Electronic Supplementary Material (ESI) for Organic & Biomolecular Chemistry.


# An asymmetric pericyclic cascade approach to 3-alkyl-3-aryloxindoles; generality, applications and mechanistic investigations

## Electronic Supplementary Information for Synthetic Studies

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**1. General Information**

Reactions involving moisture sensitive reagents were performed under an argon atmosphere using standard vacuum line techniques with anhydrous solvents. In this instance, glassware was flame dried and allowed to cool under vacuum prior to use. Solvents (THF, $CH_2Cl_2$, toluene, hexane and $Et_2O$) were obtained anhydrous and purified by an alumina column (Mbraun SPS-800). Petroleum ether is defined as petroleum ether 40-60 °C. Benzaldehyde was purified by washing with 2M NaOH solution, followed by 10% $Na_2CO_3$ solution and finally $H_2O$. It was then dried over $MgSO_4$ and distilled under reduced pressure. $Et_3N$ was dried by distillation from $CaH_2$ and stored under an atmosphere of argon. All other solvents and commercial reagents were used as supplied without further purification unless stated otherwise.

Room temperature (rt) refers to 20-25 °C. Temperatures of 0 °C and -78 °C were obtained using ice/water and $CO_2$(s)/acetone baths respectively. Any other cryogenic temperatures used are described within the procedures. Reflux conditions were obtained using DrySyn heating apparatus and a contact thermometer.

*In vacuo* refers to the use of a Büchi Rotavapor R-2000 rotary evaporator with a Vacubrand CVC2 vacuum controller or a Heidolph Laborota 4001 rotary evaporator with a vacuum controller. Kugelrohr distillations were performed on an apparatus with a Büchi glass oven and drive unit operating at high vacuum (2-3 mmHg).

Analytical thin layer chromatography was performed on pre-coated aluminium plates (Kieselgel 60 F254 silica). TLC visualisation was carried out with ultraviolet light (254 nm), followed by staining with a 1% aqueous $KMnO_4$ solution. Flash column chromatography was performed on Kieselgel 60 silica eluting with the solvent system stated.

$^1H$, $^{13}C$ and $^{19}F$ nuclear magnetic resonance (NMR) spectra were acquired on either a Bruker Avance 300 (300 MHz $^1H$, 75 MHz $^{13}C$, 282 MHz $^{19}F$), Bruker Avance II 400 (400 MHz $^1H$, 100 MHz $^{13}C$, 376 MHz $^{19}F$) or a Bruker Avance II 500 (500 MHz $^1H$, 125 MHz $^{13}C$, 470 MHz $^{19}F$) spectrometer at ambient temperature in the deuterated solvent stated. All chemical shifts are quoted in parts per million (ppm) relative to the residual solvent as the internal standard. All coupling constants, *J*, are quoted in Hz to the nearest 0.1 Hz. Multiplicities are indicated by: s (singlet), d (doublet), t (triplet), q (quartet), quint (quintet), sept (septet), oct (octet), m (multiplet), dd (doublet of doublets) etc. The abbreviation br denotes broad and app. denotes apparent. The abbreviation Ar is used to denote aromatic, and Ph used to denote a singularly substituted phenyl ring for reasons of clarity when it may otherwise be ambiguous. $CH_aH_b$ is used to denote diastereotopic vicinal protons. Infrared spectra ($\nu_{max}$) were either recorded on a Perkin-Elmer Spectrum GX FT-IR spectrometer using thin-films on KBr discs or a Shimadzu ATR (attenuated total reflectance) zinc-selenide cell FTIR 8400S. Only the characteristic peaks are quoted. Melting points were recorded on an Electrothermal 9100 apparatus. The abbreviation (decomp.) denotes decomposition. HPLC analyses were obtained on a Gilson HPLC consisting of a Gilson 305 pump, Gilson 306 pump, Gilson 811C dynamic mixer, Gilson 805 manometric module, Gilson 401C dilutor, Gilson 213XL sample injector and sample detection was performed with a Gilson 118 UV/vis detector. Separation was achieved using Chiralcel OD-H and OJ-H columns or a Chiralpak AD-H and AS-H column using the eluent system and flow rate stated. Mass spectrometry (m/z) data were acquired by electrospray ionisation (ES),

electron impact (EI) or nanospray ionisation (NSI) either at the University of St Andrews or the EPSRC National Mass Spectrometry Service Centre, Swansea. At the University of St Andrews, low and high resolution ESI-MS were carried out on a Micromass LCT spectrometer. At the EPSRC National Mass Spectrometry Service Centre, low resolution NSI-MS was carried out on a Micromass Quattro II spectrometer and high resolution NSI-MS on a Thermofisher LTQ Orbitrap XL spectrometer. Optical rotations were measured on a Perkin Elmer Precisely/Model-341 polarimeter operating at the sodium D line with a 100 mm path cell.

**2. General Procedures**

**General Procedure A for Alkylarylketene Preparation** All alkylarylketenes were prepared from the corresponding acid chlorides according to literature procedures and with analytical data in accordance with the literature.[1] **Representative Procedure:** To a stirred solution of the requisite acid chloride (1.0 eq) in dry $Et_2O$ (1 mmol/mL) at 0 °C was added *N,N*-dimethylethylamine (1.1 eq) dropwise and the reaction stirred for 16 h at 0 °C. After this time, the reaction mixture was allowed to warm to rt before being filtered under argon. The $Et_2O$ was then removed under reduced pressure and the resulting crude oil purified *via* Kugelrohr distillation under reduced pressure to furnish the ketene which was stored under nitrogen in the freezer.

**General Procedure B for Hydroxylamine Preparation** To a stirred solution of nitro-aromatic compound (1.0 eq) in THF (1 mmol/mL) at 0 °C was added Rh/C (ca. 10 mol %), followed by hydrazine monohydrate (1.2 eq) dropwise and the reaction stirred rapidly for 3 h allowing to warm to rt. The reaction mixture was filtered through a celite plug, the residue rinsed with $CH_2Cl_2$ and the filtrate concentrated *in vacuo*. The crude solid was purified *via* recrystallisation from $CH_2Cl_2$:petroleum ether to yield a solid which was stored in the freezer.

**General Procedure C for Nitrone Preparation** To a stirred solution of the requisite nitro-aromatic compound (1.0 eq) in EtOH:$H_2O$ (1:1 – 0.5 mmol/mL) was added the requisite aldehyde (1.0 eq) and $NH_4Cl$ (1.3 eq). The reaction mixture was cooled to 0 °C and zinc powder (2.0 eq) added portionwise over 1h, before being stirred 16 h, allowing to warm to rt. The reaction mixture was filtered through a celite plug that was rinsed several times with $CH_2Cl_2$ and the phases separated. The aqueous phase was extracted with $CH_2Cl_2$ (× 3) and the combined organic phases concentrated *in vacuo*. The crude solid was purified *via* recrystallisation from $CH_2Cl_2$:petroleum ether to yield a solid which was stored on the benchtop unless otherwise stated.

**General Procedure D for Nitrone Preparation** To a stirred solution of the requisite aldehyde (1.0 eq) in $CH_2Cl_2$ (0.25 mmol/mL) under argon was added $MgSO_4$ (1.1 eq) and the reaction mixture stirred for 5 min at rt. After this time, the requisite hydroxylamine (1.0 eq) was added and the reaction stirred until analysis by TLC showed consumption of starting material. The mixture was filtered to remove $MgSO_4$ and concentrated *in vacuo*. The crude nitrones were either purified by column chromatography over silica (10-50% EtOAc in petroleum ether) or used crude with no further purification.

**General Procedure E for Racemic Oxindole Synthesis** To a stirred solution of the requisite diarylnitrone (1.0 eq) in dry THF (0.15 mmol/mL) under argon was added dropwise a solution of the

requisite ketene (1.0 eq) in dry THF (1 mL) and the reaction stirred at rt for 30 min. The reaction was quenched with aq. 2M HCl (ca. 0.5 mL) and stirred for a further 15 min before being extracted with $Et_2O$ (3 × 10 mL). The combined organic phases were washed with sat. aq. $NaHCO_3$, dried over $Na_2SO_4$, filtered and concentrated *in vacuo* to give a crude oil which was purified by column chromatography over silica (0-40% EtOAc in petroleum ether) to yield the oxindole.

**General Procedure F for Asymmetric Oxindole Synthesis** A stirred solution of the requisite enantiopure nitrone (1.0 eq) in dry THF (0.15 mmol/mL) under argon was cooled to -78 °C. To the reaction was added dropwise a solution of the requisite ketene (1.0 - 2.0 eq) in dry THF (1 mL) and the reaction stirred at -78 °C until analysis by TLC showed consumption of nitrone. The reaction was quenched with aq. 2M HCl (ca. 0.5 mL) and stirred for 30 min, allowing to warm to rt before being extracted with $Et_2O$ (3 × 10 mL). The combined organic phases were washed with sat. aq. $NaHCO_3$, dried over $Na_2SO_4$, filtered and concentrated *in vacuo* to give a crude oil which was purified by column chromatography over silica (0-40% EtOAc in petroleum ether) to yield the oxindole.

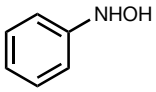
**General Procedure G for Alkylation of Arylacetic acids** A stirred solution of the requisite arylacetic acid (1.0 eq) in dry THF (0.2 mmol/mL) under argon was cooled to -78 °C. A solution of *n*-butyllithium (2.1 eq, 2.5 M in hexanes) was added dropwise and the reaction stirred at -78 °C for 35 min. The cooling bath was then removed and the reaction mixture allowed to warm to ambient temperature for ca. 45 min. The requisite alkyl bromide or chloride (1.2 - 2.0 eq) was added slowly and the reaction mixture stirred 16 h at rt. After such time, the resulting suspension was quenched with $H_2O$ and diluted with $Et_2O$. The resulting layers were separated and the aqueous phase acified with 2M HCl. The aqueous phase was extracted with $Et_2O$ (× 3) and the combined organic phases washed with brine, dried over $MgSO_4$, filtered and concentrated *in vacuo* to yield the crude disubstituted acids as solids, or as viscous oils which crystallised on standing. The crude acids were generally used without purification, unless otherwise stated, however if necessary were triturated with warm petroleum ether before filtering and washing repeatedly with hexane to yield the solid disubstituted acids.

**General Procedure H for Acid Chloride Preparation** To a stirred solution of the requisite carboxylic acid (1.0 eq) in toluene (0.5 mmol/mL) was added thionyl chloride (2.0 eq) dropwise and the reaction mixture heated to 80 °C for 3-16 h. After such time, the reaction mixture was filtered and concentrated *in vacuo* to yield crude brown oils which were either used crude without purification or purified by Kugelrohr distillation to yield the acid chlorides as colourless or pale yellow liquids which were stored under argon in the fridge.

**General Procedure I for Acid Chloride Preparation** A stirred solution of the requisite carboxylic acid (1.0 eq) and catalytic DMF (2 drops) in toluene (0.5 mmol/mL) was cooled to 0 °C. Oxalyl chloride (1.0 - 2.0 eq) was added dropwsie to the reaction mixture which was stirred for between 1-4 h at 0 °C. The reaction mixture was filtered and concentrated *in vacuo* to yield crude brown oils which were either used crude without purification or purified by Kugelrohr distillation to yield the acid chlorides as colourless or pale yellow liquids which were stored under argon in the fridge.

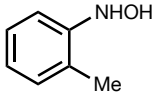
**3. Hydroxylamines**

***N*-Phenylhydroxylamine 66**



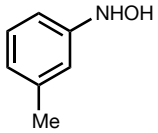

The hydroxylamine was prepared according to general procedure **B** from nitrobenzene (2.00 g, 16.4 mmol), Rh/C (0.020 g, cat.) and hydrazine monohydrate (0.88 mL, 1.2 eq, 19.7 mmol) in THF (20 mL) to give **66** (1.47 g, 82%) as a white solid; mp 82-83 °C {lit.[2] 80-81 °C}; $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 7.30-7.26 (2H, m, Ar*H*), 7.05-7.01 (3H, m, Ar*H*), 6.82 (1H, *br* s), 5.68 (1H, *br* s).

***N*-(*o*-Tolyl)hydroxylamine 67**



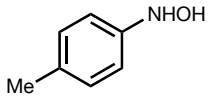

The hydroxylamine was obtained from 2-nitrotoluene (2.00 g, 14.5 mmol), Rh/C (0.020 g, cat.) and hydrazine monohydrate (0.84 mL, 1.2 eq, 17.4 mmol) in THF (20 mL) following general procedure **B** to yield **67** (1.25 g, 70%) as a white solid; mp 36-37 °C {lit.[3] 44 °C}; $^1$H NMR (300 MHz, $CDCl_3$) $\delta$ 7.32-7.26 (2H, m, Ar*H*), 7.13 (1H, d, *J* = 7.2, Ar*H*), 6.97 (1H, td, *J* = 7.2, 1.7, Ar*H*), 6.80 (1H, br s), 5.80 (1H, br s), 2.20 (3H, s, Ar$CH_3$).

***N*-(*m*-Tolyl)hydroxylamine 68**



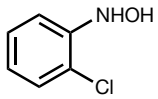

The hydroxylamine was obtained from 3-nitrotoluene (2.00 g, 14.5 mmol), Rh/C (0.020 g, cat.) and hydrazine monohydrate (0.84 mL, 1.2 eq, 17.4 mmol) in THF (20 mL) following general procedure **B** to yield **68** (1.52 g, 85%) as an off-white solid; mp 66-67 °C {lit.[4] 66-68 °C}; $^1$H NMR (300 MHz, $CDCl_3$) $\delta$ 7.17 (1H, t, *J* = 7.8, Ar*H*), 6.85-6.81 (3H, m, Ar*H*), 6.80 (1H, *br* s), 5.79 (1H, *br* s), 2.33 (3H, s, Ar$CH_3$).

***N*-(*p*-Tolyl)hydroxylamine 69**




The hydroxylamine was obtained from 4-nitrotoluene (2.00 g, 14.5 mmol), Rh/C (0.020 g, cat.) and hydrazine monohydrate (0.84 mL, 1.2 eq, 17.4 mmol) in THF (20 mL) following general procedure **B** to yield **69** (1.20 g, 67%) as a white solid; mp 82-83 °C {lit.[5] 82-84 °C}; $^1$H NMR (300 MHz, $CDCl_3$) $\delta$ 7.10 (2H, d, *J* = 8.3, Ar*H*(3,5)), 6.92 (2H, d, *J* = 8.3, Ar*H*(2,6)), 6.70 (1H, br s), 5.48 (1H, br s), 2.30 (3H, s, Ar$CH_3$).

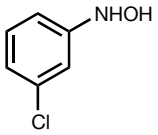
***N*-(2-Chlorophenyl)hydroxylamine 70**




The hydroxylamine was prepared according to general procedure **B** from 1-chloro-2-nitrobenzene (7.00 g, 44.4 mmol), Rh/C (0.100 g, cat.) and hydrazine monohydrate (2.59 mL, 1.2 eq, 53.3 mmol) in THF (60 mL). The crude product was purified by recrystallisation from ice-cold

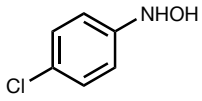
$CH_2Cl_2$:petroleum ether to yield **70** (5.03 g, 78%) as a white solid; mp 43-44 °C {lit.[6] 52 °C}; $^1$H NMR (300 MHz, $CDCl_3$) $\delta$ 7.07-6.96 (4H, m, Ar*H*).

***N*-(3-Chlorophenyl)hydroxylamine 71**



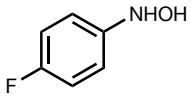

The hydroxylamine was prepared according to general procedure **B** from 1-chloro-3-nitrobenzene (7.00 g, 44.4 mmol), Rh/C (0.080 g, cat.) and hydrazine monohydrate solution (2.59 mL, 1.2 eq, 53.3 mmol) in THF (60 mL). The crude product was recrystallised from ice cold $CH_2Cl_2$:petroleum ether to yield **71** (4.25 g, 67%) as a white solid; mp 56-57 °C {lit.[6] 49 °C}; $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 7.19 (1H, t, *J* = 8.0, Ar*H*(5)), 7.04 (1H, t, *J* = 2.0, Ar*H*(2)), 6.94 (1H, ddd, *J* = 8.0, 2.0, 0.9, Ar*H*(6)), 6.83 (1H, ddd, *J* = 8.0, 2.0, 0.9, Ar*H*(4)), 6.80 (1H, br s), 5.47 (1H, br s).

***N*-(4-Chlorophenyl)hydroxylamine 72**



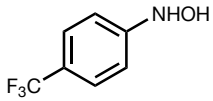

The hydroxylamine was prepared according to general procedure **B** from 1-chloro-4-nitrobenzene (2.00 g, 12.7 mmol), Rh/C (0.020g, cat.) and hydrazine monohydrate (0.47 mL, 1.2 eq, 15.2 mmol) in THF (20 mL) to yield **72** (0.590 g, 32%) as a white solid; mp 80-81 °C {lit.[6] 88 °C}; $^1$H NMR (300 MHz, $CDCl_3$) $\delta$ 7.27-7.23 (2H, m, Ar*H*(3,5)), 6.96-6.92 (2H, m, Ar*H*(2,6)).

***N*-(4-Fluorophenyl)hydroxylamine 73**



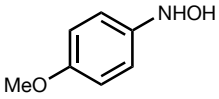

The hydroxylamine was prepared according to general procedure **B** from 1-fluoro-4-nitrobenzene (7.00 g, 49.6 mmol), Rh/C (0.100 g, cat.) and hydrazine monohydrate (2.89 mL, 1.2 eq, 59.5 mmol) in THF (60 mL) to leave a crude yellow solid that was purified by trituration from petroleum ether to leave **73** (4.74 g, 92%) as a grey solid; mp 84-85 °C {lit.[6] 100 °C}; $^1$H NMR (300 MHz, $CDCl_3$) $\delta$ 7.03-6.99 (2H, m, Ar*H*(3,5)), 6.97-6.94 (2H, m, Ar*H*(2,6)).

***N*-(4-(Trifluoromethyl)phenyl)hydroxylamine 74**



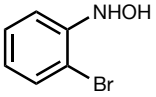

The hydroxylamine was prepared according to general procedure **B** from 4-nitrobenzotrifluoride (6.00 g, 31.4 mmol), Rh/C (0.080 g, cat.) and hydrazine monohydrate (1.83 mL, 1.2 eq, 37.7 mmol) in THF (65 mL) to yield **74** (3.85 g, 69%) as a white solid; mp 83-84 °C; $^1$H NMR (300 MHz, $CDCl_3$) $\delta$ 7.53 (2H, d, *J* = 8.5, Ar*H*(3,5)), 7.05 (2H, d, *J* = 8.5, Ar*H*(2,6)); $^{19}$F NMR (282 MHz, $CDCl_3$) $\delta$ -63.7 (ArC*F*$_3$).

***N*-(4-Methoxyphenyl)hydroxylamine 75**



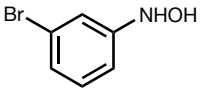

The hydroxylamine was prepared according to general procedure **B** from 4-nitroanisole (1.00 g, 6.53 mmol), Rh/C (0.010 g, cat.) and hydrazine monohydrate (0.69 mL, 1.2 eq, 7.84 mmol) in THF (10 mL) to yield **75** (0.505 g, 56%) as an off-white solid; mp 84-85 °C {lit.[7] 86-94 °C}; $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 7.03-7.00 (2H, m, Ar*H*(3,5)), 6.89-6.87 (2H, m, Ar*H*(2,6)), 5.70 (1H, *br* s), 3.81 (3H, s, O*Me*).

***N*-(2-Bromophenyl)hydroxylamine 76**



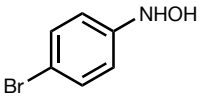

The hydroxylamine was obtained from 1-bromo-3-nitrobenzene (1.50 g, 7.43 mmol), Rh/C (0.030 g, cat.) and hydrazine monohydrate (0.43 mL, 1.2 eq, 8.91 mmol) in THF (20 mL) following general procedure **B** to yield **76** (0.991 g, 72%) as an off-white solid; mp 60-61 °C {lit.[6] 34 °C}; $^1$H NMR (300 MHz, $CDCl_3$) $\delta$ 7.45 (1H, d, $J$ = 7.8, Ar*H*), 7.32-7.29 (2H, m, Ar*H*), 7.10 (1H, *br* s), 6.86-6.84 (1H, m, Ar*H*), 5.39 (1H, *br* s).

***N*-(3-Bromophenyl)hydroxylamine 77**




The hydroxylamine was obtained from 1-bromo-3-nitrobenzene (1.50 g, 7.43 mmol), Rh/C (0.030 g, cat.) and hydrazine monohydrate (0.43 mL, 1.2 eq, 8.91 mmol) in THF (20 mL) following general procedure **B** to yield **77** (1.08 g, 78%) as an off-white solid; mp 67-68 °C {lit.[6] 66 °C}; $^1$H NMR (300 MHz, $CDCl_3$) $\delta$ 7.21-7.19 (1H, m, Ar*H*), 7.11-7.08 (2H, m, Ar*H*), 6.90-6.87 (1H, m, Ar*H*), 6.78 (1H, *br* s), 5.27 (1H, app. d, $J$ = 2.4).

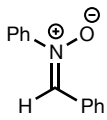
***N*-(4-Bromophenyl)hydroxylamine 78**




The hydroxylamine was prepared according to general procedure **B** from 1-bromo-4-nitrobenzene (1.50 g, 7.43 mmol), Rh/C (0.030 g, cat.) and hydrazine monohydrate (0.43 mL, 1.2 eq, 8.91 mmol) in THF (20 mL) to yield **78** (1.17 g, 85%) as an off-white solid; mp 94-95 °C {lit.[6] 91 °C}; $^1$H NMR (300 MHz, $CDCl_3$) $\delta$ 7.38 (2H, d, $J$ = 9.0, Ar*H*(3,5)), 6.87 (2H, d, $J$ = 9.0, Ar*H*(2,6)), 6.76 (1H, *br* s), 5.44 (1H, *br* s).

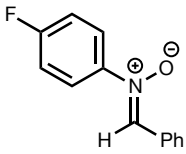
**4. Diarylnitrone Preparation**

**(*Z*)-*N*-Benzylideneaniline oxide 79**



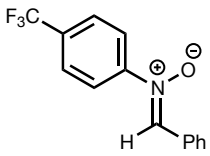
The nitrone was prepared according to general procedure **C** from nitrobenzene (10.3 mL, 100 mmol), benzaldehyde (10.2 mL, 1.0 eq, 100 mmol), $NH_4Cl$ (6.96 g, 1.2 eq, 120 mmol) and zinc powder (13.1 g, 2.0 eq, 200 mmol) in EtOH:$H_2O$ (1:1 400 mL) to yield **79** (10.5 g, 53%) as a white solid; mp 115-116 °C {lit.[8] 110-112 °C}; $^1$H NMR (300 MHz, $CDCl_3$) $\delta$ 8.42-8.39 (2H, m, $^+$N-Ar$H_{ortho}$), 7.93 (1H, s, $^+$N=C*H*), 7.80-7.77 (2H, m, Ar*H*), 7.51-7.47 (6H, m, Ar*H*).

**(*Z*)-*N*-Benzylidene-4-fluoroaniline oxide 80**



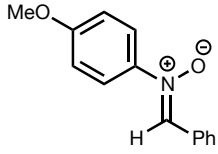
The nitrone was prepared according to general procedure **D** from **73** (4.74 g, 37.3 mmol), $MgSO_4$ (0.500 g, 1.1 eq, 41.0 mmol) and benzaldehyde (3.69 mL, 0.97 eq, 36.2 mmol) in $CH_2Cl_2$ (35 mL) and the reaction mixture stirred 2 h at rt before filtering and concentrating *in vacuo* to yield **80** (5.17 g, 64%) as a grey solid which was used without further purification; mp 154-155 °C {lit.[9] 169-170.3 °C}; $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 8.42-8.40 (2H, m, $^+$N-Ar$H_{ortho}$), 7.91 (1H, s, $^+$N=C*H*), 7.83-7.80 (2H, m, Ar*H*), 7.52-7.51 (3H, m, Ar*H*), 7.22-7.17 (2H, m, Ar*H*).

**(*Z*)-*N*-Benzylidene-4-(trifluoromethyl)aniline oxide 81**



The nitrone was prepared according to general procedure **D** from **74** (3.00 g, 16.9 mmol), $MgSO_4$ (0.400g, 1.1 eq, 18.6 mmol) and benzaldehyde (1.72 mL, 0.97 eq, 16.4 mmol) in $CH_2Cl_2$ (30 mL) and the reaction mixture stirred for 2 h at rt. After this time, the reaction mixture was filtered and concentrated *in vacuo* to yield an off-white solid which was triturated with petroleum ether to yield **81** (4.38 g, 98%) as a white solid; mp 150 °C {lit.[10] 54-56 °C}; $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 8.42-8.39 (2H, m, $^+$N-Ar$H_{ortho}$), 7.91 (1H, s, $^+$N=C*H*), 7.83-7.80 (2H, m, Ar*H*), 7.52-7.51 (3H, m, Ar*H*), 7.22-7.17 (2H, m, Ar*H*).

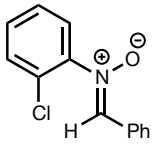
**(*Z*)-*N*-Benzylidene-4-methoxyaniline oxide 82**



The nitrone was prepared according to general procedure **C** from *p*-nitroanisole (5.00 g, 1.0 eq, 32.2 mmol), benzaldehyde (3.29 mL, 1.0 eq, 32.2 mmol), $NH_4Cl$ (2.27 g, 1.3 eq, 42.0 mmol) and zinc powder (4.26 g, 2.0 eq, 64.4 mmol) in EtOH:$H_2O$ (1:1 200 mL) to yield **82** (7.10 g, 97%) as a grey solid; mp 122-123 °C {lit.[10] 129-130 °C}; $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 8.39-8.37 (2H, m, $^+$N-

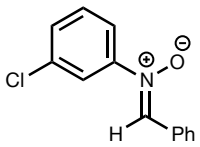
Ar$H_{ortho}$), 7.88 (1H, s, $^{+}$N=C*H*), 7.75-7.72 (2H, m, Ar*H*), 7.49-7.45 (3H, m, Ar*H*), 6.99-6.95 (2H, m, Ar*H*), 3.87 (3H, s, O*Me*).

**(*Z*)-*N*-Benzylidene-2-chloroaniline oxide 83**



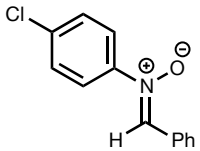
The nitrone was prepared according to general procedure **D** from **70** (2.50 g, 17.4 mmol), $MgSO_4$ (2.30 g, 1.1 eq, 19.1 mmol) and benzaldehyde (0.89 mL, 0.5 eq, 8.70 mmol) in $CH_2Cl_2$ (25 mL) to yield **83** as a yellow oil (3.86 g, quant.); $^1$H NMR (300 MHz, $CDCl_3$) $\delta$ 8.43-8.40 (2H, m, Ar*H*), 7.68-7.65 (2H, m, Ar*H*), 7.62 (1H, s, $^{+}$N=C*H*), 7.57-7.53 (3H, m, Ar*H*), 7.45-7.42 (2H, m, Ar*H*).

**(*Z*)-*N*-Benzylidene-3-chloroaniline oxide 84**



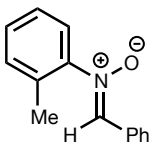
The nitrone was prepared according to general procedure **D** from hydroxylamine **71** (3.10 g, 21.6 mmol), $MgSO_4$ (2.37 g, 1.1 eq, 23.8 mmol) and benzaldehyde (2.01 mL, 0.9 eq, 19.6 mmol) in $CH_2Cl_2$. (30 mL) to give **84** (4.80 g, quant.) as a pale yellow solid; mp 69-70 °C {lit.[11] 96-96.5 °C}; $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 8.43-8.40 (2H, m, $^{+}$N-Ar$H_{ortho}$), 7.93 (1H, s, $^{+}$N=C*H*), 7.85 (1H, td, *J* = 6.9, 0.7, Ar*H*), 7.71 (1H, dt, *J* = 6.9, 2.2, Ar*H*), 7.53-7.45 (5H, m, Ar*H*).

**(*Z*)-*N*-Benzylidene-4-chloroaniline oxide 85**



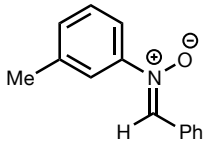
The nitrone was prepared according to general procedure **C** from benzaldehyde (1.29 mL, 12.7 mmol), 1-chloro-4-nitrobenzene (2.00 g, 1.0 eq, 12.7 mmol), $NH_4Cl$ (0.88 g, 1.3 eq, 16.5 mmol) and zinc (1.66 g, 2.0 eq, 25.4 mmol) in EtOH:$H_2O$ (1:1 40 mL) to yield **85** (1.36 g, 47%) as an off-white solid; mp 152-153 °C {lit.[10] 164-166 °C}; $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 8.40-8.37 (2H, m, $^{+}$N-Ar$H_{ortho}$), 7.91 (1H, s, $^{+}$N=C*H*), 7.76-7.74 (2H, m, Ar*H*), 7.50-7.45 (5H, m, Ar*H*).

**(*Z*)-*N*-Benzylidene-4-methylaniline oxide 86**



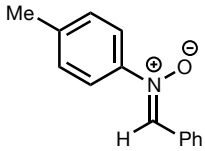
The nitrone was prepared according to general procedure **D** from **67** (0.234 g, 1.89 mmol), benzaldehyde (0.200 mL, 1.0 eq, 1.89 mmol) and $MgSO_4$ (0.250 g, 1.0 eq, 2.26 mmol) in $CH_2Cl_2$ (7 mL) to yield **86** (0.406 g, quant.) as a yellow solid; mp 101-102 °C {lit.[13] 95-96 °C}; $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 8.40-8.38 (2H, m, Ar*H*), 7.60 (1H, s, $^{+}$N=C*H*), 7.54-7.50 (3H, m, Ar*H*), 7.43-7.41 (1H, m, Ar*H*), 7.38-7.30 (3H, m, Ar*H*), 2.47 (3H, s, Ar$CH_3$).

**(*Z*)-*N*-Benzylidene-3-methylaniline oxide 87**




The nitrone was prepared according to general procedure **D** from **68** (0.234 g, 1.89 mmol), benzaldehyde (0.200 mL, 1.0 eq, 1.89 mmol) and $MgSO_4$ (0.250 g, 1.2 eq, 2.26 mmol) in $CH_2Cl_2$ (7 mL) to yield a yellow oil, which after extended standing in the fridge crystallised to give **87** (0.502 g, quant.) as a yellow solid; mp 58-59 °C {lit.[13] 91-92 °C}; $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 8.43-8.41 (2H, m, $^+$N-Ar$H_{ortho}$), 7.90 (1H, s, $^+$N=C*H*), 7.55 (2H, d, *J* = 8.2, Ar*H*), 7.50-7.47 (3H, m, Ar*H*), 7.36 (1H, t, *J* = 8.2, Ar*H*), 7.28 (1H, s, Ar*H*), 2.44 (3H, s, ArC$H_3$).

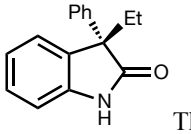
**(*Z*)-*N*-Benzylidene-4-methylaniline oxide 88**




The nitrone was prepared according to general procedure **D** from **69** (0.234 g, 1.89 mmol), benzaldehyde (0.200 mL, 1.0 eq, 1.89 mmol) and $MgSO_4$ (0.250 g, 1.2 eq, 2.26 mmol) in $CH_2Cl_2$ (7 mL) to yield **88** (0.489 g, quant.) as an off-white solid; mp 105-106 °C {lit.[14] 114-115 °C}; $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 8.39 (2H, dd, *J* = 8.0, 2.2, $^+$N-Ar$H_{ortho}$), 7.90 (1H, s, $^+$N=C*H*), 7.67 (2H, d, *J* = 8.0, Ar*H*), 7.47 (3H, dd, *J* = 5.3, 2.2, Ar*H*), 7.28-7.25 (2H, m, Ar*H*), 2.42 (3H, s, ArC$H_3$).

## 5. Alternative Stereodirecting Nitrones

**Summary of yields and enantiomeric excesses obtained for 3-Ethyl-3-phenylindolin-2-one 10 using Nitrones Prepared in the Following Section**

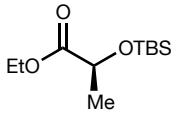



The oxindole was obtained according to general procedure **F** as an off-white solid; HPLC analysis: (Daicel Chiralcel OD-H column, eluent: hexane/*i*-PrOH 80:20, flow 1.5 mL/min, wavelength: 254 nm, retention times: 4.1 min (major) and 8.1 min (minor)). The results of the HPLC analyses are given in the table below.

| Nitrone Used | Oxindole Yield (%) | Oxindole e.e. (%) |
|---|---|---|
| **11** | 43 | 27 (ent.) |
| **12** | 78 | 70 (ent.) |
| **13** | 25 | (±) (<5%) |
| **14** | 32 | 60 |
| **15** | 70 | 80 |
| **16** | 38 | 32 |
| **17** | 21 | 70 |
| **18** | 60 | 20 |
| **4** | 83 | 84 |
| **19** | 75 | 91 |
| **20** | 60 | 96 |

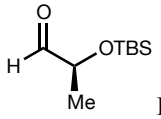
**Preparation of Enantiopure Nitrones**

**(*S*)-Ethyl 2-((*tert*-butyldimethylsilyl)oxy)propanoate 89**



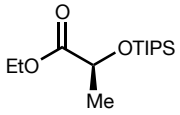

To a stirred solution of the commercially available (*S*)-ethyl 2-hydroxypropanoate (3.70 g, 22.3 mmol) in DMF (23 mL) was added imidazole (2.05 g, 1.35 eq, 30.1 mmol) and TBSCl (4.20 g, 1.25 eq, 27.8 mmol) and the reaction mixture stirred for 16 h at rt. The reaction mixture was then diluted with $Et_2O$ (30 mL) and washed successively with $H_2O$ (30 mL), aq. 0.1M HCl (30 mL) and brine (2 × 25 mL). The organic phase was dried over $Na_2SO_4$, filtered and concentrated *in vacuo* to yield **89** as a yellow oil (6.26 g, quant.); $[\alpha]_D^{20}$-23.3° (*c* = 0.96, $CHCl_3$) {lit.[15] $[\alpha]_D^{20}$ -29.6° (*c* = 1.57, $CHCl_3$)}; $^1$H NMR (300 MHz, $CDCl_3$) $\delta$ 4.31 (1H, q, *J* = 6.8, C*H*(Me)), 4.22-4.13 (2H, m, OC$H_2$CH$_3$), 1.39 (3H, d, *J* = 6.8, C(H)*Me*), 1.28 (3H, t, *J* = 7.1, OCH$_2$C$H_3$), 0.90 (9H, t, *J* = 3.4, $^t$*Bu*), 0.09 (6H, d, *J* = 11.8, di*Me*).

**(*S*)-2-((*tert*-Butyldimethylsilyl)oxy)propanal 90**



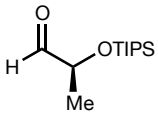
Dry toluene (10 mL) was charged with DIBAL-H (1M in toluene, 2.80 mL, 2.80 mmol) under nitrogen and the resulting suspension cooled to -78 °C. A solution of **89** (0.500 g, 2.15 mmol) in dry toluene (2 mL) was then added dropwise. The reaction was stirred at -78 °C for 1 h 30 min before being quenched with MeOH (1 mL). A saturated Rochelle salt solution (7 mL) was added to the reaction which was stirred rapidly for 10 min allowing to warm to rt. The reaction mixture was then extracted with $Et_2O$ (3 × 20 mL) and the organic phase washed with sat. aq. $NaHCO_3$, dried over $Na_2SO_4$, filtered and concentrated *in vacuo* to yield **90** as a colourless oil (0.29 g, 70%); $[\alpha]_D^{20}$ +11.3° (*c* = 0.96, $CHCl_3$) {lit.[16] $[\alpha]_D^{20}$ +12.8° (*c* = 1.59, $CHCl_3$)}; $^1$H NMR (300 MHz, $CDCl_3$) $\delta$ 9.61 (1H, d, *J* = 1.3, C*H*O), 4.09 (1H, qd, *J* = 6.9, 1.3, C*H*(Me)), 1.28 (3H, d, *J* = 6.9, C(H)*Me*), 0.92 (9H, s, $^t$*Bu*), 0.10 (6H, d, *J* = 3.5, di*Me*).

**(*S*)-Ethyl 2-((triisopropylsilyl)oxy)propanoate 91**



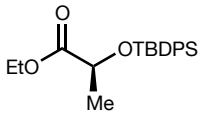
To a stirred solution of the commercially available (*S*)-ethyl 2-hydroxypropanoate (1.00 mL, 8.75 mmol) in DMF (10 mL) was added imidazole (0.775 g, 1.3 eq, 11.3 mmol) and TIPSCl (2.25 mL, 1.2 eq, 10.5 mmol) and the reaction mixture stirred for 16 h at rt. The reaction mixture was then diluted with $Et_2O$ (15 mL) and washed successively with $H_2O$ (15 mL), 0.1M HCl (15 mL) and brine (2 × 10 mL). The organic phase was then dried over $Na_2SO_4$, filtered and concentrated *in vacuo* to yield **91** as a colourless oil (2.88 g, quant.) which was used without further purification; $[\alpha]_D^{20}$-11.8° (*c* = 1.11, $CHCl_3$) {lit.[17] $[\alpha]_D^{20}$ -16.5° (*c* = 1.95, $CHCl_3$)}; $^1$H NMR (300 MHz, $CDCl_3$) $\delta$ 4.41 (1H, q, *J* = 6.7, C*H*(Me)), 4.18 (2H, dq, *J* = 7.1, 1.7, O$CH_2$$CH_3$), 1.42 (3H, d, *J* = 6.7, CH(*Me*)), 1.28 (3H, t, *J* = 7.1, $OCH_2CH_3$), 1.10 (3H, *br* s, *i*Pr*H*), 1.07-1.05 (18H, m, *i*Pr$CH_3$).

**(*S*)-2-((Triisopropylsilyl)oxy)propanal 92**



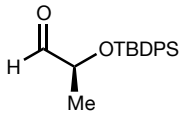
Dry toluene (10 mL) was charged with DIBAL-H (1M in toluene, 3.79 mL, 3.79 mmol) under nitrogen and the resulting suspension cooled to -78 °C. A solution of **91** (0.800 g, 2.92 mmol) in dry toluene (2 mL) was then added dropwise. The reaction was stirred at -78 °C for 1 h 30 min before being quenched with MeOH (1 mL). A saturated Rochelle salt solution (7 mL) was then added to the reaction which was stirred rapidly for 10 min allowing to warm to rt. The reaction was then extracted with $Et_2O$ (3 × 20 mL) and the organic phase washed with sat. aq. $NaHCO_3$, dried over $Na_2SO_4$, filtered and concentrated *in vacuo* to yield **92** as a colourless oil (0.66 g, 98%); $[\alpha]_D^{20}$ -5.2° (*c* = 1.16, $CHCl_3$) {lit.[18] $[\alpha]_D^{20}$ -8.4° (*c* = 2.72, $CHCl_3$)}; $^1$H NMR (300 MHz, $CDCl_3$) $\delta$ 9.66 (1H, d, *J* = 1.7, C*H*O), 4.18 (1H, qd, *J* = 6.8, 1.7, C*H*Me), 1.31 (3H, d, *J* = 6.8, CH*Me*), 1.08-1.05 (21H, m, *i*Pr).

**(*S*)-Ethyl 2-((tert-butyldiphenylsilyl)oxy)propanoate 93**



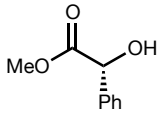

To a stirred solution of the commercially available (*S*)-ethyl 2-hydroxypropanoate (1.20 g, 10.2 mmol) in DMF (12 mL) was added imidazole (0.899 g, 1.3 eq, 13.3 mmol) and TBDPSCl (2.65 mL, 1.2 eq, 12.2 mmol) and the reaction mixture stirred for 16 h at rt. The reaction mixture was then diluted with $Et_2O$ (15 mL) and washed successively with $H_2O$ (15 mL), aq. 0.1M HCl (15 mL) and brine (2 × 10 mL). The organic phase was dried over $Na_2SO_4$, filtered and concentrated *in vacuo* to yield a colourless oil which was purified *via* column chromatography over silica (0-20% EtOAc in petroleum ether) to yield **93** as a colourless oil (2.00 g, 55%); $[\alpha]_D^{20}$ +27.5° (*c* = 1.03, EtOH) {lit.[19] $[\alpha]_D^{20}$ +46° (*c* = 1.97, EtOH)}; $^1$H NMR (300 MHz, $CDCl_3$) $\delta$ 7.73-7.64 (4H, m, Ar*H*), 7.46-7.33 (6H, m, Ar*H*), 4.27 (1H, q, *J* = 6.7, C*H*Me), 4.02 (2H, qd, *J* = 7.0, 0.6, O*C*$H_2$C$H_3$), 1.37 (3H, d, *J* = 6.7, CH*Me*), 1.15 (3H, t, *J* = 7.0, OCH$_2$C*H*$_3$), 1.10-1.09 (9H, m, $^t$*Bu*).

**(*S*)-2-((*tert*-Butyldiphenylsilyl)oxy)propanal 94**



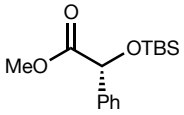

Dry toluene (10 mL) was charged with DIBAL-H (1M in toluene, 1.82 mL, 1.82 mmol) under nitrogen and the resulting suspension cooled to -78 °C. A solution of **93** (0.500 g, 1.40 mmol) in dry toluene (2 mL) was then added dropwise. The reaction was stirred at -78 °C for 1 h 30 min before being quenched with MeOH (1 mL). A saturated Rochelle salt solution (7 mL) was then added to the reaction which was stirred rapidly for 10 min allowing to warm to rt. The reaction mixture was extracted with $Et_2O$ (3 × 20 mL) and the organic phase washed with sat. aq. $NaHCO_3$, dried over $Na_2SO_4$, filtered and concentrated *in vacuo* to yield **94** as a colourless oil (0.484 g, quant.); $[\alpha]_D^{20}$-6.9° (*c* = 1.02, $CHCl_3$) {lit.[20] $[\alpha]_D^{20}$ -15.0° (*c* = 1.07, $CHCl_3$)}; $^1$H NMR (300 MHz, $CDCl_3$) $\delta$ 9.65 (1H, d, *J* = 1.2, C*H*O), 7.74-7.63 (4H, m, Ar*H*), 7.49-7.33 (6H, m, Ar*H*), 4.09 (1H, qd, *J* = 6.9, 1.2, C*H*Me), 1.22 (3H, d, *J* = 6.9, CH*Me*), 1.11 (9H, s, $^t$*Bu*).

**(*R*)-Methyl 2-hydroxy-2-phenylacetate 95**



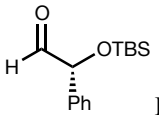

A stirred solution of the commercially available (*R*)-mandelic acid (4.0 g, 26.3 mmol) in MeOH (32 mL) was cooled to 0 °C. To this solution was added thionyl chloride (0.29 mL, 0.15 eq, 3.95 mmol) dropwise. The ice bath was then removed and the reaction heated at reflux for 1 h 30 min. After allowing to cool, the reaction was quenched with $H_2O$ (10 mL) and extracted with $Et_2O$ (3 × 30 mL). The organic phase was washed with sat. aq. $NaHCO_3$ (40 mL), dried over $Na_2SO_4$, filtered and concentrated *in vacuo* to yield **95** as a white solid (4.18 g, 96%) which was used without further purification; mp 60-61 °C {lit.[21] 58 °C}; $[\alpha]_D^{20}$-138.0° (*c* = 1.02, $CHCl_3$) {lit.[22] $[\alpha]_D^{20}$ -116° (*c* = 1.0, $CHCl_3$)}; $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 7.43-7.31 (5H, m, Ar*H*), 5.11 (1H, d, *J* = 5.6, O*H*), 3.77 (3H, s, O*Me*), 3.42 (1H, d, *J* = 5.6, C*H*(OH)).

**(*R*)-Methyl 2-((*tert*-butyldimethylsilyl)oxy)-2-phenylacetate 96**



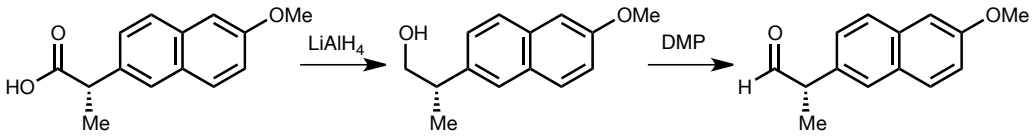

To a stirred solution of **95** (3.70 g, 22.3 mmol) in DMF (23 mL) was added imidazole (2.05 g, 1.35 eq, 30.1 mmol) and TBSCl (4.20 g, 1.25 eq, 27.9 mmol) and the reaction mixture stirred for 16 h at rt. The reaction mixture was then diluted with $Et_2O$ (30 mL) and washed successively with $H_2O$ (30 mL), aq. 0.1M HCl (30 mL) and brine (2 × 25 mL). The organic phase was then dried over $Na_2SO_4$, filtered and concentrated *in vacuo* to yield **96** as a yellow oil (5.92 g, quant.); $[\alpha]_D^{20}$-57.3° (*c* = 1.00, $CHCl_3$) {lit.[23] $[\alpha]_D^{20}$ -50.0° (*c* = 1.04, $CHCl_3$)}; $^1$H NMR (300 MHz, $CDCl_3$) $\delta$ 7.49-7.45 (2H, m, Ar*H*), 7.32 (3H, td, *J* = 4.5, 1.6, Ar*H*), 5.24 (1H, s, C*H*(OTBS)), 3.69 (3H, s, O*Me*), 0.92-0.91 (9H, m, $^t$*Bu*), 0.11 (3H, s, Si*Me*), 0.03 (3H, s, Si*Me*).

**(*R*)-2-((*tert*-Butyldimethylsilyl)oxy)-2-phenylacetaldehyde 97**




Dry toluene (10 mL) was charged with DIBAL-H (1M in toluene, 2.32 mL, 2.32 mmol) under nitrogen and the resulting suspension cooled to -78 °C. A solution of **96** (0.500 g, 1.78 mmol) in dry toluene (2 mL) was then added dropwise. The reaction was stirred at -78 °C for 1 h 30 min before being quenched with MeOH (1 mL). A saturated Rochelle salt solution (7 mL) was then added to the reaction which was stirred rapidly for 10 min allowing to warm to rt. The reaction mixture was extracted with $Et_2O$ (3 × 20 mL) and the organic phase washed with sat. aq. $NaHCO_3$, dried over $Na_2SO_4$, filtered and concentrated *in vacuo* to yield **97** as a colourless oil (0.460 g, quant.); $[\alpha]_D^{20}$+8.0° (*c* = 1.07, $CHCl_3$) {lit.[24] $[\alpha]_D^{20}$ +3.1° (*c* = 1.22, $CHCl_3$)}; $^1$H NMR (300 MHz, $CDCl_3$) $\delta$ 9.51 (1H, d, *J* = 2.1, C*H*O), 7.39-7.38 (4H, m, Ar*H*), 7.36-7.31 (1H, m, Ar*H*), 5.01 (1H, d, *J* = 2.1, C*H*(OTBS)), 0.96-0.94 (9H, m, $^t$*Bu*), 0.12 (3H, s, Si*Me*), 0.04 (3H, s, Si*Me*).

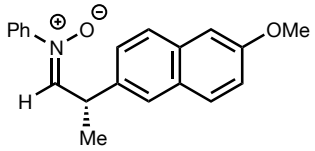
**(*S*)-2-(6-Methoxynaphthalen-2-yl)propanal 99**




Dry $Et_2O$ (10 mL) was charged with $LiAlH_4$ (2.0 M in THF) (3.91 mL, 1.8 eq, 7.82 mmol) and the reaction cooled to 0 °C. A solution of Naproxen (1.00 g, 1.0 eq, 4.34 mmol) in THF (2 mL) was then added dropwise and the reaction stirred for 16 h allowing to warm to rt. The reaction was then recooled to 0 °C and quenched with dropwise addition of $H_2O$ (2 mL) followed by 1M $NaOH_{(aq)}$ solution (10 mL). After stirring for 15 min, the reaction mixture was saturated with MeOH (25 mL), filtered through a celite plug and the solids washed thoroughly with MeOH (25 mL). The MeOH was then removed under reduced pressure, the residue taken up in $Et_2O$ (25 mL) and washed with brine (3 × 15 mL). The organic phase was dried over $Na_2SO_4$, filtered and concentrated *in vacuo* to yield **98** (0.762 g, 82 %) as a white solid; $[\alpha]_D^{20}$-19.6° (*c* = 0.94, $CHCl_3$) {lit.[25] $[\alpha]_D^{20}$ -17.7° (*c* = 2.20, $CHCl_3$)}. Alcohol **98** (0.700 g, 3.25

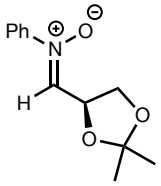
mmol) was then suspended in $CH_2Cl_2$ (30 mL) at rt to which Dess-Martin periodinane (1.65 g, 1.2 eq, 3.90 mmol) was added and the reaction stirred for 40 min at rt. A solution of sodium thiosulfate (8.80 g, 11.0 eq, 35.8 mmol) in sat. aq. $NaHCO_3$ (30 mL) was then added to the reaction followed by $Et_2O$ (30 mL) and the reaction mixture stirred rapidly for ca. 10 mins until it became biphasic and both phases colourless. The phases were separated and the aqueous phase extracted with $Et_2O$ (3 × 20 mL). The combined organic extracts were then washed sequentially with sat. aq. $NaHCO_3$ (20 mL), $H_2O$ (20 mL) and brine (20 mL) before being dried over $Na_2SO_4$, and concentrated *in vacuo* to yield **99** (0.720 g, quant.) as a light brown solid; mp 73-74 °C {lit.[26] 71-72 °C}; $[\alpha]_D^{20}$ +5.8° (*c* = 1.00, $CHCl_3$) {lit.[26] $[\alpha]_D^{20}$ + 37° (*c* = 1.00, $CHCl_3$)}; $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 9.75 (1H, d, *J* = 1.5, C*H*O), 7.74 (2H, dd, *J* = 13.8, 8.6, Ar*H*), 7.60 (1H, d, *J* = 1.1, Ar*H*), 7.28 (1H, dd, *J* = 8.6, 1.8, Ar*H*), 7.17 (1H, dd, *J* = 8.6, 2.4, Ar*H*), 7.13 (1H, d, *J* = 2.4, Ar*H*), 3.93 (3H, s, O*Me*), 3.77 (1H, q, *J* = 6.6, C*H*(Me)), 1.52 (3H, d, *J* = 7.0, CH(*Me*)).

**(*S*,*Z*)-*N*-(2-(6-Methoxynaphthalen-2-yl)propylidene)aniline oxide 11**




To a solution of **99** (0.173 g, 6.18 mmol) dissolved in a minimum quantity of ethanol (ca. 1.5 mL) was added phenylhydroxyalmine **66** (0.130 g, 2.0 eq, 12.4 mmol), then the reaction vessel sealed and stored in the fridge for 40 h to yield a white precipitate. This precipitate was filtered, washed with EtOH (2 × 5 mL), and dried to yield nitrone **11** (0.105 g, 56%) as a white solid; mp 115-116 °C; $[\alpha]_D^{20}$ -77.1° (*c* = 0.96, $CHCl_3$); $^1$H NMR (300 MHz, $CD_2Cl_2$) $\delta$ 7.67-7.56 (5H, m, Ar*H*), 7.40-7.32 (5H, m, Ar*H*), 7.07-7.05 (2H, m, Ar*H* & *H*(R)C=N$^+$), 4.64 (1H, quint., *J* = 7.2, C*H*Me), 3.82 (3H, s, O*Me*), 1.55 (3H, d, *J* = 7.2, CH*Me*); $^{13}$C NMR (75 MHz, $CD_2Cl_2$) $\delta$ 158.4 ($4^{ry}$ Ar*C*), 156.7 (Ar*C*), 147.7 ($4^{ry}$ Ar*C*), 142.4 (Ar*C*), 138.3 (H*C*=N$^+$), 130.6 (Ar*C*), 129.9 (Ar*C*), 129.8 (Ar*C*), 128.0 (Ar*C*), 127.3 (Ar*C*), 126.2 (Ar*C*), 122.4 (Ar*C*), 119.7 (Ar*C*), 118.4 ($4^{ry}$ Ar*C*), 106.3 (Ar*C*), 56.1 (O*Me*), 38.0 (*C*H(CH$_3$)), 18.6 (CH(*C*H$_3$)); *m/z* (EI$^+$) 306 ([M+H]$^+$, 100%); HRMS (EI$^+$) $C_{20}H_{20}O_2N^+$ ([M+H]$^+$) found 306.1491 requires 306.1489 (+ 0.2 ppm).

**(*S*,*Z*)-*N*-((2,2-Dimethyl-1,3-dioxolan-4-yl)methylene)aniline oxide 12**

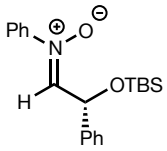



Nitrone **12** was prepared according to a modified literature procedure.[27] To a stirred solution of $MgSO_4$ (2.82 g, 1.1 eq, 23.5 mmol) in $CH_2Cl_2$ (200 mL) was added a solution of freshly distilled (*R*)-glyceraldehyde (2.78 g, 1.0 eq, 21.3 mmol) under nitrogen and the reaction mixture stirred 5 min at rt. *N*-phenylhydroxylamine (2.33 g, 1.0 eq, 21.3 mmol) was added as a solid and the reaction mixture stirred 16 h at rt. $MgSO_4$ was removed by filtration under nitrogen and the filtrate concentrated under reduced pressure. The air sensitive nitrone was used without any further purification. An authentic sample could be obtained by column chromatography ($Et_2O$) to give a colourless oil. $^1$H NMR (300 MHz,

$CDCl_3$) $\delta$ 7.70-7.67 (2H, m) 7.47-7.43 (4H, m), 5.35 (1H, dt, $J$ = 6.8, 5.3), 4.51 (1H, dd, $J$ = 8.7, 7.1), 4.06 (1H, dd, $J$ = 8.7, 5.6), 1.47 (3H, s), 1.42 (3H, s).

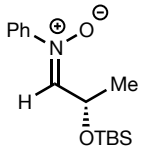
*The following β-silyloxy nitrones were found to be unstable with respect to aqueous work-up and purification by silica gel column chromatography. Therefore, they were formed invariably in more than quantitative yield due to contamination by impurities that were not removed prior to evaluation in our oxindole preparation studies. As a consequence, limited characterisation data was obtained.*

**(*R*,*Z*)-*N*-(2-((*tert*-Butyldimethylsilyl)oxy)-2-phenylethylidene)aniline oxide 13**



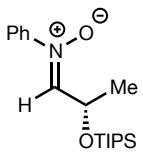

The nitrone was obtained from aldehyde **97** (0.320 g, 1.23 mmol), phenylhydroxylamine **66** (0.167 g, 1.25 eq, 1.53 mmol) and $MgSO_4$ (0.163 g, 1.1 eq, 1.35 mmol) according to general procedure **D** to yield **13** (0.422 g, 97%) as a crude yellow oil; $^1$H NMR (300 MHz, $CDCl_3$) $\delta$ 7.55-7.38 (11H, m, Ar*H* & *H*CN$^+$), 5.07-5.00 (1H, m, C*H*(OTBS)), 0.93-0.90 (9H, m, $^t$*Bu*), 0.10-0.05 (6H, m, di*Me*).

**(*S*,*Z*)-*N*-(2-((*tert*-Butyldimethylsilyl)oxy)propylidene)aniline oxide 14**



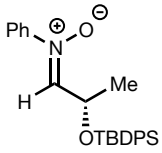

The nitrone was obtained from aldehyde **90** (0.163 g, 0.87 mmol), phenylhydroxylamine **66** (0.113 g, 1.2 eq, 1.04 mmol) and $MgSO_4$ (0.124 g, 1.1 eq, 0.96 mmol) according to general procedure **D** to yield **14** (0.284 g, quant.) as a crude yellow oil which was used without further purification; $^1$H NMR (300 MHz, $CDCl_3$) $\delta$ 7.70-7.64 (1H, m, Ar*H*), 7.46-7.40 (4H, m, Ar*H*), 7.30-7.27 (1H, m, *H*(R)C=N$^+$), 5.19 (1H, quint., $J$ = 6.3, C*H*Me), 1.48 (3H, d, $J$ = 6.3, CH*Me*), 0.92-0.88 (9H, m, $^t$*Bu*), 0.12 (6H, d, $J$ = 6.9, C*Me*$_2$).

**(*S*,*Z*)-*N*-(2-((Triisopropylsilyl)oxy)propylidene)aniline oxide 15**



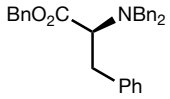

The nitrone was obtained from aldehyde **92** (0.300 g, 1.30 mmol), phenylhydroxylamine **66** (0.142 g, 1.0 eq, 1.30 mmol) and $MgSO_4$ (0.172 g, 1.1 eq, 1.40 mmol) according to general procedure **D** to yield **15** (0.424 g, quant.) as a crude yellow oil which was used without further purification; $^1$H NMR (300 MHz, $CDCl_3$) $\delta$ 7.70-7.64 (2H, m, Ar*H*), 7.48-7.42 (3H, m, Ar*H*), 7.00 (1H, m, *H*(R)C=N$^+$), 5.27 (1H, quint., $J$ = 6.3, C*H*Me), 1.51 (3H, d, $J$ = 6.3, CH*Me*), 1.09-1.04 (21H, m, $^i$*Pr*).

**(*S*,*Z*)-*N*-(2-((*tert*-Butyldiphenylsilyl)oxy)propylidene)aniline oxide 16**



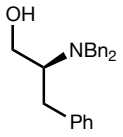

The nitrone was obtained from aldehyde **94** (0.450 g, 1.44 mmol), phenylhydroxylamine **66** (0.189 g, 1.2 eq, 1.73 mmol) and $MgSO_4$ (0.191 g, 1.1 eq, 1.58 mmol) according to general procedure **D** to yield **16** (0.663 g, quant.) as a crude yellow oil which was used without further purification; $^1$H NMR (300 MHz, $CDCl_3$) $\delta$ 7.71-7.64 (3H, m, Ar*H*), 7.41-7.32 (12H, m, Ar*H*), 7.14 (1H, d, $J$ = 5.6, *H*(R)C=N$^+$), 5.30-5.22 (1H, m, C*H*Me), 1.50 (3H, d, $J$ = 6.4, CH*Me*), 1.12-1.06 (9H, m, $^t$*Bu*).

**(*S*)-Benzyl 2-(dibenzylamino)-3-phenylpropanoate 100**



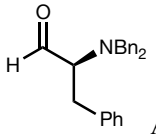

To a stirred solution of $K_2CO_3$ (8.30 g, 60.0 mmol) and sodium hydroxide (2.40 g, 60.0 mmol) in water (50 mL) was added (*S*)-phenyl alanine (4.95 g, 30.0 mmol) in $Et_2O$ (75 mL). The suspension was heated under reflux until a clear solution formed before dropwise addition of distilled benzyl bromide (14.20 mL, 4.0 eq, 120 mmol) followed by heating to reflux for a further 1h. After cooling to room temperature, the organic layer was separated and the aqueous phase was extracted with diethyl ether (200 mL x 3). The combined organic phases were washed with brine (400 mL), dried over magnesium sulfate and concentrated *in vacuo* to a crude yellow oil which was purified by column chromatography (10-50% EtOAc in petroleum ether) to yield **100** (11.23 g, 86%) as a colourless viscous oil; $[\alpha]_D^{20}$ - 9.9° ($c$ = 1.0, $CHCl_3$) {lit.[28] $[\alpha]_D^{20}$ - 72.9° ($c$ = 1.8, $CHCl_3$)}; $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 7.01-7.26 (20H, m, Ar*H*), 5.34 (2H, s, R(O)C$H_2$-Ph), 3.97 (2H, d, $J$ = 16.2, R-N-C$H_2$), 3.74 (1H, t, $J$ = 12.4, 2.6, C*H*), 3.58 (2H, d, $J$ = 16.2, R-N-C$H_2$), 3.15-3.13 (2H, m, R-C$H_2$-Ph).

**(*S*)-2-(Dibenzylamino)-3-phenylpropan-1-ol 101**



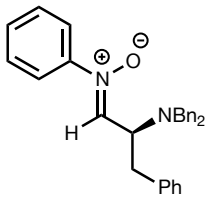

(*S*)-Benzyl 2-(dibenzylamino)-3-phenylpropanoate **100** (2.00 g, 1.0 eq, 4.50 mmol) in $Et_2O$ (20 mL) was treated dropwise with $LiAlH_4$ (2.0 M in THF) (2.7 mL, 1.2 eq, 5.40 mmol). The reaction mixture was stirred 3 h, allowing to warm to rt, before quenching with MeOH (2 mL). A saturated Rochelle salt solution (7 mL) was then added to the reaction which was stirred rapidly for 10 min and then extracted with $Et_2O$ (3 x 25 mL). The combined organic layers were then washed with brine (30 mL) and concentrated *in vacuo* to yield a crude yellow viscous oil which was purified by column chromatography over silica (0-50% EtOAc in petroleum ether) to give **101** (2.50 g, 82 %) as a colourless oil; $[\alpha]_D^{20}$ + 7.6° ($c$ = 1.0, MeOH) {lit.[29] $[\alpha]_D^{20}$ + 8.0° ($c$ = 1.0, MeOH)}; $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 7.26-7.01 (15H, m, Ar*H*), 3.88-3.84 (2H, d, $J$ = 17.7, C$H_2$-OH), 3.44-3.40 (4H, m, 2 x N-C$H_2$), 3.27-3.20 (1H, m, C*H*), 3.07-2.99 (2H, m, R-C$H_2$-Ph).

**(*S*)-2-(Dibenzylamino)-3-phenylpropanal 102**



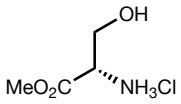
A solution of DMSO (0.24 mL, 2.0 eq, 3.00 mmol) in $CH_2Cl_2$ (10 mL) was added dropwise to a stirred solution of oxalyl chloride (0.16 mL, 1.2 eq, 1.81 mmol) in $CH_2Cl_2$ (5 mL) cooled to -78 °C using a dry ice/acetone bath and stirred at -78 °C for 15 min. A solution of **101** (0.500 g, 1.0 eq, 1.50 mmol) in $CH_2Cl_2$ (10 mL) was then added slowly and the reaction stirred for 35 min. At -78 °C was added $Et_3N$ (0.84 mL, 6.00 mmol, 4.0 eq) and the reaction mixture stirred allowing to warm to rt before being quenched with sat. aq. $NH_4Cl$ (25 mL). The organic phase was then separated and washed in succession with sat. aq. $NaHCO_3$ (30 mL) and brine (2 × 30 mL) before being dried over $Na_2SO_4$, filtered and concentrated *in vacuo* to yield **102** (0.493 g, 99%) as a viscous yellow oil which was used without further purification; $[\alpha]_D^{20}$ - 90.0° (*c* = 1.0, $CHCl_3$) {lit.[30] $[\alpha]_D^{20}$ - 92.9° (*c* = 1.87, $CH_2Cl_2$)}; $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 9.65 (1H, s, C*H*O), 7.23-7.07 (15H, m, Ar*H*), 3.68 (2H, d, *J* =13.6, 2 x N-C$H_2$), 3.58 (2H, d, *J* =13.6, 2 x N-C$H_2$), 3.49 (1H, t, *J* = 6.5, C*H*), 3.10-2.85 (2H, m, R-C$H_2$-Ph).

**(*S*,*Z*)-*N*-(2-(Dibenzylamino)-3-phenylpropylidene)aniline oxide 103**



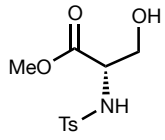
The nitrone was prepared according to general procedure **D** from (*S*)-2-(dibenzylamino)-3-phenylpropanal **102** (0.493 g, 1.50 mmol, 1.0 eq) and phenyl hydroxylamine **66** (0.164 g. 1.50 mmol, 1.0 eq) to give a crude yellow oil (0.085 g, 14%) which was used without further purification; $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 7.51-7.25 (16 H, m), 7.04-7.00 (5H, m), 4.78-4.71 (1H, m), 3.85 (2H, d, *J* = 13.9), 3.78 (2H, d, *J* = 13.9), 3.21 (1H, dd, *J* = 14.1, 6.2), 3.02 (1H, dd, *J* = 14.1, 8.9).

**(*S*)-Methyl 2-amino-3-hydroxypropanoate hydrochloride 104**



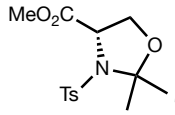
To a stirred solution of (L)-Serine (44.0 g, 0.419 mol) in MeOH (900 mL) cooled to < 0 °C using a salted ice bath was added thionyl chloride (153.0 mL, 6.0 eq, 2.10 mol) dropwise and the reaction stirred for 16 h allowing to warm to rt. The reaction mixture was then concentrated *in vacuo* and the residue taken up in $Et_2O$ (500 mL) and re-concentrated several times before being taken up in $Et_2O$ (500 mL) a final time and cooled with an ice bath to allow formation of a white precipitate. This precipitate was filtered and washed with cold $Et_2O$ (3 × 150 mL) to yield **104** (59.20 g, 92%) as a white solid; mp 157-158 °C {lit.[31] 163-165 °C}; $[\alpha]_D^{20}$ +3.9° (*c* = 1.14, MeOH) {lit.[31] $[\alpha]_D^{20}$ +3.7° (*c* = 4.0, MeOH)}; $^1$H NMR (300 MHz, $D_2O$) $\delta$ 4.29 (1H, t, *J* = 3.8, C*H*($NH_2$)), 4.08 (2H, dq, *J* = 12.5, 3.8, C$H_2$OH), 3.87 (3H, s, $CO_2$*Me*).

**(*S*)-Methyl 3-hydroxy-2-(4-methylphenylsulfonamido) propanoate 105**



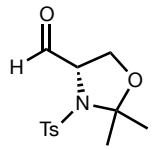
To a stirred solution of **104** (2.33 g, 1.0 eq, 15.0 mmol) in $CH_2Cl_2$ (50 mL) at 0 °C, was added $Et_3N$ (3.60 g, 2.4 eq, 35.0 mmol) and the reaction mixture stirred for 5 min at 0 °C. Tosyl chloride (3.15 g, 1.1 eq, 16.5 mmol) was added and the reaction mixture stirred for 16 h, allowing to warm to rt. The reaction was quenched by addition of $H_2O$ (50 mL), the layers separated and the aqueous layer extracted with $CH_2Cl_2$ (3 × 30 mL). The combined organic layers were washed in succession with sat. aq. $NaHCO_3$ (30 mL), 10% aq. citric acid (30 mL), $H_2O$ (30 mL) and brine (30 mL), dried over $MgSO_4$, filtered and concentrated *in vacuo* to yield **105** (2.01 g, 43%) as a white solid; mp 84-86 °C {lit.[32] mp 84-85 °C}; $[\alpha]_D^{20}$ + 3.0 (*c* = 1.0, MeOH) {lit.[32] $[\alpha]_D^{20}$ + 12.2 (*c* = 0.83, $CHCl_3$)}; $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 7.77 (2H, d, *J* = 8.3, Ar*H*), 7.34 (2H, d, *J* = 8.0, Ar*H*), 5.35 (1H, d, *J* = 6.7, N*H*), 4.02 (1H, dt, *J* = 7.3, 3.6, NC*H*), 3.93-3.91 (2H, m, C$H_2$), 3.65 (3H, s, OC$H_3$), 2.45 (3H, s, ArC$H_3$).

**(*S*)-Methyl 2,2-dimethyl-3-tosyloxazolidine-4-carboxylate 106**



To a stirred solution of **105** (1.00 g, 1.0 eq, 3.25 mmol) and 2,2-dimethoxypropane (6.26 mL, 15.0 eq, 48.0 mmol) in acetone was added $BF_3.Et_2O$ (0.08 mL, 0.2 eq, 0.600 mmol) and the reaction mixture stirred for 3 h at rt. The reaction was treated with $Et_3N$ (0.09 mL, 0.2 eq, 0.675 mmol), stirred for 15 min at rt and then concentrated *in vacuo*. The residue was then taken up in $Et_2O$ (25 mL) and washed with sat. aq. $NaHCO_3$ (25 mL). The phases were separated and the aqueous layer extracted with $Et_2O$ (3 × 25 mL). The combined organic layers were dried over $MgSO_4$, filtered and concentrated *in vacuo* to yield the crude product as a yellow oil which was purified *via* column chromatography over silica (0-30% EtOAc in petroleum ether) to yield **106** (0.050 g, 45%) as a white solid; mp 98-102 °C {lit.[33] mp 95-97 °C}; $[\alpha]_D^{20}$ -86.0 (*c* = 1.0, $CH_2Cl_2$) {lit.[33] $[\alpha]_D^{20}$ -80.2 (*c* = 1.0, $CH_2Cl_2$)}; $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 7.80 (2H, d, *J* = 8.3, Ar*H*), 7.32 (2H, d, *J* = 7.9, Ar*H*), 4.46 (1H, dd, *J* = 6.7, 2.8, C*H*), 4.16 (1H, dd, *J* = 9.2, 6.7, C$H_a$H$_b$), 4.08 (1H, dd, *J* = 9.2, 2.8, CH$_a$$H_b$), 3.64 (3H, s, OC$H_3$), 2.45 (3H, s, ArC$H_3$), 1.73 (3H, s, C$H_3$), 1.61 (3H, s, C$H_3$).

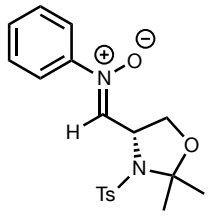
**(*S*)-2,2-Dimethyl-3-tosyloxazolidine-4-carbaldehyde 107**



To a stirred solution of **106** (0.200 g, 1.0 eq, 0.70 mmol) in toluene at -78 °C was added DIBAL-H (0.85 mL, 1.2 eq, 0.85 mmol) dropwise and the reaction stirred at -78 °C for 2 h. The reaction was quenched by slow addition of a saturated Rochelle salt solution (5 mL) followed by rapid stirring for 30 min, allowing to warm to rt. The reaction mixture was extracted with $Et_2O$ (3 × 10 mL). The combined organic layers were then washed with sat. aq. $NaHCO_3$, dried over $MgSO_4$, filtered and concentrated *in*

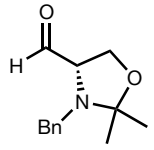
*vacuo* to yield a crude yellow oil which was purified *via* column chromatography over silica (0-15% EtOAc in petroleum ether) to yield **107** (0.168 g, 94%) as a colourless oil which was used immediately in the next reaction; $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 9.49-9.48 (1H, m, C*H*O), 7.74 (2H, d, $J$ = 8.3, Ar*H*), 7.32 (2H, d, $J$ = 7.8, Ar*H*), 4.12 (1H, dd, $J$ = 9.2, 6.7, C*H*N), 4.11-4.06 (1H, m, C$H_aH_b$), 4.05-4.00 (1H, m, C$H_aH_b$), 2.44 (3H, s, ArC$H_3$), 1.73 (3H, s, C$H_3$), 1.53 (3H, s, C$H_3$).

**(*R*,*Z*)-*N*-((2,2-Dimethyl-3-tosyloxazolidin-4-yl)methylene)aniline oxide 19**



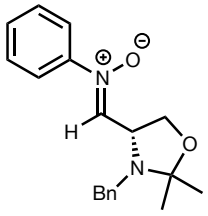
To a stirred solution of **107** (0.160 g, 1.0 eq, 0.64 mmol) and $MgSO_4$ (0.084 g, 1.1 eq, 0.70 mmol) in $CH_2Cl_2$ (5 mL) was added phenylhydroxylamine **66** (0.138 g, 2.0 eq, 1.30 mmol) and the reaction mixture stirred 16 h at rt. The reaction mixture was concentrated *in vacuo* to yield the crude product as a yellow oil which was purified by column chromatography over silica (10-60% EtOAc in petroleum ether) to yield **19** (0.152 g, 72 %) as a yellow foam; mp 48-49 °C; $[\alpha]_D^{20}$ -174.5° ($c$ = 1.09, $CHCl_3$); $\nu_{max}$ cm$^{-1}$ (thin-film) 3446, 2310, 1924, 1733, 1458, 1339; $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 7.83 (2H, d, $J$ = 8.3, Ts*H*), 7.64 (2H, d, $J$ = 8.5, Ts*H*), 7.49-7.41 (3H, m, Ar*H*), 7.34 (2H, d, $J$ = 7.9, Ar*H*), 7.28 (1H, d, $J$ = 6.0, $^+$N=C*H*), 5.07-5.11 (1H, m, C*H*), 4.23 (1H, dd, $J$ = 9.1, 4.8, C$H_aH_b$), 4.17 (1H, dd, $J$ = 11.4, 5.1, C$H_aH_b$), 2.40 (3H, s, ArC$H_3$), 1.74 (3H, s, C$H_3$), 1.55 (3H, s, C$H_3$); $^{13}$C NMR (125 MHz, $CDCl_3$) $\delta$ 147.0 (Ar*C*N$^+$), 144.6 (Ar*C*), 138.8 (Ar*C*), 137.7 (Ar*C*), 130.8 (Ar*C*), 130.2 (Ar*C*), 129.4 (Ar*C*), 128.0 (Ar*C*), 121.7 (Ar*C*), 99.0 (*C*(Me$_2$)), 67.6 (*C*H$_2$), 56.7 (*C*HN), 29.2 (C*Me$_2$*), 24.8 (C*Me$_2$*), 21.6 (Ar*C*H$_3$); *m/z* (ES$^+$) 397 ([M+Na]$^+$, 100%), 398 ([M+Na+H]$^+$, 40%); HRMS (ES$^+$) $C_{19}H_{22}O_4N_2SNa^+$ ([M+Na]$^+$) found 397.1198 requires 397.1199 (+ 0.2 ppm).

**(*S*)-3-Benzyl-2,2-dimethyloxazolidine-4-carbaldehyde 108**



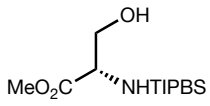
(*S*)-3-Benzyl-2,2-dimethyloxazolidine-4-carbaldehyde **108** was prepared from (*S*)-methyl 2-amino-3-hydroxypropanoate hydrochloride **104** according to a known literature procedure[34] to yield **108** as a yellow oil (0.206 g, quant.) with data in accordance with the literature and used without further purification; $[\alpha]_D^{20}$ + 3.0° ($c$ = 0.60, $CHCl_3$) {$[\alpha]_D^{20}$ lit.[34] + 5.96° ($c$ = 0.95, $CHCl_3$)}; $^1$H NMR (300 MHz, $CDCl_3$) $\delta$ 8.94 (1H, d, $J$ = 4.2, C*H*O), 7.33-7.28 (5H, m, Ar*H*), 4.08 (1H, app. t, $J$ = 8.9, CHC$H_aH_b$), 3.98 (1H, d, $J$ = 12.7, C$H_aH_b$Ph), 3.87 (1H, dd, $J$ = 8.9, 5.8, CHC$H_aH_b$), 3.45 (1H, d, $J$ = 12.7, C$H_aH_b$Ph), 3.36 (1H, ddd, $J$ = 8.9, 5.8, 4.2, C*H*CH$_2$), 1.46 (3H, s, C$H_3$), 1.32 (3H, s, C$H_3$).

**(*R*,*Z*)-*N*-((3-Benzyl-2,2-dimethyloxazolidin-4-yl)methylene)aniline oxide 18**



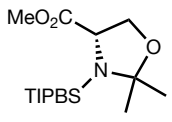
To a stirred solution of **108** (0.206 g, 0.94 mmol) and $MgSO_4$ (0.125 g, 1.1 eq, 1.03 mmol) in $CH_2Cl_2$ (5 mL) was added PhNHOH **66** (0.120 g, 1.2 eq, 1.13 mmol) and the reaction stirred for 2 h at rt. The reaction mixture was then concentrated *in vacuo* and purified *via* column chromatography over silica (0-100% EtOAc in petroleum ether) to yield **18** (0.101 g, 35 %) as a yellow solid; mp 72-73 °C; $[\alpha]_D^{20}$ +31.7° (*c* = 0.58, $CH_2Cl_2$); $\nu_{max}$ $cm^{-1}$ (KBr); $^1H$ NMR (300 MHz, $CDCl_3$) $\delta$ 7.43-7.40 (2H, m, $^+$N-Ar$H_{ortho}$), 7.35-7.22 (6H, m, Ar*H*), 7.00-6.97 (2H, m, Ar*H*), 6.67 (1H, d, *J* = 5.5, $^+$NC=*H*), 4.50-4.42 (2H, m, CHC$H_2$), 3.96 (1H, d, *J* = 12.8, C$H_2$Ph), 3.83 (1H, td, *J* = 5.5, 2.0, C*H*$CH_2$), 3.46 (1H, d, *J* = 12.8, C$H_2$Ph), 1.50 (3H, s, C$H_3$), 1.34 (3H, s, C$H_3$); $^{13}C$ NMR (75 MHz, $CDCl_3$) $\delta$ 146.5 (Ar*C*N$^+$), 141.7 (Ar*C*$CH_2$N), 139.6 (H*C*=N$^+$), 129.9 (Ar*C*), 129.1 (Ar*C*), 128.7 (Ar*C*), 127.5 (Ar*C*), 125.6 (Ar*C*), 121.3 (Ar*C*), 96.1 (*C*$Me_2$), 67.2 (*C*$H_2$O), 60.1 (*C*$H_2$Ph), 54.2 (*C*HN), 26.9 (1 x C*Me*$_2$), 19.6 (1 x C*Me*$_2$).

**(*S*)-Methyl 3-hydroxy-2-(2,4,6-triisopropylphenylsulfonamido)propanoate 109**



To a stirred solution of **104** (4.67 g, 0.030 mol) in $CH_2Cl_2$ (60 mL) was added dropwise $Et_3N$ (9.98 mL, 2.4 eq, 0.07 mol) at 0 °C and the reaction mixture stirred for 5 min at 0 °C. After this time, 2,4,6-triisopropylbenzenesulfonyl chloride (9.54 g, 1.05 eq, 0.032 mol) was added in one portion and the reaction stirred for 16 h allowing to warm to rt. The reaction was quenched with $H_2O$ (100 mL) before being extracted with $CH_2Cl_2$ (3 × 120 mL). The combined organic layers were then washed in succession with sat. aq. $NaHCO_3$ (100 mL), 10% citric acid solution (100 mL), $H_2O$ (100 mL) and brine (100 mL) before being dried over $MgSO_4$, filtered and concentrated *in vacuo* to yield **109** (11.23 g, 97%) as an off-white solid; mp 109-111 °C; $[\alpha]_D^{20}$ +4.3° (*c* = 0.91, $CHCl_3$); $\nu_{max}$ $cm^{-1}$ (KBr) 3359 (N-H), 3356 (O-H), 2959 (C-H), 1733 (C=O); $^1H$ NMR (400 MHz, $CDCl_3$) $\delta$ 7.17 (2H, s, Ar*H*), 4.12-4.06 (3H, m, *o*-*i*Pr*H* & C*H*NR), 3.91-3.90 (2H, m, C$H_2$), 3.66 (3H, s, COO*Me*), 2.90 (1H, dt, *J* = 13.8, 6.9), 1.29-1.24 (18H, m, *i*PrC$H_3$); $^{13}C$ NMR (75 MHz, $CDCl_3$) $\delta$ 170.4 (*C*=O), 153.3 (4$^{ry}$Ar*C*(*p*-*i*Pr)), 150.3 (4$^{ry}$Ar*C*(*o*-*i*Pr)), 132.2 (4$^{ry}$Ar*C*$SO_2$), 124.0 (Ar*C*H), 101.3 (*C*$Me_2$), 63.7 (*C*H(COOMe), 57.2 (*C*$H_2$), 53.0 (COO*Me*), 34.2 (*p*-*i*Pr*C*$(CH_3)_2$), 30.0 (*o*-*i*Pr*C*$(CH_3)_2$), 24.9 (C*Me*$_2$, d, *J* = 12.9), 23.6 (*p*-*i*PrC(*C*$H_3)_2$), 23.6 (*o*-*i*PrC(*C*$H_3)_2$); *m/z* (EI$^+$) 386 ([M+H]$^+$, 100%); HRMS (EI$^+$) $C_{19}H_{32}O_5NS^+$ ([M+H]$^+$) found 386.1998 requires 386.1996 (+ 0.2 ppm).

***(S)*-Methyl 2,2-dimethyl-3-((2,4,6-triisopropylphenyl)sulfonyl)oxazolidine-4-carboxylate 110**

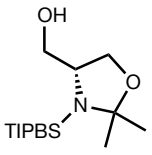


To a stirred solution of **109** (5.78 g, 0.015 mol) and pyridinium *para*-toluenesulfonate (0.94 g, 0.25 eq, 3.75 mmol) in toluene (200 mL) was added 2,2-dimethoxypropane (27.7 mL, 15.0 eq,

0.225 mol) and the reaction stirred at 80 °C for 16 h. After cooling, the reaction mixture was concentrated *in vacuo* to yield a crude light-brown oil which was purified by column chromatography over silica (0-20% EtOAc in petroleum ether) to yield **110** (3.00 g, 47 %) as a white solid; mp 106-107 °C; $[\alpha]_D^{20}$ -32.8° (*c* = 1.02, $CHCl_3$); $\nu_{max}$ $cm^{-1}$ (KBr) 2963 (C-H), 1763 (C=O); $^1H$ NMR (300 MHz, $CDCl_3$) $\delta$ 7.15 (2H, s, Ar*H*), 4.40 (1H, dd, *J* = 7.4, 2.1, 1 × C$H_2$), 4.31-4.24 (3H, m, C*H*NR & *o*-*i*Pr*H*), 4.06 (1H, dd, *J* = 9.2, 2.1, 1 × C$H_2$), 3.23 (3H, s, COO*Me*), 2.89 (1H, dt, *J* = 13.8, 6.9, *p*-*i*Pr*H*), 1.80 (6H, d, *J* =11.6), 1.30-1.22 (18H, m, *i*PrC$H_3$); $^{13}C$ NMR (75 MHz, $CDCl_3$) $\delta$ 170.4 (*C*=O), 153.8 ($4^{ry}$Ar*C*(*p*-*i*Pr)), 151.8 ($4^{ry}$Ar*C*(*o*-*i*Pr)), 131.9 ($4^{ry}$ Ar*C*$SO_2$), 100.7 (*C*$Me_2$), 67.5 (*C*H(COOMe)), 59.1 (*C*$H_2$OR), 51.9 (COO*Me*), 34.2 (*p*-*i*Pr*C*$(CH_3)_2$), 29.5 (*o*-*i*Pr*C*$(CH_3)_2$), 27.6 (*p*-*i*PrC(*C*$H_3)_2$), 24.8 (C$Me_2$, d, *J* = 6.7), 23.6 (*o*-*i*PrC(*C*$H_3)_2$); *m/z* ($EI^+$) 426 ($[M+H]^+$, 100%); HRMS ($EI^+$) $C_{22}H_{36}O_5NS^+$ ($[M+H]^+$) found 426.2312 requires 426.2309 (+ 0.3 ppm).

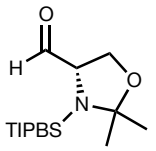
*Alternative preparation of **110** (avoiding column chromatography):* To a stirred solution of **109** (5.78 g, 0.015 mol) and pyridinium *para*-toluenesulfonate (0.94 g, 0.25 eq, 3.75 mmol) in toluene (200 mL) was added 2,2-dimethoxypropane (27.7 mL, 15.0 eq, 0.225 mol) and the reaction stirred at 100 °C for 16 h under Dean-Stark conditions. After cooling, the reaction mixture was poured into water, the layers partitioned, the organic layer diluted with EtOAc (400 mL) and washed sequentially with sat. aq. $NaHCO_3$ (300 mL) and brine (300 mL). The organic layer was then dried over $MgSO_4$, filtered and concentrated *in vacuo* to give a yellow semi-solid which was purified *via* recrystallisation from hexane to give **110** as a white solid in yields of between 40-60% based on multiple preparations.

**(*R*)-(2,2-Dimethyl-3-((2,4,6-triisopropylphenyl)sulfonyl)oxazolidin-4-yl)methanol 111**




To a stirred solution of **110** (2.55 g, 6.00 mmol) in THF (18 mL) was added dropwise $LiAlH_4$ (2.0M in THF) (4.50 mL, 1.5 eq, 9.00 mmol) at 0 °C, and the reaction stirred at 0 °C for 30 min. The reaction was then quenched with dropwise addition of $H_2O$ (1 mL), followed by addition of 40% KOH (1 mL), $H_2O$ (3 mL) and EtOAc (5 mL). The resulting slurry was then stirred vigorously for 1 h allowing to warm to rt before being filtered through a celite plug and the residue washed with EtOAc (30 mL). The reaction mixture was then dried over $MgSO_4$ before being filtered and concentrated *in vacuo* to yield **111** (2.39 g, quant.) as a very viscous colourless oil which crystallised as a white solid on standing; mp 80-82 °C; $[\alpha]_D^{20}$ +5.5° (*c* = 1.01, $CHCl_3$); $\nu_{max}$ $cm^{-1}$ (thin-film) 3527 (O-H), 2960 (C-H); $^1H$ NMR (300 MHz, $C_6D_6$) $\delta$ 7.18 (2H, s, Ar*H*), 4.67 (2H, dt, *J* = 13.6, 6.8, *o*-*i*Pr*H*), 3.87-3.80 (3H, m, C$H_2$ & C*H*NR), 2.92 (1H, t, *J* = 9.3, 1 × C$H_2$OH), 2.70-2.58 (2H, m, *p*-*i*Pr*H* & 1 × C$H_2$OH), 1.88 (3H, s, C*Me*), 1.77 (3H, s, C*Me*), 1.36 (3H, d, *J* = 6.8, *o*-*i*PrC$H_3$), 1.30 (3H, d, *J* = 6.8, *o*-*i*PrC$H_3$), 1.09 (3H, d, *J* = 6.9, *p*-*i*PrC$H_3$); $^{13}C$ NMR (75 MHz, $C_6D_6$) $\delta$ 153.7 ($4^{ry}$Ar*C*), 151.9 ($4^{ry}$Ar*C*), 134.2 ($4^{ry}$Ar*C*$SO_2$), 124.3 (Ar*C*H), 99.8 (*C*$Me_2$), 66.2 (*C*$H_2$), 62.8 (*C*H(C$H_2$OH), 59.0 (*C*$H_2$OH), 34.3 (*p*-*i*Pr*C*$(CH_3)$), 29.3 (*o*-*i*Pr*C*$(CH_3)_2$), 28.8 (*p*-*i*PrC(*C*$H_3)_2$), 25.0 (C*Me*), 24.8 (C*Me*), 23.6 (*o*-*i*PrC(*C*$H_3$)), 23.6 (*o*-*i*PrC(*C*$H_3$)); *m/z* ($EI^+$) 398 ($[M+H]^+$, 100%); HRMS ($EI^+$) $C_{21}H_{36}O_4NS^+$ ($[M+H]^+$) found 398.2363 requires 398.2360 (+ 0.3 ppm).

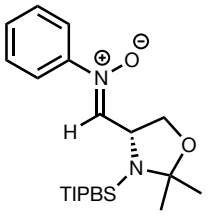
***(S)*-2,2-Dimethyl-3-((2,4,6-triisopropylphenyl)sulfonyl)oxazolidine-4-carbaldehyde 112**



A solution of DMSO (1.43 mL, 4.0 eq, 20.1 mmol) in $CH_2Cl_2$ (25 mL) was added dropwise to a stirred solution of oxalyl chloride (0.88 mL, 2.0 eq, 10.1 mmol) in $CH_2Cl_2$ (15 mL) cooled to -78 °C and stirred for 15 min. A solution of **111** (2.00 g, 1.0 eq, 5.03 mmol) in $CH_2Cl_2$ (30 mL) was then added slowly and the reaction stirred for 35 min. At -78 °C was added DIPEA (5.22 mL, 6.0 eq, 30.2 mmol) and the reaction mixture stirred, allowing to warm to rt before being quenched with sat. aq. $NH_4Cl$ (25 mL). The organic phase was then separated and washed with sat. aq. $NaHCO_3$ (30 mL), then brine (2 × 30 mL) before being dried over $Na_2SO_4$, filtered and concentrated *in vacuo* to yield **112** (2.03 g, quant.) as a viscous yellow oil which was used without further purification; $[\alpha]_D^{20}$ -23.5° (*c* = 1.22, $CHCl_3$); $\nu_{max}$ $cm^{-1}$ (thin-film) 2363 (C-H), 1701 (C=O); $^1$H NMR (300 MHz, $CDCl_3$) $\delta$ 9.00 (1H, d, *J* = 2.7, C*H*O), 7.16 (2H, s, Ar*H*), 4.33-4.09 (5H, m, *o*-*i*Pr*H* & C$H_2$ & C*H*NR), 2.93-2.84 (1H, dt, *J* = 13.8, 7.1, *p*-*i*Pr*H*), 1.81 (6H, d, *J* = 3.7, C$Me_2$), 1.25 (18H, t, *J* = 7.1); $^{13}$C NMR (75 MHz, $CDCl_3$) $\delta$ 199.3 (*C*=O), 154.6 ($4^{ry}$Ar*C*(*p*-*i*Pr)), 151.4 ($4^{ry}$Ar*C*(*o*-*i*Pr)), 131.6 ($4^{ry}$Ar*C*$SO_2$), 124.4 (Ar*C*H), 100.7 (*C*$Me_2$), 65.8 (*C*H(CHO)), 64.6 (*C*H2), 34.2 (*p*-*i*Pr*C*($CH_3$)), 29.3 (*o*-*i*Pr*C*($CH_3$)), 27.9 (*p*-*i*PrC(*C*$H_3$)$_2$), 24.7 (C$Me_2$, d, *J* = 26.8), 23.5 (*p*-*i*PrC(*C*$H_3$)$_2$); *m/z* ($CI^+$) 396 ($[M+H]^+$, 100%); HRMS ($CI^+$) $C_{21}H_{33}NO_4S^+$ ($[M+H]^+$) found 396.2209 requires 396.2209 (+ 0.1 ppm).

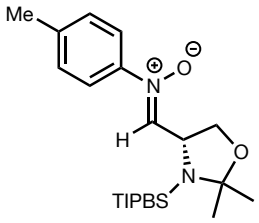
**6. *N*-TIPBS Nitrones**

**(*R*,*Z*)-*N*-((2,2-Dimethyl-3-((2,4,6-triisopropylphenyl)sulfonyl)oxazolidin-4-yl)methylene)aniline oxide 20**



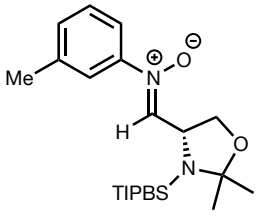
Nitrone **20** was prepared according to general procedure **D** from **112** (1.00 g, 2.52 mmol), $MgSO_4$ (0.334 g, 1.1 eq, 2.77 mmol) and phenylhydroxylamine **66** (0.330 g, 1.2 eq, 3.02 mmol) in $CH_2Cl_2$ (20 mL). The reaction mixture was then filtered and concentrated *in vacuo* to yield a crude brown semi-solid which was triturated from $Et_2O$ to yield **20** (0.558 g, 45%) as an off-white solid; mp 112-113 °C (decomp.); $[\alpha]_D^{20}$ -12.5° (*c* = 0.97, $CHCl_3$); $\nu_{max}$ $cm^{-1}$ (KBr) 3274 (N-O), 2958 (C-H), 2959 (C-H), 1733 (C=O); $^1$H NMR (300 MHz, $CDCl_3$) $\delta$ 7.41-7.31 (3H, m, Ph*H*), 7.21 (2H, s, Ar*H*(TIPBS)), 7.06-7.03 (2H, m, Ph*H*), 6.75 (1H, d, *J* = 5.3, *H*C=$N^+$), 5.11 (1H, ddd, *J* = 7.2, 5.3, 1.9, C*H*NR), 4.51-4.23 (4H, m, $CH_2$ & *o*-*i*PrH), 2.89 (1H, dt, *J* = 13.8, 6.9, *p*-*i*PrH), 1.84 (6H, d, *J* = 3.2, di*Me*), 1.29-1.20 (18H, m, *i*PrC$H_3$); $^{13}$C NMR (75 MHz, $CDCl_3$) $\delta$ 154.2 ($4^{ry}$Ar*C*), 151.8 (Ar*C*), 146.3 ($4^{ry}$Ar*C*), 139.1 (Ar*C*), 132.4 (H*C*=$N^+$), 130.4 (Ar*C*), 129.0 (Ar*C*), 124.4 (Ar*C*), 121.0 (Ar*C*), 100.2 (*C*$Me_2$), 68.0 (*C*$H_2$), 56.1 (*C*HNR), 34.2 (*p*-*i*Pr*C*), 29.2 (*p*-*i*Pr*C*$H_3$), 28.0 (*o*-*i*Pr*C*), 25.1 (C$Me_2$), 24.8 (C$Me_2$), 24.6 (*o*-*i*Pr*C*), 23.6 (*o*-*i*Pr*C*$H_3$); *m/z* ($EI^+$) 487 ($[M+H]^+$, 100%); HRMS ($EI^+$) $C_{27}H_{39}O_4N_2S^+$ ($[M+H]^+$) found 487.2633 requires 487.2625 (+ 0.8 ppm).

**(*R*,*Z*)-*N*-((2,2-Dimethyl-3-((2,4,6-triisopropylphenyl)sulfonyl)oxazolidin-4-yl)methylene)-4-methylaniline oxide 39**




The nitrone was obtained from hydroxylamine **69** (0.051 g, 1.1 eq, 4.12 mmol), $MgSO_4$ (0.050 g, 1.1 eq, 4.12 mmol) and aldehyde **112** (0.150 g, 3.79 mmol) in $CH_2Cl_2$ (20 mL) according to general procedure **D** to yield a crude a yellow semi-solid which was purified by column chromatography to give **39** (0.082 g, 43%) as an off-white solid; $[\alpha]_D^{20}$ -101.4° (*c* = 0.96, $CHCl_3$); mp 44-45 °C; $\nu_{max}$ $cm^{-1}$ (ATR) 2957, 2932, 1601; $^1H$ NMR (300 MHz, $CDCl_3$) $\delta$ 7.19 (2H, s, Ar*H*(TIPBS)), 7.06 (2H, dd, *J* = 8.6, 0.6, Ar*H*(2,6)), 6.91 (2H, d, *J* = 8.6, Ar*H*(3,5)), 6.71 (1H, d, *J* = 5.3, $^+$N=C*H*), 5.10-5.05 (1H, m, C*H*$CH_2$), 4.46 (1H, dd, *J* = 9.5, 7.2, CHC*H*$_2$), 4.35 (2H, app. quint., *J* = 6.8, $^i$Pr*H*), 4.24 (1H, dd, *J* = 9.5, 2.0, CHC*H*$_2$), 2.88 (1H, dt, *J* = 13.8, 6.9, $^i$Pr*H*), 2.33 (3H, s, ArC*H*$_3$), 1.83 (6H, d, *J* = 3.9, di*Me*), 1.27-1.18 (18H, m, $^i$PrC*H*$_3$); $^{13}C$ NMR (75 MHz, $CDCl_3$) $\delta$ 154.5 (Ar$C_{ipso}$-$N^+$), 152.1 (Ar*C*), 144.5 ($4^{ry}$ Ar*C*), 141.1 ($4^{ry}$ Ar*C*), 138.9 ($4^{ry}$ Ar*C*), 132.8 (H*C*=$N^+$), 129.9 (Ar*C*), 124.7 (Ar*C*), 121.2 (Ar*C*), 100.5 (*C*$Me_2$), 68.5 (*C*$H_2$), 56.4 (*C*HNR), 34.6 (*p*-*i*Pr*C*), 29.5 (*p*-*i*Pr*C*$H_3$), 28.4 (*o*-*i*Pr*C*), 25.4 (*o*-*i*Pr*C*$H_3$), 25.2 (*o*-*i*Pr*C*$H_3$), 25.0 (*o*-*i*Pr*C*), 24.0 (C*Me*$_2$), 24.0 (C*Me*$_2$), 21.5 (Ar*C*$H_3$); *m/z* (ESI$^+$) 501 ([M+H]$^+$, 95%), 443 (100%); HRMS (EI$^+$) $C_{28}H_{41}O_4N_2S^+$ ([M+H]$^+$) found 501.2784 requires 501.2782 (+ 0.5 ppm).

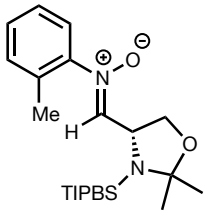
**(*R*,*Z*)-*N*-((2,2-Dimethyl-3-((2,4,6-triisopropylphenyl)sulfonyl)oxazolidin-4-yl)methylene)-3-methylaniline oxide 47**




The nitrone was obtained from hydroxylamine **68** (0.051 g, 1.1 eq, 4.12 mmol), $MgSO_4$ (0.050 g, 1.1 eq, 4.12 mmol) and aldehyde **112** (0.150 g, 3.79 mmol) in $CH_2Cl_2$ (20 mL) according to general procedure **D** to yield a crude a yellow semi-solid which was purified by column chromatography to give **47** (0.124 g, 65%) as a yellow solid; $[\alpha]_D^{20}$ -87.9° (*c* = 0.96, $CHCl_3$); mp 40-42 °C; $\nu_{max}$ $cm^{-1}$ (ATR) 2959, 2866; $^1H$ NMR (300 MHz, $CDCl_3$) $\delta$ 7.19 (2H, s, Ar*H*(TIPBS)), 7.16-7.08 (3H, m, Ar*H*), 6.76 (1H, d, *J* = 5.3, $^+$N=C*H*), 6.62-6.60 (1H, m, Ar*H*(2)), 5.07 (1H, ddd, *J* = 7.1, 5.3, 1.8, C*H*$CH_2$), 4.45 (1H, dd, *J* = 9.5, 7.1, CHC*H*$_2$), 4.35 (2H, dt, *J* = 13.5, 6.8, $^i$Pr*H*), 4.23 (1H, dd, *J* = 9.5, 1.8, CHC*H*$_2$), 2.87 (1H, dt, *J* = 13.8, 6.9, $^i$Pr*H*), 2.31 (3H, s, ArC*H*$_3$), 1.83 (6H, d, *J* = 2.7, di*Me*), 1.26 (12H, dd, *J* = 6.7, 5.1, $^i$PrC*H*$_3$), 1.19 (6H, dd, *J* = 6.9, 4.7, $^i$PrC*H*$_3$)**;** $^{13}C$ NMR (75 MHz, $CDCl_3$) $\delta$ 154.5 (Ar$C_{ipso}$-$N^+$), 152.1 (Ar*C*), 146.7 ($4^{ry}$ Ar*C*), 139.9 ($4^{ry}$ Ar*C*), 139.4 ($4^{ry}$ Ar*C*), 132.8 (H*C*=$N^+$), 131.5 ($4^{ry}$ Ar*C*), 129.0 (Ar*C*), 124.7 (Ar*C*), 122.3 (Ar*C*), 118.1 (Ar*C*), 100.5 (*C*$Me_2$), 68.5 (*C*$H_2$), 56.4 (*C*HNR), 34.6 (*p*-$^i$Pr*C*), 29.6 (*p*-$^i$Pr*C*$H_3$), 28.5 (*o*-$^i$Pr*C*), 25.4 (C*Me*$_2$), 25.2 (C*Me*$_2$), 25.0 (*o*-$^i$Pr*C*), 24.0 (*o*-$^i$Pr*C*$H_3$),

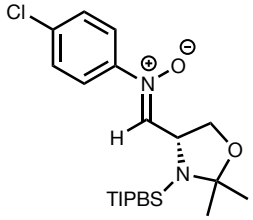
23.8 (*o*-$^{i}$Pr*C*H$_3$), 21.7 (Ar*C*H$_3$); *m/z* (ESI$^+$) 501 ([M+H]$^+$, 80%), 443 (100%); HRMS (EI$^+$) $C_{28}H_{41}O_4N_2S^+$ ([M+H]$^+$) found 501.2783 requires 501.2782 (+ 0.3 ppm).

**(*R*,*Z*)-*N*-((2,2-Dimethyl-3-((2,4,6-triisopropylphenyl)sulfonyl)oxazolidin-4-yl)methylene)-2-methylaniline oxide 43**




The nitrone was prepared according to general procedure **D** from **112** (0.150 g, 3.79 mmol), $MgSO_4$ (0.050 g, 1.1 eq, 4.12 mmol) and hydroxylamine **67** (0.051 g, 1.1 eq, 4.12 mmol) in $CH_2Cl_2$ (10 mL). The reaction mixture was filtered and concentrated *in vacuo* to yield a brown foam which was purified *via* column chromatography over silica (10-30% EtOAc in petroleum ether) to yield **43** (0.100 g, 52 %) as an off-white solid; mp 51-53 °C; $[\alpha]_D^{20}$ +37.1° (*c* = 0.99, $CH_2Cl_2$); $\nu_{max}$ cm$^{-1}$ (ATR) 2957, 2928, 1599, 1568, 1460; $^1$H NMR (500 MHz, $CD_2Cl_2$) $\delta$ 7.24 (2H, s, Ar*H*(TIPBS)), 7.23 (1H, d, *J* = 8.2, Ar*H*(6)), 7.15 (1H, t, *J* = 7.6, Ar*H*(4)), 7.02 (1H, t, *J* = 7.6, Ar*H*(5)), 6.48 (1H, d, *J* = 5.5, $^+$N=C*H*), 6.23 (1H, d, *J* = 7.7, Ar*H*(3)), 5.08 (1H, t, *J* = 5.5, C*H*CH$_2$), 4.45 (1H, dd, *J* = 9.4, 6.9, CHC*H*$_2$), 4.32 (2H, sept., *J* = 6.8, $^{i}$Pr*H*), 4.20 (1H, dd, *J* = 9.4, 1.3, $^{i}$Pr*H*), 2.94 (1H, sept., *J* = 6.9, $^{i}$Pr*H*), 2.09 (3H, s, ArC*H*$_3$), 1.80 (3H, s, C*Me*), 1.76 (3H, s, C*Me*), 1.28-1.26 (12H, m, $^{i}$PrC*H*$_3$), 1.20 (6H, d, *J* = 6.7, $^{i}$PrC*H*$_3$); $^{13}$C NMR (125 MHz, $CD_2Cl_2$) $\delta$ 154.3 (Ar*C*$_{ipso}$-N$^+$), 151.7 (Ar*C*), 146.2 (4$^{ry}$ Ar*C*), 142.1 (4$^{ry}$ Ar*C*), 132.3 (H*C*=N$^+$), 131.9 (Ar*C*Me), 131.4 (Ar*C*), 129.5 (Ar*C*), 126.2 (Ar*C*), 124.5 (Ar*C*(TIPBS)), 122.7 (Ar*C*), 100.1 (*C*Me$_2$), 68.6 (*C*H$_2$), 55.5 (*C*HNR), 34.3 (*p*-$^{i}$Pr*C*), 29.1 (*p*-$^{i}$Pr*C*H$_3$), 28.1 (*o*-$^{i}$Pr*C*), 24.7 (C*Me*$_2$), 24.5 (C*Me*$_2$), 24.4 (*o*-$^{i}$Pr*C*), 23.4 (*o*-$^{i}$Pr*C*H$_3$), 23.3 (*o*-$^{i}$Pr*C*H$_3$), 16.6 (Ar*C*H$_3$); *m/z* (ESI$^+$) 501 ([M+H]$^+$, 85%), 443 (100%); HRMS (EI$^+$) $C_{28}H_{41}O_4N_2S^+$ ([M+H]$^+$) found 501.2785 requires 501.2782 (+ 0.7 ppm).

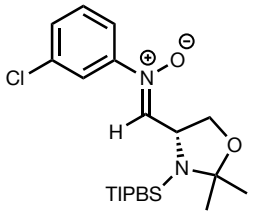
**(*Z*)-4-Chloro-*N*-((2,2-dimethyl-3-((2,4,6-triisopropylphenyl)sulfonyl)oxazolidin-4-yl)methylene)aniline oxide 40**




The nitrone was prepared according to general procedure **D** from **112** (0.100 g, 2.53 mmol), $MgSO_4$ (0.033 g, 1.1 eq, 2.78 mmol) and hydroxylamine **72** (0.040 g, 1.1 eq, 2.78 mmol) in $CH_2Cl_2$ (10 mL). The reaction mixture was then filtered and concentrated *in vacuo* to yield a pale yellow foam which was purified *via* frit column chromatography over silica (10-30% EtOAc in petroleum ether) to yield **40** (0.100 g, 76%) as a pale yellow solid; mp 95-96 °C; $[\alpha]_D^{20}$ -19.6° (*c* = 1.0, $CHCl_3$); $\nu_{max}$ cm$^{-1}$ (ATR) 2957, 1599, 1483; $^1$H NMR (500 MHz, $CDCl_3$) $\delta$ 7.29 (2H, d, *J* = 8.5, Ar*H*(2,6)), 7.22 (2H, s, Ar*H*(TIPBS)), 7.03 (2H, d, *J* = 8.5, Ar*H*(3,5)), 6.76 (1H, d, *J* = 5.4, $^+$N=C*H*), 5.11-5.09 (1H, br t, *J* = 5.4, C*H*CH$_2$), 4.51-4.48 (1H, dd, *J* = 9.4, 7.5, C*H*$_a$H$_b$), 4.38 (2H, dt, *J* = 13.5, 6.7, *o*-$^{i}$PrC*H*), 4.26-4.24 (1H, dd, *J* = 9.4, 1.5, CH$_a$*H*$_b$), 2.91 (1H, dt, *J* = 13.8, 6.9, *p*-$^{i}$PrC*H*), 1.86 (6H, d, *J* = 8.9, C*Me*$_2$), 1.30-1.23

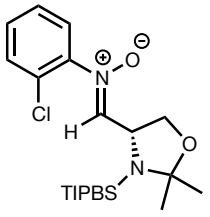
(18H, m, $^{i}$-PrC$H_3$); $^{13}$C NMR (125 MHz, $CDCl_3$) $\delta$ 154.2 (Ar$C_{ipso}$-$N^+$), 151.8 (Ar*C*), 144.7 ($4^{ry}$ Ar*C*), 139.3 ($4^{ry}$ Ar*C*), 136.4 (Ar*C*Cl), 132.4 (H*C*=$N^+$), 129.2 (Ar*C*), 124.3 (Ar*C*), 122.3 (Ar*C*), 100.3 (*C*$Me_2$), 68.0 ($CH_2$), 56.0 (*C*HNR), 34.2 (*p*-$^{i}$Pr*C*), 29.2 (*p*-$^{i}$Pr*C*$H_3$), 28.0 (*o*-$^{i}$Pr*C*), 25.1 (C$Me_2$), 24.8 (C$Me_2$), 24.5 (*o*-$^{i}$Pr*C*), 23.6 (2 x *o*-$^{i}$Pr*C*$H_3$ – observed as a single peak); *m/z* ($EI^+$) 521 ([M($^{35}$Cl)+H]$^+$, 100%); HRMS ($ESI^+$) $C_{27}H_{38}O_4N_2S^{35}Cl^+$ ([M+H]$^+$) found 521.2223 requires 521.2235 (-2.4 ppm).

**(*Z*)-3-Chloro-*N*-((2,2-dimethyl-3-((2,4,6-triisopropylphenyl)sulfonyl)oxazolidin-4-yl)methylene)aniline oxide 48**




The nitrone was prepared according to general procedure **D** from **112** (1.00 g, 2.53 mmol), $MgSO_4$ (0.334 g, 1.1 eq, 2.78 mmol) and hydroxylamine **71** (0.545g, 1.5 eq, 3.80 mmol) in $CH_2Cl_2$ (15 mL). The reaction mixture was then filtered and concentrated *in vacuo* to yield a pale yellow foam which was purified *via* frit column chromatography over silica (10-30% EtOAc in petroleum ether) to yield **48** (0.923 g, 71%) as a pale yellow solid; mp 91-92 °C; $[\alpha]_D^{20}$ -23.8° (*c* = 0.95, $CHCl_3$); $\nu_{max}$ cm$^{-1}$ (ATR) 2959, 1597, 1462; $^1$H NMR (300 MHz, $CDCl_3$) $\delta$ 7.36 (1H, ddd, *J* = 8.1, 2.0, 1.0, Ar*H*(6)), 7.20 (2H, s, Ar*H*(TIPBS)), 7.18-7.16 (1H, m, Ar*H*(5)), 6.97-6.93 (1H, m, Ar*H*(2)) 6.89 (1H, ddd, *J* = 8.1, 2.1, 1.0, Ar*H*(4)), 6.76 (1H, d, *J* = 5.4, *H*C=$N^+$), 5.07 (1H, ddd, *J* = 7.2, 5.4, 1.8, C*H*$CH_2$), 4.45 (1H, dd, *J* = 9.6, 7.2, C$H_a$H$_b$), 4.35 (2H, app. quint., *J* = 6.8, *o*-$^{i}$PrC*H*), 4.20 (1H, dd, *J* = 9.6, 2.0, CH$_a$$H_b$), 2.90 (1H, dt, *J* = 13.8, 6.9, *p*-$^{i}$PrC*H*), 1.83 (6H, d, *J* = 3.7, C$Me_2$), 1.27 (12H, t, *J* = 6.8, *o*-$^{i}$PrC$H_3$), 1.19 (6H, dd, *J* = 6.9, 4.6, *p*-$^{i}$PrC$H_3$); $^{13}$C NMR (125 MHz, $CDCl_3$) $\delta$ 154.3 (Ar$C_{ipso}$-$N^+$), 151.7 (Ar*C*), 147.0 ($4^{ry}$ Ar*C*), 139.7 ($4^{ry}$ Ar*C*), 135.0 (H*C*=$N^+$), 130.7 ($4^{ry}$ Ar*C*), 130.0 ($4^{ry}$ Ar*C*), 124.4 (Ar*C*H(TIPBS)), 121.7 (Ar*C*), 119.0 (Ar*C*), 100.2 (*C*$Me_2$), 67.9 (*C*$H_2$), 56.0 (*C*HNR), 34.1 (*p*-*i*Pr*C*), 29.2 (*p*-*i*Pr*C*$H_3$), 28.1 (*o*-*i*Pr*C*), 25.1 (C$Me_2$), 24.8 (C$Me_2$), 24.6 (*o*-*i*Pr*C*), 23.7 (*o*-*i*Pr*C*$H_3$), 23.3 (*o*-*i*Pr*C*$H_3$); *m/z* ($EI^+$) 521 ([M($^{35}$Cl)+H]$^+$, 100%); HRMS ($ESI^+$) $C_{27}H_{38}O_4N_2S^{35}Cl^+$ ([M+H]$^+$) found 521.2222 requires 521.2235 (-2.6 ppm).

**(*Z*)-2-Chloro-*N*-((2,2-dimethyl-3-((2,4,6-triisopropylphenyl)sulfonyl)oxazolidin-4-yl)methylene)aniline oxide 44**

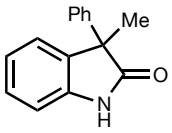



The nitrone was prepared according to general procedure **D** from **112** (0.136 g, 0.343 mmol), $MgSO_4$ (0.046 g, 1.1 eq, 0.377 mmol) and hydroxylamine **70** (0.054 g, 1.1 eq, 0.377 mmol) in $CH_2Cl_2$ (10 mL). The reaction mixture was then filtered and concentrated *in vacuo* to yield a pale yellow foam which was purified *via* frit column chromatography over silica (10-30% EtOAc in petroleum ether) to yield **44** (0.037 g, 19%) as a white foam in greater than 80% purity (contamination with residual aldehyde); mp 53-54 °C; $[\alpha]_D^{20}$ -8.9° (*c* = 1.13, $CHCl_3$); $\nu_{max}$ cm$^{-1}$ (ATR) 2959, 1599, 1460; $^1$H NMR (500

MHz, $CDCl_3$) $\delta$ 7.36 (1H, dd, $J$ = 8.1, 2.6), 7.30 (1H, td, $J$ = 7.7, 1.5), 7.21 (2H, s, Ar*H*(TIPBS)), 7.18 (1H, td, $J$ = 7.7, 1.2), 6.69 (1H, dd, $J$ = 7.9, 1.4), 6.50 (1H, d, $J$ = 5.6), 5.11-5.08 (1H, m), 4.44 (1H, dd, $J$ = 9.4, 6.9), 4.32 (2H, sept., $J$ = 6.8), 4.25 (1H, dd, $J$ = 9.4, 6.9), 2.91 (1H, sept., $J$ = 6.9), 1.78 (6H, d, $J$ = 19.5), 1.28 (6H, d, $J$ = 6.8), 1.24 (6H, dd, $J$ = 6.9, 4.2), 1.21 (6H, d, $J$ = 6.8); $^{13}$C NMR (125 MHz, $CDCl_3$) $\delta$ 154.2 (Ar$C_{ipso}$-$N^+$), 151.7 (Ar*C*), 144.4 ($4^{ry}$ Ar*C*), 143.6 ($4^{ry}$ Ar*C*), 132.2 (H*C*=$N^+$), 130.8 ($4^{ry}$ Ar*C*), 130.6 (Ar*C*), 127.6 (Ar*C*), 126.9 (Ar*C*), 125.0 (Ar*C*), 124.4 (Ar*C*(TIPBS)), 100.2 (*C*$Me_2$), 68.2 (*C*$H_2$), 55.6 (*C*HNR), 34.2 (*p*-$^i$Pr*C*), 29.1 (*p*-$^i$Pr*C*$H_3$), 28.0 (*o*-$^i$Pr*C*), 24.7 (*C*$Me_2$), 24.5 (*C*$Me_2$), 24.4 (*o*-$^i$Pr*C*), 23.4 (*o*-$^i$Pr*C*$H_3$), 23.3 (*o*-$^i$Pr*C*$H_3$); *m/z* ($EI^+$) 521 ([M($^{35}$Cl)+H]$^+$, 100%); HRMS ($ESI^+$) $C_{27}H_{38}O_4N_2S^{35}Cl^+$ ([M+H]$^+$) found 521.2224 requires 521.2235 (-2.2 ppm).

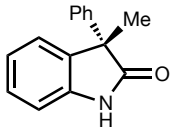
**7. 3,3-Disubstituted Oxindoles**

**(±)-3-Methyl-3-phenylindolin-2-one 21**

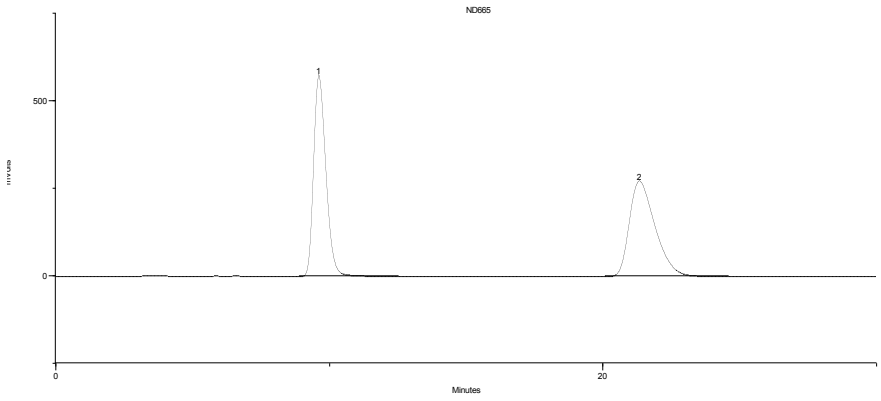



The oxindole was obtained from nitrone **79** (0.093 g, 0.400 mmol) and methylphenylketene (0.053 g, 1.0 eq, 0.400 mmol) following general procedure **E**, to yield (±)-**21** (0.076 g, 85%) as a white solid; mp 139-140 °C {lit.[13]150-152 °C}; $^1$H NMR (300 MHz, $CDCl_3$) $\delta$ 8.88 (1H, *br* s, N*H*), 7.35-7.25 (5H, m, Ar*H*), 7.24 (1H, dd, *J* = 7.6, 1.2, Ar*H*), 7.15 (1H, dd, *J* = 7.4, 0.6, Ar*H*), 7.07 (1H, td, *J* = 7.5, 0.9, Ar*H*), 6.99 (1H, d, *J* = 7.8, Ar*H*(7)), 1.84 (3H, s, *Me*); HPLC analysis: racemic (Daicel Chiralcel OD-H column, eluent: hexane/*i*-PrOH 90:10, flow 1.0 mL/min, wavelength: 254 nm, retention times: 9.6 min and 19.9 min).

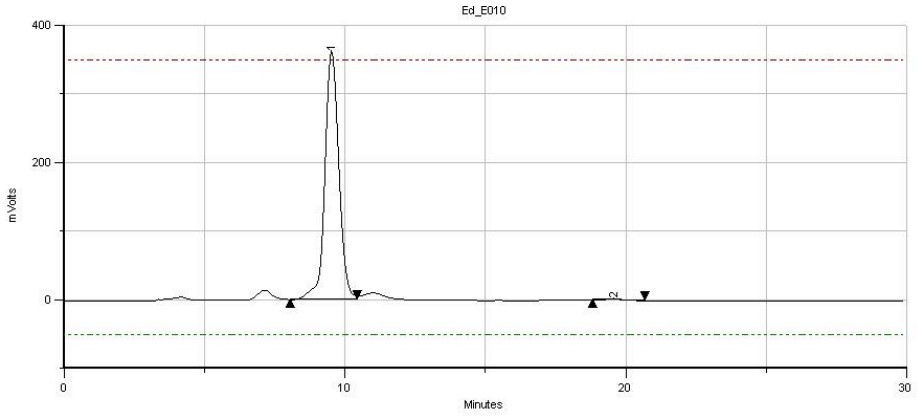
**(*S*)-3-Methyl-3-phenylindolin-2-one 21**




The oxindole was obtained from chiral nitrone **20** (0.070 g, 0.144 mmol) and methylphenylketene (0.038 g, 2.0 eq, 0.288 mmol) following general procedure **F**, to yield **21** (0.019 g, 60%) as an off-white solid; $[\alpha]_D^{20}$ -24.7° (*c* = 1.00, $CHCl_3$); HPLC analysis: 98% e.e. (Daicel Chiralcel OD-H column, eluent: hexane/*i*-PrOH 90:10, flow 1.0 mL/min, wavelength: 254 nm, retention times: 9.6 min (major) and 20.0 min (minor)).

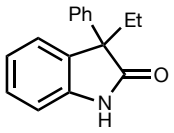



| Peak | $t_R$ (min) | Area (%) |
|---|---|---|
| 1 | 9.62 | 50.01 |
| 2 | 21.33 | 49.99 |



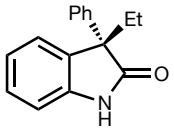

| Peak | $t_R$ (min) | Area (%) |
|---|---|---|
| 1 | 9.52 | 99.15 |
| 2 | 19.58 | 0.85 |

**(±)-3-Ethyl-3-phenylindolin-2-one 10**

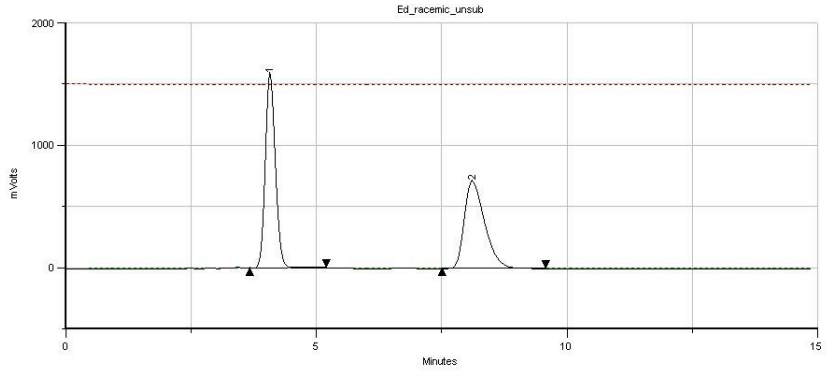



The oxindole was obtained from nitrone **79** (0.078 g, 0.400 mmol) and ethylphenylketene (0.059 g, 1.0 eq, 0.400 mmol) following general procedure **E**, to yield (±)-**10** (0.090 g, 95%) as a white solid; mp 151-152 °C {lit.[13] 149-150 °C}; $^1$H NMR (300 MHz, $CDCl_3$) $\delta$ 8.61 (1H, *br* s, N*H*), 7.42-7.36 (2H, m, Ar*H*), 7.35-7.23 (4H, m, Ar*H*), 7.19 (1H, dt, *J* = 7.5, 0.7, Ar*H*), 7.10 (1H, dt, *J* = 7.5, 1.1, Ar*H*), 6.97 (1H, ddd, *J* = 7.8, 0.9, 0.6, Ar*H*(7)), 2.47 (1H, dq, *J* = 14.7, 7.5, C$H_a$H$_b$), 2.26 (1H, dq, *J* = 14.7, 7.5, CH$_a$$H_b$), 0.77 (3H, t, *J* = 7.4, C$H_3$); HPLC analysis: racemic (Daicel Chiralcel OD-H column, eluent: hexane/*i*-PrOH 80:20, flow 1.5 mL/min, wavelength: 254 nm, retention times: 4.0 min and 8.5 min).

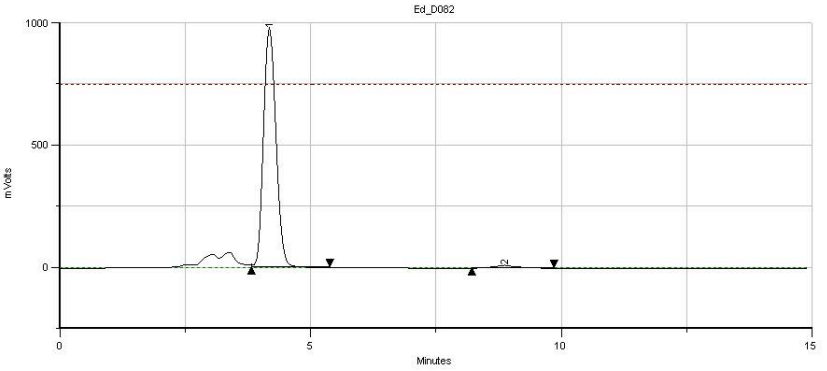
**(*S*)-3-Ethyl-3-phenylindolin-2-one 10**




The oxindole was obtained from chiral nitrone **20** (0.050 g, 0.103 mmol) and ethylphenylketene (0.030 g, 2.0 eq, 0.206 mmol) following general procedure **F**, to yield **10** (0.021 g, 86%) as an off-white solid; $[\alpha]_D^{20}$ -12.4° (*c* = 0.95, $CHCl_3$); HPLC analysis: 96% e.e. (Daicel Chiralcel OD-H column, eluent: hexane/*i*-PrOH 80:20, flow 1.5 mL/min, wavelength: 254 nm, retention times: 4.1 min (major) and 8.5 min (minor)).

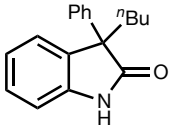



| Peak | $t_R$ (min) | Area (%) |
|---|---|---|
| 1 | 4.07 | 52.51 |
| 2 | 8.11 | 47.49 |



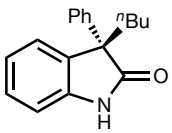

| Peak | $t_R$ (min) | Area (%) |
|---|---|---|
| 1 | 4.17 | 98.07 |
| 2 | 8.86 | 1.93 |

**(±)-3-Butyl-3-phenylindolin-2-one 22**



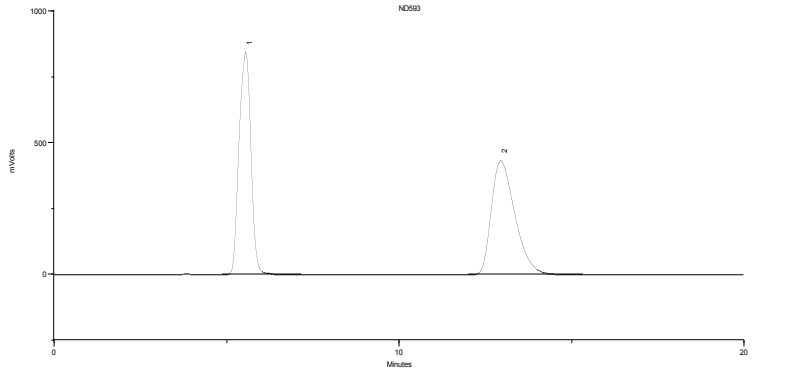

For determination of ee, the racemic sample of (±)-**22** prepared in our prior publication[13] used for HPLC analysis; $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 7.92 (1H, *br* s, N*H*), 7.37 (2H, dd, $J$ = 8.4, 1.2, Ar*H*), 7.22- 7.32 (4H, m, Ar*H*), 7.19 (1H, d, $J$ = 7.1, Ar*H*), 7.09 (1H, td, $J$ = 7.5, 0.9, Ar*H*), 6.94 (1H, d, $J$ = 7.7, Ar*H*), 2.39 (1H, td, $J$ = 12.7, 4.2, C$H_a$H$_b$), 2.19 (1H, td, $J$ = 12.6, 3.9, CH$_a$$H_b$), 1.15-1.35 (3H, m, C$H_2$), 0.88-0.97 (1H, m, C$H_2$), 0.81 (3H, t, $J$ = 7.2, C$H_3$); HPLC analysis: racemic (Daicel Chiralcel OD-H column, eluent: hexane/*i*-PrOH 90:10, flow 1.0 mL/min, wavelength: 254 nm, retention times: 5.4 min and 13.1 min).

**(*S*)-3-Butyl-3-phenylindolin-2-one 22**

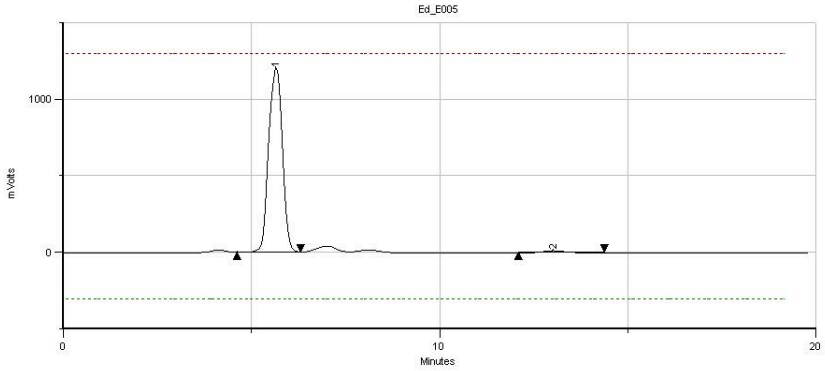



The oxindole was obtained from chiral nitrone **20** (0.070 g, 0.144 mmol) and *n*-butylphenylketene (0.076 g, 2.0 eq, 0.288 mmol) following general procedure **F**, to yield **22** (0.041 g,

94%) as a colourless oil; $[\alpha]_D^{20}$ -19.1° ($c$ = 0.95, $CHCl_3$); HPLC analysis: 96% e.e. (Daicel Chiralcel OD-H column, eluent: hexane/*i*-PrOH 90:10, flow 1.0 mL/min, wavelength: 254 nm, retention times: 5.6 min (major) and 13.0 min (minor)).

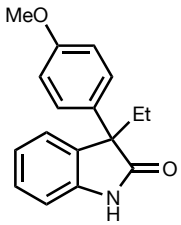



| Peak | $t_R$ (min) | Area (%) |
|---|---|---|
| 1 | 5.56 | 49.48 |
| 2 | 12.95 | 50.52 |




| Peak | $t_R$ (min) | Area (%) |
|---|---|---|
| 1 | 5.66 | 97.80 |
| 2 | 13.01 | 2.20 |

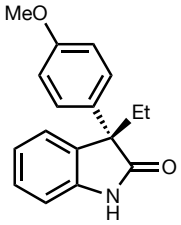
**(±)-3-Ethyl-3-(4-methoxyphenyl)indolin-2-one 23**



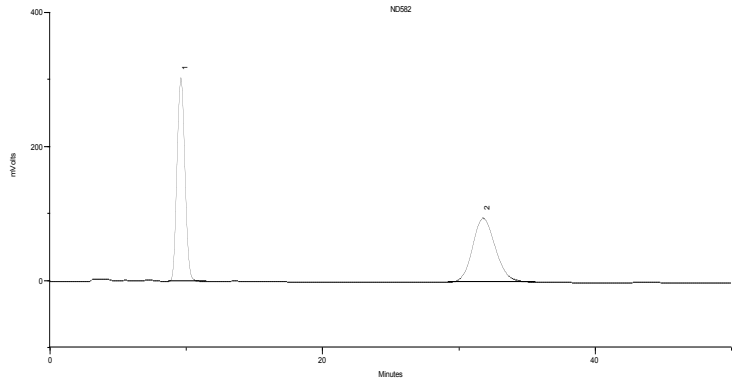

For determination of ee, the racemic sample of (±)-**23** prepared in our prior publication[13] used for HPLC analysis; $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 8.73 (1H, *br* s, N*H*), 7.27 (2H, d, $J$ = 8.9, Ar*H*), 7.23 (1H, td, $J$ = 7.6, 0.8, Ar*H*), 7.15 (1H, d, $J$ = 7.1, Ar*H*), 7.06 (1H, t, $J$ = 7.5, Ar*H*), 6.94 (1H, d, $J$ = 7.7, Ar*H*), 6.83 (2H, d, $J$ = 8.9, Ar*H*), 3.76 (3H, s, O*Me*), 2.41 (1H, dq, $J$ = 13.7, 7.0, C$H_a$H$_b$), 2.20 (1H, dq, $J$ = 13.8, 7.0, CH$_a$$H_b$), 0.74 (3H, t, $J$ = 7.3, C$H_3$); HPLC analysis: racemic (Daicel Chiralcel

OD-H column, eluent: hexane/*i*-PrOH 80:20, flow 1.0 mL/min, wavelength: 254 nm, retention times: 10.2 min and 30.4 min).

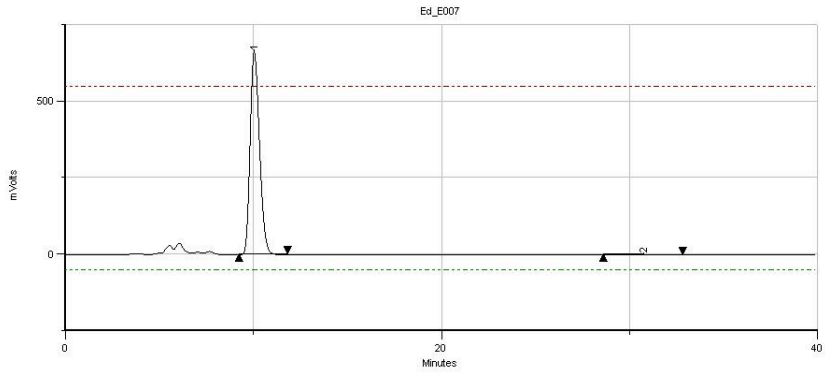
**(*S*)-3-Ethyl-3-(4-methoxyphenyl)indolin-2-one 23**




The oxindole was obtained from chiral nitrone **20** (0.070 g, 0.144 mmol) and ethyl(*p*-methoxyphenyl)ketene (0.043 g, 1.8 eq, 0.259 mmol) following general procedure **F**, to yield **23** (0.031 g, 81%) as an off-white solid; $[\alpha]_D^{20}$ -44.9° (*c* = 1.10, $CHCl_3$); HPLC analysis: 98% e.e. (Daicel Chiralcel OD-H column, eluent: hexane/*i*-PrOH 80:20, flow 1.0 mL/min, wavelength: 254 nm, retention times: 10.0 min (major) and 30.7 min (minor)).

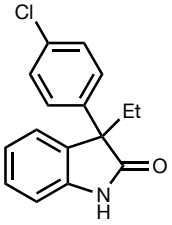



| Peak | $t_R$ (min) | Area (%) |
|---|---|---|
| 1 | 9.60 | 52.26 |
| 2 | 31.78 | 47.74 |



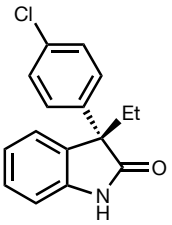

| Peak | $t_R$ (min) | Area (%) |
|---|---|---|
| 1 | 10.04 | 98.70 |
| 2 | 30.81 | 1.30 |

**(±)-3-(4-Chlorophenyl)-3-ethylindolin-2-one 28**

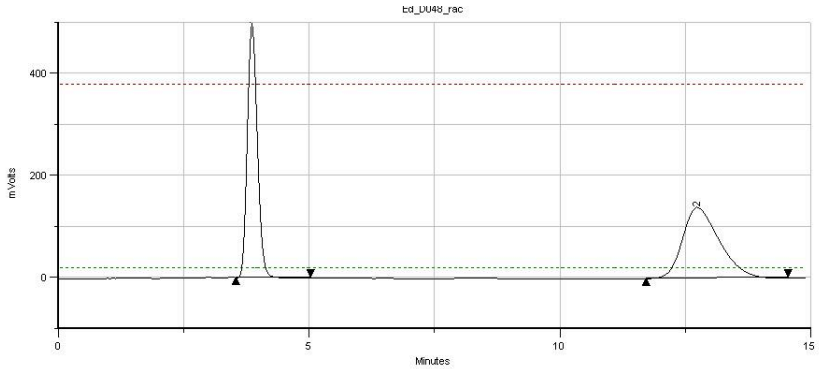



The oxindole was obtained from nitrone **79** (0.075 g, 0.380 mmol) and ethyl(*p*-chlorophenyl)ketene (0.069 g, 1.0 eq, 0.380 mmol) following general procedure **E**, to yield (±)-**28** (0.043 g, 42%) as a white solid; mp 147-148 °C; $\nu_{max}$ $cm^{-1}$ (KBr) 3186 (NH), 3084, 2968, 2929, 1705, 1613, 1492, 1470, 1398, 1320; $^1$H NMR (300 MHz, $CDCl_3$) $\delta$ 7.84 (1H, *br* s, N*H*), 7.28-7.21 (5H, m, Ar*H*), 7.13 (1H, d, *J* = 6.8, Ar*H*), 7.07 (1H, td, *J* = 7.5, 0.9, Ar*H*), 6.92 (1H, d, *J* = 7.8, Ar*H*(7)), 2.37 (1H, dq, *J* = 13.7, 7.2, C$H_a$H$_b$), 2.16 (1H, dq, *J* = 13.7, 7.2, CH$_a$$H_b$), 0.71 (3H, t, *J* = 7.2, C$H_3$); $^{13}$C NMR (75 MHz, $CDCl_3$) $\delta$ 180.1 (C=O), 141.0 (4$^{ry}$ Ar*C*), 138.6 (4$^{ry}$ Ar*C*), 133.3 (4$^{ry}$ Ar*C*), 132.1 (4$^{ry}$ Ar*C*), 128.7 (Ar'*C*), 128.5 (Ar'*C*), 128.4 (Ar*C*), 125.1 (Ar*C*), 122.8 (Ar*C*), 110.0 (Ar*C*(7)), 57.2 (*C*3), 30.8 (*C*H$_2$), 9.0 (*C*H$_3$); *m/z* (EI$^+$) 272 ([M+H]$^+$, 100%); HRMS (EI$^+$) $C_{16}H_{15}ClON$ ([M+H]$^+$) found 272.0840 requires 272.0837 (+ 0.3 ppm); HPLC analysis: racemic (Daicel Chiralcel OD-H column, eluent: hexane/*i*-PrOH 80:20, flow 1.5 mL/min, wavelength: 254 nm, retention times: 4.1 min and 12.7 min).

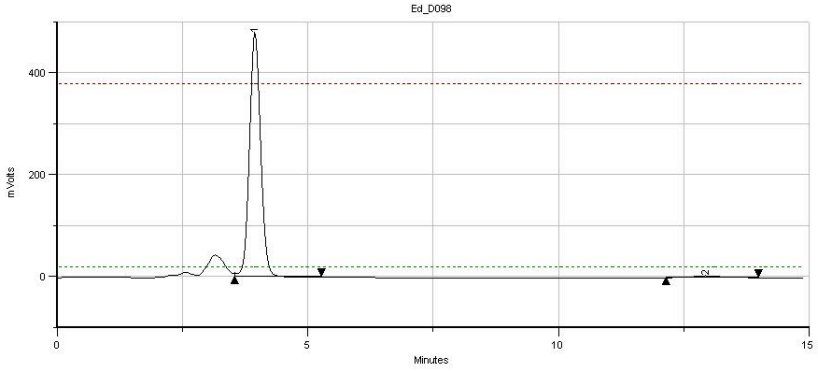
**(*S*)-3-(4-Chlorophenyl)-3-ethylindolin-2-one 28**




The oxindole was obtained from chiral nitrone **20** (0.050 g, 0.103 mmol) and ethyl(*p*-chlorophenyl)ketene (0.037 g, 2.0 eq, 0.206 mmol) following general procedure **F**, to yield **28** (0.025 g, 89%) as an off-white solid; $[\alpha]_D^{20}$ -38.5° (*c* = 1.10, $CHCl_3$); HPLC analysis: 96% e.e. (Daicel Chiralcel OD-H column, eluent: hexane/*i*-PrOH 80:20, flow 1.5 mL/min, wavelength: 254 nm, retention times: 3.9 min (major) and 12.8 min (minor)).

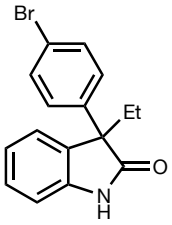



| Peak | $t_R$ (min) | Area (%) |
|---|---|---|
| 1 | 3.86 | 49.54 |
| 2 | 12.74 | 50.46 |



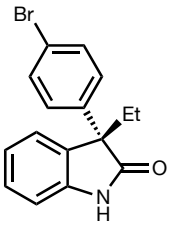

| Peak | $t_R$ (min) | Area (%) |
|---|---|---|
| 1 | 3.94 | 98.14 |
| 2 | 12.94 | 1.86 |

**(±)-3-(4-Bromophenyl)-3-ethylindolin-2-one 30**

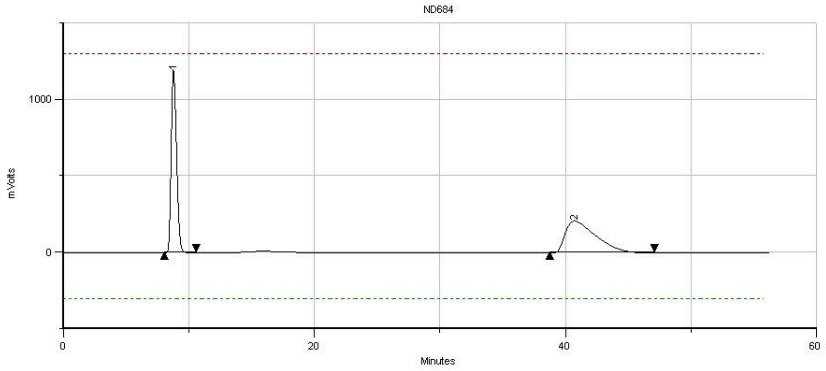



For determination of ee, the racemic sample of (±)-**30** prepared in our prior publication[13] used for HPLC analysis; $^1$H NMR (300 MHz, $CDCl_3$) $\delta$ 9.41 (1H, *br* s, N*H*), 7.45-7.42 (2H, m, Ar*H*), 7.34-7.22 (3H, m, Ar*H*), 7.16 (1H, d, $J$ = 6.1, Ar*H*), 7.11 (1H, td, $J$ = 7.3, 0.7, Ar*H*), 6.99 (1H, d, $J$ = 7.7, Ar*H*), 2.43 (1H, dq, $J$ = 13.7, 7.0, C$H_a$H$_b$), 2.23 (1H, dq, $J$ = 13.7, 7.0, CH$_a$$H_b$), 0.77 (3H, t, $J$ = 7.3, C$H_3$); HPLC analysis: racemic (Daicel Chiralcel OD-H column, eluent: hexane/*i*-PrOH 90:10, flow 1.0 mL/min, wavelength: 254 nm, retention times: 8.6 min and 41.1 min).

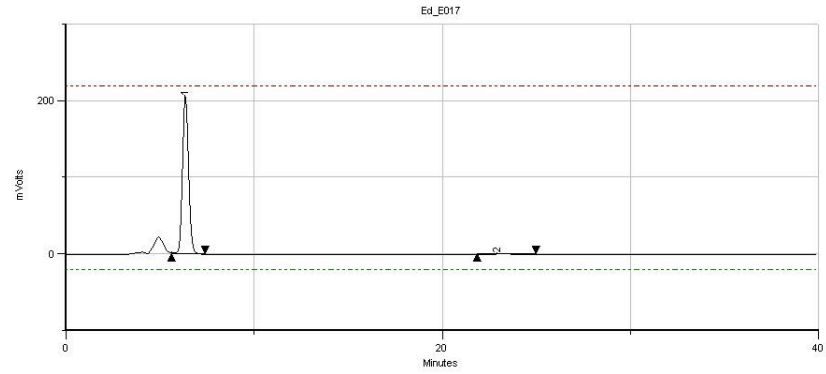
**(*S*)-3-(4-Bromophenyl)-3-ethylindolin-2-one 30**




The oxindole was obtained from chiral nitrone **20** (0.080 g, 0.164 mmol) and ethyl(*p*-bromophenyl)ketene (0.074 g, 2.0 eq, 0.328 mmol) following general procedure **F**, to yield **30** (0.021 g, 40%) as a white foam; $[\alpha]_D^{20}$ -35.2° ($c$ = 1.15, $CHCl_3$); HPLC analysis: 94% e.e. (Daicel Chiralcel OD-H column, eluent: hexane/*i*-PrOH 90:10, flow 1.0 mL/min, wavelength: 254 nm, retention times: 8.8 min (major) and 40.7 min (minor)).

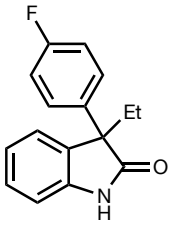



| Peak | $t_R$ (min) | Area (%) |
|---|---|---|
| 1 | 8.76 | 49.63 |
| 2 | 40.72 | 50.37 |



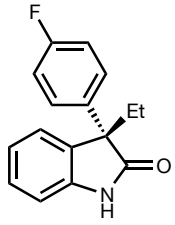

| Peak | $t_R$ (min) | Area (%) |
|---|---|---|
| 1 | 6.35 | 97.39 |
| 2 | 23.17 | 2.61 |

**(±)-3-Ethyl-3-(4-fluorophenyl)indolin-2-one 26**

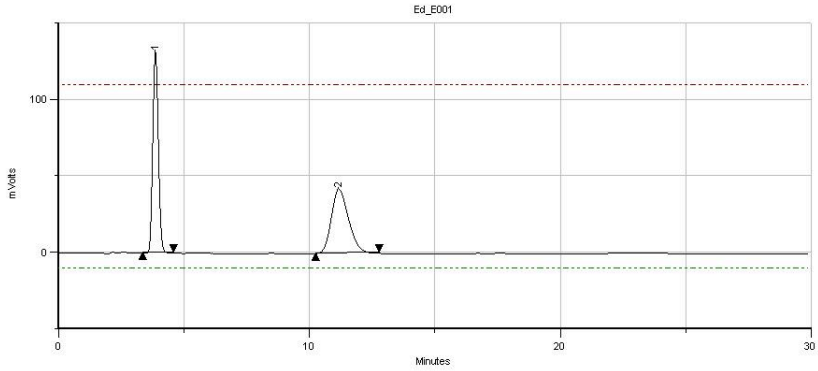



The oxindole was obtained from nitrone **79** (0.060g, 0.304 mmol) and ethyl(*p*-fluorophenyl)ketene (0.050 g, 1.0 eq, 0.304 mmol) following general procedure **E**, to yield (±)-**26** (0.052 g, 67%) as a white solid; mp 179-180 °C {lit.[13] 180 °C}; $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 8.12 (1H, br s, N*H*), 7.36-7.32 (2H, m, Ar*H*), 7.30-7.25 (1H, m, Ar*H*), 7.18-7.16 (1H, m, Ar*H*), 7.10 (1H, td, $J$ = 7.5, 0.9, Ar*H*), 7.00-6.95 (3H, m, Ar*H*), 2.41 (1H, dq, $J$ = 13.8, 7.1, C$H_a$H$_b$), 2.20 (1H, dq, $J$ = 13.8, 7.1, CH$_a$$H_b$), 0.75 (3H, t, $J$ = 7.1, C$H_3$); HPLC analysis: racemic (Daicel Chiralcel OD-H column, eluent: hexane/*i*-PrOH 80:20, flow 1.5 mL/min, wavelength: 254 nm, retention times: 4.0 min and 11.0 min).

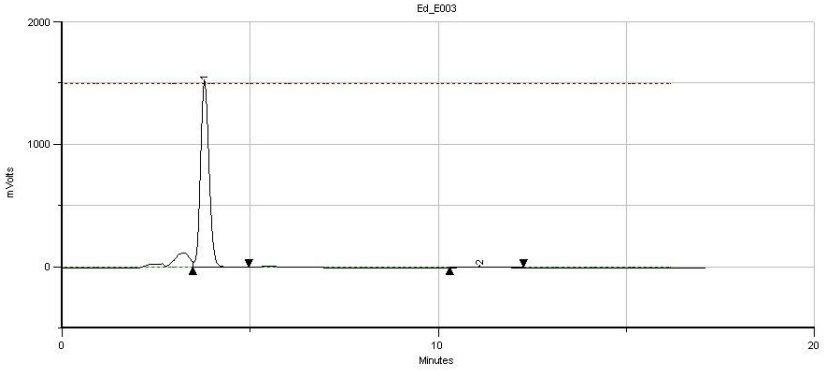
**(*S*)-3-Ethyl-3-(4-fluorophenyl)indolin-2-one 26**




The oxindole was obtained from chiral nitrone **20** (0.070 g, 0.144 mmol) and ethyl(*p*-fluorophenyl)ketene (0.047 g, 2.0 eq, 0.288 mmol) following general procedure **F**, to yield **26** (0.029 g, 79%) as an off-white solid; $[\alpha]_D^{20}$ -32.4° (*c* = 1.00, $CHCl_3$); HPLC analysis: 98% e.e. (Daicel Chiralcel OD-H column, eluent: hexane/*i*-PrOH 80:20, flow 1.5 mL/min, wavelength: 254 nm, retention times: 3.8 min (major) and 11.1 min (minor)).

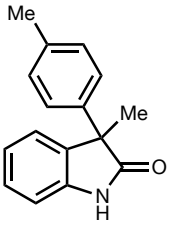



| Peak | $t_R$ (min) | Area (%) |
|---|---|---|
| 1 | 3.86 | 50.29 |
| 2 | 11.17 | 49.71 |



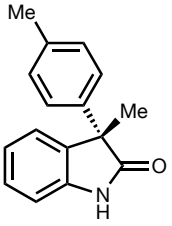

| Peak | $t_R$ (min) | Area (%) |
|---|---|---|
| 1 | 3.79 | 96.88 |
| 2 | 11.11 | 1.12 |

**(±)-3-Methyl-3-(*p*-tolyl)indolin-2-one 25**

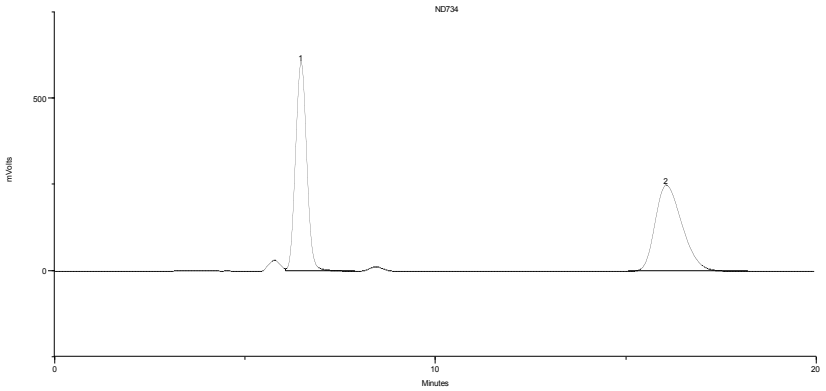



The oxindole was obtained from nitrone **79** (0.093 g, 0.400 mmol) and methyl(*p*-tolyl)ketene (0.059 g, 1.0 eq, 0.400 mmol) following general procedure **E**, to yield (±)-**25** (0.079 g, 83%) as a white solid; mp 118-119°C {lit.[13] 118-120°C}; $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 8.44 (1H, *br* s, N*H*), 7.26-7.20 (3H, m, Ar*H*), 7.14-7.10 (3H, m, Ar*H*), 7.07-7.03 (1H, m, Ar*H*), 6.96 (1H, d, $J$ = 7.7, Ar*H*(7)), 2.31 (3H, s, ArC$H_3$), 1.80 (3H, s, C$H_3$); HPLC analysis: racemic (Daicel Chiralcel OD-H column, eluent: hexane/*i*-PrOH 80:20, flow 1.0 mL/min, wavelength: 254 nm, retention times: 6.4 min and 15.6 min).

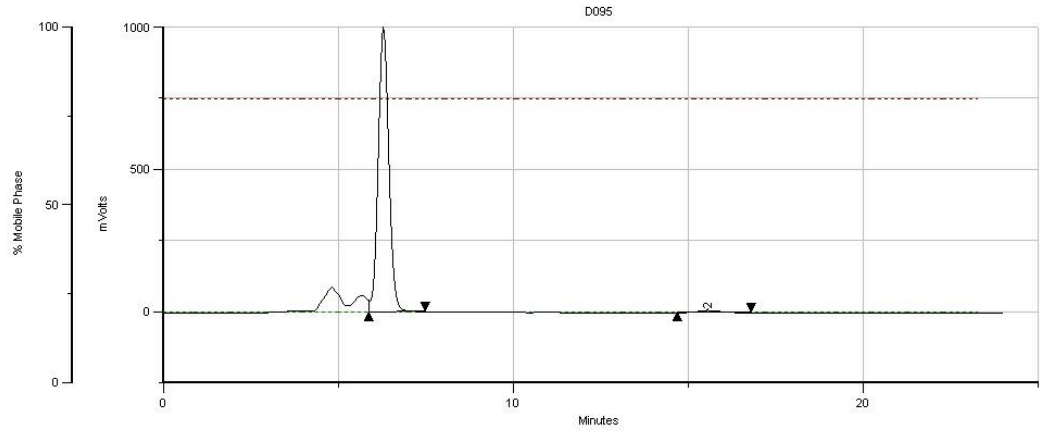
**(*S*)-3-Methyl-3-(*p*-tolyl)indolin-2-one 25**




The oxindole was obtained from chiral nitrone **20** (0.050 g, 0.103 mmol) and methyl(*p*-tolyl)ketene (0.030 g, 1.0 eq, 0.103 mmol) following general procedure **F**, to yield **25** (0.016 g, 66%) as an off-white solid; $[\alpha]_D^{20}$ -10.5° ($c$ = 0.80, $CHCl_3$); HPLC analysis: 96% e.e. (Daicel Chiralcel OD-H column, eluent: hexane/*i*-PrOH 80:20, flow 1.0 mL/min, wavelength: 254 nm, retention times: 6.3 min (major) and 15.6 min (minor)).

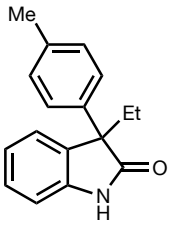



| Peak | $t_R$ (min) | Area (%) |
|---|---|---|
| 1 | 6.40 | 50.26 |
| 2 | 16.05 | 49.74 |



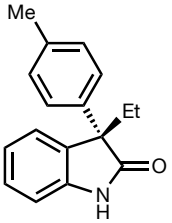

| Peak | $t_R$ (min) | Area (%) |
|---|---|---|
| 1 | 6.28 | 98.29 |
| 2 | 15.57 | 1.71 |

**(±)-3-Ethyl-3-(*p*-tolyl)indolin-2-one 24**

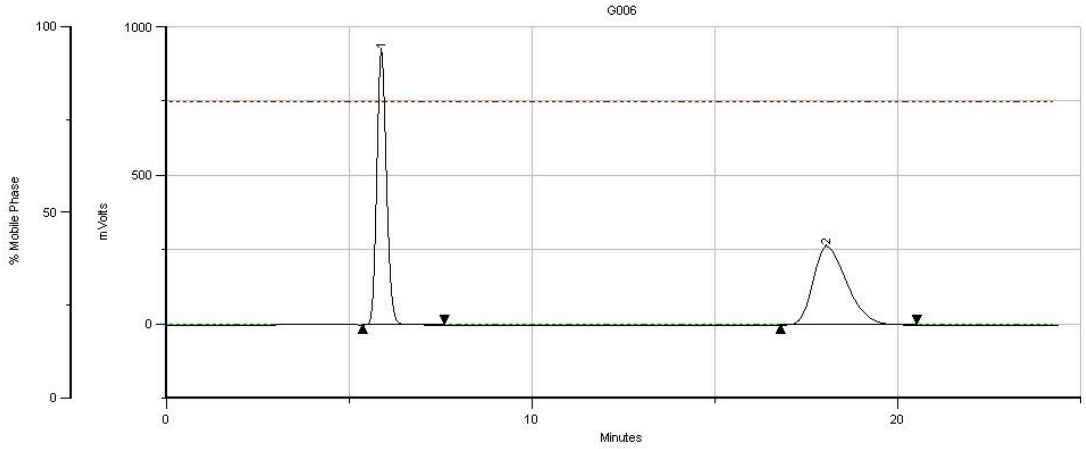



The oxindole was obtained from nitrone **79** (0.078 g, 0.396 mmol) and ethyl(*p*-tolyl)ketene (0.063 g, 1.0 eq, 0.396 mmol) following general procedure **E**, to yield (±)-**24** (0.085 g, 85%) as a white solid; mp 104-106 °C {lit.[13] 105-106 °C}; $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 7.32 (1H, *br* s, N*H*), 7.32-7.27 (3H, m, Ar*H*), 7.17 (1H, dt, *J* = 7.4, 0.2, Ar*H*), 7.17-7.06 (3H, m, Ar*H*), 6.93 (1H, d, *J* = 7.7, Ar*H*(7)), 2.44 (1H, dq, *J* = 13.7, 7.2, C$H_a$H$_b$), 2.29 (3H, s, ArC$H_3$), 2.24 (1H, dq, *J* = 13.7, 7.2, CH$_a$$H_b$), 0.75 (3H, t, *J* = 7.2, C$H_3$); HPLC analysis: racemic (Daicel Chiralcel OD-H column, eluent: hexane/*i*-PrOH 80:20, flow 1.0 mL/min, wavelength: 254 nm, retention times: 5.8 min and 17.7 min).

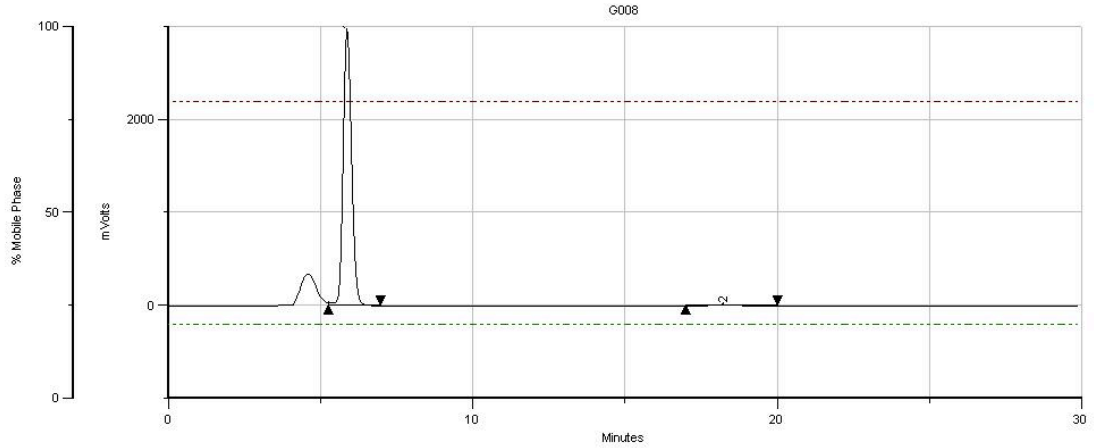
**(*S*)-3-Ethyl-3-(*p*-tolyl)indolin-2-one 24**




The oxindole was obtained from chiral nitrone **20** (0.070 g, 0.144 mmol) and ethyl(*p*-tolyl)ketene (0.035 g, 1.0 eq, 0.144 mmol) following general procedure **F**, to yield **24** (0.029 g, 85%) as an off-white solid; HPLC analysis: $[\alpha]_D^{20}$ -40.6° (*c* = 1.10, $CHCl_3$); 96% e.e. (Daicel Chiralcel OD-H column, eluent: hexane/*i*-PrOH 80:20, flow 1.0 mL/min, wavelength: 254 nm, retention times: 5.9 min (major) and 18.1 min (minor)).

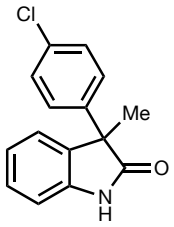



| Peak | $t_R$ (min) | Area (%) |
|---|---|---|
| 1 | 5.87 | 50.02 |
| 2 | 18.07 | 49.98 |




| Peak | $t_R$ (min) | Area (%) |
|---|---|---|
| 1 | 5.86 | 97.78 |
| 2 | 18.24 | 2.22 |

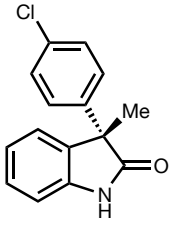
**(±)-3-(4-Chlorophenyl)-3-methylindolin-2-one 29**



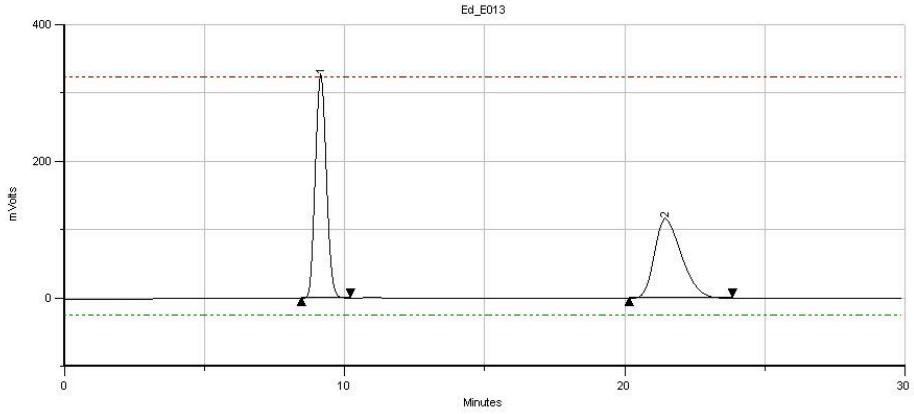

The oxindole was obtained from nitrone **79** (0.080 g, 0.406 mmol) and methyl(*p*-chlorophenyl)ketene (0.068 g, 1.0 eq, 0.406 mmol) following general procedure **E**, to yield (±)-**29** (0.102 g, 97%) as an off-white solid; mp 132-134 °C; $\nu_{max}$ $cm^{-1}$ (KBr) 3148 (NH), 3087, 2979, 1706 (C=O), 1619, 1474, 1457, 1398, 1373, 1324; $^1$H NMR (300 MHz, $CDCl_3$) $\delta$ 8.75 (1H, *br* s, N*H*), 7.27-7.23 (5H, m, Ar*H*), 7.11-7.07 (2H, m, Ar*H*), 6.98 (1H, d, *J* = 7.7, Ar*H*(7)), 1.80 (3H, s, *Me*); $^{13}$C NMR (75 MHz, $CDCl_3$) $\delta$ 182.1 (C=O), 140.7 ($4^{ry}$ Ar*C*), 139.4 ($4^{ry}$ Ar*C*), 135.4 ($4^{ry}$ Ar*C*), 133.8 ($4^{ry}$ Ar*C*), 129.2 (Ar'*C*),

128.8 (Ar'*C*), 128.6 (Ar*C*), 124.8 (Ar*C*), 123.4 (Ar*C*), 110.8 (Ar*C*(7)), 52.7 (*C*3), 24.0 (*C*$H_3$); *m/z* ($EI^+$) 258 ($[M+H]^+$, 100%); HRMS ($EI^+$) $C_{15}H_{13}ONCl$ ($[M+H]^+$) found 258.0682 requires 258.0680 (+ 0.2 ppm); HPLC analysis: racemic (Daicel Chiralcel OD-H column, eluent: hexane/*i*-PrOH 95:5, flow 1.0 mL/min, wavelength: 254 nm, retention times: 8.9 min and 21.1 min).

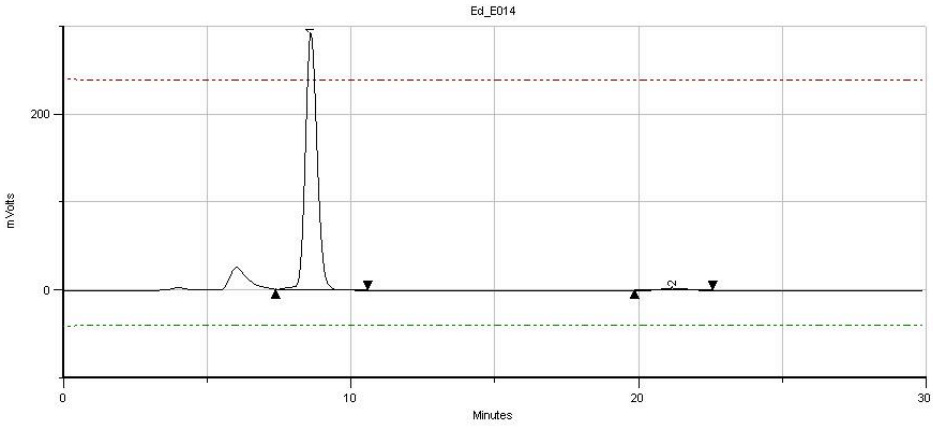
**(*S*)-3-(4-Chlorophenyl)-3-methylindolin-2-one 29**




The oxindole was obtained from chiral nitrone **20** (0.090 g, 0.185 mmol) and methyl(*p*-chlorophenyl)ketene (0.062 g, 2.0 eq, 0.370 mmol) following general procedure **F**, to yield **29** (0.021 g, 44%) as an off-white solid; $[\alpha]_D^{20}$ -28.5° (*c* = 0.90, $CHCl_3$); HPLC analysis: 94% e.e. (Daicel Chiralcel AD-H column, eluent: hexane/*i*-PrOH 95:5, flow 1.0 mL/min, wavelength: 254 nm, retention times: 9.0 min (major) and 21.3 min (minor)).

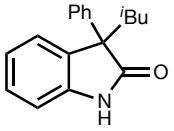



| Peak | $t_R$ (min) | Area (%) |
|---|---|---|
| 1 | 9.14 | 53.34 |
| 2 | 21.45 | 46.68 |



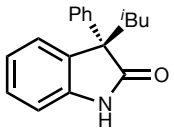

| Peak | $t_R$ (min) | Area (%) |
|---|---|---|
| 1 | 8.80 | 96.88 |
| 2 | 21.25 | 3.12 |

**(±)-3-Isobutyl-3-phenylindolin-2-one 27**

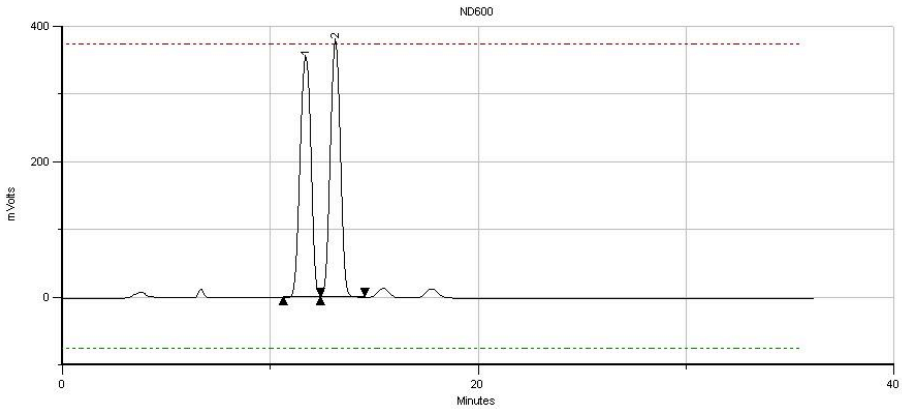



For determination of ee, the racemic sample of (±)-**27** prepared in our prior publication[13] used for HPLC analysis; $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 9.27 (1H, *br* s, N*H*), 7.37-7.35 (2H, m, Ar*H*), 7.28-7.20 (4H, m, Ar*H*), 7.17 (1H, d, $J$ = 7.1, Ar*H*), 7.06 (1H, td, $J$ = 7.5, 0.8, Ar*H*), 6.95 (1H, d, $J$ = 7.7, Ar*H*), 2.44 (1H, dd, $J$ = 13.8, 7.4, C$H_a$H$_b$), 2.17 (1H, dd, $J$ = 13.8, 5.2, CH$_a$$H_b$), 1.46 (1H, app. dquint, $J$ = 12.7, 6.4, C*H*), 0.80 (3H, d, $J$ = 6.6, C$H_3$), 0.67 (3H, d, $J$ = 6.7, C$H_3$); HPLC analysis: racemic (Daicel Chiralcel OD-H column, eluent: hexane/*i*-PrOH 95:5, flow 1.0 mL/min, wavelength: 254 nm, retention times: 12.0 min and 13.0 min).

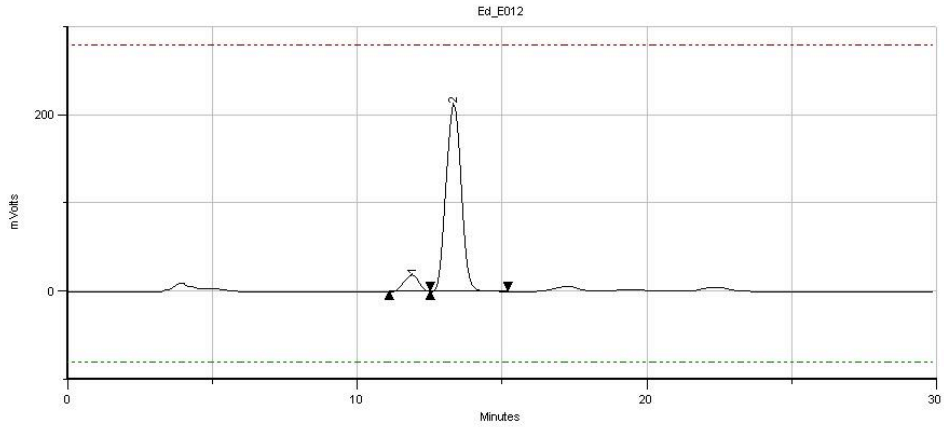
**(*S*)-3-Isobutyl-3-phenylindolin-2-one 27**




The oxindole was obtained from chiral nitrone **20** (0.070 g, 0.144 mmol) and isobutylphenylketene (0.050 g, 2.0 eq, 0.288 mmol) following general procedure **F**, to yield **27** (0.034 g, 89%) as an off-white solid; $[\alpha]_D^{20}$ -37.5° ($c$ = 1.20, $CHCl_3$); HPLC analysis: 84% e.e. (Daicel Chiralcel AD-H column, eluent: hexane/*i*-PrOH 95:5, flow 1.0 mL/min, wavelength: 254 nm, retention times: 11.8 min (minor) and 13.2 min (major)).

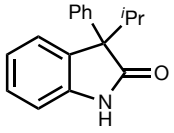



| Peak | $t_R$ (min) | Area (%) |
|---|---|---|
| 1 | 11.71 | 50.32 |
| 2 | 13.14 | 49.68 |



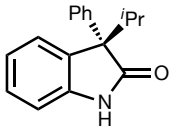

| Peak | $t_R$ (min) | Area (%) |
|---|---|---|
| 1 | 11.90 | 8.12 |
| 2 | 13.33 | 91.88 |

**(±)-3-Isopropyl-3-phenylindolin-2-one 36**

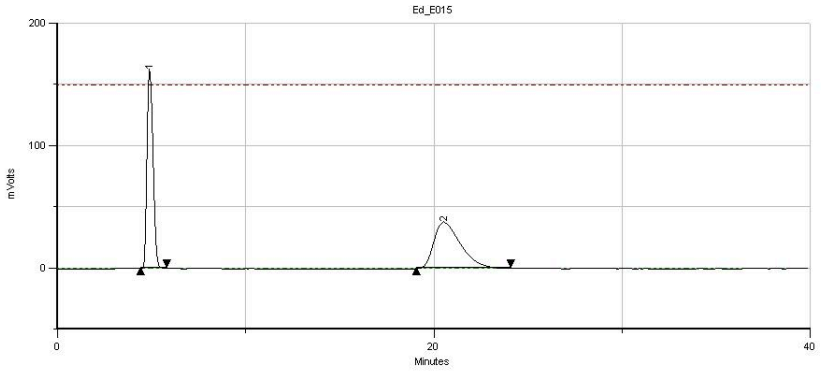



The oxindole was obtained from nitrone **79** (0.080 g, 0.406 mmol) and isopropylphenylketene (0.065 g, 1.0 eq, 0.406 mmol) following general procedure **E**, to yield (±)-**36** (0.055 g, 54%) as an off-white solid; mp 139-140 °C {lit.[35] 159-160 °C}; $^1$H NMR (300 MHz, $CDCl_3$) $\delta$ 8.24 (1H, *br* s, N*H*), 7.47-7.44 (2H, m, Ar*H*), 7.36-7.26 (5H, m, Ar*H*), 7.12 (1H, dd, $J$ = 7.6, 1.0, Ar*H*), 6.95 (1H, d, $J$ = 7.4, Ar*H*(7)), 2.93 (1H, sept., $J$ = 6.8, $^i$PrC*H*), 0.97 (3H, d, $J$ = 6.7, $^i$PrC*H*$_3$), 0.77 (3H, d, $J$ = 6.7, $^i$PrC*H*$_3$); $^{13}$C NMR (75 MHz, $CDCl_3$) $\delta$ 180.5, 141.4, 139.0, 130.2, 128.5, 128.2, 127.5, 127.2, 126.6, 122.1, 109.9, 61.3, 35.8, 17.6, 17.5; HPLC analysis: racemic (Daicel Chiralcel AD-H column, eluent: hexane/*i*-PrOH 95:5, flow 1.0 mL/min, wavelength: 254 nm, retention times: 4.6 min and 20.2 min).

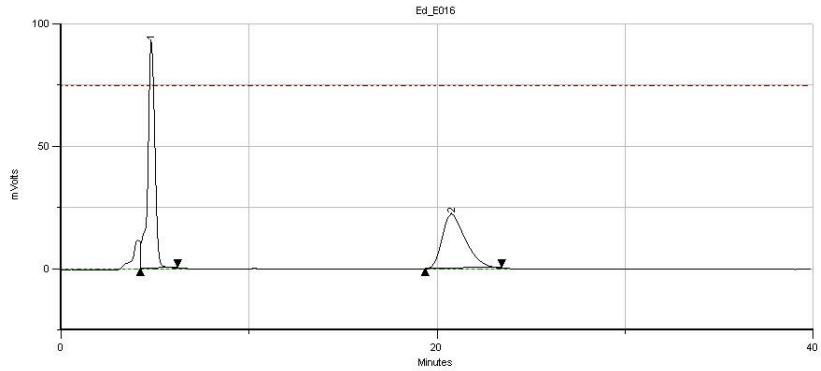
**(*S*)-3-Isopropyl-3-phenylindolin-2-one 36**




The oxindole was obtained from chiral nitrone **20** (0.080 g, 0.164 mmol) and isopropylphenylketene (0.053 g, 2.0 eq, 0.328 mmol) following general procedure **F**, to yield **36** (0.021 g, 51%) as an off-white solid; HPLC analysis: <5% e.e. (Daicel Chiralcel AD-H column, eluent: hexane/*i*-PrOH 95:5, flow 1.0 mL/min, wavelength: 254 nm, retention times: 4.8 min (major) and 20.6 min (minor)).

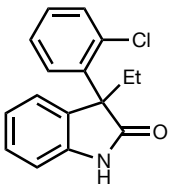



| Peak | $t_R$ (min) | Area (%) |
|---|---|---|
| 1 | 4.89 | 49.12 |
| 2 | 20.53 | 50.88 |



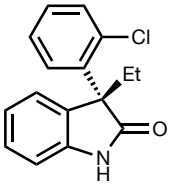

| Peak | $t_R$ (min) | Area (%) |
|---|---|---|
| 1 | 4.79 | 55.29 |
| 2 | 20.77 | 44.71 |

**(±)-3-(2-Chlorophenyl)-3-ethylindolin-2-one 34**

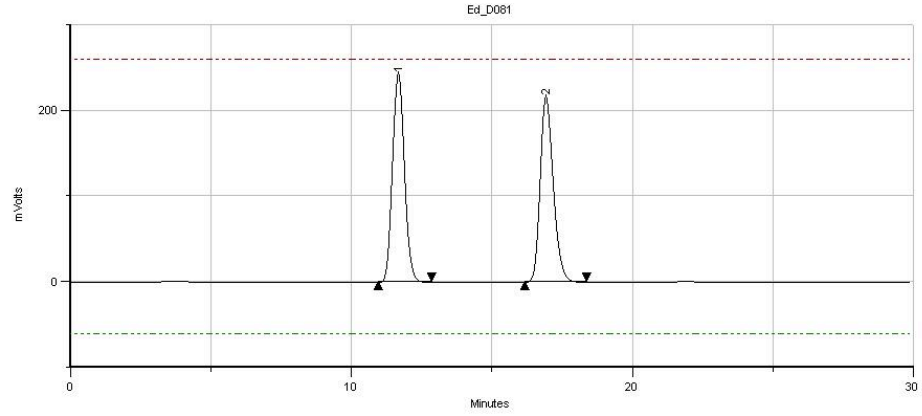



The oxindole was obtained from nitrone **79** (0.080 g, 0.406 mmol) and ethyl-(2-chlorophenyl)ketene (0.073 g, 1.0 eq, 0.406 mmol) following general procedure **E**, to yield (±)-**34** (0.102 g, 92%) as a white solid; mp 136-137 °C {lit.[13] 138-140 °C}; $^1$H NMR (300 MHz, $CDCl_3$) $\delta$ 8.87 (1H, *br* s, N*H*), 7.72 (1H, dd, *J* = 8.0, 1.3, Ar*H*), 7.37-7.16 (4H, m, Ar*H*), 6.97-6.88 (2H, m, Ar*H*), 6.74 (1H, dd, *J* = 7.4, 0.6, Ar*H*(7)), 2.43-2.23 (2H, m, C$H_2$), 0.78 (3H, t, *J* = 7.3, $CH_2CH_3$); HPLC analysis: racemic (Daicel Chiralcel AD-H column, eluent: hexane/*i*-PrOH 90:10, flow 1.0 mL/min, wavelength: 254 nm, retention times: 11.7 min and 17.2 min).

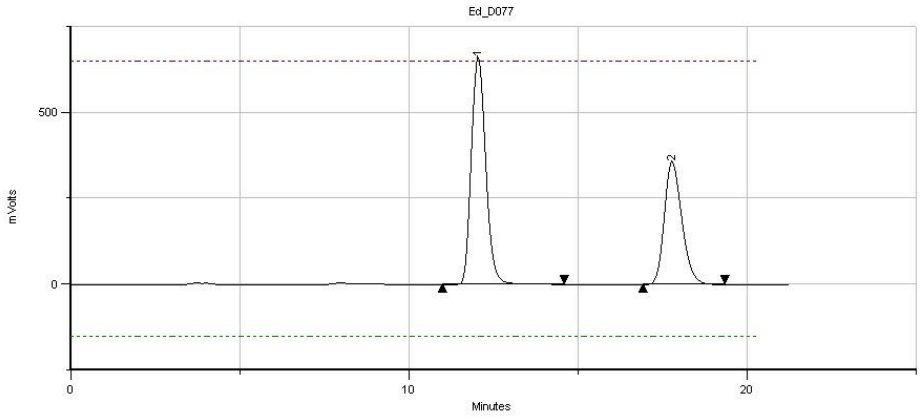
**(*S*)-3-(2-Chlorophenyl)-3-ethylindolin-2-one 34**




The oxindole was obtained from chiral nitrone **20** (0.050 g, 0.103 mmol) and ethyl-(2-chlorophenyl)ketene (0.037 g, 2.0 eq, 0.206 mmol) following general procedure **F**, to yield **34** (0.020 g, 72%) as an off-white solid; $[\alpha]_D^{20}$ +4.1° (*c* = 1.00, $CHCl_3$); HPLC analysis: 20% e.e. (Daicel Chiralcel AD-H column, eluent: hexane/*i*-PrOH 90:10, flow 1.0 mL/min, wavelength: 254 nm, retention times: 11.8 min (major) and 17.5 min (minor)).

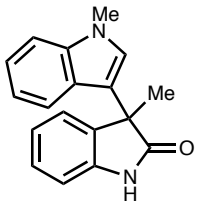



| Peak | $t_R$ (min) | Area (%) |
|---|---|---|
| 1 | 11.67 | 50.72 |
| 2 | 16.92 | 49.28 |



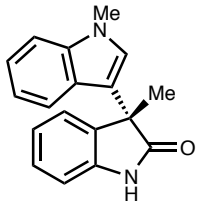

| Peak | $t_R$ (min) | Area (%) |
|---|---|---|
| 1 | 12.05 | 60.34 |
| 2 | 17.78 | 39.66 |

**(±)-3-Methyl-3-(1-methyl-1*H*-indol-3-yl)indolin-2-one 32**

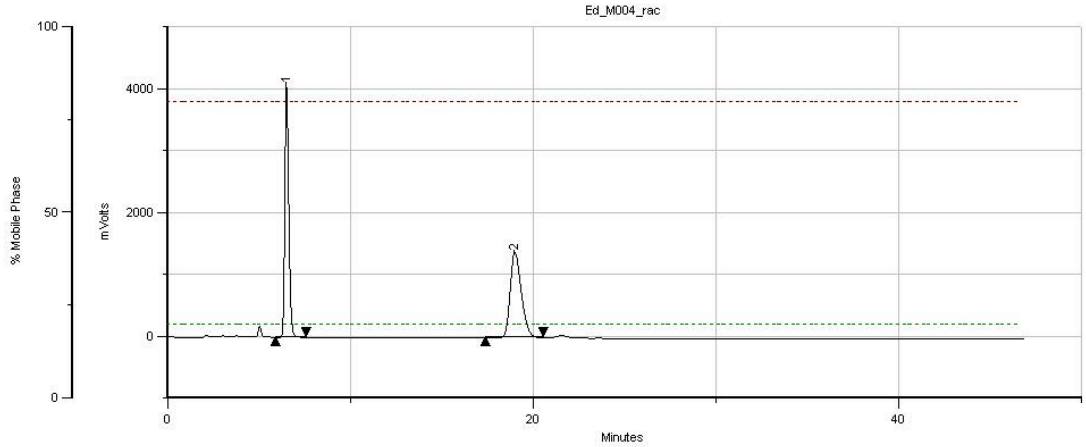


The oxindole was obtained from nitrone **79** (0.070 g, 0.355 mmol) and a crude solution of methyl(1-methyl-1*H*-indol-3-yl)ketene (2.0 mL) according to general procedure **E** as a crude brown oil. Purification *via* column chromatography (0-50% EtOAc in petrol) gave (±)-**32** (0.050 g, 51%) as an off-white solid; mp 251-253 °C {lit.[36] 255-257 °C}; $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 8.33 (1H, br s, N*H*), 7.24-7.21 (2H, m, Ar*H*), 7.15-7.09 (3H, m, Ar*H*), 7.01-6.93 (3H, m, Ar*H*), 6.90-6.86 (1H, m, Ar*H*), 3.77 (3H, s, C$H_3$), 1.88 (3H, s, N*Me*); HPLC analysis: racemic (Daicel Chiralcel AD-H column, eluent: hexane/*i*-PrOH 80:20, flow 1.5 mL/min, wavelength: 211 nm, retention times: 6.52 min (minor) and 19.6 min (major)).

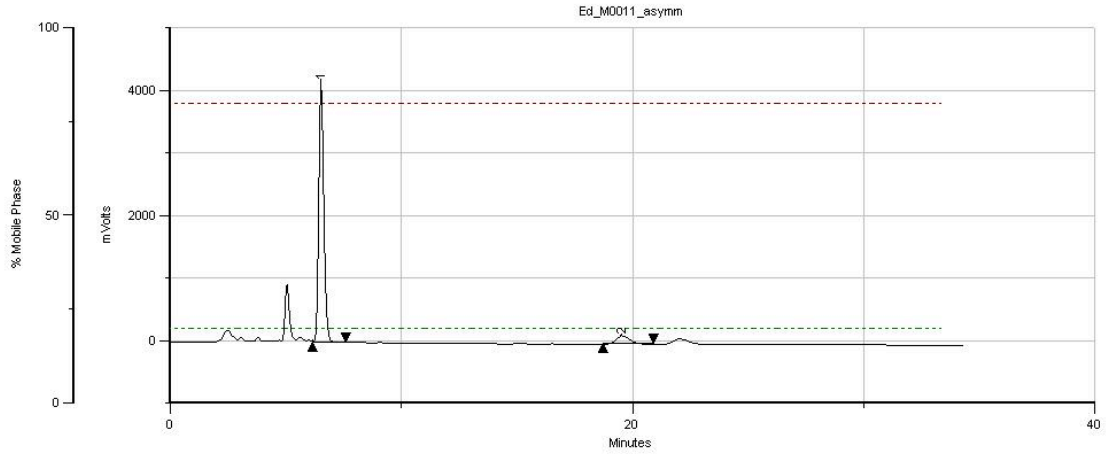
**(*S*)-3-Methyl-3-(1-methyl-1*H*-indol-3-yl)indolin-2-one 32**



The oxindole was obtained from *N*-TIPBS nitrone **20** (0.118 g, 0.242 mmol) and a crude solution of methyl(1-methyl-1*H*-indol-3-yl)ketene (2.0 mL) according to general procedure **F** as a crude brown oil. Purification *via* column chromatography (0-50% EtOAc in petrol) gave **32** (0.039 g, 58 %) as a yellow oil; $[\alpha]_D^{20}$ -36.2° ($c$ = 0.40, $CHCl_3$); HPLC analysis: 84% e.e. (Daicel Chiralcel AD-H column, eluent: hexane/*i*-PrOH 80:20, flow 1.5 mL/min, wavelength: 211 nm, retention times: 6.52 min (minor) and 19.6 min (major)).

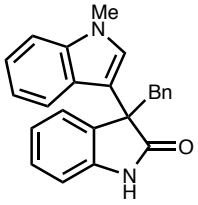



| Peak | $t_R$ (min) | Area (%) |
|---|---|---|
| 1 | 6.50 | 50.11 |
| 2 | 19.00 | 49.89 |



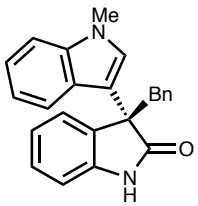

| Peak | $t_R$ (min) | Area (%) |
|---|---|---|
| 1 | 6.52 | 92.05 |
| 2 | 19.57 | 7.95 |

**(±)-3-Benzyl-3-(1-methyl-1*H*-indol-3-yl)indolin-2-one 31**



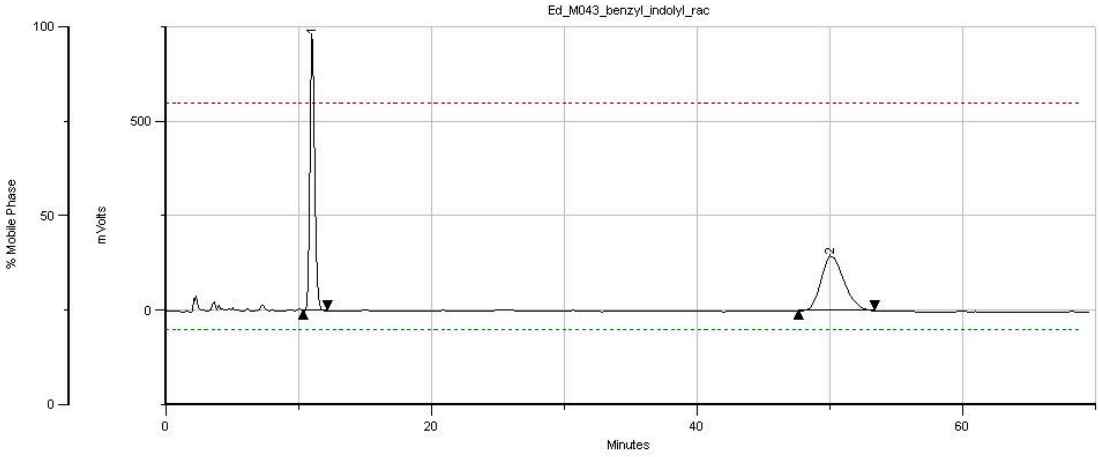

The oxindole was obtained from nitrone **79** (0.060 g, 0.304 mmol) and a crude solution of benzyl(1-methyl-1*H*-indol-3-yl)ketene (3.5 mL) according to general procedure **E** as a crude brown oil. Purification *via* column chromatography (0-50% EtOAc in petrol) gave (±)-**31** (0.038 g, 36%) as a yellow solid; mp 219-221 °C; $\nu_{max}$ $cm^{-1}$ (ATR) 3057, 2351, 1701, 1618, 1470; $^1$H NMR (300 MHz, $CDCl_3$) $\delta$ 7.63 (1H, br s, N*H*), 7.34-7.30 (1H, m, Ar*H*), 7.25-7.16 (5H, m, Ar*H*), 7.13-7.05 (4H, m, Ar*H*), 7.02-6.94 (3H, m, Ar*H*), 6.72 (1H, d, $J$ = 7.7, Ar*H*(7)), 3.92 (1H, d, $J$ = 12.6, C$H_a$H$_b$), 3.82 (3H, s, N*Me*), 3.60 (1H, d, $J$ = 12.6, CH$_a$$H_b$); $^{13}$C NMR (75 MHz, $CDCl_3$) $\delta$ 179.8 (*C*=O), 140.6 (4$^{ry}$ Ar*C*), 137.6 (4$^{ry}$ Ar*C*), 135.4 (4$^{ry}$ Ar*C*), 132.5 (4$^{ry}$ Ar*C*), 130.3 (Ar*C*(Bn)), 128.1 (Ar*C*), 127.6 (Ar*C*(Bn)), 127.5 (Ar*C*), 126.6 (4$^{ry}$ Ar*C*), 126.0 (Ar*C*), 125.2 (Ar*C*), 122.3 (Ar*C*), 121.9 (Ar*C*), 120.5 (Ar*C*), 119.3 (Ar*C*), 113.7 (4$^{ry}$ Ar*C*(3')), 109.5 (Ar*C*), 109.4 (Ar*C*), 54.5 (*C*H$_2$), 42.5 (*C*(3)), 32.9 (N*Me*); *m/z* (EI$^+$) 353 ([M+H]$^+$, 100%); HRMS (EI$^+$) $C_{24}H_{21}N_2O$ ([M+H]$^+$) found 353.1648 requires 353.1648 (- 0.1 ppm); HPLC analysis: racemic (Daicel Chiralcel AD-H column, eluent: hexane/*i*-PrOH 80:20, flow 1.5 mL/min, wavelength: 211 nm, retention times: 11.0 min (major) and 50.1min (minor)).

**(*S*)-3-Benzyl-3-(1-methyl-1*H*-indol-3-yl)indolin-2-one 31**

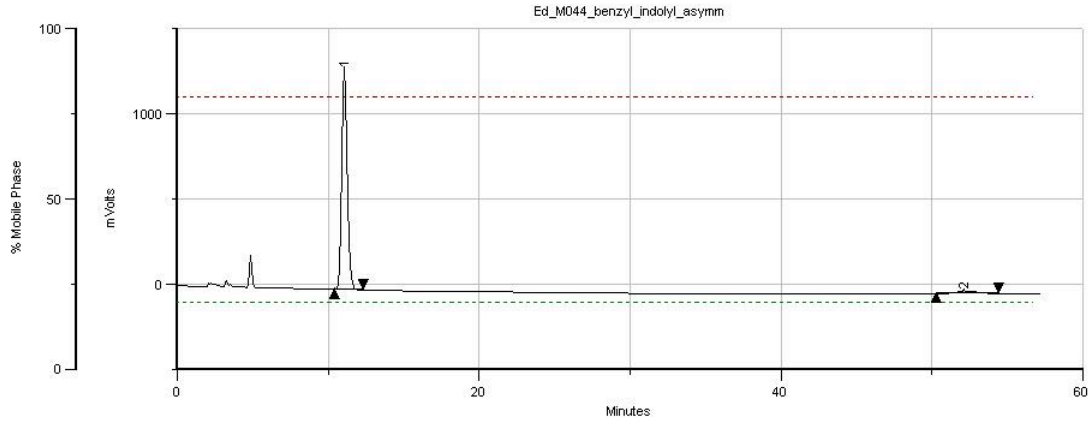



The oxindole was obtained from *N*-TIPBS nitrone **20** (0.060 g, 0.123 mmol) and a crude solution of benzyl(1-methyl-1*H*-indol-3-yl)ketene (2.5 mL) according to general procedure **F** as a

crude brown oil. Purification *via* column chromatography (0-50% EtOAc in petrol) gave **31** (0.038 g, 88 %) as a yellow semi-solid; $[\alpha]_D^{20}$ -48.8° (*c* = 0.25, $CHCl_3$); HPLC analysis: 88% e.e. (Daicel Chiralcel AD-H column, eluent: hexane/*i*-PrOH 80:20, flow 1.5 mL/min, wavelength: 211 nm, retention times: 11.0 min (major) and 52.1min (minor)).

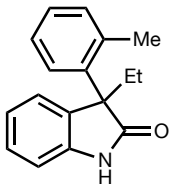



| Peak | $t_R$ (min) | Area (%) |
|---|---|---|
| 1 | 11.00 | 50.05 |
| 2 | 50.07 | 49.95 |



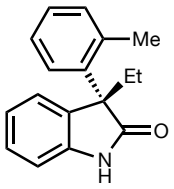

| Peak | $t_R$ (min) | Area (%) |
|---|---|---|
| 1 | 11.06 | 93.81 |
| 2 | 52.12 | 6.19 |

**(±)-3-Ethyl-3-(*o*-tolyl)indolin-2-one 33**

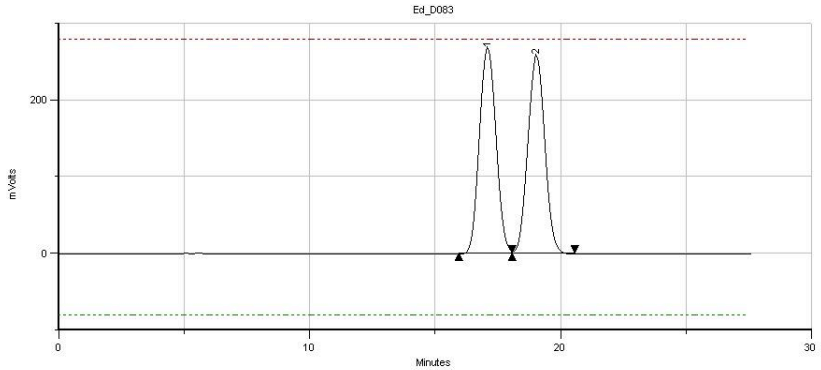



The oxindole was obtained from nitrone **79** (0.080 g, 0.406 mmol) and ethyl(2-tolyl)ketene (0.065 g, 1.0 eq, 0.406 mmol) following general procedure **E**, to yield (±)-**33** (0.077 g, 75%) as a white solid; mp 136-137 °C; $\nu_{max}$ $cm^{-1}$ (KBr) 3447, 3140 (NH), 3077, 3028, 2973, 2880, 1701 (C=O), 1618, 1470, 1456, 1338; $^1$H NMR (300 MHz, $CDCl_3$) $\delta$ 9.02 (1H, *br* s, N*H*), 7.69 (1H, dd, *J* =7.9, 0.8, Ar*H*), 7.30 (1H, td, *J* = 7.6, 1.1, Ar*H*), 7.20 (2H, td, *J* = 7.7, 1.1, Ar*H*), 7.06 (1H, d, *J* = 7.3, Ar*H*), 6.99-6.91 (2H, m, Ar*H*), 6.80 (1H, d, *J* = 7.4, Ar*H*(7)), 2.48-2.29 (2H, m, C$H_2$), 1.80 (3H, s, ArC$H_3$), 0.78 (3H, t, *J* =7.3, C$H_3$); $^{13}$C NMR (75 MHz, $CDCl_3$) $\delta$ 181.5 (C=O), 141.3 ($4^{ry}$ Ar*C*), 138.1 ($4^{ry}$ Ar*C*), 137.5 ($4^{ry}$ Ar*C*), 133.5 ($4^{ry}$ Ar*C*), 132.0 (Ar*C*), 127.9 (Ar*C*), 127.6 (Ar*C*), 127.5 (Ar*C*), 126.0 (Ar*C*), 123.5 (Ar*C*), 129.9 (Ar*C*), 109.6 (Ar*C*(7)), 57.0 (*C*3), 31.3 (*C*$H_2$), 19.6 (Ar*C*$H_3$), 8.0 ($CH_2CH_3$); *m/z* ($EI^+$) 252 ($[M+H]^+$, 100%); HRMS ($EI^+$) $C_{17}H_{18}ON^+$ ($[M+H]^+$) found 252.1383 requires 252.1383 (+ 0.0 ppm); HPLC analysis: racemic (Daicel Chiralcel AD-H column, eluent: hexane/*i*-PrOH 95:5, flow 1.0 mL/min, wavelength: 254 nm, retention times: 16.8 min and 19.0 min).

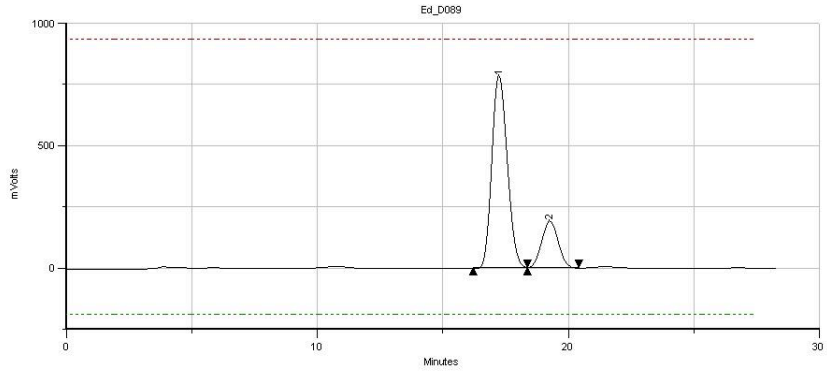
**(*S*)-3-Ethyl-3-(*o*-tolyl)indolin-2-one 33**




The oxindole was obtained from chiral nitrone **20** (0.050 g, 0.103 mmol) and ethyl(2-tolyl)ketene (0.033 g, 2.0 eq, 0.206 mmol) following general procedure **F**, to yield **33** (0.024 g, 93%) as an off-white solid; $[\alpha]_D^{20}$ +0.6° (*c* = 1.00, $CHCl_3$); HPLC analysis: 58% e.e. (Daicel Chiralcel AD-H column, eluent: hexane/*i*-PrOH 95:5, flow 1.0 mL/min, wavelength: 254 nm, retention times: 17.1 min (major) and 19.1 min (minor)).

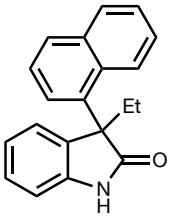



| Peak | $t_R$ (min) | Area (%) |
|---|---|---|
| 1 | 17.09 | 50.53 |
| 2 | 19.04 | 49.47 |



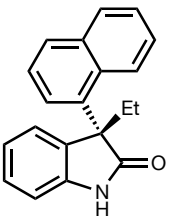

| Peak | $t_R$ (min) | Area (%) |
|---|---|---|
| 1 | 17.23 | 78.90 |
| 2 | 19.26 | 21.10 |

**(±)-3-Ethyl-3-(naphthalen-1-yl)indolin-2-one 35**



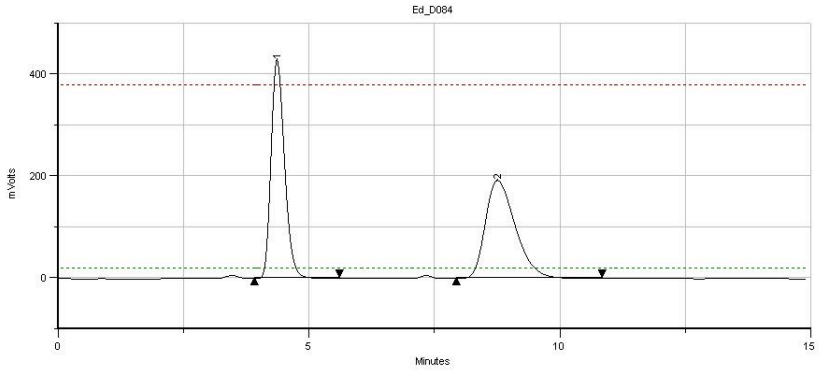

The oxindole was obtained from nitrone **79** (0.060 g, 0.304 mmol) and ethyl(naphthalen-1-yl)ketene (0.060 g, 1.0 eq, 0.304 mmol) following general procedure **E**, to yield (±)-**35** (0.064 g, 73%) as a white solid; mp 191-192 °C; $\nu_{max}$ $cm^{-1}$ (KBr) 3185 (NH), 1715 (C=O), 1471, 751; $^1$H NMR (300 MHz, $CDCl_3$) $\delta$ 9.14 (1H, *br* s, N*H*), 7.91 (1H, d, *J* = 7.4, Ar*H*), 7.83 (2H, t, *J* = 7.7, Ar*H*), 7.56 (1H, t, *J* = 7.8, Ar*H*), 7.36-7.31 (2H, m, Ar*H*), 7.18 (2H, qd, *J* = 8.0, 1.2, Ar*H*), 6.97 (1H, d, *J* =7.7, Ar*H*), 6.90 (1H, td, *J* = 7.5, 0.9, Ar*H*), 6.78 (1H, d, *J* = 7.4, Ar*H*), 2.66-2.41 (2H, m, C$H_2$), 0.85 (3H, t, *J* = 7.3, C$H_3$); $^{13}$C NMR (75 MHz, $CDCl_3$) $\delta$ 182.1 (C=O), 140.5 ($4^{ry}$ Ar*C*), 135.3 ($4^{ry}$ Ar*C*), 135.2 ($4^{ry}$ Ar*C*), 134.6 ($4^{ry}$ Ar*C*), 131.8 ($4^{ry}$ Ar*C*), 129.2 (Ar*C*), 128.0 (Ar*C*), 126.4 (Ar*C*), 126.2 (Ar*C*), 125.4 (Ar*C*), 125.2 (Ar*C*), 123.6 (Ar*C*), 123.5 (Ar*C*), 123.1 (Ar*C*), 110.1 (Ar*C*(7)), 57.0 (*C*3), 32.1 (*C*$H_2$), 8.1 (*C*$H_3$), (one Ar*C* is not observed presumably due to overlapping signals in the naphthyl region); *m/z* ($EI^+$) 288 ($[M+H]^+$, 100%); HRMS ($EI^+$) $C_{20}H_{18}ON$ ($[M+H]^+$) found 288.1386 requires 288.1383 (+ 0.3 ppm); HPLC analysis: racemic (Daicel Chiralcel OD-H column, eluent: hexane/*i*-PrOH 80:20, flow 1.5 mL/min, wavelength: 254 nm, retention times: 4.4 min and 8.7 min.

**(*S*)-3-Ethyl-3-(naphthalen-1-yl)indolin-2-one 35**

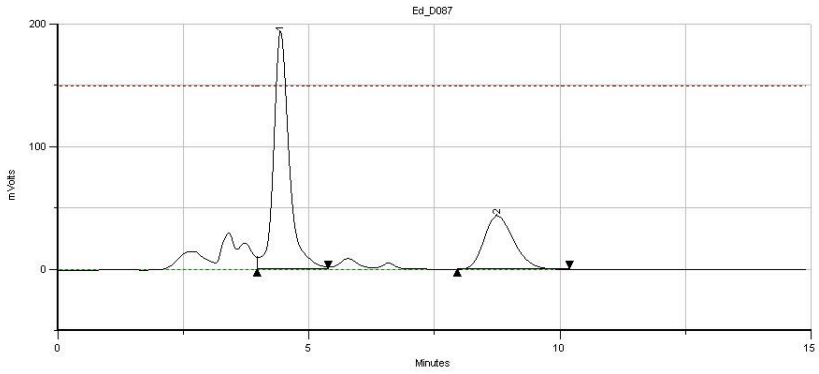



The oxindole was obtained from chiral nitrone **20** (0.050 g, 0.103 mmol) and ethyl(naphthalen-1-yl)ketene (0.040 g, 2.0 eq, 0.206 mmol) following general procedure **F**, to yield **35** (0.009 g, 30%) as an off-white solid; $[\alpha]_D^{20}$ +1.4° (*c* = 1.05, $CHCl_3$); HPLC analysis: 40% e.e. (Daicel

Chiralcel OD-H column, eluent: hexane/*i*-PrOH 80:20, flow 1.5 mL/min, wavelength: 254 nm, retention times: 4.4 min (major) and 8.8 min (minor)).

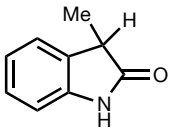



| Peak | $t_R$ (min) | Area (%) |
|---|---|---|
| 1 | 4.36 | 49.96 |
| 2 | 8.76 | 50.04 |



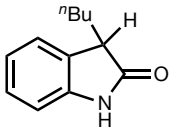

| Peak | $t_R$ (min) | Area (%) |
|---|---|---|
| 1 | 4.43 | 69.89 |
| 2 | 8.75 | 30.11 |

**(±)-3-Methylindolin-2-one 38**



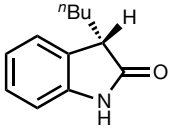

The oxindole was obtained from nitrone **79** (0.250 g, 1.27 mmol) and an excess of methylketene solution following general procedure **E**, to yield (±)-**38** (0.100 g, 54%) as an off-white solid; mp 107-109 °C {lit.[37] 100-102 °C}; $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 8.54 (1H, *br* s, N*H*), 7.23-7.19 (2H, m, Ar*H*), 7.03 (1H, td, *J* = 7.3, 1.0, Ar*H*), 6.91-6.89 (1H, m, Ar*H*(7)), 3.47 (1H, q, *J* = 7.7, C*H*(3)), 1.51 (3H, d, *J* = 7.7, CH*Me*).

**(±)-3-Butylindolin-2-one 37**

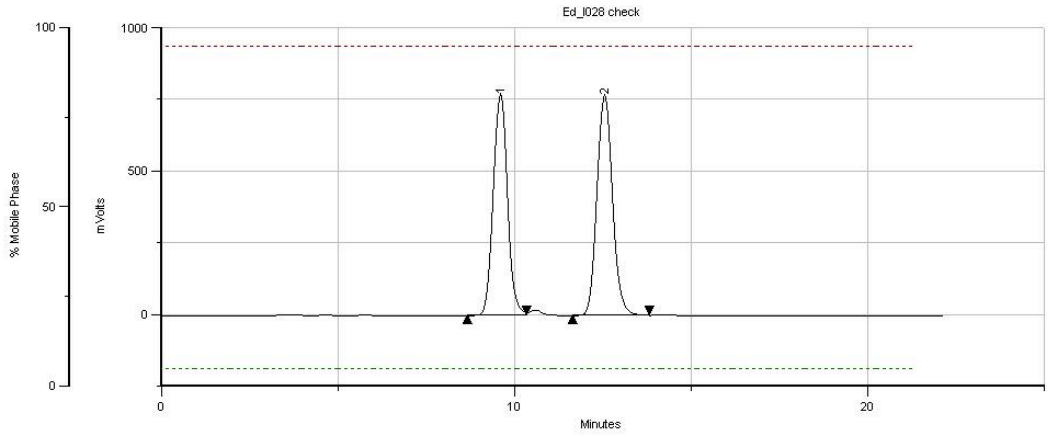


The oxindole was obtained from nitrone **79** (0.040 g, 0.203 mmol) and an excess of *n*-butylketene solution following general procedure **E**, to yield (±)-**37** (0.032 g, 83%) as a colourless oil with data in accordance with the literature;[38] $^1$H NMR (300 MHz, $CDCl_3$) $\delta$ 8.54 (1H, *br* s, N*H*), 7.24-7.18 (2H, m, Ar*H*), 7.05-7.00 (1H, m, Ar*H*), 6.90 (1H, d, $J$ = 7.6, Ar*H*(7)), 3.47 (1H, t, $J$ = 6.0, C*H*(3)), 2.02-1.91 (2H, m, CHC$H_2$), 1.41-1.27 (4H, m, -C$H_2$C$H_2$-), 0.88 (3H, t, $J$ = 7.1, $CH_2CH_3$); HPLC analysis: racemic (Daicel Chiralcel AD-H column, eluent: hexane/*i*-PrOH 95:5, flow 1.0 mL/min, wavelength: 254 nm, retention times: 9.1 min and 12.6 min).

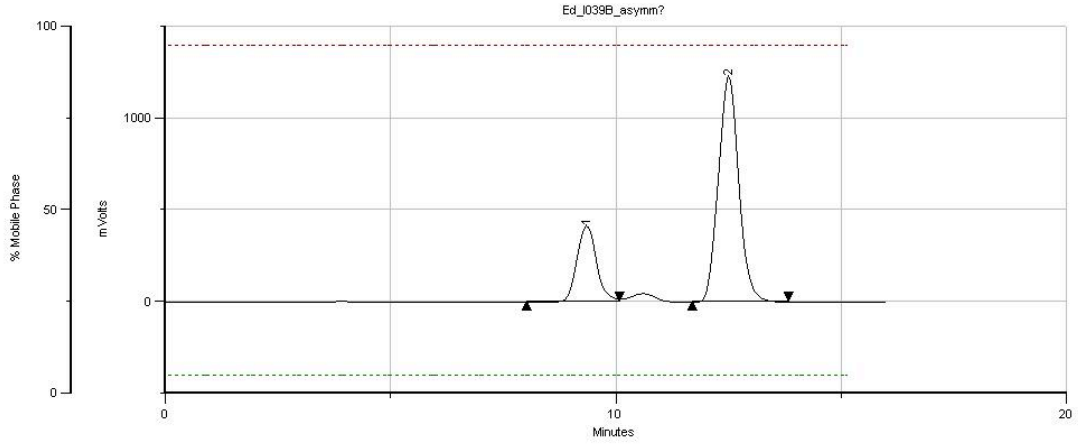
**(*S*)-3-Butylindolin-2-one 37**



The oxindole was obtained from nitrone **20** (0.050 g, 0.103 mmol) and an excess of *n*-butylketene solution following general procedure **F**, to yield **37** (0.014 g, 72%) as a pale orange oil; HPLC analysis: 50% e.e. (Daicel Chiralcel AD-H column, eluent: hexane/*i*-PrOH 95:5, flow 1.0 mL/min, wavelength: 254 nm, retention times: 9.5 min (minor) and 12.5 min (major)).

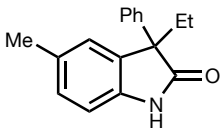



| Peak | $t_R$ (min) | Area (%) |
|---|---|---|
| 1 | 9.60 | 47.67 |
| 2 | 12.55 | 52.13 |



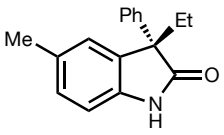

| Peak | $t_R$ (min) | Area (%) |
|---|---|---|
| 1 | 9.46 | 24.77 |
| 2 | 12.51 | 75.23 |

**(±)-3-Ethyl-5-methyl-3-phenylindolin-2-one 41**

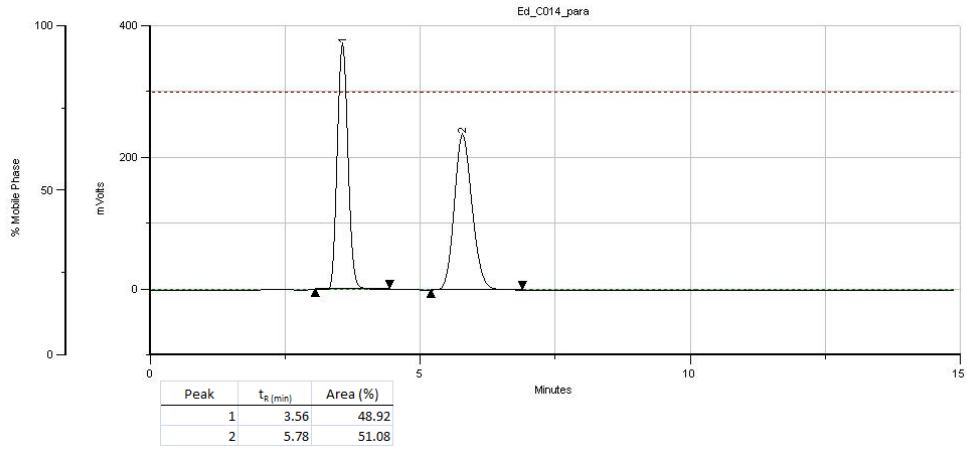



The oxindole was obtained from **88** (0.090 g, 0.430 mmol) and ethylphenylketene (0.062 g, 1.0 eq, 0.430 mmol) following general procedure **E**, to yield (±)-**41** (0.064 g, 60%) as a white solid; mp 158-159 °C {lit.[39] 160-161 °C}; $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 8.73 (1H, br s, N*H*), 7.39-7.24 (5H, m, Ar*H*), 7.04 (1H, ddd, *J* = 7.9, 1.7, 0.6, Ar*H*), 6.96 (1H, t, *J* = 0.6, Ar*H*), 6.85 (1H, d, *J* = 7.9, Ar*H*), 2.45 (1H, dq, *J* = 13.4, 7.3, C$H_2$CH$_3$), 2.33 (3H, s, ArC$H_3$), 2.23 (1H, dq, *J* = 13.4, 7.3, C$H_2$CH$_3$), 0.76 (3H, t, *J* = 7.3, CH$_2$C$H_3$); HPLC analysis: racemic (Daicel Chiralcel OD-H column, eluent: hexane/*i*-PrOH 80:20, flow 1.5 mL/min, wavelength: 254 nm, retention times: 3.6 min and 5.8 min).

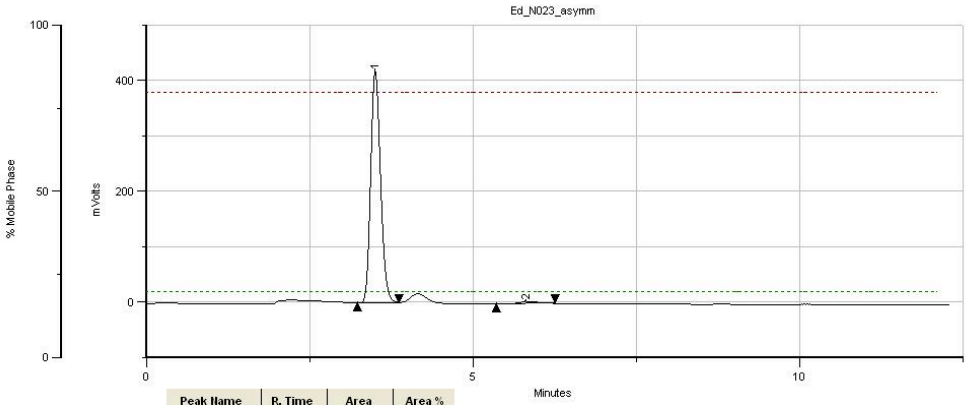
**(*S*)-3-Ethyl-5-methyl-3-phenylindolin-2-one 41**




The oxindole was obtained from chiral nitrone **39** (0.045 g, 0.090 mmol) and ethylphenylketene (0.013 g, 1.0 eq, 0.090 mmol) following general procedure **F**, to yield **41** (0.016 g, 48%) as an off-white solid; $[\alpha]_D^{20}$ -21.2° (*c* = 0.95, $CHCl_3$); HPLC analysis: 94% e.e. (Daicel Chiralcel OD-H column, eluent: hexane/*i*-PrOH 80:20, flow 1.5 mL/min, wavelength: 254 nm, retention times: 3.6 min (major) and 5.8 min (minor)).

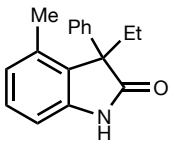


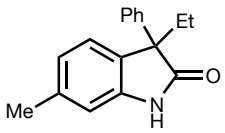

| Peak | $t_{R\,(min)}$ | Area (%) |
|---|---|---|
| 1 | 3.56 | 48.92 |
| 2 | 5.78 | 51.08 |




| Peak Name | R. Time | Area | Area % |
|---|---|---|---|
| *1 | 3.50 | 7429268.00 | 96.98 |
| *2 | 5.85 | 231062.72 | 3.02 |

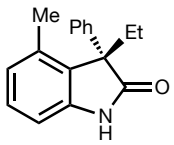
**(±)-3-Ethyl-4-methyl-3-phenylindolin-2-one 49 and (±)-3-ethyl-6-methyl-3-phenylindolin-2-one 50**

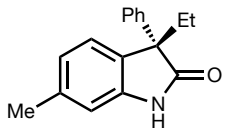



The oxindoles were obtained from **88** (0.080 g, 0.380 mmol) and ethylphenylketene (0.055 g, 1.0 eq, 0.380 mmol) following general procedure **E**, to yield **49** and **50** (combined yield; 0.040 g, 42%) as a 40:60 mixture of (±)-**49** to (±)-**50** based upon $^{1}$H NMR integration and separation *via* chiral HPLC. HPLC analysis: racemic (Daicel Chiralcel OD-H column, eluent: hexane/*i*-PrOH 80:20, flow 1.5 mL/min, wavelength: 254 nm, retention times: (±)-**50**; 4.0 min and 13.1 min; (±)-**49**; 4.8 min and 9.7 min).

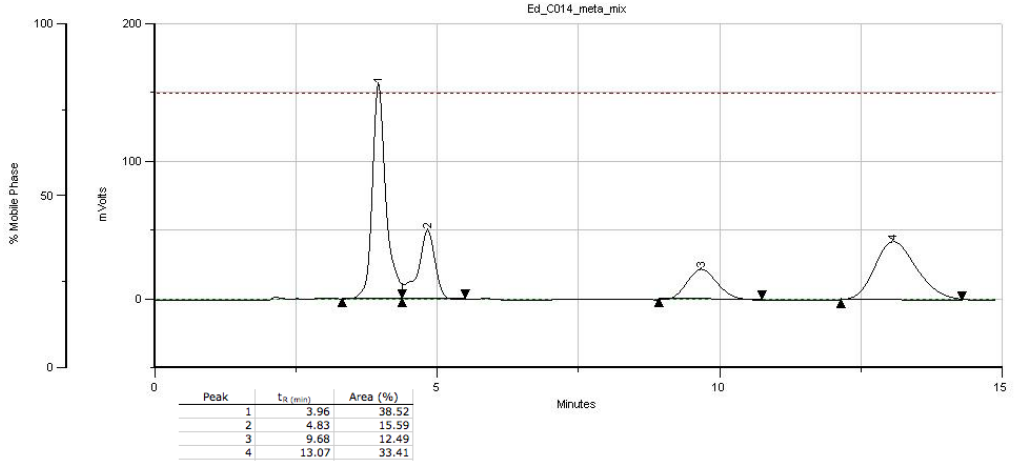
**(*S*)-3-Ethyl-4-methyl-3-phenylindolin-2-one 49 and (*S*)-3-ethyl-6-methyl-3-phenylindolin-2-one 50**



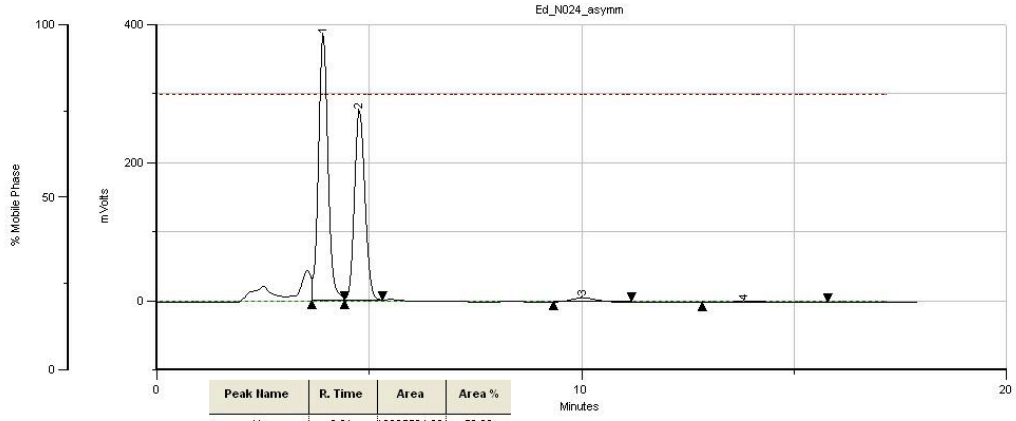




The oxindoles were obtained from chiral nitrone **47** (0.075 g, 0.150 mmol) and ethylphenylketene (0.022 g, 1.0 eq, 0.150 mmol) following general procedure **F**, to yield a mixture of **49** and **50** (0.036 g, 88%) as an off-white foam in 40:60 ratio of **49** to **50** based upon $^{1}$H NMR integration and separation *via* chiral HPLC. HPLC analysis: **49** 91% e.e. & **50** 91% e.e. (Daicel

Chiralcel OD-H column, eluent: hexane/*i*-PrOH 80:20, flow 1.5 mL/min, wavelength: 254 nm, retention times: **50**; 4.0 min (major) and 13.2 min (minor); **49**; 4.8 min (major) and 10.0 min (minor)).

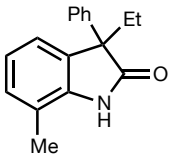



| Peak | $t_R$ (min) | Area (%) |
|---|---|---|
| 1 | 3.96 | 38.52 |
| 2 | 4.83 | 15.59 |
| 3 | 9.68 | 12.49 |
| 4 | 13.07 | 33.41 |



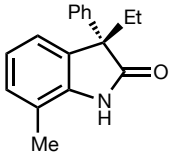

| Peak Name | R. Time | Area | Area % |
|---|---|---|---|
| *1 | 3.91 | 10085564.00 | 53.20 |
| 2 | 4.77 | 8022982.50 | 42.32 |
| *3 | 10.02 | 400858.78 | 2.11 |
| *4 | 13.97 | 448949.28 | 2.37 |

**(±)-3-Ethyl-7-methyl-3-phenylindolin-2-one 45**

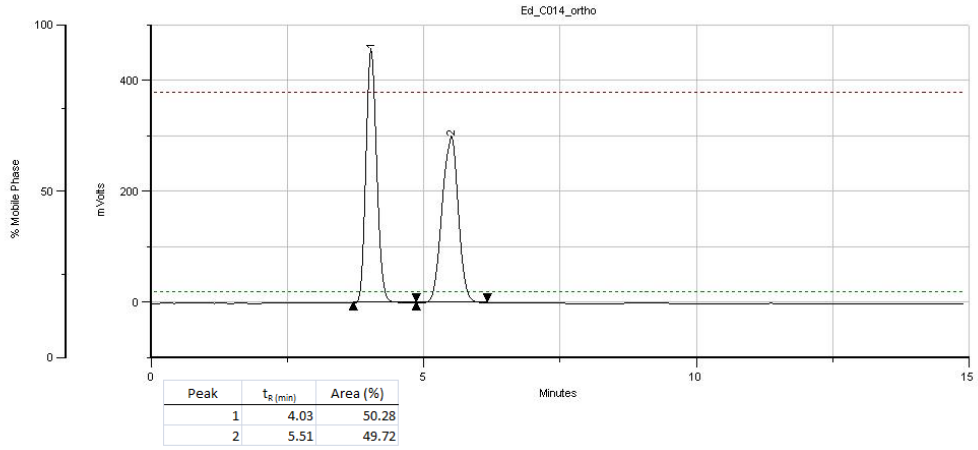



The oxindole was obtained from **86** (0.080 g, 0.380 mmol) and ethylphenylketene (0.055 g, 1.0 eq, 0.380 mmol) following general procedure **E**, to yield (±)-**45** (0.061 g, 64%) as an off-white solid; mp 136-137 °C {lit.[39] 138-139 °C}; $^1$H NMR (300 MHz, $CDCl_3$) $\delta$ 9.29 (1H, br s, N*H*), 7.39 (2H, dt, *J* = 6.7, 1.6, Ar*H*), 7.31-7.22 (3H, m, Ar*H*), 7.07-6.98 (3H, m, Ar*H*), 2.44 (1H, dq, *J* = 13.7, 7.1, C*H*$_2$CH$_3$), 2.28 (3H, s, ArC*H*$_3$), 2.23 (1H, dq, *J* = 13.7, 7.1, C*H*$_2$CH$_3$), 0.75 (3H, t, *J* = 7.1, CH$_2$C*H*$_3$); HPLC analysis: racemic (Daicel Chiralcel OD-H column, eluent: hexane/*i*-PrOH 80:20, flow 1.5 mL/min, wavelength: 254 nm, retention times: 4.0 min and 5.5 min).

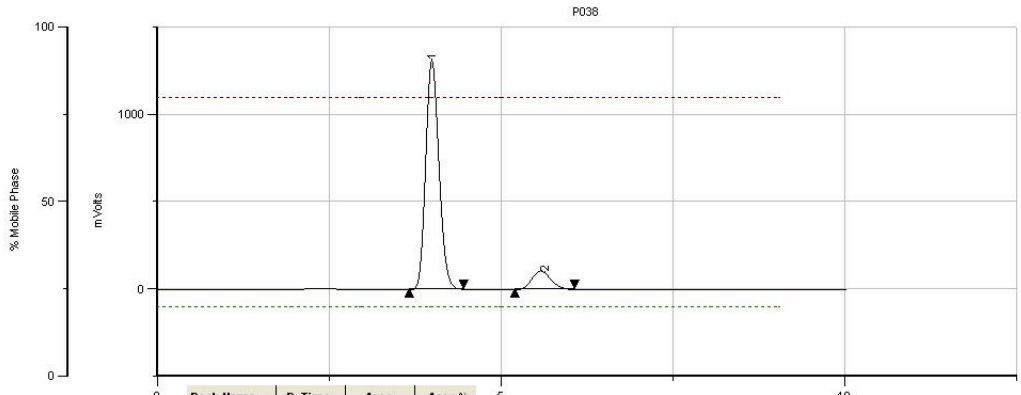
**(*S*)-3-Ethyl-7-methyl-3-phenylindolin-2-one 45**




The oxindole was obtained from chiral nitrone **43** (0.040 g, 0.060 mmol) and ethylphenylketene (0.012 g, 1.0 eq, 0.060 mmol) following general procedure **F**, to yield **45** (0.016 g, 80%) as an off-white solid; $[\alpha]_D^{20}$ -22.6° (*c* = 0.90, $CHCl_3$); HPLC analysis: 80 % e.e. (Daicel Chiralcel OD-H column, eluent: hexane/*i*-PrOH 80:20, flow 1.5 mL/min, wavelength: 254 nm, retention times: 4.0 min (major) and 5.6 min (minor)).

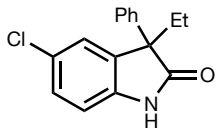



| Peak | $t_{R\,(min)}$ | Area (%) |
|---|---|---|
| 1 | 4.03 | 50.28 |
| 2 | 5.51 | 49.72 |




| Peak Name | R. Time | Area | Area % |
|---|---|---|---|
| *1 | 3.99 | 29471768.00 | 89.64 |
| *2 | 5.57 | 3405306.25 | 10.36 |

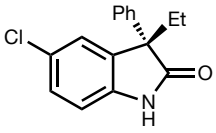
**(±)-5-Chloro-3-ethyl-3-phenylindolin-2-one 42**



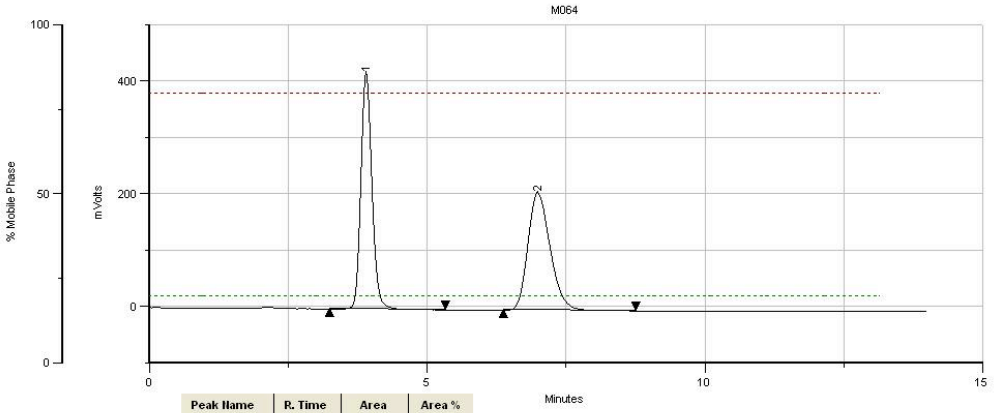

The oxindole was prepared according to general procedure **E** from **85** (0.050 g, 0.216 mmol) and ethylphenylketene (0.032 g, 1.0 eq, 0.216 mmol) to yield (±)-**42** (0.053 g, 90%) as a white solid; mp 126-127 °C {lit.[40] 152-153 °C}; $^1$H NMR (300 MHz, $CDCl_3$) $\delta$ 8.73 (1H, *br* s, N*H*), 7.29-7.19 (5H, m, Ar*H*), 7.17 (1H, dd, *J* = 8.3, 2.1, Ar*H*(6)), 7.08 (1H, d, *J* = 2.1, Ar*H*(4)), 6.83 (1H, d, *J* = 8.3, Ar*H*(7)), 2.39 (1H, dq, *J* = 13.8, 7.0, C$H_a$H$_b$), 2.17 (1H, dq, *J* = 13.8, 7.0, CH$_a$$H_b$), 0.71 (3H, t, *J* =

7.4, C$H_3$); HPLC analysis: racemic (Daicel Chiralcel OD-H column, eluent: hexane/*i*-PrOH 80:20, flow 1.5 mL/min, wavelength: 254 nm, retention times: 3.6 min and 7.0 min).

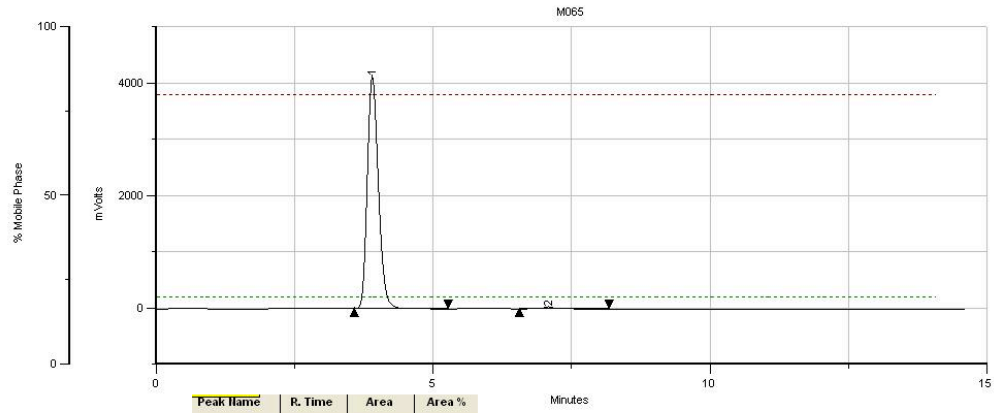
**(*S*)-5-Chloro-3-ethyl-3-phenylindolin-2-one 42**




The oxindole was prepared according to general procedure **F** from **40** (0.060 g, 0.115 mmol) and ethylphenylketene (0.017 g, 1.0 eq, 0.115 mmol) to yield **42** (0.027 g, 87%) as a white solid; $[\alpha]_D^{20}$ -54.2° (*c* = 1.20, $CHCl_3$); HPLC analysis: 97% ee (Daicel Chiralcel OD-H column, eluent: hexane/*i*-PrOH 80:20, flow 1.5 mL/min, wavelength: 254 nm, retention times: 3.6 min and 7.0 min).

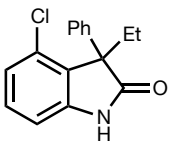


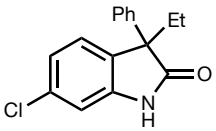

| Peak Name | R. Time | Area | Area % |
|---|---|---|---|
| *1 | 3.90 | 9711005.00 | 50.01 |
| 2 | 6.99 | 9706449.00 | 49.99 |




| Peak Name | R. Time | Area | Area % |
|---|---|---|---|
| *1 | 3.90 | 36648104.00 | 98.84 |
| *2 | 7.08 | 1131038.75 | 1.16 |

**(±)-6-Chloro-3-ethyl-3-phenylindolin-2-one 51 and (±)-4-Chloro-3-ethyl-3-phenylindolin-2-one 52**




The oxindoles were obtained from **84** (0.100 g, 0.432 mmol) and ethylphenylketene (0.064 g, 0.432 mmol) according to general procedure **E**, to yield (±)-**51** and (±)-**52** in a crude 60:40 ratio based on $^1$H NMR integration. The regioisomers were separated by column

chromatography over silica to yield (±)-**52** (0.052 g, 44%) as a white solid and (±)-**51** (0.046 g, 39%) as a white solid.

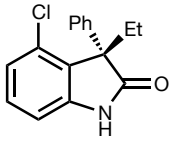
**(±)-6-Chloro-3-ethyl-3-phenylindolin-2-one 52**

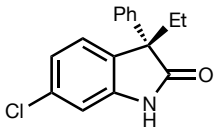
mp 142-143 °C; $\nu_{max}$ $cm^{-1}$ (ATR) 3190, 3167, 3048, 2970, 2940, 1713, 1611, 1595; $^1$H NMR (500 MHz, $CDCl_3$) $\delta$ 8.78 (1H, *br* s, N*H*), 7.35-7.30 (4H, m, Ar*H*), 7.28-7.26 (1H, m, Ar*H*), 7.10-7.06 (2H, m, Ar*H*), 6.99 (1H, s, Ar*H*(7)), 2.50 (1H, dq, *J* = 13.8, 6.9, C$H_a$H$_b$), 2.23 (1H, dq, *J* = 13.9, 7.0, C$H_a$H$_b$), 0.76 (3H, t, *J* = 7.3, C$H_3$); $^{13}$C NMR (125 MHz, $CDCl_3$) $\delta$ 181.1 (C=O), 142.3 ($4^{ry}$ Ar*C*), 139.5 ($4^{ry}$ Ar*C*), 133.8 ($4^{ry}$ Ar*C*), 131.2 ($4^{ry}$ Ar*C*), 128.7 (Ar*C*), 127.6 (Ar*C*), 126.9 (Ar*C*), 126.0 (Ar*C*), 122.7 (Ar*C*), 110.7 (Ar*C*(7)), 57.6 (*C*3), 30.4 (*C*H$_2$), 9.0 (*C*H$_3$); *m/z* (ESI$^+$) 272 ([M($^{35}$Cl)+H]$^+$, 100%); HRMS (ESI$^+$) $C_{16}H_{15}ON^{35}Cl^+$ ([M+H]$^+$) found 272.0838 requires 272.0837 (+ 0.5 ppm); HPLC analysis: racemic (Daicel Chiralcel OD-H column, eluent: hexane/*i*-PrOH 80:20, flow 1.5 mL/min, wavelength: 254 nm, retention times: 4.3 min and 14.4 min).

**(±)-4-Chloro-3-ethyl-3-phenylindolin-2-one 51**

mp 198-199 °C; $\nu_{max}$ $cm^{-1}$ (ATR) 3188, 3163, 2974, 2938, 1711, 1611, 1585, 1443; $^1$H NMR (500 MHz, $CDCl_3$) $\delta$ 8.82 (1H, *br* s, N*H*), 7.38-7.29 (5H, m, Ar*H*), 7.27 (1H, d, *J* = 8.0, Ar*H*(6)), 7.08 (1H, d, *J* = 8.0, Ar*H*(5)), 6.93 (1H, d, *J* = 8.0, Ar*H*(7)), 2.71 (2H, app. qq, *J* = 15.1, 7.5, C$H_2$), 0.78 (3H, t, *J* = 7.4, C$H_3$); $^{13}$C NMR (125 MHz, $CDCl_3$) $\delta$ 180.4 (C=O), 143.2 ($4^{ry}$ Ar*C*), 138.2 ($4^{ry}$ Ar*C*), 131.6 ($4^{ry}$ Ar*C*), 129.6 (Ar*C*), 129.3 ($4^{ry}$ Ar*C*), 128.6 (Ar*C*), 127.6 (Ar*C*), 126.7 (Ar*C*), 123.8 (Ar*C*), 108.5 (Ar*C*(7)), 59.2 (*C*3), 26.5 (*C*H$_2$), 9.1 (*C*H$_3$); *m/z* (ESI$^+$) 272 ([M($^{35}$Cl)+H]$^+$, 100%); HRMS (ESI$^+$) $C_{16}H_{15}ON^{35}Cl^+$ ([M+H]$^+$) found 272.0840 requires 272.0837 (+ 1.2 ppm); HPLC analysis: racemic (Daicel Chiralcel OD-H column, eluent: hexane/*i*-PrOH 80:20, flow 1.5 mL/min, wavelength: 254 nm, retention times: 4.9 min and 12.1 min).

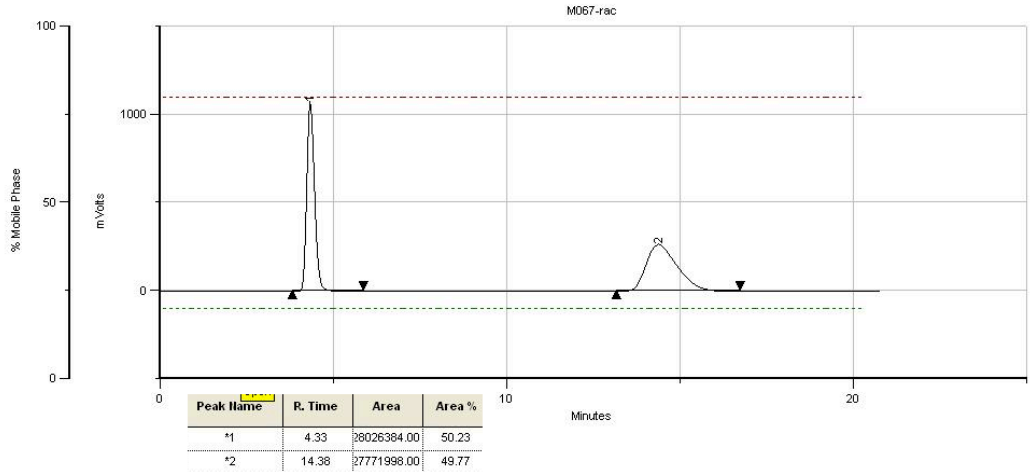
**(*S*)-6-Chloro-3-ethyl-3-phenylindolin-2-one 51 and (*S*)-4-Chloro-3-ethyl-3-phenylindolin-2-one 52**

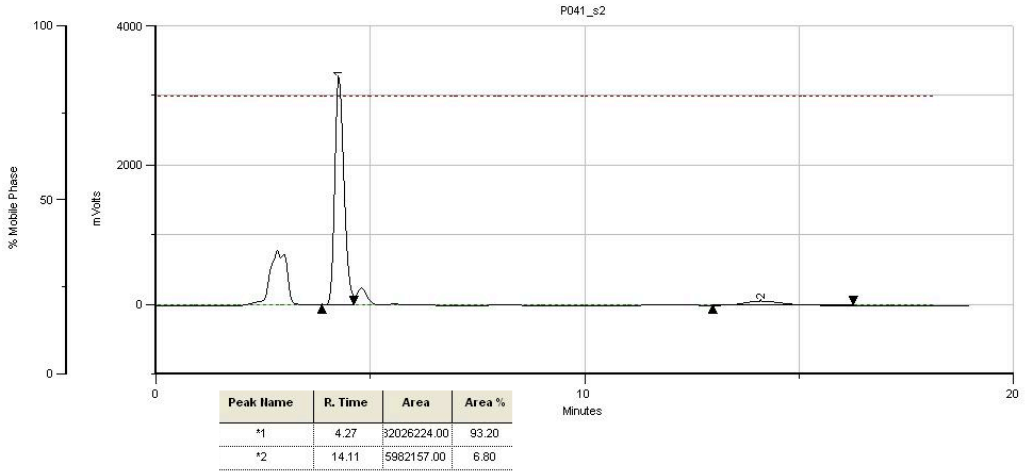




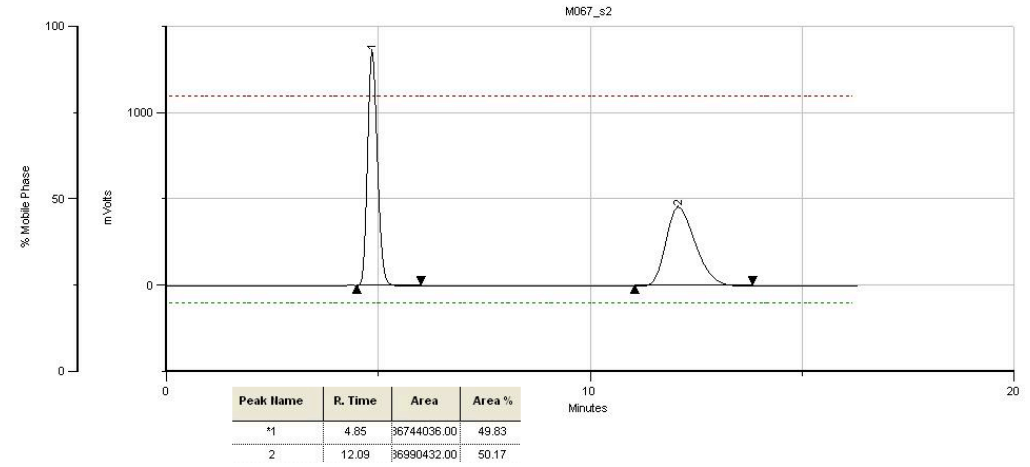

The oxindoles were prepared according to general procedure **F** from **48** (0.065 g, 0.125 mmol) and ethylphenylketene (0.018 g, 1.0 eq, 0.125 mmol) to give oxindoles **52** and **51** in a crude 60:40 ratio based on $^1$H NMR integration. The crude oxindoles were purified and separated *via* column chromatography over silica to yield **51** (0.011 g, 32%) as a white solid and **52** (0.016 g, 47%) as a white solid.

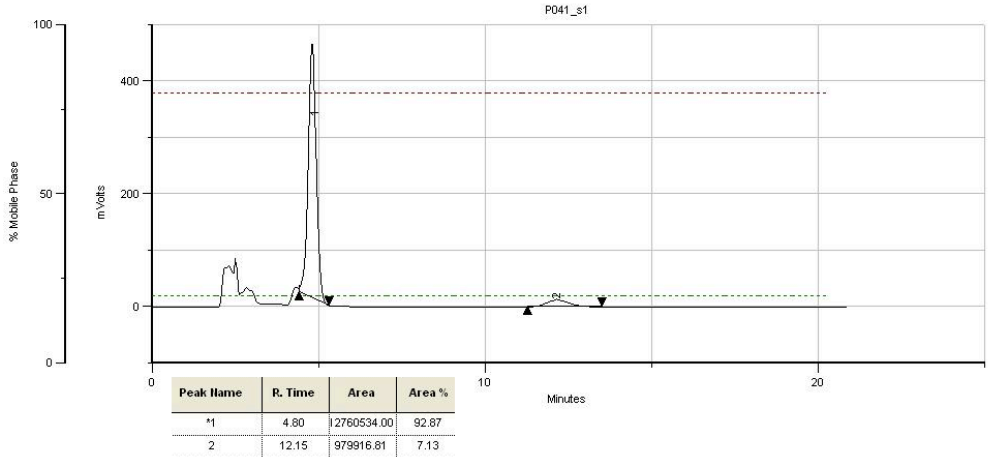
**(*S*)-6-Chloro-3-ethyl-3-phenylindolin-2-one 52** HPLC analysis: racemic (Daicel Chiralcel OD-H column, eluent: hexane/*i*-PrOH 80:20, flow 1.5 mL/min, wavelength: 254 nm, retention times: 4.3 min (major) and 14.1 min (minor)).



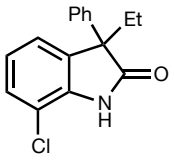




**(*S*)-4-Chloro-3-ethyl-3-phenylindolin-2-one 51** HPLC analysis: racemic (Daicel Chiralcel OD-H column, eluent: hexane/*i*-PrOH 80:20, flow 1.5 mL/min, wavelength: 254 nm, retention times: 4.8 min (major) and 12.2 min (minor)).



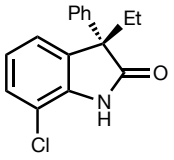



**(±)-7-Chloro-3-ethyl-3-phenylindolin-2-one 46**

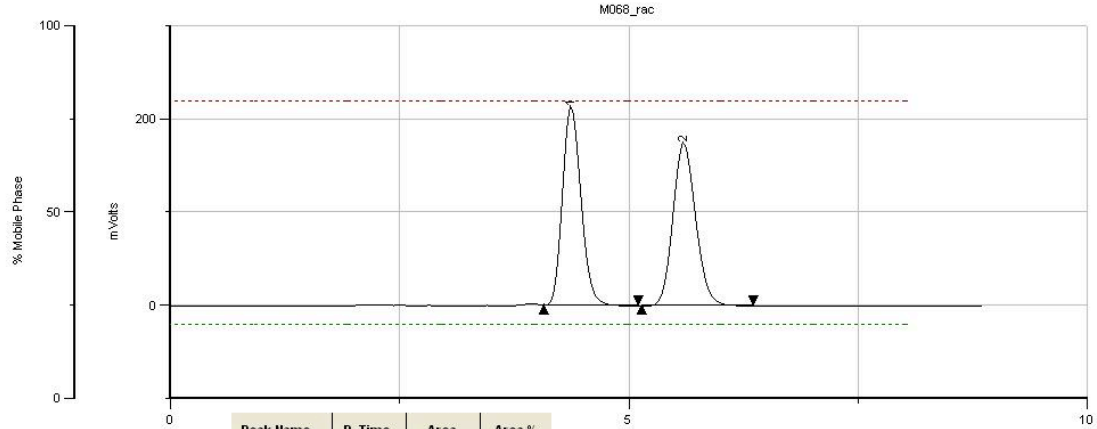



The oxindole was obtained from **83** (0.050 g, 0.216 mmol) and ethylphenylketene (0.032 g, 1.0 eq, 0.216 mmol) according to general procedure **E** to give (±)-**46** (0.051 g, 86%) as a white solid; mp 128-130 °C; $\nu_{max}$ $cm^{-1}$ (ATR) 3182, 3154, 3076, 2916, 2848, 1705, 1616, 1597, 1474; $^{1}H$ NMR (300 MHz, $CDCl_3$) $\delta$ 8.00 (1H, *br* s, N*H*), 7.41-7.25 (6H, m, Ar*H*), 7.13 (1H, ddd, $J$ = 7.5, 1.5, 0.5, Ar*H*), 7.10-7.05 (1H, m, Ar*H*), 2.50 (1H, dq, $J$ = 13.5, 7.3, C$H_a$H$_b$), 2.33-2.21 (1H, m, C$H_a$H$_b$), 0.80 (3H, t, $J$ = 7.4, C$H_3$); $^{13}C$ NMR (75 MHz, $CDCl_3$) $\delta$ 179.1 (C=O), 139.4 ($4^{ry}$ Ar*C*), 138.8 ($4^{ry}$ Ar*C*), 134.0 ($4^{ry}$ Ar*C*), 128.7 (Ar*C*), 128.1 (Ar*C*), 127.6 (Ar*C*), 126.8 (Ar*C*), 123.5 (Ar*C*), 123.4 (Ar*C*), 115.1 (Ar*C*Cl), 59.0 (*C*3), 30.8 (*C*H$_2$), 9.1 (*C*H$_3$); *m/z* (ESI$^+$) 272 ([M($^{35}$Cl)+H]$^+$, 100%); HRMS (ESI$^+$) $C_{16}H_{15}ON^{35}Cl^+$ ([M+H]$^+$) found 272.0840 requires 272.0837 (+ 1.2 ppm); HPLC analysis: racemic (Daicel Chiralcel OD-H column, eluent: hexane/*i*-PrOH 80:20, flow 1.5 mL/min, wavelength: 254 nm, retention times: 4.4 min and 5.6 min).

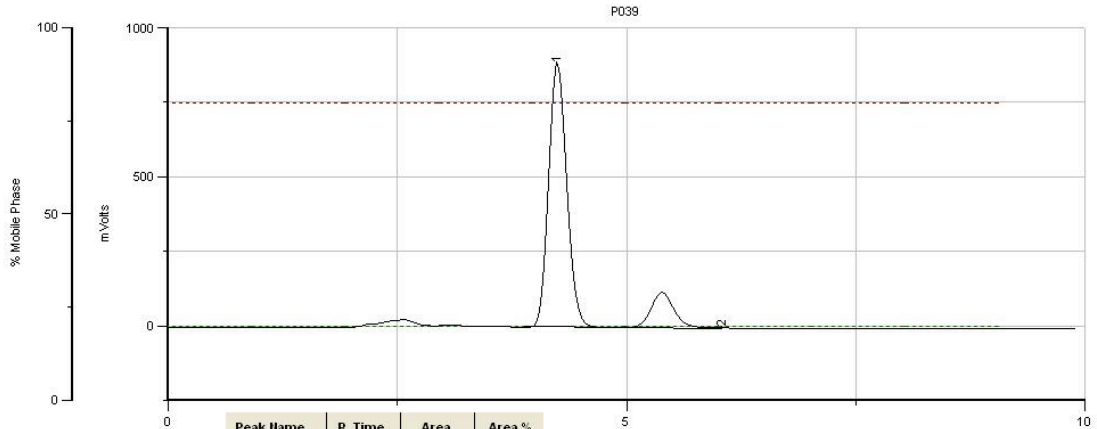
**(*S*)-7-Chloro-3-ethyl-3-phenylindolin-2-one 46**




The oxindole was prepared according to general procedure **F** from nitrone **44** (0.029 g, 0.056 mmol) and ethylphenylketene (0.008 g, 1.0 eq, 0.056 mmol) to yield **46** (0.010g, 66%) as a colourless oil; $[\alpha]_D^{20}$ -12.4° ($c$ = 1.00, $CHCl_3$); HPLC analysis: 68% ee (Daicel Chiralcel OD-H column, eluent: hexane/*i*-PrOH 80:20, flow 1.5 mL/min, wavelength: 254 nm, retention times: 4.3 min (major) and 5.4 min (minor)).



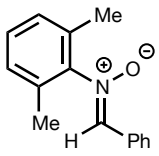

| Peak Name | R. Time | Area | Area % |
|---|---|---|---|
| *1 | 4.37 | 5066072.50 | 50.16 |
| 2 | 5.60 | 5033395.00 | 49.84 |




| Peak Name | R. Time | Area | Area % |
|---|---|---|---|
| *1 | 4.24 | 20554578.00 | 84.39 |
| *2 | 5.39 | 3803366.25 | 15.61 |

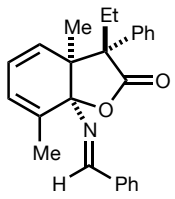
## 8. Mechanistic Probes

### (*Z*)-*N*-Benzylidene-2,6-dimethylaniline oxide 54



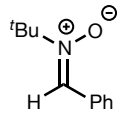
**54** was obtained according to general procedure **C** from 1,3-dimethyl-2-nitrobenzene (8.10 mL, 59.0 mmol), benzaldehyde (6.00 mL, 1.0 eq, 59.0 mmol), $NH_4Cl$ (4.14 g, 1.3 eq, 76.7 mmol) and zinc powder (7.80 g, 2.0 eq, 118 mmol) in EtOH:$H_2O$ (1:1 360 mL) to yield **54** (7.89 g, 59%) as an off-white solid; mp 110-111 °C {lit.[41] 127-128 °C}; $^1$H NMR (300 MHz, $CDCl_3$) $\delta$ 8.38-8.35 (2H, m, Ar*H*), 7.50-7.48 (3H, m, Ar*H*), 7.46 (1H, s, *H*C=N$^+$), 7.22-7.19 (1H, m, Ar*H*), 7.14-7.11 (2H, m, Ar*H*), 2.37 (6H, s, ArC$H_3$).

### (±)-(3*RS*,3a*RS*,7a*RS*)-7a-((*E*)-Benzylideneamino)-3-ethyl-3a,7-dimethyl-3-phenyl-3,3a-dihydrobenzofuran-2(7a*H*)-one 55



**55** was obtained according to general procedure **E** from nitrone **54** (0.050 g, 0.022 mmol) and ethylphenylketene (0.045 g, 1.4 eq, 0.031 mmol). Concentration of the organic material gave a crude mixture of compounds with **55** as the major component, in approximately 3.5:1 dr as an off-white foam. Recrystallisation from MeOH gave major diastereomer **55** (0.054 g, 66%) as a white solid; mp 128-130 °C (dec.); $\nu_{max}$ cm$^{-1}$ (ATR) 3061, 2976, 2918, 1748, 1497, 1449; $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 8.45 (1H, s, *H*C=N), 7.80 (2H, dd, *J* = 7.9, 1.6, N=CHAr*H*(2,6)), 7.47-7.39 (3H, m, Ar*H*), 7.36-7.33 (3H, m, Ar*H*), 7.27-7.25 (2H, m, Ar*H*), 6.20 (1H, dd, *J* = 9.8, 5.6, *C*(4)), 5.90 (1H, ddd, *J* = 5.6, 1.6, 0.8, *C*(5)), 5.50 (1H, dt, *J* = 9.8, 0.7, *C*(6)), 2.55 (1H, dq, *J* = 14.8, 7.4, C$H_a$H$_b$(C$H_2$CH$_3$)), 2.44 (1H, dq, *J* = 14.7, 7.4, CH$_a$$H_b$(C$H_2$CH$_3$)), 1.75 (3H, d, *J* = 1.5, C=CC$H_3$), 0.73 (3H, t, *J* = 7.4, CH$_2$C$H_3$), 0.56 (3H, s); $^{13}$C NMR (100 MHz, $CDCl_3$) $\delta$ 175.3 (*C*=O), 155.7 (H*C*=N), 136.7 (*C*(4)), 135.5 (Ar*C*), 134.0 (Ar*C*), 131.3 (Ar*C*), 128.9 (Ar*C*), 128.7 (Ar*C*), 128.6 (Ar*C*), 128.3 (Ar*C*), 126.9 (Ar*C*), 124.6 (Ar*C*), 122.4 (Ar*C*), 99.4 (*C*(6)), 77.2 (*C*(7a)) 61.2 (*C*(3)), 50.9 (*C*(3a)), 25.9 (*C*H$_2$), 22.7 (C(3a)*Me*), 15.3 (C(7)*Me*), 9.0 (CH$_2$C$H_3$); *m/z* (CI$^+$) 370 ([M-H]$^+$, 100%); HRMS (EI$^+$) $C_{25}H_{24}O_2N$ ([M-H]$^+$) found 370.1804 requires 370.1802 (+0.7 ppm)

**(*Z*)-*N*-Benzylidene-2-methylpropan-2-amine oxide 56**

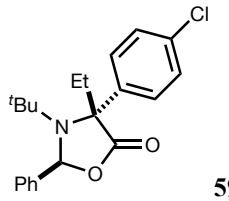


To a stirred solution of benzaldehyde (0.347 mL, 3.41 mmol) in THF:$H_2O$ (1:1 6 mL) was added $^t$Bu-hydroxylamine hydrochloride (0.570 g, 1.5 eq, 5.12 mmol) and $Na_2CO_3$ (0.271 g, 0.75 eq, 2.58 mmol) and the reaction mixture heated to 60 °C for 48 h. After allowing to cool, the reaction mixture was partitioned between $Et_2O$ (25 mL) and $H_2O$ (25 mL) and the aqueous layer extracted with $Et_2O$ (3 × 25 mL) and the combined organic layers dried over $MgSO_4$, filtered and concentrated *in vacuo* to give a crude semi-solid which was triturated from petroleum ether to give **56** (0.537 g, 89%) as a pale yellow solid; mp 79-80 °C {lit.[42] 68-70 °C}; $^1$H NMR (500 MHz, $CDCl_3$) $\delta$ 8.29 (2H, dd, $J$ = 7.7, 1.9, Ar*H*(2,6)), 7.54 (1H, s, *H*CN$^+$), 7.42-7.39 (3H, m, Ar*H*), 1.62 (9H, s, $^t$BuC*H*$_3$).

**(±)-*anti*-(2*SR*,4*RS*)-3-(*tert*-butyl)-4-(4-chlorophenyl)-4-ethyl-2-phenyloxazolidin-5-one 59 and (±)-*syn*-(2*RS*,4*RS*)-3-(*tert*-butyl)-4-(4-chlorophenyl)-4-ethyl-2-phenyloxazolidin-5-one 59a**

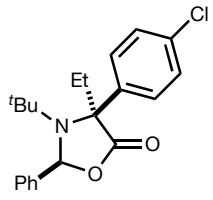
The oxazolidinones were prepared according to general procedure **E** from nitrone **56** (0.025 g, 0.141 mmol) and ethyl(*p*-chlorophenyl)ketene **57** (0.026 g, 1.0 eq, 0.141 mmol), however the reaction mixture was stirred for 5 min at rt before quenching with $H_2O$ (0.5 mL). The aqueous layer was then extracted with $Et_2O$ (3 × 20 mL), the combined organic layers dried over $MgSO_4$, filtered and concentrated *in vacuo* to yield a crude colourless oil. The major product (ca. 55%) in the crude $^1$H NMR was determined to be *N*-$^t$Bu imine **60**, however due to decomposition upon purification, this species was not isolated. The crude dr was determined as 3:1 based on the crude $^1$H NMR integration of the characteristic C(2) singlet protons. Purification by column chromatography over silica (0-10% EtOAc in petroleum ether gave **59** (0.018 g, 36%) as a white solid and **59a** (0.006 g, 12%) as a colourless oil.

*Major 'anti' diastereomer:*



**59** a white solid; mp 152-153 °C; $\nu_{max}$ cm$^{-1}$ (ATR) 2960, 1776, 1494; $^1$H NMR (300 MHz, $CDCl_3$) $\delta$ 7.61-7.58 (2H, m, ClAr*H*), 7.45-7.35 (7H, m, Ar*H*), 6.32 (1H, s, C*H*(2)), 2.64 (1H, dq, $J$ = 14.1, 7.0, C$H_a$H$_b$), 2.39 (1H, dq, $J$ = 14.1, 7.0, CH$_a$$H_b$), 1.34 (3H, t, $J$ = 7.0, C$H_3$), 0.80 (9H, s, $^t$BuCH$_3$); $^{13}$C NMR (125 MHz, $CDCl_3$) $\delta$ 175.3 (*C*=O), 141.0 (4$^{ry}$ Ar*C*), 140.0 (4$^{ry}$ Ar*C*), 134.3 (4$^{ry}$ Ar*C*), 129.9 (Ph*C*(5)), 129.4 (Ar*C*), 128.8 (Ar*C*), 128.6 (Ar*C*), 128.3 (Ar*C*), 92.5 (*C*(2)), 70.4 (*C*(4)), 55.1 ($^t$BuC), 29.8 (*C*H$_2$), 29.7 ($^t$BuC*CH*$_3$), 10.4 (*C*H$_3$); *m/z* (EI$^+$) 358 ([M($^{35}$Cl)+H]$^+$, 55%), 302 (100%); HRMS (EI$^+$) $C_{21}H_{25}O_2N^{35}Cl$ ([M+H]$^+$) found 358.1573 requires 358.1568 (+ 1.3 ppm).

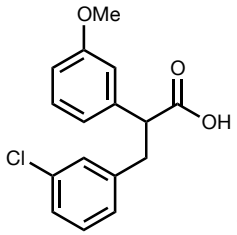
*Minor 'syn' diastereomer:*




**59a** a colourless oil; $\nu_{max}$ $cm^{-1}$ (ATR) 2976, 1771, 1489; $^1H$ NMR (300 MHz, $CDCl_3$) $\delta$ 7.67 (2H, d, $J$ = 8.7, ClAr*H*(3,5)), 7.62-7.59 (2H, m, Ar*H*), 7.45-7.37 (5H, m, Ar*H* & ClAr*H*(2,6)), 6.26 (1H, s, C*H*(2)), 2.64 (1H, dq, $J$ = 14.5, 7.3, $CH_aH_b$), 2.48 (1H, dq, $J$ = 14.5, 7.3, $CH_aH_b$), 1.30 (3H, t, $J$ = 7.3, $CH_3$), 0.90 (9H, s, $^t$BuC$H_3$); $^{13}C$ NMR (125 MHz, $CDCl_3$) $\delta$ 174.5 (*C*=O), 142.6 ($4^{ry}$ Ar*C*), 140.3 ($4^{ry}$ Ar*C*), 133.5 ($4^{ry}$ Ar*C*), 130.0 (Ph*C*(5)), 129.4 (Ar*C*), 128.6 (Ar*C*), 128.5 (Ar*C*), 128.4 (Ar*C*), 92.4 (*C*(2)), 70.9 (*C*(4)), 55.0 ($^t$Bu*C*), 30.9 ($^t$BuC$CH_3$), 27.0 ($CH_2$), 10.8 ($CH_3$); *m/z* ($EI^+$) 358 ($[M(^{35}Cl)+H]^+$, 35%), 302 (100%); HRMS ($EI^+$) $C_{21}H_{25}O_2N^{35}Cl$ ($[M+H]^+$) found 358.1571 requires 358.1568 (+ 0.7 ppm).

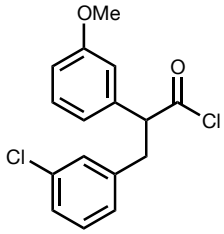
**9. Roche p53 inhibitor**

**(±)-3-(3-Chlorophenyl)-2-(3-methoxyphenyl)propanoic acid 62a**




To a stirred solution of 3-methoxyphenylacetic acid (10.03 g, 60.2 mmol) in THF (200 mL) at -78 °C was added *n*-BuLi (60 mL, 2.5 eq, 2.5M in hexanes) dropwise and the reaction then allowed to warm to rt. 3-Chlorobenzyl bromide (8.75 mL, 1.1 eq, 66.2 mmol) was then added slowly and the reaction stirred 6 h at rt before quenching with aq. 1M HCl (60 mL). The reaction mixture was then extracted with $Et_2O$ (2 × 250 mL) and the combined organic layers washed with brine (300 mL), dried over $MgSO_4$, filtered and concentrated *in vacuo* to yield a crude yellow oil which was purifed *via* column chromatography over silica (0-50% EtOAc in petroleum ether) to yield the title compound as a viscous yellow oil (15.21 g, 87%) which slowly crystallised to an off-white solid upon standing, with analytical data in accordance with the literature;[43] $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 7.30-7.28 (1H, m, MeOAr*H*(5)), 7.21-7.17 (3H, m, Ar*H*), 7.02-6.97 (1H, m, Ar*H*), 6.94-6.85 (3H, m, MeOAr*H*(2,4,6), 3.85-3.83 (1H, m, C*H*), 3.84 (3H, s, ArO*Me*), 3.40 (1H, dd, $J$ = 13.8, 7.5, C$H_a$H$_b$), 3.04 (1H, dd, $J$ = 13.8, 7.5, CH$_a$$H_b$).

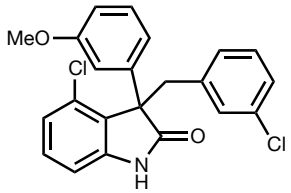
**(±)-3-(3-Chlorophenyl)-2-(3-methoxyphenyl)propanoyl chloride 63**

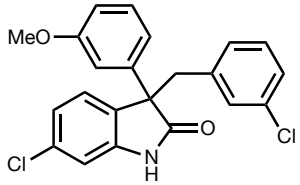



According to a literature procedure,[43] a stirred solution of acid **62a** (8.00 g, 27.5 mmol) in toluene (80 mL) was treated with thionyl chloride (4.00 mL, 2.0 eq, 55.0 mmol), and the reaction mixture stirred at 80 °C for 16 h. After cooling to rt, the reaction mixture was concentrated *in vacuo* to leave **63** (8.74 g, quant.) as a light brown oil which was used without further purification; $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 7.27-7.24 (3H, m, Ar*H*), 7.06-7.02 (1H, m, Ar*H*), 6.97-6.89 (3H, m, Ar*H*), 6.85-6.84 (1H, m, Ar*H*), 4.28 (1H, t, $J$ = 7.5, C*H*), 3.88 (3H, s, ArO*Me*), 3.51 (1H, dd, $J$ = 14.0, 7.5, C$H_a$H$_b$), 3.11 (1H, dd, $J$ = 14.0, 7.5, CH$_a$$H_b$).

**(±)-4-Chloro-3-(3-chlorobenzyl)-3-(3-methoxyphenyl)indolin-2-one (±)-65 &**

**(±)-6-Chloro-3-(3-chlorobenzyl)-3-(3-methoxyphenyl)indolin-2-one (±)-1**




To a stirred solution of acid chloride **63** (3.00 g, 9.70 mmol) in $Et_2O$ (40 mL) at 0 °C was added *N,N*-dimethylethylamine (1.10 mL, 1.05 eq, 10.2

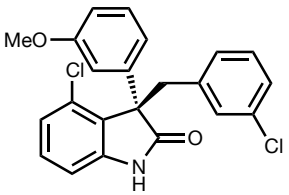
mmol) dropwise over 15 min and the reaction mixture stirred at 0 °C for 16 h. After this time, the reaction mixture was allowed to warm to rt before being filtered under nitrogen to remove the amine hydrochloride salts and then concentrated *in vacuo*. The resulting orange liquid (assumed as a 50% yield of ketene with respect to the acid chloride starting material) was then re-suspended in THF (20 mL) under nitrogen and cooled to -78 °C. A solution of nitrone **84** (1.12 g**,** 4.85 mmol) in THF (30 mL) was then added slowly over 15 min and the reaction mixture stirred at -78 °C for 4 h. The reaction was then quenched with aq. 1M HCl (5 mL) and stirred for 2 h allowing to warm to rt. The reaction mixture was then partitioned between $Et_2O$ (100 mL) and $H_2O$ (50 mL), the layers separated and the aqueous layer extracted once more with $Et_2O$ (75 mL). The combined organic layers were then washed with $NaHCO_3$ (2 × 100 mL), brine (75 mL), dried over $MgSO_4$, filtered and concentrated *in vacuo* to yield a crude dark orange oil. The crude product was purified *via* column chromatography over silica (0-30% EtOAc in petrol) to yield a mixture of the two oxindole regioisomers (1.41 g, 73% as a pale yellow foam). The regioisomers were separated *via* a second column chromatography over silica (10% $Et_2O$ in toluene) to analytical samples for chiral HPLC analysis.

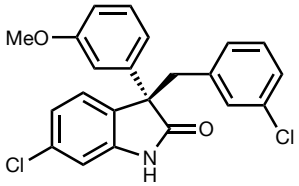
**(±)-1 (6-substituted isomer)** as a white solid: mp 152-153 °C; $\nu_{max}$ $cm^{-1}$ (ATR) 3204, 1717, 1613, 1580; $^1H$ NMR (300 MHz, $CDCl_3$) $\delta$ 7.53 (1H, br s, N*H*), 7.27 (1H, t, *J* = 8.0, Ar*H*), 7.12-6.97 (6H, m, Ar*H*), 6.91-6.74 (4H, m, Ar*H*), 3.77 (3H, s, O*Me*), 3.65 (1H, d, *J* = 13.0, C$H_a$$H_b$Ph), 3.40 (1H, d, *J* = 13.0, CH$_a$$H_b$Ph); $^{13}C$ NMR (125 MHz, $CDCl_3$) $\delta$ 178.9 (*C*=O), 159.8 (Ar*C*OMe), 141.6 (4$^{ry}$ Ar*C*), 140.4 (4$^{ry}$ Ar*C*), 137.4 (4$^{ry}$ Ar*C*), 134.1 (Ar*C*Cl), 133.6 (Ar*C*Cl), 130.2 (Ar*C*), 129.8 (Ar*C*), 129.8 (Ar*C*), 129.1 (Ar*C*), 128.3 (Ar*C*), 127.1 (Ar*C*), 126.8 (Ar*C*), 122.5 (Ar*C*), 119.3 (Ar*C*), 113.6 (Ar*C*), 112.6 (Ar*C*), 110.5 (Ar*C*(7)), 57.6 (*C*(3)), 55.3 (O*Me*), 43.0 (*C*H$_2$Ph); *m/z* (EI$^+$) 398 ([M($^{35}Cl^{35}Cl$)+H]$^+$, 100%); HRMS (EI$^+$) $C_{22}H_{18}O_2N^{35}Cl_2$ ([M+H]$^+$) found 398.0710 requires 398.0709 (+ 0.2 ppm).

**(±)-65 (4-substituted isomer)** as a white solid: mp 110-111 °C; $\nu_{max}$ $cm^{-1}$ (ATR) 3159, 1715, 1614; $^1H$ NMR (300 MHz, $CDCl_3$) $\delta$ 7.52 (1H, br s, N*H*), 7.27-7.24 (1H, m, Ar*H*), 7.12 (1H, t, *J* = 7.8, Ar*H*), 7.06-7.00 (3H, m, Ar*H*), 6.98-6.95 (2H, m, Ar*H*), 6.91-6.81 (3H, m, Ar*H*), 6.59 (1H, dd, *J* = 7.8, 0.9, Ar*H*), 3.83 (1H, d, *J* = 5.5, C$H_a$$H_b$Ph), 3.79 (3H, s, O*Me*), 3.78 (1H, d, *J* = 5.5, CH$_a$$H_b$Ph); $^{13}C$ NMR (125 MHz, $CDCl_3$) $\delta$ 178.3 (*C*=O), 159.8 (Ar*C*OMe), 142.4 (4$^{ry}$ Ar*C*), 138.9 (4$^{ry}$ Ar*C*), 137.7 (4$^{ry}$ Ar*C*), 133.6 (4$^{ry}$ Ar*C*), 131.8 (Ar*C*), 130.0 (Ar*C*), 129.7 (Ar*C*), 129.6 (Ar*C*), 129.6 (Ar*C*), 129.1 (Ar*C*), 127.9 (Ar*C*), 127.0 (Ar*C*), 123.8 (Ar*C*), 119.2 (Ar*C*), 113.6 (Ar*C*), 112.5 (Ar*C*), 108.2 (Ar*C*(7)), 59.6 (*C*(3)), 55.3 (O*Me*), 38.2 (*C*H$_2$); *m/z* (EI$^+$) 398 ([M($^{35}Cl^{35}Cl$)+H]$^+$, 100%); HRMS (EI$^+$) $C_{22}H_{18}O_2N^{35}Cl_2$ ([M+H]$^+$) found 398.0709 requires 398.0709 (+ 0.0 ppm).

**(*S*)-6-Chloro-3-(3-chlorobenzyl)-3-(3-methoxyphenyl)indolin-2-one 1 &**

**(*S*)-4-Chloro-3-(3-chlorobenzyl)-3-(3-methoxyphenyl)indolin-2-one 65**

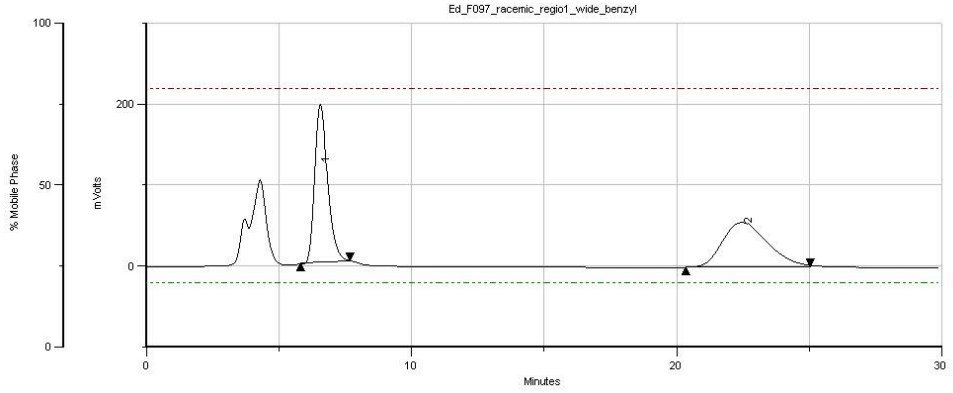


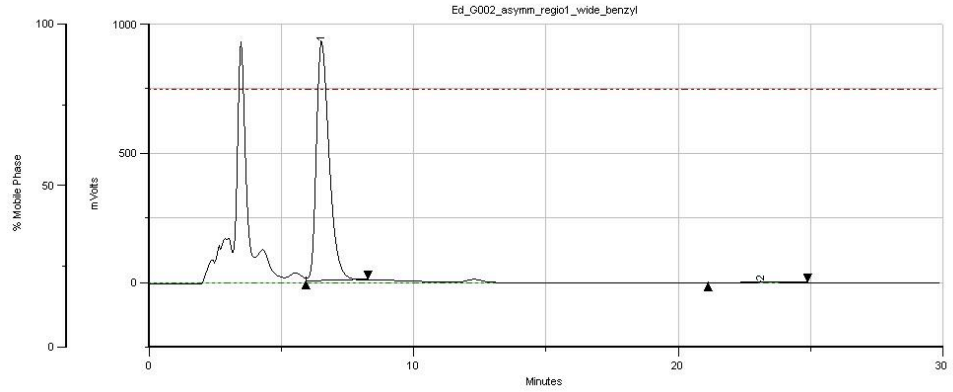

To a stirred solution of acid chloride **63** (0.800 g, 2.59 mmol) in $Et_2O$ (15 mL) at 0 °C was added *N,N*-dimethylethylamine (0.294 mL, 1.05 eq,

2.72 mmol) dropwise over 15 min and the reaction mixture stirred at 0 °C for 16 h. After this time, the reaction mixture was allowed to warm to rt before being filtered under nitrogen to remove the amine hydrochloride salts and then concentrated *in vacuo*. The resulting orange liquid (assumed as a 50% yield of ketene with respect to the acid chloride starting material) was then re-suspended in THF (6 mL) under nitrogen and cooled to -78 °C. A solution of nitrone **48** (0.575 g, 1.10 mmol) in THF (10 mL) was then added slowly over 15 min and the reaction mixture stirred at -78 °C for 4 h. The reaction was then quenched with aq. 8M HCl (3 mL) and stirred for 2 h allowing to warm to rt. The reaction mixture was then partitioned between $Et_2O$ (30 mL) and $H_2O$ (20 mL), the layers separated and the aqueous layer extracted once more with $Et_2O$ (30 mL). The combined organic layers were then washed with $NaHCO_3$ (2 x 20 mL), brine (25 mL), dried over $MgSO_4$, filtered and concentrated *in vacuo* to yield a crude viscous yellow oil which was purified *via* column chromatography over silica to yield a mixture of both regioisomeric products. A second column chromatography of 0.124 g of this material over silica (10% $Et_2O$ in toluene) gave (*S*)-**1** (0.064 g, 52%) and (*S*)-**65** (0.045 g, 36%).

**1 as an off-white foam (6-substituted isomer)** HPLC analysis: 96% e.e. (Daicel Chiralcel OD-H column, eluent: hexane/*i*-PrOH 80:20, flow 1.5 mL/min, wavelength: 254 nm, retention times: 6.5 min (major) and 23.0 min (minor)); $[\alpha]_D^{20}$ -22.8° (*c* = 0.45, $CHCl_3$).



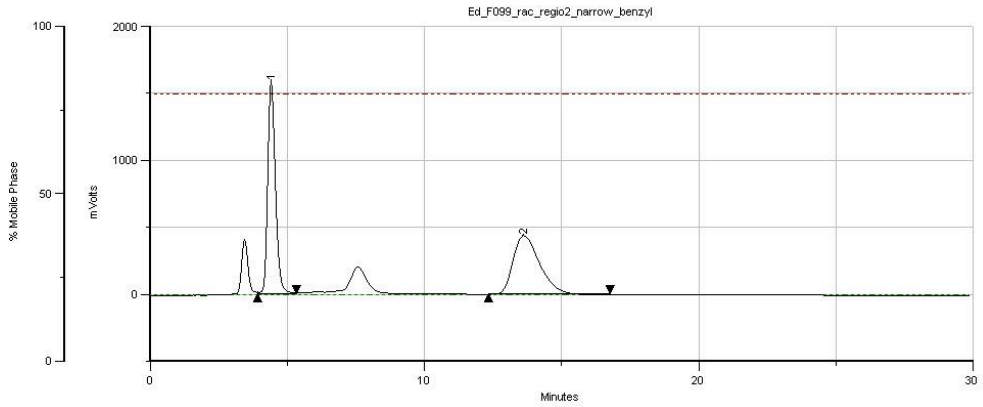

| Peak | $t_R$ (min) | Area (%) |
|---|---|---|
| 1 | 6.55 | 50.28 |
| 2 | 22.45 | 49.72 |



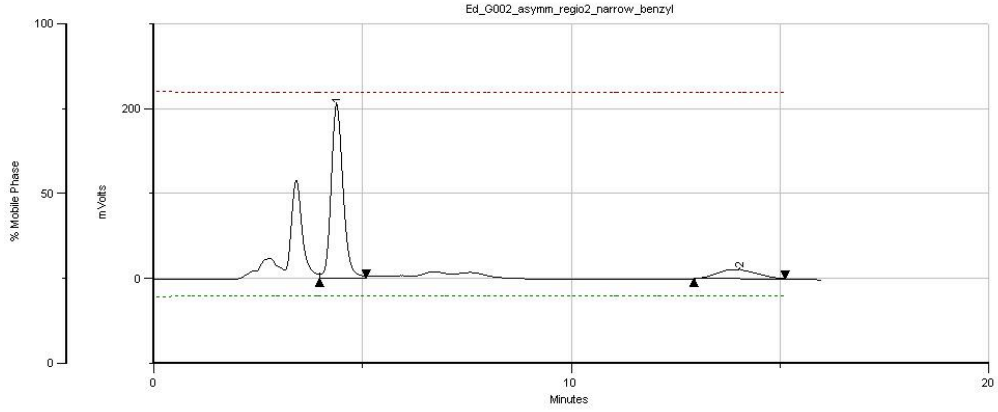

| Peak | $t_R$ (min) | Area (%) |
|---|---|---|
| 1 | 6.51 | 97.73 |
| 2 | 23.12 | 2.27 |

The assigned absolute configuration of (*S*)-**1** is consistent with the chiral HPLC analysis performed by Kuendig and co-workers on the *(R)*-enantiomer, which exhibits the *opposite* major/minor arrangement of peaks: HPLC analysis: 96% e.e. (Daicel Chiralcel OD-H column, eluent: hexane/*i*-PrOH 70:30, flow 1.0 mL/min, wavelength: 254 nm, retention times: 7.0 min (minor) and 23.9 min (major)). See reference [43] for further details.

**65 as a pale-yellow oil (4-substituted isomer)** HPLC analysis: 65% e.e. (Daicel Chiralcel OD-H column, eluent: hexane/*i*-PrOH 80:20, flow 1.5 mL/min, wavelength: 254 nm, retention times: 4.4 min (major) and 13.6 min (minor)); $[\alpha]_D^{20}$ -39.3° (*c* = 0.58, $CHCl_3$).




| Peak | $t_R$ (min) | Area (%) |
|---|---|---|
| 1 | 4.40 | 51.61 |
| 2 | 13.62 | 48.39 |




| Peak | $t_R$ (min) | Area (%) |
|---|---|---|
| 1 | 4.38 | 82.52 |
| 2 | 13.92 | 17.48 |

**10. References**

1. a) Douglas, J.; Taylor, J. E.; Churchill, G.; Slawin, A. M. Z.; Smith, A. D. *J. Org. Chem.* **2013,** *78,* 3925-3938. b) Houdous B. L.; Fu G. C. *J. Am. Chem. Soc.* **2002**, *124*, 1578-1579. c) Baigrie L. M.; Seiklay H. R.; Tidwell T. T. *J. Am. Chem. Soc.* **1985**, *107*, 5391-5396. d) Pracejus H.; Wallura G. *J. Prakt. Chem.* **1963**, *19*, 33-38. e) Sudo, A.; Uchino, S.; Endo, T. *J. Polym. Sci. Part A: Polym. Chem.* **2001**, *39*, 2093-2102.

2. Maresh, J.; Zhang, J.; Tzeng, Y-L.; Goodman, N. A.; Lynn, D. G. *Bioorg. Med. Chem. Lett.* **2007**, *17*, 3281-3286.

3. Bamberger, R. *Justus Liebigs Ann.* **1901**, *316*, 279-280.

4. Patrick, T. B.; Schield, J. A.; Kirchner, D. G. *J. Org. Chem.* **1974**, *39*, 1758-1761.

5. Liu, S.; Wang, Y.; Jiang, J.; Jin, Z. *Green Chem.* **2009**, *11*, 1397-1400.

6. Peltier, G. *Bull. Soc. Chim. Fr.* **1969**, 264-269.

7. Cheng, S. *J. Org. Chem.* **1974**, *39*, 2835-2837.

8. Andrade, M. M.; Barros, M. T.; Pinto, R.C. *Tetrahedron*, **2008**, *64*, 10521-10530.

9. Sadownik, J. W.; Philp, D. *Angew. Chem., Int. Ed.* **2008**, *47,* 9965-9970.

10. Nelson, D. W.; Owens, J.; Hiraldo, D. *J. Org. Chem.* **2001**, *66*, 2572-2582.

11. DellaColetta, B. A.; Frye, J. G.; Youngless, T. L.; Ziegler, J. P.; Landolt, R. G. *J. Org. Chem.* **1977**, *42*, 3057-3059.

12. Suda, K.; Tsujimoto, T.; Yamauchi, M. *Bull. Chem. Soc. Jap.* **1987**, *10*, 3607-3612.

13. Duguet, N.; Slawin, A. M. Z.; Smith, A. D. *Org. Lett.* **2009**, *11*, 3858-3861.

14. Beckmann, E. *Liebigs Ann.* **1909**, *367*, 273-279.

15. Shi, B.; Merten, S.; Wong, D. K. Y.; Chu, J. C. K.; Liu, L. L.; Lam, S. K.; Jäger, A.; Wong, W.-T.; Chiu, P.; Metz, P. *Adv. Synth. Catal.* **2009**, *351*, 3128-3132.

16. Marshal, J. A.; Shiping, X. *J. Org. Chem.* **1995**, *60,* 7230-7237.

17. Cainelli, G.; Panunzio, M.; Bandini, E.; MartelIi, G.; Spunta, G. *Tetrahedron* **1996**, *52*, 1685-1698.

18. Overman, L. E.; Bell, K. L.; Ito, F. *J. Am. Chem. Soc.* **1984**, *106,* 4192-4201.

19. Chiacchio, U.; Corsaro, A.; Gumina, G.; Rescifina, A.; Iannazzo, D.; Piperno, A.; Romeo, G.; Romeo, R. *J. Org. Chem.* **1999**, *64*, 9321-9327.

20. Purdie, I.; Irvine, J. C. *J. Chem. Soc.* **1899**, *75,* 483-493.

21. Tanaka, K., *J. Org. Chem.* **1990**, *55,* 181-185.

22. Huang, X.; Ying, J. Y. *Chem. Comm.* **2007**, *18*, 1825-1827.

23. Kobayashi, Y.; Takemoto, Y.; Ito, Y.; Terashima, S. *Tetrahedron Lett.* **1990**, *31*, 3031-3034.

24. Kobayashi, Y.; Takemoto, Y.; Kamijo, T.; Harada, H.; Ito, Y.; Terashima, S. *Tetrahedron* **1992**, *48*, 1853-1868.

25. Coulbeck, E.; Eames, J. *Tetrahedron: Asymmetry* **2007**, *18*, 2313-2325.

26. Schloemer, G. C. *EP 81993 A2*, **1983**.

27. Gallos, J. K.; Stathakis, C. I.; Kotoulas, S. S.; Koumbis, A. E. *J. Org. Chem.* **2005**, *70*, 6884-6890.

28. O'Brien, P.; R. Powell, H.; R. Raithby, P.; Warren, S. *J. Chem. Soc., Perkin Trans. 1* **1997**, 1031-1040.

29. Wu, J.; Gao, S.; Liao, G.; Lin, H.; Nie, A. *Synthetic Commun*. **2012**, *42*, 2907-2916.

30. Ng, J. S.; Przybyla, C. A.; Liu, C.; Yen, J. C.; Muellner, F. W.; Weyker, C. L. *Tetrahedron* **1995**, *51*, 6397-6410.

31. Fenster, E.; Fehl, C.; Aubé, J. *Org. Lett.* **2011**, *13*, 2614-2617.

32. Baldwin, J. E.; Spivey, A. C.; Schofield, C. J.; Sweeney, J. B. *Tetrahedron* **1993**, *49*, 6309-6330.

33. Donohoe, T. J.; Wheelhouse, K. M. P.; Lindsay-Scott, P. J.; Glossop, P. A.; Nash, I. A.; Parker, J. S. *Angew. Chem., Int. Ed.* **2008**, *47*, 2872-2875.

34. Barco, A.; Benetti, S.; Casolari, A.; Pollini, G. P.; Spalluto, G. *Tetrahedron Lett.* **1990**, *31*, 4917-4920.

35. Künzle, F.; Schmutz, J. *Helv. Chim. Acta* **1970**, *53*, 798-804.

36. Zhou, F.; Cao, Z-Y.; Zhang, J.; Yang, H-B.; Zhou, J. *Chem.-Asian J.* **2012**, *7*, 233-241.

37. Alvarez, R. G.; Hunter, I. S.; Suckling, C. J.; Thomas, M.; Vitinius, U. *Tetrahedron* **2001**, *57*, 8581-8587.

38. Galzerano, P.; Bencivenni, G.; Pesciaioli, F.; Mazzanti, A.; Giannichi, B.; Sambri, L.; Bartoli, G.; Melchiorre, P. *Chem. Eur. J.* **2009**, *15*, 7846-7849.

39. Li, C. Y.; Zhu, B-H.; Ye, L-W.; Jing, Q.; Sun, X-L.; Tang, Y.; Shen, Q. *Tetrahedron*, **2007**, *63*, 8046-8053.

40. Schmittel, M.; Seggern, H. *J. Am. Chem. Soc.* **1993**, *115*, 2165-2177.

41. Heine, H. W.; Zibuck, R.; VandenHeuvel, W. J. A. *J. Am. Chem. Soc.* **1982**, *104*, 3691-3694.

42. Newcomb, M.; Reeder, R. A. *J. Org. Chem.* **1980**, *45*, 1489-1493.

43. Katayev, D.; Kuendig, E. P. *Helv. Chim. Acta* **2012**, *95,* 2287-2295.