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Total Synthesis of (–)-Colchicine via a Rh-triggered Cycloaddition Cascade

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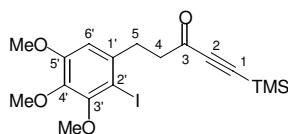
Supporting Information

General Procedures	2	Tropolones 21 and 22	17
		Tropolonemethyl ethers 24 and 25	18
Characterizations		7-Hydroxydesacetamidocolchicine 26	20
Propargylic ketone 6	2	7-Hydroxydesacetamido-	
Propargylic alcohol 8	3	-isocolchicine 27	21
Silyl ether 9	4	Methanesulfonic acid 28	22
4-oxobutyric acid 10	5	Azide 30	23
Diazoketone 11	6	Colchicine 1	24
TBS-protected Cycloadduct 12	7	Crystallographic Data	
Cycloadduct 13	8	Compound 8	25
Tropone 14	10	Compound 12	27
oxa-bridged compound 15	11	Compound 25	28
Diol 16	12	Compound 32	29
Aminotropones 17 and 18	13		
Aminotropones 19 and 20	15		

General Procedures. Reactions were conducted in flame-dried glassware under an atmosphere of argon using freshly distilled anhydrous solvents. NMR spectra were recorded at 25 °C on Bruker DRX 500, Bruker DPX 300 or Bruker AC 250 spectrometers. Proton chemical shifts are reported in ppm (δ) relative to the solvent reference downfield from TMS and were determined by reference to the residual solvent peaks (CDCl_3 : δ 7.24 ppm, DMSO [d6]: 2.50 ppm). Data are reported as follows: chemical shift (multiplicity [singlet (s), doublet (d), triplet (t), quartet (q) and multiplet (m)], coupling constants [Hz], integration). Carbon NMR spectra were recorded with complete proton decoupling and the multiplicity was assessed by DEPT measurements. Carbon chemical shifts are reported in ppm (δ) relative to solvent resonance as the internal standard (CDCl_3 : δ 77.0 ppm, DMSO [d6]: 39.5 ppm). Infrared spectra were obtained on Perkin Elmer FT-IR Paragon 1000 spectrometer. Melting points were recorded on a Büchi B-545 and are not corrected. Optical rotations were recorded on a Perkin Elmer Polarimeter 343 *plus* at the given wavelengths (path length 100 mm). Mass spectra were obtained on Finnigan MAT Incos 50 Galaxy System (DIP-MS) (EI) or Finnigan MAT 900 (ESI) spectrometers, high resolution mass spectra on a Finnigan HSQ-30 (HR-EI-MS) or on a Finnigan MAT 900 (HR-ESI-MS). The method of ionisation is given in parentheses.

Characterizations

5-(2-Iodo-3,4,5-trimethoxyphenyl)-1-(trimethylsilyl)pent-1-yn-3-one (6)



To a solution of TMS-acetylene (15.5 mL, 112 mmol, 1.53 equiv.) in abs. THF (215 mL) was slowly added a solution of *n*-BuLi (68.1 mL, 106 mmol, 1.45 equiv., 1.56 M in hexane) under argon at -78 °C. After 30 min, the resulting solution was warmed to 0 °C and cooled then back to -78 °C. The lithiumacetylid-solution obtained was added dropwise through a canula to a solution of Weinreb amide (**7**) (30.0 g, 73.3 mmol) in abs. THF (215 mL) at -78 °C. The resulting solution was warmed to -10 °C over 1 h, after 60 min cooled to -40 °C and then added to a mixture of ice and phosphate-buffer (pH 7, 500 mL). After extraction with CH_2Cl_2 (2 \times 500 mL), the combined organic extracts were dried under ice-cooling over Na_2SO_4 . Filtration over a short bed of Celite and removing of the solvents under vacuum at room temperature afforded 32.2 g (98 %) of a colorless oil.

R_f (SiO₂, EtOAc/*n*-hexane 1:6) = 0.29

IR (ATR): $\tilde{\nu}$ [cm⁻¹] = 2958 (s), 2934 (s), 2845 (w), 2148 (w), 1673 (ss), 1580 (w), 1558 (m), 1478 (s), 1425 (m), 1386 (s), 1339 (s), 1250 (s), 1197 (m), 1163 (m), 1100 (ss), 1047 (m), 1006 (s), 845 (ss), 761 (m), 703 (w).

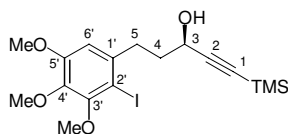
¹H-NMR (300 MHz, CDCl₃): δ [ppm] = 0.21 (s, 9H, SiMe₃), 2.86 (m, 2H), 3.05 (m, 2H), 3.81 (s, 6H, 2 OMe), 3.84 (s, 3H, OMe), 6.65 (s, 1H, 6'-H).

¹³C-NMR (75 MHz, CDCl₃): δ [ppm] = -0.79 (q, SiMe₃), 34.97 (t), 45.43 (t), 56.09 (q, OMe), 60.69 (q, OMe), 60.91 (q, OMe), 87.67 (s), 98.44 (s), 101.71 (s), 109.10 (d, C-6'), 138.46 (s), 140.54 (s), 153.13 (s), 153.57 (s), 186.11 (s, C-3).

MS (DIP-EI70 eV): m/z (%) = 446 (45) [M]⁺, 374 (17), 319 (100) [-I], 307 (34), 277 (41), 247 (9), 194 (18), 125 (47), 97 (43), 83 (40).

HRMS (ED): calc. for [M]⁺ (¹²C₁₇H₂₃¹²⁷I¹⁶O₄²⁸Si): 446.0410, found: 446.041.

(3*R*)-5-(2-Iodo-3,4,5-trimethoxyphenyl)-1-(trimethylsilyl)pent-1-yn-3-ol (**8**)



To a solution of alkyne (**6**) (31.8 g, 71.2 mmol) in *i*PrOH (71 mL, HPLC-grade) under argon was added 1 mol % of (*R,R*)-ruthenium-catalyst (**7**) (427 mg, 712 μ mol). The color of the solution turns to brown with the total dissolution of the catalyst. After 16 h, the solvent was removed under vacuum and the residue was purified by flash-chromatography (EtOAc/cyclohexane 1:5, 1:4, 1:3). Crystallisation from *n*-hexane afforded 30.5 g (96 %) of colorless quadratic crystalline solid.

R_f (SiO₂, EtOAc/cyclohexane 1:3) = 0.26

mp.: 75 °C (*n*-hexane)

IR (ATR): $\tilde{\nu}$ [cm⁻¹] = 3425 (ss, br.), 2954 (m), 2935 (m), 2169 (w), 1560 (m), 1478 (s), 1425 (m), 1358 (s), 1332 (s), 1247 (s), 1197 (m), 1162 (m), 1103 (s), 1063 (m), 1042 (m), 1005 (s), 841 (ss), 759 (m).

¹H-NMR (300 MHz, CDCl₃): δ [ppm] = 0.17 (s, 9H, SiMe₃), 1.91 (d, ³*J* = 5.5 Hz, 1 OH), 1.95 (m, 2H, 4-H₂), 2.89 (m, 2H, 5-H₂), 3.82 (s, 3H, OMe), 3.83 (s, 3H, OMe), 3.85 (s, 3H, OMe), 4.38 (dq_{tt}, *J*_d = 5.5 Hz, *J*_t = 6.5 Hz, 1H, 3-H), 6.65 (s, 1H, 6'-H).

$^{13}\text{C-NMR}$ (75 MHz, CDCl_3): δ [ppm] = -0.11 (q, SiMe_3), 36.67 (t), 37.81 (t), 56.11 (q, OMe), 60.69 (q, OMe), 60.94 (q, OMe), 62.09 (d, C-3), 87.96 (s), 90.05 (s), 106.23 (s), 108.90 (d, C-6'), 139.59 (s), 140.40 (s), 153.11 (s), 153.53 (s).

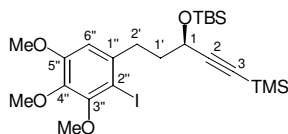
MS (DIP-EI70 eV): m/z (%) = 448 (7) $[\text{M}]^+$, 321 (13) $[-\text{I}]$, 308 (20), 277 (7), 205 (15), 191 (6), 181 (100), 165 (5), 99 (5), 75 (7), 73 (16).

HRMS (ED): calc. for $[\text{M}]^+$ ($^{12}\text{C}_{17}\text{H}_{25}^{127}\text{I}^{16}\text{O}_4^{28}\text{Si}$): 448.0567, found.: 448.056.

$[\alpha]_{\text{D}} = -21.5$, $[\alpha]_{546} = -26.2$, $[\alpha]_{405} = -59.8$, $[\alpha]_{365} = -83.0$ ($c = 1.00$, CHCl_3 , 20°C).

HPLC (Diacel Chiralpak AD-H, hexane/*i*PrOH 98:2, $v = 1.0$ ml/min, $\lambda = 254$ nm, $\sim 25^\circ\text{C}$): $t_{\text{R}} = 20.36$ min (100 %), $>99\%$ *ee*.

***tert*-Butyl(dimethyl)silyl[(1*R*)-1-[(2-iodo-3,4,5-trimethoxyphenyl)ethyl]-3-(trimethylsilyl)prop-2-ynyl]ether (9)**



Propargylalcohol (**8**) (30.0 g, 66.9 mmol), imidazole (11.4 g, 167 mmol, 2.5 equiv.) and TBSCl (12.1 g, 80.3 mmol, 1.2 equiv.) were solubilized in abs. DMF (100 mL) and stirred under argon overnight. H_2O (300 mL) was then added and the resulting mixture was extracted with MTBE (3 \times 300 mL). The combined organic extracts were washed with saturated NH_4Cl (300 mL) and dried over Na_2SO_4 . After filtration over a short bed of Celite and removal of the solvent under vacuum, the raw product was purified by flash-chromatography (EtOAc/cyclohexane 1:20). Subsequent crystallisation from *n*-hexane afforded 35.1 g (93 %) of colorless crystals.

R_f (SiO_2 , EtOAc/*n*-hexane 1:10) = 0.33

mp.: $50\text{--}51^\circ\text{C}$ (*n*-hexane)

IR (ATR): $\tilde{\nu}$ [cm^{-1}] = 2953 (s), 2931 (s), 2852 (m), 2169 (w), 1561 (w), 1478 (s), 1425 (m), 1385 (s), 1332 (m), 1248 (s), 1197 (m), 1162 (m), 1103 (ss), 1006 (s), 838 (ss), 776 (m).

$^1\text{H-NMR}$ (300 MHz, CDCl_3): δ [ppm] = 0.13 (s, 3H, OSiMe), 0.15 (s, 3H, OSiMe), 0.15 (s, 9H, SiMe_3), 0.91 (s, 9H, OSi*t*Bu), 1.91 (m, 2H, 1'- H_2), 2.84 (m, 2H, 2'- H_2), 3.83 (s, 6H, 2 OMe), 3.85 (s, 3H, OMe), 4.40 (qt, $^3J = 6.5$ Hz, 1H, 1-H), 6.62 (s, 1H, 6''-H).

$^{13}\text{C-NMR}$ (75 MHz, CDCl_3): δ [ppm] = -4.83 (q, OSiMe), -4.36 (q, OSiMe), -0.16 (q, SiMe_3), 18.30 (s, OSi CMe_3), 25.86 (q, OSi CMe_3), 37.03 (d), 38.77 (d), 56.11 (q, OMe), 60.68

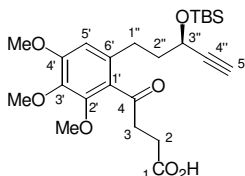
(q, OMe), 60.95 (q, OMe), 62.82 (d, C-1), 88.03 (s), 89.13 (s), 107.21 (s), 108.78 (d, C-6''), 140.16 (s), 140.30 (s), 153.08 (s), 153.50 (s).

MS (DIP-EL, 70 eV): m/z (%) = 562 (6) [M]⁺, 505 (9) [-C₄H₉], 435 (18) [-I], 420 (14), 378 (32), 363 (100), 348 (14), 307 (78), 305 (41), 181 (61), 155 (20), 75 (14), 73 (26).

HRMS (ED): calc. for [M]⁺ (¹²C₂₃H₃₉¹²⁷I¹⁶O₄²⁸Si₂): 562.1432, found.: 562.142.

[α]_D = +8.2, [α]₅₄₆ = +9.3, [α]₄₀₅ = +15.3, [α]₃₆₅ = +17.1 (c = 0.995, CHCl₃, 20 °C).

4-[6-((3R)-3-[[*tert*-Butyl(dimethyl)silyl]oxy]pent-4-ynyl)-2,3,4-trimethoxyphenyl]-4-oxobutyric acid (**10**)



To a solution of aryl iodide (**9**) (14.7 g, 26.1 mmol) in abs. THF (275 mL) under argon was added dropwise a solution of *i*PrMgCl (26.1 mL, 52.2 mmol, 2 equiv., 2M in THF) at -25 °C. After 4 h, the Grignard solution was cooled to -40 °C and added rapidly through a canula to a stirred suspension of succinic anhydride (10.4 g, 104 mmol, 4 equiv.) in abs. THF (275 mL). The resulting mixture was warmed to RT over 1.5 h, added to a of saturated NH₄Cl solution (450 mL) and extracted with CH₂Cl₂ (3×250 mL). The combined organic extracts were dried over Na₂SO₄. After filtration and removal of the solvent under vacuum, the raw product was dissolved in abs. MeOH (750 mL). K₂CO₃ (34.8 g, 261 mmol, 10 equiv.) was added to the resulting solution and the mixture was stirred 1.5 h at RT, then added to a saturated NH₄Cl solution (750 mL) and extracted CH₂Cl₂ (3×300 mL). The combined organic extracts were dried over Na₂SO₄. After filtration and removal of the solvent under vacuum, the raw product was purified by flash-chromatography (EtOAc/cyclohexane 1:3, 1:2, 1:1, 2:1) to afford 8.91 g (73 %) of a colorless viscose oil.

R_f (SiO₂, EtOAc/cyclohexane 1:1) = 0.35

IR (ATR): $\tilde{\nu}$ [cm⁻¹] = 3282 (m), 2930 (s), 2854 (w), 2109 (w), 1734 (m), 1708 (ss), 1593 (m), 1493 (m), 1455 (m), 1399 (s), 1335 (s), 1249 (s), 1129 (s), 1091 (s), 999 (m), 836 (s), 777 (m), 667 (m).

¹H-NMR (500 MHz, CDCl₃): δ [ppm] = 0.09 (s, 3H, OSiMe), 0.12 (s, 3H, OSiMe), 0.88 (s, 9H, OSi*t*Bu), 1.90 (m, 2H, 2''-H₂), 2.40 (d, ⁴J = 2 Hz, 1H, 5''-H), 2.58 (m, 2H, 1''-H₂), 2.73 (m, 2H, 2-H₂), 3.10 (m, 2H, 3-H₂), 3.83 (s, 3H, OMe at C-3'), 3.837^{**} (s, 3H, OMe at C-4'),

3.839^{**}) (s, 3H, OMe at C-2'), 4.34 (dt, ⁴J = 2 Hz, ³J = 6.5 Hz, 1H, 3''-H), 6.50 (s, 1H, 5'-H).*)

¹³C-NMR (75 MHz, CDCl₃): δ [ppm] = -5.09 (q, OSiMe), -4.59 (q, OSiMe), 18.18 (s, OSiCMe₃), 25.74 (q, OSiCMe₃), 28.12 (t, C-2), 28.67 (t, C-1''), 39.51 (t, C-3), 40.52 (t, C-2''), 56.01^{**}) (q, OMe at C-4'), 60.88 (q, OMe at C-3'), 61.67^{**}) (q, OMe at C-2'), 62.26 (d, C-3''), 72.56 (d, C-5''), 85.02 (d, C-4''), 108.73 (d, C-5'), 127.94 (s, C-1'), 134.81 (s, C-6'), 139.75 (s, C-3'), 150.62^{**}) (s, C-2'), 154.31^{**}) (s, C-4'), 178.52 (s, C-1), 203.89 (s, C-4).*)

MS (DIP-El, 70 eV): m/z (%) = 407 (16) [M⁺-C₄H₉], 307 (21), 287 (16), 263 (12), 250 (44), 235 (17), 231 (26), 219 (14), 182 (100), 167 (21), 151 (29), 101 (18), 97 (21), 83 (20).

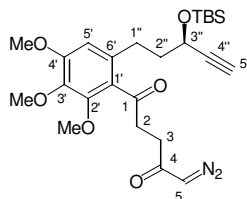
HRMS (ED): calc. for [M]⁺ (¹²C₂₀H₂₇¹⁶O₇²⁸Si): 407.1526, found.: 407.153.

[α]_D = +12.6, [α]₅₄₆ = +14.1, [α]₄₀₅ = +26.7, [α]₃₆₅ = +38.0 (c = 1.00, CHCl₃, 20 °C).

*) The peaks in ¹H-NMR- and ¹³C-NMR-Spectrum were assigned with the help of H,H-Cosy-, HMQC-, HMBC- und NOESY-spectra.

***) The assignments of the peaks at 3.837/56.01/154.31 ppm und 3.839/61.67/150.62 ppm in ¹H-NMR- und ¹³C-NMR-spectra were made based on the comparison with the corresponding signals of **13**.

(3R)-5-Diazo-1-[6-[3-[[*tert*-butyl(dimethyl)silyl]oxy]pent-4-ynyl]-2,3,4-trimethoxyphenyl]-pentan-1,4-dione (**11**)



To a solution of γ -oxocarboxylic acid (**10**) (8.81 g, 19.0 mmol) in THF (160 mL) and Et₂O (160 mL) under argon were sequentially added at -20 °C NEt₃ (2.65 mL, 19.0 mmol, 1.0 equiv.) and ClC(O)OiBu (2.49 mL, 19.0 mmol, 1.0 eq). After 1 h, the mixture was warmed to -10 °C and a solution of CH₂N₂ (380 mL, 87.4 mmol, 4.6 eq, 0.23M in Et₂O) was added dropwise. After stirring at -5 °C overnight, the solution was warmed to RT and silica was added to destroy the excess of diazomethane. After filtration, the solution was washed with water (200 mL), saturated NaHCO₃ (200 mL) and brine (200 mL). The organic phase was dried over Na₂SO₄ and the solvent was removed under vacuum. Purification by flash-chromatography (EtOAc/cyclohexane 1:5, 1:4, 1:3, 1:2) afforded 6.59 g (71 %) of a light yellow oil.

R_f (SiO₂, EtOAc/cyclohexane 1:3) = 0.24

IR (ATR): $\tilde{\nu}$ [cm⁻¹] = 3272 (w), 3095 (w), 2928 (s), 2853 (m), 2100 (ss, C=N=N), 1696 (m), 1643 (s), 1593 (m), 1571 (w), 1492 (m), 1461 (s), 1400 (s), 1376 (s), 1344 (ss), 1316 (s), 1250 (s), 1128 (s), 1093 (ss), 835 (ss), 777 (s), 665 (w).

¹H-NMR (500 MHz, CDCl₃): δ [ppm] = 0.09 (s, 3H, OSiMe), 0.12 (s, 3H, OSiMe), 0.88 (s, 9H, OSi^tBu), 1.89 (m, 2H, 2''-H₂), 2.38 (d, ⁴*J* = 2 Hz, 1H, 5''-H), 2.58 (m, 2H, 1''-H₂), 2.68 (br. m, 2H, 3-H₂), 3.10 (m, 2H, 2-H₂), 3.80 (s, 3H, OMe at C-3'), 3.82 (s, 3H, OMe at C-4'), 3.83 (s, 3H, OMe at C-2'), 4.36 (dt, ⁴*J* = 2 Hz, ³*J* = 6.5 Hz, 1H, 3''-H), 5.31 (br. s, 1H, 5-H), 6.48 (s, 1H, 5'-H).*)

¹³C-NMR (62.5 MHz, CDCl₃): δ [ppm] = -5.10 (q, OSiMe), -4.64 (q, OSiMe), 18.15 (s, OSiCMe₃), 25.72 (q, OSiCMe₃), 28.70 (t, C-1''), 34.23 (br. t, C-3), 39.54 (br. t, C-2), 40.52 (t, C-2''), 54.39 (br. d, C-5), 55.96 (q, OMe at C-4'), 60.81 (q, OMe at C-3'), 61.59 (q, OMe at C-2'), 62.26 (d, C-3''), 72.45 (d, C-5''), 85.05 (d, C-4''), 108.64 (d, C-5'), 128.04 (s, C-1'), 134.66 (s, C-6'), 139.65 (s, C-3'), 150.49 (s, C-2'), 154.21 (s, C-4'), 193.15 (s, C-4), 204.41 (C-1).*)

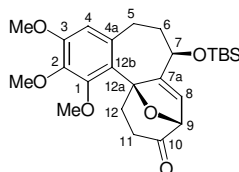
MS (DIP-EI, 70 eV): *m/z* (%) = 488 (4) [M]⁺, 460 (45) [-N₂], 403 (10) [-N₂ -C₄H₉], 351 (9), 305 (7), 231 (56), 219 (15), 207 (14), 181 (20), 129 (48), 115 (15), 83 (30), 75 (92), 73 (86).

HRMS (EI): calc. for [M]⁺ (¹²C₂₅H₃₆¹⁴N₂¹⁶O₆²⁸Si): 488.2343, found.: 488.235.

[α]_D = +11.3, [α]₅₄₆ = +13.0 (*c* = 1.00, CHCl₃, 20 °C).

*) Peaks in ¹H-NMR- und ¹³C-NMR-spectra were assigned with the help of H,H-Cosy-, HMQC-, HMBC- und NOESY-spectra.

(7*R*,9*R*,12*aR*)-7-[[*tert*-Butyl(dimethyl)silyl]oxy]-1,2,3-trimethoxy-9,12*a*-epoxy-6,7,9,11,12,12*a*-hexahydrobenzo[*a*]heptalen-10(5*H*)-one (12)



To a stirred suspension of Rh₂(OAc)₄ (132 mg, 298 μ mol, 3 mol %) in abs. toluene (200 mL), was added over 6 h through *via* a syringe pump a solution of diazoketone (**11**) (4.86 g, 9.95 mmol) in abs. toluene (300 mL). After 60 min under reflux, the solution was cooled to RT and the solvent was removed under vacuum. The raw product was purified by flash-chromatography (EtOAc/cyclohexane 1:5) to afford 2.94 g (64 %) of a colorless viscose oil.

R_f (SiO₂, EtOAc/cyclohexane 1:5) = 0.24

IR (ATR): $\tilde{\nu}$ [cm⁻¹] = 2932 (m), 2854 (w), 1726 (ss, C=O ketone), 1592 (m), 1493 (m), 1451 (s), 1402 (m), 1347 (m), 1320 (m), 1291 (m), 1249 (s), 1197 (w), 1129 (s), 1087 (ss), 1031 (m), 1003 (m), 921 (m), 881 (m), 834 (s), 807 (m), 775 (m), 666 (w).

¹H-NMR (500 MHz, CDCl₃): δ [ppm] = 0.01 (s, 3H, OSiMe), 0.03 (s, 3H, OSiMe), 0.88 (s, 9H, OSi*t*Bu), 1.83 (ddd, ³*J*₁ = 6.5 Hz, ³*J*₂ = 7.5 Hz, ²*J* = 13.5 Hz, 1H, 12-H_a), 1.86 (dddd, ³*J*₁ = 4.0 Hz, ³*J*₂ = 4.5 Hz, ³*J*₃ = 5.5 Hz, ²*J* = 13.5 Hz, 1H, 6-H_a), 2.32 (dddd, ³*J*₁ = 3.5 Hz, ³*J*₂ = 8.5 Hz, ³*J*₃ = 13.5 Hz, ²*J* = 13.5 Hz, 1H, 6-H_b), 2.41 (ddd, ³*J*₁ = 3.5 Hz, ³*J*₂ = 4 Hz, ²*J* = 14.5 Hz, 1H, 5-H_a), 2.60 (ddd, ³*J*₁ = 3.5 Hz, ³*J*₂ = 7.5 Hz, ²*J* = 17 Hz, 1H, 11-H_a), 2.92 (ddd, ³*J*₁ = 6.5 Hz, ³*J*₂ = 9 Hz, ²*J* = 17 Hz, 1H, 11-H_b), 3.08 (ddd, ³*J*₁ = 4.5 Hz, ³*J*₂ = 13.5 Hz, ²*J* = 14.5 Hz, 1H, 5-H_b), 3.33 (ddd, ³*J*₁ = 3.5 Hz, ³*J*₂ = 9 Hz, ²*J* = 13.5 Hz, 1H, 12-H_b), 3.83 (s, 3H, OMe at C-3), 3.85 (s, 3H, OMe at C-2), 3.95 (s, 3H, OMe at C-1), 4.51 (ddd, ⁴*J* = 2 Hz, ³*J*₁ = 5.5 Hz, ³*J*₂ = 8.5 Hz, 1H, 7-H), 4.72 (d, ³*J* = 2 Hz, 1H, 9-H), 6.00 (ψt, *J* = 2 Hz, 1H, C-8), 6.39 (s, 1H, 4-H).*)

¹³C-NMR (75 MHz, CDCl₃): δ [ppm] = -4.83 (q, OSiMe₂), 18.05 (s, OSiCMe₃), 25.72 (q, OSiCMe₃), 30.55 (t, C-12), 32.20 (t, C-5), 35.63 (t, C-11), 37.00 (t, C-6), 55.84 (q, OMe an C-3), 60.74 (q, OMe an C-2), 62.29 (q, OMe an C-1), 67.46 (d, C-7), 85.55 (d, C-9), 88.30 (s, C-12a), 109.68 (d, C-4), 120.05 (d, C-8), 123.69 (s, C-12b), 137.12 (s, C-4a), 141.86 (s, C-2), 153.27 (s, C-3), 154.88 (s, C-1), 156.54 (s, C-7a), 204.41 (s, C-10).*)

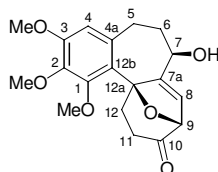
MS (DIP-EL, 70 eV): *m/z* (%) = 460 (15) [M]⁺, 403 (100) [-C₄H₉], 375 (16), 361 (9), 329 (40), 285 (9), 273 (58), 181 (11), 75 (16), 73 (18).

HRMS (EI): calc. for [M]⁺ (¹²C₂₅H₃₆¹⁶O₆²⁸Si): 460.2281, found.: 460.228.

[α]_D = +125.5, [α]₅₄₆ = +161.9, [α]₄₀₅ = +660.5, [α]₃₆₅ = +1450 [α]₃₃₄ = +5110 (*c* = 1.05, CHCl₃, 20 °C).

*) Peaks in ¹H-NMR- und ¹³C-NMR-spectra were assigned with the help of H,H-Cosy-, HMQC-, HMBC- und NOESY-spectra.

(7*R*,9*R*,12*aR*)-7-Hydroxy-1,2,3-trimethoxy-9,12*a*-epoxy-6,7,9,11,12,12*a*-hexahydrobenzo[*a*]heptalen-10(5*H*)-one (13)



To a solution of silylether (**12**) (98 mg, 213 μmol) in abs. THF (2 mL) under argon was added at 0 °C a solution of TBAF (0.64 mL, 640 μmol, 3 equiv., 1M in THF). After 30 min, water

(10 mL) was added and the solution was extracted with CH₂Cl₂ (3×4 mL). The combined organic extracts were filtered over a short bed of Celite in a Pasteur-pipette and the solvent was removed under vacuum. After radial chromatography over silica-gel (EtOAc/cyclohexane 2:1), 68 mg (92 %) of a colorless solid were obtained.

R_f (SiO₂, EtOAc/cyclohexane 3:1) = 0.36

mp.: 154-155 °C (EtOAc/cyclohexane)

IR (ATR): $\tilde{\nu}$ [cm⁻¹] = 3443 (s, br., OH), 2936 (m), 2854 (w), 1722 (ss, C=O ketone), 1592 (m), 1492 (m), 1451 (s), 1401 (m), 1320 (m), 1241 (w), 1195 (w), 1127 (s), 1088 (m), 1027 (s), 1002 (m), 918 (w), 833 (w), 808 (w), 750 (s), 665 (w).

¹H-NMR (500 MHz, CDCl₃): δ [ppm] = 1.84 (m, 1H, 12-H_a), 1.87 (m, 1H, 6-H_a), 2.37 (dddd, ³J₁ = 3.5 Hz, ³J₂ = 8 Hz, ³J₃ = 13 Hz, ²J = 13.5 Hz, 1H, 6-H_b), 2.46 (ddd, ³J₁ = 3.5 Hz, ³J₂ = 4 Hz, ²J = 14.5 Hz, 1H, 5-H_a), 2.60 (ddd, ³J₁ = 3 Hz, ³J₂ = 7.5 Hz, ²J = 17 Hz, 1H, 11-H_a), 2.95 (ddd, ³J₁ = 7 Hz, ³J₂ = 9.5 Hz, ²J = 17 Hz, 1H, 11-H_b), 3.04 (ddd, ³J₁ = 4 Hz, ³J₂ = 13 Hz, ²J = 14.5 Hz, 1H, 5-H_b), 3.26 (ddd, ³J₁ = 3 Hz, ³J₂ = 9.5 Hz, ²J = 13 Hz, 1H, 12-H_b), 3.83 (s, 3H, OMe an C-3), 3.84 (s, 3H, OMe an C-2), 3.95 (s, 3H, OMe an C-1), 4.61 (ddd, ⁴J = 2 Hz, ³J₁ = 5.5 Hz, ³J₂ = 8 Hz, 1H, 7-H), 4.74 (d, ³J = 2 Hz, 1H, 9-H), 6.06 (ψ t, *J* = 2 Hz, 1H, C-8), 6.40 (s, 1H, 4-H).*)

¹³C-NMR (75 MHz, CDCl₃): δ [ppm] = 30.94 (t, C-12), 31.87 (t, C-5), 35.65 (t, C-6), 36.00 (t, C-11), 55.85 (q, OMe at C-3), 60.73 (q, OMe at C-2), 62.26 (q, OMe at C-1), 67.16 (d, C-7), 85.45 (d, C-9), 88.40 (s, C-12a), 109.69 (d, C-4), 120.10 (d, C-8), 123.82 (s, C-12b), 136.74 (s, C-4a), 141.88 (s, C-2), 153.21 (s, C-3), 154.82 (s, C-1), 156.62 (s, C-7a), 204.72 (s, C-10).*)

MS (DIP-EI, 70 eV): *m/z* (%) = 346 (38) [M]⁺, 329 (15), 318 (39) [-CO], 299 (20), 290 (30), 273 (21), 259 (26), 220 (33), 181 (100), 128 (23), 115 (39), 91 (20), 77 (24).

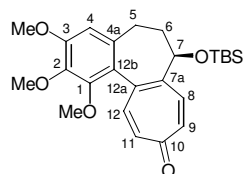
HRMS (EI): calc. for [M]⁺ (¹²C₁₉H₂₂¹⁶O₆): 346.1416, found.: 346.142.

[α]_D = +217.5, [α]₅₄₆ = +283.5, [α]₄₀₅ = +1117.7, [α]₃₆₅ = +2438.0 (*c* = 0.990, CHCl₃, 20 °C).

HPLC (Macherey-Nagel Nucleosil pre-column, Diacel Chiralpak AD-H, Hexane/*i*PrOH 90:10, *v* = 1.0 ml/min, λ = 254 nm, ~25 °C): *t_R* = 9.45 min (100 %), > 99 % *ee*.

*) Peaks in ¹H-NMR- und ¹³C-NMR-spectra were assigned according to the data of the corresponding (*rac*) compound, with the help of H,H-Cosy-, HMQC-, HMBC- und NOESY-spectra.

(7*RS*)-7-[[*tert*-Butyl(dimethyl)silyl]oxy]-1,2,3-trimethoxy-6,7-dihydrobenzo[*a*]heptalen-10(5*H*)-one (*rac*-14)



To a solution of ketone (*rac*-**12**) (400 mg, 869 μmol) in abs. CH_2Cl_2 (20 mL) under argon was added dropwise at -78°C a solution of Et_2AlCl (4.35 mL, 4.35 mmol, 5 equiv., 1M in *n*-hexane). The solution was warmed to 0°C over 2 h and cooled again to -78°C . After addition of MeOH (5 mL), the solution was slowly warmed to RT and saturated NH_4Cl (50 mL) was added. The aqueous phase was extracted CH_2Cl_2 (2 \times 50 mL) and the combined organic extracts were dried over Na_2SO_4 . After filtration and removal of the solvent under vacuum, the raw product was purified by flash-chromatography (EtOAc/cyclohexane 1:4, 1:3, 1:2, 1:1) to afford 199 mg (52 %) of a yellow oil.

R_f (SiO_2 , EtOAc/cyclohexane 1:2) = 0.20

IR (ATR): $\tilde{\nu}$ [cm^{-1}] = 2928 (s), 2853 (m), 1623 (s), 1562 (ss), 1488 (m), 1454 (s), 1401 (m), 1341 (m), 1320 (m), 1234 (m), 1134 (s), 1093 (ss), 1003 (s), 876 (s), 835 (ss), 777 (s), 730 (w), 670 (w).

$^1\text{H-NMR}$ (300 MHz, CDCl_3): δ [ppm] = -0.13 (s, 3H, OSiMe), -0.09 (s, 3H, OSiMe), 0.82 (s, 9H, OSi*t*Bu), 1.95 (m, 1H, 6- H_a), 2.32 (m, 1H, 6- H_b), 2.35 (m, 2H, 5- H_2), 3.64 (s, 3H, OMe an C-1), 3.89 (s, 3H, OMe an C-2), 3.90 (s, 3H, OMe an C-3), 4.27 (m, 1H, 7-H), 6.54 (s, 1H, 4-H), 6.95 (dd, $^4J = 3$ Hz, $^3J = 12.5$ Hz, 11-H), 7.10 (dd, $^4J = 3$ Hz, $^3J = 13$ Hz, 9-H), 7.23 (d, $^3J = 12.5$ Hz, 12-H), 7.77 (d, $^3J = 13$ Hz, 8-H).^{*)}

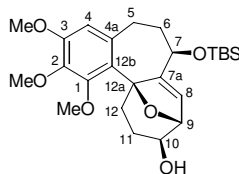
$^{13}\text{C-NMR}$ (75 MHz, CDCl_3): δ [ppm] = -5.09 (q, OSiMe), -4.95 (q, OSiMe), 18.16 (s, OSiCMe₃), 25.75 (q, OSiCMe₃), 29.99 (t, C-5), 42.16 (t, C-6), 56.01 (q, OMe an C-3), 61.00 (q, OMe an C-1), 61.23 (q, OMe an C-2), 71.80 (d, C-7), 107.24 (d, C-4), 124.93 (s, C-12b), 134.19 (d, C-8), 136.02 (s, C-4a), 138.23 (d, C-11), 139.05 (s, C-12a), 140.13 (d, C-9), 141.17 (s, C-2), 141.28 (d, C-12), 147.67 (s, C-7a), 150.72 (s, C-1), 153.96 (s, C-3), 187.43 (s, C-10).^{*)}

MS (DIP-EI, 70 eV): m/z (%) = 442 (23) [$\text{M}]^+$, 385 (100) [$-\text{C}_4\text{H}_9$], 357 (59) [$-\text{C}_4\text{H}_9 - \text{CO}$], 342 (27), 252 (16), 126 (65), 73 (42).

HRMS (EI): calc. für [$\text{M}]^+$ ($^{12}\text{C}_{25}\text{H}_{34}^{16}\text{O}_5^{28}\text{Si}$): 442.2176, found.: 442.217.

^{*)} Peaks in $^1\text{H-NMR}$ - und $^{13}\text{C-NMR}$ -spectra were assigned with the help of H,H-Cosy-, HMQC-, HMBC- und NOESY-spectra.

(7*R*,9*R*,10*S*,12*aR*)-7-[[*tert*-Butyl(dimethyl)silyl]oxy]-1,2,3-trimethoxy-9,12*a*-epoxy-5,6,7,9,10,11,12,12*a*-octahydrobenzo[*a*]heptalen-10-ol (15)



To a solution of ketone (**12**) (1.40 g, 3.04 mmol) in abs. THF (30 mL) under argon was added dropwise at $-78\text{ }^{\circ}\text{C}$ a solution of L-Selectride (7.6 mL, 2.5 equiv., 1M in THF). After 3 h, MeOH (5 mL) was added and the reaction mixture was slowly warmed to RT, gas evolution was observed. After addition of saturated NH_4Cl (50 mL), the mixture was extracted with MTBE (3 \times 50 mL) and the combined organic extracts were dried over Na_2SO_4 . After filtration and removal of the solvent under vacuum, the raw product was purified by flash-chromatography (EtOAc/cyclohexane 1:4, 1:3, 1:2) to afford 1.13 g (80%) of a colorless faum.

R_f (SiO_2 , EtOAc/*n*-hexane 1:2) = 0.19

IR (ATR): $\tilde{\nu}$ [cm^{-1}] = 3425 (w, br.), 2930 (ss), 2854 (m), 1591 (m), 1490 (m), 1452 (s), 1399 (s), 1346 (m), 1319 (s), 1255 (s), 1197 (m), 1130 (s), 1088 (ss), 1017 (m), 950 (w), 883 (w), 835 (ss), 774 (m), 665 (w).

$^1\text{H-NMR}$ (300 MHz, CDCl_3): δ [ppm] = 0.044 (s, 3H, OSiMe), 0.045 (s, 3H, OSiMe), 0.91 (s, 9H, OSi*t*Bu), 1.18 (dd, $^3J = 6.5$ Hz, $^2J = 14$ Hz, 1H, 12- H_a), 1.71 (dd, $^3J = 6.5$ Hz, $^2J = 14$ Hz, 1H, 11- H_a), 1.85 (m, 1H, 6- H_a), 1.88 (m, 1H, 11- H_b), 2.19 (dddd, $^3J_1 = 3$ Hz, $^3J_2 = 7.5$ Hz, $^3J_3 = 12.5$ Hz, $^2J = 13.5$ Hz, 1H, 6- H_b), 2.40 (ddd, $^3J_1 = 3$ Hz, $^3J_2 = 5$ Hz, $^2J = 14.5$ Hz, 1H, 5- H_a), 2.90 (br. d, $J = 10$ Hz, 1 OH), 3.14 (ddd, $^3J_1 = 4$ Hz, $^3J_2 = 12.5$ Hz, $^2J = 14.5$ Hz, 1H, 5- H_b), 3.35 (ddd, $^3J_1 = 6.5$ Hz, $^3J_2 = 11.5$ Hz, $^2J = 14$ Hz, 1H, 12- H_b), 3.48 (s, 1H, 10-H), 3.81 (s, 3H, OMe an C-3), 3.84 (s, 3H, OMe an C-2), 3.93 (s, 3H, OMe an C-1), 4.30 (ddd, $^4J = 2$ Hz, $^3J_1 = 5.5$ Hz, $^3J_2 = 7.5$ Hz, 1H, 7-H), 4.64 (s, 1H, 9-H), 6.10 (q, $J = 2$ Hz, 1H, 8-H), 6.36 (s, 1H, 4-H).^{*)}

$^{13}\text{C-NMR}$ (75 MHz, CDCl_3): δ [ppm] = -4.88 (q, OSiMe), -4.62 (q, OSiMe), 18.06 (s, OSiMe₃), 22.32 (t, C-12), 25.78 (q, OSiMe₃), 26.43 (t, C-11), 32.65 (t, C-5), 37.14 (t, C-6), 55.79 (q, OMe an C-3), 60.69 (q, OMe an C-2), 61.63 (q, OMe an C-1), 63.67 (d, C-10), 68.38 (d, C-7), 82.51 (d, C-9), 89.55 (s, C-12a), 109.76 (d, C-4), 122.85 (d, C-8), 124.31 (s, C-12b), 137.07 (s, C-4a), 141.91 (s, C-2), 149.12 (s, C-7a), 152.71 (s, C-3), 155.36 (s, C-1).^{*)}

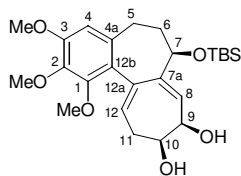
MS (DIP-El, 70 eV): m/z (%) = 462 (16) [M]⁺, 405 (7) [$-\text{C}_4\text{H}_9$], 387 (8), 331 (77), 273 (21), 207 (26), 181 (23), 126 (20), 75 (26), 73 (38).

$[\alpha]_{\text{D}} = -103.3$, $[\alpha]_{546} = -123.4$, $[\alpha]_{405} = -262.8$, $[\alpha]_{365} = -355.0$ ($c = 1.01$, CHCl_3 , 20°C).

HRMS (ED): calc. for $[\text{M}]^+$ ($^{12}\text{C}_{25}\text{H}_{38}^{16}\text{O}_6^{28}\text{Si}$): 462.2438, found.: 462.243.

*) Peaks in ^1H -NMR- und ^{13}C -NMR-spectra were assigned according to the data of the corresponding (*rac*) compound, with the help of H,H-Cosy-, HMQC-, HMBC- und NOESY-spectra.

(7*R*,9*R*,10*S*)-7-[[*tert*-Butyl(dimethyl)silyl]oxy]-1,2,3-trimethoxy-5,6,7,9,10,11-hexahydrobenzo[*a*]heptalen-9,10-diol (16)



To a solution of endoxide (**15**) (455 mg, 983 μmol) in CH_2Cl_2 (20 mL) under argon were subsequently dropwise added at -50°C NEt_3 (0.68 mL, 4.9 mmol, 5 equiv.) and TMSOTf (0.89 mL, 4.9 mmol, 5 equiv.). The reaction mixture was warmed to -10°C over 45 min and then cooled to -50°C . Abs. MeOH (1 mL) was then added and the reaction mixture was warmed to RT. The solvent was removed under vacuum at RT and the residue was solved in abs. MeOH (30 mL). K_2CO_3 (1.36 g, 9.84 mmol, 10 equiv.) was added at 0°C and the reaction mixture was warmed to RT over 45 min before addition of saturated NH_4Cl (50 mL). After extraction with CH_2Cl_2 (3×25 mL), the combined organic extracts were dried over Na_2SO_4 , filtered and the solvent was removed under vacuum at RT. The raw product was purified by flash-chromatography (EtOAc/cyclohexane 1:8, 1:6, 1:2, 1:1) to afford 287 mg (63 %) of colorless oil.

R_f (SiO_2 , EtOAc/cyclohexane 1:1) = 0.21

IR (ATR): $\tilde{\nu}$ [cm^{-1}] = 3408 (ss, br., OH), 2929 (s), 2853 (m), 1594 (m), 1483 (m), 1458 (s), 1406 (m), 1343 (m), 1322 (m), 1310 (m), 1249 (s), 1127 (s), 1093 (ss), 1004 (m), 886 (m), 833 (s), 775 (s), 668 (w).

^1H -NMR (250 MHz, CDCl_3): δ [ppm] = -0.09 (s, 3H, OSiMe), -0.07 (s, 3H, OSiMe), 0.82 (s, 9H, OSi*t*Bu), 1.68 (m, 1H), 1.95 (m, 1H), 2.36 (m, 2H), 2.66 (m, 2H), 3.63 (s, 3H, OMe), 3.83 (s, 6H, 2 OMe), 3.96 (m, 1H), 4.29 (m, 1H), 4.36 (m, 1H), 5.89 (dd, $J_1 = 6$ Hz, $J_2 = 7$ Hz, 1H, 12-H), 6.10 (d, $J = 4$ Hz, 1H, 8-H), 6.43 (s, 1H, 4-H).

^{13}C -NMR (62.5 MHz, CDCl_3): δ [ppm] = -5.09 (q, OSiMe), -4.98 (q, OSiMe), 18.23 (s, OSiMe₃), 25.83 (q, OSiMe₃), 29.65 (t), 34.51 (t), 36.39 (t), 55.98 (q, OMe), 60.86 (q,

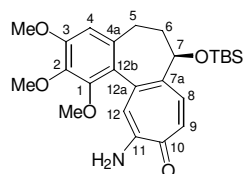
OMe), 61.05 (q, OMe), 71.98 (d), 72.63 (d), 78.67 (d), 107.01 (d, C-4), 126.81 (s), 127.12 (d), 130.61 (d), 134.65 (s), 135.18 (s), 140.23 (s), 140.76 (s), 150.51 (s), 152.07.

MS (DIP-EL, 70 eV): m/z (%) = 462 (7) [M]⁺, 405 (19) [–C₄H₉], 387 (24), 361 (12), 313 (21), 285 (22), 271 (18), 254 (12), 233 (11), 207 (23), 181 (28), 129 (17), 115 (14), 75 (88), 73 (100).

HRMS (ED): calc. for [M]⁺ (¹²C₂₅H₃₈¹⁶O₆²⁸Si): 462.2438, found.: 462.244.

[α]_D = –81.3, [α]₅₄₆ = –96.2, [α]₄₀₅ = –196.5, (c = 1.31, CHCl₃, 20 °C).

(7RS)-11-Amino-7-[[*tert*-butyl(dimethyl)silyl]oxy]-1,2,3-trimethoxy-6,7-dihydrobenzo[*a*]heptalen-10(5H)-one (*rac*-17)



To a solution of tropone (*rac*-14) (180 mg, 407 μ mol) in abs. EtOH (8 mL) under argon was added dropwise N₂H₄·H₂O (0.89 ml, 18 mmol, 45 equiv.) at 0 °C. The solution was warmed to RT and stirred 4.5 h. Solvent and liquid reagents were removed under vacuum. Radial chromatography (EtOAc/cyclohexane 1:4 + 2 % NEt₃, 1:3 + 2 % NEt₃) afforded in the first fraction a yellow oil and in the second fraction a orange-yellow oil. Crystallisation of the second fraction in EtOAc/cyclohexane afforded 72 mg (39 %) of orange-yellow needles.

R_f (SiO₂, EtOAc/cyclohexane 1:3 + 2 % NEt₃) = 0.31

mp.: 173 °C (EtOAc/cyclohexane)

IR (ATR): $\tilde{\nu}$ [cm⁻¹] = 3419 (w), 3288 (s, br.), 3187 (w), 2929 (m), 2853 (w), 1591 (s), 1523 (s), 1461 (m), 1433 (w), 1399 (w), 1359 (s), 1309 (w), 1249 (m), 1193 (m), 1123 (s), 1094 (ss), 1003 (m), 881 (s), 835 (s), 776 (m), 731 (m), 668 (w).

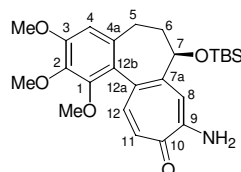
¹H-NMR (250 MHz, CDCl₃): δ [ppm] = –0.15 (s, 3H, OSiMe), –0.10 (s, 3H, OSiMe), 0.82 (s, 9H, OSi t Bu), 1.84 (m, 1H), 2.29 (m, 3H), 3.54 (s, 3H, OMe), 3.89 (s, 3H, OMe), 3.90 (s, 3H, OMe), 4.29 (m, 1H, 7-H), 5.75 (br. s, 2 NH), 6.52 (s, 1H, 4-H), 7.01 (s, 1H, 12-H), 7.25 (d, 1H, ³J = 12.5 Hz), 7.83 (d, 1H, ³J = 12.5 Hz).

¹³C-NMR (62.5 MHz, CDCl₃): δ [ppm] = –5.10 (q, OSiMe), –5.03 (q, OSiMe), 18.14 (s, OSiCMe₃), 25.75 (q, OSiCMe₃), 30.10 (t), 41.83 (t), 55.95 (q, OMe), 60.86 (q, OMe), 61.23 (q, OMe), 71.76 (d, C-7), 107.12 (d, C-4), 117.31 (d), 126.35 (s), 130.12 (d), 133.28 (d), 135.75 (s), 137.71 (s), 140.78 (s), 141.13 (s), 150.50 (s), 153.43 (s), 154.04 (s), 175.88 (s, C-10).

MS (DIP-El, 70 eV): m/z (%) = 457 (21) $[M]^+$, 426 (36) $[-OMe]$, 400 (12) $[-C_4H_9]$, 326 (12), 298 (10), 207 (19), 75 (30), 73 (100).

HRMS (EI): calc. for $[M]^+$ ($^{12}C_{25}H_{35}^{14}N^{16}O_5^{28}Si$): 457.2285, found.: 457.228.

(7RS)-9-Amino-7-[[tert-butyl(dimethyl)silyl]oxy]-1,2,3-trimethoxy-6,7-dihydrobenzo[*a*]heptalen-10(5H)-one (*rac*-18)



By the synthesis of (*rac*-17) from tropone (*rac*-14) (180 mg, 407 μ mol), a yellow oil was obtained after chromatography in a first fraction. Crystallisation in EtOAc/cyclohexane afforded 78 mg (42 %) of yellow crystals.

R_f (SiO₂, EtOAc/cyclohexane 1:3 + 2 % NEt₃) = 0.37

mp.: 219-220 °C (destr.) (EtOAc/cyclohexane)

IR (ATR): $\tilde{\nu}$ [cm^{-1}] = 3412 (w), 3285 (s, br.), 2928 (m), 2852 (w), 1598 (s), 1522 (s), 1485 (m), 1444 (m), 1403 (m), 1341 (s), 1318 (m), 1258 (m), 1138 (m), 1095 (ss), 1004 (m), 885 (s), 835 (s), 777 (s), 668 (w).

¹H-NMR (300 MHz, CDCl₃): δ [ppm] = -0.12 (s, 3H, OSiMe), -0.08 (s, 3H, OSiMe), 0.84 (s, 9H, OSi t Bu), 1.88 (m, 1H, 6-H_a), 2.31 (m, 3H, 6-H_b and 5-H₂), 3.54 (s, 3H, OMe an C-1), 3.89 (s, 3H, OMe an C-3), 3.89 (s, 3H, OMe an C-2), 4.35 (m, 1H, 7-H), 5.88 (br. s, 2 NH), 6.51 (s, 1H, 4-H), 7.12 (d, 3J = 12.5 Hz, 11-H), 7.38 (d, 3J = 12.5 Hz, 12-H), 7.50 (s, 8-H).*)

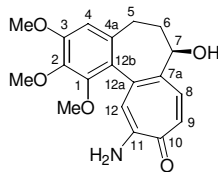
¹³C-NMR (75 MHz, CDCl₃): δ [ppm] = -5.09 (q, OSiMe), -4.95 (q, OSiMe), 18.24 (s, OSiCMe₃), 25.80 (q, OSiCMe₃), 30.03 (t, C-5), 41.95 (t, C-6), 55.99 (q, OMe at C-3), 60.62 (q, OMe at C-1), 61.24 (q, OMe at C-2), 72.34 (d, C-7), 107.00 (d, C-4), 109.51 (d, C-8), 125.93 (s, C-12b), 128.70 (d, C-11), 129.14 (s, C-12a), 135.58 (s, C-4a), 140.73 (d, C-12), 141.16 (s, C-2), 149.90 (s, C-7a), 150.57 (s, C-1), 152.96 (s, C-3), 155.23 (s, C-9), 175.72 (s, C-10).*)

MS (DIP-El, 70 eV): m/z (%) = 457 (17) $[M]^+$, 400 (9) $[-C_4H_9]$, 287 (10), 167 (20), 149 (48), 126 (100), 97 (28), 83 (21), 71 (38).

HRMS (EI): calc. for $[M]^+$ ($^{12}C_{25}H_{35}^{14}N^{16}O_5^{28}Si$): 457.2285, found.: 457.229.

*) Peaks in ¹H-NMR- und ¹³C-NMR-spectra were assigned with the help of H,H-Cosy-, HMQC-, HMBC- und NOESY-spectra.

(7*RS*)-11-Amino-7-hydroxy-1,2,3-trimethoxy-6,7-dihydrobenzo[*a*]heptalen-10(5*H*)-one
(*rac*-19)



To a solution of silylether (*rac*-17) (54 mg, 0.12 mmol) in abs. THF (1 mL) under argon was added dropwise at 0°C a solution of TBAF (0.35 mL, 0.35 mmol, 2.9 equiv., 1M in THF). After 45 min, water (5 mL) was added and the mixture was extracted with CH₂Cl₂ (4×4 mL). The combined organic extracts were filtered in a Pasteur-pipette over a short bed of Celite and the solvent was removed under vacuum. The raw product was purified by radial chromatography (EtOAc/cyclohexane 5:1 + 1 % NEt₃) to afford 39 mg (96 %) of a yellow oil.

R_f (SiO₂, EtOAc/cyclohexane 10:1) = 0.13

IR (ATR): $\tilde{\nu}$ [cm⁻¹] = 3433 (m), 3323 (s, br.), 3194 (m), 2924 (s), 2850 (w), 1707 (w), 1592 (ss), 1517 (s), 1490 (s), 1445 (ss), 1402 (m), 1345 (s), 1313 (m), 1234 (m), 1194 (m), 1123 (ss), 1089 (m), 848 (w), 746 (w).

¹H-NMR (250 MHz, CDCl₃): δ [ppm] = 1.85 (m, 1H), 2.35 (m, 3H), 3.56 (s, 3H, OMe), 3.87 (s, 3H, OMe), 3.88 (s, 3H, OMe), 4.41 (dd, $J_1 = 5.5$ Hz, $J_2 = 10.5$ Hz, 1H, 7-H), 5.77 (br. s, 2 NH), 6.53 (s, 1H, 4-H), 7.00 (s, 1H, C-12), 7.18^{*)} (d, $^3J = 12.5$ Hz, 1H), 7.84 (d, $^3J = 12.5$ Hz, 1H).

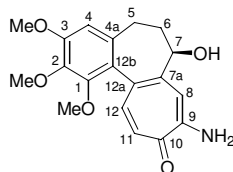
¹³C-NMR (62.5 MHz, CDCl₃): δ [ppm] = 30.07 (t), 40.66 (t), 56.02 (q, OMe), 61.00 (q, OMe), 61.20 (q, OMe), 70.78 (d, C-7), 107.21 (d, C-4), 117.93 (d), 126.26 (s), 130.11 (d), 132.82 (d), 135.76 (s), 138.24 (s), 141.03 (s), 141.51 (s), 150.47 (s), 153.50 (s), 154.19 (s), 175.46 (s, C-10).

MS (DIP-EI, 70 eV): m/z (%) = 343 (100) [M]⁺, 325 (12) [-H₂O], 312 (34) [-OMe], 284 (10), 267 (17), 256 (10), 207 (40), 181 (20), 128 (9), 115 (13), 83 (13) 77 (14).

HRMS (EI): calc. for [M]⁺ (¹²C₁₉H₂₁¹⁴N¹⁶O₅): 343.1420, found.: 343.142.

*) The doublet-signal at 7.18 ppm in ¹H-NMR-Spectrum is strongly dependent on the concentration.

(7RS)-9-Amino-7-hydroxy-1,2,3-trimethoxy-6,7-dihydrobenzo[*a*]heptalen-10(5H)-one
(*rac*-20)



To a solution of silylether (*rac*-**18**) (51 mg, 0.11 mmol) in abs. THF (1 mL) under argon was added dropwise at 0°C a solution of TBAF (0.30 mL, 0.30 mmol, 2.7 equiv., 1M in THF). After 45 min, water (5 mL) was added and the mixture was extracted with CH₂Cl₂ (4×4 mL). The combined organic extracts were filtered in a Pasteur-pipette over a short bed of Celite and the solvent was removed under vacuum. The raw product was purified by radial chromatography (EtOAc/Cyclohexane 5:1 + 2 % NEt₃, 10:1+ 2 % NEt₃) to afford 35 mg (91 %) of a light yellow solid.

R_f (SiO₂, EtOAc/cyclohexane 10:1 + 2 % NEt₃) = 0.14

IR (ATR): $\tilde{\nu}$ [cm⁻¹] = 3353 (s), 3288 (m), 3211 (m), 2932 (w), 1643 (w), 1602 (s), 1518 (s), 1476 (s), 1444 (ss), 1402 (m), 1338 (s), 1292 (m), 1195 (m), 1137 (s), 1097 (ss), 1054 (m), 857 (m), 726 (s), 648 (w).

¹H-NMR (250 MHz, DMSO-[D₆]): δ [ppm] = 1.72 (m, 1H), 2.19 (m, 2H), 2.46 (m, 1H), 3.53 (s, 3H, OMe), 3.75 (s, 3H, OMe), 3.82 (s, 3H, OMe), 4.19 (m, 1H, 7-H), 5.51 (d, 1 OH), 6.74 (s, 1H, 4-H), 6.84 (d, ³J = 12 Hz, 1H), 7.14 (d, ³J = 12 Hz, 1H), 7.44 (br. s, 2 NH), 7.62 (s, 1H, C-8).

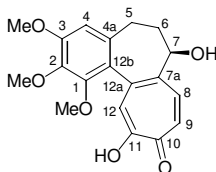
¹³C-NMR (62.5 MHz, DMSO-[D₆]): δ [ppm] = 29.28 (t), 40.43^{*)} (t), 55.73 (q, OMe), 60.24 (q, OMe), 60.44 (q, OMe), 69.97 (d, C-7), 107.29 (d), 107.82 (d), 125.82 (d), 125.91 (s), 126.47 (s), 135.11 (s), 139.18 (d), 140.35 (s), 149.77 (s), 150.98 (s), 152.22 (s), 156.89 (s), 174.20 (s, C-10).

MS (DIP-EI, 70 eV): m/z (%) = 344 (21), 343 (100) [M]⁺, 315 (15), 256 (12), 181 (52), 128 (10), 115 (10), 84 (12).

HRMS (EI): calc. für [M]⁺ (¹²C₁₉H₂₁¹⁴N¹⁶O₅): 343.1420, found.: 343.142.

*) The signal at 40.43 ppm in ¹³C-NMR-spectrum was overlapped by the solvent signal and was determined using a DEPT-spectrum.

(7*RS*)-7,11-Dihydroxy-1,2,3-trimethoxy-6,7-dihydrobenzo[*a*]heptalen-10(5*H*)-one (rac-21)



A solution of aminotropone (*rac*-**19**) (38 mg, 0.11 mmol) in a mixture of EtOH (2 mL) and aq. KOH (2 mL, 2N) was heated overnight at 110 °C under argon. The solution was then cooled to 0°C, neutralized with HCL 1N and extracted with CH₂Cl₂ (3×4 mL). The combined organic extracts were filtered in a Pasteur-pipette over a short bed of Celite. Removal of the solvent under vacuum afforded 32 mg (82%) of a yellow oil, containing ~5% impurities (according to NMR).

IR (ATR): $\tilde{\nu}$ [cm⁻¹] = 3378 (ss, br.), 3215 (s, br.), 2934 (s), 2853 (w), 1591 (ss), 1540 (m), 1456 (ss), 1399 (m), 1345 (m), 1316 (m), 1266 (s), 1236 (s), 1193 (m), 1130 (s), 1109 (s), 1088 (s), 1050 (m), 997 (m), 970 (w), 919 (w), 850 (m), 733 (s).

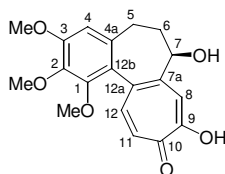
¹H-NMR (300 MHz, DMSO-[D₆]): δ [ppm] = 1.69 (m, 1H), 2.20 (m, 2H), 2.45 (m, 1H), 3.60 (s, 3H, OMe), 3.78 (s, 3H, OMe), 3.85 (s, 3H, OMe), 4.16 (dd, $J_1 = 6.5$, $J_2 = 10.5$ Hz, 1H, 7-H), 5.51 (br. s, 1 OH), 6.79 (s, 1H, 4-H), 7.15 (s, 1H, 12-H), 7.33 (d, $^3J = 12$ Hz, 1H, 9-H), 7.91 (d, $^3J = 12$ Hz, 1H, 8-H).

¹³C-NMR (75 MHz, DMSO-[D₆]): δ [ppm] = 29.10 (t), 40.19 (t), 55.78 (q, OMe), 60.49 (q, OMe), 60.72 (q, OMe), 69.40 (d, C-7), 107.45 (d, C-4), 124.98 (s), 125.36 (d), 126.26 (d), 132.84 (d), 135.17 (s), 140.35 (s), 141.42 (s), 142.69 (s), 149.80 (s), 153.38 (s), 166.27 (s, C-11), 172.49 (s, C-10).

MS (DIP-EI, 70 eV): m/z (%) = 344 (34) [M]⁺, 298 (12) [-H₂O -CO], 207 (9), 181 (16), 167 (16), 149 (36), 126 (20), 111 (32), 97 (48), 84 (75), 71 (53).

HRMS (EI): calc. for [M]⁺ (¹²C₁₉H₂₀¹⁶O₆): 344.1260, found.: 344.126.

(7*RS*)-7,9-Dihydroxy-1,2,3-trimethoxy-6,7-dihydrobenzo[*a*]heptalen-10(5*H*)-one (rac-22) ((±)-7-Hydroxydesacetamidocolchicin)



A solution of aminotropone (*rac*-**20**) (31 mg, 90 μ mol) in a mixture of EtOH (2 mL) and aq.KOH (2 mL, 2N) was heated overnight at 110 °C under argon. The solution was then cooled to 0°C, neutralized with HCL 1N and extracted with CH₂Cl₂ (3×4 mL). The combined organic extracts were filtered in a Pasteur-pipette over a short bed of Celite. Removal of the solvent under vacuum afforded 23 mg (74%) of a yellow oil.

IR (ATR): $\tilde{\nu}$ [cm⁻¹] = 3340 (ss, br., OH), 3215 (s, br.), 2922 (s), 2850 (w), 1596 (ss), 1545 (m), 1487 (s), 1453 (m), 1401 (m), 1344 (m), 1318 (m), 1273 (s), 1231 (s), 1194 (m), 1137 (s), 1092 (ss), 1001 (m), 923 (m), 857 (w), 753 (w).

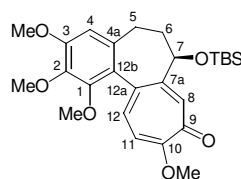
¹H-NMR (250 MHz, CDCl₃): δ [ppm] = 1.84 (m, 1H), 2.28 (m, 1H), 2.40 (m, 2H), 3.68 (s, 3H, OMe), 3.85 (s, 3H, OMe), 3.88 (s, 3H, OMe), 4.44 (m, 1H, 7-H), 5.57 (br. s, 1 OH), 6.52 (s, 1H, 4-H), 7.34 (d, ³*J* = 12 Hz, 1H), 7.43 (s, 1H, C-12), 8.02 (d, ³*J* = 12 Hz, 1H).

¹³C-NMR (75 MHz, DMSO-[D₆]): δ [ppm] = 29.05 (t), 40.34 (t), 55.77 (q, OMe), 60.47 (q, OMe), 60.54 (q, OMe), 69.84 (d, C-7), 107.42 (d, C-4), 118.10 (d), 124.33 (d), 124.81 (s), 132.94 (s), 135.11 (s), 140.16 (d), 140.35 (s), 149.82 (s), 151.84 (s), 152.94 (s), 168.18 (s), 172.03 (s).

MS (DIP-El, 70 eV): *m/z* (%) = 344 (100) [M]⁺, 316 (20) [-CO], 257 (15), 197 (10), 181 (60), 169 (10), 152 (10), 128 (13), 115 (20), 99 (13), 77 (15), 71 (13), 69 (16).

HRMS (EI): calc. for [M]⁺ (¹²C₁₉H₂₀¹⁶O₆): 344.1260, found.: 344.125.

(7*R*)-7-[[*tert*-Butyl(dimethyl)silyl]oxy]-1,2,3,10-tetramethoxy-6,7-dihydrobenzo[*a*]heptalen-9(5*H*)-one (24)



To a solution of DMSO (0.70 mL, 9.8 mmol, 36 equiv.) in CH₂Cl₂ (35 mL) under argon was added dropwise at -60 °C TFAA (1.10 mL, 7.9 mmol, 29 equiv.). After 10 min, a solution of diol (**16**) (125 mg, 270 μ mol) in CH₂Cl₂ (5 mL) was added and the resulting solution was stirred 1.5 h at -60 °C. NEt₃ (2.73 mL, 19.7 mmol, 73 equiv.) was added and the solution was allowed to warm to RT overnight. HCl 0,1N was then added to the pale-orange resulting solution and the phases were separated. The aqueous phase was extracted CH₂Cl₂ (2×10 mL) and the combined organic extracts were filtrated through a short bed of Celite. The solvent was removed under vacuum and the residue was solubilized in MeOH (15 mL). To this

solution, CH₂N₂ (8 mL, 2.4 mmol, 9 equiv., 0.3 M in Et₂O) was added at 0 °C. The resulting mixture was stirred 1 h. Silica was then added until no more gas evolution was observed. After filtration, the solvent was removed under vacuum. The raw product was purified by flash-chromatography (EtOAc/cyclohexane 1:2, 1:1, 2:1, 3:1) to afford 38 mg of a yellow oil in a first fraction, 20.5 mg of a colorless oil in a second fraction, 14.2 mg of a mixed fraction and 26.8 mg of a last fraction. Radial chromatography (EtOAc/cyclohexane 1:2, 1:1) of the mixed fraction and of the last fraction together afforded 25.5 mg (20%) of a yellow oil (the less polar compound).

R_f (SiO₂, EtOAc/*n*-hexane 1:2) = 0.20

IR (ATR): $\tilde{\nu}$ [cm⁻¹] = 2928 (s), 2853 (w), 1616 (m), 1586 (ss), 1486 (m), 1458 (s), 1343 (m), 1317 (m), 1248 (ss), 1193 (w), 1137 (m), 1118 (m), 1096 (ss), 1005 (m), 889 (m), 836 (ss), 778 (m), 671 (w).

¹H-NMR (300 MHz, CDCl₃): δ [ppm] = -0.09 (s, 6H, OSiMe₂), 0.83 (s, 9H, OSi^tBu), 1.80 (m, 1H, 6-H_a), 2.21 (m, 1H, 6-H_b), 2.39 (m, 2H, 5-H₂), 3.57 (s, 3H, OMe an C-1), 3.912 (s, 3H, OMe at C-3), 3.917 (s, 3H, OMe at C-2), 3.97 (s, 3H, OMe at C-9), 4.32 (dd, $J_1 = 7$ Hz, $J_2 = 10$ Hz, 1H, 7-H), 6.52 (s, 1H, 4-H), 6.76 (d, $^3J = 11$ Hz, 1H, 11-H), 7.19 (d, $^3J = 11$ Hz, 1H, 12-H), 7.81 (s, 1H, 8-H).*)

¹³C-NMR (75 MHz, CDCl₃): δ [ppm] = -5.01 (q, OSiMe₂), 18.24 (s, OSiCMe₃), 25.82 (q, OSiCMe₃), 29.99 (t, C-5), 40.46 (t, C-6), 55.99 (q, OMe at C-3), 56.17 (q, OMe at C-10), 60.78 (q, OMe at C-1), 61.22 (q, OMe at C-2), 72.12 (d, C-7), 107.02 (d, C-4), 111.53 (d, C-11), 125.08 (s, C-12b), 132.21 (d, C-8), 134.32 (d, C-12), 134.71 (s, C-12a), 135.22 (s, C-4a), 141.19 (s, C-2), 150.75 (s, C-1), 152.29 (s, C-7a), 153.27 (s, C-3), 164.02 (s, C-10), 179.65 (s, C-9).*)

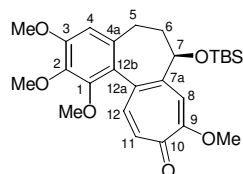
MS (DIP-EI, 70 eV): m/z (%) = 472 (43) [M]⁺, 415 (65) [-C₄H₉], 387 (62) [-C₄H₉-CO], 372 (27), 356 (17), 341 (10), 313 (16), 282 (16), 219 (12), 209 (24), 97 (17), 89 (50), 75 (68), 73 (100).

HRMS (EI): calc. for [M]⁺ (¹²C₂₆H₃₆¹⁶O₆²⁸Si): 472.2281, found.: 472.228.

[α]_D = +137.8, **[α]₅₄₆** = +182.1 ($c = 0.95$, CHCl₃, 20 °C).

*) Peaks in ¹H-NMR- und ¹³C-NMR-spectra were assigned with the help of H,H-Cosy-, HMQC-, HMBC- und NOESY-spectra.

(7R)-7-[[*tert*-Butyl(dimethyl)silyl]oxy]-1,2,3,9-tetramethoxy-6,7-dihydrobenzo[*a*]heptalen-10(5H)-one (25)



The second fraction obtained from the precedent synthesis of **24** and the more polar fraction obtained after chromatography of the mixed fraction afforded together 28.1 mg (22%) of a colorless oil.

R_f (SiO₂, EtOAc/*n*-hexane 1:2) = 0.27

IR (ATR): $\tilde{\nu}$ [cm⁻¹] = 2928 (m), 2853 (w), 2148 (w), 1619 (s), 1575 (ss), 1488 (m), 1458 (s), 1402 (m), 1343 (m), 1320 (m), 1254 (s), 1191 (w), 1160 (m), 1139 (s), 1096 (ss), 1004 (m), 893 (m), 836 (ss), 778 (m), 671 (w).

¹H-NMR (300 MHz, CDCl₃): δ [ppm] = -0.10 (s, 3H, OSiMe), -0.07 (s, 3H, OSiMe), 0.84 (s, 9H, OSi*t*Bu), 1.98 (m, 1H, 6-H_a), 2.30 (m, 1H, 6-H_b), 2.35 (m, 2H, 5-H₂), 3.59 (s, 3H, OMe at C-1), 3.891 (s, 3H, OMe at C-2), 3.894 (s, 3H, OMe at C-3), 3.99 (s, 3H, OMe at C-9), 4.39 (m, 1H, 7-H), 6.53 (s, 1H, 4-H), 7.15 (d, ³*J* = 12.5 Hz, 1H, 11-H), 7.34 (d, ³*J* = 12.5 Hz, 1H, 12-H), 7.55 (s, 1H, 8-H).^{*)}

¹³C-NMR (75 MHz, CDCl₃): δ [ppm] = -4.97 (q, OSiMe), -4.91 (q, OSiMe), 18.12 (s, OSiCMe₃), 25.77 (q, OSiCMe₃), 29.96 (t, C-5), 42.21 (t, C-6), 56.01^{**)} (q, OMe an C-3), 56.06^{**)} (q, OMe an C-9), 60.80 (q, OMe an C-1), 61.23 (q, OMe an C-2), 72.30 (d, C-7), 107.12 (d, C-4), 110.16 (d, C-8), 125.11 (s, C-12b), 132.61 (s, C-12a), 133.85 (d, C-11), 135.69 (s, C-4a), 141.00 (d, C-12), 141.18 (s, C-2), 146.03 (s, C-7a), 150.57 (s, C-1), 153.52 (s, C-3), 163.74 (s, C-9), 179.60 (s, C-10).^{*)}

MS (DIP-EI, 70 eV): *m/z* (%) = 472 (26) [M]⁺, 415 (49) [-C₄H₉], 387 (27) [-C₄H₉-CO], 372 (11), 341 (10), 313 (12), 285 (10), 97 (13), 83 (14), 75 (42), 73 (100).

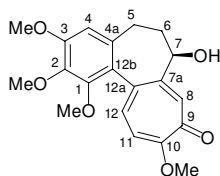
HRMS (ED): calc. for [M]⁺ (¹²C₂₆H₃₆¹⁶O₆²⁸Si): 472.2281, found.: 472.228.

[α]_D = +231.6, [α]₅₄₆ = +313.6 (*c* = 0.80, CHCl₃, 20 °C).

*) Peaks in ¹H-NMR- und ¹³C-NMR-spectra were assigned with the help of H,H-Cosy-, HMQC-, HMBC- und NOESY-spectra.

***) The assignments of the signals at 56.01 ppm und 56.06 ppm in ¹³C-NMR-spectra could be exchanged.

(7R)-7-Hydroxy-1,2,3,10-tetramethoxy-6,7-dihydrobenzo[*a*]heptalen-9(5H)-one (26)
(7-Hydroxydesacetamidocolchicine)



To a solution of silylether (**24**) (20 mg, 42 μ mol) in abs. THF (2 mL), HF.Py (0.50 mL, 1M in THF) was added at 0 °C. After 30 min the solution was warmed to RT and HF.Py (1.0 mL, 1M in THF) was once more added. After 2 h, saturated NH_4Cl (5mL) was added and the solution was extracted with CH_2Cl_2 (3 \times 4 mL). The combined organic extracts were washed with HCl 0.1 N (5 mL), filtrated over a short bed of Celite and the solvent was removed under vacuum. Purification by radial chromatography on (EtOAc/cyclohexane 15:1, EtOAc, $\text{CHCl}_3/\text{MeOH}$ 20:1) afforded 13 mg (86%) of a colorless oil.

R_f (SiO_2 , $\text{CHCl}_3/\text{MeOH}$ 20:1) = 0.10

IR (ATR): $\tilde{\nu}$ [cm^{-1}] = 3363 (s, br.), 2921 (s), 2829 (m), 1612 (m), 1586 (s), 1555 (ss), 1486 (m), 1459 (m), 1344 (m), 1317 (m), 1250 (ss), 1192 (w), 1137 (m), 1092 (ss), 1013 (w), 1000 (w), 921 (w), 842 (w).

$^1\text{H-NMR}$ (250 MHz, CDCl_3): δ [ppm] = 1.80 (m, 1H), 1.96 (d, 1 OH), 2.43 (m, 3H), 3.57 (s, 3H, OMe), 3.89 (s, 3H, OMe), 3.90 (s, 1H, OMe), 3.94 (s, 3H, OMe), 4.47 (m, 1H, 7-H), 6.54 (s, 1H, 4-H), 6.79 (d, $^3J = 11$ Hz, 1H), 7.18 (d, $^3J = 11$ Hz, 1H), 7.97 (s, 1H, 8-H).

$^{13}\text{C-NMR}$ (62.5 MHz, CDCl_3): δ [ppm] = 29.85 (t), 39.0 (t), 56.07 (q, OMe), 56.20 (q, OMe), 60.96 (q, OMe), 61.17 (q, OMe), 71.23 (d, C-7), 107.08 (d, C-4), 112.20 (d), 124.91 (s), 131.35 (d), 134.87 (d), 135.11 (s), 135.50 (s), 141.14 (s), 150.71 (s), 153.40 (s), 153.47 (s), 163.90 (s, C-10), 179.56 (s, C-9).

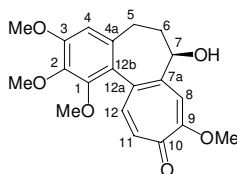
MS (DIP-EI, 70 eV): m/z (%) = 358 (56) [M^+], 330 (46) [-CO], 271 (21), 255 (12), 241 (11), 181 (100), 152 (14), 128 (16), 115(19), 55 (12).

HRMS (EI): calc. for [M] $^+$ ($^{12}\text{C}_{20}\text{H}_{22}^{16}\text{O}_6$): 358.1416, found: 358.141.

$[\alpha]_D = +109$, $[\alpha]_{546} = +162$ ($c = 1.05$, CHCl_3 , 20 °C).

(7R)-7-Hydroxy-1,2,3,9-tetramethoxy-6,7-dihydrobenzo[a]heptalen-10(5H)-one (27)

(7-Hydroxydesacetamidoisocolchicine)



To a solution of silylether (**25**) (45 mg, 95 μ mol) in abs. THF (5 mL), HF.Py (0.50 mL, 1M in THF) was added at 0 °C. After 30 min the solution was warmed to RT and HF.Py (1.0 mL, 1M in THF) was once more added. After 2 h, saturated NH₄Cl (5mL) was added and the solution was extracted with CH₂Cl₂ (3 \times 4 mL). The combined organic extracts were washed with HCl 0.1 N (5 mL), filtrated through a short bed of Celite and the solvent was removed under vacuum. Purification by radial chromatography (EtOAc/cyclohexane 20:1, EtOAc, CHCl₃/MeOH 10:0.4) afforded 34 mg (98%) of a pale yellow powder.

R_f (SiO₂, CHCl₃/MeOH 10:0.6) = 0.29

IR (ATR): $\tilde{\nu}$ [cm⁻¹] = 3347 (s, br.), 2929 (s), 2850 (m), 1606 (m), 1555 (ss), 1487 (m), 1453 (m), 1402 (m), 1344 (m), 1318 (m), 1255 (m), 1234 (w), 1192 (w), 1161 (w), 1138 (m), 1093 (ss), 1048 (w), 999 (w), 977 (w), 918 (w), 851 (w).

¹H-NMR (300 MHz, CDCl₃): δ [ppm] = 1.98 (m, 1H), 2.43 (m, 4H), 3.65 (s, 3H, OMe), 3.865 (s, 3H, OMe), 3.878 (s, 1H, OMe), 3.981 (s, 3H, OMe), 4.49 (m, 1H, 7-H), 6.53 (s, 1H, 4-H), 7.08 (d, ³J = 12.5 Hz, 1H), 7.30 (d, ³J = 12.5 Hz, 1H), 7.62 (s, 1H, 8-H).

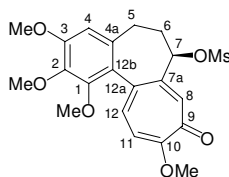
¹³C-NMR (75 MHz, CDCl₃): δ [ppm] = 29.93 (t, C-5), 41.04 (t, C-6), 56.04 (q, OMe), 56.25 (q, OMe), 61.01 (q, OMe), 61.13 (q, OMe), 71.29 (d, C-7), 107.17 (d, C-4), 110.60 (d, C-8), 124.92 (s, C-12b), 131.30, 133.46, 133.50, 135.71, 141.03 (s, C-2), 141.44 (s, C-7a), 150.55 (s, C-1), 153.61 (s, C-3), 163.79 (s, C-9), 179.35 (s, C-10).

MS (DIP-EI, 70 eV): m/z (%) = 358 (56) [M⁺], 330 (46) [-CO], 271 (21), 255 (12), 241 (11), 181 (100), 152 (14), 128 (16), 115(19), 83 (12).

HRMS (EI): calc. for [M]⁺ (¹²C₂₀H₂₂¹⁶O₆): 358.1416, found: 358.141.

[α]_D = +170, **[α]₅₄₆** = +239 (c = 1.037, CHCl₃, 20 °C).

(7RS)-Methanesulfonic acid 1,2,3,10-tetramethoxy-9-oxo-5,6,7-trihydro-benzo-[a]heptalen-7-yl ester (rac-28)



To a solution of alcohol (*rac*-**26**) (316 mg, 0.88 mmol) in abs. CH₂Cl₂ (20 mL) under argon were sequently added NEt₃ (0.8 mL, 5.73 mmol, 6.5 equiv.) and freshly distilled MsCl (0.11 mL, 1.41 mmol, 1.4 equiv.) at 0°C. After 2 h, ice-water (5 mL) was added and the solution was extracted with CH₂Cl₂ (3 \times 10 mL). The combined organic extracts were washed with HCl

1 N (10 mL), saturated NaHCO₃ (10 mL) and brine (10 mL), dried over Na₂SO₄ and filtered. The solvent was removed in vacuum and the raw product was purified by flash chromatography (CH₂Cl₂/acetone 1:1) to afford 317.1 mg (82%) of a yellow oil.

R_f (SiO₂, CH₂Cl₂/acetone 1:1) = 0.32

IR (ATR): $\tilde{\nu}$ [cm⁻¹] = 2934 (s, br.), 2832 (m), 2235 (m), 1617 (m), 1566 (ss), 1485 (m), 1454 (m), 1431 (w), 1398 (m), 1344 (ss), 1319 (m), 1282 (w), 1248 (ss), 1172 (ss), 1136 (ss), 1087 (ss), 1064 (w), 1021 (m), 983 (m), 954 (m), 910 (m), 877 (m), 824 (m), 725 (ss), 643 (m).

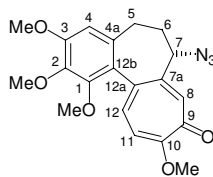
¹H-NMR (300 MHz, CDCl₃): δ [ppm] = 2.0 (m, 1H), 2.45 (m, 3H), 2.94 (s, 3H, OMe), 3.54 (s, 3H, OMe), 3.84 (s, 3H, OMe), 3.85 (s, 1H, OMe), 3.94 (s, 3H, OMe), 5.18 (m, 1H, 7-H), 6.48 (s, 1H, 4-H), 6.78 (d, ³J = 10.8 Hz, 1H), 7.20 (d, ³J = 10.8 Hz, 1H), 7.55 (s, 1H, 8-H).

¹³C-NMR (75 MHz, CDCl₃): δ [ppm] = 29.13 (t, C-5), 37.59 (t, C-6), 38.79 (q, SO₂Me), 55.89 (q, OMe), 56.31 (q, OMe), 61.05 (2×q, OMe), 78.27 (d, C-7), 107.39 (d, C-4), 112.13 (d, C-11), 123.98 (s), 130.98 (d, C-8), 133.55 (s), 133.85 (s), 135.60 (d, C-12), 141.48 (s), 146.55 (s), 150.85 (s), 153.69 (s), 164.24 (s, C-10), 178.73 (s, C-9).

MS (DIP-EI, 70 eV): *m/z* (%) = 436 (26) [M⁺], 312 (100), 297 (28), 281 (25), 269 (10), 254 (15), 79 (33).

HRMS (EI): calc. for [M]⁺ (¹²C₂₁H₂₄¹⁶O₈³²S): 436.1192, found: 436.119.

(7*RS*)-7-Azido-1,2,3,10-tetramethoxy-6,7-dihydrobenzo[*a*]heptalen-9(5*H*)-one (rac-30)



A solution of mesylether (*rac*-**28**) (180 mg, 0.41 mmol) and NaN₃ (293 mg, 11 equiv.) in abs. DMSO (20 mL) was heated three days at 50 °C. Water (5 mL) was then added and the solution was extracted with CH₂Cl₂ (3×10 mL). The combined organic extracts were then washed with saturated NaHCO₃ (10 mL) and brine (10 mL) and dried over Na₂SO₄. The raw product was purified by flash chromatography (CH₂Cl₂/acetone 1:1) to afford 122 mg (77%) of a yellow oil.

R_f (SiO₂, CHCl₃/MeOH 20:1) = 0.30

IR (ATR): $\tilde{\nu}$ [cm⁻¹] = 2936 (s, br.), 2103 (ss, N₃), 1614 (m), 1585 (ss), 1486 (m), 1454 (m), 1431 (w), 1395 (m), 1346 (m), 1319 (m), 1248 (ss), 1137 (m), 1088 (m), 1064 (w), 1021 (m), 983 (w), 910 (w), 877 (w), 730 (m).

MS (DIP-EL, 70 eV): m/z (%) = 357 (86) [M^+], 328 (25), 312 (78), 298 (100), 281 (34), 254 (27), 239 (15), 207 (53), 181 (20), 165 (16), 152 (20), 141 (26), 115 (25), 77 (25).

HRMS (ED): calc. for [M]⁺ ($^{12}C_{20}H_{23}^{16}O_5^{14}N$): 357.401, found: 357.157

To a solution of this product (20 mg, 0.056 mmol) in distilled pyridine (2 mL) was added freshly distilled acetic anhydride (0.21 mL, 2.23 mmol) under argon. After 10 min, pyridine is evaporated under vacuum to give a brown oil. Purification by radial chromatography afforded 17.9 mg of a pale yellow solid (0.045 mmol). NMR data were compared to those of commercially available (–)-colchicine.

R_f (SiO₂, acetone) = 0.25

¹H-NMR (300 MHz, CDCl₃): δ [ppm] = 1.88 (s, 3H, CH₃-Ac), 2.20 (m, 3H), 2.46 (m, 1H), 3.58 (s, 3H, OMe), 3.83 (s, 3H, OMe), 3.87 (s, 3H, OMe), 3.94 (s, 3H, OMe), 4.57 (m, 1H, 7-H), 6.47 (s, 1H, 4-H), 6.84 (d, ³ J = 11 Hz, 1H), 7.29 (d, ³ J = 11 Hz, 1H), 7.59 (s, 1H, 8-H).

¹³C-NMR (75 MHz, CDCl₃): δ [ppm] = 22.49 (q, Ac), 29.72 (t, C-5), 36.07 (t, C-6), 52.68 (d, C-7), 55.96 (q, OMe), 56.30 (q, OMe), 61.20 (q, OMe), 61.40 (q, OMe), 107.14 (d, C-4), 112.90 (d, C-11), 125.40 (s), 130.18 (d, C-8), 134.15 (s), 135.56 (d, C-12), 136.94 (s), 141.40 (s), 150.94 (s), 152.76 (s), 153.36 (s), 163.83 (s, C-10), 170.06 (s, CO-Ac), 179.32 (s, C-9).

Crystallographic data

(3*R*)-5-(2-Iodo-3,4,5-trimethoxyphenyl)-1-(trimethylsilyl)pent-1-yn-3-ol (**8**)



Table 1. Crystal data and structure refinement for **8**.

Identification code	tgr283
Empirical formula	C ₁₇ H ₂₅ I O ₄ Si ₁
Formula weight	896.72
Temperature	100(2) K
Wavelength	0.71073 Å
Crystal system, space group	Triclinic, P1
Unit cell dimensions	a = 8.8676(2) Å alpha = 93.8080(10) deg. b = 10.1283(2) Å beta = 106.9720(10) deg. c = 12.0789(3) Å gamma = 98.8980(10) deg.
Volume	1017.95(4) Å ³
Z, Calculated density	2, 1.463 Mg/m ³
Absorption coefficient	1.647 mm ⁻¹
F(000)	452
Crystal size	0.1 x 0.07 x 0.07 mm
Theta range for data collection	1.78 to 31.99 deg.
Limiting indices	-13<=h<=13, -15<=k<=15, -18<=l<=17
Reflections collected / unique	13817 / 13817 [R(int) = 0.0000]
Reflection observed [I>2sigma(I)]	11690
Completeness to theta = 31.99	99.8 %
Absorption correction	None

Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	13817 / 3 / 434
Goodness-of-fit on F^2	0.671
Final R indices [$I > 2\sigma(I)$]	R1 = 0.0308, wR2 = 0.0836
R indices (all data)	R1 = 0.0427, wR2 = 0.0950
Absolute structure parameter	-0.007(12)
Largest diff. peak and hole	0.501 and -0.837 e. \AA^{-3}

(7*R*,9*R*,12*aR*)-7-[[*tert*-Butyl(dimethyl)silyl]oxy]-1,2,3-trimethoxy-9,12a-epoxy-6,7,9,11,12,12a-hexahydrobenzo[*a*]heptalen-10(5*H*)-one (12)



Table 2. Crystal data and structure refinement for **12**.

Identification code	tgr175u
Empirical formula	C ₂₅ H ₃₆ O ₆ Si
Formula weight	460.63
Temperature	293(2) K
Wavelength	0.71073 \AA
Crystal system, space group	triclinic, P-1
Unit cell dimensions	a = 7.296(1) \AA alpha = 86.86(1) deg. b = 11.663(1) \AA beta = 81.56(1) deg. c = 15.376(1) \AA gamma = 88.52(1) deg.
Volume	1292.1(2) \AA^3
Z, Calculated density	2, 1.184 g/cm ³
Absorption coefficient	0.126 mm ⁻¹
F(000)	496
Crystal size	0.20 x 0.15 x 0.10 mm

Theta range for data collection	1.34 to 27.00 deg.
Limiting indices	-7<=h<=9, -14<=k<=14, -19<=l<=19
Reflections collected / unique	8682 / 5518 [R(int) = 0.0616]
Reflection observed [I>2sigma(I)]	2103
Completeness to theta = 27.00	97.7 %
Refinement method	Full-matrix least-squares on F ²
Data / restraints / parameters	5518 / 0 / 401
Goodness-of-fit on F ²	0.948
Final R indices [I>2sigma(I)]	R1 = 0.0662, wR2 = 0.1287
R indices (all data)	R1 = 0.2112, wR2 = 0.1737
Largest diff. peak and hole	0.175 and -0.234 e.A ⁻³

(7R)-7-[[*tert*-Butyl(dimethyl)silyl]oxy]-1,2,3,9-tetramethoxy-6,7-dihydrobenzo[*a*]heptalen-10(5H)-one (25)



Table 3. Crystal data and structure refinement for **25**.

Identification code	trg348
Empirical formula	C ₂₆ H ₃₆ O ₆ Si
Formula weight	472.64
Temperature	100(2) K
Wavelength	0.71073 Å
Crystal system, space group	Orthorhombic, P212121
Unit cell dimensions	a = 7.45890(10) Å alpha = 90 deg. b = 12.9937(2) Å beta = 90 deg. c = 26.1200(5) Å gamma = 90 deg.
Volume	2531.52(7) Å ³
Z, Calculated density	4, 1.240 Mg/m ³

Absorption coefficient	0.131 mm ⁻¹
F(000)	1016
Crystal size	0.2 x 0.1 x 0.1 mm
Theta range for data collection	1.56 to 30.00 deg.
Limiting indices	-10<=h<=10, -18<=k<=18, -36<=l<=36
Reflections collected / unique	7361 / 7361 [R(int) = 0.0000]
Reflection observed [I>2sigma(I)]	5410
Completeness to theta = 30.00	100.0 %
Absorption correction	None
Refinement method	Full-matrix least-squares on F ²
Data / restraints / parameters	7361 / 0 / 442
Goodness-of-fit on F ²	1.021
Final R indices [I>2sigma(I)]	R1 = 0.0405, wR2 = 0.0803
R indices (all data)	R1 = 0.0731, wR2 = 0.1024
Absolute structure parameter	-0.12(11)
Largest diff. peak and hole	0.291 and -0.286 e.A ⁻³

(7R)-7-Acetamino-1,2,3,10-tetramethoxy-6,7-dihydrobenzo[a]heptalen-9(5H)-one (32)



Table 4. Crystal data and structure refinement for **32**.

Identification code	vb48
Empirical formula	C ₃₂ H ₅₁ N O ₉
Formula weight	593.74
Temperature	100(2) K
Wavelength	0.71073 Å

Crystal system, space group	Monoclinic, P21
Unit cell dimensions	a = 10.4972(19) Å alpha = 90 deg. b = 12.7999(14) Å beta = 73.381(5) deg.
Volume	1686.5(5) Å ³
Z, Calculated density	2, 1.169 Mg/m ³
Absorption coefficient	0.084 mm ⁻¹
F(000)	644
Crystal size	0.3 x 0.2 x 0.05 mm
Theta range for data collection	2.02 to 25.00 deg.
Limiting indices	-12<=h<=12, -11<=k<=15, -13<=l<=15
Reflections collected / unique	7065 / 3080 [R(int) = 0.0786]
Reflection observed [I>2sigma(I)]	1593
Completeness to theta = 25.00	98.7 %
Absorption correction	None
Refinement method	Full-matrix least-squares on F ²
Data / restraints / parameters	3080 / 1 / 404
Goodness-of-fit on F ²	1.011
Final R indices [I>2sigma(I)]	R1 = 0.0818, wR2 = 0.1871
R indices (all data)	R1 = 0.1691, wR2 = 0.2284
Absolute structure parameter	0(3)
Largest diff. peak and hole	0.405 and -0.315 e.Å ⁻³