Open flask and scaleable catalytic asymmetric α-amination of carboxylic acids using isothioureas at low catalyst loadings

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SUPPORTING INFORMATION

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Appendix I: ¹H and ¹³C NMR Spectra for Novel Compounds and HPLC data
1.1 General Information

Reactions involving moisture sensitive reagents were carried out under an argon atmosphere using standard vacuum line techniques in addition to freshly distilled solvents. All glassware used was flame dried and cooled under vacuum.

Solvents (THF, CH₂Cl₂, toluene, hexane and Et₂O) were obtained anhydrous and purified by an alumina column (Mbraun SPS-800). Petrol is defined as petroleum ether 40-60 °C. 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 CO₂(s)/acetone baths respectively. Temperatures of 0 °C to -50 °C for overnight reactions were obtained using an immersion cooler (HAAKE EK 90). Reflux conditions were obtained using an oil bath equipped with 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.

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 KMnO₄ solution. Flash column chromatography was performed on Kieselgel 60 silica in the solvent system stated.

¹H and ¹³C nuclear magnetic resonance (NMR) spectra were acquired on either a Bruker Avance 300 (300 MHz, ¹H, 75 MHz ¹³C), Bruker Avance II 400 (400 MHz, ¹H, 100 MHz ¹³C) or a Bruker Avance II 400 (500 MHz, ¹H, 125 MHz ¹³C) 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. Multiplicities are indicated by: s (singlet), d (doublet), t (triplet), q (quartet), ABq (AB quartet), sept (septet), oct (octet), m (multiplet), dd (doublet of doublets), ddd (doublet of doublet of doublets), dt (doublet of triplets) and td (triplet of doublets). The abbreviation Ar is used to denote aromatic, br to denote broad and app. to denote apparent.

Infrared spectra (ν max) were recorded on a Perkin-Elmer Spectrum GX FT-IR spectrometer using either thin films on NaCl plates or KBr discs. Only the characteristic peaks are quoted. Melting points were recorded on an Electrothermal apparatus and are uncorrected.

HPLC analyses were obtained on two separate machines; 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 while the temperature was assumed to be 20 °C; a Shimadzu HPLC consisting of a DGU-20A5 degasser, LC-20AT liquid chromatograph, SIL-20AHT autosampler, CMB-20A communications bus module, SPD-M20A diode array detector and a CTO-20A column oven which allowed the temperature to be set from 25-40
°C. Separation was achieved using Chiralcel OD-H and OJ-H columns or Chiralpak AD-H, AS-H, IA, IB, IC and ID columns.

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.

1.2 General Experimental Procedures

General procedure A: Cu(I) mediated N-arylation.

To a flask under inert atmosphere was charged the requisite aryl iodide, copper iodide, 1,10-phenanthroline, cesium carbonate, benzyl carbazate and anhydrous dimethyl formamide and the reaction mixture was heated at 80 °C for 1 h. Once cool the reaction mixture was filtered and concentrated in vacuo to give the crude reaction mixture.

General procedure B: Hydrazine acylation.

Following the procedure outlined by Bowman et al.,1 to a solution of requisite hydrazine and triethylamine in Et2O at 0 °C was added the requisite acid chloride dropwise. The reaction mixture was stirred at 0 °C for 30 minutes before being filtered. The residue was washed with water and recrystallised from ethanol to give the hydrazide.

General procedure C: Diazene formation.

Following the procedure outlined by Bowman et al.,1 to a solution of requisite hydrazide and pyridine in CH2Cl2 at -78 °C was added N-bromosuccinimide portion wise. The reaction mixture was warmed to rt and stirred for 30 minutes before being filtered. The filtrate was concentrated in vacuo and the resulting solid was triturated with Et2O. The mixture was filtered and the filtrate was washed with 1M HCl followed by sat. aq. NaHCO3. The organic layer was dried (MgSO4), filtered and concentrated in vacuo to give the crude reaction mixture.

General procedure D: Michael addition-lactonization (racemic).

To a solution of requisite acid in DCM were added DIPEA and either benzoyl chloride or p-methoxybenzoyl chloride at rt. The reaction mixture was allowed to stir at rt for 20 minutes.
The requisite Michael acceptor, Lewis base (1-20 mol%), and DIPEA were then added in that order at the required temperature. The reaction mixture was stirred at the required temperature until complete by TLC and was subsequently quenched by addition of 1M HCl. Once warmed to rt, the reaction mixture was poured into water and extracted twice with CH₂Cl₂. The combined organics were dried (MgSO₄), filtered and concentrated in vacuo to give the crude reaction mixture.

**General procedure E: Michael addition-lactonization (asymmetric).**

To a solution of requisite acid in DCM were added DIPEA and either benzoyl chloride or p-methoxybenzoyl chloride at rt. The reaction mixture was allowed to stir at rt for 20 minutes. The requisite Lewis base (1-20 mol%), Michael acceptor and DIPEA were then added in that order at the required temperature. The reaction mixture was stirred at the required temperature until complete by TLC and was subsequently quenched by addition of 1M HCl. Once warmed to rt, the reaction mixture was poured into water and extracted twice with CH₂Cl₂. The combined organics were dried (MgSO₄), filtered and concentrated in vacuo to give the crude reaction mixture.

**General procedure F: Samarium iodide N-N bond cleavage.**

To a solution of starting material in MeOH was added 0.1M SmI₂ and the reaction mixture was allowed to stir at -78 °C for 10 minutes. The reaction mixture was poured into sat. aq. NaHCO₃ and extracted twice with ethyl acetate. The combined organics were dried (MgSO₄), filtered and concentrated in vacuo to give the crude reaction mixture.

1.3 Experimental Procedures

**benzyl 1-(4-(trifluoromethyl)phenyl)hydrazinecarboxylate**

Following general procedure A 4-iodobenzotrifluoride (1.08 mL, 7.35 mmol), copper iodide (140 mg, 0.74 mmol), 1,10-phenanthroline (265 mg, 1.47 mmol), cesium carbonate (3.35 g, 10.3 mmol), benzyl carbazate (1.46 g, 8.82 mmol) and anhydrous dimethyl formamide (10 mL) gave, after chromatographic purification (eluent Et₂O:petrol 25:75), amine 46 as a white solid (1.02 g, 45%); mp 62-64 °C; νmax (KBr) 3367 (N-H), 2956 (C-H), 1684 (C=O), 1616, 1512; δH (500 MHz, CDCl₃) 4.52 (2H, s, NH₂), 5.29 (2H, s, CH₂), 7.38-7.41 (5H, m,
ArH), 7.58 (2H, d, J 8.7, ArH), 7.74 (2H, d, J 7.8, ArH); δ_C (125 MHz, CDCl₃) 68.7 (CH₃), 122.4 (ArC), 124.2 (q, J 270, CF₃), 125.5 (q, J 3.5, ArC), 126.3 (q, J 32.1, 4ry ArC), 128.4 (ArC), 128.6 (ArC), 153.5 (4ry ArC), 145.6 (4ry ArC), 155.5 (C=O); m/z (Cl⁺) 311 ([M+H]⁺, 100%); HRMS (Cl⁺) C₁₅H₁₄F₃N₂O₂⁺ ([M+H]⁺) requires 311.1002; found 311.1005 (+1.0 ppm).

**benzyl 1-(4-methoxyphenyl)hydrazinecarboxylate**

![Chemical Structure](Image)

Following general procedure A, 4-idoanisole (10.0 g, 42.7 mmol), copper iodide (0.81 g, 4.27 mmol), 1,10-phenanthroline (1.54 g, 8.55 mmol), cesium carbonate (19.5 g, 59.8 mmol), benzyl carbazole (8.51 g, 51.3 mmol) and anhydrous dimethyl formamide (45 mL) gave, after chromatographic purification (eluent Et₂O:petrol 50:50), amine 47 as a yellow solid (11.2 g, 96%); mp 69-71 °C; {lit.⁷ mp 74-75 °C}; δ_H (300 MHz, CDCl₃) 3.73 (3H, s, CH₃), 4.30 (2H, br s, NH₂), 5.13 (2H, s, CH₂), 6.77-6.80 (2H, m, ArH), 7.23-7.29 (7H, m, ArH).

**N’-phenylbenzohydrazide**

![Chemical Structure](Image)

Following general procedure B, phenylhydrazine (1.82 mL, 18.5 mmol), triethylamine (2.58 mL, 18.5 mmol) and benzoil chloride (2.18 mL, 15.6 mmol) in Et₂O (35 mL) gave, after recrystallisation from ethanol, hydrazide 48 as a white solid (1.60 g, 45%); mp 163-165 °C; {lit.¹ mp 171-172 °C}; δ_H (400 MHz, CDCl₃) 6.30 (1H, br s, NH), 6.84-6.86 (3H, m, ArH), 7.15-7.19 (2H, m, ArH), 7.40 (2H, t, J 7.6, ArH), 7.49 (1H, t, J 7.4, ArH), 7.77 (2H, d, J 7.4, ArH), 7.94 (1H, br s, NH).

**4-fluoro-N’-phenylbenzohydrazide**

![Chemical Structure](Image)

Following general procedure B, phenylhydrazine (0.55 mL, 5.59 mmol), triethylamine (0.78 mL, 5.59 mmol) and 4-fluorobenzoyl chloride (0.60 mL, 5.08 mmol) in Et₂O (20 mL) gave, after recrystallisation from ethanol, hydrazide 49 as a white solid (378 mg, 32%); mp 171-
173 °C; {lit.¹ mp 177-179 °C}; δ_H (300 MHz, CDCl₃) 6.35 (1H, d, J 3.5, NH), 6.96-7.00 (3H, m, ArH), 7.20 (2H, t, J 8.6, ArH), 7.27-7.33 (2H, m, ArH), 7.85-7.93 (3H, m, ArH and NH).

4-fluoro-N'-phenylbenzohydrazide

Following general procedure B, phenylhydrazine (0.91 mL, 9.25 mmol), triethylamine (1.29 mL, 9.25 mmol) and 3-fluorobenzoyl chloride (1.01 mL, 8.41 mmol) in Et₂O (20 mL) gave, after recrystallisation from ethanol, hydrazide 50 as a white solid (654 mg, 34%); mp 120-122 °C; ν_max (KBr) 3251 (N-H), 3026 (C-H), 1646 (C=O), 1588, 1551; δ_H (300 MHz, CD₃OD) 6.79-6.88 (3H, m, ArH), 7.16-7.22 (2H, m, ArH), 7.29-7.35 (1H, m, ArH), 7.51 (1H, td, J 8.0, 5.7, ArH), 7.62 (1H, dt, J 9.6, 2.0, ArH), 7.71-7.74 (1H, m, ArH); δ_C (75 MHz, CD₃OD) 114.3 (ArC), 115.5 (d, J 30.9, ArC), 119.9 (d, J 28.5, ArC), 121.3 (ArC), 124.3 (d, J 3.9, ArC), 130.0 (ArC), 131.8 (d, J 10.6, ArC), 136.5 (d, J 9.2, 4ry ArC), 150.0 (4ry ArC), 164.2 (d, J 326, 4ry ArC), 168.8 (C=O); m/z (NSI⁺) 231 ([M+H]⁺, 100%); HRMS (NSI⁺) C₁₃H₁₂FN₂O⁺ ([M+H]⁺) requires 231.0928; found 231.0930 (+0.8 ppm).

4-fluoro-N'-phenylbenzohydrazide

Following general procedure B, phenylhydrazine (0.91 mL, 9.25 mmol), triethylamine (1.29 mL, 9.25 mmol) and 2-fluorobenzoyl chloride (1.01 mL, 8.41 mmol) in Et₂O (20 mL) gave, after recrystallisation from ethanol, hydrazide 51 as a white solid (1.07 mg, 55%); mp 107-109 °C; ν_max (KBr) 3272 (N-H), 3024 (C-H), 1639 (C=O), 1546, 1499; δ_H (400 MHz, CD₃OD) 6.80-6.84 (1H, m, ArH), 6.91 (2H, m, ArH), 7.18-7.31 (4H, m, ArH), 7.53-7.58 (1H, m, ArH), 7.72-7.76 (1H, m, ArH); δ_C (75 MHz, CD₃OD) 114.3 (ArC), 117.3 (d, J 29.9, ArC), 121.3 (ArC), 123.1 (d, J 19.7, 4ry ArC), 125.8 (d, J 4.6, ArC), 130.1 (ArC), 131.5 (d, J 3.3, ArC), 134.5 (d, J 11.4, ArC), 149.9 (4ry ArC), 161.4 (d, J 331, 4ry ArC), 167.2 (C=O); m/z (NSI⁺) 231 ([M+H]⁺, 100%); HRMS (NSI⁺) C₁₃H₁₂FN₂O⁺ ([M+H]⁺) requires 231.0928; found 231.0930 (+0.8 ppm).
4-bromo-N'-phenylbenzohydrazide

Following general procedure B, phenylhydrazine (0.91 mL, 9.25 mmol), triethylamine (1.29 mL, 9.25 mmol) and 4-bromobenzoyl chloride (1.85 g, 8.41 mmol) in Et₂O (20 mL) gave, after recrystallisation from ethanol, hydazide 52 as a white solid (828 mg, 34%); mp 196-198 °C; \{lit.\(^1\) mp 198-199 °C\}; \(\delta_H\) (400 MHz, CDCl\(_3\)) 6.35 (1H, d, J 3.4, NH), 6.94-6.98 (3H, m, Ar\(H\)), 7.26-7.30 (2H, m, Ar\(H\)), 7.65 (2H, d, J 8.5 Ar\(H\)), 7.74 (2H, d, J 8.5, Ar\(H\)), 7.96 (1H, br s, NH).

4-chloro-N'-phenylbenzohydrazide

Following general procedure B, phenylhydrazine (0.91 mL, 9.25 mmol), triethylamine (1.29 mL, 9.25 mmol) and 4-chlorobenzoyl chloride (1.08 mL, 8.41 mmol) in Et₂O (20 mL) gave, after recrystallisation from ethanol, hydazide 53 as a white solid (1.17 g, 56%); mp 166-168 °C; \{lit.\(^1\) mp 193-195 °C\}; \(\delta_H\) (400 MHz, CDCl\(_3\)) 6.35 (1H, d, J 3.5, NH), 6.94-6.99 (3H, m, Ar\(H\)), 7.27-7.31 (2H, m, Ar\(H\)), 7.49 (2H, d, J 8.5 Ar\(H\)), 7.82 (2H, d, J 8.5, Ar\(H\)), 7.93 (1H, br s, NH).

N'-phenyl-1-naphthohydrazide

Following general procedure B, phenylhydrazine (0.91 mL, 9.25 mmol), triethylamine (1.29 mL, 9.25 mmol) and 1-naphthoyl chloride (1.27 mL, 8.41 mmol) in Et₂O (20 mL) gave, after recrystallisation from ethanol, hydazide 54 as a white solid (740 mg, 34%); mp 194-196 °C; \{lit.\(^5\) mp 240 °C\}; \(\delta_H\) (300 MHz, CDCl\(_3\)) 6.52 (1H, d, J 4.3, NH), 6.99-7.05 (3H, m, Ar\(H\)), 7.32-7.37 (2H, m, Ar\(H\)), 7.52-7.64 (3H, m, Ar\(H\)), 7.77-7.79 (2H, m, Ar\(H\)), 7.92-7.96 (1H, m, Ar\(H\)), 8.03 (1H, d, J 8.3, Ar\(H\)), 8.36-8.39 (1H, m, NH).
4-nitro-N'-phenylbenzohydrazide

Following general procedure B, phenylhydrazine (1.82 mL, 18.5 mmol), triethylamine (2.58 mL, 16.8 mmol) and 4-nitrobenzoyl chloride (3.12 g, 16.8 mmol) in Et2O (35 mL) gave, after recrystallisation from ethanol, hydrazide 55 as an orange solid (2.06 g, 48%); mp 198-200 °C; \{lit.\} \(\text{mp } 206 \, ^\circ\text{C}\}; \delta_{\text{H}} (400 \text{ MHz, CDCl}_3) 6.37 (1H, d, J 3.0, NH), 6.96-7.00 (3H, m, \text{ArH}), 7.31-7.33 (2H, m, \text{ArH}), 8.01-8.06 (3H, m, \text{ArH and NH}), 8.38 (2H, d, J 8.8, \text{ArH}).

4-methyl-N'-phenylbenzohydrazide

Following general procedure B, phenylhydrazine (0.91 mL, 9.25 mmol), triethylamine (1.29 mL, 9.25 mmol) and p-toluoyl chloride (1.11 mL, 8.41 mmol) in Et2O (20 mL) gave, after recrystallisation from ethanol, hydrazide 56 as a white solid (0.83 g, 44%); mp 166-167 °C; \{lit.\} \(\text{mp } 172 \, ^\circ\text{C}\}; \delta_{\text{H}} (300 \text{ MHz, CDCl}_3) 2.36 (3H, s, CH₃), 6.26 (1H, d, J 3.5, NH), 6.87 (2H, d, J 8.2, \text{ArH}), 7.15-7.22 (5H, m, \text{ArH}), 7.68 (2H, d, J 8.2, \text{ArH}), 7.76 (1H, br s, NH).

N'-phenylfuran-2-carbohydrazide

Following general procedure B, phenylhydrazine (0.91 mL, 9.25 mmol), triethylamine (1.29 mL, 9.25 mmol) and 2-furoyl chloride (0.83 mL, 8.41 mmol) in Et2O (20 mL) gave, after recrystallisation from ethanol, hydrazide 57 as a white solid (0.80 g, 47%); mp 141-142 °C; \{lit.\} \(\text{mp } 144-145 \, ^\circ\text{C}\}; \delta_{\text{H}} (300 \text{ MHz, CDCl}_3) 6.24 (1H, br s, NH), 6.60 (1H, dd, J 3.5, 1.7, \text{ArH}), 6.94-6.98 (3H, m, \text{ArH}), 7.24-7.35 (3H, m, \text{ArH}), 7.56 (1H, d, J 1.0, \text{ArH}), 8.10 (1H, br s, NH).
N’-(4-methoxyphenyl)-4-(trifluoromethyl)benzohydrazide

\[
\begin{align*}
\text{47} & \quad \text{MeO} \quad \text{BnO} \quad \text{N} \quad \text{H} \\
\rightarrow & \quad \text{MeO} \quad \text{BnO} \quad \text{N} \quad \text{H} \\
\text{58} & \quad \text{MeO} \quad \text{BnO} \quad \text{N} \quad \text{H} \\
\rightarrow & \quad \text{MeO} \quad \text{BnO} \quad \text{N} \quad \text{H}
\end{align*}
\]

To a solution of 47 (11.1 g, 40.8 mmol) and triethylamine (6.25 mL, 44.9 mmol) in EtOAc (100 mL) at 0 °C was added 4-trifluoromethylbenzoyl chloride (6.06 mL, 40.8 mmol). The reaction mixture was stirred at rt for 1 h. The reaction mixture was washed with 1M HCl and sat. aq. NaHCO₃. The organic layer was dried (MgSO₄), filtered and concentrated in vacuo to give the crude acylated product 58 which was used without purification. To a solution of crude acylated product 58 (17.7 g, 40.8 mmol assuming 100% conversion) and 10% palladium on charcoal (4.27 g, 4.08 mmol, 10 mol%) in EtOAc (100 mL) was appended a balloon of hydrogen gas. The hydrogen gas was allowed to bubble through the reaction mixture at rt for 4 h. The reaction mixture was filtered through celite and concentrated in vacuo. Recrystallisation from ethanol gave hydrazide 59 as a white solid (7.95 g, 63% over 2 steps); mp 158-160 °C; ν max (KBr) 3270 (N-H), 3068 (C-H), 1649 (C=O), 1551, 1510; δH (300 MHz, (CH₃)₂S=O) 3.67 (3H, s, CH₃), 6.79 (4H, s, ArH), 7.69 (1H, d, J 2.5, NH), 7.89 (2H, d, J 8.2, ArH), 8.11 (2H, d, J 8.1, ArH), 10.6 (1H, d, J 2.2, NH); δc (75 MHz, (CH₃)₂S=O) 55.2 (CH₃), 113.9 (ArC), 114.3 (ArC), 123.9 (q, J 271, CF₃), 125.5 (q, J 3.7, ArC), 128.2 (ArC), 131.4 (q, J 31.7, 4ry ArC), 136.9 (4ry ArC), 143.0 (4ry ArC), 152.8 (4ry ArC), 165.1 (C=O); m/z (NSI⁻) 311 ([M+H]+, 100%); HRMS (NSI⁻) C₁₅H₁₄F₃N₂O₂⁻ ([M+H]+) requires 311.1002; found 311.1005 (+1.0 ppm).

(E)-phenyl(phenyldiazemyl)methanone

\[
\begin{align*}
\text{60} & \quad \text{Ph} \quad \text{N} \quad \text{N} \quad \text{Ph}
\end{align*}
\]

Following general procedure C, hydrazide 48 (1.5 g, 7.08 mmol), pyridine (0.63 mL, 7.79 mmol) and N-bromosuccinimide (1.26 g, 7.08 mmol) in CH₂Cl₂ (7 mL) gave, after chromatographic purification (eluent Et₂O:petrol 20:80), diazene 60 as a red oil (1.17 g, 79%); δH (400 MHz, CDCl₃) 7.43-7.63 (6H, m, ArH), 7.91-8.02 (4H, m, ArH).

(E)-((4-fluorophenyl)diazemyl)(phenyl)methanone

\[
\begin{align*}
\text{61} & \quad \text{F} \quad \text{NH}_2\text{HCl} \quad \rightarrow \quad \text{F} \quad \text{NH} \quad \text{Ph} \\
\rightarrow & \quad \text{F} \quad \text{NH} \quad \text{Ph} \\
\text{62} & \quad \text{F} \quad \text{NH} \quad \text{Ph} \\
\rightarrow & \quad \text{F} \quad \text{NH} \quad \text{Ph}
\end{align*}
\]

S9
To a solution of 4-fluorophenylhydrazine hydrochloride 61 (2.00 g, 12.3 mmol) and triethylamine (3.43 mL, 24.6 mmol) in EtO (30 mL) at 0 °C was slowly added benzoyl chloride (1.29 mL, 11.2 mmol). After stirring at rt for 30 minutes the reaction mixture was concentration in vacuo. The solid was dissolved in CH₂Cl₂ and washed with 1M HCl. The organic layer was dried (MgSO₄), filtered and concentrated in vacuo to give a crude hydrazide 62 which was used without purification. Following general procedure C, hydrazide 62 (2.57 g, 11.2 mmol assuming 100% conversion), pyridine (1.07 mL, 12.3 mmol) and N-bromosuccinimide (1.98 g, 11.2 mmol) in CH₂Cl₂ (15 mL) gave, after chromatographic purification (eluent EtO:petrol 20:80), diazene 63 as a red solid (545 mg, 21% over 2 steps); mp 48-50 °C; νmax (KBr) 3067 (C-H), 1702 (C=O), 1591, 1503; δH (300 MHz, CDCl₃) 7.26-7.32 (2H, m, ArH), 7.54-7.60 (2H, m, ArH), 7.68-7.74 (1H, m, ArH), 8.06-8.12 (4H, m, ArH); δC (75 MHz, CDCl₃) 116.5 (d, J 23.0, ArC), 126.0 (d, J 9.5, ArC), 128.9 (ArC), 130.6 (ArC), 130.9 (4ry ArC), 134.6 (ArC), 148.7 (d, 2.9, 4ry ArC), 165.9 (d, J 254, 4ry ArC), 181.7 (C=O); m/z (ES⁺) 251 ([M+Na]⁺, 100%); HRMS (ES⁺) C₁₃H₉FN₂NaO⁺ ([M+Na]⁺) requires 251.0597; found 251.0590 (-2.5 ppm).

**(E)-(4-fluorophenyl)(phenyldiazenyl)methanone**

![Chemical structure of 64](image)

Following general procedure C, hydrazide 49 (370 mg, 1.61 mmol), pyridine (0.14 mL, 1.77 mmol) and N-bromosuccinimide (0.29 g, 1.61 mmol) in CH₂Cl₂ (5 mL) gave, after chromatographic purification (eluent EtO:petrol 20:80), diazene 64 as a red oil (280 mg, 76%); νmax (thin film) 3068 (C-H), 1707 (C=O), 1597, 1507; δH (400 MHz, CDCl₃) 7.20-7.26 (2H, m, ArH), 7.58-7.67 (3H, m, ArH), 8.02-8.05 (2H, m, ArH), 8.12-8.17 (2H, m, ArH); δC (100 MHz, CDCl₃) 116.3 (d, J 21.9, ArC), 123.7 (ArC), 127.4 (d, J 2.7, 4ry ArC), 129.4 (ArC), 133.4 (d, J 9.7, ArC), 135.7 (ArC), 152.1 (4ry ArC), 166.6 (d, J 256, 4ry ArC), 180.5 (C=O); m/z (ES⁺) 251 ([M+Na]⁺, 100%); HRMS (ES⁺) C₁₃H₉FN₂NaO⁺ ([M+Na]⁺) requires 251.0597; found 251.0602 (+2.1 ppm).

***(E)-(3-fluorophenyl)(phenyldiazenyl)methanone***

![Chemical structure of 65](image)

Following general procedure C, hydrazide 50 (488 mg, 2.13 mmol), pyridine (0.19 mL, 2.34 mmol) and N-bromosuccinimide (0.38 g, 2.13 mmol) in CH₂Cl₂ (5 mL) gave, after
chromatographic purification (eluent Et₂O:petrol 20:80), diazene 65 as a red oil (362 mg, 75%); ν<sub>max</sub> (thin film) 3073 (C-H), 1716 (C=O), 1589, 1499; δ<sub>H</sub> (400 MHz, CDCl₃) 7.37-7.42 (1H, m, ArH), 7.54 (1H, td, J 8.0, 5.4, ArH), 7.58-7.68 (3H, m, ArH), 7.81 (1H, ddd, J 9.0, 2.6, 1.5, ArH), 7.88-7.90 (1H, m, ArH), 8.02-8.05 (2H, m, ArH); δ<sub>C</sub> (100 MHz, CDCl₃) 117.2 (d, J 22.8, ArC), 121.7 (d, J 21.3, ArC), 123.8 (ArC), 126.4 (d, J 3.0, ArC), 129.5 (ArC), 130.7 (d, J 7.4, ArC), 133.0 (d, J 6.7, 4ry ArC), 133.8 (ArC), 152.1 (4ry ArC), 162.7 (d, J 247, 4ry ArC), 180.6 (C=O); m/z (ES<sup>+</sup>) 251 ([M+Na]<sup>+</sup>, 100%); HRMS (ES<sup>+</sup>) C<sub>13</sub>H<sub>9</sub>FN₂NaO⁺ ([M+Na]<sup>+</sup>) requires 251.0597; found 251.0602 (+2.1 ppm).

(E)-(2-fluorophenyl)(phenyldiazazenyl)methanone

![Chemical Structure](image)

Following general procedure C, hydrazide 51 (800 mg, 3.49 mmol), pyridine (0.31 mL, 3.84 mmol) and N-bromosuccinimide (0.62 g, 3.49 mmol) in CH₂Cl₂ (5 mL) gave, after chromatographic purification (eluent Et₂O:petrol 20:80), diazene 66 as a red oil (540 mg, 68%); ν<sub>max</sub> (thin film) 3066 (C-H), 1695 (C=O), 1609, 1586, 1505; δ<sub>H</sub> (300 MHz, CDCl₃) 7.20 (1H, ddd, J 10.6, 8.4, 1.0, ArH), 7.36 (1H, td, J 7.6, 0.9, ArH), 7.56-7.71 (4H, m, ArH), 7.98-8.02 (2H, m, ArH), 8.13 (1H, ddd, J 7.8, 7.1, 1.8, ArH); δ<sub>C</sub> (75 MHz, CDCl₃) 117.2 (d, J 29.3, ArC), 119.3 (d, J 15.0, 4ry ArC), 123.6 (ArC), 124.6 (d, J 4.8, ArC), 129.4 (ArC), 132.5 (ArC), 133.4 (ArC), 136.4 (d, J 12.0, ArC), 152.1 (4ry ArC), 162.5 (d, J 346, 4ry ArC), 180.9 (d, J 7.8, C=O); m/z (ES<sup>+</sup>) 251 ([M+Na]<sup>+</sup>, 100%); HRMS (ES<sup>+</sup>) C<sub>13</sub>H<sub>9</sub>FN₂NaO⁺ ([M+Na]<sup>+</sup>) requires 251.0597; found 251.0593 (-1.4 ppm).

(E)-(4-bromophenyl)(phenyldiazazenyl)methanone

![Chemical Structure](image)

Following general procedure C, hydrazide 52 (0.82 g, 2.82 mmol), pyridine (0.26 mL, 3.10 mmol) and N-bromosuccinimide (0.50 g, 2.82 mmol) in CH₂Cl₂ (5 mL) gave, after chromatographic purification (eluent Et₂O:petrol 20:80), diazene 67 as a red solid (669 mg, 82%); mp 39-40 °C; {lit<sup>4</sup> mp 38-39.5 °C}; δ<sub>H</sub> (300 MHz, CDCl₃) 7.57-7.66 (3H, m, ArH), 7.68-7.72 (2H, m, ArH), 7.95-7.99 (2H, m, ArH), 8.01-8.04 (2H, m, ArH).
(E)-(4-chlorophenyl)(phenyl diazenyl)methanone

![Structure of 68]

Following general procedure C, hydrazide 53 (1.16 g, 4.71 mmol), pyridine (0.42 mL, 5.18 mmol) and N-bromosuccinimide (0.84 g, 4.71 mmol) in CH₂Cl₂ (5 mL) gave, after chromatographic purification (eluent Et₂O:petrol 20:80), diazene 68 as a red oil (0.91 g, 76%); ν_max (thin film) 3064 (C-H), 1701 (C=O), 1591, 1500; δ_H (300 MHz, CDCl₃) 7.50-7.55 (2H, m, ArH), 7.57-7.67 (3H, m, ArH), 8.01-8.07 (4H, m, ArH); δ_C (75 MHz, CDCl₃) 123.8 (ArC), 129.4 (ArC), 129.5 (ArC), 131.9 (ArC), 131.9 (ArC), 133.7 (ArC), 141.2 (ArC), 152.1 (ArC), 180.8 (C=O); m/z (ES⁺) 267 ([M+Na]⁺, 100%); HRMS (ES⁺) C₉H₁₃ClN₂NaO₃⁻ ([M+Na]⁻) requires 267.0303; found 267.0302 (-0.3 ppm).

(E)-naphthalen-1-yl(phenyl diazenyl)methanone

![Structure of 69]

Following general procedure C, hydrazide 54 (0.74 g, 2.81 mmol), pyridine (0.26 mL, 3.10 mmol) and N-bromosuccinimide (0.50 g, 2.81 mmol) in CH₂Cl₂ (5 mL) gave, after chromatographic purification (eluent Et₂O:petrol 20:80), diazene 69 as a red solid (575 mg, 79%); mp 76-78 °C; ν_max (KBr) 3061 (C-H), 1697 (C=O), 1591, 1500; δ_H (400 MHz, CDCl₃) 7.54-7.66 (5H, m, ArH), 7.76 (1H, ddd, J 8.6, 7.0, 1.4, ArH), 7.96 (1H, dd, J 8.2, 0.4, ArH), 8.05-8.07 (2H, m, ArH), 8.15 (1H, d, J 8.2, ArH), 8.31 (1H, dd, J 7.3, 1.2, ArH), 9.25 (1H, d, J 8.7, ArH); δ_C (100 MHz, CDCl₃) 123.7 (ArC), 124.4 (ArC), 126.2 (ArC), 126.9 (ArC), 127.1 (ArC), 128.8 (ArC), 129.0 (ArC), 129.4 (ArC), 131.6 (ArC), 133.3 (ArC), 133.4 (ArC), 134.1 (ArC), 135.6 (ArC), 152.1 (ArC), 183.1 (C=O); m/z (ES⁺) 283 ([M+Na]⁺, 100%); HRMS (ES⁺) C₁₁H₁₂N₂NaO⁻ ([M+Na]⁻) requires 283.0847; found 283.0848 (+0.2 ppm).

(E)-(4-nitrophenyl)(phenyl diazenyl)methanone

![Structure of 70]

Following general procedure C, hydrazide 55 (2.00 g, 7.78 mmol), pyridine (0.69 mL, 8.56 mmol) and N-bromosuccinimide (1.39 g, 7.78 mmol) in CH₂Cl₂ (10 mL) gave, after
chromatographic purification (eluent Et$_2$O:petrol 50:50), diazene 70 as a red solid (0.91 g, 46%); mp 127-129 °C; $\nu_{\text{max}}$ (KBr) 3080 (C-H), 1711 (C=O), 1605, 1529, 1499; $\delta_{\text{H}}$ (300 MHz, CDCl$_3$) 7.50-7.62 (3H, m, ArH), 7.94-7.97 (2H, m, ArH), 8.19-8.23 (2H, m, ArH), 8.29-8.33 (2H, m, ArH); $\delta_{\text{C}}$ (100 MHz, CDCl$_3$) 124.0 (ArC), 124.0 (ArC), 129.6 (ArC), 131.7 (ArC), 134.3 (ArC), 136.1 (4ry ArC), 151.1 (4ry ArC), 152.1 (4ry ArC), 179.7 (C=O); m/z (APCI$^+$) 256 ([M+H]$^+$, 100%); HRMS (APCI$^+$) C$_{13}$H$_{16}$N$_2$O$^+$ ([M+H]$^+$) requires 256.0717; found 256.0714 (-1.0 ppm).

(E)-(phenyldiazenyl)(p-tolyl)methanone

\[
\begin{align*}
\text{Ph}^+ & \text{N} \equiv \text{N} \text{O} \\
\text{CH}_3
\end{align*}
\]

Following general procedure C, hydrazide 56 (0.82 g, 3.63 mmol), pyridine (0.32 mL, 4.00 mmol) and N-bromosuccinimide (0.65 g, 3.63 mmol) in CH$_2$Cl$_2$ (5 mL) gave, after chromatographic purification (eluent Et$_2$O:petrol 15:85), diazene 71 as a red oil (0.63 g, 77%); $\delta_{\text{H}}$ (400 MHz, CDCl$_3$) 2.38 (3H, s, CH$_3$), 7.25 (2H, d, J 8.0, ArH), 7.47-7.55 (3H, m, ArH), 7.87-7.94 (4H, m, ArH).

(E)-furan-2-yl(phenyldiazenyl)methanone

\[
\begin{align*}
\text{Ph}^+ & \text{N} \equiv \text{N} \text{O} \\
\text{O}
\end{align*}
\]

Following general procedure C, hydrazide 57 (0.79 g, 3.91 mmol), pyridine (0.35 mL, 4.30 mmol) and N-bromosuccinimide (0.69 g, 3.91 mmol) in CH$_2$Cl$_2$ (5 mL) gave, after chromatographic purification (eluent Et$_2$O:petrol 20:80), diazene 72 as a red oil (405 mg, 52%); $\delta_{\text{H}}$ (300 MHz, CDCl$_3$) 6.70 (1H, dd, J 3.6, 1.7, ArH), 7.45 (1H, dd, J 3.6, 0.7, ArH), 7.58-7.69 (3H, m, ArH), 7.84 (1H, dd, J 1.7, 0.7, ArH), 8.03-8.07 (2H, m, ArH).

(E)-4-(benzoyldiazenyl)benzonitrile

\[
\begin{align*}
\text{Ph} & \text{N} \equiv \text{N} \text{H}_2\text{Cl} \\
\rightarrow & \\
\text{Ph} & \text{N} \equiv \text{N} \text{O} \text{Ph} \\
\rightarrow & \\
\text{Ph} & \text{N} \equiv \text{O} \text{Ph}
\end{align*}
\]

To a solution of 4-cyanophenylhydrazine hydrochloride 73 (2.00 g, 11.8 mmol) and triethylamine (3.29 mL, 23.6 mmol) in Et$_2$O (30 mL) at 0 °C was slowly added benzoyl chloride (1.24 mL, 10.7 mmol). After stirring at rt for 30 minutes the reaction mixture was
concentration in vacuo. The solid was dissolved in CH$_2$Cl$_2$ and washed with 1M HCl. The organic layer was dried (MgSO$_4$), filtered and concentrated in vacuo to give a crude hydrazide 74 which was used without purification. Following general procedure C, hydrazide 74 (2.54 g, 10.7 mmol assuming 100% conversion), pyridine (0.97 mL, 11.8 mmol) and N-bromosuccinimide (1.90 g, 10.7 mmol) in CH$_2$Cl$_2$ (15 mL) gave, after chromatographic purification (eluent Et$_2$O:petrol 20:80), diazene 75 as a purple solid (258 mg, 10% over 2 steps); mp 110-112 °C; $\nu_{\text{max}}$ (KBr) 3043 (C-H), 1722 (C=O), 1508, 1506; $\delta_{\text{H}}$ (400 MHz, CDCl$_3$) 7.57 (2H, t, J 7.7, ArH), 7.73 (1H, t, J 7.4, ArH), 7.91 (2H, d, J 8.4, ArH), 8.05 (2H, d, J 7.3, ArH), 8.09 (2H, d, J 8.4, ArH); $\delta_{\text{C}}$ (75 MHz, CDCl$_3$) 116.5 (C=N), 117.9 (4ry ArC), 123.9 (ArC), 129.1 (ArC), 130.2 (4ry ArC), 130.6 (ArC), 133.5 (ArC), 135.0 (ArC), 153.5 (4ry ArC), 181.5 (C=O); m/z (ES$^+$) 236 ([M+H]$^+$, 100%); HRMS (ES$^+$) C$_{14}$H$_{10}$N$_3$O$^+$ ([M+H]$^+$) requires 236.0824; found 236.0824 (+0.2 ppm).

(E)-phenyl((4-(trifluoromethyl)phenyl)diazenyl)methanone

![Chemical structures](image)

To a solution of 46 (1.00 g, 3.226 mmol) and triethylamine (0.49 mL, 3.55 mmol) in EtOAc (10 mL) at 0 °C was added benzoyl chloride (0.37 mL, 3.23 mmol). The reaction mixture was stirred at rt for 1 h. The reaction mixture was washed with 1M HCl and sat. aq. NaHCO$_3$. The organic layer was dried (MgSO$_4$), filtered and concentrated in vacuo to give the crude acylated product 76 which was used without purification. To a solution of crude acylated product 76 (1.34 g, 3.23 mmol assuming 100% conversion) and 10% palladium on charcoal (0.34 g, 0.32 mmol, 10 mol%) in EtOAc (10 mL) was appended a balloon of hydrogen gas. The hydrogen gas was allowed to bubble through the reaction mixture at rt for 4 h. The reaction mixture was filtered through celite and concentrated in vacuo to give the hydrazide 77 which was used without purification. Following general procedure C, hydrazide 77 (903 mg, 3.23 mmol assuming 100% conversion), pyridine (0.29 mL, 3.55 mmol) and N-bromosuccinimide (0.57 g, 3.23 mmol) in CH$_2$Cl$_2$ (10 mL) gave, after chromatographic purification (eluent Et$_2$O:petrol 10:90), diazene 78 as a red oil (601 mg, 66% over 3 steps); $\nu_{\text{max}}$ (thin film) 3070 (C-H), 1716 (C=O), 1599; $\delta_{\text{H}}$ (500 MHz, CDCl$_3$) 7.46 (2H, t, J 7.8, ArH), 7.61 (1H, t, J 7.5, ArH), 7.70 (2H, d, J 8.3, ArH), 7.94-7.96 (2H, m, ArH), 8.00 (2H, d, J 8.2, ArH); $\delta_{\text{C}}$ (125 MHz, CDCl$_3$) 123.6 (q, J 271, CF$_3$), 123.7 (ArC), 126.7 (q, J 3.5, ArC), 129.0 (ArC), 130.3 (4ry ArC), 130.6 (ArC), 134.4 (q, J 32.5, 4ry ArC), 134.9 (ArC), 153.6 (4ry ArC), 181.7 (C=O); m/z (ES$^+$) 301 ([M+Na]$^+$, 100%); HRMS (ES$^+$) C$_{14}$H$_2$F$_3$N$_2$NaO$^+$ ([M+Na]$^+$) requires 301.0565; found 301.0566 (+0.4 ppm).
(E)-((4-methoxyphenyl)diazenyl)(4-(trifluoromethyl)phenyl)methanone

Following general procedure C, hydrazide 59 (3.50 g, 11.3 mmol), pyridine (1.02 mL, 12.4 mmol) and N-bromosuccinimide (2.00 g, 11.3 mmol) in CH$_2$Cl$_2$ (50 mL) gave, after chromatographic purification (eluent Et$_2$O:petrol 20:80), diazene 79 as a red solid (2.57 g, 74%) mp 56-58 °C; v$_{\text{max}}$ (KBr) 2936 (C-H), 1696 (C=O), 1597, 1504; δ$_{\text{H}}$ (300 MHz, CDCl$_3$) 3.97 (3H, s, CH$_3$), 7.07-7.11 (2H, m, ArH), 7.82 (2H, d, J 8.2, ArH), 8.04-8.10 (2H, m, ArH), 8.29 (2H, d, J 8.1, ArH); δ$_{\text{C}}$ (100 MHz, CDCl$_3$) 55.8 (CH$_3$), 114.7 (ArC), 123.5 (q, J 271, CF$_3$), 125.8 (q, J 3.6, ArC), 126.6 (ArC), 131.0 (ArC), 134.9 (4ry ArC), 135.3 (q, J 32.7, 4ry ArC), 146.8 (4ry ArC), 164.8 (4ry ArC), 179.9 (C=O); m/z (ES$^+$) 331 ([M+Na]$^+$, 100%); HRMS (ES$^+$) C$_{13}$H$_{11}$N$_2$NaO$_2$F$_3$ $^+$ ([M+Na]$^+$) requires 331.0670; found 331.0675 (+1.4 ppm).

Isothioureia catalysts used

Optimization studies on compound 3

triphenyl-4H-1,3,4-oxadiazin-6(5H)-one

Following general procedure D, phenylacetic acid (54.5 mg, 0.40 mmol), DIPEA (104 μL, 0.60 mmol) and p-methoxybenzoyl chloride (102 mg, 0.60 mmol) in DCM (2 mL), diazene 60 (42.0 mg, 0.20 mmol), DHPB 80 (7.60 mg, 0.04 mmol) and DIPEA (52 μL, 0.3 mmol) for 1 h at rt gave, after chromatographic purification (eluent Et$_2$O:petrol 2:98) (±)-3 as a colourless oil (41.0 mg, 63%); v$_{\text{max}}$ (thin film) 3063, 2977 (C-H), 1791 (C=O), 1596, 1495; δ$_{\text{H}}$ (400 MHz, CDCl$_3$) 5.96 (1H, s, C(5)H), 6.89-6.92 (1H, m, ArH), 7.15-7.28 (9H, m, ArH), 7.31-7.34 (3H, m, ArH), 7.86-7.89 (2H, m, ArH); δ$_{\text{C}}$ (100 MHz, CDCl$_3$) 59.5 (C(5)), 114.5 (ArC), 121.9 (ArC), 125.6 (ArC), 126.7 (ArC), 128.6 (ArC), 128.9 (4ry ArC), 129.1 (ArC), 129.4 (ArC), 129.4 (ArC), 130.3 (ArC), 131.2 (4ry ArC), 141.0 (C(2)), 144.3 (ArC), 160.4
(C(6)); m/z (APCI+) 328 ([M]+, 12%); HRMS (APCI+) C_{19}H_{16}N_{2}O_{2}^{+} ([M]+) requires 328.1206; found 328.1201 (-1.6 ppm).

**Asymmetric Catalyst Screen:**
Tetramisole hydrochloride (2S)-81 (4.82 mg, 0.02 mmol, 10 mol%) gave approximately 65% conversion to the desired product after 16 h at rt.

Benzotetramisole (2R)-82 (5.04 mg, 0.02 mmol, 10 mol%) gave approximately 20% conversion to the desired product after 16 h at rt.

Ph/i-Pr isothiourea catalyst (2S,3R)-5 (6.17 mg, 0.02 mmol, 10 mol%) gave full conversion to the desired product after 1 h at rt. Chromatographic purification (eluent Et_{2}O:petrol 2:98) gave (5R)-3 as a colourless oil (43.0 mg, 66%); Chiral HPLC Chiralpak AD-H (5% IPA:hexane, flow rate 1 mL min^{-1}, 211 nm, 20 °C) t_{R}(5S): 8.9 min, t_{R}(5R): 14.6 min, 95% ee.

**Temperature Screen:**
All reactions with Ph/i-Pr isothiourea catalyst (2S,3R)-5 (6.17 mg, 0.02 mmol, 10 mol%)

Reaction for 2 h at 0 °C gave, after chromatographic purification (eluent Et_{2}O:petrol 2:98) (5R)-3 as a colourless oil (42.3 mg, 65%); Chiral HPLC Chiralpak AD-H (5% IPA:hexane, flow rate 1 mL min^{-1}, 211 nm, 20 °C) t_{R}(5S): 8.8 min, t_{R}(5R): 14.4 min, 98% ee.

Reaction for 16 h at -30 °C gave, after chromatographic purification (eluent Et_{2}O:petrol 2:98) (5R)-3 as a colourless oil (39.7 mg, 61%); Chiral HPLC Chiralpak AD-H (5% IPA:hexane, flow rate 1 mL min^{-1}, 211 nm, 20 °C) t_{R}(5S): 8.8 min, t_{R}(5R): 14.5 min, 99% ee.

Reaction for 16 h at -78 °C gave, after chromatographic purification (eluent Et_{2}O:petrol 2:98) (5R)-3 as a colourless oil (53.2 mg, 81%); Chiral HPLC Chiralpak AD-H (5% IPA:hexane, flow rate 1 mL min^{-1}, 211 nm, 20 °C) t_{R}(5S): 9.0 min, t_{R}(5R): 14.8 min, 99% ee.

**Catalyst Loading Screen:**
All reactions at -78 °C for 16 h.

Ph/i-Pr isothiourea catalyst (2S,3R)-5 (3.09 mg, 0.01 mmol, 5 mol%) gave, after chromatographic purification (eluent Et_{2}O:petrol 2:98) (5R)-3 as a colourless oil (54.3 mg,
83%); Chiral HPLC Chiralpak AD-H (5% IPA:hexane, flow rate 1 mL min⁻¹, 211 nm, 20 °C) 
tᵣ(S5): 8.8 min, tᵣ(R₅): 15.2 min, >99% ee.

Ph/i-Pr isothiourea catalyst (2S,3R)-5 (1.23 mg, 0.004 mmol, 1 mol%) gave, after 
chromatographic purification (eluuent Et₂O:petrol 2:98) (5R)-3 as a colourless oil (58.6 mg, 
89%); [α]D²⁰⁻621.7 (c 1.075, CH₂Cl₂); Chiral HPLC Chiralpak AD-H (5% IPA:hexane, flow 
rate 1 mL min⁻¹, 211 nm, 20 °C) tᵣ(S5): 8.8 min, tᵣ(R₅): 14.8 min, >99% ee.

**Optimal asymmetric reaction conditions for compound 3**

(R)-2,4,5-triphenyl-4H-1,3,4-oxadiazin-6(5H)-one

Following general procedure E, phenylacetic acid (40.8 mg, 0.30 mmol), DIPEA (78 µL, 0.45 
mmol) and p-methoxybenzoyl chloride (77 mg, 0.45 mmol) in DCM (2 mL), Ph/i-Pr 
isothiourea catalyst (2S,3R)-5 (0.62 mg, 0.002 mmol, 1 mol%), diazene 60 (42.0 mg, 0.20 
mmol) and DIPEA (52 µL, 0.3 mmol) for 16 h at -78 °C gave, after chromatographic 
purification (eluuent Et₂O:petrol 2:98) (5R)-3 as a colourless oil (57.0 mg, 87%); [α]D²⁰⁻621.7 
(c 1.075, CH₂Cl₂); Chiral HPLC Chiralpak AD-H (5% IPA:hexane, flow rate 1 mL min⁻¹, 211 
nm, 20 °C) tᵣ(S5): 8.8 min, tᵣ(R₅): 14.8 min, >99% ee.

**methyl 2-(2-benzoyl-1-phenylhydrazinyl)-2-phenylacetate**

Following general procedure D, phenylacetic acid (40.9 mg, 0.30 mmol), DIPEA (78 µL, 0.45 
mmol) and benzoyl chloride (52 µL, 0.45 mmol) in DCM (2 mL), diazene 60 (42.0 mg, 0.20 
mmol), DHPB 80 (7.60 mg, 0.04 mmol) and DIPEA (52 µL, 0.3 mmol) for 1 h at rt followed 
by addition of MeOH (2 mL) and stirring for 1 h at rt gave, after chromatographic purification 
(eluuent EtOAc:petrol 25:75) a rotameric mixture (ratio 91:9) of (±)-4 as a white solid (67.8 
mg, 94%); mp 148-150 °C; νmax (KBr) 3355 (N-H), 3075, 2950 (C-H), 1729 (C=O), 1687 
(C=O), 1599; Data for major rotamer δ₁ (300 MHz, CDCl₃) 3.74 (3H, s, CH₃), 5.82 (1H, s, 
C(2)H), 6.90-6.96 (3H, m, ArH), 7.18-7.31 (7H, m, ArH), 7.36-7.42 (3H, m, ArH), 7.44-7.48 
(2H, m, ArH), 8.43 (1H, s, NH); Selected data for minor rotamer δ₁ (300 MHz, CDCl₃) 3.62 
(3H, s, CH₃), 5.50 (1H, s, C(2)H), 7.90 (1H, s, NH); Data for major rotamer δₑ (100 MHz,
CDCl$_3$ 52.5 (CH$_3$), 66.7 (C(2)), 114.8 (ArC), 121.7 (ArC), 127.0 (ArC), 128.6 (ArC), 128.6 (ArC), 128.9 (ArC), 129.1 (ArC), 129.5 (ArC), 131.8 (ArC), 133.0 (4ry ArC), 133.3 (4ry ArC), 148.4 (4ry ArC), 166.6 (C=O), 173.1 (C=O); Selected data for minor rotamer δC (100 MHz, CDCl$_3$) 52.4 (CH$_3$), 68.0 (C(2)), 115.4 (ArC), 122.3 (ArC), 127.8 (ArC), 129.9 (ArC), 130.2 (ArC), 130.4 (ArC); m/z (NSI) 361 ([M+H]$^+$, 100%); HRMS (NSI) C$_{22}$H$_{17}$N$_2$O$_3$ $^+$ ([M+H]$^+$) requires 361.1547; found 361.1546 (-0.2 ppm).

**(R)-methyl 2-(2-benzoyl-1-phenylhydrazinyl)-2-phenylacetate**

![Image](image.png)

Following general procedure E, phenylacetic acid (40.9 mg, 0.30 mmol), DIPEA (78 µL, 0.45 mmol) and benzoyl chloride (52.2 µL, 0.45 mmol) in DCM (2 mL), Ph/i-Pr isothioureacatalyst (2S,3R)-5 (0.62 mg, 0.002 mmol, 1 mol%), diazene 60 (42.0 mg, 0.20 mmol) andDIPEA (52 µL, 0.3 mmol) for 16 h at -78 °C followed by addition of MeOH (2 mL) andstirring for 1 h at rt gave, after chromatographic purification (eluent EtOAc:petrol 25:75) arotameric mixture (ratio 91:9) of (2R)-4 as a white solid (67.8 mg, 94%); [α]$_D^{20}$ -37.6 (c 0.5,CH$_2$Cl$_2$); Chiral HPLC Chiralpak IB (10% IPA:hexane, flow rate 1 mL min$^{-1}$, 211 nm, 20 °C)t$_R$(2S): 12.7 min, t$_R$(2R): 15.0 min, 99% ee.

The same procedure using Ph/i-Pr isothiourea catalyst (2S,3R)-5 (0.31 mg, 0.001 mmol, 0.5 mol%) for 16 h at -78 °C gave (2R)-4 as a white solid (61.0 mg, 85%), >99% ee.

The same procedure using Ph/i-Pr isothiourea catalyst (2S,3R)-5 (0.16 mg, 0.0005 mmol, 0.25 mol%) for 40 h at -78 °C gave (2R)-4 as a white solid (60.0 mg, 83%), >99% ee.

The same procedure using Ph/i-Pr isothiourea catalyst (2S,3R)-5 (0.062 mg, 0.0002 mmol, 0.1 mol%) for 40 h at -78 °C gave (2R)-4 as a white solid (43.0 mg, 60%), 99% ee. The conversion was determined to be 65% by analysis of the crude $^1$H NMR.

**2,4-diphenyl-5-(p-tolyl)-4H-1,3,4-oxadiazin-6(5H)-one**

![Image](image.png)

The same procedure using Ph/i-Pr isothiourea catalyst (2S,3R)-5 (0.062 mg, 0.0002 mmol, 0.1 mol%) for 40 h at -78 °C gave (2R)-4 as a white solid (43.0 mg, 60%), 99% ee. The conversion was determined to be 65% by analysis of the crude $^1$H NMR.
Following general procedure D, p-tolylacetic acid (45.1 mg, 0.30 mmol), DIPEA (78 μL, 0.45 mmol) and p-methoxybenzoyl chloride (77 mg, 0.45 mmol) in DCM (2 mL), diazene 60 (42.0 mg, 0.20 mmol), DHPB 80 (7.60 mg, 0.04 mmol) and DIPEA (52 μL, 0.3 mmol) for 1 h at rt gave, after chromatographic purification (eluent Et₂O:petrol 1:99) (±)-6 as a white solid (45.1 mg, 66%); mp 120-122 °C; ν_{max} (KBr) 3059, 2931 (C-H), 1789 (C=O), 1597, 1494; δ_{H} (400 MHz, CDCl₃) 2.18 (3H, s, CH₃), 5.92 (1H, s, C(5)H), 6.89-6.93 (1H, m, ArH), 7.01 (2H, d, J 8.1, ArH), 7.13-7.18 (4H, m, ArH), 7.21-7.25 (2H, m, ArH), 7.31-7.35 (3H, m, ArH), 7.85-7.90 (2H, m, ArH); δ_{C} (100 MHz, CDCl₃) 21.1 (CH₃), 59.3 (C(5)), 114.5 (ArC), 121.8 (ArC), 125.6 (ArC), 126.6 (ArC), 128.1 (4ry ArC), 128.6 (ArC), 128.9 (4ry ArC), 129.4 (ArC), 130.0 (ArC), 130.2 (ArC), 139.0 (4ry ArC), 140.9 (C(2)), 144.4 (4ry ArC), 160.6 (C(6)); m/z (APCI⁺) 343 ([M+H]⁺, 23%); HRMS (APCI⁺) C₂₃H₁₉N₂O₂⁺ ([M+H]⁺) requires 343.1441; found 343.1438 (-0.9 ppm).

(R)-2,4-diphenyl-5-(p-tolyl)-4H-1,3,4-oxadiazin-6(5H)-one

Following general procedure E, p-tolylacetic acid (45.1 mg, 0.30 mmol), DIPEA (78 μL, 0.45 mmol) and p-methoxybenzoyl chloride (77 mg, 0.45 mmol) in DCM (2 mL), Ph/i-Pr isothiourea catalyst (2S,3R)-5 (0.62 mg, 0.002 mmol, 1 mol%), diazene 60 (42.0 mg, 0.20 mmol) and DIPEA (52 μL, 0.3 mmol) for 16 h at -78 °C gave, after chromatographic purification (eluent Et₂O:petrol 1:99) (5R)-6 as a white solid (53.3 mg, 78%); [α]_{D}^{20} -603.3 (c 0.75, CH₂Cl₂); Chiral HPLC Chiralpak AD-H (5% IPA:hexane, flow rate 1 mL min⁻¹, 211 nm, 20 °C) tₘ(5S): 8.7 min, tₘ(5R): 20.2 min, >99% ee.

5-(4-bromophenyl)-2,4-diphenyl-4H-1,3,4-oxadiazin-6(5H)-one

Following general procedure E, p-bromophenylacetic acid (64.5 mg, 0.30 mmol), DIPEA (78 μL, 0.45 mmol) and p-methoxybenzoyl chloride (77 mg, 0.45 mmol) in DCM (2 mL), diazene 60 (42.0 mg, 0.20 mmol), DHPB 80 (7.60 mg, 0.04 mmol) and DIPEA (52 μL, 0.3 mmol) for 1 h at rt gave, after chromatographic purification (eluent Et₂O:petrol 1:99) (±)-7 as a white solid (41.2 mg, 51%); mp 38-40 °C; ν_{max} (KBr) 3060, 2934 (C-H), 1789 (C=O), 1597,
1486; δ_H (300 MHz, CDCl_3) 5.92 (1H, s, C(5)H), 6.92-6.97 (1H, m, ArH), 7.13-7.18 (4H, m, ArH), 7.22-7.28 (2H, m, ArH), 7.33-7.37 (5H, m, ArH), 7.86-7.89 (2H, m, ArH); δ_C (100 MHz, CDCl_3) 59.1 (C(5)), 114.5 (ArC), 122.1 (ArC), 123.4 (4ry ArC), 125.6 (ArC), 128.4 (ArC), 128.6 (4ry ArC), 129.6 (ArC), 129.5 (ArC), 130.2 (4ry ArC), 130.5 (ArC), 132.5 (ArC), 141.2 (C(2)), 144.0 (4ry ArC), 160.0 (C(6)); m/z (NSI') 439 ([M+CH_3O]^+, 95%); HRMS (NSI') C_22H_30^+BrN_2O_5^+ ([M+CH_3O]^+) requires 439.0652; found 439.0655 (+0.7 ppm).

(R)-5-(4-bromophenyl)-2,4-diphenyl-1H,1,3,4-oxadiazin-6(5H)-one

Following general procedure E, p-bromophenylacetic acid (64.5 mg, 0.30 mmol), DIPEA (78 μL, 0.45 mmol) and p-methoxybenzoyl chloride (77 mg, 0.45 mmol) in DCM (2 mL), Ph/i-Pr isothiourea catalyst (2S,3R)-5 (0.62 mg, 0.002 mmol, 1 mol%), diazene 60 (42.0 mg, 0.20 mmol) and DIPEA (52 μL, 0.3 mmol) for 16 h at -78 °C gave, after chromatographic purification (eluent Et_2O:petrol 1:99) (5R)-7 as a white solid (64.9 mg, 80%); [α]_D^10 -572.0 (c 0.50, CH_2Cl_2); Chiral HPLC Chiralpak AD-H (5% IPA:hexane, flow rate 1 mL min^-1, 211 nm, 20 °C) t_R(5S): 10.1 min, t_R(5R): 19.0 min, 99% ee.

5-(4-chlorophenyl)-2,4-diphenyl-1H,1,3,4-oxadiazin-6(5H)-one

Following general procedure D, p-chlorophenylacetic acid (51.2 mg, 0.30 mmol), DIPEA (78 μL, 0.45 mmol) and p-methoxybenzoyl chloride (77 mg, 0.45 mmol) in DCM (2 mL), diazene 60 (42.0 mg, 0.20 mmol), DHPB 80 (7.60 mg, 0.04 mmol) and DIPEA (52 μL, 0.3 mmol) for 1 h at rt gave, after chromatographic purification (eluent Et_2O:petrol 1:99) (±)-8 as a white solid (38.9 mg, 54%); mp 40-42 °C; ν_max (KBr) 2933 (C-H), 1790 (C=O), 1598, 1490; δ_H (300 MHz, CDCl_3) 5.93 (1H, s, C(5)H), 6.93 (1H, t, J 7.2, ArH), 7.13-7.28 (8H, m, ArH), 7.30-7.38 (3H, m, ArH), 7.84-7.90 (2H, m, ArH); δ_C (100 MHz, CDCl_3) 59.0 (C(5)), 114.5 (ArC), 122.1 (ArC), 125.6 (ArC), 128.1 (ArC), 128.6 (4ry ArC), 128.6 (ArC), 129.5 (ArC), 129.6 (ArC), 129.6 (4ry ArC), 130.5 (ArC), 135.2 (4ry ArC), 141.2 (C(2)), 144.1 (4ry ArC), 160.1 (C(6)); m/z (NSI') 395 ([M+CH_3O]^+, 100%); HRMS (NSI') C_22H_30^+ClN_2O_5^+ ([M+CH_3O]^+) requires 395.1157; found 395.1157 (+0.0 ppm).
(R)-5-(4-chlorophenyl)-2,4-diphenyl-4H-1,3,4-oxadiazin-6(5H)-one

![Chemical Structure](image)

Following general procedure E, p-chlorophenylacetic acid (51.2 mg, 0.30 mmol), DIPEA (78 μL, 0.45 mmol) and p-methoxybenzoyl chloride (77 mg, 0.45 mmol) in DCM (2 mL), Ph/i-Pr isothioure catalyst (25:3R)-5 (0.62 mg, 0.002 mmol, 1 mol%), diazene 60 (42.0 mg, 0.20 mmol) and DIPEA (52 μL, 0.3 mmol) for 16 h at -78 °C gave, after chromatographic purification (eluent Et₂O:petrol 1:99) (5R)-8 as a white solid (47.8 mg, 66%); [α]D 20°−613.5 (c 0.2, CH₂Cl₂); Chiral HPLC Chiralpak AD-H (5% IPA:hexane, flow rate 1 mL min⁻¹, 211 nm, 20 °C) tₚ(5S): 9.2 min, tₚ(5R): 16.9 min, >99% ee.

5-(4-fluorophenyl)-2,4-diphenyl-4H-1,3,4-oxadiazin-6(5H)-one

![Chemical Structure](image)

Following general procedure D, p-fluorophenylacetic acid (46.2 mg, 0.30 mmol), DIPEA (78 μL, 0.45 mmol) and p-methoxybenzoyl chloride (77 mg, 0.45 mmol) in DCM (2 mL), diazene 60 (42.0 mg, 0.20 mmol), DHPB 80 (7.60 mg, 0.04 mmol) and DIPEA (52 μL, 0.3 mmol) for 1 h at rt gave, after chromatographic purification (eluent Et₂O:petrol 1.5:98.5) (±)-9 as a colourless oil (37.2 mg, 54%); v_max (thin film) 3063, 2928 (C-H), 1791 (C=O), 1597, 1506; δ_H (400 MHz, CDCl₃) 5.94 (1H, s, C(5)H), 6.89-6.96 (3H, m, ArH), 7.15-7.28 (2H, m, ArH), 7.23-7.27 (4H, m, ArH), 7.33-7.37 (3H, m, ArH), 7.87-7.90 (2H, m, ArH); δ_C (100 MHz, CDCl₃) 58.9 (C(5)), 114.5 (ArC), 116.4 (d, J 21.8, ArC), 122.0 (ArC), 125.6 (ArC), 126.9 (d, J 3.0, 4ry ArC), 128.5 (ArC), 128.6 (ArC), 128.7 (4ry ArC), 129.4 (ArC), 130.4 (ArC), 141.1 (C(2)), 144.1 (4ry ArC), 160.3 (C(6)), 163.1 (d, J 247, 4ry ArC); m/z (NOESY) 379 ([M+CH₃O]⁺, 100%); HRMS (NOESY) C₂₂H₂₀FN₂O₅⁺ ([M+ CH₃O]⁺) requires 379.1452; found 379.1454 (+0.4 ppm).

(R)-5-(4-fluorophenyl)-2,4-diphenyl-4H-1,3,4-oxadiazin-6(5H)-one

![Chemical Structure](image)

S21
Following general procedure E, p-fluorophenylacetic acid (46.2 mg, 0.30 mmol), DIPEA (78 μL, 0.45 mmol) and p-methoxybenzoyl chloride (77 mg, 0.45 mmol) in DCM (2 mL), Ph/i-Pr isothiourea catalyst (2S,3R)-5 (0.62 mg, 0.002 mmol, 1 mol%), diazene 60 (42.0 mg, 0.20 mmol) and DIPEA (52 μL, 0.3 mmol) for 16 h at -78 °C gave, after chromatographic purification (eluent Et₂O:petrol 1.5:98.5) (5R)-9 as a colourless oil (53.6 mg, 77%); [α]D 20 -634.2 (c 0.5, CH₂Cl₂); Chiral HPLC Chiralpak AD-H (5% IPA:hexane, flow rate 1 mL min⁻¹, 211 nm, 20 °C) tₚ(5S): 8.5 min, tₚ(5R): 12.7 min, >99% ee.

5-([1,1'-biphenyl]-4-yl)-2,4-diphenyl-4H-1,3,4-oxadiazin-6(5H)-one

Following general procedure D, biphenylacetic acid (63.6 mg, 0.30 mmol), DIPEA (78 μL, 0.45 mmol) and p-methoxybenzoyl chloride (77 mg, 0.45 mmol) in DCM (2 mL), diazene 60 (42.0 mg, 0.20 mmol), DHPB 80 (7.60 mg, 0.04 mmol) and DIPEA (52 μL, 0.3 mmol) for 1 h at rt gave, after chromatographic purification (eluent Et₂O:petrol 1:99) (+)-10 as a white solid (40.3 mg, 53%); mp 39-41 °C; νmax (KBr) 3059, 2925 (C-H), 1790 (C=O), 1597, 1494; δH (400 MHz, CDCl₃) 6.01 (1H, s, C(5)H), 6.92-6.96 (1H, m, ArH), 7.20-7.37 (12H, m, ArH), 7.40-7.44 (4H, m, ArH), 7.90-7.92 (2H, m, ArH); δC (100 MHz, CDCl₃) 59.3 (C(5)), 114.5 (ArC), 121.9 (ArC), 125.6 (ArC), 127.1 (ArC), 127.7 (ArC), 128.1 (ArC), 128.6 (ArC), 128.8 (ArC), 128.9 (ArC), 130.1 (ArC), 130.3 (ArC), 140.1 (4ry ArC), 141.1 (C(2)), 142.0 (4ry ArC), 144.3 (4ry ArC), 160.4 (C(6)); m/z (APCI⁺) 405 ([M+H]⁺, 100%); HRMS (APCI⁺) C₂₇H₂₁N₂O₂⁺ ([M+H]⁺) requires 405.1598; found 405.1591 (-1.6 ppm).

(R)-5-([1,1'-biphenyl]-4-yl)-2,4-diphenyl-4H-1,3,4-oxadiazin-6(5H)-one

Following general procedure E, biphenylacetic acid (63.6 mg, 0.30 mmol), DIPEA (78 μL, 0.45 mmol) and p-methoxybenzoyl chloride (77 mg, 0.45 mmol) in DCM (2 mL), Ph/i-Pr isothiourea catalyst (2S,3R)-5 (0.62 mg, 0.002 mmol, 1 mol%), diazene 60 (42.0 mg, 0.20
mmol) and DIPEA (52 µL, 0.3 mmol) for 16 h at -78 °C gave, after chromatographic purification (eluent Et₂O:petrol 1:99) (5R)-10 as a white solid (70.8 mg, 88%); [α]_D^{20} -532.2 (c 0.5, CH₂Cl₂); Chiral HPLC Chiralpak AD-H (5% IPA:hexane, flow rate 1 mL min⁻¹, 211 nm, 20 °C) tₖ(5S): 13.5 min, tₖ(5R): 16.7 min, 98% ee.

2,4-diphenyl-5-(m-tolyl)-4H-1,3,4-oxadiazin-6(5H)-one

Following general procedure D, m-tolylacetic acid (45.1 mg, 0.30 mmol), DIPEA (78 µL, 0.45 mmol) and p-methoxybenzoyl chloride (77 mg, 0.45 mmol) in DCM (2 mL), diazene 60 (42.0 mg, 0.20 mmol), DHPB 80 (7.60 mg, 0.04 mmol) and DIPEA (52 µL, 0.3 mmol) for 1 h at rt gave, after chromatographic purification (eluent Et₂O:petrol 1:99) (±)-11 as a white solid (44.8 mg, 65%); mp 130-132 °C; ν_max (KBr) 3030, 2926 (C-H), 1789 (C=O), 1597, 1494; δ_H (400 MHz, CDCl₃) 2.19 (3H, s, CH₃), 5.91 (1H, s, C(5)H), 6.91 (1H, tt, J 7.2, 1.1, ArH), 7.00-7.03 (2H, m, ArH), 7.06-7.11 (2H, m, ArH), 7.14-7.17 (2H, m, ArH), 7.21-7.26 (2H, m, ArH), 7.31-7.35 (3H, m, ArH), 7.86-7.90 (2H, m, ArH); δ_C (100 MHz, CDCl₃) 21.5 (CH₃), 59.5 (C(5)), 114.5 (ArC), 121.8 (ArC), 123.6 (ArC), 125.6 (ArC), 127.2 (ArC), 128.6 (ArC), 128.9 (4ry ArC), 129.2 (ArC), 129.4 (ArC), 129.9 (ArC), 130.2 (ArC), 131.2 (4ry ArC), 139.3 (4ry ArC), 140.9 (C(2)), 144.3 (4ry ArC), 160.5 (C(6)); m/z (APCI⁺) 343 ([M+H⁺], 92%); HRMS (APCI⁺) C_{22}H_{19}N₂O₂⁺ ([M+H⁺]) requires 343.1441; found 343.1438 (-0.9 ppm).

(R)-2,4-diphenyl-5-(m-tolyl)-4H-1,3,4-oxadiazin-6(5H)-one

Following general procedure E, m-tolylacetic acid (45.1 mg, 0.30 mmol), DIPEA (78 µL, 0.45 mmol) and p-methoxybenzoyl chloride (77 mg, 0.45 mmol) in DCM (2 mL), Ph/i-Pr isothiourea catalyst (2S,3R)-5 (0.62 mg, 0.002 mmol, 1 mol%), diazene 60 (42.0 mg, 0.20 mmol) and DIPEA (52 µL, 0.3 mmol) for 16 h at -78 °C gave, after chromatographic purification (eluent Et₂O:petrol 1:99) (5R)-11 as a white solid (53.8 mg, 79%); [α]_D^{20} -651.6 (c 0.25, CH₂Cl₂); Chiral HPLC Chiralpak AD-H (5% IPA:hexane, flow rate 1 mL min⁻¹, 211 nm, 20 °C) tₖ(5S): 7.7 min, tₖ(5R): 8.9 min, >99% ee.
5-(naphthalen-2-yl)-2,4-diphenyl-4H-1,3,4-oxadiazin-6(5H)-one

Following general procedure D, 2-naphthylacetic acid (55.9 mg, 0.30 mmol), DIPEA (78 µL, 0.45 mmol) and p-methoxybenzoyl chloride (77 mg, 0.45 mmol) in DCM (2 mL), diazene 60 (42.0 mg, 0.20 mmol), DHPB 80 (7.60 mg, 0.04 mmol) and DIPEA (52 µL, 0.3 mmol) for 1 h at rt gave, after chromatographic purification (eluent Et2O:petrol 1:99) (±)-12 as a white solid (40.3 mg, 53%); mp 40-42 °C; νmax (KBr) 3058, 2935 (C-H), 1788 (C=O), 1596, 1494; δH (400 MHz, CDCl3) 6.12 (1H, s, C(5)H), 6.90-6.94 (1H, m, ArH), 7.20-7.27 (4H, m, ArH), 7.32-7.42 (6H, m, ArH), 7.64-7.74 (4H, m, ArH), 7.88-7.91 (2H, m, ArH); δC (100 MHz, CDCl3) 59.8 (C(5)), 114.6 (ArC), 121.9 (ArC), 123.7 (ArC), 125.6 (ArC), 126.2 (ArC), 126.7 (ArC), 126.8 (ArC), 127.7 (ArC), 128.2 (ArC), 128.6 (4ry ArC), 128.8 (ArC), 129.4 (ArC), 129.5 (ArC), 130.3 (ArC), 133.2 (4ry ArC), 133.4 (4ry ArC), 141.1 (C(2)), 144.3 (4ry ArC), 160.4 (C(6)); m/z (APCI⁺) 379 ([M+H]⁺, 100%); HRMS (APCI⁺) C23H19N2O2⁺ ([M+H]⁺) requires 379.1441; found 379.1433 (-2.1 ppm).

(R)-5-(naphthalen-2-yl)-2,4-diphenyl-4H-1,3,4-oxadiazin-6(5H)-one

Following general procedure E, 2-naphthylacetic acid (55.9 mg, 0.30 mmol), DIPEA (78 µL, 0.45 mmol) and p-methoxybenzoyl chloride (77 mg, 0.45 mmol) in DCM (2 mL), Ph/i-Pr isothiourea catalyst (2S,3R)-5 (0.62 mg, 0.002 mmol, 1 mol%), diazene 60 (42.0 mg, 0.20 mmol) and DIPEA (52 µL, 0.3 mmol) for 16 h at -78 °C gave, after chromatographic purification (eluent Et2O:petrol 1:99) (5R)-12 as a white solid (57.6 mg, 76%); [α]D20 -540.4 (c 0.5, CH2Cl2); Chiral HPLC Chiralpak AD-H (5% IPA:hexane, flow rate 1 mL min⁻¹, 211 nm, 20 °C) t₈(5S): 13.0 min, t₈(5R): 22.5 min, 99% ee.

4-(4-fluorophenyl)-2,5-diphenyl-4H-1,3,4-oxadiazin-6(5H)-one

S24
Following general procedure D, phenylacetic acid (40.9 mg, 0.30 mmol), DIPEA (78 μL, 0.45 mmol) and p-methoxybenzoyl chloride (77 mg, 0.45 mmol) in DCM (2 mL), diazene 63 (45.4 mg, 0.20 mmol), DHPB 80 (7.60 mg, 0.04 mmol) and DIPEA (52 μL, 0.3 mmol) for 1 h at rt gave, after chromatographic purification (eluend Et₂O:petrol 1:99) (±)-13 as a white solid (49.6 mg, 72%); mp 48-50 °C; νmax (thin film) 3062, 2924 (C-H), 1791 (C=O), 1600, 1506; δH (400 MHz, CDCl₃) 5.88 (1H, s, C(5)H), 6.90-6.95 (2H, m, ArH), 7.08-7.12 (2H, m, ArH), 7.20-7.26 (5H, m, ArH), 7.31-7.35 (3H, m, ArH), 7.85-7.87 (2H, m, ArH); δC (75 MHz, CDCl₃) 59.9 (C(5)), 116.0 (d, J 22.6, ArC), 116.0 (d, J 7.7, ArC), 125.6 (ArC), 126.7 (ArC), 128.6 (ArC), 128.7 (4ry ArC), 129.2 (ArC), 129.4 (ArC), 130.4 (ArC), 131.0 (4ry ArC), 140.7 (d, J 2.1, 4ry ArC), 141.1 (C(2)), 158.4 (d, J 240, 4ry ArC), 160.3 (C(6)); m/z (NSI⁺) 379 ([M+CH₃O]⁺, 100%); HRMS (NSI⁺) C₂₂H₂₀F₅N₂O₃⁺ ([M+CH₃O]⁺) requires 379.1452; found 379.1450 (+0.7 ppm).

**(R)-4-(4-fluorophenyl)-2,5-diphenyl-4H-1,3,4-oxadiazin-6(5H)-one**

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(5R)-13

Following general procedure E, phenylacetic acid (40.9 mg, 0.30 mmol), DIPEA (78 μL, 0.45 mmol) and p-methoxybenzoyl chloride (77 mg, 0.45 mmol) in DCM (2 mL), Ph/i-Pr isothiourea catalyst (2S,3R)-5 (0.62 mg, 0.002 mmol, 1 mol%), diazene 63 (45.4 mg, 0.20 mmol) and DIPEA (52 μL, 0.3 mmol) for 16 h at -78 °C gave, after chromatographic purification (eluend Et₂O:petrol 1:99) (5R)-13 as a white solid (56.7 mg, 82%); [α]D²⁰ -604.2 (c 0.5, CH₂Cl₂); Chiral HPLC Chiralpak AD-H (5% IPA:hexane, flow rate 1 mL min⁻¹, 211 nm, 20 °C) tₘ(5S): 11.9 min, tₘ(5R): 16.5 min, >99% ee.

**2-(4-fluorophenyl)-4,5-diphenyl-4H-1,3,4-oxadiazin-6(5H)-one**

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(±)-14

Following general procedure D, phenylacetic acid (40.9 mg, 0.30 mmol), DIPEA (78 μL, 0.45 mmol) and p-methoxybenzoyl chloride (77 mg, 0.45 mmol) in DCM (2 mL), diazene 64 (45.4 mg, 0.20 mmol), DHPB 80 (7.60 mg, 0.04 mmol) and DIPEA (52 μL, 0.3 mmol) for 1 h at rt gave, after chromatographic purification (eluend Et₂O:petrol 1:99) (±)-14 as a colourless oil.
(48.5 mg, 70%); \(\nu_{\text{max}}\) (thin film) 3064, 2920 (C-H), 1790 (C=O), 1597, 1496; \(\delta_{\text{H}}\) (300 MHz, CDCl\(_3\)) 5.96 (1H, s, C(5)H), 6.89-6.94 (1H, m, ArH), 6.98-7.04 (2H, m, ArH), 7.13-7.17 (2H, m, ArH), 7.20-7.28 (7H, m, ArH), 7.83-7.89 (2H, m, ArH); \(\delta_{C}\) (100 MHz, CDCl\(_3\)) 59.5 (C(5)), 114.4 (ArC), 115.8 (d, J 21.9, ArC), 121.9 (ArC), 125.0 (d, J 3.2, 4ry ArC), 126.6 (ArC), 127.7 (d, J 8.4, ArC), 129.1 (ArC), 129.4 (ArC), 129.4 (ArC), 131.1 (4ry ArC), 140.4 (C(2)), 144.2 (4ry ArC), 160.2 (C(6)), 164.0 (d, J 250, 4ry ArC); \(m/z\) (NSI\(^+\)) 379 ([M+CH\(_3\)O\(^+\)], 100%); HRMS (NSI\(^+\)) \(\text{C}_{22}\text{H}_{20}\text{FN}_2\text{O}_3^+\) ([M+CH\(_3\)O\(^+\)] requires 379.1452; found 379.1456 (+0.9 ppm).

(R)-2-(4-fluorophenyl)-4,5-diphenyl-4H-1,3,4-oxadiazin-6(5H)-one

Following general procedure E, phenylacetic acid (40.9 mg, 0.30 mmol), DIPEA (78 \(\mu\)L, 0.45 mmol) and p-methoxybenzoyl chloride (77 mg, 0.45 mmol) in DCM (2 mL), Ph/i-Pr isothiourea catalyst (2S,3R)-5 (0.62 mg, 0.002 mmol, 1 mol%), diazene 64 (45.4 mg, 0.20 mmol) and DIPEA (52 \(\mu\)L, 0.3 mmol) for 16 h at -78 °C gave, after chromatographic purification (eluent Et\(_2\)O:petrol 1:99) (R)-14 as a colourless oil (60.9 mg, 88%); \([\alpha]_D^{20}\) -609.2 (c 0.5, CH\(_2\)Cl\(_2\)); Chiral HPLC Chiralpak AD-H (5% IPA:hexane, flow rate 1 mL min\(^{-1}\), 211 nm, 20 °C) \(t_{R}(5S): 9.9\) min, \(t_{R}(5R): 18.6\) min, 99% ee.

2-(3-fluorophenyl)-4,5-diphenyl-4H-1,3,4-oxadiazin-6(5H)-one

Following general procedure D, phenylacetic acid (40.9 mg, 0.30 mmol), DIPEA (78 \(\mu\)L, 0.45 mmol) and p-methoxybenzoyl chloride (77 mg, 0.45 mmol) in DCM (2 mL), diazene 65 (45.4 mg, 0.20 mmol), DHPB 80 (7.60 mg, 0.04 mmol) and DIPEA (52 \(\mu\)L, 0.3 mmol) for 1 h at rt gave, after chromatographic purification (eluent Et\(_2\)O:petrol 1:99) (±)-15 as a colourless oil (39.4 mg, 57%); \(\nu_{\text{max}}\) (thin film) 3062 (C-H), 1792 (C=O), 1597, 1498; \(\delta_{\text{H}}\) (400 MHz, CDCl\(_3\)) 5.96 (1H, s, C(5)H), 6.91-6.95 (1H, m, ArH), 7.02 (1H, tdd, J 8.3, 2.6, 0.9, ArH), 7.14-7.17 (2H, m, ArH), 7.20-7.31 (8H, m, ArH), 7.56-7.59 (1H, m, ArH), 7.63-7.65 (1H, m, ArH); \(\delta_{C}\) (100 MHz, CDCl\(_3\)) 59.5 (C(5)), 112.6 (d, J 24.4, ArC), 114.6 (ArC), 117.2 (d, J 21.4, ArC), 121.2 (d, J 2.7, ArC), 122.2 (ArC), 126.6 (ArC), 129.2 (ArC), 129.4 (ArC), 129.4 (ArC), 130.2
(d, J 8.1, ArC), 131.0 (d, J 5.6, 4ry ArC), 131.0 (4ry ArC), 139.9 (4ry ArC), 144.1 (4ry ArC), 160.0 (C(6)), 162.9 (d, J 245, 4ry ArC); m/z (NSI') 379 ([M+CH3O]+, 100%); HRMS (NSI') C22H20FN2O3+ ([M+CH3O]+) requires 379.1452; found 379.1456 (+0.9 ppm).

(R)-2-(3-fluorophenyl)-4,5-diphenyl-4H-1,3,4-oxadiazin-6(5H)-one

![Chemical structure](image)

Following general procedure E, phenylacetic acid (40.9 mg, 0.30 mmol), DIPEA (78 μL, 0.45 mmol) and p-methoxybenzoyl chloride (77 mg, 0.45 mmol) in DCM (2 mL), Ph/i-Pr isothiourea catalyst (25,3R)-5 (0.62 mg, 0.002 mmol, 1 mol%), diazene 65 (45.4 mg, 0.20 mmol) and DIPEA (52 μL, 0.3 mmol) for 16 h at -78 °C gave, after chromatographic purification (eluent Et3O:petrol 1:99) (5R)-15 as a colourless oil (52.5 mg, 76%); [α]D20 - 608.0 (c 0.5, CH2Cl2); Chiral HPLC Chiralpak AD-H (5% IPA:hexane, flow rate 1 mL min⁻¹, 211 nm, 20 °C) tR(5R): 8.1 min, tR(5S): 10.5 min, 99% ee.

2-(3-fluorophenyl)-4,5-diphenyl-4H-1,3,4-oxadiazin-6(5H)-one

![Chemical structure](image)

Following general procedure D, phenylacetic acid (40.9 mg, 0.30 mmol), DIPEA (78 μL, 0.45 mmol) and p-methoxybenzoyl chloride (77 mg, 0.45 mmol) in DCM (2 mL), diazene 66 (45.4 mg, 0.20 mmol), DHPB 80 (7.60 mg, 0.04 mmol) and DIPEA (52 μL, 0.3 mmol) for 1 h at rt gave, after chromatographic purification (eluent Et3O:petrol 1:99) (±)-16 as a colourless oil (40.3 mg, 58%); νmax (thin film) 3064 (C-H), 2925, 1791 (C=O), 1597, 1495; δH (300 MHz, CDCl3) 5.99 (1H, s, C(5)H), 6.92 (1H, tt, J 6.9, 1.4, ArH), 7.04-7.12 (2H, m, ArH), 7.16-7.34 (10H, m, ArH), 7.69 (1H, td, J 7.7, 1.7, ArH); δC (75 MHz, CDCl3) 59.6 (C(5)), 114.5 (ArC), 117.0 (d, J 28.8, ArC), 117.3 (d, J 12.8, 4ry ArC), 122.1 (ArC), 124.1 (d, J 5.1, ArC), 126.7 (ArC), 128.7 (ArC), 129.1 (ArC), 129.4 (ArC), 129.4 (ArC), 131.1 (4ry ArC), 131.7 (d, J 11.2, ArC), 137.7 (d, J 9.1, 4ry ArC), 144.2 (4ry ArC), 160.2 (C(6)), 160.3 (d, J 342, 4ry ArC); m/z (NSI') 379 ([M+CH3O]+, 100%); HRMS (NSI') C22H20FN2O3+ ([M+CH3O]+) requires 379.1452; found 379.1456 (+0.9 ppm).
(R)-2-(2-fluorophenyl)-4,5-diphenyl-4H-1,3,4-oxadiazin-6(5H)-one

![Chemical Structure](image)

Following general procedure E, phenylacetic acid (40.9 mg, 0.30 mmol), DIPEA (78 µL, 0.45 mmol) and p-methoxybenzoyl chloride (77 mg, 0.45 mmol) in DCM (2 mL), Ph/i-Pr isothiourea catalyst (2S,3R)-5 (0.62 mg, 0.002 mmol, 1 mol%), diazene 66 (45.4 mg, 0.20 mmol) and DIPEA (52 µL, 0.3 mmol) for 16 h at -78 °C gave, after chromatographic purification (elucent Et₂O:petrol 1:99) (5R)-**16** as a colourless oil (48.5 mg, 70%); [α]D<sup>20</sup> - 599.4 (c 0.5, CH₂Cl₂); Chiral HPLC Chiralpak AD-H (5% IPA:hexane, flow rate 1 mL min⁻¹, 211 nm, 20 °C) t<sub>R</sub>(S): 10.4 min, t<sub>R</sub>(R): 13.0 min, 99% ee.

2-(4-bromophenyl)-4,5-diphenyl-4H-1,3,4-oxadiazin-6(5H)-one

![Chemical Structure](image)

Following general procedure D, phenylacetic acid (40.9 mg, 0.30 mmol), DIPEA (78 µL, 0.45 mmol) and p-methoxybenzoyl chloride (77 mg, 0.45 mmol) in DCM (2 mL), diazene 67 (57.8 mg, 0.20 mmol), DHPB 80 (7.60 mg, 0.04 mmol) and DIPEA (52 µL, 0.3 mmol) for 1 h at rt gave, after chromatographic purification (elucent Et₂O:petrol 1:99) (±)-**17** as a white solid (51.4 mg, 63%); mp 44-46 °C; ν<sub>max</sub> (KBr) 3062 (C-H), 1789 (C=O), 1597, 1497; δ<sub>δ</sub> (300 MHz, CDCl₃) 5.95 (1H, s, C(5)H), 6.89-6.95 (1H, m, ArH), 7.13-7.27 (9H, m, ArH), 7.42-7.47 (2H, m, ArH), 7.70-7.75 (2H, m, ArH); δ<sub>C</sub> (100 MHz, CDCl₃) 59.5 (C(5)), 114.5 (ArC), 122.1 (ArC), 124.7 (4ry ArC), 126.6 (ArC), 127.0 (ArC), 127.8 (4ry ArC), 129.2 (ArC), 129.4 (ArC), 131.0 (4ry ArC), 131.8 (ArC), 140.3 (C(2)), 144.1 (4ry ArC), 160.1 (C(6)); m/z (NSI⁺) 439 ([M+CH₃O⁺], 100%); HRMS (NSI⁺) C<sub>22</sub>H₁₇⁷⁹BrN₂O₃⁺ ([M+CH₃O⁺]) requires 439.0652; found 439.0655 (+0.7 ppm).

(R)-2-(4-bromophenyl)-4,5-diphenyl-4H-1,3,4-oxadiazin-6(5H)-one

![Chemical Structure](image)
Following general procedure E, phenylacetic acid (40.9 mg, 0.30 mmol), DIPEA (78 μL, 0.45 mmol) and p-methoxybenzoyl chloride (77 mg, 0.45 mmol) in DCM (2 mL), Ph/i-Pr isothiourea catalyst (2S,3R)-5 (0.62 mg, 0.002 mmol, 1 mol%), diazene 67 (57.8 mg, 0.20 mmol) and DIPEA (52 μL, 0.3 mmol) for 16 h at -78 °C gave, after chromatographic purification (eluent Et₂O:petrol 1:99) (5R)-17 as an off-white solid (63.3 mg, 78%); [α]D 20 -609.0 (c 0.5, CH₂Cl₂); Chiral HPLC Chiralpak AD-H (5% IPA:hexane, flow rate 1 mL min⁻¹, 211 nm, 20 °C) tR(5S): 12.8 min, tR(5R): 24.1 min, >99% ee.

2-(4-chlorophenyl)-4,5-diphenyl-4H-1,3,4-oxadiazin-6(5H)-one

Following general procedure D, phenylacetic acid (40.9 mg, 0.30 mmol), DIPEA (78 μL, 0.45 mmol) and p-methoxybenzoyl chloride (77 mg, 0.45 mmol) in DCM (2 mL), diazene 68 (48.9 mg, 0.20 mmol), DHPB 80 (7.60 mg, 0.04 mmol) and DIPEA (52 μL, 0.3 mmol) for 1 h at rt gave, after chromatographic purification (eluent Et₂O:petrol 1:99) (±)-18 as an off-white solid (48.9 mg, 67%); mp 80-82 °C; νmax (KBr) 2966 (C-H), 1777 (C=O), 1595, 1497; δH (300 MHz, CDCl₃) 5.95 (1H, s, C(5)H), 6.89-6.95 (1H, m, ArH), 7.13-7.32 (11H, m, ArH), 7.77-7.82 (2H, m, ArH); δC (75 MHz, CDCl₃) 59.5 (C(5)), 114.5 (ArC), 122.1 (ArC), 126.6 (ArC), 126.8 (ArC), 127.3 (4ry ArC), 128.9 (ArC), 129.2 (ArC), 129.4 (ArC), 131.1 (4ry ArC), 136.4 (4ry ArC), 140.2 (C(2)), 144.1 (4ry ArC), 160.1 (C(6)); m/z (NSI⁺) 395 ([M+CH₃O]⁺, 100%); HRMS (NSI⁺) C₂₂H₂₀ClN₂O₃⁺ ([M+CH₃O]⁺) requires 395.1157; found 395.1158 (+0.3 ppm).

(R)-2-(4-chlorophenyl)-4,5-diphenyl-4H-1,3,4-oxadiazin-6(5H)-one

Following general procedure E, phenylacetic acid (40.9 mg, 0.30 mmol), DIPEA (78 μL, 0.45 mmol) and p-methoxybenzoyl chloride (77 mg, 0.45 mmol) in DCM (2 mL), Ph/i-Pr isothiourea catalyst (2S,3R)-5 (0.62 mg, 0.002 mmol, 1 mol%), diazene 68 (48.9 mg, 0.20 mmol) and DIPEA (52 μL, 0.3 mmol) for 16 h at -78 °C gave, after chromatographic purification (eluent Et₂O:petrol 1:99) (5R)-18 as an off-white solid (56.3 mg, 78%); [α]D 20 -
614.4 (c 0.5, CH₂Cl₂); Chiral HPLC Chiralpak AD-H (5% IPA:hexane, flow rate 1 mL min⁻¹, 211 nm, 20 °C) tₘₜ(5S): 11.5 min, tₘₜ(5R): 22.8 min, >99% ee.

2-(4-bromophenyl)-4,5-diphenyl-4H-1,3,4-oxadiazin-6(5H)-one

Following general procedure D, phenylacetic acid (40.9 mg, 0.30 mmol), DIPEA (78 μL, 0.45 mmol) and p-methoxybenzoyl chloride (77 mg, 0.45 mmol) in DCM (2 mL), diazene 69 (52.0 mg, 0.20 mmol), DHPB 80 (7.60 mg, 0.04 mmol) and DIPEA (52 μL, 0.3 mmol) for 1 h at rt gave, after chromatographic purification (eluent Et₂O:petrol 1:99) (±)-19 as an off-white solid (45.5 mg, 60%); mp 138-140 °C; νₗₛₐₓ (KBr) 3063 (C-H), 1791 (C=O), 1599, 1506; δH (400 MHz, CDCl₃) 6.05 (1H, s, C(5)H), 6.93 (1H, tt, J 6.9, 1.4, ArH), 7.20-7.28 (7H, m, ArH), 7.33-7.40 (3H, m, ArH), 7.44 (1H, ddd, J 8.0, 6.9, 1.2, ArH), 7.51 (1H, ddd, J 8.5, 6.9, 1.6, ArH), 7.78-7.83 (2H, m, ArH), 7.86 (1H, dd, J 7.4, 1.2, ArH), 8.80-8.82 (1H, m, ArH); δC (75 MHz, CDCl₃) 59.5 (C(5)), 114.6 (ArC), 122.1 (ArC), 124.9 (ArC), 125.4 (4r ArC), 125.8 (ArC), 126.3 (ArC), 126.8 (4r ArC), 127.4 (ArC), 127.5 (ArC), 128.9 (ArC), 129.2 (ArC), 129.4 (ArC), 129.5 (ArC), 130.3 (4r ArC), 131.2 (4r ArC), 131.4 (ArC), 134.1 (4r ArC), 141.5 (C(2)), 144.5 (4r ArC), 160.6 (C(6)); m/z (NSI⁻) 397 ([M+H₂O]⁻, 100%); HRMS (NSI⁻) C₁₂H₁¹N₂O₃⁺ ([M+H₂O]⁻) requires 397.1547; found 397.1548 (+0.3 ppm).

(R)-2-(naphthalen-1-yl)-4,5-diphenyl-4H-1,3,4-oxadiazin-6(5H)-one

Following general procedure E, phenylacetic acid (40.9 mg, 0.30 mmol), DIPEA (78 μL, 0.45 mmol) and p-methoxybenzoyl chloride (77 mg, 0.45 mmol) in DCM (2 mL), Ph/i-Pr isothiourea catalyst (2S,3R)-5 (0.62 mg, 0.002 mmol, 1 mol%), diazene 69 (52.0 mg, 0.20 mmol) and DIPEA (52 μL, 0.3 mmol) for 16 h at -78 °C gave, after chromatographic purification (eluent Et₂O:petrol 1:99) (5R)-19 as an off-white solid (53.5 mg, 71%); [α]D20 - 611.5 (c 1.0, CH₂Cl₂); Chiral HPLC Chiralpak AD-H (2% IPA:hexane, flow rate 1 mL min⁻¹, 211 nm, 20 °C) tₘₜ(5S): 15.7 min, tₘₜ(5R): 16.9 min, >99% ee.
allyl 2-(2-benzyloxy-1-phenylhydrazinyl)-2-phenylacetate

Following general procedure D, phenylacetic acid (40.9 mg, 0.30 mmol), DIPEA (78 µL, 0.45 mmol) and benzoyl chloride (52 µL, 0.45 mmol) in DCM (2 mL), diazene 60 (42.0 mg, 0.20 mmol), DHPB 80 (7.60 mg, 0.04 mmol) and DIPEA (52 µL, 0.3 mmol) for 1 h at rt followed by addition of allyl alcohol (2 mL) and stirring for 1 h at rt gave, after chromatographic purification (eluent Et₃O:petrol 40:60) a rotameric mixture (ratio 91:9) of (±)-20 as a colourless oil (48.6 mg, 63%); ν_max (thin film) 3287 (N-H), 3064, 2948 (C-H), 1733 (C=O), 1683 (C=O), 1599; Data for major rotamer δ_H (500 MHz, CDCl₃) 4.75 (2H, d, J 5.1, CH₂), 5.26-5.32 (2H, m, CH₂=CH), 5.87-5.93 (2H, m, C(2)H and CH₂=CH), 6.98-7.06 (3H, m, ArH), 7.31-7.43 (7H, m, ArH), 7.48-7.59 (5H, m, ArH), 8.51 (1H, s, NH); Selected data for minor rotamer δ_H (500 MHz, CDCl₃) 5.61 (1H, s, C(2)H), 7.98 (1H, s, NH); Data for major rotamer δ_C (100 MHz, CDCl₃) 66.2 (CH₂), 66.8 (C(2)), 114.9 (ArC), 119.6 (CH₂=CH), 121.7 (ArC), 127.0 (ArC), 128.6 (ArC), 128.6 (ArC), 128.9 (ArC), 129.1 (ArC), 129.4 (ArC), 131.2 (CH₂=CH), 131.7 (ArC), 133.0 (4ry ArC), 133.2 (4ry ArC), 148.3 (4ry ArC), 166.5 (C=O), 172.3 (C=O); Selected data for minor rotamer δ_C (100 MHz, CDCl₃) 65.8 (CH₂), 68.1 (C(2)), 115.4 (ArC), 122.3 (ArC), 127.8 (ArC), 129.8 (ArC), 130.2 (ArC); m/z (NSI⁺) 387 ([M+H]⁺, 100%); HRMS (NSI⁺) C₂₄H₂₃N₂O₃⁺ ([M+H]⁺) requires 387.1703; found 387.1711 (+2.0 ppm).

(R)-allyl 2-(2-benzyloxy-1-phenylhydrazinyl)-2-phenylacetate

Following general procedure E, phenylacetic acid (40.9 mg, 0.30 mmol), DIPEA (78 µL, 0.45 mmol) and benzoyl chloride (52.2 µL, 0.45 mmol) in DCM (2 mL), Ph/i-Pr isothiourea catalyst (2S,3R)-5 (0.62 mg, 0.002 mmol, 1 mol%), diazene 60 (42.0 mg, 0.20 mmol) and DIPEA (52 µL, 0.3 mmol) for 16 h at -78 °C followed by addition of allyl alcohol (2 mL) and stirring for 1 h at rt gave, after chromatographic purification (eluent Et₃O:petrol 40:60) a rotameric mixture (ratio 91:9) of (R)-20 as a colourless oil (63.8 mg, 83%); [α]_D²⁰ -30.0 (c 0.5, CH₂Cl₂); Chiral HPLC Chiralpak IB (10% IPA:hexane, flow rate 1 mL min⁻¹, 211 nm, 20 °C) t_R(2R): 18.1 min, t_R(2S): 21.8 min, 98% ee.
2-(2-benzooyl-1-phenylhydrazinyl)-N-isopropyl-2-phenylacetamide

![Chemical Structure](image)

(±)-21

Following general procedure D, phenylacetic acid (40.9 mg, 0.30 mmol), DIPEA (78 µL, 0.45 mmol) and benzooyl chloride (52 µL, 0.45 mmol) in DCM (2 mL), diazene 60 (42.0 mg, 0.20 mmol), DHPB 80 (7.60 mg, 0.04 mmol) and DIPEA (52 µL, 0.3 mmol) for 1 h at rt followed by addition of isopropylamine (2 mL) and stirring for 1 h at rt gave, after chromatographic purification (eluent Et₂O:petrol 75:25) a rotameric mixture (ratio 93:7) of (±)-21 as a white solid (53.4 mg, 69%); mp 64-66 °C; ν_{max} (KBr) 3235 (N-H), 3064, 2971 (C-H), 1653 (C=O), 1598; Data for major rotamer δ_{H} (500 MHz, CDCl₃) 1.15 (3H, d, J 6.6, CH₃), 1.21-1.26 (3H, m, CH₃), 4.13 (1H, s, J 6.5, CH), 5.29 (1H, s, C(2)H), 6.85 (2H, d, J 6.8, ArH), 7.00 (1H, t, J 7.3, ArH), 7.20-7.35 (11H, m, ArH), 7.50 (1H, t, J 7.3, ArH), 7.59 (1H, s, NH), 9.38 (1H, s, NH); Selected data for minor rotamer δ_{H} (500 MHz, CDCl₃) 1.04 (6H, d, J 6.6, CH₃), 3.96-4.03 (1H, m, CH); Data for major rotamer δ_{C} (100 MHz, CDCl₃) 22.4 (CH₃), 22.5 (CH₃), 41.6 (CH), 72.0 (C(2)), 112.5 (ArC), 120.7 (ArC), 127.0 (ArC), 128.7 (ArC), 128.9 (ArC), 129.0 (ArC), 129.5 (ArC), 129.7 (ArC), 132.0 (4ry ArC), 132.3 (4ry ArC), 134.2 (4ry ArC), 147.3 (4ry ArC), 168.9 (C=O), 169.5 (C=O); Selected data for minor rotamer δ_{C} (100 MHz, CDCl₃) 22.6 (CH₃), 41.5 (CH); m/z (NSI⁺) 388 ([M+H]⁺, 100%); HRMS (NSI⁺) C_{21}H_{26}N_{2}O_{2}⁺ ([M+H]⁺) requires 388.2020; found 388.2027 (+1.9 ppm).

(R)-2-(2-benzooyl-1-phenylhydrazinyl)-N-isopropyl-2-phenylacetamide

![Chemical Structure](image)

(2R)-21

Following general procedure E, phenylacetic acid (40.9 mg, 0.30 mmol), DIPEA (78 µL, 0.45 mmol) and benzooyl chloride (52.2 µL, 0.45 mmol) in DCM (2 mL), Ph/i-Pr isothiourea catalyst (2S,3R)-5 (0.62 mg, 0.002 mmol, 1 mol%), diazene 60 (42.0 mg, 0.20 mmol) and DIPEA (52 µL, 0.3 mmol) for 16 h at -78 °C followed by addition of pyrrolidine (2 mL) and stirring for 1 h at rt gave, after chromatographic purification (eluent Et₂O:petrol 75:25) a rotameric mixture (ratio 93:7) of (2R)-21 as a white solid (71.0 mg, 92%); [α]₀^{20} -132 (c 0.125, CH₂Cl₂); Chiral HPLC Chiralpak IB (20% IPA:hexane, flow rate 1 mL min⁻¹, 211 nm, 20 °C) tₘ(2S): 6.6 min, tₘ(2R): 7.6 min, 99% ee.
N’-(2-oxo-1-phenyl-2-(pyrrolidin-1-yl)ethyl)-N’-phenylbenzohydrazide

![Chemical Structure of N’-(2-oxo-1-phenyl-2-(pyrrolidin-1-yl)ethyl)-N’-phenylbenzohydrazide](image)

Following general procedure E, phenylacetic acid (40.9 mg, 0.30 mmol), DIPEA (78 μL, 0.45 mmol) and benzoyl chloride (52 μL, 0.45 mmol) in DCM (2 mL), diazene 60 (42.0 mg, 0.20 mmol), DHPB 80 (7.60 mg, 0.04 mmol) and DIPEA (52 μL, 0.3 mmol) for 1 h at rt followed by addition of pyrrolidine (2 mL) and stirring for 1 h at rt gave, after chromatographic purification (eluent Et₂O) a rotameric mixture (ratio 96:4) of (±)-22 as a colourless oil (71.3 mg, 89%); νmax (thin film) 3344 (N-H), 3063 (C-H), 1687 (C=O), 1582; Data for major rotamer δH (500 MHZ, CDCl₃) 1.74-1.92 (4H, m, 2CH₂), 3.07-3.10 (1H, m, CHH), 3.42-3.54 (3H, m, CH₂ and CHH), 5.77 (1H, s, C(2)H), 6.85-6.93 (3H, m, ArH), 7.19-7.27 (7H, m, ArH), 7.36 (1H, t, J 7.1, ArH), 7.45 (2H, d, J 7.1, ArH), 7.50 (2H, d, J 7.4, ArH), 9.41 (1H, s, NH); Selected data for minor rotamer δH (500 MHZ, CDCl₃) 5.44 (1H, s, C(2)H), 8.65 (1H, s, NH); Data for major rotamer δC (100 MHz, CDCl₃) 24.1 (CH₂), 26.1 (CH₂), 45.8 (CH₂), 46.3 (CH₂), 65.7 (C(2)), 114.9 (ArC), 121.4 (ArC), 127.1 (ArC), 128.4 (ArC), 128.7 (ArC), 128.8 (ArC), 129.4 (ArC), 129.5 (ArC), 131.5 (ArC), 133.2 (4ry ArC), 133.4 (4ry ArC), 149.2 (4ry ArC), 166.4 (C=O), 170.7 (C=O); Selected data for minor rotamer δC (100 MHz, CDCl₃) 23.9 (CH₂), 26.0 (CH₂), 67.7 (C(2)), 115.7 (ArC), 121.8 (ArC), 126.9 (ArC), 127.8 (ArC), 129.7 (ArC), 130.5 (ArC); m/z (NSI⁺) 400 ([M+H⁺], 100%); HRMS (NSI⁺) C₂₀H₂₂N₂O₂⁺ ([M+H⁺]) requires 400.2020; found 400.2026 (+1.6 ppm).

(R)-N’-(2-oxo-1-phenyl-2-(pyrrolidin-1-yl)ethyl)-N’-phenylbenzohydrazide

![Chemical Structure of (R)-N’-(2-oxo-1-phenyl-2-(pyrrolidin-1-yl)ethyl)-N’-phenylbenzohydrazide](image)

Following general procedure E, phenylacetic acid (40.9 mg, 0.30 mmol), DIPEA (78 μL, 0.45 mmol) and benzoyl chloride (52.2 μL, 0.45 mmol) in DCM (2 mL), Ph/i-Pr isothiourea catalyst (2S,3R)-5 (0.62 mg, 0.002 mmol, 1 mol%), diazene 60 (42.0 mg, 0.20 mmol) and DIPEA (52 μL, 0.3 mmol) for 16 h at -78 °C followed by addition of pyrrolidine (2 mL) and stirring for 1 h at rt gave, after chromatographic purification (eluent Et₂O) a rotameric mixture (ratio 96:4) of (2R)-22 as a colourless oil (69.7 mg, 87%); [α]D²⁰ -96.6 (c 0.5, CH₂Cl₂); Chiral HPLC Chiralpak IB (40% IPA:hexane, flow rate 1 mL min⁻¹, 211 nm, 20 °C) tR(2S): 6.3 min, tR(2R): 11.1 min, 99% ee.
methyl 2-(2-benzoyl-1-phenylhydrazinyl)-2-(4-methoxyphenyl)acetate

(±)-23

Following general procedure D, 4-methoxyphenylacetic acid (49.9 mg, 0.30 mmol), DIPEA (78 µL, 0.45 mmol) and benzooyl chloride (52 µL, 0.45 mmol) in DCM (2 mL), diazene 60 (42.0 mg, 0.20 mmol), DHPB 80 (7.60 mg, 0.04 mmol) and DIPEA (52 µL, 0.3 mmol) for 1 h at rt followed by addition of MeOH (2 mL) and stirring for 1 h at rt gave, after chromatographic purification (eluent EtOAc:petrol 35:65) a rotameric mixture (ratio 89:11) of (±)-23 as a light yellow solid (58.3 mg, 75%); mp 36-38 °C; \( \nu_{\text{max}} \) (KBr) 3368 (N-H), 3060, 2952 (C-H), 1734 (C=O), 1675 (C=O), 1612, 1514; Data for major rotamer \( \delta_{\text{H}} \) (300 MHz, CDCl\( _3 \)) 3.66 (3H, s, CH\( _3 \)), 3.71 (3H, s, CH\( _3 \)), 5.75 (1H, s, C(2)H), 6.75-6.79 (2H, m, ArH), 6.85-6.95 (3H, m, ArH), 7.18-7.24 (2H, m, ArH), 7.26-7.34 (4H, m, ArH), 7.36-7.42 (1H, m, ArH), 7.48-7.52 (2H, m, ArH), 8.43 (1H, s, NH); Selected data for minor rotamer \( \delta_{\text{H}} \) (300 MHz, CDCl\( _3 \)) 3.60 (3H, s, CH\( _3 \)), 3.71 (3H, s, CH\( _3 \)), 5.45 (1H, s, C(2)H), 6.56-6.59 (2H, m, ArH), 7.85 (1H, s, NH); Data for major rotamer \( \delta_{\text{C}} \) (75 MHz, CDCl\( _3 \)) 52.5 (CH\( _3 \)), 55.2 (CH\( _3 \)), 66.1 (C(2)), 114.0 (ArC), 114.8 (ArC), 121.6 (ArC), 125.2 (4r ArC), 127.1 (ArC), 128.6 (ArC), 129.5 (ArC), 130.4 (ArC), 131.8 (ArC), 133.0 (4r ArC), 148.4 (4r ArC), 159.9 (4r ArC), 166.6 (C=O), 173.3 (C=O); Selected data for minor rotamer \( \delta_{\text{C}} \) (75 MHz, CDCl\( _3 \)) 52.4 (CH\( _3 \)), 55.4 (CH\( _3 \)), 67.2 (C(2)), 115.3 (ArC), 122.2 (ArC), 127.8 (ArC), 129.9 (ArC), 131.4 (ArC); \( \text{m/z (NSI)} \) 391 ([M+H\( ^{+} \), 100%); HRMS (NSI) \( \text{C}_{23}\text{H}_{23}\text{N}_{2}\text{O}_{4}^{+} \) ([M+H\( ^{+} \)]) requires 391.1652; found 391.1655 (+0.7 ppm).

(R)-methyl 2-(2-benzoyl-1-phenylhydrazinyl)-2-(4-methoxyphenyl)acetate

(2R)-23

Following general procedure E, 4-methoxyphenylacetic acid (49.9 mg, 0.30 mmol), DIPEA (78 µL, 0.45 mmol) and benzooyl chloride (52.2 µL, 0.45 mmol) in DCM (2 mL), Ph/\( \text{i-Pr} \) isothiourea catalyst (2S,3R)-5 (0.62 mg, 0.002 mmol, 1 mol%), diazene 60 (42.0 mg, 0.20 mmol) and DIPEA (52 µL, 0.3 mmol) for 16 h at -78 °C followed by addition of MeOH (2
mL) and stirring for 1 h at rt gave, after chromatographic purification (eluent EtOAc:petrol 30:70) a rotameric mixture (ratio 89:11) of (2R)-23 as a light yellow oil (59.3 mg, 76%); \([\alpha]_D^{20} -30.8\) (c 0.5, CHCl\(_3\)); Chiral HPLC Chiralpak IB (10% IPA:hexane, flow rate 1 mL min\(^{-1}\), 211 nm, 20 °C) \(t_R(2S)\): 19.3 min, \(t_R(2R)\): 26.2 min, 98% ee.

methyl 2-(2-benzoyl-1-phenylhydrazinyl)-2-(thiophen-3-yl)acetate

Following general procedure D, thiophene-3-acetic acid (42.7 mg, 0.30 mmol), DIPEA (78 \(\mu\)L, 0.45 mmol) and benzoyl chloride (52 \(\mu\)L, 0.45 mmol) in DCM (2 mL), diazene 60 (42.0 mg, 0.20 mmol), DHPB 80 (7.60 mg, 0.04 mmol) and DIPEA (52 \(\mu\)L, 0.3 mmol) for 1 h at rt followed by addition of MeOH (2 mL) and stirring for 1 h at rt gave, after chromatographic purification (eluent EtOAc:petrol 25:75) a rotameric mixture (ratio 92:8) of (+)-24 as a light yellow solid (67.2 mg, 92%); mp 128-130 °C; \(\nu_{\text{max}}\) (KBr) 3355 (N-H), 3078, 2952 (C-H), 1727 (C=O), 1685 (C=O), 1600, 1514; Data for major rotamer \(\delta_{\text{n}}\) (400 MHz, CDCl\(_3\)) 3.72 (3H, s, CH\(_3\)), 5.83 (1H, s, C(2)H), 6.87-6.95 (3H, m, ArH), 7.16-7.23 (4H, m, ArH), 7.28-7.33 (3H, m, ArH), 7.38-7.42 (1H, m, ArH), 7.49-7.51 (2H, m, ArH), 8.47 (1H, s, NH); Selected data for minor rotamer \(\delta_{\text{n}}\) (400 MHz, CDCl\(_3\)) 3.59 (3H, s, CH\(_3\)), 5.56 (1H, s, C(2)H), 6.57 (1H, dd, \(J\) 5.0, 1.3, ArH), 7.89 (1H, s, NH); Data for major rotamer \(\delta_{\text{c}}\) (75 MHz, CDCl\(_3\)) 52.6 (CH\(_3\)), 62.7 (C(2)), 114.8 (ArC), 121.8 (ArC), 125.0 (ArC), 126.3 (ArC), 127.1 (ArC), 128.2 (ArC), 128.7 (ArC), 129.5 (ArC), 131.9 (ArC), 133.0 (4ry ArC), 133.8 (4ry ArC), 148.1 (4ry ArC), 166.8 (C=O), 173.0 (C=O); Selected data for minor rotamer \(\delta_{\text{c}}\) (100 MHz, CDCl\(_3\)) 52.5 (CH\(_3\)), 62.8 (C(2)), 115.4 (ArC), 122.3 (ArC), 126.1 (ArC), 127.8 (ArC), 129.9 (ArC), 130.6 (ArC); \(m/z\) (NSI') 367 ([M+H]\(^+\), 100%); HRMS (NSI') \(C_{26}H_{10}N_2O_2S^+\) ([M+H]\(^+\)) requires 367.1111; found 367.1114 (+0.8 ppm).

(R)-methyl 2-(2-benzoyl-1-phenylhydrazinyl)-2-(thiophen-3-yl)acetate

Following general procedure E, thiophene-3-acetic acid (42.7 mg, 0.30 mmol), DIPEA (78 \(\mu\)L, 0.45 mmol) and benzoyl chloride (52.2 \(\mu\)L, 0.45 mmol) in DCM (2 mL), Ph/i-Pr isothiourea catalyst (2S,3R)-5 (0.62 mg, 0.002 mmol, 1 mol%), diazene 60 (42.0 mg, 0.20
mmol) and DIPEA (52 μL, 0.3 mmol) for 16 h at -78 °C followed by addition of MeOH (2 mL) and stirring for 1 h at rt gave, after chromatographic purification (eluent EtOAc:petrol 25:75) a rotameric mixture (ratio 91:9) of (2R)-24 as a light yellow oil (63.1 mg, 86%); [α]D 20 
-26.2 (c 0.5, CH₂Cl₂); Chiral HPLC Chiralel OD-H (10% IPA:hexane, flow rate 1 mL min⁻¹, 211 nm, 20 °C) t₀(2S): 28.0 min, t₀(2R): 31.5 min, >99% ee.

**methyl 2-(2-(4-methylbenzoyl)-1-phenylhydrazinyl)-2-phenylacetate**

![Chemical structure of (±)-25]

Following general procedure D, phenylacetic acid (81.7 mg, 0.60 mmol), DIPEA (156 μL, 0.90 mmol) and benzoyl chloride (104 μL, 0.90 mmol) in DCM (2 mL), diazene 71 (44.8 mg, 0.20 mmol), DHPB 80 (7.60 mg, 0.04 mmol) and DIPEA (52 μL, 0.3 mmol) for 2 h at rt followed by addition of MeOH (2 mL) and stirring for 1 h at rt gave, after chromatographic purification (eluent Et₂O:petrol 40:60) a rotameric mixture (ratio 92:8) of (±)-25 as a white solid (66.0 mg, 88%); mp 36-38 °C; νmax (KBr) 3374 (N-H), 3030, 2924 (C-H), 1750 (C=O), 1708 (C=O), 1599; Data for major rotamer δH (400 MHz, CDCl₃) 2.28 (3H, s, CH₃), 3.73 (3H, s, CH₃), 5.80 (1H, s, C(2)H), 6.86-6.95 (3H, m, ArH), 7.08 (2H, d, J 7.9, ArH), 7.19-7.27 (5H, m, ArH), 7.34-7.39 (4H, m, ArH), 8.40 (1H, s, NH); Selected data for minor rotamer δH (400 MHz, CDCl₃) 2.18 (3H, s, CH₃), 3.61 (3H, s, CH₃), 5.51 (1H, s, C(2)H), 6.70-6.80 (2H, m, ArH), 7.84 (1H, s, NH); Data for major rotamer δC (75 MHz, CDCl₃) 21.5 (CH₃), 52.5 (CH₃), 66.7 (C(2)), 114.8 (ArC), 121.6 (ArC), 127.1 (ArC), 128.6 (ArC), 128.9 (ArC), 129.1 (ArC), 129.2 (ArC), 129.5 (ArC), 130.0 (4ry ArC), 133.3 (4ry ArC), 142.3 (4ry ArC), 148.5 (4ry ArC), 166.5 (C=O), 173.1 (C=O); Selected data for minor rotamer δC (100 MHz, CDCl₃) 22.7 (CH₃), 52.4 (CH₃), 68.0 (C(2)), 115.4 (ArC), 122.2 (ArC), 127.8 (ArC), 128.0 (ArC), 129.8 (ArC), 130.2 (ArC); m/z (NSI⁺) 375 ([M+H]⁺, 100%); HRMS (NSI⁺) C₂₃H₂₃N₂O₃⁺ ([M+H]⁺) requires 375.1703; found 375.1706 (+0.7 ppm).

**(R)-methyl 2-(2-(4-methylbenzoyl)-1-phenylhydrazinyl)-2-phenylacetate**

![Chemical structure of (2R)-25]

Following general procedure E, phenylacetic acid (81.7 mg, 0.60 mmol), DIPEA (156 μL, 0.90 mmol) and benzoyl chloride (104 μL, 0.90 mmol) in DCM (2 mL), Ph/i-Pr isothiourea catalyst (2S,3R)-5 (0.62 mg, 0.002 mmol, 1 mol%), diazene 71 (44.8 mg, 0.20 mmol) and
DIPEA (52 μL, 0.3 mmol) for 16 h at -78 °C followed by addition of MeOH (2 mL) and stirring for 1 h at rt gave, after chromatographic purification (eluent Et₂O:petrol 40:60) a rotameric mixture (ratio 92:8) of (2R)-26 as a white solid (49.2 mg, 66%); [α]_D<sup>20</sup> -24.3 (c 1.0, CH₂Cl₂); Chiral HPLC Chiralcel OD-H (10% IPA:hexane, flow rate 1 mL min⁻¹, 211 nm, 20 °C) t<sub>R</sub>(2S): 11.9 min, t<sub>R</sub>(2R): 14.3 min, >99% ee.

**methyl 2-(2-(furan-2-carbonyl)-1-phenylhydrazinyl)-2-phenylacetate**

![Image](https://example.com/image)

(±)-26

Following general procedure D, phenylacetic acid (40.9 mg, 0.30 mmol), DIPEA (78.0 μL, 0.45 mmol) and benzoyl chloride (52.2 μL, 0.90 mmol) in DCM (2 mL), diazene 72 (40.0 mg, 0.20 mmol), DHPB 80 (7.60 mg, 0.04 mmol) and DIPEA (52 μL, 0.3 mmol) for 1 h at rt followed by addition of MeOH (2 mL) and stirring for 1 h at rt gave, after chromatographic purification (eluent Et₂O:petrol 50:50) a rotameric mixture (ratio 93:7) of (±)-26 as a white solid (50.3 mg, 72%); mp 148-150 °C; ν<sub>max</sub> (KBr) 3345 (N-H), 3097, 2950 (C-H), 1729 (C=O), 1695 (C=O), 1598; Data for major rotamer δ<sub>H</sub> (300 MHz, CDCl₃) 3.72 (3H, s, CH₃), 5.77 (1H, s, C(2)H), 6.36 (1H, dd, J 3.5, 1.8, ArH), 6.86-6.96 (4H, m, ArH), 7.18-7.24 (5H, m, ArH), 7.34-7.38 (3H, m, ArH), 8.67 (1H, s, NH); Selected data for minor rotamer δ<sub>H</sub> (300 MHz, CDCl₃) 3.65 (3H, s, CH₃), 5.65 (1H, s, C(2)H), 6.14 (1H, dd, J 3.5, 1.7, ArH), 7.82 (1H, s, NH); Data for major rotamer δ<sub>C</sub> (75 MHz, CDCl₃) 52.5 (CH₃), 66.7 (C(2)), 112.0 (ArC), 115.0 (ArC), 115.5 (ArC), 121.8 (ArC), 128.6 (ArC), 128.9 (ArC), 129.2 (ArC), 129.4 (ArC), 133.1 (4ry ArC), 144.4 (4ry ArC), 146.6 (4ry ArC), 148.4 (4ry ArC), 157.2 (C=O), 172.7 (C=O); Selected data for minor rotamer δ<sub>C</sub> (75 MHz, CDCl₃) 52.5 (CH₃), 67.6 (C(2)), 112.0 (ArC), 115.2 (ArC), 117.2 (ArC), 122.4 (ArC), 128.5 (ArC), 129.8 (ArC), 130.0 (ArC), 144.9 (ArC); m/z (NSI⁺) 351 ([M+H]⁺, 100%); HRMS (NSI⁺) C₂₀H₁₉N₂O₄⁺ ([M+H]⁺) requires 351.1339; found 351.1339 (-0.1 ppm).

**(R)-methyl 2-(2-(furan-2-carbonyl)-1-phenylhydrazinyl)-2-phenylacetate**

![Image](https://example.com/image)

(2R)-26

Following general procedure E, phenylacetic acid (40.9 mg, 0.30 mmol), DIPEA (78.0 μL, 0.45 mmol) and benzoyl chloride (52.2 μL, 0.45 mmol) in DCM (2 mL), Ph/i-Pr isothiourea catalyst (2S,3R)-5 (0.62 mg, 0.002 mmol, 1 mol%), diazene 72 (40.0 mg, 0.20 mmol) and
DIPEA (52 µL, 0.3 mmol) for 16 h at -78 °C followed by addition of MeOH (2 mL) and stirring for 1 h at rt gave, after chromatographic purification (eluent Et₂O:petrol 50:50) a rotameric mixture (ratio 93:7) of (2R)-26 as a white solid (59.5 mg, 85%); [α]D30 -38.8 (c 0.5, CH₂Cl₂); Chiral HPLC Chiralpak IB (10% IPA:hexane, flow rate 1 mL min⁻¹, 211 nm, 20 °C) tR(2S): 16.2 min, tR(2R): 21.5 min, 99% ee.

methyl 2-(2-(4-nitrobenzoyl)-1-phenylhydrazinyl)-2-phenylacetate

Following general procedure D, phenylacetic acid (40.9 mg, 0.30 mmol), DIPEA (78 µL, 0.45 mmol) and benzoyl chloride (52 µL, 0.45 mmol) in DCM (2 mL), diazene 70 (51.0 mg, 0.20 mmol), DHPB 80 (7.60 mg, 0.04 mmol) and DIPEA (52 µL, 0.3 mmol) for 1 h at rt followed by addition of MeOH (2 mL) and stirring for 1 h at rt, gave, after chromatographic purification (eluent Et₂O:petrol 50:50) a rotameric mixture (ratio 69:31) of (±)-27 as a light yellow solid (66.0 mg, 81%); mp 58-56 °C; νmax (KBr) 3412 (N-H), 3075, 2953 (C-H), 1735 (C=O), 1678 (C=O), 1599, 1525 (N-O), 1346 (N-O); Data for major rotamer δH (300 MHz, CDCl₃) 3.74 (3H, s, CH₃), 5.81 (1H, s, C(2)H), 6.91-6.95 (3H, m, ArH), 7.21-7.28 (5H, m, ArH), 7.35-7.39 (2H, m, ArH), 7.55-7.58 (2H, m, ArH), 8.10-8.13 (2H, m, ArH), 8.62 (1H, s, NH); Selected data for minor rotamer δH (300 MHz, CDCl₃) 3.61 (3H, s, CH₃), 5.46 (1H, s, C(2)H), 7.77-7.80 (2H, m, ArH), 8.12 (1H, s, NH); Data for major rotamer δC (75 MHz, CDCl₃) 52.6 (CH₃), 66.8 (C(2)), 114.9 (ArC), 122.1 (ArC), 123.8 (ArC), 128.3 (ArC), 128.7 (ArC), 129.1 (ArC), 129.6 (ArC), 133.1 (4ry ArC), 138.5 (4ry ArC), 148.0 (4ry ArC), 148.6 (4ry ArC), 164.8 (C=O), 173.1 (C=O); Selected data for minor rotamer δC (75 MHz, CDCl₃) 52.6 (CH₃), 68.4 (C(2)), 115.8 (ArC), 122.3 (ArC), 123.0 (ArC), 128.6 (ArC), 128.9 (ArC), 130.1 (ArC), 130.3 (ArC), 132.4 (4ry ArC), 138.6 (4ry ArC), 149.7 (4ry ArC), 171.4 (C=O), 171.5 (C=O); m/z (NSI) 406 ([M+H]+, 100%); HRMS (NSI) C₂₂H₂₀N₃O₅⁺ ([M+H]+) requires 406.1397; found 406.1399 (+0.4 ppm).

(R)-methyl 2-(2-(4-nitrobenzoyl)-1-phenylhydrazinyl)-2-phenylacetate

Following general procedure E, phenylacetic acid (40.9 mg, 0.30 mmol), DIPEA (78 µL, 0.45 mmol) and benzoyl chloride (52.2 µL, 0.45 mmol) in DCM (2 mL), Ph/i-Pr isothiourea
catalyst (2S,3R)-5 (0.62 mg, 0.002 mmol, 1 mol%), diazene 70 (51.0 mg, 0.20 mmol) and DIPEA (52 μL, 0.3 mmol) for 16 h at -78 °C followed by addition of MeOH (2 mL) and stirring for 1 h at rt gave, after chromatographic purification (eluent Et2O:petrol 50:50) a rotameric mixture (ratio 69:31) of (2R)-27 as a light yellow solid (67.8 mg, 84%); [α]D
20
 = -47.0 (c 0.5, CH2Cl2); Chiral HPLC Chiralpak IA (40% IPA:hexane, flow rate 1 mL min⁻¹, 211 nm, 20 °C) tR(2S): 20.9 min, tR(2R): 30.6 min, 99% ee.

methyl 2-(2-(4-nitrobenzoyl)-1-phenylhydrazinyl)-2-(o-tolyl)acetate

Following general procedure D, o-tolylacetic acid (45.1 mg, 0.30 mmol), DIPEA (78 μL, 0.45 mmol) and benzoyl chloride (52 μL, 0.45 mmol) in DCM (2 mL), diazene 70 (51.0 mg, 0.20 mmol), DHPB 80 (7.60 mg, 0.04 mmol) and DIPEA (52 μL, 0.3 mmol) for 1 h at rt followed by addition of MeOH (2 mL) and stirring for 1 h at rt gave, after chromatographic purification (eluent Et2O:petrol 50:50) a rotameric mixture (ratio 55:45) of (±)-28 as a light yellow solid (63.0 mg, 75%); mp 56-58 °C; νmax (KBr) 3333 (N-H), 3085, 2962 (C-H), 1721 (C=O), 1679 (C=O), 1598, 1529 (N-O), 1348 (N-O); Data for both rotamers δH (400 MHz, CDCl3) 1.69 (3H, s, CH3), 2.53 (3H, s, CH3), 3.60 (3H, s, CH3), 3.73 (3H, s, CH3), 5.64 (1H, s, C(2)H), 5.91 (1H, s, C(2)H), 6.74-6.76 (1H, m, ArH), 6.82-6.85 (2H, m, ArH), 6.90-7.07 (7H, m, ArH), 7.12-7.21 (6H, m, ArH), 7.23-7.27 (2H, m, ArH), 7.36-7.40 (2H, m, ArH), 7.55-7.58 (2H, m, ArH), 7.79-7.82 (2H, m, ArH), 8.10-8.13 (2H, m, ArH), 8.18 (1H, s, NH), 8.50 (1H, s, NH); Data for both rotamers δC (100 MHz, CDCl3) 18.5 (CH3), 19.2 (CH3), 52.5 (CH3), 52.6 (CH3), 63.8 (C(2)), 65.2 (C(2)), 114.3 (ArC), 115.5 (ArC), 121.7 (ArC), 122.3 (ArC), 123.0 (ArC), 123.8 (ArC), 125.5 (ArC), 126.7 (ArC), 127.7 (ArC), 128.2 (ArC), 128.4 (ArC), 129.3 (ArC), 129.6 (ArC), 129.7 (ArC), 129.9 (ArC), 130.2 (ArC), 130.8 (ArC), 130.8 (4ry ArC), 131.2 (ArC), 131.3 (4ry ArC), 138.2 (4ry ArC), 138.6 (4ry ArC), 138.7 (4ry ArC), 139.8 (4ry ArC), 148.0 (4ry ArC), 148.6 (4ry ArC), 148.8 (4ry ArC), 149.7 (4ry ArC), 164.7 (C=O), 171.7 (C=O), 171.9 (C=O), 173.6 (C=O); m/z (NSI) 442 ([M+Na]+, 42%); HRMS (NSI) C23H23N3NaO6+ ([M+Na]+) requires 442.1373; found 442.1375 (+0.4 ppm).
(R)-methyl 2-(2-(4-nitrobenzoyl)-1-phenylhydrazinyl)-2-(o-tolyl)acetate

Following general procedure E, o-tolylacetic acid (45.1 mg, 0.30 mmol), DIPEA (78 μL, 0.45 mmol) and benzoyl chloride (52.2 μL, 0.45 mmol) in DCM (2 mL), Ph/i-Pr isothiourea catalyst (2S,3R)-5 (0.62 mg, 0.002 mmol, 1 mol%), diazene 70 (51.0 mg, 0.20 mmol) and DIPEA (52 μL, 0.3 mmol) for 16 h at -78 °C followed by addition of MeOH (2 mL) and stirring for 1 h at rt gave, after chromatographic purification (eluent Et₂O:petrol 50:50) a rotameric mixture (ratio 55:45) of (2R)-28 as a light yellow solid (67.7 mg, 81%); [α]_D²⁰ -30.0 (c 0.25, CH₂Cl₂); Chiral HPLC Chiralpak IA (40% IPA:hexane, flow rate 1 mL min⁻¹, 211 nm, 20 °C) t_R(2S): 11.7 min, t_R(2R): 16.1 min, 99% ee.

methyl 2-(naphthalen-1-yl)-2-(2-(4-nitrobenzoyl)-1-phenylhydrazinyl)acetate

Following general procedure D, 1-naphthylacetic acid (55.9 mg, 0.30 mmol), DIPEA (78 μL, 0.45 mmol) and benzoyl chloride (52 μL, 0.45 mmol) in DCM (2 mL), diazene 70 (51.0 mg, 0.20 mmol), DHPB 80 (7.60 mg, 0.04 mmol) and DIPEA (52 μL, 0.3 mmol) for 1 h at rt followed by addition of MeOH (2 mL) and stirring for 1 h at rt gave, after chromatographic purification (eluent Et₂O:petrol 50:50) a rotameric mixture (ratio 78:22) of (±)-29 as a light yellow solid (68.0 mg, 75%); mp 74-76 °C; ν_max (KBr) 3415 (N-H), 3062, 2953 (C-H), 1735 (C=O), 1670 (C=O), 1599, 1522 (N-O), 1344 (N-O); Data for major rotamer δ_H (400 MHz, CDCl₃) 3.66 (3H, s, CH₃), 6.30 (1H, s, C(2)H), 6.53-6.56 (2H, m, ArH), 6.96-7.00 (1H, m, ArH), 7.10 (1H, t, J 7.3, ArH), 7.16-7.19 (1H, m, ArH), 7.23-7.32 (6H, m, ArH), 7.41-7.47 (3H, m, ArH), 7.59 (1H, d, J 8.1, ArH), 7.75-7.79 (1H, m, ArH), 8.16 (1H, s, NH); Selected data for minor rotamer δ_H (400 MHz, CDCl₃) 3.76 (3H, s, CH₃), 6.52 (1H, s, C(2)H), 7.03-7.05 (2H, m, ArH), 8.04-8.07 (2H, m, ArH), 8.18 (1H, d, J 8.7, ArH), 8.57 (1H, s, NH); Data for both rotamers δ_C (100 MHz, CDCl₃) 52.7 (CH₃), 52.7 (CH₂), 63.5 (C(2)), 63.9 (C(2)), 114.5 (ArC), 115.0 (ArC), 122.0 (ArC), 122.1 (ArC), 122.9 (ArC), 123.7 (ArC), 123.7 (ArC), 124.3 (ArC), 125.3 (ArC), 125.8 (ArC), 126.2 (ArC), 126.6 (ArC), 126.8 (ArC), 127.3 (ArC), 127.4 (ArC), 128.2 (ArC), 128.5 (ArC), 128.7 (ArC), 128.7
(ArC), 129.3 (4ry ArC), 129.8 (ArC), 130.4 (ArC), 130.4 (ArC), 130.5 (ArC), 131.7 (4ry ArC), 132.3 (4ry ArC), 133.6 (4ry ArC), 133.8 (4ry ArC), 137.5 (4ry ArC), 138.5 (4ry ArC), 148.0 (4ry ArC), 148.0 (4ry ArC), 148.5 (4ry ArC), 149.6 (4ry ArC), 164.3 (C=O), 171.6 (C=O), 172.0 (C=O), 173.5 (C=O); m/z (NSI') 478 ([M+Na]', 97%); HRMS (NSI') C_{36}H_{22}N_{3}NaO_{5}^{-} ([M+Na]') requires 478.1373; found 478.1377 (+0.7 ppm).

(R)-methyl 2-(naphthalen-1-yl)-2-(2-(4-nitrobenzoyl)-1-phenylhydrazinyl)acetate

Following general procedure E, 1-naphthylacetic acid (55.9 mg, 0.30 mmol), DIPEA (78 μL, 0.45 mmol) and benzoyl chloride (52.2 μL, 0.45 mmol) in DCM (2 mL), Ph/i-Pr isothiourea catalyst (2S,3R)-5 (0.62 mg, 0.002 mmol, 1 mol%), diazene 70 (51.0 mg, 0.20 mmol) and DIPEA (52 μL, 0.3 mmol) for 16 h at -78 °C followed by addition of MeOH (2 mL) and stirring for 1 h at rt gave, after chromatographic purification (eluent Et₂O:petrol 50:50) a rotameric mixture (ratio 78:22) of (2R)-29 as a light yellow solid (72.0 mg, 79%); [α]_{D}^{20} +20.0 (c 0.5, CH₂Cl₂); Chiral HPLC Chiralpak IA (40% IPA:hexane, flow rate 1 mL min⁻¹, 211 nm, 20 °C) tₘ(2S): 13.2 min, tₘ(2R): 29.0 min, 99% ee.

methyl 2-(2-(4-nitrobenzoyl)-1-phenylhydrazinyl)-2-(4-(trifluoromethyl)phenyl)acetate

Following general procedure D, 4-trifluoromethylphenylacetic acid (61.3 mg, 0.30 mmol), DIPEA (78 μL, 0.45 mmol) and benzoyl chloride (52 μL, 0.45 mmol) in DCM (2 mL), diazene 70 (51.0 mg, 0.20 mmol), DHPB 80 (7.60 mg, 0.04 mmol) and DIPEA (52 μL, 0.3 mmol) for 1 h at rt followed by addition of MeOH (2 mL) and stirring for 1 h at rt gave, after chromatographic purification (eluent Et₂O:petrol 50:50) a rotameric mixture (ratio 74:26) of (±)-30 as a light yellow solid (74.0 mg, 78%); mp 150-152 °C; ν<sub>max</sub> (KBr) 3412 (N-H), 3085, 2956 (C-H), 1735 (C=O), 1680 (C=O), 1600, 1524 (N-O), 1323 (N-O); Data for major rotamer δ<sub>H</sub> (400 MHz, CDCl₃) 3.77 (3H, s, CH₃), 5.83 (1H, s, C(2)H), 6.93-6.97 (2H, m, ArH), 7.23-7.28 (2H, m, ArH), 7.34-7.41 (1H, m, ArH), 7.52 (4H, s, ArH), 7.58-7.61 (2H, m,
ArH), 8.11-8.15 (2H, m, ArH), 8.71 (1H, s, NH); Selected data for minor rotamer δH (400 MHz, CDCl₃) 3.65 (3H, s, CH₃), 5.12 (1H, s, C(2)H), 6.90-6.92 (2H, m, ArH), 7.03-7.10 (3H, m, ArH), 7.15-7.18 (2H, m, ArH), 7.78-7.81 (2H, m, ArH), 8.17 (1H, s, NH); Data for both rotamers δC (100 MHz, CDCl₃) 52.8 (CH₃), 52.9 (CH₃), 66.4 (C(2)), 67.9 (C(2)), 115.1 (ArC), 115.8 (ArC), 122.4 (ArC), 122.6 (ArC), 123.4 (ArC), 123.9 (ArC), 125.1 (4ry ArC), 125.6 (q, J 3.6, ArC), 125.7 (q, J 3.6, ArC), 128.2 (ArC), 128.4 (ArC), 129.4 (ArC), 129.7 (ArC), 130.2 (ArC), 130.6 (ArC), 131.0 (4ry ArC), 131.3 (4ry ArC), 136.4 (4ry ArC), 137.3 (4ry ArC), 138.1 (4ry ArC), 147.7 (4ry ArC), 148.2 (4ry ArC), 148.8 (4ry ArC), 149.9 (4ry ArC), 164.6 (C=O), 170.7 (C=O), 171.1 (C=O), 172.5 (C=O); m/z (NSI') 396 ([M+Na]⁺, 65%); HRMS (NSI') C₂₆H₁₈F₃N₃NaO₂⁺ ([M+Na]⁺) requires 496.1091; found 496.1094 (+0.7 ppm).

(R)-methyl 2-(2-(4-nitrobenzoyl)-1-phenylhydrazinyl)-2-(4-(trifluoromethyl)phenyl)acetate

Following general procedure E, 4-trifluoromethylphenylacetic acid (61.3 mg, 0.30 mmol), DIPEA (78 µL, 0.45 mmol) and benzoyl chloride (52.2 µL, 0.45 mmol) in DCM (2 mL), Ph/i-Pr isothiourea catalyst (2S,3R)-5 (0.62 mg, 0.002 mmol, 1 mol%), diazene 70 (51.0 mg, 0.20 mmol) and DIPEA (52 µL, 0.3 mmol) for 16 h at -78 °C followed by addition of MeOH (2 mL) and stirring for 1 h at -78 °C gave, after chromatographic purification (eluent Et₂O:petrol 50:50) a rotameric mixture (ratio 74:26) of (2R)-30 as a light yellow solid (78.5 mg, 83%); [α]D²⁰ -26.6 (c 0.5, CH₂Cl₂); Chiral HPLC Chiralpak IA (80% IPA:hexane, flow rate 1 mL min⁻¹, 211 nm, 40 °C) tₚ(2S): 7.5 min, tₚ(2R): 17.8 min, 97% ee.

* Enantiomeric excess was 92% when methanolysis carried out at rt. When the product is re-subjected to the reaction conditions at rt the ee drops with time.

methyl 2-(2-benzoyl-1-(4-cyanophenyl)hydrazinyl)-2-phenylacetate

S42
Following general procedure D, phenylacetic acid (40.9 mg, 0.30 mmol), DIPEA (78 μL, 0.45 mmol) and benzoyl chloride (52 μL, 0.45 mmol) in DCM (2 mL), diazene 75 (47.0 mg, 0.20 mmol), DHPB 80 (7.60 mg, 0.04 mmol) and DIPEA (52 μL, 0.3 mmol) for 1 h at rt followed by addition of MeOH (2 mL) and stirring for 1 h at rt gave, after chromatographic purification (eluent Et₂O:petrol 60:00) a rotameric mixture (ratio 94:6) of (±)-31 as a white solid (52.5 mg, 68%); mp 72-74 °C; ν_max (KBr) 3412 (N-H), 2954 (C-H), 2220 (C≡N), 1748 (C=O), 1684 (C=O), 1604, 1508; Data for major rotamer δ_H (300 MHz, CDCl₃) 3.76 (3H, s, CH₃), 5.83 (1H, s, C(2)H), 6.89-6.94 (2H, m, ArH), 7.21-7.49 (12H, m, ArH), 8.37 (1H, s, NH); Selected data for minor rotamer δ_H (300 MHz, CDCl₃) 3.65 (3H, s, CH₃), 5.56 (1H, s, C(2)H), 6.78 (2H, dd, J 8.2, 1.0, ArH), 7.81 (1H, s, NH); Data for major rotamer δ_C (75 MHz, CDCl₃) 52.9 (CH₃), 66.4 (C(2)), 103.7 (4ry ArC), 114.1 (ArC), 119.4 (C≡N), 127.0 (ArC), 128.7 (ArC), 128.8 (ArC), 129.3 (ArC), 129.4 (ArC), 132.0 (4ry ArC), 132.1 (4ry ArC), 132.2 (ArC), 133.8 (ArC), 151.5 (4ry ArC), 166.4 (C=O), 172.2 (C=O); Selected data for minor rotamer δ_C (75 MHz, CDCl₃) 52.9 (CH₃), 67.5 (C(2)), 115.2 (ArC), 127.3 (ArC), 127.5 (ArC), 130.4 (ArC), 134.2 (ArC); m/z (NSI⁺) 386 ([M+H]⁺, 100%); HRMS (NSI⁺) C_{26}H_{29}N_{3}O_{5}⁺ ([M+H]⁺) requires 386.1499; found 386.1502 (+0.7 ppm).

(R)-methyl 2-(1-(4-methoxyphenyl)-2-(4-(trifluoromethyl)benzoyl)hydrazinyl)-2-phenylacetate

Following general procedure E, phenylacetic acid (40.9 mg, 0.30 mmol), DIPEA (78 μL, 0.45 mmol) and benzoyl chloride (52.2 μL, 0.45 mmol) in DCM (2 mL), Ph/i-Pr isothiourea catalyst (2S,3R)-5 (0.62 mg, 0.002 mmol, 1 mol%), diazene 75 (47.0 mg, 0.20 mmol) and DIPEA (52 μL, 0.3 mmol) for 16 h at -78 °C followed by addition of MeOH (2 mL) and stirring for 1 h at -78 °C gave, after chromatographic purification (eluent Et₂O:petrol 60:40) a rotameric mixture (ratio 94:6) of (2R)-31 as a white solid (71.5 mg, 93%); [α]_D^{20} -46.8 (c 0.5, CH₂Cl₂); Chiral HPLC Chiralpak IA (80% IPA:hexane, flow rate 1 mL min⁻¹, 254 nm, 40 °C) tᵣ(2R): 5.8 min, tᵣ(2S): 12.9 min, 98% ee.

* Enantiomeric excess was 91% when methanolation is carried out at rt. When the product is re-subjected to the reaction conditions at rt the ee drops with time.
methyl 2-(2-benzoyl-1-(4-(trifluoromethyl)phenyl)hydrazinyl)-2-phenylacetate

\[
\begin{align*}
\text{CF}_3 \\
\text{MeO} & \text{N} \text{N} \\
\text{Ph} & \text{Ph} \\
\end{align*}
\]

(±)-32

Following general procedure D, phenylacetic acid (204 mg, 1.50 mmol), DIPEA (0.39 mL, 2.25 mmol) and benzoyl chloride (0.26 mL, 2.25 mmol) in DCM (10 mL), diazene 78 (278 mg, 1.00 mmol), DHPB 80 (38.0 mg, 0.20 mmol) and DIPEA (0.26 mL, 1.5 mmol) for 1 h at rt followed by addition of MeOH (10 mL) and stirring for 1 h at rt gave, after chromatographic purification (eluent Et₂O:petrol 30:70) a rotameric mixture (ratio 94:6) of (±)-32 as a white solid (278 mg, 65%); mp 120-122 °C; ν₂₅₀ (KBr) 3392 (N-H), 2952 (C-H), 1738 (C=O), 1682 (C=O), 1616; Data for major rotamer δH (300 MHz, CDCl₃) 3.82 (3H, s, CH₃), 5.97 (1H, s, C(2)H), 7.07 (2H, d, J 8.6, ArH), 7.32-7.38 (5H, m, ArH), 7.47-7.58 (7H, m, ArH), 8.67 (1H, s, NH); Selected data for minor rotamer δH (300 MHz, CDCl₃) 3.72 (3H, s, CH₃), 5.70 (1H, s, C(2)H), 8.04 (1H, s, NH); Data for major rotamer δC (75 MHz, CDCl₃) 52.7 (CH₃), 66.8 (C(2)), 114.0 (ArC), 122.8 (q, J 32.9, 4ry ArC), 124.5 (q, J 269, CF₃), 126.8 (q, J 3.5, ArC), 127.1 (ArC), 128.7 (ArC), 128.7 (ArC), 129.2 (ArC), 129.3 (ArC), 132.1 (ArC), 132.4 (4ry ArC), 132.7 (4ry ArC), 151.0 (4ry ArC), 166.6 (C=O), 172.4 (C=O); Selected data for minor rotamer δC (75 MHz, CDCl₃) 52.7 (CH₃), 67.8 (C(2)), 114.9 (ArC), 127.3 (ArC), 127.7 (ArC), 130.3 (ArC), 130.8 (ArC); m/z (NSI⁻) 429 ([M+H]⁺, 100%); HRMS (NSI⁻) C₂₃H₂₈F₃N₂O₃⁻ ([M+H]⁺) requires 429.1421; found 429.1422 (+0.3 ppm).

(R)-methyl 2-(2-benzoyl-1-(4-(trifluoromethyl)phenyl)hydrazinyl)-2-phenylacetate

\[
\begin{align*}
\text{CF}_3 \\
\text{MeO} & \text{N} \text{N} \\
\text{Ph} & \text{Ph} \\
\end{align*}
\]

(2R)-32

Following general procedure E, phenylacetic acid (204 mg, 1.50 mmol), DIPEA (0.39 mL, 2.25 mmol) and benzoyl chloride (0.26 mL, 2.25 mmol) in DCM (10 mL), Ph/i-Pr isothiourea catalyst (2S,3R)-5 (3.08 mg, 0.01 mmol, 1 mol%), diazene 78 (278 mg, 1.00 mmol) and DIPEA (0.26 mL, 1.5 mmol) for 16 h at -78 °C followed by addition of MeOH (10 mL) and stirring for 1 h at rt gave, after chromatographic purification (eluent Et₂O:petrol 30:70) a rotameric mixture (ratio 94:6) of (2R)-32 as a white solid (336 mg, 86%); [α]D²⁰ -48.6 (c 0.5,
CH₂Cl₂); Chiral HPLC Chiralpak IA (30% IPA:hexane, flow rate 1 mL min⁻¹, 211 nm, 20 °C) 
tₜᵣ(2R): 9.0 min, tₜᵣ(2S): 15.5 min, 99% ee.

**methyl 2-(1-(4-methoxyphenyl)-2-(4-(trifluoromethyl)benzoyl)hydrazinyl)-2-phenoxyacetate**

Following general procedure D, phenylacetic acid (40.9 mg, 0.30 mmol), DIPEA (78 μL, 0.45 mmol) and benzoyl chloride (52 μL, 0.45 mmol) in DCM (2 mL), diazene 79 (61.6 mg, 0.20 mmol), DHPB 80 (7.60 mg, 0.04 mmol) and DIPEA (52 μL, 0.3 mmol) for 1 h at rt followed by addition of MeOH (2 mL) and stirring for 1 h at rt gave, after chromatographic purification (eluent Et₂O:petrol 50:50) a rotamic mixture (ratio 76:24) of (±)-33 as a light yellow oil (69.3 mg, 76%); ν_max (thin film) 3283 (N-H), 2955 (C-H), 1737 (C=O), 1674 (C=O), 1511; Data for major rotamer δ_H (400 MHz, CDCl₃) 3.69 (3H, s, CH₃), 3.72 (3H, s, CH₃), 5.69 (1H, s, C(2)H), 6.77-6.79 (2H, m, ArH), 6.93-6.95 (2H, m, ArH), 7.07-7.11 (1H, m, ArH), 7.21-7.28 (3H, m, ArH), 7.37-7.39 (1H, m, ArH), 7.54 (4H, m, ArH), 8.63 (1H, s, NH); Selected data for minor rotamer δ_H (400 MHz, CDCl₃) 3.60 (3H, s, CH₃), 3.75 (3H, s, CH₃), 5.32 (1H, s, C(2)H), 6.87-6.92 (2H, m, ArH), 8.15 (1H, s, NH); Data for both rotamers δ_C (100 MHz, CDCl₃) 52.4 (CH₃), 52.5 (CH₃) 55.6 (CH₃), 55.6 (CH₃), 67.7 (C(2)), 69.3 (C(2)), 114.7 (ArC), 115.1 (ArC), 117.3 (ArC), 117.7 (ArC), 124.0 (q, J 3.8, ArC), 125.6 (q, J 3.5, ArC), 127.5 (ArC), 128.1 (ArC), 128.7 (ArC), 128.8 (ArC), 128.9 (ArC), 129.0 (ArC), 130.0 (ArC), 131.7 (4ry ArC), 132.6 (4ry ArC), 133.2 (4ry ArC), 133.5 (4ry ArC), 136.2 (4ry ArC), 136.4 (4ry ArC), 142.0 (4ry ArC), 142.4 (4ry ArC), 155.2 (4ry ArC), 158.9 (4ry ArC), 165.3 (C=O), 171.6 (C=O), 172.3 (C=O), 173.3 (C=O); m/z (NSI⁺) 459 ([M+H]^+, 100%); HRMS (NSI⁺) C₂₉H₂₃F₃N₂O₄⁺ ([M+H]^+) requires 459.1526; found 459.1520 (-1.3 ppm).
(R)-methyl 2-(1-(4-methoxyphenyl)-2-(4-(trifluoromethyl)benzoyl)hydrazinyl)-2-phenylacetate

Following general procedure E, phenylacetic acid (40.9 mg, 0.30 mmol), DIPEA (78 µL, 0.45 mmol) and benzoyl chloride (52.2 µL, 0.45 mmol) in DCM (2 mL), Ph/i-Pr isothiourea catalyst (2S,3R)-5 (0.62 mg, 0.002 mmol, 1 mol%), diazene 79 (61.6 mg, 0.20 mmol) and DIPEA (52 µL, 0.3 mmol) for 16 h at -78 °C followed by addition of MeOH (2 mL) and stirring for 1 h at rt gave, after chromatographic purification (eluent Et₂O:petrol 50:50) a rotameric mixture (ratio 76:24) of (2R)-33 as a light yellow oil (68.8 mg, 75%); [α]D 20 -34.6 (c 0.5, CH₂Cl₂); Chiral HPLC Chiralpak IA (50% IPA:hexane, flow rate 1 mL min⁻¹, 211 nm, 20 °C) tₘ(2R): 19.0 min, tₘ(2S): 34.7 min, 99% ee.

Scale-up:
Following general procedure E, phenylacetic acid (1.33 g, 9.74 mmol), DIPEA (2.53 mL, 14.6 mmol) and benzoyl chloride (1.70 mL, 14.6 mmol) in DCM (40 mL), Ph/i-Pr isothiourea catalyst (2S,3R)-5 (20.0 mg, 0.065 mmol, 1 mol%), diazene 79 (2.00 g, 6.49 mmol) and DIPEA (1.69 mL, 9.74 mmol) for 16 h at -78 °C rt followed by addition of MeOH (10 mL) and stirring for 1 h at rt gave, after chromatographic purification (eluent Et₂O:petrol 50:50) a rotameric mixture (ratio 76:24) of (2R)-33 as a light yellow oil (2.83 g, 95%); 99% ee.

methyl 2-(4-fluorophenyl)-2-(1-(4-methoxyphenyl)-2-(4-(trifluoromethyl)benzoyl)hydrazinyl)acetate

Following general procedure D, 4-fluorophenylacetic acid (231 mg, 1.50 mmol), DIPEA (0.39 mL, 2.25 mmol) and benzoyl chloride (0.26 mL, 2.25 mmol) in DCM (10 mL), diazene
79 (308 mg, 1.00 mmol), DHPB 80 (38.0 mg, 0.20 mmol) and DIPEA (0.26 mL, 1.5 mmol) for 1 h at rt followed by addition of MeOH (10 mL) and stirring for 1 h at rt gave, after chromatographic purification (eluent Et₂O:petrol 40:60) a rotameric mixture (ratio 81:19) of (+)-34 as a white solid (347 mg, 73%); mp 68-70 °C; \( \nu_{\text{max}} \) (KBr) 3363 (N-H), 2956 (C-H), 1741 (C=O), 1674 (C=O), 1513; Data for major rotamer \( \delta_{\text{H}} \) (400 MHz, CDCl₃) 3.75 (3H, s, CH₃), 3.78 (3H, s, CH₃), 5.77 (1H, s, C(2)H), 6.86 (2H, d, J 9.0, ArH), 6.98-7.05 (4H, m, ArH), 7.47 (2H, dd, J 8.4, 5.3, ArH), 7.59 (2H, d, J 8.2, ArH), 7.66 (2H, d, J 8.2, ArH), 8.96 (1H, s, NH); Selected data for minor rotamer \( \delta_{\text{H}} \) (400 MHz, CDCl₃) 3.68 (3H, s, CH₃), 3.81 (3H, s, CH₃), 5.43 (1H, s, C(2)H), 7.19 (2H, d, J 9.0 ArH), 7.36 (2H, d, J 8.1, ArH), 8.29 (1H, s, NH); Data for both rotamers \( \delta_{\text{C}} \) (75 MHz, CDCl₃) 52.4 (CH₃), 52.5 (CH₃), 55.4 (CH₃), 55.5 (CH₃), 67.1 (C(2)), 68.5 (C(2)), 114.7 (ArC); 115.1 (ArC), 115.7 (d, J 21.7, ArC), 117.6 (ArC), 117.7 (ArC), 123.6 (q, J 271, CF₃), 124.0 (q, J 3.5, ArC), 125.6 (q, J 3.6, ArC), 127.6 (ArC), 128.2 (ArC), 128.7 (d, J 3.2, 4ry ArC), 129.6 (d, J 3.2, 4ry ArC), 130.8 (d, J 8.3, ArC), 131.9 (d, J 8.5, ArC), 133.4 (q, J 32.5, 4ry ArC), 136.2 (4ry ArC), 136.2 (4ry ArC), 141.9 (4ry ArC), 142.1 (4ry ArC), 155.3 (4ry ArC), 155.7 (4ry ArC), 162.8 (d, J 247, 4ry ArC), 162.8 (d, J 248 4ry ArC), 165.4 (C=O), 171.7 (C=O), 172.0 (C=O), 172.9 (C=O); \( m/z \) (NSI⁺) 477 ([M+H]⁺, 100%); HRMS (NSI⁺) \( C_{24}H_{25}F_{2}N_{2}O_{4}^{+} \) ([M+H]⁺) requires 477.1432; found 477.1420 (-2.5 ppm).

(R)-methyl 2-(4-fluorophenyl)-2-(1-(4-methoxyphenyl)-2-(4-(trifluoromethyl)benzoyl)hydrazinyl)acetate

\[
\begin{align*}
\text{OMe} & \quad \text{O} \\
\text{MeO} & \quad \text{N} \quad \text{N} \\
\text{F} & \quad \text{(2R)-34} \\
\end{align*}
\]

Following general procedure E, 4-fluorophenylacetic acid (231 mg, 1.50 mmol), DIPEA (0.39 mL, 2.25 mmol) and benzoyl chloride (0.26 mL, 2.25 mmol) in DCM (10 mL), Ph/i-Pr isothiourea catalyst (2S,3R)-5 (3.08 mg, 0.01 mmol, 1 mol%), diazene 79 (308 mg, 1.00 mmol) and DIPEA (0.26 mL, 1.5 mmol) for 16 h at -78 °C followed by addition of MeOH (10 mL) and stirring for 1 h at rt gave, after chromatographic purification (eluent Et₂O:petrol 40:60) a rotameric mixture (ratio 79:21) of (2R)-34 as a white solid (377 mg, 79%); \( [\alpha]_{D}^{20} \) - 43.8 (c 0.5, CH₂Cl₂); Chiral HPLC Chiralpak IA (50% IPA:hexane, flow rate 1 mL min⁻¹, 211 nm, 20 °C) \( t_{R}(2S) \): 17.0 min, \( t_{R}(2R) \): 26.4 min, 99% ee.
methyl 2-(1-(4-methoxyphenyl)-2-(4-(trifluoromethyl)benzoyl)hydrazinyl)-2-(naphthalen-2-yl)acetate

Following general procedure D, 2-naphthylacetic acid (279 mg, 1.50 mmol), DIPEA (0.39 mL, 2.25 mmol) and benzoyl chloride (0.26 mL, 2.25 mmol) in DCM (10 mL), diazene 79 (308 mg, 1.00 mmol), DHPB 80 (38.0 mg, 0.20 mmol) and DIPEA (0.26 mL, 1.5 mmol) for 1 h at rt followed by addition of MeOH (10 mL) and stirring for 1 h at rt gave, after chromatographic purification (eluent Et₂O:petro 45:55) a rotameric mixture (ratio 75:25) of (±)-35 as a light yellow solid (302 mg, 59%); mp 74-76 °C; ν<sub>max</sub>(KBr) 3414 (N-H), 2954 (C-H), 1735 (C=O), 1670 (C=O), 1510; Data for major rotamer δ<sub>H</sub> (300 MHz, CDCl₃) 3.79 (3H, s, CH₃), 3.85 (3H, s, CH₃), 6.03 (1H, s, C(2)H), 6.92 (2H, d, J 9.0, ArH), 7.16 (2H, d, J 9.1, ArH), 7.48-7.59 (6H, m, ArH), 7.73-7.93 (5H, m, ArH), 9.07 (1H, s, NH); Selected data for minor rotamer δ<sub>H</sub> (300 MHz, CDCl₃) 3.76 (3H, s, CH₃), 3.85 (3H, s, CH₃), 5.68 (1H, s, C(2)H), 6.77 (2H, d, J 8.1 ArH), 7.04 (2H, d, J 9.0, ArH), 7.29 (2H, d, J 9.0, ArH), 7.66 (2H, d, J 8.3, ArH), 8.42 (1H, s, NH); Data for both rotamers δ<sub>C</sub> (75 MHz, CDCl₃) 52.5 (CH₃), 52.6 (CH₃), 55.5 (CH₃), 55.6 (CH₃), 68.1 (C(2)), 69.2 (C(2)), 114.7 (ArC), 115.2 (ArC), 117.6 (ArC), 123.8 (q, J 3.5, ArC), 125.5 (q, J 3.6, ArC), 126.5 (ArC), 126.6 (ArC), 126.7 (ArC), 126.7 (ArC), 126.7 (ArC), 126.8 (ArC), 127.2 (ArC), 127.5 (ArC), 127.8 (ArC), 127.9 (ArC), 128.1 (ArC), 128.2 (ArC), 128.2 (ArC), 128.4 (ArC), 128.6 (ArC), 129.9 (4ry ArC), 130.1 (ArC), 131.3 (4ry ArC), 133.0 (4ry ArC), 133.1 (4ry ArC), 133.3 (4ry ArC), 133.4 (4ry ArC), 136.0 (4ry ArC), 136.4 (4ry ArC), 142.2 (4ry ArC), 142.4 (4ry ArC), 155.3 (4ry ArC), 155.6 (4ry ArC), 165.5 (C=O), 171.7 (C=O), 172.1 (C=O), 173.1 (C=O); m/z (NSI-<sup>+</sup>) 509 ([M+H]<sup>+</sup>, 100%); HRMS (NSI-<sup>+</sup>) C<sub>23</sub>H<sub>24</sub>F₃N₄O₄<sup>+</sup> ([M+H]<sup>+</sup>) requires 509.1683; found 509.1680 (-0.5 ppm).
(R)-methyl 2-(1-(4-methoxyphenyl)-2-(4-(trifluoromethyl)benzoyl)hydrazinyl)-2-(naphthalen-2-yl)acetate

![Chemical Structure](image)

Following general procedure E, 2-naphthylacetic acid (279 mg, 1.50 mmol), DIPEA (0.39 mL, 2.25 mmol) and benzoyl chloride (0.26 mL, 2.25 mmol) in DCM (10 mL), Ph/i-Pr iso thiourea catalyst (25.3R)-5 (3.08 mg, 0.01 mmol, 1 mol%), diazene 79 (308 mg, 1.00 mmol) and DIPEA (0.26 mL, 1.5 mmol) for 16 h at -78 °C followed by addition of MeOH (10 mL) and stirring for 1 h at rt gave, after chromatographic purification (eluent Et₂O:petrol 45:55) a rotameric mixture (ratio 70:30) of (2R)-35 as a light yellow solid (408 mg, 80%); [α]D 20° -75.8 (c 0.5, CH₂Cl₂); Chiral HPLC Chiralpak IB (20% IPA:hexane, flow rate 1 mL min⁻¹, 211 nm, 20 °C) tᵣ(2S): 12.5 min, tᵣ(2R): 14.5 min, 98% ee.

methyl 2-(2-(4-nitrobenzoyl)-1-phenylhydrazinyl)-2-(phenylthio)acetate

![Chemical Structure](image)

Following general procedure D, (phenylthio)acetic acid (50.5 mg, 0.30 mmol), DIPEA (78 µL, 0.45 mmol) and benzoyl chloride (52 µL, 0.45 mmol) in DCM (2 mL), diazene 70 (51.0 mg, 0.20 mmol), DHPB 80 (7.60 mg, 0.04 mmol) and DIPEA (52 µL, 0.3 mmol) for 1 h at rt followed by addition of MeOH (2 mL) and stirring for 1 h at rt gave, after chromatographic purification (eluent Et₂O:petrol 50:50) a rotameric mixture (ratio 87:13) of (±)-36 as an orange oil (62.8 mg, 72%); ν max (Diamond Cell) 3269 (N-H), 3061, 2953 (C-H), 1736 (C=O), 1682 (C=O), 1597, 1523 (N-O), 1348 (N-O); Data for major rotamer δH (300 MHz, CDCl₃) 3.70 (3H, s, CH₃), 5.69 (1H, s, C(2)H), 6.82-6.91 (3H, m, ArH), 7.13-7.25 (5H, m, ArH), 7.60-7.64 (2H, m, ArH), 7.95-8.00 (2H, m, ArH), 8.22-8.25 (2H, m, ArH), 8.81 (1H, s, NH); Selected data for minor rotamer δH (300 MHz, CDCl₃) 3.57 (3H, s, CH₃), 5.60 (1H, s, C(2)H), 7.50 (2H, d, J 8.8, ArH), 7.83 (2H, d, J 8.8, ArH), 8.17 (1H, s, NH); Data for major rotamer δC (100 MHz, CDCl₃) 53.1 (CH₃), 72.1 (C(2)), 115.7 (ArC), 122.7 (ArC), 124.0 (ArC), 128.8 (ArC), 129.1 (ArC), 129.4 (ArC), 129.5 (ArC), 132.6 (4ry ArC), 133.7 (ArC), 138.6 (4ry ArC),
146.8 (4ry ArC), 150.0 (4ry ArC), 165.2 (C=O), 169.7 (C=O); Selected data for minor rotamer δC (100 MHz, CDCl₃) 53.1 (CH₃), 72.3 (C(2)), 116.4 (ArC), 122.8 (ArC), 123.8 (ArC), 127.3 (ArC), 127.8 (ArC), 130.2 (ArC), 139.4 (4ry ArC), 147.5 (4ry ArC), 168.6 (C=O), 172.4 (C=O); m/z (ES⁺) 460 ([M+Na⁺], 100%); HRMS (ES⁺) C₂₂H₁₆N₂NaO₃S⁺ ([M+Na⁺]) requires 460.0943; found 460.0932 (-2.4 ppm).

(R)-methyl 2-(2-(4-nitrobenzoyl)-1-phenylhydrazinyl)-2-(phenylthio)acetate

Following general procedure E, (phenylthio)acetic acid (50.5 mg, 0.30 mmol), DIPEA (78 μL, 0.45 mmol) and benzyol chloride (52.2 μL, 0.45 mmol) in DCM (2 mL), Ph/3-Pr isothiourea catalyst (2S,3R)-5 (0.62 mg, 0.002 mmol, 1 mol%), diazene 70 (51.0 mg, 0.20 mmol) and DIPEA (52 μL, 0.3 mmol) for 16 h at -78 °C followed by addition of MeOH (2 mL) and stirring for 1 h at -78 °C gave, after chromatographic purification (eluent Et₂O:petrol 50:50) a rotameric mixture (ratio 87:13) of (2R)-36 as an orange oil (72.7 mg, 83%); [α]D²⁰

+m5.0 (c 0.2, CH₂Cl₂); Chiral HPLC Chiralpak IA (40% IPA:hexane, flow rate 1 mL min⁻¹, 211 nm, 30 °C) tr(R): 13.1 min, tr(S): 20.2 min, 98% ee.

methyl 2-methoxy-2-(2-(4-nitrobenzoyl)-1-phenylhydrazinyl)acetate

Following general procedure D, methoxycetic acid (23.0 μL, 0.30 mmol), DIPEA (78 μL, 0.45 mmol) and benzoyl chloride (52 μL, 0.45 mmol) in DCM (2 mL), diazene 70 (51.0 mg, 0.20 mmol), DHPB 80 (7.60 mg, 0.04 mmol) and PS-BEMP (227 mg, 0.5 mmol) for 1 h at rt followed by addition of MeOH (2 mL) and stirring for 1 h at rt gave, after chromatographic purification (eluent Et₂O:petrol 70:30) a rotameric mixture (ratio 94:6) of (±)-37 as an orange solid (38.9 mg, 54%); mp 122-124 °C; v max (Diamond Cell) 3278 (N-H), 3071, 2960 (C-H), 1748 (C=O), 1676 (C=O), 1597, 1525 (N-O), 1346 (N-O); Data for major rotamer δH (400 MHz, CDCl₃) 3.56 (3H, s, CH₃), 3.73 (3H, s, CH₃), 5.28 (1H, s, C(2)H), 6.93-7.00 (3H, m, ArH), 7.22-7.26 (2H, m, ArH), 7.93-7.96 (2H, m, ArH), 8.21-8.24 (2H, m, ArH), 8.41 (1H, s, NH); Selected data for minor rotamer δH (400 MHz, CDCl₃) 3.45 (3H, s, CH₃); 3.67 (3H, s, CH₃), 4.93 (1H, s, C(2)H); Data for major rotamer δC (100 MHz, CDCl₃) 53.0 (CH₃), 57.5 (CH₃), 89.3 (C(2)), 115.8 (ArC), 122.8 (ArC), 124.0 (ArC), 128.7 (ArC), 129.5 (ArC), 138.4
(4ry ArC), 146.2 (4ry ArC), 150.0 (4ry ArC), 165.2 (C=O), 168.3 (C=O); Selected data for minor rotamer $\delta_c$ (100 MHz, CDCl$_3$) 53.4 (CH$_3$), 90.7 (C(2)), 114.0 (ArC), 121.9 (ArC), 127.3 (ArC); m/z (ES$^+$) 382 ([M+Na]$^+$, 100%); HRMS (ES$^+$) C$_{17}$H$_{17}$N$_2$NaO$_6$ $^+$ ([M+Na]$^+$) requires 382.1015; found 382.1023 (+2.0 ppm).

(R)-methyl 2-methoxy-2-(2-(4-nitrobenzoyl)-1-phenylhydrazinyl)acetate

Following general procedure E, methoxyacetic acid (23.0 µL, 0.30 mmol), DIPEA (78 µL, 0.45 mmol) and benzoyl chloride (52.2 µL, 0.45 mmol) in DCM (2 mL), Ph/i-Pr isothiourea catalyst (2S,3R)-5 (6.16 mg, 0.02 mmol, 10 mol%), diazene 70 (51.0 mg, 0.20 mmol) and PS-BEMP (227 mg, 0.5 mmol) for 16 h at rt followed by addition of MeOH (2 mL) and stirring for 1 h at rt gave, after chromatographic purification (eluent Et$_2$O:petrol 70:30) a rotameric mixture (ratio 95:5) of (2R)-37 as an orange solid (38.7 mg, 54%); $[\alpha]_D^{20} +15.5$ (c 0.2, CH$_2$Cl$_2$); Chiral HPLC Chiralpak AD-H (20% IPA:hexane, flow rate 1 mL min$^{-1}$, 211 nm, 30 °C) $t_R(2S)$: 22.4 min, $t_R(2R)$: 24.7 min, 83% ee.

methyl 2-(2-(4-nitrobenzoyl)-1-phenylhydrazinyl)-3-phenylpropanoate

Following general procedure D, 3-phenylpropanoic acid (45.1 mg, 0.30 mmol), DIPEA (78 µL, 0.45 mmol) and benzoyl chloride (52 µL, 0.45 mmol) in DCM (2 mL), diazene 70 (51.0 mg, 0.20 mmol), DHPB 80 (7.60 mg, 0.04 mmol) and PS-BEMP (227 mg, 0.5 mmol) for 1 h at rt followed by addition of MeOH (2 mL) and stirring for 1 h at rt gave, after chromatographic purification (eluent Et$_2$O:petrol 35:65) a rotameric mixture (ratio 90:10) of (±)-38 as a light yellow solid (44.3 mg, 53%); mp 42-44 °C; $\nu_{\text{max}}$ (Diamond Cell) 3279 (N-H), 3065, 2943 (C-H), 1728 (C=O), 1686 (C=O), 1597, 1522 (N-O), 1344 (N-O); Data for major rotamer $\delta_h$ (400 MHz, CDCl$_3$) 3.10 (1H, dd, J 13.6, 8.2, CHH), 3.39 (1H, dd, J 13.6, 6.1, CHH), 3.52 (3H, s, CH$_3$), 4.71 (1H, dd, J 8.2, 6.1 CHH), 6.83-6.92 (3H, m, ArH), 7.16-7.26 (7H, m, ArH), 7.99-8.02 (2H, m, ArH), 8.26-8.29 (2H, m, ArH), 8.86 (1H, s, NH); Data for minor rotamer $\delta_h$(400 MHz, CDCl$_3$) 3.47 (3H, s, CH$_3$), 7.42 (2H, d, J 8.9, ArH), 8.20 (1H, s, NH); Data for major rotamer $\delta_c$ (100 MHz, CDCl$_3$) 37.1 (CH$_3$), 52.1 (CH$_3$), 65.2 (C(2)), 115.3 (ArC), 122.3 (ArC), 124.1 (ArC), 127.2 (ArC), 128.6 (ArC), 128.7 (ArC), 129.2
(ArC), 129.5 (ArC), 136.5 (4ry ArC), 138.2 (4ry ArC), 147.9 (4ry ArC), 150.1 (4ry ArC), 164.8 (C=O), 174.2 (C=O); Selected data for minor rotamer δ C (100 MHz, CDCl3) 35.6 (CH3), 52.1 (CH3), 66.3 (C(2)), 116.4 (ArC), 122.8 (ArC), 128.2 (ArC), 128.5 (ArC), 130.0 (ArC); m/z (ES+) 442 ([M+Na]+, 100%); HRMS (ES+) C23H21N3NaO5+ ([M+Na]+) requires 442.1379; found 442.1363 (-3.6 ppm).

(R)-methyl 2-(2-(4-nitrobenzoyl)-1-phenylhydrazinyl)-3-phenylpropanoate

\[
\text{MeO} \quad \text{PhNHN} \quad \text{O} \\
\text{O} \quad \text{NHN} \quad \text{O} \\
\text{Ph} \quad \text{Ar} \quad \text{Ph} \\
(2R)-38
\]

Following general procedure E, 3-phenylpropanionic acid (45.1 mg, 0.30 mmol), DIPEA (78 μL, 0.45 mmol) and benzoyl chloride (52.2 μL, 0.45 mmol) in DCM (2 mL), Ph/i-Pr isothiourea catalyst (2S,3R)-5 (6.16 mg, 0.02 mmol, 10 mol%), diazene 70 (51.0 mg, 0.20 mmol) and PS-BEMP (227 mg, 0.5 mmol) for 16 h at rt followed by addition of MeOH (2 mL) and stirring for 1 h at rt gave, after chromatographic purification (eluent Et2O:petrol 40:60) a rotameric mixture (ratio 90:10) of (2R)-38 as a light yellow solid (51.8 mg, 62%); [α]D20 -28.4 (c 0.5, CH2Cl2); Chiral HPLC Chiralpak IA (40% IPA:hexane, flow rate 1 mL min⁻¹, 211 nm, 30 °C) tR(2R): 9.8 min, tR(2S): 18.1 min, 99% ee.

N’-(2-hydroxy-1-(p-tolyl)ethyl)-N’-phenylbenzohydrazide

\[
\text{HO} \quad \text{NHN} \quad \text{O} \\
\text{NHN} \quad \text{O} \\
\text{Ph} \quad \text{Ar} \quad \text{Ph} \\
(±)-39
\]

To a solution of (±)-6 (68.4 mg, 0.20 mmol) in THF (1 mL) was added 2M LiAlH4 (1.0 mL, 2.0 mmol) and the reaction mixture was allowed to stir at rt for 10 mins. The reaction mixture was quenched by addition of sat. aq. NH4Cl and extracted with Et2O. The organic layer was dried (MgSO4), filtered and concentrated in vacuo. Chromatographic purification (eluent Et2O:petrol 60:40) gave (±)-39 as a white solid (67.8 mg, 98%); mp 148-150 °C; νmax (KBr) 3551 (O-H), 3412 (N-H), 2933 (C-H), 1662 (C=O), 1597, 1497; δH (500 MHz, CDCl3) 2.23 (3H, s, CH3), 3.78 (1H, td, J 11.7, 3.6, C(2)H3), 3.94 (1H, t, J 10.5, C(2)H2H), 4.61 (1H, br s, OH), 5.18 (1H, d, J 7.2, C(1)H)), 6.82 (1H, t, J 7.3, ArH), 6.94 (2H, d, J 8.1, ArH), 7.02-7.05 (4H, m, ArH), 7.17-7.20 (2H, m, ArH), 7.41 (2H, t, J 7.6 ArH), 7.51 (1H, t, J 7.4, ArH), 7.74 (2H, d, J 7.6, ArH); δ C (125 MHz, CDCl3) 21.1 (CH3), 61.2 (C(2)), 65.2 (C(1)), 114.2 (ArC),

S52
120.6 (ArC), 127.3 (ArC), 127.5 (ArC), 129.0 (ArC), 129.5 (ArC), 129.7 (ArC), 131.8 (4ry ArC), 132.4 (4ry ArC), 132.7 (ArC), 138.3 (4ry ArC), 148.6 (4ry ArC), 168.7 (C=O); m/z (NSI') 347 ([M+H']

(R)-N'-(2-hydroxy-1-(p-tolyl)ethyl)-N'-phenylbenzohydrazide

To a solution of (2R)-6 (33.9 mg, 0.10 mmol) in THF (1 mL) was added 2M LiAlH₄ (0.5 mL, 1.0 mmol) and the reaction mixture was allowed to stir at rt for 10 mins. The reaction mixture was quenched by addition of sat. aq. NH₄Cl and extracted with Et₂O. The organic layer was dried (MgSO₄), filtered and concentrated in vacuo. Chromatographic purification (eluent Et₂O:petrol 60:40) gave (±)-39 as a white solid (33.6 mg, 97%); [α]D₂⁰ -73.2 (c 0.25, CH₂Cl₂); Chiral HPLC Chiralpak AD-H (30% IPA:hexane, flow rate 1 mL min⁻¹, 254 nm, 30 °C) tᵣ(1R): 7.4 min, tᵣ(1S): 10.7 min, >99% ee.

methyl 2-((4-methoxyphenyl)amino)-2-phenylacetate

Following general procedure F, ester (±)-33 (400 mg, 0.88 mmol) and 0.1M SmI₂ (26.4 mL, 2.64 mmol) in MeOH (10 mL) gave, after chromatographic purification (eluent Et₂O:petrol 20:80) (±)-40 as a light yellow solid (167 mg, 70%); mp 104-106 °C; [lit.⁸ mp 107-108 °C]; δH (300 MHz, CDCl₃) 3.73 (3H, s, CH₃), 3.75 (3H, s, CH₃), 4.69 (1H, br s, N/H), 5.05 (1H, s, C(2)H), 6.54-6.59 (2H, m, ArH), 6.72-6.76 (2H, m, ArH), 7.33-7.41 (3H, m, ArH), 7.50-7.53 (2H, m, ArH).
(R)-methyl 2-((4-methoxyphenyl)amino)-2-phenylacetate

Following general procedure F, ester (2R)-33 (229 mg, 0.50 mmol) and 0.1M SmI₂ (15.0 mL, 1.50 mmol) in MeOH (5 mL) gave, after chromatographic purification (eluent Et₂O:petrol 20:80) (2R)-40 as a colourless oil (112 mg, 83%); [α]₀ 20° -99.2 (c 0.125, CHCl₃); [lit.⁹ [α]° _D +97.6 (c 1.29 in CHCl₃) for a 98% ee sample (2S)-configuration}; Chiral HPLC Chiralcel OJ-H (30% IPA:hexane, flow rate 1 mL min⁻¹, 220 nm, 30 °C) tₘ₉(2R): 28.1 min, tₘ₉(2S): 30.9 min, 99% ee.

* Enantiomeric excess was 91% when reaction carried out at rt.

methyl 2-(4-fluorophenyl)-2-((4-methoxyphenyl)amino)acetate

Following general procedure F, ester (±)-34 (238 mg, 0.50 mmol) and 0.1M SmI₂ (15.0 mL, 1.50 mmol) in MeOH (5 mL) gave, after chromatographic purification (eluent Et₂O:petrol 25:75) (±)-41 as a light yellow solid (107.9 mg, 75%); mp 102-104 °C; [lit.⁸ mp 99-100 °C}; δH (300 MHz, CDCl₃) 3.64 (3H, s, CH₃), 3.66 (3H, s, CH₃), 4.60 (1H, br s, NH), 4.92 (1H, s, C(2)H), 6.42-6.45 (2H, m, ArH), 6.64-6.67 (2H, m, ArH), 6.94-7.00 (2H, m, ArH), 7.37-7.42 (2H, m, ArH).

(R)-methyl 2-(4-fluorophenyl)-2-((4-methoxyphenyl)amino)acetate

Following general procedure F, ester (2R)-34 (238 mg, 0.50 mmol) and 0.1M SmI₂ (15.0 mL, 1.50 mmol) in MeOH (5 mL) gave, after chromatographic purification (eluent Et₂O:petrol 25:75) (2R)-41 as a light yellow solid (110 mg, 76%); [α]₀ 20° -86.8 (c 0.25, CH₂Cl₂); [lit.⁹ [α]° _D +70.4 (c 1.40 in CHCl₃) for a 93% ee sample (2S)-configuration}; Chiral HPLC
Chiralpak AD-H (10% IPA:hexane, flow rate 1 mL min⁻¹, 211 nm, 30 °C) tᵣ(2S): 13.7 min, tᵣ(2R): 15.9 min, 98% ee.

**methyl 2-((4-methoxyphenyl)amino)-2-(naphthalen-2-yl)acetate**

![Chemical Structure](image)

Following general procedure F, ester (±)-35 (254 mg, 0.50 mmol) and 0.1M SmI₂ (15.0 mL, 1.50 mmol) in MeOH (5 mL) gave, after chromatographic purification (elucent Et₂O:petrol 25:75) (±)-42 as a light yellow oil (111 mg, 69%); δ_H (300 MHz, CDCl₃) 3.59 (3H, s, CH₃), 3.62 (3H, s, CH₃), 4.73 (1H, br s, NH), 5.09 (1H, s, C(2)H), 6.47-6.51 (2H, m, ArH), 6.59-6.65 (2H, m, ArH), 7.36-7.41 (2H, m, ArH), 7.51 (1H, dd, J 8.6, 1.8, ArH), 7.71-7.76 (3H, m, ArH), 7.87 (1H, s, ArH).

**(R)-methyl 2-((4-methoxyphenyl)amino)-2-(naphthalen-2-yl)acetate**

![Chemical Structure](image)

Following general procedure F, ester (2R)-35 (254 mg, 0.50 mmol) and 0.1M SmI₂ (15.0 mL, 1.50 mmol) in MeOH (5 mL) gave, after chromatographic purification (elucent Et₂O:petrol 25:75) (2R)-42 as a colourless oil (131 mg, 82%); [α]_D²⁰ +180.4 (c 0.25, CH₂Cl₂); [lit.⁹ [α]_D²⁰ +130.6 (c 1.60 in CHCl₃) for a 97% ee sample (2S)-configuration); Chiral HPLC Chiralcel OJ-H (30% IPA:hexane, flow rate 1 mL min⁻¹, 220 nm, 30 °C) tᵣ(2R): 30.4 min, tᵣ(2S): 33.0 min, 98% ee.

**methyl 2-phenyl-2-(phenylamino)acetate**

![Chemical Structure](image)

Following general procedure F, ester (±)-4 (150 mg, 0.42 mmol) and 0.1M SmI₂ (12.5 mL, 1.25 mmol) in MeOH (5 mL) gave, after chromatographic purification (elucent Et₂O:petrol 25:75) (±)-43 as a white solid (59.8 mg, 60%); mp 73-74 °C; [lit.¹² mp 79-80 °C]; δ_H (300
MHz, CDCl₃) 3.63 (3H, s, CH₃), 4.87 (1H, d, J 5.7, NH), 5.00 (1H, d, J 5.9, C(2)H), 6.47 (2H, dd, J 8.6, 0.9, ArH), 6.58-6.64 (1H, m, ArH), 7.00-7.06 (2H, m, ArH), 7.21-7.29 (3H, m, ArH), 7.39-7.43 (2H, m, ArH).

(R)-methyl 2-phenyl-2-(phenylamino)acetate

Following general procedure F, ester (2R)-4 (180 mg, 0.50 mmol) and 0.1M SmI₂ (15.0 mL, 1.50 mmol) in MeOH (5 mL) gave, after chromatographic purification (eluent Et₂O:petrol 25:75) (2R)-43 as a colourless oil (109.7 mg, 91%); [α]D²⁰ ⁰ -51.5 (c 0.2, CH₂Cl₂); [lit.⁹ [α]D²⁰ +49.9 (c 0.9 in CHCl₃) for a 97% ee sample (2S)-configuration]; Chiral HPLC Chiracel OD-H (1% IPA:hexane, flow rate 1 mL min⁻¹, 211 nm, 30 °C) tR(2S): 23.7 min, tR(2R): 26.1 min, 99% ee.

methyl 2-phenyl-2-((4-(trifluoromethyl)phenylamino)acetate

Following general procedure F, ester (±)-32 (214 mg, 0.50 mmol) and 0.1M SmI₂ (15.0 mL, 1.50 mmol) in MeOH (5 mL) gave, after chromatographic purification (eluent Et₂O:petrol 25:75) (±)-44 as a colourless oil (133 mg, 86%); δH (300 MHz, CDCl₃) 3.66 (3H, s, CH₃), 5.01 (1H, d, J 5.7, C(2)H), 5.28 (1H, d, J 5.5, NH), 6.47 (2H, d, J 8.5, ArH), 7.23-7.31 (5H, m, ArH), 7.37-7.40 (2H, m, ArH).

(R)-methyl 2-phenyl-2-((4-(trifluoromethyl)phenylamino)acetate

Following general procedure F, ester (2R)-32 (214 mg, 0.50 mmol) and 0.1M SmI₂ (15.0 mL, 1.50 mmol) in MeOH (5 mL) gave, after chromatographic purification (eluent Et₂O:petrol 25:75) (2R)-44 as a colourless oil (117 mg, 76%); [α]D²⁰ ⁰ -98.0 (c 0.25, CH₂Cl₂); Chiral HPLC
Chiralcel OD-H (1% IPA:hexane, flow rate 1 mL min⁻¹, 211 nm, 30 °C) tᵣ(2R): 13.6 min, tᵣ(2S): 14.7 min, 98% ee.

**methyl 2-amino-2-phenylacetate**

![Structure](image)

To a solution of PMP protected amine (±)-40 (84.0 mg, 0.31 mmol) in MeCN:H₂O (1:1, 10 mL) was added periodic acid (70.5 mg, 0.31 mmol) and 1M H₂SO₄ (0.31 mL, 0.31 mmol) and the reaction mixture was allowed to stir for 16 h at rt. The reaction mixture was washed with CH₂Cl₂. The aqueous layer was retained, basified with sat. aq. NaHCO₃ and extracted twice with ethyl acetate. The combined organics were dried (MgSO₄), filtered and concentrated in vacuo to give (±)-45 as a yellow oil (16.0 mg, 31%); δH (300 MHz, CDCl₃) 1.97 (2H, br s, NH₂), 3.63 (3H, s, CH₃), 4.55 (1H, s, C(2)H), 7.23-7.30 (5H, m, ArH).

**((R))-methyl 2-amino-2-phenylacetate**

![Structure](image)

To a solution of PMP protected amine (2R)-40 (34.5 mg, 0.13 mmol) in MeCN:H₂O (1:1, 10 mL) was added periodic acid (28.9 mg, 0.13 mmol) and 1M H₂SO₄ (0.13 mL, 0.13 mmol) and the reaction mixture was allowed to stir for 16 h at rt. The reaction mixture was washed with CH₂Cl₂. The aqueous layer was retained, basified with sat. aq. NaHCO₃ and extracted twice with ethyl acetate. The combined organics were dried (MgSO₄), filtered and concentrated in vacuo to give (2R)-45 as a yellow oil (9.8 mg, 47%); [α]D₂⁰ -192 (c 0.025, CH₂Cl₂); {lit.¹⁰ [α]D₂⁰ +202.3 (c 0.49 in CHCl₃) for a 91% ee sample (2S)-configuration}.

**methyl 2-acetamido-2-phenylacetate**

![Structure](image)

To a solution of amine (±)-45 (15.0 mg, 0.09 mmol) and triethylamine (14.0 μL, 0.1 mmol) in CH₂Cl₂ (1 mL) at 0 °C was added acetic anhydride (9.44 μL, 0.1 mmol) and the reaction mixture was stirred at rt for 30 minutes. The reaction mixture was washed several times with
water and the organic layer was dried (MgSO₄), filtered and concentrated in vacuo to give acylated amine (±-83 as a yellow oil (15.1 mg, 80%); δ_H (300 MHz, CDCl₃) 1.97 (3H, s, CH₃), 3.66 (3H, s, OCH₃), 5.52 (1H, d, J 7.3, C(2)H), 6.42 (1H, br s, NH), 7.27-7.29 (5H, m, ArH).

(R)-methyl 2-acetamido-2-phenylacetate

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\begin{center}
\includegraphics[width=0.2\textwidth]{Figure.png}
\end{center}
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To a solution of amine (2R)-45 (6.0 mg, 0.036 mmol) and triethylamine (5.58 µL, 0.04 mmol) in CH₂Cl₂ (1 mL) at 0 °C was added acetic anhydride (3.78 µL, 0.04 mmol) and the reaction mixture was stirred at rt for 30 minutes. The reaction mixture was washed several times with water and the organic layer was dried (MgSO₄), filtered and concentrated in vacuo to give acylated amine (±-83 as a yellow oil (6.8 mg, 90%); [α]_D^{20} -188 (c 0.05, CH₂Cl₂); {lit.}^{11} [α]_D^{20} -36 (c 1.00 in CHCl₃) for a 24% ee sample (2R)-configuration; Chiral HPLC Chiralcel OJ-H (10% IPA:hexane, flow rate 1 mL min⁻¹, 211 nm, 30 °C) t_R(2S): 16.1 min, t_R(2R): 17.9 min, 90% ee.
1.4 NMR Analysis

NMR analysis illustrating that hydrazide 4 and its analogues are rotameric

Fig. 1 a) Expansion of $^1$H NMR spectrum of compound 4. b) 1D gs-NOESY/EXSY spectrum acquired upon selective irradiation of aliphatic CH resonance at 5.89 ppm. The positive phased peak at 5.58 ppm indicates that hydrazide 4 exists in solution in the form of two fast exchanging species, likely rotamers. The negative phased doublets at 7.03 and 7.48 ppm appear in the spectrum due to NOE between the aliphatic CH resonance and adjacent ortho-phenyl protons for both major and minor rotamer.

1.4 References and Notes


HPLC Data

HPLC data compound 3: Chiralpak AD-H 5% IPA:hexane, 1 mL min⁻¹, 211 nm, 20 °C, >99% ee
HPLC data compound 4: Chiralpak IB 10% IPA:hexane, 1 mL min⁻¹, 211 nm, 20 °C, 99% ee
HPLC data compound 6: Chiralpak AD-H 5% IPA:hexane, 1 mL min\(^{-1}\), 211 nm, 20 °C, >99% ee
HPLC data compound 7: Chiralpak AD-H 5% IPA:hexane, 1 mL min⁻¹, 211 nm, 20 °C, 99% ee
HPLC data compound 8: Chiralpak AD-H 5% IPA:hexane, 1 mL min⁻¹, 211 nm, 20 °C, >99% ee
HPLC data compound 9: Chiralpak AD-H 5% IPA:hexane, 2 mL min⁻¹, 211 nm, 20 °C, >99% ee
HPLC data compound 10: Chiralpak AD-H 5% IPA:hexane, 2 mL min⁻¹, 211 nm, 20 °C, 98% ee
HPLC data compound 11: Chiralpak AD-H 5% IPA:hexane, 1 mL min⁻¹, 211 nm, 20 °C, >99% ee
HPLC data compound 12: Chiralpak AD-H 5% IPA:hexane, 1 mL min⁻¹, 211 nm, 20 °C, 99% ee

**Table 1: Retention Times and Areas**

<table>
<thead>
<tr>
<th>Peak Number</th>
<th>Peak Name</th>
<th>R. Time</th>
<th>Area</th>
<th>Area %</th>
</tr>
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<tbody>
<tr>
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<td>13.00</td>
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<td>51.03</td>
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</table>

**Table 2: Retention Times and Areas**

<table>
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<th>R. Time</th>
<th>Area</th>
<th>Area %</th>
</tr>
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<tbody>
<tr>
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<td>11715293.45</td>
<td>98.83</td>
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</table>
HPLC data compound 13: Chiralpak AD-H 5% IPA:hexane, 2 mL min⁻¹, 211 nm, 20 °C, >99% ee

![HPLC diagram]

<table>
<thead>
<tr>
<th>Inj. Number</th>
<th>Peak Name</th>
<th>R. Time</th>
<th>Area</th>
<th>Area %</th>
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<tbody>
<tr>
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<td>11.68</td>
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</table>

![HPLC diagram]

<table>
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<th>Peak Name</th>
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<th>Area</th>
<th>Area %</th>
</tr>
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HPLC data compound 14: Chiralpak AD-H 5% IPA:hexane, 1 mL min\(^{-1}\), 211 nm, 20 °C, 99% ee

![Chemical Structure Image]

<table>
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</table>

![Graph Image]

<table>
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<th>Area</th>
<th>Area %</th>
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<tr>
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</table>

![Graph Image]
HPLC data compound 15: Chiralpak AD-H 5% IPA:hexane, 1 mL min⁻¹, 211 nm, 20 °C, 99% ee

<table>
<thead>
<tr>
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<th>R. Time</th>
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% Mobile Phase

<table>
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<td>2</td>
<td>*2</td>
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<td>25337235</td>
<td>99.50</td>
</tr>
</tbody>
</table>
HPLC data compound 16: Chiralpak AD-H 5% IPA:hexane, 1 mL min⁻¹, 211 nm, 20 °C, 99% ee

<table>
<thead>
<tr>
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<th>Peak Name</th>
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<th>Area</th>
<th>Area %</th>
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<tbody>
<tr>
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<table>
<thead>
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<th>Area</th>
<th>Area %</th>
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</thead>
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<tr>
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<td>13.90</td>
<td>6079017.19</td>
<td>0.65</td>
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<tr>
<td>2</td>
<td>&quot;2&quot;</td>
<td>13.90</td>
<td>6079017.19</td>
<td>99.35</td>
</tr>
</tbody>
</table>
HPLC data compound 17: Chiralpak AD-H 5% IPA:hexane, 1 mL min⁻¹, 211 nm, 20 °C, >99% ee
HPLC data compound 18: Chiralpak AD-H 5% IPA:hexane, 2 mL min⁻¹, 211 nm, 20 °C, >99% ee
HPLC data compound 19: Chiralpak AD-H 2% IPA:hexane, 1 mL min$^{-1}$, 211 nm, 20 °C, >99% ee

![Chemical structure image]

<table>
<thead>
<tr>
<th>Inj. Number</th>
<th>Peak Name</th>
<th>Ret. Time</th>
<th>Area</th>
<th>Area %</th>
</tr>
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<tbody>
<tr>
<td>1</td>
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<td>15.71</td>
<td>15736230.60</td>
<td>49.90</td>
</tr>
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<td>2</td>
<td>16.66</td>
<td>5019113.60</td>
<td>50.10</td>
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</table>

![Graph 1]

<table>
<thead>
<tr>
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<th>Peak Name</th>
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<th>Area %</th>
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<td>2</td>
<td>16.95</td>
<td>30862794.0</td>
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</table>

![Graph 2]
HPLC data compound 20: Chiralpak IB 10% IPA:hexane, 1 mL min⁻¹, 211 nm, 20 °C, 98% ee
HPLC data compound 21: Chiralpak IB 20% IPA:hexane, 1 mL min\(^{-1}\), 211 nm, 20 °C, 99% ee
HPLC data compound 22: Chiralpak IB 40% IPA: hexane, 1 mL min⁻¹, 211 nm, 20 °C, 99% ee
HPLC data compound 23: Chiralpak IB 10% IPA:hexane, 2 mL min⁻¹, 211 nm, 20 °C, 98% ee
HPLC data compound 24: Chiralcel OD-H 10% IPA:hexane, 1 mL min\(^{-1}\), 211 nm, 20 °C, >99% ee
HPLC data compound 25: Chiralcel OD-H 10% IPA:hexane, 2 mL min\(^{-1}\), 211 nm, 20 °C, >99% ee
HPLC data compound 26: Chiralpak IB 10% IPA:hexane, 1 mL min⁻¹, 211 nm, 20 °C, 99% ee

<table>
<thead>
<tr>
<th>Inj. Number</th>
<th>Peak Name</th>
<th>R. Time</th>
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<th>Area %</th>
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<table>
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<th>Area</th>
<th>Area %</th>
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<tbody>
<tr>
<td>1</td>
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<td>*2</td>
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<td>3030531.05</td>
<td>99.56</td>
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</tbody>
</table>

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HPLC data compound 27: Chiralpak IA 40% IPA:hexane, 2 mL min⁻¹, 211 nm, 20 °C, 99% ee

```
<table>
<thead>
<tr>
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<tr>
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<table>
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<tr>
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<tr>
<td>2</td>
<td>2.00</td>
<td>43330590.25</td>
<td>99.67</td>
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</tbody>
</table>
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HPLC data compound 28: Chiralpak IA 40% IPA:hexane, 1 mL min⁻¹, 211 nm, 20 °C, 99% ee
HPLC data compound 29: Chiralpak IA 40% IPA:hexane, 1 mL min\(^{-1}\), 211 nm, 20 °C, 99% ee

![Chemical structure of compound 29]

<table>
<thead>
<tr>
<th>Inj. Number</th>
<th>Peak Name</th>
<th>R. Time</th>
<th>Area</th>
<th>Area %</th>
</tr>
</thead>
<tbody>
<tr>
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<td>*1</td>
<td>13.22</td>
<td>4355492.0</td>
<td>59.27</td>
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<tr>
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<td>4235096.0</td>
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</table>

![HPLC chromatogram for compound 29]

<table>
<thead>
<tr>
<th>Inj. Number</th>
<th>Peak Name</th>
<th>R. Time</th>
<th>Area</th>
<th>Area %</th>
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<td>57490475.0</td>
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</tbody>
</table>
HPLC data compound 30: Chiralpak IA 80% IPA:hexane, 1 mL min\(^{-1}\), 211 nm, 40 °C, 97% ee
HPLC data compound 31: Chiralpak IA 80% IPA:hexane, 1 mL min⁻¹, 254 nm, 40 °C, 98% ee
HPLC data compound 32: Chiralpak IA 30% IPA:hexane, 2 mL min⁻¹, 211 nm, 20 °C, 99% ee
HPLC data compound 33: Chiralpak IA 50% IPA:hexane, 2 mL min$^{-1}$, 211 nm, 20 °C, 99% ee
HPLC data compound 34: Chiralpak IA 50% IPA:hexane, 1 mL min⁻¹, 211 nm, 20 °C, 99% ee
HPLC data compound 35: Chiralpak IB 20% IPA:hexane, 1 mL min⁻¹, 211 nm, 20 °C, 98% ee
HPLC data compound 36: Chiralpak IA 40% IPA:hexane, 1 mL min⁻¹, 211 nm, 30 °C, 98% ee
HPLC data compound 37: Chiralpak AD-H 20% IPA:hexane, 1 mL min⁻¹, 211 nm, 30 °C, 83% ee

![Graph of HPLC data compound 37](image)
HPLC data compound 38: Chiralpak IA 40% IPA:hexane, 1 mL min⁻¹, 211 nm, 30 °C, 99% ee
HPLC data compound 39: Chiralpak AD-H 30% IPA:hexane, 1 mL min⁻¹, 254 nm, 30 °C, >99% ee
HPLC data compound 40: Chiralcel OJ-H 30% IPA:hexane, 1 mL min\(^{-1}\), 220 nm, 30 °C, 99% ee

![HPLC chromatogram](image)

<table>
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<tr>
<th>Peak</th>
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<tbody>
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<tr>
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<td>49.98</td>
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<td>Total</td>
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<td>100.00</td>
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</table>

![HPLC chromatogram](image)

<table>
<thead>
<tr>
<th>Peak</th>
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<th>Area %</th>
</tr>
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<tr>
<td>1</td>
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<tr>
<td>Total</td>
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<td>100.00</td>
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</tbody>
</table>
HPLC data compound 41: Chiralpak AD-H 10% IPA:hexane, 1 mL min⁻¹, 211 nm, 30 °C, 98% ee
HPLC data compound 42: Chiralpak IB 20% IPA:hexane, 1 mL min⁻¹, 220 nm, 30 °C, 98% ee
HPLC data compound 43: Chiralcel OD-H 1% IPA:hexane, 1 mL min⁻¹, 211 nm, 30 °C, 99% ee

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HPLC data compound 44: Chiralcel OD-H 1% IPA:hexane, 1 mL min$^{-1}$, 211 nm, 30 °C, 98% ee
HPLC data compound 83: Chiralcel OJ-H 10% IPA:hexane, 1 mL min⁻¹, 211 nm, 30 °C, 90% ee
$^1$H, CDCl$_3$, 400 MHz
$^{13}$C, CDCl$_3$, 100 MHz
$\text{Me} - \text{Ph} \overset{\text{N}}{-\text{N}} \overset{\text{O}}{-\text{O}} \overset{\text{Ph}}{6}$

$^1\text{H}, \text{CDCl}_3, 400 \text{ MHz}$
$\text{Br} \quad \text{Ph}$

$\text{N} - \text{N} - \text{O}$

$\text{Ph}$

$^1\text{H}, \text{CDCl}_3, 300 \text{ MHz}$
$^{13}$C, CDCl$_3$, 100 MHz

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$^{13}$C, CDCl$_3$, 100 MHz
$^{13}$C, CDCl$_3$, 100 MHz
$^{13}$C, CDCl$_3$, 75 MHz
$^{13}$C, CDCl$_3$, 100 MHz
15

$^{13}$C, CDCl$_3$, 100 MHz
$^{13}$C, CDCl$_3$, 75 MHz
$^{13}$C, CDCl$_3$, 75 MHz
$^{13}$C, CDCl$_3$, 75 MHz

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$^1$H, CDCl$_3$, 500 MHz
13C, CDCl₃, 100 MHz
$^{13}$C, CDCl₃, 100 MHz
$^{1}$H, CDCl$_3$, 300 MHz
1H, CDCl₃, 400 MHz
$^{13}$C, CDCl$_3$, 75 MHz
$^{13}C$, CDCl$_3$, 75 MHz
$^1$H, CDCl$_3$, 300 MHz
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1H, CDCl3, 400 MHz

0.80 1.64 1.75 5.59 1.72 0.98 2.48 2.98
0.97 2.02 2.02 2.14 7.03 0.819 2.49
$^{1}H$, CDCl$_3$, 400 MHz
$\text{MeO}$ $\text{Ph}$ $\text{CF}_3$

$^1$H, CDCl$_3$, 400 MHz

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$^{13}$C, CDCl$_3$, 100 MHz
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$^1$H, CDCl$_3$, 300 MHz
$^1$H, CDCl$_3$, 400 MHz

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$^{13}$C, CDCl$_3$, 75 MHz
N N
H
O
Ph
SPh
O
MeO
NO2

$^{13}$C, CDCl$_3$, 100 MHz
+MeO
<table>
<thead>
<tr>
<th>N</th>
<th>37</th>
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<tbody>
<tr>
<td>O</td>
<td>Ph</td>
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<tr>
<td>OMe</td>
<td>NO2</td>
</tr>
</tbody>
</table>

$^{13}$C, CDCl$_3$, 100 MHz

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{$\text{MeO}$}$\text{Bn}$ $\text{N}$ $\text{N}$ $\text{O}$ $\text{Ph}$ $\text{O}$

$^{1}$H, CDCl$_3$, 400 MHz
$^1$H, CDCl$_3$, 500 MHz
$^{13}$C, CDCl₃, 100 MHz
$^1$H, CDCl$_3$, 300 MHz
$^{13}$C, CDCl$_3$, 75 MHz
Ph$_2$N$\equiv$N$\equiv$O

$^1$H, CDCl$_3$, 300 MHz
$^{13}$C, CDCl$_3$, 100 MHz
Ph₃N⁺N⁻O⁻NO₂

¹H, CDCl₃, 300 MHz