Nucleophilic Addition of α-Metallated Carbamates to Planar Chiral Cationic \( \eta^3 \)-Allylmolybdenum Complexes: A Stereochemical Study

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Abstract: Chiral \( \alpha\)-(\(O\)-carbamoyl)alkyl- and \(\alpha\)-(\(N\)-carbamoyl)alkylcopper(I) reagents derived from (–)-sparteine-mediated asymmetric lithiation of hindered carbamates react with cationic \(\eta^3\)-allylmolybdenum complexes with retention of configuration.

Key words: (–)-sparteine, nucleophilic addition, \(\eta^3\)-allylmolybdenum complexes, asymmetric deprotonation, carbamates, \(\alpha\)-(\(O\)-carbamoyl)alkylcopper(I), \(\alpha\)-(\(N\)-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 \(\eta^3\)-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 \(\alpha\)-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-butylphenylide (LDBB)\(^3\) to give the axial organo-lithium \(2\) 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 \(\eta^3\)-allylmolybdenum complexes occurs with high and predictable stereoselectivity. We now report that chiral \(\alpha\)-(\(O\)-carbamoyl)alkyl- and \(\alpha\)-(\(N\)-carbamoyl)alkylcopper(I) reagents derived from hindered carbamates react with cationic \(\eta^3\)-allylmolybdenum complexes with retention of configuration to provide an acyclic variant of the chemistry described above.

At the heart of our work is the convenient and general synthesis of enantioenriched \(\alpha\)-(\(O\)-carbamoyl)alkyllithiums invented by Hoppe and co-workers.\(^10,11\) The procedure is illustrated by the synthesis of the \(\alpha\)-(\(O\)-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 \(15,2S\)-stannane \(12\) in 23% yield (er = >97:3), the \((15,2R)\)-stannane (46%, er = 88:12) and recovered starting material \(11\) (14%) after column chromatography. The minor \((15,2S)\)-isomer was used in the next step owing to its higher enantiopurity. Thus treatment of stannane \(12\) with BuLi in Et\(_2\)O–THF (1:1) at \(-78^\circ\text{C}\) fol-
ollowed by addition of CuBr·SMe 2 generated the organo-
copper(I) reagent 14 to which was added a freshly
prepared solution of the cationic complex (2S,4R)-4 in
acetonitrile. After aqueous workup, the crude η 2-adduct
was treated with oxygen in chloroform to give the crystal-
line 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-(2S,4R)-4 with retention of configuration.

![Figure 1 X-ray crystal structure of adduct 15](image)

(Scheme 2)

The organocopper(I) reagent 14 was also added to the enantiomeric η 2-allylmolybdenum complex (2R,4S)-4 in
order to establish that the stereoselectivity of the addition
was not a consequence of matched-pair effects. The dia-
stereoisomeric 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. Methanalysis of the carbamate 16
(79% yield) followed by ozonolysis of the alkene 17 re-
turned (2R,3R,4S)-diol 18 after reductive workup
(Scheme 2). The 1H NMR spectrum of (2R,3R,4S)-18
compared favourably with data reported by Matsumoto
and co-workers for the racemic modification.14

The second α-(O-carbamoyl)alkylocopper(I) nucleophile
in this study was selected to determine the consequence,
if any, of a chelating heteroatom substituent β to the car-
bonic centre. The requisite stannane 19, easily pre-
pared by the procedure of Hoppe and co-workers,15 was
converted to the organocopper(I) reagent as before. Addi-
tion of the η 2-allylmolybdenum complex (2R,4S)-4 in
MeCN gave olefin 20 in 57% overall yield from stannane
19 after oxidative decomplexation (Scheme 3). 1H 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 add-
uct 20 was assigned on the assumption that the nucleo-
phile 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)alkylocopper(I) intermediate derived from stan-
nane 19 was treated with the simple η 1-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 1H and 13C NMR spectroscopic
data correlated with literature values.16,17

The regiochemistry of ligand-directed carbamate metalla-
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-car-
bamoyl)alkyl lithiums.18 Thus asymmetric metallation of
N-Boc-indoline 24 with s-BuLi and (−)-sparteine fol-
lowed by alkylation with allyl chloride and DMPU gave

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2-allylindoline (S)-25 in 15% yield (S:R = 99:1) as shown in Scheme 4. 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 \( \eta^1 \)-allylmolybdenum complex 21. Asymmetric lithiation of N-Boc-indoline 24 with \( \text{s-BuLi}/(\text{--})\text{-sparteine} \) 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 \(^1\)H 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·SMe\(_2\), to give the organocupper(I) reagent 31. Addition of 31 to cationic \( \eta^3 \)-allylmolybdenum complex (2R,4S)-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 3

![Scheme 3](image)

### Scheme 4

![Scheme 4](image)

### Scheme 5

![Scheme 5](image)

#### Synthesis of the Cationic \( \eta^3 \)-Allylmolybdenum Complexes (2R,4S)-4 and (2S,4R)-4

We previously prepared the cationic complex (2R,4S)-4 by a 4-step sequence first described by Faller and Linebarger\(^{21} \) (Scheme 6). The principal detractor 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.
A more efficient and scalable route to (2R,4S)-4 and its enantiomer has been achieved (Scheme 7) featuring two significant improvements. Firstly, the Sharpeless 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 (–)-(2R,4S)-35 and (+)-(2S,4R)-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), 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 complexes with clean retention of configuration.26 In the case of complexes (2R,4S)-4 and (2S,4R)-4, the addition occurred regioselectively at the less hindered terminus anti to the molybdenum in accord with previous observations.19 The method provides a potentially useful chain extension in which two adjacent stereogenic centres are connected forming an axially chiral cationic complex derived from the asymmetric metallation of hindered carbanion equivalents (Figure 2). Compared with the reductive cleavage and transmetallation procedures used previously to generate the α-alkoxalkyllithiums, 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.

(–)-Sparteine was purified by Kugelrohr distillation immediately prior to use. CuBr·SMe₂ was prepared by the procedure of Theis and Townsend25 and purified by recrystallisation before use. Commercial n-BuLi and s-BuLi solutions were titrated against 1,3-diphenylisobenzofuran and benzophenone.26 Organic extracts were dried over MgSO₄ and concentrated using a rotary evaporator. 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 H₂SO₄, KMnO₄ or cerium(IV) sulfate solutions.

Specific optical rotations ([α]D) were measured on an Optical Activity polAAr2000 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 13C NMR spectra were recorded in Fourier Transform mode at the field strength specified. All spectra were obtained in CDCl₃ or CD₂CN solution in 5 mm diameter tubes, and the chemical shift in ppm is quoted relative to the residual signals of CHCl₃ (δH 7.26, δC 77.2) or MeCN (δH 2.00, δC 117.7) unless specified otherwise. Coupling constants (J) are reported in Hz. The number of protons attached to the carbon in the 13C 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 HMOC 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 x 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 (15, 2S)-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] $[\alpha]_D^{20}$ -22.4 ($c = 1.2$, acetone) [Lit. $[\alpha]_D^{20}$ -20.3 ($c = 1.2$, acetone)].

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

Stannane (27.1 mg, 35%) as colourless crystals; mp 79–81 °C (CH$_2$Cl$_2$) and (S)-15 (15.1 mg, 26%) as a colourless oil; $[\alpha]_D^{20}$ +38.6 ($c = 0.80$, CHCl$_3$).

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

$^1$H NMR (500 MHz, CDCl$_3$): $\delta$ (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, C1OH), 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$_3$): $\delta$ (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), 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 (C1OH$_2$), 60.9/59.9 (C9), 43.0 (C1H, Ar), 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 calc'd for C$_{24}$H$_{37}$NO$_3$Na: 410.2671; found: 410.2675.

Anal. Calc'd 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, $b = 20.3854(10)$ Å, $c = 7.9378(4)$ Å, $\beta = 103.1410(19)^\circ$, $V = 1160.01(10)$ Å$^3$, $Z = 2$, $\rho_{\text{calc}} = 1.11$ Mg/m$^3$, $\mu = 0.072$ mm$^{-1}$; crystal size: 0.13 × 0.12 × 0.02 mm, data collection range: 2.82 ≤ $\theta$ ≤ 26°, 6320 measured reflections, final $R$(refl) values: 0.1155, (0.3059) for 3503 independent data and 279 parameters [$I > 2\sigma(I)$].

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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=CHCHMe₂ 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 Fiedel pairs merged.

2,2,4,4-Tetramethyloxazolidine-3-carboxylic Acid (3E,15Z,20) 2,5-Dimethyl-1-(1S)-1-phenylethyl)hex-3-enyl Ester (16)

The title compound was prepared from reaction 12n with catonic 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; [α]D₂₀ = 0.97 (c = 1.07, CHCl₃).

IR (film): 1695 (s) cm⁻¹.

1H NMR (500 MHz, CDCl₃): 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, C8), 4.76–4.61 (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 CH₃), 1.29–1.24 (3 H, m, C1CH₃), 1.02–0.95 (3 H, m, C7H₃), 0.92 (6 H, d, J = 6.8 Hz, CH₃CH₃, and C6CH₃).

13C NMR (75 MHz, CDCl₃): δ = 144.8 (C, Ar), 128.8 (2 CH, Ar), 127.6 (2, CH, Ar), 126.6 (CH, Ar), 79.2 (C2H), 68.4 (C1H), 44.0 (C4H), 36.1 (C2H), 19.3 (C1CH₃), 9.1 (C2CH₃).

For the atom numbering scheme see Figure 2.

HRMS (ES): m/z calculated for C₁₉H₂₃NO₃: 310.1677; found: 310.1676 (19)

Carbamate 40 was prepared in 91% yield on a 32 mmol scale by the method of Hoppe. 11H NMR spectroscopic data were in accordance with literature data; 15 [α]D₂₀ = -11.4 (c = 5.3, MeOH).

Carbamate 140 (100 MHz, CDCl₃): 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), 76.2 (0.45 C, C₇H), 73.4 (C₄H), 69.5 (C₆H), 61.6 (C₇H), 60.7 (0.45 C, C₈), 59.8 (0.55 C, C₈), 33.3 (C₂H), 27.1 (2 CH), 26.7 (CH₃), 25.8 (CH₃), 25.4 (CH₃), 24.3 (CH₃).

13C NMR (100 MHz, CDCl₃): 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, 24.3 (C₂H), 14.3/14.1 (C₃H₆).

For the atom numbering scheme see Figure 2.
J = 3.1, 7.4 Hz, C4H (H2), 2.31–2.20 (1 H, m, C2H (H2)), 1.95 (1 H, ddd, J = 14.4, 6.8, 4.1 Hz, C2H (H2)), 1.55–1.26 (30 H, m), 0.92–0.85 (15 H, m).

13C NMR (100 MHz, CDCl3): 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 (C8H), 69.6 (C4H), 67.7 (C1H), 60.8 (0.4 C, NCMe2C), 59.6 (0.6 C, NCMe3C), 38.5 (C2H), 29.3 (3 x C11H, JCSa = 28.8), 27.7 (3 x C10H, JCSa = 28.8), 27.2 (0.5 C, CH3), 26.9 (0.5 C, CH3), 25.8 (CH3), 25.5 (2 CH3), 24.4 (0.5 C, CH3), 24.3 (0.5 C, CH3), 13.9 (3 x C12H), 10.1 (3 x C9H, JCSa = 162.9, 155.9).

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 C25H32NO3: C, 66.7; H, 9.89; N, 3.52. Found: C, 66.56; H, 9.83; N, 3.47. 2,2,4,4-Tetramethyloxazolidine-3-carboxylic Acid (1S)-(−)(4S)-2,2-Dimethyl-1,3-dioxolan-4-ylmethylbut-3-ene (22)

A solution of stannane \( \text{Me}_2\text{Sn} \) (4.6 mL of a 1.42 M solution in hexanes, 6.5 mmol) and NOBF4 (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 30 min, the mixture was cooled to \( –78 \) °C under \( \text{N}_2 \). The light yellow solution was added dropwise to a solution of stannane \( \text{Me}_2\text{Sn} \) (4.6 mL of a 1.42 M solution in hexanes, 6.5 mmol) in THF (35 mL) at \( 0 \) °C under \( \text{N}_2 \). The mixture was then re-description above for olefin 20.

Concentration in vacuo and purification by column chromatography (SiO2, Et2O–hexanes, 1:4) yielded the title compound 22 (1.45 g, 61%) as a pale yellow oil; \([\alpha]_D^{22}=+22.1 \) (c = 1.02, CHCl3).

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+1)+, 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 \( \text{C}_{25}\text{H}_{32}\text{O}_3\text{N} \) [M+H]+: 342.2280; found: 342.2283.

(2S)-1-(4S)-2,2-Dimethyl[1,3]dioxolan-4-ylpent-4-ene-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 LiAIH4 (480 mg, 12.7 mmol) in THF (35 mL) at \( 0 \) °C under \( \text{N}_2 \). The mixture was then refluxed for 4 d (with the addition of a further 480 mg of LiAIH4 after 44 h) and cooled to \( 0 \) °C. \( \text{H}_2\text{O} \) (0.9 mL) was then added, followed by 15% \( \text{aq} \) NaOH (0.9 mL) and \( \text{H}_2\text{O} \) (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

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with THF (3 × 15 mL). The filtrate was concentrated in vacuo and the residue was purified by column chromatography (Et2O–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 18F 2311.19 (c = 3.20) [Lit.13 18F 2311.5 +14.6 (c = 3.33, CHCl3)].

**N-tert-Butoxy carbonyl-2,3-dihydroindole (24)**

The title compound was prepared on a 75 mmol scale according to the procedure of Iwao and co-workers,15 mp 43–45 °C (hexanes) (Lit.15 mp 42–45 °C).

13C NMR (100 MHz, CDCl3): δ = 152.8 (C), 142.9 (C), 131.4 (C), 127.5 (CH), 124.8 (CH2), 122.3 (CH), 115.0 (CH), 80.9 (CMe2), 47.8 (C2H2), 28.71 (C(CH3)3), 27.5 (C3H7).

(2S)-2-Allyl-2-N-tert-butyloxycarbonyl-2,3-dihydroindole (25) and 7- Allyl-N-tert-butoxy carbonyl-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, 6.44 mmol) and (−)-sparteine (1.93 g, 8.25 mmol) in tert-butyl methyl ether (65 mL) at −78 °C under N2. The light yellow solution was stirred at −78 °C for 3.25 h before cooling to approximately −90 °C. A solution of CuBr2·Me2S (1.83 g, 8.89 mmol) in disisopro pyl 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 (η5-cyclopentadienyl)(η6-propenyl)(di carbonyl)molydbdenum (2.69 g, 10.4 mmol) and NOBF4 (1.34 g, 11.4 mmol) in MeCN (20 mL) at 0 °C for 10 min] was added drop wise over 10 min. The dark-brown solution was allowed to warm slowly to r.t. under N2 overnight, before aqueous workup in an identical manner to that described above for olefin 20. Decomplexation was performed using the CAN-mediated procedure described above for olefin 20. Purification by column chromatography (SiO2, Et2O–toluene, 2:98 to 5:95) yielded a mixture of 25 and 26 as a pale yellow oil (901 mg, 55%; Rf 0.39 in tolucene) and recovered indoline 24 (130 mg, 9%; Rf 0.24 in toluene).

1H NMR spectroscopy revealed an approximately equimolar ratio of 25 and 26.14 1H and 13C NMR spectroscopic data for 25 and 26 were in accordance with literature data:19 18F 2311.19 (c = 0.55, CHCl3).

IR (film): 1739 (s), 1670 (s) cm−1.

13C NMR (100 MHz, CDCl3): δ = 171.0 (C=O), 165.8 (C=O), 142.1 (C), 133.9 (C), 130.0 (C=O), 130.3 (C), 129.9 (C=O), 129.4 (2 CH), 128.9 (2 CH), 127.8 (CH), 125.0 (CH), 124.7 (CH), 119.0 (C=O), 118.2 (CH), 75.0 (C11H), 58.3 (C2H2), 39.1 (C8H2), 33.7 (C3H7), 21.0 (OCOCH3).

For the atom numbering scheme see Figure 2.


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

**N-tert-Butoxy carbonyl-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 Karusishi,35 mp 84.5–85.5 °C (pentane) [Lit.35 mp 84.5–85.0 °C (pentane)].

13C NMR (100 MHz, CDCl3): δ = 153.4 (C=O), 140.7 (C=O), 137.2 (C=O), 129.1 (CH=CH), 125.3 (CH=CH), 124.2 (C=O), 122.9 (CH=CH), 81.6 (CMe2), 51.5 (C2H2), 30.1 (C3H7), 28.3 (C3H7).

(2R)-N-tert-Butoxy carbonyl-7-chloro-2-(15,3E)-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 N2. 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 that 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 CuBr2·Me2S (1.23 g, 6.01 mmol) in disisopropyl 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 (2R,4S)-4 [which had been freshly prepared from neutral complex (−)-35 (1.21 g, 3.85 mmol) and NOBF4 (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

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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·3H2O (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 Et2O (100 mL) and H2O (100 mL). After stirring for 10 min, the mixture was filtered through Celite, the phases were separated and the aqueous phase was extracted with Et2O (2 × 50 mL). The combined organic phases were washed with brine (50 mL), dried, filtered and concentrated in vacuo to yield a pale yellow oil. The residue was purified by column chromatography (SiO2, hexanes–Et2O, 20:1) to give the title compound (2.09 g, 11.9 mmol) was added H2O (30 mL) and the aqueous layer was extracted with CH2Cl2 (2 × 20 mL). The combined organic layers were dried and concentrated in vacuo. The residue was purified by column chromatography (SiO2, hexanes–Et2O, 20:1) to give the title compound (3.55 g, 44%) both as colourless liquids.

(5)-37
R = 0.15 (hexanes–Et2O, 4:1); [α]25 +81.6 (c = 1.14, CHCl3).

(4)-38
R = 0.60 (hexanes–Et2O, 4:1); [α]25 +76.9 (c = 1.35, MeOH).

The 1H and 13C NMR spectroscopic data for both (5)-37 and (4)-38 were in accordance with the literature data.6

Benzoic Acid (2E,5S)-5-Methylhex-3-en-2-yl Ester ([S]-39)
To a solution of alcohol (4)-37 (2.50 g, 21.9 mmol) in CH2Cl2 (150 mL) was added Et3N (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 H2O (30 mL) was added and the aqueous layer was extracted with CH2Cl2 (2 × 20 mL). The combined organic layers were dried and concentrated in vacuo. The residue was purified by column chromatography (SiO2, hexanes–Et2O, 20:1) to give the title compound (3.9 g, 86%) as a colourless oil; Rf = 0.73 (hexanes–Et2O, 4:1); ee = 98.7% (chiral HPLC); [α]25 +24.1 (c = 1.14, CHCl3).

IR (film): 1717 (s) cm–1.

1H NMR (500 MHz, CDCl3): 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 quartet, 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), 1.01 (6 H, d, J = 6.8 Hz, C6H, and C7H).

Anal. Calcd for C21H22O2: C, 78.97; H, 7.73. Found: C, 78.95; H, 7.81.

Benzoic Acid (3E,5R)-5-Methylhex-3-en-2-yl Ester ([S]-39)
To a solution of acetate (4)-38 (5.00 g, 32.0 mmol) in MeOH (180 mL) was added K2CO3 (5.31 g, 38.4 mmol) in one portion. The white suspension was stirred at r.t. for 3 h. H2O (300 mL) and CH2Cl2 (400 mL) were added and the aqueous layer was extracted with CH2Cl2 (3 × 100 mL). The combined organic layers were dried and concentrated in vacuo to give alcohol (4)-38 (2.09 g, 57%) as a colourless oil which was converted to benzoate (4)-39 (3.84 g, 96%) according to the procedure described above for benzoate ([S]-39; [α]25 +23.3 (c = 1.18, CHCl3); ee = 93% (chiral HPLC).

(n)-Cyclopentadienyl(5-methyl-2,3,4,4',5'R)-η4-hex-3-en-2-yl(di carboxyln) molybdenum ([4+]-35)
The title compound and its enantiomer were prepared by a modification1 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 (3)-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, 7.15 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 LiCl 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 (+)-(25,4R)-35 as yellow needles (2.60 g, 21.9 mmol) in pentane (60 mL) was added freshly activated 4Å molecular sieves (crushed, 4.00 g, 50 wt%). After filtration through Celite, the solution was concentrated in vacuo. The residue was purified by column chromatography (SiO2, hexanes–Et2O, 6:1, then 4:1, then 2:1) to give ester (5)-38 (5.42 g, 49%) and (4)-37 (3.55 g, 44%) both as colourless liquids.

(5)-37
R = 0.15 (hexanes–Et2O, 4:1); [α]25 +81.6 (c = 1.14, CHCl3).

(4)-38
R = 0.60 (hexanes–Et2O, 4:1); [α]25 +76.9 (c = 1.35, MeOH).

The 1H and 13C NMR spectroscopic data for both (5)-37 and (4)-38 were in accordance with the literature data.6

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judged by the integration of the C3H signals at 

For the atom numbering scheme see Figure 2.

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References

(24) Attempts to accomplish a similar enzymatic resolution of (±)-33 failed.
(30) The supplementary crystallographic data for this structure (CCDC 247732) can be obtained free of charge via www.ccdc.cam.ac.uk/data_request/cif, by emailing data_request@ccdc.cam.ac.uk, or by contacting The Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge CB2 1EZ, UK.