Exploring Rhodium-Catalysed Conjugate Addition of Chiral Alkenylboronates Using Chiral Olefin Ligands

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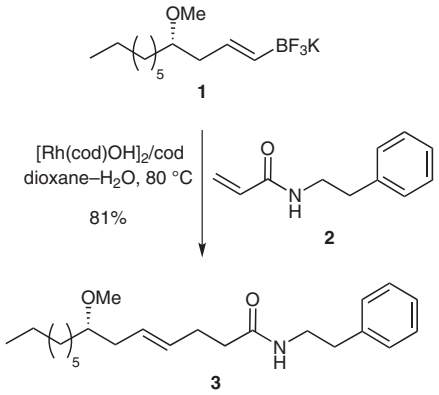
Abstract: The rhodium-catalysed addition of chiral alkenylboron reagents to prochiral α,β-unsaturated carbonyl acceptors are demonstrated to proceed under ligand control. The highest activities were obtained with chiral olefin ligands and the configuration of the new stereocentre can be predicted by using established models.

Key words: alkenylboronate, conjugate addition, rhodium, catalysis, chiral olefin ligands

The transition-metal-catalysed conjugate addition of organometallics is regarded as a fundamental methodology for organic synthesis.[1] In particular, the introduction of a practical protocol for rhodium-catalysed addition of organoboron reagents to activated alkenes with predictable stereocontrol has transformed the way synthetic chemists can employ this reaction in organic synthesis.[2] In the large majority of reported additions to prochiral acceptors, a single stereocentre is established by an asymmetric carbometalation under the control of an enantiopure rhodium complex. The sense of asymmetric induction can be reliably predicted by means of simple stereochemical models when using chiral atropisomeric diphosphine[3] and chiral olefin ligands.[4] If the rhodium-catalysed conjugate addition reaction is going to be commonly employed in the synthesis of complex target molecules, it is crucial to gain an understanding of the stereoselectivity issues involved in joining together enantiopure fragments. In this context, both substrate-control[5] and ligand-control[6] have been established as useful strategies in the addition of arylboron donors to enantiopure acceptors. Despite the considerable advances in catalyst design and substrate (acceptor) diversity, the structure of the organometallic donor remains surprisingly limited to aryl (and a number of alkenyl) derivatives.[7] Although there are a number of useful methods available for the preparation of complex enantiopure organoboron derivatives, only isolated examples of conjugate addition reactions have been reported.[8] In a notable example, the synthesis of hermitamides A and B (natural products isolated from the marine cyanobacterium *Lyngbya majuscula*) have been completed using rhodium-catalysed addition of an enantiopure alkenylboron reagent to an acrylamide.[9] The optimised conditions for the addition required the use of the commercially available $[Rh(cod)(OH)]_2$ catalyst with added cyclooctadiene ligand to limit catalyst decomposition. In the challenging coupling to acrylamide **2**, the use of the trifluoro(alkenyl)borate salt **1** was required because significant amounts of protodeboronation product was noted with other boron reagents. It is important to note that no new chiral centre is formed during the reaction, and hermitamide A (**3**) was isolated in good yield without loss of stereochemical integrity (Scheme 1). In this article we demonstrate that the rhodium-catalysed addition of a chiral alkenylboron reagent to prochiral α,β-unsaturated carbonyl acceptors is an efficient process and, importantly, proceeds under ligand-control, thus opening the door to new applications in stereoselective synthesis.



Scheme 1 The catalytic synthesis of hermitamide A

For the preliminary studies, we chose to employ chiral alkenyltrifluoroborate salt **8**, which is an analogue of the donor used in the synthesis of hermitamides A and B. We have previously noted that alkenyltrifluoroborate salts offer practical advantages in terms of stability and product yield in rhodium-catalysed conjugate addition reactions. This is proposed to be due to the slow release of alkenylboronic acid and a concomitant reduction in competing protodeboronation pathways.[9] The chiral alkenyltrifluoroborate salt **8** was prepared by the route shown in Scheme 2. Initial addition of the alkynyllithium salt to the commercially available chiral epoxide **4** furnished the alcohol product, which was subsequently methylated to afford **5** in excellent yield over the two steps. The *syn*-addition of pinacolborane was achieved using the zirconi-

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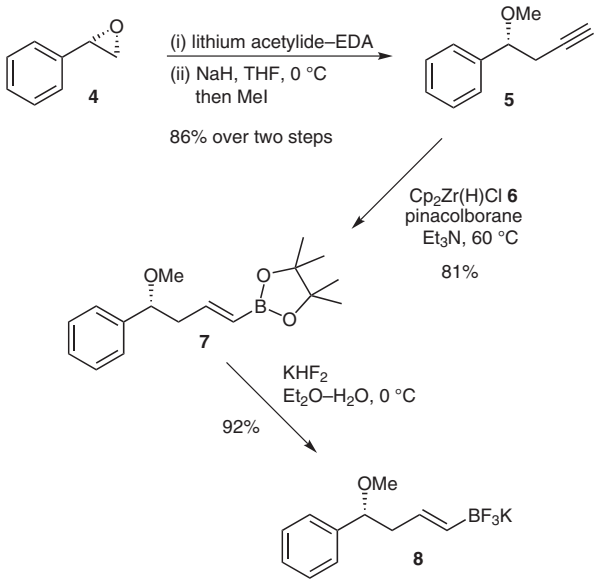
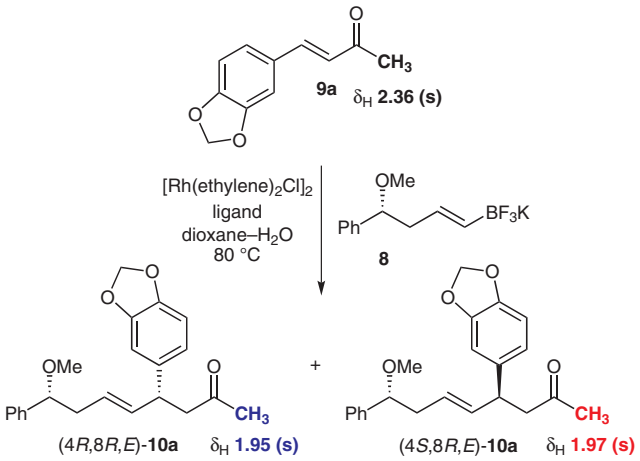
um-mediated procedure reported by Pereira and Srebnik.[10] Following this protocol, alkyne **5** was treated with 0.1 equivalents of Schwartz reagent **6** and anhydrous triethylamine in neat pinacolborane. The reaction proceeded with complete conversion into the chiral alkenylpinacol boronic ester **7**. After purification, an 81% yield of **7** with high *E*/*Z* selectivity (98:2) was obtained. This product could be directly converted into the trifluoro(alkenyl)borate salt **8** by treatment with potassium difluorohydride.



Scheme 2 The synthesis of chiral alkenylboron reagent

With the desired alkenylboron species in hand, rhodium-catalysed conjugate additions could now be investigated. The acyclic enone **9a** was selected as a substrate to benchmark the selectivity of the conjugate addition (Scheme 3). The two diastereomers of product (4*R*,8*R*,*E*)-**10a** and (4*S*,8*R*,*E*)-**10a** could be distinguished by ^{1}H NMR spectroscopy and, interestingly, in the absence of added ligand, a 50:50 mixture was observed with a range of rhodium pre-catalysts. A brief study revealed that $[Rh(ethylene)_2Cl]_2$ in dioxane/water at 80 °C afforded satisfactory conversion into the product (up to 55%) alongside a competing protodeboronation process. Notably, the remote stereocentre on the alkenylboron donor did not induce any stereoselectivity in the formation of the new carbon–carbon bond. This presented the opportunity to introduce the chiral alkene fragment using ligand control and switching the diastereoselectivity of the process by changing the enantiomer of ligand employed in the addition. A range of enantiopure ligands (Figure 1) were tested and ^{1}H NMR spectroscopic analysis was used to facilitate the identification of the optimum system (Table 1). The application of (*R*)-BINAP as ligand demonstrated a preference for the (4*R*,8*R*,*E*)-diastereomer of **10a**. As expected, with (*S*)-BINAP the stereoselectivity switched to afford the (4*S*,8*R*,*E*)-diastereomer of **10a** with comparable activity. Other atropisomeric bidentate phosphine ligands such as tol-BINAP, SYNPHOS, and DIFLUORPHOS afforded similar selectivities to BINAP and the same sense of asymmetric induction, albeit with slightly lower conversions. Other privileged ligand structures such as Me-DUPHOS and H_8-MONOPHOS were less effective in this particular reaction. The highest conversion into product was observed with the commercially available chiral bicyclo[2.2.2]octadiene (DOLEFIN) ligands described by Carreira and co-workers.[11] Thus, the (*R*,*R*,*R*)-ligand provided the (4*R*,8*R*,*E*)-diastereomer with good diastereoselectivity. For both the chiral diphosphine and chiral olefin ligands, the configuration of the new stereocentre was consistent with the simple predictive models presented in the literature.[4]



Scheme 3 Stereoselective addition of chiral alkenylboron reagent

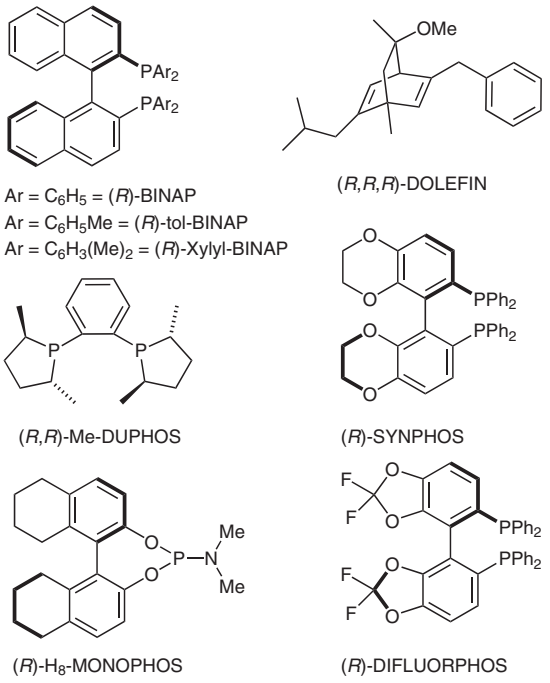
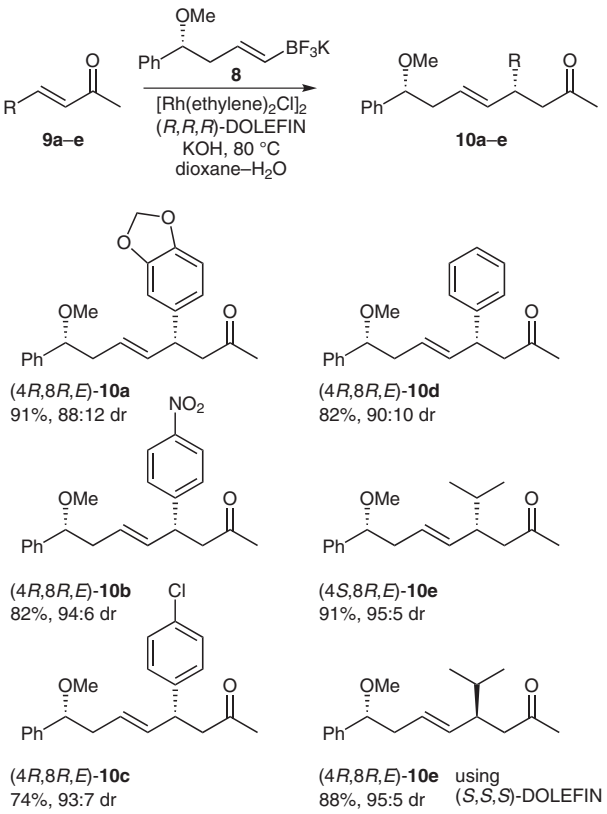


Figure 1 Chiral ligands used in stereoselective additions

Table 1 Ligand Control of Stereoselectivity

Ligand	Conv. (%)[a]	dr (4*R*/4*S*)-**10a**[a]
none	55	50:50
(*R*)-BINAP	62	87:13
(*S*)-BINAP	62	13:87
(*R*)-tol-BINAP	53	85:15
(*R*)-xylyl-BINAP	58	82:18
(*R*)-SYNPHOS	43	89:11
(*R*)-DIFLUORPHOS	41	87:13
(*R*,*R*,*R*)-DOLEFIN	82	87:13
(*R*,*R*)-Me-DUPHOS	24	52:48
(*R*)-H_8-MONOPHOS	69	66:34
(*R*,*R*,*R*)-DOLEFIN[c]	98 (91[b])	88:12
(*R*,*R*,*R*)-DOLEFIN[d]	89	89:11
(*R*,*R*,*R*)-DOLEFIN[e]	82	88:12

[a] Determined by ^{1}H NMR analysis of the crude reaction mixture.
[b] Isolated yield after flash chromatography.
[c] Aqueous KOH (1.5 M, 0.1 mL) added.
[d] Aqueous K_2CO_3 (1.5 M, 0.1 mL) added.
[e] Aqueous K_3PO_4 (1.5 M, 0.1 mL) added.



Scheme 4 Exploring the scope of the addition

The introduction of a base resulted in further improvements to the efficiency of the process. In particular, the use of potassium hydroxide afforded excellent conversion into product (4*R*,8*R*,*E*)-**10a** with good diastereoselectivity and, importantly, a high isolated yield. Given that the chiral alkenylboron donor is the most valuable component of the reaction mixture, the results suggest that chiral olefin ligands are superior to phosphine-based systems for this particular application.

With the optimised set of reaction conditions, we next explored the scope of the process with respect to the acyclic enones **10a–e**; in all cases the chiral alkenylboron reagent **8** was employed as donor (Scheme 4).

The diastereoselectivity was consistently high for acyclic substrates featuring aryl and an alkyl substituent on the alkene. In all cases, isolated yields were excellent. It is useful to note that both electron-donating and electron-withdrawing substituents were tolerated on the aryl group (**10a–d**). The highest selectivity was observed with the isopropyl-substituted substrate **10e**, again, this is consistent with literature precedent for the enantioselective addition of arylboron reagents to this class of compound. Thus, the (*R*,*R*,*R*)-ligand gave the (4*S*,8*R*,*E*)-diastereomer of **10e** in high yield and with 95:5 dr. The (*S*,*S*,*S*)-ligand provided the complementary (4*R*,8*R*,*E*)-diastereomer of **10e** with identical selectivity.

In conclusion, we have demonstrated that the rhodium-catalysed addition of a chiral alkenylboron reagent to prochiral α,β-unsaturated carbonyl acceptors can be an efficient process that enables the construction of highly functionalised alkenes under ligand control. Central to the success of this approach was the use of chiral olefin ligands to provide high stereoselectivity and superior activity in the carbometalation step.

IR spectra were recorded on a Perkin-Elmer 1600 FT IR spectrophotometer, using NaCl discs. ^{1}H NMR spectra were obtained on a Bruker Avance 300 spectrometer operating at 300 MHz, unless otherwise noted, with tetramethylsilane as an internal standard. *J* values are given in Hz. ^{13}C NMR spectra were obtained on a Bruker Avance 300 spectrometer operating at 75 MHz, unless otherwise noted. Mass spectra were obtained on a Bruker Time-of-Flight mass spectrometer (ESI-TOF). Enantiomeric excesses were determined using HPLC (see individual compounds for details) with a UV detector at 254 nm. All dry solvents were freshly distilled under nitrogen prior to use. Tetrahydrofuran was distilled over an alumina column. Petroleum ether refers to that fraction obtained between 40–60 °C. All other reagents were obtained from commercial suppliers and used as received. All glassware used under anhydrous conditions was dried in an oven and allowed to cool under nitrogen prior to use. All reactions were carried out under argon unless otherwise stated. Flash chromatography was conducted under medium pressure, using matrix 60 silica.

2-[(*E*)-(*R*)-4-Methoxy-4-phenylbut-1-enyl]-4,4,5,5-tetramethyl[1,3,2]dioxaborolane (7)

[(*R*)-1-Methoxybut-3-ynyl]benzene[12] (**5**; 4.00 g, 25.0 mmol) and pinacolborane (3.36 g, 26.3 mmol) were charged to a 25-mL Schlenk tube under a positive pressure of dry argon. To the resulting solution was added sequentially bis(cyclopentadienyl)zirconium(IV) chloride hydride (**6**; 0.65 g, 2.5 mmol) followed by Et_3N (0.25 g, 2.5

mmol), the mixture was capped then heated at 60 °C for 16 h with protection from light. Upon completion, hexane (5 mL) was added and the mixture was stirred for 10 min in air. The material was isolated through a short silica pad (elution with hexanes) to give the title product.

Yield: 5.83 g (81%); colourless oil; R_f = 0.15 (PE–EtOAc, 9:1); $[\alpha]_D^{20}$ +12.9 (*c* 0.95, CH_3OH).

IR (neat): 2980, 2931 (C=C), 1640 (C–O), 1358, 1323 (B–O) cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 6.62–6.48 (m, 5 H, PhH), 6.55 (dt, *J* = 19.6, 6.41 Hz, 1 H, C*H* alkene), 5.43 (dt, *J* = 19.6, 1.51 Hz, 1 H, C*H* alkene), 4.15 (dd, *J* = 8.29, 5.28 Hz, 1 H, C*H*OCH_3), 3.13 (s, 3 H, OCH_3), 2.59 (ddt, *J* = 15.1, 6.41, 1.51 Hz, 1 H, CHCH_2CHCH), 2.40 (ddt, *J* = 15.1, 8.29, 1.51 Hz, 1 H, CHCH_2CHCH), 1.18 (s, 12 H, 4 × CH_3).

^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 150.1, 141.7, 128.3, 127.5, 126.6, 83.0, 82.9, 56.6, 44.5, 24.7; C–B peak not observed.

^{11}B NMR (96.3 MHz, $CDCl_3$): δ = 31.2.

HRMS (ESI^+): *m*/*z* [M + Na^+] calcd for $C_{17}H_{25}B_1Na_1O_3$: 311.1794; found: 311.1791.

Potassium (*R*,*E*)-4-Methoxy-4-phenylbut-1-enyl Trifluoroborate (8)

2-[(*E*)-(*R*)-4-Methoxy-4-phenylbut-1-enyl)-4,4,5,5-tetramethyl[1,3,2]dioxaborolane (**7**; 2.31 g, 8.0 mmol) in Et_2O (25 mL), was charged to a 100-mL round-bottom flask. The flask was cooled to 0 °C (ice/salt) and to the resulting solution was added sequentially potassium hydrogen difluoride (2.34 g, 30 mmol) followed by H_2O (5 mL). The mixture was warmed to r.t. and stirred for 3 h until a thick white precipitate formed. Upon completion, the reaction mixture was concentrated in vacuo and thoroughly dried under high vacuum (0.01 mmHg). The solids were then washed with acetone (250 mL) and filtered to remove inorganic salts. The solvent was concentrated to approximately 20 mL, Et_2O (100 mL) was added and the suspension was triturated to precipitate the product. Storage overnight at –20 °C in a freezer gave the product.

Yield: 1.97 g (92%); white solid; mp 185 °C (acetone) (dec.); $[\alpha]_D^{20}$ +13.4 (*c* 0.65, MeOH).

IR (KBr): 2992, 2931 (C=C), 1652 (C–O), 1107, 946 (B–F) cm^{-1}.

^1H NMR (300 MHz, CD_3OD): δ = 8.32–8.15 (m, 5 H, PhH), 6.69 (dt, *J* = 17.7, 6.78 Hz, 1 H, C*H* alkene), 6.39 (dt, *J* = 17.7, 3.77 Hz, 1 H, C*H* alkene), 5.10–4.24 (dd, *J* = 7.54, 6.03 Hz, 1 H, C*H*OCH_3), 4.12 (s, 3 H, OCH_3), 3.44 (ddt, *J* = 15.5, 6.41, 1.51 Hz, 1 H, CHCH_2CHCH), 3.44 (ddt, *J* = 15.5, 7.54, 1.51 Hz, 1 H, CHCH_2CHCH).

^{13}C NMR (75.5 MHz, CD_3OD): δ = 143.5, 133.7, 133.7, 129.3, 128.5, 127.9, 86.0, 56.7, 45.7; C–B peak not observed.

^{11}B NMR (96.3 MHz, CD_3OD): δ = 4.12

HRMS (ESI^-): *m*/*z* [M + H^+] calcd for $C_{11}H_{14}BF_3O$: 229.1011; found: 229.1009.

Rhodium-Catalysed Addition of Chiral Alkenylboron Reagent 8; General Procedure

A 24-mL screw-capped vial equipped with a rubber septum was charged with rhodium(bisethylene)chloride dimer (3 mol%) and ligand (7 mol%), potassium (*R*,*E*)-4-methoxy-4-phenylbut-1-enyl trifluoroborate (**8**; 0.40 mmol) and aq KOH (1.5 M, 0.1 mL) were added by syringe and the vessel was purged with argon. After 10 min stirring at r.t., enone **10** (0.20 mmol) in dioxane (0.5 mL) was added in a single portion via syringe. The mixture was transferred with stirring to a preheated hotplate at 80 °C for 20 h. The crude reaction mixture was taken up in Et_2O (5 mL) and filtered through a short plug of silica (Et_2O) and the solvent was removed in vacuo. The crude residue was purified by flash column chromatography on silica gel (PE–EtOAc, 9:1) to give the product.

(4*R*,8*R*,*E*)-4-(Benzo[*d*][1,3]dioxol-5-yl)-7-methoxy-7-phenylhept-5-en-2-one (10a)

The crude residue was purified by flash column chromatography on silica gel (petrol–EtOAc, 4:1) to give the title product.

Yield: 0.058 g (91%); 88:12 ratio of diastereomers; colourless oil; R_f = 0.20 (petrol–EtOAc, 4:1); $[\alpha]_D^{20}$ –28.2 (*c* 0.80, $CHCl_3$).

IR (KBr): 2897, 2824, 1715 (C=O), 1504, 1488 cm^{-1}.

^1H NMR (500 MHz, C_6D_6): δ = 7.33–7.10 (m, 5 H, PhH), 6.62 (d, *J* = 7.91 Hz, 1 H, ArH), 6.52 (d, *J* = 1.51 Hz, 1 H, ArH), 6.47 (dd, *J* = 7.91, 1.51 Hz, 1 H, ArH), 5.83 (s, 2 H, OCH_2O), 5.40 (dd, *J* = 15.5, 6.78 Hz, 1 H, C*H* alkene), 5.21 (dt, *J* = 15.5, 6.78 Hz, 1 H, C*H* alkene), 4.02 (t, *J* = 6.78 Hz, 1 H, C*H*OCH_3), 3.66 (q, *J* = 7.16 Hz, 1 H, CH), 3.12 (s, 3 H, OCH_3), 2.68–2.53 (m, 2 H, CH_2), 2.51–2.35 (m, 1 H, CH), 2.34–2.15 (m, 1 H, CH), 1.97 (s, 1 H, $COCH_3$, minor diastereomer), 1.95 (s, 3 H, $COCH_3$, major diastereomer).

^{13}C NMR (125.8 MHz, $CDCl_3$): δ = 207.5, 148.0, 146.4, 141.8, 137.6, 135.3, 128.7, 128.7, 127.9, 127.2, 126.4, 120.8, 108.5, 108.3, 101.2, 84.2, 56.9, 49.9, 43.6, 41.3, 31.0, 15.6.

HRMS (ESI^+): *m*/*z* [M + Na^+] calcd for $C_{22}H_{24}NaO_4$: 375.1572; found: 375.1558.

(4*R*,8*R*,*E*)-7-Methoxy-4-(4-nitrophenyl)-7-phenylhept-5-en-2-one (10b)

The crude residue was purified by flash column chromatography on silica gel (petrol–EtOAc 4:1) to give the title product.

Yield: 0.052 g (82%); 94:6 ratio of diastereomers; colourless oil; R_f = 0.20 (petrol–EtOAc, 9:1); $[\alpha]_D^{20}$ –38.2 (*c* 0.95, $CHCl_3$).

IR (KBr): 2937, 1717 (C=O), 1643 (NO_2), 1520, 1348 cm^{-1}.

^1H NMR (500 MHz, C_6D_6): δ = 8.10–8.0 (m, 2 H, PhH), 7.33–7.10 (m, 7 H, PhH), 5.39 (dd, *J* = 15.5, 6.78 Hz, 1 H, C*H* alkene), 5.19 (dt, *J* = 15.5, 6.78 Hz, 1 H, C*H* alkene), 4.04 (t, *J* = 6.78 Hz, 1 H, C*H*OCH_3), 3.72 (q, *J* = 7.16 Hz, 1 H, CH), 3.12 (s, 3 H, OCH_3), 2.80–2.62 (m, 2 H, CH_2), 2.53–2.34 (m, 1 H, CH), 2.28–2.17 (m, 1 H, CH), 2.01 (s, 3 H, $COCH_3$, minor diastereomer), 1.99 (s, 1 H, $COCH_3$, major diastereomer).

^{13}C NMR (125.8 MHz, $CDCl_3$): δ = 206.2, 151.5, 141.6, 133.7, 128.8, 128.8, 128.7, 128.1, 128.0, 128.0, 127.1, 127.1, 124.1, 83.9, 57.0, 49.1, 43.4, 41.3, 31.0, 30.9.

HRMS (ESI^+): *m*/*z* [M + Na^+] calcd for $C_{21}H_{23}NNaO_4$: 376.1524; found: 376.1514.

(4*R*,8*R*,*E*)-4-(4-Chlorophenyl)-7-methoxy-7-phenylhept-5-en-2-one (10c)

The crude residue was purified by flash column chromatography on silica gel (petrol–EtOAc 9:1) to give the title product.

Yield: 0.048 g (74%); 93:7 ratio of diastereomers; colourless oil; R_f = 0.20 (petrol–EtOAc, 9:1); $[\alpha]_D^{20}$ –48.6 (*c* 0.90, $CHCl_3$).

IR (KBr): 3029, 2934, 2824, 1717 (C=O), 1492, 1360, 1093 cm^{-1}.

^1H NMR (500 MHz, C_6D_6): δ = 7.36–7.16 (m, 7 H, PhH), 7.15–6.98 (m, 2 H, PhH), 5.40 (dd, *J* = 15.5, 6.78 Hz, 1 H, C*H* alkene), 5.22 (dt, *J* = 15.5, 6.78 Hz, 1 H, C*H* alkene), 4.02 (t, *J* = 6.78 Hz, 1 H, C*H*OCH_3), 3.72 (q, *J* = 7.16 Hz, 1 H, CH), 3.12 (s, 3 H, OCH_3), 2.71–2.61 (m, 2 H, CH_2), 2.52–2.34 (m, 1 H, CH), 2.31–2.20 (m, 1 H, CH), 1.97 (s, 3 H, $COCH_3$, major diastereomer), 1.94 (s, 1 H, $COCH_3$, minor diastereomer).

^{13}C NMR (125.8 MHz, $CDCl_3$): δ = 207.1, 142.2, 141.8, 134.8, 132.4, 129.5, 129.2, 128.9, 128.7, 128.4, 127.9, 127.2, 127.2, 127.1, 127.0, 127.0, 84.0, 57.0, 57.0, 50.5, 49.6, 43.3, 41.4, 31.0, 31.0.

HRMS (ESI$^+$): *m*/*z* [M + Na$^+$] calcd for $C_{21}H_{23}ClNaO_2$: 365.1284; found: 365.1280.

(4*R*,8*R*,*E*)-7-Methoxy-4,7-diphenylhept-5-en-2-one (10d)

The crude residue was purified by flash column chromatography on silica gel (petrol–EtOAc, 9:1) to give the title product.

Yield: 0.049 g (82%); 90:10 ratio of diastereomers; colourless oil; R_f = 0.25 (petrol–EtOAc, 9:1); $[\alpha]_D^{20}$ +46.1 (*c* 1.0, $CHCl_3$).

IR (neat): 2979, 2935, 2824, 1722 (C=O), 1367, 1145, 1102 cm^{-1}.

^{1}H NMR (500 MHz, C_6D_6): δ = 7.36–7.16 (m, 8 H, PhH), 7.15–6.98 (m, 2 H, PhH), 5.44 (dd, *J* = 15.4, 7.16 Hz, 1 H, C*H* alkene), 5.22 (dt, *J* = 15.4, 6.78 Hz, 1 H, C*H* alkene), 4.03 (t, *J* = 6.78 Hz, 1 H, C*H*OCH$_3$), 3.74 (q, *J* = 7.16 Hz, 1 H, CH), 3.12 (s, 3 H, OCH$_3$), 2.71–2.61 (m, 2 H, CH$_2$), 2.52–2.34 (m, 1 H, CH), 2.31–2.20 (m, 1 H, CH), 1.97 (s, 1 H, COCH$_3$, major diastereomer), 1.94 (s, 3 H, COCH$_3$, minor diastereomer).

^{13}C NMR (125.8 MHz, $CDCl_3$): δ = 208.8, 208.7, 141.6, 133.2, 133.2, 128.3, 127.6, 127.5, 126.8, 126.8, 84.1, 84.0, 56.6, 46.9, 46.8, 41.2, 31.7, 30.5, 30.5, 20.4, 20.3, 18.8, 16.7.

HRMS (ESI$^+$): *m*/*z* [M + Na$^+$] calcd for $C_{21}H_{24}NaO_2$: 331.1764; found: 331.1760.

(4*R*,8*R*,*E*)-4-Isopropyl-7-methoxy-7-phenylhept-5-en-2-one (10e)

The crude residue was purified by flash column chromatography on silica gel (petrol–EtOAc, 20:1) to give the title product.

Yield: 0.051 g (91%); 95:5 ratio of diastereomers; colourless oil; R_f = 0.3 (petrol–EtOAc, 20:1); $[\alpha]_D^{20}$ –53.2 (*c* 0.81, $CHCl_3$).

IR (neat): 2959, 2931, 2822, 1711 (C=O), 1357, 1101.

^{1}H NMR (500 MHz, C_6D_6): δ = 7.36–7.31 (m, 2 H, PhH), 7.29–7.23 (m, 3 H, PhH), 5.30 (dt, *J* = 15.4, 6.62 Hz, 1 H, C*H* alkene), 5.22 (dd, *J* = 15.5, 7.88 Hz, 1 H, C*H* alkene), 4.08 (t, *J* = 6.62 Hz, 1 H, C*H*OCH$_3$), 3.21 (s, 3 H, OCH$_3$), 2.52 (dt, *J* = 13.6, 6.94 Hz, 1 H, CH), 2.44–2.28 (m, 4 H), 2.06 (s, 1 H, COCH$_3$, minor diastereomer), 2.04 (s, 3 H, COCH$_3$, major diastereomer), 1.51 [sept, *J* = 6.62 Hz, 1 H, C*H*(CH$_3$)$_2$], 0.83 [dd, *J* = 19.9, 6.62 Hz, 6 H, CH(C*H*$_3$)$_2$, major diastereomer], 0.76 [dd, *J* = 19.9, 6.62 Hz, 0.6 H, CH(C*H*$_3$)$_2$, minor diastereomer].

^{13}C NMR (125.8 MHz, $CDCl_3$): δ = 208.8, 208.7, 141.6, 133.2, 133.2, 128.3, 127.6, 127.5, 126.8, 126.8, 84.1, 84.0, 56.6, 46.9, 46.8, 41.2, 31.7, 30.5, 30.5, 20.4, 20.3, 18.8, 16.7

HRMS (ESI$^+$): *m*/*z* [M + Na$^+$] calcd for $C_{18}H_{26}NaO_2$: 297.1831; found: 297.1826.

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