An Improved Dienophile-Induced Access to Enantiopure 2,4-Dideoxysugar Lactones via Hetero Diels–Alder Reaction: Synthesis of the (+)-Lactone Moiety of Compactin

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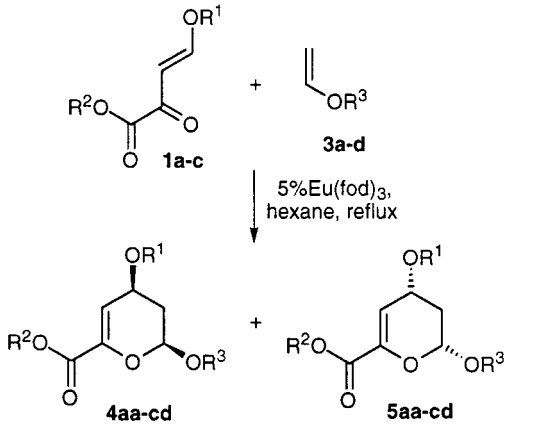
Dedicated to the memory of Professor J. M. Poirier

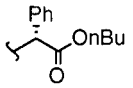
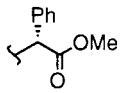
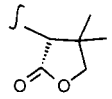
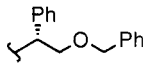
Abstract: Polystereocontrolled access to **4**-type heterocycloadducts was consistently improved by using a new 4-oxy-substituted 1-oxabutadiene, methyl (*E*)-*tert*-butoxymethylenepyruvate (**1c**). Obtained in both enantiomeric forms with high diastereomerical purity, these adducts led to diprotected 2,4-dideoxyglucose **10** and -gluconolactone **12** in both L and D series in high yields. Epimerization of (–)-**12** via intramolecular Mitsunobu inversion gave a straightforward access to the lactone moiety (+)-**16** of compactin.

Key words: methyl (*E*)-*tert*-butoxymethylenepyruvate, chiral enol ethers, (4+2) heterocycloaddition, intramolecular Mitsunobu reaction, (+)-compactin lactone

In the course of our stereochemical investigations in the field of inverse electron demand hetero Diels–Alder (IEDHDA) reactions,[1] we have reported since 1993 on the use of *O*-vinylmandelic esters to effect efficient asymmetric *endo*-selective cycloaddition with various 2-activated 1-oxabutadienes in Danishefsky-type[2] catalytic conditions.[3] In a context where promising enantioselective approaches are few,[4] this dienophile-induced methodology proved interesting when applied to unsubstituted vinyl ethers. Heterodiene-induced methodologies, of great value for various types of dienophiles (e.g. β-substituted enol ethers,[5] styrenic compounds[6, 7]), did not give good results in this specific case (dr ca. 2:1).[5c, 6, 8] Thus, starting from both enantiomers of butyl *O*-vinylmandelate (**3a**) and heterodiene **1b**, we recently disclosed an asymmetric route to protected L- and D-2-deoxysugars via diastereopure adduct **4ba** (Scheme 1, Table 1).[3c]

The fair diversity concerning the functionalization of type-4 adducts together with the ability to perform selective *O*-protections prompted us to investigate other valuable applications, namely in the 2,4-dideoxy series. For this purpose, we searched for a new analog of **1b**, that



1	R^1	R^2	3	R^3	4/5
1a	Et	Et	**(-)-3a**		**aa**
1b	Bn	Me	**(-)-3a**		**ba**
1c	*t*-Bu	Me	**(-)-3a**		**ca**
1c	*t*-Bu	Me	**(-)-3b**		**cb**
1c	*t*-Bu	Me	**(+)-3c**		**cc**
1c	*t*-Bu	Me	**(-)-3d**		**cd**

Scheme 1

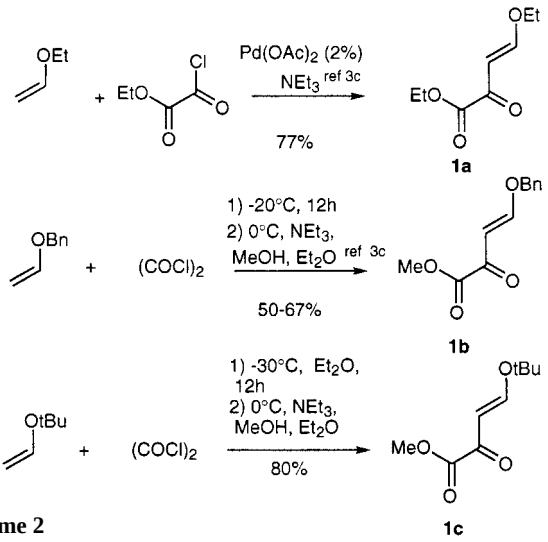
Table 1. Syntheses of Heteroadducts **4** from l-Oxabutadienes **1a–c** and Vinyl Ethers **3a–d**

Entry	Adduct	Starting Material (Equiv)	Time (d)	Global Adduct			Major adduct		
				Yield[a] (%)	Diastereomeric Ratio		Yield[a] (%)	Diastereomeric Ratio	
					endo/*exo*	Facial		*endo*/*exo*	Facial
1	**4aa**	**1a** (1.0) + (–)-**3a**	3	87	> 99:1	95:5	87	> 99:1	95:5
2	**4ba**	**1b** (1.7) + (–)-**3a**	3	75	> 99:1	93:7	61	> 99:1	> 99:1
3	**4ca**	**1c** (1.0) + (–)-**3a**	3	81	93:7	93:7	54	> 99:1	> 99:1
4	**4cb**	**1c** (1.0) + (–)-**3b**	3	85	> 99:1	90:10	70	> 99:1	98:2[b]
5	**4cc** or **5cc**	**1c** (1.0) + (+)-**3c**	7	70	> 99:1	77:23	53	> 99:1	> 99:1
6	**4cd** or **5cd**	**1c** (1.0) + (–)-**3d**	3	82	> 99:1	78:22	82	> 99:1	78:22

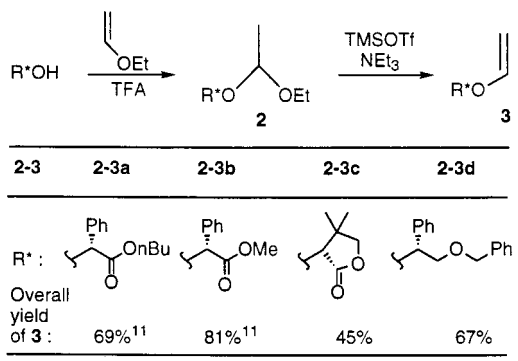
[a] Isolated yield after chromatography. [b] Adduct **4cb** had a facial dr > 99:1 after one recrystallization from petroleum ether (yield 63%).

would be more effective and liable to introduce the 3-hydroxy group in a non-hydrogenolizable protected form on the carbohydrate skeleton. We now report that methyl (*E*)-*tert*-butoxymethylenepyruvate (**1c**), readily obtained in high yield from commercial *tert*-butyl vinyl ether, acted as a superior electron-deficient heterodiene.

The preparation of the new compound **1c** was based, as for **1b**, on Effenberger's method[9] with some modifications related to the higher reactivity of **1c** towards oxalyl chloride: addition of *tert*-butyl vinyl ether to oxalyl chloride in diethyl ether was carried out at –30 °C and the intermediate monochloride was then quenched with methanol at 0 °C in excess triethylamine[10] (Scheme 2). Starting from stoichiometric amounts of both reactants, rapid chromatography of the crude product gave the desired **1c** in 76% yield; the side products, separable from the latter, being the (*Z*)-isomer of **1c** (8%) and dimethyl oxalate (12%). Yields were somewhat improved when using a slight excess of oxalyl chloride, but contamination of the purified product by dimethyl oxalate also increased. Nevertheless, none of these byproducts was found to exert a negative influence or interfere during the further cycloaddition step and, besides, they could be easily removed at this stage. This preparation method has been successfully scaled-up to over 100 mmol without an effect on the rate level. Product **1c** is more stable than its benzyl analog **1b**: it was completely characterized by spectroscopic and elemental data and may be stored in its frozen form for several months.



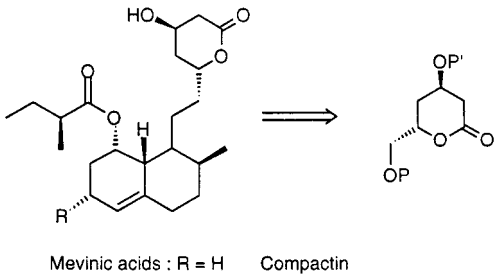
Scheme 2



Scheme 3

All the enol ethers **3** were prepared via the corresponding mixed acetals **2** according the mercury-free preparation method we recently described (Scheme 3).[11] $Eu(fod)_3$-catalyzed *endo*-heterocycloaddition of **1c** with chiral enol ethers **3a,b** occurred under mild conditions (60 °C) and with efficient facial diastereocontrol (Scheme 1, Table 1). These reaction conditions were found to be nondegradative towards oxabutadiene **1c** even after a 3-day period. Consequently, high yields were obtained in all cases without using an excess of this component (Table 1, entries 3, 4). Moreover, decreasing the relative amount of catalyst from typically 5% to less than 2% only affected the reaction time. Facial selectivities remained at comparable levels as for adducts prepared from heterodiene **1a** and **lb** and interestingly the major isomer **4** was isolated with high diastereomeric purity in fair to good yields. Although vinyl ethers derived from mandelic acid proved to be efficient in achieving asymmetric induction,[12] we looked at other new chiral vinyl ethers **3c** and **3d**, prepared respectively in 45% and 67% yield from the corresponding alcohols by our standard method. With the vinyl ether **3c** derived from pantolactone, the reaction was sluggish and facial control was lower, nevertheless diastereomeric separation by chromatography was easily performed (entry 5). Finally, vinyl ether **3d** of monoprotected phenyl ethanediol **11** proved to be inefficient (entry 6). These results confirm the crucial role played by the ester function of the dienophile in the production of a stereodifferentiating transition state relayed by intermolecular Eu complexation. Its absence in the reduced analog **3d** of benzyl α-phenyl-α-(vinyloxy) acetate had a negative influence on the facial control during the cycloaddition process. Moreover, the conformational strain attributed to the carbonyl function in a five-membered ring as in **3c** might be responsible for the lack of reactivity and selectivity observed.

Considering the double stereocontrolled large-scale access to compounds **4ca**, **4cb**, and **4cc** in 37, 57, and 24% overall yields, respectively, from *tert*-butyl vinyl ether (or mandelic acid) and in both enantiomeric forms for the former two adducts, we anticipated using this asymmetric IEDHDA methodology as the key step for a short and convenient synthesis of the lactonic moiety of (+)-compactin and (+)-mevinolin (Scheme 4).

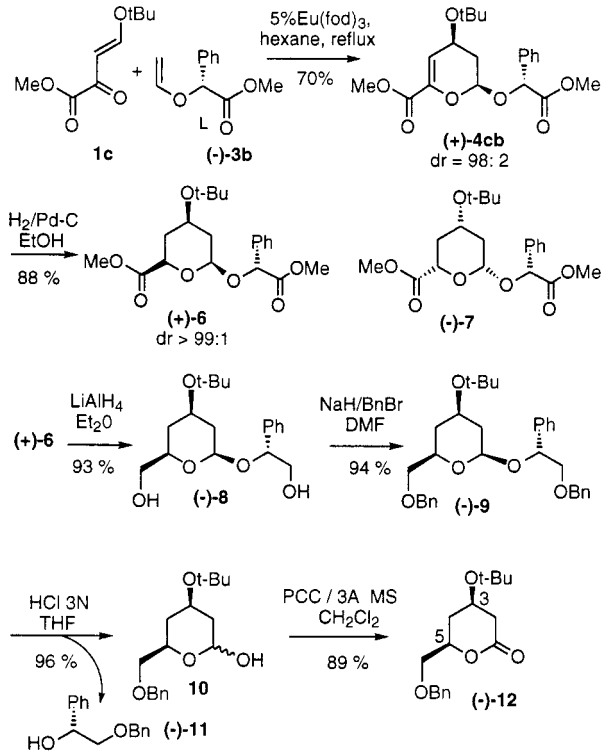


Scheme 4

Although widely investigated by the chiral pool approach or asymmetric processes,[13] syntheses of this type of lactone by new synthetic ways remains of interest owing to the importance of mevinic acids as potent inhibitors of

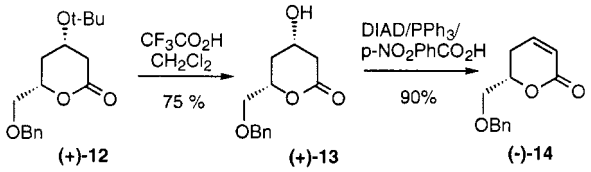
HMGCoA reductase in the biosynthesis of cholesterol.[14] Specifically acting in its open form as a mimic of mevalonic acid, this lactonic part has been retained in the elaboration of valuable and more accessible analogs of (+)-compactin, in which the decalin moiety was replaced by an achiral aromatic subunit. In order to elaborate such structures in a convergent way, orthogonal OH-protection is required on the starting dihydroxylactonic synthon, which is easily and precisely arranged in a *de novo* synthetic plan such as ours.

Starting from the most accessible adduct **4cb** in each enantiomeric form, catalytic hydrogenation afforded the *cis* tetrahydropyranyl derivative **6** as a single crystalline diastereomer in high yield (Scheme 5). This total diastereomeric purity was established after identification of the hydrogenated product **7** of diastereomer **5cb**, obtained by catalytic hydrogenation of a 90:10 mixture of **4cb**/**5cb** and chromatographic separation from **6**. After $LiAlH_4$ reduction of diester **6** to the diol **8**, benzylation gave high yields of **9**. Removal of the chiral auxiliary in a reduced form (e.g. **11**) by acidic hydrolysis followed by PCC oxidation of the resulting lactol **10** led to the diprotected *cis* lactone **12** in 66% overall yield from adduct **4cb**.



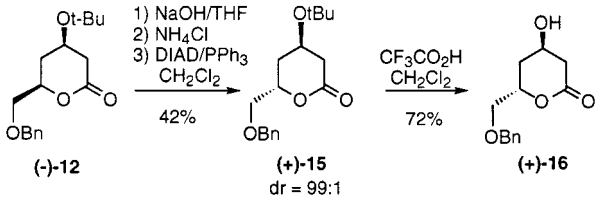
Scheme 5

At this stage, we had to perform the critical transformation of **12** into its *trans* isomer. For this purpose, inversion of the configuration at C-5 in lactone (–)-**12** or at C-3 in lactone (+)-**12** were successively investigated. Starting from lactone (+)-**12** removal of the *O-tert*-butyl group readily occurred using trifluoroacetic acid in dichloromethane (Scheme 6). Not so surprisingly, all our attempts to effect Mitsunobu inversion at C-3 using either standard (PPh_3, benzoic acid, DIAD) or modified (PPh_3, *p*-nitrobenzoic acid, DIAD)[15] conditions failed, leading in all cases to dehydration product (–)-**14**. Moriarty's alternative procedure[16] in which an intermediate triflate is treated with KNO_2 in DMF in the presence of 18-crown-6 gave the same result. Considering the efficiency of this transformation using an acetal analog,[17] we must conclude that the α-proton acidity of lactone (+)-**12** favors the elimination of the intermediate oxyphosphonium salt (or of the triflate in the last attempt) over the S_N2 process.



Scheme 6

On the other hand, a successful approach consisted of effecting inversion at C-5 in lactone (–)-**12** by means of an intramolecular Mitsunobu reaction on the corresponding δ-hydroxy acid (Scheme 7). This last intermediate was readily produced after saponification of (–)-**12** in excess aqueous NaOH and careful regeneration of the acidic function with ammonium chloride. Treatment of this δ-hydroxy acid with PPh_3 and DIAD cleanly led to a mixture of the desired *trans* lactone (+)-**15** and starting lactone (–)-**12** in a 9:1 ratio. Chromatographic purification afforded the *trans* lactone (+)-**15** with high diastereomeric purity (99:1) in a 42% unoptimized yield (more than 80% yield with regard to the consumed starting material). Noteworthy, to the best of our knowledge, this interconversion between *cis* and *trans* lactones via intramolecular Mitsunobu inversion at the C-5 stereogenic center seems to have been only performed in the opposite way (from *trans* to *cis*)[18] in which the final product has the more stable configuration. Finally, CF_3CO_2H removal of the *tert*-butyl protection at C-3 gave the β-hydroxylactone (+)-**16**, whose properties were found to be in full accordance with literature data.[19]



Scheme 7

All reagents were of commercial quality from freshly opened source or distilled before use. Mps were determined on a Reichert Thermovar apparatus and are uncorrected. ^1H (400 MHz) and ^{13}C (100 MHz) NMR spectra were recorded on a Bruker AC 400 instrument in $CDCl_3$ using TMS for ^1H spectra and the solvent for ^{13}C spectra as internal references. IR spectra were recorded on a Mattson Genesis spectrophotometer. Specific optical rotations were measured with a Per-

kin–Elmer Model 241 polarimeter. HRMS were performed on a Varian MAT311 at the C. R. M. P. O. (Rennes). Low resolution MS were run on a Fisons MD 800 detector. Elemental analyses were performed at the C. N. R.S (Gif-sur-Yvette). Flash chromatography was run on SDS silica gel A C. C. (230–400 mesh).

Ethyl (*E*)-Ethoxymethylenepyruvate (1a):[20]
To a solution of $Pd(OAc)_2$ (46 mg, 0.2 mmol) and Et_3N (4.2 mL, 30 mmol) in ethyl vinyl ether (10 mL, 110 mmol) was added dropwise ethyl oxalyl chloride (2.3 mL, 20 mmol). After refluxing for 18 h followed by dilution with Et_2O, filtration and evaporation, the crude product was distilled (bp 90 °C/0.7 Torr; Lit.[20] bp 89–90 °C/0.6 Torr) to afford heterodiene **3a**, as a yellow oil (3.95 g, 77%).

Methyl (*E*)-Benzyloxymethylenepyruvate (1b):
To vigorously stirred oxalyl chloride (4.76 g, 37.5 mmol) was added dropwise benzyl vinyl ether (3.35 g, 25 mmol) at –20 °C. After stirring at –20 °C overnight, the resulting dark yellow oil was transferred dropwise with a needle into an ice-cooled solution of MeOH (2.5 mL) and Et_3N (25 mL) in Et_2O (100 mL). The white thick suspension so obtained was quickly filtered and the white solid was removed. After evaporation of volatile materials, the yellow crude product was rapidly chromatographed (EtOAc/cyclohexane, from 2:8 to 4:6), giving a mixture of **3b** (yellow oil, 3.3 g, 60%) (R_f 0.60, EtOAc/cyclohexane, 4:6) together with 20 to 40 mol% of dimethyl oxalate.

Methyl (*E*)-tert-Butoxymethylenepyruvate (1c):
To a stirred solution of oxalyl chloride (15.2 g, 120 mmol) in Et_2O (5 mL), was added a solution of *tert*-butyl vinyl ether (12.0 g, 120 mmol) in Et_2O (5 mL) at –30 °C. After stirring at –30 °C overnight, the yellow oily reaction medium was transferred dropwise with a needle into an ice-cooled solution of MeOH (10 mL) and Et_3N (80 mL) in Et_2O (600 mL). The white thick suspension so obtained was quickly filtered and the white solid was removed. After evaporation of volatile materials, the yellow crude product was rapidly chromatographed (EtOAc/cyclohexane 6:4), giving **3c** (R_f 0.50, EtOAc/cyclohexane, 6:4, 17.1 g corrected mass, 76%) as a yellow oil contaminated by less than 10 mol% of dimethyl oxalate (**3c** was used without further purification in all cycloadditions described above). For analytical requirements, further chromatography using Et_2O/petroleum ether 1:1 as the eluent gave a sample of **3c** (R_f 0.32, Et_2O/petroleum ether 1:1) free from dimethyl oxalate.
Anal. Calcd for $C_9H_{14}O_4$: C 58.05; H 7.58; Found: C 58.04; H 7.69.

Methyl (–)-(*R*)-α-Phenyl-α-(Vinyloxy)acetate (3b); Typical Procedure:
To a solution of methyl (–)-(*R*)-mandelate, $[\alpha]_D^{20}$ –144 (*c* = 1, MeOH), (6.7 g, 40 mmol) in ethyl vinyl ether (75 mL) were slowly added a few drops of trifluoroacetic acid (~0.25 mL). After stirring for 5 d, addition of an excess of anhyd Na_2CO_3, filtration and evaporation gave mixed acetal **2b** as a colorless oil (9 g, 95%) which was next used without further purification.
2b: 2 isomers ratio 1:1; bp 108–112 °C/0.05 Torr.
^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.12 (m, 3H), 1.35 (d, 3H), 3.40–3.60 (m, 2H), 3.72 (s, 3H), 4.80 and 4.95 (g, 1H), 5.70 and 5.78 (s, 1H), 7.30–7.50 (m, 5H).
To a solution of mixed acetal **2b** (9 g, 37.5 mmol) in anhyd CH_2Cl_2 (40 mL) was added under argon at 0 °C, Et_3N (6.1 g, 60 mmol, 1.6 equiv) and then dropwise TMSOTf (10.8 g, 48.7 mmol, 1.3 equiv). After stirring overnight with slow warming to r.t., 1 M aq NaOH (12 mL) was added and the mixture was then diluted with petroleum ether (400 mL). After decanting, the organic layers were dried ($MgSO_4$) and evaporated and the product purified by column chromatography (5% EtOAc/cyclohexane), thus giving pure vinyl ether **3b** as a colorless oil (6.12 g, 85%) which crystallized on freezing; mp 35 °C; $[\alpha]_D^{20}$ –106 (*c* = 1.01, MeOH) (Lit[3b] $[\alpha]_D^{20}$ –106 (*c* = 1.43, MeOH)).
Anal. Calcd for $C_{11}H_{12}O_3$: C 68.73; H 6.29; Found: C 68.63; H 6.06.

Table 2. Selected ^{1}H NMR Data [δ, *J* (Hz)] of *endo*-Adducts **4** and **5**.

Product	$\delta_{1\text{-H}}$	$^3J_{1,2a}$	$^3J_{1,2e}$	$\delta_{3\text{-H}}$	$\delta_{4\text{-H}}$
4aa	5.43	5.1	2.9	4.16	6.21
5aa	5.05	6.0	3.0	4.28	6.19
4ba	5.40	4.5	2.9	4.19	6.23
5ba	5.05	6.0	2.5	4.40	6.21
4ca	5.34	6.7	2.6	4.33	6.02
5ca	5.06	2.9	1.5	4.40	6.02
exo-**ca**[a]	5.45	5.2	2.9	4.33	6.23
4cb	5.36	6.6	2.5	4.31	6.00
5cb	4.98	7.9	2.4	4.26	5.96
4cc	5.63	5.8	2.7	4.26	6.08
5cc	5.38	7.9	2.3	4.33	6.02

[a] Derived from **1c** and **3a**

Cycloadduct (+)-(2*S*,4*S*,1′*R*)-(4cb); Typical Procedure:
Vinyl ether (–)-(*R*)-**3b** (5.8 g, 30 mmol), heterodiene **1c** (5.6 g, 30 mmol) and Eu(fod)$_3$ (0.93 g, 0.9 mmol) in a mixture of petroleum ether (90 mL) and toluene (10 mL) were stirred for 60 h under reflux. After cooling and evaporation of the solvents, the brownish oily residue was chromatographed on silica gel as described below:
(a) Using EtOAc/cyclohexane (3:7) as the eluent furnished a mixture of *endo* adducts **4cb** and **5cb** (9.5 g, 85%, **4cb**/**5cb** 90:10) as an oil (R_f 0.44, EtOAc/cyclohexane 4:6).
(b) Using Et_2O/petroleum ether (6:4) as the eluent furnished quasi-pure adduct (+)-**4cb** (8.0 g, 70%, **4cb**/**5cb** 98:2) as a solid; mp 93–95 °C; $[\alpha]_D^{20}$ +11.0 (*c* = 0.55, acetone); R_f 0.51 (Et_2O/petroleum ether 8:2). A single recrystallization from petroleum ether gave pure adduct (+)-**4cb** (7.2 g, 63%, dr >99:1) ; mp 94–96 °C; $[\alpha]_D^{20}$ +11.5 (*c* = 0.55, acetone).
Anal. Calcd for $C_{20}H_{26}O_7$: C 63.48; H 6.93; Found: C 63.31; H 6.84.

Spectral data for diastereomer (2*R*,4*R*,1,*R*)-**5cb**: R_f 0.44 (Et_2O/petroleum ether 8:2).
^{1}H NMR ($CDCl_3$): δ = 1.20 (s, 9H, *t*-Bu), 2.1–2.2 (m, 2H, 2-H), 3.69 (s, 3H), 3.78 (s, 3H), 4.26 (dt, 1H, 3-H), 4.98 (dd, 1H, *J* = 7.9, 2.4 Hz, 1-H), 5.38 (s, 1H, 1′-H), 5.96 (d, 1H, *J* = 2.8 Hz, 4-H), 7.3–7.55 (m, 5H, Ar-H).
^{13}C NMR ($CDCl_3$): δ = 28.1, 35.8, 52.2, 52.4, 61.3, 74.6, 78.2, 96.8, 114.7, 127.7, 128.6, 129.0, 135.2, 141.6, 162.7, 170.3.

Enantiomer (–)-(2*R*,4*R*, 1′*S*)-**4cb**; $[\alpha]_D^{20}$ –11 (*c* = 0.55, acetone), was obtained from (+)-(*S*)-**3b** and **1c** by the same procedure as above.

Tetrahydropyranyl Diester (+)-(2*S*,4*R*,6*R*,1′*R*)-6:
A solution of dihydropyran (+)-(2*S*,4*S*,1′*R*)-**4cb** (7.6 g, 20 mmol, dr **4**/**5** 98:2) in 95% EtOH (80 mL) was stirred with 10% Pd/C (0.5 g) under H_2 (3 bar) for 15 h at r.t. After filtration through Celite and drying ($MgSO_4$), the concentrated product was diluted in boiling petroleum ether, and gave after cooling pure diester (+)-**6** (6.7 g, 88%, dr >99:1) as a crystalline solid; mp 131 °C; white needles; $[\alpha]_D^{20}$ + 10 (*c* = 0.65, acetone).
^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.21 (s, 9H, Me_3C), 1.56 (≃ q, J ≃ 12 Hz, 1H), 1.58 (m, 1H), 2.08 (m, 1H), 2.22 (m, 1H), 3.72 (m, 1H), 3.73 (s, 3H), 3.77 (s, 3H), 4.01 (dd, *J* = 12.2 and 1.2 Hz, 1H), 4.68 (dd, *J* = 9.6 and 1.9 Hz, 1H), 5.52 (s, 1H), 7.32 (m, 3H), 7.44 (m, 2H).
^{13}C NMR (100 MHz, $CDCl_3$): δ = 28.4, 36.9, 40.1, 52.3, 52.3, 65.9, 71.7, 74.2, 76.7, 98.8, 127.3, 128.4, 128.6, 135.9, 170.4, 171.5.
Anal. Calcd for $C_{20}H_{28}O_7$: C 63.14; H 7.42; Found: C 62.95; H 7.44.
MS(EI): *m/z* (%) = 215 (M^+-OCH(Ph)CO_2Me, 32), 159 (39), 149 (36), 141 (100), 57 (64).

Table 3. Spectroscopic Data and Physical Constants of New Compounds **1**, **3**, **4** and **5**

Product	R_f[a]	$[\alpha]_D^{20}$ (*c*, Solvent)	IR ν (cm^{-1})	MS *m/z* (%)	^1H NMR ($CDCl_3$) δ, *J* (Hz)	^{13}C NMR ($CDCl_3$) δ
1b	0.60 (A: 6:4)	–	1748, 1691 (C=O), 1654, 1608 (C=C)	–	3.88 (s, 3H, MeO), 5.05 (s, 2H, CH_2O), 6.33 (d, 1H, *J* = 12.5, 3-H), 7.35–7.43 (m, 5H, Ar-H), 8.00 (d, 1H, *J* = 12.5, 4-H)	52.9 (Me), 74.1 (CH_2Ph), 102.6 (C-3), 127–135 (C-Ar), 162.7 (C-1), 166.9 (C-4), 181.7 (C-2)
1c	0.50 (A: 6:4)	–	1733 (C=O), 1668 (C=C)	–	1.41 (s, 9H, *t*-Bu), 3.88 (s, 3H, MeO), 6.26 (d, 1H, *J* = 11.9, 3-H), 8.08 (d, 1H, *J* = 11.9, 4-H)	28.2 (Me_3C), 52.8 (MeO), 82.2 (C-O), 104.4 (C-3), 163.0 (C-1), 163.8 (C-4), 181.8 (C-2)
3c	0.45 (A: 8:2)	+ 54 (2.2, acetone) + 34.7 (0.95, CH_2Cl_2)	1791 (C=O), 1641, 1625 (C=C)	(EI): 156 (M+, 16), 141 (57), 113 (22), 41 (100). HRMS calcd for $C_8H_{12}O_3$ 156.0786, found: 156.0780	1.15 (s, 3H, Me), 1.25 (s, 3H, Me), 3.95 (d, 1H, *J* = 8.9, 4-H), 4.03 (d, 1H, *J* = 8.9, 4-H), 4.17 (s, 1H, 2-H), 4.20 (dd, 1H, *J* = 2.3, 6.5, 2′-H_{cis}), 4.54 (dd, 1H, *J* = 2.3, 13.9, 2′-H_{trans}), 6.46 (dd, 1H, *J* = 6.5, 13.9, 1′-H)	19.2 (Me), 23.1 (Me), 40.4 (C-3), 76.0, (C-4), 81.1 (C-2), 90.9 (C-2′), 150.6 (C-1′), 173.4 (C=O)
3d	0.70 (A: 8:2)	–34 (1.5, MeOH)	1637, 1617 (C=C)	(CI): 211 (MH^+-OC_2H_3, 5), 193 (15), 133 (5), 121 (9), 105 (8), 91 (100)	3.60 and 3.63 (dd, 1H, *J* = 3.7, 10.7, 2-H), 4.00 (dd, 1H, *J* = 1.7, 6.6, 2′-H_{cis}), 4.26 (dd, 1H, *J* = 1.7, 14.2, 2′-H_{trans}), 4.54 and 4.65 (d, 1H, *J* = 12.2, CH_2Ph), 4.98 (dd, 1H, *j* = 3.7, 7.8, 1-H), 6.40 (dd, 1H, *J* = 6.6, 14.2, 1′-H), 7.30 (m, 10H, Ph)	73.4, 74.1 (CH_2O), 80.6 (C-1), 89.6 (C-1′), 126–128 (CH-Ar), 138.0 (C-Ar), 138.6 (C-Ar), 150.7 (C-2′)
4aa/ 5aa (95:5)	0.56 (A: 6:4)	+ 21.9 (1.12, MeOH)	1747 (C=O), 1654 (C=C)	–	0.85 (t, 3H, *J* = 7.4), 1.25 (m, 2H), 1.24 (t, 3H, *J* = 7.0), 1.29 (t, 3H, *J* = 7.0), 2.25 (m, 2H), 3.60 (s, 3H), 4.13 (t, 2H, *J* = 6.6), 4.21 (q, 2H, *J* = 7.0), 5.40 (dd, 1H, *J* = 3.0, 5.1, 1-H), 5.45 (s, 1H, 1′-H), 6.22 (d, 1H, *J* =3.7, 4-H) 7.2–7.5 (m, 5H)[b]	13.6, 14.1, 15.5 (3 × Me), 19.0 (C-5′), 30.5 (C-4′), 32.4 (C-2), 61.3 (C-3), 63.7, 65.2, 67.0 (3 × CH_2O), 77.0 (C-1), 96.7 (C-1), 111.4 (C-4), 127–129 (HC-Ar), 136.0 (C-Ar), 142.0 (C-5), 162.4 (C=O), 170.8 (C=O)[b]
4ba	0.55 (A: 6:4)	+ 31.7 (1.42, CH_2Cl_2)	1733 (C=O), 1754 (C=C)	HRMS calcd for $C_{26}H_{20}O_7$ 454.1891, found: 454.1984	0.84 (t, 3H, *J* = 7.4), 1.23 (m, 2H), 1.52 (m, 2H), 2.21 (ddd, 1H, *J* = 2.9, 6.4, 14.3, 2-H_{ax}), 2.43 (dt, 1H, *J* = 4.5, 14.3, 2-H_{eq}), 3.71 (s, 3H), 4.08 (t, 2H, *J* = 6.6, 3′-H), 4.19 (m, 1H, 3-H), 4.57 (m, 2H, CH_2Ph), 5.43 (m, 2H, 1-H and 1′-H), 6.23 (d, 1H, *J* = 4.0, 4-H), 7.15–7.50 (m, 10H, Ar-H)	13.6 (Me), 18.5 (C-5′), 30.5 (C-4′), 32.3 (C-2), 52.3 (MeO), 65.2 (C-3′), 66.0 (C-3), 70.1 (CH_2Ph), 77.2 (C-1′), 96.3 (C-1), 111.3 (C-4), 125–129 (CH-Ar), 136.0, 138.2 (C-Ar), 141.9 (C-5), 162.8 (C=O), 170.7 (C=O)
4ca	0.59 (A: 6:4)	+ 12.1 (0.95, CH_2Cl_2)	1735 (C=O), 1648 (C=C)	HRMS calcd for $C_{19}H_{24}O_7$ 364.1522, found: 364.1522	0.85 (t, 3H), 1.25 (s, 9H), 1.29 (m, 2H), 1.58 (m, 2H), 2.15 (m, 1H, 2-H_{ax}), 2.27 (ddd, 1H, *J* = 2.6, 6.6, 13.8, 1-H_{eq}), 3.75 (s, 3H), 4.12 (m, 2H), 4.32 (m, 1H, 3-H), 4.37 (dd, 1H, *J* = 2.5, 6.7, 1-H), 5.50 (s, 1H, 1′-H), 6.01 (d, 1H, *J* = 2.5, 4-H), 7.28–7.46 (m, 3H, Ar-H), 7.52 (m, 2H, Ar-H)	13.6 (Me), 18.9 (C-5′), 26.9, 28.1 (Me_3C), 30.4 (C-4′), 35.6 (C-2), 52.2 (MeO), 60.5 (C-3), 65.2 (C-3′), 74.4 (CMe_3), 76.7 (C-1′), 97.1 (C-1), 114.8 (C-4), 127–128.3 (CH-Ar), 135.9 (C-Ar), 141.5 (C-5), 162.9 (C=O), 170.8 (C=O)

Table 3. (continued)

Product	R_f[a]	$[\alpha]_D^{20}$ (*c*, Solvent)	IR ν (cm^{-1})	MS *m/z* (%)	^1H NMR ($CDCl_3$) δ, *J* (Hz)	^{13}C NMR ($CDCl_3$) δ
4cb	0.44 (A: 6:4) 0.51 (B: 2:8)	+ 11.5 (0.55, acetone)	1747, 1739 (C=O), 1648 (C=C)	(EI): 322 (M-CH_2:CMe_2^+, 4), 212 (3), 191 (3), 166 (10), 149 (78), 57 (100)	1.24 (s, 9H, *t*-Bu), 2.15 (dt, 1H, *J* = 6.6, 13.4, 2-H), 2.27 (ddd, 1H, *J* = 2.5, 6.6, 13.4, 2-H), 3.71 (s, 3H), 3.73 (s, 3H), 4.31 (dt, 1H, *J* = 3.5, 6.6, 3-H), 5.36 (dd, 1H, *J* = 2.5, 6.6, 1-H), 5.51 (s, 1H, 1′-H), 6.00 (d, 1H, *J* = 3.5, 4-H), 7.3–7.55 (m, 5H, Ar-H)	28.2 (Me_3C), 35.6 (C-2), 52.2, 52.4 (MeO), 60.5 (C-3), 74.5 (CMe_3), 76.6 (C-1′), 97.0 (C-1), 114.8 (C-4), 127–128.4 (CH-Ar), 135.8 (C-Ar), 141.3 (C-5), 162.9 (C=O), 171.2 (C=O)
4cc	0.55 (A: 6:4)	+ 29.0 (1.0, $CHCl_3$)	1789, 1735 (C=O), 1648 (C=C)	(EI): 342 (M^+, 1), 286 (7), 268 (3), 254 (4), 157 (27), 113 (57), 71 (53), 57 (100) HRMS calcd for $C_{17}H_{26}O_7$ 342.1678, found: 342.1683	1.08 (s, 3H, Me), 1.16 (s, 3H, Me), 1.21 (s, 9H, Me_3C), 2.09 (td, 1H, *J* = 5.6, 14.0, 2-H_0), 2.21 (ddd, 1H, *J* = 2.7, 6.6, 14.0, 2-H), 3.80 (s, 3H, MeO), 3.95 (dd, 1H, *J* = 8.8, CH_2Ph), 4.01 (dd, 1H, *J* = 8.8, CH_2Ph), 4.26 (ddd, 1H, *J* = 3.9, 5.6, 6.6, 3-H), 5.63 (dd, 1H, *J* = 2.7, 5.8, 1-H), 6.08 (d, 1H, *J*=3.9, 4-H)	19.3 (Me), 22.6 (Me), 28.1 (Me_3C), 35.4 (C-2), 40.1 (C-Me_2), 52.2 (MeO), 59.7 (C-3), 74.3 (CMe_3), 76.4 (CH_2O), 78.3 (C-1′), 96.7 (C-1), 115.3 (C-4), 140.7 (C-5), 163.0 (C=O), 175.2 ($C=O_{lact}$)
5cc	0.40 (A: 6:4)	–	342.1678, found: 342.1683	–	1.13 (s, 3H, Me), 1.23 (s, 3H, Me), 1.23 (s, 9H, Me_3C), 2.04 (ddd, 1H, *J* = 6.8, 7.9, 13.5, 2-H), 2.28 (ddd, 1H, *J* = 2.3, 6.6, 13.5, 2-H), 3.80 (s, 3H, MeO), 3.90 (d, 1H, *J* = 8.8, CH_2Ph), 4.00 (d, 1H, *J* = 8.8, CH_2Ph), 4.33 (dt, 1H, *J* = 3.2, 6.7, 3-H), 5.38 (dd, 1H, *J* = 2.3, 7.9, 1-H), 6.02 (d, 1H, *J* = 3.2, 4-H)	19.3 (Me), 22.9 (Me), 28.0 (Me_3C), 35.1 (C-2), 40.3 (C-Me_2), 52.1 (MeO), 60.9 (C-3), 74.3 (CMe_3), 75.9 (CH_2O), 78.9 (C-1′), 98.2 (C-1), 114.5 (C-4), 141.5 (C-5), 162.6 (C=O), 173.9 ($C=O_{lact}$)
4cd/ 5cd (*M*/*m* 78:22)	0.50 (B: 5:5)	+ 31.0 (1.1, acetone)	1747, 1739 (C=O), 1648 (C=C)	(EI): 384 (M-CH_2:CMe_2^+, < 1), 225 (4), 173 (5), 107 (31), 105 (49), 91 (69), 57 (100)	1.21 (*M*) and 1.26 (*m*) (s, 9H, Me_3C), 2.10 (m, 1H, 2H), 2.19 (br s, 1H, 2-H), 3.64 (*M*) and 3.80 (*m*) (s, 3H, MeO), 3.80 (m, 2H, 2′-H), 4.28 (m, 1H, 3-H), 4.62 (s, 2H, CH_2Ph), 5.11 (m) and 5.21 (*M*) (m, 1H), 5.27 (*m*) and 5.71 (*M*) (m, 1H), 6.03 (*m*) and 6.09 (*M*) (s, 1H, 1-H)	28.0 (Me_3C), 35.9 (C-2), 51.8 (MeO), 60.5 (C-3), 73.2 (CH_2O), 73.6 (CMe_3), 79.9 (C′-1), 99.3 (C-1), 114.3 (C-4), 127–128 (CH-Ar), 138.1 (C-Ar), 139.4 (C-Ar), 141.9 (C-5), 163.3 (C=O)[c]

[a] Eluent A: cyclohexane/EtOAc; B: petroleum ether/Et_2O.
[b] For **4aa**.
[c] For major (*M*) diastereomer.

The same procedure, applied to a 90:10 mixture of adducts **4cb** and **5cb** (7.6 g, 20 mmol), gave a crude product (6.8 g, 90%) from which the pure major isomer (+)-**6** (5.2 g, 68%) spontaneously crystallized from Et_2O/petroleum ether solution. Careful chromatography of the oily residue (EtOAc/toluene 2:8) afforded both solid products **6** [(0.62 g, 8%); R_f 0.36 (EtOAc/toluene 3:7)] and **7** [(0.61 g, 8%); R_f 0.23 (EtOAc/toluene 3:7)].

(–)-(2*R*,4*S*,6*S*,1′*R*)-**7**: mp 121 °C (Et_2O); white needles; $[\alpha]_D^{20}$ > –1 13 (*c* = 0.65, acetone).

^1H NMR (400 MHz, $CDCl_3$): δ = 1.17 (s, 9H), 1.52 (≃ q, 1H, J ≃ 12 Hz), 1.66 (ddd, 1H), 2.08 (m, 2H), 3.61 (m, 1H), 3.71 (s, 3H), 3.78 (s, 3H), 3.87 (dd, *J* = 12.2 and 2.1 Hz), 4.32 (dd, *J* = 9.9 and 1.8 Hz, 1H), 5.40 (s, 1H), 7.38 (m, 3H), 7.44 (m, 2H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 28.4, 36.8, 40.0, 52.3, 52.3, 65.8, 71.5, 74.1, 77.8, 97.7, 127.7, 128.8, 129.0, 135.4, 170.3, 170.5.

Tetrahydropyranyl Diol (–)-(2*S*,4*R*,6*R*,1′*R*)-(8):

To a suspension of $LiAlH_4$ (4.2 g, 113 mmol) in Et_2O (60 mL) was added dropwise at 0°C a warmed solution of diester (+)-**6** (5.7 g, 15 mmol) in Et_2O (300 mL). After stirring for 15 h at r.t., followed by cautious dropwise addition of sat. aq Na_2SO_4 (18 mL) at 0 °C and stirring again for 15 h at r.t., the precipitated aluminum salts were removed by filtration and washed with hot EtOAc (60 mL). The combined organic layers were dried ($MgSO_4$) and evaporated, giving the crude diol (–)-**8** (4.62 g, 93%) which was next used without further purification; R_f 0.55 (EtOH/toluene 1:5); $[\alpha]_D^{20}$ –8.8 (*c* = 1.7, acetone).

IR (neat): ν = 3421 cm^{-1} (OH).

^1H NMR (400 MHz, $CDCl_3$): δ = 1.19 (s, 9H, Me_3C), 1.21 (≃ q, 1H, *J* ≃ 12 Hz), 1.31 (dd, 1H, *J* = 9.5 and 2.5 Hz), 1.53 (m, 2H), 2.06 (m, 1H), 2.32 (dd, 1H, *J* = 9.5 and 3.6Hz), 3.28 (m, 3H), 3.64 (m, 2H), 3.79 (m, 1H), 4.63 (dd, 1H, *J* = 9.9 and 1.9 Hz), 4.67 (dd, 1H, *J* = 8.7 and 3.7 Hz), 7.25–7.4 (m, 5H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 28.4, 35.7, 40.6, 65.3, 66.2, 66.7, 73.0, 74.0, 83.1, 101.1, 126.8, 128.3, 128.5, 139.3.

MS(EI): *m/z* (%) = 237 (M^+-CH_2OH – CH_2=CMe_2, 1), 187 (15), 149 (3), 131 (58), 113 (100), 57 (99).

Tetrahydropyranyl Dibenzyl Ether (–)-(2*S*,4*R*,6*R*,1′*R*)-(9):
To a suspension of NaH (prewashed from mineral oil with hexane, 0.87 g, 36 mmol) in DMF (30 mL) was successively added dropwise at 0 °C a solution of unpurified diol (-)-**8** (4.62 g, 14 mmol) in DMF (60 mL) and benzyl bromide (4.1 mL, 34 mmol). After stirring over a 24–48 h period at r.t. (meanwhile gas evolution had ceased and medium had become nearly clear yellow), quenching with H_2O (150 mL), extraction with Et_2O (200 mL), and drying ($MgSO_4$), the evaporated product was chromatographed (Et_2O/petroleum ether 1:1), giving dibenzyl ether (–)-**9** (6.42 g, 93%, 85% from diester (+)-**6**) as a thick white oil; R_f 0.60 (Et_2O/petroleum ether 1:1); $[\alpha]_D^{20}$ –4.8 (*c* = 4.3, MeOH).
^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.19 (s, 9H, Me_3C), 1.23 (≃ q, 1H, *J* ≃ 12 Hz), 1.51 (ddd, 1H, *J* = 11, 13 Hz), 1.82 (m, 1H), 2.12 (m, 1H), 3.38–3.56 (m, 3H), 3.57–3.74 (m, 3H), 4.39 (d, 1H, *J* = 12.1 Hz, benzyl), 4.44 (d, 1H, *J* = 12.1 Hz, benzyl), 4.54 (d, 1H, *J* = 12.1 Hz, benzyl), 4.59 (d, 1H, *J* = 12.1 Hz, benzyl), 4.77 (dd, 1H, *J* = 9.8 and 1.8 Hz), 4.95 (dd, 1H, *J* = 8.0 and 3.7 Hz), 7.3–7.5 (m, 15H).
^{13}C NMR (100 MHz, $CDCl_3$): δ = 28.4, 37.0, 40.9, 66.4, 72.1, 73.0, 73.3, 73.4, 73.7, 75.1, 79.3, 100.8, 126.8, 127.4, 127.5, 127.6, 128.1, 128.3, 128.4, 138.3, 138.5, 139.8.
MS(EI): *m/z* (%) = 341 (M^+-CH_2OH – CH_2=CMe_2, 1), 277 (1), 251 (2), 235 (2), 219 (5), 203 (5), 157 (14), 107 (27), 91 (100), 57 (43).

6-*O*-Benzyl-3-*O*-*tert*-butyl-L-2,4-dideoxyglucopyranose (10):
To a solution of (–)-**9** (6.06 g, 12 mmol) in THF (120 mL) was added 3 N aq HCl (80 mL) at r.t. After stirring for 48 h (meanwhile clearness of the medium was maintained by THF dilution), the mixture was poured into sat. aq $NaHCO_3$ (350 mL) and extensively extracted with hot EtOAc (10 × 80 mL). The combined organic layers were washed with sat. brine (20 mL), dried ($MgSO_4$) and the concentrated product was chromatographed (EtOAc/cyclohexane 4:6), giving benzyloxyphenylethanol (–)-**11** (R_f 0.44, 2.58 g) and then lactol L-**10** (R_f 0.26, 3.37 g, 91%) as clear oily mixture of anomers (α/β 70:30) which slowly crystallized; mp 50–54 °C.
IR (neat): ν = 3400 cm^{-1} (OH).
^{1}H NMR (400 MHz, $CDCl_3$): δ = α anomer: 1.20 (s, 9H, Me_3C), 1.32 (≃ q, 1H, *J* ≃ 12 Hz), 1.55 (m, 1H), 1.75 (m, 1H), 1.92 (m, 1H), 3.10 (m, 1H), 3.41 (dd, 1H, *J* = 10.0 and 3.5 Hz), 3.47 (dd, 1H, *J* = 10.0 and 6.7 Hz), 4.01 (m, 1H), 4.23 (m, 1H), 4.53 (d, 1H, *J* = 12.0 Hz, benzyl), 4.57 (d, 1H, *J* = 12.0 Hz, benzyl), 5.41 (m, 1H), 7.3–7.5 (m, 5H). β anomer: 1.19 (s, 9H, Me_3C), 1.35 (≃ q, 1H, *J* ≃ 12 Hz), 1.75 (m, 2H), 2.06 (m, 1H), 3.43 (m, 1H), 3.60 (m, 3H), 3.73 (m, 1H), 4.53 (d, 1H, *J* = 12.2 Hz, benzyl), 4.59 (d, 1H, *J* = 12.2 Hz, benzyl), 4.72 (m, 1H), 7.3–7.5 (m, 5H).
^{13}C NMR (100 MHz, $CDCl_3$): δ = α anomer: 28.4, 37.3, 39.1, 62.7, 67.2, 73.4, 73.4, 73.9, 93.1, 127.7, 127.8, 128.4, 138.1. β anomer: 28.4, 36.5, 42.1, 60.4, 66.1, 71.8, 72.9, 74.0, 94.8, 127.7, 127.8, 128.4, 138.1.
Anal. Calcd for $C_{17}H_{26}O_4$: C 69.36; H 8.90; Found: C 69.01; H 8.71.

***O*-6-Benzyl-*O*-3-*tert*-butyl-L-2,4-dideoxygluconolactone [(–)-12]:**
To a solution of lactol L-**10** (3.23 g, 11 mmol) in CH_2Cl_2 (80 mL) were successively added PCC (7.76 g, 36 mmol) and 3A powdered molecular sieves. After stirring for 15 h at r.t., the mixture was diluted with Et_2O (150 mL) and filtered. The filtrate was dried ($MgSO_4$) and evaporated, and the crude residue was chromatographed (Et_2O/petroleum ether from 1:1 to 2:1), giving lactone (–)-**12** (2.86 g, 89%,) as an oil; R_f 0.44 (Et_2O/petroleum ether 2:1); $[\alpha]_D^{20}$ –19.5 (*c* = 2.4, MeOH).
IR (neat): ν = 1741 cm^{-1} (C=O).
^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.20 (s, 9H, Me_3C), 1.74 (ddd, 1H, *J* = 10.0, 11.7 and 13.7 Hz, 4-H_{ax}), 2.12 (dddd, 1H, *J* = 1.5, 3.3, 4.9 and 13.7 Hz, 4-H_{eq}), 2.43 (dd, 1H, *J* = 8.4 and 17.4 Hz, 2-H_{ax}), 2.80 (ddd, 1H, *J* = 1.5, 6.0 and 17.4 Hz, 2-H_{eq}), 3.61 (dd, 1H, *J* = 4.8 and 10.3 Hz, 6-H), 3.65 (dd, 1H, *J* = 4.9 and 10.3 Hz, 6-H), 3.97 (dddd, 1H, 3-H), 4.38 (m, 1H, 5-H), 4.58 (s, 2H, benzyl), 7.32 (m, 5H, Ar-H).
^{13}C NMR (100 MHz, $CDCl_3$): δ – 28.2 (Me_3C), 34.5 (C-4), 39.7 (C-2), 63.3 (C-3), 71.7, 73.5, 74.4 (CMe_3), 76.1 (C-5), 127.7, 127.8, 128.4, 137.7, 170.4 (C-1).
Anal. Calcd for $C_{17}H_{24}O_4$: C 69.84; H 8.27; Found: C 69.92; H 8.28.
MS (CI): *m/z* (%) = 293 (MH^+, 3), 237 (4), 219 (9), 157 (3), 129 (8), 91 (100).

D-2,4-dideoxygluconolactone (+)-**12**; $[\alpha]_D^{20}$ +19.5 (*c* = 2.4, MeOH) was obtained from adduct (–)-(2*R*,4*R*,1′*S*)-**4cb** by the same five-step procedure.

***O*-6-Benzyl-L-2,4-dideoxygluconolactone [(+)-13]:**
To a solution oflactone (+)-**12** (0.292 g, 1.0 mmol) in CH_2Cl_2 (2 mL) was added trifluoroacetic acid (1 mL) at r.t. After stirring for 24 h, the mixture was diluted with CH_2Cl_2 (50 mL), washed with sat. aq $NaHCO_3$, dried and the concentrated oily residue was extracted with boiling Et_2O. After evaporation, the crude product was chromatographed (EtOAc/cyclohexane 4:6), giving lactone (+)-**13**; (0.175 g, 75%,) as an oil; R_f 0.10 (EtOAc/cyclohexane 4:6); $[\alpha]_D^{20}$ +19.4 (*c* = 1.03, MeOH).
IR (neat): ν = 3430 (OH), 1735 cm^{-1} (C=O).
^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.76 (ddd, 1H, *J* = 8.0, 9.8 and 14.0 Hz, 4-H_{ax}), 2.22 (dddd, 1H, 4-H_{eq}), 2.47 (dd, 1H, *J* = 7.4 and 17.2 Hz, 2-H_{ax}), 2.80 (ddd, 1H, *J* = 1.5, 5.4 and 17.2 Hz, 2-H_{eq}), 3.30 (br s, 1H, OH), 3.62 (m, 2H, 6-H), 4.18 (m, 1H), 4.39 (m, 1H), 4.58 (s, 2H, benzyl), 7.32 (m, 5H, Ar-H).
^{13}C NMR (100 MHz, $CDCl_3$): δ = 33.8 (C-4), 39.4 (C-2), 62.6 (C-3), 71.0, 73.0, 75.7 (C-5), 127.8, 128.0, 128.5, 137.4, 170.6 (C-1).
HRMS for $C_{13}H_{17}O_4$ (CI), $(M+H)^+$ Calcd: 237.1127. Found: 237.1127.

(4*R*,6*S*)-6-Benzyloxymethyl-4-*tert*-butoxytetrahydro-2*H*-pyran-2-one [(+)-15]:
A solution of lactone (–)-**12** (0.59 g, 2 mmol) in THF (30 mL) was treated with 1 M aq NaOH (10 mL) for 1 h at 4 °C. The mixture was next treated with excess sat. aq NH_4Cl (5 mL) then solid NH_4Cl (1 g), and diluted with CH_2Cl_2 (50 mL). After rapid extraction with cold CH_2Cl_2 (5 × 50 mL), the dried solution ($MgSO_4$) was concentrated (× 10) at 4 °C. To the resulting solution (ca. 30 mL) were added PPh_3 (0.50 g) and then, at 4 °C, dropwise diisopropyl azodicarboxylate (420 μL). After stirring for 60 h, the concentrated product was chromatographed (Et_2O/petroleum ether 4:6), giving *trans*-lactone (+)-**15** (0.25 g, 42%,) as a solid; needles; mp 79–80 °C); R_f 0.30 (Et_2O/petroleum ether 4:1); $[\alpha]_D^{20}$ +10.5 (*c* = 1.03, MeOH).
IR (neat): ν = 1740 cm^{-1} (C=O).
^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.17 (s, 9H, Me_3C), 1.82 (ddt, 1H, 4-H_{ax}), 2.12 (dddd, 1H, *J* = 1.5, 4.7, 8.2 and 8.2 Hz, 4-H_{eq}), 2.53 (ddd, 1H, *J* = 1.3, 4.5 and 17.2 Hz, 2-H_{eq}), 2.62 (dd, 1H, *J* = 4.9 and 17.2 Hz, 2-H_{ax}), 3.62 (dd, 1H, *J* = 4.3 and 10.6 Hz, 6-H), 3.68 (dd, 1H, *J* = 4.0 and 10.6 Hz, 6-H), 4.13 (m, 1H, 3-H), 4.58 (d, 2H, benzyl), 4.80 (m, 1H, 5-H), 7.32 (m, 5H, Ar-H).
^{13}C NMR (100 MHz, $CDCl_3$): δ = 28.2 (Me_3C), 32.9 (C-4), 38.9 (C-2), 62.0 (C-3), 71.8, 73.6, 74.4 (CMe_3), 75.6 (C-5), 127.7, 127.8, 128.4, 137.8, 170.6 (C-1).
Anal. Calcd for $C_{17}H_{24}O_4$: C 69.84; H 8.27; Found: C 69.54; H 8.13
MS (CI): *m/z* (%) = 293 ($M+H^+$, 8), 237 (4), 219 (19), 157 (4), 129 (9), 91 (100).

(4*R*,6*S*)-6-Benzyloxymethyl-4-hydroxytetrahydro-2*H*-pyran-2-one [(+)-16]:
To a solution of lactone (+)-**15** (0.292 g, 1 mmol) in CH_2Cl_2 (2 mL) was added trifluoroacetic acid (1 mL) at r.t. After stirring for 24 h, the mixture was diluted with CH_2Cl_2 (50 mL), washed with sat. aq $NaHCO_3$, dried and the concentrated oily residue was extracted with boiling Et_2O. After evaporation, the crude product was chromatographed, giving lactone (+)-**16** (0.17 g, 72%); $[\alpha]_D^{20}$ + 6.5 (*c* = 1.0, $CHCl_3$); R_f 0.15 (Et_2O); as an oily product whose physiochemical properties were in good agreement with reported data, (Lit.[19] $[\alpha]_D^{29}$+ 6.59 (*c* = 1.032, $CHCl_3$).

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