)



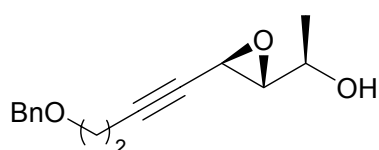
δ H (500 MHz, $CDCl_3$): 7.36–7.29 (m, 5 H, ArH), 6.11 (dd, $J = 15.9$ Hz, $J = 6.0$ Hz, 1 H, $CH=CHC-OH$), 5.68 (dd, $J = 15.9$ Hz, $J = 1.5$ Hz, 1 H, $CH=CHC-OH$), 4.57 (s, 2 H, $PhCH_2$), 4.33 (m, 1 H, CH_2OH), 3.61 (t, $J = 7.0$ Hz, 2 H, OCH_2), 2.63 (dt, $J = 7.0$ Hz, $J = 2.0$ Hz, 2 H, OCH_2CH_2 7–H), 1.79 (s, 1 H, OH), 1.29 (d, $J = 6.5$ Hz, 3 H, CH_3).

δ C (125 MHz, $CDCl_3$): 145.7 (+, $CHOH$), 138.0 (x, quaternary ArC), 128.4 (+, 2 x *m*-ArC), 127.6 (+, 2 x *o*-ArC), 127.6 (+, 1 x *p*-ArC), 109.4 (+, $CH=CHC-OH$), 87.5 (x, $CH_2C\equiv C$), 79.3 (x, $CH_2C\equiv C$), 72.9 (–, $PhCH_2$), 68.3 (–, OCH_2CH_2), 68.2 (+, $CHOH$), 23.0 (+, CH_3), 20.8 (–, OCH_2CH_2).

FAB–MS: m/z (%) = 229 (10, $[M-H]^+$), 213 (22), 199 (5), 183 (9), 169 (13), 165 (5), 92 (100), 44 (15), 41 (4).

FAB–HRMS: $C_{15}H_{18}O_2$ (230.1307), calcd.: 229.1229 ($[M-H]^+$), found: 215.1243.

(*R,R,R*)-1-[(4-Benzyloxybut-1-ynyl)oxiran-2-yl]ethanol (**9**)



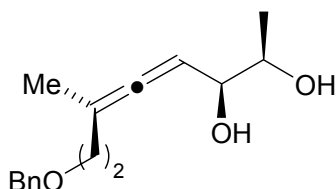
δ H (400 MHz, CDCl₃) = 7.36–7.29 (m, 5 H, ArH), 4.55 (s, 2 H, PhCH₂), 3.96 (dq, J = 6.5 Hz, J = 3.0 Hz, 1 H, CH(OH)), 3.58 (t, J = 7.0 Hz, 2 H, OCH₂CH₂), 3.43 (d, J = 1.5 Hz, 1 H, CH(O)CHCHOH), 3.14 (t, J = 2.5 Hz, 1 H, CH(O)CHCHOH), 2.53 (dt, J = 6.5 Hz, J = 1.5 Hz, 2H, OCH₂CH₂), 2.18 (s, 1H, OH), 1.27 (d, J = 6.5 Hz, 3 H, CH₃).

δ C (100 MHz, CDCl₃) = 137.8 (x, quaternary ArC), 128.3 (+, 2 x *m*-ArC), 127.7 (+, 1 x *p*-ArC), 127.6 (+, 2 x *o*-ArC), 81.9 (x, CH₂C≡C), 77.2 (x, CH₂C≡C), 72.9 (–, PhCH₂), 67.8 (–, OCH₂CH₂), 64.0 (+, CH(O)CHCHOH), 63.0 (+, CHOH), 42.1 (+, CH(O)CHCHOH), 20.1 (–, OCH₂CH₂), 18.4 (+, CH₃).

FAB–MS: m/z (%) = 245 (3, [M–H]⁺), 244 (2), 203 (6), 92 (40), 58 (8), 44 (5), 28 (2).

FAB–HRMS: C₁₅H₁₈O₃ (246.1256), calcd.: 245.1178 ([M–H]⁺), found: 245.1141.

(2*R*,3*S*,5*S*)-8-Benzyloxy-6-methylocta-4,5-diene-2,3-diol (**10**)



δ H (400 MHz, CDCl₃): 7.36–7.28 (m, 5 H, ArH), 5.20 (m, 1 H, C=C=CH), 4.51 (dd, J = 12.0 Hz, 2 H, PhCH₂), 4.01 (m, 1 H, CH(OH)CHMe(OH)), 3.77 (m, 1 H, CH(OH)CHMe(OH)), 3.58 (m, 2 H, OCH₂CH₂), 2.90 (s, 2 H, OH), 2.32/2.22 (m, 2H, OCH₂CH₂), 1.72 (d, J = 2.8 Hz, 3 H, CH₃C=C=C), 1.24 (d, J = 6.3 Hz, 3 H, CH(OH)CH₃).

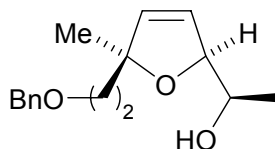
δ C (100 MHz, CDCl₃): 200.8 (x, C=C=C), 137.7 (x, quaternary ArC), 128.3 (+, 2 x *m*-ArC), 127.8 (+, 2 x *o*-ArC), 127.6 (+, 1 x *p*-ArC), 99.9 (x, C=C=CH), 90.7 (+, C=C=CH), 73.0 (+, CH(OH)CHMe(OH)), 72.7 (–, PhCH₂), 70.3 (+, CH(OH)CHMe(OH)).

(OH), 67.3 (–, OCH₂CH₂), 33.9 (–, OCH₂CH₂), 18.7 (+, CH₃C=C=C CH), 17.5 (+, CH₃CHOH).

FAB–MS: m/z (%) = 263 (6, [M+H]⁺), 245 (11, [M–OH]⁺), 227 (9), 217 (6), 215 (1), 201 (30), 92 (100), 78 (27), 44 (24).

FAB–HRMS: C₁₆H₂₂O₃ (262.1569), calcd.: 263.1647 ([M+H]⁺), found: 263.1652.

(*R*)-1-[(*S,S*)-5-(2-Benzyloxyethyl)-2,5-dihydro-5-methylfuran-2-yl]ethanol
(11)



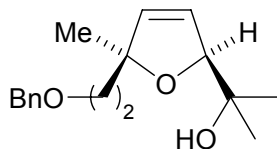
δH (400 MHz, CDCl₃ppm): 7.34–7.28 (m, ArH), 5.89 (dd, J = 6.0 Hz, J = 2.1 Hz, 1 H, CH=CH-CH), 5.82 (d, J = 6.0 Hz, 1 H, CH=CH-CH), 4.70 (s, 1 H, CH=CH-CH), 4.51 (dd, J = 12.2 Hz, 2 H, PhCH₂), 3.88 (m, 1 H, CHOH), 3.64/3.54 (m, 2 H, OCH₂CH₂), 2.09/1.85 (m, 2H, OCH₂CH₂), 1.29 (s, 3 H, furane-CH₃), 1.20 (d, J = 6.5 Hz, 3 H, CH₃CHOH).

δC (100 MHz, CDCl₃): 137.9 (x, quaternary ArC), 136.3 (+, CH=CH-CH), 128.3 (+, 2 x *m*-ArC), 127.8 (+, 2 x *o*-ArC), 127.6 (+, 1 x *p*-ArC), 89.1 (x, quaternary furane-C), 89.0 (+, CH=CH-CH), 72.7 (–, PhCH₂), 68.0 (+, CHOH), 66.4 (–, OCH₂CH₂), 39.8 (–, OCH₂CH₂), 26.6 (+, furane-CH₃), 18.1 (+, CH₃CHOH).

FAB–MS: m/z (%) = 263 (55, [M+H]⁺), 261 (11, [M–H]⁺), 92 (100), 84 (15), 56 (10).

FAB–HRMS: C₁₆H₂₂O₃ (262.1569), calcd.: 263.1647 ([M+H]⁺), found: 263.1677.

2-[(*S,S*)-5-(2-Benzyloxyethyl)-2,5-dihydro-5-methylfuran-2-yl]propan-2-ol
(12)



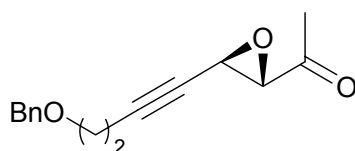
δ H (400 MHz, CDCl₃): 7.35–7.28 (m, 5 H, ArH), 5.90 (dd, *J* = 6.0 Hz, *J* = 2.3 Hz, 1 H, CH=CH-CH), 5.76 (d, *J* = 6.0 Hz, 1 H, CH=CH-CH), 4.60 (s, 1 H, CH=CH-CH), 4.51 (dd, *J* = 12.0 Hz, 2 H, PhCH₂), 3.62 (m, 2 H, OCH₂CH₂), 3.00 (s, 1 H, OH), 2.07/1.89 (m, 2H, OCH₂CH₂), 1.29 (s, 3 H, furane-CH₃), 1.21 (s, 3 H, (CH₃)₂COH), 1.17 (s, 3 H, (CH₃)₂COH).

δ C (100 MHz, CDCl₃): 138.0 (x, quaternary ArC), 136.4 (+, CH=CH-CH), 128.3 (+, 2 x *m*-ArC), 127.7 (+, 2 x *o*-ArC), 127.5 (+, 1 x *p*-ArC), 125.6 (+, CH=CH-CH), 91.6 (+, CH=CH-CH), 89.0 (x, quaternary furane C), 72.7 (–, PhCH₂), 71.0 (x, C(CH₃)₂), 66.5 (–, OCH₂CH₂), 40.0 (–, OCH₂CH₂), 26.8 (+, furane-CH₃), 26.2 (+, (CH₃)₂COH), 25.0 (+, (CH₃)₂COH).

FAB–MS: *m/z* (%) = 277 (30, [M+H]⁺), 259 (11), 92 (73), 60 (13), 40 (7).

FAB–HRMS: C₁₇H₂₄O₃ (276.1725), calcd.: 277.1804 ([M+H]⁺), found: 277.1762.

1-[(2*S*,3*R*)-3-(4-Benzyloxybut-1-ynyl)oxiran-2-yl]ethanone (13)



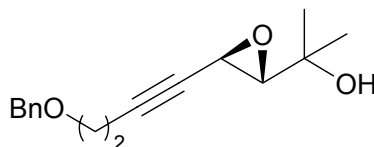
δ H (400 MHz, CDCl₃): 7.38–7.29 (m, 5 H, ArH), 4.55 (s, 2H, PhCH₂), 3.58 (t, J = 6.9 Hz, 2H, OCH₂CH₂), 3.55 (d, J = 1.5 Hz, 1 H, CH(O)CHC=O), 3.49 (d, J = 1.5 Hz, 1 H, CH(O)CHC=O), 2.54 (t, J = 6.8 Hz, 2 H, OCH₂CH₂), 2.09 (s, 3 H, CH₃).

δ C (100 MHz, CDCl₃): 203.0 (x, C=O), 137.8 (x, quaternary ArC), 128.4 (+, 2 x *m*-ArC), 127.7 (+, 1 x *p*-ArC), 127.6 (+, 2 x *o*-ArC), 83.1 (x, CH₂C≡C), 75.6 (x, CH₂C≡C), 72.9 (–, PhCH₂), 67.6 (–, OCH₂CH₂), 60.3 (+, CH(O)CHC=O), 45.0 (+, CH(O)CHC=O), 24.8 (+, CH₃), 20.1 (–, OCH₂CH₂).

FAB–MS: *m/z* (%) = 243 (4, [M–H]⁺), 242 (2), 226 (1), 225 (1), 222 (1), 92 (30), 52 (8), 44 (11).

FAB–HRMS: C₁₅H₁₆O₃ (244.1099), calcd.: 244.1099 ([M]⁺), found: 244.1075

2-((2*S*,3*R*)-3-(4-Benzyloxybut-1-ynyl)oxiran-2-yl)propan-2-ol (**14**)



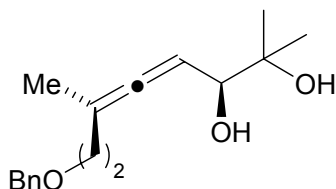
δ H (400 MHz, CDCl₃): 7.36–7.29 (m, 5 H, ArH), 4.55 (s, 2H, PhCH₂), 3.59 (t, J = 7.0 Hz, 2H, OCH₂CH₂), 3.43 (d, J = 1.5 Hz, 1 H, CH(O)CHCOH), 3.07 (d, J = 2.3 Hz, 1 H, CH(O)CHCOH), 2.54 (dt, J = 7.0 Hz, J = 1.0 Hz, 2 H, OCH₂CH₂), 1.77 (s, 1 H, OH), 1.31 (s, 3 H, CH₃), 1.26 (s, 3 H, CH₃).

δ C (100 MHz, CDCl₃): 137.9 (x, quaternary ArC), 128.4 (+, 2 x *m*-ArC), 127.7 (+, 1 x *p*-ArC), 127.6 (+, 2 x *o*-ArC), 81.9 (x, CH₂C≡C), 72.9 (–, PhCH₂), 67.8 (–, OCH₂CH₂), 67.4 (x, CH₂C≡C), 66.0 (+, CH(O)CHCOH), 42.9 (+, CH(O)CHCOH), 27.5 (+, CH₃), 24.8 (+, CH₃), 20.1 (–, OCH₂CH₂).

FAB–MS: *m/z* (%) = 261 (4, [M+H]⁺), 259 (10), 92 (100), 60 (60), 44 (40), 28 (7).

FAB–HRMS: C₁₆H₂₀O₃ (260.1412), calcd.: 261.1491 ([M+H]⁺), found: 261.1463

(*S,S*)-8-Benzyloxy-2,6-dimethylocta-4,5-diene-2,3-diol (**15**)



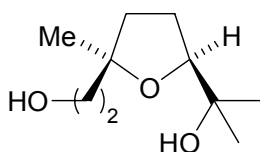
δ H (400 MHz, CDCl₃): 7.36–7.30 (m, 5 H, ArH), 5.22 (m, 1 H, C=C=CH), 4.53 (dd, J = 11.8 Hz, 2 H, PhCH₂), 3.85 (d, J = 3.0 Hz, 1 H, CHOH), 3.60 (m, 2 H, OCH₂CH₂), 2.91 (s, 2 H, OH), 2.28 (m, 2H, OCH₂CH₂), 1.74 (d, J = 2.8 Hz, 3 H, CH₃C=C=C), 1.18 (s, 3 H, CH₃), 1.11 (s, 3 H, CH₃).

δ C (100 MHz, CDCl₃): 200.6 (x, C=C=C), 137.7 (x, C-10), 128.4 (+, 2 x *m*-ArC), 128.1 (+, 2 x *o*-ArC), 127.8 (+, 1 x *p*-ArC), 100.8 (x, C=C=CH), 91.3 (+, C=C=CH), 75.7 (+, CHOH), 73.0 (–, PhCH₂), 72.9 (x, C(CH₃)₂), 67.3 (–, OCH₂CH₂), 34.4 (–, OCH₂CH₂), 25.4 (+, CH₃C=C=C), 23.8 (+, CH₃), 18.6 (+, CH₃).

FAB–MS: *m/z* (%) = 277 (4, [M+H]⁺), 273 (2), 272 (1), 267 (1), 201 (10), 92 (15), 40 (18).

FAB–HRMS: C₁₇H₂₄O₃ (276.1725), calcd.: 277.1804 ([M+H]⁺), found.: 277.1818.

2-((2*S*,5*R*)-Tetrahydro-5-(2-hydroxyethyl)-5-methylfuran-2-yl)propan-2-ol
(**16**)



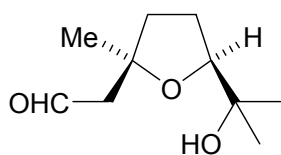
δ H (400 MHz, CDCl₃): 3.97–3.91 (m, 1 H, CH), 3.86–3.75 (m, 2 H, OCH₂CH₂), 2.54 (s, 1 H, OH), 2.02–1.68 (m, 6 H, CH₂CH₂C(CH₃)CH₂), 1.29 (s, 3 H, furane-CH₃), 1.24 (s, 3 H, CH₃), 1.13 (s, 3 H, CH₃).

δ C (100 MHz, CDCl₃): 85.7 (+, CH), 83.9 (x, CH₂C(CH₃)O), 70.9 (x, C(CH₃)₂), 59.8 (–, OCH₂CH₂), 41.8 (–, OCH₂CH₂), 38.2 (–, CH₂CH₂CH), 27.7 (+, furane-CH₃), 25.9 (–, CH₂CH₂CH), 25.4 (+, CH₃), 25.0 (+, CH₃).

FAB–MS: m/z (%) = 189 (64, [M+H]⁺), 171 (100, [M–OH]⁺), 154 (57), 82 (53).

FAB–HRMS: C₁₀H₂₀O₃ (188.1412), calcd.: 171.1351 ([M–OH]⁺), found: 171.1385

2-((2R,5S)-Tetrahydro-5-(2-hydroxypropan-2-yl)-2-methylfuran-2-yl)acetaldehyde (**3**)



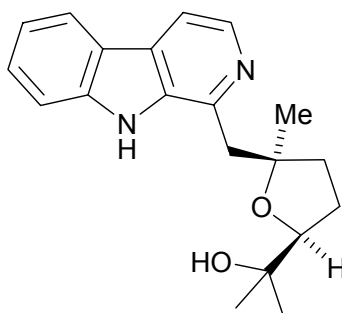
δ H (400 MHz, CDCl₃): 9.84 (t, J = 2.9 Hz, 1 H, HC=O), 3.83 (m, 1 H, CH), 2.62 (d, J = 2.8 Hz, 2 H, C=OCH₂), 1.95–1.78 (m, 4 H, CH₂CH₂CH), 1.37 (s, 3 H, furane-CH₃), 1.21 (s, 3 H, CH₃), 1.11 (s, 3 H, CH₃).

δ C (100 MHz, CDCl₃): 202.3 (+, C=O), 85.7 (+, CH), 81.2 (x, CH₂C(CH₃)O), 70.9 (x, C(CH₃)₂), 54.2 (–, C=OCH₂), 38.2 (–, CH₂CH₂CH), 27.4 (+, furane-CH₃), 26.8 (+, CH₃), 26.0 (–, CH₂CH₂CH), 24.4 (+, CH₃).

FAB–MS: m/z (%) = 187 (12, [M+H]⁺), 185 (20, [M–H]⁺), 169 (82, [M–OH]⁺), 143 (100), 56.0 (35), 42 (20).

FAB–HRMS: C₁₀H₁₈O₃ (186.1256), calcd.: 187.1334 ([M+H]⁺), found: 187.1375.

(-)-Isocyclocapitelline (2)



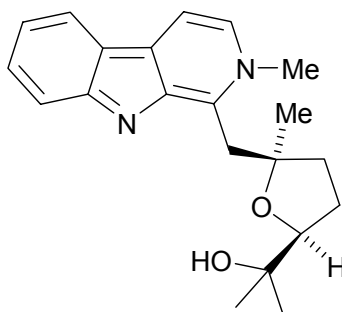
δ H (500 MHz, CDCl₃): 10.41 (s, 1 H, NH), 8.35 (d, J = 4.7 Hz, 1 H, 8-H), 8.09 (d, J = 7.6 Hz, 1 H, 12-H), 7.83 (d, J = 4.7 Hz, 1 H, 9-H), 7.50 (s, 1 H, 14-H), 7.50 (s, 1 H, 15-H), 7.24 (pt, J = 6.5 Hz, 1 H, 13-H), 3.89 (m, 1 H, 2-H), 3.48/3.21 (dd, J = 13.6 Hz, 2 H, 6-H), 2.08 (m, 2 H, 3-H, 4-H), 1.91 (m, 2 H, 3-H, 4-H), 1.33 (s, 3 H, 1'-H), 1.23 (s, 3 H, 5'-H), 1.21 (s, 3 H, 1''-H).

δ C (125 MHz, CDCl₃): 142.8 (x, C-7), 140.8 (x, C-16), 137.4 (+, C-8), 135.9 (x, C-17), 128.7 (x, C-10), 127.9 (+, C-14), 121.6 (x, C-11), 121.6 (+, C-12), 119.4 (+, C-13), 113.2 (+, C-9), 111.8 (+, C-15), 86.4 (+, C-2), 84.0 (x, C-5), 71.2 (x, C-1), 46.6 (-, C-6), 39.0 (-, C-4), 27.9 (+, C-1'), 26.1 (-, C-3), 25.9 (+, C-1''), 25.8 (+, C-5').

FAB-MS: m/z (%) = 325 (20, [M+H]⁺), 165 (4), 52 (6).

FAB-HRMS: C₂₀H₂₄N₂O₂ (324.1838), calcd.: 325.1916 ([M+H]⁺), found: 325.1900.

(-)-Isochrysotricine (1)



δ H (500 MHz, CDCl₃): 8.11 (d, J = 7.7 Hz, 1 H, 10-H), 7.96 (d, J = 8.5 Hz, 1 H, 9-H), 7.93 (d, J = 6.2 Hz, 1 H, 13-H), 7.53 (t, J = 7.6 Hz, 1 H, 15-H), 7.33 (d, J = 6.2 Hz, 1 H, 16-H), 7.13 (t, J = 7.1 Hz, 1 H, 14-H), 4.91 (s, 1H, OH), 4.32/3.19 (dd, J = 14.2 Hz, 2 H, 6-H), 4.12 (s, 3 H, 8'-H), 3.83 (m, 1 H, 2-H), 2.22-1.84 (m, 4 H, 3-H, 4-H), 1.27 (s, 3 H, 1'-H), 1.09 (s, 3 H, 1''-H), 1.03 (s, 3 H, 5'-H).

δ C (125 MHz, CDCl₃): 157.3 (x, C-17), 146.2 (x, C-18), 141.8 (x, C-7), 131.0 (x, C-11), 128.2 (+, C-15), 124.6 (+, C-9), 121.8 (+, C-13), 121.6 (x, C-12), 119.3 (+, C-14), 117.6 (+, C-16), 114.0 (+, C-10), 87.4 (+, C-2), 84.2 (+, C-6), 78.1 (x, C-5), 70.1 (x, C-1), 44.4 (+, C-8'), 39.4 (-, C-4), 27.4 (-, C-3), 27.0 (+, C-5'), 25.9 (+, C-1'), 25.5 (+, C-1'').

FAB-MS: m/z (%) = 339 (2, [M+H]⁺), 273 (3), 229 (2), 40 (7), 32 (3).

FAB-HRMS: C₂₁H₂₆N₂O₂ (338.1994), calcd.: 339.2073 ([M+H]⁺), found: 339.2103.