159. Facile Preparation of (±)-12-Epiprostaglandins from 7-Oxabicyclo[2.2.1]hept-5-en-2-one *via* an all-*cis*-Formyllactone Related to *Corey* Lactone[1])

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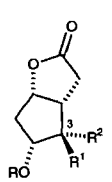
The bicyclic monoselenoacetal **7**, easily obtained from (±)-7-oxabicyclo[2.2.1]hept-5-en-2-one (**6**) *via* a radical addition-acyl migration sequence, was converted to racemic 12-epiprostaglandins **3** and **4**. The key intermediate was the all-*cis*-formyllactone **2b** related to *Corey* lactone (see **12**; *Scheme 1*). The presence of a (*tert*-butyl)-dimethylsilyl protective group for the 11-OH substituent (prostaglandin numbering) was found to be crucial in avoiding β-elimination and epimerization during the *Wittig-Horner* reaction (*Scheme 2*). Epimerization at C(12) at the formyllactone stage (see **2b**) was also possible and gave the known precursor **1b** of naturally occurring prostaglandins and analogs.

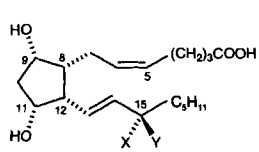
Introduction. – The synthesis of prostanoids, such as type-F prostaglandins (PGF), has been a distinguished field of investigation during the last 25 years [2]. A very successful approach was developed by *Corey* and coworkers *via* formyllactone **1** [3] [4]. The 12-epiprostaglandins (12-epi-PGF) are currently being screened for biological activity [5], and only a few syntheses of this class of compounds were reported [6] [7]. Surprisingly, the very logical approach toward these prostanoids, starting from the isomeric all-*cis*-formyllactone **2**, was never reported[2]).

We now report a stereoselective and facile synthesis of racemic all-*cis*-formyllactone **2** (which is related to *Corey* lactone) using an effective radical addition-acyl migration procedure and the conversion of this key intermediate, *i.e.*, of **2b**, to (±)-12-epi-$PGF_{2\alpha}$ (**3**) and (±)-12,15-diepi-$PGF_{2\alpha}$ (**4**). The inversion of configuration at C(12) (PGF numbering) is also described so that our approach is also a formal synthesis of $PGF_{2\alpha}$ (**5**). A known precursor of PGC_2 is also prepared.

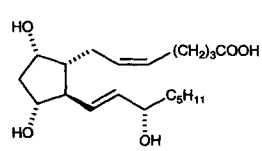
Recently, we became interested in the introduction of C-moieties into 7-oxabicyclo-[2.2.1]hept-5-en-2-one (**6**) by using radical-based methodologies [1] [9] [10]. The bicyclic



1 R^1 = CHO, R^2 = H
2 R^1 = H, R^2 = CHO



3 X = OH, Y = H; 12-epi-$PGF_{2\alpha}$
4 X = H, Y = OH; 12,15-diepi-$PGF_{2\alpha}$



5 $PGF_{2\alpha}$

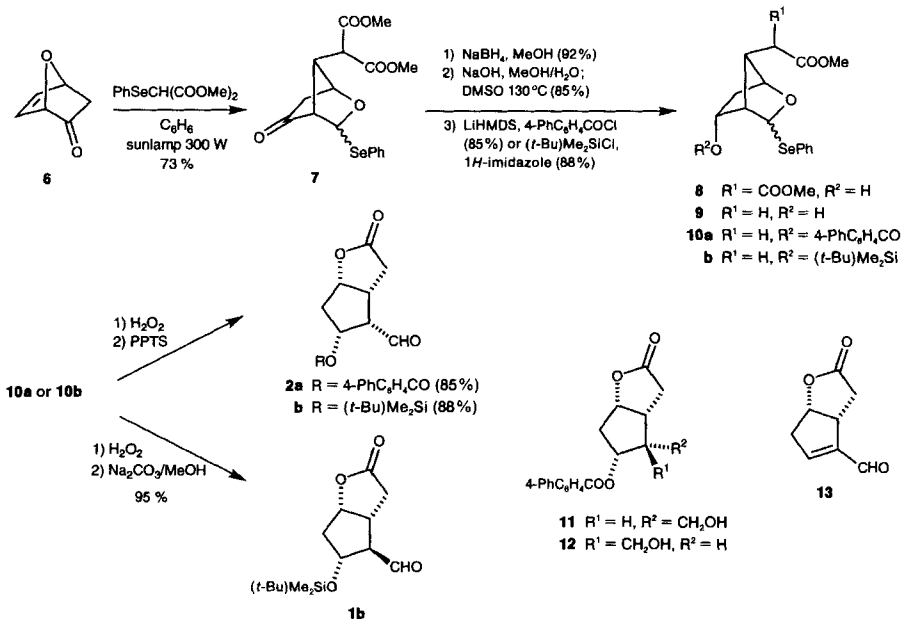
[1]) A preliminary communication of one part of this work was published [1].

[2]) However, during the writing of this manuscript, such an approach was published [8].

unsaturated ketone **6**, readily available in both enantiomeric forms [11] [12], attracted much attention for the preparation of sugar derivatives, natural products, C-branched carbohydrates, and other products of biological interest [11]. We already demonstrated that radical additions to **6** are completely *exo*-stereoselective, and that good regioselectivity can be obtained with electrophilic radicals [10]. The stereoselective synthesis of prostanoids which is presented here is based on this methodology.

Results. – *all-*cis-*Formyllactone* **2** (*Scheme 1*). Our retrosynthetic approach to **2** is based on the prediction that the substituted dimethyl malonate **7** can be easily obtained from **6** by regioselective addition of a bis(methoxycarbonyl)methyl radical at C(5) followed by migration of the acyl group employing a slow phenylselenenyl-group transfer. Indeed, irradiation (300-W sunlamp) over a period of 12 h of a solution of (±)-**6** and dimethyl 2-(phenylselenenyl)propanedioate[3]) in benzene gave mainly the rearranged product **7** in 73% yield after chromatography and recrystallization (*endo*/*exo* 3:1). Full details about the mechanistic aspect of this rearrangement will be published in a forthcoming paper. Treatment of **7** with $NaBH_4$ in MeOH afforded exclusively the *endo*-hydroxy derivative **8** (92%) which was then saponified (NaOH/MeOH) and decarboxylated (DMSO, 140°) to give **9** (85%). Protection of the *endo*-OH group by deprotonation with lithium bis(trimethylsilyl)amide (LiHMDS) and treatment with 4-phenylbenzoyl chloride (4-PhC_6H_4COCl) afforded **10a** (85% yield). Acetal hydrolysis (H_2O_2, acetone/H_2O) and lactonization (pyridinium toluene-4-sulfonate (PPTS)/$CHCl_3$) were carried out under extremely mild conditions, and the all-*cis*-formyllactone **2a** was isolated in good

Scheme 1



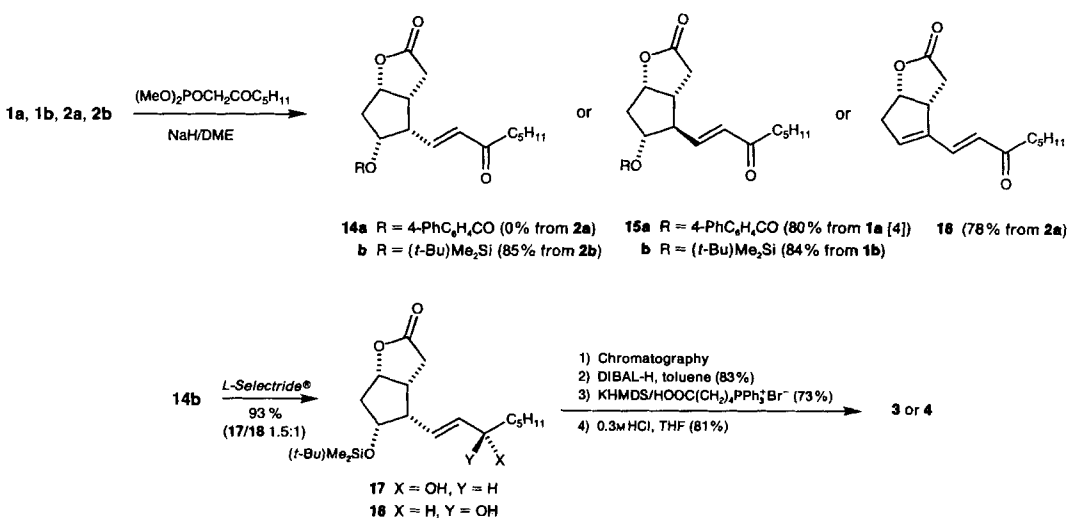
[3]) This reagent was recently introduced by *Byers* and *Lane* and proved to be very efficient for radical-mediated phenylselenenyl-group transfer reactions [13].

yield (95%) containing less than 5% of β-elimination product **13**. Reduction of **2a** with $NaBH_4$/MeOH gave all-*cis*-(hydroxymethyl)lactone (**11**; 91%) which showed physical and spectral data clearly different from commercially available racemic *Corey* lactone **12**. Filtration of **2a** through silica gel gave the unsatured formyllactone **13** (95%), identical in every respect with an authentic sample prepared from **12** [14] [15]. The (*tert*-butyl)-dimethylsilyl-protected all-*cis*-formyllactone **2b** was also prepared from **9** by reaction with (*t*-Bu)Me_2SiCl/1*H*-imidazole (→ **10b** (85%)), followed by acetal hydrolysis and lactonization (95%).

To have access to naturally occurring prostaglandins, we examined the epimerization of all-*cis*-formyllactone **2b**. A precedent, *i.e.*, the epimerization of the (tetrahydro-2*H*-pyran-2-yl)-protected all-*cis*-formyllactone under basic conditions (cat. Na_2CO_3 in MeOH), was reported by *Libit* [16][4]). Treating **2b** with a catalytic amount of Na_2CO_3 in MeOH gave the epimerized formyllactone **1b**. An even more convenient procedure was found starting directly from **10b** *via* O,Se-acetal opening (H_2O_2) and direct treatment of the monocyclic hydroxy ester with Na_2CO_3 in MeOH to achieve a one-pot lactonization and epimerization sequence. The conversion of formyllactone **1b** to several natural prostaglandins and analogs such as $PGF_{2\alpha}$ (**5**) was reported [19].

12-Epiprostaglandins (*Scheme 2*). Our first attempts to introduce the ω-chain was based on the work of *Chen* and *Ghosez* who reported that a mixture **1a**/**2a** (R = 4-PhC_6H_4CO) was converted exclusively to **15a** by treatment with dimethyl 2-oxoheptylphosphonate/NaH [20]. The *Wittig-Horner* condensation was accompanied by an epimerization leading to the more stable product **15a**. However, starting from diastereoisomerically pure **2a**, we never observed the formation of either **14a** or **15a**, despite intensive efforts. Only oxodienelactone **16** arising from the β-elimination of 4-phenylbenzoate was isolated. Oxodienelactone **16** was reported as an intermediate for

Scheme 2



[4]) Epimerization of monocyclic systems were also reported [17] [18].

the synthesis of PGC_2 [14] [21]. As expected, under similar reaction conditions, a pure sample of **1a**, prepared from commercially available *Corey* lactone, gave **15a** in 80% yield [4]. We believe that *Chen* and *Ghosez*'s observation of the selective formation of **15a** may in fact been caused by β-elimination of the minor isomer **2a** rather than by epimerization.

To avoid β-elimination, we used the diastereoisomerically pure formyllactone **2b**. Its *Wittig-Horner* reaction gave **14b** (85%) without elimination or epimerization. This last point was confirmed by running the *Wittig-Horner* reaction with **1b**, prepared from commercially available *Corey* lactone (±)-**12**. The product **15b** was clearly different from **14b**. The choice of a silyl protective group proved to be of crucial importance for avoiding both elimination and epimerization[5][6].

The conversion of **14b** to 12-epi-$PGF_{2\alpha}$ (**3**) was accomplished similarly to the original method reported for the synthesis of $PGF_{2\alpha}$ [3] [4], *i.e.*, reduction of the keto function with *L-Selectride*® [23] which gave the epimeric hydroxy derivatives **17** and **18** as a 1.5:1 mixture, easily separated by flash chromatography[7]. The major isomer **17** possesses the correct relative configuration for the preparation of 12-epi-$PGF_{2\alpha}$ (**3**). Both isomers **17** and **18** were separately reduced with diisobutylaluminium hydride (DIBAL-H) to the lactol, and the α-chain was introduced by a *Wittig* reaction. After deprotection of the silyl ether with dilute HCl in THF, 12-epi-$PGF_{2\alpha}$ (**3**) and 12,15-diepi-$PGF_{2\alpha}$ (**4**) were isolated. The ^1H- and ^{13}C-NMR spectra of **3** were in close agreement to those reported [7]. To our knowledge, the preparation of 12,15-diepi-$PGF_{2\alpha}$ (**4**) was never described before.

Conclusions. – We have demonstrated that all-*cis*-formyllactone **2b**, which is related to *Corey* lactone and easily obtained from 7-oxabicyclo[2.2.1]hept-5-en-2-one (**6**), is a convenient precursor for the preparation of all-*cis*-prostanoids, a class of compounds which has received little attention in the past. The reaction sequence is short and characterized by an easy and complete stereocontrol. Moreover, epimerization at C(12) (PGF numbering) at the formyllactone stage (see **2b**) is possible making this approach also convenient for the preparation of naturally occurring prostanoids and their analogs.

We thank the *Swiss National Science Foundation* and the *Fondation Herbette* for financial support. *P.R.* thanks also the *Stiftung für Stipendien auf dem Gebiet der Chemie* for the *Alfred Werner* stipend. We thank Prof. *Ghosez* for providing us with unpublished experimental details of his work.

Experimental Part

General. THF was freshly distilled from K under N_2, 1,2-dimethoxyethane (DME) distilled from Na/benzophenone, CH_2Cl_2 from P_2O_5, and benzene from CaH_2 under N_2. Irradiations were conducted using a sunlamp *Osram Ultra-Vitalux 300 W*. Bulb-to-bulb distillations: *Büchi-GKR-50* apparatus; b.p. refer to air-bath temp. Flash column chromatography (FC) and filtration: *Merck* silica gel *60* (70–230 mesh), AcOEt and petroleum ether

[5] Indeed, the use of a tetrahydro-2*H*-pyranyl group was reported to lead mainly to epimerization [17].

[6] To prepare naturally occurring prostaglandins, we also investigated the epimerization of the hydroxylactone obtained by deprotection of **14b** in dilute HCl solution. Using the *Corey* epimerization conditions (AcOH/morpholine) [22], we isolated only oxodienelactone **16** along with unreacted starting material. No trace of epimerized product was observed.

[7] We are confident that by working with optically active compounds the stereoselectivity of this step could be easily controlled by using a chiral reducing agent [24]. Such a control in the 12-epiprostaglandin series was reported [7].

(p.e.) as eluents.TLC: *Merck* silica gel *60* F_{254} anal. plates; detection with UV, I_2, or by spraying with a soln. of phosphomolybdic acid (25 g), $Ce(SO_4)_2 \cdot 4\ H_2O$ (10 g), conc. H_2SO_4 (60 ml), and H_2O (940 ml) with subsequent heating. GC: *Carlo Erba, DB-WAX*, 29 m (capillary column). M.p.: *Büchi Tottoli* apparatus; not corrected. IR: *Perkin-Elmer-297* spectrophotometer; in cm^{-1}. NMR: *Bruker AC-250 FT* at 250 (^1H) and ^{13}C/62.9 MHz (^{13}C), *Bruker AMX-400 FT* at 400 (^1H) and 100.6 MHz (^{13}C), and *Bruker AMX2-600* at 600 MHz (^1H); unless otherwise indicated, $CDCl_3$ solns. and chemical shifts δ in ppm rel. to $SiMe_4$ (= 0 ppm). MS: *Finnigan 1020* and *Nermag R10-10C;* chemical ionization (CI) with NH_3; electron ionization (EI) at 70 eV. Elemental analysis: *Ilse Beetz*, Mikroanalytisches Laboratorium, D–96317 Kronach, Germany.

all-*cis*-Formyllactone. – *Dimethyl 2-[(1*RS,*3*RS *and 3*SR,*4*RS,*7*SR*)-5-Oxo-3-(phenylselenenyl)-2-oxabicyclo[2.2.1]hept-7-yl]propanedioate* (**7**). A soln. of (±)-**6** (1.00 g, 9.1 mmol) and dimethyl 2-(phenylselenenyl)propanedioate [13] (5.4 g, 15.5 mmol) in anh. benzene (30 ml) was irradiated with a 300-W sunlamp for 12 h under N_2. The temp. of the mixture raised to 50°. After evaporation, FC (AcOEt/p.e., 1:4) and recrystallization (AcOEt/p.e.) gave **7** (2.63 g, 73%; 3*SR*/3*RS* or *endo*/*exo* 3:1). Isomeric compounds (612 mg, 17%) resulting mainly from radical addition at C(6) were separated during FC. **7**: M.p. 104–105°. IR (KBr): 3010*w*, 2960*w*, 2920*w*, 1750*s*, 1740*s*, 1480*m*, 1435*m*, 1320*m*, 1260*m*, 1210*m*, 1180*m*, 1150*m*, 1120*m*, 990*m*, 940*w*, 930*m*, 900*m*, 740*m*, 690*m*. ^1H-NMR (250 MHz, $CDCl_3$): 3-*endo*-**7** ((1*RS*,3*RS*,4*RS*,7*SR*)): 7.52 (*m*, 2 arom. H); 7.32 (*m*, 3 arom. H); 5.80 (*dd*, ^3J = 3.0, 0.8, H–C(3)); 4.73 (*m*, H–C(1)); 3.77, 3.74 (2*s*, COOMe); 3.64 (*d*, ^3J = 11.0, C*H*COOMe); 3.08 (*m*, H–C(4)); 2.87 (br. *d*, ^3J = 11.0, H–C(7)); 2.76 (*d*, ^2J = 18.0, H_{endo}–C(6)); 2.40 (*ddd*, ^3J = 2.0, 1.0, ^2J = 18.0, H_{exo}–C(6)); (3-*exo*)-**7** ((1*RS*,3*RS*,4*RS*,7*SR*); significant peaks): 7.52 (*m*, 2 arom. H); 7.30 (*m*, 3 arom. H); 5.50 (*s*, H–C(3)); 4.85 (*m*, H–C(1)); 4.32 (*d*, ^3J = 11.0, C*H*COOMe); 3.86, 3.85 (2*s*, COOMe); 3.30 (*m*, H–C(4)); 2.85 (*d*, ^3J = 11.0, H–C(7)). EI-MS: 398 (1.93, $[M + 1]^+$), 397 (0.15, M^+), 396 (1), 316 (9), 314 (27), 312 (23), 241 (5), 234 (10), 157 (29), 139 (11), 117 (8), 101 (13), 94 (13), 81 (59), 78 (82), 77 (100), 59 (38). Anal. calc. for $C_{17}H_{18}O_6Se$ (397.29): C 51.40, H 4.57, Se 19.87; found: C 51.42, H 4.58, Se 19.89.

*Dimethyl 2-[(1*RS,*3*RS *and 3*SR,*4*RS,*5*SR,*7*SR*)-5-Hydroxy-3-(phenylselenenyl)-2-oxabicyclo[2.2.1]hept-7-yl]propanedioate* (**8**). To a cooled (−10°) suspension of **7** (9.4 g, 23 mmol) in MeOH (30 ml) was added $NaBH_4$ (0.89 g, 24 mmol) in portions. The mixture was stirred for 5 min at −10° until it became clear, then allowed to warm to r.t., poured into cold H_2O, and neutralized with 0.1M HCl. The neutral aq. layer was extracted with AcOEt (3 × 30 ml) and the combined org. layer washed with brine, dried ($MgSO_4$), and evaporated: **8** (9.2 g, 98%). Colorless oil. Recrystallization from AcOEt/p.e. gave pure *endo*-**8**[8]) for anal. purposes. M.p. 122–123°. IR (KBr): 3480*s* (br.), 3080*w*, 3020*w*, 2980*w*, 2950*s*, 1760*s*, 1740*s*, 1580*m*, 1480*m*, 1440*s*, 1430*s*, 1280*s*, 1220*s*. ^1H-NMR (250 MHz, $CDCl_3$): 7.64 (*m*, 2 arom. H); 7.30 (*m*, 3 arom. H); 5.8 (*dd*, ^3J = 2.0, 1.8, H–C(3)); 4.60 (*m*, H–C(5)); 4.26 (*d*, ^3J = 2.5, H–C(1)); 3.74, 3.76 (2*s*, COOMe); 3.62 (*d*, ^3J = 11.5, C*H*COOMe); 2.78 (br. *s*, H–C(4)); 2.49 (br. *d*, ^3J = 11.5, H–C(7)); 2.34 (*ddd*, ^2J = 14.0, ^3J = 10.0, 3.0, H_{exo}–C(6)); 2.21 (br. *s*, OH); 1.88 (*dd*, ^2J = 14.0, ^3J = 5.0, H_{endo}-C(6)). ^{13}C-NMR (62.9 MHz, $CDCl_3$); 168.74 (*s*); 168.62 (*s*); 133.93 (*s*); 132.78 (*d*); 129.10 (*d*); 127.16 (*d*); 83.07 (*d*); 79.91 (*d*); 71.95 (*d*); 52.83 (*q*); 50.84 (*d*); 48.33 (*d*); 39.01 (*t*). EI-MS: 400 (1.63, $[M + 1]^+$), 369 (3), 275 (3), 243 (67), 211 (4), 199 (6), 161 (7), 157 (11), 139 (25), 133 (33), 123 (13), 111 (100), 83 (27), 77 (33), 69 (29), 66 (89). Anal. calc. for $C_{17}H_{20}O_6Se$ (399.30): C 51.14, H 5.05, Se 19.77; found: C 51.11, H 5.11, Se 19.65.

*Methyl 2-[(1*RS,*3*RS *and 3*SR,*4*RS,*5*SR,*7*SR*)-5-Hydroxy-3-(phenylselenenyl)-2-oxabicyclo[2.2.1]hept-7-yl]acetate* (**9**. To a soln. of **8** (6.6 g, 16.5 mmol) in MeOH (40 ml), 1M aq. NaOH (20 ml) was added. The mixture was stirred at r.t. for 2 h, neutralized with 1M HCl, and poured into H_2O (150 ml). The aq. layer was extracted with CH_2Cl_2 (3 × 80 ml), the combined org. phase washed with H_2O (3 × 30 ml), dried ($MgSO_4$), and evaporated, and the residue (6.0 g), dissolved in dry DMSO (20 ml) and heated at 130° under N_2 for 30 min until CO_2 evolution stopped. After cooling to r.t., the mixture was poured into CH_2Cl_2 and washed with H_2O to remove the DMSO. Drying ($MgSO_4$), evaporation, and FC (AcOEt/p.e. 1:1) afforded **9**[8]) which crystallized from AcOEt/p.e. (4.6 g, 86%). Colorless crystals. M.p. 90–91°. IR (KBr): 3400*s* (br.), 3060*w*, 3000*w*, 2980*m*, 1730*s*, 1570*m*, 1430*s*, 1340*s*, 1230*s*, 1200*s*, 1150*s*, 1090*s*, 1050*w*, 920*s*, 750*s*. ^1H-NMR (250 MHz, $CDCl_3$): 7.53 (*m*, 2 arom. H); 7.29 (*m*, 3 arom. H); 5.74 (*dd*, ^3J = 2.0, 1.8, H–C(3)); 4.58 (*m*, H–C(5)); 4.19 (*d*, ^3J = 2.5, H–C(1)); 3.68 (*s*, COOMe); 2.78 (br. *s*, H–C(4)); 2.54 (*d*, ^2J = 11.0, 1 H, CH_2COOMe); 2.49 (*d*, ^2J = 11.0, 1 H, CH_2COOMe); 2.4 (*s*, OH); 2.29 (br. *s*, H–C(7)); 2.28 (*ddd*, ^3J = 5.0, 2.5, ^2J = 17.5, H_{exo}–C(6)); 1.83 (*dd*, ^3J = 5.0, ^2J = 17.5, H_{endo}–C(6)). ^{13}C-NMR (62.9 MHz, $CDCl_3$): 172.69 (*s*); 134.19 (*s*); 132.75 (*d*); 129.04 (*d*); 127.05 (*d*); 83.68 (*d*); 80.53 (*d*); 72.17 (*d*); 51.70 (*d*,*q*); 45.14 (*d*); 39.80 (*t*); 30.83 (*t*). CI-MS: 342 (1.47, $[M + 1]^+$), 341 (0.22, M^+), 340 (2), 311 (3), 307 (5), 195 (2),

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[8]) For convenience, physical data and spectra of pure 3-*endo*-**8**–**10** are given, although both diastereoisomers were suitable for preparative purposes.

185 (100), 157 (6), 135 (6), 111 (8), 81 (65), 79 (27). Anal. calc. for $C_{15}H_{18}O_4Se$ (341.26): C 52.79, H 5.32, Se 23.14; found: C 52.86, H 5.33, Se 23.08.

Methyl 2-{(1RS,3RS and 3SR,4RS,5SR,7SR)-5-[(1,1'-Biphenyl-4-yl)carbonyloxy]-3-(phenylselenenyl)-2-oxabicyclo[2.2.1]hept-7-yl}acetate (**10a**). To a cooled (−78°) soln. of **9** (1.0 g, 2.9 mmol) in THF (20 ml) was added 0.7M LiHMDS (4.2 ml, 2.9 mmol) in THF/hexanes 1.3:1. The soln. was stirred for 15 min, a soln. of (1,1'-biphenyl-4-yl)carbonyl chloride (0.70 g, 3.2 mmol) in THF (5 ml) added, and the mixture allowed to warm to r.t. The mixture was poured into Et_2O (60 ml) and the org. soln. washed with 1M NH_4Cl (20 ml) and brine (20 ml), dried ($MgSO_4$), and evaporated. FC (AcOEt/p.e., 1:4) and recrystallization (AcOEt/p.e.) gave **10a**[8]) (1.25 g, 85%). M.p. 105–106°. IR (KBr): 3080*w*, 2960*m*, 1730*s*, 1715*s*, 1610*s*, 1480*m*, 1450*m*, 1440*s*, 1270*s*, 1200*m*, 1010*s*, 750*s*. ^{1}H-NMR (250 MHz, $CDCl_3$): 8.3 (*m*, 2 arom. H); 7.78–7.55 (*m*, 6 arom. H); 7.54–7.40 (*m*, 3 arom. H); 7.33–7.22 (*m*, 3 arom. H); 5.78 (*dd*, ^3J = 2.0, 2,0, H–C(3)); 5.5 (*m*, H–C(5)); 4.31 (*d*, ^3J = 2.0, H–C(1)); 3.70 (*s*, COOMe); 3.17 (br. *s*, H–C(4)); 2.59 (*d*, ^2J = 10.0, 1 H, CH_2COOMe); 2.57 (*d*, ^2J = 10.0, 1 H, CH_2COOMe); 2.48 (br. *s*, H–C(7)); 2.46 (*m*, H_{exo}–C(6)); 2.18 (*dd*, ^3J = 5.0, ^2J = 14.5, H_{endo}–C(6)). ^{13}C-NMR (62.9 MHz, $CDCl_3$): 172.31 (*s*); 166.33 (*s*); 145.87 (*s*); 139.87 (*s*); 133.57 (*s*); 133.17 (*d*); 130.70 (*d*); 130.02 (*d*); 129.05 (*d*); 128.86 (*d*); 128.30 (*d*); 128.11 (*s*); 127.49 (*d*); 127.23 (*d*); 127.32 (*d*); 127.05 (*d*); 83.65 (*d*); 80.16 (*d*); 73.59 (*d*); 51.80 (*q*); 49.79 (*d*); 45.228 (*d*); 39.98 (*t*); 30.69 (*t*). EI-MS: 366 (15), 365 (45), 198 (3), 181 (100), 152 (5), 107 (2), 97 (3), 85 (29), 83 (53), 78 (18). Anal. calc. for $C_{28}H_{26}O_5Se$ (521.47): C 64.49, H 5.03, Se 15.14; found: C 64.37, H 5.07, Se 15.01.

(1RS,5SR,6RS,7SR)-7-[(1,1'-Biphenyl-4-yl)carbonyloxy]-3-oxo-2-oxabicyclo[3.3.0]octane-6-carbaldehyde (= *(3aRS,4SR,5RS,6aSR)-4-Formyl-3,3a,4,5,6,6a-hexahydro-2-oxo-2H-cyclopenta[b]furan-5-yl 1,1'-Biphenyl-4-carboxylate*; **2a**). A soln. of **10a** (521 mg, 1.0 mmol) in acetone/H_2O 5:1 (6 ml) was treated with a 30% H_2O_2 soln. (160 mg, 1.4 mmol). The mixture was stirred at r.t. for 1 h. After addition of 5% Pd/C (cat.) to decompose unreacted H_2O_2, the soln. was stirred for 10 min and filtered through *Celite*, and CH_2Cl_2 (10 ml) was added to the filtrate. The org. phase was washed with a 1M NaOH (5 ml) and dried ($MgSO_4$). Evaporation gave the hydroxy ester (370 mg) as a foaming oil which was dissolved in $CHCl_3$ (5 ml) and stirred for 2 h at 40° with pyridinium toluene-4-sulfonate (cat.). The mixture was poured into CH_2Cl_2 (10 ml) and washed with 1M NaOH (5 ml). Evaporation and recrystallization (Et_2O/p.e., −78°) gave **2a** (316 mg, 90%) which was used crude in the next step. ^{1}H-NMR (250 MHz, $CDCl_3$): 9.92 (*s*, CHO); 7.98 (*m*, 2 arom. H); 7.65 (*m*, 4 arom. H); 7.47 (*m*, arom. H); 6.12 (*dd*, ^3J = 4.5, 4.0, H–C(7)); 5.26 (*dd*, ^3J = 8.0, 6.5, H–C(1)); 3.52 (*m*, H–C(5)); 3.18 (*dd*, ^3J = 4.0, ^2J = 8.0, 1 H–C(4)); 3.01 (*m*, H–C(6)); 2.98 (*d*, ^2J = 8.0, 1 H–C(4)); 2.61 (*d*, ^2J = 16, 1 H–C(8)); 2.31 (*ddd*, ^3J = 7.0, 4.0, ^2J = 16.0, 1 H–C(8)).

(1RS,5SR,6SR,7SR)-7-[(1,1'-Biphenyl-4-yl)carbonyloxy]-6-(hydroxymethyl)-2-oxabicyclo[3.3.0]octan-3-one (= *(3aRS,4RS,5RS,6aSR)-3-3a,4,5,6,6a-Hexahydro-4-(hydroxymethyl)-2-oxo-2H-cyclopenta[b]furan-5-yl 1,1'-Biphenyl-4-carboxylate*; **11**). To a cooled (−10°) soln. of **2a** (316 mg, 0.90 mmol) in MeOH (5 ml) was added $NaBH_4$ (34 mg, 0.90 mmol). The soln. was stirred for 5 min at −10° (→clear) and finally allowed to warm to r.t. The mixture was poured into cold H_2O and neutralized with 0.1M HCl, the aq. layer extracted with AcOEt (3 × 10 ml), the combined org. phase washed with brine, dried ($MgSO_4$), and evaporated, and the residue purified by FC (AcOEt/p.e. 2:1): **11** (290 mg, 91%). Colorless oil. IR ($CHCl_3$): 3500*s*, 3020*w*, 2960*m*, 1760*s*, 1700*s*, 1610*s*, 1410*m*, 1280*s*, 1030*s*, 810*m*. ^{1}H-NMR (250 MHz, $CDCl_3$): 8.08 (*m*, 2 arom. H); 7.67 (*m*, 4 arom. H); 7.48 (*m*, 3 arom. H); 5.69 (*dd*, ^3J = 5.0, 4.0, H–C(7)); 5.29 (*dd*, ^3J = 6.0, 7.0, H–C(1)); 3.72 (*m*, CH_2OH); 3.29 (*m*, H–C(5)); 2.78 (br. *s*, OH); 2.62 (*m*, 2 H–C(4)); 2.55 (*d*, ^2J = 16.0, 1 H–C(8)); 2.49 (*m*, H–C(6)); 2.21 (*ddd*, ^3J = 6.0, 4.0, ^2J = 16.0, 1 H–C(8)). ^{13}C-NMR (62.9 MHz, $CDCl_3$); 177.18 (*s*); 166.89 (*s*); 146.35 (*s*); 139.63 (*s*); 130.34 (*d*); 128.89 (*d*); 128.22 (*d*); 127.33 (*d*); 127.21 (*d*); 84.39 (*d*); 76.29 (*d*); 58.61 (*t*); 49.33 (*d*); 39.49 (*t*); 38.21 (*d*); 29.81 (*t*). CI-MS: 353 (45, $[M + 1]^+$), 352 (100, M^+), 336 (5), 315 (2), 252 (2), 239 (2), 229 (3), 198 (45), 181 (96), 152 (17), 85 (41), 83 (65), 77 (22). Anal. calc. for $C_{21}H_{20}O_5$ (352.39): C 71.58, H 5.72; found: C 71.49, H 5.73.

(1RS,5SR)-3-Oxo-2-oxabicyclo[3.3.0]oct-6-ene-6-carbaldehyde (= *(3aRS,6aSR)-3,3a,6,6a-Tetrahydro-2H-cyclopenta[b]furan-4-carbaldehyde*; **13**). Filtration through silica gel (AcOEt) of **2a** (35 mg, 0.1 mmol) gave **13** (13 mg, 85%). ^{1}H-NMR (200 MHz, $CDCl_3$): 9.80 (*s*, CHO); 6.90 (br. *d*, *J* = 2.5, H–C(7)); 5.22 (*dt*, *J* = 6.2, 3.1, H–C(1)); 3.75 (*m*, H–C(5)); 3.0 (*m*, 2 H–C(8)); 2.90 (*dd*, *J* = 18.7, 9.2, 1 H–C(4)); 2.71 (*dd*, *J* = 18.7, 3.7, 1 H–C(4)). Anal. calc. for $C_8H_8O_3$ (238.24): C 63.15, H 5.30; found: C 63.01, H 5.18.

Methyl 2-{(1RS,3RS and 3SR,4RS,5SR,7SR)-5-(tert-butyl)dimethylsilyloxy]-3-(phenylselenenyl)-2-oxabicyclo[2.2.1]hept-7-yl}acetate (**10b**). To a soln. of **9** (4.10 g, 12.0 mmol) in CH_2Cl_2 (60 ml) was added successively 1*H*-imidazole (1.14 g, 16.8 mmol) and (*t*-Bu)Me_2SiCl (2.71 g, 18.0 mmol). The mixture was stirred at r.t. for 12 h, and CH_2Cl_2 (50 ml) was added. The org. layer was washed with H_2O (2 × 20 ml), dried ($MgSO_4$), and evaporated. FC (AcOEt/p.e. 1:20) and recrystallization (Et_2O/p.e.) gave **10b**[8]) (4.81 g, 88%). M.p. 72–73°. IR (KBr): 3060*w*, 2960*m*, 2920*m*, 1740*s*, 1480*m*, 1250*m*, 1110*s*, 1000*m*. ^{1}H-NMR (250 MHz, $CDCl_3$): 7.69–7.59 (*m*, 2 arom. H); 7.32–7.20 (*m*, 3 arom. H); 5.73 (*dd*, ^3J = 3.0, 2.5, H–C(3)); 4.48 (*m*, H–C(5)); 4.16 (*d*, ^3J = 2.5, H–C(1)); 3.68 (*s*,

COOMe); 2.69 (br. *s*, H–C(4)); 2.57 (*A* of *ABX*, $^3J_{AX}$ = 8.0, $^2J_{AB}$ = 16.0, 1 H, C*H*COOMe); 2.43 (*B* of *ABX*, $^3J_{BX}$ = 7.5, $^2J_{AB}$ = 16.0, 1 H, C*H*COOMe); 2.22 (br. *t*, ^3J = 8.0, H–C(7)); 2.12 (*ddd*, ^3J = 10.0, 2.5, ^2J = 13.5, H_{exo}–C(6)); 1.82 (*dd*, ^3J = 4.5, ^2J = 13.5, H_{endo}–C(6)); 0.98 (*s*, *t*-BuSi); 0.15, 0.11 (2*s*, Me_2Si). ^{13}C-NMR (62.9 MHz, $CDCl_3$): 172.69 (*s*); 135.46 (*s*); 132.43 (*d*); 128.81 (*d*); 126.55 (*d*); 83.50 (*d*); 80.42 (*d*); 72.18 (*d*); 51.99 (*d*); 51.65 (*q*); 44.52 (*d*); 40.06 (*t*); 30.77 (*t*); 25.92 (*q*); 18.12 (*s*); –4.73 (*q*); –4.89 (*q*). EI-MS: 299 (15), 267 (2), 241 (2), 167 (28), 157 (8), 141 (54), 139 (18), 135 (24), 107 (25), 81 (100), 79 (22), 75 (34), 73 (73), 59 (24). Anal. calc. for $C_{21}H_{32}SeSiO_4$ (455.53): C 55.37, H 7.08; found: C 55.41, H 7.14.

*(1RS,5SR,6SR,7SR)-7-[(*tert*-Butyl)dimethylsilyloxy]-3-oxo-2-oxabicyclo[3.3.0]octane-6-carbaldehyde* (= *3aRS,4RS,5RS,6aSR)-5-[(*tert*-Butyl)dimethylsilyloxy]-3,3a,4,5,6,6a-hexahydro-2-oxo-2*H*-cyclopenta[b]furan-4-carbaldehyde*; **2b**). As described for **2a**, with **10b** (2 g, 4.39 mmol), acetone/H_2O 5:1 (8 ml), and 30% H_2O_2 soln. (700 mg, 6.14 mmol). The hydroxy ester (1.36 g) in $CHCl_3$ (5 ml) was stirred for 4 h at 40° with PPTS (cat.) and the mixture poured into CH_2Cl_2 (20 ml) and worked up as described for **2a** (10 ml of 1M NaOH): **2b** (1.18 g, 95%) which was used crude in the next step. Colorless oil. ^{1}H-NMR (250 MHz, $CDCl_3$): 9.88 (*s*, CHO); 5.10 (*t*, ^3J = 7.5, H–C(1)); 4.82 (*t*, ^3J = 4.0, H–C(7)); 3.30 (*m*, H–C(5)); 2.88 (*A* of *ABX*, $^3J_{AX}$ = 6.0, $^2J_{AB}$ = 18.5, 1 H–C(4)); 2.80 (*m*, H–C(6)); 2.75 (*B* of *ABX*, $^3J_{BX}$ = 11.0, $^2J_{AB}$ = 18.5, 1 H–C(4)); 2.20 (*d*, ^2J = 15.0, H_{endo}–C(8)); 1.98 (*ddd*, ^3J = 7.5, 4.0, ^2J = 15.0, H_{exo}–C(8)); 0.83 (*s*, *t*-BuSi); 0.07–0.06 (2*s*, Me_2Si). ^{13}C-NMR (62.9 MHz, $CDCl_3$): 200.24 (*d*); 177.21 (*s*); 83.79 (*d*); 74.10 (*d*); 42.05 (*d*, *t*); 37.40 (*d*); 32.18 (*t*); 25.42 (*q*); 17.71 (*s*); –4.70 (*q*); –5.47 (*q*).

*(1RS,5SR,6RS,7SR)-7-[(*tert*-Butyl)dimethylsilyloxy]-3-oxo-2-oxabicyclo[3.3.0]octane-6-carbaldehyde* (= *(3aRS,4SR,5RS,6aSR)-5-[(*tert*-Butyl)dimethylsilyloxy]-3,3a,4,5,6,6a-hexahydro-2-oxo-2*H*-cyclopenta[b]-furan-4-carbaldehyde*; **1b**). *From* **2b**: To a soln. of **2b** (60 mg, 0.21 mmol) in MeOH (2 ml) was added Na_2CO_3 (cat.), and the mixture was stirred at r.t. for 4 days. The soln. was poured into CH_2Cl_2 (6 ml), washed with 1M NaCl (2 × 3 ml), and dried ($MgSO_4$). Evaporation gave **1b** (55 mg, 92%).

From **10b**: As described for **2a**, with **10b** (200 mg, 0.44 mmol), acetone/H_2O 5:1 (2 ml), and 30% H_2O_2 (70 mg, 0.61 mmol; dilution of the filtrate with CH_2Cl_2 (4 ml) and washing with 1M NaOH (2 ml)). The hydroxy ester (136 mg) was dissolved in MeOH (2 ml) and stirred for 4 days at r.t. with Na_2CO_3 (cat.), the mixture poured into CH_2Cl_2 (6 ml), and the soln. washed with 1M NaCl (2 × 3 ml), dried ($MgSO_4$), and evaporated: **1b** (114 mg, 95%). Colorless oil.

*From (±)-***12**: As described for **10b**, with (±)-**12** (1.00 g, 2.83 mmol; commercially available), CH_2Cl_2 (10 ml), 1*H*-imidazole (232 mg, 3.40 mmol), and (*t*-Bu)Me_2SiCl (641 mg, 4.25 mmol). Workup with CH_2Cl_2 (30 ml) and 1M NaCl and FC (AcOEt/p.e. 1:4) gave the 6-(silyloxymethyl) derivative (1.25 g, 95%). Colorless crystallizing oil. ^{1}H-NMR (250 MHz, $CDCl_3$): 8.1–8.04 (*m*, 2 arom. H); 7.70–7.57 (*m*, 4 arom. H); 7.48–7.33 (*m*, 3 arom. H); 5.38 (*m*, H–C(7)); 5.09 (br. *t*, ^3J = 5.5, H–C(1)); 3.7 (*m*, CH_2OSi); 3.0–2.83 (*m*, 2 H–C(4)); 2.66–2.52 (*m*, H–C(5)); 2.50 (*dt*, ^3J = 6.0, ^2J = 16.5, H–C(8)); 2.4–2.28 (*dm*, ^2J = 16.5, H–C(8), H–C(6)); 0.88 (*s*, *t*-BuSi); 0.08 (*s*, Me_2Si).

To a soln. of the above obtained 6-(silyloxymethyl) derivative (1.25 g, 2.67 mmol) in MeOH (10 ml) was added at r.t. K_2CO_3 (370 mg, 2.67 mmol). The mixture was stirred 4 h at r.t., poured into CH_2Cl_2 (100 ml), and washed with 1M NaCl (2 × 20 ml). The org. layer was dried ($MgSO_4$) and evaporated: 7-hydroxy-6-(silyloxymethyl) derivative (765 mg, quant.) which was used without purification in the next step. White solid. ^{1}H-NMR (250 MHz, $CDCl_3$): 4.92 (*dt*, ^3J = 7.0, 3.0, H–C(1)); 4.11 (br. *q*, ^3J = 6.5, H–C(7)); 3.72–3.52 (*m*, CH_2OSi); 2.8 (*dd*, ^3J = 9.5, ^2J = 17.5, H–C(4)); 2.68–2.55 (*m*, H–C(5)); 2.58 (br. *s*, OH); 2.52 (*dd*, ^3J = 2.0, ^2J = 17.5, H–C(4)); 2.4 (*ddd*, ^4J = 2.0, ^3J = 7.0, 6.5, ^2J = 15.0, H_{exo}–C(8)); 2.05–1.92 (*m*, H_{endo}–C(8), H–C(6)); 0.88 (*s*, *t*-BuSi); 0.05 (*s*, Me_2Si).

The 7-hydroxy-6-(silyloxymethyl) derivative (715 mg, 2.66 mmol) in CH_2Cl_2 (5 ml) was treated with 1*H*-imidazole (218 mg, 3.2 mmol) and (*t*-Bu)Me_2SiCl (600 mg, 4.0 mmol), as described for **10b**. Workup with CH_2Cl_2 (10 ml) and 1M NaCl and FC (AcOEt/p.e. 1:5) gave the 7-(silyloxy)-6-(silyloxymethyl) derivative (1.0 g, 94%). White crystals. ^{1}H-NMR (250 MHz, $CDCl_3$): 4.94 (*dt*, ^3J = 7.0, 2.5, H–C(1)); 4.13 (br. *q*, ^3J = 6.0, H–C(7)); 3.53 (*m*, CH_2OSi); 2.8 (*dd*, ^3J = 11.0, ^2J = 17.0, 1 H–C(4)); 2.75–2.50 (*m*, H–C(5)); 2.53 (*dd*, ^3J = 2.0, ^2J = 17.0, 1 H–C(4)); 2.23 (*ddd*, ^3J = 7.0, 6.0, ^2J = 15.0, H_{exo}–C(8)); 2.05–1.92 (*m*, H_{endo}–C(8), H–C(6)); 0.88 (*s*, 2 *t*-BuSi); 0.07 (*s*, 2 Me_2Si).

A soln. of the 7-(silyloxy)-6-(silyloxymethyl) derivative (1.00 g, 2.48 mmol) in AcOH/THF/H_2O 13:3:7 (10 ml) was stirred at r.t. for 12 h [25]. The mixture was poured in AcOEt (50 ml), washed with 1M NaOH (2 × 10 ml), and dried ($MgSO_4$). Evaporation and FC (AcOEt/p.e. 1:2) gave after recrystallization (Et_2O/p.e.), the 6-(hydroxymethyl)-7-(silyloxy) derivative (533 mg, 75%). White crystals. M.p. 105–107°. IR (KBr): 3460*s*, 2980*w*, 2940*s*, 2920*s*, 1730*s*, 1470*m*, 1460*m*, 1300*m*, 1170*s*, 1130*s*, 960*s*, 880*s*, 840*s*, 770*s*. ^{1}H-NMR (250 MHz, $CDCl_3$): 4.94 (*dt*, ^3J = 7.0, 2.8, H–C(1)); 4.14 (*q*, ^3J = 6.0, H–C(7)); 3.6 (*d*, ^2J = 6.0, CH_2OH); 2.8 (*dd*, ^3J = 11.0, ^2J = 17.0, 1 H–C(4)); 2.75–2.60 (*m*, H–C(5)); 2.53 (*dd*, ^3J = 2.0, ^2J = 17.0, 1 H–C(4)); 2.29 (*ddd*, ^3J = 7.0, 6.0, ^2J = 15.0, H_{exo}–C(8)); 2.07–1.92 (*m*, H_{endo}–C(8), H–C(6)); 1.82 (br. *s*, OH); 0.88 (*s*, *t*-BuSi); 0.07 (*s*, Me_2Si). ^{13}C-NMR

(62.9 MHz, $CDCl_3$): 177.45 (*s*); 83.84 (*d*); 74.88 (*d*); 62.65 (*t*), 56.37 (*d*); 40.87 (*t*); 38.89 (*d*), 35.53 (*t*); 25.60 (*q*); 17.82 (*s*); −4.72, −5.12 (*q*). EI-MS: 285 (1.25, $[M-1]^+$), 235 (4), 229 (3), 193 (3), 188 (6), 129 (2), 1111 (7), 105 (3), 93 (19), 91 (15), 77 (10), 75 (100), 73 (20), 59 (13), 57 (30), 55 (24). Anal. calc. for $C_{14}H_{26}O_4Si$ (286.44): C 58.70, H 9.15, Si 9.80; found: C 58.77, H 9.09, Si 9.93.

To a soln. of the 6-(hydroxymethyl)-7-(silyloxy) derivative (300 mg, 1.04 mmol) in dry benzene (5 ml) were added successively under N_2 at r.t. dry DMSO (1 ml), DCC (860 mg, 4.16 mmol), and pyridinium trifluoroacetate (200 mg, 1.04 mmol). The mixture was stirred at r.t. for 4 h, AcOEt (40 ml) added, and the mixture filtered. The org. layer was successively washed with H_2O (10 ml) and brine (10 ml), dried ($MgSO_4$), and evaporated: crude **1b** (280 mg, 94%) which was used without purification for the *Wittig-Horner* reaction. ^{1}H-NMR (400 MHz, $CDCl_3$): 9.72 (*s*, CHO); 5.03 (*t*, ^3J = 6.6, H–C(1)); 4.59 (*m*, H–C(7)); 3.38 (*ddd*, ^3J = 11.0, 6.9, 3.3, H–C(5)); 2.98 (br. *s*, H–C(6)); 2.90 (*dd*, ^3J = 11.0, ^2J = 18.5, 1 H–C(4)); 2.53 (*dd*, ^3J = 3.3, ^2J = 18.5, 1 H–C(4)); 2.16 (br. *d*, ^2J = 15.0, H_{endo}–C(8)); 1.88 (*ddd*, ^3J = 6.5, 4.5, ^2J = 15.0, H_{exo}–C(8)); 0.97 (*s*, *t*-BuSi); 0.12 (*s*, Me_2Si).

12-Epiprostaglandins. – *(1RS,5SR)-6-[(E)-3-Oxooct-1-en-1-yl]-2-oxabicyclo[3.3.0]oct-6-en-3-one* (= *(3aRS,6aSR)-3,3a,6,6a-Tetrahydro-4-[(E)-3-oxooct-1-en-1-yl]-2H-cyclopenta[b]furan-2-one*; **16**). A soln. of dimethyl (2-oxoheptyl)phosphonate (122 mg, 0.55 mmol) in dry DME (2 ml) was added under N_2 to a suspension of NaH (12.5 mg, 0.52 mmol) in DME (4 ml) at r.t. The mixture was stirred at r.t. for 1 h and cooled (0°), a soln. of **2a** (180 mg, 0.51 mmol) in DME (1 ml) added, and the mixture stirred at r.t. for 4 h, neutralized (AcOH), and evaporated FC (AcOEt/p.e. 1:1) and recrystallization (Et_2O/p.e.) gave **16** (111 mg, 87%). White crystals. M.p. 77–78°. IR (KBr): 2960*m*, 2920*m*, 1770*s*, 1690*s*, 1620*s*, 1470*m*, 1180*s*, 980*s*. ^{1}H-NMR (250 MHz, $CDCl_3$): 7.28 (*d*, ^3J = 16.5, H–C(1′)); 6.21 (br. *s*, H–C(7)); 5.98 (*d*, ^3J = 16.5, H–C(2′)); 5.27 (*ddd*, ^3J = 7.0, 5.0, 2.0, H–C(1)); 3.68 (*m*, H–C(5)); 2.92 (*m*, 2 H–C(8)); 2.9 (*dd*, ^2J = 18.0, ^3J = 10.0, 1 H–C(4)); 2.6 (*t*, ^3J = 7.0, 2 H–C(4′)); 2.56 (*dd*, ^2J = 18.0, ^3J = 2.5, 1 H–C(4)); 1.63 (*m*, 2 H–C(5′)); 1.34 (*m*, 2 H–C(6′), 2 H–C(7′)); 0.91 (*m*, 3 H–C(8′)). ^{13}C-NMR (62.9 MHz, $CDCl_3$): 200.49 (*s*); 175.95 (*s*); 140.84 (*s*); 137.90 (*d*), 135.78 (*d*); 127.75 (*d*); 82.65 (*d*); 44.0 (*d*); 40.47 (*t*); 40.23 (*t*); 32.17 (*t*); 31.41 (*t*); 23.91 (*t*), 22.44 (*t*); 13.92 (*q*). EI-MS: 249 (3, $[M+1]^+$), 248 (7, M^+), 240 (4), 233 (6), 229 (6), 219 (17), 192 (64), 177 (21), 133 (24), 121 (32), 108 (20), 107 (53), 103 (27), 93 (53), 77 (98), 65 (44), 55 (100). Anal. calc. for $C_{15}H_{20}O_3$ (248.32): C 72.56, H 8.12; found: C 72.47, H 8.12.

(1RS,5SR,6RS,7SR)-7-[(tert-Butyl)dimethylsilyloxy]-6-[(E)-3-oxooct-1-en-1yl]-2-oxabicyclo[3.3.0]octan-3-one (= *(3aRS,4SR,5RS,6aSR)-5-[(tert-Butyl)dimethylsilyloxy]-3,3a,4,5,6,6a-hexahydro-4-[(E)-3-oxooct-1-en-1-yl]-2H-cyclopenta[b]furan-2-one*; **14b**). To a clear, cooled (0°) soln. of the Na^+ salt of dimethyl (2-oxoheptyl)phosphonate (353 mg, 1.44 mmol) in dry DME (10 ml) was added a soln. of **2b** (373 mg, 1.31 mmol) in dry DME (5 ml). The mixture was stirred at r.t. for 4 h and neutralized with AcOH. Evaporation and FC (AcOEt/p.e. 1:3) gave **14b** (424 mg, 85%). Colorless oil. IR (Film): 2960*s*, 2920*s*, 1770*s*, 1670*s*, 1630*m*, 1180*s*, 1090*s*, 840*s*, 780*s*. ^{1}H-NMR (250 MHz, $CDCl_3$): 6.90 (*dd*, ^3J = 16.0, 7.5, H–C(1′)); 6.1 (*dd*, ^3J = 16.0, ^4J = 1.0, H–C(2′)); 5.08 (*tm*, ^3J = 7.0, H–C(1)); 4.23 (*dm*, ^3J = 4.0, H–C(7)); 3.13 (*m*, H–C(5)); 2.75 (*dd*, ^3J = 5.0, ^2J = 18.5, 1 H–C(4)); 2.63 (*td*, ^3J = 8.0, 3.0, H–C(6)); 2.56–2.40 (*m*, 1 H–C(4)); 2.49 (*t*, ^3J = 7.0, 2 H–C(4′)); 2.16 (*d*, ^2J = 15.0, 1 H–C(8)); 1.92 (*ddd*, ^3J = 7.0, 4.0, ^2J = 15.0, 1 H–C(8)); 1.57 (*m*, 2 H–C(5′)); 1.23 (*m*, 2 H–C(6′), 2 H–C(7′)); 0.87–0.76 (*m*, *t*-BuSi, 3 H–C(8′)); 0.01, −0.01 (2*s*, Me_2Si). ^{13}C-NMR (62.9 MHz, $CDCl_3$): 200.01 (*s*); 176.83 (*s*); 142.63 (*d*); 135.67 (*d*); 84.52 (*d*); 76.53 (*d*); 50.20 (*d*); 42.18 (*t*); 41.38 (*d*); 39.47 (*t*); 31.20 (*t*); 30.98 (*t*); 25.41 (*q*); 23.66 (*t*); 22.22 (*t*); 17.74 (*s*); 13.72 (*q*); −4.96 (*q*); −5.5 (*q*). EI-MS: 323 (33), 305 (3), 279 (2), 231 (4), 225 (6), 223 (5), 199 (4), 133 (4), 99 (24), 75 (100), 57 (15). Anal. calc. for $C_{21}H_{36}SiO_4$ (380.60): C 66.27, H 9.53, Si 7.38; found: C 66.18, H 9.50, Si 7.32.

(1RS,5SR,6SR,7SR)-7-[(tert-Butyl)dimethylsilyloxy]-6-[(E)-3-oxooct-1-en-1-yl]-2-oxabicyclo[3.3.0]octan-3-one (= *(3aRS,4RS,5RS,6aSR)-5-[(tert-Butyl)dimethylsilyloxy]-3,3a,4,5,6,6a-hexadryo-4-[(E)-3-oxooct-1-en-1-yl]-2H-cyclopenta[b]furan-2-one;* **15b**). As described for **14b**, with dimethyl (2-oxoheptyl)phosphonate (263 mg, 1.08 mmol), DME (10 ml), **1b** (280 mg, 0.98 mmol) and DME (5 ml). FC (AcOEt/p.e. 1:4) gave **15b** (312 mg, 84%). Viscous colorless oil. IR (film): 2960*s*, 2940*s*, 2860*s*, 1775*s*, 1700*m*, 1680*m*, 1630*m*, 1470*m*, 1255*m*, 1220*m*, 1170*m*, 1130*m*, 840*s*, 780*s*. ^{1}H-NMR (250 MHz, $CDCl_3$): 6.54 (*dd*, ^3J = 16.0, 8.5, H–C(1′)); 6.27 (*dd*, ^3J = 16.0, ^4J = 1.0, H–C(2′)); 4.98 (*dt*, ^3J = 7.0, 3.0, H–C(1)); 4.04 (*q*, ^3J = 6.0, H–C(7)); 2.78 (*dd*, *A* of *ABX*, ^3J = 10.0, ^2J = 15.0, 1 H–C(4)); 2.78–2.67 (*m*, H–C(5)); 2.52 (*t*, ^3J = 6.5, 2 H–C(4′)); 2.52–2.44 (*m*, H–C(6)); 2.45 (*dm*, *B* of *ABX* system, ^2J = 15.0, 1 H–C(4)); 2.37 (*dddd*, ^3J = 7.0, 6.0, ^2J = 14.8, ^4J = 1.5, 1 H–C(8)); 2.20 (*ddd*, ^3J = 6.0, 3.0, ^2J = 14.8, 1 H–C(8)); 1.61 (*m*, 2 H–C(5′)); 1.30 (*m*, 2 H–C(6′), 2 H–C(7)); 0.90 (*t*, 3 H–C(8′)); 0.88 (*s*, *t*-BuSi); 0.05, 0.03 (2*s*, Me_2Si). ^{13}C-NMR (62.9 MHz, $CDCl_3$): 199.80 (*s*); 176.30 (*s*); 144.10 (*d*); 131.16 (*d*); 82.66 (*d*); 77.15 (*d*); 56.51 (*d*); 41.61 (*d*); 40.79 (*t*); 34.52 (*t*); 31.30 (*t*); 25.54 (*q*); 23.63 (*t*); 22.36 (*t*); 17.89 (*s*); 13.86 (*q*); −4.98 (*q*); −5.15 (*q*); 1 CH_2 is missing. EI-MS: 325 (3), 324 (11), 323 (39), 279 (5), 249 (3), 225 (6), 199 (7), 101 (13), 99 (31), 95 (30), 94 (24), 79 (39), 75 (100), 73 (82), 59 (72). Anal. calc. for $C_{21}H_{36}SiO_4$ (380.60): C 66.27, H 9.53, Si 7.38; found: C 66.15, H 9.53, Si 7.29.

(1RS,5SR,6RS,7SR,3'RS)- and (1RS,5SR,6RS,7SR,3'SR)-7-[(tert-Butyl)dimethylsilyloxy]-6-[(E)-3-hydroxyoct-1-en-1-yl]-2-oxabicyclo[3.3.0]octan-3-one ((3aRS,4SR,5RS,6aSR,3'SR)- and (3aRS,4SR,5RS,6aSR,3'RS)-5-[(tert-Butyl)dimethylsilyloxy]-3,3a,4,5,6,6a-hexahydro-4-[(E)-3-hydroxyoct-1-en-1-yl]-2H-cyclopenta[b]furan-2-one; **17** and **18**, resp.). To a cooled (−78°) soln. of **14b** (1.09 g, 2.86 mmol) in dry THF (20 ml), 1M *L-Selectride*® in THF (3.15 ml, 3.15 mmol) was added. The mixture was stirred at −78° for 20 min and quenched with MeOH (0.5 ml). Et_2O (30 ml) was added and the org. layer washed with 1M NH_4Cl (2 × 10 ml), dried ($MgSO_4$), and evaporated FC (AcOEt/p.e. 1:3) **17**/**18** (1.5:1; 1.02 g, 93%) which were easily separated by FC (AcOEt/p.e. 1:4).

17: Colorless oil. ^{1}H-NMR (250 MHz, $CDCl_3$): 5.78 (*dd*, ^3J = 16.0, 8.0, H–C(1')); 5.55 (*dd*, ^3J = 16.0, 6.5, H–C(2')); 5.04 (br. *t*, ^3J = 7.0, H–C(1)); 4.15 (*t*, ^3J = 3.5, H–C(7)); 4.04 (br. *q*, ^3J = 6.5, H–C(3')); 3.02 (*m*, H–C(5)); 2.75 (*dd*, ^3J = 5.0, ^2J = 18.5, 1 H–C(4)); 2.50 (*m*, H–C(6)); 2.42 (*dd*, ^3J = 11.5, ^2J = 18.5, 1 H–C(4)); 2.10 (*d*, ^2J = 15, H_{endo}–C(8)); 1.88 (*ddd*, ^3J = 7.0, 3.5, ^2J = 15, H_{exo}–C(8)); 1.59–1.49 (*m*, 2 H–C(4')); 1.48–1.15 (*m*, 2 H–C(5'), 2 H–C(6'), 2 H–C(7')); 0.82 (*m*, 3 H–C(8')); 0.80 (*s*, *t*-BuSi); 0.01, 0.00 (2*s*, Me_2Si). ^{1}H-NMR (250 MHz, C_6D_6): 4.51 (*t*, ^3J = 7.0, H–C(1)); 4.06 (br. *q*, ^3J = 6.0, H–C(3')); 3.80 (*t*, ^3J = 3.5, H–C(7)); 1.98 (*dt*, ^3J = 8.5, 3.5, H–C(6)). ^{13}C-NMR (62.9 MHz, $CDCl_3$): 177.57 (*s*); 136.57 (*d*); 126.96 (*d*); 84.69 (*d*); 76.53 (*d*); 72.62 (*d*); 50.20 (*d*); 42.05 (*t*); 41.48 (*d*); 37.00 (*t*); 31.53 (*t*); 31.04 (*t*); 25.49 (*q*); 24.94 (*t*); 22.40 (*t*); 17.83 (*s*); 13.86 (*q*); −5.12 (*q*).

18: Colorless oil. ^{1}H-NMR (250 MHz, $CDCl_3$): 5.82 (*dd*, ^3J = 8.5, 15.5, H–C(1')); 5.59 (*dd*, ^3J = 7.0, 15.5, H–C(2')); 5.08 (br. *t*, ^3J = 7.0, H–C(1)); 4.17 (*t*, ^3J = 3.6, H–C(7)); 4.09 (br. *q*, ^3J = 6.5, H–C(3')); 3.04 (*m*, H–C(5)); 2.82 (*dd*, ^3J = 5.0, ^2J = 18.5, 1 H–C(4)); 2.50 (*m*, H–C(6)); 2.49 (*dd*, ^3J = 11.5, ^2J = 18.5, 1 H–C(4)); 2.13 (*d*, ^2J = 15.0, H_{endo}–C(8)); 1.90 (*ddd*, ^3J = 7.0, 3.6, ^2J = 15, H_{exo}–C(8)); 1.75 (br. *s*, OH); 1.62–1.41 (*m*, 2 H–C(4')); 1.40–1.18 (*m*, 2 H–C(5'), 2 H–C(6'), 2 H–C(7')); 0.86 (*m*, 3 H–C(8')); 0.85 (*s*, *t*-BuSi); 0.03, 0.01 (2*s*, $2Me_2Si$). ^{1}H-NMR (250 MHz, C_6D_6): 4.55 (*t*, ^3J = 7.0, H–C(1)); 4.08 (br. *q*, ^3J = 7.0, H–C(3')); 3.79 (*t*, ^3J = 3.5, H–C(7)); 2.00 (*dt*, ^3J = 8.5, 3.5, H–C(6)). ^{13}C-NMR (62.9 MHz, $CDCl_3$): 177.68 (*s*); 136.68 (*d*); 127.47 (*d*); 84.80 (*d*); 76.99 (*d*); 72.95 (*d*); 50.51 (*d*); 42.18 (*t*); 41.59 (*d*); 37.17 (*t*); 31.68 (*t*); 31.11 (*t*); 25.62 (*q*); 25.14 (*t*); 22.52 (*t*); 17.97 (*s*); 13.97 (*q*); −4.72 (*q*); −4.99 (*q*).

17/**18**: Anal. calc. for $C_{21}H_{38}SiO_4$ (382.62): C 65.92, H 10.01, Si 7.34; found: C 65.87, H 9.95, Si 7.36.

(±)-12-Epi-PGF$_{2\alpha}$ (= (9RS,11SR,15RS,5Z,13E)-9,11,15-Trihydroxy-12-epiprosta-5,13-dien-1-oic Acid; **3**). To a cooled (−60°) soln. of **17** (1.00 g, 2.61 mmol) in dry toluene (20 ml) was added under N_2 1.2M DIBAL-H in toluene (4.8 ml, 5.7 mmol). The mixture was stirred at −60° for 15 min and poured into Et_2O (20 ml). Then 1M aq. potassium sodium tartrate (10 ml) was added to complex aluminium salts. The mixture was stirred for 1 h and filtered through *Celite*. The org. layer was dried ($MgSO_4$) and evaporated. FC (AcOEt/p.e. 1:3) gave the lactol (791 mg, 83%). Colorless oil which was used without purification in the next step. To a suspension of (4-carboxybutyl)triphenylphosphonium bromide (461 mg, 1.04 mmol) in dry toluene (30 ml) was added dropwise at r.t. 15% KHMDS in toluene (2.07 ml, 1.56 mmol). The red-orange ylide was stirred for 30 min and a soln. of the crude lactol (100 mg, 0.26 mmol) in toluene (5 ml) added. The mixture was stirred for 4 h and quenched with 1M NaCl (20 ml). The aq. layer was acidified with 2M HCl and extracted with CH_2Cl_2 (2 × 10 ml). The org. layers were dried ($MgSO_4$) and evaporated FC (AcOEt/p.e. 1:1) gave *11-O*-silylated 12-epi-PGF$_{2\alpha}$ (89 mg, 73%). ^{1}H-NMR (400 MHz, $CDCl_3$): 5.81 (*dd*, ^3J = 15.6, 10.5, H–C(13)); 5.58–5.48 (*m*, H–C(14), *H*C=CH); 5.40–5.30 (*m*, HC=C*H*); 4.60 (br. *s*, 2 OH); 4.29–4.09 (*m*, H–C(9), H–C(11), H–C(15)); 2.66 (*dt*, ^3J = 10.0, 5.6, H–C(8)); 2.32 (*dt*, *J* = 7.0, 2.8, 2 H); 2.29–1.88 (*m*, 7 H); 1.62–1.48 (*m*, 2 H); 1.38–1.20 (*m*, 6 H); 0.92–0.80 (*m*, 3 H–C(20), *t*-BuSi); 0.06, 0.02 (2*s*, Me_2Si).

A soln. of the crude 11-*O*-silylated 12-epi-PGF$_{2\alpha}$ (85 mg, 0.18 mmol) was treated with 0.33M aq. THF/HCl 2:1.5 (5 ml) and stirred overnight. Then 2M HCl (3 ml) and brine (1 ml) were added the aq. layer was extracted with CH_2Cl_2 (3 × 5 ml) and the combined org. phase dried ($MgSO_4$) and evaporated. FC (AcOEt/MeOH/AcOH 90:10:0.5) gave **3** (52 mg, 81%). White solid. M.p. 79–80°. ^{1}H-NMR (400 MHz, $CDCl_3$): 5.84 (*dd*, ^3J = 15.1, 10.4, H–C(13)); 5.53 (*dd*, ^3J = 15.1, 6.2, H–C(14)); 5.49–5.32 (*m*, H–C(5), H–C(6)); 4.22 (*m*, H–C(9), H–C(11)); 4.16 (br. *q*, ^3J = 6.4, H–C(15)); 3.75 (br. *s*, 3 OH); 2.77 (*m*, H–C(12)); 2.33 (*t*, ^3J = 6.5, 2 H); 2.37–2.27 (*m*, H–C(7)); 2.22–1.92 (*m*, 5 H); 1.89 (*ddd*, ^3J = 4.0, 1.5, ^2J = 16.1, H_{exo}–C(10)); 1.70 (*m*, 2 H); 1.52 (*m*, 2 H); 1.40–1.22 (*m*, 6 H); 0.88 (*t*, ^3J = 6.8, 3 H–C(20)). ^{13}C-NMR (62.9 MHz, $CDCl_3$): 177.77 (*s*); 136.99 (*d*); 129.87 (*d*); 129.31 (*d*); 128.67 (*d*); 75.40 (*d*); 73.53 (*d*); 72.64 (*d*); 49.95 (*d*); 47.67 (*d*); 42.51 (*t*); 36.83 (*t*); 32.97 (*t*); 31.77 (*t*); 26.37 (*t*); 25.24 (*t*); 24.45 (*t*); 24.24 (*t*); 22.65 (*t*); 14.67 (*q*). These spectra are in good agreement with the ones reported [7].

(±)-12,15-Diepi-PGF$_{2\alpha}$ (= (9RS,11SR,15SR,5Z,13E)-9,11,15-Trihydroxy-12-epiprosta-5,13-dien-1-oic Acid; **4**). As described for **3**, **18** (1.00 g, 2.61 mmol) was treated with DIBAL-H and (4-carboxybutyl)-triphenylphosphonium bromide/KHMDS: 11-*O*-silylated 12,15-diepi-PGF$_{2\alpha}$ (89 mg, 73%). ^{1}H-NMR (400 MHz, $CDCl_3$): 5.82 (*dd*, ^3J = 15.2, 10.2, H–C(13)); 5.59 (*m*, *H*C=CH); 5.43 (*dd*, ^3J = 15.2, 8.2, H–C(14)); 5.39 (*m*,

HC=C*H*); 4.90 (br. *s*, 2 OH); 4.28–4.11 (*m*, H–C(9), H–C(11), H–C(15)); 2.63 (*dt*, ^3J = 10.0, 5.3, H–C(8)); 2.32 (*dt*, ^3J = 7.2, 2.0, 2 H); 2.24–2.16 (*m*, H); 2.11 (br. *q*, ^3J = 7.4, 2 H); 2.07–1.95 (*m*, 1 H); 1.95 (*t*, ^3J = 3.7, 2 H); 1.72–1.42 (*m*, 4 H); 1.40–1.23 (*m*, 6 H); 1.01–0.82 (*m*, 3 H–C(20), *t*-BuSi); 0.07, 0.02 (2*s*, Me_2Si).

The crude 11-*O*-silylated 12,15-diepi-$PGF_{2\alpha}$ (85 mg, 0.18 mmol) was treated with THF/0.33M aq. HCl 2:1.5 (5 ml) and worked up as described for **3**, yielding **4** (52 mg, 81%). Colorless oil. ^{1}H-NMR (600 MHz, $CDCl_3$): 5.88 (*dd*, ^3J = 15.1, 10.5, H–C(13)); 5.58 (*dd*, ^3J = 15.1, 5.7, H–C(14)); 5.46 (*m*, *H*C=CH); 5.38 (*m*, HC=C*H*); 4.73 (br. *s*, 3 OH); 4.28–4.10 (*m*, H–C(9), H–C(11), H–C(15)); 2.73 (*ddd*, ^3J = 10.5, 8.5, 6.5, H–C(12)); 2.36–2.23 (*m*, 1 H); 2.31 (*t*, ^3J = 6.5, 2 H); 2.19 (*dt*, ^3J = 6.0, ^3J = 14.5, H–C(10)); 2.15–2.09 (*m*, 2 H); 2.09–2.02 (*m*, 1 H); 1.86 (*ddd*, ^3J = 4.5, 1.8, ^2J = 14.4, H–C(10)); 1.72–1.61 (*m*, 2 H); 1.58–1.47 (*m*, 2 H); 1.45–1.20 (*m*, 6 H); 0.86 (*t*, ^3J = 6.6, 3 H–C(20)). ^{13}C-NMR (62.9 MHz, $CDCl_3$): 177.18 (*s*); 136.78 (*d*); 129.99 (*d*); 129.29 (*d*); 127.62 (*d*); 75.26 (*d*); 73.29 (*d*); 72.33 (*d*); 50.18 (*d*); 47.03 (*d*); 45.54 (*t*); 37.07 (*t*); 32.65 (*t*); 31.75 (*t*); 26.23 (*t*); 25.14 (*t*); 24.33 (*t*); 24.22 (*t*); 22.58 (*t*); 14.03 (*q*). Anal. calc. for $C_{20}H_{34}O_5$ (354.49): C 67.77, H 9.67; found C 67.84, H 9.59.

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