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The dienolate aldol reaction of (*E*)-*N*-crotonoyl C(4)-isopropyl SuperQuat: asymmetric synthesis of α-vinyl-β-hydroxycarboxylic acid derivatives and conversion to α-ethylidene-β-hydroxyesters (β-substituted Baylis–Hillman products)

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ABSTRACT

The synthesis of α-vinyl-β-hydroxyesters and α-ethylidene-β-hydroxyesters (β-substituted Baylis–Hillman products) via the dienolate aldol reaction of (*E*)-*N*-crotonoyl C(4)-isopropyl SuperQuat is described. High levels of *syn*-diastereoselectivity (up to >98% de) are observed for the dienolate aldol reaction with boron enolates, generated either directly with Bu_2BOTf or by transmetalation of the potassium enolate with *B*-bromocatecholborane. Cleavage of the resultant *syn*-aldol products from the auxiliary gives α-vinyl-β-hydroxyesters in >98% de and >98% ee. Subsequent isomerisation of the double bond into conjugation provides α-ethylidene-β-hydroxyesters (β-substituted Baylis–Hillman products) in high diastereo- and enantiopurity (≥91:9 [(*E*):(*Z*)] and >98% ee).

1. Introduction

The Morita–Baylis–Hillman reaction has been used extensively in organic synthesis as a key carbon–carbon bond forming reaction.[1] This reaction employs either tertiary amines[2] or phosphines[3] to catalyse the condensation of an aldehyde and an acrylate ester to give α-methylene-β-hydroxy-esters. These compounds have proven to be useful synthetic intermediates, often used to provide practical synthons in stereoselective synthesis.[4] As this efficient reaction produces polyfunctional chiral molecules in a single step, various endeavours seeking to develop asymmetric versions of this reaction to afford allylic alcohols in enantiomerically enriched form have been reported: for example, chiral acrylates,[5] chiral aldehydes,[6] chiral amines[7] and chiral phosphines[8] have been used. Although efficient, these approaches are restricted to the use of acrylate components, generating α-methylene-β-hydroxy compounds. Methods for the preparation of α-alkylidene-β-hydroxycarboxylic acid derivatives (β-substituted Baylis–Hillman products) have been reported, although examples are limited. Racemic β-substituted Baylis–Hillman products may be prepared from α-silyl-alkenoates but with low levels of (*E*):(*Z*) stereocontrol,[9] whilst hydroalumination of β-propiolates in the presence of HMPA and subsequent reaction with an aldehyde gives the desired products with high (*Z*)-stereocontrol.[10] Enantiomerically enriched β-substituted Baylis–Hillman products may be prepared by α-functionalisation of chiral α,β-unsaturated sulfoxides with aldehydes,[11] and through the reaction of silyl allenolates with aldehydes catalysed by a chiral oxazaborolidine,[12] although the synthetic generality of these procedures has yet to be demonstrated. In order to address this structural limitation, we became interested in the development of methodology that is capable of the stereoselective synthesis of enantiomerically pure β-substituted Baylis–Hillman products, and have recently reported an asymmetric protocol[13] in which the highly diastereoselective conjugate addition of a homochiral lithium amide[14] to an α,β-unsaturated ester was used as the key step for the introduction of stereochemistry. For example, addition of lithium (*R*)-*N*-methyl-*N*-(α-methylbenzyl)amide **2** to *tert*-butyl crotonate **1** gave β-aminoester **3** in 84% yield and >98% de. Subsequent asymmetric aldol reaction via deprotonation with LDA, transmetallation with $B(OMe)_3$, and addition of acetaldehyde gave *syn*-aldol product **4** in good yield, which was isolated as a single diastereoisomer (>98% de). Tandem N-oxidation and Cope elimination then gave the desired β-substituted Baylis–Hillman product (*S*,*E*)-**5** in good yield and high de and ee (Scheme 1).

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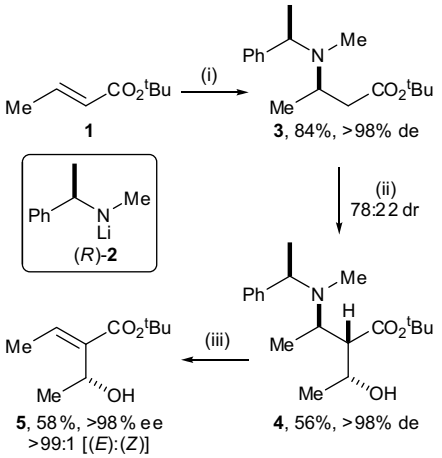


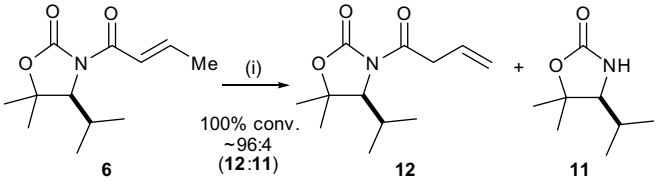
Scheme 1. Reagents and conditions: (i) lithium (*R*)-*N*-methyl-*N*-(α-methylbenzyl)amide **2** (1.6 equiv), THF, −78 °C then NH_4Cl (satd aq); (ii) LDA (3.0 equiv), THF, −78 to 0 °C, then $B(OMe)_3$, then CH_3CHO; (iii) *m*CPBA, $CHCl_3$, rt.

We also proposed that homochiral β-substituted Baylis–Hillman products **9** could be accessed via a diastereoselective dienolate aldol reaction of (*E*)-*N*-crotonoyl oxazolidinone **6**. Either cleavage of the auxiliary from the aldol product **7** and subsequent isomerisation of the double bond within the corresponding α-vinyl-β-hydroxyester **8**, or isomerisation of the double bond within **7** followed by cleavage of the auxiliary from **10**, would then afford the desired β-substituted Baylis–Hillman products **9** directly (Fig. 1). The enhanced exocyclic cleavage capacity and the high levels of diastereofacial control observed in reactions of *N*-acyl SuperQuat derivatives made the L-valine derived SuperQuat auxiliary **11** an ideal choice for this transformation.[15,16] We delineate herein our investigations within this area.

2. Results and discussion

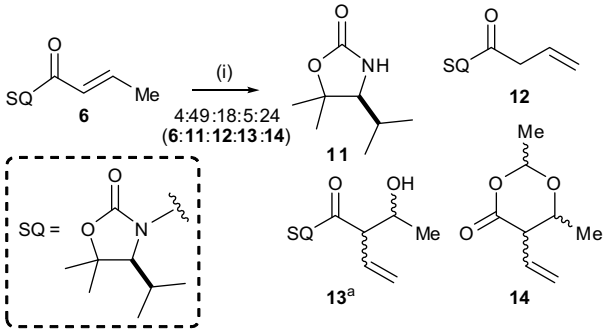
2.1. Dienolate aldol reaction

The reaction of enolates with electrophiles is a powerful strategy for carbon–carbon bond formation,[17] although lithium amide bases such as LDA (which are commonly used for enolisation of carbonyl compounds) are also known to add to α,β-unsaturated esters in a conjugate fashion unless carcinogenic additives such as HMPA are used.[18,19] Initial studies therefore focused on preparing dienolates of (*E*)-*N*-crotonoyl SuperQuat **6**[20] via deprotonation with the non-nucleophilic base KHMDS. Thus, **6** was stirred at −78 °C with KHMDS for 1 h then satd aq NH_4Cl was added to assess the extent of dienolate formation. ^1H NMR spectroscopic analysis of the crude reaction mixture indicated that all starting material had been consumed, and that the *N*-acyl fragment had been converted to the corresponding β,γ-unsaturated isomer **12**, consistent with dienolate formation followed by regioselective (kinetic) protonation at C(2′).[21,22] Non-acylated SuperQuat **11** was also detected as a minor side product (∼4%), which is consistent with a ketene decomposition pathway occurring as a side reaction (Scheme 2).



Scheme 2. Reagents and conditions: (i) KHMDS, THF, −78 °C, 1 h then NH_4Cl (satd, aq).

The level of diastereoselectivity in the asymmetric dienolate aldol reactions of the potassium dienolate of (*E*)-*N*-crotonoyl SuperQuat **6** was next assessed by reaction with acetaldehyde. ^1H NMR spectroscopic analysis of the crude reaction mixture indicated that a complex mixture of products was obtained with poor conversion (∼5%) to the desired aldol products **13**, with poor diastereoselectivity (20% de). Protonation at C(2′) of the dienolate (to give **12**), ketene decomposition (to give SuperQuat **11**), and formation of dioxanone **14** (presumably by reaction of the product alkoxide with excess acetaldehyde) were identified as the major side reactions in this system (Scheme 3).[5e]



Scheme 3. Reagents and conditions: (i) KHMDS, THF, −78 °C, 1 h then CH_3CHO, −78 °C, 1 h [[a]20% de (only two diastereoisomers were detected)].

Subsequent efforts to promote the dienolate aldol reaction focused on transmetallation of the potassium dienolate to give the

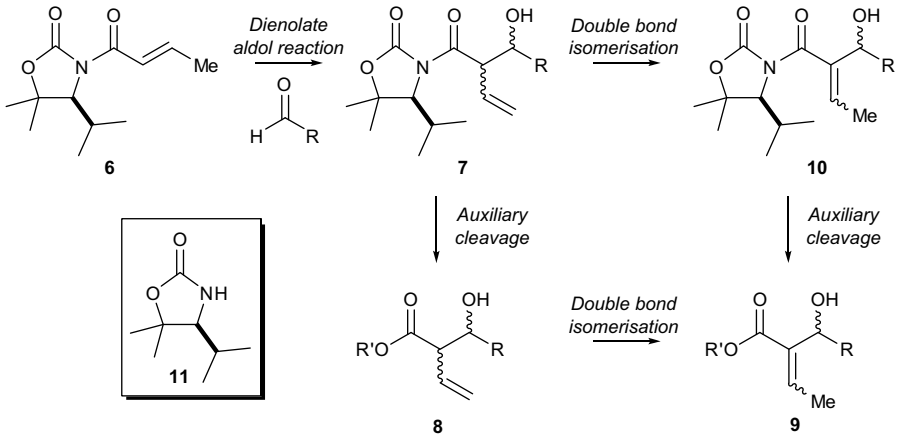
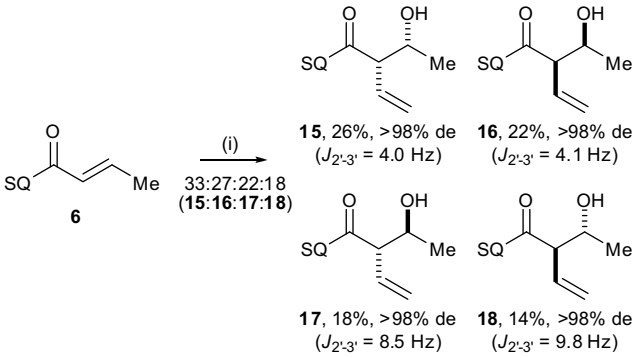


Figure 1. Potential route to β-substituted Baylis–Hillman products **9**.

less reactive zinc dienolate. Transmetallation of the potassium dienolate of (*E*)-*N*-crotonoyl SuperQuat **6** with $ZnCl_2$ followed by addition of acetaldehyde gave good conversion (80%) to aldol products **15**–**18**, with no traces of side products **11**, **12** or **14** being detected. ^{1}H NMR spectroscopic analysis of the crude reaction mixture revealed that all four aldol products had been formed in a ratio of 33:27:22:18 for **15**:**16**:**17**:**18**, respectively. Chromatographic purification allowed separation of all the diastereoisomers, which were individually isolated in 14–26% yield, and in >98% de in each case (Scheme 4).[23] The relative configurations within aldol products **15**–**18** were initially assigned by ^{1}H NMR ^3J coupling constant analyses: *N*-acyl oxazolidinone derived *syn*- and *anti*-aldol products have been shown to display indicative coupling constants between the C(2′)*H* and C(3′)*H* protons.[24] The accepted model for the explanation of this finding postulates that hydrogen bonding between the C(3′)-hydroxyl group and the C(1′)-carbonyl group forms a chair-like conformation with the largest possible number of substituents in equatorial positions. The coupling constants then follow from the Karplus equation, with diagnostic ^3J coupling constants of 2–4 Hz for the *syn*-diastereoisomers and 8–10 Hz for the *anti*-diastereoisomers. Furthermore, the relative *anti*-configuration of **17** was established via X-ray crystallographic analysis, with the (4*S*,2′*S*,3′*S*)-absolute configuration assigned relative to the known (*S*)-configuration of the C(4)-stereogenic centre (Fig. 2).[25]



Scheme 4. Reagents and conditions: (i) KHMDS, THF, −78 °C, 30 min then $ZnCl_2$, Et_2O, 30 min then CH_3CHO, −78 °C, 1 h.

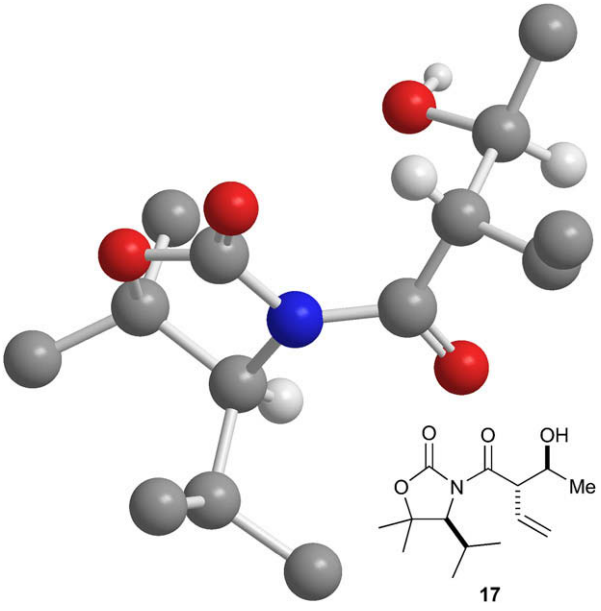
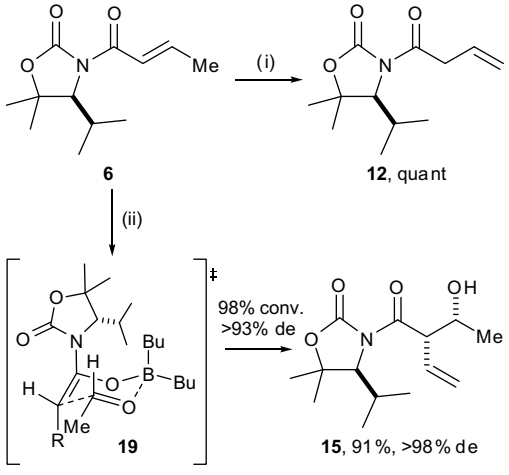


Figure 2. Chem3D representation of the single crystal X-ray structure of **17** (some H atoms have been omitted for clarity).

The configurations within the two remaining *syn*-aldol products **15** and **16** were subsequently assigned by comparison with an authentic sample of **15** (vide infra).

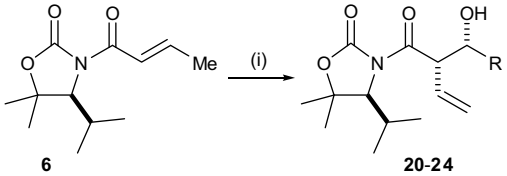
These data suggest that employing a less reactive enolate suppresses the formation of the undesired side products **11**, **12** and **14**, although the diastereoselectivity was poor in the case of the zinc dienolate. The corresponding boron dienolate was therefore investigated. Formation of the boron dienolate may either be achieved by transmetallation of the potassium dienolate or by direct formation by treatment of (*E*)-*N*-crotonoyl oxazolidinone **6** with Bu_2BOTf in the presence of Et_3N. Evans et al. have shown that direct boron enolisation with Bu_2BOTf is applicable to (*E*)-*N*-crotonoyl oxazolidinones giving β,γ-unsaturated aldol products in high de.[26] Application of this protocol to (*E*)-*N*-crotonoyl oxazolidinone **6** via addition of Bu_2BOTf and Et_3N at −78 °C, followed by warming to 0 °C for 30 min, and re-cooling to −78 °C with subsequent addition of aldehyde (1.0 equiv) led to a complex mixture of products, indicating that (*E*)-*N*-crotonoyl SuperQuat **6** behaves somewhat differently to (*E*)-*N*-crotonoyl Evans oxazolidinones. To confirm that dienolate formation occurs at −78 °C, without the need to warm the solution to 0 °C, Bu_2BOTf and Et_3N were added to (*E*)-*N*-crotonoyl oxazolidinone **6** at −78 °C followed by the addition of satd aq NH_4Cl after 30 min which gave **12** in quantitative yield. This modified dienolate formation protocol was therefore applied to the aldol reaction with acetaldehyde: Bu_2BOTf and Et_3N were added to **6** in CH_2Cl_2 at −78 °C; after 30 min acetaldehyde was added and the reaction mixture was stirred at −78 °C for 1 h before the addition of satd aq NH_4Cl to give *syn*-aldol product **15** in 98% conversion and >93% de. Purification via flash column chromatography gave **15** as a single diastereoisomer (>98% de) in 91% isolated yield (Scheme 5). The relative configuration within *syn*-**15**, which displayed a diagnostic ^3J coupling constant of 4.0 Hz between the C(2′)*H* and C(3′)*H* protons (indicative of a *syn*-configuration), was assigned by analogy to the well established aldol reaction of dienolates derived from *N*-acyl oxazolidinones, presumably proceeding via chair-like transition state **19**.[26,27] Within this transition state the dipole–dipole interactions within the imide are minimised, with the stereodirecting isopropyl group blocking the *Si* face of the dienolate; the aldehyde then presents its *Si* face towards the dienolate, with the sterically more demanding methyl group occupying an equatorial position within the transition state, giving rise to *syn*-aldol product **15**.



Scheme 5. Reagents and conditions: (i) Bu_2BOTf, Et_3N, CH_2Cl_2, −78 °C, 30 min then satd aq NH_4Cl; (ii) Bu_2BOTf, Et_3N, CH_2Cl_2, −78 °C, 1 h then CH_3CHO, −78 °C, 1 h [R = CH=CH_2].

The generality of this aldol protocol was next established by reaction with a range of aldehydes: treatment of the boron dienolate derived from (*E*)-*N*-crotonoyl SuperQuat **6** with

propionaldehyde, isobutyraldehyde, pivalaldehyde, benzaldehyde and phenylacetaldehyde was investigated. Extended reaction times (2–4 h) were required for the reactions to proceed to good conversion, with the increasing steric bulk having a marked effect on both yield and diastereoselectivity of the reaction. *syn*-Aldol products **20**–**24** were formed with moderate to good diastereoselectivity (52–98% de), with chromatographic purification giving **20**–**24** as single diastereoisomers (>98% de) in 40–95% isolated yield (Scheme 6).[28] Recrystallisation of the major diastereoisomers arising from reaction with pivalaldehyde and benzaldehyde allowed unambiguous assignment of the *syn*-relative configuration of aldol products **22** and **23** by single crystal X-ray analysis, with the absolute (4*S*,2′*S*,3′*S*)-configurations assigned from the known (*S*)-configuration of the C(4)-stereogenic centre within the L-valine derived SuperQuat auxiliary (Figs. 3 and 4).[29] This stereochemical outcome is consistent with the dienolate aldol reaction of substrates **22** and **23** proceeding via a transition state analogous to **19**, and giving the expected *syn*-Evans aldol products. The configurations within **20**, **21**, and **24** were thus assigned by analogy to those of **22** and **23**.



Conv. (%)	Product	de (%)[a]	Yield (%)[b]	$J_{2'\text{-}3'}$ (Hz)
92	**20** R = Et	86	86	3.7
88	**21** R = ^{i}Pr	76	88	4.0
53	**22** R = ^{t}Bu	52	40	4.4
95	**23** R = Ph	98	95	9.0
95	**24** R = Bn	92	95	3.2

Scheme 6. Reagents and conditions: (i) Bu_2BOTf, Et_3N, CH_2Cl_2, −78 °C, 60 min then RCHO, −78 °C, 2–4 h [[a]crude; [b]isolated as single diastereoisomers (>98% de)].

Transmetallation of the potassium dienolate of (*E*)-*N*-crotonoyl SuperQuat **6** to the corresponding boron dienolate was next investigated: treatment of the potassium dienolate with $B(OMe)_3$ followed by the addition of acetaldehyde gave a complex mixture of products. However, treatment of the potassium dienolate with a pre-made solution of *B*-bromocatechol borane

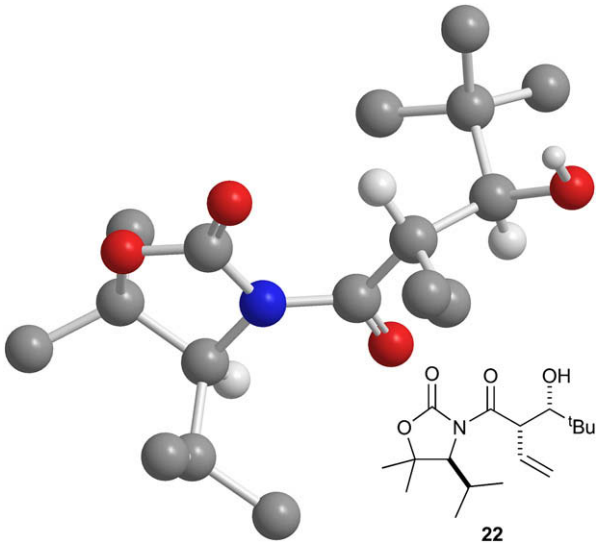


Figure 3. Chem3D representation of the single crystal X-ray structure of **22** (some H atoms have been omitted for clarity).

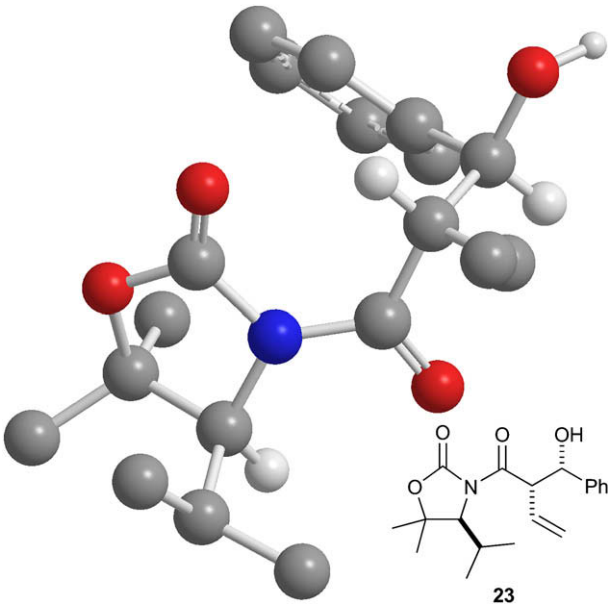
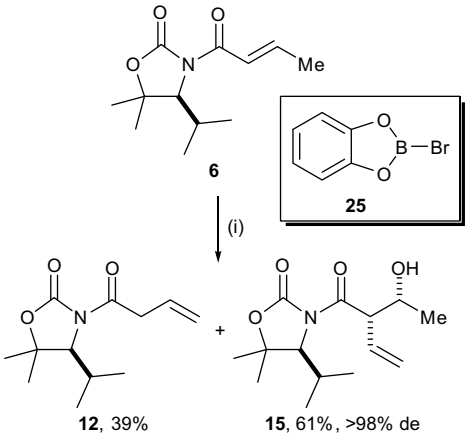


Figure 4. Chem3D representation of the single crystal X-ray structure of **23** (some H atoms have been omitted for clarity).

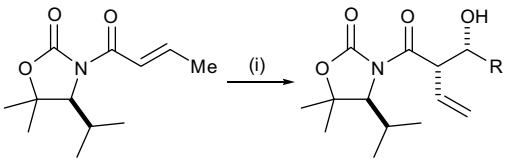
25 in CH_2Cl_2, followed by the addition of acetaldehyde gave a 39:61 mixture of β,γ-unsaturated *N*-acyl SuperQuat **12** and *syn*-aldol product **15** in >98% de. Chromatographic purification of this mixture gave **12** in 39% yield, and *syn*-**15** in 61% yield and >98% de (Scheme 7).



Scheme 7. Reagents and conditions: (i) KHMDS, THF, −78 °C, 30 min then **25**, 30 min then CH_3CHO, −78 °C, 1 h.

The generality of this highly diastereoselective transmetallation/boron enolisation protocol was next established by application of these conditions to a range of aldehydes. Upon treatment of the boron dienolate of (*E*)-*N*-crotonoyl SuperQuat **6** with propionaldehyde, isobutyraldehyde, benzaldehyde and phenylacetaldehyde complete consumption of starting material was observed with the major products being the desired *syn*-aldol products **20**, **21**, **23** and **24** (>98% de in each case).[30] Chromatographic purification gave *syn*-aldol products **20**, **21**, **23** and **24** in 57–78% isolated yield and in >98% de (Scheme 8).[31]

With a range of *syn*-aldol products **15** and **20**–**24** (as single diastereoisomers) in hand their conversion to the corresponding α-vinyl-β-hydroxycarboxylic acid derivatives and α-ethylidene-β-hydroxyesters (β-substituted Baylis–Hillman products) was next investigated.

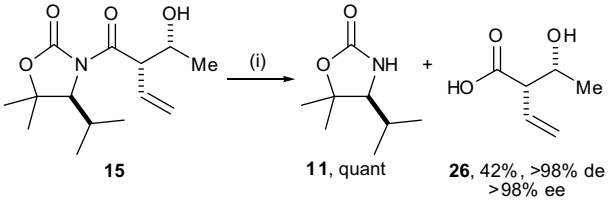


Product	de (%)[a]	Yield (%)[b]	$J_{2'\text{-}3'}$ (Hz)
20 R = Et	>98	66	3.7
21 R = ^{i}Pr	>98	57	4.0
23 R = Ph	>98	78	9.0
24 R = Bn	>98	64	3.2

Scheme 8. Reagents and conditions: (i) KHMDS, THF, −78 °C, 30 min then **25**, 30 min then RCHO, −78 °C, 1–4 h [[a]crude; [b]isolated as single diastereoisomers (>98% de)].

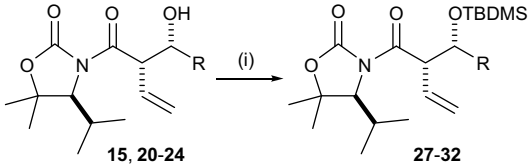
2.2. Synthesis of α-vinyl-β-hydroxycarboxylic acid derivatives

Initial studies showed that treatment of **15** with lithium hydroperoxide (under the standard conditions for auxiliary cleavage)[19] gave SuperQuat **11** in quantitative yield, and the desired β-hydroxy acid product **26**, although **26** was found to be highly water soluble (even at very low pH) and was isolated in only 42% yield (in >98% de and >98% ee[32]) (Scheme 9).



Scheme 9. Reagents and conditions: (i) LiOH, H_2O_2, H_2O, MeOH, 0 °C to rt, 18 h.

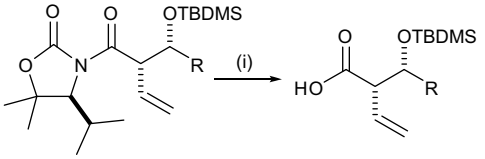
An alternative protocol employing *O*-silyl protection of the β-hydroxy substituent was next investigated. Aldol products **15**, **20**, **23** and **24** were treated with TBDMSCl and imidazole in DMF to give quantitative conversion to the desired *O*-TBDMS protected products **27**, **28**, **31** and **32**, which were isolated in 40–98% yield; attempted silylation of **21** and **22** (R=^{i}Pr and ^{t}Bu) failed to give the desired products **29** and **30**, even employing more forcing conditions (TBDMSOTf and DMAP), and returned starting material in each case presumably as a result of the steric bulk of the C(2′)-alkyl substituent reducing the nucleophilicity of the alcohol (Scheme 10).



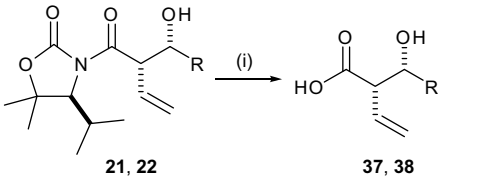
		Yield (%)	de (%)
15 R = Me	**27** R = Me	97	>98
20 R = Et	**28** R = Et	98	>98
21 R = ^{i}Pr	**29** R = ^{i}Pr	0	--
22 R = ^{t}Bu	**30** R = ^{t}Bu	0	--
23 R = Ph	**31** R = Ph	40	>98
24 R = Bn	**32** R = Bn	96	>98

Scheme 10. Reagents and conditions: (i) TBDMSCl, imidazole, DMF, rt, 12 h.

With *O*-silyl protected material **27**, **28**, **31** and **32** in hand, cleavage to give the corresponding carboxylic acids was attempted. Treatment of **27**, **28**, **31** and **32** with LiOOH in MeOH gave carboxylic acids **33**–**36** in 73–92% yield (>98% de and >98% ee[32] in each case). Furthermore, the substrates with α-branched C(2′)-substituents **21** and **22** (where O-silylation was not successful) were also subjected to the same cleavage conditions and cleanly gave carboxylic acids **37** and **38** (both in >98% de and >98% ee[32]) in 89 and 92% yield, respectively (Scheme 11).



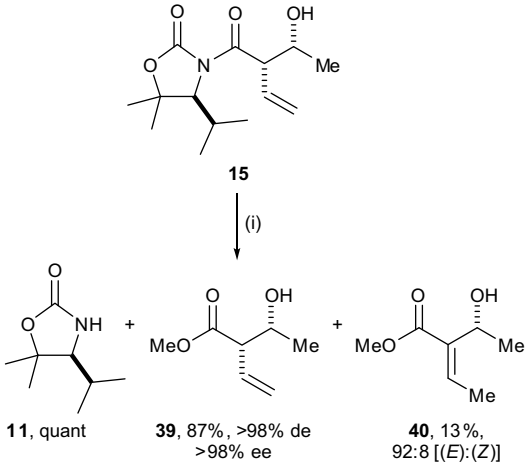
		Yield (%)	de (%)	ee (%)
27 R = Me	**33** R = Me	73	>98	>98
28 R = Et	**34** R = Et	85	>98	>98
31 R = Ph	**35** R = Ph	92	>98	>98
32 R = Bn	**36** R = Bn	90	>98	>98



		Yield (%)	de (%)	ee (%)
21 R = ^{i}Pr	**37** R = ^{i}Pr	89	>98	>98
22 R = ^{t}Bu	**38** R = ^{t}Bu	92	>98	>98

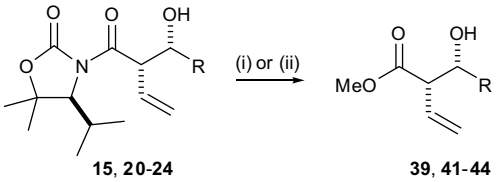
Scheme 11. Reagents and conditions: (i) LiOH, H_2O_2, H_2O, MeOH, 0 °C to rt, 18 h.

Methanolysis of the *syn*-aldol products was also investigated as it would afford synthetically more useful methyl esters directly and potentially provide access to β-methyl Baylis–Hillman products. Thus, treatment of a solution of **15** in MeOH with BuLi at −78 °C gave, in addition to SuperQuat **11**, an 87:13 mixture of **39** and **40** indicating that partial isomerisation of the double bond had occurred under these conditions. Following chromatographic purification of the mixture **39** was isolated in 87% yield (in >98% de and >98% ee[32]), and **40** was isolated in 13% yield as a 92:8 [(*E*):(*Z*)] mixture of geometric isomers (Scheme 12).



Scheme 12. Reagents and conditions: (i) MeOH, BuLi, −78 °C, 3 h.

Further optimisation revealed that a reaction temperature of −20 °C proved advantageous for controlled methanolysis and this protocol was successfully applied to *syn*-aldol products **15** and **20**–**24**. β,γ-Unsaturated esters **39** and **41**–**44** were isolated in 79–91% yield, and in >98% de and >98% ee[32] in each case, although **45** could not be separated from its α,β-unsaturated isomer (Scheme 13).

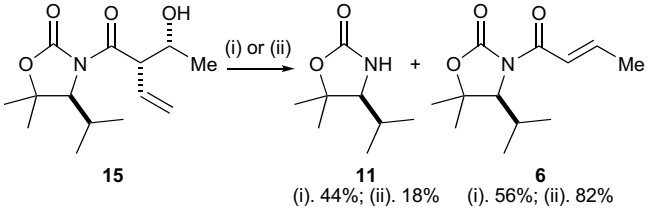


			Yield (%)	de (%)	ee (%)
15 R = Me	**39** R = Me		81	>98	>98
20 R = Et	**41** R = Et		87	>98	>98
21 R = ^{i}Pr	**42** R = ^{i}Pr		79	>98	>98
22 R = ^{t}Bu	**43** R = ^{t}Bu		91	>98	>98
23 R = Ph	**44** R = Ph		83	>98	>98
24 R = Bn	**45** R = Bn		quant[a]	--	--

Scheme 13. Reagents and conditions: (i) MeOH, BuLi, −78 °C, 3 h [[a]76:24 mixture of α,β- and β,γ-unsaturated isomers].

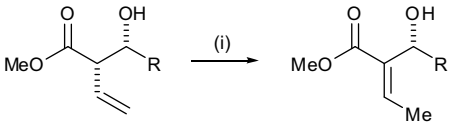
2.3. Synthesis of α-ethylidene-β-hydroxyesters (β-substituted Baylis–Hillman products)

While there appear to be no reports concerning the direct isomerisation of β-hydroxy-β,γ-unsaturated amides to their α,β-unsaturated derivatives, a number of protocols exist for the isomerisation of α-branched-β,γ-unsaturated carbonyl compounds by treatment with either Et_3N or DBU.[33,34] Thus, a solution of **15** in THF was treated with Et_3N and stirred for for 2 h, but returned only starting material.[22] Treatment of **15** with a number of different bases including piperidine, DBU and DABCO was then attempted with no reaction noted even upon extended reaction times (up to 24 h). Attempts to promote the isomerisation via heating under more forcing conditions (KO^{t}Bu) also proved unsuccessful, resulting in the formation of (*E*)-*N*-crotonoyl **6**, presumably as a result of a retro-aldol-type process under the basic conditions of the reaction; similar reactivity was noted upon treatment with KO^{t}Bu at rt (Scheme 14). Treatment of the *O*-TBDMS protected silyl ether **27** with either DBU or KO^{t}Bu at elevated temperatures was also unsuccessful: in both cases no reaction was observed, with only starting material returned. The use of acidic conditions was next investigated, but treatment of a solution of **15** in CH_2Cl_2 or toluene with acid (TFA, *p*-TsOH or CSA) was found to only result in the return of staring material.



Scheme 14. Reagents and conditions: (i) KO^{t}Bu, THF, rt, 24 h; (ii) KO^{t}Bu, THF, reflux, 24 h.

Having previously shown that isomerisation of β,γ-unsaturated methyl esters to α,β-unsaturated methyl esters is possible under basic conditions (vide supra), treatment of methyl ester **39** with DBU at rt was investigated and found to isomerise the double bond into conjugation at similar rate in THF, Et_2O or CH_2Cl_2. After 1 h, **40** was isolated in 88% yield as an inseparable 83:17 mixture of (*E*):(*Z*) isomers. The major component was determined to be the (*E*)-isomer by ^{1}H NMR NOE studies. While changing the solvent to Et_2O, CH_2Cl_2 or pentane had no effect on the (*E*):(*Z*) selectivity, lowering the temperature to −20 °C increased the (*E*):(*Z*) ratio to 92:8, with a concomitant increase in the reaction time to 48 h. Application of this protocol to β,γ-unsaturated methyl esters **41**–**45** also proved successful and gave the desired β-substituted Baylis–Hillman products **46**–**50** in excellent yield and high diastereoisomeric purity [≥91:9 (*E*):(*Z*) ratio]. However, in the case of the benzaldehyde derived material **49** (R=Ph), the yield was greatly reduced as dehydration competed with isomerisation (Scheme 15). The enantiopurity of α,β-unsaturated compounds **40** and **46**–**50** was assessed by ^{1}H NMR analysis in the presence of chiral solvating agent Eu(hfc)$_3$, and comparison with authentic racemic samples. In each case, β-substituted Baylis–Hillman products **40** and **46**–**50** were found to be >98% ee, confirming that the stereochemical integrity of these substrates had not been compromised during the deprotection protocol.



		Yield (%)	(*E*):(*Z*)	ee (%)
39 R = Me	**40** R = Me	95	92:8	>98
41 R = Et	**46** R = Et	89	92:8	>98
42 R = ^{i}Pr	**47** R = ^{i}Pr	98	92:8	>98
43 R = ^{t}Bu	**48** R = ^{t}Bu	97	91:9	>98
44 R = Ph	**49** R = Ph	43	94:6	>98
45 R = Bn[a]	**50** R = Bn	97[b]	92:8	>98

Scheme 15. Reagents and conditions: (i) DBU, THF, −20 °C, 48 h [[a]76:24 mixture of α,β- and β,γ-unsaturated isomers; [b]yield from **24** (two steps)].

3. Conclusion

The aldol reaction of the boron dienolate derived from (*E*)-*N*-crotonoyl C(4)-isopropyl SuperQuat (generated either directly with Bu_2BOTf or by transmetalation of the potassium enolate with *B*-bromocatecholborane) with a range of aldehydes proceeds in high yield and with excellent *syn*-diastereoselectivity (up to >98% de). Cleavage of the resultant *syn*-aldol products from the auxiliary gives α-vinyl-β-hydroxy-esters, and subsequent isomerisation of the double bond into conjugation provides a range of α-ethylidene-β-hydroxy-esters (β-substituted Baylis–Hillman products) in high diastereo- and enantiopurity (≥91:9 [(*E*):(*Z*)] and >98% ee).

4. Experimental

4.1. General experimental

All reactions involving organometallic or other moisture-sensitive reagents were carried out under a nitrogen or argon atmosphere using standard vacuum line techniques and glassware that was flame dried and cooled under nitrogen before use. Solvents were dried according to the procedure outlined by Grubbs et al.[35] Water was purified by a Millipore Elix® UV-10 system. All other solvents were used as supplied (analytical or HPLC grade) without prior purification. Organic layers were dried over $MgSO_4$. Thin layer chromatography was performed on aluminium plates coated with 60 F_{254} silica. Plates were visualised using UV light (254 nm), iodine, 1% aq $KMnO_4$, or 10% ethanolic phosphomolybdic acid. Flash column chromatography was performed on Kieselgel 60 silica.

Elemental analyses were recorded by the microanalysis service of the Inorganic Chemistry Laboratory, University of Oxford, UK. Melting points were recorded on a Gallenkamp Hot Stage apparatus and are uncorrected. Optical rotations were recorded on a Perkin–Elmer 241 polarimeter with a water-jacketed 10 cm cell. Specific rotations are reported in 10^{-1} deg cm^2 g^{-1} and concentrations in g/100 mL. IR spectra were recorded on a Bruker Tensor 27 FT-IR spectrometer as either a thin film on NaCl plates (film) or a KBr disc (KBr), as stated. Selected characteristic peaks are reported in cm^{-1}. NMR spectra were recorded on Bruker Avance spectrometers in the deuterated solvent stated. The field was locked by external referencing to the relevant deuteron resonance. Low-resolution mass

spectra were recorded on either a VG MassLab 20-250 or a Micromass Platform 1 spectrometer. Accurate mass measurements were run on either a Bruker MicroTOF internally calibrated with polyalanine, or a Micromass GCT instrument fitted with a Scientific Glass Instruments BPX5 column (15 m×0.25 mm) using amyl acetate as a lock mass.

4.2. General procedure 1 for dibutylborontriflate aldol reaction

Bu_2BOTf (1.3 equiv, 1.0 M in CH_2Cl_2) and Et_3N (1.5 equiv) were added to a solution of (*E*)-*N*-crotonoyl SuperQuat **6** (1.0 equiv) in CH_2Cl_2 at −78 °C and the resultant mixture was stirred at −78 °C for 1 h. Freshly distilled aldehyde (1.5 equiv) was then added and the reaction mixture was allowed to warm to rt and stirred for 1 h. Satd aq NH_4Cl (1 mL) solution was then added, the resultant mixture was cooled to 0 °C, and H_2O_2 (2 mL, 35% in water) and MeOH (2 mL) were added. The resultant mixture was allowed to warm to rt, stirred for 1 h, and then concentrated in vacuo. The residue was triturated with 40–60 °C petrol, and the organic extracts were washed with satd aq $NaHCO_3$, then dried, filtered and concentrated in vacuo.

4.3. General procedure 2 for *B*-bromocatecholborane aldol reaction

KHMDS (1.1 equiv, 0.5 M in toluene) was added to a solution of (*E*)-*N*-crotonoyl SuperQuat **6** (1.0 equiv) in THF at −78 °C and the reaction mixture was stirred for 1 h at −78 °C. A pre-made solution of *B*-bromocatecholborane **25** (1.1 equiv) in THF (1.25 M) was then added and the resultant mixture was stirred for 30 min before freshly distilled aldehyde (1.5 equiv) was added. The reaction mixture was then stirred at −78 °C for 30 min before it was allowed warm to rt and stirred for 1 h. Satd aq NH_4Cl was then added and the resultant mixture was partitioned between Et_2O and brine. The organic phase was then dried, filtered and concentrated in vacuo.

4.4. General procedure 3 for *O*-silyl protection

TBDMSCl (1.5 equiv) and imidazole (2.0 equiv) were added to a solution of the alcohol (1.0 equiv) in DMF (0.2 M) at rt and the resultant solution was stirred at rt for 16 h. The reaction was monitored by TLC and upon completion, the mixture was partitioned between satd aq NH_4Cl and pentane. The organic phase was then dried, filtered and concentrated in vacuo.

4.5. General procedure 4 for lithium hydroperoxide auxiliary cleavage

Satd aq LiOH in hydrogen peroxide (30% w/w) was added to a stirred solution of the substrate (1.0 equiv) in methanol (2.0 M) at 0 °C. The resulting suspension was allowed to warm to rt and stirred for 18 h. The mixture was then concentrated in vacuo and the residue was triturated with Et_2O. The combined organic extracts were acidified to pH 2 with 1.0 M aq HCl and extracted with CH_2Cl_2. The combined organic extracts were then dried, filtered and concentrated in vacuo.

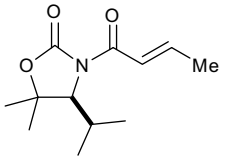
4.6. General procedure 5 for lithium methoxide auxiliary cleavage

BuLi (1.0 equiv) was added to a solution of alcohol (1.0 equiv) in MeOH (0.2 M) at −78 °C over a period of 5 min. The resultant mixture was allowed to warm to −20 °C and was monitored by TLC analysis. After completion, the mixture was partitioned between satd aq NH_4Cl and pentane, the organic phase was then dried, filtered and concentrated in vacuo.

4.7. General procedure 6 for double dond isomerisation

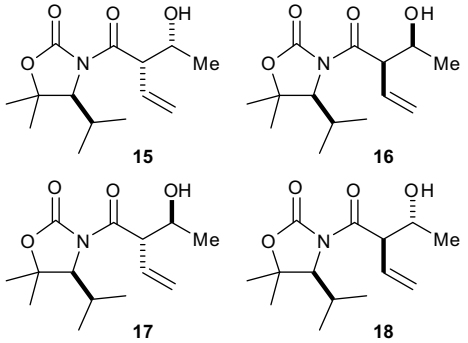
DBU (4.0 equiv) was added to a solution of the requisite α-vinyl-β-hydroxyester (1.0 equiv) in CH_2Cl_2 (2.0 M) and the resultant solution was stirred at −20 °C for 36 h. The reaction mixture was then diluted with pentane and the organic layer was washed with satd aq NH_4Cl then dried, filtered and concentrated in vacuo.

4.7.1. (4S,2′E)-N(3)-But-2-enoyl-4-isopropyl-5,5-dimethyl-oxazolidin-2-one ***6***



BuLi (2.5 M in hexanes, 62 mL, 0.16 mol) was added dropwise via syringe to a solution of SuperQuat **11** (20.0 g, 0.13 mol) in THF (200 mL) at −78 °C. The reaction mixture was stirred at −78 °C for 10 min then *trans*-crotonoyl chloride (21.3 mL, 90%, 0.2 mol) was added and the resultant mixture was allowed to warm to rt over 2 h. Satd aq NH_4Cl (250 mL) was then added and the resultant mixture was extracted with EtOAc (2×250 mL). The combined organic extracts were washed with satd aq $NaHCO_3$ (300 mL), then dried, filtered and concentrated in vacuo. The residue was recrystallised from 40–60 °C petrol/Et_2O to give **6** as a white crystalline solid (24.3 g, 85%);[15b] mp 69–70 °C; {lit.[15b] mp 71–72 °C}; $[\alpha]_D^{23}$ +13.9 (*c* 0.85, $CHCl_3$); {lit.[15b] $[\alpha]_D^{22}$ +14.5 (*c* 1.0, $CHCl_3$); δ_H (500 MHz, $CDCl_3$) 0.94 (3H, d, *J* 6.9, $CH(CH_3)_A(CH_3)_B$), 1.01 (3H, d, *J* 6.9, $CH(CH_3)_A(CH_3)_B$), 1.37 (3H, s, $C(CH_3)_A(CH_3)_B$), 1.49 (3H, s, $C(CH_3)_A(CH_3)_B$), 1.94 (3H, dd, *J* 6.9, 1.6, C(4′)H_3), 2.13 (1H, septd, *J* 6.9, 3.4, $CH(CH_3)_2$), 4.19 (1H, d, *J* 3.4, C(4)*H*), 7.13 (1H, qd, *J* 15.2, 6.9, C(3′)*H*), 7.30 (1H, qd, *J* 15.2, 1.6, C(2′)*H*); δ_C (50 MHz, $CDCl_3$) 16.9, 18.4, 21.2, 21.2 ($C(CH_3)_2$, $CH(CH_3)_2$), 28.7 (C(4′)H_3), 29.5 ($CH(CH_3)_2$), 66.3 (C(4)H), 82.8 ($C(CH_3)_2$), 122.1 (C(2′)H), 146.8 (C(3′)H), 153.8 (C(2)), 165.9 (C(1′)); *m*/*z* (GC Tof CI^+) 226 ($[M+H]^+$, 37%), 158 ($[M-C_4H_3O]^+$, 100).

4.7.2. (4S,2′S,3′R)-, (4S,2′R,3′S)-, (4S,2′S,3′S)- and (4S,2′R,3′R)-N(3)-(2′-Vinyl-3′-hydroxybutanoyl)-4-isopropyl-5,5-dimethyl-oxazolidin-2-one (4S,2′S,3′R)- ***15****, (4S,2′R,3′S)-* ***16****, (4S,2′S,3′S)-* ***17*** *and (4S,2′R,3′R)-* ***18***



A solution of **6** (3.00 g, 11.8 mmol) in THF (50 mL) was stirred at −78 °C for 5 min then KHMDS (23.6 mL, 13.0 mmol, 0.5 M in toluene) was added via syringe. The resultant mixture was stirred at −78 °C for 1 h then $ZnCl_2$ (23.6 mL, 13.0 mmol, 0.5 M in THF) was added and the reaction mixture was stirred for another 30 min before freshly distilled acetaldehyde (1.00 mL, 17.7 mmol) was also added. The resultant mixture was stirred for 30 min, allowed to

warm to rt then stirred for a further 1 h. Satd aq NH_4Cl (80 mL) was then added and the resultant mixture was partitioned between Et_2O (300 mL) and brine (300 mL). The organic phase was separated and then dried, filtered and concentrated in vacuo. The residue was purified by flash column chromatography (eluent Et_2O/pentane, 3:7) to give (4*S*,2′*S*,3′*R*)-**15** (823 mg, 26%, >98% de), (4*S*,2′*R*,3′*S*)-**16** (696 mg, 22%, >98% de) and (4*S*,2′*R*,3′*R*)-**18** (443 mg, 14%, >98% de) as colourless oils, and (4*S*,2′*S*,3′*S*)-**17** as a white crystalline solid (570 mg, 18%, >98% de).

Data for (4*S*,2′*S*,3′*R*)-**15**. $[\alpha]_D^{22}$ −43.5 (*c* 1.0, $CHCl_3$); ν_{max} (film) 1770 (C=O, exocyclic), 1702 (C=O, endocyclic), 1635 (C=C); δ_H (500 MHz, $CDCl_3$) 0.93 (3H, d, *J* 6.9, CH(CH_3)$_A$(CH$_3$)$_B$), 1.00 (3H, d, *J* 6.9, CH(CH$_3$)$_A$(CH_3)$_B$), 1.20 (3H, d, *J* 6.3, C(4′)H_3), 1.41 (3H, s, C(CH_3)$_A$(CH$_3$)$_B$), 1.52 (3H, s, C(CH$_3$)$_A$(CH_3)$_B$), 2.13 (1H, septd, *J* 6.9, 3.2, C*H*(CH$_3$)$_2$), 3.06 (1H, s, O*H*), 4.13–4.19 (1H, m, C(3′)*H*), 4.22 (1H, d, *J* 3.2, C(4)*H*), 4.60 (1H, dd, *J* 9.1, 4.0, C(2′)*H*), 5.40 (1H, app dd, *J* 10.1, 1.4, CH=C*H*$_A$H$_B$), 5.49 (1H, d, *J* 17.1, CH=CH$_A$*H*$_B$), 5.99 (1H, ddd, *J* 17.1, 10.1, 9.1, C*H*=CH$_2$); δ_C (50 MHz, $CDCl_3$) 16.5, 19.6, 21.7, 28.6 (CH(*C*H$_3$)$_2$, C(*C*H$_3$)$_2$), 21.2 (*C*(4′)H$_3$), 29.7 (*C*H(CH$_3$)$_2$), 53.2 (*C*(2′)H), 66.0 (*C*(4)H), 67.9 (*C*(3′)H), 82.8 (*C*(CH$_3$)$_2$), 121.9 (*C*H=CH$_2$), 131.9 (CH=*C*H$_2$), 153.4 (*C*(2)), 175.1 (*C*(1′)); *m*/*z* (GC Tof CI$^+$) 270 ([M+H]$^+$, 15%) 158 ([M−C$_6$H$_7$O$_2$]$^+$, 100); HRMS (GC Tof CI$^+$) $C_{14}H_{24}NO_4^+$ ([M+H]$^+$) requires 270.1700; found 270.1698.

Data for (4*S*,2′*R*,3′*S*)-**16**. $[\alpha]_D^{22}$ +92.3 (*c* 1.5, $CHCl_3$); ν_{max} (film) 3516 (O–H), 1770 (C=O, exocyclic), 1694 (C=O, endocyclic), 1635 (C=C); δ_H (500 MHz, $CDCl_3$) 0.98 (3H, d, *J* 6.9, CH(CH_3)$_A$(CH$_3$)$_B$), 1.06 (3H, d, *J* 6.9, CH(CH$_3$)$_A$(CH_3)$_B$), 1.23 (3H, d, *J* 6.4, C(4′)H_3), 1.35 (3H, s, C(CH_3)$_A$(CH$_3$)$_B$), 1.52 (3H, s, C(CH$_3$)$_A$(CH_3)$_B$), 2.10 (1H, septd, *J* 6.9, 3.4, C*H*(CH$_3$)$_2$), 3.12 (1H, br s, O*H*), 4.13 (1H, d, *J* 3.4, C(4)*H*), 4.23 (1H, dq, *J* 6.4, 4.1, C(3′)*H*), 4.55 (1H, dd, *J* 9.1, 4.1, C(2′)*H*), 5.30 (1H, d, *J* 17.2, CH=C*H*$_A$H$_B$), 5.33 (1H, d, *J* 10.3, CH=CH$_A$*H*$_B$), 5.97 (1H, ddd, *J* 17.2, 10.3, 9.1, C*H*=CH$_2$); δ_C (125 MHz, $CDCl_3$) 16.8, 19.6, 21.5, 28.6 (C(*C*H$_3$)$_2$, CH(*C*H$_3$)$_2$), 21.2 (*C*(4′)H$_3$), 29.4 (*C*H(CH$_3$)$_2$), 53.0 (*C*(2′)H), 66.6 (*C*(4)H), 68.3 (*C*(3′)H), 83.1 (*C*(CH$_3$)$_2$), 121.0 (CH=*C*H$_2$), 131.3 (*C*H=CH$_2$), 153.4 (*C*(2)), 174.1 (*C*(1′)); *m*/*z* (APCI$^+$) 270 ([M+H]$^+$, 4%), 252 ([M−OH]$^+$, 26), 158 ([SQ+H]$^+$, 100); HRMS (CI$^+$) $C_{14}H_{24}NO_4^+$ ([M+H]$^+$) requires 270.1700; found 270.1700.

Data for (4*S*,2′*S*,3′*S*)-**17**. Found: C, 62.4; H, 8.7; N, 5.2%; $C_{14}H_{25}NO_4$ requires C, 62.4; H, 8.6; N, 5.2%; mp 99–100 °C; $[\alpha]_D^{21}$ +4.4 (*c* 1.0, $CHCl_3$); ν_{max} (KBr) 3466 (O–H), 1770 (C=O, exocyclic), 1680 (C=O, endocyclic), 1633 (C=C); δ_H (400 MHz, $CDCl_3$) 0.90 (3H, d, *J* 6.8, CH(CH_3)$_A$(CH$_3$)$_B$), 0.98 (3H, d, *J* 6.8, CH(CH$_3$)$_A$(CH_3)$_B$), 1.23 (3H, d, *J* 6.6, C(4′)H_3), 1.34 (3H, s, C(CH_3)$_A$(CH$_3$)$_B$), 1.49 (3H, s, C(CH$_3$)$_A$(CH_3)$_B$), 2.10 (1H, septd, *J* 6.8, 3.2, C*H*(CH$_3$)$_2$), 2.44 (1H, app d, *J* 6.2, O*H*), 4.08 (1H, dq, *J* 8.5, 6.6, C(3′)*H*), 4.20 (1H, d, *J* 3.2, C(4)*H*), 4.54 (1H, dd, *J* 9.7, 8.5, C(2′)*H*), 5.24 (1H, d, *J* 9.8, CH=C*H*$_A$H$_B$), 5.37 (1H, d, *J* 17.3, CH=CH$_A$*H*$_B$), 5.89 (1H, app dd, *J* 17.3, 9.7, C*H*=CH$_2$); δ_C (100 MHz, $CDCl_3$) 16.7, 20.9, 21.7, 28.6 (CH(*C*H$_3$)$_2$, C(*C*H$_3$)$_2$), 21.2 (*C*(4′)H$_3$), 29.8 (*C*H(CH$_3$)$_2$), 55.4 (*C*(2′)H), 66.0 (*C*(4)H), 69.5 (*C*(3′)H), 82.8 (*C*(CH$_3$)$_2$), 119.8 (CH=CH$_2$), 133.7 (*C*H=CH$_2$), 153.4 (*C*(2)), 174.2 (*C*(1′)); *m*/*z* (GC Tof CI$^+$) 270 ([M+H]$^+$, 5%), 226 ([M−C$_2$H$_3$O]$^+$, 100), 158 ([SQ+H]$^+$, 73).

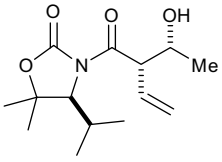
Data for (4*S*,2′*R*,3′*R*)-**18**. ν_{max} (KBr) 3466 (O–H), 1765 (C=O, exocyclic), 1685 (C=O, endocyclic), 1635 (C=C); δ_H (400 MHz, $CDCl_3$) 0.95 (3H, d, *J* 6.9, CH(CH_3)$_A$(CH$_3$)$_B$), 1.03 (3H, d, *J* 6.9, CH(CH$_3$)$_A$(CH_3)$_B$), 1.25 (3H, d, *J* 6.8, C(4′)H_3), 1.38 (3H, s, C(CH_3)$_A$(CH$_3$)$_B$), 1.51 (3H, s, C(CH$_3$)$_A$(CH_3)$_B$), 1.97 (1H, app s, O*H*), 2.14 (1H, septd, *J* 6.9, 3.2, C*H*(CH$_3$)$_2$), 3.73 (1H, dq, *J* 9.8, 6.8, C(3′)*H*), 3.81 (1H, dd, *J* 9.8, 9.3, C(2′)*H*), 4.15 (1H, d, *J* 3.2, C(4)*H*), 5.24 (1H, d, *J* 10.1, CH=C*H*$_A$H$_B$), 5.29 (1H, d, *J* 17.0, CH=CH$_A$*H*$_B$), 6.00 (1H, ddd, *J* 17.0, 10.1, 9.3, C*H*=CH$_2$); δ_C (100 MHz, $CDCl_3$) 20.1, 21.0, 21.6, 29.3 (CH(*C*H$_3$)$_2$, C(*C*H$_3$)$_2$), 22.9 (*C*(4′)H$_3$), 30.3 (*C*H(CH$_3$)$_2$), 50.0 (*C*(2′)H), 65.6 (*C*(4)H), 69.7 (*C*(3′)H), 85.5 (*C*(CH$_3$)$_2$), 134.2 (CH=*C*H$_2$), 146.8 (*C*H=CH$_2$), 153.2 (*C*(2)), 174.5 (*C*(1′)); *m*/*z* (APCI$^+$) 270 ([M+H]$^+$, 10%), 252 ([M−OH]$^+$, 32), 158 ([SQ+H]$^+$, 100); HRMS (CI$^+$) $C_{14}H_{24}NO_4^+$ ([M+H]$^+$) requires 270.1700; found 270.1703.

4.7.2.1. X-ray crystal structure determination for ***17***. Data were collected using an Enraf-Nonius κ-CCD diffractometer with graphite monochromated Mo Kα radiation using standard procedures at 190 K. The structure was solved by direct methods (SIR92); all non-hydrogen atoms were refined with anisotropic thermal parameters. Hydrogen atoms were added at idealised positions. The structure was refined using CRYSTALS.[36]

X-ray crystal structure data for **17** [$C_{14}H_{23}NO_4$]: M=269.34, orthorhombic, space group $P2_12_12_1$, a=7.9067(2) Å, b=12.5456(3) Å, c=15.3428(3) Å, V=1521.9(6) Å^3, Z=4, μ=0.085 mm^{-1}, colourless block, crystal dimensions=0.4×0.4×0.4 mm^3. A total of 3365 unique reflections were measured for $5<\theta<27$ and 2930 reflections were used in the refinement. The final parameters were wR_2=0.084 and R_1=0.036 [$I>3.0\sigma(I)$].

Crystallographic data (excluding structure factors) has been deposited with the Cambridge Crystallographic Data Centre as supplementary publication number CCDC 720350. Copies of the data can be obtained, free of charge, on application to CCDC, 12 Union Road, Cambridge CB2 1EZ, UK [fax: +44(0) 1223 336033 or e-mail: deposit@ccdc.cam.ac.uk].

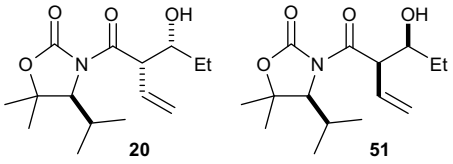
4.7.3. (4S,2′S,3′R)-N(3)-(2′-Vinyl-3′-hydroxybutanoyl)-4-isopropyl-5,5-dimethyl-oxazolidin-2-one ***15***



Method A. Following *general procedure 1*, **6** (500 mg, 2.22 mmol) gave, after purification by flash column chromatography (eluent Et_2O/pentane, 3:7), **15** as a colourless oil (539 mg, 91%, >98% de); $[\alpha]_D^{22}$ −43 (*c* 1.0, $CHCl_3$).

Method B. Following *general procedure 2*, **6** (500 mg, 2.22 mmol) gave, after purification by flash column chromatography (eluent Et_2O/pentane, 3:7), **15** as a colourless oil (385 mg, 65%, >98% de); $[\alpha]_D^{22}$ −42 (*c* 1.0, $CHCl_3$).

4.7.4. (4S,2′S,3′R)- and (4S,2′R,3′S)-N(3)-(2′-Vinyl-3′-hydroxy-pentanoyl)-4-isopropyl-5,5-dimethyl-oxazolidin-2-one (4S,2′S,3′R)- ***20*** *and (4S,2′R,3′S)-* ***51***



Method A. Following *general procedure 1*, **6** (3.00 g, 13.2 mmol) gave, after purification by flash column chromatography (eluent Et_2O/pentane, 4:6), (4*S*,2′*S*,3′*R*)-**20** (3.20 g, 86%, >98% de) and (4*S*,2′*R*,3′*S*)-**51** (342 mg, 9%, >98% de) as colourless oils.

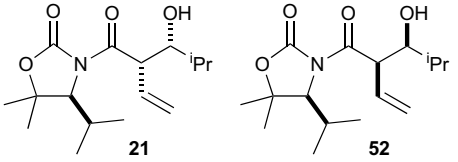
Data for (4*S*,2′*S*,3′*R*)-**20**. $[\alpha]_D^{24}$ −44 (*c* 1.0, $CHCl_3$); ν_{max} (film) 3518 (O–H), 1775 (C=O, exocyclic), 1692 (C=O, endocyclic), 1635 (C=C); δ_H (400 MHz, $CDCl_3$) 0.92 (3H, d, *J* 6.9, CH(CH_3)$_A$(CH$_3$)$_B$), 0.97 (3H, d, *J* 7.6, C(5′)H_3), 0.99 (3H, d, *J* 6.9, CH(CH$_3$)$_A$(CH_3)$_B$), 1.40 (3H, s, C(CH_3)$_A$(CH$_3$)$_B$), 1.43–1.59 (2H, m, C(4′)H_2), 1.51 (3H, s, C(CH$_3$)$_A$(CH_3)$_B$), 2.13 (1H, septd, *J* 6.9, 3.1, C*H*(CH$_3$)$_2$), 3.11 (1H, br s, O*H*), 3.83–3.89 (1H, m, C(3′)*H*), 4.21 (1H, d, *J* 3.1, C(4)*H*), 4.66 (1H, dd, *J* 9.1, 3.7, C(2′)*H*), 5.38 (1H, dd, *J* 10.2, 1.4, CH=C*H*$_A$H$_B$), 5.48 (1H, dd, *J* 17.3, 1.4, CH=CH$_A$*H*$_B$), 5.98 (1H, ddd, *J* 17.3, 10.2, 9.1, C*H*=CH$_2$); δ_C (100 MHz, $CDCl_3$) 10.1 (*C*(5′)H$_3$), 16.6, 21.3, 21.5, 28.8 (C(*C*H$_3$)$_2$, CH(*C*H$_3$)$_2$), 26.9 (*C*(4′)H$_2$), 29.8

(*C*H(CH$_3$)$_2$), 51.6 (*C*(2′)H), 66.0 (*C*(4)H), 73.0 (*C*(3′)H), 82.7 (*C*(CH$_3$)$_2$), 121.6 (CH=*C*H$_2$), 131.6 (*C*H=CH$_2$), 153.0 (*C*(2)), 175.0 (*C*(1′)); *m*/*z* (APCI$^+$) 284 ([M+H]$^+$, 5%), 266 ([M−OH]$^+$, 20), 158 ([SQ+H]$^+$, 100); HRMS (CI$^+$) $C_{15}H_{26}NO_4^+$ ([M+H]$^+$) requires 284.1856; found 284.1856.

Data for (4*S*,2′*R*,3′*S*)-**51**. ν_{max} (film) 3515 (O–H), 1775 (C=O, exocyclic), 1693 (C=O, endocyclic), 1635 (C=C); δ_H (400 MHz, CDCl$_3$) 0.98 (3H, d, *J* 7.0, CH(C*H*$_3$)$_A$(CH$_3$)$_B$), 1.00 (3H, t, *J* 7.4, C(5′)*H*$_3$), 1.05 (3H, d, *J* 7.0, CH(CH$_3$)$_A$(C*H*$_3$)$_B$), 1.34 (3H, s, C(C*H*$_3$)$_A$(CH$_3$)$_B$), 1.43–1.59 (2H, m, C(4′)*H*$_2$), 1.51 (3H, s, C(CH$_3$)$_A$(C*H*$_3$)$_B$), 2.16 (1H, septd, *J* 7.0, 3.3, C*H*(CH$_3$)$_2$), 3.05 (1H, d, *J* 2.7, O*H*), 3.92–3.97 (1H, m, C(3′)*H*), 4.13 (1H, d, *J* 3.3, C(4)*H*), 4.63 (1H, dd, *J* 9.3, 3.6, C(2′)*H*), 5.30 (1H, d, *J* 17.2, CH=C*H*$_A$H$_B$), 5.32 (1H, d, *J* 10.2, CH=CH$_A$*H*$_B$), 5.97 (1H, ddd, *J* 17.2, 10.2, 9.3, C*H*=CH$_2$); δ_C (100 MHz, CDCl$_3$) 10.0 (*C*(5′)H$_3$), 17.0, 21.3, 21.5, 21.5 (C(*C*H$_3$)$_2$, CH(*C*H$_3$)$_2$), 27.0 (*C*(4′)H$_2$), 29.5 (*C*H(CH$_3$)$_2$), 51.6 (*C*(2′)H), 66.7 (*C*(4)H), 73.4 (*C*(3′)H), 83.1 (*C*(CH$_3$)$_2$), 121.1 (CH=*C*H$_2$), 131.2 (*C*H=CH$_2$), 153.3 (*C*(2)), 174.6 (*C*(1′)); *m*/*z* (APCI$^+$) 284 ([M+H]$^+$, 7%), 266 ([M−OH]$^+$, 23), 158 ([SQ+H]$^+$, 100); HRMS (CI$^+$) $C_{15}H_{26}NO_4^+$ ([M+H]$^+$) requires 284.1856; found 284.1858.

Method B. Following *general procedure 2*, **6** (500 mg, 1.95 mmol) gave, after purification by flash column chromatography (eluent Et$_2$O/pentane, 4:6), **20** as colourless oil (348 g, 66%, >98% de); $[\alpha]_D^{24}$ −44 (*c* 1.0, CHCl$_3$).

4.7.5. (4*S*,2′*S*,3′*R*)- and (4*S*,2′*R*,3′*S*)-N(3)-(2′-Vinyl-3′-hydroxy-4′-methylpentanoyl)-4-isopropyl-5,5-dimethyl-oxazolidin-2-one (4*S*,2′*S*,3′*R*)-***21*** and (4*S*,2′*R*,3′*S*)-***52***



Method A. Following *general procedure 1*, **6** (500 mg, 2.22 mmol) gave, after purification by flash column chromatography (eluent Et$_2$O/pentane, 3:7), (4*S*,2′*S*,3′*R*)-**21** (575 mg, 88%, >98% de) and (4*S*,2′*R*,3′*S*)-**52** (31 mg, 5%, >98% de) as white crystalline solids.

Data for (4*S*,2′*S*,3′*R*)-**21**. Found: C, 64.6; H, 9.4; N, 4.8%; $C_{16}H_{27}NO_4$ requires C, 64.6, H, 9.15, N, 4.7%; mp 46–47 °C; $[\alpha]_D^{26}$ −53.2 (*c* 1.0, CHCl$_3$); ν_{max} (KBr disc) 3510 (O–H), 1762 (C=O, endocyclic), 1686 (C=O, exocyclic), 1631 (C=C); δ_H (400 MHz, CDCl$_3$) 0.90 (6H, app t, *J* 6.7, C(4)H(C*H*$_3$)$_2$), 0.96 (6H, app d, *J* 7.0, C(4′)H(CH$_3$)$_2$), 1.37 (3H, s, C(C*H*$_3$)$_A$(CH$_3$)$_B$), 1.49 (3H, s, C(CH$_3$)$_A$(C*H*$_3$)$_B$), 1.68 (1H, app octet, *J* 6.7, C(4)C*H*(CH$_3$)$_2$), 2.10 (1H, septd, *J* 7.0, 3.1, C(4′)*H*), 3.14 (1H, d, *J* 2.3, O*H*), 3.58–3.62 (1H, m, C(3′)*H*), 4.18 (1H, d, *J* 3.1, C(4)*H*), 4.82 (1H, dd, *J* 9.1, 4.0, C(2′)*H*), 5.35 (1H, dd, *J* 10.2, 1.4, CH=C*H*$_A$H$_B$), 5.48 (1H, dd, *J* 17.3, 1.4, CH=CH$_A$*H*$_B$), 5.97 (1H, ddd, *J* 17.3, 10.2, 9.1, C*H*=CH$_2$); δ_C (100 MHz, CDCl$_3$) 14.0, 16.6, 19.0, 21.0, 21.3, 28.7, (C(*C*H$_3$)$_2$, C(4)CH(*C*H$_3$)$_2$, C(4′)H(*C*H$_3$)$_2$), 30.0, 30.9 (C(4)*C*H(CH$_3$)$_2$, *C*(4′)H), 49.6 (*C*(2′)H), 65.9 (*C*(4)H), 76.3 (*C*(3′)H), 82.7 (*C*(CH$_3$)$_2$), 121.3 (CH=*C*H$_2$), 131.9 (*C*H=CH$_2$), 152.9 (*C*(2)), 175.1 (*C*(1′)); *m*/*z* (GC Tof CI$^+$) 298 ([M+H]$^+$, 11%), 280 ([M−OH]$^+$, 76).

Data for (4*S*,2′*R*,3′*S*)-**52**. Found: C, 64.6; H, 9.15; N, 4.7%; $C_{16}H_{27}NO_4$ requires C, 64.6, H, 9.15, N, 4.7%; mp 102–103 °C; $[\alpha]_D^{22}$ +115 (*c* 1.0, CHCl$_3$); ν_{max} (KBr disc) 3579 (O–H), 1770 (C=O, endocyclic), 1686 (C=O, exocyclic), 1646 (C=C); δ_H (400 MHz, CDCl$_3$) 0.94–1.00 (9H, m, C(4)CH(C*H*$_3$)$_A$, C(4′)H(C*H*$_3$)$_2$), 1.04 (3H, d, *J* 6.9, C(4)CH(C*H*$_3$)$_B$), 1.32 (3H, s, C(C*H*$_3$)$_A$(CH$_3$)$_B$), 1.50 (3H, s, CH(CH$_3$)$_A$(C*H*$_3$)$_B$), 1.80 (1H, septd, *J* 7.3, 4.0, C(4′)*H*), 2.14 (1H, septd, *J* 6.9, 3.2, C(4)C*H*(CH$_3$)$_2$), 2.75 (1H, d, *J* 2.3, O*H*), 3.68 (1H, td, *J* 8.6, 4.0, C(3′)*H*), 4.11 (1H, d, *J* 3.2, C(4)*H*), 4.75 (1H, app t, *J* 8.6, C(2′)*H*), 5.18 (1H, dd, *J* 9.9, 1.1, CH=C*H*$_A$H$_B$), 5.23 (1H, dd, *J* 17.2, 1.1, CH=CH$_A$*H*$_B$), 5.89 (1H, ddd, *J* 17.2, 9.9, 8.6, C*H*=CH$_2$); δ_C (100 MHz, CDCl$_3$) 15.3, 16.9, 19.9, 21.2, 21.6, 28.6 (C(*C*H$_3$)$_2$, C(4)CH(*C*H$_3$)$_2$, C(4′)H(*C*H$_3$)$_2$), 29.6, 30.4 (C(4)*C*H(CH$_3$)$_2$, *C*(4′)H), 50.9 (*C*(2′)H), 66.9 (*C*(4)H), 77.9 (*C*(3′)H), 83.1 (*C*(CH$_3$)$_2$), 119.0 (CH=*C*H$_2$), 133.9 (*C*H=CH$_2$), 153.9 (*C*(2)), 174.4 (*C*(1′)); *m*/*z* (APCI$^+$) 298 ([M+H]$^+$, 10%), 280 ([M−OH]$^+$, 34), 158 ([SQ+H]$^+$, 100).

Method B. Following *general procedure 2*, **6** (500 mg, 2.22 mmol) gave, after purification by flash column chromatography (eluent Et$_2$O/pentane, 3:7), **21** as a white solid (372 mg, 57%, >98% de); mp 46–47 °C; $[\alpha]_D^{26}$ −54.8 (*c* 1.0, CHCl$_3$).

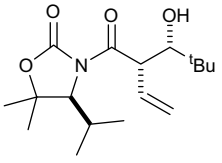
4.7.5.1. *X-ray crystal structure determination for* ***52***.

Data were collected using an Enraf-Nonius κ-CCD diffractometer with graphite monochromated Mo Kα radiation using standard procedures at 190 K. The structure was solved by direct methods (SIR92); all non-hydrogen atoms were refined with anisotropic thermal parameters. Hydrogen atoms were added at idealised positions. The structure was refined using CRYSTALS.[36]

X-ray crystal structure data for **52** [$C_{16}H_{27}NO_4$]: *M*=297.39, orthorhombic, space group $P2_12_12_1$, *a*=7.9367(1) Å, *b*=11.1016(2) Å, *c*=19.1260(5) Å, *V*=1685.2(12) Å^3, *Z*=4, μ=0.083 mm^{-1}, colourless plate, crystal dimensions=0.2×0.2×0.2 mm^3. A total of 2205 unique reflections were measured for $5<\theta<27$ and 1936 reflections were used in the refinement. The final parameters were wR_2=0.025 and R_1=0.031 [$I>3.0\sigma(I)$].

Crystallographic data (excluding structure factors) has been deposited with the Cambridge Crystallographic Data Centre as supplementary publication number CCDC 720191. Copies of the data can be obtained, free of charge, on application to CCDC, 12 Union Road, Cambridge CB2 1EZ, UK [fax: +44(0) 1223 336033 or e-mail: deposit@ccdc.cam.ac.uk].

4.7.6. (4*S*,2′*R*,3′*S*)-N(3)-(2′-Vinyl-3′-hydroxy-4′,4′-dimethylpentanoyl)-4-isopropyl-5,5-dimethyl-oxazolidin-2-one ***22***



Following *general procedure 1*, **6** (500 mg, 2.22 mmol) gave, after purification by flash column chromatography (eluent Et$_2$O/pentane, 3:7) **22** as a white crystalline solid (274 mg, 40%, >98% de); Found: C, 65.6; H, 9.4; N, 4.55%; $C_{17}H_{29}NO_4$ requires C, 65.6, H, 9.4, N, 4.5%; mp 64–66 °C; $[\alpha]_D^{27}$ −75.0 (*c* 1.0, CHCl$_3$); ν_{max} (film) 3523 (O–H), 1774 (C=O, exocyclic), 1693 (C=O, endocyclic), 1632 (C=C); δ_H (400 MHz, CDCl$_3$) 0.92 (3H, d, *J* 6.9, CH(C*H*$_3$)$_A$(CH$_3$)$_B$), 0.95 (9H, s, C(C*H*$_3$)$_3$), 0.97 (3H, d, *J* 6.9, CH(CH$_3$)$_A$(C*H*$_3$)$_B$), 1.39 (3H, s, C(C*H*$_3$)$_A$(CH$_3$)$_B$), 1.51 (3H, s, C(CH$_3$)$_A$(C*H*$_3$)$_B$), 2.12 (1H, septd, *J* 6.9, 3.0, C*H*(CH$_3$)$_2$), 2.82 (1H, d, *J* 3.2, O*H*), 3.73 (1H, dd, *J* 4.4, 3.2, C(3′)*H*), 4.21 (1H, d, *J* 3.0, C(4)*H*), 5.07 (1H, dd, *J* 9.4, 4.4, C(2′)*H*), 5.34 (1H, d, *J* 9.4, CH=C*H*$_A$H$_B$), 5.54 (1H, d, *J* 17.2, CH=CH$_A$*H*$_B$), 6.04 (1H, app dt, *J*, 9.4, 17.2, C*H*=CH$_2$); δ_C (100 MHz, CDCl$_3$) 16.5, 21.3, 21.4, 28.8 (C(*C*H$_3$)$_2$, CH(*C*H$_3$)$_2$), 26.5 (*C*(CH$_3$)$_3$), 30.0 (*C*H(CH$_3$)$_2$), 35.6 (C(*C*H$_3$)$_3$), 48.5 (*C*(2′)H), 65.8 (*C*(4)H), 77.7 (*C*(3′)H), 82.5 (*C*(CH$_3$)$_2$), 120.8 (CH=*C*H$_2$), 133.7 (*C*H=CH$_2$), 153.0 (*C*(2)), 175.2 (*C*(1′)); *m*/*z* (APCI$^+$) 312 ([M+H]$^+$, 3%), 158 ([SQ+H]$^+$, 100).

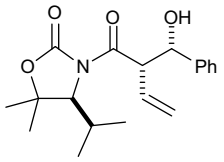
4.7.6.1. *X-ray crystal structure determination for* ***22***.

Data were collected using an Enraf-Nonius κ-CCD diffractometer with graphite monochromated Mo Kα radiation using standard procedures at 190 K. The structure was solved by direct methods (SIR92); all non-hydrogen atoms were refined with anisotropic thermal parameters. Hydrogen atoms were added at idealised positions. The structure was refined using CRYSTALS.[36]

X-ray crystal structure data for **22** [$C_{34}H_{58}N_2O_8$]: M=622.84, orthorhombic, space group $P2_12_12_1$, a=10.4670(1) Å, b=11.0940(1) Å, c=31.2650(4) Å, V=3630.5(12) Å^3, Z=4, μ=0.080 mm^{-1}, colourless plate, crystal dimensions=0.3×0.4×0.5 mm^3. A total of 4380 unique reflections were measured for $5<\theta<27$ and 3352 reflections were used in the refinement. The final parameters were wR_2=0.033 and R_1=0.030 [$I>3.0\sigma(I)$].

Crystallographic data (excluding structure factors) has been deposited with the Cambridge Crystallographic Data Centre as supplementary publication number CCDC 720190. Copies of the data can be obtained, free of charge, on application to CCDC, 12 Union Road, Cambridge CB2 1EZ, UK [fax: +44(0) 1223 336033 or e-mail: deposit@ccdc.cam.ac.uk].

4.7.7. (4S,2′R,3′S)-N(3)-(2′-Vinyl-3′-hydroxy-3′-phenylpropanoyl)-4-isopropyl-5,5-dimethyl-oxazolidin-2-one ***23***



Method A. Following *general procedure 1*, **6** (3.00 g, 13.2 mmol) gave, after purification by flash column chromatography (eluent Et_2O/pentane, 1:1), **23** as a white crystalline solid (4.14 g, 95%, >98% de); Found: C, 68.9; H, 7.6; N, 4.2%; $C_{19}H_{25}NO_4$ requires C, 68.9, H, 7.6, N, 4.2%; mp 99–101 °C; $[\alpha]_D^{27}$ −41 (c 1.0, $CHCl_3$); ν_{max} (film) 3487 (O–H), 1779 (C=O, exocyclic), 1667 (C=O, endocyclic), 1639 (C=C); δ_H (400 MHz, $CDCl_3$) 0.86 (3H, s, C(CH_3)$_A$(CH$_3$)$_B$), 0.87 (3H, d, J 7.0, CH(CH_3)$_A$(CH$_3$)$_B$), 0.96 (3H, d, J 7.0, CH(CH$_3$)$_A$(CH_3)$_B$), 1.41 (3H, s, C(CH_3)$_A$(CH$_3$)$_B$), 2.05 (1H, dsept, J 7.0, 3.4, CH(CH$_3$)$_2$), 2.78 (1H, d, J 2.3, OH), 3.94 (1H, d, J 3.4, C(4)H), 5.01 (1H, d, J 7.5, 2.3, C(3′)H), 5.09 (1H, dd, J 9.0, 7.5, C(2′)H), 5.40 (1H, dd, J 10.0, CH=CH_AH$_B$), 5.51 (1H, dd, J 17.4, CH=CH$_A$$H_B$), 6.03 (1H, ddd, J 17.4, 10.0, 9.0, CH=CH$_2$), 7.24–7.40 (5H, m, *Ph*); δ_C (100 MHz, $CDCl_3$) 16.7, 21.2, 21.4, 27.8 (C(CH_3)$_2$, CH(CH_3)$_2$), 29.6 (CH(CH$_3$)$_2$), 55.1 (C(2′)H), 65.9 (C(4)H), 74.5 (C(3′)H), 82.6 (C(CH$_3$)$_2$), 121.9 (CH=CH_2), 127.1 (*p-Ph*), 128.0, 128.4 (*o,m-Ph*), 133.1 (*i-Ph*), 140.7 (CH=CH$_2$), 152.9 (C(2)), 172.9 (C(1′)); m/z (APCI$^+$) 331 ([M]$^+$, 3%); HRMS (CI$^+$) $C_{19}H_{25}NNaO_4^+$ ([M+Na]$^+$) requires 354.1676; found 354.1681.

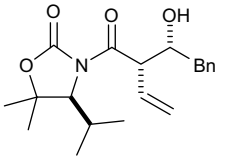
Method B. Following *general procedure 2*, **6** (500 mg, 2.22 mmol) gave, after purification by flash column chromatography (eluent Et_2O/pentane, 1:1), **23** as a white crystalline solid (571 mg, 78%, >98% de); mp 99–101 °C; $[\alpha]_D^{27}$ −41 (c 1.0, $CHCl_3$).

4.7.7.1. X-ray crystal structure determination for ***23****.* Data were collected using an Enraf-Nonius κ-CCD diffractometer with graphite monochromated Mo Kα radiation using standard procedures at 190 K. The structure was solved by direct methods (SIR92); all non-hydrogen atoms were refined with anisotropic thermal parameters. Hydrogen atoms were added at idealised positions. The structure was refined using CRYSTALS.[36]

X-ray crystal structure data for **23** [$C_{19}H_{25}NO_4$]: M=331.41, tetragonal, space group $P4_12_12$, a=8.8433(1) Å, b=8.8433(1) Å, c=46.7682(4) Å, V=3657.46(7) Å^3, Z=8, μ=0.084 mm^{-1}, colourless plate, crystal dimensions=0.2×0.2×0.2 mm^3. A total of 2528 unique reflections were measured for $5<\theta<27$ and 1796 reflections were used in the refinement. The final parameters were wR_2=0.034 and R_1=0.030 [$I>3.0\sigma(I)$].

Crystallographic data (excluding structure factors) has been deposited with the Cambridge Crystallographic Data Centre as supplementary publication number CCDC 720193. Copies of the data can be obtained, free of charge, on application to CCDC, 12 Union Road, Cambridge CB2 1EZ, UK [fax: +44(0) 1223 336033 or e-mail: deposit@ccdc.cam.ac.uk].

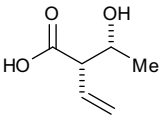
4.7.8. (4S,2′R,3′S)-N(3)-(2′-Vinyl-3′-hydroxy-4′-phenylbutanoyl)-4-isopropyl-5,5-dimethyl-oxazolidin-2-one ***24***



Method A. Following *general procedure 1*, **6** (3.00 g, 13.2 mmol) gave, after purification by flash column chromatography (eluent Et_2O/pentane, 1:1), **24** as a colourless oil (4.24 g, 95%, >98% de); $[\alpha]_D^{24}$ −21.6 (c 1.0, $CHCl_3$); ν_{max} (film) 3520 (O–H), 1770 (C=O, exocyclic), 1694 (C=O, endocyclic), 1633 (C=C); δ_H (400 MHz, $CDCl_3$) 0.92 (3H, d, J 6.8, CH(CH_3)$_A$(CH$_3$)$_B$), 1.00 (3H, d, J 6.8, CH(CH$_3$)$_A$(CH_3)$_B$), 1.39 (3H, s, C(CH_3)$_A$(CH$_3$)$_B$), 1.52 (3H, s, C(CH$_3$)$_A$(CH_3)$_B$), 1.70–1.73 (1H, m, C(4′)H_A), 1.83–1.87 (1H, m, C(4′)H_B), 2.13 (1H, septd, J 6.8, 3.0, CH(CH$_3$)$_2$), 3.30 (1H, s, OH), 3.97–4.01 (1H, m, C(3′)H), 4.21 (1H, d, J 3.0, C(4)H), 4.65 (1H, dd, J 8.9, 3.2, C(2′)H), 5.40 (1H, dd, J 10.3, 1.4, CH=CH_AH$_B$), 5.50 (1H, dd, J 17.3, 1.4, CH=CH$_A$$H_B$), 6.00 (1H, ddd, J 17.3, 10.3, 8.9, CH=CH$_2$), 7.23–7.35 (5H, m, *Ph*); δ_C (50 MHz, $CDCl_3$) 16.7, 21.3, 21.5, 28.8 (C(CH$_3$)$_2$, CH(CH_3)$_2$), 29.9 (CH(CH$_3$)$_2$), 35.6 (C(4′)H$_2$), 52.0 (C(2′)H), 66.0 (C(4)H), 70.7 (C(3′)H), 82.8 (C(CH$_3$)$_2$), 121.8 (CH=CH_2), 125.8 (*p-Ph*), 128.3, 128.5 (*o,m-Ph*), 131.4 (*i-Ph*), 141.8 (CH=CH$_2$), 153.0 (C(2)), 175.0 (C(1′)); m/z (ESI$^+$) 382 ([M+Na]$^+$, 100%); HRMS (ESI$^+$) $C_{20}H_{27}NNaO_4^+$ ([M+Na]$^+$) requires 368.1832; found 368.1843.

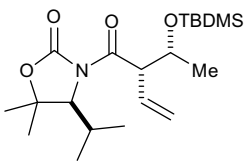
Method B. Following *general procedure 2*, **6** (500 mg, 2.22 mmol) gave, after purification by flash column chromatography (eluent Et_2O/pentane, 1:1), **24** as a colourless oil (487 mg, 64%, >98% de); $[\alpha]_D^{24}$ −22 (c 1.0, $CHCl_3$).

4.7.9. (2S,3R)-2-Vinyl-3-hydroxybutanoic acid ***26***



Following *general procedure 4*, **15** (200 mg, 0.52 mmol) gave, after purification by flash column chromatography (eluent $CHCl_3$/MeOH, 1:10), **26** as a colourless oil (39 mg, 42%, >98% de, >98% ee);[37] $[\alpha]_D^{24}$ −2.2 (c 0.2, MeOH); δ_H (400 MHz, $CDCl_3$) 1.23 (3H, d, J 6.4, C(4)H_3), 3.07 (1H, dd, J 9.2, 4.5, C(2)H), 4.14–4.19 (1H, m, C(3)H), 5.30 (1H, d, J 17.2, CH=CH_AH$_B$), 5.37 (1H, d, J 9.9, CH=CH$_A$$H_B$), 5.95 (1H, app dt, J 17.2, 9.9, CH=CH$_2$); δ_C (100 MHz, $CDCl_3$) 19.9 (C(4)H$_3$), 56.7 (C(2)H), 67.6 (C(3)H), 121.0 (CH=CH$_2$), 131.1 (CH=CH$_2$), 177.4 (C(1)); m/z (ESI$^-$) 129 ([M−H]$^-$, 100%); HRMS (ESI$^-$) $C_6H_9O_3^-$ ([M−H]$^-$) requires 129.0557; found 129.0554.

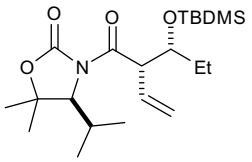
4.7.10. (4S,2′R,3′S)-N(3)-[2′-Vinyl-3′-(tert-butyldimethylsilyloxy)-butanoyl]-4-iso-propyl-5,5-dimethyl-oxazolidin-2-one ***27***



Following *general procedure 3*, **15** (2.00 g, 7.42 mmol) gave **27** as a pale yellow oil (2.76 g, 97%, >98% de); $[\alpha]_D^{23}$ −3.5 (c 1.0, $CHCl_3$); ν_{max} (film) 1778 (C=O, exocyclic), 1694 (C=O, endocyclic), 1638

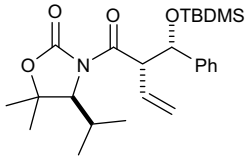
(C=C); δ_H (400 MHz, $CDCl_3$) 0.03 (3H, s, Si(CH_3)$_A$), 0.05 (3H, s, Si(CH_3)$_B$), 0.85 (9H, s, C(CH_3)$_3$), 0.92 (3H, d, *J* 7.0, CH(CH_3)$_A$(CH_3)$_B$), 1.00 (3H, d, *J* 7.0, CH(CH_3)$_A$(CH_3)$_B$), 1.18 (3H, d, *J* 6.5, C(4′)H_3), 1.34 (3H, s, C(CH_3)$_A$(CH_3)$_B$), 1.50 (3H, s, C(CH_3)$_A$(CH_3)$_B$), 2.13 (1H, septd, *J* 7.0, 3.2, C*H*(CH_3)$_2$), 4.13 (1H, app quintet, *J* 6.5, C(3′)*H*), 4.17 (1H, d, *J* 3.2, C(4)*H*), 4.65 (1H, dd, *J* 8.8, 6.5, C(2′)*H*), 5.23 (1H, dd, *J* 10.2, 1.4, CH=CH_AH$_B$), 5.31 (1H, app d, *J* 17.2, CH=CH$_A$$H_B$), 5.94 (1H, ddd, *J* 17.2, 10.2, 8.8, C*H*=CH$_2$); δ_C (100 MHz, $CDCl_3$) −4.7, −4.5 (Si(CH_3)$_2$), 16.8, 21.3, 21.4, 28.7 (C(CH_3)$_2$, CH(CH_3)$_2$), 21.8 (*C*(4′)H$_3$), 25.8 (C(CH_3)$_3$), 29.7 (*C*H(CH_3)$_2$), 55.1 (*C*(2′)H), 66.2 (*C*(4)H), 70.1 (*C*(3′)H), 82.4 (*C*(CH_3)$_2$), 119.2 (CH=*C*H$_2$), 134.8 (*C*H=CH$_2$), 153.1 (*C*(2)), 173.1 (*C*(1′)); *m*/*z* (GC Tof CI$^+$) 384 ([M+H]$^+$, 32%), 252 ([M−C$_6$H$_{15}$OSi]$^+$, 34), 158 ([SQ+H]$^+$, 85); HRMS (GC Tof CI$^+$) $C_{20}H_{38}NO_4Si^+$ ([M+H]$^+$) requires 384.2565; found 384.2579.

4.7.11. (4S,2′R,3′S)-N(3)-[2′-Vinyl-3′-(tert-butyldimethylsilyloxy)-pentanoyl]-4-isopropyl-5,5-dimethyl-oxazolidin-2-one ***28***



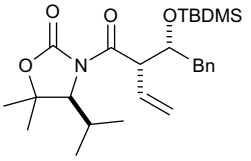
Following *general procedure 3*, **20** (200 mg, 0.74 mmol) gave **28** as a colourless wax (288 mg, 98%, >98% de); $[\alpha]_D^{21}$ −7.6 (*c* 1.0, $CHCl_3$); ν_{max} (film) 1778 (C=O, exocyclic), 1695 (C=O, endocyclic), 1636 (C=C); δ_H (400 MHz, $CDCl_3$) 0.03 (3H, s, Si(CH_3)$_A$), 0.05 (3H, s, Si(CH_3)$_B$), 0.88 (9H, s, C(CH_3)$_3$), 0.89 (3H, t, *J* 7.5, C(5′)H_3), 0.92 (3H, d, *J* 7.0, CH(CH_3)$_A$(CH_3)$_B$), 1.01 (3H, d, *J* 7.0, CH(CH_3)$_A$(CH_3)$_B$), 1.39 (3H, s, C(CH_3)$_A$(CH_3)$_B$), 1.51 (3H, s, C(CH_3)$_A$(CH_3)$_B$), 1.54–1.65 (2H, m, C(4′)H_2), 2.14 (1H, septd, *J* 7.0, 3.2, C*H*(CH_3)$_2$), 4.08 (1H, dt, *J* 7.3, 5.0, C(3′)*H*), 4.16 (1H, d, *J* 3.2, C(4)*H*), 4.71 (1H, dd, *J* 8.9, 7.3, C(2′)*H*), 5.24 (1H, dd, *J* 10.2, 1.6, CH=CH_AH$_B$), 5.38 (1H, dd, *J* 17.2, 1.6, CH=CH$_A$$H_B$), 5.97 (1H, ddd, *J* 17.2, 10.2, 8.9, C*H*=CH$_2$); δ_C (100 MHz, $CDCl_3$) −4.2, −4.2 (Si(CH_3)$_2$), 8.6 (*C*(5′)H$_3$), 16.8, 21.4, 21.4, 28.7 (C(CH_3)$_2$, CH(CH_3)$_2$), 18.1 (*C*(CH_3)$_3$), 25.9 (C(CH_3)$_3$), 28.2 (*C*(4′)H$_2$), 29.8 (*C*H(CH_3)$_2$), 52.6 (*C*(2′)H), 66.2 (*C*(4)H), 73.7 (*C*(3′)H), 82.4 (*C*(CH_3)$_2$), 119.4 (CH=*C*H$_2$), 135.1 (*C*H=CH$_2$), 153.0 (*C*(2)), 175.2 (*C*(1′)); *m*/*z* (GC Tof CI$^+$) 398 ([M+H]$^+$, 100%), 266 ([M−C$_6$H$_{15}$OSi]$^+$, 90); HRMS (GC Tof CI$^+$) $C_{21}H_{40}NO_4Si^+$ ([M+H]$^+$) requires 398.2721; found 398.2740.

4.7.12. (4S,2′R,3′S)-N(3)-[2′-Vinyl-3′-(tert-butyldimethylsilyloxy)-3′-phenylpropanoyl]-4-isopropyl-5,5-dimethyl-oxazolidin-2-one ***31***



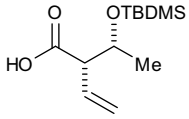
Following *general procedure 3*, **23** (100 mg, 0.35 mmol) gave **31** as a colourless wax (56 mg, 40%, >98% de); $[\alpha]_D^{21}$ −22.1 (*c* 0.9, $CHCl_3$); ν_{max} (film) 1781 (C=O, exocyclic), 1694 (C=O, endocyclic); δ_H (400 MHz, $CDCl_3$) −0.25 (3H, s, Si(CH_3)$_A$), 0.01 (3H, s, Si(CH_3)$_B$), 0.59 (3H, s, C(CH_3)$_A$(CH_3)$_B$), 0.81 (9H, s, C(CH_3)$_3$), 0.85 (3H, d, *J* 6.9, CH(CH_3)$_A$(CH_3)$_B$), 0.94 (3H, d, *J* 6.9, CH(CH_3)$_A$(CH_3)$_B$), 1.34 (3H, s, C(CH_3)$_A$(CH_3)$_B$), 2.00 (1H, septd, *J* 6.9, 3.4, C*H*(CH_3)$_2$), 3.80 (1H, d, *J* 3.4, C(4)*H*), 4.92 (1H, d, *J* 9.2, C(3′)*H*), 5.09 (1H, app t, *J* 8.5, C(2′)*H*), 5.29 (1H, dd, *J* 10.1, 1.5, CH=CH_AH$_B$), 5.43 (1H, dd, *J* 17.3, 1.5, CH=CH$_A$$H_B$), 6.02 (1H, ddd, *J* 17.3, 10.1, 8.5, C*H*=CH$_2$), 7.15–7.35 (5H, m, *Ph*); δ_C (100 MHz, $CDCl_3$) −4.9, −4.7 (Si(CH_3)$_2$), 16.8, 21.1, 21.4, 27.3 (C(CH_3)$_2$, CH(CH_3)$_2$), 18.3 (*C*(CH_3)$_3$), 25.6 (C(CH_3)$_3$), 29.5 (*C*H(CH_3)$_2$), 56.4 (*C*(2′)H), 65.8 (*C*(4)H), 76.4 (*C*(3′)H), 82.2 (*C*(CH_3)$_2$), 119.6 (CH=*C*H$_2$), 127.5 (*p*-*Ph*), 127.6, 128.0 (*o*,*m*-*Ph*), 135.1 (*i*-*Ph*), 142.7 (*C*H=CH$_2$), 152.8 (*C*(2)), 172.4 (*C*(1′)); *m*/*z* (ESI$^+$) 446 ([M+H]$^+$, 100%); HRMS (ESI$^+$) $C_{25}H_{39}NNaO_4Si^+$ ([M+Na]$^+$) requires 468.2541; found 468.2563.

4.7.13. (4S,2′R,3′S)-N(3)-[2′-Vinyl-3′-(tert-butyldimethylsilyloxy)-4′-phenylbutanoyl]-4-isopropyl-5,5-dimethyl-oxazolidin-2-one ***32***



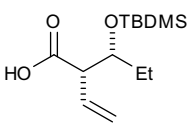
Following *general procedure 3*, **24** (200 mg, 0.56 mmol) gave **32** as a colourless wax (253 mg, 96%, >98% de); $[\alpha]_D^{24}$ −20.0 (*c* 1.0, $CHCl_3$); ν_{max} (film) 1770 (C=O, exocyclic), 1694 (C=O, endocyclic), 1635 (C=C); δ_H (400 MHz, $CDCl_3$) 0.06 (3H, s, Si(CH_3)$_A$), 0.08 (3H, s, Si(CH_3)$_B$), 0.91 (9H, s, C(CH_3)$_3$), 0.93 (3H, d, *J* 6.9, CH(CH_3)$_A$(CH_3)$_B$), 1.01 (3H, d, *J* 6.9, CH(CH_3)$_A$(CH_3)$_B$), 1.36 (3H, s, C(CH_3)$_A$(CH_3)$_B$), 1.51 (3H, s, C(CH_3)$_A$(CH_3)$_B$), 1.75–1.95 (2H, m, C(4′)H_2), 2.14 (1H, septd, *J* 6.9, 3.0, C*H*(CH_3)$_2$), 4.18 (1H, d, *J* 3.0, C(4)*H*), 4.22 (1H, dt 7.1, 5.1, C(3′)*H*), 4.84 (1H, dd, *J* 9.0, 7.1, C(2′)*H*), 5.28 (1H, dd, *J* 10.1, 1.4, CH=CH_AH$_B$), 5.39 (1H, dd, *J* 17.3, 1.4, CH=CH$_A$$H_B$), 5.96 (1H, ddd, *J* 17.3, 10.1, 9.0, C*H*=CH$_2$), 7.23–7.34 (5H, m, *Ph*); δ_C (50 MHz, $CDCl_3$) −4.15, −4.1 (Si(CH_3)$_2$), 16.8, 21.4, 21.5, 28.8 (C(CH_3)$_2$, CH(CH_3)$_2$), 18.1 (*C*(CH_3)$_3$), 25.7 (C(CH_3)$_3$), 29.8 (*C*H(CH_3)$_2$), 37.6 (*C*(4′)H$_2$), 53.0 (*C*(2′)H), 66.1 (*C*(4)H), 72.7 (*C*(3′)H), 82.4 (*C*(CH_3)$_2$), 119.7 (CH=*C*H$_2$), 125.7 (*p*-*Ph*), 128.3, 128.4 (*o*,*m*-*Ph*), 135.0 (*i*-*Ph*), 142.4 (*C*H=CH$_2$), 153.0 (*C*(2)), 173.0 (*C*(1′)); *m*/*z* (APCI$^+$) 460 ([M+H]$^+$, 6%), 228 ([M−C$_6$H$_{15}$OSi]$^+$, 100); HRMS (CI$^+$) $C_{26}H_{42}NO_4Si^+$ ([M+H]$^+$) requires 460.2878; found 460.2880.

4.7.14. (2S,3R)-2-Vinyl-3-(tert-butyldimethylsilyloxy)butanoic acid ***33***



Following *general procedure 4*, **27** (200 mg, 0.52 mmol) gave, after purification by flash column chromatography (eluent Et_2O), **33** as a colourless oil (92 mg, 73%, >98% de, >98% ee); $[\alpha]_D^{21}$ +1.7 (*c* 1.1, $CHCl_3$); ν_{max} (film) 3300–2500 (O–H), 1712 (C=O), 1643 (C=C); δ_H (400 MHz, $CDCl_3$) 0.07 (3H, s, Si(CH_3)$_A$), 0.08 (3H, s, Si(CH_3)$_B$), 0.88 (9H, s, C(CH_3)$_3$), 1.18 (3H, d, *J* 6.3, C(4)H_3), 3.04 (1H, dd, *J* 9.4, 4.8, C(2)*H*), 4.23 (1H, dq, *J* 6.3, 4.8, C(3)*H*), 5.15 (1H, br d, *J* 17.4, CH=CH_AH$_B$), 5.28 (1H, dd, *J* 10.4, 1.5, CH=CH$_A$$H_B$), 5.94 (1H, ddd, *J* 17.4, 10.4, 9.4, C*H*=CH$_2$); δ_C (100 MHz, $CDCl_3$) −4.5, −4.1 (Si(CH_3)$_2$), 17.9 (*C*(4)H$_3$), 21.1 (*C*(CH_3)$_3$), 25.6 (C(CH_3)$_3$), 57.6 (*C*(2)H), 69.6 (*C*(3)H), 119.5 (CH=*C*H$_2$), 132.2 (*C*H=CH$_2$), 177.3 (*C*(1)); *m*/*z* (APCI$^-$) 243 ([M−H]$^-$, 6%), 129 ([M−C$_6$H$_{14}$Si]$^-$, 100); HRMS (ESI$^-$) $C_{12}H_{23}O_3Si^-$ ([M−H]$^-$) requires 243.1422; found 243.1417.

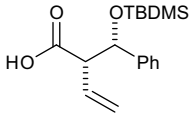
4.7.15. (2S,3R)-2-Vinyl-3-(tert-butyldimethylsilyloxy)pentanoic acid ***34***



Following *general procedure 4*, **28** (150 mg, 0.38 mmol) gave, after purification by flash column chromatography (eluent Et_2O), **34** as a colourless oil (83 mg, 85%, >98% de, >98% ee); $[\alpha]_D^{24}$ +4.2 (*c*

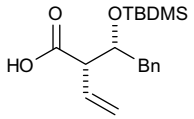
1.3, $CHCl_3$); ν_{max} (film) 3300–2500 (O–H), 1710 (C=O), 1642 (C=C); δ_H (400 MHz, $CDCl_3$) 0.07 (3H, t, *J* 5.0, C(5)H_3), 0.08 (3H, s, Si(CH_3)$_A$), 0.89 (9H, s, C(CH_3)$_3$), 0.90 (3H, s, Si(CH_3)$_B$), 1.53–1.56 (2H, m, C(4)H_2), 3.17 (1H, dd, *J* 9.2, 4.5, C(2)*H*), 4.01 (1H, dt, *J* 6.2, 4.5, C(3)*H*), 5.15 (1H, br d, *J* 17.3, CH=CH_AH$_B$), 5.27 (1H, dd, *J* 10.3, 1.6, CH=CH$_A$$H_B$), 5.96 (1H, ddd, *J* 17.3, 10.3, 9.2, C*H*=CH$_2$); δ_C (100 MHz, $CDCl_3$) −4.8, −4.4 (Si(CH_3)$_2$), 9.6 (*C*(5)H_3), 18.0 (*C*(CH_3)$_3$), 25.7 (C(CH_3)$_3$), 29.7 (*C*(4)H_2), 54.9 (*C*(2)H), 74.8 (*C*(3)H), 119.4 (CH=H_2), 132.1 (*C*H=CH$_2$), 177.3 (*C*(1)); *m*/*z* (APCI$^+$) 259 ([M+H]$^+$, 12%), 114 ([$C_6H_{14}Si$]$^+$, 100); HRMS (CI$^+$) $C_{13}H_{27}O_3Si^+$ ([M+H]$^+$) requires 259.1724; found 259.1719.

4.7.16. (2S,1′S)-2-Vinyl-3-(tert-butyldimethylsilyloxy)-3-phenylpropanoic acid **35**



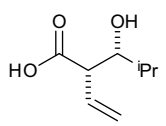
Following *general procedure 4*, **31** (100 mg, 0.32 mmol) gave, after purification by flash column chromatography (eluent Et_2O), **35** as a colourless oil (50 mg, 92%, >98% de, >98% ee); $[\alpha]_D^{24}$ +33.6 (*c* 1.0, $CHCl_3$); ν_{max} (film) 2600–3200 (O–H), 1710 (C=O), 1641 (C=C); δ_H (400 MHz, $CDCl_3$) −0.20 (3H, s, Si(CH_3)$_A$), 0.03 (3H, s, Si(CH_3)$_B$), 0.87 (9H, s, C(CH_3)$_3$), 3.26 (1H, dd, *J* 9.2, 5.7, C(2)*H*), 4.96 (1H, d, *J* 17.4, CH=CH_AH$_B$), 5.11 (1H, d, *J* 5.7, C(3)*H*), 5.18 (1H, app dd, *J* 10.3, 1.3, CH=CH$_A$$H_B$), 5.98 (1H, ddd, *J* 17.4, 10.3, 9.2, C*H*=CH$_2$), 7.24–7.30 (5H, m, *Ph*); δ_C (100 MHz, $CDCl_3$) −5.3, −4.7 (Si(CH_3)$_2$), 18.1 (*C*(CH_3)$_3$), 25.7 (C(CH_3)$_3$), 59.5 (*C*(2)H), 75.7 (*C*H=CH$_2$), 119.8 (CH=*C*H$_2$), 126.6 (*p*-*Ph*), 127.6, 127.9 (*o*,*m*-*Ph*), 128.0 (*p*-*Ph*), 141.8 (*C*H=CH$_2$), 177.7 (*C*(1)); *m*/*z* (ESI$^-$) 305 ([M−H]$^-$, 100%); HRMS (ESI$^-$) $C_{17}H_{25}O_3Si^-$ ([M−H]$^-$) requires 305.1578; found 305.1564.

4.7.17. (2S,3R)-2-Vinyl-3-(tert-butyldimethylsilyloxy)-4-phenylbutanoic acid **36**



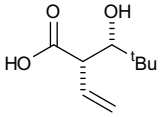
Following *general procedure 4*, **32** (200 mg, 0.56 mmol) gave, after purification by flash column chromatography (eluent Et_2O), **36** as a colourless oil (167 mg, 90%, >98% de, >98% ee); $[\alpha]_D^{23}$ +4.1 (*c* 1.0, $CHCl_3$); ν_{max} (film) 2500–3400 (O–H), 1709 (C=O), 1642 (C=C); δ_H (400 MHz, $CDCl_3$) 0.06 (3H, s, Si(CH_3)$_A$), 0.09 (3H, s, Si(CH_3)$_B$), 0.90 (9H, s, C(CH_3)$_3$), 1.83–1.88 (2H, m, C(4)H_2), 3.23 (1H, dd, *J* 9.4, 4.4, C(2)*H*), 4.17 (1H, dt, *J* 6.0, 4.4, C(3)*H*), 5.19 (1H, br d, *J* 17.4, CH=CH_AH$_B$), 5.32 (1H, dd, *J* 10.3, 1.3, CH=H$_A$$H_B$), 6.00 (1H, ddd, *J* 17.4, 10.3, 9.4, C*H*=CH$_2$), 7.16–7.31 (5H, m, *Ph*); δ_C (100 MHz, $CDCl_3$) −4.7, −4.4 (Si(CH_3)$_2$), 18.0 (*C*(CH_3)$_3$), 25.8 (C(CH_3)$_3$), 31.6 (*C*(4)H_2), 55.4 (*C*(2)H), 73.2 (*C*(3)H), 119.7 (CH=*C*H$_2$), 125.9 (*p*-*Ph*), 128.3, 128.4 (*o*,*m*-*Ph*), 128.4 (*i*-*Ph*), 141.6 (*C*(1′)H), 177.8 (*C*(1)); *m*/*z* (APCI$^-$) 333 ([M−H]$^-$, 5%), 131 ([$C_6H_{15}OSi$]$^-$, 100%); HRMS (ESI$^+$) $C_{18}H_{29}O_3Si^+$ ([M+H]$^+$) requires 321.1880; found 321.1882.

4.7.18. (2S,3R)-2-Vinyl-3-hydroxy-4-methylpentanoic acid **37**



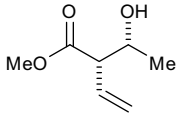
Following *general procedure 4*, **21** (200 mg, 0.67 mmol) gave, after purification by flash column chromatography (eluent Et_2O), **37** as a colourless oil (95 mg, 89%, >98% de, >98% ee); $[\alpha]_D^{24}$ −78.0 (*c* 1.0, $CHCl_3$); ν_{max} (film) 3420 (O–H), 3500–2500 (O–H), 1713 (C=O), 1637 (C=O); δ_H (400 MHz, $CDCl_3$) 0.93 (3H, d, *J* 7.0, CH(CH_3)$_A$(CH$_3$)$_B$), 1.01 (3H, d, *J* 7.0, CH(CH$_3$)$_A$(CH_3)$_B$), 1.73 (1H, app octet, *J* 6.8, C*H*(CH$_3$)$_2$), 3.28 (1H, dd, *J* 9.3, 4.5, C(2)*H*), 3.68 (1H, dd, *J* 7.0, 4.5, C(3)*H*), 5.31 (1H, dd, *J* 17.2, 1.3, CH=CH_AH$_B$), 5.36 (1H, dd, *J* 10.3, 1.3, CH=CH$_A$$H_B$), 5.97 (1H, ddd, *J* 17.2, 10.3, 9.3, C*H*=CH$_2$); δ_C (100 MHz, $CDCl_3$) 17.8, 19.0 (CH(*C*H$_3$)$_2$), 30.8 (*C*(4)H), 53.3 (*C*(2)H), 76.3 (*C*(3)H), 120.8 (CH=*C*H$_2$), 131.1 (*C*H=CH$_2$), 178.8 (*C*(1)); *m*/*z* (ESI$^-$) 157 ([M−H]$^-$, 100%); HRMS (ESI$^-$) $C_8H_{13}O_3^-$ ([M−H]$^-$) requires 157.0870; found 157.0862.

4.7.19. (2S,3R)-2-Vinyl-3-hydroxy-4,4-dimethylpentanoic acid **38**



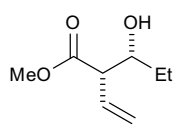
Following *general procedure 4*, **22** (100 mg, 0.32 mmol) gave, after purification by flash column chromatography (eluent Et_2O), **38** as a colourless oil (50 mg, 92%, >98% de, >98% ee); $[\alpha]_D^{24}$ −0.7 (*c* 0.9, $CHCl_3$); ν_{max} (film) 3700–3000 (O–H), 1682 (C=O), 1633 (C=C); δ_H (400 MHz, $CDCl_3$) 0.97 (9H, s, C(CH_3)$_3$), 3.36 (1H, dd, *J* 9.5, 4.4, C(2)*H*), 3.74 (1H, d, *J* 4.4, C(3)*H*), 5.29–5.33 (1H, m, CH=CH_AH$_B$), 5.34 (1H, d, *J* 6.0, CH=CH$_A$$H_B$), 6.05 (1H, dt, *J* 17.4, 9.5, C*H*=CH$_2$); δ_C (100 MHz, $CDCl_3$) 25.4 (C(*C*H$_3$)$_3$), 34.6 (*C*(CH$_3$)$_3$), 52.3 (*C*(2)H), 77.8 (*C*(3)H), 120.4 (CH=*C*H$_2$), 132.4 (*C*H=CH$_2$), 177.9 (*C*(1)); *m*/*z* (ESI$^-$) 171 ([M−H]$^-$, 100%); HRMS (ESI$^-$) $C_9H_{15}O_3^-$ ([M−H]$^-$) requires 171.1027; found 171.1024.

4.7.20. Methyl (2S,3R)-2-vinyl-3-hydroxybutanoate **39**



Following *general procedure 5*, **15** (500 mg, 1.86 mmol) gave, after purification by flash column chromatography (eluent Et_2O), **39** as a colourless oil (217 mg, 81%, >98% de, >98% ee); $[\alpha]_D^{25}$ −110 (*c* 1.0, $CHCl_3$); ν_{max} (film) 3444 (O–H), 1732 (C=O), 1641 (C=C); δ_H (400 MHz, $CDCl_3$) 1.18 (3H, d, *J* 6.2, C(4)H_3), 2.64 (1H, br s, O*H*), 3.02 (1H, dd, *J* 9.1, 4.9, C(2)*H*), 3.72 (3H, s, OCH_3), 4.10 (1H, app quintet, *J* 5.8, C(3)*H*), 5.25 (1H, dd, *J* 17.2, 1.4, CH=CH_AH$_B$), 5.33 (1H, dd, *J* 10.2, 1.4, CH=CH$_A$$H_B$), 5.93 (1H, ddd, *J* 17.2, 10.2, 9.1, C*H*=CH$_2$); δ_C (100 MHz, $CDCl_3$) 20.0 (*C*(4)H_3), 52.1 (O*C*H$_3$), 57.1 (*C*(2)H), 67.6 (*C*(3)H), 120.7 (*C*(2′)H_2), 131.7 (*C*(1′)H), 173.6 (*C*(1)); *m*/*z* (GC Tof CI$^+$) 145 ([M+H]$^+$, 100%); HRMS (GC Tof CI$^+$) $C_7H_{13}O_3^+$ ([M+H]$^+$) requires 145.0859; found 145.0867.

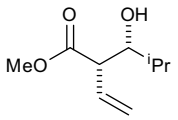
4.7.21. Methyl (2S,3R)-2-vinyl-3-hydroxypentanoate **41**



Following *general procedure 5*, **20** (500 mg, 1.77 mmol) gave, after purification by flash column chromatography (eluent Et_2O), **41** as a colourless oil (243 mg, 87%, >98% de, >98% ee); $[\alpha]_D^{24}$ −96.8 (*c* 1.0, $CHCl_3$); ν_{max} (film) 3454 (O–H), 1732 (C=O), 1640 (C=C); δ_H (400 MHz, $CDCl_3$) 0.93 (3H, t, *J* 7.4, C(5)H_3), 1.41–1.46 (2H, m, C(4)H_2), 2.70 (1H, br s, O*H*), 3.06 (1H, dd, *J* 9.3, 4.8, C(2)*H*), 3.69 (3H, s, OCH_3), 3.82 (1H, dt, *J* 7.6, 4.8, C(3)*H*), 5.20 (1H, dd, *J* 17.2, 1.5,

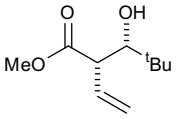
CH=CH_AH$_B$), 5.27 (1H, dd, *J* 10.3, 1.5, CH=CH$_A$$H_B$), 5.91 (1H, ddd, *J* 17.2, 10.3, 9.3, C*H*=CH$_2$); δ_C (100 MHz, $CDCl_3$) 9.9 (*C*(5)H$_3$), 27.0 (*C*(4)H$_2$), 52.0 (O*C*H$_3$), 55.3 (*C*(2)H), 72.7 (*C*(3)H), 120.2 (CH=*C*H$_2$), 131.7 (*C*H=CH$_2$), 173.8 (*C*(1)); *m*/*z* (GC Tof CI$^+$) 176 ([M+NH$_4$]$^+$, 100%), 159 ([M+H]$^+$, 92); HRMS (GC Tof CI$^+$) $C_8H_{15}O_3^+$ ([M+H]$^+$) requires 159.1016; found 159.1020.

4.7.22. Methyl (2S,3R)-2-vinyl-3-hydroxy-4-methylpentanoate ***42***



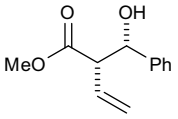
Following *general procedure 5*, **21** (200 mg, 0.67 mmol) gave, after purification by flash column chromatography (eluent Et$_2$O), **42** as a colourless oil (92 mg, 79%, >98% de, >98% ee); $[\alpha]_D^{24}$ −99.9 (*c* 0.95, $CHCl_3$); ν_{max} (film) 3452 (O–H), 1731 (C=O), 1642 (C=C); δ_H (400 MHz, $CDCl_3$) 0.93 (3H, d, *J* 6.8, CH(C*H*$_3$)$_A$(CH$_3$)$_B$), 0.98 (3H, d, *J* 6.8, CH(CH$_3$)$_A$(C*H*$_3$)$_B$), 1.81–1.85 (1H, m, C(4)*H*), 2.64 (1H, d, *J* 3.3, O*H*), 3.25 (1H, dd, *J* 9.3, 4.5, C(2)*H*), 3.60–3.64 (1H, m, C(3)*H*), 3.72 (3H, s, OC*H*$_3$), 5.26 (1H, br dd, *J* 17.3, 1.4, CH=CH_AH$_B$), 5.31 (1H, dd, *J* 10.2, 1.4, CH=CH$_A$$H_B$), 5.96 (1H, ddd, *J* 17.3, 10.2, 9.3, C*H*=CH$_2$); δ_C (100 MHz, $CDCl_3$) 17.4, 19.5 (CH(*C*H$_3$)$_2$), 29.2 (*C*(4)H), 51.8 (O*C*H$_3$), 56.4 (*C*(2)H), 76.4 (*C*(3)H), 120.1 (CH=*C*H$_2$), 131.6 (*C*H=CH$_2$), 173.0 (*C*(1)); *m*/*z* (GC Tof CI$^+$) 173 ([M+H]$^+$, 100); HRMS (GC Tof CI$^+$) $C_9H_{17}O_3^+$ ([M+H]$^+$) requires 173.1172; found 173.1169.

4.7.23. Methyl (2S,3R)-2-vinyl-3-hydroxy-4,4-dimethylpentanoate ***43***



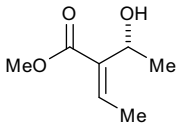
Following *general procedure 5*, **22** (400 mg, 1.29 mmol) gave, after purification by flash column chromatography (eluent Et$_2$O), **43** as a colourless oil (218 mg, 91%, >98% de, >98% ee); $[\alpha]_D^{25}$ −121 (*c* 1.0, $CHCl_3$); ν_{max} (film) 3534 (O–H), 1738 (C=O), 1636 (C=C); δ_H (400 MHz, $CDCl_3$) 0.94 (9H, s, C(C*H*$_3$)$_3$), 2.49 (1H, d, *J* 3.6, O*H*), 3.31 (1H, dd, *J* 9.6, 4.5, C(2)*H*), 3.68 (1H, dd, *J* 4.5, 3.6, C(3)*H*), 3.70 (3H, s, OC*H*$_3$), 5.22–5.27 (1H, m, CH=CH_AH$_B$), 5.28–5.31 (1H, m, CH=CH$_A$$H_B$), 6.02 (1H, app dt, *J* 17.6, 9.6, C*H*=CH$_2$); δ_C (100 MHz, $CDCl_3$) 26.3 (C(*C*H$_3$)$_3$), 35.5 (*C*(CH$_3$)$_3$), 52.1 (O*C*H$_3$), 52.6 (*C*(2)H), 77.8 (*C*(3)H), 119.8 (CH=*C*H$_2$), 133.2 (*C*H=CH$_2$), 174.3 (*C*(1)); *m*/*z* (GC Tof CI$^+$) 204 ([M+NH$_4$]$^+$, 96%), 187 ([M+H]$^+$, 100), 169 ([M−OH]$^+$, 45); HRMS (GC Tof CI$^+$) $C_{10}H_{22}NO_3^+$ ([M+NH$_4$]$^+$) requires 204.1594; found 204.1597.

4.7.24. Methyl (2S,1′R)-2-vinyl-3-hydroxyl-3-phenylpropanoate ***44***



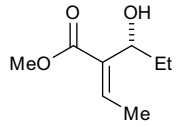
Following *general procedure 5*, **23** (500 mg, 1.41 mmol) gave, after purification by flash column chromatography (eluent Et$_2$O), **44** as a colourless oil (241 mg, 83%, >98% de, >98% ee);[38] $[\alpha]_D^{22}$ −87.5 (*c* 0.5, $CHCl_3$); ν_{max} (film) 3480 (O–H), 1732 (C=O), 1639 (C=C); δ_H (400 MHz, $CDCl_3$) 2.99 (1H, d, *J* 2.8, O*H*), 3.35 (1H, dd, *J* 8.9, 6.0, C(2)*H*), 3.61 (3H, s, OC*H*$_3$), 5.03 (1H, dd, *J* 6.0, 2.8, C(3)*H*), 5.16 (1H, br dt, *J* 17.3, 1.3, CH=CH_AH$_B$), 5.27 (1H, br dd, *J* 10.2, 1.3, CH=CH$_A$$H_B$), 5.92 (1H, ddd, *J* 17.3, 10.2, 8.9, C*H*=CH$_2$), 7.26–7.33 (5H, m, *Ph*); δ_C (100 MHz, $CDCl_3$) 52.4 (O*C*H$_3$), 58.2 (*C*(2)H), 73.8 (*C*(3)H), 120.7 (*C*(2′)H$_2$), 126.3 (*p*-*Ph*), 127.9, 128.2 (*o*,*m*-*Ph*), 131.7 (*i*-*Ph*), 140.7 (*C*(1′)H), 172.9 (*C*(1)); *m*/*z* (GC Tof CI$^+$) 207 ([M+H]$^+$, 11%), 189 ([M−OH]$^+$, 76).

4.7.25. Methyl (2E,3R)-2-ethylidene-3-hydroxybutanoate ***40***



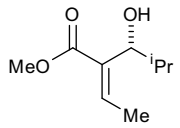
Following *general procedure 5*, **39** (200 mg, 1.39 mmol) gave, after purification by flash column chromatography (eluent Et$_2$O), **40** as a colourless oil (188 mg, 95%, 92:8 [(*E*):(*Z*)], >98% ee);[13b,37] $[\alpha]_D^{24}$ +36.6 (*c* 1.0, $CHCl_3$); ν_{max} (film) 3430 (O–H), 1706 (C=O), 1653 (C=C); δ_H (400 MHz, $CDCl_3$) 1.39 (3H, d, *J* 6.7, C(4)*H*$_3$), 1.83 (1H, d, *J* 7.3, C(2′)*H*$_3$), 3.75 (3H, s, OC*H*$_3$), 4.75 (1H, q, *J* 6.7, C(3)*H*), 6.81 (1H, q, *J* 7.3, C(1′)*H*); δ_C (100 MHz, $CDCl_3$) 13.7 (*C*(4)H$_3$), 21.0 (*C*(2′)H$_3$), 51.7 (O*C*H$_3$), 64.6 (*C*(3)H), 134.6 (*C*(1′)H), 138.1 (*C*(2)), 167.6 (*C*(1)); *m*/*z* (APCI$^+$) 145 ([M+H]$^+$, 100%), 127 ([M−OH]$^+$, 32); HRMS (CI$^+$) $C_7H_{13}O_3^+$ ([M+H]$^+$) requires 145.0859; found 145.0869.

4.7.26. Methyl (2E,3R)-2-ethylidene-3-hydroxypentanoate ***46***



Following *general procedure 5*, **41** (200 mg, 1.27 mmol) gave, after purification by flash column chromatography (eluent Et$_2$O), **46** as a colourless oil (178 mg, 89%, 92:8 [(*E*):(*Z*)], >98% ee);[38] $[\alpha]_D^{24}$ +22.4 (*c* 1.0, $CHCl_3$); ν_{max} (film) 3516 (O–H), 1697 (C=O), 1644 (C=C); δ_H (400 MHz, $CDCl_3$) 0.90 (3H, t, *J* 7.4, C(5)*H*$_3$), 1.60–1.65 (1H, m, C(4)*H*$_A$), 1.81–1.84 (1H, m, C(4)*H*$_B$), 1.84 (1H, d, *J* 7.3, C(2′)*H*$_3$), 3.51 (1H, br d, *J* 7.4, O*H*), 3.74 (3H, s, OC*H*$_3$), 4.44 (1H, app t, *J* 7.3, C(3)*H*), 6.90 (1H, q, *J* 7.3, C(1′)*H*); δ_C (100 MHz, $CDCl_3$) 10.4 (*C*(4)H$_2$), 14.0 (*C*(5)H$_3$), 29.9 (*C*(2′)H$_3$), 51.6 (O*C*H$_3$), 70.1 (*C*(3)H), 133.5 (*C*(1′)H), 139.1 (*C*(2)), 167.8 (*C*(1)); *m*/*z* (GC Tof CI$^+$) 159 ([M+H]$^+$, 82%), 141 ([M−OH]$^+$, 100); HRMS (CI$^+$) $C_8H_{18}NO_3^+$ ([M+NH$_4$]$^+$) requires 176.1281; found 176.1293.

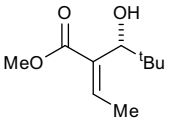
4.7.27. Methyl (2E,3R)-2-ethylidene-3-hydroxy-4-methylpentanoate ***47***



Following *general procedure 5*, **42** (200 mg, 1.16 mmol) gave, after purification by flash column chromatography (eluent Et$_2$O), **47** as colourless oil (197 mg, 98%, 92:8 [(*E*):(*Z*)], >98% ee); $[\alpha]_D^{21}$ +15.5 (*c* 1.0, $CHCl_3$); ν_{max} (film) 3520 (O–H), 1697 (C=O), 1644 (C=C); δ_H (400 MHz, $CDCl_3$) 0.78 (3H, d, *J* 6.6, CH(C*H*$_3$)$_A$(CH$_3$)$_B$), 1.10 (3H, d, *J* 6.6, CH(CH$_3$)$_A$(C*H*$_3$)$_B$), 1.86 (3H, d, *J* 7.3, C(2′)*H*$_3$), 1.98 (1H, septd, *J* 9.3, 6.6, C(4)*H*) 3.48 (1H, d, *J* 11.0, O*H*), 3.76 (3H, s, OC*H*$_3$), 4.10 (1H, dd, *J* 11.0, 9.3, C(3)*H*), 6.97 (1H, app qd, *J* 7.3, 0.5, C(1′)*H*); δ_C (100 MHz, $CDCl_3$) 14.4, 19.2 (CH(*C*H$_3$)$_2$), 19.5 (*C*(2′)H$_3$), 33.8 (*C*(4)H), 51.7 (O*C*H$_3$), 74.4 (*C*(3)H), 132.9 (*C*(1′)H), 139.9 (*C*(2)), 168.1 (*C*(1)); *m*/*z* (GC Tof CI$^+$) 173 ([M+H]$^+$, 42%), 155 ([M−OH]$^+$,

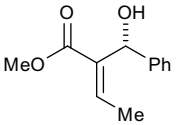
100); HRMS (GC Tof CI$^+$) $C_9H_{17}O_3^+$ ([M+H]$^+$) requires 173.1172; found 173.1180.

4.7.28. Methyl (2E,3R)-2-ethylidene-3-hydroxy-4,4-dimethylpentanoate ***48***



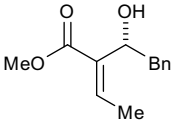
Following *general procedure 5*, **43** (200 mg, 1.07 mmol) gave, after purification by flash column chromatography (eluent Et_2O), **48** as a colourless oil (193 mg, 97%, 91:9 [(*E*):(*Z*)], >98% ee); $[\alpha]_D^{23}$ +28.5 (*c* 1.1, $CHCl_3$); ν_{max} (film) 3479 (O–H), 1694 (C=O), 1649 (C=C); δ_H (400 MHz, $CDCl_3$) 0.90 (9H, s, C(CH_3)$_3$), 1.85 (3H, d, *J* 7.3, C(2′)H_3), 3.75 (3H, s, OCH_3), 4.30 (1H, dd, *J* 10.0, 0.5, C(3)*H*), 4.70 (1H, br d, *J* 10.0, O*H*), 6.95 (1H, qd, *J* 7.3, 0.5, C(1′)*H*); δ_C (100 MHz, $CDCl_3$) 15.0 (*C*(2′)H_3), 26.3 (C(*C*H_3)$_3$), 37.5 (*C*(4)), 51.9 (O*C*H_3), 76.4 (*C*(3)H), 130.9 (*C*(1′)H), 140.8 (*C*(2)), 169.8 (*C*(1)); *m*/*z* (GC Tof CI$^+$) 187 ([M+H]$^+$, 54%), 169 ([M−OH]$^+$, 100); HRMS (GC Tof CI$^+$) $C_{10}H_{19}O_3^+$ ([M+H]$^+$) requires 187.1329; found 187.1340.

4.7.29. Methyl (2E,1′R)-2-hydroxybenzyl-but-2-enoate ***49***



Following *general procedure 6*, **44** (300 mg, 0.91 mmol) gave, after purification by flash column chromatography (eluent Et_2O), **49** as a colourless oil (86 mg, 43%, 94:6 [(*E*):(*Z*)], >98% ee);[13b,39] $[\alpha]_D^{21}$ +38.5 (*c* 1.0, $CHCl_3$); ν_{max} (film) 3492 (O–H), 1698 (C=O), 1645 (C=C); δ_H (400 MHz, $CDCl_3$) 2.00 (3H, d, *J* 7.4, C(2′)H_3), 3.69 (3H, s, OCH_3), 4.23 (1H, br d, *J* 9.4, O*H*), 5.74 (1H, d, *J* 9.4, C(3)*H*), 7.11 (1H, q, *J* 7.4, C(1′)*H*), 7.23–7.40 (5H, m, *Ph*); δ_C (100 MHz, $CDCl_3$) 14.3 (*C*(2′)H_3), 51.8 (O*C*H_3), 69.2 (*C*(3)H), 125.2 (*p*-*Ph*), 127.1, 128.3 (*o*,*m*-*Ph*), 133.3 (*i*-*Ph*), 140.0 (*C*(1′)H), 143.7 (*C*(2)), 167.6 (*C*(1)); *m*/*z* (APCI$^+$) 224 ([M+Na]$^+$, 4%); HRMS (CI$^+$) $C_{12}H_{18}NO_3^+$ ([M+NH_4]$^+$) requires 224.1281; found 224.1291.

4.7.30. Methyl (2E,3R)-2-ethylidene-3-hydroxy-4-phenyl-butanoate ***50***



Following *general procedure 5*, **24** (400 mg, 1.16 mmol) gave a 76:24 mixture of **45** and **50**, respectively (225 mg, quant). This mixture was treated with DBU (0.7 mL, 4.64 mmol) according to *general procedure 6* to give, after purification by flash column chromatography (eluent Et_2O), **50** as a colourless oil (194 mg, 97% (two steps), 92:8 [(*E*):(*Z*)], >98% ee); $[\alpha]_D^{25}$ +64.0 (*c* 1.0, $CHCl_3$); ν_{max} (film) 3515 (O–H), 1694 (C=O), 1644 (C=O), 1603 (C=C); δ_H (400 MHz, $CDCl_3$) 1.74 (3H, d, *J* 7.3, C(2′)H_3), 1.82–1.86 (1H, m, C(4)H_A), 2.00 (1H, m, C(4)H_B), 3.59 (1H, d, *J* 10.8, O*H*), 3.77 (3H, s, OCH_3), 4.55 (1H, ddd, *J* 10.8, 8.8, 5.4, C(3)*H*), 6.88 (1H, q, *J* 7.3, C(1′)*H*), 7.23–7.35 (5H, m, *Ph*); δ_C (100 MHz, $CDCl_3$) 13.9 (*C*(2′)H_3), 32.1 (*C*(4)H_2), 51.7 (OCH_3), 67.9 (*C*(3)H), 125.8 (*p*-*Ph*), 128.3, 128.4 (*o*,*m*-*Ph*), 133.6 (*i*-*Ph*), 139.0 (*C*(1′)H), 141.6 (*C*(2)), 167.8 (*C*(1)); *m*/*z* (APCI$^+$) 221 ([M+H]$^+$, 90%); HRMS (CI$^+$) $C_{13}H_{20}NO_3^+$ ([M+NH_4]$^+$) requires 238.1438; found 238.1440.

Acknowledgements

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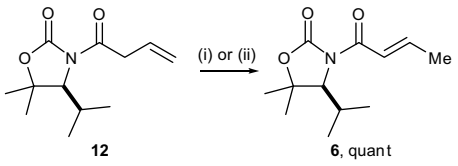
22. Isomerisation of β,γ-unsaturated *N*-acyl SuperQuat **12** to give *N*-crotonoyl SuperQuat **6** with either Et_3N or DBU rapidly promoted full conversion to the desired product as a single geometric isomer [(*E*):(*Z*) ratio >99:1], with chromatographic purification giving **6** in quantitative yield.



Reagents and conditions: (i) Et_3N, THF, rt, 2 h; (ii) DBU, THF, rt, 2 h.

23. SuperQuat **11** was also isolated in 9% yield.
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25. Within the crystal lattice for compound **17** intermolecular hydrogen bonding is observed between the C(3′)-hydroxyl groups and the C(1′)-carbonyl groups.
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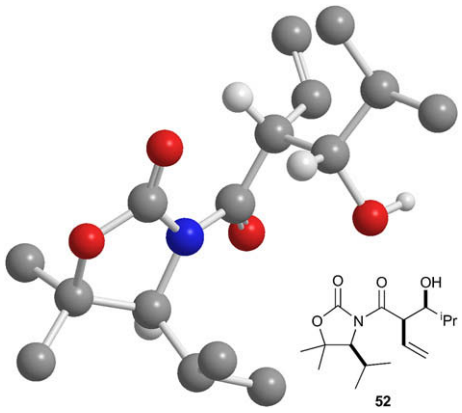
28. In the case of the C(3′)-ethyl and C(3′)-isopropyl substrates **20** and **21** the corresponding non-Evans *syn*-aldol products **51** and **52** were isolated as the minor diastereoisomers in 9 and 5% yield, respectively (in >98% de in each case); no minor diastereoisomers were isolated from reaction of substrates **22**–**24**. The relative configurations within **51** and **52** were initially based on ^3J ^{1}H NMR coupling constant analysis with **51** and **52** displaying diagnostic coupling constants of 3.6 and 4.0 Hz, respectively between the C(2′)H and C(3′)*H* protons, indicative of a *syn*-configuration. Furthermore, recrystallisation of the minor diastereoisomeric product of the reaction with isobutyraldehyde allowed the *syn*-relative configuration of the minor aldol product **52** to be unambiguously determined by X-ray crystallographic analysis, with the absolute (4*S*,2′*R*,3′*S*)-configuration assigned relative to the known (*S*)-configuration of the C(4)-stereogenic centre. Within the crystal lattice for compound **52** intermolecular hydrogen bonding is observed between the C(3′)-hydroxyl groups and the C(1′)-carbonyl groups.



Chem3D representation of the single crystal X-ray structure of **52** (some H atoms have been omitted for clarity).

29. Within the crystal lattice for compound **22** intermolecular hydrogen bonding is observed between the C(3′)-hydroxyl groups and the C(2)-carbonyl groups, whereas for compound **23** intermolecular hydrogen bonding is observed between the C(3′)-hydroxyl groups and the C(1′)-carbonyl groups.
30. No aldol products were isolated upon reaction with pivalaldehyde, presumably due to its steric bulk precluding reaction.
31. In each case, β,γ-unsaturated **12** was isolated (typically in ~20% yield), along with small amounts (<5%) of SuperQuat auxiliary **11**.
32. Given the known enantiomeric purity (i.e., >98% ee) of the SuperQuat chiral auxiliary (*S*)-**11**, the enantiomeric purity of **26**, **33**–**39** and **41**–**45** was assigned from the diastereoisomeric purity (determined by peak integration of the ^{1}H NMR spectrum of the crude reaction mixture and the pure product).
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