Polyketide Synthesis Using the Boron-Mediated, *anti*-Aldol Reactions of Lactate-Derived Ketones: Total Synthesis of (–)-ACRL Toxin IIIB

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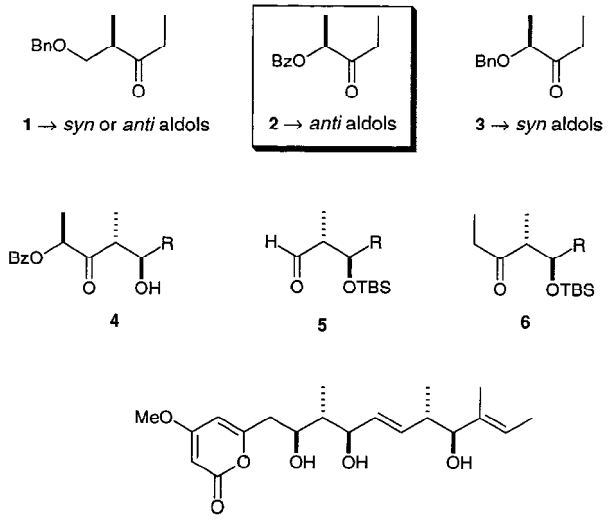
Abstract: The boron-mediated, *anti*-selective, aldol reactions of ketone **2** (and related derivatives) proceed with high levels of asymmetric induction, diastereoselectivities of up to 200:1 in favour of the aldol adducts **4** are obtained with achiral aldehydes and reagent control operates with chiral aldehydes. These lactate-derived ketones provide a versatile chiral auxiliary for the synthesis of β-hydroxy carbonyl compounds. Oxidative removal of the auxiliary provides enantiomerically pure aldehydes **5**, while reductive deoxygenation gives the corresponding ethyl ketones **6**. This practical asymmetric methodology for generating *anti*-aldols is illustrated by an efficient total synthesis of (–)-ACRL toxin IIIB (**7**), which proceeds in 15 steps from **2** with 21% overall yield and 88% diastereoselectivity.

Key words: chiral auxiliary, lactate, enol borinate, *anti*-aldol, (–)-ACRL toxin IIIB

The polyketides represent an important reservoir of natural product diversity, which is associated with a wide range of biological activity. These polyoxygenated compounds continue to stimulate the development of new synthetic methods and strategies, particularly for the installation of the characteristic stereochemical arrays of alternating methyl and hydroxyl groups. Asymmetric aldol reactions, which can combine the formation of carbon-carbon bonds with the generation of two stereogenic centres, have emerged as especially powerful tools for the efficient synthesis of polyketides.[1] In particular, the use of a temporary chiral auxiliary attached to a stereodefined enolate is a popular tactic, with removal of the auxiliary after the aldol step. However, while such *syn*-selective asymmetric aldol reactions can be used with confidence, the analogous *anti*-selective transformation is generally much less straightforward.[1,2]

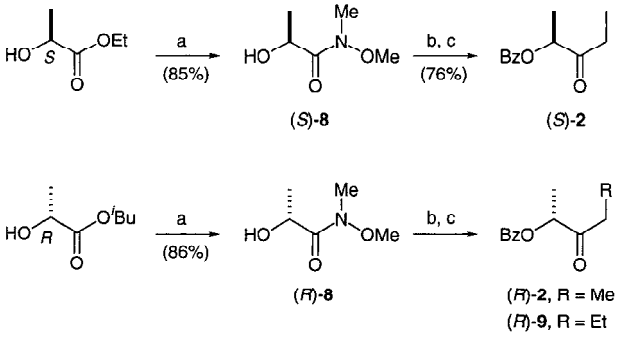
We have previously developed the use of β-alkoxy ketones such as **1** (Figure), where high levels of π-face selectivity can be readily achieved in both *syn*- and *anti*-selective aldol reactions by appropriate choice of the metal enolate derivative.[3] As a recent extension, we introduced the related α-alkoxy ketones **2** and **3** for boron-mediated aldol reactions, where the simple choice of hydroxyl protecting group determines the enolate geometry and resulting *syn vs anti* diastereoselectivity.[4–6] Hence, these lactate-derived, chiral ketones[7,8] function as versatile new reagents for stereocontrolled polyketide synthesis.[9,10]

We now report our preferred synthesis of ketone **2** and provide full details of its *anti*-selective, asymmetric aldol reactions with aldehydes. The resulting aldol adducts **4** can be elaborated into a wide range of enantiomerically pure carbonyl compounds, *e.g.* by transformation into aldehydes **5** and ethyl ketones **6**. The ready availability of the auxiliary group, the general efficiency and mildness of the boron-mediated aldol reaction, and the versatility of the resulting adducts, make this method advantageous. Finally, we illustrate this novel aldol methodology by its application to the total synthesis of (–)-ACRL toxin IIIB (**7**), as a representative polyketide derivative having *anti*-configured propionate units.[9]



Figure

Synthesis of **2**: Our initial multi-step synthesis[4] of the ethyl ketone **2** *via* the corresponding benzyl ether **3** has been superseded by a shorter, more convenient route. Both enantiomers of ketone **2** are now readily available in three routine steps (65% overall) from the commercially available lactate esters (Scheme 1). Ethyl (*S*)-(–)-lactate was first reacted with *N*,*O*-dimethylhydroxylamine hydrochloride, in the presence of *i*-PrMgCl, to give the Weinreb amide (*S*)-**8** in 85% yield. This improved procedure[11] is

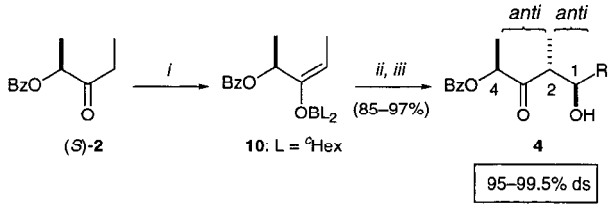


Reagents: (a) MeONHMe.HCl, ^{i}PrMgCl, THF, –20 → 0°C, 1.5 h. (b) EtMgBr (or PrMgBr), THF, 0 °C, 2 h. (c) Bz_2O, $^{i}Pr_2NEt$, DMAP, CH_2Cl_2, 14 h

Scheme 1

experimentally straightforward and avoids the use of pyrophoric Me_3Al. Addition of EtMgBr to (*S*)-**8**, followed by benzoylation of the resulting (volatile) α-hydroxy ketone with benzoic anhydride (Bz_2O), then provided (*S*)-**2**, $[\alpha]_D^{20}$ +25.1 (*c* = 4.6, $CHCl_3$). In an identical manner, isobutyl (*R*)-(+)-lactate was converted into (*R*)-**2** *via* the enantiomeric amide (*R*)-**8**. A variety of related alkyl ketones, *e.g.* (*R*)-**9**, can be prepared in enantiomerically pure form by suitable choice of Grignard or organolithium reagents. These ketones are configurationally stable and can be stored for extended periods.

anti-Selective, Asymmetric Aldol Reactions of **2**: From experience already gained with the *anti*-aldol reactions of ethyl ketone **1**,[3] we sought to achieve selective enolisation of **2** to generate the corresponding (*E*)-enol dicyclohexylborinate **10** (Scheme 2). This can be achieved[12] using Brown's dicyclohexylboron chloride (*c*-Hex_2BCl), as a mild Lewis acid, in conjunction with a sterically undemanding, tertiary amine base. Indeed, the optimal conditions for the *anti*-aldol reaction of **2** were enolisation by *c*-Hex_2BCl and Me_2NEt in Et_2O at 0 °C for 2 hours to generate **10** *in situ*, prior to cooling to –78 °C, and addition of the required aldehyde. Storing the reaction mixture at –26 °C (freezer) over a period of 14 hours ensured complete conversion, whilst maintaining high levels of selectivity, before normal oxidative workup (H_2O_2, pH 7 buffer). As shown in Table 1, this procedure led to high yields for a range of aliphatic, aromatic and unsaturated aldehydes, accompanied by excellent diastereoselectivities. The crystalline 1,2-*anti*-2,4-*anti* adducts **4a–e** were isolated in 85–97% yield with ≥ 95% ds.



Reagents: (*i*) $^cHex_2BCl$, Me_2NEt, Et_2O, 0 °C, 2 h. (*ii*) RCHO, –78 → –26 °C, 14 h. (*iii*) H_2O_2, pH7 buffer, MeOH, 0 °C, 1 h

Scheme 2

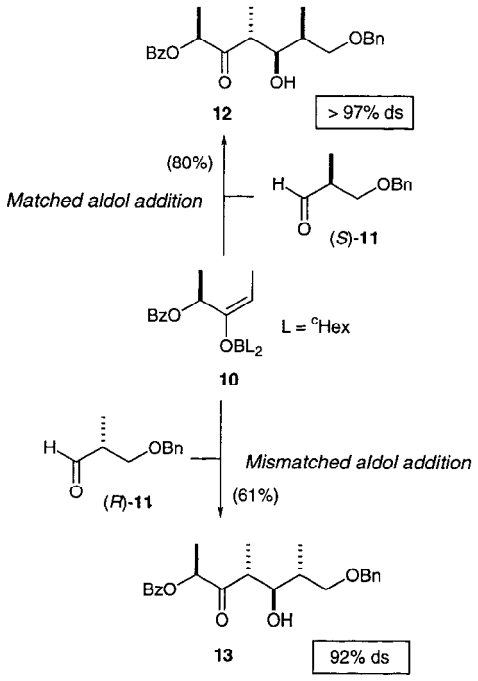
Table 1. *anti*-Aldol Reactions of (*S*)-**2** with RCHO[a]

RCHO R	Product[b]	ds[c]	Yield[d] (%)
i-Pr	**4a**	97:3	95
Ph	**4b**	99.5:0.5	85
Et	**4c**	99.5:0.5	82
CH_2=C(Me)	**4d**	98:2	97
(*E*)-MeCH=CH	**4e**	95:5	85

[a] Reaction conditions: *c*-Hex_2BCl/Me_2NEt/Et_2O, 0 °C, 2 h; RCHO, –78 → –26 °C, 14 h.
[b] Enantiomeric purity (> 97% ee) and hydroxyl configuration determined by ^{19}F and ^1H NMR analysis of (*R*)- and (*S*)-MTPA esters.
[c] Ratio of major isomer to sum of minor isomers by HPLC.
[d] Isolated yield of aldol adducts after chromatography.

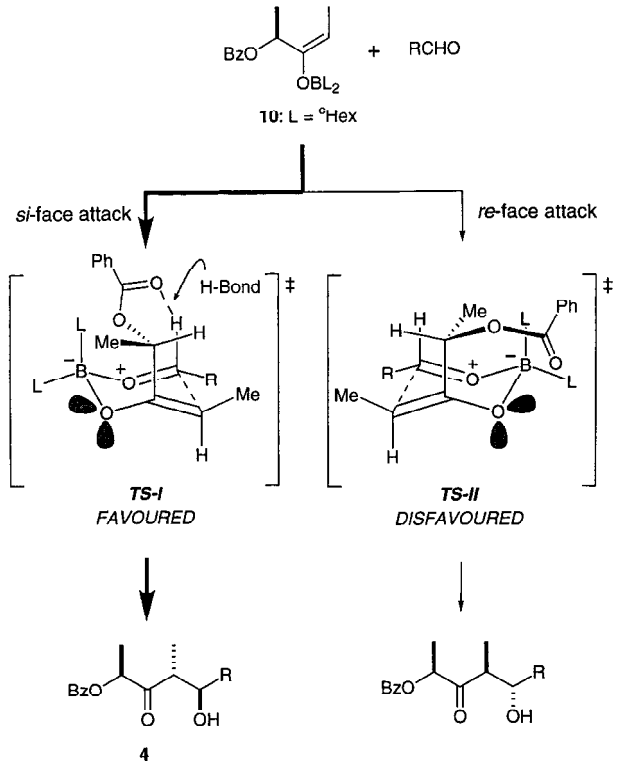
In each case, the stereoselectivity of the aldol reaction was determined by HPLC and/or ^1H NMR (400 MHz) analysis of the crude reaction mixture. A single recrystallisation usually sufficed to give the stereochemically homogeneous aldol adduct. The relative and absolute configurations of the aldol adducts **4a–e** were assigned by various means. The 1,2-*anti* relationship was ascertained from the diagnostic large vicinal coupling constant, $J_{1,2}$ = 7.0–8.8 Hz (*cf.* $J_{1,2}$ = 3–5 Hz for the *syn*-aldol isomers). The absolute configuration at the new secondary hydroxyl centre was determined using the advanced Mosher method[13] through comparison of the relevant ^1H NMR chemical shifts of the diastereomeric (*R*)- and (*S*)-MTPA esters. The enantiomeric purity of the aldol products was assessed as >97% ee by ^{19}F NMR spectroscopy of these same Mosher esters, indicating that no racemisation had occurred.

The high levels of selectivity obtained with these simple aldehydes led us next to examine reagent control in aldol additions to chiral aldehydes (Scheme 3). Following enolisation of ketone (*S*)-**2**, the derived (*E*)-enol borinate **10** was reacted separately with the enantiomeric aldehydes (*S*)- and (*R*)-**11**, leading to the formation of adducts **12** and **13** with > 97% ds (matched) and 92% ds (mismatched), respectively. This latter result indicates that the high π-facial selectivity of the enolate **10** overrides the Felkin–Anh type induction from the aldehyde, which bodes well for general application in the stereocontrolled synthesis of complex polyketide systems. All of these auxiliary-controlled aldol reactions employ *c*-Hex_2BCl as a mild enolising reagent, which is easy to prepare[12] as well as being commercially available. Under the conditions of the aldol reaction, this reagent is compatible with most functional groups and can be used with sensitive aldehydes.[10,14,15]



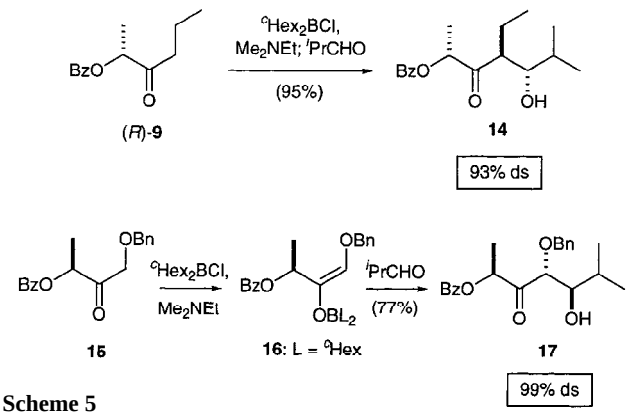
Scheme 3

The origin of the high levels of π-face selectivity in the reactions of **10** can be traced to the relative steric and electronic contributions of the substituents (H, Me, OBz) at the enolate stereocentre in the chair transition state for the aldol addition (Scheme 4).[16] For such (*E*)-enol borinates, there is a strong preference for the proton to eclipse the double bond to minimise A(1,3) allylic strain. In the competing transition structures, ***TS-I*** and ***TS-II***, the benzoate group is directed either inwards or outwards in the chair arrangement. In ***TS-II*** (*re*-face attack on aldehyde), there is likely to be a destabilising lone-pair repulsion between the benzoate and enolate oxygens. Based on the formyl hydrogen bond model recently espoused by Corey *et al.*[17] to explain the facial selectivity in a number of asymmetric addition processes, ***TS-I*** (*si*-face attack on aldehyde) may be favoured due to a stabilising H-bond between the benzoate oxygen with the aldehyde proton. Taken together, this analysis accounts for the apparent contra-steric preference for the benzoate to occupy the inside position.



Scheme 4

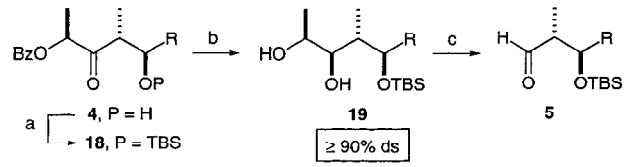
In addition to these results for ethyl ketone **2**, comparable stereoselectivities can also be obtained in the boron-mediated, *anti*-aldol reactions of related ketones (Scheme 5). For example, addition of the propyl ketone (*R*)-**9** to isobutyraldehyde gave **14** in 95% yield with 93% ds. In an analogous manner to **2**, the alkoxymethyl ketone **15** was cleanly enolised by *c*-Hex_2BCl and Me_2NEt to give the enol borinate **16**, which gave the corresponding *anti* aldol adduct **17** on addition to isobutyraldehyde, with high levels of asymmetric induction (≥ 99% ds). These more highly oxygenated ketones should prove useful for the asymmetric synthesis of contiguous polyols. In other studies from our laboratory, they have already been used in



Scheme 5

synthetic approaches to zaragozic acid C[10] and concanamycin A.[14]

Manipulation of the Aldol Adducts: These *anti*-aldol adducts can be transformed into a range of useful intermediates for the synthesis of polyketide natural products. As shown in Scheme 6, the most widely used transformation is to give the α-methyl-β-siloxy aldehydes **5**.[5,10] This can be accomplished in a high yielding, three-step sequence (Table 2).



Reagents: (a) TBSOTf, 2,6-lutidine, CH_2Cl_2, –78 °C, 1 h. (b) $LiBH_4$, THF, –78 → 20 °C, 24 h. (c) $NaIO_4$, MeOH, H_2O, 30 min

Scheme 6

Table 2. Preparation of Aldehydes **5**[a]

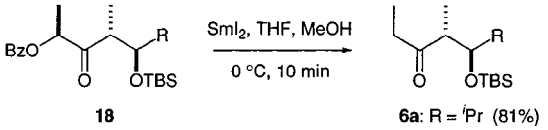
Aldol Adduct	R	Product[b]	Yield[c] (%)
4a	*i*-Pr	**5a**	74
4b	Ph	**5b**	85
4e	(*E*)-MeCH=CH	**5c**	82[d]
12	(*S*)-$BnOCH_2CH(Me)$	**5d**	70
13	(*R*)-$BnOCH_2CH(Me)$	**5e**	83

[a] Reaction conditions as in Scheme 6 unless otherwise stated.
[b] Diastereomeric purity (> 99%) by HPLC analysis and ^1H NMR spectroscopy.
[c] Isolated overall yield after chromatography.
[d] $NaBH_4$ reduction followed by K_2CO_3 hydrolysis was used.[18]

First, silylation of **4** with *tert*-butyldimethylsilyl triflate (TBSOTf) gave the corresponding silyl ether **18**. Subsequently, ketone reduction with $LiBH_4$ was accompanied by cleavage of the benzoate group, **18** → **19**, which (although not essential here) proceeded with good levels of diastereoselectivity (≥ 90 ds). Alternatively, $NaBH_4$ reduction followed by K_2CO_3 hydrolysis of the benzoate also gave the 1,2-diol **19** in high yield. In several cases,

the predominating 1,2-diol stereochemistry in **19** was determined by appropriate NOE analysis of the derived *cis*-acetonide. While the reduction stereoselectivity here can be influenced to varying extents by the substituents on either side of the ketone, it appears largely to arise by Felkin–Anh control associated with the sterically demanding TBS-containing residue.[19] The resulting monoprotected 1,2,4-triols **19** have four contiguous stereocentres, which may be exploited if required. For our present purposes, two of these stereocentres are discarded in the next step, whereby glycol cleavage with $NaIO_4$ gave the aldehydes **5**.

As an alternative to this oxidative cleavage sequence, reductive removal[20] of the α–benzoate substituent in **18** by SmI_2 gave a high yield of the corresponding ethyl ketones **6a** and **6b** (Scheme 7). Notably, this asymmetric synthesis of diethyl ketone *anti*-aldol adducts is experimentally convenient and complements alternative routes using chiral boron reagents.[1] By using a second aldol reaction on the ethyl side, such ketones permit the highly stereocontrolled synthesis of elaborate polypropionate systems.[15,21]



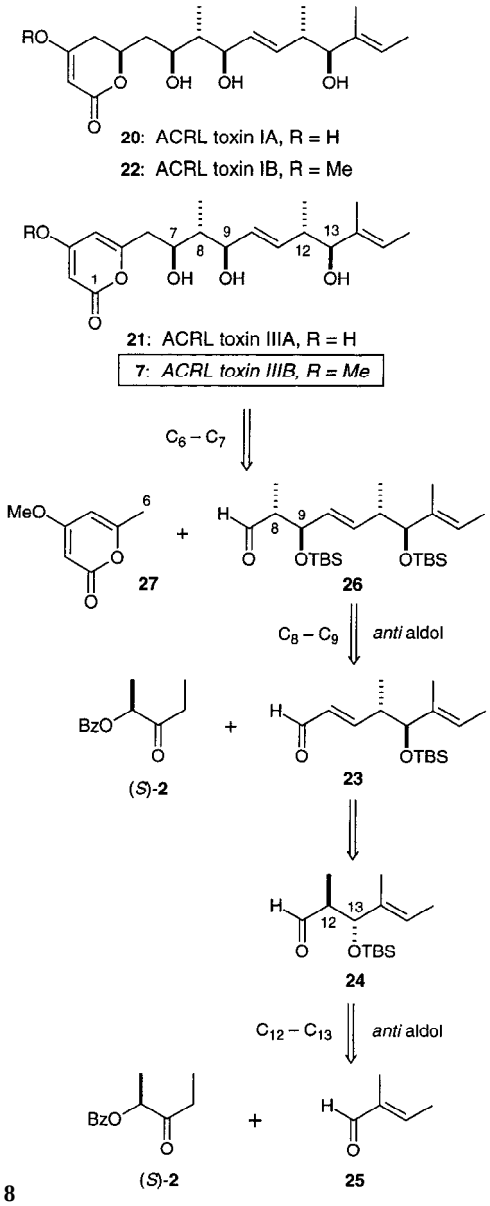
18 **6a**: R = ^{i}Pr (81%) **6b**: R = Ph (96%)

Scheme 7

Total Synthesis of (–)-ACRL Toxin IIIB: The phytopathogenic fungus *Alternaria citri*, which causes brown spot disease of citrus, produces several host specific toxins (Scheme 8) that damage the leaves of rough lemon and Rangpur lime plants. The major component, ACRL toxin IA (**20**), is the most active toxin, with ACRL toxin IIIA (**21**) being isolated in smaller quantities, along with other minor components.[22] Full structural characterisation of the toxins was only possible from their methyl ether derivatives ACRL toxin IB (**22**) and IIIB (**7**). We were attracted to these fungal polyketides as synthetic targets[23] due to the two *anti*-configured propionate units present in the side chain. As already mentioned, these are generally more difficult to control than the corresponding *syn*-relationships. As such, ACRL toxin IIIB (**7**) was selected to demonstrate the utility of our new *anti*-aldol methodology.

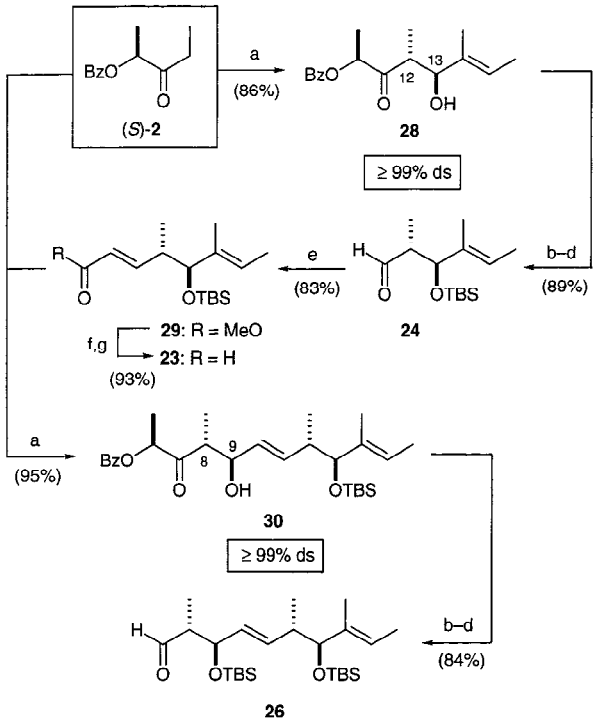
Our retrosynthetic analysis (Scheme 8) is based on three disconnections which, in the forward sense, involve the control of stereochemistry in addition reactions to aldehydes. We planned to use the ketone (*S*)-**2** to control both the stereochemistry at C_8–C_9 and C_{12}–C_{13} *via anti*-aldol additions to aldehyde **23** (derived from **24**) and tiglic aldehyde (**25**), respectively. The final coupling step planned between aldehyde **26** and α-pyrone **27**, while having some precedent in a previous synthesis of ACRL toxin IIIB by Mulzer *et al.*,[23a] presented greater uncertainty in the sense and degree of stereoinduction.

As shown in Scheme 9, the C_{12} and C_{13} stereocentres were first installed together by a boron-mediated, *anti*-al-



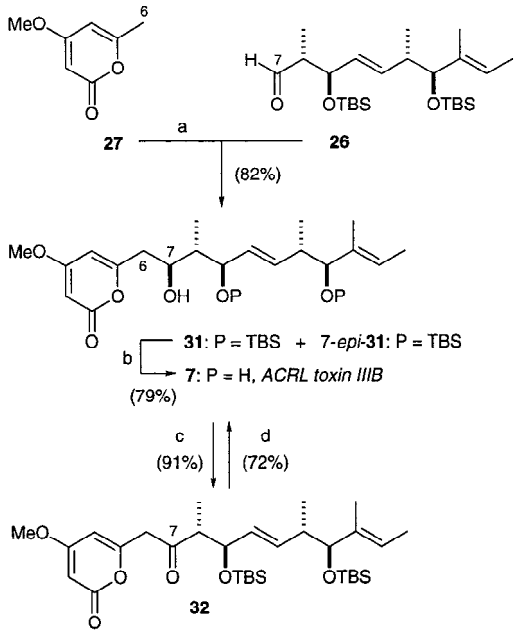
Scheme 8

dol reaction between ethyl ketone (*S*)-**2** and tiglic aldehyde (**25**). Under standard conditions, the reaction proceeded with excellent diastereoselectivity (≥99% ds) and, following a single recrystallisation, the aldol adduct **28** was obtained in 86% yield. HPLC analysis of the crude product indicated that < 1% of other isomers were produced. This β-hydroxy ketone was then converted into aldehyde **24** (88%) *via* the usual three-step sequence of protection, reduction and oxidative cleavage. Next, chain extension by a $Ba(OH)_2$-promoted HWE reaction[24] gave solely the (*E*)-alkene **29** (83%). The use of stronger bases led to some epimerisation at C_{12}, as well as traces of the (*Z*)-alkene. Subsequent DIBAL reduction of this ester, followed by Dess–Martin oxidation,[25] gave the enal **23** (93%). In an analogous manner, the *anti*-aldol reaction of (*S*)-**2** with enal **23** gave the adduct **30** (95%). As before, ^{1}H NMR and HPLC analysis indicated ≥99% ds. Repeating the highly reproducible, three-step sequence then gave the aldehyde **26** (84%). This aldol-based synthesis is no-



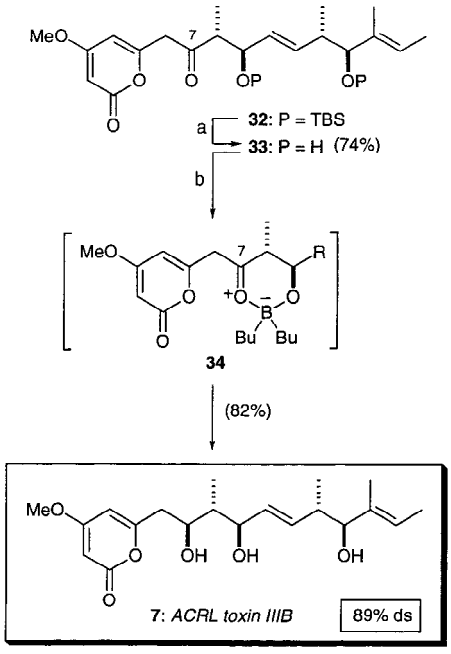
Reagents: (a) $^{c}Hex_2BCl$, Me_2NEt, Et_2O, 0 °C, 2 h; **25** or **23**, –78 → –26 °C, 16 h, H_2O_2, MeOH, pH7 buffer, 0 °C, 1 h. (b) TBSOTf, 2,6-lutidine, CH_2Cl_2, –78 °C, 1 h. (c) $LiBH_4$, THF, –78 → 20 °C, 24 h. (d) $NaIO_4$, MeOH, H_2O, 20 °C, 1 h. (e) $(MeO)_2P(=O)CH_2CO_2Me$, $Ba(OH)_2$, THF:H_2O, 40:1, 20 °C, 16 h. (f) DIBAL, Et_2O, –40 °C, 2 h. (g) Dess-Martin periodinane, CH_2Cl_2, 20 °C, 1 h

Scheme 9



Reagents: (a) KHMDS, Et_2O, –100 °C, 1 h; **26**, 2 h. (b) HF•pyridine, THF, 0 → 20 °C, 2 h. (c) Dess-Martin periodinane, CH_2Cl_2, 20 °C, 2 h. (d) $NaBH_4$, EtOH, 0 °C

Scheme 10



Reagents: (a) HF•pyridine, THF, 0 → 20 °C, 2 h. (b) $^{n}Bu_2BOMe$, THF, MeOH, –78 °C, 20 min; $LiBH_4$, 2 h; H_2O_2, pH7 buffer, 20 °C, 1 h

Scheme 11

table for achieving essentially complete control of the four stereocentres in the ACRL toxin side chain and proceeds in 46% yield from ketone (*S*)-**2**.

As shown in Scheme 10, completion of the synthesis required the C_6–C_7 coupling between aldehyde **26** and the commercially available α-pyrone **27**. In order to generate the correct configuration at C_7, addition of the metallated α-pyrone **27** is required to occur on the opposite face of the α-chiral aldehyde to that normally predicted by the Felkin–Anh model. Although there was some precedent[23a] for this, in our hands, deprotonation of α-pyrone **27** (KHMDS, Et_2O, –100 °C) and addition of **26** gave, at best, a 71 : 29 ratio of adducts. Following HPLC separation, the major product **31** was isolated in 48% yield along with 19% of 7-*epi*-**31**. Subsequent deprotection of **31** and recrystallisation gave pure (–)-ACRL toxin IIIB (**7**) in 79% yield.

In an attempt to improve the product distribution resulting from the modestly selective pyrone addition, we chose to explore the reduction of the C_7 ketone. The mixture of epimeric alcohols at C_7 was oxidised with Dess–Martin periodinane[25] to give ketone **32** (91%). Conversion of this ketone to the correct alcohol **31** now required selective hydride addition in the Felkin–Anh sense. While $NaBH_4$ or DIBAL both led to predominant formation of **31**, the selectivity obtained was disappointing (ca. 2:1).

A more rewarding strategy (Scheme 11) was to exploit the chelation controlled, 1,3-*syn* reduction of the β-hydroxy ketone **33**. Removal of the two silyl protecting groups from ketone **32** was achieved with HF•pyridine to give **33** (74%). Precomplexation with Bu_2BOMe,[26] followed by reduction of the intermediate boron chelate **34** with $LiBH_4$ then led to a 94% yield of ACRL toxin IIIB (**7**) and its C_7 epimer. Analysis of the 400 MHz ^1H NMR spectrum showed that the ratio of alcohols was now much im-

proved at 89 : 11. A single recrystallisation gave pure (–)-ACRL toxin IIIB (**7**), obtained in 82% isolated yield, which had ^{1}H and ^{13}C NMR data in full agreement with that reported for the authentic compound. The specific rotation recorded for **7**, $[\alpha]_D^{20}$ –47.0 (*c* = 0.6, $CHCl_3$), was in good agreement with that obtained by Mulzer *et al.*, $[\alpha]^{20}_D$ –49.0 (*c* = 0.8, $CHCl_3$). This improved synthesis of (–)-ACRL toxin IIIB proceeds in 15 steps with 21% overall yield and an acceptable 88% diastereoselectivity for the installation of the five stereocentres.

Conclusions: The boron-mediated, *anti*-aldol chemistry of ketone **2** enables the efficient asymmetric synthesis of a wide range of valuable polyketide intermediates, as illustrated here by its application to the total synthesis of (–)-ACRL toxin IIIB **(7)**. Key features of this method are: (*i*) the use of an auxiliary from readily available (*R*)- or (*S*)-lactate; (*ii*) the ability to introduce other α-substituents; and (*iii*) the operation of reagent control from the enolate in additions to chiral aldehydes. The subsequent manipulation of the aldol products to give aldehydes and ethyl ketones demonstrates the use of the lactate-derived HCMe(OBz) group as a versatile chiral auxiliary. Moreover, this stereoinducing group should be considered as an *optional* auxiliary for asymmetric synthesis, which may be retained if desired. For example, the reduction of ketones **18** with $LiBH_4$ provides useful monoprotected 1,2,4-triols **19** having four contiguous stereocentres.

This new *anti*-selective aldol methodology, combined with the related *syn*-selective transformations using the analogous benzyl ether **3**,[4–6] should have general utility for the synthesis of a variety of polyketide natural products.

^{1}H NMR spectra were recorded at either 250, 400 or 500 MHz on Bruker AC and DPX250, AM400 or DRX500 spectrometers and ^{13}C spectra were recorded at either 62.9 or 100.6 MHz on Bruker AC and DPX250 or AM400 spectrometers. All spectra were obtained using $CDCl_3$ as solvent and referenced to $CHCl_3$ (δ = 7.26) for ^{1}H NMR and $CDCl_3$ (δ = 77.0) for ^{13}C NMR. The numbering of carbon atoms for assignment refers to the numbering of the carbon skeleton of the target product **7**. Optical rotations were measured at 20 °C. Except for aqueous reactions, all experiments were carried out under an argon atmosphere with anhydrous solvents. Silica gel was used to perform the column chromatography. The following solvents and reagents were purified and dried according to recommended procedures: THF, Et_2O, CH_2Cl_2, Me_2NEt, 2,6-lutidine and *i*-Pr_2NEt.[27]

***(S)*-2-Hydroxy-*N*-methoxy-*N*-methylpropionamide [(*S*)-8]:**
To a cooled (–20 °C) mixture of ethyl (*S*)-lactate (2.0 g, 16.9 mmol) and MeON(Me)H•HCl (4.1 g, 42 mmol) in THF (50 mL), was added a 2 M solution of *i*-PrMgCl in Et_2O (42 mL) dropwise over 30 min. The reaction mixture was stirred at –20 °C for 30 min and at 0 °C for a further 30 min before satd aq NH_4Cl solution (150 mL) was added. The mixture was extracted with Et_2O (4 × 50 mL), followed by CH_2Cl_2 (4 x 50 mL). The combined organic extracts were dried ($MgSO_4$), concentrated *in vacuo*, and the residue purified by column chromatography (50% EtOAc in hexanes → EtOAc) to give the amide **8** (1.91 g, 85%) as a colourless oil. On a larger scale, purification was achieved by distillation; bp 63–65 °C/0.5 Torr; $[\alpha]_D$ –50.0 (*c* = 2.2, $CHCl_3$).
IR (film): ν = 3440 (br), 1658 cm^{-1} (s).
^{1}H NMR (400 MHz): δ = 1.33 [d, 3 H, *J* = 6.7 Hz, CH(C*H*$_3$)OH], 3.22 (s, 3 H, NCH_3); 3.35 (d, 1H, *J* = 6.7 Hz, OH), 3.69 (s, 3 H, OCH_3), 4.47 [qn, 1H, *J* = 6.7 Hz, C*H*(CH$_3$)OH].
^{13}C NMR (100.6 MHz): δ = 20.8, 32.2, 61.1, 64.7, 175.6.
HRMS (CI, NH_3): *m*/*z* $[M+H]^+$ found 134.0817, $C_5H_{12}O_3N$ requires 134.0817.
LRMS (CI, NH_3): *m*/*z* = 34 ($[M+H]^+$, 100).

***(S)*-2-Benzoyloxypentan-3-one [(*S*)-2]; Typical Procedure:**
To a cooled (0 °C) solution of amide (*S*)-**8** (1.0 g, 7.5 mmol) in THF (30 mL) was added a 3 M solution of EtMgBr in Et_2O (8 mL) and the reaction mixture was allowed to warm to r.t. After 1 h, satd aq NH_4Cl solution (40 mL) was added and the mixture was extracted with Et_2O (20 mL) followed by CH_2Cl_2 (2 × 20 mL). The combined organic extracts were dried ($MgSO_4$) and concentrated to *ca.* 50 mL. To this solution was added Bz_2O (2.55 g, 11.3 mmol), DMAP (0.10 g, 0.82 mmol) and *i*-Pr_2NEt (2.5 mL, 14.3 mmol). After stirring for 14 h, excess Bz_2O was removed by addition of ethylenediamine (0.5 g, 8.3 mmol). H_2O (40 mL) was added, the mixture extracted with Et_2O (4 x 20 mL), then the organic extracts were dried ($MgSO_4$) and concentrated to an oil. Column chromatography (20% EtOAc in hexane) afforded (*S*)-**2** (1.18 g, 76%) as a colourless oil; $[\alpha]_D$ +25.1 (*c* = 4.6, $CHCl_3$).
IR (film) ν = 1718 (s), 1601 cm^{-1} (w).
^{1}H NMR (400 MHz): δ = 1.05 (t, 3 H, *J* = 7.4 Hz, CH_2CH_3), 1.52 [d, 3 H, *J* = 7.0 Hz, CH(C*H*$_3$)OBz], 2.56 (dq, 1 H, *J* = 14.6, 7.4 Hz, $CH_AH_BCH_3$), 2.64 (dq, 1 H, *J* = 14.6, 7.4 Hz, $CH_AH_BCH_3$), 5.33 [q, 1 H, *J* = 7.0 Hz, C*H*(CH$_3$)OBz], 7.52 (t, 2 H, *J* = 6.8 Hz, Ar*H*), 7.58 (tt, 1 H, *J* = 6.8, 1.2 Hz, Ar*H*), 8.07 (dd, 2 H, *J* = 6.8, 1.2 Hz, Ar*H*).
^{13}C NMR (100.6 MHz): δ = 7.4, 16.7, 31.7, 75.3, 128.6, 129.6, 130.0, 133.6, 166.1, 208.7.
HRMS (CI, NH_3): *m*/*z* $[M+H]^+$ found 207.1021, $C_{12}H_{15}O_3$ requires 207.1021.
LRMS (CI, NH_3): *m*/*z* 207 ($[M+H]^+$ 100), 105 (30).
Analysis: found C, 70.18; H, 6.88; $C_{12}H_{14}O_3$ requires C, 69.88; H, 6.84.

In a related manner, following the typical procedure for the preparation of **2**, the ketones (*R*)-**9** and **15** were obtained using PrMgBr and $BnOCH_2Li/MgBr_2$, respectively, in the reactions.

(R)-2-Benzoyloxyhexan-3-one **[(*R*)-9]:**
R_f (40% Et_2O in hexane) 0.48; $[\alpha]_D$ –12.8 (*c* = 0.8, $CHCl_3$).
IR (film): ν = 1719 (s), 1609, 1595 cm^{-1} (w).
^{1}H NMR (400 MHz): δ = 0.92 (t, 3 H, *J* = 7.2 Hz, $CH_2CH_2CH_3$), 1.52 [d, 3 H, *J* = 7.1 Hz, CH(C*H*$_3$)OBz], 1.66 (sextet, 2 H, *J* = 7.2 Hz, $CH_2CH_2CH_3$), 2.47 (dt, 1 H, *J* = 17.4, 7.2 Hz, $CH_AH_BCH_2CH_3$), 2.59 (dt, 1 H, *J* = 17.4, 7.2 Hz, $CH_AH_BCH_2CH_3$), 5.32 [q, 1 H, J = 7.1 Hz, C*H*(CH$_3$)OBz], 7.46 (dd, 2 H, *J* = 7.9, 7.3 Hz, Ar*H*), 7.59 (tt, 1 H, *J* = 7.3, 1.6 Hz, Ar*H*), 8.07 (dd, 2 H, *J* = 7.9, 1.6 Hz, Ar*H*).
^{13}C NMR (100.6 MHz): δ = 13.7, 16.3, 16.7, 40.1, 75.2, 128.5, 129.6, 129.8, 133.4, 165.9, 207.9.
HRMS (+FAB): *m*/*z* $[M+H]^+$ found 221.1170, $C_{13}H_{17}O_3$ requires 221.1178.
LRMS (+FAB): *m*/*z* = 221 ($[M+H]^+$, 60), 154 (26), 105.

(S)-3-Benzoyloxy-1-benzyloxybutan-2-one **[(*S*)-(15)]:**
R_f (CH_2Cl_2) 0.24; $[\alpha]_D$ +23.8 (*c* = 1.4, $CHCl_3$).
IR (film): ν =1712 (s), 1602, 1584, 1558 cm^{-1} (w).
^{1}H NMR (250 MHz): δ = 1.57 [d, 3 H, *J* = 7.0 Hz, CH(C*H*$_3$)OBz], 4.28 (d, 1 H, *J* = 15.1 Hz, CH_AH_BOBn), 4.37 (d, 1 H, *J* = 15.1 Hz, CH_AH_BOBn), 4.61 (d, 1 H, *J* = 11.7 Hz, OCH_AH_BPh), 4.65 (d, 1 H, *J* = 11.7 Hz, OCH_AH_BPh), 5.54 [q, 1 H, *J* = 7.0 Hz, C*H*(CH$_3$)OBz], 7.37–7.25 (m, 5H, Ar*H*), 7.45 (dd, 2 H, *J* = 8.2, 7.0 Hz, Ar*H*), 7.58 (tt, 1 H, *J* = 7.0, 1.4 Hz, Ar*H*), 8.04 (dd, 2 H, *J* = 8.2, 1.4 Hz, Ar*H*).
^{13}C NMR (62.9 MHz): δ = 16.2, 72.7, 73.3, 128.0, 128.1, 128.5, 129.3, 129.8, 133.4, 137.0, 165.9, 205.2.
HRMS (CI, NH_3): *m*/*z* $[M+H]^+$ found 299.1283, $C_{18}H_{19}O_4$ requires 299.1283.
LRMS (CI, NH_3): *m*/*z* 316 ($[M+NH_4]^+$, 53), 299 ($[M+H]^+$, 64), 208 (50), 196 (100).

***anti*-Aldol Reaction of (*S*)-2 Using *c*-Hex_2BCl; Synthesis of 4a–e, 12–14, 17, 28 and 30; General Procedure A:**
To a cooled (–78 °C) solution of *c*-Hex_2BCl (0.16 g, 0.75 mmol) in Et_2O (2 mL) was added Me_2NEt (96 mg, 0.9 mmol), followed by ke-

tone (*S*)-**2** (0.10 g, 0.5 mmol) in Et_2O (2 mL). The reaction mixture was warmed to 0 °C and stirred for 2 h before recooling to –78 °C. The required aldehyde (2.0 mmol for achiral aldehydes) was added and the stirring continued for a further 2 h, before being transferred to the freezer (–26 °C) for 14 h. The reaction was quenched at 0 °C by addition of MeOH (2 mL) and pH 7 buffer (2 mL), H_2O_2 (2 mL, 30%) was then added and the stirring continued for 1 h. The mixture was partitioned between H_2O (30 mL) and CH_2Cl_2 (3 × 30 mL). The combined organic extracts were dried ($MgSO_4$) and concentrated *in vacuo*. Isolation of the aldol products was achieved by column chromatography and diastereomeric ratios determined by 400 MHz ^{1}H NMR analysis and/or HPLC separation. The yields and diasteromeric ratios for **4a–e** are given in Table 1.

(2S,4R,5R)-2-Benzoyloxy-5-hydroxy-4,6-dimethylheptan-3-one **(4a):**
R_f (50% Et_2O in hexane) 0.39; mp 93–94 °C; $[\alpha]_D$ +41.6 (*c* = 1.0, $CHCl_3$).
IR ($CHCl_3$): ν = 3545 (br), 1733 (s), 1699 (s), 1601, 1584, 1492 cm^{-1} (w).
^{1}H NMR (400 MHz): δ = 0.87 [d, 3 H, *J* = 6.8 Hz, CH(CH_3)CH_3], 0.94 [d, 3 H, *J* = 6.8 Hz, CH(CH_3)CH_3], 1.20 [d, 3 H, *J* = 7.2 Hz, CH(CH_3)CHOH], 1.55 [d, 3 H, *J* = 7.1 Hz, CH(CH_3)OBz], 1.77 [septet d, 1 H, *J* = 6.8, 4.1 Hz, C*H*(CH_3)$_2$], 2.33 (d, 1 H, *J* = 6.4 Hz, OH), 2.99 [br quintet, 1 H, *J* = 7.2 Hz, C*H*(CH_3)CHOH], 3.57 (ddd, 1 H, *J* = 7.2, 6.4, 4.1 Hz, C*H*OH), 5.43 [q, 1 H, *J* = 7.1 Hz, C*H*(CH_3)OBz], 7.43 (dd, 2 H, *J* = 7.9, 7.6 Hz, Ar*H*), 7.57 (t, 1 H, *J* = 7.6 Hz, Ar*H*), 8.05 (d, 2 H, *J* = 7.9 Hz, Ar*H*).
^{13}C NMR (100.6 MHz): δ = 14.4, 15.2, 15.9, 20.0, 29.8, 54.5, 74.8, 77.7, 128.5, 129.5, 129.8, 133.3, 165.9, 212.0.
HRMS (CI, NH_3): *m/z* $[M+H]^+$ found 279.1596, $C_{16}H_{23}O_4$ requires 279.1596.
LRMS (CI, NH_3): *m/z* = 279 ($[M+H]^+$,100), 261 (32), 207 (100), 159 (64), 141 (43), 105 (60).
Analysis: found C, 69.10; H, 7.82; $C_{16}H_{22}O_4$ requires C, 69.04; H, 7.94.

(1S,2R,4S)-4-Benzoyloxy-1-hydroxy-2-methyl-1-phenylpentan-3-one **(4b):**
R_f (50% Et_2O in hexane) 0.35; mp 133–135 °C; $[\alpha]_D$ –19.0 (*c* = 0.8, $CHCl_3$).
IR ($CHCl_3$): ν = 3396 (br), 1720 (s), 1495 cm^{-1} (w).
^{1}H NMR (400 MHz): δ = 1.06 [d, 3 H, *J* = 7.2 Hz, CH(CH_3)CHOH], 1.49 [d, 3 H, *J* = 7.1 Hz, CH(CH_3)OBz], 2.78 (br, s, 1 H, OH), 3.14 [dq, 1 H, *J* = 8.4, 7.2 Hz, C*H*(CH_3)CHOH], 4.81 [d, 1 H, *J* = 8.4 Hz, C*H*(OH)Ph], 5.40 [q, 1 H, *J* = 7.1 Hz, C*H*(CH_3)OBz], 7.35–7.27 (m, 5 H, Ar*H*), 7.43 (dd, 2 H, *J* = 7.4, 7.3 Hz, Ar*H*), 7.58 (tt, 1 H, *J* = 7.4, 1.3 Hz, Ar*H*), 8.07 (dd, 2 H, *J* = 7.3, 1.3 Hz, Ar*H*).
^{13}C NMR (100.6 MHz): δ = 14.9, 15.3, 49.8, 75.0, 76.5, 126.6, 128.1, 128.4, 128.5, 129.6, 129.8, 133.3, 142.1, 165.9, 211.3.
HRMS (+FAB): *m/z* $[M+H]^+$ found 313.1443, $C_{19}H_{21}O_4$ requires 313.1440.
LRMS (+FAB): *m/z* = 313 ($[M+H]^+$, 75), 289 (52), 177 (100), 154 (92), 136 (85).

(2S,4R,5R)-2-Benzoyloxy-5-hydroxy-4-methylheptan-3-one **(4c):**
R_f (50% Et_2O in hexane) 0.28; mp 64–65 °C; $[\alpha]_D$ +41.6 (*c* = 1.0, $CHCl_3$).
IR ($CHCl_3$): ν = 3412 (br), 1722 (s), 1602, 1584 cm^{-1} (w).
^{1}H NMR (400 MHz): δ = 0.96 (t, 3 H, *J* = 7.4 Hz, CH_2CH_3), 1.24 [d, 3 H, *J* = 7.2 Hz, CH(CH_3)CHOH], 1.34–1.45 (m, 1 H, C$H_A$$CH_B$$CH_3$), 1.55 [d, 3 H, *J* = 7.1 Hz, CH(CH_3)OBz], 1.63–1.57 (m, 1 H, $CH_A$$H_B$$CH_3$), 2.50 (br, s, 1 H, OH), 2.87 [qn, 1 H, *J* = 7.2 Hz, C*H*(CH_3)CHOH], 3.68 (ddd, 1 H, *J* = 10.1, 7.2, 3.2 Hz, C*H*OH), 5.42 [q, 1 H, *J* = 7.1 Hz, C*H*(CH_3)OBz], 7.44 (dd, 2 H, *J* = 8.0, 7.5 Hz, Ar*H*) 7.57 (tt, 1 H, *J* = 7.5, 1.0 Hz, Ar*H*), 8.06 (dd, 2 H, *J* = 8.0, 1.0 Hz, Ar*H*).
^{13}C NMR (100.6 MHz): δ = 14.5, 15.9, 27.3, 47.8, 74.7, 128.5, 129.5, 129.8, 133.3, 165.9, 211.9.
HRMS (+FAB): *m/z* $[M+H]^+$ found 265.1451, $C_{15}H_{21}O_4$ requires 265.1440.
LRMS (+FAB): *m/z* = 265 ($[M+H]^+$, 60), 154 (100), 136 (95), 105 (80), 71 (45).

(2S,4R,5S)-2-Benzoyloxy-5-hydroxy-4,6-dimethylhept-6-en-3-one **(4d):**
R_f (50% Et_2O in hexane) 0.35; mp 59–60 °C; $[\alpha]_D$ +29.0 (*c* = 0.6 $CHCl_3$).
IR ($CHCl_3$): ν = 3509 (br), 1718 (s), 1601 cm^{-1} (w).
^{1}H NMR (400 MHz): δ = 1.03 [d, 3 H, *J* = 7.2 Hz, CH(CH_3)CHOH], 1.56 [d, 3 H, *J* = 7.0 Hz, CH(CH_3)OBz], 1.71 [s, 3 H, C(=CH_2)CH_3], 2.28 (br s, 1 H, OH), 3.01 [dq, 1 H, *J* = 8.8, 7.2 Hz, C*H*(CH_3)CHOH], 4.25 (d, 1 H, *J* = 8.8 Hz, C*H*OH), 4.92 (s, 1 H, =C$H_A$$H_B$), 4.95 (s, 1 H, =$CH_A$$H_B$), 5.44 [q, 1 H, *J* = 7.0 Hz, C*H*(CH_3)OBz], 7.44 (t, 2 H, *J* = 7.4 Hz, Ar*H*) 7.56 (t, 1 H, *J* = 7.4 Hz, Ar*H*), 8.07 (d, 2 H, *J* = 7.4 Hz, Ar*H*).
^{13}C NMR (100.6 MHz): δ = 14.5, 15.6, 16.6, 45.5, 75.0, 78.3, 114.5, 128.5, 129.6, 129.8, 133.3, 144.4, 165.9, 211.0.
HRMS (+FAB): *m/z* $[M+H]^+$ found 277.1413, $C_{16}H_{21}O_4$ requires 277.1440.
LRMS (+FAB): *m/z* = 277 ($[M+H]^+$, 78), 154 (100), 136 (80), 105 (70).

(2S,4R,5R,6E)-2-Benzoyloxy-5-hydroxy-4-methyloct-6-en-3-one **(4e):**
R_f (50% Et_2O in hexane) 0.30; mp 130–132 °C; $[\alpha]_D$ +34.6 (*c* = 0.5, $CHCl_3$).
IR ($CHCl_3$): ν = 3416 (br), 1732 (s), 1718 cm^{-1} (s).
^{1}H NMR (400 MHz): δ = 1.17 [d, 3 H, *J* = 7.2 Hz, CH(CH_3)CHOH], 1.55 [d, 3 H, *J* = 7.0 Hz, CH(CH_3)OBz], 1.69 (dd, 3 H, *J* = 6.4, 1.4 Hz, =CHCH_3), 2.24 (br, s, 1 H, OH), 2.88 [qn, 1 H, *J* = 7.2 Hz, C*H*(CH_3)CHOH], 4.20 (dd, 1 H, *J* = 7.8, 7.2 Hz, C*H*OH), 5.46–5.39 [m, 2 H, =C*H*(CH)OH and C*H*(CH_3)OBz], 5.72 (dq, 1 H, *J* = 15.2, 6.4 Hz, =C*H*CH_3), 7.46 (dd, 2 H, *J* = 7.4, 8.0 Hz, Ar*H*), 7.57 (tt, 1 H, *J* = 7.4, 1.3 Hz, Ar*H*), 8.07 (dd, 2 H, *J* = 8.0, 1.3 Hz, Ar*H*).
^{13}C NMR (100.6 MHz): δ = 14.5, 15.9, 17.7, 48.2, 74.9, 75.0, 128.5, 129.3, 129.6, 129.8, 131.4, 133.3, 165.9, 211.3.
HRMS (+FAB): *m/z* $[M+H]^+$ found 277.1447, $C_{16}H_{21}O_4$ requires 277.1440.
LRMS (+FAB): *m/z* = 277 ($[M+H]^+$, 18), 259 (20), 154 (100), 136 (65).

(2*S*,4*R*,5*R*,6*S*)-2-Benzoyloxy-7-benzyloxy-5-hydroxy-4,6-dimethylheptan-3-one (12):
General procedure A was followed with ketone (*S*)-**2** (97.3 mg, 0.472 mmol), *c*-Hex_2BCl (153 μL, 0.706 mmol), Me_2NEt (92 μL, 0.848 mmol) and aldehyde (*S*)-**11** (54.0 mg, 0.272 mmol). Standard workup and column chromatography (50% Et_2O in hexane) afforded the aldol product as a colourless oil (83.5 mg, 80%); R_f (50% Et_2O in hexane) 0.34; $[\alpha]_D$ +11.5 (*c* = 3.8, $CHCl_3$).
IR (film): ν =3505 (br), 1716 (s), 1602 cm^{-1} (w).
^{1}H NMR (400 MHz): δ = 0.96 [d, 3 H, *J* = 7.1 Hz, CH(CH_3)CH_2OBn], 1.12 [d, 3 H, *J* = 7.1 Hz, CH(CH_3)O], 1.55 [d, 3 H, *J* = 7.0 Hz, CH(CH_3)OBz], 1.89 [m, 1 H, C*H*(CH_3)CH_2OBn], 2.82 (d, 1 H, *J* = 3.3 Hz, OH), 3.00 [dq, 1 H, *J* = 9.2, 7.1 Hz, C*H*(CH_3)CO], 3.52 (dd, 1 H, *J* = 9.0, 5.4 Hz, C$H_A$$H_B$OBn), 3.55 (dd, 1 H, *J* = 9.0, 4.3 Hz, $CH_A$$H_B$OBn), 4.08 (ddd, 1 H, *J* = 9.2, 4.9, 3.3 Hz, C*H*OH), 4.45 (d, 1 H, *J* = 12.0 Hz, OC$H_A$$H_B$Ph), 4.50 (d, 1 H, *J* = 12.0 Hz, OC$H_A$$H_B$Ph), 5.43 [q, 1 H, *J* = 7.0 Hz, C*H*(CH_3)OBz], 7.36–7.26 (m, 5H, Ar*H*), 7.43 (dd, 2 H, *J* = 8.3, 7.5 Hz, Ar*H*), 7.59 (tt, 1 H, *J* = 7.5, 1.3 Hz, Ar*H*), 8.08 (dd, 2 H, *J* = 8.3, 1.3 Hz, Ar*H*).
13C NMR (100.6 MHz): δ = 9.6, 13.9, 15.6, 35.6, 45.7, 73.5, 75.0, 75.1(2), 75.1(4), 127.6, 127.7, 128.4, 128.5, 129.7, 129.8, 133.2, 138.0, 165.9, 211.2.
HRMS (+FAB): *m/z* $[M+H]^+$ found 385.2028, C_{23} $H_{29}O_5$ requires 385.2015.
LRMS (+FAB): *m/z* = 407 ($[M+Na]^+$, 40), 385 ($[M+H]^+$, 100).

(2*S*,4*R*,5*R*,6*R*)-2-Benzoyloxy-7-benzyloxy-5-hydroxy-4,6-dimethylheptan-3-one (13):
General procedure A was followed with ketone (*S*)-**2** (111 mg, 0.539 mmol), *c*-Hex_2BCl (175 μL, 0.808 mmol), Me_2NEt (105 μL,

0.970 mmol) and aldehyde (*R*)-**11** (43.0 mg, 0.217 mmol). Standard workup and column chromatography (50% Et_2O in hexane) afforded the aldol product as a colourless oil (51.0 mg, 61%); R_f (50% Et_2O in hexane) 0.34; $[\alpha]_D$ +8.0 (*c* = 2.0, $CHCl_3$).
IR (film): ν = 3504 (br), 1718 (s), 1602 cm^{-1} (w).
^{1}H NMR (400 MHz): δ = 1.07 [d, 3 H, *J* = 7.1 Hz, CH(C*H*$_3$)CH$_2$OBn], 1.21 [d, 3 H, *J* = 7.1 Hz, CH(C*H*$_3$)CO], 1.52 [d, 3 H, *J* = 7.0 Hz, CH(C*H*$_3$)OBz], 1.96 [m, 1 H, C*H*(CH$_3$CH$_2$OBn], 3.07 (d, 1 H, *J* = 7.7 Hz, OH), 3.13 [qn, 1 H, *J* = 7.1 Hz, C*H*(CH$_3$)CO], 3.55 (m, 2 H, C*H*$_2$OBn), 3.69 (ddd, 1 H, *J* = 7.7, 7.1, 4.4 Hz, C*H*OH), 4.46 (s, 2 H, OCH$_2$Ph), 5.43 [q, 1 H, *J* = 7.0 Hz, C*H*(CH$_3$)OBz], 7.27–7.34 (m, 5H, Ar*H*), 7.44 (d, 2 H, *J* = 7.3 Hz, Ar*H*), 7.58 (t, 1 H, *J* = 7.3 Hz, Ar*H*), 8.08 (d, 2 H, *J* = 7.3 Hz, Ar*H*).
^{13}C NMR (100.6 MHz): δ = 14.4, 15.6, 35.1, 46.2, 72.0, 73.4, 75.0, 77.0, 127.6, 127.7, 128.4, 128.5, 129.6, 129.8, 133.3, 138.0, 165.8, 211.5.
HRMS (CI, NH_3): *m/z* $[M+H]^+$ found 385.2023, $C_{23}H_{29}O_5$ requires 385.2015.
LRMS (CI, NH_3): *m/z* = 385 ($[M+H]^+$, 18), 207 (100), 196 (98), 108 (40).

(2*R*,4*S*,5*S*)-2-Benzoyloxy-4-ethyl-5-hydroxy-6-methylheptan-3-one (14):
General procedure A was followed with *c*-Hex$_2$BCl (128 μL, 0.590 mmol), Me$_2$NEt (77 μL, 0.708 mmol), ketone (*R*)-**9** (86.5 mg, 0.393 mmol) and *i*-PrCHO (143 μL, 1.57 mmol). Standard workup and column chromatography (40% Et_2O in hexane) gave **14** as a white crystalline solid (109.6 mg, 95%): mp 86–88 °C; R_f (40% Et_2O in hexane) 0.25; $[\alpha]_D$ –39 (*c* = 1.3, $CHCl_3$).
IR ($CHCl_3$): ν = 3555 (br), 1725 (s), 1698 (s), 1601, 1585 cm^{-1} (w).
^{1}H NMR (250 MHz): δ = 0.90 [d, 3 H, *J* = 6.7 Hz, CH(CH)$_3$ C*H*$_3$], 0.92 [d, 3 H, *J* = 6.8 Hz, CH(C*H*$_3$)CH$_3$], 0.98 (t, 3 H, *J* = 7.4 Hz, CH$_2$C*H*$_3$), 1.56 [d, 3 H, *J* = 7.1 Hz, CH(C*H*$_3$)OBz], 1.75–1.74 [m, 3 H, C*H*(CH$_3$)$_2$ and C*H*$_2$CH$_3$], 2.37 (d, 1 H, *J* = 7.5 Hz, OH), 2.94 [q, 1 H, *J* = 6.5 Hz, C*H*CH$_2$(CH$_3$)CHOH], 3.55 (ddd, 1 H, *J* = 7.5, 6.5, 5.2 Hz, C*H*OH), 5.49 [q, 1 H, *J* = 7.1 Hz, C*H*(CH$_3$)OBz], 7.47 (dd, 2 H, *J* = 8.0, 7.6 Hz, Ar*H*), 7.59 (tt, 1 H, *J* = 7.6, 1.3 Hz, Ar*H*), 8.09 (dd, 2 H, *J* = 8.0, 1.3 Hz, Ar*H*).
^{13}C NMR (100.6 MHz): δ = 11.7, 16.0, 16.2, 20.0, 22.4, 30.7, 51.3, 75.4, 76.6, 128.5, 129.6, 129.8, 133.4, 165.8, 212.1.
HRMS (+FAB): *m/z* $[M+H]^+$ found 293.1734, $C_{17}H_{25}O_4$ requires 293.1753.
LRMS (+FAB): *m/z* = 293 ($[M+H]^+$, 96), 153 (100), 136 (52).
Analysis: found C, 70.07; H, 8.42; $C_{17}H_{24}O_4$ requires C, 69.84; H, 8.27.

(2*S*,4*R*,5*R*)-2-Benzoyloxy-4-benzyloxy-5-hydroxy-6-methylheptan-3-one (17):
General procedure A was followed with *c*-Hex$_2$BCl (70 μL, 0.325 mmol), Me$_2$NEt (44 μL, 0.406 mmol), ketone **15** (48.4 mg, 0.162 mmol) and *i*-PrCHO (59 μL, 0.650 mmol). Standard workup and column chromatography (50% Et_2O in hexane) afforded **17** as an oil (46.4 mg, 77%); R_f (50% Et_2O in hexane) 0.38; $[\alpha]_D$ +60.0 (*c* = 2.2, $CHCl_3$).
IR (film): ν = 3490 (br), 1719 (s), 1601, 1584, 1496 cm^{-1} (w).
^{1}H NMR (400 MHz): δ = 0.86 [d, 3 H, *J* = 6.8 Hz, CH(CH$_3$)C*H*$_3$], 0.98 [d, 3 H, *J* = 6.9 Hz, CH(C*H*$_3$)CH$_3$], 1.58 [d, 3 H, *J* = 6.9 Hz, CH(C*H*$_3$)OBz], 1.95 [m, 1 H, C*H*(CH$_3$)$_2$], 2.87 (d, 1 H, *J* = 6.7 Hz, OH), 3.80 (m, 1 H, C*H*OH), 4.09 [d, 1 H, *J* = 6.9 Hz, C*H*(OBn)CHOH], 4.53 (d, 1 H,*J* = 11.5 Hz, OCH$_A$*H*$_B$Ph), 4.62 (d, 1 H, *J* = 11.5 Hz, OC*H*$_A$H$_B$Ph), 5.66 [q, 1 H, *J* = 6.9 Hz, C*H*(CH$_3$)OBz], 7.35–7.29 (m, 5H, Ar*H*), 7.45 (dd, 2 H, *J* = 8.1, 7.0 Hz, Ar*H*), 7.57 (tt, 1 H, *J* = 7.0, 1.1 Hz, Ar*H*), 8.05 (dd, 2 H, *J* = 8.1, 1.1 Hz, Ar*H*).
^{13}C NMR (100.6 MHz): δ = 16.3, 16.9, 19.9, 29.4, 72.8, 73.9, 76.2, 84.4, 128.2, 128.5, 128.6, 128.7, 129.3, 130.0, 133.6, 136.9, 166.6, 207.9.
HRMS (CI, NH_3): *m/z* $[M+H]^+$ found 371.1858, $C_{22}H_{27}O_5$ requires 371.1858.
LRMS (CI, NH_3): *m/z* = 371 ($[M+H]^+$, 24), 290 (28), 212 (26), 196 (64), 108 (75), 105 (40), 52 (100).

TBS Protection of Aldol Products; Synthesis of 18; General Procedure B:
To a cooled (–78 °C) solution of the aldol product **4** (0.5 mmol) in CH_2Cl_2 (3 mL) was added 2,6-lutidine (214 mg, 2 mmol) followed by TBSOTf (397 mg, 1.5 mmol). The reaction mixture was quenched with satd aq $NaHCO_3$ solution (10 mL) after 1 h or until TLC analysis showed consumption of the starting material. It was then allowed to warm to r.t., partitioned between H_2O (10 mL) and CH_2Cl_2 (3 × 25 mL) and the combined organic extracts were dried ($MgSO_4$), concentrated *in vacuo* and purified by column chromatography.

(2S,4R,5R)-2-Benzoyloxy-5-tert-butyldimethylsilyloxy-4,6-dimethylheptan-3-one (**18**, *R = i-Pr*):
R_f (20% Et_2O in hexane) 0.52; $[\alpha]_D$ +1.8 (*c* = 1.0, $CHCl_3$).
IR (film): ν = 1724 (s), 1603, 1585 cm^{-1} (w).
^{1}H NMR (250 MHz): δ = –0.07 (s, 3 H, SiCH$_3$), 0.03 (s, 3 H, SiCH$_3$), 0.87–0.84 [m, 12 H, CH(CH$_3$)C*H*$_3$ and SiC(CH$_3$)$_3$], 0.94 [d, 3 H, *J* = 6.8 Hz, CH(C*H*$_3$)CH$_3$], 1.10 [d, 3 H, *J* = 7.1 Hz, CH(CH$_3$)CHOTBS], 1.51 [d, 3 H, *J* = 7.0 Hz, CH(C*H*$_3$)OBz], 1.78 [septet, d, 1 H, *J* = 6.8, 2.3 Hz, C*H*(CH$_3$)$_2$], 3.06 [dq, 1 H, *J* = 8.6, 7.1 Hz, C*H*(CH$_3$)CHOTBS], 3.88 (dd, 1 H, *J* = 8.6, 2.3 Hz, C*H*OTBS), 5.46 [q, 1 H, *J* = 7.0 Hz, C*H*(CH$_3$)OBz], 7.45 (dd, 2 H, *J* = 8.1, 7.3 Hz, Ar*H*), 7.56 (tt, 1 H, *J* = 7.3, 1.0 Hz, Ar*H*), 8.07 (dd, 2 H, *J* = 8.1, 1.0 Hz, Ar*H*).
^{13}C NMR (62.9 MHz): δ = –4.5, –3.5, 14.4, 15.7, 16.1, 18.6, 19.8, 26.4, 31.2, 46.6, 75.1, 77.6, 128.6, 129.8, 129.9, 133.4, 165.8, 209.2.
HRMS (CI, NH_3): *m/z* $[M+H]^+$ found 393.2461, $C_{22}H_{37}O_4Si$ requires 393.2461.
LRMS (CI, NH_3): *m/z* = 393 ($[M+H]^+$, 55), 261 (20), 187 (60), 132 (100).

(1S,2R,4S)-4-Benzoyloxy-1-tert-butyldimethylsilyloxy-2-methyl-1-phenylpentan-3-one (**18**, *R = Ph*):
R_f (20% Et_2O in hexane) 0.46; $[\alpha]_D$ +43.6 (*c* = 2.8, $CHCl_3$).
IR (film): ν = 1720 (s), 1602, 1558, 1507 cm^{-1} (w).
^{1}H NMR (250 MHz): δ = –0.30 (s, 3 H, SiCH$_3$), –0.07 (s, 3 H, SiCH$_3$), 0.79 [s, 9 H, SiC(CH$_3$)$_3$], 0.83 [d, 3 H, *J* = 7.1 Hz, CH(C*H*$_3$)CHOTBS], 1.60 [d, 3 H, *J* = 7.0 Hz, CH(C*H*$_3$)OBz], 3.10 [dq, 1 H, *J* = 9.6, 7.1 Hz, C*H*(CH$_3$)CHOTBS], 4.78 [d, 1 H, *J* = 9.6 Hz, C*H*(OTBS)Ph], 5.48 [q, 1 H, *J* = 7.0 Hz, C*H*(CH$_3$)OBz], 7.27–7.31 (m, 5 H, Ar*H*), 7.46 (dd, 2 H, *J* = 8.6, 7.4 Hz, Ar*H*), 7.58 (tt, 1 H, *J* = 7.4, 1.3 Hz, Ar*H*), 8.09 (dd, 2 H, *J* = 8.6, 1.3 Hz, Ar*H*).
^{13}C NMR (62.9 MHz): δ = –5.1, –4.8, 14.6, 15.2, 18.0, 25.7, 51.2, 75.3, 77.6, 127.2, 127.8, 128.2, 128.4, 129.7, 129.8, 133.2, 142.6, 165.8, 209.4.
HRMS (CI, NH_3): *m/z* $[M+H]^+$ found 427.2305, $C_{25}H_{35}O_4Si$ requires 427.2305.
LRMS (CI, NH_3): *m/z* = 427 ($[M+H]^+$, 18), 211 (40), 177 (100).

(2S,4R,5R,6E)-2-Benzoyloxy-5-tert-butyldimethylsilyloxy-4-methyloct-6-en-3-one (**18**, *R = (E)-CH=CHMe*):
R_f (20% Et_2O in hexane) 0.55; $[\alpha]_D$ –1.4 (*c* = 1.4, $CHCl_3$).
IR (film): ν = 1722 (s), 1602 cm^{-1} (w).
^{1}H NMR (250 MHz): δ = 0.00 (s, 3 H, SiCH$_3$), , 0.09 (s, 3 H, SiCH$_3$), 0.81 [s, 9 H, SiC(CH$_3$)$_3$], 1.02 [d, 3 H, *J* = 7.1 Hz, CH(C*H*$_3$)CHOTBS], 1.52 [d, 3 H, *J* = 7.0 Hz, CH(C*H*$_3$)OBz], 1.68 (dd, 3 H, *J* = 6.5, 1.5 Hz, =CHC*H*$_3$), 2.87 [dq, 1 H, *J* = 9.2, 7.1 Hz, C*H*(CH$_3$)CHOTBS], 4.23 (dd, 1 H, *J* = 9.2, 8.6 Hz, C*H*OTBS), 5.28 (ddq ,1 H, *J* = 15.3, 8.6, 1.5 Hz, C*H*=CHCH$_3$), 5.42 [q, 1 H, *J* = 7.0 Hz, C*H*(CH$_3$)OBz], 5.60 (dq, 1 H, *J* = 15.3, 6.5 Hz, =C*H*CH$_3$), , 7.45 (dd, 2 H, *J* = 7.3, 7.1 Hz, Ar*H*), 7.58 (tt, 1 H, *J* = 7.1, 1.2 Hz, Ar*H*), 8.08 (dd, 2 H, *J* = 7.3, 1.2 Hz, Ar*H*).
^{13}C NMR (62.9 MHz): δ = –4.6, –4.0, 14.4, 15.3, 17.7, 18.2, 26.0, 49.1, 75.7, 76.6, 128.5, 128.6, 129.9, 130.0, 132.6, 133.3, 165.9, 209.6.
HRMS (CI, NH_3): *m/z* $[M+H]^+$ found 391.2305, $C_{22}H_{35}O_4Si$ requires 391.2305.
LRMS (CI, NH_3): *m/z* = 391 ($[M+H]^+$, 10), 259 (100), 177 (20), 137 (30).

(2S,4R,5R,6S)-2-Benzoyloxy-7-benzyloxy-5-tert-butyldimethylsilyloxy-4,6-dimethylheptan-3-one (**18**, *R = (S)-CH(Me)CH$_2$OBn*):
R_f (30% Et_2O in hexane) 0.46; $[\alpha]_D$ –6.4 (*c* = 1.6, $CHCl_3$).
IR (film): ν = 1721 (s,), 1602, 1585, 1548, 1512, 1494 cm^{-1} (w).
^{1}H NMR (400 MHz): δ = –0.09 (s, 3 H, $SiCH_3$), 0.01 (s, 3 H, $SiCH_3$), 0.82 [s, 9 H, $SiC(CH_3)_3$], 0.89 [d, 3 H, *J* = 7.1 Hz, CH(C*H*$_3$)CH$_2$OBn], 1.11 [d, 3 H, *J* = 7.2 Hz, CH(C*H*$_3$)CO], 1.50 [d, 3 H, *J* = 7.0 Hz, CH(C*H*$_3$)OBz], 1.95 [m, 1 H, C*H*(CH$_3$)CH$_2$OBn], 3.10 [dq, 1 H, *J* = 8.5, 7.2 Hz, C*H*(CH$_3$)CO], 3.27 (dd, 1 H, *J* = 8.8, 6.7 Hz, CH$_A$*H*$_B$ OBn), 3.41 (dd, 1 H, *J* = 8.8, 7.4 Hz, C*H*$_A$H$_B$OBn), 4.22 (dd, 1 H, *J* = 8.5, 1.3 Hz, C*H*OTBS), 4.42 (d, 1 H, *J* = 12.0 Hz, OC*H*$_A$H$_B$Ph), 4.50 (d, 1 H, *J* = 12.0 Hz, OCH$_A$*H*$_B$Ph), 5.47 [q, 1 H, *J* = 7.0 Hz, C*H*(CH$_3$)OBz], 7.26–7.34 (m, 5H, Ar*H*), 7.45 (t, 2 H, *J* = 7.4 Hz, Ar*H*), 7.58 (t, 1 H, *J* = 7.4 Hz, Ar*H*), 8.06 (d, 2 H, *J* = 7.4 Hz, Ar*H*).
^{13}C NMR (100.6 MHz): δ = –5.0, –3.6, 10.5, 14.0, 15.6, 18.5, 26.2, 36.1, 46.9, 65.9, 72.9, 73.0, 127.4, 127.5, 127.6, 128.3, 128.5, 129.8, 133.3, 165.7, 209.0.
HRMS (+FAB): *m/z* [M+H]$^+$ found 499.2876, $C_{29}H_{43}O_5Si$ requires 499.2880.
LRMS (+FAB): *m/z* = 499 ([M+H]$^+$, 24), 441 (51), 349 (25), 293 (50), 259 (75), 179 (100).

(2S,4R,5R,6R)-2-Benzoyloxy-7-benzyloxy-5-tert-butyldimethylsilyloxy-4,6-dimethylheptan-3-one (**18**, *R = (R)-CH(Me)CH$_2$OBn*):
R_f (30% Et_2O in hexane) 0.46; $[\alpha]_D$ –5.9 (*c* = 1.4, $CHCl_3$).
IR (film): ν = 1721 (s), 1602, 1584, 1495 cm^{-1} (w).
^{1}H NMR (400 MHz): δ = –0.07 (s, 3 H, $SiCH_3$), 0.05 (s, 3 H, $SiCH_3$) 0.84 [s, 9 H, $SiC(CH_3)_3$], 0.98 [d, 3 H, *J* = 7.1 Hz, CH(C*H*$_3$)CH$_2$OBn], 1.11 [d, 3 H, *J* = 7.1 Hz, CH(C*H*$_3$)CO], 1.49 [d, 3 H, *J* = 7.0 Hz, CH(C*H*$_3$)OBz], 2.08 [m, 1 H, C*H*(CH$_3$)CH$_2$OBn], 3.21 [dq, 1 H, *J* = 8.7, 7.1 Hz, C*H*(CH$_3$)CO], 3.25 (dd, 1 H, *J* = 9.3, 6.8 Hz, C*H*$_A$-H$_B$OBn), 3.58 (dd, 1 H, *J* = 9.3, 6.4 Hz, CH$_A$*H*$_B$OBn), 4.04 (dd, 1 H, *J* = 8.7, 2.2 Hz, C*H*OTBS), 4.44 (s, 2 H, OC*H*$_2$Ph), 5.44 [q, 1 H, *J* = 7.0 Hz, C*H*(CH$_3$)OBz], 7.26–7.32 (m, 5H, Ar*H*), 7.43 (d, 2 H, *J* = 7.4 Hz, Ar*H*), 7.55 (t, 1 H, *J* = 7.4 Hz, Ar*H*), 8.05 (d, 2 H, *J* = 7.4 Hz, Ar*H*).
^{13}C NMR (100.6 MHz): δ = –4.9, –3.9, 14.2, 14.9, 15.5, 18.3, 26.1, 37.1, 46.3, 71.7, 72.9, 74.9, 75.9, 127.4, 128.2, 128.3, 128.4, 129.7, 129.8, 133.2, 138.5, 165.7, 209.0.
HRMS (CI, NH_3): *m/z* [M+H]$^+$ found 499.2880, $C_{29}H_{43}O_5Si$ requires 499.2880.
LRMS (CI, NH_3): *m/z* = 516 ([M+NH$_4$]$^+$, 100), 499 ([M+H]$^+$ 44), 391 (38), 367 (35), 177 (40).

LiBH$_4$ Reduction of 18; Synthesis of Diols 19; General Procedure C:
To a cooled (–78°C) solution of the protected aldol product **18** (0.5 mmol) in THF (6 mL) was added a 2 M THF solution of $LiBH_4$ (5.0 mL, 10.0 mmol). The reaction mixture was warmed slowly to r.t. and stirring was continued for 24 h, before cooling to 0°C and careful quenching with H_2O. The mixture was partitioned between H_2O (15 mL) and Et_2O (4 × 25 mL) and the combined organic extracts washed with brine (30 mL), dried ($MgSO_4$) and concentrated *in vacuo*. Column chromatography gave the required 1,2-diol.

(2S,3R,4S,5R)-5-tert-Butyldimethylsilyloxy-4,6-dimethylheptan-2,3-diol (**19**, *R = i-Pr*):
R_f (50% Et_2O in hexane) 0.22; $[\alpha]_D$ –7.5 (*c* = 1.6, $CHCl_3$).
IR (film): ν = 3418 cm^{-1} (s br).
^{1}H NMR (400 MHz): δ = 0.09 (s, 3 H, $SiCH_3$), 0.12 (s, 3 H, $SiCH_3$) 0.83 [d, 3 H, *J* = 7.0 Hz, CH(CH$_3$)C*H*$_3$], 0.89 [d, 3 H, *J* = 6.9 Hz, CH(C*H*$_3$)CH$_3$], 0.92 [d, 3 H, *J* = 6.7 Hz, CH(C*H*$_3$)CHOH], 0.93 [s, 9H, $SiC(CH_3)_3$], 1.16 [d, 3 H, *J* = 6.3 Hz, CH(C*H*$_3$)OH], 1.70 [m, 1 H, C*H*(CH$_3$)$_2$], 1.84 [m, 1 H, C*H*(CH$_3$)CHOH], 2.63 [d, 1 H, *J* = 7.0 Hz, CH(CH$_3$)O*H*], 3.45 (t, 1 H, *J* = 4.8 Hz, C*H*OTBS), 3.48 (d, 1 H, *J* = 3.0 Hz, CHO*H*), 3.63 (ddd, 1 H, *J* = 9.4, 3.0, 1.2 Hz, C*H*OH), 3.77 [m, 1 H, C*H*(CH$_3$)OH].
^{13}C NMR (100.6 MHz): δ = –4.2, –3.9, 15.6, 15.9, 18.2, 18.3, 19.0, 26.0, 33.6, 38.3, 67.9, 72.6, 82.6.
HRMS (CI, NH_3): *m/z* [M+H]$^+$ found 291.2355, $C_{15}H_{35}O_3Si$ requires 291.2356.
LRMS (CI, NH_3): *m/z* = 291 ([M+H]$^+$ 90), 176 (30), 159 (32), 141 (100).

(1S,2S,3R,4S)-1-tert-Butyldimethylsilyloxy-2-methyl-1-phenylpentan-3,4-diol (**19**, *R = Ph*):
R_f (60% Et_2O in hexane) 0.25; $[\alpha]_D$ –77.7 (*c* = 1.6, $CHCl_3$).
IR (film): ν = 3417 (br), 1603, 1492 cm^{-1} (w).
^{1}H NMR (400 MHz): δ = –0.30 (s, 3 H, $SiCH_3$), 0.02 (s, 3 H, $SiCH_3$), 0.61 [d, 3 H, *J* = 6.9 Hz, CH(C*H*$_3$)CHOTBS], 0.87 [s, 9H, $SiC(CH_3)_3$], 1.15 [d, 3 H, *J* = 6.3 Hz, CH(C*H*$_3$)OH], 1.84 [br sextet, 1 H, *J* = 7.8 Hz, C*H*(CH$_3$)CHOTBS], 2.51 [d, 1 H, *J* = 8.0 Hz, CH(CH$_3$)O*H*], 3.61 [ddd, 1 H, *J* = 7.8, 3.5, 1.6 Hz C*H*(OH)CH(CH$_3$)OH], 3.77 [m, 1 H, C*H*(CH$_3$)OH], 4.01 (d, 1 H, *J* = 1.6 Hz, CHO*H*), 4.62 [d, 1 H, *J* = 7.8 Hz, C*H*(OTBS)Ph], 7.32–7.26 (m, 5 H, Ar*H*).
^{13}C NMR (100.6 MHz): δ = –5.1, –4.5, 12.0, 16.1, 18.0, 25.8, 43.7, 68.3, 77.5, 80.8, 127.4, 128.1, 142.8.
HRMS (+FAB): *m/z* [M+H]$^+$ found 325.2230, $C_{18}H_{33}O_3Si$ requires 325.2199.
LRMS (+FAB): *m/z* = 347 ([M+Na]$^+$ 55), 325 ([M+H]$^+$, 84), 249 (40), 221 (100), 193 (85).

(2S,3R,4S,5S,6E)-5-tert-Butyldimethylsilyloxy-4-methyloct-6-en-2,3-diol (**19**, *R = (E)-CH=CHMe*):
R_f (30% Et_2O in CH_2Cl_2) 0.33; $[\alpha]_D$ –18.0 (*c* = 1.0, $CHCl_3$).
IR (film): ν = 3380 (s br), 1670 cm^{-1} (w).
^{1}H NMR (250 MHz): δ = 0.08 (s, 3 H, $SiCH_3$), 0.04 (s, 3 H, $SiCH_3$), 0.75 [d, 3 H, *J* = 6.9 Hz, CH(C*H*$_3$)CHOTBS], 0.89 [s, 9H, $SiC(CH_3)_3$], 1.15 [d, 3 H, *J* = 6.3 Hz, CH(C*H*$_3$)OH], 1.58 [m, 1 H, C*H*(CH$_3$)CHOTBS], 1.70 (dd, 3 H, *J* = 6.3, 1.3 Hz, =CHC*H*$_3$), 2.58 [d, 1 H, *J* = 8.1 Hz, CH(CH$_3$)O*H*], 3.60 [ddd, 1 H, *J* = 8.3, 3.5, 2.1 Hz, C*H*(OH)CH(CH$_3$)OH], 3.80 [obscured, 1 H, C*H*(CH$_3$)OH], 3.80 (d, 1 H, *J* = 2.1 Hz, CHO*H*), 4.06 (t, 1 H, *J* = 7.8 Hz, C*H*OTBS), 5.38 (ddq, 1 H, *J* = 15.4, 7.8, 1.3 Hz, C*H*=CHCH$_3$), 5.51 (dq, 1 H, *J* = 15.4, 6.3 Hz, =C*H*CH$_3$).
HRMS (CI, NH_3): *m/z* [M+H]$^+$ found 289.2199, $C_{15}H_{33}O_3Si$ requires 289.2199.
LRMS (CI, NH_3): *m/z* = 289 ([M+H]$^+$ 6), 174 (100), 157 (20), 139 (40).

(2S,3R,4R,5R,6S)-7-Benzyloxy-5-tert-butyldimethylsilyloxy-4,6-dimethylheptan-2,3-diol (**19**, *R = (S)-CHMeCH$_2$OBn*):
R_f (30% Et_2O in CH_2Cl_2) 0.38; $[\alpha]_D$ +8.9 (*c* = 1.4, $CHCl_3$).
IR (film): ν = 3440 (br), 1558, 1540, 1496 cm^{-1} (w).
^{1}H NMR (400 MHz): δ = –0.01 (s, 3 H, $SiCH_3$), 0.05 (s, 3 H, $SiCH_3$), 0.80 (d, 3 H, *J* = 7.0 Hz, CHC*H*$_3$), 0.88 (d, 3 H, *J* = 7.0 Hz, CHC*H*$_3$), 0.90 [s, 9H, $SiC(CH_3)_3$], 1.11 [d, 3 H, *J* = 6.4 Hz, CH(C*H*$_3$)OH], 1.65–1.69 [m, 1 H, C*H*(CH$_3$)CH$_2$OBn], 2.00–2.03 [m, 1 H, C*H*(CH$_3$)CHOH], 2.51 (br, s, 1 H, OH), 3.28–3.31 (m, 1 H, C*H*OH), 3.54–3.63 (m, 2 H, C*H*$_2$OBn), 3.79 (m, 1 H, C*H*OH), 4.00 (dd, 1 H, *J* = 4.5, 2.6 Hz, C*H*OTBS), 4.48 (d, 1 H, *J* = 12.0 Hz, OC*H*$_A$H$_B$Ph), 4.50 (d, 1 H, *J* = 12.0 Hz, OCH$_A$*H*$_B$Ph), 7.28–7.34 (m, 5 H, Ar*H*).
^{13}C NMR (100.6 MHz): δ = –4.8, –4.3, 11.4, 12.5, 15.7, 18.1, 25.9, 35.3, 41.6, 67.7, 73.2, 73.5, 74.2, 75.8, 127.7, 127.8, 128.4, 137.7.
HRMS (+FAB): *m/z* [M+H]$^+$ found 397.2784, $C_{22}H_{41}O_4Si$ requires 397.2774.
LRMS (+FAB): *m/z* = 419 ([M+Na]$^+$, 25), 397 ([M+H]$^+$, 100), 265 (40), 187 (38), 157 (50).

(2S,3R,4S,5R,6R)-7-Benzyloxy-5-tert-butyldimethylsilyloxy-4,6-dimethylheptan-2,3-diol (19, *R = (R)-CHMeCH$_2$OBn)*:
R_f (30% Et_2O in CH_2Cl_2) 0.38; $[\alpha]_D$ –2.4 (*c* = 1.7, $CHCl_3$).
IR (film): ν = 3440 (br), 1558, 1540, 1496 cm^{-1} (w).
^{1}H NMR (400 MHz): δ = 0.08 (s, 3 H, $SiCH_3$), 0.14 (s, 3 H, $SiCH_3$), 0.82 (d, 3 H, *J* = 7.0 Hz, CHC*H*$_3$), 0.90 [s, 9H, $SiC(CH_3)_3$], 0.99 (d, 3 H, *J* = 6.9 Hz, CHC*H*$_3$), 1.13 [d, 3 H, *J* = 6.4 Hz, CH(C*H*$_3$)OH], 1.74–1.78 [m, 1 H, C*H*(CH$_3$)CH$_2$OBn], 2.09–2.13 [m, 1 H, C*H*(CH$_3$)CHOH], 2.68 (br s, 1 H, OH), 3.30 (dd, 1 H, *J* = 9.2, 6.7 Hz, CH$_A$*H*$_B$OBn), 3.48 (dd, 1 H, *J* = 9.2, 6.3 Hz, C*H*$_A$H$_B$OBn), 3.51 (br, s, 1 H, OH), 3.63 (dd, 1 H, *J* = 9.3, 3.2 Hz, C*H*OTBS), 3.75–3.78 (m, 2 H, 2 x C*H*OH), 4.68 (d, 1 H, *J* = 17.6 Hz, OCH$_A$*H*$_B$Ph), 4.70 (d, 1 H, *J* = 17.6 Hz, OC*H*$_A$H$_B$Ph), 7.26–7.40 (m, 5 H, Ar*H*).
^{13}C NMR (100.6 MHz): δ = –4.5, –4.1, 13.9, 14.9, 15.9, 18.2, 26.0, 38.0, 39.3, 67.9, 72.4, 73.1, 76.2, 78.9, 127.0, 127.7, 128.4, 138.5.

HRMS (+FAB): *m/z* $[M+H]^+$ found 397.2766, $C_{22}H_{41}O_4Si$ requires 397.2774.
LRMS (+FAB): *m/z* = 419 ($[M+Na]^+$, 23), 397 ($[M+H]^+$,100), 265 (35), 173 (40).

$NaIO_4$ Cleavage; Synthesis of Aldehydes 5a–e, 24 and 26; General Procedure D:
To a stirred solution of 1,2-diol (0.2 mmol) in MeOH (2 mL) and H_2O (1 mL) at r.t. was added $NaIO_4$ (257 mg; 1.2 mmol). The reaction mixture was stirred at r.t. for 30 min or until TLC analysis showed consumption of starting material. The reaction mixture was diluted with H_2O (6 mL), extracted with Et_2O (3 × 15 mL) and then the combined organic extracts were dried ($MgSO_4$), concentrated *in vacuo* and purified by column chromatography.

(2R,3R)-3-tert-Butyldimethylsilyloxy-2,4-dimethylpentanal **(5a)**:[28]
R_f (10% Et_2O in hexane) 0.61; $[\alpha]_D$ –49.1 (*c* = 1.4, CH_2Cl_2).
IR (film): ν = 1725 cm^{-1} (s).
^1H NMR (400 MHz): δ = 0.03 (s, 3 H, $SiCH_3$), 0.50 (s, 3 H, $SiCH_3$), 0.86–0.85 [m, 15 H, $CH(CH_3)_2$ and $SiC(CH_3)_3$], 1.07 [d, 3 H, *J* = 7.1 Hz, $CH(CH_3)CHO$], 1.82 [m, 1 H, $CH(CH_3)_2$], 2.51 [m, 1 H, $CH(CH_3)CHO$], 3.65 (dd, 1 H, *J* = 5.0, 4.1 Hz, CHOTBS), 9.76 (d, 1 H, *J* = 3.3 Hz, CHO).
^{13}C NMR (100.6 MHz): δ = –4.3,–4.1, 12.0, 18.2, 18.3, 18.7, 25.9, 32.9, 49.9, 79.2, 205.1.

(2R,3S)-3-tert-Butyldimethylsilyloxy-2-methyl-3-phenylpropanal **(5b):**
R_f (50% Et_2O in hexane) 0.60; $[\alpha]_D$ –60.0 (*c* = 0.9, $CHCl_3$).
IR (film): ν = 1726 (s), 1490 cm^{-1} (w).
^1H NMR (400 MHz): δ = –0.26 (s, 3 H, $SiCH_3$), 0.00 (s, 3 H, $SiCH_3$), 0.84 [s, 9 H, $SiC(CH_3)_3$], 0.87 [d, 3 H, *J* = 7.1 Hz, $CH(CH_3)CHO$], 2.68 [qnd, 1 H, *J* = 7.1, 2.7 Hz, $CH(CH_3)CHO$], 4.75 [d, 1 H, *J* = 7.6 Hz, CH(OTBS)Ph], 7.26–7.35 (m, 5 H, Ar*H*), 9.81 (d, 1 H, *J* = 2.7 Hz, CHO).
^{13}C NMR (100.6 MHz): δ = –5.2, –4.5, 11.1, 18.1, 25.7, 54.6, 76.8, 126.7, 127.8, 128.3, 142.3, 204.5.

(2R,3R,4E)-3-tert-Butyldimethylsilyloxy-2-methylhex-4-enal **(5c):**
R_f (10% Et_2O in hexane) 0.59; $[\alpha]_D$ –51.7 (*c* = 1.5, $CHCl_3$).
IR (film): ν = 1729 cm^{-1} (s).
^1H NMR (400 MHz): δ = –0.01 (s, 3 H, $SiCH_3$), 0.02 (s, 3 H, $SiCH_3$), 0.84 [s, 9H, $SiC(CH_3)_3$], 0.97 [d, 3 H, *J* = 6.9 Hz, $CH(CH_3)CHO$], 1.69 (m, 3 H, $=CHCH_3$), 2.42 [dqd, 1 H, *J* = 7.1, 6.9, 2.5 Hz, $CH(CH_3)CHO$], 4.21 (dd, 1 H, *J* = 7.5, 7.1 Hz, CHOTBS), 5.40 (ddq, 1 H, *J* = 15.3, 7.5, 1.6 Hz, $CH=CHCH_3$), 5.61 (dq, 1 H, *J* = 15.3, 6.6, Hz, $=CHCH_3$), 9.72 (d, 1 H, *J* = 2.5 Hz, CHO).
^{13}C NMR (100.6 MHz): δ = –5.0, –3.9, 10.7, 17.5, 18.1, 25.7, 52.7, 75.4, 127.8, 132.0, 205.0.
HRMS (CI, NH_3): *m/z* $[M+H]^+$ found 243.1780, $C_{13}H_{27}O_2Si^+$ requires 243.1780.
LRMS (CI, NH_3): *m/z* = 243 ($[M+H]^+$ 4), 225 (6), 185 (17), 128 (43), 111 (100).

(2R,3R,4S)-5-Benzyloxy-3-tert-butyldimethylsilyloxy-2,4-dimethylpentanal **(5d):**
R_f (50% CH_2Cl_2 in hexane) 0.31.
IR (film): ν = 1725 (s), 1496 cm^{-1} (w).
^1H NMR (250 MHz): δ = 0.03 (s, 3 H, $SiCH_3$), 0.04 (s, 3 H, $SiCH_3$), 0.86 [s, 9H, $SiC(CH_3)_3$], 0.94 [d, 3 H, *J* = 7.0 Hz, $CH(CH_3)CH_2$], 1.07 [d, 3 H, *J* = 7.1 Hz, $CH(CH_3)CHO$], 1.97 [m, 1 H, $CH(CH_3)CH_2OBn$], 2.56 [qdd, 1 H, *J* = 7.1, 5.4, 2.5 Hz, $CH(CH_3)COH$], 3.28 (dd, 1 H, *J* = 9.1, 5.7 Hz, CH_AH_BOBn), 3.37 (dd, 1 H, *J* = 9.1, 7.0 Hz, CH_AH_BOBn), 4.06 (dd, 1 H, *J* = 5.4, 3.9 Hz, CHOTBS), 4.44 (s, 2 H, OCH_2Ph), 7.26–7.37 (m, 5 H, Ar*H*), 9.70 (d, 1 H, *J* = 2.5 Hz, CHO).
Due to the unstable nature of aldehyde **5d** full characterisation was not obtained but, instead, $NaBH_4$ reduction of **5d** and removal of the TBS group with aq HCl afforded the known (2*S*,3*S*,4*S*)-5-benzyloxy-2,4-dimethylpentan-1,3-diol.[29]

(2R,3R,4R)-5-Benzyloxy-3-tert-butyldimethylsilyloxy-2,4-dimethylpentanal **(5e)**:[30]
R_f (50% CH_2Cl_2 in hexane) 0.31.
IR (film): ν = 1724 (s), 1496 cm^{-1} (w).
^1H NMR (250 MHz): δ = 0.06 [s, 6 H, $Si(CH_3)_2$], 0.87 [s, 9 H, $SiC(CH_3)_3$], 0.92 [d, 3 H, *J* = 7.1 Hz, $CH(CH_3)CH_2OBn$], 1.10 [d, 3 H, *J* = 7.0 Hz, $CH(CH_3)CHO$], 2.05 [m, 1 H, $CH(CH_3)CH_2OBn$], 2.54 [qdd, 1 H, *J* = 7.0, 3.6, 2.5 Hz, $CH(CH_3)CHO$], 3.35 (dd, 1 H, *J* = 9.2, 6.1 Hz, CH_AH_BOBn), 3.46 (dd, 1 H, *J* = 9.2, 6.2 Hz CH_AH_BOBn), 3.98 (dd, 1 H, *J* = 5.6, 3.6 Hz, CHOTBS), 4.45 (1 H, d, *J* = 12.1 Hz, OCH_AH_BPh), 4.47 (1 H, d, *J* = 12.1 Hz, OCH_AH_BPh), 7.26–7.37 (5 H, m, Ar*H*), 9.77 (1 H, d, *J* = 2.5 Hz, CHO).

SmI_2 Reduction; Synthesis of 6a,b; General Procedure:
To a cooled (0 °C) solution of the protected aldol product **18** (0.05 mmol) in THF (0.6 mL) and MeOH (0.3 mL) was added a 0.1 M solution of SmI_2 in THF until the green colour persisted in the reaction mixture (typically 3–4 equiv of SmI_2 were used). Satd aq K_2CO_3 solution (3 mL) was added and the mixture extracted with Et_2O (3 × 10 mL). The combined organic extracts were dried ($MgSO_4$), concentrated *in vacuo* and purified by column chromatography.

(4R,5R)-5-tert-Butyldimethylsilyloxy-4,6-dimethylheptan-3-one **(6a)**:[31]
R_f (5% Et_2O in hexane) 0.5; $[\alpha]_D$ +12.3 (*c* = 0.6, $CHCl_3$).
IR (film): ν = 1719 cm^{-1} (s).
^1H NMR (250 MHz): δ = –0.08 (s, 3 H, $SiCH_3$), 0.03 (s, 3 H, $SiCH_3$), 0.85 [s, 9 H, $SiC(CH_3)_3$], 0.88 [d, 3 H, *J* = 6.9 Hz, $CH(CH_3)CH_3$], 0.89 [d, 3 H, *J* = 6.9 Hz, $CH(CH_3)CH_3$], 0.94 [d, 3 H, *J* = 7.1 Hz, $CH(CH_3)CO$], 1.01 (t, 3 H, *J* = 7.2 Hz, CH_2CH_3), 1.73 [septet d, 1 H, *J* = 6.9, 3.1 Hz, $CH(CH_3)_2$], 2.46 (dq, 1 H, *J* = 18.7, 7.2 Hz, $CH_AH_BCH_3$), 2.51 (dq, 1 H, *J* = 18.7, 7.2 Hz, $CH_AH_BCH_3$), 2.68 [dq, 1 H, *J* = 7.7, 7.1 Hz, $CH(CH_3)CO$], 3.77 (dd, 1 H, *J* = 7.7, 3.1 Hz, CHOTBS).
^{13}C NMR (62.9 MHz): δ = –4.4, –4.2, 7.4, 13.8, 18.4, 19.7, 26.1, 31.2, 36.8, 50.2, 78.3, 214.3.

(1S,2R)-1-tert-Butyldimethylsilyloxy-2-methyl-1-phenylpentan-3-one **(6b):**
R_f (5% EtOAc in hexane) 0.38; $[\alpha]_D$ +80.4 (*c* = 2.2, $CHCl_3$).
IR (film): ν = 1718 (s), 1603, 1515, 1493 cm^{-1} (w).
^1H NMR (250 MHz): δ = –0.35 (s, 3 H, $SiCH_3$), –0.08 (s, 3 H, $SiCH_3$), 0.64 [d, 3 H, *J* = 7.0 Hz, $CH(CH_3)CO$], 0.76 [s, 9 H,$SiC(CH_3)_3$], 1.05 (t, 3 H, *J* = 7.3 Hz, CH_2CH_3), 2.57 (dd, 1 H, *J* = 18.5, 7.3 Hz, $CH_AH_BCH_3$), 2.63 (dd, 1 H, *J* = 18.5, 7.3 Hz, $CH_AH_BCH_3$), 2.88 [dq, 1 H, *J* = 9.5, 7.0 Hz, $CH(CH_3)CHOTBS$], 4.64 (d, 1 H, *J* = 9.5 Hz, CHOTBS), 7.21–7.34 (m, 5 H, Ar*H*).
^{13}C NMR (62.9 MHz): δ = –5.4, –4.7, 7.3, 13.8, 17.9, 25.6, 37.9, 53.9, 78.4, 127.0, 127.6, 128.1, 142.8, 214.7.

(2*S*,4*R*,5*S*,6*E*)-2-Benzoyloxy-5-hydroxy-4,6-dimethyloct-6-en-3-one (28):
General procedure A was followed with (*S*)-**2** (540 mg, 2.62 mmol), *c*-Hex_2BCl (0.852 mL, 3.93 mmol), Me_2NEt (0.510 mL, 4.72 mmol) and freshly distilled *trans*-2-methylbut-2-enal (0.758 mL, 7.86 mmol). Standard workup followed by recrystallisation (Et_2O in hexane) afforded **28** as a crystalline white solid (659 mg, 86%); mp 92–94 °C; $[\alpha]_D$ +28.1 (*c* = 1.8, $CHCl_3$).
IR $CHCl_3$): ν = 3517 (br), 1718 (s), 1601 cm^{-1} (w).
^1H NMR (400 MHz): δ = 1.02 (d, 3 H, *J* = 7.0 Hz, C_{12}-CH_3), 1.56 (d, 3 H, *J* = 7.0 Hz, H-16),1.58 (d, 3 H, *J* = 1.0 Hz, C_{14}-CH_3), 1.60 [d, 3 H, *J* = 6.7 Hz, $CH(CH_3)OBz$], 2.00 (d, 1 H, *J* = 3.2 Hz, C_{13}-OH), 3.03 (dq, 1 H, *J* = 9.2, 7.0 Hz, H-12), 4.18 (dd, 1 H, *J* = 9.2, 3.2 Hz, H-13), 5.43 (q, 1 H, *J* = 7.0 Hz, H-15), 5.50 [q, 1 H, *J* = 6.7 Hz, $CH(CH_3)OBz$], 7.45 (t, 2 H, *J* = 7.5 Hz, Ar*H*), 7.55 (t, 1 H, *J* = 7.5 Hz, Ar*H*), 8.02 (d, 2 H, *J* = 7.5 Hz, Ar*H*).
^{13}C NMR (100.6 MHz): δ = 10.4, 13.1, 14.5, 15.6, 45.6, 75.1, 80.1, 124.1, 128.4, 129.6, 129.8, 133.3, 135.1, 166.1, 211.2.
HRMS (CI, NH_3): *m/z* $[M+NH_4]^+$ found 308.1862, $C_{17}H_{26}O_4N$ requires 308.1862.

LRMS (CI, NH_3): *m/z* = 308 ($[M+NH_4]^+$, 4), 290 (37), 207 (100), 105 (20).
Analysis: found C, 70.12; H, 7.63; $C_{17}H_{22}O_4$ requires C, 70.32; H, 7.64.

(2*S*,4*R*,5*S*,6*E*)-2-Benzoyloxy-5-*tert*-butyldimethylsilyloxy-4,6-dimethyloct-6-en-3-one:
General procedure B was followed with **28** (824 mg, 2.84 mmol), 2,6-lutidine (1.00 mL, 8.52 mmol) and TBSOTf (1.30 mL, 5.68 mmol). Standard workup and column chromatography (20% Et_2O in hexanes) afforded the title compound as a colourless oil (1.12 g, 98%); $[\alpha]_D$ –7.1 (*c* = 1.7, $CHCl_3$).
IR (film): ν = 1722 (s), 1602, 1585 cm^{-1} (w).
^1H NMR (250 MHz): δ = –0.07 (s, 3 H, $SiCH_3$), –0.05 (s, 3 H, $SiCH_3$), 0.80 [s, 9 H, $SiC(CH_3)_3$], 0.94 (d, 3 H, *J* = 7.1 Hz C_{12}-CH_3), 1.51–1.55 (m, 6 H, H-16 and C_{14}-CH_3), 1.59 [d, 3 H, *J* = 7.0 Hz, CH(C*H*$_3$)OBz], 2.99 (dq, 1 H, *J* = 9.7, 7.1 Hz, H-12), 4.20 (d, 1 H, *J* = 9.7 Hz, H-13), 5.42 [q, 2 H, *J* = 7.0 Hz, C*H*(CH_3)OBz and H-15, overlapping signals], 7.46 (dd, 2 H, *J* = 7.4, 6.7 Hz, Ar*H*), 7.59 (tt, 1 H, *J* = 6.7, 1.3 Hz, Ar*H*), 8.02 (dd, 2 H, *J* = 7.4, 1.3 Hz, Ar*H*).
^{13}C NMR (62.9 MHz): δ = –5.2, –4.9, 10.1, 12.9, 14.5, 15.2, 18.1, 25.8, 47.3, 75.3, 81.3, 123.7, 128.4, 129.7, 129.8, 133.1, 135.3, 165.7, 209.5.
HRMS (+FAB): *m/z* $[M+H]^+$ found 405.2462, $C_{23}H_{37}O_4Si$ requires 405.2461.
LRMS (+FAB): *m/z* = 405 ($[M+H]^+$, 40), 403 ($[M–H]^+$, 60), 347 (80), 199 (90), 179 (100).

(2*S*,3*R*,4*S*,5*S*,6*E*)-5-*tert*-Butyldimethylsilyloxy-4,6-dimethyloct-6-en-2,3-diol:
General procedure C was followed with the above protected aldol product (1.31 g, 3.24 mmol) and a 2 M THF solution of $LiBH_4$ (32.4 mL). Column chromatography (30% EtOAc in hexane) afforded the diol as a colourless oil (944 mg, 96%, 90% ds); $[\alpha]_D$ +28.5 (*c* = 2.6, $CHCl_3$).
IR (film): ν = 3432 (s br), 1670 cm^{-1} (w).
^1H NMR (400 MHz): δ = –0.01 (s, 3 H, $SiCH_3$), 0.09 (s, 3 H, $SiCH_3$), 0.63 (d, 3 H, *J* = 6.9 Hz, C_{12}-CH_3), 0.88 [s, 9H, $SiC(CH_3)_3$], 1.15 [d, 3 H, *J* = 6.4 Hz, CH(C*H*$_3$)OH], 1.54 (s, 3 H, C_{14}-CH_3), 1.58 (d, 3 H, *J* = 6.6 Hz, H-16), 1.63 (m, 1 H, H-12), 2.60 [d, 1 H, *J* = 9.7 Hz, CH(CH_3)O*H*], 3.64 (dd, 1 H, *J* = 8.4, 3.2 Hz, H-11), 3.77 [m, 1 H, C*H*(CH_3)OH], 3.88 (d, 1 H, *J* = 9.1 Hz, H-13), 4.44 (br s, 1 H, C_{11}–OH), 5.38 (q, 1 H, *J* = 6.6 Hz, H-15).
^{13}C NMR (100.6 MHz): δ = –5.2, –4.3, 10.8, 12.8, 13.0, 10.0, 16.1, 25.9, 38.6, 68.6, 78.1, 86.6, 123.8, 136.0.
HRMS (CI, NH_3): *m/z* $[M+H]^+$ found 303.2355, $C_{16}H_{35}O_3Si$ requires 303.2355.
LRMS (CI, NH_3): *m/z* = 303 ($[M+H]^+$, 14), 287 (42), 273 (20), 188 (33), 171 (100), 153 (42).

(2*R*,3*S*,4*E*)-3-*tert*-Butyldimethylsilyloxy-2,6-dimethylhex-4-enal (24):[32]
General procedure D was followed with the above diol (360 mg, 1.19 mmol) and $NaIO_4$ (1.53 g, 7.15 mmol). Rapid column chromatography (20% Et_2O in hexane) afforded aldehyde **24** as a colourless oil (283 mg, 93%); $[\alpha]_D$ +30.6 (*c* = 1.7, $CHCl_3$).
IR (film): ν = 1729 (s), 1670 cm^{-1} (w).
^1H NMR (400 MHz): δ = –0.06 (s, 3 H, $SiCH_3$), 0.00 (s, 3 H, $SiCH_3$), 0.82–0.84 [m, 12 H, $SiC(CH_3)_3$ and C_{12}-CH_3], 1.55 (s, 3 H, C_{14}-CH_3), 1.60 (d, 3 H, *J* = 6.7 Hz, H-16), 2.54 (dqd, 1 H, *J* = 8.8, 7.2, 2.8 Hz, H-12), 4.04 (d, 1 H, *J* = 8.8 Hz, H-13), 5.43 (q, 1 H, *J* = 6.7 Hz, H-15), 9.73 (d, 1 H, *J* = 2.8 Hz, H-11).
^{13}C NMR (100.6 MHz): δ = –5.2, –4.4, 10.7, 11.1, 13.1, 16.2, 25.9, 50.4, 80.7, 123.3, 135.5, 205.7.
HRMS (CI, NH_3): *m/z* $[M+H]^+$ found 257.1937, $C_{14}H_{29}O_2Si$ requires 257.1937.
LRMS (CI, NH_3): *m/z* = 257 ($[M+H]^+$,12), 199 (66), 142 (100), 125 (100).

Methyl (4*S*,5*S*,2*E*,6*E*)-5-*tert*-Butyldimethylsilyloxy-4,6-dimethylocta-2,6-dienoate (29):
A mixture of $(MeO)_2P(O)CH_2CO_2Me$ (0.358 mL, 2.21 mmol) and $Ba(OH)_2$•$8H_2O$ (662 mg, 2.10 mmol, heated to 120 °C under vacuum for 2 h prior to use) in THF (5 mL) was stirred at r.t. for 20 min. A solution of the aldehyde **24** (283 mg, 1.11 mmol) in THF/H_2O (5 mL, 40:1) was added and the pale yellow suspension stirred at r.t. for 16 h. The reaction mixture was diluted with CH_2Cl_2 (150 mL), washed with satd aq $NaHCO_3$ solution (70 mL) and brine (70 mL). The organic layer was dried ($MgSO_4$), concentrated *in vacuo* and purified by column chromatography (5% Et_2O in hexane) to give ester **29** (287 mg, 83%); $[\alpha]_D$ +16.2 (*c* = 2.6, $CHCl_3$).
IR (film): ν = 1728 (s), 1659 cm^{-1} (m).
^1H NMR (400 MHz): δ = –0.09 (s, 3 H, $SiCH_3$) , –0.03 (s, 3 H, $SiCH_3$), 0.85–0.87 [m, 12 H, C_{12}-CH_3 and $SiC(CH_3)_3$], 1.52 (s, 3 H, C_{14}-CH_3), 1.58 (d, 3 H, *J* = 6.6 Hz, H-16), 2.42 (m, 1 H, H-12), 3.66 (d, 1 H, *J* = 8.2 Hz, H-13), 3.70 (s, 3 H,OCH_3), 5.34 (q, 1 H, *J* = 6.6 Hz, H-15), 5.76 (dd, 1 H, *J* = 15.8, 1.0 Hz, H-10), 7.00 (dd, 1 H, *J* = 15.8, 7.8 Hz, H-11).
^{13}C NMR (100.6 MHz): δ = –5.2, –4.7, 10.6, 12.9, 15.8, 18.1, 25.7, 41.1, 51.3, 82.7, 120.2, 122.2, 136.3, 153.3, 167.2.
HRMS (CI, NH_3): *m/z* $[M+H]^+$ found 313.2199, $C_{17}H_{33}O_3Si^+$ requires 313.2199.
LRMS (CI, NH_3): *m/z* = 313 ($[M+H]^+$, 3), 255 (8), 198 (100), 181 (95).

(4*S*,5*S*,2*E*,6*E*)-5-*tert*-Butyldimethylsilyloxy-4,6-dimethylocta-2,6-dienol:
To a cooled (–78 °C) solution of **29** (322 mg, 1.03 mmol) in Et_2O (15 mL) was added a 1 M solution of DIBAL in hexanes (3.09 mL, 3.09 mmol). The reaction mixture was warmed to –40 °C, the stirring continued for 2 h and then the mixture was quenched with H_2O (25 mL) and extracted with Et_2O (4 × 25 mL). The combined organic extracts were dried ($MgSO_4$), concentrated *in vacuo* and the resulting oil was purified by column chromatography (40% Et_2O in hexane) to give the alcohol as a colourless oil (286 mg, 98%); $[\alpha]_D$ +7.6 (*c* = 1.5, $CHCl_3$).
IR (film): ν = 3321 (br s), 1669 cm^{-1} (w).
^1H NMR (400 MHz): δ = –0.08 (s, 3 H, $SiCH_3$), –0.03 (s, 3 H, $SiCH_3$), 0.80 (d, 3 H, *J* = 6.8 Hz, C_{12}-CH_3), 0.84 [s, 9 H, $SiC(CH_3)_3$], 1.52 (s, 3 H, C_{14}-CH_3), 1.57 (d, 3 H, *J* = 6.6 Hz, H-16), 2.25 (m, 1 H, H-12), 3.60 (d, 1 H, *J* = 8.1 Hz, H-13), 4.08 (d, 2 H, *J* = 5.4 Hz, H-9), 5.31 (q, 1 H, *J* = 6.6 Hz, H-15), 5.60 (dt, 1 H, *J* = 15.8, 5.4 Hz, H-10), 5.68 (dd, 1 H, *J* = 15.8, 7.2 Hz, H-11).
^{13}C NMR (100.6 MHz): δ = –4.79, –4.38, 11.1, 13.1, 17.0, 18.3, 26.1, 41.0, 64.4, 83.5, 121.7, 128.5, 137.29, 137.30.
HRMS (+FAB): *m/z* $[M–H]^+$ found 283.2199, $C_{16}H_{31}O_2Si^+$ requires 283.2093.
LRMS (+FAB): *m/z* = 283 ($[M–H]^+$, 70), 267 (50), 227 (35), 199 (100), 159 (60).

(4*S*,5*S*,2*E*,6*E*)-5-*tert*-Butyldimethylsilyloxy-4,6-dimethylocta-2,6-dienal (23):
To a solution of Dess–Martin periodinane (592 mg, 1.38 mmol) in CH_2Cl_2 (5 mL) at r.t. was added the above alcohol (262 mg, 0.923 mmol) in CH_2Cl_2 (10 mL) *via* cannula. The mixture was stirred for 1 h before pouring into a 1:1 mixture of satd aq $NaHCO_3$/$Na_2S_2O_3$ solution (15 mL). The separated aqueous layer was extracted with Et_2O (4 × 30 mL) and the combined organic extracts dried ($MgSO_4$) and concentrated *in vacuo*. The crude mixture was purified by column chromatography (30% Et_2O in hexane) to afford aldehyde **23** as a colourless oil (246 mg, 95%); $[\alpha]_D$ –19.6 (*c* = 2.5, $CHCl_3$).
IR (film): ν = 1695 (s), 1636 cm^{-1} (w).
^1H NMR (400 MHz): δ = –0.07 (s, 3 H, $SiCH_3$), –0.02 (s, 3 H, $SiCH_3$), 0.85 [s, 9 H, $SiC(CH_3)_3$], 0.91 (d, 3 H, *J* = 6.8 Hz, C_{12}-CH_3), 1.54 (s, 3 H, C_{14}-CH_3), 1.58 (d, 3 H, *J* = 6.7 Hz, H-16), 2.57 (m, 1 H, H-12), 3.73 (d, 1 H, *J* = 7.9 Hz, H-13), 5.38 (q, 1 H, *J* = 6.7 Hz, H-15), 6.09 (ddd, 1 H, *J* = 15.7, 7.9, 1.1 Hz, H-10), 6.92 (dd, 1 H, *J* = 15.7, 7.4 Hz, H-11), 9.48 (d, 1 H, *J* = 7.9 Hz, H-9).
^{13}C NMR (100.6 MHz): δ = –5.2, –4.6, 10.8, 12.9, 18.1, 25.7, 41.5, 82.6, 122.6, 132.3, 136.1, 162.6, 194.2.
HRMS (+FAB): *m/z* $[M]^+$ found 282.2025, $C_{16}H_{30}O_2Si$ requires 282.2015.
LRMS (+FAB): *m/z* = 282 ($[M]^+$, 40), 225 (55), 199 (100).

(2*S*,4*R*,5*R*,8*S*,9*S*,6*E*,10*E*)-2-Benzoyloxy-9-*tert*-butyldimethylsilyloxy-5-hydroxy-4,8,10-trimethyldodeca-6,10-dien-3-one (30):
General procedure A was followed with ketone (*S*)-**2** (140 mg, 0.680 mmol), *c*-Hex_2BCl (221 μL, 1.02 mmol), Me_2NEt (132 μL, 1.22 mmol) and aldehyde **23** (101 mg, 0.358 mmol). Standard workup and column chromatography (1% Et_2O in CH_2Cl_2) afforded **30** as a colourless oil (166 mg, 95%); $[\alpha]_D$ +4.2 (*c* = 0.9, $CHCl_3$).
IR (film): ν = 3524 (br m), 1720 (s), 1602, 1558 cm^{-1} (w).
^1H NMR (400 MHz): δ = –0.09 (s, 3 H, $SiCH_3$), –0.04 (s, 3 H, $SiCH_3$), 0.80 (d, 3 H, *J* = 6.9 Hz, C_{12}-CH_3), 0.83 [s, 9 H, $SiC(CH_3)_3$], 1.12 (d, 3 H, *J* = 7.1 Hz, C_8-CH_3), 1.50 (s, 3 H, C_{14}-CH_3), 1.55 [d, 3 H, *J* = 7.0 Hz, CH(C*H*$_3$)OBz], 1.56 (d, 3 H, *J* = 6.6 Hz, H-16), 1.97 (d, 1 H, *J* = 3.1 Hz, C_9-OH), 2.27 (m, 1 H, H-12), 2.87 (dq, 1 H, *J* = 8.4, 7.1 Hz, H-8), 3.61 (d, 1 H, *J* = 7.7 Hz, H-13), 4.20 (m, 1 H, H-9), 5.31 (q, 1 H, *J* = 6.6 Hz, H-15), 5.36 (dd, 1 H, *J* = 15.5, 7.9 Hz, H-10), 5.42 [q, 1 H, *J* = 7.0 Hz, C*H*(CH$_3$)OBz], 5.76 (dd, 1 H, *J* = 15.5, 7.1 Hz, H-11), 7.43 (t, 2 H, *J* = 7.4 Hz, Ar*H*), 7.56 (t, 1 H, *J* = 7.4 Hz, Ar*H*), 8.02 (d, 2 H, *J* = 7.4 Hz, Ar*H*).
^{13}C NMR (100.6 MHz): δ = –5.1, –4.7, 11.0, 12.8, 14.5, 15.5, 16.7, 18.2, 25.8, 40.6, 48.2, 75.0, 75.5, 83.0, 121.4, 128.4, 129.1, 129.4, 129.8, 133.2, 136.6, 138.3, 165.3, 210.9.
HRMS (+FAB): *m*/*z* $[M+H]^+$ found 489.3006, $C_{28}H_{45}O_5Si$ requires 489.3036.
LRMS (+FAB): *m*/*z* = 489 ($[M+H]^+$, 20), 487 ($[M–H]^+$, 50), 471 (80), 357 (80), 199 (100).

(2*S*,4*R*,5*R*,8*S*,9*S*,6*E*,10*E*)-2-Benzoyloxy-5,9-di-*tert*-butyldimethylsilyloxy-4,8,10-trimethyldodeca-6,10-dien-3-one:
General procedure B was followed with **30** (166 mg, 0.340 mmol), 2,6-lutidine (100 μL, 0.848 mmol) and TBSOTf (156 μL, 0.679 mmol). Standard workup and column chromatography (7% EtOAc in hexane) afforded the silyl ether as a colourless oil (203 mg, 99%); $[\alpha]_D$ –1.2 (*c* = 1.7, $CHCl_3$).
IR (film): ν = 1723 (s), 1602, 1585 cm^{-1} (w).
^1H NMR (100.6 MHz): δ = –0.07 (s, 3 H, $SiCH_3$), –0.03 (s, 3 H, $SiCH_3$), –0.02 (s, 3 H, $SiCH_3$), –0.01 (s, 3 H, $SiCH_3$), 0.81 [s, 9 H, $SiC(CH_3)_3$], 0.87–0.90 [m, 12 H, C_{12}-CH_3 and $SiC(CH_3)_3$], 1.01 (d, 3 H, *J* = 7.1 Hz, C_8-CH_3), 1.49 (s, 3 H, C_{14}-CH_3), 1.53 [d, 3 H, *J* = 6.9 Hz, CH(C*H*$_3$)OBz], 1.57 (d, 3 H, *J* = 6.7 Hz, H-16), 2.27 (m, 1 H, H-12), 2.85 (dq, 1 H, *J* = 8.2, 7.1 Hz H-8), 3.69 (d, 1 H, *J* = 6.6 Hz, H-13), 4.23 (t, 1 H, *J* = 8.2 Hz, H-9), 5.20 (q, 1 H, *J* = 6.7 Hz, H-15), 5.20 (dd, 1 H, *J* = 15.5, 8.2 Hz, H-10), 5.41 [q, 1 H, *J* = 6.9 Hz, C*H*(CH$_3$)OBz], 5.67 (dd, 1 H, *J* = 15.7, 6.6 Hz, H-11), 7.44 (dd, 2 H, *J* = 7.8, 7.4 Hz, Ar*H*), 7.56 (tt, 1 H, *J* = 7.4, 1.1 Hz, Ar*H*), 8.07 (dd, 2 H, *J* = 7.8, 1.1 Hz, Ar*H*).
^{13}C NMR (100.6 MHz):δ = –5.0, –4.7, –4.5, –3.9, 11.8, 12.8, 14.5, 15.1, 17.1, 18.0, 18.3, 25.9, 26.0, 40.5, 49.0, 75.4, 76.9, 82.2, 120.8, 128.3, 128.4, 129.8, 130.3, 133.2, 136.3, 136.7, 165.8, 209.5.
HRMS (+FAB): *m*/*z* $[M–H]^+$ found 601.3723, $C_{34}H_{57}O_5Si_2$ requires 601.3744.
LRMS (+FAB): *m*/*z* = 601 ($[M–H]^+$, 40), 546 (35), 341 (75), 295 (90), 199 (100), 179 (80).

(2*S*,3*R*,4*S*,5*R*,8*S*,9*S*,6*E*,10*E*)-5,9-Di-*tert*-butyldimethylsilyloxy-4,8,10-trimethyldodeca-6,10-diene-2,3-diol:
General procedure C was followed with the above protected aldol product (219 mg, 0.364 mmol) and a 2 M THF solution of $LiBH_4$ (3.64 mL, 7.27 mmol). Column chromatography (30% EtOAc in hexane) afforded the diol as a colourless oil (166 mg, 91%, 90% ds); $[\alpha]_D$ –24 (*c* = 1.0, $CHCl_3$).
IR (film): ν = 3422 (br s), 1669 cm^{-1} (w).
^1H NMR (400 MHz): δ = –0.07 (s, 3 H, $SiCH_3$), –0.02 (s, 3 H, $SiCH_3$), 0.03 (s, 3 H, $SiCH_3$), 0.08 (s, 3 H, $SiCH_3$), 0.74 (d, 3 H, *J* = 6.9 Hz, C_8-CH_3), 0.87 [s, 9 H, $SiC(CH_3)_3$], 0.88–0.90 [m, 12 H, C_{12}-CH_3 and $SiC(CH_3)_3$], 1.15 [d, 3 H, *J* = 6.3 Hz, CH(C*H*$_3$)OH], 1.52 (s, 3 H, C_{14}-CH_3), 1.56 (d, 3 H, *J* = 6.7 Hz, H-16), 2.32–2.33 (m, 2 H, H-8,12), 3.60 (dd, 1 H, *J*= 8.1, 3.6 Hz, H-7), 3.67 (br s, 1 H, OH), 3.68 (d, 1 H, *J* = 4.3 Hz, H-13), 3.78 [qd, 1 H, *J* = 6.3, 3.6 Hz, C*H*(CH$_3$)OH], 3.88 (br, s, 1 H, OH), 4.06 (t, 1 H, *J* = 7.6 Hz, H-9), 5.34–5.35 (m, 2 H, H-10,15), 5.78 (dd, 1 H,*J* = 15.9, 5.9 Hz, H-11).
^{13}C NMR (100.6 MHz): δ = –5.1, –4.8, –4.6, –3.6, 11.8, 12.6, 12.9, 16.2, 16.6, 18.2, 18.3, 25.8, 39.8, 41.9, 68.3, 77.4, 80.0, 82.4, 120.9, 130.4, 135.7, 136.8.
HRMS (+FAB): *m*/*z* $[M–H]^+$ found 499.3667, $C_{27}H_{55}O_4Si_2$ requires 499.3639.
LRMS (+FAB): *m*/*z* = 523 ($[M+Na]^+$, 30), 499 ($[M–H]^+$, 55), 369 (95), 199 (100).

(2*R*,3*R*,6*S*,7*S*,4*E*,8*E*)-3,7-Di-*tert*-butyldimethylsilyloxy-2,6,8-trimethyldeca-4,8-dienal (26):
General procedure D was followed with the above diol (80.0 mg, 0.160 mmol) and $NaIO_4$ (1.03 g, 4.80 mmol). Column chromatography (20% Et_2O in hexane) afforded **26** as a colourless oil (68 mg, 94%); $[\alpha]_D$ –33.6 (*c* = 2.2, $CHCl_3$).
IR (film): ν = 1729 (s), 1668 cm^{-1} (w).
^1H NMR (400 MHz): δ = –0.07 (s, 3 H, $SiCH_3$), –0.02 (s, 3 H, $SiCH_3$), –0.01 (s, 3 H, $SiCH_3$), 0.02 (s, 3 H, $SiCH_3$), 0.85 [s, 9 H, $SiC(CH_3)_3$], 0.87 [s, 9 H, $SiC(CH_3)_3$], 0.87 (d, 3 H, *J* = 6.6 Hz, C_{12}-CH_3), 0.97 (d, 3 H, *J* = 7.0 Hz, C_8-CH_3), 1.52 (s, 3 H, C_{14}-CH_3), 1.56 (d, 3 H, *J* = 7.1 Hz, H-16), 2.32 (m, 1 H, H-12), 2.42 (qn d, 1 H, *J* = 7.0, 2.6 Hz, H-8), 3.68 (d, 1 H, *J* = 6.4 Hz, H-13), 4.21 (t, 1 H, *J* = 7.0 Hz, H-9) 5.31–5.37, (m, 2 H, H-10,15), 5.81 (dd, 1 H, *J* = 15.7, 6.6 Hz, H-11), 9.72 (d, 1 H, *J* = 2.6 Hz, H-7).
^{13}C NMR (100.6 MHz): δ = –5.1, –5.0, –4.6, –3.8, 10.8, 11.8, 12.9, 17.1, 18.0, 18.2, 25.8, 25.9, 40.1, 52.9, 75.7, 82.4, 120.8, 129.6, 135.8, 136.8, 205.0.
HRMS (+FAB): *m*/*z* $[M–H]^+$ found 453.3189, $C_{25}H_{49}O_3Si_2$ requires 453.3220.
LRMS (+FAB): *m*/*z* = 453 ($[M–H]^+$, 90), 395 (65), 381 (50), 341 (75), 301 (60), 199 (100).

(2'*S*,3'*S*,4'*R*,7'*S*,8'*S*,5'*E*,9'*E*)-4-Methoxy-6-(4',8'-di-*tert*-butyldimethylsilyloxy-3',7',9'-trimethylundeca-5',9'-dien-2'-ol)-2*H*-pyran-2-one (31):
To a cooled (–100 °C) solution of **27** (167 mg, 1.19 mmol) in Et_2O (6 mL), was added a 0.5 M solution of potassium bis(trimethylsilyl)amide (KHMDS) in toluene (2.08 mL, 1.04 mmol) and the stirring was continued at –100 °C for 1 h. A cooled (–78 °C) solution of **26** (63.0 mg, 0.139 mmol) in Et_2O (6 mL) was added *via* cannula, and stirring was continued for a further 2 h. The reaction was quenched by the addition of MeOH (5 mL) at –100 °C and allowed to warm to r.t., whereupon the mixture was diluted with H_2O (10 mL) and extracted with CH_2Cl_2 (3 × 20 mL). The combined organic extracts were dried ($MgSO_4$) and concentrated *in vacuo*. Column chromatography (40% EtOAc in hexane) yielded the protected toxin (67.4 mg, 82%) as a 2.5:1 ratio of epimers at C_7. HPLC separation (40% EtOAc in hexane) gave **31** (39.2 mg, 48%) and 7-*epi*-**31** (16 mg, 19%).

31: $[\alpha]_D$ –46.0 (*c* = 2.0, $CHCl_3$).
IR (film): ν = 3432 (br s), 1701 (s), 1648 cm^{-1} (m).
^1H NMR (400 MHz): δ = –0.08 (s, 3 H, $SiCH_3$)., –0.03 (s, 3 H, $SiCH_3$), 0.01 (s, 3 H, $SiCH_3$), 0.07 (s, 3 H, $SiCH_3$), 0.80 (d, 3 H, *J* = 6.9 Hz, C_8-CH_3), 0.85–0.87 [m, 21 H, 2 x $SiC(CH_3)_3$ and C_{12}-CH_3], 1.51 (s, 3 H, C_{14}-CH_3), 1.55 (d, 3 H, *J* = 6.6 Hz, H-16), 1.64 (m, 1 H, H-8), 2.33 (m, 1 H, H-12), 2.45 (dd, 1 H, *J* = 14.8, 9.4 Hz, C_6-H_AH_B), 2.74 (dd, 1 H, *J* = 14.8, 2.2 Hz, C_6-H_AH_B), 3.66 (d, 1 H, *J* = 6.6 Hz, H-13), 3.77 (s, 3 H, OCH_3), 3.96–4.02 (m, 3 H, H-7 and C_7-OH and H-9), 5.31 (dd, 1 H, *J* = 15.9, 7.9 Hz, H-10), 5.35 (q, 1 H, *J* = 6.6 Hz, H-15), 5.40 (d, 1 H, *J* = 2.1 Hz, H-2), 5.80 (dd, 1 H, *J* = 15.9, 5.9 Hz, H-11), 5.95 (d, 1 H, *J* = 2.1 Hz, H-4).
^{13}C NMR (100.6 MHz): δ = –5.1, –4.7, –4.6, –3.5, 11.7, 12.9, 13.5, 16.5, 18.0, 18.2, 25.9, 25.9, 39.2, 39.7, 44.5, 55.7, 72.3, 80.3, 82.5, 87.8, 101.7, 121.0, 130.5, 135.9, 136.8, 136.3, 165.1, 171.3.
HRMS (+FAB): *m*/*z* $[M–H]^+$ found 593.3715, $C_{32}H_{57}O_6Si_2$ requires 593.3694.
LRMS (+FAB): *m*/*z* = 593 ($[M–H]^+$, 5), 537 (50), 379 (60), 331 (80), 199 (100).

(3'*R*,4'*R*,7'*S*,8'*S*,5'*E*,9'*E*)-4-Methoxy-6-(4',8'-di-*tert*-butyldimethylsilyloxy-3',7',9'-trimethylundeca-5',9'-dien-2'-one)-2*H*-pyran-2-one (32):

To a solution of Dess–Martin periodinane (179 mg, 0.418 mmol) in CH_2Cl_2 (3 mL) at r.t. was added a mixture of alcohols **31** and 7-*epi*-**31** (124 mg, 0.209 mmol) in CH_2Cl_2 (2 mL) *via* cannula. The reaction mixture was stirred for 2 h, before pouring into a 1:1 mixture of satd aq $NaHCO_3/Na_2S_2O_3$ solution (8 mL). The separated aqueous layer was extracted with CH_2Cl_2 (3 × 25 mL) and the combined organic extracts were dried ($MgSO_4$) and concentrated *in vacuo*. Column chromatography (40% EtOAc in hexane) afforded ketone **32** as a colourless oil (112 mg, 91%); $[\alpha]_D$ –54.2 (*c* = 1.5, $CHCl_3$).
IR (film): ν = 1729 (s), 1654 cm^{-1} (m).
^1H NMR (400 MHz): δ = –0.08 (s, 3 H, $SiCH_3$), –0.04 (s, 3 H, $SiCH_3$), –0.03 (3s, H, $SiCH_3$), –0.02 (s, 3 H, $SiCH_3$), 0.82 [s, 9 H, $SiC(CH_3)_3$], 0.87 [s, 9 H, $SiC(CH_3)_3$], 0.87 (d, 3 H, *J* = 6.7 Hz, C_{12}-CH_3), 0.92 (d, 3 H, *J* = 7.0 Hz, C_8-CH_3), 1.53 (s, 3 H, C_{14}-CH_3), 1.55 (d, 3 H, *J* = 6.7 Hz, H-16), 2.30 (sextet, 1 H, *J* = 6.7 Hz, H-12), 2.71 (dq, 1 H, *J* = 8.1, 7.0 Hz, H-8), 3.60 (d, 1 H, *J* = 17.1 Hz, C_6-H_AH_B), 3.63 (d, 1 H, *J* = 17.1 Hz, C_6-H_AH_B), 3.66 (d, 1 H, *J* = 6.7 Hz, H-13), 3.78 (s, 3 H, CH_3O), 4.10 (t, 1 H, *J* = 8.1 Hz, H-9), 5.21 (ddd, 1 H, *J* = 15.8, 8.1, 1.2 Hz, H-10), 5.35 (q, 1 H, *J* = 6.7 Hz, H-15), 5.43 (d, 1 H, *J* = 2.2 Hz, H-2), 5.80 (dd, 1 H, *J* = 15.8, 6.7 Hz, H-11), 5.91 (d, 1 H, *J* = 2.2 Hz, H-4).
^{13}C NMR (100.6 MHz): δ = –5.1, –5.0, –4.6, –3.9, 11.7, 12.9, 13.6, 16.7, 18.0, 18.2, 25.8, 25.9, 39.2, 48.5, 52.6, 55.8, 77.7, 82.3, 88.4, 102.9, 120.9, 129.6, 136.5, 136.7, 158.0, 164.3, 170.8, 206.9.

(3'*R*,4'*R*,7'*S*,8'*S*,5'*E*,9'*E*)-4-Methoxy-6-(4',8'-dihydroxy-3',7',9'-trimethylundeca-5',9'-dien-2'-one)-2*H*-pyran-2-one (33):

To a cooled (0 °C) solution of **32** (14.1 mg, 0.0238 mmol) in THF (2 mL) was added HF•pyridine (0.4 mL). The stirring was continued for 1 h at 0 °C, followed by 1 h at r.t. H_2O (5 mL) was added and the mixture extracted with Et_2O (4 × 8 mL). The combined organic extracts were washed with satd aq $NaHCO_3$ solution (2 × 5 mL), dried (Na_2SO_4) and concentrated *in vacuo*. Column chromatography (EtOAc) yielded ketone **33** as a crystalline white solid (6.4 mg, 74%); mp 144–146 °C; $[\alpha]_D$ –35.7 (*c* = 0.3, $CHCl_3$).
IR ($CHCl_3$): ν = 3378 (br s), 1716, 1681 (s), 1643 cm^{-1} (m).
^1H NMR (400 MHz): δ = 0.78 (d, 3 H, *J* = 7.0 Hz, C_{12}-CH_3), 1.00 (d, 3 H, *J* = 7.1 Hz, C_8-CH_3), 1.56 (s, 3 H, C_{14}-CH_3), 1.59 (d, 3 H, *J* = 6.8 Hz, H-16), 2.29 (dqn, 1 H, *J* = 8.3, 7.0 Hz, H-12), 2.71 (qn, 1 H, *J* = 7.1 Hz, H-8), 3.60 (d, 1 H, *J* = 7.0 Hz, H-11), 3.65 (d, 1 H, *J* = 17.2 Hz, C_6-H_AH_B), 3.69 (d, 1 H, *J* = 17.2 Hz, C_6-H_AH_B), 3.78 (s, 3 H, CH_3O), 4.10 (dd, 1 H, *J* = 7.7, 7.1 Hz, H-9), 5.47–5.42 (m, 3 H, H-2,10,15), 5.55 (dd, 1 H, *J* = 15.3, 8.3 Hz, H-11), 5.95 (d, 1 H, *J* = 2.3 Hz, H-4).
^{13}C NMR (100.6 MHz): δ = 10.4., 13.1, 13.5, 17.3, 40.5, 47.4, 51.5, 55.9, 75.7, 82.2, 88.3, 103.2, 123.4, 131.5, 136.0, 137.7, 158.1, 164.6, 171.0, 207.4.
HRMS (+FAB): *m/z* $[M+H]^+$ found 365.1986, $C_{20}H_{29}O_6$ requires 365.1964.
LRMS (+FAB): *m/z* = 387 ($[M+Na]^+$, 47), 365 ($[M+H]^+$, 30), 347 (75), 329 (100), 154 (80).

(–)-ACRL Toxin IIIB (7):

To a cooled (–78 °C) solution of **33** (6.8 mg, 0.0187 mmol) in THF (1 mL) and MeOH (0.2 mL) was added a 2.9 M MeOH solution of Bu_2BOMe (26 μL, 0.0747 mmol), and the stirring was continued for 20 min to allow complex formation. A 2 M THF solution of $LiBH_4$ (37 μL, 0.0747 mmol) was added and the reaction mixture stirred at –78 °C for 2 h after which time TLC analysis showed consumption of starting material. The reaction mixture was quenched by addition of pH 7 buffer (1 mL), MeOH (1 mL) and then 30% H_2O_2 (0.5 mL) was added and the resulting mixture stirred at r.t. for 1 h, whereupon it was partitioned between H_2O (5 mL) and CH_2Cl_2 (3 × 5 mL). The combined organic extracts were dried (Na_2SO_4), concentrated *in vacuo* and column chromatography (10% MeOH in $CHCl_3$) afforded (–)-ACRL toxin IIIB **(7)** and 7-*epi*-**7** as an 89:11 mixture (6.4 mg, 94%). Recrystallisation (EtOAc) gave pure **7** (5.6 mg, 82%); mp 153–155 °C (Lit.[23a] 152 °C); $[\alpha]_D$ –47.0 (*c* = 0.6, $CHCl_3$).
IR ($CHCl_3$): ν = 3410 (br s), 1699 (s), 1640 cm^{-1} (m).
^1H NMR (400 MHz): δ = 0.84 (d, 3 H, *J* = 6.8 Hz, C_8-CH_3), 0.85 (d, 3 H, *J* = 6.9 Hz, C_{12}-CH_3), 1.58 (s, 3 H, C_{14}-CH_3), 1.63 (d, 3 H, *J* = 6.9 Hz, H-16) 1.71 (m, 1 H, H-8), 2.32 (m, 1 H, H-12), 2.47 (dd, 1 H, *J* = 14.8, 9.4 Hz, C_6-H_AH_B), 2.80 (dd, 1 H, *J* = 14.8, 2.2 Hz, C_6-H_AH_B), 3.65 (d, 1 H, *J* = 6.9 Hz, H-13), 3.78 (s, 3 H, CH_3O), 4.07 (m, 1 H, H-7), 4.09 (m, 1 H, H-9), 5.41 (d, 1 H, *J* = 2.1 Hz, H-2), 5.46 (q, 1 H, *J* = 7.2 Hz, H-15), 5.57 (m, 1 H, H-10), 5.61 (m, 1 H, H-11), 5.94 (d, 1 H, *J* = 2.1 Hz, H-4).
^{13}C NMR (100.6 MHz): δ = 10.5, 13.1, 13.4, 17.2, 39.4, 40.4, 43.4, 55.8, 72.7, 77.9, 82.3, 87.8, 101.9, 123.3, 132.8, 135.9, 136.5, 163.2, 165.2, 171.4.
HRMS (+FAB): *m/z* $[M+H]^+$ found 367.2121, $C_{20}H_{31}O_6$ requires 367.2121.
LRMS (+FAB): *m/z* = 367 ($[M+H]^+$, 70), 331 (90), 265 (50), 169 (100).

7-*epi*-ACRL Toxin IIIB:

mp 162–165 °C; $[\alpha]_D$ +66.7 (*c* = 0.3, $CHCl_3$).
IR ($CHCl_3$): ν = 3408 (br s), 1698 (s), 1644 cm^{-1} (m).
^1H NMR (250 MHz): δ = 0.82 (d, 3 H, *J* = 6.8 Hz, C_{12}-CH_3), 0.97 (d, 3 H, *J* = 7.1 Hz, C_8-CH_3), 1.60 (s, 3 H, C_{14}-CH_3), 1.62 (d, 3 H, *J* = 6.8 Hz, H-16), 1.68 (m, 1 H, H-8), 2.34 (m, 1 H, H-12), 2.51 (dd, 1 H, *J* = 14.4, 3.1 Hz, C_6-H_AH_B), 2.62 (dd, 1 H, *J* = 14.4, 9.6 Hz, C_6-H_AH_B), 3.62 (d, 1 H, *J* = 9.1 Hz, H-13), 3.78 (s, 3 H, CH_3O), 4.10 (m, 1 H, H-7), 4.41–4.32 (m, 1 H, H-9), 5.41 (d, 1 H, *J* = 2.2 Hz, H-2), 5.62–5.44 (m, 3 H, H-10,11,15), 5.92 (d, 1 H, *J* = 2.2 Hz, H-4).
HRMS (+FAB): *m/z* $[MH–H_2O]^+$ found 349.2024, $C_{20}H_{29}O_5$ requires 349.2015.
LRMS (+FAB): *m/z* = 367 ($[M+H]^+$, 18), 349 ($[MH–H_2O]^+$, 20), 331 (70), 199 (100).

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