Enantioselective Synthesis of Sterically Hindered $\alpha$-Allyl-$\alpha$-Aryl Oxindoles via Palladium-Catalysed Decarboxylative Asymmetric Allylic Alkylation

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General Information

Materials and Methods

Unless otherwise noted, reactions were performed with rigorous exclusion of air and moisture, under an inert atmosphere of nitrogen in flame-dried glassware with magnetic stirring. N₂-flushed stainless steel cannulas or plastic syringes were used to transfer air- and moisture-sensitive reagents. All reagents were obtained from commercial sources and used without further purification unless otherwise stated. Anhydrous tetrahydrofuran (THF), diethyl ether (Et₂O) and dichloromethane (CH₂Cl₂) were obtained from a dry solvent dispenser. Tris(dibenzylideneacetone)dipalladium(0) chloroform adduct was prepared via the method of Zalesskiy.¹ L1 and L2 were prepared according to previously reported methods.² L3 and L4 were purchased from Sigma Aldrich and used as received. Allyl 3-(methyl(phenyl)amino)-3-oxopropionate (4) and N-methyloxindole (6) were prepared according to literature procedures.³ Aryllead triacetates used in the preparation of α-aryl β-amido allyl esters ³a-³m were also prepared according to the literature.⁴ Thin-layer chromatography (TLC) was performed on aluminium plates pre-coated with silica gel F254. They were visualised with UV-light (254 nm) fluorescence quenching, or by charring with an acidic vanillin solution (vanillin, H₂SO₄ in ethanol). Flash column chromatography was carried out using 40-63 μm, 230-400 mesh silica gel.

Instrumentation

¹H NMR spectra were recorded on a 400 or 500 MHz spectrometer. ¹³C NMR spectra were recorded a 400 or 500 MHz spectrometer at 101 or 126 MHz. Chemical shifts (δ) are reported in parts per million (ppm) downfield from tetramethylsilane and are referenced to residual proton in the NMR solvent (CDCl₃ = δ 7.26 ppm). ¹³C-NMR are referenced to the residual solvent peak (CDCl₃ = δ 77.0 ppm). All ¹³C spectra are ¹H decoupled. NMR data are represented as follows: chemical shift (δ ppm), coupling constant (J) in Hertz (Hz), integration. High resolution mass spectra [electrospray ionisation (ESI-TOF)] (HRMS) were measured on a micromass LCT orthogonal time-of-flight mass spectrometer with leucine enkephalin (Tyr-Gly-Phe-Leu) as an internal lock mass. Infrared spectra were recorded on a Bruker Platinum ATR spectrometer and are reported in terms wavenumbers (νmax) with units of reciprocal centimetres (cm⁻¹). Optical rotation (α) values were measured at room temperature and specific rotation ([α]D) values are given in degrees (°). Melting points were determined in open capillary tubes. Supercritical fluid chromatography (SFC) was performed on waters UPC² using a Chiralpak-IA3, IB3, IC3 or ID3 columns. HPLC was performed using a Chiralcel OD column.
References:


$^1$H NMR, $^{13}$C NMR and $^{19}$F NMR Spectra of New Compounds

$^1$H NMR (500 MHz, CDCl$_3$)
$^1$H NMR (400 MHz, CDCl$_3$)

$^{13}$C NMR (126 MHz, CDCl$_3$)
$^1$H NMR (500 MHz, CDCl$_3$)
$^1$H NMR (500 MHz, CDCl$_3$)

$^{13}$C NMR (126 MHz, CDCl$_3$)
$^1$H NMR (500 MHz, CDCl$_3$)

$^{13}$C NMR (126 MHz, CDCl$_3$)
$^1$H NMR (500 MHz, CDCl$_3$)

$^{13}$C NMR (126 MHz, CDCl$_3$)
$^1$H NMR (500 MHz, CDCl$_3$)

$^{13}$C NMR (126 MHz, CDCl$_3$)
$^{1}H$ NMR (400 MHz, CDCl$_3$)

$^{13}C$ NMR (126 MHz, CDCl$_3$)
$^1$H NMR (500 MHz, CDCl$_3$)

$^{13}$C NMR (126 MHz, CDCl$_3$)
$^1$H NMR (500 MHz, DMSO-D$_3$, 80°C)

$^{13}$C NMR (126 MHz, DMSO-D$_3$, 80°C)
$^1$H NMR (400 MHz, CDCl$_3$)

![NMR spectrum of 3k]

$^{13}$C NMR (101 MHz, CDCl$_3$)

![NMR spectrum of 3k]
MISSING SPECTRA (3I)
$^1$H NMR (500 MHz, CDCl$_3$)

$^{13}$C NMR (126 MHz, CDCl$_3$)
$^{19}$F NMR (470 MHz, CDCl$_3$)
$^1$H NMR (400 MHz, CDCl$_3$)

$^{13}$C NMR (101 MHz, CDCl$_3$)
$^1$H NMR (400 MHz, CDCl$_3$)

$^{13}$C NMR (101 MHz, CDCl$_3$)
$^1$H NMR (500 MHz, CDCl$_3$)

$^{13}$C NMR (126 MHz, CDCl$_3$)
$^1$H NMR (500 MHz, CDCl$_3$)

$^{13}$C NMR (126 MHz, CDCl$_3$)
MISSING SPECTRA (11e)
$^1$H NMR (400 MHz, CDCl$_3$)

$^{13}$C NMR (101 MHz, CDCl$_3$)
$^1$H NMR (400 MHz, CDCl$_3$)

$^{13}$C NMR (101 MHz, CDCl$_3$)
$^1$H NMR (500 MHz, CDCl$_3$)

$^{13}$C NMR (126 MHz, CDCl$_3$)
$^1$H NMR (400 MHz, CDCl$_3$)

$^{13}$C NMR (101 MHz, CDCl$_3$)
$^1$H NMR (500 MHz, CDCl$_3$)

$^{13}$C NMR (126 MHz, CDCl$_3$)
MISSING SPECTRA (11k)
MISSING SPECTRA (11I)
$^1$H NMR (500 MHz, CDCl$_3$)

$^{13}$C NMR (126 MHz, CDCl$_3$)
$^{19}$F NMR (470 MHz, CDCl$_3$)
SFC Chromatograms

**Auto-Scaled Chromatogram**

Peak Results

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**Auto-Scaled Chromatogram**

Peak Results

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Peak Results

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Auto-Scaled Chromatogram

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X-ray Data for compound 11a

Table 1. Crystal data and structure refinement for compound 11a.

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<td></td>
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<td></td>
<td>c = 24.7460(2) Å  (\gamma=90^\circ).</td>
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<td>Volume</td>
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Z 4

Density (calculated) 1.223 Mg/m³

Absorption coefficient 0.686 mm⁻¹

F(000) 752

Crystal size 0.3749 x 0.1296 x 0.0915 mm³

Theta range for data collection 3.57 to 76.90°.

Index ranges −8<=h<=10, −11<=k<=11, −31<=l<=31

Reflections collected 19851

Independent reflections 3983 [R(int) = 0.0309]

Completeness to theta = 76.90° 99.0 %

Absorption correction Analytical

Max. and min. transmission 0.947 and 0.858

Refinement method Full-matrix least-squares on F²

Data / restraints / parameters 3983 / 0 / 239

Goodness-of-fit on F² 1.041

Final R indices [I>2sigma(I)] R1 = 0.0287, wR2 = 0.0711

R indices (all data) R1 = 0.0309, wR2 = 0.0729

Absolute structure parameter −0.02(13)

Largest diff. peak and hole 0.158 and −0.178 e.Å⁻³