Supplementary Material

Novel Bifunctional Chiral Squaramide-Amine Catalysts for Highly Enantioselective Addition of Mono and Diketones to Nitroalkenes

Ze Dong,a Xiaoqing Jin,a Pengcheng Wang,a Chang Min,a Jin Zhang,a Zhe Chen,a Hai-Bing Zhou,a,b and Chune Donga,b,*

*aState Key Laboratory of Virology, College of Pharmacy, Wuhan University, 430071 China
bKey Laboratory of Organofluorine Chemistry, Shanghai Institute of Organic Chemistry, Chinese Academy of Sciences, Shanghai 200032 China

E-mail: cdong@whu.edu.cn

Table of Contents

1 General information S2
2 Characterization data of catalysts 1-3 S2
3 Characterization data of Michael adducts 12a-m S5
4 Characterization data of Michael adducts 14a-l S10
5 Synthesis and Characterization data of 15 S15
6 References S16
7 NMR spectra S17
8 Representative HPLC spectra S40
1. General information

Tetrahydrofuran, diethyl ether and toluene were dried over Na/benzophenone, dichloromethane was dried over CaH$_2$ and distilled prior to use. Reaction progress was monitored using analytical thin-layer chromatography (TLC) on 0.25mm Merck F-254 silica gel glass plates. Visualization was achieved by UV light (254 nm). Flash chromatography was performed with silica gel (Merck, 230-400 mesh). Unless otherwise noted, all NMR spectra were recorded using CDCl$_3$ as the solvent with reference to residual CHCl$_3$ ($^1$H at 7.24 ppm and $^{13}$C at 77.0 ppm). Optical rotations were measured at room temperature on a Perkin–Elmer 241MC automatic polarimeter (concentration in g/100 mL). Melting points were obtained on a micro-melting apparatus and the data were uncorrected. Determination of % ee was achieved using a chiral HPLC equipped with a chiralpak AD column with 99:1 n-hexanes: 2-propanol as the mobile phase at a flow rate of 1 mL/min. Catalyst 4 was synthesized according to the literature.$^{1a}$

2. Characterization of catalysts (1-3)

**General procedure for preparation of bifunctional organocatalysts (1-3).** Preparation of 1a is typical

![Diagram of the reaction](image)

The pure (S)-2-amino-1-\(N\)-Boc-pyrrolidine 6 was obtained as a colorless oil according to the reported procedures.$^2$ To a solution of diethylsquarate 5 (0.1 mmol) in EtOH (5 mL) with TEA was
added (S)-2-amino-1-N-Boc-pyrrolidine 6 (0.11 mmol) EtOH (5 mL) at rt. The reaction mixture was stirred overnight and subjected to column chromatography to afford 7 (87%). To a solution of 7 (0.1 mmol) and amine 8 (0.12 mmol) in EtOH (10 mL) was added TEA (0.1 mmol). After 36 h, the reaction mixture was concentrated and subjected to column chromatography to afford squaramide 9 (72%) as a yellow solid: $^1$H NMR (400 MHz CDCl$_3$) $\delta$ 1.03-1.18 (m, 9H), 1.53 (s, 9H), 3.0-3.73 (m, 11H), 5.05 (m, 1H), 5.7 (m, 1H), 7.5-8.7 (m, 4H). $^{13}$C NMR (100Hz CDCl$_3$) 183.6, 181.7, 171.2, 168.2, 167.7, 155.5, 150.0, 148.6, 139.9, 139.0, 130.1, 129.5, 127.1, 124.1, 115.0, 114.6, 80.6, 59.2, 49.4, 46.9, 46.5, 45.8, 42.0, 39.2, 28.6, 27.9, 25.1, 24.2, 23.0, 21.0, 14.1.

The above Boc-protected squaramide 9 was dissolved in a mixture of HCl/EtOH (12 mL/60 mL) and stirred for 12 h at room temperature. The mixture was basified with concentrated ammonia solution and extracted with CH$_2$Cl$_2$ (2x40 mL). After the removal of the solvent in vacuo, the residue was purified through flash column chromatography on silica gel (eluent: methanol / TEA = 10:1), gave 1a as a white solid in 55% yield.

Catalyst (1a)

![Catalyst 1a](image)

$^1$H NMR (400 MHz, CDCl$_3$) $\delta$ = 0.80-1.87 (m, 9H), 2.10-3.95 (m, 13H), 5.01-5.11 (m, 2H), 5.72-5.80 (m, 1H), 6.25 (s, br, 1H), 7.57-8.79 (m, 6H) ppm; $^{13}$C NMR (100Hz, CDCl$_3$) $\square \delta$: 183.7, 182.5, 167.9, 150.4, 150.2, 148.8, 147.2, 140.0, 130.4, 129.9, 127.6, 127.1, 124.0, 119.5, 115.4, 60.5, 49.7, 46.6, 45.5, 44.8, 39.3, 29.8, 28.5, 27.9, 26.7, 25.7, 24.2. HRMS (ESI) calcd for C$_{28}$H$_{33}$N$_5$O$_2$H [M + H]$^+$ 472.2713; found 472.2703; m.p. 159-161 °C.

Catalyst (1b)

![Catalyst 1b](image)

$^1$H NMR (400 MHz, CDCl$_3$) $\delta$ = 0.78-1.93 (m, 9H), 2.0-4.05 (m, 13H), 5.11-5.19 (m, 2H),...
5.65-5.83 (m, 1H), 6.25 (s, br, 1H), 7.50-8.73 (m, 6H) ppm; $^{13}$C NMR (100Hz, CDCl$_3$) δ: 183.9, 180.7, 168.2, 166.7, 155.4, 149.9, 139.9, 138.8, 130.1, 129.5, 126.8, 124.1, 115.0, 114.6, 59.2, 49.4, 46.9, 46.5, 45.8, 42.0, 39.2, 28.6, 27.9, 25.1, 24.2, 23.3. HRMS (ESI) calcd for C$_{28}$H$_{33}$N$_5$O$_2$H [M + H]$^+$ 472.2713; found 472.2707; m.p. 177-180 °C.

Catalyst (1c)

$^1$H NMR (400 MHz, CDCl$_3$) δ = 8.91 (d, 1H), 8.53 (d, 1H), 8.13 (d, 1H), 7.85 – 7.52 (m, 3H), 6.22 (s, 3H), 5.78 (s, 1H), 5.19 – 4.91 (m, 2H), 3.64 (d, 4H), 3.19 (d, 2H), 2.75 (t, 3H), 2.36 (s, 1H), 1.99 (s, 5H), 1.65 (d, 3H), 1.44 (s, 1H), 1.25 (s, 1H), 1.11 (t, 1H); $^{13}$C NMR (100 MHz, CDCl$_3$) δ 182.85, 182.09, 178.96, 168.09, 167.82, 150.28, 148.36, 145.38, 140.63, 130.34, 129.66, 127.49, 126.69, 123.30, 115.21, 60.13, 55.42, 45.58, 44.99, 40.59, 38.88, 27.62, 27.26, 27.07, 25.73, 24.44, 23.72, 9.63; HRMS (ESI) calcd for C$_{28}$H$_{33}$N$_5$O$_2$H [M + H]$^+$ 472.26343; found 472.27070; m.p. 188-193 °C

Catalyst (1d)

$^1$H NMR (400 MHz, CDCl$_3$) δ = 11.81 (s, 4H), 10.15 – 9.27 (m, 2H), 9.05 (s, 1H), 8.56 (s, 1H), 8.28 (s, 1H), 7.81 (d, 1H), 5.80 (s, 1H), 5.58 (s, 1H), 5.35 (d, 1H), 3.91 (d, 3H), 3.60 (s, 4H), 3.27 (s, 2H), 2.78 (s, 1H), 1.98 (s, 5H), 1.48 (s, 3H), 1.40 (s, 4H), 1.26 (s, 1H), 1.14 (s, 1H); $^{13}$C NMR (100 MHz, CDCl$_3$) δ 182.79, 182.35, 168.25, 167.61, 150.25, 148.29, 139.78, 139.69, 130.02, 129.60, 127.33, 126.72, 115.13, 115.02, 60.35, 57.68, 49.11, 48.60, 46.50, 46.19, 45.47, 38.84, 27.42, 26.09, 25.10, 24.00, 23.94, 18.34. HRMS (ESI) calcd for C$_{28}$H$_{33}$N$_5$O$_2$H [M + H]$^+$ 472.26343; found 472.27070; m.p. 151-154 °C
**Catalyst (2a)**

\[\text{H NMR (400 MHz, DMSO-}d_6\text{)} \delta = 0.78-0.91 \text{ (m, 2H), 0.99-1.04 \text{ (m, 1H), 1.48-1.54 \text{ (m, 3H),}}
2.18-2.23 \text{ (m, 1H), 2.63 - 2.93 \text{ (m, 4H), 3.06-3.09 \text{ (m, 1H), 4.96 \text{ (d, } J = 4.5 \text{ Hz, 1H), 5.05 \text{ (d, } J = 10.5 \text{ Hz, 1H), 5.14 \text{ (d, } J = 17.4 \text{ Hz, 1H), 5.20-5.23 \text{ (m, 1H), 5.76-5.84 \text{ (m, 1H), 6.01 \text{ (d, } J = 11.0 \text{ Hz, 1H), 7.03-7.22 \text{ (m, 9H), 7.62 \text{ (d, } J = 4.5 \text{ Hz, 1H), 7.71 \text{ (t, } J = 7.4 \text{ Hz, 1H), 7.81 \text{ (t, } J = 7.5 \text{ Hz, 1H), 7.97 \text{ (t, } J = 7.7 \text{ Hz, 1H), 8.10 \text{ (d, } J = 8.5 \text{ Hz, 1H), 8.40 \text{ (d, } J = 8.4 \text{ Hz, 1H), 8.98 \text{ (d, } J = 4.5 \text{ Hz, 1H).}}\]

\[\text{\textsuperscript{13}C NMR (100MHz, DMSO-}d_6\text{)} \delta 182.8, 182.6, 167.6, 163.5, 151.1, 148.6, 145.7, 143.3, 141.5, 139.5, 136.5, 135.4, 131.6, 131.1, 130.6, 129.5, 128.6, 128.0, 127.0, 126.7, 124.0, 115.3, 75.6, 73.2, 63.1, 59.9, 49.6, 49.4, 27.9, 26.8, 25.9. HRMS (ESI) calcd for C\textsubscript{37}H\textsubscript{36}N\textsubscript{4}O\textsubscript{3}H [M + H]\textsuperscript{+} 585.2866; found 585.2876; m.p. 286-189 °C.\]

**Catalyst (2b)**

\[\text{H NMR (400 MHz, DMSO-}d_6\text{)} \delta = 0.80-0.90 \text{ (m, 2H), 0.98-1.04 \text{ (m, 1H), 1.51-1.52 \text{ (m, 3H),}}
2.2 (s, br, 1H), 2.60 - 3.23 (m, 4H), 5.12 (d, } J = 4.5 \text{ Hz, 1H), 5.16 (d, } J = 10.5 \text{ Hz, 1H), 5.19 (d, } J = 17.4 \text{ Hz, 1H), 5.20-5.23 \text{ (m, 1H), 5.81-5.84 \text{ (m, 1H), 5.95-5.97 \text{ (m, 1H), 6.07, (s, br, 1H),}}
7.00-7.18 \text{ (m, 9H), 7.64-7.76 \text{ (m, 2H), 7.78 \text{ (t, } J = 7.5 \text{ Hz, 1H), 8.04 \text{ (d, } J = 8.5 \text{ Hz, 1H), 8.10-8.13 \text{ (m, 1H), 8.40 \text{ (d, } J = 8.5 \text{ Hz, 1H), 8.96 \text{ (d, } J = 5.0 \text{ Hz, 1H).}}\]

\[\text{\textsuperscript{13}C NMR (100MHz, DMSO-}d_6\text{)} \delta 182.9, 182.4, 167.3, 163.3, 150.9, 148.5, 142.3, 141.3, 139.5, 139.0, 133.4, 132.6, 131.1, 130.6, 129.9, 128.6, 128.0, 127.6, 126.8, 123.6, 115.1, 81.3, 75.4, 73.5, 62.7, 59.5, 49.4, 27.7, 26.0, 25.5. HRMS (ESI) calcd for C\textsubscript{37}H\textsubscript{36}N\textsubscript{4}O\textsubscript{3}H [M + H]\textsuperscript{+} 585.2866; found 585.2876; m.p. 279-283 °C.\]
Catalyst (3)

\[
\text{Ph} \quad \text{OH} \\
\text{N} \quad \text{O} \quad \text{N} \\
\text{Ph} \quad \text{N} \\
\text{N} \\
\text{Ph}
\]

\(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta = 8.45\) (s, 1H), 8.11 (s, 1H), 7.81 – 7.43 (m, 3H), 7.43 – 6.97 (m, 11H), 5.54 – 5.12 (m, 3H), 3.65 (s, 1H), 3.33 (s, 4H), 2.63 (s, 1H), 2.17 (s, 1H), 2.07 (s, 2H), 1.85 (s, 5H), 1.54 (s, 2H), 1.36–1.08 (m, 3H), 1.03 – 0.81 (m, 2H). \(^{13}\)C NMR (100MHz, CDCl\(_3\)) \(\delta\): 183.9, 178.9, 169.5, 132.4, 130.0, 129.8, 128.2, 128.1, 127.9, 127.6, 123.2, 49.9, 49.1, 45.4, 29.7, 26.9, 24.9, 23.7. HRMS (ESI) calcd for C\(_{40}\)H\(_{40}\)N\(_4\)O\(_3\)H [M + H]\(^+\) 625.3179; found 625.3176; m.p. 192-195 °C.

3. Characterization data of Michael products (12a-m)

Representative procedure for the Asymmetric Michael Reaction of Nitroolefin 11a with Cyclohexanone (10)

\[
\begin{array}{ccc}
\text{O} & + & \text{Ph} \equiv \text{NO}_2 \\
\text{10} & & \text{11a} \\
\end{array}
\]

\[
\begin{array}{c}
\text{10 mol\% 1a} \\
\text{10 mol\% PhCOOH} \\
\text{THF, rt} \\
\end{array}
\]

\[
\begin{array}{c}
\text{O} \quad \text{Ph} \\
\quad \text{NO}_2
\end{array}
\]

\[
\text{12a}
\]

The organocatalyst 1a (23.5 mg, 0.05 mmol), PhCO\(_2\)H (6.0 mg, 0.05 mmol) and cyclohexanone 10 (490.7 mg, 5.0 mmol) were stirred in 2 mL of THF for 10 min at room temperature. trans-\(\beta\)-Nitrostyrene 11a (75.0 mg, 0.5 mmol) was then added and the reaction mixture was stirred for 48 h. The reaction mixture was concentrated under reduced pressure, and the residue was purified by column chromatography on silica gel (petroleum ether / ethyl acetate (6:1)) to give the corresponding pure Michael product 12a (29.5 mg, 60%) as a white solid. Compounds 12a-l are known \(^3\).
2-(2-nitro-1-phenylethyl) cyclohexanone (12a)

The ee was determined by HPLC (Chiralpak AD column, hexane/i-PrOH 90:10, flow rate 1.0 mL/min, $\lambda = 220$ nm, 25 °C). $t_R$ (minor) = 20.0 min; $t_R$ (major) = 24.8 min, syn/anti = 88/12, syn: ee = 93%.

$^1$H NMR (400 MHz, CDCl$_3$) $\delta$ = 7.36 – 7.23 (m, 3H), 7.18 – 7.15 (m, 2H), 4.94 (dd, $J = 12.5, 4.5$ Hz, 1H), 4.64 (dd, $J = 12.5, 9.9$ Hz, 1H), 3.76 (td, $J = 9.9, 4.5$ Hz, 1H), 2.74 – 2.64 (m, 1H), 2.54 – 2.33 (m, 2H), 2.13 – 2.02 (m, 1H), 1.83 – 1.63 (m, 3H), 1.58 – 1.48 (m, 1H), 1.33 – 1.13 (m, 1H).

$^{13}$C NMR (100 MHz, CDCl$_3$) □212.0, 137.9, 129.2, 128.4, 128.1, 79.1, 52.8, 44.2, 43.0, 33.5, 28.6, 25.2; m.p. 125-127 °C.

2-(1-(4-fluorophenyl)-2-nitroethyl) cyclohexanone (12b)

The ee was determined by HPLC (Chiralpak OD column, hexane/i-PrOH 98:2, flow rate 1.0 mL/min, $\lambda = 220$ nm, 25 °C). $t_R$ (minor) = 25.4 min; $t_R$ (major) = 27.0 min, syn/anti = 86/14, syn: ee = 82%.

$^1$H NMR (400 MHz, CDCl$_3$) $\delta$ = 7.15 (dd, $J = 8.7, 5.3$ Hz, 2H), 7.01 (t, $J = 8.6$ Hz, 2H), 4.93 (dd, $J = 12.5, 4.5$ Hz, 1H), 4.59 (dd, $J = 12.5, 10.1$ Hz, 1H), 3.77 (td, $J = 9.9, 4.5$ Hz, 1H), 2.65 (ddd, $J = 12.0, 10.2, 5.1$ Hz, 1H), 2.51 – 2.43 (m, 1H), 2.42 – 2.33 (m, 1H), 2.14 – 2.03 (m, 1H), 1.84 – 1.53 (m, 3H), 1.25 – 1.15 (m, 1H). $^{13}$C NMR (100 MHz, CDCl$_3$): $\delta$ 211.7, 163.4, 160.9, 133.5, 133.4, 129.8, 129.7, 116.0, 115.8, 78.8, 52.5, 43.3, 42.7, 33.2, 28.5, 25.0; m.p. 72-74 °C.
2-(1-(4-bromophenyl)-2-nitroethyl) cyclohexanone (12c)

The ee was determined by HPLC (Chiralpak AD column, hexane/i-PrOH 90:10, flow rate 1.0 mL/min, \( \lambda = 220 \text{ nm, } 20^\circ\text{C} \)). \( t_R \) (minor) = 12.8 min; \( t_R \) (major) = 20.4 min, syn/anti = 87/13, syn: ee = 83%.

\(^1\text{H} \text{NMR (400 MHz, CDCl}_3) \delta = 7.45 \text{ (d, } J = 8.4 \text{ Hz, 2H)}, 7.06 \text{ (d, } J = 8.4 \text{ Hz, 2H)}, 4.93 \text{ (dd, } J = 12.6, 4.5 \text{ Hz, 1H}), 4.60 \text{ (dd, } J = 12.6, 10.0 \text{ Hz, 1H)}, 3.75 \text{ (td, } J = 9.9, 4.5 \text{ Hz, 1H}), 2.65 \text{ (ddd, } J = 11.6, 9.9, 5.1 \text{ Hz, 1H}), 2.50 - 2.43 \text{ (m, 1H)}, 2.42 - 2.32 \text{ (m, 1H)}, 2.13 - 2.03 \text{ (m, 1H)}, 1.84 - 1.53 \text{ (m, 4H)}, 1.26 - 1.16 \text{ (m, 1H)).} \(^1\text{C} \text{NMR (100 MHz, CDCl}_3): \delta 221.5, 136.8, 131.7, 129.9, 121.7, 78.5, 52.4, 43.4, 42.8, 33.2, 28.4, 25.1; \text{m.p. 120-122} \text{ °C.}

2-(1-(2-bromophenyl)-2-nitroethyl) cyclohexanone (12d)

The ee was determined by HPLC (Chiralpak AD column, hexane/i-PrOH 85:15, flow rate 0.8 mL/min, \( \lambda = 220 \text{ nm, } 20^\circ\text{C} \)). \( t_R \) (minor) = 10.4 min; \( t_R \) (major) = 16.1 min, syn/anti = 97/3, syn: ee = 84%.

\(^1\text{H} \text{NMR (400 MHz, CDCl}_3) \delta = 7.57 \text{ (dd, } J = 8.0, 1.0 \text{ Hz, 1H)}, 7.30 \text{ (t, } J = 7.9 \text{ Hz, 1H}), 7.22 \text{ (dd, } J = 7.8, 1.7 \text{ Hz, 1H}), 7.12 \text{ (td, } J = 7.9, 1.7 \text{ Hz, 1H}), 4.94 - 4.85 \text{ (m, 2H)}, 4.32 \text{ (dd, } J = 15.3, 7.1 \text{ Hz, 1H}), 2.90 \text{ (s, 1H)}, 2.50 - 2.43 \text{ (m, } 1\text{H}), 2.43 - 2.33 \text{ (m, 1H)}, 2.14 - 2.05 \text{ (m, 1H)}, 1.86 - 1.53 \text{ (m, 4H)}, 1.44 - 1.30 \text{ (m, 1H)).} \(^1\text{C} \text{NMR (100 MHz, CDCl}_3): 211.7, 137.3, 133.7, 129.1, 128.0, 42.8, 33.0, 28.5, 25.3; \text{m.p. 80-81} \text{ °C.}
2-(1-(2-chlorophenyl)-2-nitroethyl) cyclohexanone (12e)

![Chemical Structure](image)

The ee was determined by HPLC (Chiralpak AD column, hexane/i-PrOH 95:5, flow rate 1.0 mL/min, \( \lambda = 220 \text{ nm} \), 20°C). \( t_R \) (minor) = 11.7 min; \( t_R \) (major) = 20.5 min, syn/anti = 98/2, syn: ee = 93%.

\(^1\)H NMR (400 MHz, CDCl\(_3\)) \( \delta = 7.40 - 7.35 \) (m, 1H), 7.28 - 7.18 (m, 3H), 4.92 - 4.88 (m, 2H), 4.29 (dd, \( J = 16.6, 7.0 \text{ Hz} \), 1H), 2.92 (td, \( J = 12.1, 4.9 \text{ Hz} \), 1H), 2.52 - 2.45 (m, 1H), 2.44 - 2.35 (m, 1H), 2.14 - 2.07 (m, 1H), 1.85 - 1.54 (m, 4H), 1.33 (ddd, \( J = 24.9, 12.5, 3.5 \text{ Hz} \), 1H). \(^{13}\)C NMR (100 MHz, CDCl\(_3\)): 211.7, 138.8, 135.4, 133.6, 130.4, 128.9, 127.4, 77.1, 51.7, 42.8, 33.1, 30.9, 28.5, 25.3.

2-(1-(2,4-dichlorophenyl)-2-nitroethyl)cyclohexanone (12f)

The ee was determined by HPLC (Chiralpak AD column, hexane/i-PrOH 90:10, flow rate 1.0 mL/min, \( \lambda = 220 \text{ nm} \), 20°C). \( t_R \) (minor) = 9.3 min; \( t_R \) (major) = 13.1 min, syn/anti = 80/20, syn: ee = 85%.

\(^1\)H NMR (400 MHz, CDCl\(_3\)) \( \delta = 7.41 \) (d, \( J = 2.1 \text{ Hz} \), 1H), 7.23 (d, \( J = 2.1 \text{ Hz} \), 1H), 7.19 (s, 1H), 4.89 (d, \( J = 2.1 \text{ Hz} \), 1H), 4.87 (s, 1H), 4.24 (dd, \( J = 15.7, 7.9 \text{ Hz} \), 1H), 2.92 - 2.82 (m, 1H), 2.52 - 2.44 (m, 1H), 2.43 - 2.33 (m, 1H), 2.16 - 2.07 (m, 1H), 1.87 - 1.61 (m, 4H), 1.39 - 1.29 (m, 1H). \(^{13}\)C NMR (100 MHz, CDCl\(_3\)): 211.3, 135.1, 134.1, 133.5, 130.2, 127.7, 51.6, 42.8, 40.3, 33.1, 28.5, 27.2, 25.3, m.p. 105-107 °C.
2-(1-(4-trifluorophenyl)-2-nitroethyl) cyclohexanone (12g)

The ee was determined by HPLC (Chiralpak AD column, hexane/i-PrOH 95:5, flow rate 0.8 mL/min, λ = 220 nm, 20°C). \( t_R \) (minor) = 18.4 min; \( t_R \) (major) = 39.7 min, syn/anti = 88/12, syn: ee = 80%.

\(^1\)H NMR (400 MHz, CDCl\(_3\)) \( \delta = 7.59 \) (d, \( J = 8.1 \) Hz, 2H), 7.32 (d, \( J = 8.1 \) Hz, 2H), 4.98 (dd, \( J = 12.8, 4.5 \) Hz, 1H), 4.67 (dd, \( J = 12.8, 10.1 \) Hz, 1H), 3.86 (td, \( J = 9.8, 4.5 \) Hz, 1H), 2.70 (ddd, \( J = 12.9, 9.9, 5.1 \) Hz, 1H), 2.52 – 2.44 (m, 1H), 2.43 – 2.33 (m, 1H), 2.14 – 2.05 (m, 1H), 1.84 – 1.77 (m, 1H), 1.74 – 1.57 (m, 3H), 1.30 – 1.19 (m, 1H). \(^{13}\)C NMR (100 MHz, CDCl\(_3\)): \( \square 211.2, 142.1, 132.3 \) (q, \( J = 38.5 \) Hz), 128.6, 125.7, 109.3 (q, \( J = 275.5 \) Hz ), 78.3, 52.3, 43.7, 42.7, 33.2, 28.4, 25.1; m.p. 85-86 °C.

2-(1-(3-nitrophenyl)-2-nitroethyl) cyclohexanone (12h)

The ee was determined by HPLC (Chiralpak AD column, hexane/i-PrOH 95:5, flow rate 0.8 mL/min, λ = 220 nm, 20°C). \( t_R \) (minor) = 12.0 min; \( t_R \) (major) = 16.1 min, syn/anti = 86/14, syn: ee = 86%.

\(^1\)H NMR (400 MHz, CDCl\(_3\)) \( \delta = 8.17 – 8.13 \) (m, 1H), 8.09 (t, \( J = 1.9 \) Hz, 1H), 7.56 – 7.52 (m, 2H), 5.01 (dd, \( J = 13.0, 4.4 \) Hz, 1H), 4.71 (dd, \( J = 13.0, 10.2 \) Hz, 1H), 3.95 (td, \( J = 9.8, 4.4 \) Hz, 1H), 2.75 (ddd, \( J = 14.1, 9.4, 5.1 \) Hz, 1H), 2.53 – 2.47 (m, 1H), 2.44 – 2.38 (m, 1H), 2.13 – 2.09 (m, 1H), 1.84 – 1.79 (m, 1H), 1.65 – 1.54 (m, 3H), 1.34 – 1.27 (m, \( J = 12.6, 4.0 \) Hz, 1H). \(^{13}\)C NMR
(100 MHz, CDCl$_3$): δ 211.0, 148.6, 143.9, 140.2, 134.9, 130.0, 122.9, 78.1, 52.2, 43.7, 42.8, 33.2, 30.9, 28.3, 25.1; m.p. 77-79 °C.

2-(1-(2-methoxyphenyl)-2-nitroethyl) cyclohexanone (12i)

![Chemical Structure](image)

The ee was determined by HPLC (Chiralpak AD column, hexane/i-PrOH 99:1, flow rate 1.0 mL/min, λ = 220 nm, 20°C). $t_R$ (minor) = 22.5 min; $t_R$ (major) = 23.5 min, syn/anti = 97/3, syn: ee = 81%.

$^1$H NMR (400 MHz, CDCl$_3$) δ = 7.27 – 7.22 (m, 1H), 7.08 (dd, $J = 7.4$, 1.7 Hz, 1H), 6.88 (t, $J = 8.4$ Hz, 2H), 4.83 (dd, $J = 7.0$, 4.7 Hz, 1H), 4.00 – 3.92 (m, 1H), 3.84 (s, 3H), 2.98 (td, $J = 11.6$, 5.2 Hz, 1H), 2.51 – 2.44 (m, 1H), 2.43 – 2.34 (m, 1H), 2.11 – 2.03 (m, 1H), 1.80 – 1.54 (m, 4H), 1.20 (dd, $J = 13.0$, 3.7 Hz, 1H). $^{13}$C NMR (100 MHz, CDCl$_3$): δ 212.6, 157.6, 131.0, 129.0, 125.4, 120.9, 111.0, 55.4, 50.6, 41.3, 40.2, 33.3, 28.6, 25.2; m.p. 98-100 °C.

2-(2-nitro-1-p-tolylethyl) cyclohexanone (12j)

![Chemical Structure](image)

The ee was determined by HPLC (Chiralpak AD column, hexane/i-PrOH 95:5, flow rate 1.0 mL/min, λ = 220 nm, 20°C). $t_R$ (minor) = 21.1 min; $t_R$ (major) = 32.2 min, syn/anti = 83/7, syn: ee = 80%.

$^1$H NMR (400 MHz, CDCl$_3$) δ = 7.12 (d, $J = 7.9$ Hz, 2H), 7.04 (d, $J = 8.1$ Hz, 2H), 4.91 (dd, $J = 12.4$, 4.6 Hz, 1H), 4.61 (dd, $J = 12.3$, 9.9 Hz, 1H), 3.72 (td, $J = 9.9$, 4.5 Hz, 1H), 2.71 – 2.62 (m, 1H), 2.50 – 2.44 (m, 1H), 2.43 – 2.33 (m, 1H), 2.11 – 2.03 (m, 1H), 1.81 – 1.64 (m, 3H), 1.62 – 1.51 (m, 1H), 1.25 – 1.19 (m, 1H). $^{13}$C NMR (100 MHz, CDCl$_3$): δ 212.1, 137.5, 134.6, 129.6, 128.0, 79.0, 52.6, 43.6, 42.7, 33.2, 28.5, 25.0, 21.1; m.p. 123-127 °C.
2-(1-(furan-2-yl)-2-nitroethyl) cyclohexanone (12k)

![Chemical Structure of 2-(1-(furan-2-yl)-2-nitroethyl) cyclohexanone (12k)](attachment)

The ee was determined by HPLC (Chiralpak AD column, hexane/i-PrOH 90:10, flow rate 1.0 mL/min, λ = 220 nm, 20°C). \( t_R \) (minor) = 26.9 min; \( t_R \) (major) = 20.9 min, \textit{syn/anti} = 80/20, \textit{syn}: ee = 81%.

\(^1\)H NMR (400 MHz, CDCl\(_3\)) \( \delta = 7.34 \) (d, \( J = 1.5 \) Hz, 1H), 6.29 (dd, \( J = 3.2, 1.9 \) Hz, 1H), 6.18 (d, \( J = 3.2 \) Hz, 1H), 4.79 (dd, \( J = 12.5, 4.8 \) Hz, 1H), 4.67 (dd, \( J = 12.5, 9.4 \) Hz, 1H), 3.97 (td, \( J = 9.2, 4.8 \) Hz, 1H), 2.79 – 2.71 (m, 1H), 2.49 – 2.42 (m, 1H), 2.41 – 2.31 (m, 1H), 2.13 – 2.06 (m, 1H), 1.87 – 1.80 (m, 1H), 1.79 – 1.72 (m, 1H), 1.69 – 1.59 (m, 2H), 1.31 – 1.26 (m, 1H). \(^{13}\)C NMR (100 MHz, CDCl\(_3\)) □ 211.0, 151.0, 142.3, 110.3, 109.0, 76.7, 51.1, 42.6, 37.6, 32.5, 28.2, 25.1.

2-(1-(thiophen-2-yl)-2-nitroethyl) cyclohexanone (12l)

![Chemical Structure of 2-(1-(thiophen-2-yl)-2-nitroethyl) cyclohexanone (12l)](attachment)

The ee was determined by HPLC (Chiralpak AD column, hexane/i-PrOH 95:5, flow rate 1.0 mL/min, λ = 220 nm, 20°C). \( t_R \) (minor) = 20.1 min; \( t_R \) (major) = 23.6 min, \textit{syn/anti} = 83/7, \textit{syn}: ee = 75%.

\(^1\)H NMR (400 MHz, CDCl\(_3\)) \( \delta = 7.21 \) (dd, \( J = 7.1, 4.1 \) Hz, 1H), 6.93 (dd, \( J = 5.1, 3.5 \) Hz, 1H), 6.87 (dd, \( J = 3.5, 0.7 \) Hz, 1H), 4.89 (dd, \( J = 12.6, 4.7 \) Hz, 1H), 4.65 (dd, \( J = 12.6, 9.4 \) Hz, 1H), 4.13 (td, \( J = 9.1, 4.7 \) Hz, 1H), 2.72 – 2.64 (m, 1H), 2.50 – 2.43 (m, 1H), 2.41 – 2.31 (m, 1H), 2.14 – 2.04 (m, 1H), 1.95 – 1.87 (m, 1H), 1.87 – 1.80 (m, 1H), 1.67 – 1.60 (m, 2H), 1.32 (dd, \( J = 12.8, 3.4 \) Hz, 1H). \(^{13}\)C NMR (100 MHz, CDCl\(_3\)): □ 211.3, 140.5, 126.9, 126.6, 125.0, 79.2, 53.4, 42.6, 39.4, 32.8, 28.3, 25.1; m.p. 84-86 °C.
4. Characterization data of Michael products (14a-l)

General procedure for the Asymmetric Michael Reaction of Nitroolefin 11 with diketones (13)

To a solution of nitroolefin 11 (0.5 mmol) in CH$_2$Cl$_2$ (1.5 mL) was added catalyst 1a (0.005 mmol) and 1,3-dicarbonyl compound 13 (5.0 mmol). Upon consumption of nitroolefin substrate (monitored by TLC), the reaction mixture was concentrated and purified by column chromatography to afford the conjugate addition product 14. Relative and absolute configurations of the products were determined by comparison of $^1$H NMR, $^{13}$C NMR spectra and HPLC data with the known literature. Compounds 14a-l are known.

3-(2-nitro-1-phenylethyl)pentane-2,4-dione (14a)

The ee was determined by HPLC (Chiralpak AD column, hexane/EtOH 90:10, flow rate 1.0 mL/min, $\lambda = 220$ nm, 25°C). $t_R$ (minor) = 28.3 min; $t_R$ (major) = 30.4 min, ee = 93%.

$^1$H NMR (400 MHz, CDCl$_3$) $\delta = 7.36 – 7.26$ (m, 3H), 7.19 (dd, $J = 7.9$, 1.5 Hz, 2H), 4.69 – 4.59 (m, 2H), 4.37 (d, $J = 10.8$ Hz, 1H), 4.24 (ddd, $J = 10.8$, 7.6, 5.1 Hz, 1H), 2.29 (s, 3H), 1.94 (s, 3H).

$^{13}$C NMR (100 MHz, CDCl$_3$): 201.8, 201.0, 136.0, 129.3, 128.6, 128.0, 78.2, 70.7, 42.8, 30.4, 29.6; m.p. 115-118 °C.
3-(1-(4-fluorophenyl)-2-nitroethyl)pentane-2,4-dione (14b)

![Chemical Structure]

The ee was determined by HPLC (Chiralpak AD column, hexane/i-PrOH 90:10, flow rate 1.0 mL/min, λ = 220 nm, 25°C). _t_R_(minor) = 10.8 min; _t_R_(major) = 22.9 min, ee = 88%.

^1^H NMR (400 MHz, CDCl₃): δ = 7.18 (dd, *J* = 8.7, 5.1 Hz, 2H), 7.03 (t, *J* = 8.6 Hz, 2H), 4.63 – 4.59 (m, 2H), 4.34 (d, *J* = 10.8 Hz, 1H), 4.24 (ddd, *J* = 10.9, 7.0, 5.5 Hz, 1H), 2.30 (s, 3H), 1.97 (s, 3H). ^1^3^C NMR (100 MHz, CDCl₃): 221.4, 169.4, 137.6, 128.7, 126.8, 126.1, 77.62, 62.4, 62.3, 42.2, 38.0, 31.6, 19.4, 14.0.

3-(1-(4-bromophenyl)-2-nitroethyl)pentane-2,4-dione (14c)

![Chemical Structure]

The ee was determined by HPLC (Chiralpak AD column, hexane/i-PrOH 90:10, flow rate 1.0 mL/min, λ = 220 nm, 25°C). _t_R_(minor) = 32.5 min; _t_R_(major) = 35.1 min, ee = 81%.

^1^H NMR (400 MHz, CDCl₃): δ = 7.40 (d, *J* = 8.5 Hz, 2H), 7.01 (d, *J* = 8.5 Hz, 2H), 4.56 – 4.52 (m, 2H), 4.26 (d, *J* = 10.7 Hz, 1H), 4.18 – 4.11 (m, 1H), 2.23 (s, 3H), 1.91 (s, 3H). ^1^3^C NMR (100 MHz, CDCl₃): 200.4, 199.5, 134.1, 131.5, 128.6, 121.7, 76.8, 69.4, 41.2, 29.4, 28.6.

3-(2-nitro-1-(p-tolyl)ethyl)pentane-2,4-dione (14d)

![Chemical Structure]

The ee was determined by HPLC (Chiralpak AD column, hexane/i-PrOH 90:10, flow rate 1.0 mL/min, λ = 220 nm, 25 °C). _t_R_(minor) = 10.6 min; _t_R_(major) = 18.0 min, ee = 88%.

^1^H NMR (400 MHz, CDCl₃): δ = 7.12 (d, *J* = 8.0 Hz, 2H), 7.06 (d, *J* = 8.2 Hz, 2H), 4.63 – 4.58 (m, 2H), 4.35 (d, *J* = 10.8 Hz, 1H), 4.25 – 4.17 (m, 1H), 2.30 (s, 3H), 2.28 (s, 3H), 1.94 (s, 3H). ^1^3^C
NMR (100 MHz, CDCl₃): 201.9, 201.2, 138.3, 132.9, 130.0, 127.8, 78.4, 70.7, 42.5, 30.4, 29.6, 21.0; m.p. 101-103 °C.

3-(2-nitro-1-(thiophen-2-yl) ethyl)pentane-2,4-dione (14e)

![Structural formula](image)

The ee was determined by HPLC (Chiralpak AD column, hexane/i-PrOH 90:10, flow rate 1.0 mL/min, λ = 220 nm, 25°C). tᵣ (minor) = 16.3 min; tᵣ (major) = 21.9 min, ee = 83%.

¹H NMR (400 MHz, CDCl₃): δ = 7.17 (dd, J = 5.1, 0.9 Hz, 1H), 6.87 (dd, J = 5.1, 3.6 Hz, 1H), 6.82 (d, J = 3.3 Hz, 1H), 4.61 – 4.58 (m, 2H), 4.51 – 4.44 (m, 1H), 4.33 (d, J = 10.1 Hz, 1H), 2.23 (s, 3H), 2.01 (s, 3H). ¹³C NMR (100 MHz, CDCl₃): 200.5, 199.6, 137.4, 126.4, 126.0, 124.7, 77.5, 70.0, 37.2, 29.5, 28.6.

2-benzoyl-4-nitro-3-phenylbutyric acid ethyl ester (14f)

![Structural formula](image)

The ee was determined by HPLC (Chiralpak AD column, hexane/i-PrOH 90:10, flow rate 1.0 mL/min, λ = 220 nm, 25°C) (1:1 mixture of diastereomers). Major diastereomer: tᵣ (minor) = 14.3 min; tᵣ (major) = 17.5 min, ee = 85%; minor diastereomer: tᵣ (minor) = 16.8 min; tᵣ (major) = 34.6 min, ee = 84%.

major diastereomer: ¹H NMR (400 MHz, CDCl₃): δ = 7.85 (d, J = 7.2 Hz, 2H), 7.58 – 7.53 (m, 1H), 7.42 (t, J = 7.8 Hz, 2H), 7.34 – 7.28 (m, 3H), 7.23 – 7.17 (m, 3H), 4.96 (d, J = 1.7 Hz, 1H), 4.95 – 4.90 (m, 2H), 4.46 – 4.40 (m, 1H), 4.18 (q, J = 7.1 Hz, 2H), 1.18 (t, J = 7.1 Hz, 3H).

minor diastereomer: ¹H NMR (400 MHz, CDCl₃) δ = 8.05 (d, J = 7.2 Hz, 2H), 7.62 (t, J = 7.9 Hz, 1H), 7.49 (t, J = 7.8 Hz, 2H), 7.33 – 7.28 (m, 2H), 7.24 – 7.16 (m, 3H), 4.95 – 4.90 (m, 1H), 4.79 (t, J = 6.4 Hz, 2H), 4.49 (ddd, J = 8.4, 7.4, 4.2 Hz, 1H), 3.87 (qd, J = 7.1, 2.0 Hz, 2H), 0.90 (t, J = 7.1 Hz, 3H); m.p. 94-96 °C.
2-acetyl-2-(2-nitro-1-phenylethyl)cyclopentanone (14g)

\[
\begin{align*}
\text{Ph} & \quad \text{COMe} \\
\text{H} & \quad \text{NO}_2
\end{align*}
\]

The ee was determined by HPLC (Chiralpak AD column, hexane/i-PrOH 90:10, flow rate 1.0 mL/min, λ = 220 nm, 25°C) (1:1 mixture of diastereomers). Major diastereomer: \( t_R \) (minor) = 14.5 min; \( t_R \) (major) = 24.0 min, ee = 88%; minor diastereomer: \( t_R \) (minor) = 12.6 min; \( t_R \) (major) = 18.5 min, ee = 86%.

major diastereomer: \( ^1H \) NMR (400 MHz, CDCl\(_3\)): \( \delta = 7.28 - 7.17 \) (m, 4H), 7.11 (dd, \( J = 7.2, 2.2 \) Hz, 1H), 4.95 (dd, \( J = 13.1, 11.0 \) Hz, 1H), 4.53 (dd, \( J = 13.1, 3.8 \) Hz, 1H), 4.21 (dd, \( J = 11.0, 3.8 \) Hz, 1H), 2.43 – 2.27 (m, 2H), 2.11 (s, 3H), 1.96 – 1.86 (m, 2H), 1.71 – 1.60 (m, 1H), 1.37 – 1.28 (m, 1H).

minor diastereomer: \( ^1H \) NMR (400 MHz, CDCl\(_3\)): \( \delta = 7.28 - 7.17 \) (m, 4H), 7.11 (dd, \( J = 7.2, 2.2 \) Hz, 1H), 4.79 (dd, \( J = 13.5, 11.6 \) Hz, 1H), 4.44 (dd, \( J = 13.5, 3.9 \) Hz, 1H), 4.32 (dd, \( J = 11.6, 3.8 \) Hz, 1H), 2.54 – 2.45 (m, 1H), 2.26 (s, 3H), 2.17 – 1.96 (m, 2H), 1.71 – 1.61 (m, 3H).

1-(2-nitro-1-phenylethyl)-2-oxocyclopentanecarboxylic acid ethyl ester (14h)

\[
\begin{align*}
\text{Ph} & \quad \text{CO}_2\text{Et} \\
\text{H} & \quad \text{NO}_2
\end{align*}
\]

The ee was determined by HPLC (Chiralpak AD column, hexane/i-PrOH 90:10, flow rate 1.0 mL/min, λ = 220 nm, 25°C) (24:1 mixture of diastereomers). Major diastereomer: \( t_R \) (minor) = 15.6 min; \( t_R \) (major) = 26.3 min, ee = 83%; minor diastereomer: \( t_R \) (minor) = 13.6 min; \( t_R \) (major) = 20.6 min, ee = 87%.

major diastereomer: \( ^1H \) NMR (400 MHz, CDCl\(_3\)): \( \delta = 7.33 – 7.23 \) (m, 5H), 5.17 (dd, \( J = 13.6, 3.9 \) Hz, 1H), 5.01 (dd, \( J = 13.6, 11.0 \) Hz, 1H), 4.25 – 4.18 (m, 2H), 4.08 (dd, \( J = 11.0, 3.9 \) Hz, 1H), 2.42 – 2.26 (m, 2H), 2.08 – 1.77 (m, 4H), 1.27 (t, \( J = 7.1 \) Hz, 3H).
minor diastereomer: $^1$H NMR (400 MHz, CDCl$_3$): $\delta = 7.33 – 7.23$ (m, 5H), 5.29 (dd, $J = 13.4$, 11.1 Hz, 1H), 4.84 (dd, $J = 13.5$, 3.5 Hz, 1H), 4.33 – 4.26 (m, 2H), 4.14 (dd, $J = 12.5$, 5.4 Hz, 1H), 2.54 – 2.43 (m, 2H), 2.19 – 2.08 (m, 6H), 1.29 (t, $J = 7.1$ Hz, 3H).

$\text{2-acetyl-4-nitro-3-phenylbutyric acid methyl ester (14i)}$

![Image of 2-acetyl-4-nitro-3-phenylbutyric acid methyl ester](image)

The ee was determined by HPLC (Chiralpak AD column, hexane/i-PrOH 90:10, flow rate 1.0 mL/min, $\lambda = 220$ nm, 25°C) (1.1:1 mixture of diastereomers). Major diastereomer: $t_R$ (minor) = 27.6 min; $t_R$ (major) = 23.9 min, ee = 86%; minor diastereomer: $t_R$ (minor) = 33.6 min; $t_R$ (major) = 42.8 min, ee = 80%.

major diastereomer: $^1$H NMR (400 MHz, CDCl$_3$): $\delta = 7.35 – 7.27$ (m, 3H), 7.22 – 7.18 (m, 2H), 4.82 (d, $J = 4.7$ Hz, 1H), 4.78 (d, $J = 1.5$ Hz, 1H), 4.27 – 4.17 (m, 1H), 4.14 (d, $J = 9.6$ Hz, 1H), 3.53 (s, 3H), 2.30 (s, 3H).

minor diastereomer: $^1$H NMR (400 MHz, CDCl$_3$): $\delta = 7.35 – 7.27$ (m, 3H), 7.22 – 7.18 (m, 2H), 4.84 (d, $J = 2.0$ Hz, 1H), 4.77 (s, 1H), 4.27 – 4.17 (m, 1H), 4.05 (d, $J = 9.8$ Hz, 1H), 3.78 (s, 3H), 2.05 (s, 3H); m.p. 100-102 °C.

$\text{2-acetyl-4-nitro-3-phenylbutyric acid ethyl ester (14j)}$

![Image of 2-acetyl-4-nitro-3-phenylbutyric acid ethyl ester](image)

The ee was determined by HPLC (Chiralpak AD column, hexane/i-PrOH 90:10, flow rate 1.0 mL/min, $\lambda = 220$ nm, 25°C) (1.1:1 mixture of diastereomers). Major diastereomer: $t_R$ (minor) = 32.4 min; $t_R$ (major) = 29.6 min, ee = 87%; minor diastereomer: $t_R$ (minor) = 35.3 min; $t_R$ (major) = 39.8 min, ee = 86%.

major diastereomer: $^1$H NMR (400 MHz, CDCl$_3$): $\delta = 7.34 – 7.26$ (m, 3H), 7.20 (d, $J = 7.5$ Hz, 2H), 4.84 (dd, $J = 6.9$, 4.6 Hz, 1H), 4.75 (d, $J = 6.2$ Hz, 1H), 4.27 – 4.16 (m, 2H), 4.12 (d, $J = 10.0$ Hz, 1H), 3.97 (q, $J = 7.1$ Hz, 1H), 2.30 (s, 3H), 1.00 (t, $J = 7.1$ Hz, 3H).
minor diastereomer: $^1$H NMR (400 MHz, CDCl$_3$): $\delta =$ 7.34 – 7.26 (m, 3H), 7.20 (d, $J =$ 7.5 Hz, 2H), 4.84 (dd, $J =$ 6.9, 4.6 Hz, 1H), 4.75 (d, $J =$ 6.2 Hz, 1H), 4.27 – 4.16 (m, 2H), 4.03 (d, $J =$ 9.7 Hz, 1H), 3.97 (q, $J =$ 7.1 Hz, 1H), 2.06 (s, 3H), 1.28 (t, $J =$ 7.1 Hz, 3H).

2-acetyl-4-nitro-3-phenylbutyric acid tert-butyl ester (14k)

![Structure](image)

The ee was determined by HPLC (Chiralpak AD column, hexane/i-PrOH 90:10, flow rate 1.0 mL/min, $\lambda =$ 220 nm, 25°C) (12:1 mixture of diastereomers). Major diastereomer: $t_R$ (minor) = 9.4 min; $t_R$ (major) = 12.6 min, ee = 86%; minor diastereomer: $t_R$ (minor) = 18.2 min; $t_R$ (major) = 15.3 min, ee = 86%.

major diastereomer: $^1$H NMR (400 MHz, CDCl$_3$): $\delta =$ 7.34 – 7.27 (m, 3H), 7.21 (dd, $J =$ 7.9, 1.5 Hz, 2H), 4.71 (dd, $J =$ 8.3, 6.3 Hz, 2H), 4.17 – 4.07 (m, 1H), 4.02 (d, $J =$ 10.4 Hz, 1H), 2.31 (s, 3H), 1.16 (s, 9H); m.p. 128-132 °C.

minor diastereomer: $^1$H NMR (400 MHz, CDCl$_3$): $\delta =$ 7.34 – 7.27 (m, 3H), 7.21 (dd, $J =$ 7.9, 1.5 Hz, 2H), 4.86 – 4.81 (m, 2H), 4.19 (dd, $J =$ 9.2, 4.1 Hz, 1H), 3.92 (d, $J =$ 9.6 Hz, 1H), 2.06 (s, 3H), 1.47 (s, 9H).

2-((2-nitro-1-phenylethyl)-3-oxopentanoic methyl ester (14l)

![Structure](image)

The ee was determined by HPLC (Chiralpak AD column, hexane/i-PrOH 90:10, flow rate 1.0 mL/min, $\lambda =$ 220 nm, 25°C) (1:1 mixture of diastereomers). Major diastereomer: $t_R$ (minor) = 19.7 min; $t_R$ (major) = 31.5 min, ee = 86%; minor diastereomer: $t_R$ (minor) = 28.9 min; $t_R$ (major) = 36.5 min, ee = 80%.

major diastereomer: $^1$H NMR (400 MHz, CDCl$_3$): $\delta =$ 7.34 – 7.26 (m, 3H), 7.19 (d, $J =$ 7.0 Hz, 2H), 4.85 (dd, $J =$ 8.2, 7.0 Hz, 1H), 4.79 (d, $J =$ 6.4 Hz, 1H), 4.28 – 4.20 (m, 1H), 4.03 (d, $J =$ 9.9 Hz, 1H), 3.75 (s, 3H), 2.67 (dq, $J =$ 18.5, 7.2 Hz, 1H), 2.53 – 2.42 (m, 1H), 0.83 (t, $J =$ 7.2 Hz, 3H).
minor diastereomer: $^1$H NMR (400 MHz, CDCl$_3$): $\delta = 7.34 – 7.26$ (m, 3H), 7.19 (d, $J = 7.0$ Hz, 2H), 4.85 (dd, $J = 8.2, 7.0$ Hz, 1H), 4.79 (d, $J = 6.4$ Hz, 1H), 4.28 – 4.20 (m, 1H), 4.14 (d, $J = 9.3$ Hz, 1H), 3.52 (s, 3H), 2.52 – 2.42 (m, 1H), 2.13 (dq, $J = 18.5, 7.2$ Hz, 1H), 1.06 (t, $J = 7.2$ Hz, 3H).

5. Synthesis and Characterization data of (15)

A suspension of 14j (0.2 mmol) and zinc powder (5.0 mmol, 25 eq.) in 5 mL of ethanol was heated at 70 °C with stirring, and 2 mL of acetate acid was added dropwise and the resulting mixture was then refluxed for 30 min. Upon completion as shown by TLC, the reaction mixture was cooled to room temperature. Saturated aqueous ammonia was added dropwise to the reaction mixture till the pH>8, which was then extracted with CH$_2$Cl$_2$ (3 × 25 mL). The CH$_2$Cl$_2$ extracts were washed with water, dried (MgSO$_4$), filtered, and were removed by rotary evaporation. The remaining material was purified by flash chromatography on silica gel using a 10-30% EtOAc/hexane to give 15 as a yellow viscous oil. $^1$H NMR (400 MHz, CDCl$_3$): $\delta = 7.36$ (m, 3H), 7.15 (m, 2H), 4.46 (m, 1H), 4.22 (m, 1H), 3.70 (m, 1H), 2.31 (m, 2H), 1.98 (s, 3H), 1.86 (m, 3H), 1.36 (m, 1H). MS m/z: 245 (M$^+$).

6. References

7. Representative NMR spectra
8. Representative HPLC spectra

<table>
<thead>
<tr>
<th>Peak</th>
<th>Ret. Time (min)</th>
<th>Height (mV)</th>
<th>Area (mV*min)</th>
<th>Area (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>19.965</td>
<td>8874.243</td>
<td>305330.188</td>
<td>3.39</td>
</tr>
<tr>
<td>2</td>
<td>24.798</td>
<td>230911.078</td>
<td>8699720.000</td>
<td>96.61</td>
</tr>
<tr>
<td>Totals</td>
<td></td>
<td></td>
<td>9333120.188</td>
<td></td>
</tr>
</tbody>
</table>

Et OMe
O O
Ph NO2
H
H

H

©ARKAT-USA, Inc.
<table>
<thead>
<tr>
<th>Peak</th>
<th>Ret. Time (min)</th>
<th>Height (mV)</th>
<th>Area (mV*min)</th>
<th>Area (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>19.628</td>
<td>22368.396</td>
<td>846535.813</td>
<td>9.24</td>
</tr>
<tr>
<td>2</td>
<td>21.618</td>
<td>165169.391</td>
<td>8320523.000</td>
<td>90.76</td>
</tr>
<tr>
<td><strong>Totals</strong></td>
<td></td>
<td></td>
<td><strong>82</strong></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Peak</th>
<th>Ret. Time (min)</th>
<th>Height (mV)</th>
<th>Area (mV*min)</th>
<th>Area (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>12.798</td>
<td>65527.676</td>
<td>1060722.500</td>
<td>8.63</td>
</tr>
<tr>
<td>2</td>
<td>20.457</td>
<td>395572.406</td>
<td>11234555.000</td>
<td>91.37</td>
</tr>
<tr>
<td><strong>Totals</strong></td>
<td></td>
<td></td>
<td><strong>83</strong></td>
<td></td>
</tr>
</tbody>
</table>
Peak | Ret. Time (min) | Height (mV) | Area (mV*min) | Area (%)  
--- | --- | --- | --- | --- 
1   | 11.215 | 85210.547 | 2285664.250 | 7.80  
2   | 18.395 | 905982.563 | 27020646.000 | 92.20  
Totals | | | | 84  

Peak | Ret. Time (min) | Height (mV) | Area (mV*min) | Area (%)  
--- | --- | --- | --- | --- 
1   | 18.442 | 67089.438 | 2720848.250 | 10.18
<table>
<thead>
<tr>
<th>Peak</th>
<th>Ret. Time (min)</th>
<th>Height (mV)</th>
<th>Area (mV*min)</th>
<th>Area (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>17.442</td>
<td>39133.758</td>
<td>1508271.000</td>
<td>10.31</td>
</tr>
<tr>
<td>2</td>
<td>31.945</td>
<td>151902.250</td>
<td>13115318.000</td>
<td>89.69</td>
</tr>
<tr>
<td>Totals</td>
<td></td>
<td></td>
<td>80</td>
<td></td>
</tr>
<tr>
<td>Peak</td>
<td>Ret. Time (min)</td>
<td>Height (mV)</td>
<td>Area (mV*min)</td>
<td>Area (%)</td>
</tr>
<tr>
<td>------</td>
<td>----------------</td>
<td>-------------</td>
<td>---------------</td>
<td>----------</td>
</tr>
<tr>
<td>1</td>
<td>25.760</td>
<td>9084.296</td>
<td>375649.031</td>
<td>3.42</td>
</tr>
<tr>
<td>2</td>
<td>27.475</td>
<td>164236.344</td>
<td>10620019.000</td>
<td>96.58</td>
</tr>
<tr>
<td>Totals</td>
<td></td>
<td></td>
<td>93</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Peak</th>
<th>Ret. Time (min)</th>
<th>Height (mV)</th>
<th>Area (mV*min)</th>
<th>Area (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>15.938</td>
<td>20368.398</td>
<td>588482.000</td>
<td>6.33</td>
</tr>
<tr>
<td>Peak</td>
<td>Ret. Time (min)</td>
<td>Height (mV)</td>
<td>Area (mV*min)</td>
<td>Area (%)</td>
</tr>
<tr>
<td>------</td>
<td>-----------------</td>
<td>-------------</td>
<td>---------------</td>
<td>----------</td>
</tr>
<tr>
<td>1</td>
<td>39.692</td>
<td>98558.008</td>
<td>8353256.000</td>
<td>9.72</td>
</tr>
<tr>
<td>2</td>
<td>43.227</td>
<td>833338.500</td>
<td>77555608.000</td>
<td>90.28</td>
</tr>
<tr>
<td>totals</td>
<td></td>
<td></td>
<td></td>
<td>81</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Peak</th>
<th>Ret. Time (min)</th>
<th>Height (mV)</th>
<th>Area (mV*min)</th>
<th>Area (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>20.147</td>
<td>24718.764</td>
<td>869847.375</td>
<td>1.89</td>
</tr>
<tr>
<td>2</td>
<td>32.038</td>
<td>847358.875</td>
<td>45104788.000</td>
<td>98.11</td>
</tr>
<tr>
<td>Totals</td>
<td></td>
<td></td>
<td></td>
<td>96</td>
</tr>
</tbody>
</table>