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Vitamin B_{12}, a Catalyst in the Synthesis of Prostaglandins

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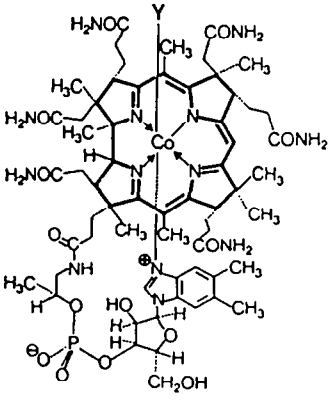
Dedicated to Professor Wang Yu on the occasion of his 80th birthday

(*Received in Japan* 2 *November* 1989)

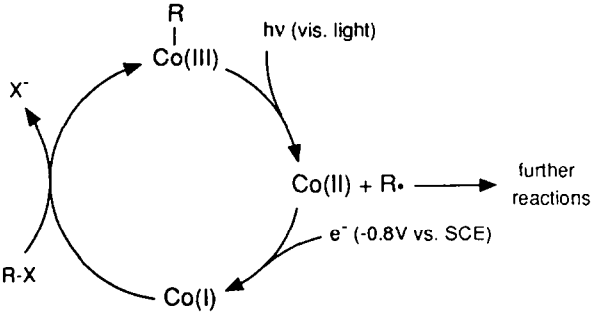
Abstract. - A prostaglandin $F_{2\alpha}$ precursor containing all structural features from C_6 to C_{20} with 8*R*, 9*S*, 11*R* and 12*R* chirality is obtained by the one step formation of two C-C bonds in the B_{12}-catalyzed radical cyclization-addition sequence starting from a chiral cyclopentene bromoacetal and 1-octyne-3-one. The B_{12}-catalyzed radical cyclization-elimination sequence of a chiral cyclopentene precursor leads to (-)-(3a*R*,6a*S*)-3,3a,6,6a-tetrahydro-2*H*-cyclopenta[*b*]furan-2-one. Its (+)-(3a*S*,6a*R*)-enantiomer is obtained *via* B_{12}-catalyzed, enantioselective isomerization of cyclopentene oxide to (*R*)-2-cyclopentene-1-ol followed by the B_{12}-catalyzed radical cyclization-elimination sequence of its bromoacetal.

Introduction. - Recent years have seen an impressive development of radical chemistry directed towards organic synthesis[1]. The commonly used reagents are organotin compounds, in particular tri-*n*-butyltin hydride[2]. Mainly for ecological, but also for economic reasons these compounds should be replaced by less toxic and more specifically acting reagents or catalysts. A salient candidate is vitamin B_{12}[3], a coenzyme known to promote a series of biological transformations *via* radical intermediates[4]. Since B_{12} is produced industrially in large-scale fermentation processes[5], it is commercially available at a reasonable price. B_{12} and related Co-complexes have been applied as catalysts for various reaction types such as: oxidations, hydrogenations, reductions of functional groups, reductive eliminations, rearrangements and reductive C-C bond formations[6]. Of special interest in organic synthesis is the B_{12}-catalyzed, photochemically induced radical C-C bond formation[7]. The mode of action of these catalysts is known to some extent[8] (Scheme 1).

Scheme 1. Generation of Carbon Centered Free Radicals by B_{12}-Photo-Electro-Catalysis



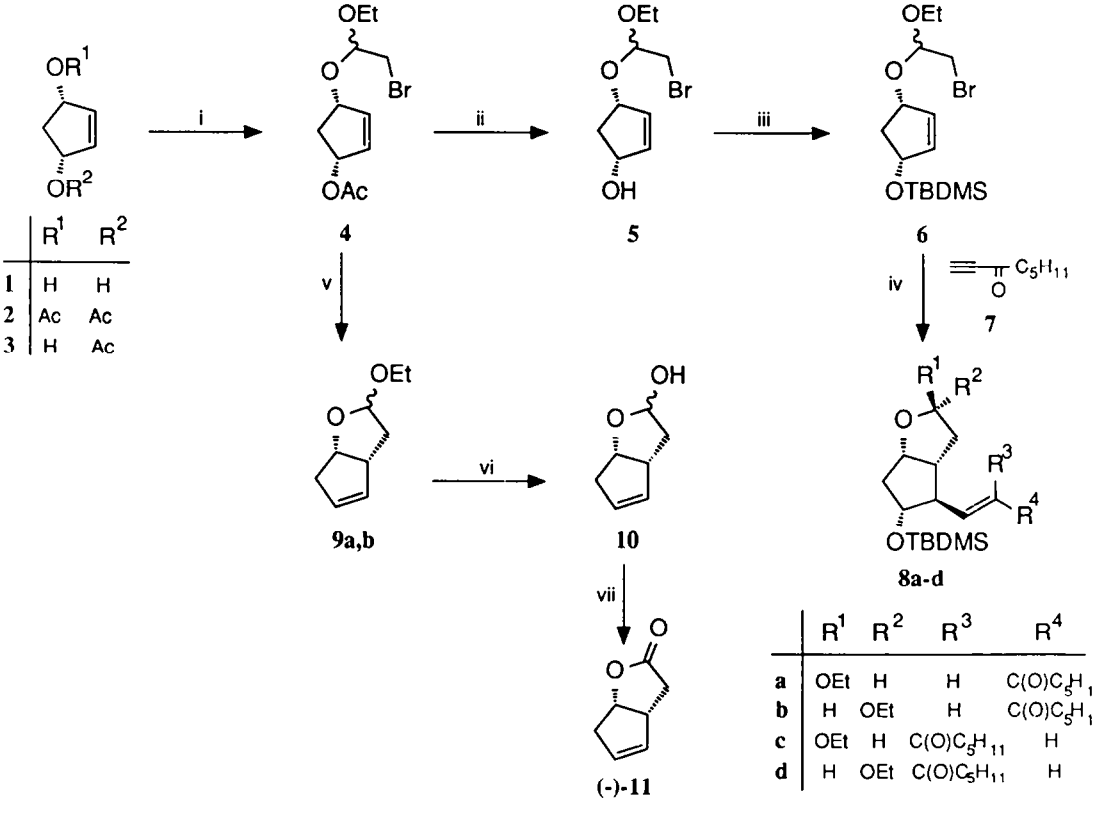
Y = OH•HCl Hydroxocobalamine hydrochloride (B_{12a})



The catalytically active species is cob(I)alamin (B_{12s}), which is obtained by reduction of hydroxocob(III)alamin (B_{12a}) in two consecutive one-electron reductions. The first reduction to cob(II)alamin (B_{12r}) occurs at *ca.* 0 V (*vs.* SCE), the second to B_{12s} at *ca.* -0.8 V [9]. B_{12s} is (different from B_{12r}) a highly reactive species and undergoes rapid bimolecular nucleophilic substitution with primary alkyl bromides RX to form organocob(III)alamins[10]. Photochemically induced Co-C bond homolysis with visible light (λ = 400-600 nm)[11] affords the persistent radical B_{12r}[12] and the transient carbon radical R•[12]. B_{12r} is recycled to B_{12s} by a one-electron reduction, whilst the carbon radical undergoes typical "free radical" reactions, *e.g.* addition to olefins[1].

Synthesis of $PGF_{2\alpha}$-precursors[13]. - Numerous approaches in PG-syntheses start from chiral cyclopentane precursors bearing functionalities ready to be elaborated into side chains[14]. The key feature of two recent reports on $PGF_{2\alpha}$-syntheses from *Stork et al.*[15] and *Keck* and *Burnett*[16] is the cyclization of free radicals generated from a cyclopentene iodoacetal with trapping of the intermediate secondary carbon radical by a precursor of the C_{13}-C_{20} side chain in a single step. Both cyclization-trapping sequences[1a,17] are based on radical generation using organotin compounds.

Scheme 2. B_{12}-Catalyzed Synthesis of PG-Precursors from Optically Active Cyclopentene Diol Derivatives



	R^1	R^2
1	H	H
2	Ac	Ac
3	H	Ac

	R^1	R^2	R^3	R^4
a	OEt	H	H	$C(O)C_5H_{11}$
b	H	OEt	H	$C(O)C_5H_{11}$
c	OEt	H	$C(O)C_5H_{11}$	H
d	H	OEt	$C(O)C_5H_{11}$	H

i) **3** + ethylvinylether, NBS, CH_2Cl_2, -40° to r.t., 16h (88%); ii) KOH, 90% EtOH, r.t. (83%); iii) TBDMSCl, imidazole, DMF, r.t. (98%); or i to iii without isolation of intermediates in 96%; iv) 6 equiv. **7**, 0.018 equiv. B_{12a}, electrolysis in 0.3M $LiClO_4$/DMF at -0.9V (vs. SCE), vis. light (>55% **8** as a mixture of four isomers (GC)); cis-trans-equilibration: I_2, hexane, hv → trans isomers **8a,b** (47%); v) 0.01 equiv. B_{12a}, Zn, NH_4Cl/EtOH, r.t., 6h (73%); vi) 1.5% HCl/THF, r.t., 48h (37%, not optimized); vii) CrO_3, acetone/H_2SO_4/H_2O (63%, e.e.>98%, not optimized).

Our synthesis of $PGF_{2\alpha}$-precursors relies on the original work on B_{12}-catalyzed, reductive radical cyclization[18], *Tada's* report concerning the cobaloxim-mediated synthesis of γ-lactones[19] and the knowledge of the B_{12}-catalyzed radical addition to activated alkynes[7] (Scheme 2).

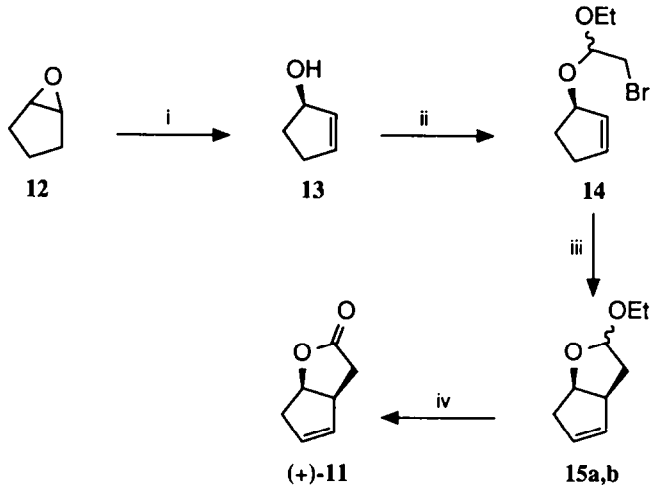
The *cis*-diol **1** was obtained by a slight modification of the procedure of *Kaneko et al.*[20] starting from cyclopentadiene. Acetylation[21] gave the diacetate **2**, which was hydrolyzed enantioselectively with porcine pancreas lipase according to *Laumen* and *Schneider*[22] to afford **(+)-3** (e.e. > 98%) in 37% yield from cyclopentadiene. Reaction with ethylvinyl ether and N-bromosuccinimide (NBS)[15,19] gave the bromoacetal **4**. Since the acetoxy function in **4** is a potential leaving group, it was replaced by a silyloxy function *via* basic hydrolysis to **5** and silylation with *tert.*-butyldimethylchlorosilane (TBDMS-Cl)[23] affording **6** in 72% yield with respect to **3**. The key-step of the synthesis is the reductive B_{12}-catalyzed radical cyclization of **6** with concomitant trapping of the intermediate secondary radical by 1-octyne-3-one **7**[24], affording **8** in one operation. The electrolysis of **6** in the presence of a fivefold excess of **7** was performed in a specially designed H-type electrochemical cell[25] under irradiation with visible light at a constant cathode potential of -0.9V (*vs.* SCE) and in the presence of 0.018 equiv. of B_{12a} (with respect to **6**) in 0.3 M $LiClO_4$/ DMF. Under these conditions a mixture of the four diastereomers of **8** (differing in the configuration at the double bond and of the acetal function) was obtained in *ca.* 55% yield. All four isomers were separated by chromatography and characterized individually. Quantitative isomerization to the *trans*-olefins **8a,b** was achieved by exposing a solution of the mixture of diastereomers in hexane, containing some iodine, to visible light. **8a** and **8b** were separated by chromatography and isolated as pure materials in 26% and 21% yield, respectively, with respect to **6**. The two diastereomeric acetals easily underwent acid-catalyzed interconversion. The mixture **8a,b** is an advanced intermediate, from which $PGF_{2\alpha}$ had been obtained in three further steps[15].

The B_{12}-catalyzed cyclization-addition step **6** + **7** → **8** needs some comments: in the absence of either B_{12} or light, no product **8** is formed at -0.9V; at a more negative potential or with Zn/NH_4Cl as a chemical reducing agent, **7** is reduced to 1-octene-3-one, which traps the intermediate radical affording products lacking the $\Delta^{13,14}$ double bond[26]; as a by-product of the described synthesis 1,3,5-trihexanoylbenzene (the product of B_{12}-catalyzed radical trimerization of **7**) was formed in *ca.* 12% with respect to the total amount of **7**.

B_{12}-catalzyed electrolysis of the acetoxy bromoacetal **4** in DMF at -1.0V afforded the diastereomeric acetals **9a,b** as products of a cyclization-elimination sequence. The same compounds were obtained in 73% yield on treatment of **4** in ethanol with Zn/NH_4Cl in the presence of 0.01 equiv. B_{12a}. Acid hydrolysis gave the crystalline hemiacetal **10**, which on *Jones*-oxidation afforded the known[27] lactone **(-)-11** (m.p. 44-45°, e.e. > 98%), an important intermediate in PG-syntheses[28].

The enantiomer **(+)-11** was prepared in five steps from cyclopentene oxide **12** (Scheme 3). The achiral epoxide **12** was first transformed to (*R*)-2-cyclopentene-1-ol **13** (67% yield, 62% e.e.) by the recently discovered enantioselective isomerization with catalytic amounts of B_{12a} (0.01 equiv.) and Zn in methanol[29]. **14** was then obtained quantitatively in the usual way. The B_{12}-catalyzed cyclization of **14** with $NaBH_4$ in ethanol at 60° afforded the diastereomeric acetals **15a,b** in 71% yield. *Jones*-oxidation followed by crystallization finally gave **(+)-11**[30] in 45% yield and an e.e. > 99%. The straightforward transformation of the achiral epoxide **12** to essentially pure **(+)-11** illustrates the power and versatility of vitamin B_{12} as catalyst in organic synthesis.

Scheme 3. Synthesis of Optically Active Cyclopenta[b]furans by Enantioselective B_{12}-Catalysis

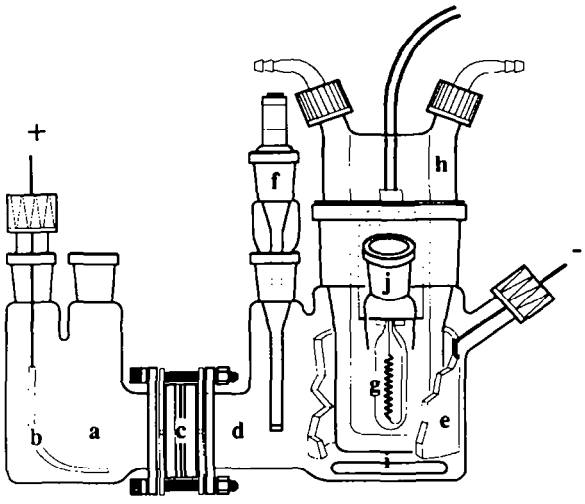


i) 0 01 equiv. B_{12a}, Zn/NH_4Cl, MeOH, r.t., 8d (67%, e.e.=62%); ii) ethylvinylether, NBS, CH_2Cl_2, -40° to r.t., 16h (100%); iii) 0.035 equiv. B_{12a}, $NaBH_4$, EtOH, 60°, 70min. (71%); iv) CrO_3, acetone/H_2SO_4/H_2O, 0°, 1h, then crystallization and 2 x recrystallization (45%, e.e.>99%).

Experimental Section

General: Vitamin B_{12a} (hydroxocobalamine hydrochloride, pyrogen-free *Fr. Ph. BP*, 10.7% loss on drying, < 2% cyanocobalamine) from *Roussel Uclaf*, rose bengal (*standard*), thiourea (*purum*), pyridine (*puriss.*), acetic anhydride (*puriss.*), porcine pancreas lipase PPL (cat. no. 62300), N-bromosuccinimide (*purum*), *tert.*-butyldimethylchlorosilane (*purum*), imidazole (*puriss.*), 1-octyne-3-ol (*purum*), $LiClO_4$ (*purum*) and *p*-toluenesulfonic acid monohydrate (*pract.*) from *Fluka*, CrO_3 (*p.a.*) from *Merck*, NH_4Cl (*purum*), HOAc (98%), H_2SO_4 (*puriss.* 95%) and THF (*purum*) from *Siegfried* and O_2 from *Carba* were used as purchased. CH_2Cl_2 from *Fluka* was distilled over P_2O_5. Cyclopentadiene was freshly distilled from its dimer (*pract.*) from *Fluka* over a 30 cm vigreux column. 4-Dimethylaminopyridine (*purum*) from *Fluka* was recrystallized from ethylacetate. Ethylvinylether (*purum*) from *Fluka* was freshly distilled over sodium. Cyclopentene oxide from *Merck* was distilled, b.p. 98-99°/715 mbar (important: the oxide should be free of chlorinated solvents). 0.1M P-buffers were prepared from $Na_2HPO_4 \cdot H_2O$ (*puriss.*) from *Fluka* and $NaH_2PO_4 \cdot 12H_2O$ (*p.a.*) from *Merck*. Zn-wool (*puriss.*) from *Siegfried* was activated before use: Zn (*ca.* 1 g) in 2N HCl (*ca.* 10 ml) was stirred for 15 min at r.t., followed by washing with H_2O, MeOH and Et_2O (3 x 10 ml each). DMF (*puriss.*) from *Fluka* was filtered through basic Alox from *Merck* before use, except for the electrochemical experiment yielding PG-precursor **8**, where best results were obtained with dry DMF (either *puriss. absolute, < 0.01% H_2O* from *Fluka*, filtered through basic Alox, or distillation of *puriss.* from *Fluka* over P_2O_5, filtered through basic Alox). The electrochemical experiment was carried out in an H-type cell under potentiostatic conditions (see *Fig.*). GC: *Hewlett-Packard 5890* gas chromatograph, 20 m *Duran* glass cap. column coated with *SE-54*, temp. program from 40° to 200° at a rate of 3°/min. ^{1}H-NMR: *Varian EM 360L* (60 MHz) and *Bruker AM-400WB* (400 MHz), TMS (= 0 ppm) as internal standard. IR: *Perkin-Elmer 782* infrared spectrometer. MS: *Varian MAT CH-7A* mass spectrometer, ionization energy 70 eV. UV: *Hewlett-Packard 8451A* diode array spectrophotometer. $[\alpha]_D$: *Perkin-Elmer 241* polarimeter. n_D: *Carl Zeiss* refractometer. Melting points: *Büchi 510*. Elemental analysis: performed by

Org.-chem. Mikrolabor ETH, Zürich. TLC: precoated plates, silica gel *60* F_{254} from *Merck* developed with H_2SO_4/vanilline. Flash chromatography: silica gel for flash chromatography from *Baker*. HPLC: silica gel 7 μm, column diameter 23 mm, column length 25 cm.



a) anode compartment under Ar
b) anode (graphitized carbon felt GFA5 from Sigri Elektrographit GmbH)
c) diaphragm (Nafion 423 membrane from Du Pont)
d) cathode compartment under Ar
e) cathode (carbon felt, arranged cylindrically around cooling jacket **h**), distance ca. 2 mm)
f) reference electrode (saturated calomel electrode SCE from Metrohm)
g) light source (250 W halogen lamp)
h) water cooling jacket for g)
i) stirrer bar
j) inlet for substances and Ar

Electrical equipment:
Potentiostat AMEL Model 550
Analog Integrator AMEL Model 721
Chart Recorder Linseis

Fig. Equipment for Photo Electro Catalysis
(conceived by Ch. Weymuth [25])

cis-*4-Cyclopentene-1,3-diol* (**1**). A solution of cyclopentadiene (16.0 ml, 193.6 mmol), thiourea (10.0 g, 131.4 mmol) and rose bengal (300 mg, 0.3 mmol) in distilled methanol (1600 ml) was purged with oxygen and irradiated with a 100 W halogen lamp at r.t. for 8 h. After stirring for another 12 h without light, the obtained pink suspension was concentrated *in vacuo* to *ca.* 100 ml and filtered through *Celite*. Methanol (50 ml) was added to the filtrate and the newly formed suspension filtered again through *Celite* after standing at r.t. for 12 h. The solvent was removed and distillation (100° - 130° (bath temp.)/$2 \cdot 10^{-2}$ mbar) afforded **1** (11.20 g, 58%) as a pale yellow liquid, which solidified upon standing. It was used without further purification. ^{1}H-NMR (60 MHz, $CDCl_3$): 1.56 (*dt*, *J* = 15 and 3, HC(2)); 2.73 (*m*, HC(2)); 3.93 (*s*, OH); 4.68 (*m*, HC(1), HC(3)); 6.05 (*s*, HC(4), HC(5)). IR (KBr): 3280*s*, 3060*s*, 2975*s*, 2935*m*, 2875*s*, 2250*m*, 2230*m*, 1445*m*, 1350*s*, 1315*s*, 1290*m*, 1270*m*, 1165*m*, 1120*s*, 1090*s*, 1065*s*, 1015*s*, 995*s*, 950*m*, 880*m*, 845*m*, 780*s*, 760*s*.

cis-*4-Cyclopentene-1,3-diol diacetate* (**2**). To an ice cooled solution of diol **1** (10.01 g, 0.1 mol) and 4-dimethylaminopyridine (1.25 g, 10.0 mmol) in pyridine (100 ml) under N_2 was added acetic anhydride (37.74 ml, 0.4 mol) over 45 min. After stirring for 30 min at r.t. the solution was poured into ice water (200 ml) and extracted with Et_2O (3 x 100 ml). The org. soln. was washed with 10% HCl (2 x 50 ml), 5% $NaHCO_3$ (2 x 50 ml) and brine (3 x 50 ml), dried (Na_2SO_4) and the solvent removed. Bulb-to-bulb distillation (105° (oven temp.)/$2 \cdot 10^{-2}$ mbar) of the residue afforded **2** (14.57 g, 79%) as a pale yellow liquid. ^{1}H-NMR (60 MHz, $CDCl_3$): 1.73 (*dt*, *J* = 15 and 4, HC(2)); 2.05 (*s*, CH_3); 2.90 (*m*, HC(2)); 5.59 (*dd*, *J* = 4 and 7.5, HC(1), HC(3)); 6.13 (*s*, HC(4), HC(5)). IR (neat): 2950*w*, 1740*s*, 1435*w*, 1365*m*, 1260*s*, 1180*w*, 1075*m*, 1020*m*, 990*w*, 960*w*, 910*w*, 770*w*.

(1R,4S)-4-Cyclopentene-1,3-diol monoacetate (**3**). To an emulsion of diacetate **2** (3.26 g, 17.7 mmol) in 0.1M P-buffer of pH = 7.00 (70 ml) was added a suspension of porcine pancreas lipase PPL (4.00 g) in the same buffer (30 ml). Whilst stirring at r.t., the pH was kept at 7.0 by continuous addition of 1M NaOH. After 48 h 19.12 ml

base had been consumed. The suspension was continuously extracted in a *Kutscher-Steudel* extractor with Et_2O (150 ml) for 24 h. The org. soln. was dried ($MgSO_4$) and the solvent removed. The remaining white solid was recrystallized from Et_2O/low boiling petroleum ether to yield **3** (2.02 g, 80%) as colorless needles. M.p. 49° - 51°. ^{1}H-NMR (60 MHz, $CDCl_3$): 1.65 (*dt*, *J* = 15 and 4, HC(2)); 2.07 (*s*, CH_3); 2.84 (*m*, HC(2)); 2.63 (*s*, OH); 4.77 (*m*, HC(3)); 5.53 (*m*, HC(1)); 6.07 (*m*, HC(4), HC(5)). IR (KBr): 3390*m*, 2920*w*, 2900*w*, 1825*w*, 1730*s*, 1445*m*, 1415*m*, 1380*m*, 1360*s*, 1325*m*, 1255*s*, 1180*m*, 1085*s*, 1060*s*, 1020*s*, 980*m*, 970*m*, 910*w*, 880*w*, 840*w*, 790*m*. $[\alpha]_D^{20}$: + 68°.0 (c = 1.64, $CHCl_3$; e.e.>98% by comparison with an authentic sample (e.e.>99%) kindly submitted by *M. Schneider* and *K. Laumen*.). Higher concentrations of substrate and enzyme gave considerably shorter reaction times, but also lower yields (60% - 70%).

(1R,4S)-4-(1-Ethoxy-2-bromoethoxy)-2-cyclopentene-1-ol acetate (**4**). To a suspension of alcohol **3** (1.30 g, 9.1 mmol) and N-bromosuccinimide (1.87 g, 10.5 mmol) in dry CH_2Cl_2 (20 ml) under N_2 at -40° was added ethylvinylether (1.24 ml, 13 mmol) dissolved in CH_2Cl_2 (3 ml) over 30 min. After 2 h the solution was allowed to warm to r.t. and stirred for additional 21 h. It was poured into ice water (30 ml) and washed with brine (2 x 30 ml). The brine was extracted with CH_2Cl_2 (50 ml), the combined org. soln. dried (Na_2SO_4) and the solvent removed. The residue was flash chromatographed (120 g silica gel; hexane/ ethylacetate 6:4) and bulb-to-bulb distilled (130° (oven temp.)/$2 \cdot 10^{-2}$ mbar) to give **4** (2.35 g, 88%) as a practically colorless, lachrymatory liquid (1:1 mixture of diastereomers as determined by GC and 400 MHz ^{1}H-NMR). ^{1}H-NMR (60 MHz, $CDCl_3$): 1.25 (*t*, *J* = 7, ethoxy-CH_3); 1.80 (*dtd*, *J* = 15 and 5 and 2, HC(5)); 2.06 (*s*, acetate CH_3); 2.87 (*m*, HC(5)); 3.40 (*d*, *J* = 6, CH_2Br); 3.70 (*m*, ethoxy-CH_2); 4.78 (*m*, HC(4), OCHO); 5.53 (*m*, HC(1)); 6.10 (AB-system, HC(2), HC(3)). IR (neat): 2980*m*, 2930*w*, 2900*w*, 1740*s*, 1430*w*, 1365*m*, 1240*s*, 1190*w*, 1115*m*, 1060*m*, 1020*s*, 910*w*, 770*w*. MS (20°): a.o. 169(5), 167(5), 153(33), 151(33), 126(7), 125(91), 123(30), 83(31), 82(21), 81(5), 73(7), 72(9), 43(100).

(1R,4S)-4-(1-Ethoxy-2-bromoethoxy)-2-cyclopentene-1-ol (**5**). A solution of bromoacetal **4** (1.125 g, 3.8 mmol) in 0.25M KOH in 90% ethanol (100 ml) was stirred in the dark at r.t. for 1.5 h. It was neutralized (pH = 7 to 8) by dropwise addition of 98% acetic acid. After concentrating *in vacuo* to *ca.* 10 ml, the resulting two phases were poured into ice water (40 ml) and extracted with Et_2O (3 x 50 ml). The org. soln. was washed with brine (40 ml), dried (Na_2SO_4) and the solvent evaporated. The residue was flash chromatographed (100 g silica gel; hexane/ethylacetate 6:4) and bulb-to-bulb distilled (130° (oven temp.)/$2 \cdot 10^{-2}$ mbar) to give **5** (0.798 g, 83%) as a pale yellow liquid. ^{1}H-NMR (60 MHz, $CDCl_3$): 1.23 (*t*, *J* = 7.5, ethoxy-CH_3); 1.70 (*dtd*, *J* = 14.5 and 4 and 1.5, HC(5)); 2.35 (*s*, OH); 2.75 (*md*, *J* = 2, HC(5)); 3.37 (*d*, *J* = 5.5, CH_2Br); 3.40 - 3.95 (*m*, ethoxy-CH_2); 4.53 - 4.80 (*m*, HC(4), OCHO); 4.83 (*t*, *J* = 5.5, HC(1)); 6.07 (AB-system, HC(2), HC(3)). IR (neat): 3410*m*, 3060*w*, 2980*m*, 2950*m*, 2890*m*, 1445*w*, 1425*m*, 1370*m*, 1355*m*, 1320*w*, 1190*m*, 1120*s*, 1060*s*, 1030*s*, 890*w*, 765*w*. MS (20°): a.o. 154(17), 152(17), 126(19), 124(20), 85(6), 84(100), 83(6), 76(6), 74(13), 73(8), 56(13), 48(7), 46(12), 44(10), 29(10).

(1,1-Dimethylethyl){[(1R,4S)-4-(1-ethoxy-2-bromoethoxy)-2-cyclopentene-1-yl]oxy}dimethylsilane (**6**). To a solution of *tert.*-butyldimethylchlorosilane (0.33 g, 2.2 mmol) and imidazole (0.32 g, 4.6 mmol) in DMF (2 ml) under N_2 was added bromoacetal **5** (0.465 g, 1.9 mmol). After stirring at r.t. for 1.5 h the clear solution was poured into ice water (50 ml) and extracted with Et_2O (3 x 30 ml). The org. soln. was washed with 0.1M P-buffer (pH = 6; 2 x 30 ml) and H_2O (30 ml), dried (Na_2SO_4) and the solvent removed. Bulb-to-bulb distillation (30 min at 60° (oven temp.)/ $2 \cdot 10^{-2}$ mbar to remove volatile impurities, then 140°/$2 \cdot 10^{-2}$mbar) afforded **6** (0.661 g, 98%) as a colorless and odorless liquid. ^{1}H-NMR (60 MHz, $CDCl_3$): 0.08 (*s*, $SiCH_3$); 0.91 (*s*, Si-*tert.*-butyl); 1.25 (*t*, *J* = 7, ethoxy-CH_3); 1.40 - 1.95 (*m*, HC(5')); 2.50 - 3.00 (*m*, HC(5')); 3.38 (*d*, *J* = 5.5, CH_2Br); 3.47 - 3.94 (*m*,

ethoxy-CH_2); 4.50 - 4.95 (*m*, HC(1'), HC(4'), OCHO); 5.95 (AB-system, HC(2'), HC(3')). IR (neat): 2960*m*, 2930*s*, 2890*m*, 2860*m*, 1470*w*, 1460*w*, 1370*m*, 1250*m*, 1125*s*, 1100*s*, 1060*s*, 1030*s*, 1005*m*, 940*w*, 905*m*, 835*s*, 775*m*, 670*w*. MS (20°): a.o. 263(5), 261(5), 198(5), 197(31), 185(23), 183(21), 181(21), 157(44), 153(94), 151(100), 141(15), 125(66), 123(71), 115(9), 104(8), 103(79), 75(90), 73(91), 72(25), 66(13), 59(14), 57(21), 44(9), 43(9). **6** can also be prepared from **3** in 96% overall yield without chromatography of **4** and **5** respectively. The only purification is the bulb-to-bulb distillation of **6**.

1-Octyne-3-one (**7**). To an ice cooled solution of 1-octyne-3-ol (8.00 g, 63.4 mmol) in distilled acetone (30 ml) was added a solution of CrO_3 (5.49 g, 54.9 mmol) in 95% H_2SO_4 (5 ml) and H_2O (15.7 ml) with the temp. not exceeding 10°. After stirring at r.t. for 1 h H_2O (30 ml) was added to dissolve the precipitate. The resulting two liquid phases were poured into ice water (140 ml) and extracted with Et_2O (3 x 50 ml and 2 x 25 ml). The org. soln. was washed with 5% $NaHCO_3$ (50 ml) and brine (3 x 50 ml), dried ($MgSO_4$) and the solvent removed. Distillation (60° - 62°/*ca.* 10 mbar) afforded **7** (7.26 g, 92%) as a pale yellow liquid with an intense, characteristic odor. ^{1}H-NMR (60 MHz, $CDCl_3$): 0.69 - 2.05 (*m*, H on C(5) to C(8)); 2.60 (*t*, *J* = 7, HC(4)); 3.24 (*s*, HC(1)). IR (neat): 3260*m*, 2960*m*, 2930*m*, 2880*m*, 2090*m*, 1680*s*, 1460*w*, 1405*w*, 1380*w*, 1220*w*, 1130*w*, 1080*w*, 700*w*. n_D^{20}: 1.4330.

B_{12}-catalyzed electrosynthesis of the prostaglandin precursors **8**:
trans-*1-[(2R/S,3aR,4R,5R,6aS)-5-{[(1,1-Dimethylethyl)dimethylsilyl]oxy}-2-ethoxyhexahydro-2H-cyclopenta[b]-furan-4-yl]-1-octene-3-one* (**8a,b**). The cathode compartment of the electrochemical cell, containing C-felt (2.77 g) as cathode material, was charged with a solution of vitamin B_{12a} (250 mg, 0.18 mmol) in 0.3M $LiClO_4$/DMF (250 ml). The anode compartment was charged with 0.3M $LiClO_4$/DMF (*ca.* 50 ml). B_{12} was reduced to Co(I) at a constant cathode potential of -1.4 V (*vs.* SCE) until the initial current of *ca.* 50 mA had diminished to a stable background level and the color had changed from red to dark green. On reducing the potential to -0.9 V a stable background level of *ca.* 3.5 mA was observed. Keeping the potential at -0.9 V, 1-octyne-3-one **7** (3.72 g, 30 mmol) was added, followed by bromoacetal **6** (3.65 g, 10 mmol) after 15 min. Thereby the color changed to dark red and the current remained on a low level. After switching on the 250 W halogen lamp the current rose to 30 mA and the temperature to 40° - 41°, which was maintained throughout the reaction. Additional **7** was added after 5 h (2.48 g, 20 mmol) and 25 h (1.24 g, 10 mmol). After 44 h the current had diminished to a constant background level of 9 mA and 1543 Cb e^- (16.0 mmol) had been consumed. The solution was poured into ice water (750 ml) and extracted with Et_2O (6 x 100 ml). The org. soln. was washed with brine (3 x 100 ml), dried (Na_2SO_4) and the solvent removed. Excess **7** (*ca.* 1.8 g) was removed by bulb-to-bulb distillation (45° (oven temp.)/$5 \cdot 10^{-2}$ mbar) and the residual dark brown liquid (8.86 g) was filtered through silica gel (70 g; low boiling petroleum ether/Et_2O 8:2; an attempt to accomplish *cis-trans*-isomerization at this stage with a trace of I_2 in hexane and irradiating with sunlight was unsuccessful). Flash chromatography of the crude product (210 g silica gel; low boiling petroleum ether/Et_2O 19:1 to 8:2) afforded two main fractions: 1,3,5-tri(hexane-1-one-1-yl)benzene (0.30 g, 0.8 mmol; data see below) and 3.50 g of a yellow liquid comprising the four isomers of **8** (containing at least 65% **8** (GC), corresponding to at least 55% with respect to **6**). For *cis-trans*-isomerization the latter fraction was dissolved in hexane (50 ml) containing I_2 (90 mg) and irradiated with a halogen lamp for 50 min at r.t. The solution was then poured into ice water (25 ml), washed with brine, containing a small amount of Na-thiosulfate (2 x 25 ml), and brine (25 ml), dried (Na_2SO_4) and the solvent removed. Flash chromatography (150 g silica gel; low boiling petroleum ether/Et_2O 19:1 to 8:2) of the remaining dark liquid (3.36 g) afforded essentially pure **8a** (1.07 g, 26%) and **8b** (0.85 g, 21%) as slightly yellow oils (assignment of configuration based on NOE-experiments; each of the pure diastereomers **8a** and **8b** yielded a equilibrium mixture of both in ethanol containing a trace amount of

p-toluenesulfonic acid monohydrate). For elemental analysis a sample of **8a** was distilled in a glass tube at 150° (oven temp.)/ $5 \cdot 10^{-3}$ mbar. $C_{23}H_{42}O_4Si$: calculated C 67.27%, H 10.31%; found C 67.27%, H 10.23%.

Data of **8a** (R_f-value = 0.51 in low boiling petroleum ether/Et_2O 8:2): ^{1}H-NMR (400 MHz, $CDCl_3$): -0.04 (*s*, Si-CH_3); -0.02 (*s*, Si-CH_3); 0.82 (*s*, Si-*tert.*-butyl); 0.70 - 0.95 (*m*, HC(8)), 1.15 (*td*, *J* = 7.07 and 0.77, ethoxy-CH_3); 1.10 - 1.35 (*m*, HC(6), HC(7)); 1.50 - 1.65 (*m*, HC(5)); 1.72 (*ddd*, *J* = 13.48 and 8.86 and 4.34, HC(6')); 1.84 (*ddd*, *J* =13.48 and 4.83 and 4.83, HC(3')); 2.01 (*ddd*, *J* = 13.52 and 8.82 and <1, HC(3')), 2.25 - 2.45 (*m*, HC(3*a*'), HC(4'), HC(6')); 2.48 (*t*, *J* = 7.45, HC(4)); 3.34 - 3.48 (*m*, ethoxy-CH_2); 3.67 (*dqd*, *J* = 9.61 and 7.11 and 0.76, ethoxy-CH_2); 3.89 (*ddd*, *J* = 8.15 and 8.15 and 8.15, HC(5')); 4.42 (*ddd*, *J* = 7.02 and 7.02 and 4.20, HC(6*a*')); 5.19 (*d*, *J* = 4.91, HC(2')); 6.09 (*dd*, *J* = 15.84 and 0.96, HC(2)); 6.64 (*dd*, *J* = 15.83 and 8.05, HC(1)). ^{13}C-NMR (25.2 MHz, $CDCl_3$): -4.7*u*, -4.5*u*, 13.9*u*, 15.2*u*, 18.0*g*, 22.5*g*, 24.0*g*, 25.7*u*, 31.5*g*, 38.4*g*, 40.4*g*, 41.0*g*, 44.3*u*, 57.0*u*, 62.6*g*, 78.1*u*, 79.5*u*, 105.1*u*, 130.8*u*, 146.2*u*. IR (neat): 3450*w*, 2960*s*, 2930*s*, 2860*m*, 2250*w*, 1695*m*, 1680*m*, 1630*w*, 1465*m*, 1405*w*, 1380*m*, 1360*w*, 1335*w*, 1250*m*, 1115*m*, 1050*m*, 1005*m*, 910*m*, 865*w*, 835*m*, 775*m*, 730*s*, 670*w*, 645*w*. MS (90°): a.o. 365(10), 354(11), 353(43), 309(11), 308(12), 307(50), 281(17), 234(15), 233(70), 199(12), 189(13), 187(23), 178(11), 161(14), 153(12), 151(13), 136(14), 135(11), 133(14), 131(11), 129(11), 117(29), 107(18), 105(10), 101(23), 99(100), 91(15), 81(14), 79(15), 75(63), 73(62), 72(21), 71(48), 59(14), 55(12), 44(11), 43(49), 41(11). UV (CCl_4): 266(3.29).

Data of **8b** (R_f = 0.29): ^{1}H-NMR (400 MHz, $CDCl_3$): -0.03 (*s*, Si-CH_3); -0.01 (*s*, Si-CH_3); 0.83 (*s*, Si-*tert.*-butyl); 0.75 - 0.98 (*m*, HC(8)); 1.18 (*t*, *J* = 7.10, ethoxy-CH_3); 1.15 - 1.40 (*m*, HC(6), HC(7)); 1.52 - 1.64 (*m*, HC(5)); 1.76 (*ddd*, *J* = 12.61 and 10.73 and 6.36, HC(6')); 1.84 (*d*, *J* = 13.32, HC(3')); 1.99 (*ddd*, *J* = 13.36 and 9.36 and 5.29, HC(3')); 2.30 - 2.40 (*m*, HC(3*a*')); 2.37 - 2.45 (*m*, HC(6')); 2.49 (*t*, *J* = 7.47, HC(4)); 2.86 (*ddd*, *J* = 9.23 and 9.23 and 9.23, HC(4')); 3.40 (*dq*, *J* = 9.55 and 7.03, ethoxy-CH_2); 3.71 - 3.80 (*m*, ethoxy-CH_2, HC(5')); 4.49 (*dd*, *J* = 14.35 and 7.70, HC(6*a*')); 5.15 (*d*, *J* = 5.20, HC(2')); 6.17 (*dd*, *J* = 15.83 and 0.99, HC(2)); 6.69 (*dd*, *J* = 15.83 and 8.10, HC(1)). ^{13}C-NMR (25.2 MHz, $CDCl_3$): -4.6*u*, -4.4*u*, 13.9*u*, 15.1*u*, 18.0*g*, 22.5*g*, 24.0*g*, 25.7*u*, 31.5*g*, 37.1*g*, 40.4*g*, 43.4*g*, 44.0*u*, 55.5*u*, 62.5*g*, 76.8*u*, 81.0*u*, 105.5*u*, 130.8*u*, 147.1*u*. IR (neat): 3460*w*, 2960*s*, 2930*s*, 2860*m*, 2250*w*, 1695*m*, 1675*m*, 1630*m*, 1465*m*, 1410*w*, 1375*m*, 1255*m*, 1120*m*, 1055*m*, 1005*m*, 980*m*, 910*m*, 865*m*, 835*m*, 775*m*, 730*s*, 665*w*, 645*w*. MS (80°): a.o. 365(4), 353(6), 309(18), 308(24), 307(100), 234(10), 233(44), 189(11), 187(24), 133(14), 117(20), 107(11), 103(11), 101(13), 99(62), 91(10), 81(12), 79(10), 75(41), 73(41), 72(14), 71(30), 59(10), 43(34). UV (CCl_4): 268(3.41).

Data of *1,3,5-tri(hexane-1-one-1-yl)benzene*: ^{1}H-NMR (60 MHz, $CDCl_3$): 0.70 - 1.20 (*m*, HC(6')); 1.20 - 2.20 (*m*, H on C(3') to C(5')); 3.10 (*t*, *J* = 7, HC(2')); 8.76 (*s*, aromatic H). IR (neat): 2860*s*, 2830*s*, 2770*s*, 2760*s*, 1695*s*, 1595*w*, 1470*m*, 1460*m*, 1440*w*, 1410*w*, 1380*m*, 1315*w*, 1295*w*, 1240*m*, 1170*s*, 1115*w*, 1055*w*, 915*m*, 840*w*, 775*w*, 730*s*, 680*w*, 645*w*. MS (90°): a.o. 372(26), 317(7), 316(27), 302(13), 301(61), 272(11), 261(17), 260(89), 245(23), 217(12), 205(13), 204(100), 203(11), 99(33), 71(24), 43(17). UV (EtOH): 228(4.37), 300(3.19).

cis-*1-[(2*R/S,*3*aR,*4*R,*5*R,*6a*S)-5-{[(1,1-Dimethylethyl)dimethylsilyl]oxy}-2-ethoxyhexahydro-*2H*-cyclopenta[*b*]-furan-4-yl]-1-octene-3-one* (**8c,d**). In a parallel experiment under the same conditions, but without *cis-trans*-isomerization, all four isomers of **8** were separated by flash chromatography (320 g silica gel; low boiling petroleum ether/Et_2O 19:1 to 8:2) affording **8a** (0.54 g, R_f = 0.51 in low boiling petroleum ether/Et_2O 8:2), **8b** (0.51 g, R_f = 0.29), **8c** (0.34 g, R_f = 0.66) and **8d** (0.52 g, R_f = 0.37).

Data of **8c** (R_f = 0.66): ^{1}H-NMR (400 MHz, $CDCl_3$): *ca.* 0 (*s*, Si-CH_3); 0.83 (*s*, Si-*tert.*-butyl); 0.85 - 1.00 (*m*, HC(8)); 1.19 (*t*, *J* = 7.08, ethoxy-CH_3); 1.21 - 1.42 (*m*, HC(6), HC(7)); 1.55 - 1.63 (*m*, HC(5)); 1.74 - 1.81 (*m*, HC(3'), HC(6')); 1.97 (*ddd*, *J* = 13.3 and 9.0 and 1.6, HC(3')); 2.21 - 2.40 (*m*, HC(3*a*'), HC(4'), HC(6')); 2.45 (*t*, *J* = 7.43, HC(4)); 3.44 (*dq*, *J* = 9.61 and 7.04, ethoxy-CH_2); 3.72 (*dq*, *J* = 9.66 and 7.11, ethoxy-CH_2); 3.87 (*ddd*, *J*

= 8.29 and 8.29 and 6.95, HC(5')); 4.47 (*ddd*, *J* = 7.05 and 7.05 and 4.24, HC(6*a*')); 5.29 (*dd*, *J* = 5.20 and 1.59, HC(2')); 5.72 (*dd*, *J* = 11.44 and 10.53, HC(1)); 6.21 (*dd*, *J* = 11.47 and 0.69, HC(2)). IR (neat): 3450*w*, 2960*s*, 2930*s*, 2860*s*, 1695*s*, 1625*w*, 1465*m*, 1410*w*, 1375*w*, 1335*w*, 1295*w*, 1250*m*, 1130*m*, 1110*m*, 1055*m*, 1030*m*, 1000*m*, 940*w*, 905*w*, 835*m*, 775*m*, 730*w*, 670*w*. MS (65°): a.o. 365(9), 354(27), 353(100), 308(20), 307(83), 281(27), 279(10), 261(16), 234(13), 233(58), 215(10), 206(12), 199(11), 189(16), 187(35), 181(10), 178(11), 151(17), 153(12), 151(37), 136(14), 133(15), 131(14), 117(27), 107(20), 101(22), 99(94), 91(16), 81(14), 79(13), 75(70), 73(55), 71(52), 59(14), 55(12), 43(52), 41(12), 18(12).

Data of **8d** (R_f = 0.37): ^{1}H-NMR (400 MHz, $CDCl_3$): *ca.* 0 (*s*, Si-CH_3); 0.84 (*s*, Si-*tert.*-butyl); 0.85 - 1.00 (*m*, HC(8)); 1.22 (*t*, *J* = 7.04, ethoxy-CH_3); 1.25 - 1.40 (*m*, HC(6), HC(7)); 1.50 - 1.70 (*m*, HC(5)); 1.83 (*ddd*, *J* = 12.48 and 10.65 and 6.49, HC(6')); 1.96 (*ddd*, *J* = 13.31 and 9.36 and 5.20, HC(3')); 2.08 (*d*, *J* = 13.27, HC(3')); 2.20 - 2.80 (*m*, HC(4), HC(3*a*'), HC(4'), HC(6')); 3.49 (*q*, *J* = 7.02, ethoxy-CH_2); 3.70 - 3.90 (*m*, HC(5')); 4.52 (*dd*, *J* = 14.82 and 7.57, HC(6*a*')); 5.19 (*d*, *J* = 5.16, HC(2')); 5.74 (*dd*, *J* = 10.82 and 11.77, HC(1)); 6.13 (*dd*, *J* = 11.83 and 0.59, HC(2)). IR (neat): 3450*w*, 2960*s*, 2930*s*, 2860*s*, 1715*m*, 1680*m*, 1625*w*, 1465*m*, 1410*w*, 1380*m*, 1250*m*, 1180*w*, 1120*s*, 1055*s*, 1005*m*, 980*w*, 910*w*, 870*w*, 835*m*, 775*m*, 730*m*, 670*w*, 645*w*. MS (70°): a.o. 365(2), 364(2), 353(5), 309(17), 308(24), 307(100), 233(18), 189(9), 187(26), 151(11), 134(6), 117(13), 101(7), 99(38), 81(6), 75(29), 73(25), 72(10), 71(24), 43(31).

*(3a*R,*6a*S*)-2-Ethoxy-3,3a,6,6a-tetrahydro-*2H*-cyclopenta[*b*]furan* (**9a,b**). A suspension of vitamin B_{12a} (55 mg, 0.04 mmol) and NH_4Cl (3.21 g, 60 mmol) in ethanol (30 ml) was stirred at r.t. under Ar with activated Zn-wool (3.00 g, 46 mmol) wrapped around the stirrer bar. After 10 to 20 min the color of the solution changed from red to dark green. Bromoacetal **4** (1.173 g, 4 mmol) was added and and the mixture stirred at r.t. for 6 h. Then the red-brown suspension was poured into a solution of 25% NH_3 (5 ml) in ice water (150 ml) and extracted with Et_2O (5 x 30 ml). The org. soln. was washed with brine (5 x 30 ml), dried (Na_2SO_4) and the solvent removed. Bulb-to-bulb distillation (r.t./$5 \cdot 10^{-2}$ mbar) afforded **9** (0.453 g, 73%) as a clear liquid with a characteristic odor (1:1 mixture of diastereomers **9a** and **9b** as determined by GC). For elemental analysis a sample was purified by preparative GC. $C_9H_{14}O_2$: calculated C 70.10%, H 9.15%; found C 69.86%, H 9.12%. IR (neat): 3060*w*, 2980*m*, 2920*m*, 2870*m*, 1445*w*, 1370*w*, 1330*m*, 1190*w*, 1170*w*, 1120*m*, 1100*m*, 1060*s*, 1040*s*, 1005*m*, 990*s*, 865*m*, 820*w*. MS (20°): a.o. 154(8), 126(6), 125(5), 110(9), 109(60), 108(68), 98(10), 88(10), 83(11), 81(66), 80(67), 79(100), 77(17), 73(9), 72(67), 70(8), 67(22), 66(20), 53(10), 44(28), 43(22), 41(20), 39(9), 29(8), 18(10). For ^{1}H-NMR the two diastereomers were separated by flash chromatography (silica gel; hexane/ethylacetate 9:1). ^{1}H-NMR (60 MHz, $CDCl_3$): 1. diastereomer (R_f = 0.53): 1.20 (*t*, *J* = 7, ethoxy-CH_3); 1.57 - 2.45 (*m*, HC(6)); 2.57 (*m*, HC(3)); 3.19 - 4.10 (*m*, HC(3*a*), ethoxy-CH_2); 4.78 (*m*, HC(6*a*)); 5.18 (*dd*, *J* = 4.5 and 2, OCHO); 5.63 (AB-system, HC(4), HC(5)); 2. diastereomer (R_f = 0.42): 1.12 (*t*, *J* = 7, ethoxy-CH_3); 1.65 - 2.45 (*m*, HC(6)); 2.61 (*m*, HC(3)); 3.13 - 4.00 (*m*, HC(3*a*), ethoxy-CH_2); 4.87 (*m*, HC(6*a*)); 5.14 (*dd*, *J* = 4.5 and 2, OCHO); 5.67 (AB-system, HC(4), HC(5)).

*(3a*R,*6a*S*)-3,3a,6,6a-Tetrahydro-2*H*-cyclopenta[*b*]furan-2-ol* (**10**). A solution of acetal **9** (0.326 g, 2.1 mmol) in 1.5% HCl/THF (3:2; 20 ml) was stirred at r.t. for 48 h. It was poured into ice water (80 ml) and extracted with Et_2O (5 x 25 ml). The org. soln. was washed with 5% $NaHCO_3$ (25 ml) and brine (3 x 25 ml), dried (Na_2SO_4) and the solvent removed. Recrystallization from low boiling petroleum ether afforded **10** (0.098 g, 37%) as colorless crystals. M.p. 54° - 56°. ^{1}H-NMR (60 MHz, $CDCl_3$): 1.60 - 2.40 (*m*, HC(6)); 2.30 - 2.90 (*m*, HC(3)); 3.20 - 3.77 (*m*, HC(3*a*)); 4.37 (*s*, OH); 4.91 (*m*, HC(6*a*)); 5.32 - 5.90 (*m*, OCHO, HC(4), HC(5)). IR (KBr): 3380*s*, 3050*m*, 3000*m*, 2950*m*, 2930*m*, 2850*m*, 1445*w*, 1430*w*, 1360*w*, 1330*w*, 1310*w*, 1285*w*, 1265*m*, 1250*m*, 1220*w*, 1190*m*, 1175*m*, 1110*m*, 1090*m*, 1060*m*, 1035*s*, 995*m*, 975*s*, 920*w*, 890*m*, 860*m*, 820*m*, 770*w*, 710*m*. MS: a.o. 126(5),

108(37), 83(47), 81(11), 80(39), 79(100), 77(26), 70(8), 67(30), 66(36), 65(8), 55(22), 54(13), 53(16), 51(11), 44(8), 43(11), 41(21), 39(22), 28(13), 27(14), 18(24). $C_7H_{10}O_2$: calculated C 66.65%, H 7.99%; found C 66.23%, H 7.96%.

*(-)-(3*aR,*6a*S*)-3,3a,6,6a-Tetrahydro-2*H*-cyclopenta[b]furan-2-on* (**(-)-11**). To an ice cooled solution of lactol **10** (0.082g, 0.65 mmol) in distilled acetone (2 ml) was added a solution of CrO_3 (0.048 g, 0.48 mmol) and 95% H_2SO_4 (0.04 ml) in H_2O (0.14 ml). After stirring at r.t. for 2 h H_2O (3 ml) was added to dissolve the precipitate and the solution poured into ice water (40 ml) and extracted with Et_2O (3 x 20 ml). The org. soln. was washed with 5% $NaHCO_3$ (20 ml) and brine (3 x 20 ml), dried (Na_2SO_4) and the solvent removed. The residue was sublimed in a bulb-to-bulb distillation apparatus (70°(oven temp.)/$4 \cdot 10^{-2}$ mbar) affording **(-)-11** (0.051 g, 63%) as colorless crystals. M.p. 44° - 45°. ^{1}H-NMR (60 MHz, $CDCl_3$): 2.20 - 3.04 (*m*, HC(3), HC(6)); 3.30 - 3.80 (*m*, HC(3*a*)); 5.18 (*ddd*, *J* = 6 and 3 and 3, HC(6*a*)); 5.45 - 6.03 (*m*, HC(4), HC(5)). IR (KBr): 3500*w*, 3080*w*, 3060*w*, 3000*m*, 2960*w*, 2930*m*, 2910*m*, 2830*w*, 1765*s*, 1430*m*, 1420*m*, 1365*m*, 1350*m*, 1295*m*, 1255*s*, 1230*m*, 1190*s*, 1170*s*, 1150*s*, 1110*w*, 1040*s*, 1015*m*, 955*m*, 940*m*, 920*s*, 895*s*, 865*m*, 825*m*, 805*m*, 775*m*, 730*s*. MS (250°): a.o. 125(3), 124(29), 96(39), 95(83), 91(9), 81(43), 79(27), 77(18), 68(22), 67(100), 66(10), 65(19), 54(29), 53(25), 52(9), 51(17), 50(16), 42(10), 41(39), 40(13), 39(65), 38(13), 37(10), 32(18), 28(51), 27(21), 18(84). $[\alpha]_D^{25}$: -103° (c = 0.80, CH_3OH; Lit.value[27]: $[\alpha]_D^{25}$: -106° (c = 0.80, CH_3OH)). $C_7H_8O_2$: calculated C 67.73%, H 6.50%; found C 67.45%, H 6.51%.

(+)-(R)-2-Cyclopentene-1-ol (**13**). A 100 ml flask under Ar, containing MeOH (35 ml), was charged with vitamin B_{12a} (1.29 g, 0.83 mmol), NH_4Cl (1.0 g) and Zn-wool (1.5 g) wrapped around a magnetic stirrer bar. After stirring for 30 min the color changed from red (B_{12a}) to dark green (B_{12s}). To this mixture was added cyclopentene oxide **12** (6.96 g, 82.7 mmol) *via* syringe. The color immediately changed to red (alkyl-Co(III)). After stirring for 8 days at r.t. (*ca.* 22°) under Ar, the solution had turned dark brown. The flask was opened, the strirrer bar (together with excess Zn-wool) removed and Et_2O (100 ml) added. A red-brown precipitate (B_{12}) formed. The solution was decanted and the precipitate extracted with Et_2O (5 x 50 ml). The combined etheral fractions were washed with brine (2 x 60 ml), dried (Na_2SO_4) and the solvent evaporated. The remaining oil was bulb-to-bulb distilled (30° (oven temp.)/*ca.* $2 \cdot 10^{-2}$ mbar) affording **13** (5.01 g of a purity of 93% (GC), corresponding to 67% with respect to **12**) as a colorless oil. $[\alpha]_D^{22}$: +91.0° (neat), corresponding to 62% e.e.[29].

1-(1-Ethoxy-2-bromoethoxy)-2-cyclopentene (**14**). A suspension of crude cyclopentenol **13** (5.01 g, 59.5 mmol, $[\alpha]_D^{22}$: +91.0°, e.e.=62%) and N-bromosuccinimide (10.8 g, 65.0 mmol) in CH_2Cl_2 (80 ml) was cooled to -50° under Ar. Ethylvinylether (6.43 g, 89.3 mmol) was added dropwise over a period of 20 min. The mixture was stirred for 2 h at -40° to -50° and then at r.t. for 16 h. The suspension was poured into ice water (100 ml) and extracted with CH_2Cl_2 (6 x 100 ml). The combined organic fractions were washed with brine (3 x 50 ml), dried (Na_2SO_4) and the solvent removed. Bulb-to-bulb distillation (95° (oven temp.)/*ca.* $2 \cdot 10^{-2}$ mbar) of the residue afforded bromoacetal **14** (15.0 g of a purity of 93% (GC), corresponding to 100% with respect to **13**) as a colorless oil. ^{1}H-NMR (60 MHz, $CDCl_3$): 1.23 (*t*, 3H), 1.70 - 2.80 (*m*, 4H), 3.20 - 3.90 (*m*, 4H), 4.60 - 5.00 (*m*, 2H), 5.60 - 6.20 (*m* , 2H). IR (neat): 3060*w*, 2980*s*, 2930*m*, 2900*m*, 2860*m*, 1725*w*, 1620*w*, 1485*w*. 1425*w*, 1360*w*, 1325*w*, 1190*w*, 1120*s*, 1040*s*, 920*w*. MS: 153(12), 151(12), 125(17), 123(17), 109(5), 103(12), 84(6), 83(4), 77(5), 67(100).

*(3a*S*,6a*R*)-2-Ethoxy-3,3a,6,6a-tetrahydro-2*H*-cyclopenta[b]furan* (**15a,b**). To a solution of crude bromoacetal **14** (0.94 g, 4.0 mmol) in ethanol (20 ml) was added vitamin B_{12a} (0.20 g, 0.14 mmol). The solution was heated to 60° under Ar and powdered sodium borohydride (0.23 g, 6.0 mmol) added batchwise over a period of 1 h. The

temperature of the reaction was kept at 60° to 65°. After additional 10 min the mixture was allowed to cool to r.t. and ice water (20 ml) was added. The mixture was extracted with Et_2O (6 x 40 ml). The ethereal fraction was washed with 2N $NaHSO_4$ (20 ml), brine (2 x 60 ml), dried (Na_2SO_4) and the solvent removed *in vacuo* affording **15** (0.51 g of a purity of 85% (GC), corresponding to 71% with respect to **14** as a 1:1 mixture of diastereomers **15a** and **15b** (GC)) as a yellowish oil. IR (neat): 3060w, 2980m, 2920m, 2870m, 1445w, 1370w, 1330m, 1190w, 1170w, 1120m, 1100m, 1060s, 1040s, 1005m, 990s, 865m, 820w. MS: 154(8),110(9), 109(60), 108(68), 98(10), 88(10), 83(11), 81(66), 80(67), 79(100), 77(17), 73(9), 72(67), 70(8), 67(22), 66(20), 5310), 44(28), 43(22), 41(20), 39(9), 29(8), 18(10). For ^{1}H-NMR the two diastereomers were separated by flash chromatography (silicagel; Et_2O/hexane 1:1). ^{1}H-NMR (60 MHz, $CDCl_3$): 1. diastereomer (R_f = 0.63 in Et_2O/hexane): 1.20 (*t*, *J* = 7, ethoxy-CH_3); 1.5 - 2.4 (*m*, HC(6)); 2.57 (*m*, HC(3)); 3.1 - 4.1 (*m*, HC(3*a*), ethoxy-CH_2); 4.78 (*m*, HC(6*a*)); 5.16 (*dd*, *J* = 4.5 and 2, OCHO); 5.63 (AB-system, HC(4), HC(5)); 2. diastereomer (R_f = 0.56): 1.12 (*t*, *J* = 7, ethoxy-CH_3); 1.6 - 2.5 (*m*, HC(6)); 2.61 (*m*, HC(3)); 3.1 - 4.0 (*m*, HC(3*a*), ethoxy-CH_2); 4.87 (*m*, HC(6*a*)); 5.14 (*dd*, *J* = 4.5 and 2, OCHO); 5.67 (AB-system, HC(4), HC(5))

*(+)-(3*aS,*6a*R*)-3,3a,6,6a-Tetrahydro-*2H*-cyclopenta[*b*]furan-2-on* ((+)-**11**). To an ice cooled solution of crude acetal **15** (2.46 g, 16.0 mmol) in distilled acetone (90 ml) was added dropwise a solution of CrO_3 (3.2 g, 32 mmol) in 95% H_2SO_4 (3.37 ml) dissolved in H_2O (13 ml) over a period of 60 min. After stirring at 0° for 1 h and at r.t. for 2 h, ice water (50 ml) was added to dissolve the precipitate. The solution was poured into ice water (50 ml) and extracted with Et_2O (6 x 150 ml). The combined organic solution was washed with 5% $NaHCO_3$ (2 x 60 ml), brine (3 x 100 ml), dried (Na_2SO_4) and the solvent removed *in vacuo*. Bulb-to-bulb distillation (70° (oven temp.)/*ca.* $4 \cdot 10^{-2}$ mbar) afforded (+)-**11** (1.67 g of a purity of 93% (GC), corresponding to 78% with respect to **15**) as a colorless oil ($[\alpha]_D$: +91.0°, 62% e.e.). For crystallization the oil was dissolved in Et_2O/hexane *ca.* 1:1 (*ca.* 40 ml) and cooled gradually to 10° (20 min), 0° (2 h), -20° (24 h), affording colorless crystals which were recrystallized twice from Et_2O/hexane giving pure (+)-**11** (0.89 g, 45%). M.p. 44.5 - 45.5°. $[\alpha]_D^{22}$: +104.4° (c = 0.802, CH_3OH). The e.e. was found to be >99.5% by analytical GC with heptakis(2,3,6-tri-O-pentyl)-β-cyclodextrine as chiral stationary phase. ^{1}H-NMR, IR and MS of (+)-**11** are virtually superimposable to those of (-)-**11** described above. $C_7H_8O_2$: calculated C 67.73%, H 6.50%; found C 67.45%, H 6.59%.

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