Nucleophilic Addition of α-Metallated Carbamates to Planar Chiral Cationic η³-Allylmolybdenum Complexes: A Stereochemical Study

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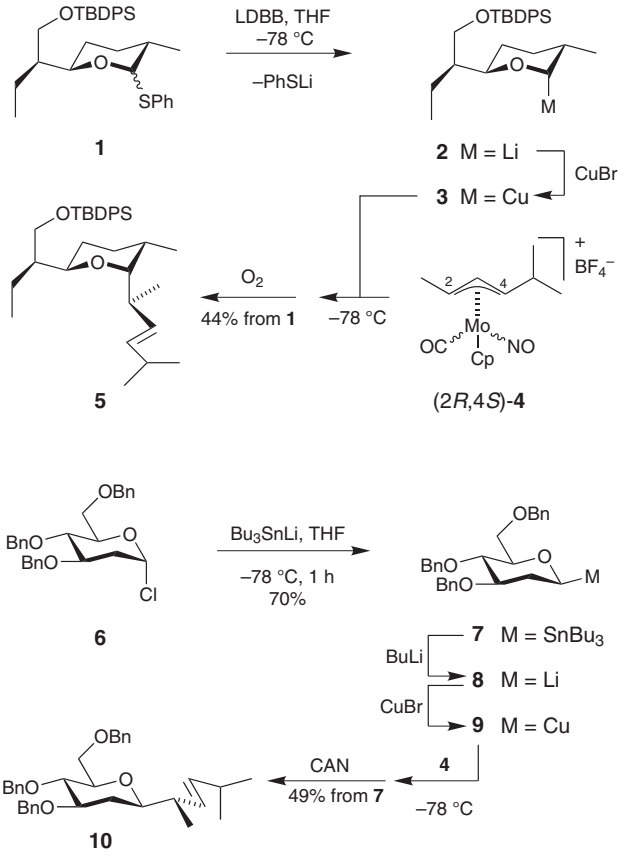
Abstract: Chiral α-(*O*-carbamoyl)alkyl- and α-(*N*-carbamoyl)alkylcopper(I) reagents derived from (–)-sparteine-mediated asymmetric lithiation of hindered carbamates react with cationic η³-allylmolybdenum complexes with retention of configuration.

Key words: (–)-sparteine, nucleophilic addition, η³-allylmolybdenum complexes, asymmetric deprotonation, carbamates, α-(*O*-carbamoyl)alkylcopper(I), α-(*N*-carbamoyl)alkylcopper(I)

A powerful method for the stereoselective appendage of a carbon chain to an oxacyclic ring with simultaneous creation of two stereogenic centres is exemplified by the addition of tetrahydropyran-2-ylcopper(I) reagent **3** to the cationic planar chiral η³-allylmolybdenum complex **4** to give adduct **5** after oxidative decomplexation (Scheme 1).[1] The reaction occurs with clean retention in the organocopper(I) nucleophile which adds regioselectively to the allyl ligand *anti* to the molybdenum. The requisite α-alkoxyalkylcopper(I) reagent **3** was generated stereoselectively by a 2-step sequence involving first reductive lithiation of the *O*,*S*-acetal **1**[2] using lithium di-*tert*-butylbiphenylide (LDBB)[3] to give the axial organolithium **2** owing to the radical anomeric effect.[4,5] The second step, transmetallation with CuBr, occurred with retention of configuration.[6,7] However, the reductive lithiation is only stereoselective when the oxygen atom is contained in a six-membered ring and many functional groups are incompatible with the powerful reductive conditions.[8] A milder alternative is illustrated by the generation of organocopper(I) reagent **9** from the enantiomerically pure stannane **7** by two sequential transmetallation reactions, both of which occurred with retention of configuration.[9] In order to extend the scope of the chemistry depicted in Scheme 1, especially to *acyclic* systems, we required access to a readily available configurationally stable carbon nucleophile whose addition to cationic η³-allylmolybdenum complexes occurs with high and predictable stereoselectivity. We now report that chiral α-(*O*-carbamoyl)alkyl- and α-(*N*-carbamoyl)alkylcopper(I) reagents derived from hindered carbamates react with cationic η³-allylmolybdenum complexes with retention of configuration to provide an acyclic variant of the chemistry described above.



Scheme 1

At the heart of our work is the convenient and general synthesis of enantioenriched α-(*O*-carbamoyl)alkyllithiums invented by Hoppe and co-workers.[10,11] The procedure is illustrated by the synthesis of the α-(*O*-carbamoyl)alkylstannane **11**:[12] ligand-directed deprotonation of the pro-*S* proton of the *racemic* carbamate **11** with *s*-butyllithium and (–)-sparteine followed by addition of chlorotributylstannane gave the (1*S*,2*S*)-stannane **12** in 23% yield (er = >97:3), the (1*S*,2*R*)-stannane (46%, er = 88:12) and recovered starting material **11** (14%) after column chromatography. The minor (1*S*,2*S*)-isomer was used in the next step owing to its higher enantiopurity. Thus treatment of stannane **12** with BuLi in Et_2O–THF (1:1) at –78 °C fol-

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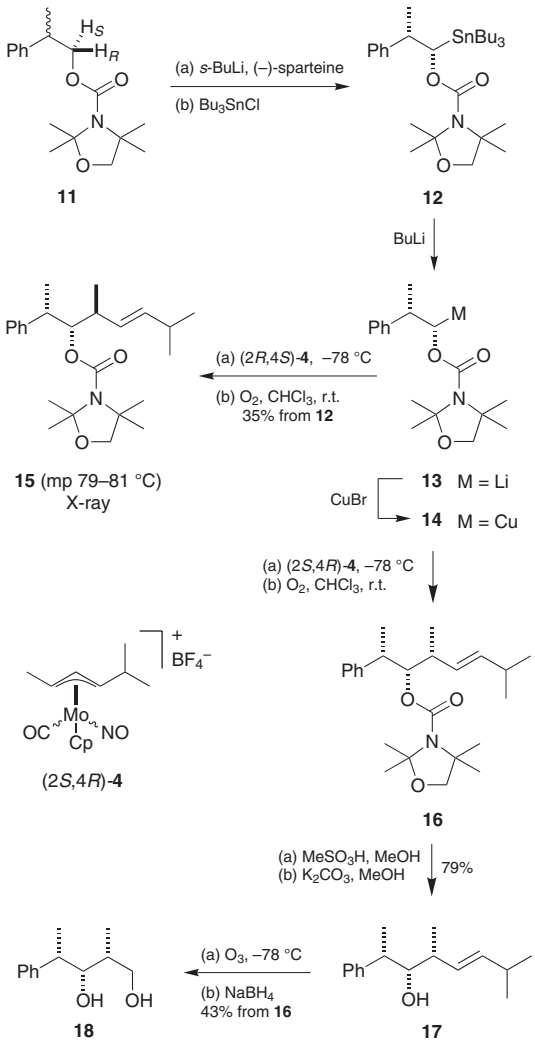
lowed by addition of $CuBr{\cdot}SMe_2$ generated the organocopper(I) reagent **14** to which was added a freshly prepared solution of the cationic complex (2*S*,4*R*)-**4** in acetonitrile. After aqueous workup, the crude η^2-adduct was treated with oxygen in chloroform to give the crystalline adduct **15** in 35% overall yield from stannane **12** (Scheme 2). An X-ray crystal structure of adduct **15** (Figure 1) revealed the relative stereochemistry to be 1,2-*syn*-2,3-*anti* indicating that the transmetallation of lithium to copper(I) occurred with retention[13] and the α-(*O*-carbamoyl)alkylcopper(I) reagent **14** added to the cationic η^3-allylmolybdenum complex (2*S*,4*R*)-**4** with retention of configuration.



Scheme 2

The organocopper(I) reagent **14** was also added to the enantiomeric η^3-allylmolybdenum complex (2*R*,4*S*)-**4** in order to establish that the stereoselectivity of the addition was not a consequence of matched-pair effects. The diastereoisomeric 1,2-*syn*-2,3-*syn* adduct **16** was isolated in 52% overall yield from stannane **12** along with 15% of (*S*)-**11**. Adduct **16** was not crystalline and hence its relative configuration was established by correlation with a known compound. Methanolysis of the carbamate **16**

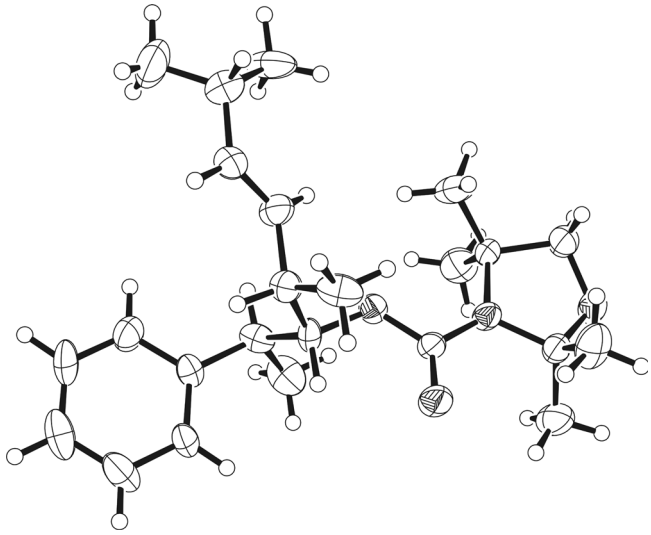


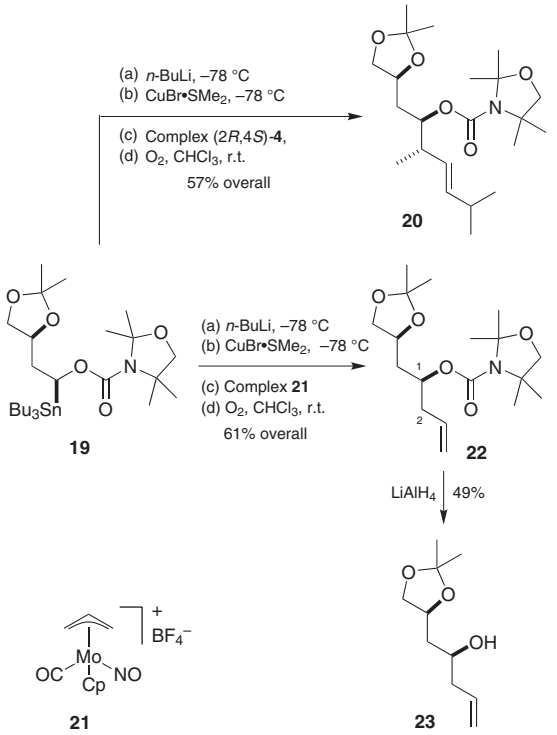
Figure 1 X-ray crystal structure of adduct **15**

(79% yield) followed by ozonolysis of the alkene **17** returned (2*R*,3*R*,4*S*)-diol **18** after reductive workup (Scheme 2). The ^{1}H NMR spectrum of (2*R*,3*R*,4*S*)-**18** compared favourably with data reported by Matsumoto and co-workers for the racemic modification.[14]

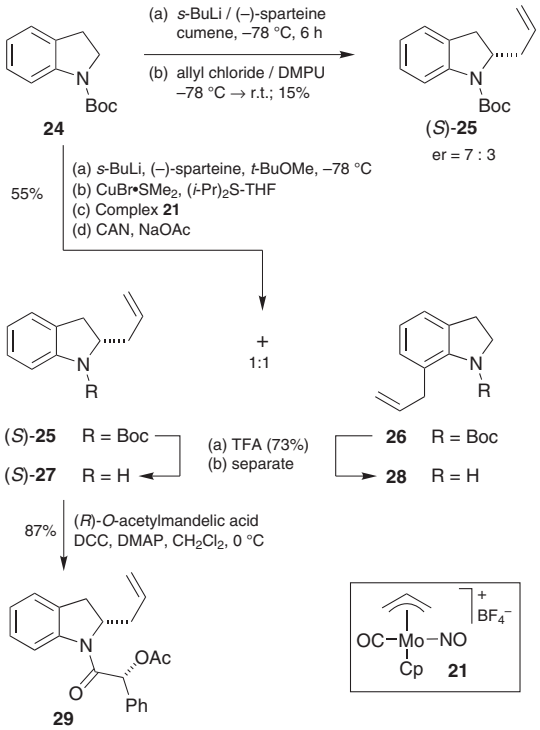
The second α-(*O*-carbamoyl)alkylcopper(I) nucleophile in this study was selected to determine the consequence, if any, of a chelating heteroatom substitutent β to the carbanionic centre. The requisite stannane **19**, easily prepared by the procedure of Hoppe and co-workers,[15] was converted to the organocopper(I) reagent as before. Addition of the η^3-allylmolybdenum complex (2*R*,4*S*)-**4** in MeCN gave olefin **20** in 57% overall yield from stannane **19** after oxidative decomplexation (Scheme 3). ^{1}H NMR spectroscopy and GC/MS of the crude reaction mixture revealed a mixture of 4 isomers in the approximate ratio 95:2:2:1. The 1,2-*anti* stereochemistry of the major adduct **20** was assigned on the assumption that the nucleophile added with retention of configuration *anti* to the molybdenum.

Proof that the alkylation reaction proceeds with retention of configuration in the nucleophile was obtained once again by correlation with a known compound. The α-(*O*-carbamoyl)alkylcopper(I) intermediate derived from stannane **19** was treated with the simple η^3-allylmolybdenum complex **21**. The resultant adduct **22** (dr = 50:1) was obtained in 61% overall yield from **19**. Reductive cleavage of the carbamate group gave the (*S*)-alcohol **23** (49%) whose optical rotation and ^{1}H and ^{13}C NMR spectroscopic data correlated with literature values.[16,17]

The regiochemistry of ligand-directed carbamate metallation is structure dependent. Beak and co-workers showed that carbamates devoid of a proton adjacent to oxygen metallate adjacent to nitrogen instead to give α-(*N*-carbamoyl)alkyllithiums.[18] Thus asymmetric metallation of *N*-Boc-indoline **24** with *s*-BuLi and (–)-sparteine followed by alkylation with allyl chloride and DMPU gave



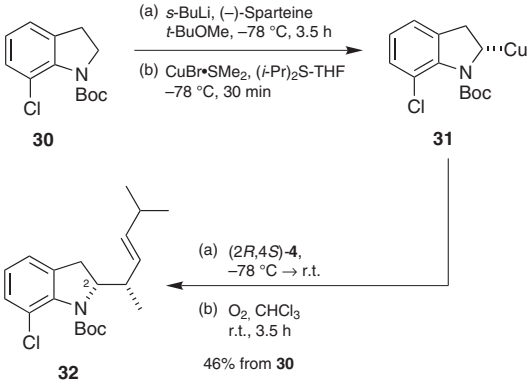
Scheme 3



Scheme 4

2-allylindoline (*S*)-**25** in 15% yield (*S*:*R* = 99:1) as shown in Scheme 4.[19] By using allyl bromide as the alkylating agent, the yield improved to 28% but the er of the reaction plummeted (*S*:*R* = 7:3). The low yield and variable enantioselectivity in this reaction prompted us to examine the alkylation of *N*-Boc-indoline **24** with the simple cationic η^3-allylmolybdenum complex **21**.[20] Asymmetric lithiation of *N*-Boc-indoline **24** with *s*-BuLi/(–)-sparteine, transmetallation to the organocopper(I) reagent, and reaction with **21** gave an inseparable equimolar mixture of 2- and 7-substituted indolines **25** and **26** (55%) together with 9% of recovered indoline **24**. Comparison of the sign of optical rotation of the mixture **25** and **26** [+44.2, (*c* = 0.55, $CHCl_3$)] with that reported by Beak[19] [+29 (*c* = 0.01, $CHCl_3$), 36% ee] indicated that the lithiation–transmetallation–allylation sequence returned **25** with the (*S*)-configuration. Protonolysis of the *N*-Boc group gave the separable amines (*S*)-**27** and **28**. The 2-allyl derivative (*S*)-**27** gave (*R*)-*O*-acetylmandelamide **29** as a single diastereoisomer according to ^1H and ^{13}C NMR spectroscopy and GC/MS. Hence, the transmetallation (Li to Cu) and nucleophilic addition reactions occurred with clean retention of stereochemistry.

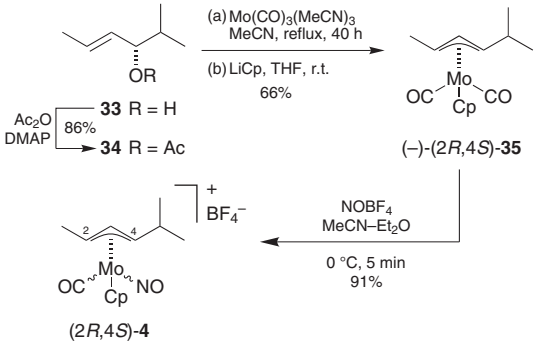
In order to avoid the complications of arene metallation observed with *N*-Boc indoline, we performed an asymmetric lithiation of *N*-Boc-7-chloroindoline **30** and its transmetallation with $CuBr{\cdot}SMe_2$, to give the organocopper(I) reagent **31**. Addition of **31** to cationic η^3-allylmolybdenum complex (2*R*,4*S*)-**4** gave an inseparable mixture of 4 isomeric adducts (57%) in the ratio 4:9:81:6 according to GC/MS. The major product was assigned the absolute stereochemistry depicted in **32** based on the precedent provided in the three preceding examples (Scheme 5).



Scheme 5

Synthesis of the Cationic η^3-Allylmolybdenum Complexes (2*R*,4*S*)-4 and (2*S*,4*R*)-4

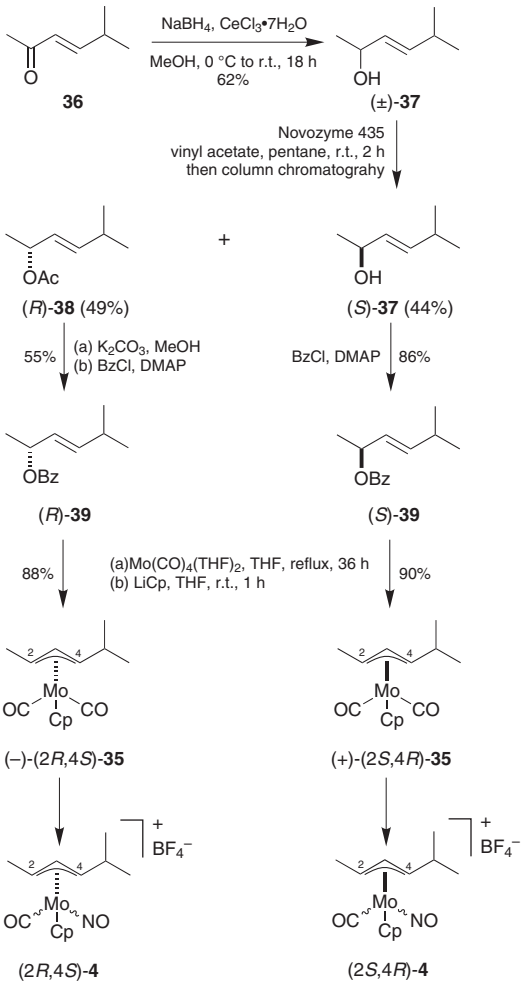
We previously prepared the cationic complex (2*R*,4*S*)-**4** by a 4-step sequence first described by Faller and Linebarrier[21] (Scheme 6). The principal detraction to this route was the Sharpless kinetic resolution[22] used to prepare the allylic alcohol **33**. Although the enantiomeric purity of **33** was excellent (er = 97:3), the yield was low (26%) and the reaction was awkward to conduct on a large scale. Moreover, two separate kinetic resolutions were required to prepare both enantiomers of **33**.



Scheme 6

A more efficient and scalable route to (2*R*,4*S*)-**4** and its enantiomer has been achieved (Scheme 7) featuring two significant improvements. Firstly, the Sharpless kinetic resolution has been replaced by a much faster, easier and more convenient enzymatic resolution of the racemic alcohol (±)-**37** using Novozyme 435 and vinyl acetate.[23] The easily separable allylic alcohol (*S*)-**37** and the allylic acetate (*R*)-**38** were obtained in 44% yield (er = 99:1) and 49% yield (er = 96:4) respectively. Note that both products of the single kinetic resolution were transformed to the desired enantiomeric complexes.[24] Secondly, the yield and quality of the neutral complexes (–)-(2*R*,4*S*)-**35** and (+)-(2*S*,4*R*)-**35** were enhanced by the use of allylic benzoates (*R*)-**39** and (*S*)-**39** as precursors instead of the corresponding allylic acetates and $Mo(CO)_4(THF)_2$ instead of $Mo(CO)_3(MeCN)_3$ as the Mo(0) source.[25]

In summary, we have established that α-(*O*-carbamoyl)alkyl- and α-(*N*-carbamoyl)alkylcopper(I) reagents derived from the asymmetric metallation of hindered carbamates add to planar chiral cationic η^3-allylmolybdenum complexes with clean retention of configuration.[26] In the case of complexes (2*R*,4*S*)-**4** and (2*S*,4*R*)-**4**, the addition occurred regioselectively at the less hindered terminus *anti* to the molybdenum in accord with previous observations.[1,9] The method provides a potentially useful chain extension in which two adjacent stereogenic centres are created in a single step and it represents a relatively rare procedure in asymmetric synthesis, the direct and stereospecific connection of a carbocation equivalent and a carbanion equivalent[27] (Figure 2). Compared with the reductive cleavage and transmetallation procedures used previously to generate the α-alkoxyalkyllithiums, Hoppe's asymmetric metallation protocol provides a more general and versatile route to enantioenriched carbon nucleophiles. Although the stereoselectivity of the addition is excellent, the yield is modest at best and needs improvement.



Scheme 7

(–)-Sparteine was purified by Kugelrohr distillation immediately prior to use. $CuBr{\cdot}SMe_2$ was prepared by the procedure of Theis and Townsend[28] and purified by recrystallisation before use. Commercial *n*-BuLi and *s*-BuLi solutions were titrated against 1,3-diphenylacetone-*p*-tosylhydrazone.[29] Organic extracts were dried over $MgSO_4$ and concentrated using a rotary evaporator at diaphragm pump pressure (5–20 mmHg). All reactions were magnetically stirred and were monitored by TLC using silica gel pre-coated aluminum foil sheets, layer thickness 0.25 mm. Compounds were visualised by UV (254 nm), 20 wt% phosphomolybdic acid in EtOH, anisaldehyde, vanillin followed by H_2SO_4, $KMnO_4$ or cerium(IV) sulfate solutions.

Specific optical rotations ($[\alpha]_D$) were measured on an Optical Activity polAAr 2000 polarimeter using a 5 mL cell with a 1 dm path length or a 0.5 mL cell with a 0.05 dm path length. IR spectra were recorded on a Nicolet Impact 410 FT-IR spectrometer using a thin film supported between NaCl plates or a KBr disk, unless otherwise specified. ^1H and ^{13}C NMR spectra were recorded in Fourier Transform mode at the field strength specified. All spectra were obtained in $CDCl_3$ or CD_3CN solution in 5 mm diameter tubes, and the chemical shift in ppm is quoted relative to the residual signals of $CHCl_3$ (δ_H 7.27, δ_C 77.2) or MeCN (δ_H 2.00, δ_C 117.7) unless specified otherwise. Coupling constants (*J*) are reported in Hz. The number of protons attached to the carbon in the ^{13}C spectra was ascertained by the Distortionless Enhancement by Phase Transfer (DEPT) technique with secondary pulses at 90° and 135°. Signal assignments are based on COSY and HMQC correlations. Low- and high-resolution mass spectra were run on a JEOL MStation JMS-700 spectrometer. Ion mass/charge (*m*/*z*) ratios are reported as values in atomic mass units followed, in parenthesis, by the peak intensity relative to the base peak (100%). GC/MS was performed on the above spectrometer, using a Chrompack WCOT Fused Silica column (25 m × 0.25mm, CP-SIL 8CB-MS stationary phase), initial temperature and heating rates are specified for individual cases.

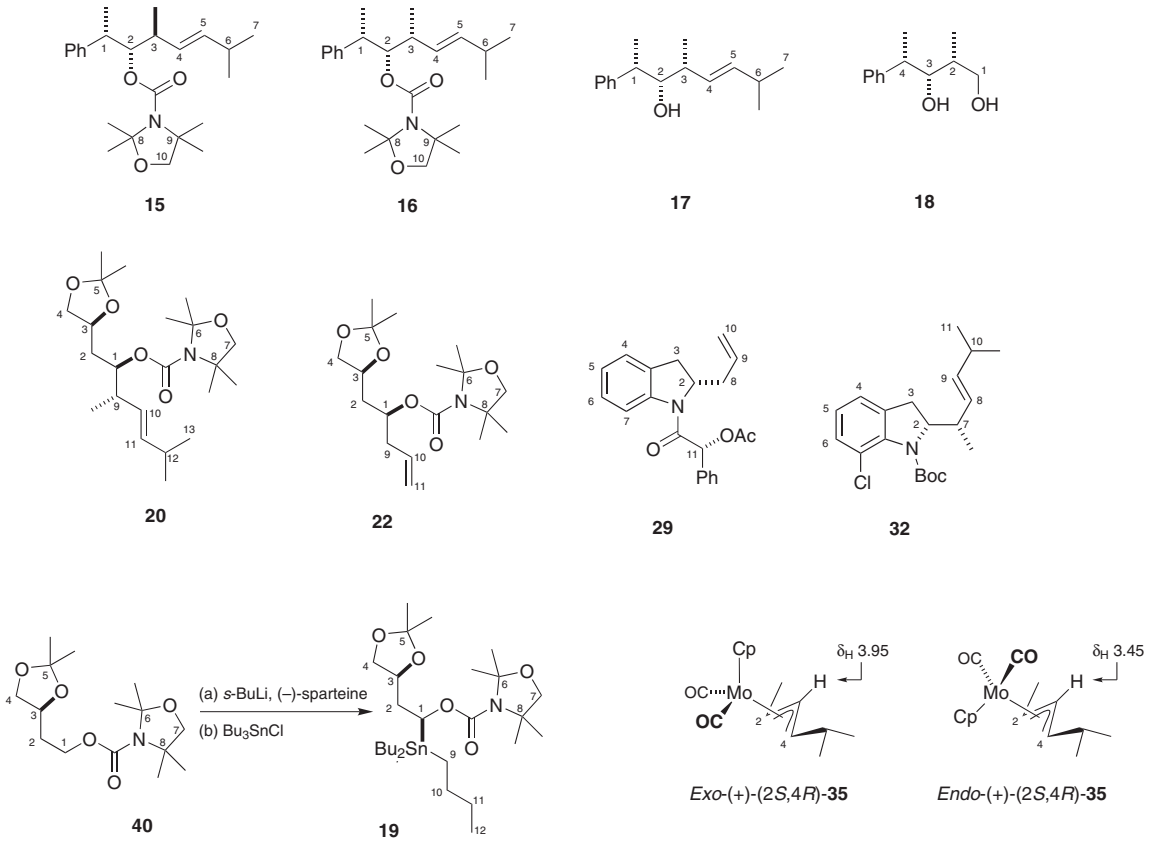


Figure 2 Atom numbering scheme used in assigning the ^{1}H and ^{13}C NMR data in the experimental section

2,2,4,4-Tetramethyloxazolidine-3-carboxylic Acid (1*S*,2*S*)-1-Tributylstannyl-2-phenylpropyl Ester (12)

The title compound was prepared in 22% yield from racemic 2,2,4,4-tetramethyloxazolidine-3-carboxylic acid 2-phenylpropyl ester (**11**) according to the procedure of Hoppe and co-workers;[12] $[\alpha]_D^{18}$ –22.4 (*c* = 1.2, acetone) {Lit.[12] $[\alpha]_D^{20}$ –20.3 (*c* = 1.2, acetone)}.

2,2,4,4-Tetramethyloxazolidine-3-carboxylic Acid (1*S*,2*S*,3*E*)-2,5-Dimethyl-1-[(1*S*)-1-phenylethyl]hex-3-enyl Ester (15)

Stannane **12** (116 mg, 0.200 mmol) was dissolved in THF (2 mL) and Et_2O (2 mL) and the solution was stirred at –78 °C for 10 min. *n*-BuLi (0.15 mL, 0.22 mmol, 1.51 M in hexane) was added dropwise and the resulting colourless solution was stirred for 40 min at –78 °C. A solution of CuBr·SMe_2 (49 mg, 0.240 mmol) in Et_2O (0.3 mL) and diisopropyl sulfide (0.25 mL) was then added dropwise. The resulting brown solution was stirred for 4 h at –78 °C. In another flask neutral molybdenum complex (+)-(2*S*,4*R*)-**35** (94 mg, 0.30 mmol) was dissolved in MeCN (1 mL) and cooled to 0 °C. Nitrosonium tetrafluoroborate (43 mg, 0.36 mmol) was added in one portion and the mixture was stirred for 10 min at 0 °C before adding to the organocopper(I) reagent via syringe. The resulting brown solution was stirred for 1 h at –78 °C and then warmed to r.t. whereupon aq NH_4Cl (5 mL), Et_2O (10 mL) and ammonia (5 mL) were added sequentially. The blue aqueous layer was extracted with Et_2O (2 × 10 mL) and the combined organic layers were washed with brine (10 mL), dried and concentrated. The crude product was dissolved in $CHCl_3$ (30 mL) and oxygen was bubbled through the solution. After 15 h, the mixture was concentrated and the residue purified by column chromatography (SiO_2, hexanes–Et_2O, 20:1 to 8:1) to give the title compound **15** (27.1 mg, 35%) as colourless crystals; mp 79–81 °C (CH_2Cl_2) and (*S*)-**15** (15.1 mg, 26%) as a colourless oil; $[\alpha]_D^{22}$ +38.6 (*c* = 0.80, $CHCl_3$).

IR (film): 1690 (s) cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ (mixture of rotamers) = 7.32–7.27 (2 H, m, Ar), 7.24–7.18 (3 H, m, Ar), 5.41–5.29 (1 H, m, C4H), 5.22 (1 H, dd, *J* = 6.4 15.4 Hz, C5H), 5.16 (1 H, dd, *J* = 2.3 10.1 Hz, C2H), 3.76 (2 H, s, $C10H_2$), 3.01–2.91 (1 H, m, C1H), 2.26 (1 H, apparent octet, *J* = 6.6 Hz, C6H), 2.14–2.05 (1 H, m, C3H), 1.63/1.61, 1.60/1.56, 1.47/1.46 and 1.45/1.42 (3 H each, s, 4 CH_3), 1.25–1.20 (3 H, m, $C1CH_3$), 1.01 (3 H, d, *J* = 6.7 Hz, $C7H_3$), 0.98 (3 H, d, *J* = 6.7 Hz, $C6CH_3$), 0.95–0.90 (3 H, m, $C3CH_3$).

^{13}C NMR (75 MHz, $CDCl_3$,): δ (mixture of rotamers) = 153.3/152.5 (C=O), 144.2 (C, Ar), 139.6/139.5 (C5H), 128.7 (2 CH, Ar), 128.1 (2 CH, Ar), 127.3/127.1 (C4H), 126.6 (CH, Ar), 96.2/94.9 (C8), 81.3 (C2H), 76.6/76.3 ($C10H_2$), 60.9/59.9 (C9), 43.0 (C1H), 38.6/38.5 (C3H), 31.3 (C6H), 27.3/26.9, 25.8, 25.7/25.8 and 24.5/24.4 (4 CH_3), 22.8 ($C6CH_3$), 22.7 ($C7H_3$), 19.4 ($C1CH_3$), 18.8 ($C3CH_3$).

For the atom numbering scheme see Figure 2.

HRMS (ES); *m*/*z* calcd for $C_{24}H_{37}NO_3Na$: 410.2671; found: 410.2675.

Anal. Calcd for $C_{24}H_{37}NO_3$: C, 74.38; H, 9.62; N, 3.61. Found: C, 74.3; H, 9.3; N, 3.55.

X-ray structure of 15[30]

$C_{24}H_{37}NO_3$, monoclinic, space group $P2_1$, *a* = 7.3615(4) Å, *b* = 20.3854(8) Å, *c* = 7.9378(4) Å, β = 103.1410(19)°, *V* = 1160.01(10) $Å^3$, *Z* = 2, ρ_{calc} = 1.11 Mg/m^3, μ = 0.072 mm^{-1}, crystal size: 0.13 × 0.12 × 0.02 mm, data collection range: 2.82 ≤ θ ≤ 26°, 6320 measured reflections, final *R*(*wR*) values: 0.1155, (0.3059) for 3503 independent data and 279 parameters [$I > 2\sigma(I)$],

largest residual peak and hole: 0.432, –0.473 e Å^{-3}. Reflections were weak possibly because of the poor crystal quality. This factor, together with the disorder of the CH=CHCHMe$_2$ group, which was modelled over two equally occupied positions, led to a structure of only moderate precision. All hydrogen atoms were placed in idealised positions with the following C–H distances: aromatic, 0.95 Å; olefinic, 0.95 Å; methyl, 0.98 Å; methylene, 0.99 Å; methine, 1.00 Å. In the absence of significant anomalous scattering effects, only the relative stereochemistry was determined and Friedel pairs merged.

2,2,4,4-Tetramethyloxazolidine-3-carboxylic Acid (3*E*,1*S*,2*R*)-2,5-Dimethyl-1-[(1*S*)-1-phenylethyl)hex-3-enyl Ester (16)

The title compound was prepared reaction of stannane **12** with cationic complex **4** was performed on a 0.20 mmol scale according to the procedure described above. Compound **16** (40 mg, 52%) was obtained as a colourless oil together with (*S*)-**11** (8.5 mg, 15%); $[\alpha]_D^{22}$ +34.3 (*c* = 0.97, $CHCl_3$).

IR (film): 1695 (s) cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ (mixture of rotamers) = 7.32–7.17 (5 H, m, Ar), 5.37–5.26 (2 H, m, C4H and C5H), 5.24–5.18 (1 H, m, C2H), 3.73 (2 H, s, C10H$_2$), 3.08–2.98 (1 H, m, C1H), 2.26–2.13 (2 H, m, C3H and C6H), 1.62/1.57, 1.55/1.50, 1.47/1.42 and 1.40/1.37 (3 H each, s, 4 CH$_3$), 1.29–1.24 (3 H, m, C1CH$_3$), 1.02–0.95 (3 H, m, C3CH$_3$), 0.92 (6 H, d, *J* = 6.8 Hz, C6CH$_3$ and C7H$_3$).

^{13}C NMR (75 MHz, $CDCl_3$): δ (mixture of rotamers) = 152.9/152.1 (C=O), 144.3 (C, Ar), 137.4 (C5H), 129.6 (C4H), 128.7 (2 CH, Ar), 127.8 (2 CH, Ar), 126.6 (CH, Ar), 96.1/94.8 (C8), 80.6/80.5 (C2H), 76.6/76.2 (C10H$_2$), 60.8/59.8 (C9), 42.2 (C1H), 37.8/37.8 (C3H), 31.2 (C6H), 27.6/27.0, 25.9/25.8, 25.6/25.3 and 24.4/24.3 (4 CH$_3$), 22.7/22.7 (C7H$_3$ and C6CH$_3$), 18.4/18.3 (C1CH$_3$), 14.3/14.1 (C3CH$_3$).

For the atom numbering scheme see Figure 2.

HRMS (ES): *m*/*z* calcd for $C_{24}H_{37}NO_3Na$: 410.2671; found: 410.2677.

Anal. Calcd for $C_{24}H_{37}NO_3$: C, 74.38; H, 9.62; N, 3.61. Found: C, 74.1; H, 9.35; N, 3.65.

(2*S*,3*S*,4*R*,5*E*)-4,7-Dimethyl-2-phenyloct-5-en-3-ol (17)

Carbamate **16** (38 mg, 0.098 mmol) in MeOH (2 mL) containing $MeSO_3H$ (10.4 mg, 0.108 mmol) was refluxed for 3 h and the solvent was evaporated. The residue was dissolved in Et_2O (12 mL) and extracted with aq NH_4Cl (2 × 5 mL). The aqueous layer was extracted with Et_2O (3 × 5 mL). The combined organic layers were dried and evaporated. The crude product (31.3 mg, 0.90 mmol) was dissolved in MeOH (3 mL) and K_2CO_3 (20 mg, 0.144 mmol) was added. The reaction mixture was refluxed for 2 h. The solvent was evaporated and the residue was dissolved in CH_2Cl_2 (10 mL) and extracted with aq 2 M HCl (2 × 10 mL). The aqueous layer was extracted with CH_2Cl_2 (3 × 10 mL). The combined organic layers were dried and evaporated and the residue purified by column chromatography (SiO_2, hexanes–Et_2O, 20:1) to give the title compound **17** (18.0 mg, 79%) as a colourless oil; $[\alpha]_D^{22}$ +5.3 (*c* = 0.72, $CHCl_3$).

IR (film): 3456 (br m) cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.33–7.28 (2 H, m, Ar), 7.24–7.18 (3 H, m, Ar), 5.45 (1 H, dd, *J* = 6.6 15.8 Hz, C5H), 5.33 (1 H, dd, *J* = 7.2 15.4 Hz, C4H), 3.56–3.51 (1 H, m, C2H), 2.90 (1 H, apparent quintet, *J* = 6.7 Hz, C1H), 2.27 (1 H, apparent octet, *J* = 6.7 Hz, C6H), 2.12 (1 H, apparent octet, *J* = 6.6 Hz, C3H), 1.47 (1 H, br s, OH), 1.30 (3 H, d, *J* = 6.8 Hz, C1CH$_3$), 1.01–0.95 (9 H, m, C7H$_3$, C3H$_3$, C6CH$_3$).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 145.4 (C, Ar), 138.4 (C5H), 130.1 (C4H), 128.7 (2 CH, Ar), 127.8 (2 CH, Ar), 126.5 (CH, Ar), 79.5 (C2H), 42.7 (C1H), 39.3 (C3H), 31.2 (C6H), 22.8 (C7H$_3$ and C6CH$_3$), 15.8 (C1CH$_3$), 14.6 (C3CH$_3$).

For the atom numbering scheme see Figure 2.

HRMS (ES): *m*/*z* calcd for $(M - OH)^+$: 215.1800; found: 215.1799.

Anal. Calcd for $C_{16}H_{24}O$: C, 82.70; H, 10.41. Found: C, 82.5; H, 10.24.

(2*R*,3*R*,4*S*)-2-Methyl-4-phenylpentane-1,3-diol (18)

Ozone was bubbled through a solution of alcohol **17** (18 mg, 0.077 mmol) in CH_2Cl_2 (5 mL) at –78 °C. After 5 min, the solution turned blue and oxygen was bubbled through the solution for 20 min. $NaBH_4$ (31 mg, 0.82 mmol) in MeOH (1 mL) was added at –78 °C and the resulting mixture was stirred for 2 h at 0 °C. Aq NH_4Cl (5 mL) and CH_2Cl_2 (5 mL) were added and the aqueous layer was extracted with CH_2Cl_2 (2 × 5 mL). The combined organic layers were dried and evaporated. The residue was purified by column chromatography (SiO_2, hexanes–Et_2O, 4:1 then 1:1, followed by 1:2) to give the title compound **18** (9.3 mg, 62%) as a colourless solid: mp 61–63 °C (hexane) (Lit.[14] mp 98.0–98.5 °C); $[\alpha]_D^{24}$ –6.7 (*c* = 0.67, $CHCl_3$). The ^{1}H NMR spectroscopic data were in accordance with the literature data.[14]

^{13}C NMR (75 MHz, $CDCl_3$): δ = 144.8 (C, Ar), 128.8 (2 CH, Ar), 127.6 (2 CH, Ar), 126.6 (CH, Ar), 79.2 (C3H), 68.4 (C1H$_2$), 44.0 (C4H), 36.1 (C2H), 19.3 (C4CH$_3$), 9.1 (C2CH$_3$).

For the atom numbering scheme see Figure 2.

2,2,4,4-Tetramethyloxazolidine-3-carboxylic Acid (1*S*)-2-[(4*S*)-2,2-Dimethyl-[1,3]dioxolan-4-yl]-1-(tributylstannyl)ethyl Ester (19)

Carbamate **40** was prepared in 91% yield on a 32 mmol scale by the method of Hoppe.[31] ^{1}H NMR spectroscopic data were in accordance with literature data;[15] $[\alpha]_D$ –9.47 (*c* = 5.08, MeOH) {Lit.[15] $[\alpha]_D^{20}$ –11.4 (*c* = 5.3, MeOH)}.

Carbamate 40

^{13}C NMR (100 MHz, $CDCl_3$): δ (mixture of rotamers) = 153.4 (0.55 C, C=O), 152.8 (0.45 C, C=O), 109.1 (C5), 96.0 (0.55 C, C6), 94.9 (0.45 C, C6), 76.5 (0.55 C, C7H$_2$), 76.2 (0.45 C, C7H$_2$), 73.4 (C3H), 69.5 (C4H$_2$), 61.6 (C1H$_2$), 60.7 (0.45 C, C8), 59.8 (0.55 C, C8), 33.3 (C2H$_2$), 27.1 (2 CH$_3$), 26.7 (CH$_3$), 25.8 (CH$_3$), 25.4 (CH$_3$), 24.3 (CH$_3$).

^{13}C NMR (100 MHz, $CDCl_3$, 52 °C): δ = 138.4, 109.2, 76.6, 73.6, 69.6, 61.7, 33.5, 27.2, 26.8, 25.8, 25.6, 24.4.

Three quaternary signals were not observed. For the atom numbering scheme see Figure 2.

s-BuLi [22.9 mL of a 1.28 M solution in cyclohexane–hexane (92:8), 29.4 mmol] was added dropwise to a solution of carbamate **40** (8.04 g, 26.7 mmol) and (–)-sparteine (6.88 g, 29.4 mmol) in Et_2O (140 mL) at –78 °C under N_2. The clear yellow solution was stirred at –78 °C for 3 h before the dropwise addition of Bu_3SnCl (10.9 mL, 40.0 mmol) and the solution was allowed to warm gradually to r.t. over 12 h. Aq 1 M HCl (100 mL) and Et_2O (50 mL) were added and after stirring for 10 min, the phases were separated. The aqueous phase was extracted with Et_2O (2 × 50 mL), and the combined organic phases were washed with brine (50 mL), dried, filtered and concentrated in vacuo. The residue was purified by column chromatography (SiO_2, Et_2O–hexanes, 1:4) to give the title compound **19** (10.8 g, 69%) as a colourless oil; $[\alpha]_D$ +15.3 (*c* = 0.85, $CHCl_3$).

IR (film): 1680 (s) cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 4.76 (1 H, dt, *J* = 9.6, 4.1 Hz, C1H), 4.17 (1 H, apparent septet, *J* = 6.2 Hz, C3H), 4.10 (1 H, dd, *J* = 6.0, 6.0 Hz, C4H_AH$_B$), 3.72 (2 H, s, C7H$_2$), 3.55 (1 H, dt,

J = 3.1, 7.4 Hz, C4H$_A$$H_B$), 2.31–2.20 (1 H, m, C2$H_AH_B$), 1.95 (1 H, ddd, J = 14.4, 6.8, 4.1 Hz, C2H$_A$$H_B$), 1.55–1.26 (30 H, m), 0.92–0.85 (15 H, m).

^{13}C NMR (100 MHz, $CDCl_3$): δ (mixture of rotamers) = 153.3 (0.6 C, C=O), 152.6 (0.4 C, C=O), 109.1 (C5), 96.1 (0.6 C, C6), 94.8 (0.4 C, C6), 76.5 (0.6 C, C7), 76.2 (0.4 C, C7), 74.7 (C3H), 69.6 (C4H$_2$), 67.7 (C1H), 60.8 (0.4 C, N*C*Me$_2$CH$_2$), 59.6 (0.6 C, N*C*Me$_2$CH$_2$), 38.5 (C2H$_2$), 29.3 (3 × C11H$_2$, $^3J_{C,Sn}$ 9.8), 27.7 (3 × C10H$_2$, $^2J_{C,Sn}$ 28.8), 27.2 (CH$_3$), 26.9 (0.5 C, CH$_3$), 26.7 (0.5 C, CH$_3$), 25.8 (CH$_3$), 25.5 (2 CH$_3$), 24.4 (0.5 C, CH$_3$), 24.3 (0.5 C, CH$_3$), 13.9 (3 × C12H$_3$), 10.1 (3 × C9H$_2$, $^1J_{C,Sn}$ 162.9, 155.9).

For the atom numbering scheme see Figure 2.

LRMS (CI mode, isobutane): m/z = 592.0 [(M + H)$^+$, 11%], 590.1 (10), 534.0 (100), 532.0 (75), 476.0 (8), 474.0 (6), 291.0 (6), 289.0 (5).

Anal. Calcd for $C_{27}H_{53}NO_5Sn$: C, 54.92; H, 9.05; N, 2.37. Found: C, 54.99; H, 9.04; N, 2.28.

2,2,4,4-Tetramethyloxazolidine-3-carboxylic Acid (1*R*,2*S*,3*E*)-1-[(4*S*)-2,2-Dimethyl-1,3-dioxolan-4-ylmethyl)-2,5-dimethylhex-3-enyl Ester (20)

n-BuLi (4.6 mL of a 1.42 M solution in hexanes, 6.5 mmol) was added dropwise to a solution of stannane **19** (3.49 g, 5.92 mmol) in THF (100 mL) at –78 °C under N_2. The light yellow solution was stirred at –78 °C for 30 min. The mixture was cooled to approximately –90 °C whereupon a solution of CuBr·SMe_2 (1.46 g, 7.10 mmol) in diisopropyl sulfide (2.5 mL) and THF (10 mL) was added dropwise. The brown-orange solution was allowed to warm to –78 °C over 45 min before re-cooling to approximately –90 °C. A solution of cationic complex (2*R*,4*S*)-**4** [which had been freshly prepared from neutral complex (–)-(2*R*,4*S*)-**35** (1.55 g, 4.93 mmol) and $NOBF_4$ (633 mg, 5.42 mmol) in MeCN (10 mL) at 0 °C for 10 min] was added dropwise. After warming to –78 °C and stirring for 1.5 h, aq NH_4Cl (40 mL), Et_2O (30 mL) and aq NH_3 (5 mL) were added and the mixture warmed to r.t. After filtration of the mixture through Celite, and thorough washing of the Celite with Et_2O (2 × 30 mL), the phases were separated and the aqueous phase was extracted with Et_2O (3 × 30 mL). The combined organic phases were washed with brine (50 mL), dried, filtered and concentrated in vacuo. The resulting yellow-brown oil was dissolved in $CHCl_3$ (250 mL) and stirred at r.t. while bubbling oxygen through the solution for 44 h with irradiation from a standard household light-bulb (150 W) for the last 26 h. The dark-brown mixture was concentrated in vacuo, dissolved in CH_2Cl_2 (5 mL) and flushed through a plug of SiO_2 (4 cm depth, Et_2O) before purification by column chromatography (SiO_2, Et_2O–hexanes, 0:1 to 1:1) to yield the title olefin **20** (1.12 g, 57%) as a pale yellow oil. GC/MS (160 °C, 1 min, 3 °C min^{-1} to 200 °C, 5 °C to 250 °C) showed 4 isomers in the ratio 1:95:2:2 with retention times of 9.32, 10.03, 10.19, 10.36 min respectively; $[\alpha]_D$ +10.3 (c = 1.3, $CHCl_3$). Stannane **19** (93 mg, 4%) was also recovered.

IR (film): 1694 (s) cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 5.45 (1 H, dd, J = 15.6, 6.3 Hz, C11H), 5.31 (1 H, dd, J = 15.6, 7.9 Hz, C10H), 4.83 (1 H, dt, J = 9.9, 3.9 Hz, C1H), 4.15–4.07 (2 H, m, C3H, C4H_AH$_B$), 3.75 (2 H, s, C7H$_2$), 3.58–3.52 (1 H, m, C4H$_A$$H_B$), 2.44–2.34 (1 H, m, C9H), 2.25 (1 H, apparent octet, J = 6.8 Hz, C12H), 1.98 (1 H, dt, J = 9.9, 4.7 Hz, C2H_AH$_B$), 1.70–1.63 (1 H, m, C2H$_A$$H_B$), 1.55 (6 H, br s, CH$_3$), 1.41 (3 H, s, CH$_3$), 1.40 (3 H, s, CH$_3$), 1.38 (3 H, s, CH$_3$), 1.32 (3 H, s, CH$_3$), 1.03 (1.5 H, d, J = 6.8 Hz, C9CH$_3$), 1.02 (1.5 H, d, J = 6.8 Hz, C9CH$_3$), 0.96 (6 H, d, J = 6.8 Hz, C13H$_3$, C12CH$_3$).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 152.7 (0.6 C, C=O), 152.6 (0.4 C, C=O), 139.4 (C10H or C11H), 127.9 (0.6 C, C10H or C11H), 127.8 (0.4 C, C10H or C11H), 108.9 (C5), 96.1 (0.6 C, C6), 95.0 (0.4 C, C6), 76.6 (0.6 C, C7H$_2$), 76.2 (0.4 C, C7H$_2$), 74.9 (C1H or C3H), 73.7 (C1H or C3H), 69.7 (C4H$_2$), 60.8 (0.4 C, C8), 59.9 (0.6 C, C8), 41.0 (C9H), 36.3 (C2H$_2$), 31.2 (C12H), 27.1 (CH$_3$), 26.8 (CH$_3$), 25.8 (CH$_3$), 25.7 (0.5 C, CH$_3$), 25.6 (0.5 C, CH$_3$), 25.4 (CH$_3$), 24.4 (CH$_3$), 22.7 (C13H$_3$), 22.6 (C12CH$_3$), 17.0 (C9CH$_3$).

For the atom numbering scheme see Figure 2.

LRMS (CI mode, isobutane): m/z = 398.2 [(M + H)$^+$, 95%], 340.2 (100), 225.2 (62), 167.2 (59).

Anal Calcd for $C_{22}H_{39}NO_5$: C, 66.47; H, 9.89; N, 3.52. Found: C, 66.56; H, 9.83; N, 3.47.

2,2,4,4-Tetramethyloxazolidine-3-carboxylic Acid (1*S*)-1-[(4*S*)-2,2-Dimethyl-1,3-dioxolan-4-ylmethyl]but-3-enyl Ester (22)

To a solution of stannane **19** (4.09 g, 6.93 mmol) in THF (100 mL) at –78 °C under N_2 was added *n*-BuLi (5.4 mL of a 1.42 M solution in hexanes, 7.6 mmol) dropwise and the resulting light-yellow solution was stirred at –78 °C for 20 min. The mixture was cooled to approximately –90 °C and a solution of CuBr·SMe_2 (1.71 g, 8.32 mmol) in diisopropyl sulfide (3 mL) and THF (10 mL) was added dropwise. After stirring at –78 °C for 30 min, the orange-brown solution was re-cooled to –90 °C and a solution of cationic complex **21** [which had been freshly prepared from (η^5-cyclopentadienyl)(η^3-propenyl)(dicarbonyl)molybdenum (1.12 g, 4.34 mmol) and $NOBF_4$ (558 mg, 4.77 mmol) in MeCN (12 mL) at 0 °C for 10 min] was added via cannula keeping the internal temperature below –75 °C. The brown solution was stirred at –78 °C for 1 h before aqueous workup and decomplexation (O_2, light, r.t., 19 h) as described above for olefin **20**. Concentration in vacuo and purification of the residue by column chromatography (SiO_2, Et_2O–hexanes, 1:4) yielded the title compound **22** (1.45 g, 61%) as a pale yellow oil; $[\alpha]_D$ +22.1 (c = 1.02, $CHCl_3$).

IR (film): 1696 (s) cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 5.84–5.72 (1 H, m, C10H), 5.10 (1 H, d, J = 17.9 Hz, C11H_AH$_B$), 5.09 (1 H, d, J = 9.5 Hz, C11H$_A$$H_B$), 4.99–4.93 (1 H, m, C1H), 4.15 (1 H, br quintet, J = 6.4 Hz, C3H), 4.09 (1 H, dd, J = 7.6, 5.8 Hz, C4H_AH$_B$), 3.72 (2 H, s, C7H$_2$), 3.56 (1 H, t, J = 7.6 Hz, C4H$_A$$H_B$), 4.47–4.37 (2 H, m, C9H$_2$), 2.03–1.93 (1 H, m, C2H_AH$_B$), 1.81–1.71 (1 H, m, C2H$_A$$H_B$), 1.55 (3 H, s, CH$_3$), 1.53 (3 H, s, CH$_3$), 1.51 (3 H, s, CH$_3$), 1.41–1.33 (9 H, 3 CH$_3$).

^{13}C NMR (100 MHz, $CDCl_3$): δ (mixture of rotamers) = 152.4 (0.6 C, C = O), 151.6 (0.4 C C=O), 133.8 (C10H), 118.3 (C11H$_2$), 109.1 (C6), 96.1 (0.6 C, C5), 95.0 (0.4 C, C5), 76.5 (0.6 C, C7H$_2$), 76.2 (0.4 C, C7H$_2$), 73.3 (C3H), 71.1 (C1H), 69.6 (C4H$_2$), 60.8 (0.4C, C8), 59.9 (0.6 C, C8), 39.5 (0.6 C, C9H$_2$), 39.4 (0.4 C, C9H$_2$), 38.0 (0.6 C, C2H$_2$), 37.9 (0.4 C, C2H$_2$), 27.2 (CH$_3$), 26.9 (CH$_3$), 25.8 (CH$_3$), 25.7 (0.5 C, CH$_3$), 25.6 (0.5 C, CH$_3$), 25.5 (0.5 C, CH$_3$), 25.4 (0.5 C, CH$_3$), 24.4 (CH$_3$).

For the atom numbering scheme see Figure 2.

LRMS (EI mode GC/MS, 150 °C, 2 min, 5 °C/min to 200 °C, 10 °C/min to 250 °C, retention time = 6.31 min): m/z = 341 [(M$^+$), 2%], 326 (100), 158 (85), 156 (35), 101 (87). A minor diastereoisomer (2%) was observed, with a retention time of 6.47 min.

HRMS (CI mode, isobutane): m/z calcd for $C_{18}H_{32}O_5N$ [MH]$^+$: 342.2280; found: 342.2283.

(2*S*)-1-[(4*S*)-2,2-Dimethyl[1,3]dioxolan-4-yl]pent-4-en-2-ol (23)

A solution of olefin **22** (1.08 g, 3.16 mmol) in THF (25 mL) was added dropwise over 5 min to a suspension of $LiAlH_4$ (480 mg, 12.7 mmol) in THF (35 mL) at 0 °C under N_2. The mixture was then refluxed for 4 d (with the addition of a further 480 mg of $LiAlH_4$ after 44 h) and cooled to 0 °C. H_2O (0.9 mL) was then added, followed by 15% aq NaOH (0.9 mL) and H_2O (2.7 mL). The mixture was brought back to reflux for 30 min. After cooling to r.t., the mixture was filtered through Celite and the Celite was washed thoroughly

with THF (3 × 15 mL). The filtrate was concentrated in vacuo and the residue was purified by column chromatography (Et_2O–hexanes, 3:7 to 1:1) to give the title compound **23** (475 mg, 81%) as a colourless oil. Spectroscopic data were in accordance with literature data;[16,17] $[\alpha]_D$ +11.9 (*c* = 3.20) {Lit.[17] $[\alpha]_D$ +14.6 (*c* = 3.33, $CHCl_3$)}.

***N-tert*-Butoxycarbonyl-2,3-dihydroindole (24)**

The title compound was prepared on a 75 mmol scale according to the procedure of Iwao and co-workers,[32] mp 43–45 °C (hexanes) (Lit.[32] mp 42–45 °C).

^{13}C NMR (100 MHz, $CDCl_3$, 52 °C): δ = 152.8 (C), 142.9 (C), 131.4 (C), 127.5 (CH), 124.8 (CH), 122.3 (CH), 115.0 (CH), 80.9 (CMe_3), 47.8 ($C2H_2$), 28.7 [$C(CH_3)_3$], 27.5 ($C3H_2$).

(2*S*)-2-Allyl-*N*-*tert*-butoxycarbonyl-2,3-dihydroindole (25) and 7-Allyl-*N*-*tert*-butoxycarbonyl-2,3-dihydroindole (26)

s-BuLi [6.4 mL of a 1.30 M solution in cyclohexane–hexane (92: 8), 8.25 mmol] was added dropwise to a solution of indoline **24** (1.39 g, 6.4 mmol) and (–)-sparteine (1.93 g, 8.25 mmol) in *tert*-butyl methyl ether (65 mL) at –78 °C under N_2. The light yellow solution was stirred at –78 °C for 3.25 h before cooling to approximately –90 °C. A solution of CuBr·SMe_2 (1.83 g, 8.89 mmol) in diisopropyl sulfide (5 mL) and THF (7 mL) was added dropwise, ensuring that the internal solution temperature did not rise above –75 °C. After stirring for 40 min at –78 °C, the solution was cooled to approximately –85 °C and a solution of cationic complex **21** [which had been freshly prepared from (η^5-cyclopentadienyl)(η^3-propenyl)(dicarbonyl)molybdenum (2.69 g, 10.4 mmol) and $NOBF_4$ (1.34 g, 11.4 mmol) in MeCN (20 mL) at 0 °C for 10 min] was added dropwise over 10 min. The dark-brown solution was allowed to warm slowly to r.t. under N_2 overnight, before aqueous workup in an identical fashion to that described above for olefin **20**. Decomplexation was performed using the CAN-mediated procedure described above for olefin **20**. Purification by column chromatography (SiO_2, toluene–hexanes, 1:1 to 100:0 followed by Et_2O–hexanes, 1:9) yielded a mixture of **25** and **26** as a pale yellow oil (901 mg, 55%; R_f 0.39 in toluene) and recovered indoline **24** (130 mg, 9%; R_f 0.24 in toluene). ^1H NMR spectroscopy revealed an approximately equimolar ratio of **25** and **26**. ^1H and ^{13}C NMR spectroscopic data for **25** and ^1H NMR data for **26** were in accordance with literature data;[19] $[\alpha]_D$ +44.2 (*c* = 0.55, $CHCl_3$).

IR (film, 1:1 mixture of **25** and **26**): 1703 (s) cm^{-1}.

26

^{13}C NMR (100 MHz, $CDCl_3$): δ = 154.0 (C=O), 142.3 (C, C_6H_5), 138.3 (C, C_6H_5), 137.1 ($CH{=}CH_2$), 134.8 (C, C_6H_5), 128.8 (CH, C_6H_5), 124.7 (CH, C_6H_5), 116.0 ($CH{=}CH_2$), 115.4 (CH, C_6H_5), 80.8 (CMe_3), 51.2 ($C2H_2$), 37.9 ($CH_2CH{=}CH_2$), 29.8 ($C3H_2$), 28.6 [$C(CH_3)_3$].

(2*S*)-2-Allyl-2,3-dihydro-1*H*-indole (27) and 7-Allyl-2,3-dihydro-1*H*-indole (28)

Trifluoroacetic acid (2 mL) was added to a solution of indolines **25** and **26** (ca. 1:1, 742 mg, 2.86 mmol) in CH_2Cl_2 (8 mL) at 0 °C under N_2. The orange-brown solution was stirred at 0 °C for 30 min and then at r.t. for 1.5 h. The mixture was concentrated in vacuo to give a purple oil, which was dissolved in Et_2O (25 mL) and washed with NaOH (0.5 M, 2 × 25 mL). The combined aqueous phases were extracted with Et_2O (2 × 25 mL) and CH_2Cl_2 (3 × 25 mL) and the combined organic phases washed with brine (25 mL), dried, filtered and concentrated in vacuo. The residue was purified by column chromatography (SiO_2, Et_2O–toluene, 2:98 to 5:95) to give indoline **27** (233 mg, 51%; R_f 0.51 in Et_2O–toluene, 5:95) and indoline **28** (100 mg, 22%; R_f 0.34 in Et_2O–toluene, 5: 95) as clear oils. Spectroscopic data for **27**[33] {$[\alpha]_D$ –54.3 (*c* = 1.18, $CHCl_3$)} and for **28**[34] were in accordance with literature data.

(2*S*)-[*N*-(*R*)-α-Acetoxyphenylacetyl]-2-allyl-2,3-dihydroindole (29)

A solution of DCC (87 mg, 0.42 mmol) and (*R*)-*O*-acetylmandelic acid (82 mg, 0.42 mmol) in CH_2Cl_2 (5 mL) was cooled to 0 °C under N_2 and stirred for 15 min before the addition via cannula of a solution of indoline **27** (56 mg, 0.35 mmol) in CH_2Cl_2 (10 mL). The cloudy mixture was stirred at 0 °C under N_2 for 1 h and concentrated in vacuo. EtOAc (25 mL) was added to the residue and the mixture was filtered before the addition of 0.5 M HCl (15 mL). The phases were separated and the organic phase was washed with 0.5 M HCl (15 mL) and aqueous $NaHCO_3$ (2 × 15 mL). The two aqueous phases were extracted separately with EtOAc (2 × 15 mL) and the combined organic phases dried, filtered and concentrated in vacuo. The residue was purified by column chromatography (SiO_2, Et_2O–hexanes, 4:6) to give the title amide **29** (102 mg, 87%) as a colourless oil. ^1H and ^{13}C NMR spectroscopic analysis indicated the presence of a single diastereoisomer within the limits of detection; $[\alpha]_D$ –121.9 (*c* = 2.04, $CHCl_3$).

IR (film): 1739 (s), 1670 (s) cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 8.24 (1 H, d, *J* = 8.1 Hz), 7.52 (2 H, t, *J* = 2.9 Hz), 7.46–7.38 (3 H, m), 7.23 (1 H, t, *J* = 7.7 Hz), 7.15 (1 H, d, *J* = 7.2 Hz), 7.05 (1 H, t, *J* = 7.4 Hz), 6.18 (1 H, s, C11H), 5.79 (1 H, ddt, *J* = 17.0, 10.0, 7.0 Hz, C9H), 5.19 (1 H, d, *J* = 17.0 Hz, C10H_AH_B), 5.16 (1 H, d, *J* = 10.0 Hz, C10H_AH_B), 4.32 (1 H, br t, *J* = 8.5 Hz, C2H), 3.02 (1 H, dd, *J* = 15.8, 8.5 Hz, C3H_AH_B), 2.86–2.72 (2 H, m, C8H_AH_B, C3H_AH_B), 2.49 (1 H, dt, *J* = 14.4, 7.9 Hz, C8H_AH_B), 2.24 (3 H, s, $OCOCH_3$).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 171.0 (C=O), 165.8 (C=O), 142.1 (C), 133.9 (C), 133.0 (C9H), 130.3 (C), 129.9 (CH), 129.4 (2 CH), 128.9 (2 CH), 127.8 (CH), 125.0 (CH), 124.7 (CH), 119.0 ($C10H_2$), 118.2 (CH), 75.0 (C11H), 58.3 (C2H), 39.1 ($C8H_2$), 33.7 ($C3H_2$), 21.0 ($OCOCH_3$).

For the atom numbering scheme see Figure 2.

HRMS (EI^+ mode): *m*/*z* calcd for $C_{21}H_{21}NO_3$ [$M^{+\cdot}$]: 335.1521; found: 335.1521.

GC/MS (150 °C, 1 min/5 °C to 250 °C, R_t 14.73 min) indicated the presence of a single amide diastereomer, within the limits of detection.

***N-tert*-Butoxycarbonyl-7-chloro-2,3-dihydroindole (30)**

The title compound was prepared in 72% yield on a 15 mmol scale according to the method of Iwao and Kuraishi,[35] mp 84.5–85.5 °C (pentane) [Lit.[35] mp 84.5–85.0 °C (pentane)].

^3C NMR (100 MHz, $CDCl_3$): δ = 153.4 (C=O), 140.7 (C, Ar), 137.2 (C, Ar), 129.1 (CH, Ar), 125.3 (CH, Ar), 124.2 (C, Ar), 122.9 (CH, Ar), 81.6 (CMe_3), 51.5 ($C2H_2$), 30.1 ($C3H_2$), 28.3 [$C(CH_3)_3$].

(2*R*)-*N*-*tert*-Butoxycarbonyl-7-chloro-2-[(1*S*,3*E*)-1,4-dimethylpent-2-enyl]-2,3-dihydroindole (32)

s-BuLi (4.3 mL of a 1.28 M solution in cyclohexane–hexane (92:8), 5.54 mmol) was added dropwise to a solution of (–)-sparteine (1.30 g, 5.54 mmol) in *tert*-butyl methyl ether (70 mL) at –78 °C under N_2. The solution was stirred for 10 min before the slow addition of a precooled (–78 °C) solution of indoline **30** (1.17 g, 4.62 mmol) in *tert*-butyl methyl ether (50 mL) via cannula, ensuring the internal solution temperature did not rise above –75 °C. The solution was stirred at –78 °C for 3.5 h before cooling to approximately –85 °C. A solution of CuBr·SMe_2 (1.23 g, 6.01 mmol) in diisopropyl sulfide (4 mL) and THF (6 mL) was then added ensuring that the internal solution temperature did not rise above –75 °C. The orange solution was stirred at –78 °C for 30 min and cooled to approximately –85 °C. A solution of complex (2*R*,4*S*)-**4** [which had been freshly prepared from neutral complex (–)-**35** (1.21 g, 3.85 mmol) and $NOBF_4$ (495 mg, 4.24 mmol) in MeCN (10 mL) at 0 °C for 10 min] was then added via cannula. The brown solution was allowed to

warm gradually to r.t. over 14 h before aqueous workup in an identical fashion to that described above for olefin **20**. To the crude material following aqueous workup dissolved in acetone (250 mL) was added $NaOAc·3H_2O$ (7.5 g) added, followed by CAN (2.5 g). The orange-brown mixture was stirred at r.t. for 3 h before concentration in vacuo and addition of Et_2O (100 mL) and H_2O (100 mL). After stirring for 10 min, the mixture was filtered through Celite, the phases were separated and the aqueous phase was extracted with Et_2O (2 × 50 mL). The combined organic phases were washed with brine (50 mL), dried, filtered and concentrated in vacuo to yield a brown oil. The residue was purified by column chromatography (SiO_2, Et_2O–hexanes, 5: 95 to 10: 90) to give an inseparable mixture of 4 isomeric adducts (766 mg, 57% from neutral complex **4**) as a pale yellow oil. ^1H NMR spectroscopy indicated that **32** was the major isomer of the whose ratio was established by GC/MS (150 °C, 2 min/5 °C to 200 °C, 10 °C/min to 250 °C) as 4:9:81:6 with retention times of 8.66, 9.11, 9.50, 9.78 min respectively. NMR spectroscopic data is quoted for the major isomer **32** recorded on the mixture; $[\alpha]_D$ +9.42 (*c* = 1.38, $CHCl_3$).

IR (film): 1702 (s) cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 7.15 (1 H, d, *J* = 8.0 Hz, C6H), 7.01 (1 H, d, *J* = 7.2, 0.4 Hz, C4H), 6.93 (1 H, t, *J* = 7.6 Hz, C5H), 5.30 (1 H, ddd, *J* = 15.3, 6.4, 0.8 Hz, C9H), 5.06 (1 H, ddd, *J* = 15.3, 8.2, 1.4 Hz, C8H), 4.45 (1 H, ddd, *J* = 8.5, 5.4, 1.2 Hz, C2H), 3.35 (1 H, dd, *J* = 16.0, 8.5 Hz, $C3H_AH_B$), 2.61 (1 H, d, *J* = 16.0 Hz, $C3H_AH_B$), 2.24 (1 H, ddq, *J* = 13.2, 1.2, 6.7 Hz, C7H), 2.08 (1 H, dseptet, *J* = 1.1, 6.7 Hz, C10H), 1.54 (9 H, s, *t*-C_4H_9), 0.99 (3 H, d, *J* = 6.8 Hz, $C7CH_3$), 0.82 and 0.80 (3 H each, d, *J* = 6.8 Hz, $C10CH_3$ and $C11H_3$).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 153.8 (C=O), 140.9 (C), 138.3 (C9H), 136.9 (C), 128.8 (CH), 127.7 (C8H), 125.2 (CH), 124.3 (C), 122.7 (CH), 81.4 (*C*Me_3), 66.9 (C2H), 42.2 (C7H), 33.4 ($C3H_2$), 31.0 (C10H), 28.4 [$C(CH_3)_3$], 22.6 and 22.3 ($C10CH_3$ and $C11H_3$), 16.7 (3, $C7CH_3$).

For the atom numbering scheme see Figure 2.

LRMS (EI mode): *m*/*z* = 349 [(M^+), 2%], 276 (3), 252 (6), 152 (100), 117 (11), 57 (97).

Anal. Calcd for $C_{20}H_{28}ClNO_2$: C, 68.65; H, 8.07; N, 4.00. Found: C, 68.50; H, 7.89; N, 3.96.

(*E*)-5-Methylhex-3-en-2-ol (37)

To a solution of enone **36** (14.7 g, 131 mmol) in MeOH (210 mL) was added $CeCl_3·7H_2O$ (53.7 g, 144 mmol) and the yellow solution was stirred at r.t. for 30 min. The reaction mixture was cooled to 0 °C and $NaBH_4$ (5.45 g, 144 mmol) was added in small portions in order to keep the temperature below 7 °C. After 1 h, the addition was complete and the white suspension was stirred at 0 °C for 1.5 h and at r.t. for 16 h. The mixture was cooled to 5 °C and aq NH_4Cl (150 mL) was added slowly. Et_2O (80 mL) was added and the aqueous layer was extracted with Et_2O (3 × 40 mL). The combined organic layers were washed with brine (30 mL), dried and concentrated in vacuo. The residue was distilled to give the title compound **37** (9.50 g, 62%) as a colourless oil; bp 57–60 °C/15 mmHg. The ^1H and ^{13}C NMR spectroscopic data were in accordance with the literature data.[36]

Enzymatic Resolution of (±)-37

To a solution of (±)-alcohol **37** (8.00 g, 70.1 mmol) and vinyl acetate (30.2 g, 350 mmol) in pentane (60 mL) was added freshly activated 4Å molecular sieves (crushed, 4.00 g, 50 wt%) and Novozyme 435 (0.80 g, 10 wt%). The reaction mixture was stirred at r.t. and after 2 h, ^1H NMR spectroscopic analysis of the crude product indicated 50% conversion. After filtration through Celite, the solution was concentrated in vacuo. The residue was purified by column chromatography (SiO_2, hexanes–Et_2O, 6:1, then 4:1, then 2:1) to give ester (*R*)-**38** (5.42 g, 49%) and (*S*)-**37** (3.55 g, 44%) both as colourless liquids.

(*S*)-37

R_f 0.15 (hexanes–Et_2O, 4: 1); $[\alpha]_D^{25}$ +81.6 (*c* = 1.14, $CHCl_3$).

(*R*)-38

R_f 0.60 (hexanes–Et_2O, 4:1); $[\alpha]_D^{23}$ +76.9 (*c* = 1.35, MeOH).

The ^1H and ^{13}C NMR spectroscopic data for both (*S*)-**37** and (*R*)-**38** were in accordance with the literature data.[36]

Benzoic Acid (2*E*,5*S*)-5-Methylhex-3-en-2-yl Ester [(*S*)-39)]

To a solution of alcohol (*S*)-**37** (2.50 g, 21.9 mmol) in CH_2Cl_2 (150 mL) were added Et_3N (3.32 g, 32.8 mmol), benzoyl chloride (4.62 g, 32.8 mmol) and DMAP (268 mg, 2.19 mmol). The reaction mixture was stirred at r.t. for 18 h whereupon H_2O (30 mL) was added and the aqueous layer was extracted with CH_2Cl_2 (2 × 20 mL). The combined organic layers were dried and concentrated in vacuo. The residue was purified by column chromatography (SiO_2, hexanes–Et_2O, 20:1) to give the title compound (*S*)-**39** (4.13 g, 86%) as a colourless oil; R_f 0.73 (hexanes–Et_2O, 4:1); ee = 98.7% (chiral HPLC); $[\alpha]_D^{25}$ +24.1 (*c* = 1.14, $CHCl_3$).

IR (film): 1717 (s) cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$): δ = 8.07 (2 H, d, *J* = 7.7 Hz, *o*-Ar), 7.55 (1 H, t, *J* = 7.3 Hz, *p*-Ar), 7.44 (2 H, t, *J* = 7.7 Hz, *m*-Ar), 5.77 (1 H, dd, *J* = 6.4, 15.0 Hz, C4H), 5.89 (1 H, apparent quintet, *J* = 6.4 Hz, C2H), 5.54 (1 H, dd, *J* = 6.8, 15.4 Hz, C3H), 2.31 (1 H, apparent octet, *J* = 6.8 Hz, C5H), 1.43 (3 H, d, *J* = 6.4 Hz, $C1H_3$), 1.01 (6 H, d, *J* = 6.8 Hz, $C6H_3$ and $C5CH_3$).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 165.9 (C=O), 140.2 (C3H), 132.8 (CH, *p*-Ar), 131.0 (C, *ipso*-Ar), 129.7 (2CH, *o*-Ar), 128.4 (2CH, *m*-Ar), 126.7 (C4H), 71.9 (C2H), 30.7 (C5H), 22.2 ($C6H_3$ and $C5CH_3$), 20.7 ($C1H_3$).

Anal. Calcd for $C_{14}H_{18}O_2$: C, 77.03; H, 8.31. Found: C, 76.95; H, 8.15.

Benzoic Acid (3*E*,5*R*)-5-Methylhex-3-en-2-yl Ester [(*R*)-39]

To a solution of acetate (*R*)-**38** (5.00 g, 32.0 mmol) in MeOH (180 mL) was added K_2CO_3 (5.31 g, 38.4 mmol) in one portion. The white suspension was stirred at r.t. for 3 h. H_2O (300 mL) and CH_2Cl_2 (400 mL) were added and the aqueous layer was extracted with CH_2Cl_2 (3 × 100 mL). The combined organic layers were dried and concentrated in vacuo to give alcohol (*R*)-**37** (2.09 g, 57%) as a colourless oil which was converted to benzoate (*R*)-**39** (3.84 g, 96%) according to the procedure described above for benzoate (*S*)-**39**; $[\alpha]_D^{25}$ –23.3 (*c* = 1.18, $CHCl_3$); ee = 93% (chiral HPLC).

(η⁵-Cyclopentadienyl)(5-methyl-(2*S*,3*R*,4*R*)-η³-hex-3-en-2-yl)(dicarbonyl)molybdenum [(+)-35]

The title compound and its enantiomer were prepared by a modification[25] of a published procedure.[1] A solution of $Mo(CO)_6$ (3.15 g, 11.9 mmol) in THF (40 mL) was refluxed for 15 min whereupon benzoate (*S*)-**39** (2.00 g, 9.17 mmol) in THF (10 mL) was added. The reaction mixture was refluxed for 3 d. The dark brown solution was allowed to cool to r.t. In a separate flask, cyclopentadiene (727 mg, 11.0 mmol) was dissolved in THF (30 mL) and cooled to 0 °C. BuLi (7.75 mL, 11.0 mmol, 1.42 M in hexane) was added dropwise and the resulting yellow solution was stirred for 15 min at 0 °C. The ice bath was removed and the LiCp solution was added dropwise at r.t. to the molybdenum complex. After 1 h, the brown solution was filtered through a pad of activated alumina and washed with THF (200 mL). The yellow filtrate was concentrated under reduced pressure to give a brown solid (2.86 g), which was recrystallised from petroleum ether (60–80 °C, 4 mL) to give the neutral complex (+)-(2*S*,4*R*)-**35** as yellow needles (2.60 g,

90%): R_f 0.77 (hexanes–Et_2O, 8:1); mp 63–65 °C (hexane) [Lit.[1] mp 65–67 °C (hexane)]; $[\alpha]_D^{23}$ +55.9 (*c* = 1.09, $CHCl_3$). ^1H NMR spectroscopy indicated a mixture of *exo*- and *endo*-isomers (5:1) as judged by the integration of the C3H signals at δ_{exo} = 3.95 and δ_{endo} = 3.45 respectively.

^{95}Mo NMR (13 MHz, THF): δ_{exo} = –1743, δ_{endo} = –1559.

^1H and ^{13}C NMR spectroscopic data have been recorded for the *exo*-isomer.[1] The signals for the *endo*-isomer (recorded on a 5:1 mixture) are:

^1H NMR (400 MHz, $CDCl_3$): δ = 5.20 (5 H, s, Cp), 3.45 (1 H, t, *J* = 10.0 Hz, C3H), 2.63 (1 H, dq, *J* = 10.0, 6.0 Hz, C2H), 2.37 (1 H, t, *J* = 9.6 Hz, C4H), 2.02 (1 H, ddt, *J* = 13.2, 9.2, 6.6 Hz, C5H), 1.88 (3 H, d, *J* = 6.0 Hz, $C1H_3$), 1.22 (3 H, d, *J* = 6.4 Hz, $C6H_3$), 1.13 (3 H, d, *J* = 6.8 Hz, $C5CH_3$).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 240.4 (2 C=O), 90.6 (5 CH, Cp), 90.5 (C3H), 67.6 (C4H), 51.0 (C2H), 33.7 (C5H), 28.1 ($C1H_3$), 25.3 ($C6H_3$), 20.5 ($C5CH_3$).

For the atom numbering scheme see Figure 2.

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