Highly diastereoselective boron and titanium mediated aldol reactions of a mannitol derived 2,3-butanediacetal ethyl ketone.

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Abstract

A mannitol derived 2,3-butanediacetal ethyl ketone displays high levels of diastereoselectivity in boron and titanium mediated aldol reactions with a range of aliphatic and aromatic aldehydes to afford *syn* aldol products in high yield. The stereochemical outcome of the reaction was determined using *J*-value analysis, NMR analysis of *O*-acetylmandelate derivatives and X-ray crystallography.

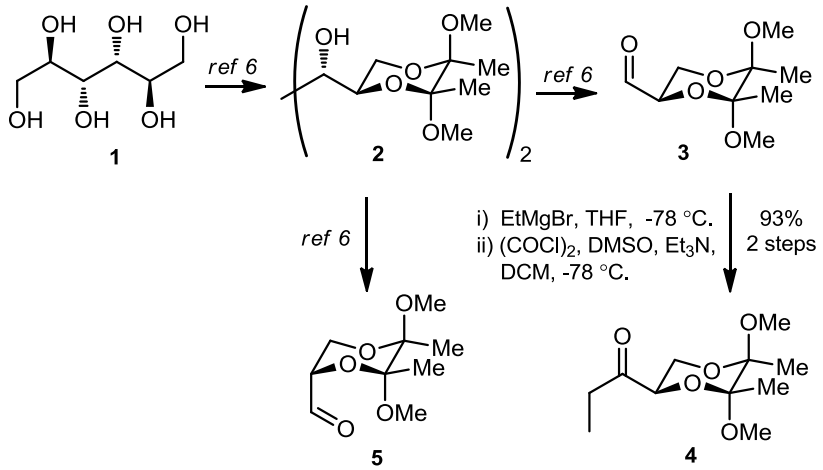
Introduction

Since its discovery by Borodin,[1] and independently by Wurtz,[2] the aldol addition reaction has become one of the most important transformations in organic synthesis.[3] Its ability to furnish *β*-hydroxy carbonyl compounds with excellent levels of stereocontrol has led to its widespread employment in the total synthesis of natural products, particularly secondary metabolites derived from the polyketide biosynthetic pathway.[4]

As part of our research exploring the synthetic utility of 2,3-butane-diacetal derivatives of polyol precursors,[5] we have previously shown that a simple synthetic sequence can be used to convert D-mannitol (**1**), *via* the selectively functionalised intermediate **2** to either the equatorial (**3**) or axial (**5**) diastereoisomer of (5*R*,6*R*)-5,6-dimethoxy-5,6-dimethyl-1,4-dioxane-2-carbaldehyde at will (Scheme 1).[6]

In many of the reactions in which they act as electrophiles, these aldehydes display excellent stereodirecting abilities, giving rise to a highly versatile stereochemical manifold.[7] Building on this, we wished to explore the use of the 2,3-butane diacetal motif as the stereodirecting

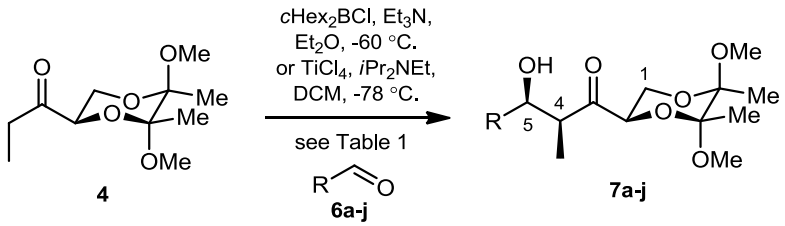
group in a nucleophilic reaction partner and chose the aldol reaction as our initial subject of investigation. To this end, the equatorial ethyl ketone **4** was synthesised in high yield from **3** using a simple Grignard-addition/Swern-oxidation sequence. In this manuscript, we report that boron and titanium mediated aldol reactions of **4** proceed with excellent levels of diastereoselectivity, furnishing *syn,syn* products with a range of aldehydes.



Scheme 1 Reagents and conditions: i. EtMgBr, THF, -78 °C. ii. $(COCl)_2$, Me_2SO, Et_3N, DCM, -78 °C.

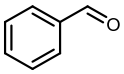
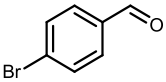
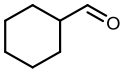
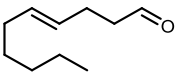
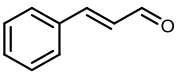
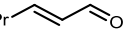
We began our investigation with benzaldehyde, **6a**, as the electrophilic reaction partner. Initially exploring the generation of dialkyl boron enolates, a brief survey of reagents and conditions identified dicyclohexylboron chloride and triethylamine in diethyl ether at -60 °C as suitable, giving rise to high levels of stereocontrol whilst allowing the reaction to proceed at an acceptable rate.

Under these conditions, using recently prepared dicyclohexyl boron chloride,[8] the coupling of **4** with benzaldehyde afforded a 98% yield of the product **7a** in a diastereomeric ratio of 96:4 as determined from ^{1}H NMR spectroscopy (Scheme 2, Table 1). Using the same conditions, **4** was then coupled with a series of aromatic and aliphatic aldehydes to afford the corresponding aldol products **7a-j** in excellent yields and with very high levels of stereocontrol (Scheme 2, Table 1). An oxidative workup with alkaline hydrogen peroxide was used to convert the cyclohexyl groups on boron to cyclohexanol prior to chromatographic purification.



Scheme 2 Reagents and conditions: **4**, *c*Hex_2BCl, Et_3N, Et_2O, -60 °C then **6a-j**, Et_2O -60 °C *OR* **4**, $TiCl_4$, iPr_2NEt, CH_2Cl_2, -78 °C, then **6a-c**.

Table 1 Results of the aldol coupling of **4**.

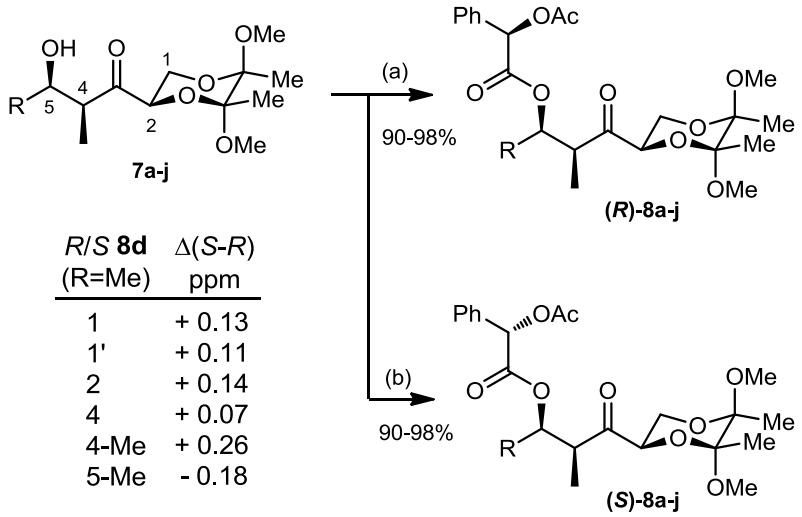
entry	**6**	Aldehyde	Product	Method[a]	$^3J_{HH}$ 4,5 (Hz)	Yield[b] (%)	d.r.
1	**6a**		**7a**	B	4.6	98	96:4
2				Ti	"	95	95:5
3	**6b**		**7b**	B	4.4	94	95:5
4				Ti	"	92	94:6
5	**6c**		**7c**	B	2.9	98	94:6
6				Ti	"	91	94:6
7	**6d**		**7d**	B	3.6	92	95:5
8	**6e**		**7e**	B	3.1	97	97:3
9	**6f**		**7f**	B	3.2	96	94:6
10	**6g**		**7g**	B	2.8	93	94:6
11	**6h**		**7h**	B	3.5	94	95:5
12	**6i**		**7i**	B	4.3	95	94:6
13	**6j**		**7j**	B	6.5	97	95:5

[a] B = Boron, Ti = Titanium. [b] isolated yield after purification by column chromatography on silica gel.

The relatively low α-β ^{1}H-^{1}H coupling constants (Table 1, 4th column) are consistent with the newly created stereocentres having a relative *syn* relationship, according to the Stiles–House model.[9] Although dicyclohexylboron chloride often leads to the formation of *E*-boron enolates, the enolate geometry is highly dependent on the substitution pattern at the α'

position and related α'-alkoxy ketones have been shown to afford exclusive formation of *Z*-boron enolates using this reagent.[10]

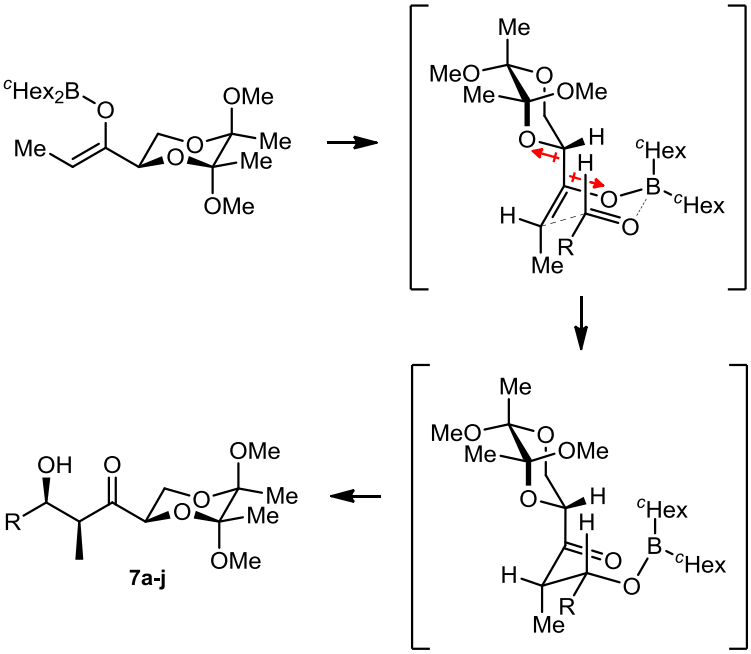
The absolute configuration of the β hydroxyl stereocentre in the aldol products was determined by comparison of the ^{1}H NMR spectra of their (*R*)- and (*S*)-*O*-acetylmandelate esters (Scheme 3, example Δ(*S*-*R*) data are shown for compound **8d**).



R/*S* **8d** (R=Me)	Δ(*S*-*R*) ppm
1	+ 0.13
1'	+ 0.11
2	+ 0.14
4	+ 0.07
4-Me	+ 0.26
5-Me	- 0.18

Scheme 3 Reagents and conditions: (a) (*R*)-*O*-acetylmandelic acid, EDCI, DMAP, DCM, 0 °C; (b) (*S*)-*O*-acetylmandelic acid, EDCI, DMAP, DCM, 0 °C.

The stereochemical outcome of the reaction can be explained on the basis of a preferred enolate conformation in which the enolate C-O bond and the α' C-O bond are aligned in an antiperiplanar orientation for dipolar reasons. The approach of the aldehyde towards the least hindered face of the enolate in a Zimmerman–Traxler transition state then leads to the observed diastereoselectivity (Scheme 4).[3k, 11]



Scheme 4. Possible transition state model for the aldol addition. Dipoles shown in red.

p-Bromobenzaldehyde **6b** was specifically chosen in the hope that the *p*-bromobenzene ring might impart crystallinity to the corresponding product **7b**. Pleasingly, this turned out to be the case and an X-ray crystal structure was obtained (Figure 1). In addition to providing further evidence for the relative *syn*-aldol stereochemistry, the presence of the heavy bromine atom also allowed the absolute stereochemistry to be determined from the X-ray data (which was in full agreement with the *O*-acetylmandelate analysis).

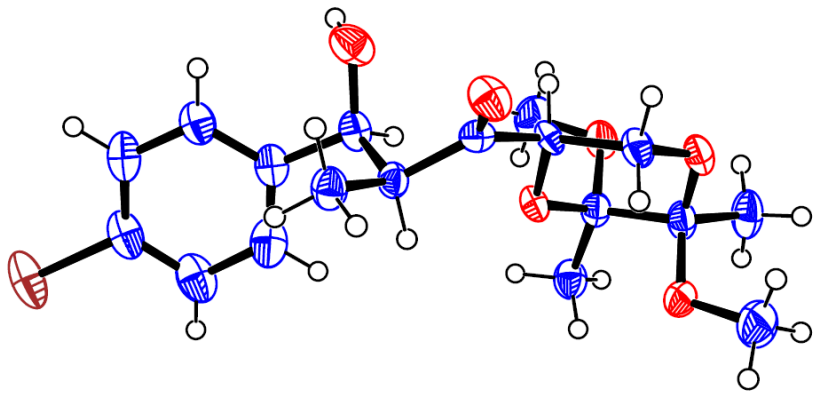


Figure 1. X-ray structure of **7b**. Thermal ellipsoids are shown at 50%.

In addition to the use of dicyclohexylboron chloride, we also briefly explored titanium reagents and found titanium tetrachloride to be equally competent in effecting these transformations (affording the same diastereomer of product) using diisopropylethylamine as the base and dichloromethane as the solvent (Table 1, entries 2,4,6). Conveniently, commercial grade material (purchased as a 1 M solution in dichloromethane) was found to be adequate, providing a possible advantage over the use of dicyclohexylboron chloride. As the titanium derived by-products are all easily hydrolysed and extracted into the aqueous phase on workup, this is also a potential advantage over the boron reagent (which leads to cyclohexyl byproducts whose removal generally necessitates additional workup steps). As the observed stereochemical outcome of the titanium mediated reaction was the same as the boron mediated aldol addition, it is also possible that the transition-state is similar to that shown in Scheme 4. Unlike the boron atom in dialkylboron enolates, the titanium metal in the enolate can bind to additional Lewis basic groups, such as the α'-alkoxy group in **4**. This might be expected to lead to the alternative *syn* aldol stereochemistry *via* an alternative enolate conformation. However, it is possible that the 2,3-butane-diacetal moiety (containing two adjacent quaternary carbons) would cause too much steric crowding to permit such a chelated structure (Figure 2). This might perhaps lead to a similar 'dipole aligned' Zimmerman-Traxler transition state as suggested for the boron mediated reaction.

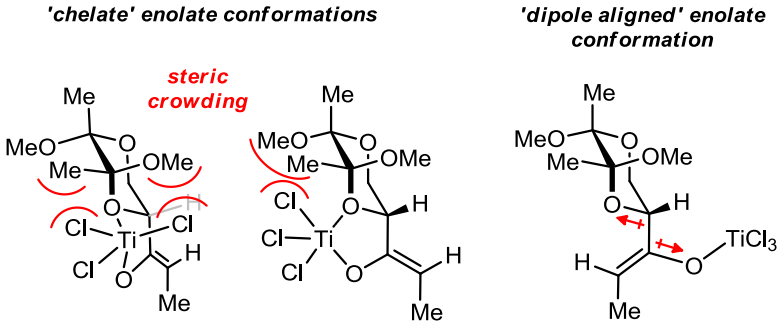
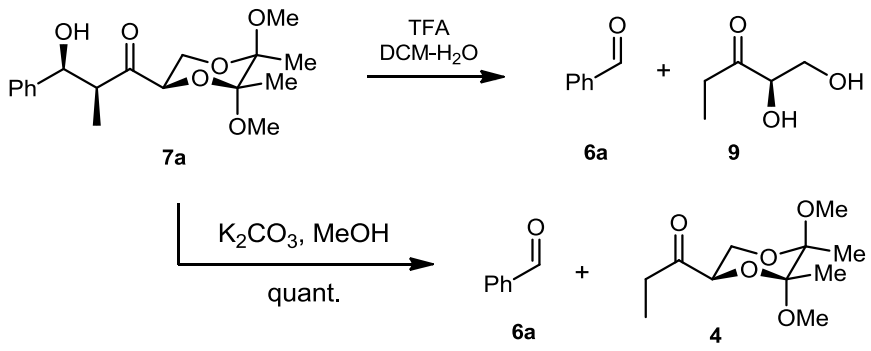


Figure 2. Potential steric crowding in hypothetical chelated titanium enolate conformations (left) and proposed favoured dipole-aligned enolate (right).

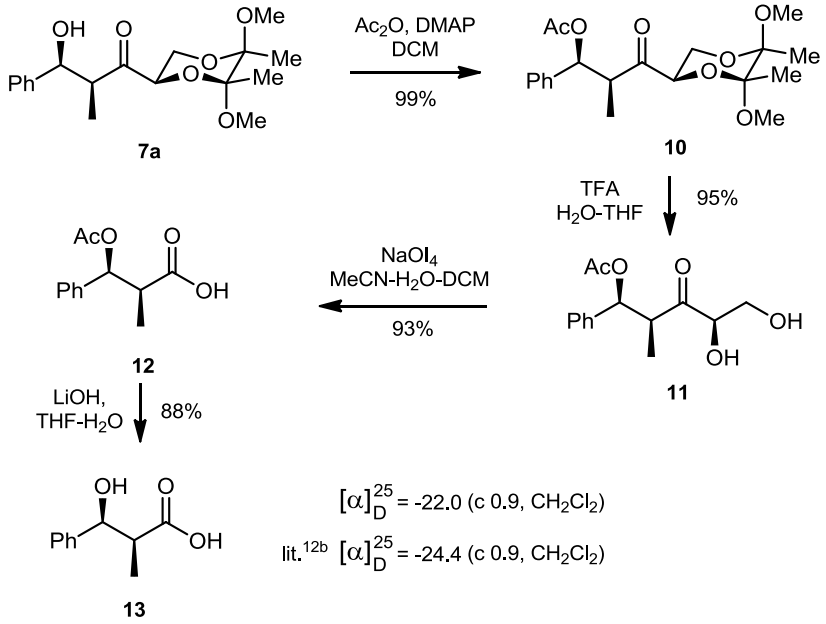
Having established the efficacy of the aldol coupling, we wanted to establish that the 2,3-butane-diacetal group could be removed in order to reveal the keto-diol functionality. Perhaps unsurprisingly, when this was attempted using trifluoroacetic acid (a reagent we have commonly used for this transformation), the reaction was also accompanied by a rapid retro-aldol cleavage (Scheme 5). We also found that the retro-aldol cleavage of **7a** was rapid at

room temperature using methanolic potassium carbonate, leading to the aldehyde and ketone in quantitative yield (Scheme 5). As yet, we have been unable to determine the order in which the butane-diacetal cleavage and retro-aldol processes occur under acidic conditions.



Scheme 5. Retro-aldol cleavage transformations of **7a**.

To prevent the possibility of the retro-aldol process, we acylated the secondary alcohol in **7a**. With this change, the butane-diacetal cleavage of the ester **10** was able to be performed in high yield (Scheme 6). We found that a THF-water solvent mixture, which provided a homogeneous reaction mixture after addition of TFA, led to the highest yield (95%) for this reaction.



Scheme 6. Butane-diacetal cleavage and conversion to known hydroxy acid **13**.

The keto-triol moiety in **11** could be cleaved to the carboxylic acid **12** in 93% yield using sodium periodate in MeCN-H_2O-DCM. Saponification of the acetate group then afforded the well known hydroxy acid **13**. Spectroscopic data and optical rotation values for this compound matched those provided in the literature,[12] further confirming the diastereoselectivity of the aldol addition.

Conclusion

In conclusion, we have demonstrated that boron and titanium mediated aldol reactions of the mannitol derived 2,3-butane-diacetal ethyl ketone **4** proceed with high levels of substrate directed stereocontrol. The relative *syn* aldol stereochemistry was determined by analysis of the *J*-coupling values between the α and β hydrogens in the ^{1}H NMR spectra. The absolute sense of stereocontrol was determined using X-ray crystallography, by NMR analysis of acetylmandelate derivatives and by conversion of aldol product **7a** to the known hydroxy acid **13**. We are currently investigating the use of this reaction in the synthesis of several polyketide natural products.

Experimental Section

General Experimental Details:

Unless otherwise stated, reactions were performed using glassware that was dried by heating with a heat-gun under a flow of argon. Argon gas was pre-dried by passing through a cartridge of granular calcium chloride. Unless otherwise stated, all reagents were used as supplied from commercial sources without further purification. Dichloromethane used in reactions was purified using continuously recycling distillation over calcium hydride under a dry argon atmosphere. Tetrahydrofuran and diethyl ether used in reactions were pre-dried over freshly pressed sodium wire and then further purified using continuously recycling distillation over a mixture of calcium hydride and lithium aluminium hydride under a dry argon atmosphere using triphenylmethane as an indicator. Triethylamine and diisopropylethylamine were purified by distillation over calcium hydride and were stored over calcium hydride under an atmosphere of dry argon. Distilled water and aqueous solutions were prepared on site. Flash column chromatography was performed using Merck 9385 grade silica gel purchased from Sigma-Aldrich. Analytical thin layer chromatography was performed using Merck Silica gel 60 F254 1 mm glass plates and visualised either by

ultraviolet radiation (254 nm) or by staining with potassium permanganate, cerium ammonium molybdate or vanillin solutions prepared by known procedures. 40/60 Petroleum ether refers to the distillate collected between 40–60 °C. ^{1}H spectra were recorded on Bruker Avance 300 (300 MHz) or Bruker Avance DPX-400 (400 MHz) spectrometers. Chemical shifts are reported in parts per million (ppm) and the spectra are calibrated to the residual protic form of the deuterated solvent (7.26 ppm $CDCl_3$; 3.31 ppm CD_3OD). The multiplicity of a signal is reported as: s – singlet; d – doublet; t – triplet; br – broad; m – multiplet. Coupling constants (*J*) are given in hertz (Hz) to 1 decimal place. Apodisation functions (Gaussian, exponential, sine bell) were used to resolve multiplets in some cases. The centre of each peak is reported with the exception of unresolved multiplet signals where a range of ppm values are given. ^{13}C NMR spectra were recorded on Bruker Avance 300 (75 MHz) or Bruker Avance DPX-400 (100 MHz) spectrometers with complete proton decoupling. Chemical shifts are reported in ppm and the spectra are calibrated to the deuterated solvent as the internal deuterium lock (77.00 ppm $CDCl_3$; 49.00 ppm CD_3OD). ^{13}C signals are singlets unless otherwise stated and are reported to 2 decimal places. Infrared Spectroscopy was carried out using a thin film (evaporated from solution) on a Thermo Scientific Nicolet iS10 ATR spectrometer. Mass Spectrometry was carried out on a Waters LCMS with electrospray ionisation and a QTOF analyser.

Synthesis and Spectroscopic Data:

1-((2*R*,5*R*,6*R*)-5,6-dimethoxy-5,6-dimethyl-1,4-dioxan-2-yl)propan-1-one **4**.

Step 1) *Grignard addition*: To a stirring solution of the starting aldehyde **3** (10.0 g, 49.0 mmol, 1.0 equiv) in dry tetrahydrofuran (300 mL) was added dropwise a solution of ethylmagnesium bromide (2.5 M in Et_2O, 98.0 mL, 98.0 mmol, 2.0 equiv) at -78 °C (acetone/dry-ice bath) under an atmosphere of dry argon. The reaction mixture was stirred at this temperature for 1 hr after which time it was quenched by the addition of saturated aqueous ammonium chloride (60 mL) followed by water (100 mL) and diethyl ether (200 mL) with rapid stirring. The reaction mixture was allowed to warm to room temperature and the layers were separated. The aqueous layer was extracted thrice with diethyl ether (3 × 60 mL) and the combined organic layers were washed with water (100 mL), brine (100 mL) and dried over magnesium sulfate. The solvent was removed under reduced pressure to afford a

crude material that was used in the next reaction without further purification or characterisation.

Step 2) *Swern oxidation*: A solution of dimethyl sulfoxide (10.44 mL, 147 mmol, 3.0 equiv) in dichloromethane (200 mL) was added dropwise to a stirring solution of oxalyl chloride (6.30 mL, 73.5 mmol, 1.5 equiv) in dichloromethane (200 mL) at -78 °C under an atmosphere of dry argon. The reaction was stirred at this temperature for 20 min. A solution of the crude material from the Grignard addition step in dichloromethane (200 mL) was added dropwise at -78 °C. The reaction mixture was stirred at this temperature for 20 min. Triethylamine (40.9 mL, 294 mmol, 6.0 equiv) was added dropwise at -78 °C. The reaction mixture was stirred at this temperature for 15 min before warming to -15 °C (acetone/ice bath) and stirring for a further 45 min. The reaction was quenched by the addition of saturated aqueous ammonium chloride (100 mL) followed by diethyl ether (600 mL). The mixture was allowed to warm to room temperature and the layers were separated. The aqueous layer was extracted thrice with diethyl ether (3 × 100 mL). The combined organic layers were washed with saturated ammonium chloride solution (200 mL), water (200 mL) and brine (200 mL) before drying over magnesium sulfate. The solvent was removed under reduced pressure and to afford a crude product which was purified by column chromatography on silica gel (Merck 9385 grade) eluting with a gradient from 40/60 petroleum ether to a 1:1 mixture of 40/60 petroleum ether to diethyl ether. After removal of solvent under reduced pressure, the product was isolated as a colourless oil (10.57 g, 93% over two steps).

^{1}H NMR (400 MHz, $CDCl_3$) δ 4.34 (dd, *J* = 10.5, 4.3 Hz, 1H), 3.73 (dd, *J* = 11.5, 4.3 Hz, 1H), 3.68 (dd, *J* = 11.5, 10.5 Hz, 1H), 3.31 (s, 3H), 3.25 (s, 3H), 2.78 (dq, *J* = 18.8, 7.2 Hz, 1H), 2.56 (dq, *J* = 18.8, 7.2 Hz, 1H), 1.35 (s, 3H), 1.28 (s, 3H), 1.03 (dd, *J* = 7.2, 7.2 Hz, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 209.3, 99.7, 98.1, 72.6, 59.7, 48.3, 48.1, 31.7, 17.7, 17.5, 6.7. **FTIR** (thin film) ν_{max} cm^{-1} 2990, 2946, 2833, 1716, 1459, 1405, 1374, 1258, 1212, 1165, 1137, 1115, 1054, 1035, 1010, 987, 944, 878, 841, 773. **HRMS** (ESI-TOF, m/z) calculated for $C_{11}H_{20}NaO_5^+$ ($[M+Na]^+$): 255.1203. Observed: 255.1213.

General procedure for boron mediated aldol reactions:

Triethylamine (179 µL, mmol, 1.29 mmol, 3.0 equiv) was added dropwise to a solution of dicyclohexylboron chloride (188 µL, 0.862 mmol, 2.0 equiv) in dry diethyl ether (1 mL) at -60 °C (chloroform/dry-ice bath) under a dry argon atmosphere. After stirring at this temperature for 2 min, a solution of the starting ketone **4** (100 mg, 0.431 mmol, 1.0 equiv) in dry diethyl ether (1 mL) was added at -60 °C. The mixture was stirred at this temperature for 30 min, during which a significant amount of white precipitate was formed. To this suspension was added a solution of the aldehyde (1.94 mmol, 4.5 equiv) in dry diethyl ether (1 mL). The mixture was stirred at -60 °C for 5 h. To the reaction mixture was added saturated aqueous ammonium chloride solution (2 mL) with rapid stirring followed by the addition of diethyl ether (10 mL). The mixture was allowed to warm to room temperature and the layers were separated. The aqueous layer was thrice extracted with diethyl ether (3 × 5 mL) and the combined organic layers were dried over magnesium sulfate before removing the solvent under reduced pressure. The organic material was then dissolved in methanol (6 mL) and pH 7 aqueous phosphate buffer (2 mL) was added to the resulting solution. Into this cloudy suspension was added aqueous hydrogen peroxide (2 mL, 30% wt/vol.) and the mixture was stirred rapidly at room temperature for 30 min. Diethyl ether (20 mL) and water (20 mL) were added and the mixture was stirred rapidly for 2 min. The layers were separated and the aqueous layer was extracted with diethyl ether (10 mL). The combined organic layers were washed with water (10 mL) before drying over magnesium sulfate. The solvent was removed under reduced pressure and the crude material was purified by column chromatography on silica gel (Merck 9385 grade), eluting with a solvent gradient from 40/60 petroleum ether to a 1:1 mixture of 40/60 petroleum ether to diethyl ether.

General procedure for titanium mediated aldol reactions:

Diisopropylethylamine (85 µL, 0.517 mmol, 1.2 equiv) was added to a solution of the starting ketone **4** (100 mg, 0.431 mmol, 1.0 equiv) in dichloromethane (4 mL) at -78 °C (acetone/dry-ice bath) under a dry argon atmosphere. To this solution was added dropwise a solution of titanium tetrachloride in dichloromethane (1.0 M, 517 µL, 0.517 mmol, 1.2 equiv) at -78 °C. The reaction mixture was stirred at this temperature for 2 min. A solution of the aldehyde (0.517 mmol, 1.2 equiv) in dichloromethane was added dropwise at -78 °C. The reaction mixture was stirred at this temperature for 10 min. Saturated aqueous sodium bicarbonate (10

mL) was added dropwise with rapid stirring, followed by diethyl ether (10 mL). The mixture was allowed to warm to room temperature and extracted thrice with diethyl ether (3 × 10 mL). The combined organic layers were washed with water (10 mL), brine (10 mL) and dried over magnesium sulfate. The solvent was removed under reduced pressure to afford the crude material which was purified was purified by column chromatography on silica gel (Merck 9385 grade), eluting with a solvent gradient from 40/60 petroleum ether to a 1:1 mixture of 40/60 petroleum ether to diethyl ether.

(2*S*,3*S*)-1-((2*R*,5*R*,6*R*)-5,6-dimethoxy-5,6-dimethyl-1,4-dioxan-2-yl)-3-hydroxy-2-methyl-3-phenylpropan-1-one **7a**.

(Boron aldol: 143 mg from 100 mg of **4**, 98%. Titanium aldol: 139 mg from 100 mg of **4**, 95%)

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.39 – 7.25 (m, 5H), 5.12 (dd, *J* = 4.6, 3.1 Hz, 1H), 4.32 (dd, *J* = 10.1, 4.8 Hz, 1H), 3.70 – 3.59 (m, 2H), 3.47 (qd, *J* = 7.0, 4.6 Hz, 1H), 3.29 (s, 3H), 3.25 (s, 3H), 2.61 (d, *J* = 3.1 Hz, 1H), 1.38 (s, 3H), 1.29 (s, 3H), 1.12 (d, *J* = 7.0 Hz, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 212.0, 141.9, 128.3, 127.6, 126.0, 99.8, 98.0, 73.4, 72.4, 59.6, 48.8, 48.5, 48.1, 17.7, 17.5, 10.1. **FTIR** (thin film) ν_{max} cm^{-1} 3484 (br), 2991, 2946, 2833, 1710, 1493, 1453, 1374, 1336, 1212, 1137, 1112, 1053, 1034, 944, 876, 840, 765, 748. **HRMS** (ESI-TOF, m/z) calculated for $C_{18}H_{26}NaO_6^+$ ($[M+Na]^+$): 361.1622. Observed: 361.1626.

(2*S*,3*S*)-3-(4-bromophenyl)-1-((2*R*,5*R*,6*R*)-5,6-dimethoxy-5,6-dimethyl-1,4-dioxan-2-yl)-3-hydroxy-2-methylpropan-1-one **7b**.

(Boron aldol: 169 mg from 100 mg of **4**, 94%. Titanium aldol: 165 mg from 100 mg of **4**, 92%).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.47 (d, *J* = 8.4 Hz, 2H), 7.21 (d, *J* = 8.4 Hz, 2H), 5.06 (dd, *J* = 4.4, 2.9 Hz, 1H), 4.34 (dd, *J* = 10.5, 4.5 Hz, 1H), 3.70-3.60 (m, 2H), 3.37 (qd, *J* = 7.0, 4.4 Hz, 1H), 3.26 (s, 3H), 3.23 (s, 3H), 2.73 (d, *J* = 2.9 Hz, 1H), 1.35 (s, 3H), 1.28 (s, 3H), 1.08 (d, *J* = 7.0 Hz, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 212.1, 140.9, 131.4, 127.7, 121.4, 99.8, 98.1, 72.7, 72.6, 59.6, 48.5, 48.5, 48.1, 17.7, 17.5, 9.8. **FTIR** (thin film) ν_{max} cm^{-1} 3470 (br),

2991, 2946, 2833, 1710, 1487, 1455, 1374, 1213, 1165, 1139, 1114, 1071, 1054, 1035, 1010, 986, 944, 878, 829, 789. **HRMS** (ESI-TOF, m/z) calculated for $C_{18}H_{25}BrKO_6^+$ ($[M+K]^+$): 455.0466. Observed: 455.0472.

(2*S*,3*R*)-1-((2*R*,5*R*,6*R*)-5,6-dimethoxy-5,6-dimethyl-1,4-dioxan-2-yl)-3-hydroxy-2,4-dimethylpentan-1-one **7c**.

(Boron aldol: 143 mg from 100 mg of **4**, 98%. Titanium aldol: 119 mg from 100 mg of **4**, 91%)

^{1}H NMR (400 MHz, $CDCl_3$) δ 4.49 (dd, *J* = 10.6, 4.4 Hz, 1H), 3.78 – 3.63 (m, 2H), 3.61 – 3.54 (m, 1H), 3.38 (qd, *J* = 7.0, 2.9 Hz, 1H), 3.32 (s, 3H), 3.24 (s, 3H), 2.12 (d, *J* = 3.9 Hz, 1H), 1.66 (m, 1H), 1.35 (s, 3H), 1.28 (s, 3H), 1.07 (d, *J* = 7.0 Hz, 3H), 1.01 (d, *J* = 6.6 Hz, 3H), 0.90 (d, *J* = 6.7 Hz, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 212.5, 99.8, 98.0, 76.4, 71.7, 59.8, 48.6, 48.1, 43.7, 31.2, 19.2, 19.1, 17.7, 17.5, 8.1. **FTIR** (thin film) ν_{max} cm^{-1} 3516 (br), 2957, 2874, 2834, 1709, 1459, 1374, 1332, 1262, 1213, 1140, 1115, 1037, 1013, 945, 878. **HRMS** (ESI-TOF, m/z) calculated for $C_{15}H_{28}KO_6^+$ ($[M+K]^+$): 343.1517. Observed: 343.1526.

(2*S*,3*R*)-1-((2*R*,5*R*,6*R*)-5,6-dimethoxy-5,6-dimethyl-1,4-dioxan-2-yl)-3-hydroxy-2-methylbutan-1-one **7d**.

(Boron aldol: 110 mg from 100 mg of **4**, 92%).

^{1}H NMR (400 MHz, $CDCl_3$) δ 4.43 (dd, *J* = 10.3, 4.7 Hz, 1H), 4.10 (qd, *J* = 6.3, 3.6 Hz, 1H), 3.75-3.60 (m, 2H), 3.30 (s, 3H), 3.24 (s, 3H), 3.13 (qd, *J* = 7.1, 3.6 Hz, 1H), 2.51 (br s, 1H), 1.35 (s, 3H), 1.28 (s, 3H), 1.16 (d, *J* = 6.3 Hz, 3H), 1.12 (d, *J* = 7.1 Hz, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 212.7, 99.8, 98.0, 72.5, 67.5, 59.7, 48.5, 48.1, 47.1, 20.1, 17.7, 17.5, 9.6. **FTIR** (thin film) ν_{max} cm^{-1} 3493 (br), 2972, 2947, 2834, 1707, 1454, 1374, 1331, 1281, 1212, 1137, 1113, 1055, 1034, 1004, 944, 911, 877, 841. **HRMS** (ESI-TOF, m/z) calculated for $C_{13}H_{24}NaO_6^+$ ($[M+Na]^+$): 299.1465. Observed: 299.1474.

(2*S*,3*R*)-1-((2*R*,5*R*,6*R*)-5,6-dimethoxy-5,6-dimethyl-1,4-dioxan-2-yl)-3-hydroxy-2-methylheptan-1-one **7e**.

(Boron aldol: 133 mg from 100 mg of **4**, 97%).

^{1}H NMR (400 MHz, $CDCl_3$) δ 4.46 (dd, *J* = 10.5, 4.5 Hz, 1H), 3.93 (s, 1H), 3.72 (dd, *J* = 11.5, 4.5 Hz, 1H), 3.67 (dd, *J* = 11.5, 10.5 Hz, 1H), 3.31 (s, 3H), 3.24 (s, 3H), 3.17 (qd, *J* = 7.1, 3.1 Hz, 1H), 2.31 (br s, 1H), 1.60-1.25 (m, 6H), 1.35 (s, 3H), 1.28 (s, 3H), 1.09 (d, *J* = 7.1 Hz, 3H), 0.89 (t, *J* = 7.0 Hz, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 212.6, 99.8, 98.0, 72.2, 71.1, 59.7, 48.5, 48.1, 46.0, 34.0, 28.2, 22.5, 17.7, 17.5, 14.0, 8.9. **FTIR** (thin film) ν_{max} cm^{-1} 3509 (br), 2935, 2834, 1708, 1456, 1374, 1212, 1165, 1137, 1114, 1036, 1008, 969, 944, 877, 842. **HRMS** (ESI-TOF, m/z) calculated for $C_{16}H_{30}NaO_6^+$ ($[M+Na]^+$): 341.1935. Observed: 341.1952.

(2*S*,3*R*)-1-((2*R*,5*R*,6*R*)-5,6-dimethoxy-5,6-dimethyl-1,4-dioxan-2-yl)-3-hydroxy-2-methylpentan-1-one **7f**.

(Boron aldol: 115 mg from 100 mg of **4**, 92%).

^{1}H NMR (400 MHz, $CDCl_3$) δ 4.48 (dd, *J* = 10.3, 4.7 Hz, 1H), 3.86 (ddd, *J* = 8.2, 5.4, 3.1 Hz, 1H), 3.77 – 3.66 (m, 2H), 3.31 (s, 3H), 3.24 (s, 3H), 3.25 – 3.19 (m, 1H), 1.60 – 1.40 (m, 2H), 1.37 (s, 3H), 1.30 (s, 3H), 1.12 (d, *J* = 7.1 Hz, 3H), 0.98 (dd, *J* = 7.4, 7.4 Hz, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 212.5, 99.8, 98.0, 72.8, 72.2, 59.8, 48.5, 48.1, 45.7, 27.3, 17.7, 17.5, 10.4, 9.0. **FTIR** (thin film) ν_{max} cm^{-1} 3516 (br), 2941, 2878, 2834, 1708, 1456, 1374, 1331, 1212, 1138, 1114, 1035, 1003, 974, 945, 878, 842. **HRMS** (ESI-TOF, m/z) calculated for $C_{14}H_{30}NO_6^+$ ($[M+NH_4]^+$): 308.2068. Observed: 308.2070.

(2*S*,3*R*)-3-cyclohexyl-1-((2*R*,5*R*,6*R*)-5,6-dimethoxy-5,6-dimethyl-1,4-dioxan-2-yl)-3-hydroxy-2-methylpropan-1-one **7g**.

(Boron aldol: 138 mg from 100 mg of **4**, 93%).

^{1}H NMR (400 MHz, $CDCl_3$) δ 4.49 (dd, *J* = 10.6, 4.4 Hz, 1H), 3.75 (dd, *J* = 11.5, 4.4 Hz, 1H), 3.69 (dd, *J* = 11.5, 10.6 Hz, 1H), 3.66 (dd, *J* = 8.4, 2.8 Hz, 1H), 3.38 (qd, *J* = 7.0, 2.8

Hz, 1H), 3.33 (s, 3H), 3.25 (s, 3H), 2.10 – 2.01 (m, 2H), 1.80 – 1.71 (m, 2H), 1.70 – 1.56 (m, 3H), 1.41 – 1.10 (m, 3H), 1.36 (s, 3H), 1.29 (s, 3H), 1.06 (d, *J* = 7.0 Hz, 3H), 1.01 – 0.89 (m, 2H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 212.6, 99.8, 98.0, 75.2, 71.7, 59.8, 48.6, 48.1, 43.3, 40.6, 29.5, 29.2, 26.3, 26.0, 25.8, 17.7, 17.5, 8.2. **FTIR** (thin film) ν_{max} cm^{-1} 3517 (br), 2991, 2925, 2851, 1709, 1449, 1374, 1212, 1141, 1115, 1057, 1038, 1011, 978, 945, 879. **HRMS** (ESI-TOF, m/z) calculated for $C_{18}H_{32}NaO_6^+$ ($[M+Na]^+$): 367.2091. Observed: 367.2098.

(2*S*,3*R*,*E*)-1-((2*R*,5*R*,6*R*)-5,6-dimethoxy-5,6-dimethyl-1,4-dioxan-2-yl)-3-hydroxy-2-methyldodec-6-en-1-one **7h**.

(Boron aldol: 157 mg from 100 mg of **4**, 94%).

^{1}H NMR (400 MHz, $CDCl_3$) δ 5.50 – 5.33 (m, 2H), 4.45 (dd, *J* = 10.2, 4.6 Hz, 1H), 3.94 (ddd, *J* = 7.7, 3.5, 3.5 Hz, 1H), 3.76 – 3.61 (m, 2H), 3.31 (s, 3H), 3.24 (s, 3H), 3.17 (qd, *J* = 7.1, 3.5 Hz, 1H), 2.33 (br s, 1H), 2.21 – 2.04 (m, 2H), 2.03-1.90 (m, 2H), 1.56 (m, 1H), 1.44 (m, 1H), 1.38 – 1.18 (m, 6H), 1.35 (s, 3H), 1.28 (s, 3H), 1.11 (d, *J* = 7.1 Hz, 3H), 0.87 (t, *J* = 6.7 Hz, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 212.4, 131.4, 129.2, 99.8, 98.0, 72.3, 70.8, 59.8, 48.5, 48.1, 46.2, 34.2, 32.5, 31.4, 29.2, 29.1, 22.5, 17.7, 17.5, 14.0, 9.3. **FTIR** (thin film) ν_{max} cm^{-1} 3516 (br), 2990, 2925, 2872, 2854, 1708, 1456, 1373, 1212, 1165, 1139, 1115, 1056, 1036, 968, 945, 878, 842. **HRMS** (ESI-TOF, m/z) calculated for $C_{21}H_{38}NaO_6^+$ ($[M+Na]^+$): 409.2561. Observed: 409.2568.

(2*S*,3*R*,*E*)-1-((2*R*,5*R*,6*R*)-5,6-dimethoxy-5,6-dimethyl-1,4-dioxan-2-yl)-3-hydroxy-2-methyl-5-phenylpent-4-en-1-one **7i**.

(Boron aldol: 149 mg from 100 mg of **4**, 95%).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.43 – 7.23 (m, 5H), 6.65 (d, *J* = 15.9 Hz, 1H), 6.19 (dd, *J* = 15.9, 6.1 Hz, 1H), 4.64 (m, 1H), 4.49 (dd, *J* = 10.5, 4.5 Hz, 1H), 3.76 (dd, *J* = 11.5, 4.5 Hz, 1H), 3.71 (dd, *J* = 11.5, 10.5 Hz, 1H), 3.40 (qd, *J* = 7.0, 4.3 Hz, 1H), 3.33 (s, 3H), 3.26 (s, 3H), 2.64 (s, 1H), 1.39 (s, 3H), 1.31 (s, 3H), 1.20 (d, *J* = 7.0 Hz, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 211.8, 136.5, 131.5, 128.9, 128.6, 127.8, 126.5, 99.9, 98.1, 72.8, 72.7, 59.7, 48.5, 48.1, 46.8, 17.7, 17.5, 10.5. **FTIR** (thin film) ν_{max} cm^{-1} 3479 (br), 2991, 2945, 2833, 1709,

1494, 1449, 1374, 1332, 1212, 1139, 1114, 1054, 1034, 966, 944, 877, 841, 747. **HRMS** (ESI-TOF, m/z) calculated for $C_{20}H_{28}NaO_6^+$ ($[M+Na]^+$): 387.1778. Observed: 387.1790.

(2*S*,3*R*,*E*)-1-((2*R*,5*R*,6R)-5,6-dimethoxy-5,6-dimethyl-1,4-dioxan-2-yl)-3-hydroxy-2-methyloct-4-en-1-one **7j**.

(Boron aldol: 138 mg from 100 mg of **4**, 97%).

^{1}H NMR (400 MHz, $CDCl_3$) δ 6.01 (dt, *J* = 15.4, 6.8, 1H), 5.75 (dd, *J* = 15.4, 6.5 Hz, 1H), 4.76 (dd, *J* = 10.5, 4.4 Hz, 1H), 4.70 (m, 1H), 4.05 (dd, *J* = 11.5, 4.3 Hz, 1H), 4.00 (dd, *J* = 11.5, 10.5 Hz, 1H), 3.66 (s, 3H), 3.64 – 3.55 (m, 1H), 3.58 (s, 3H), 2.72 (s, 1H), 2.39 – 2.28 (m, 2H), 1.77 – 1.70 (m, 2H), 1.69 (s, 3H), 1.62 (s, 3H), 1.43 (d, *J* = 7.0 Hz, 3H), 1.22 (t, *J* = 7.3 Hz, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 211.7, 133.4, 129.4, 99.8, 98.0, 73.0, 72.5, 59.7, 48.5, 48.1, 46.7, 34.3, 22.2, 17.7, 17.5, 13.6, 10.5. **FTIR** (thin film) ν_{max} cm^{-1} 3485 (br), 2956, 2932, 2873, 2834, 1709, 1456, 1374, 1212, 1165, 1138, 1114, 1055, 1035, 968, 945, 877, 841. **HRMS** (ESI-TOF, m/z) calculated for $C_{17}H_{34}NO_6^+$ ($[M+NH_4]^+$): 348.2381. Observed: 348.2396.

General procedure for the formation of (*R*)- and (*S*)-acetylmandelates:

A mixture of the starting hydroxy ketone (0.015 mmol, 1.0 equiv), the corresponding (*R*) or (*S*)-*O*-acetylmandelic acid (5.8 mg, 0.030 mmol, 2.0 equiv), *N*-(3-dimethylaminopropyl)-*N*'-ethylcarbodiimide hydrochloride (5.8 mg, 0.030 mmol, 2.0 equiv) and *N*,*N*-4-dimethylaminopyridine (3.7 mg, 0.030 mmol, 2.0 equiv) in dry dichloromethane (1 mL) was stirred at room temperature for 2 h. Diethyl ether (3 mL) and water (3 mL) were added and the mixture was stirred for 10 min. The layers were separated and the organic layer was washed with saturated aqueous sodium bicarbonate (1 mL), saturated aqueous ammonium chloride (1 mL) then dried over magnesium sulfate. The solvent was removed under reduced pressure to afford the product as a viscous colourless oil.

(*R*)-(1*S*,2*S*)-3-((2*R*,5*R*,6*R*)-5,6-dimethoxy-5,6-dimethyl-1,4-dioxan-2-yl)-2-methyl-3-oxo-1-phenylpropyl 2-acetoxy-2-phenylacetate **(*R*)-8a**.

(7.3 mg from 5.0 mg of **7a**, 95%).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.50 – 7.38 (m, 5H), 7.33 – 7.21 (m, 5H), 6.32 (d, *J* = 5.3 Hz, 1H), 5.96 (s, 1H), 4.18 (dd, *J* = 10.6, 4.3 Hz, 1H), 3.59 – 3.43 (m, 3H), 3.26 (s, 3H), 3.20 (s, 3H), 2.17 (s, 3H), 1.38 (s, 3H), 1.26 (s, 3H), 0.77 (d, *J* = 6.8 Hz, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 208.0, 170.2, 167.9, 138.3, 133.6, 129.3, 128.8, 128.5, 128.0, 127.6, 125.8, 99.9, 98.0, 76.0, 74.5, 72.0, 59.5, 48.7, 48.0, 47.9, 20.6, 17.8, 17.6, 9.5. **FTIR** (thin film) ν_{max} cm^{-1} 2991, 2947, 2834, 1745, 1716, 1497, 1455, 1373, 1227, 1168, 1141, 1114, 1053, 1036, 1011, 973, 943, 878, 737, 698. **HRMS** (ESI-TOF, m/z) calculated for $C_{28}H_{34}KO_9^+$ ($[M+K]^+$): 553.1834. Observed: 553.1850.

(*S*)-(1*S*,2*S*)-3-((2*R*,5*R*,6*R*)-5,6-dimethoxy-5,6-dimethyl-1,4-dioxan-2-yl)-2-methyl-3-oxo-1-phenylpropyl 2-acetoxy-2-phenylacetate **(*S*)-8a**.

(7.3 mg from **7a**, 96%).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.43 – 7.29 (m, 5H), 7.19 – 7.10 (m, 3H), 6.95 – 6.89 (m, 2H), 6.30 (d, *J* = 6.2 Hz, 1H), 5.98 (s, 1H), 4.23 (dd, *J* = 10.9, 4.1 Hz, 1H), 3.65 – 3.58 (m, 2H), 3.52 (dd, *J* = 11.4, 10.9 Hz, 1H), 3.23 (s, 3H), 3.21 (s, 3H), 2.18 (s, 3H), 1.38 (s, 3H), 1.26 (s, 3H), 1.06 (d, *J* = 6.8 Hz, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 208.3, 170.0, 167.7, 138.1, 133.5, 129.2, 128.7, 128.2, 127.9, 127.8, 125.9, 99.9, 98.0, 76.2, 74.3, 72.2, 59.5, 48.6, 48.0, 47.9, 20.6, 17.8, 17.5, 10.6. **FTIR** (thin film) ν_{max} cm^{-1} 2991, 2947, 2834, 1747, 1717, 1497, 1455, 1373, 1229, 1206, 1170, 1142, 1115, 1054, 1036, 973, 944, 879, 749, 699. **HRMS** (ESI-TOF, m/z) calculated for $C_{28}H_{34}KO_9^+$ ($[M+K]^+$): 553.1834. Observed: 553.1855.

(*R*)-(1*S*,2*S*)-1-(4-bromophenyl)-3-((2*R*,5*R*,6*R*)-5,6-dimethoxy-5,6-dimethyl-1,4-dioxan-2-yl)-2-methyl-3-oxopropyl 2-acetoxy-2-phenylacetate **(*R*)-8b**.

(7.9 mg from 6.0 mg **7b**, 93%).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.49 – 7.36 (m, 7H), 7.12 (d, *J* = 8.4 Hz, 2H), 6.25 (d, *J* = 5.4 Hz, 1H), 5.91 (s, 1H), 4.16 (dd, *J* = 10.7, 4.2 Hz, 1H), 3.57 – 3.43 (m, 3H), 3.24 (s, 3H), 3.21 (s, 3H), 2.17 (s, 3H), 1.37 (s, 3H), 1.26 (s, 3H), 0.78 (d, *J* = 6.8 Hz, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 207.7, 170.3, 167.9, 137.4, 133.3, 131.7, 129.4, 128.8, 127.6, 127.5, 122.0, 99.9, 98.0, 75.4, 74.6, 72.2, 59.5, 48.7, 48.1, 47.7, 20.6, 17.8, 17.6, 9.6. **FTIR** (thin film) ν_{max}

cm^{-1} 2990, 2947, 2834, 1744, 1716, 1620, 1489, 1455, 1373, 1228, 1207, 1167, 1141, 1114, 1074, 1053, 1035, 1010, 974, 942, 878. **HRMS** (ESI-TOF, m/z) calculated for $C_{28}H_{33}BrKO_9^+$ ($[M+K]^+$): 631.0940. Observed: 631.0954.

(*S*)-(1*S*,2*S*)-1-(4-bromophenyl)-3-((2*R*,5*R*,6*R*)-5,6-dimethoxy-5,6-dimethyl-1,4-dioxan-2-yl)-2-methyl-3-oxopropyl 2-acetoxy-2-phenylacetate **(*S*)-8b**.

(8.6 mg from 6.2 mg **7b**, 97%).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.44 – 7.32 (m, 4H), 7.28 – 7.23 (m, 3H), 6.77 (d, *J* = 8.4 Hz, 2H), 6.23 (d, *J* = 6.3 Hz, 1H), 5.95 (s, 1H), 4.25 (dd, *J* = 10.9, 4.0 Hz, 1H), 3.63 (dd, *J* = 11.5, 4.0 Hz, 1H), 3.57 – 3.49 (m, 2H), 3.22 (s, 6H), 2.18 (s, 3H), 1.37 (s, 3H), 1.26 (s, 3H), 1.06 (d, *J* = 6.8 Hz, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 208.1, 170.1, 167.7, 137.3, 133.4, 131.4, 129.4, 128.8, 127.8, 127.7, 122.0, 99.9, 98.1, 75.6, 74.2, 72.4, 59.5, 48.6, 48.1, 47.8, 20.6, 17.8, 17.5, 10.8. **FTIR** (thin film) ν_{max} cm^{-1} 2991, 2947, 2834, 1746, 1716, 1489, 1455, 1373, 1229, 1205, 1168, 1141, 1114, 1083, 1073, 1054, 1035, 1010, 973, 942, 878. **HRMS** (ESI-TOF, m/z) calculated for $C_{28}H_{33}BrKO_9^+$ ($[M+K]^+$): 631.0940. Observed: 631.0957.

(*R*)-(2*S*,3*R*)-1-((2*R*,5*R*,6*R*)-5,6-dimethoxy-5,6-dimethyl-1,4-dioxan-2-yl)-2,4-dimethyl-1-oxopentan-3-yl 2-acetoxy-2-phenylacetate **(*R*)-8c**.

(6.8 mg from 4.8 mg **7c**, 90%).

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.41-7.39 (m, 5H), 5.83 (s, 1H), 5.20 (dd, *J* = 8.8, 3.1 Hz, 1H), 4.49 (dd, *J* = 10.8, 4.3 Hz, 1H), 3.58 (dd, *J* = 11.5, 4.3 Hz, 1H), 3.49 (dd, *J* = 11.5, 10.8 Hz, 1H), 3.44 – 3.38 (m, 4H), 3.20 (s, 3H), 2.18 (s, 3H), 1.97 – 1.81 (m, 1H), 1.33 (s, 3H), 1.27 (s, 3H), 0.98 (d, *J* = 6.8 Hz, 3H), 0.93 (d, *J* = 6.6 Hz, 3H), 0.69 (d, *J* = 6.9 Hz, 3H). **^{13}C NMR** (75 MHz, $CDCl_3$) δ 208.6, 170.4, 168.6, 133.5, 129.3, 128.7, 127.8, 99.8, 98.0, 78.8, 74.5, 71.3, 59.7, 48.9, 48.1, 42.9, 30.3, 20.7, 19.1, 18.8, 17.8, 17.6, 7.7. **FTIR** (thin film) ν_{max} cm^{-1} 2964, 2947, 2878, 2834, 1742, 1716, 1497, 1456, 1372, 1329, 1231, 1209, 1140, 1177, 1115, 1049, 1037, 1010, 971, 943, 879. **HRMS** (ESI-TOF, m/z) calculated for $C_{25}H_{36}KO_9^+$ ($[M+K]^+$): 519.1991. Observed: 519.2003.

(*S*)-(2*S*,3*R*)-1-((2*R*,5*R*,6*R*)-5,6-dimethoxy-5,6-dimethyl-1,4-dioxan-2-yl)-2,4-dimethyl-1-oxopentan-3-yl 2-acetoxy-2-phenylacetate **(*S*)-8c**.

(7.4 mg from 5.0 mg **7c**, 94%).

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.47 – 7.34 (m, 5H), 5.87 (s, 1H), 5.21 (dd, *J* = 7.6, 4.5 Hz, 1H), 4.55 (dd, *J* = 10.9, 4.2 Hz, 1H), 3.74 (dd, *J* = 11.3, 4.2 Hz, 1H), 3.61 (dd, *J* = 11.3, 10.9 Hz, 1H), 3.52 (qd, *J* = 6.9, 4.5 Hz, 1H), 3.41 (s, 3H), 3.24 (s, 3H), 2.18 (s, 3H), 1.72 (m, 1H), 1.35 (s, 3H), 1.28 (s, 3H), 1.04 (d, *J* = 6.9 Hz, 3H), 0.76 (d, *J* = 6.8 Hz, 3H), 0.53 (d, *J* = 6.6 Hz, 3H). **^{13}C NMR** (75 MHz, $CDCl_3$) δ 209.1, 170.0, 168.6, 134.0, 129.2, 128.7, 127.7, 99.8, 98.0, 78.9, 74.3, 71.6, 59.8, 48.8, 48.1, 43.3, 30.2, 20.7, 19.1, 17.8, 17.7, 17.6, 9.3. **FTIR** (thin film) ν_{max} cm^{-1} 2963, 2878, 2834, 1745, 1716, 1497, 1456, 1373, 1332, 1231, 1210, 1176, 1141, 1116, 1055, 1037, 1011, 968, 944, 879. **HRMS** (ESI-TOF, m/z) calculated for $C_{25}H_{36}KO_9^+$ ($[M+K]^+$): 519.1991. Observed: 519.2008.

(*R*)-(2*R*,3*S*)-4-((2*R*,5*R*,6*R*)-5,6-dimethoxy-5,6-dimethyl-1,4-dioxan-2-yl)-3-methyl-4-oxobutan-2-yl 2-acetoxy-2-phenylacetate **(*R*)-8d**.

(7.6 mg from 5.1 mg **7d**, 91%).

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.44 – 7.36 (m, 5H), 5.80 (s, 1H), 5.41 (qd, *J* = 6.4, 4.7 Hz, 1H), 4.30 (dd, *J* = 10.3, 4.6 Hz, 1H), 3.59 (dd, *J* = 11.3, 4.6 Hz, 1H), 3.53 (dd, *J* = 11.3, 10.3 Hz, 1H), 3.31 (s, 3H), 3.21 (s, 3H), 3.23 – 3.13 (m, 1H), 2.18 (s, 3H), 1.32 (s, 3H), 1.29 (d, *J* = 6.4 Hz, 3H), 1.26 (s, 3H), 0.83 (d, *J* = 6.9 Hz, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 208.4, 170.4, 168.3, 133.7, 129.3, 128.8, 127.6, 99.8, 98.0, 74.7, 71.8, 71.8, 59.7, 48.7, 48.0, 46.4, 20.6, 18.3, 17.7, 17.6, 9.3. **FTIR** (thin film) ν_{max} cm^{-1} 2989, 2947, 2834, 1741, 1715, 1497, 1455, 1373, 1324, 1264, 1229, 1210, 1177, 1138, 1114, 1082, 1054, 1032, 1003, 963, 943, 878. **HRMS** (ESI-TOF, m/z) calculated for $C_{23}H_{32}KO_9^+$ ($[M+K]^+$): 491.1678. Observed: 491.1693.

(S)-(2R,3S)-4-((2R,5R,6R)-5,6-dimethoxy-5,6-dimethyl-1,4-dioxan-2-yl)-3-methyl-4-oxobutan-2-yl 2-acetoxy-2-phenylacetate **(*S*)-8d**.

(7.3 mg from 4.5 mg **7d**, 99%).

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.45 – 7.35 (m, 5H), 5.80 (s, 1H), 5.42 (qd, *J* = 6.3, 5.3 Hz, 1H), 4.44 (dd, *J* = 10.7, 4.2 Hz, 1H), 3.72 (dd, *J* = 11.5, 4.2 Hz, 1H), 3.64 (dd, *J* = 11.5, 10.7 Hz, 1H), 3.35 – 3.25 (m, 4H), 3.24 (s, 3H), 2.18 (s, 3H), 1.34 (s, 3H), 1.28 (s, 3H), 1.11 (d, *J* = 3.2 Hz, 3H), 1.09 (d, *J* = 3.8 Hz, 3H). **^{13}C NMR** (75 MHz, $CDCl_3$) δ 208.8, 170.2, 168.2, 133.6, 129.2, 128.8, 127.5, 99.8, 98.0, 74.6, 72.0, 71.8, 59.7, 48.6, 48.1, 46.3, 20.6, 17.8, 17.7, 17.6, 10.4. **FTIR** (thin film) ν_{max} cm^{-1} 2989, 2946, 2834, 1742, 1715, 1497, 1455, 1373, 1327, 1264, 1229, 1209, 1177, 1138, 1113, 1082, 1053, 1032, 1003, 963, 943, 878. **HRMS** (ESI-TOF, m/z) calculated for $C_{23}H_{32}KO_9^+$ ($[M+K]^+$): 491.1678. Observed: 491.1688.

(*R*)-(2*S*,3*R*)-1-((2*R*,5*R*,6*R*)-5,6-dimethoxy-5,6-dimethyl-1,4-dioxan-2-yl)-2-methyl-1-oxoheptan-3-yl 2-acetoxy-2-phenylacetate **(*R*)-8e**.

(7.8 mg from 5.3 mg **7e**, 94%).

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.42 – 7.36 (m, 5H), 5.80 (s, 1H), 5.43 (ddd, *J* = 7.5, 6.4, 3.5 Hz, 1H), 4.37 (dd, *J* = 10.6, 4.4 Hz, 1H), 3.59 (dd, *J* = 11.5, 4.4 Hz, 1H), 3.51 (dd, *J* = 11.5, 10.6 Hz, 1H), 3.37 (s, 3H), 3.30 – 3.23 (m, 1H), 3.21 (s, 3H), 2.18 (s, 3H), 1.77 – 1.45 (m, 2H), 1.33 – 1.20 (m, 4H), 1.32 (s, 3H), 1.26 (s, 3H), 0.88 (t, *J* = 6.9 Hz, 3H), 0.77 (d, *J* = 6.9 Hz, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 208.4, 173.5, 168.5, 133.7, 129.3, 128.7, 127.7, 99.8, 98.0, 74.6, 74.5, 71.5, 59.7, 48.8, 48.1, 44.6, 32.0, 27.5, 22.2, 20.7, 17.7, 17.6, 13.9, 8.2. **FTIR** (thin film) ν_{max} cm^{-1} 2953, 2873, 2835, 1742, 1716, 1497, 1456, 1373, 1331, 1263, 1230, 1208, 1176, 1139, 1115, 1083, 1037, 1005, 967, 944, 879. **HRMS** (ESI-TOF, m/z) calculated for $C_{26}H_{38}KO_9^+$ ($[M+K]^+$): 533.2147. Observed: 533.2170.

(*S*)-(2*S*,3*R*)-1-((2*R*,5*R*,6*R*)-5,6-dimethoxy-5,6-dimethyl-1,4-dioxan-2-yl)-2-methyl-1-oxoheptan-3-yl 2-acetoxy-2-phenylacetate **(*S*)-8e**.

(8.6 mg from 6.1 mg **7e**, 92%).

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.46 – 7.33 (m, 5H), 5.82 (s, 1H), 5.40 (ddd, *J* = 8.3, 5.0 Hz, 1H), 4.50 (dd, *J* = 10.9, 4.2 Hz, 1H), 3.73 (dd, *J* = 11.5, 4.2 Hz, 1H), 3.62 (dd, *J* = 11.5, 10.9 Hz, 1H), 3.36 (s, 3H), 3.34 – 3.29 (m, 1H), 3.24 (s, 3H), 2.17 (s, 3H), 1.51 – 1.23 (m, 2H), 1.34 (s, 3H), 1.28 (s, 3H), 1.20 – 1.05 (m, 2H), 1.06 (d, *J* = 6.9 Hz, 3H), 0.97 – 0.87 (m, 2H),

0.70 (t, *J* = 7.3 Hz, 3H). **^{13}C NMR** (75 MHz, $CDCl_3$) δ 208.9, 170.1, 168.6, 133.8, 129.2, 128.7, 127.6, 99.8, 98.0, 74.5, 74.5, 71.8, 59.7, 48.7, 48.1, 45.1, 32.0, 27.1, 22.0, 20.7, 17.7, 17.6, 13.7, 9.6. **FTIR** (thin film) ν_{max} cm^{-1} 2954, 2873, 2834, 1742, 1713, 1526, 1496, 1455, 1373, 1332, 1230, 1208, 1176, 1140, 1115, 1083, 1037, 964, 944, 879. **HRMS** (ESI-TOF, m/z) calculated for $C_{26}H_{38}KO_9^+$ ($[M+K]^+$): 533.2147. Observed: 533.2170.

(*R*)-(2*S*,3*R*)-1-((2*R*,5*R*,6*R*)-5,6-dimethoxy-5,6-dimethyl-1,4-dioxan-2-yl)-2-methyl-1-oxopentan-3-yl 2-acetoxy-2-phenylacetate **(*R*)-8f**.

(6.3 mg from 4.2 mg **7f**, 93%).

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.44 – 7.36 (m, 5H), 5.81 (s, 1H), 5.35 (ddd, *J* = 7.3, 6.9, 3.7 Hz, 1H), 4.38 (dd, *J* = 10.6, 4.5 Hz, 1H), 3.59 (dd, *J* = 11.5, 4.5 Hz, 1H), 3.52 (dd, *J* = 11.5, 10.6 Hz, 1H), 3.37 (s, 3H), 3.33 – 3.23 (m, 1H), 3.21 (s, 3H), 2.18 (s, 3H), 1.78 – 1.52 (m, 2H), 1.32 (s, 3H), 1.26 (s, 3H), 0.93 (t, *J* = 7.4 Hz, 3H), 0.76 (d, *J* = 6.9 Hz, 3H). **^{13}C NMR** (75 MHz, $CDCl_3$) δ 208.5, 170.4, 168.5, 133.5, 129.3, 128.7, 127.7, 99.8, 98.0, 75.8, 74.6, 71.4, 59.7, 48.8, 48.8, 44.2, 25.5, 20.7, 17.8, 17.6, 9.9, 8.1. **FTIR** (thin film) ν_{max} cm^{-1} 2946, 2881, 2835, 1743, 1717, 1497, 1456, 1373, 1332, 1263, 1231, 1211, 1178, 1142, 1116, 1083, 1055, 1038, 1003, 970, 946, 879. **HRMS** (ESI-TOF, m/z) calculated for $C_{24}H_{34}KO_9^+$ ($[M+K]^+$): 505.1834. Observed: 505.1843.

(*S*)-(2*S*,3*R*)-1-((2*R*,5*R*,6*R*)-5,6-dimethoxy-5,6-dimethyl-1,4-dioxan-2-yl)-2-methyl-1-oxopentan-3-yl 2-acetoxy-2-phenylacetate **(*S*)-8f**.

(7.3 mg from 4.8 mg **7f**, 94%).

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.46 – 7.34 (m, 5H), 5.82 (s, 1H), 5.34 (ddd, *J* = 7.4, 6.0, 4.6 Hz, 1H), 4.50 (dd, *J* = 10.8, 4.2 Hz, 1H), 3.73 (dd, *J* = 11.5, 4.2 Hz, 1H), 3.62 (dd, *J* = 11.5, 10.8 Hz, 1H), 3.41 – 3.33 (m, 1H), 3.36 (s, 3H), 3.24 (s, 3H), 2.17 (s, 3H), 1.53 – 1.41 (m, 2H), 1.34 (s, 3H), 1.28 (s, 3H), 1.06 (d, *J* = 6.9 Hz, 3H), 0.63 (t, *J* = 7.4 Hz, 3H). **^{13}C NMR** (75 MHz, $CDCl_3$) δ 208.9, 170.1, 168.6, 133.8, 129.2, 128.7, 127.6, 99.8, 98.0, 76.0, 74.5, 71.7, 59.7, 48.7, 48.1, 44.5, 25.4, 20.7, 17.8, 17.6, 9.6, 9.4. **FTIR** (thin film) ν_{max} cm^{-1} 2945, 2880, 2834, 1742, 1716, 1497, 1455, 1373, 1332, 1266, 1229, 1208, 1176, 1138, 1114, 1084,

1054, 1035, 1004, 969, 944, 878. **HRMS** (ESI-TOF, m/z) calculated for $C_{24}H_{34}KO_9^+$ ($[M+K]^+$): 505.1834. Observed: 505.1848.

(*R*)-(1*R*,2*S*)-1-cyclohexyl-3-((2*R*,5*R*,6*R*)-5,6-dimethoxy-5,6-dimethyl-1,4-dioxan-2-yl)-2-methyl-3-oxopropyl 2-acetoxy-2-phenylacetate **(*R*)-8g**.

(7.6 mg from 5.2 mg **7g**, 97%).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.42 – 7.36 (m, 5H), 5.85 (s, 1H), 5.27 (dd, *J* = 8.6, 3.1 Hz, 1H), 4.48 (dd, *J* = 10.8, 4.2 Hz, 1H), 3.57 (dd, *J* = 11.3, 4.2 Hz, 1H), 3.49 (dd, *J* = 11.3, 10.8 Hz, 1H), 3.44 – 3.38 (m, 1H), 3.43 (s, 3H), 3.20 (s, 3H), 2.17 (s, 3H), 1.82 – 1.62 (m, 5H), 1.33 (s, 3H), 1.27 (s, 3H), 1.26 – 0.84 (m, 6H), 0.70 (d, *J* = 6.9 Hz, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 208.6, 170.3, 168.6, 133.7, 129.3, 128.6, 127.8, 99.8, 98.0, 77.9, 74.5, 71.3, 59.7, 48.9, 48.1, 42.4, 39.6, 29.3, 29.1, 26.1, 25.9, 25.7, 20.7, 17.8, 17.6, 7.7. **FTIR** (thin film) ν_{max} cm^{-1} 2990, 2928, 2853, 1743, 1716, 1451, 1373, 1319, 1231, 1210, 1178, 1141, 1115, 1082, 1054, 1038, 1008, 975, 943, 890. **HRMS** (ESI-TOF, m/z) calculated for $C_{28}H_{40}KO_9^+$ ($[M+K]^+$): 559.2304. Observed: 559.2321.

(*S*)-(1*R*,2*S*)-1-cyclohexyl-3-((2*R*,5*R*,6*R*)-5,6-dimethoxy-5,6-dimethyl-1,4-dioxan-2-yl)-2-methyl-3-oxopropyl 2-acetoxy-2-phenylacetate **(*S*)-8g**.

(8.0 mg from 5.6 mg **7g**, %).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.47 – 7.33 (m, 5H), 5.88 (s, 1H), 5.24 (dd, *J* = 7.1, 4.9 Hz, 1H), 4.52 (dd, *J* = 10.9, 4.1 Hz, 1H), 3.72 (dd, *J* = 11.3, 4.1 Hz, 1H), 3.61 (dd, *J* = 11.3, 10.9 Hz, 1H), 3.52 (qd, *J* = 6.9, 4.9 Hz, 1H), 3.40 (s, 3H), 3.24 (s, 3H), 2.17 (s, 3H), 1.64 – 1.46 (m, 2H), 1.44 – 1.32 (m, 1H), 1.33 (s, 3H), 1.28 (s, 3H), 1.29 – 1.18 (m, 2H), 1.16 – 1.06 (m, 2H), 1.04 (d, *J* = 6.9 Hz, 3H), 0.99 – 0.82 (m, 2H), 0.78 – 0.60 (m, 2H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 209.3, 169.9, 168.6, 134.1, 129.1, 128.6, 127.7, 99.8, 98.0, 78.1, 74.3, 71.78, 59.8, 48.7, 48.1, 42.7, 39.6, 29.2, 27.8, 26.0, 25.8, 25.5, 20.7, 17.8, 17.6, 9.6. **FTIR** (thin film) ν_{max} cm^{-1} 2991, 2930, 2854, 1746, 1716, 1453, 1373, 1324, 1231, 1209, 1177, 1141, 1116, 1083, 1057, 1038, 1010, 964, 944, 880, 741, 697. **HRMS** (ESI-TOF, m/z) calculated for $C_{28}H_{40}KO_9^+$ ($[M+K]^+$): 559.2304. Observed: 559.2322.

(*R*)-(2*S*,3*R*,*E*)-1-((2*R*,5*R*,6*R*)-5,6-dimethoxy-5,6-dimethyl-1,4-dioxan-2-yl)-2-methyl-1-oxododec-6-en-3-yl 2-acetoxy-2-phenylacetate **(*R*)-8h**.

(8.9 mg from 6.2 mg **7h**, 98%).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.44 – 7.36 (m, 5H), 5.83 (s, 1H), 5.46 – 5.28 (m, 3H), 4.39 (dd, *J* = 10.5, 4.2 Hz, 1H), 3.58 (dd, *J* = 11.8, 4.2 Hz, 1H), 3.51 (dd, *J* = 11.8, 10.5 Hz, 1H), 3.36 (s, 3H), 3.27 – 3.18 (m, 4H), 2.17 (s, 3H), 2.09 – 1.85 (m, 4H), 1.79 (m, 1H), 1.65-1.50 (m, 4H), 1.34-1.24 (m, 3H), 1.32 (s, 3H), 1.26 (s, 3H), 0.89 (t, *J* = 6.8 Hz, 3H), 0.77 (d, *J* = 6.8 Hz, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 208.3, 170.3, 168.4, 133.6, 131.9, 129.3, 128.7, 128.2, 127.7, 99.7, 98.0, 74.6, 74.0, 71.5, 59.7, 48.8, 48.0, 44.8, 32.7, 32.6, 31.4, 29.2, 28.5, 22.5, 20.7, 17.8, 17.6, 14.0, 8.3. **FTIR** (thin film) ν_{max} cm^{-1} 2990, 2950, 2925, 2872, 2855, 1743, 1716, 1497, 1456, 1373, 1333, 1297, 1261, 1230, 1209, 1175, 1141, 1115, 1083, 1054, 1037, 1004, 968, 944, 879. **HRMS** (ESI-TOF, m/z) calculated for $C_{31}H_{46}KO_9^+$ ($[M+K]^+$): 601.2773. Observed: 601.2792.

(*S*)-(2*S*,3*R*,*E*)-1-((2*R*,5*R*,6*R*)-5,6-dimethoxy-5,6-dimethyl-1,4-dioxan-2-yl)-2-methyl-1-oxododec-6-en-3-yl 2-acetoxy-2-phenylacetate **(*S*)-8h**.

(8.6 mg from 5.9 mg **7h**, 100%).

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.47 – 7.35 (m, 5H), 5.83 (s, 1H), 5.39 (ddd, *J* = 8.8, 4.5, 4.5 Hz, 1H), 5.22 – 5.02 (m, 2H), 4.52 (dd, *J* = 11.0, 4.2 Hz, 1H), 3.73 (dd, *J* = 11.5, 4.2 Hz, 1H), 3.61 (dd, *J* = 11.5, 11.0 Hz, 1H), 3.35 (s, 3H), 3.34 – 3.30 (m, 1H), 3.23 (s, 3H), 2.18 (s, 3H), 1.90 – 1.81 (m, 2H), 1.66 – 1.08 (m, 10H), 1.34 (s, 3H), 1.28 (s, 3H), 1.06 (d, *J* = 6.9 Hz, 3H), 0.88 (t, *J* = 6.9 Hz, 3H). **^{13}C NMR** (75 MHz, $CDCl_3$) δ 208.7, 170.1, 168.4, 133.8, 131.8, 129.2, 128.7, 128.0, 127.6, 99.7, 98.0, 74.5, 73.9, 71.9, 59.7, 48.7, 48.1, 45.2, 32.6, 32.4, 31.4, 29.1, 28.1, 22.5, 20.7, 17.8, 17.6, 14.1, 9.5. **FTIR** (thin film) ν_{max} cm^{-1} 2989, 2926, 2872, 2855, 1745, 1716, 1455, 1373, 1333, 1262, 1230, 1209, 1174, 1141, 1116, 1055, 1037, 968, 945, 880. **HRMS** (ESI-TOF, m/z) calculated for $C_{31}H_{46}KO_9^+$ ($[M+K]^+$): 601.2773. Observed: 601.2797.

(*R*)-(3*R*,4*S*,*E*)-5-((2*R*,5*R*,6*R*)-5,6-dimethoxy-5,6-dimethyl-1,4-dioxan-2-yl)-4-methyl-5-oxo-1-phenylpent-1-en-3-yl 2-acetoxy-2-phenylacetate **(*R*)-8i**.

(8.3 mg from 5.8 mg **7i**, 97%).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.48 – 7.44 (m, 2H), 7.42 – 7.37 (m, 3H), 7.34 – 7.23 (m, 5H), 6.53 (dd, *J* = 16.0, 1.2 Hz, 1H), 6.13 (dd, *J* = 16.0, 6.3 Hz, 1H), 5.92 (s, 1H), 5.90 (ddd, *J* = 6.3, 5.9, 1.2 Hz, 1H), 4.30 (dd, *J* = 10.5, 4.5 Hz, 1H), 3.59 (dd, *J* = 11.5, 4.5 Hz, 1H), 3.54 (dd, *J* = 11.4, 10.5 Hz, 1H), 3.44 – 3.37 (m, 1H), 3.29 (s, 3H), 3.20 (s, 3H), 2.18 (s, 3H), 1.35 (s, 3H), 1.26 (s, 3H), 0.90 (d, *J* = 6.9 Hz, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 207.9, 170.3, 168.0, 136.0, 133.6, 133.1, 129.3, 128.8, 128.6, 128.1, 127.6, 126.7, 124.7, 99.8, 98.1, 75.3, 74.6, 72.1, 59.6, 48.7, 48.0, 46.0, 20.6, 17.8, 17.6, 9.9. **FTIR** (thin film) ν_{max} cm^{-1} 2991, 2943, 2834, 1744, 1716, 1496, 1454, 1373, 1229, 1207, 1169, 1141, 1115, 1054, 1036, 1009, 966, 943, 912, 879. **HRMS** (ESI-TOF, m/z) calculated for $C_{30}H_{40}NO_9^+$ ($[M+NH_4]^+$): 558.2698. Observed: 558.2702.

(*S*)-(3*R*,4*S*,*E*)-5-((2*R*,5*R*,6*R*)-5,6-dimethoxy-5,6-dimethyl-1,4-dioxan-2-yl)-4-methyl-5-oxo-1-phenylpent-1-en-3-yl 2-acetoxy-2-phenylacetate **(*S*)-8i**.

(9.8 mg from 6.1 mg **7i**, 98%).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.48 – 7.42 (m, 2H), 7.40 – 7.36 (m, 3H), 7.28 – 7.20 (m, 3H), 7.13 (d, *J* = 6.7 Hz, 2H), 6.15 (d, *J* = 15.1 Hz, 1H), 5.98 – 5.88 (m, 3H), 4.44 (dd, *J* = 10.8, 4.1 Hz, 1H), 3.72 (dd, *J* = 11.5, 4.1 Hz, 1H), 3.63 (dd, *J* = 11.5, 10.8 Hz, 1H), 3.53 – 3.45 (m, 1H), 3.30 (s, 3H), 3.22 (s, 3H), 2.19 (s, 3H), 1.36 (s, 3H), 1.28 (s, 3H), 1.14 (d, *J* = 6.9 Hz, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 208.3, 170.1, 167.9, 135.9, 133.7, 132.7, 129.3, 128.8, 128.5, 128.0, 127.8, 126.5, 124.5, 99.9, 98.1, 75.2, 74.4, 72.3, 59.7, 48.6, 48.1, 46.0, 20.6, 17.8, 17.6, 10.8. **FTIR** (thin film) ν_{max} cm^{-1} 2990, 2943, 2834, 1747, 1717, 1496, 1455, 1373, 1332, 1230, 1207, 1172, 1142, 1116, 1055, 1036, 1011, 968, 944, 879. **HRMS** (ESI-TOF, m/z) calculated for $C_{30}H_{36}KO_9^+$ ($[M+K]^+$): 579.1991. Observed: 579.2011.

(*R*)-(2*S*,3*R*,*E*)-1-((2*R*,5*R*,6*R*)-5,6-dimethoxy-5,6-dimethyl-1,4-dioxan-2-yl)-2-methyl-1-oxooct-4-en-3-yl 2-acetoxy-2-phenylacetate **(*R*)-8j**.

(7.5 mg from 5.0 mg **7j**, 98%).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.45 – 7.35 (m, 5H), 5.87 (s, 1H), 5.72 – 5.63 (m, 2H), 5.41 (dd, *J* = 15.5, 6.7 Hz, 1H), 4.28 (dd, *J* = 10.5, 4.4 Hz, 1H), 3.59 (dd, *J* = 11.5, 4.4 Hz, 1H), 3.54 (dd, *J* = 11.5, 10.5 Hz, 1H), 3.32 (s, 3H), 3.31 – 3.24 (m, 1H), 3.21 (s, 3H), 2.17 (s, 3H), 1.98 (dt, *J* = 7.0, 7.0, Hz, 2H), 1.39 – 1.34 (m, 2H), 1.33 (s, 3H), 1.26 (s, 3H), 0.92 – 0.80 (m, 6H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 208.1, 170.2, 167.9, 135.5, 133.8, 129.2, 128.7, 127.6, 125.6, 99.8, 98.0, 75.5, 74.6, 71.9, 59.7, 48.7, 48.0, 46.0, 34.2, 22.0, 20.6, 17.8, 17.6, 13.5, 9.8. **FTIR** (thin film) ν_{max} cm^{-1} 2991, 2956, 2930, 2873, 2835, 1745, 1716, 1497, 1456, 1373, 1336, 1254, 1229, 1208, 1171, 1140, 1115, 1054, 1037, 1010, 967, 943, 879. **HRMS** (ESI-TOF, m/z) calculated for $C_{27}H_{38}KO_9^+$ ($[M+K]^+$): 545.2147. Observed: 545.2160.

(*S*)-(2*S*,3*R*,*E*)-1-((2*R*,5*R*,6*R*)-5,6-dimethoxy-5,6-dimethyl-1,4-dioxan-2-yl)-2-methyl-1-oxooct-4-en-3-yl 2-acetoxy-2-phenylacetate **(*S*)-8j**.

(7.3 mg from 5.3 mg **7j**, 90%).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.44 – 7.33 (m, 5H), 5.87 (s, 1H), 5.67 (dd, *J* = 6.4, 6.4 Hz, 1H), 5.39 (ddd, *J* = 14.8, 6.6, 6.6 Hz, 1H), 5.22 (dd, *J* = 14.8, 6.4 Hz, 1H), 4.40 (dd, *J* = 11.1, 3.9 Hz, 1H), 3.71 (dd, *J* = 11.1, 3.9 Hz, 1H), 3.63 (dd, *J* = 11.1, 11.1 Hz, 1H), 3.43 – 3.35 (m, 1H), 3.33 (s, 3H), 3.23 (s, 3H), 2.17 (s, 3H), 1.88 – 1.81 (dt, *J* = 7.0, 7.0 Hz, 2H), 1.35 (s, 3H), 1.28 (s, 3H), 1.22 (m, 2H), 1.08 (d, *J* = 6.9 Hz, 3H), 0.76 (t, *J* = 7.3 Hz, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 208.5, 170.1, 167.9, 135.4, 133.7, 129.2, 128.7, 127.7, 125.2, 99.9, 98.1, 75.6, 74.5, 72.2, 59.7, 48.6, 48.1, 45.8, 34.1, 21.9, 20.6, 17.8, 17.6, 13.4, 10.8. **FTIR** (thin film) ν_{max} cm^{-1} 3066, 2956, 1740 (shoulder), 1497, 1456, 1431, 1373, 1328, 1227 (shoulder), 1170, 1141, 1114, 1082, 1048 (shoulder), 1004, 966, 944, 877. **HRMS** (ESI-TOF, m/z) calculated for $C_{27}H_{38}KO_9^+$ ($[M+K]^+$): 545.2147. Observed: 545.2159.

(1*S*,2*S*)-3-((2*R*,5*R*,6*R*)-5,6-dimethoxy-5,6-dimethyl-1,4-dioxan-2-yl)-2-methyl-3-oxo-1-phenylpropyl acetate **10**.

Acetic anhydride (111 µL, 1.18 mmol, 2.0 equiv) was added dropwise to a stirring solution of the starting material **7a** (200 mg, 0.592 mmol, 1 equiv) and *N*,*N*-4-dimethylaminopyridine (361 mg, 2.96 mmol, 5 equiv) in dichloromethane (5 mL) at 0 °C under an atmosphere of dry argon. The mixture was stirred at this temperature for 15 min. Water (50 mL) and diethyl

ether (10 mL) were added and the mixture was stirred rapidly at room temperature for 2 min. The layers were separated and the aqueous layer was extracted thrice with diethyl ether (3 × 10 mL). The combined organic layers were washed five times with saturated aqueous ammonium chloride (5 × 20 mL), water (10 mL) and brine (10 mL) and dried over magnesium sulfate. The solution was then filtered through a plug of silica gel (20 g, Merck 9385 grade) which was washed several times with diethyl ether. The solvent was removed under reduced pressure to afford the product as a colourless oil (223 mg, 99%).

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.36 – 7.23 (m, 5H), 6.35 (d, *J* = 5.3 Hz, 1H), 4.36 (dd, *J* = 10.8, 4.2 Hz, 1H), 3.67-3.62 (m, 2H), 3.55 (dd, *J* = 11.5, 10.8 Hz, 1H), 3.33 (s, 3H), 3.23 (s, 3H), 2.09 (s, 3H), 1.42 (s, 3H), 1.28 (s, 3H), 1.03 (d, *J* = 6.9 Hz, 3H). **^{13}C NMR** (75 MHz, $CDCl_3$) δ 209.0, 169.9, 139.0, 128.4, 127.9, 126.1, 99.9, 98.0, 74.3, 72.3, 59.5, 48.7, 48.1, 47.7, 20.9, 17.8, 17.6, 10.0. **FTIR** (thin film) ν_{max} cm^{-1} 2990, 2947, 2834, 1740, 1715, 1495, 1453, 1372, 1228, 1165, 1139, 1113, 1053, 1034, 1022, 969, 944, 878. **HRMS** (ESI-TOF, m/z) calculated for $C_{20}H_{28}KO_7^+$ ($[M+K]^+$): 419.1467. Observed: 419.1484.

(1*S*,2*S*,4*R*)-4,5-dihydroxy-2-methyl-3-oxo-1-phenylpentyl acetate **11**.

The starting material **10** (50.0 mg, 0.131 mmol) was dissolved in tetrahydrofuran (1 mL) and the solution was stirred at 0 °C (water/ice bath). To this was added dropwise a mixture of trifluoroacetic acid (3 mL) and water (1 mL). The reaction was stirred at 0 °C for 3 h. The reaction mixture was added portionwise to a stirring mixture of ice (10 g), saturated aqueous sodium bicarbonate (20 mL) and diethyl ether (20 mL). The mixture was extracted thrice with diethyl ether (3 × 20 mL). The combined organic layers were washed with brine and dried over magnesium sulfate. The solvent was removed under reduced pressure to afford the product as a viscous, colourless oil (33.1 mg, 95%).

^{1}H NMR (400 MHz, MeOH) δ 7.36 – 7.23 (m, 5H), 6.20 (d, *J* = 6.8 Hz, 1H), 4.08 (dd, *J* = 5.3, 4.0 Hz, 1H), 3.65 (dq, *J* = 6.8, 6.8 Hz, 1H), 3.55 (dd, *J* = 11.5, 4.0 Hz, 1H), 3.49 (dd, *J* = 11.5, 5.3 Hz, 1H), 2.08 (s, 3H), 1.09 (d, *J* = 6.8 Hz, 3H). **^{13}C NMR** (101 MHz, MeOH) δ 214.1, 171.8, 140.6, 129.4, 129.0, 127.7, 78.6, 76.3, 64.5, 48.9, 20.9, 11.7. **FTIR** (thin film) ν_{max} cm^{-1} 3447 (br), 3033, 2938, 2880, 1715 (has shoulder), 1496, 1455, 1373, 1231 (has

shoulder), 1117, 1050, 1021, 970, 916, 884, 761. **HRMS** (ESI-TOF, m/z) calculated for $C_{14}H_{18}NaO_5^+$ ($[M+Na]^+$): 289.1052. Observed: 289.1054.

(2*S*,3*S*)-3-acetoxy-2-methyl-3-phenylpropanoic acid **12**.

To a rapidly stirring mixture of the starting keto-diol **11** (50 mg, 0.188 mmol) in acetonitrile (3 mL), dichloromethane (3 mL) and water (3 mL) was added sodium periodate (400 mg, 1.87 mmol, 9.9 equiv) at 0 °C. The mixture was stirred at this temperature for 20 min. Water (10 mL) and diethyl ether (10 mL) were added and the mixture was stirred for 2 min. The layers were separated. The aqueous layer was extracted five times with diethyl ether (5 × 5 mL). The combined organic layers were washed with brine (10 mL) and dried over magnesium sulfate. The solvent was removed under reduced pressure to afford the product as a paste (38.8 mg, 93%).

^{1}H NMR (400 MHz, MeOH) δ 7.37 – 7.23 (m, 5H), 6.05 (d, *J* = 6.7 Hz, 1H), 2.94 (dq, *J* = 6.9 Hz, 1H), 2.08 (s, 3H), 1.19 (d, *J* = 7.0 Hz, 3H). **^{13}C NMR** (101 MHz, MeOH) δ 176.7, 171.7, 140.2, 129.4, 129.0, 127.7, 77.5, 46.8, 20.8, 12.8. **FTIR** (thin film) ν_{max} cm^{-1} 3032, 2983, 2945, 1736, 1710, 1496, 1431, 1456, 1373, 1227, 1116, 1095, 1021, 973, 917, 847. **HRMS** (ESI-TOF, m/z) calculated for $C_{12}H_{14}NaO_4^+$ ($[M+Na]^+$): 245.0790. Observed: 245.0795.

(2*S*,3*S*)-3-hydroxy-2-methyl-3-phenylpropanoic acid **13**.

To a solution of the starting acetate 12 (26.0 mg, 0.117 mmol, 1 equiv) in tetrahydrofuran (18 mL) was added an aqueous solution of lithium hydroxide (0.1 M, 4.5 mL, 0.450 mmol, 3.85 equiv) at room temperature. The mixture was stirred at room temperature overnight. Ether (20 mL) and dilute aqueous hydrochloric acid (1 M, 20 mL) were added and the mixture was stirred for 1 minute before separating the layers. The aqueous layer was extracted thrice with diethyl ether (3 × 20 mL). The combined organic layers were dried over magnesium sulfate. The solvent was removed under reduced pressure to afford the product as a white paste (18.6 mg, 88%).

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.38 – 7.27 (m, 5H), 5.19 (d, *J* = 3.9 Hz, 1H), 2.84 (qd, *J* = 7.2, 3.9 Hz, 1H), 1.15 (d, *J* = 7.2 Hz, 3H). **^{13}C NMR** (75 MHz, $CDCl_3$) δ 180.6, 141.0, 128.4, 127.7, 125.9, 73.3, 46.1, 10.3. **FTIR** (thin film) ν_{max} cm^{-1} 3600-3000 (v. br), 3063, 3031, 2983, 2924, 1704, 1494, 1454, 1402, 1196, 1122, 1060, 1021, 984, 909. **HRMS** (ESI-TOF, m/z) calculated for $C_{10}H_{12}NaO_3^+$ ($[M+Na]^+$): 203.0679. Observed: 203.0676. $[\alpha]_d$ = -22.0 (c = 0.9, CH_2Cl_2, α = -0.20, l = 10 cm).

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