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Synthesis of the Decalin Subunit of Coloradocin

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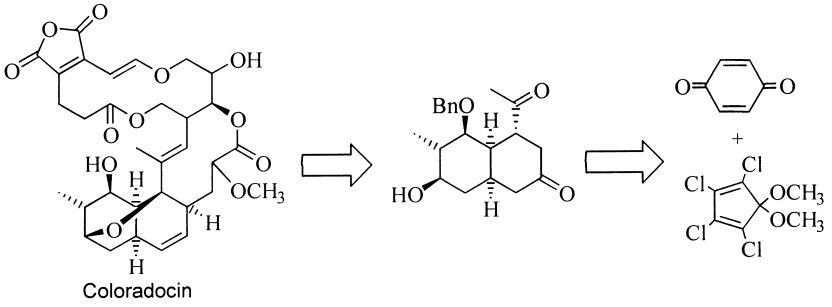
Abstract—The *cis*-decalin subunit of coloradocin is synthesized starting with an intermediate of our synthetic attempts towards nodusmicin. After transforming the additional functionalities of this tetracyclic β-diketal reductive cleavage with SmI_2 leads to a tricyclic diketone. Selective reduction is followed by acidic fragmentation to the desired *cis*-decalin derivative. The very mild conditions of this fragmentation led us to examine a synthetic variant that should allow easy connection with other subunits of the projected convergent synthesis of this antibiotic.

The increasing resistance of bacterial pathogens against antibiotics necessitates the development of new and effective antibiotic species.[1] Total synthesis can play an important role in defining the chemistry of antibiotics, often leading to their improved activity. Therefore we have chosen a small family of recently isolated antibiotics—the nargenicins and structurally related compounds—as synthetic targets.[2] The structures of these tetra- to hexacyclic macrolides differ strongly from those of the usually administered antibiotics; thus cross resistance is unlikely. Some of this group of polyketide antibiotics are even orally applicable.[3] Despite these advantages the main antibiotics of this group have not been synthesized. The efforts of several research groups[4,5] culminated in the synthesis of 18-deoxynargenicin A_1 by Kallmerten et al.[6]

Our own synthetic efforts were directed towards nodusmicin. In the present publication we extend this protocol[4g,i] to the construction of the decalin part of coloradocin (Scheme 1).

Coloradocin, the structurally as well as biosynthetically[8] most complex antibiotic of this group, has been isolated from *Actinoplanes coloradoensis*.[7] Its structure is identical with luminamicin, which previously has been isolated from bacteria of the genus bacteroides.[9] Coloradocin exhibits activity against pathogenic anaerobic and microaerophilic species, including ampicillin resistant strains of *N. gonorrhoeae* and *H. influenza*.[7] So far one synthetic attempt towards coloradocin has been reported.[5]

To convert our former synthesis of the decalinone unit of nodusmicin[4g,i] to that of the corresponding subunit of coloradocin we have focused our attention on improving the key step, the acidic fragmentation, which required rather drastic acidic conditions, thus reducing the flexibility of our synthetic plan. Experiments performed in other connections have alerted us to the fact that acidic fragmentation is achieved much easier when the cyclic acetal of tetracyclic β-diketals similar to **1** is opened prior to acidic fragmentation.[10] Starting with tetracyclic compound **1**[4g] (Scheme 2), an intermediate of the synthesis of the decalinone subunit of nodusmicin, the *t*-butyl dimethylsilyl group is exchanged



Scheme 1.

Keywords: antibiotic; total synthesis; coloradocin; acidic fragmentation; substituted *cis* decalin.

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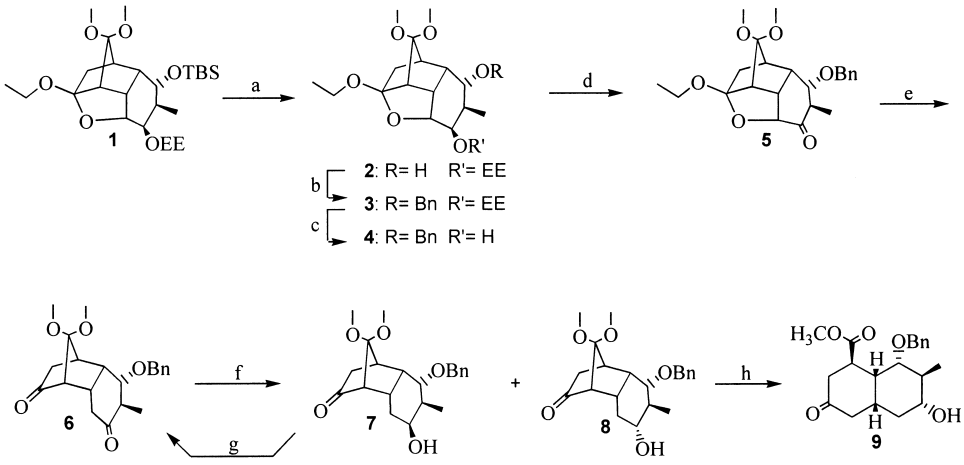
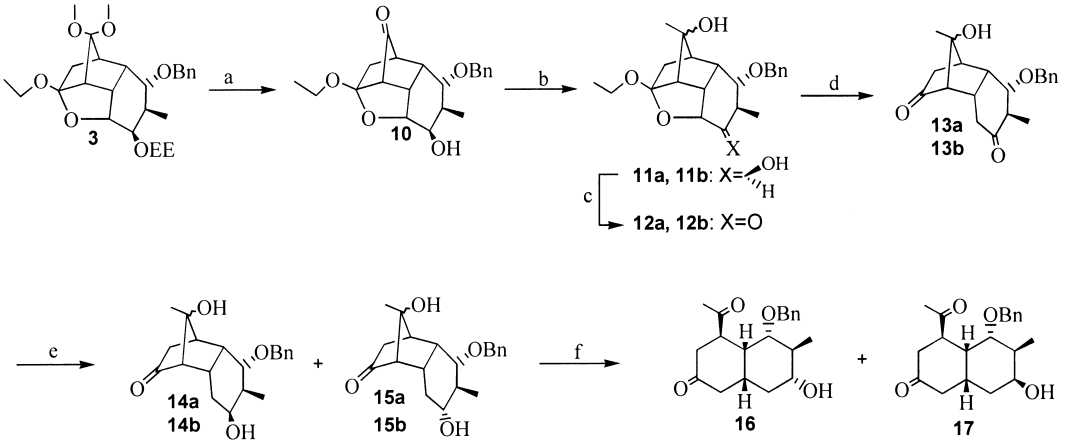


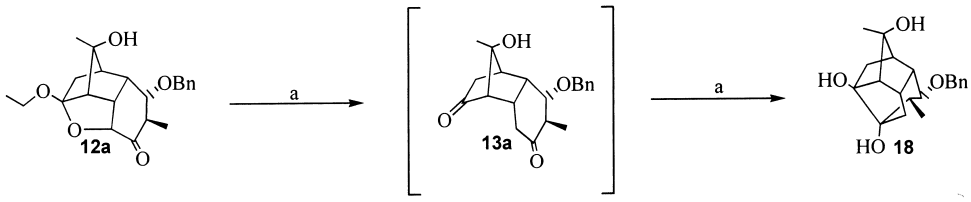
Scheme 2. (a) TBAF, THF, 40°C, 2.5 h (85%); (b) NaH, BnBr, Bu_4NI, THF, rfl. 4 h (82%); (c) 0.1% methanolic HCl–THF (1:1), 0°C, 1 h, (96%); (d) Jones reagent, 0°C, (95%); (e) SmI_2, THF–MeOH (1:1), −78°C (80%); (f) DIBAL, THF, −78°C, (67% **8**, 31% **7**); (g) Jones reagent, 0°C, (98%); (h) i: 2% aq. HCl–MeOH (1:2) rfl., 1 h; ii: CH_2N_2, Et_2O (68%, 2 steps).

for the acid stable benzyl group. Subsequently the acetal protecting group of the exo alcohol of **3** is removed and the hydroxy oxidized by Jones reagent. Ketone **5** thus obtained is the premise for cleaving the cyclic ketal by reductive deoxygenation in vicinal position to the ketone, thereby affording not only the desired tricyclic compound but also removing the surplus oxygen function. Of all the methods examined (Zn under ultrasonic conditions/HOAc, Ti(III)/HCl, lithium naphthalenide, Birch conditions), reduction with samarium diiodide[11] is by far the most efficient one. Regio- and stereoselective reduction of the tricyclic diketone **6** is now attempted. Despite the higher strain in the norbornane part the sterical hindrance proved sufficient to reduce exclusively the ketone of the cyclohexanone part under mild conditions. Contrary to the regioselectivity the stereoselectivity is lower than expected. With DIBAL a 2:1 mixture of the two epimeric alcohols is produced, which are easily separable on silica gel. Molecular modeling studies reveal[12] that the most stable conformation of **6** is the one with the cyclohexanone in boat conformation, thus approach from the α-side of the molecule is facilitated. The undesired exo-alcohol **7** can easily be recycled by Jones oxidation and subsequent reduction. Endo-alcohol **8** is treated under very mild acidic conditions producing the desired acidic decalinone derivative, which is esterified with diazomethane yielding **9**.

The mild conditions of this fragmentation reaction encouraged us to examine the possibility of introducing the second subunit of our projected convergent synthesis prior to fragmentation. As the most simple model we have chosen the methyl group. Starting material for this synthetic variant is non racemic compound **1**.[4i] Here the exchange of the protective group leading to **3** is succeeded by hydrolysis to the hydroxy ketone **10** (Scheme 3). Addition of methyl magnesium chloride yields a 1:1 mixture of the tertiary alcohols **11a** and **11b**. Jones oxidation of the secondary alcohol leads to ketones **12a** and **12b**, which are treated with samarium diiodide. Depending on the reaction conditions either the desired tricycles **13a** and **13b** are obtained in high yields without any byproducts when protic solvents are used or utilizing aprotic solvents deoxigenation is followed by a very fast pinacol reaction[13] even at very low temperatures (−100°C) yielding **18** (Scheme 4). For the regio- and stereoselective reduction of **13a** and **13b** DIBALH proves the most efficient hydride. Contrary to the nodusmicin pathway,



Scheme 3. (a) 2% aq. HCl–dioxane (1:4), 4 h, rfl (98%); (b) MeMgCl, THF, 0°C (95%); (c) Jones reagent, 0°C (95%); (d) SmI_2, THF:MeOH (1:2), −78°C (81%); (e) DIBAL, THF, −78°C; (f) $BF_3{\cdot}OEt_2$, CH_3CN, 0°C, 1 h (53% **16**; 20% **17**, 2 steps).



Scheme 4. (a) SmI_2, THF, HMPA, −100°C (97%).

both diastereomeric alcohols are easily fragmentated affording the enantiomerically pure decalinones (+)-**16** and (+)-**17**, which are separable on silica gel (Scheme 3).

Experimental

General notes

^{1}H NMR (400 MHz) and ^{13}C NMR (100 MHz) spectra were recorded on a Bruker Spektrospin AM 400-WB. Mass spectra were recorded on a spectrometer MAT 8230 (Finnigan) and IR spectra on a Perkin–Elmer 1600 FTIR spectrometer on silicon. Optical rotations were recorded on a Perkin–Elmer 241 polarimeter with the sodium D line. Melting points were obtained using a Reichert 'Kofler' hot stage microscope and are uncorrected. Silica gel (230–400 mesh ASTM, Merck) was used for flash chromatography.

(1*R,3*R**,5*R**,7*R**,8*S**,9*R**,10*S**,11*R**,12*R**)-6,6-Dimethoxy-3-ethoxy-12-(1′-ethoxyethyl)oxy-11-methyl-2-oxatetracyclo[6.4.0.0^{3,7}.0^{5,9}]dodecan-10-ol (2).** 1280 mg (2.56 mmol) of **1** and 2000 mg TBAF (6.34 mmol) are dissolved in 70 ml THF. After stirring at 40°C for 2.5 h sat. aq. NH_4Cl is added and the mixture extracted four times with ether. The organic layers are washed with brine, dried with $MgSO_4$, and concentrated, resulting in 840 mg (2.18 mmol, 85%) of **2**.

(1*R,3*R**,5*R**,7*R**,8*S**,9*R**,10*S**,11*R**,12*R**)-10-Benzyloxy-6,6-dimethoxy-3-ethoxy-12-(1′-ethoxyethyl)oxy-11-methyl-2-oxatetracyclo[6.4.0.0^{3,7}.0^{5,9}]dodecane (3).** 350 mg (0.91 mmol) **2** are dissolved in 30 ml abs. THF and 104 mg (4.5 mmol) NaH, 770 mg (4.5 mmol) benzyl bromide and 40 mg (0.11 mmol) Bu_4NI are added and refluxed for 4 h. After cooling to room temperature sat. aqu. NH_4Cl is added and the mixture is extracted four times with ether. The organic layers are washed with brine, dried with $MgSO_4$, and concentrated. Flash chromatography of the residue (petroleum ether–ethyl acetate 15:1 then 6:1) afforded 353 mg (0.75 mmol, 82%) of **3**.

(±)-(1*R,3*R**,5*R**,7*R**,8*S**,9*R**,10*S**,11*R**,12*R**)-10-Benzyloxy-6,6-dimethoxy-3-ethoxy-11-methyl-2-oxatetracyclo-[6.4.0.0^{3,7}.0^{5,9}]dodecan-12-ol (4).** 51.5 mg (0.11 mmol) of **3** are dissolved in 2 ml abs. THF and 2 ml abs. MeOH and cooled to 0°C. 80 μl methanolic HCl (0.74 M in abs. MeOH) are added and the mixture stirred for 1 h. After quenching with sat. aq. $NaHCO_3$ the mixture is extracted four times with ether. The organic layers are washed with brine, dried with $MgSO_4$ and concentrated, yielding 42 mg (0.11 mmol 96%) of **4** as colorless oil.

IR (cm^{-1}): 3427, 2978, 2932; ^{1}H NMR ($CDCl_3$, δ): 1.02 (d, 3H) $J_{CH_3,11}$=6.6 Hz C(11)CH_3; 1.16 (t, 3H) $J_{1',2'}$=7.1 Hz H(2′); 1.41 (exchangeable with D_2O) OH; 2.05 (d, 1H) $J_{4,4}$=13.1 Hz H(4*n*); 2.14 (ddq, 1H) $J_{11,10}$=11.6 Hz, J_{11,CH_3}=6.6 Hz, $J_{11,12}$=2.3 Hz H(11); 2.16 (ddd, 1H) $J_{4,4}$=13.1 Hz, J=3.8 Hz, J=2.3 Hz H(4*x*); 2.29 (m, 1H) $w_{1/2}\approx$9 Hz H(5); 2.64–2.69 (m, 2H) H(7), H(8); 2.85 (m, 1H) $w_{1/2}$=25 Hz H(9); 3.16 (s, 3H) OCH_3; 3.19 (s, 3H) OCH_3; 3.49 (dq, 1H) $J_{1',1'}$=9.1 Hz, $J_{1',2'}$=7.1 Hz H(1′a); 3.57 (dd, 1H) $J_{10,11}$=11.6 Hz, $J_{10,9}$=8.6 Hz H(10); 3.64 (dq, 1H) $J_{1',1'}$=9.4 Hz, $J_{1',2'}$=7.3 Hz H(1′b); 3.85 (m, 1H) $w_{1/2}\approx$8 Hz H(12); 4.03 (dd, 1H) $J_{1,12}$=$J_{1,8}$=4.0 Hz H(1); 4.39 (d, 1H) $J_{1'',1''}$=11.6 Hz benzyl. H; 4.6 (d, 1H) $J_{1'',1''}$=11.6 Hz benzyl. H; 7.2–7.29 (m, 5H) aromat. H; ^{13}C NMR ($CDCl_3$, δ): 139.1, 128.8, 128.4, 128 aromat. C, 114.2, 112.1 C3, C6; 77.7, 76, 73.4 C1, C10, C12; 72.6 benzyl. C; 59.2 C1′; 51.1 OCH_3; 51.0 OCH_3; 50.3 C7; 39.7 C4; 39.7, 38.9, 35.9, 33.0 C5, C8, C9, C11; 16, 15.4 CH_3(2′), CH_3(11); MS (*m*/*z*, %): 404.2 (100%, M^+); HRMS: Calcd for $C_{23}H_{32}O_6$: 404.2199. Found: 404.2217.

(±)-(1*R,3*R**,5*R**,7*R**,8*S**,9*R**,10*S**,11*R**)-10-Benzyloxy-6,6-dimethoxy-3-ethoxy-11-methyl-2-oxatetracyclo-[6.4.0.0^{3,7}.0^{5,9}]dodecan-12-one (5).** To a solution of 34.5 mg (0.08 mmol) of **4** in 15 ml acetone Jones reagent is added under stirring at 0°C until discoloration ceases. Stirring is continued for 5 min. Then sat. aq. $NaHCO_3$ is added and the mixture is extracted three times with ether. The organic layers are washed with brine, dried with $MgSO_4$ and concentrated, yielding 32.7 mg (0.076 mmol 95%) of **5** as colourless oil.

IR (cm^{-1}): 3431, 2974, 2935, 1722; ^{1}H NMR ($CDCl_3$, δ): 1.02 (d, 3H) $J_{CH_3,11}$=6.0 Hz C(11)CH_3; 1.17 (t, 3H) $J_{1',2'}$=7.0 Hz H(2′); 2.3 (d, 1H) $J_{4,4}$=12.1 Hz H(4*n*); 2.33 (dd, 1H) $J_{4,4}$=12.1 Hz, J_{lr}=1.5 Hz H(4*x*); 2.43 (m, 1H) $w_{1/2}$=7.8 Hz H(5); 2.70 (dd, 1H) $J_{7,8}$=5.0 Hz, $J_{7,5}$=2.0 Hz H(7); 2.75 (ddd, 1H) $J_{8,7}$=5.0 Hz, $J_{8,1}$=4.5 Hz, $J_{8,9}$=9.0 Hz H(8); 2.86 (dddd, 1H) $J_{9,10}$=8.0 Hz, $J_{9,8}$=9.0 Hz, $J_{9,5}$=3.0 Hz, $J_{9,4x}\cong$1 Hz H(9); 3.14 (s, 3H) OCH_3; 3.21 (s, 3H) OCH_3; 3.36 (dd, 1H) $J_{10,11}$=12.0 Hz, $J_{10,9}$=8.0 Hz H(10); 3.45 (dq, 1H) $J_{11,10}$=12.0 Hz J_{11,CH_3}=6.0 Hz H(11); 3.51 (dq, 1H) $J_{1',1'}$=9.0 Hz, $J_{1',2'}$=7.0 Hz H(1′a); 3.65 (dq, 1H) $J_{1',1'}$=9.0 Hz, $J_{1',2'}$=7.0 Hz H(1′b); 4.08 (d, 1H) $J_{1,8}$=4.5 Hz H(1); 4.43 (d, 1H) $J_{1'',1''}$=11.6 Hz benzyl. H; 4.59 (d, 1H) $J_{1'',1''}$=11.6 Hz benzyl. H; 7.2–7.32 (m, 5H) aromat. H; ^{13}C NMR ($CDCl_3$, δ): 211.7 C12; 138.2, 131.2, 129.2, 128.9 aromat. C; 116.3, 111.3 C3, C6; 83.7, 79.8 C1, C10; 73.3 benzyl. C; 59.6 C1′; 51.4 OCH_3; 51.2 OCH_3; 50.4, 44.1, 43.3, 39.8, 39.8 C7, C5, C8, C9, C11; 39.5 C4; 15.9, 11.5 CH_3(2′), CH_3(11); MS (*m*/*z*): 402.4 100%, M^+; HRMS: Calcd for $C_{23}H_{30}O_6$: 402.2042. Found: 402.2029.

(±)-(1*R,2*S**,5*R**,6*S**,7*R**,8*R**)-6-Benzyloxy-11,11-dimethoxy-5-methyltricyclo [6.2.1.0^{2,7}]undeca-4,10-dione (6).** *Preparation of the SmI_2-solution (≈1 M):* 11 ml abs. THF in a Schlenk vessel are degassed (freeze–thaw technique). The addition of 182 mg (1.2 mmol) Sm powder (40 mesh) and 88.6 μl (1.1 mmol) CH_2I_2 under a stream of argon is followed by vigorous stirring and slight warming until the blue color appears. The suspension is stirred for a further 2 h. The deeply blue solution is now ready for use and can be stored for several days.

A solution of 27 mg (0.17 mmol) of **5** in 3.5 ml abs. THF and 1.5 ml abs. MeOH is degassed at −78°C. A SmI_2 solution (≈1 M) is added dropwise (ca. 2 ml) until the starting material is no longer detectable by TLC. After the addition of a few drops of 2% aq. HCl, the mixture is extracted three times with ether. The organic layers are washed with brine, dried with $MgSO_4$ and concentrated. The residue is filtered through silica gel (petroleum ether–ethyl acetate 3:1) yielding 3 mg of starting material (**5**) and 17.2 mg of **6** (0.14 mmol, 80% related to consumed starting material) as colorless oil.

IR (cm^{-1}): 1750, 1717; ^{1}H NMR ($CDCl_3$, δ): 1.02 (d, 3H) $J_{CH_3,5}$=7.5 Hz CH_3(5); 2.23–2.75 (m, 6H) H(1), H(2), H(3), H(3), H(5), H(8); 2.28 (d, 1H) $J_{9,9}$=18.6 Hz H(9); 2.68 (dd, 1H) $J_{7,2}$=8.0 Hz, $J_{7,6}$=3.5 Hz H(7); 3.18 (s, 3H) OCH_3; 3.23 (s, 3H) OCH_3; 3.33 (d, 1H) $J_{9,9}$=18.6 Hz H(9n); 3.92 (dd, 1H) J=5.0 Hz, J=3.5 Hz H(6); 4.33 (d, 1H) $J_{1',1'}$= 12.1 Hz benzyl. H; 4.51 (d, 1H) $J_{1',1'}$=12.1 Hz benzyl. H; 7.13–7.29 (m, 5H) aromat. H; ^{13}C NMR ($CDCl_3$, δ): 212.8, 212.3 C4, C10; 137.8, 128.9, 128.3, 128 aromat. C; 111.9 C11; 80.6 C6; 71.7 benzyl. C; 58.6 C1; 51.2 OCH_3; 50.9 OCH_3; 46.5, 42.7, 35.1, 31.9 C2, C5, C7, C8; 40.9, 40.6 C3, C9; 14.6 CH_3(5); MS (*m*/*z*, %): 358 (100%, M^+), 267 (30%, $M^+-C_7H_7$), 91 (15%, $C_7H_7^+$); HRMS: Calcd for $C_{21}H_{26}O_5$: 358.1780. Found: 358.1791.

(±)-(1*R,2*R**,3*S**,4*S**,5*S**,7*S**,8*R**)-3-Benzyloxy-5-hydroxy-4-methyltricyclo [6.2.1.0^{2,7}]undecan-9-one (7) and (±)-(1*R**,2*R**,3*S**,4*S**,5*R**,7*S**,8*R**)-3-benzyloxy-5-hydroxy-4-methyltricyclo [6.2.1.0^{2,7}]undecan-9-one (8).** To a solution of 19.5 mg (0.054 mmol) of **6** in 3.5 ml abs. THF a solution of DIBAL (1 M in hexane, ~200 μl) is added at −78°C until the starting material is no longer detectable by TLC. Sat. aq. NH_4Cl is added and the mixture is extracted four times with ether. The organic layers are washed with brine, dried with $MgSO_4$ and concentrated. Flash chromatography of the residue (petroleum ether–ethyl acetate 2:1) afforded 11.6 mg (0.036 mmol, 67%) of product **8**, 5.4 mg (0.017 mmol, 31%) of byproduct **7** and 2.3 mg (0.006 mmol) of starting material.

Compound **7**: IR (cm^{-1}): 3442, 2937, 2873, 1749; ^{1}H NMR ($CDCl_3$, δ): 0.98 (d, 3H) $J_{CH_3,4}$=7.0 Hz CH_3(4); 1.11 (ddd, 1H) $J_{6,6}$=13 Hz, $J_{6,5}\cong J_{6,7}\cong$11 Hz H(6); 1.48 (br, 1H exchangeable with D_2O) OH; 1.62 (ddq, 1H) J_{4,CH_3}= 7.0 Hz, $J_{4,5}=J_{4,3}$=8.0 Hz H(4); 1.99 (ddd, 1H) $J_{6,6}$= 13.0 Hz, $J_{6,5}$=7.5 Hz, $J_{6,7}$=5.5 Hz H(6); 2.31 (dd, 1H) $J_{10,10}$=18.1 Hz, $J_{10,1}$=4.5 Hz H(10); 2.46 (dddd, 1H) $J_{7,2}=J_{7,6}$=12.2 Hz, $J_{7,8}$=6.0 Hz, $J_{7,6}$=5.5 Hz H(7); 2.50 (d, 1H) $J_{8,7}$=6.0 Hz H(8); 2.61 (dd, 1H) $J_{1,2}=J_{1,10}$=4.5 Hz H(1); 2.71 (d, 1H) $J_{10,10}$=18.1 Hz H(10); 2.71–2.77 (m, 1H) H(2); 3.16 (s, 3H) OCH_3; 3.19 (s, 3H) OCH_3; 3.17–3.23 (m, 1H) H(5); 3.48 (dd, 1H) $J_{3,2}\cong J_{3,4}\cong$8.0 Hz H(3); 4.47 (d, 1H) $J_{1',1'}$=12.1 Hz benzyl. H; 4.55 (d, 1H) $J_{1',1'}$= 12.1 Hz benzyl. H; 7.2–7.32 (m, 5H) aromat. H; ^{13}C NMR ($CDCl_3$, δ): 212.9 C9; 138.6, 128.9, 128.8, 128.1 aromat. C; 110.9 C11; 82.1, 72.6 C3, C5; 73.1 benzyl. C; 59.6, 43.8, 42.4, 35.5, 32.1 C1, C2, C4, C7, C8; 51.1 OCH_3; 50.7 OCH_3; 40.6, 35.7 C6, C10; 16.3 CH_3(4); MS (*m*/*z*; %): 360 (100%, M^+); 268 (25%, $M^+-C_7H_7$); 91 (15%, C_7H_7); HRMS: Calcd for $C_{21}H_{28}O_5$: 360.1936. Found: 360.1923.

Compound **8**: IR (cm^{-1}): 3438, 2942, 2865, 1750; ^{1}H NMR ($CDCl_3$, δ): 1.09 (d, 3H) $J_{CH_3,4}$=6.5 Hz CH_3(4); 1.25 (ddd, 1H) $J_{6,6}$=14.7 Hz, $J_{6,7}$=11.5 Hz, J=2.8 Hz H(6); 1.45 (br, exchangeable with D_2O) OH; 1.5 (ddq, 1H) J_{4,CH_3}=6.5 Hz, $J_{4,3}$=9.5 Hz, $J_{4,5}$=1 Hz H(4); 1.97 (ddd, 1H) $J_{6,6}$=14.7 Hz, $J_{6,7}$=9 Hz, $J_{6,5}$=3.6 Hz H(6); 2.46 (m, 2H) $w_{1/2}$=5 Hz H(10,10); 2.68 (dd, 1H) $J_{8,7}$=5.5 Hz, $J_{8,1}$=1.5 Hz H(8); 2.72 (m, 1H) $w_{1/2}$=8 Hz H(1); 2.84 (dddd, 1H) $J_{7,2}\cong$9 Hz, $J_{7,6}\cong$9 Hz, $J_{7,6}$=11 Hz, $J_{7,8}$=5.5 Hz H(7); 3.18 (ddd, 1H) $J_{2,3}=J_{2,7}$=10.0 Hz, $J_{2,1}$=3.5 Hz H(2); 3.25 (s, 3H) OCH_3; 3.29 (s, 3H) OCH_3; 3.82 (dd, 1H) $J_{3,2}=J_{3,4}$=9.5 Hz H(3); 3.92 (m, 1H) $w_{1/2}$=7.5 Hz H(5); 4.52 (d, 1H) $J_{1',1'}$=11.5 Hz benzyl. H; 4.73 (d, 1H) $J_{1',1'}$=11.5 Hz benzyl. H; 7.32–7.49 (m, 5H) aromat. H; ^{13}C NMR ($CDCl_3$, δ): 212.9 C9; 138.9, 128.7, 128.1, 128 aromat. C; 110.6 C11; 78.6, 72.0 C3, C5; 73.9 benzyl. C; 60.3 C8; 51.1 OCH_3; 50.7 OCH_3; 42.2, 40.8, 35.7, 31.1 C1, C2, C4, C7; 40.9, 34 C6, C10; 16.7 CH_3(4); MS (*m*/*z*, %): 360 (100%, M^+); 268 (15%, $M^+-C_7H_7$); 91 (15%, C_7H_7); HRMS: Calcd for $C_{21}H_{28}O_5$: 360.1936. Found: 360.1920.

(±)-(1*R,2*R**,6*R**,8*S**,9*R**,10*R**)-Methyl-10-benzyloxy-8-hydroxy-9-methyl-4-oxobicyclo[4.4.0]decyl-2-carboxylate (9).** 18.9 mg (0.052 mmol) of **8** are dissolved in 3 ml CH_3OH and 1 ml 1% aq. HCl and refluxed for 1 h. After removal of the solvents the residue is dissolved in 3 ml ether and an ethereal solution of CH_2N_2 is added dropwise at 0°C and the mixture stirred for 30 min. Concentration of the solution is followed by flash chromatography (petroleum ether–ethyl acetate 1:1), yielding 14.2 mg (0.035 mmol, 68%) of **9**.

IR (cm^{-1}): 3385, 2924, 1719 (br); ^{1}H NMR ($CDCl_3$, δ): 1.07 (d, 3H) $J_{CH_3,9}$=6.0 Hz CH_3(9); 1.2 (ddd, 1H) $J_{7,7}=J_{7,6}$=13.6 Hz, $J_{7,8}$=10.5 Hz H(7); 1.45 (d, 1H, exchangeable with D_2O) $J_{OH,8}$=4 Hz OH; 1.61–1.72 (m, 2H) H(7,9); 2.10–2.17 (m, 1H) H(6); 2.19 (ddd, 1H) $J_{5,5}$=14.3 Hz, $J_{5,6}=J_{5,3}$=2 Hz H(5); 2.4 (ddd, 1H) $J_{3,3}$=14.3 Hz, $J_{3,2}$= 5.0 Hz, $J_{3,5}$=2 Hz H(3); 2.49 (dd, 1H) $J_{3,3}$=14.3 Hz, $J_{3,2}$= 12.5 Hz H(3); 2.64 (dd, 1H) $J_{5,5}$=14.3 Hz, $J_{5,6}$=6.0 Hz H(5); 2.86 (ddd, 1H) $J_{1,2}$=12.5 Hz, $J_{1,10}$=5.0 Hz, $J_{1,6}$=3.0 Hz H(1); 2.99 (ddd, 1H) $J_{2,3}=J_{2,1}$=12.5 Hz, $J_{2,3}$= 5.0 Hz H(2); 3.05 (dd, 1H) $J_{10,9}$=11.1 Hz, $J_{10,1}$=5.0 Hz H(10); 3.16 (dddd, 1H) $J_{8,9}=J_{8,7}$=10.5 Hz, $J_{8,7}$=4.8 Hz, $J_{8,OH}$=4 Hz H(8); 3.31 (s, 3H) $COOCH_3$; 4.21 (d, 1H) $J_{1',1'}$=11.1 Hz benzyl. H; 4.55 (d, 1H) $J_{1',1'}$=11.1 Hz benzyl. H; 7.28–7.39 (m, 5H) aromat. H; ^{13}C NMR ($CDCl_3$, δ): 208.2 C4; 174.8 CO_2CH_3; 138.1, 128.2, 128.1, 127.6 aromat. C; 82.9 C10; 74.1 C8; 72.5 benzyl. C; 51.9 CO_2CH_3; 46.1 C5; 43.6 C3; 40.1 C9; 39.9 C2; 39.2 C1; 36.1 C7; 34.1 C6; 14.5 CH_3(9); MS (*m*/*z*, %):

346.3 (100%, M^+); 91 (5%, C_7H_7); HRMS: Calcd for $C_{20}H_{26}O_5$: 346.1780. Found: 346.1792. Anal. Calcd for $C_{20}H_{26}O_5$: C, 69.74%; H, 7.56%. Found: C, 70.03%; H, 7.61%.

(+)-(1*R*,3*R*,5*R*,7*R*,8*S*,9*R*,10*S*,11*R*,12*R*)-10-Benzyloxy-3-ethoxy-12-hydroxy-11-methyl-2-oxatetracyclo-[6.4.0.0^{3,7}.0^{5,9}]dodecan-6-one (10). 54 mg (0.12 mmol) of **3** are dissolved in 4 ml dioxane and after addition of 1.5 ml 2% aq. HCl refluxed for 4 h. After cooling to room temperature sat. aq. $NaHCO_3$ is added and the mixture is extracted four times with ether. The organic layers are washed with brine, dried with $MgSO_4$ and concentrated, resulting in 40 mg (0.12 mmol, 98%) of **10** as colorless oil.

$[\alpha]_D^{20}$=+95.2 (c=0.42 in CCl_4); IR (cm^{-1}): 3456, 2977, 2882, 1775; ^{1}H NMR ($CDCl_3$, δ): 1.06 (d, 3H) $J_{CH_3,11}$=6.5 Hz C(11)CH_3; 1.13 (t, 3H) $J_{1',2'}$=7.0 Hz H(2′); 1.6 (m, 1H, exchangeable with D_2O) OH; 2.05 (ddd, 1H) $J_{4,4}$=13.6 Hz, $J_{4,5}$=3.5 Hz, $J_{4,9}$=1.5 Hz H(4exo); 2.19 (ddq, 1H) $J_{11,10}$=12 Hz, J_{11,CH_3}=6.5 Hz, $J_{11,12}$=2 Hz H(11); 2.31 (dd, 1H) $J_{5,4}\cong J_{5,9}\cong$3.5 Hz H(5); 2.46 (d, 1H) $J_{4,4}$= 13.6 Hz H(4endo); 2.65 (dd, 1H) $J_{7,8}$=5.0 Hz, $J_{7,5}$=1.5 Hz H(7); 2.75 (dddd, 1H) $J_{9,8}$=10 Hz, $J_{9,10}$=7.2 Hz, $J_{9,5}$=3.5 Hz, $J_{9,4}$=1.5 Hz H(9); 2.9 (dt, 1H) $J_{8,9}$=10 Hz, $J_{8,7}$=$J_{8,1}$=5.0 Hz H(8); 3.47 (dq, 1H) $J_{1',1'}$=9 Hz, $J_{1',2'}$= 7 Hz H(1′a); 3.63 (dd, 1H) $J_{10,9}$=7.2 Hz, $J_{10,11}$=11.5 Hz H(10); 3.65 (dq, 1H) $J_{1',1'}$=9 Hz, $J_{1',2'}$=7 Hz H(1′b); 3.94 (m, 1H) $w_{1/2}$=9 Hz H(12); 4.14 (dd, 1H) $J_{1,8}$=$J_{1,12}$=4.5 Hz H(1); 4.35 (d, 1H) $J_{1'',1''}$=11.0 Hz benzyl. H; 4.58 (d, 1H) $J_{1'',1''}$=11.0 Hz benzyl. H; 7.2–7.31 (m, 5H) aromat.H; ^{13}C NMR ($CDCl_3$, δ): 210.3 C6; 138.5, 128.8, 128.4, 128.2 aromat. C; 111.5 C3; 76.9, 72.5, 72.3 C1, C10, C12; 72.5 benzyl. C; 59.7 C1′; 52.7 C7; 43.3, 37.9, 34.2, 33.3 C8, C9, C11, C5; 39.9 C4; 15.7, 15.5 C(11)CH_3, C2′; MS (*m/z*, %): 358 (100% M^+); 267 (45% $M^+-C_7H_7$); 106 (65%); 91 (47%); 57 (50%); HRMS Calcd for $C_{21}H_{26}O_5$: 358.1780. Found: 358.1769.

(+)-(1*R*,3*R*,5*R*,6*S*,7*S*,8*S*,9*R*,10*S*,11*R*,12*R*)-10-Benzyloxy-6,11-dimethyl-3-ethoxy-θ2-oxatetracyclo[6.4.0.0^{3,7}.0^{5,9}]-dodeca-6,12-diol (11a) and (+)-(1*R*,3*R*,5*R*,6*R*,7*S*,8*S*,9*R*,10*S*,11*R*,12*R*)-10-benzyloxy-6,11-dimethyl-3-ethoxy-2-oxatetracyclo[6.4.0.0^{3,7}.0^{5,9}]dodeca-6,12-diol (11b). A solution of 160 mg (0.45 mmol) of **10** in 20 ml abs. THF is treated with 500 μl MeMgCl (3 M in THF, 1.5 mmol) at 0°C. After 45 min sat. aq. NH_4Cl is added and the mixture is extracted four times with ether. The organic layers are washed with brine, dried with $MgSO_4$ and concentrated, yielding 158 mg (0.42 mmol, 95%) of a 1:1 mixture of the diastereomeric alcohols **11a**:**11b** as colorless oil. To characterize the alcohols a small amount of this mixture is separated by flash chromatography (petroleum ether–ethyl acetate 3:1).

Compound **11a**: mp 123–124°C $[\alpha]_D^{20}$=+112.5 (c=0.425 in CCl_4); IR (cm^{-1}): 3423, 2966, 2927, 2878; ^{1}H NMR ($CDCl_3$, δ): 1.02 (d, 3H) $J_{CH_3,11}$=6.5 Hz C(11)CH_3; 1.14 (t, 3H) $J_{1',2'}$=7.0 Hz H(2′); 1.29 (s, 1H, exchangeable with D_2O) OH; 1.35 (s, 1H, exchangeable with D_2O) OH; 1.40 (s, 3H) C(6)CH_3; 1.92–1.95 (m, 2H) H(5), H(4*n*); 2.07 (dd, 1H) $J_{4,4}$=15.1 Hz, $J_{4,5}$=2 Hz H(4*x*); 2.5 (ddq, 1H) $J_{11,10}$=11.5 Hz, J_{11,CH_3}=6.5 Hz, $J_{11,12}$=2 Hz H(11); 2.36 (dd, 1H) $J_{7,8}$=5.0 Hz, $J_{7,5}$=1.5 Hz H(7); 2.82 (dt, 1H) $J_{8,9}$=9.5 Hz, $J_{8,7}$=$J_{8,1}$=4.5 Hz H(8); 3.27 (dddd, 1H) $J_{9,8}$=9.5 Hz, $J_{9,10}$=8.7 Hz, $J_{9,5}\cong J_{9,4}\cong$3 Hz H(9); 3.47 (dq, 1H) $J_{1',1'}$=9.5 Hz, $J_{1',2'}$=7.0 Hz H(1′a); 3.61 (dq, 1H) $J_{1',1'}$=9 Hz, $J_{1',2'}$=7.0 Hz H(1′b); 3.63 (dd, 1H) $J_{10,9}$= 8.5 Hz, $J_{10,11}$=11.5 Hz H(10); 3.87 (m, 1H) $w_{1/2}$=8 Hz H(12); 4.03 (dd, 1H) $J_{1,8}\cong J_{1,12}\cong$4.2 Hz H(1); 4.37 (d, 1H) $J_{1'',1''}$=11.5 Hz benzyl. H; 4.65 (d, 1H) $J_{1'',1''}$=11.5 Hz benzyl. H; 7.19–7.3 (m, 5H) aromat. H; ^{13}C NMR ($CDCl_3$, δ) 138.5, 128.8, 128.4, 128.2 aromat. C, 114.2 C3, 82.3 C6, 77.8, 75.8, 73.7 C1, C10, C12; 72.5 benzyl. C; 59.3 C1′; 56.6 C7; 45.8 C5; 40.8 C4; 39.7, 36.2, 33.1 C8, C9, C11; 21.4 CH_3(6); 16, 15 CH_3(2′), CH_3(11); MS (*m/z*,%): 374 (100%, M^+); 283 (3%, $M^+-C_7H_7$); HRMS: Calcd for $C_{22}H_{30}O_5$: 374.2093. Found: 374.2085.

Compound **11b**: $[\alpha]_D^{20}$=+111.5 (c=0.460 in CCl_4); IR (cm^{-1}): 3459, 2970; ^{1}H NMR ($CDCl_3$, δ): 1.03 (d, 3H) $J_{CH_3,11}$=6.8 Hz C(11)CH_3; 1.15 (t, 3H) $J_{1',2'}$=7.0 Hz H(2′); 1.29 (s, 3H) C(6)CH_3; 1.35 (s, 1H, exchangeable with D_2O) OH; 1.98 (m, 1H) $w_{1/2}$=10 Hz H(5); 2.12–2.21 (m, 2H) H(4*n*), H(11); 2.27 (ddd, 1H) $J_{4,4}$=15.6 Hz, $J_{4,5}$=5 Hz, $J_{4,9}$=2.5 Hz H(4*x*); 2.29 (dd, 1H) $J_{7,8}$= 4.5 Hz, $J_{7,5}$=1.5 Hz H(7); 2.48 (s, 1H, exchangeable with D_2O) OH; 2.56 (dt, 1H) $J_{8,9}$=9.5 Hz, $J_{8,7}$=$J_{8,1}$=4.5 Hz H(8); 2.66 (dddd, 1H) $J_{9,8}$=9.5 Hz, $J_{9,10}$=11.5 Hz, $J_{9,5}$= $J_{9,4}$=2.8 Hz H(9); 3.53 (dd, 1H) $J_{10,9}$=11.5 Hz, $J_{10,11}$= 8.5 Hz H(10); 3.54 (dq, 1H) $J_{1',1'}$=9 Hz, $J_{1',2'}$=7.0 Hz H(1′a); 3.67 (dq, 1H) $J_{1',1'}$=9 Hz, $J_{1',2'}$=7.0 Hz H(1′b); 3.85 (s, 1H) $w_{1/2}$=9 Hz H(12); 4.05 (dd, 1H) $J_{1,8}$= $J_{1,12}$=4.5 Hz H(1); 4.38 (d, 1H) $J_{1'',1''}$=11.6 Hz benzyl. H; 4.57 (d, 1H) $J_{1'',1''}$=11.6 Hz benzyl. H; 7.2– 7.29 (m, 5H) aromat. H. (The configuration of C(11) was established by NOESY experiments: cross peaks between CH_3(6,) H(8) and H(9) determined the structure.) ^{13}C NMR ($CDCl_3$, δ) 139, 128.8, 128.4, 128.2 aromat. C; 116.4 C3; 83.1 C6; 77.7, 76, 72.7 C1, C10, C12; 72.3 benzyl. C; 59.7 C1′; 56.1 C7; 46 C5; 39.8 C4; 37.9, 33.2, 36.5 C9, C8, C11; 21.2 CH_3(6); 15.9, 15.5 CH_3(11), C(2′); MS (*m/z*, %): 374 (100%, M^+); 283 (2%, $M^+-C_7H_7$); HRMS: Calcd for $C_{22}H_{30}O_5$: 374.2093. Found: 374.2082.

(+)-(1*R*,3*R*,5*R*,6*S*,7*S*,8*S*,9*R*,10*S*,11*R*)-10-Benzyloxy-6,11-dimethyl-3-ethoxy-6-hydroxy-2-oxatetracyclo-[6.4.0.0^{3,7}.0^{5,9}]dodecan-12-one (12a) and (+)-(1*R*,3*R*,5*R*,6*R*,7*R*,8*S*,9*R*,10*S*,11*R*)-10-benzyloxy-6,11-dimethyl-3-ethoxy-6-hydroxy-2-oxatetracyclo[6.4.0.0^{3,7}.0^{5,9}]dodecan-12-one (12b). To a solution of 158 mg (0.422 mmol) of the diastereomeric mixture **11** in 15 ml acetone at 0°C Jones reagent is added until decoloration ceases. After stirring for a further 5 min. sat. aq. $NaHCO_3$ is added and the mixture is extracted three times with ether. The organic layers are washed with brine, dried with $MgSO_4$ and concentrated. Flash chromatography (petroleum ether–ethyl acetate 5:2) yields 74 mg of **l2a** and 75 mg of **12b** (0.40 mmol, 95%).

Compound **12a**: mp 108–110°C $[\alpha]_D^{20}$=+92.3 (c=0.22 in CCl_4); IR (cm^{-1}): 3484, 2972, 1720, 1454, 1377; ^{1}H NMR ($CDCl_3$, δ): 1.01 (d, 3H) $J_{CH_3,11}$=6.0 Hz (11)CH_3; 1.15 (t, 3H) $J_{1',2'}$=7.0 Hz H(2′); 1.32 (s, 1H, exchangeable with D_2O) OH; 1.44 (s, 3H) C(6)CH_3; 2.08 (dd, 1H) $J_{4,4}$= 16.1 Hz, $J_{4,5}$=2.5 Hz H(4); 2.1 (m, 1H) H(5); 2.35 (dd, 1H) $J_{4,4}$=16.1 Hz, $J_{4,5}$=2.5 Hz H(4); 2.42 (dd, 1H) $J_{7,8}$=

4.5 Hz, $J_{7,5}$=1.5 Hz H(7); 2.91 (dt, 1H) $J_{8,9}$=9.5 Hz, $J_{8,7}$=$J_{8,1}$=4.5 Hz H(8); 3.32 (dddd, 1H) $J_{9,8}$=$J_{9,10}$=9.5 Hz, $J_{9,5}$=$J_{9,4}$=3 Hz H(9); 3.39–3.45 (m, 2H) H(10), H(11); 3.48 (dq, 1H) $J_{1',1'}$=9.5 Hz, $J_{1',2'}$=7.0 Hz H(1′a); 3.62 (dq, 1H) $J_{1',1'}$=9.5 Hz, $J_{1',2'}$=7.0 Hz H(1′b); 4.09 (d, 1H) $J_{1,8}$=4.5 Hz H(1); 4.39 (d, 1H) $J_{1'',1''}$=11.6 Hz benzyl. H; 4.65 (d, 1H) $J_{1'',1''}$=11.6 Hz benzyl. H; 7.22–7.31 (m, 5H) aromat. H; ^{13}C NMR ($CDCl_3$, δ): 212.0 C12; 138.3, 128.8, 128.3, 128.2 aromat. C; 116.2 C3; 83.5, 79.7 C1, C10; 81.6 C6; 72.9 benzyl. C; 59.6 C1′; 57.0 C7; 45.7, 45.2, 43.4, 37.1 C5, C8, C9, C11; 40.1 C4; 21.2 CH_3(6); 15.9, 11.7 CH_3(11), CH_3(2′); MS: (*m*/*z*, %): 372.3 (100%, M^+); HRMS: Calcd for $C_{22}H_{28}O_5$: 372.1936. Found: 372.1949.

Compound **12b**: mp 101–102°C; $[\alpha]_D^{20}$=+85.7 (*c*=0.22 in CCl_4); IR (cm^{-1}): 3483, 2973, 2933, 2898, 1722; ^{1}H NMR ($CDCl_3$, δ): 1.03 (d, 3H) $J_{CH_3,11}$=6.8 Hz C(11)CH_3; 1.16 (t, 3H) $J_{1',2'}$=7.0 Hz H(2′); 1.29 (s, 3H) C(6)CH_3; 2.12 (m, 1H) $w_{1/2}$=9 Hz H(5); 2.33 (d, 1H) $J_{7,5}$=2.0 Hz H(7); 2.43 (m, 2H) $w_{1/2}$=3 Hz H(4*x*), H(4*n*); 2.64 (m, 2H) $w_{1/2}$=9 Hz H(8), H(9); 3.35 (m, 1H) $w_{1/2}$=21.1 Hz H(10); 3.46 (dq, 1H) J_{11,CH_3}=6.8 Hz, $J_{11,10}$=12.1 Hz H(11); 3.55 (dq, 1H) $J_{1',1'}$=9.1 Hz, $J_{1',2'}$=7 Hz H(1′a); 3.67 (dq, 1H) $J_{1',1'}$= 9.1 Hz, $J_{1',2'}$=7 Hz H(1′b); 4.09 (d, 1H) $J_{1,8}$=3.5 Hz H(1); 4.44 (d, 1H) $J_{1'',1''}$=11.5 Hz benzyl. H; 4.56 (d, 1H) $J_{1'',1''}$=11.5 Hz benzyl. H; 7.21–7.31 (m, 5H) aromat. H; ^{13}C NMR ($CDCl_3$, δ): 211.3 C12; 138.0, 128.9, 128.5, 128.4 aromat. C; 118.5 C3; 84.0, 79.9 C1, C10; 82.2 C6; 73.6 benzyl. C; 59.9 C1′; 56.5 C7; 45.9, 43.6, 43.4, 37.4 C5, C8, C9, C11; 39.6 C4; 21.4 CH_3(6); 15.9, 11.6 CH_3(11), C(2′); MS (*m*/*z*; %): 372.2 (100%, M^+); HRMS: Calcd for $C_{22}H_{28}O_5$: 372.1936. Found: 372.1925.

(+)-(1*S*,2*S*,5*R*,6*S*,7*R*,8*R*,11*S*)-6-Benzyloxy-5,11-dimethyl-11-hydroxytricyclo[6.2.1.0^{2,7}]undeca-4,10-dione (13a). 24 mg (0.065 mmol) of **12a** are dissolved in 2 ml abs. THF and 4 ml abs. MeOH. Degassing is followed by dropwise addition of the SmI_2 solution at −78°C under an atmosphere of argon until the starting material is no longer detectable by TLC (ca. 2 ml). The reaction mixture is quenched by addition of 2% aq. HCl and water and extracted three times with ether. The organic layers are washed with brine, dried with $MgSO_4$ and concentrated. Flash chromatography (petroleum ether–ethyl acetate 2:3) yields 17 mg of **l3a** (0.053 mmol**,** 81%) as colorless oil.

Compound **13a**: $[\alpha]_D^{20}$=+53.1 (*c*=0.08 in CCl_4); IR (cm^{-1}): 2936, 2360, 1743, 1709; ^{1}H NMR ($CDCl_3$, δ): 1.08 (d, 3H) $J_{CH_3,5}$=7.5 Hz C(5)CH_3; 1.38 (s, 3H) C(11)CH_3; 2.18 (dd, 1H) $J_{9,9}$=19.1, $J_{9,8}$=4.5 Hz H(9); 2.2–2.36 (m, 4H) H(1),H(3),H(3),H(8); 2.7 (dq, 1H) J_{5,CH_3}=7.5 Hz, $J_{5,6}$= 4.0 Hz H(5); 2.90 (dddd, 1H) $J_{2,7}$=11.0 Hz, $J_{2,3}$=13.8 Hz, $J_{2,3}$=5.4 Hz, $J_{2,1}$=5.8 Hz H(2); 3.07 (ddd, 1H) $J_{7,2}$= 11.0 Hz, $J_{7,6}$=$J_{7,8}$=3.5 Hz H(7); 3.44 (d, 1H) $J_{9,9}$=19.1 Hz H(9); 3.97 (dd, 1H) $J_{6,7}$=3.5 Hz, $J_{6,5}$=4.0 Hz H(6); 4.32 (d, 1H) $J_{1'',1''}$=12.1 Hz benzyl. H; 4.52 (d, 1H) $J_{1'',1''}$=12.1 Hz benzyl. H; 7.14–7.29 (m, 5H) aromat. H; ^{13}C NMR ($CDCl_3$, δ): 215.0, 213.4 C4, C10; 137.9, 128.9, 128.2, 127.9 aromat. C; 82.9 C11; 80.9 C6; 71.7 benzyl. C; 65.1 C1; 48.3, 46.7, 35.5, 33.0 C2, C5, C7, C8; 41.5, 41.3 C3, C9; 22.4, 14.7 CH_3(5), CH_3(11); MS (*m*/*z*, %): 328 (100%, M^+); 91 (15%, $C_7H_7^+$); HRMS: Calcd for $C_{20}H_{24}O_4$: 328.1675. Found: 328.1688.

(+)-(1*S*,2*S*,5*R*,6*S*,7*R*,8*R*,11*R*)-6-Benzyloxy-5,11-dimethyl-11-hydroxytricyclo[6.2.1.0^{2,7}]undeca-4,10-dione (13b). 34 mg (0.09 mmol) of **12b** are dissolved in 3 ml abs. THF and 1.5 ml abs. MeOH. Degassing is followed by dropwise addition of the SmI_2 solution at −78°C under an atmosphere of argon until the starting material is no longer detectable by TLC (ca. 2 ml). The reaction mixture is quenched by addition of 2% aq. HCl and water and extracted three times with ether. The organic layers are washed with brine, dried with $MgSO_4$ and concentrated. Flash chromatography (petroleum ether–ethyl acetate 2:3) yields 24 mg of **l3b** (0.072 mmol, 80%) as colourless oil. When a larger scale is adopted small amounts of byproduct **18** are isolated.

Compound **13b**: $[\alpha]_D^{20}$=+56.9 (*c*=0.05 in CCl_4); IR (cm^{-1}): 2936, 1744, 1712; ^{1}H NMR ($CDCl_3$, δ): 1.03 (d, 3H) $J_{CH_3,5}$=8 Hz C(5)CH_3; 1.46 (s, 3H) C(11)CH_3; 1.82 (s, 1H, exchangeable with D_2O) OH; 2.25 (dd, 1H) $J_{1,2}$=3.0 Hz, $J_{1,8}$=1.5 Hz H(1); 2.28–2.33 (m, 2H) H(3ax), H(3eq); 2.38 (m, 1H) H(8); 2.5–2.57 (m, 2H) H(2), H(7); 2.62 (ddd, 1H) $J_{9,9}$=18.1 Hz, $J_{9,8}$=5.0 Hz H(9); 2.68 (dq, 1H) J_{5,CH_3}=8 Hz, $J_{5,6}$=3.5 Hz H(5); 3.29 (d, 1H) $J_{9,9}$=18.1 Hz H(9); 3.91 (dd, 1H) $J_{6,5}$=3.5 Hz, $J_{6,7}$=4.0 Hz H(6); 4.35 (d, 1H) $J_{1'',1''}$=12.0 Hz benzyl. H; 4.51 (d, 1H) $J_{1'',1''}$=12.0 Hz benzyl. H; 7.15–7.29 (m, 5H) aromat. H; ^{13}C NMR ($CDCl_3$, δ): 216, 212.6 C4, C10; 137.7, 128.9, 128.3, 128.0 aromat. C; 83.3 C11; 80.4 C6; 71.9 benzyl. C; 63.9 C1; 48.3, 46.7, 35.2, 32.3 C2, C5, C7, C8; 41.1, 39.9 C3, C9; 22.1, 14.7 CH_3(5), CH_3(11); MS (*m*/*z*, %): 328 (100%, M^+); 91 (15%, $C_7H_7^+$); HRMS: Calcd for $C_{20}H_{24}O_4$: 328.1675. Found: 328.1663.

(±)-(1*S,2*S**,4*R**,5*S**,6*S**,7*S**,8*R**,9*S**,10*R**)-9-Benzyloxy-5,10-dimethyltetracyclo[5,3,1,0$^{2.6}$,0$^{4.8}$]undeca-1,2,5-triol (18).** 18 mg (0.048 mmol) of (±)-**12a** are dissolved in 3 ml abs. THF and 100 μl abs. HMPA. Degassing is followed by dropwise addition of the SmI_2 solution at −100°C under an atmosphere of argon until the starting material is no longer detectable by TLC (ca. 1.6 ml). The reaction mixture is quenched by the addition of 2% aq. HCl and water and extracted three times with ether. The organic layers are washed with brine, dried with $MgSO_4$ and concentrated. Flash chromatography (petroleum ether–ethyl acetate 1:2) yields 17.5 mg of **l8** (0.047 mmol**,** 97%) as colorless oil.

IR (cm^{-1}): 3385, 2958, 2361; ^{1}H NMR ($CDCl_3$, δ): 1.08 (d, 3H) $J_{CH_3,10}$=6.5 Hz CH_3(10); 1.17 (dd, 1H) $J_{11,11}$=11.5 Hz, $J_{11,7}$=$J_{11,10}$=2 Hz H(11); 1.32 (d, 3H) $J_{CH_3,10}$=6.5 Hz CH_3(5); 1.60 (s, 1H, exchangeable with D_2O) OH; 1.71 (dd, 1H) $J_{6,7}$=3.5 Hz, $J_{6,4}$=2.5 Hz H(6); 1.74 (dd, 1H) $J_{11,11}$=11.5 Hz, $J_{11,7}$=2 Hz H(11); 1.83 (m, 1H) $w_{1/2}$=9.5 Hz H(4); 2.12 (dddd, 1H) $J_{7,8}$=9.5 Hz, $J_{7,11}$≅ $J_{7,11}$≅$J_{7,6}$≅2.5 Hz H(7); 2.21 (ddd, 1H) $J_{3,3}$=12.5 Hz, $J_{3,4}$=$J_{3,8}$=2 Hz H(3); 2.23 (ddq, 1H) J_{10,CH_3}≅$J_{10,9}$≅6.0 Hz, $J_{10,11}$=2.0 Hz H(10); 2.42 (dddd, 1H) $J_{8,7}$=10.6 Hz, $J_{8,9}$≅$J_{8,4}$≅5.7 Hz, $J_{8,3}$=2 Hz H(8); 2.45 (dd, 1H) $J_{3,3}$= 12.0, $J_{3,4}$=1 Hz H(3); 2.8 (s, 1H, exchangeable with D_2O) OH; 3.08 (s, 1H, exchangeable with D_2O) OH; 3.16 (t, 1H) $J_{9,8}$=$J_{9,10}$=6.0 Hz H(9); 4.32 (d, 1H) $J_{1'',1''}$=11.5 Hz benzyl. H; 4.51 (d, 1H) $J_{1'',1''}$=11.5 Hz benzyl. H; 7.22–7.3 (m, 5H) aromat. H; ^{13}C NMR ($CDCl_3$, δ): 139.0, 128.8, 128.1, 128 aromat. C; 85.1, 82.9, 80.1 C1, C2, C5; 83.5 C9; 71.3

benzyl.C; 64.6 C6; 47.6, 45.6, 37.8, 34 C4, C7, C8, C10; 36.5, 33.3 C3, C11; 22.6, 16.6 CH_3(5), CH_3(10); MS (*m/z*; %): 330 (45%, M^+); 312 (100%, M^+-H_2O); 221 (3%, $M^+-H_2O-C_7H_7$); 91 (13%, C_7H_7); HRMS: Calcd for $C_{20}H_{26}O_4$: 330.1831. Found: 330.1819.

(1*R*,2*R*,3*S*,4*S*,7*S*,8*S*)-3-Benzyloxy-4,11-dimethyl-5,11-dihydroxy-tricyclo[6.2.1.0^{2,7}]undecan-9-one (14a,14b, 15a,15b). To a solution of 20 mg (0.061 mmol) of the diastereomeric mixture **13** in 2 ml abs. THF at −78°C a solution of DIBAL (1 M in hexane, ca. 150 μl) is added until the starting material is no longer detectable by TLC. Then sat. aq. NH_4Cl is added and the mixture is extracted three times with ether. The organic layers are washed with brine, dried with $MgSO_4$ and concentrated. The residue is filtered through silica gel (petroleum ether–ethyl acetate 3:2) and the resulting diastereomeric mixture (17.8 mg) is used immediately.

(+)-(1*R*,5*R*,6*R*,7*S*,8*S*,9*R*)-5-Acetyl-7-benzyloxy-9-hydroxy-8-methylbicyclo[4.4.0]decan-3-one (16) and (+)-(1*R*,5*R*,6*R*,7*S*,8*S*,9*S*)-5-acetyl-7-benzyloxy-9-hydroxy-8-methylbicyclo[4.4.0]decan-3-one (17). To a solution of 17.8 mg (0.054 mmol) of **14** and **15** in 4 ml CH_3CN 100 μl (0.79 mmol) freshly distilled $BF_3{\cdot}OEt_2$ is added at 0°C and the mixture is stirred for 1 h at 0°C. Then sat. aq. $NaHCO_3$ is added and the mixture is extracted three times with ether. The organic layers are washed with brine, dried with $MgSO_4$ and concentrated. Flash chromatography (petroleum ether–ethyl acetate 1:4) yields 10.6 mg of **16** (0.029 mmol 53% over two steps) and 4 mg of **17** (0.011 mmol 20% over two steps).

Compound **16**: mp 116–118°C; $[\alpha]_D^{20}=+29.9$ (c=0.23 in CCl_4); IR (cm^{-1}): 3567, 2924, 1708; ^1H NMR ($CDCl_3$, δ): 1.04 (d, 3H) $J_{CH_3,8}$=6.0 Hz CH_3(8); 1.22 (dd, 1H) $J_{10,10}$=13.0 Hz, $J_{10,9}$=11.6 Hz $J_{10,1}$=12 Hz H(10); 1.55 (s, 1H, exchangeable with D_2O) OH; 1.61 (ddq, 1H) J_{8,CH_3}=6.0 Hz, $J_{8,9}$=11.6 Hz, $J_{8,7}$=11 Hz H(8); 1.67 (ddd, 1H) $J_{10,10}$=13.0 Hz, $J_{10,9}\cong J_{10,1}\cong$3.8 Hz H(10); 2.02 (s, 3H) $CH_3(2')$; 2.12–2.18 (m, 2H) H(1), H(2); 2.25 (ddd, 1H) $J_{4,4}$=14.1 Hz, $J_{4,5}$=5.0 Hz, $J_{4,2}$=2.0 Hz H(4); 2.37 (dd, 1H) $J_{4,4}\cong J_{4,5}\cong$13.1 Hz H(4); 2.64 (dd, 1H) $J_{2,2}$=14.1 Hz, $J_{2,1}$=5.8 Hz H(2); 2.89 (ddd, 1H) $J_{6,5}$=11.5 Hz, $J_{6,7}=J_{6,1}$=4.3 Hz H(6); 2.99 (dd, 1H) $J_{7,8}$=11.0 Hz, $J_{7,6}$=4.3 Hz H(7); 3.16 (ddd, 1H) $J_{9,8}=J_{9,10}$=10.5 Hz, $J_{9,10}$=4.5 Hz H(9); 3.20 (ddd, 1H) $J_{5,4}=J_{5,6}$=12 Hz, $J_{5,4}$=5 Hz H(5); 4.06 (d, 1H) $J_{1'',1''}$=10.5 Hz benzyl. H; 4.37 (d, 1H) $J_{1'',1''}$=10.5 Hz benzyl. H; 7.23–7.28 (m, 5H) aromat. H; ^{13}C NMR ($CDCl_3$, δ): 209.7, 209 C1′, C3; 138.1, 128.9, 128.8, 128.6 aromat. C; 83.1, 74.3 C7, C9; 72.4 benzyl. C; 46.5, 43.5, 36.7 C2, C4, C10; 46.4, 40.8, 40.8, 34.7 C1, C5, C6, C8; 32.2, 14.9 C2′, CH_3(8); MS (*m/z*): 330.4 (100%, M^+); 91 (4%, C_7H_7); HRMS: Calcd for $C_{20}H_{26}O_4$: 330.1831. Found: 330.1839. Anal. Calcd for $C_{20}H_{26}O_4$: C, 72.70%; H, 7.93%. Found: C, 72.39%; H, 7.82%.

Compound **17**: mp 115–116°C; $[\alpha]_D^{20}=+73.3$ (c=0.41 in CCl_4); IR (cm^{-1}): 3510, 2924, 1709; ^1H NMR ($CDCl_3$, δ): 1.00 (d, 3H) $J_{CH_3,8}$=6.5 Hz C(8)CH_3; 1.37 (ddd, 1H) $J_{10,10}=J_{10,1}$=14.1 Hz, $J_{10,9}$=2.7 Hz H(10); 1.38 (s, 1H, exchangeable with D_2O) OH; 1.67 (ddd, 1H) $J_{10,10}$=14.1 Hz, $J_{10,9}=J_{10,1}$=3.0 Hz H(10); 1.76 (ddq, 1H) $J_{CH_3,8}$=6.5 Hz, $J_{8,7}$=11.1 Hz, $J_{8,9}$=3.9 H(8); 1.99 (s, 3H) $CH_3(2')$; 2.09 (ddd, 1H) $J_{2,2}$=11.6 Hz, $J_{2,1}=J_{2,4}$=2.5 Hz H(2); 2.24 (ddd,1H) $J_{4,4}$=14.1 Hz, $J_{4,5}$=4.6 Hz, $J_{4,2}$=2.5 Hz H(4); 2.4 (dd, 1H) $J_{4,4}$=14.1 Hz, $J_{4,5}$=12.1 Hz H(4); 2.61–2.66 (m, 2H) H(1), H(2); 2.96 (ddd, 1H) $J_{6,5}$=12.1 Hz, $J_{6,7}=J_{6,1}$=3.8 Hz H(6); 3.15 (ddd, 1H) $J_{5,4}=J_{5,6}$=12.1 Hz, $J_{5,4}$=4.6 Hz H(5); 3.48 (dd, 1H) $J_{7,8}$=11.1 Hz, $J_{7,6}$=3.8 Hz H(7); 3.89 (m, 1H) $w_{1/2}$=8 Hz H(9); 4.08 (d, 1H) $J_{1'',1''}$=10.5 Hz benzyl. H; 4.36 (d, 1H) $J_{1'',1''}$=10.5 Hz benzyl. H; 7.2–7.28 (m, 5H), aromat. H; ^{13}C NMR ($CDCl_3$, δ): 210.7, 209 C3, C1′; 138.4, 128.8, 128.6, 127.9 aromat. C; 83.1, 71.4 C9, C7; 72.2 benzyl. C; 46.5, 43.7, 34.9, C2, C4, C10; 45.8, 41.7, 36.8, 32.8 C1, C5, C6, C8; 31.9 C2′; 14.8 CH_3(8); MS (*m/z*, %): 330.4 (100%, M^+); 91 (3%, C_7H_7); HRMS: Calcd for $C_{20}H_{26}O_4$: 330.1831. Found: 330.1823. Anal. Calcd for $C_{20}H_{26}O_4$: C, 72.70%; H, 7.93%. Found: C, 72.39%; H, 7.82%.

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