Supporting Information for:

Unsaturated β-ketoesters as versatile electrophiles in organocatalysis

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1. General methods

$^1$H-NMR and $^{13}$C-NMR spectra were recorded at 300 MHz and 75 MHz or at 400 MHz and 100 MHz respectively. Chemical shifts are reported in ppm relative to the resonance of CHCl$_3$ ($\delta$ = 7.26) for $^1$H-NMR and to the central peak of CDCl$_3$ ($\delta$ = 77.5) for $^{13}$C-NMR. Flash chromatography (FC) was carried out using Merck silica gel 60 (230-400 mesh) using mixtures of petroleum ether 30-50 °C (PE) and diethyl ether. Diastereoisomer ratios (dr) and enantiomeric excesses (ee) of the products were determined either by CSP-GC equipped with a MEGA column (chiral stationary phase diacetyl $t$-butyl $\beta$ CAX 30%) and a flame ionization detector (FID 5890 series II Hawlett-Packard) or by HPLC, using a CHIRALPAK IB ocolumn and a refractive index detector VARIAN RI 4.

1.1 Materials

Analytical grade solvents were used as received. All commercially available reagents were used as received, including nitroalkanes $2a$, $2b$, $2c$, $2d$, $2g$ and $2h$ and Cinchona alkaloid catalysts $I$, $II$, $III$, $IV$, $V$, and $VII$. Catalyst $VI$ was prepared accordingly to ref. 11e. Nitroalkanes $2e$ [M. Cherest and X. Lusinchi, Tetrahedron, 1986, 42, 3825] and $2f$ [A. K. Ghosh and H. Lei, J. Org. Chem., 2002, 67, 8783] were prepared accordingly to standard literature procedures. Unsaturated substrates $1a$-$c$ were prepared following the procedure reported in ref. 8 and stored at -20 °C prior to use. It should be noted that no chromatographic purification should be performed on the unsaturated adducts because of their instability over silica gel.

![Chemical structures of Cinchona alkaloids and catalysts](image)

**Figure 1**

Ethyl-2-oxo-cyclopent-1-enecarboxylate ($1a$):

$^1$H NMR (300 MHz) $\delta$ (CDCl$_3$): 8.28 (t, 1H, $J = 2.7$ Hz), 4.14 (q, 2H, $J = 7.2$ Hz), 2.7-2.6 (m, 2H), 2.42-2.39 (m, 2H) 1.19 (t, 3H, $J = 7.2$ Hz).

$^{13}$C NMR (75 MHz) $\delta$ (CDCl$_3$): 203.2, 172.2, 162.1, 137.6, 61.2, 36.0, 27.0, 14.5.

Ethyl-2-oxo-cyclohexen-1-enecarboxylate ($1b$):

$^1$H NMR (300 MHz) $\delta$ (CDCl$_3$): 7.66 (m, 1H), 4.26 (q, 2H, $J = 7.2$ Hz), 2.6-1.9 (m, 6H) 1.31 (t, 3H, $J = 7.2$ Hz).

$^{13}$C NMR (75 MHz) $\delta$ (CDCl$_3$): 194.7, 164.9, 156.0, 133.6, 61.3, 39.0, 26.4, 22.5, 14.4.
2. Synthesis and characterization of compounds 3

2.1 General procedure for the preparation of products 3a-3j

Unsaturated substrate 1a-c (0.35 mmol) is dissolved in 3.5 mL of the solvent with catalyst I-VII (10% mol, an equimolar mixture of quinine and quinidine is used for the preparation of racemic samples) at the temperature indicated in table 2. When the mixture is homogeneous, the nitroalkane 2a-h (3 eq) is added. The reaction is left without stirring for a period of time that varies between a few hours (reactions at room temperature, racemic samples) and some days (reactions at -20°C). When the unsaturated β-ketoester is totally consumed (TLC), the crude reaction mixture is directly loaded on a chromatographic column filled with silica gel and packed with PE, and quickly purified by FC (PE first, then PE:Et₂O from 10:1 to 1:4) to avoid degradation. The solvent is removed in vacuo to provide the products 3a-j as dense, pale yellow oils.

3a. The ee was determined by CSP-GC (column head pressure of carrier gas nitrogen of 14 psi, column temperature 180°C); \( \tau_{\text{major}} = 24.8 \, \text{min}, \tau_{\text{minor}} = 23.8 \, \text{min} \). For ees: see table 1, entries 1-14.

\[ 1H-NMR \, (300 \, \text{MHz}) \, \delta \, (\text{CDCl}_3), \text{mixture of keto and enol forms with ratio 1:1:} \ 10.6 \, (\text{bs}, \ 1H, \text{enol form}), \ 4.71 \, (\text{dd}, \ 1H, J = 12.0 \, \text{Hz}, \ J = 4.2 \, \text{Hz}, \text{enol form}), \ 4.59 \, (\text{dd}, \ 1H, J = 12.7 \, \text{Hz}, \ J = 6.7 \, \text{Hz}, \text{keto form}), \ 4.52 \, (\text{dd}, \ 1H, J = 12.7 \, \text{Hz}, \ J = 6.7 \, \text{Hz}, \text{keto form}), \ 4.3-4.1 \, (\text{m}, \ 2H, \text{keto form}, \ 3H \text{ enol form}), \ 3.7-3.6 \, (\text{m}, \ 1H, \text{keto form}), \ 3.4-3.2 \, (\text{m}, \ 1H, \text{enol form}), \ 3.10 \, (\text{d}, \ 1H, J = 11.4 \, \text{Hz}, \text{keto form}), \ 2.8-2.0 \, (m, \ 6H), \ 1.8-1.6 \, (m, \ 2H), \ 1.32 \, (t, \ 3H, J = 7.2 \, \text{Hz}, \text{keto form}), \ 1.31 \, (t, \ 3H, J = 7.2 \, \text{Hz}, \text{enol form}). \]

\[ 13C-NMR \, (75 \, \text{MHz}) \, \delta \, (\text{CDCl}_3): \ 208.3, \ 179.0, \ 169.3, \ 167.9, \ 99.7, \ 79.2, \ 78.4, \ 62.5, \ 60.9, \ 58.7, \ 40.0, \ 39.1, \ 38.1, \ 31.4, \ 25.1, \ 24.3, \ 14.6, \ 14.7. \]

\[ [\alpha]_D = +35.4 \, (\text{sample with 79% ee}, \ \text{MeOH}, \ c = 30 \, \text{mg/mL}). \]

\[ \text{HRMS calculated for C}_9\text{H}_{13}\text{NNaO}_5: \ 238.0691; \text{found: 238.0658}. \]

3b. The ee was determined by CSP-GC (column head pressure of carrier gas nitrogen of 14 psi, column temperature 180°C); for major diastereoisomer: \( \tau_{\text{major}} = 9.6 \, \text{min}, \ \tau_{\text{minor}} = 9.2 \, \text{min} \). For ees: see table 1, entries 15-18.

\[ 1H-NMR \, (300 \, \text{MHz}) \, \delta \, (\text{CDCl}_3), \text{mixture of keto and enol forms with ratio 6:1:} \ 4.46 \, (\text{ddd}, \ 1H, J = 11.7 \, \text{Hz}, \ J = 10.5 \, \text{Hz}, \ J = 3.6 \, \text{Hz}), \ 4.25 \, (q, \ 2H), \ 2.96 \, (d, \ 1H, J = 11.7 \, \text{Hz}), \ 2.6-2.5 \, (m, \ 2H), \ 2.2-2.0 \, (m, \ 3H), \ 1.8-1.6 \, (m, \ 2H), \ 1.31 \, (t, \ 3H), \ 0.98 \, (t, \ 3H). \]

\[ 13C-NMR \, (75 \, \text{MHz}) \, \delta \, (\text{CDCl}_3): \ 208.6, \ 168.6, \ 93.1, \ 62.5, \ 58.5, \ 43.8, \ 38.2, \ 25.6, \ 24.0, \ 14.6, \ 10.8. \]

\[ \text{HRMS calculated for C}_{11}\text{H}_{17}\text{NNaO}_5; \ 266.1004; \text{found: 266.1041}. \]

3c. The ee was determined by CSP-GC (column head pressure of carrier gas nitrogen of 14 psi, column temperature 180°C); for major diastereoisomer: \( \tau_{\text{major}} = 13.1 \, \text{min}, \ \tau_{\text{minor}} = 12.1 \, \text{min}, \ ee = 94\%, \ dr = 20:1, \) table 2, entry 1.

\[ 1H-NMR \, (300 \, \text{MHz}) \, \delta \, (\text{CDCl}_3), \text{mixture of keto and enol forms with ratio 5:1:} \ 10.8 \, (\text{bs}, \ 1H, \text{enol form}), \ 5.0-4.8 \, (m, \ 1H, \text{enol form}), \ 4.8-4.6 \, (m, \ 1H, \text{keto form}), \ 4.26 \, (q, \ 4H, J = 7.2 \, \text{Hz}), \ 3.5-3.4 \, (m, \ 1H, \text{keto form}), \ 3.2-3.1 \, (m, \ 1H), \ 3.03 \, (d, \ 1H, J = 11.7 \, \text{Hz}), \ 2.6-2.1 \, (m, \ 6H), \ 1.8-1.4 \, (m, \ 2H), \ 1.58 \, (d, \ 6H, J = 6.6 \, \text{Hz}), \ 1.32 \, (t, \ 6H, J = 7.2 \, \text{Hz}). \]

\[ 13C-NMR \, (75 \, \text{MHz}) \, \delta \, (\text{CDCl}_3): \ 208.6, \ 171.6, \ 168.6, \ 100.0, \ 86.0, \ 84.4, \ 66.3, \ 62.5, \ 60.8, \ 58.3, \ 45.9, \ 44.8, \ 38.3, \ 31.4, \ 24.1, \ 17.8, \ 16.7, \ 15.7, \ 14.7, \ 14.6. \]

\[ \text{HRMS calculated for C}_{10}\text{H}_{15}\text{NNaO}_5: \ 252.0848; \text{found: 252.0859}. \]
3d. The ee was determined by CSP-GC (column head pressure of carrier gas nitrogen of 9 psi, column temperature 165°C); for major diastereoisomer using quinine as catalyst: \( \tau_{\text{major}} = 32.6 \text{ min} \), \( \tau_{\text{minor}} = 28.6 \text{ min} \), \( \text{ee} = 94\% \), \( \text{dr} = 30:1 \), table 2, entry 8. Using quinidine as catalyst: \( \text{ee} = -93\% \), \( \text{dr} = 15:1 \), table 2, entries 2-3.

\(^1H\)-NMR (300 MHz) \( \delta \) (CDCl₃), mixture of keto and enol forms 3:1: 10.6 (bs, 1H, enol form), 5.0-4.8 (m, 1H), 4.6-4.1 (m, 5H), 3.4-3.1 (m, 2H), 2.96 (d, 1H, J = 11.7 Hz), 2.6-1.9 (m, 8H), 1.8-1.1 (m, 8H), 1.28 (t, 6H, J = 6.9 Hz), 1.0-0.8 (m, 6H).

\(^{13}C\)-NMR (75 MHz) \( \delta \) (CDCl₃), keto form: 208.3, 168.6, 91.3, 62.5, 58.5, 43.9, 38.2, 34.0, 24.0, 19.6, 14.6, 13.8.

HRMS calculated for C₁₂H₁₉NNaO₅: 280.1161; found: 280.1170.

3e. The ee was determined by CSP-GC (column head pressure of carrier gas nitrogen of 15 psi, column temperature 190°C); for major diastereoisomer using quinine as catalyst: \( \tau_{\text{major}} = 61.4 \text{ min} \), \( \tau_{\text{minor}} = 53.4 \text{ min} \), \( \text{ee} = 91\% \), \( \text{dr} = 20:1 \), table 2, entry 4.

\(^1H\)-NMR (300 MHz) \( \delta \) (CDCl₃): 7.4-7.0 (m, 5H), 5.0-4.8 (m, 1H), 4.26 (q, 2H, J = 6.9 Hz), 3.5-2.9 (m, 3H), 3.08 (d, 1H, J = 11.7 Hz), 2.6-2.1 (m, 4H), 1.31 (t, 3H, J = 6.9 Hz).

\(^{13}C\)-NMR (75 MHz) \( \delta \) (CDCl₃), keto form: 207.9, 168.2, 135.0, 129.2, 129.1, 128.9, 128.8, 127.9, 92.1, 62.4, 58.2, 43.5, 38.0, 37.9, 23.4, 14.4.

HRMS calculated C₁₆H₁₉NNaO₅: 328.1161; found: 328.1133.

3f. The ee was determined by CSP-GC (column head pressure of carrier gas nitrogen of 15 psi, column temperature 190°C); for major diastereoisomer using quinine as catalyst: \( \tau_{\text{major}} = 46.7 \text{ min} \), \( \tau_{\text{minor}} = 45.3 \text{ min} \), \( \text{ee} = 98\% \), \( \text{dr} = 20:1 \), table 2, entry 5.

\(^1H\)-NMR (300 MHz) \( \delta \) (CDCl₃), mixture of keto and enol 4:1: 4.8-4.6 (m, 1H), 4.4-4.1 (m, 2H), 3.89 (dd, 1H, J = 11.1 Hz, J = 3.7 Hz), 3.03 (d, 1H, J = 11.4 Hz), 2.8-2.0 (m, 5H), 2.0-1.8 (m, 1H), 1.2-1.1 (m, 3H), 1.1-0.8 (m, 21H).

\(^{13}C\)-NMR (75 MHz) \( \delta \) (CDCl₃), keto form: 208.3, 165.8, 93.0, 63.8, 62.6, 58.5, 40.7, 38.0, 24.2, 18.3, 14.6, 12.4.

HRMS calculated for C₁₉H₃₅NNaO₆Si: 424.2131; found: 424.2135.

3g. The ee was determined by CSP-GC (column head pressure of carrier gas nitrogen of 16 psi, column temperature 180°C); for major diastereoisomer using quinine as catalyst: \( \tau_{\text{major}} = 64.6 \text{ min} \), \( \tau_{\text{minor}} = 60.3 \text{ min} \), \( \text{ee} = 91\% \), \( \text{dr} = 15:1 \), table 2, entry 6.

\(^1H\)-NMR (300 MHz) \( \delta \) (CDCl₃), mixture of keto and enol 4:1: 10.7 (bs, 1H, enol form), 4.9-4.8 (m, 1H, enol form), 4.7-4.6 (m, 1H, keto form), 4.27 (q, 2H, J = 7.2 Hz, keto form), 3.69 (s, 3H, keto form), 3.3-3.1 (m, 1H, keto form), 3.06 (d, 1H, J = 11.4 Hz, keto form), 2.8-2.0 (m, 6H, keto form), 1.8-1.6 (m, 2H, keto form), 1.33 (t, 3H, J = 7.2 Hz, keto form), 1.32 (t, 3H, J = 7.2 Hz, enol form).

\(^{13}C\)-NMR (75 MHz) \( \delta \) (CDCl₃), keto form: 208.3, 172.5, 168.5, 90.3, 62.6, 58.2, 52.4, 43.8, 38.2, 30.2, 27.1, 24.0, 14.6.
HRMS calculated for C_{13}H_{19}NNaO_{7}: 324.1059; found: 324.1066.

3h. The ee was determined by CSP-HPLC (eluant n-hexane:i-propanol, 97:3, flow 0.9 mL/min); for major diastereoisomer using quinine as catalyst: \( \tau_{\text{major}} = 42.0 \) min, \( \tau_{\text{minor}} = 36.5 \) min, ee = 92, \( dr = 35:1 \), table 2, entry 7.

\[^{1}\text{H-NMR}\] (400 MHz) \( \delta (\text{CDCl}_3) \), mixture of 3h' and 3h'': 5.18 (d, 1H, \( J = 9.4 \) Hz, 3h''), 4.45 (d, 1H, \( J = 2.8 \) Hz, 3h'), 4.18 (q, 4H, \( J = 7.2 \) Hz), 3.2-3.1 (m, 1H, 3h''), 3.0-2.9 (m, 1H, 3h'), 2.6-2.0 (m, 8H), 1.4-1.2 (m, 6H).

\[^{1}\text{H-NMR}\] (400 MHz) \( \delta (\text{CDCl}_3) \), single diastereoisomer 3h': 4.44 (d, 1H, \( J = 2.8 \) Hz), 4.18 (q, 2H, \( J = 7.2 \) Hz), 3.2-3.1 (m, 1H), 2.4-2.2 (m, 4H), 1.27 (t, 3H, \( J = 7.2 \) Hz).

\[^{13}\text{C-NMR}\] (100 MHz) \( \delta (\text{CDCl}_3) \), mixture of 3h' and 3h'': 202.8, 201.9, 172.0, 162.3, 71.2, 63.7, 62.7, 48.9, 40.5, 39.9, 33.8, 32.7, 32.6, 30.4, 21.2, 17.9, 14.0, 13.8.

\[^{13}\text{C-NMR}\] (100 MHz) \( \delta (\text{CDCl}_3) \), single diastereoisomer 5i': 202.7, 162.2, 63.9, 62.8, 48.8, 33.8, 32.7, 21.2, 13.9.

HRMS calculated for C_{9}H_{11}NNaO_{5}: 236.0535; found: 236.0541.

3i. The ee was determined by CSP-GC (column head pressure of carrier gas nitrogen of 16 psi, column temperature 180°C); using quinine as catalyst: \( \tau_{\text{major}} = 19.2 \) min, \( \tau_{\text{minor}} = 19.4 \) min, ee = 87%, table 2, entry 8.

\[^{1}\text{H-NMR}\] (300 MHz) \( \delta (\text{CDCl}_3) \), only enol form: 4.54 (dd, 1H, \( J = 11.7 \) Hz, \( J = 3.9 \) Hz), 4.4-4.2 (m, 1H), 4.26 (q, 2H, \( J = 7.2 \) Hz), 3.5-3.4 (m, 1H), 2.4-2.2 (m, 2H), 1.9-1.6 (m, 5H), 1.33 (t, 3H, \( J = 7.2 \) Hz).

\[^{13}\text{C-NMR}\] (75 MHz) \( \delta (\text{CDCl}_3) \): 176.0, 172.0, 97.1, 78.3, 61.4, 32.3, 29.4, 24.9, 17.2, 14.6.

\( [\alpha]_D^0 \): +5.3 (sample with 87% ee, CHCl$_3$, c = 45 mg/mL).

HRMS calculated C_{10}H_{15}NNaO_{5}: 252.0848; found: 252.0842.

3j. The ee was determined by CSP-HPLC (eluant hexane:i-propanol, 92.5:1.5, flow 0.9 mL/min); using quinine as catalyst: \( \tau_{\text{major}} = 43.5 \) min, \( \tau_{\text{minor}} = 38.5 \) min, ee = 52%, Table 2, entry 9.

\[^{1}\text{H-NMR}\] (300 MHz) \( \delta (\text{CDCl}_3) \): 14.0 (bs, 1H, enol), 4.5-4.6 (m, 2H, ketone), 4.3-.4.4 (m, 2H, enol), 3.6-3.8 (m, 1H, ketone), 3.3-3.5 (m, 2H, ketone), 2.0-2.7 (m, 6H), 2.41 (s, 3H, ketone), 2.09 (s, 3H, enol), 1.9-2.0 (m, 1H), 1.5-1.8 (m, 1H).

\[^{13}\text{C-NMR}\] (75 MHz) \( \delta (\text{CDCl}_3) \): 208.9, 204.4, 201.2, 179.3, 126.0, 109.6, 65.8, 64.0, 38.7, 38.6, 34.6, 31.0, 37.0, 24.9, 24.4, 21.0.

HRMS calculated C_{8}H_{11}NNaO_{4}: 208.0586; found: 208.0570.
3. One pot procedure for the synthesis of bicyclic adduct 5a and adducts 6a-f

3.1 General procedure for the preparation of products 5a and 6b-f

Unsaturated substrate 1a (0.35 mmol) is dissolved in 1 mL of toluene with quinine I (10% mol) at -20°C. To the homogeneous mixture nitroalkane 2a-g (3 eq) is added and the reaction is left without stirring for 24 h; then methyl vinyl ketone 4 is added (3 eq) and the solution is left at room temperature for additional 12 h. The crude reaction mixture is loaded on a chromatographic column packed with silica gel and purified by FC (PE first, then PE:Et₂O from 10:1 to 1:4). The solvent is removed in vacuo to provide directly bicyclic adduct 5a or adducts 6b-f as colorless oils.

5a. The ee was determined by CSP-HPLC (eluant n-hexane:i-propanol, 97.5:2.5, flow 0.9 mL/min); mixture of epimers 1.5:1; for more polar epimer τ_major = 31.7 min, τ_minor = 28.0 min, ee = 97%, table 3, entry 1.

\[ \text{1H-NMR (300 MHz) } \delta (\text{CDCl}_3) \text{, mixture of epimers 3:1: } 5.32 (d, 1H, J = 12.0 Hz), 4.18 (q, 4H, J = 7.2 Hz), 4.00 (d, 1H, J = 12.0 Hz), 3.26 (dd, 1H, J = 12.0 Hz, J = 5.7 Hz), 2.85 (ddd, 2H, J = 12.6 Hz, J = 12.6 Hz, J = 5.7 Hz), 2.6-1.5 (m, 19H), 1.35 (s, 3H), 1.24 (t, 6H, J = 7.2 Hz), 1.23 (s, 3H). \]

\[ \text{13C-NMR (75 MHz) } \delta (\text{CDCl}_3): 211.1, 208.9, 185.8, 169.9, 165.6, 93.8, 91.7, 71.1, 69.5, 62.8, 62.4, 62.1, 43.7, 41.6, 36.9, 36.5, 34.4, 33.7, 27.4, 27.3, 25.0, 22.6, 21.8, 21.7, 14.4. \]

HRMS calculated \( \text{C}_{13}\text{H}_{19}\text{NNaO}_{6} \): 308.1110; found: 308.1105.

6b. The ee was determined by CSP-HPLC (eluant n-hexane:i-propanol, 97.5:2.5, flow 0.9 mL/min); using quinine as catalyst: τ_major = 22.7 min, τ_minor = 18.2 min, ee = 96%, table 3, entry 2.

\[ \text{1H-NMR (300 MHz) } \delta (\text{CDCl}_3): 4.4-4.1 (m, 3H), 2.8-2.2 (m, 6H), 2.15 (s, 3H), 2.1-1.9 (m, 5H), 1.28 (t, 3H, J = 7.2 Hz), 0.92 (t, 3H, J = 7.2 Hz). \]

\[ \text{13C-NMR (75 MHz) } \delta (\text{CDCl}_3): 213.4, 207.5, 169.7, 93.9, 62.5, 60.9, 48.5, 38.7, 38.1, 30.4, 28.4, 26.4, 24.8, 14.6, 10.9. \]

HRMS calculated \( \text{C}_{18}\text{H}_{23}\text{NNaO}_{6} \): 336.1423; found: 336.1440.

6c. The ee was determined by CSP-HPLC (eluant n-hexane:i-propanol, 97.5:2.5, flow 0.9 mL/min); using quinine as catalyst: τ_major = 28.0 min, τ_minor = 25.6 min, ee = 95%, table 3, entry 3.

\[ \text{1H-NMR (300 MHz) } \delta (\text{CDCl}_3): 4.6-4.5 (m, 1H), 4.4-4.1 (m, 2H), 2.8-2.4 (m, 6H), 2.15 (s, 3H), 2.1-1.9 (m, 3H), 1.64 (d, 3H, J = 6.6 Hz), 1.28 (t, 3H, J = 7.2 Hz). \]

\[ \text{13C-NMR (75 MHz) } \delta (\text{CDCl}_3): 213.3, 207.6, 169.6, 86.9, 65.2, 62.6, 49.2, 38.7, 38.1, 32.6, 28.2, 24.9, 22.8, 19.4, 14.6. \]

HRMS calculated \( \text{C}_{14}\text{H}_{21}\text{NNaO}_{6} \): 322.1267; found: 322.1271.
6d. The ee was determined by CSP-HPLC (eluant n-hexane:i-propanol, 97.5:2.5, flow 0.9 mL/min); using quinine as catalyst: \( \tau_{\text{major}} = 29.5 \text{ min}, \tau_{\text{minor}} = 27.5 \text{ min}, ee = 95\% \), table 3, entry 4.

\( ^1H\)-NMR (300 MHz) \( \delta \) (CDCl\(_3\)): 7.3-7.2 (m, 3H), 7.1-7.0 (m, 2H), 4.7-4.5 (m, 1H), 4.4-4.1 (m, 2H), 3.35 (dd, 1H, J = 14.1, J = 3.0 Hz), 3.15 (dd, 1H, J = 14.1 Hz, J = 11.4 Hz), 2.8-2.2 (m, 6H), 2.15 (s, 3H), 2.1-1.9 (m, 3H), 1.30 (t, 3H, J = 7.2 Hz).

\( ^{13}C\)-NMR (75 MHz) \( \delta \) (CDCl\(_3\)): 213.2, 207.5, 169.8, 135.5, 129.4, 129.1, 128.1, 93.9, 62.7, 60.9, 48.2, 39.1, 38.7, 38.1, 30.4, 28.5, 24.7, 14.6.

6e. The ee was determined by CSP-HPLC (eluant n-hexane:i-propanol, 97.5:2.5, flow 0.9 mL/min); using quinine as catalyst: \( \tau_{\text{major}} = 13.9 \text{ min}, \tau_{\text{minor}} = 11.5 \text{ min}, ee = 93\% \), table 3, entry 5.

\( ^1H\)-NMR (300 MHz) \( \delta \) (CDCl\(_3\)): 4.6-4.5 (m, 1H), 4.3-4.0 (m, 2H), 4.14 (d, 2H, J = 6.3 Hz), 3.35 (dd, 1H, J = 14.1 Hz, J = 3.0 Hz), 3.15 (dd, 1H, J = 14.1 Hz, J = 11.4 Hz), 2.8-2.5 (m, 2H), 2.4-2.1 (m, 3H), 2.14 (s, 3H), 2.1-1.8 (m, 3H), 1.28 (t, 3H, J = 7.2 Hz), 1.2-0.9 (m, 20H).

\( ^{13}C\)-NMR (75 MHz) \( \delta \) (CDCl\(_3\)): 213.2, 207.3, 169.6, 93.0, 63.7, 62.7, 60.6, 45.2, 38.7, 38.1, 30.4, 28.0, 24.7, 18.3, 14.6, 12.3.

HRMS calculated C\(_{23}\)H\(_{41}\)NNaO\(_7\)Si: 494.2550; found: 494.2548.

6f. The ee was determined by CSP-HPLC (eluant n-hexane:i-propanol, 97.5:2.5, flow 0.9 mL/min); using quinine as catalyst: \( \tau_{\text{major}} = 43.5 \text{ min}, \tau_{\text{minor}} = 38.5 \text{ min} ee = 96\% \), Table 3, entry 6.

\( ^1H\)-NMR (300 MHz) \( \delta \) (CDCl\(_3\)): 4.8-4.6 (m, 1H), 4.3-4.1 (m, 2H), 3.7 (s, 3H), 2.8-1.9 (m, 13H), 2.13 (s, 3H), 1.27 (t, 3H, J = 7.2 Hz).

\( ^{13}C\)-NMR (75 MHz) \( \delta \) (CDCl\(_3\)): 213.1, 207.6, 171.8, 169.1, 90.5, 62.4, 60.4, 52.1, 48.5, 38.5, 37.8, 30.1, 29.9, 28.2, 27.8, 24.6, 14.2.

HRMS calculated C\(_{17}\)H\(_{25}\)NNaO\(_8\): 394.1478; found: 394.1465.
4. Determination of the configuration for the newly formed stereocenters

4.1 Determination of the stereochemistry of compounds 3

\[
\text{CO}_2\text{Et} \quad \alpha
\]
\[
\text{NO}_2 \quad \beta
\]
\[
\gamma
\]

4.1.1 Determination of the absolute configuration of the stereocenter on the \(\beta'\)-position

Upon ester cleavage and decarboxylation of adduct 3a, only compound 7 is obtained (reaction conditions: 50 mg of 5a, 200 mg of NaCl in 1 mL of DMSO at 140 °C; after 2h water was added and the mixture extracted with ethyl acetate; concentration of the organic phase and column chromatography purification afforded 7 in 75% yield). Comparison of the sign and value of optical rotation with the one reported in the literature [ref 12c-d] assigned unambiguously the configuration of the stereocenter in the \(\beta'\)-position, also ruling out the possibility of epimerization of this stereocenter.

\[
\begin{align*}
\text{CO}_2\text{Et} & \quad \alpha \\
\text{NO}_2 & \quad \beta' \\
\end{align*}
\]

4.1.2 Determination of the absolute configuration of the stereocenter on the \(\alpha\)-position

The large coupling constant observed \((J = 12.7 \text{ Hz})\) between protons Ha and Hb in compound 3a, and the similar value \((12-13\text{Hz})\) measured through all the series of compounds 3 is compatible only with the presence of the more stable \(\text{trans}\) isomer.

\[
J (\text{Ha-Hb}) = 12\text{Hz}
\]

4.1.3 Determination of the absolute configuration of the stereocenter on the \(\gamma'\)-position

When nitrobromomethane 2h is employed as the nucleophile, the outcome of the reaction is similar within the series of compounds illustrated in Table 2. Two diastereoisomers are formed, in low diastereoselectivity when the reaction is run at rt, \((dr = 4:1)\), employing as the catalyst a mixture of quinine and quinidine to produce a quasi-racemate, while high diastereoselectivity \((>20:1)\) is observed at lower temperature \((-20^\circ \text{C})\),
utilizing as the catalyst only quinine (see table 2 in the article and table 4 in SI). The major diastereoisomer shows enantiomeric excess of 92%. These dr values are in good agreement within the series studied. The resulting products are, however, not the expected nitro Michael adducts $3k'\text{-}k''$, but the cyclopropyl derivatives $3h'\text{-}h''$. The formation of $3h'\text{-}h''$ can be rationalized through an internal $S_N2$ reaction and subsequent ring closure, which would occur with inversion of configuration of the stereocenter at the $\gamma'$-position.

Epimerization of the stereocenter at the $\gamma'$-position in compound $3h'$ or $3h''$ (at -20 °C) under the reaction conditions has not been observed; moreover, only one diastereoisomer is formed at low temperature while a mixture is formed at high temperatures, indicating that this ratio is related to the diastereoselectivity of the nitro Michael reaction and not to an epimerization process.

The larger coupling constant observed ($J = 9.4 \text{ Hz}$) between protons $Hc$ and $Hb$ in compound $3h''$ in comparison with the smaller value observed for compound $3h'$ ($J=2.8 \text{ Hz}$) indicates $trans$ relationship between these protons in compound $3h''$ and $cis$ relationship in compound $3h'$. Consequently, the configuration of the stereocenter present in the $\gamma'$-position of compounds 3 has been assigned as $(R)$.

Condition A: quinine + quinidine, (racemate), rt, $3h'/3h''$=4:1
Condition B: quinine, -20 °C, $3h'/3h''$>20:1

Scheme 4
**Table 4.** Quinine I mediated addition of nitrocompounds 2b-h to 1a at rt

<table>
<thead>
<tr>
<th>Entry[^a]</th>
<th>R</th>
<th>Solvent</th>
<th>Y, [%][^b]</th>
<th>dr[^c]</th>
<th>ee, [%][^c]</th>
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<tr>
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<td>3:1</td>
<td>85/60</td>
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<tr>
<td>2[^d]</td>
<td>Et, 2b</td>
<td>DCM</td>
<td>3b, 67</td>
<td>2:1</td>
<td>-</td>
</tr>
<tr>
<td>3</td>
<td>Me, 2c</td>
<td>DCM</td>
<td>3c, 67</td>
<td>1:1</td>
<td>69/n.d.</td>
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<tr>
<td>4[^d]</td>
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<td>DCM</td>
<td>3c, 75</td>
<td>1:1</td>
<td>-</td>
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<tr>
<td>5</td>
<td>nPr, 2d</td>
<td>toluene</td>
<td>3d, 70</td>
<td>1:2</td>
<td>84/68</td>
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<tr>
<td>6[^d]</td>
<td>nPr, 2d</td>
<td>DCM</td>
<td>3d, 60</td>
<td>4:1</td>
<td>-</td>
</tr>
<tr>
<td>7[^d,^e]</td>
<td>Br, 2h</td>
<td>DCM</td>
<td>3h, 45</td>
<td>4:1</td>
<td>-</td>
</tr>
</tbody>
</table>

[^a]: Reaction condition: 0.35 mmol 1, 3 eq nitrocompund 2, 3.5 mL solvent, 10% mol catalyst I, rt, 24 h.  
[^b]: Yield referred to pure isolated compounds after FC.  
[^c]: dr and ee determined by CSP-GC.  
[^d]: mixture of quinine I and quinidine VII employed as the catalyst.  
[^e]: The isolated product is the cyclopropyl derivative 3h, see ref 15 and SI.

### 4.2 Determination of the stereochemistry of compounds 5a and 6

The stereochemistry of the newly formed stereocenters in the $\alpha$ and $\gamma'$ position has been determined via analysis of the NOESY spectra of the cyclic compound 5a. The stereochemistry of the stereocenter in the $\alpha$ position of adducts 6 has been assigned as identical.

In particular, the trans relationship between $\text{Ha}$ and $\text{Hb}$ has been determined by the large coupling constant observed ($J=12$ Hz). The stereochemistry of the quaternary stereocenter has been determined by the analysis of the NOESY spectra, which indicate no spatial proximity between $\text{Ha}$ and $\text{Hd}$ and a spatial correlation between $\text{Hb}$ and $\text{Hd}$.
4.3 Characterization of compound 7

\[ ^1\text{H-NMR} \text{ (300 MHz) } \delta (\text{CDCl}_3): 4.41 \text{ (d, 2H, } J= 7.2 \text{ Hz), 3.0-2.8 (m, 1H), 2.6-1.6 (m, 6H).} \]

\[ [\alpha]_D^\circ: +102 \text{ (sample with 79% ee, CHCl}_3, c= 10 \text{ mg/mL).} \]
4.4 High field spectra for compound 3h

$^1$H-NMR spectra of the mixture of diastereoisomers 3h'-h''
$^1$H-NMR spectra of 3h’
\(^{13}\)C-NMR spectra of 3h’

Mixture of diastereoisomers

Single diastereoisomer
$^1$H-$^1$H COSY spectra of the mixture of diastereoisomers 3h'-h''
$^1$H-$^{13}$C HMSQC spectra of the mixture of diastereoisomers 3h'-h''
4.5 High field spectra for compound 5a

$^1$H-NMR spectra of compound 5a

$^1$H-$^1$H COSY spectra of compound 5a
NOESY spectra of compound 5a
5. Copies of $^1$H and $^{13}$C-NMR spectra, and chromatograms

**$^{13}$C OBSERVE**

Pulse sequence: $\pi$ pul
Solvent: CDCl$_3$
Ambient temperature
File: $\text{m.1}$
Instrument: Mercury-500B

- Relax. delay 1.000 sec
- Pulsed 47.4 degrees
- Acq. time 1.090 sec
- Widths 6586.5 Hz
- 32 repetitions

**$^1$H OBSERVE**

Pulse sequence: $\pi$ pul
Solvent: CDCl$_3$
Ambient temperature
File: $\text{m.1}$
Instrument: Mercury-500B

- Relax. delay 1.000 sec
- Pulsed 47.4 degrees
- Acq. time 1.090 sec
- Widths 6586.5 Hz
- 32 repetitions

Total time 2 min, 47 sec.
1b

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Pulse sequence: 8xpy1
Solvent: CDCl3
Ambient temperature
File: tetramethylsilane_13C
Memory-Jupyter

Relax. Delay 1.000 sec
Pulse 57.1 degrees
Avg. time 1.950 sec
Width 4.065 Hz
1000 repetitions

Data preparation
FT time 32780
Total time 30 min, 59 sec

1H OBSERVE
Pulse sequence: 8xpy1
Solvent: CDCl3
Ambient temperature
File: tetramethylsilane_13C
Memory-Jupyter

Relax. Delay 2.000 sec
Pulse 47.1 degrees
Avg. time 1.950 sec
Width 4.441 Hz
38000 repetitions

Data preparation
FT time 32780
Total time 2 hr, 26 min, 22 sec
### Supplementary Material (ESI) for Chemical Communications
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#### Racemic Sample

![Racemic Sample](image)

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#### Pure Enantiomer

![Pure Enantiomer](image)

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S25
**Supplementary Material (ESI) for Chemical Communications**

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### Racemic Sample

**Formula:**

\[
\text{Racemic Sample}
\]

**Chemical Structure**

![Chemical Structure Diagram]

**Table 1: Area Analysis**

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**Graphical Representation**

![Graphical Representation Diagram]
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Solvent: CDC13
Ambient temperature
File: micros263k_3d

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Acq. time 1.685 sec
Width 14241.7 Hz
120000 repetitions
CARAS pH, 15.4100110 MHz
DECAYCUP: 12, 25.738020 MHz
Power 61.64
continuously on
WALTZ-16 modulated

data processing
Line broadening: 1.0 Hz
PE size 120172
Total time 164 hr, 15 min, 2 sec
Racemic Sample

\[ \text{O} \]

\[ \text{CO}_2\text{Et} \]

\[ \text{NO}_2 \]

\[ \text{Hb} \]

\[ \text{Ha} \]

\[ \text{Hc} \]

\[ \text{Ph} \]

\[ 3e \]
RUN # 10  JAN 1, 1901  03:44:24

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2.506
3.885
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STOP

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19.248

P/P ERR0

RUN#  10  JAN 1, 1901  03:44:24

AREA

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| 16.823| 2176 UV  | .164  | .01262|
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| 19.760| 59338 UV | .228  | .34425|

TOTAL AREA=1.7237E+07
MUL FACTOR=1.00000E+00
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---

**Steady State NMR**

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**Solvent:** CDCl3  
**Additional parameters:**  
**Temperature:** 25°C  
**Date:** 2010-08-15  
**HD:** 1.38 ppm 
**FT size:** 128K  
**Total time:** 0.56 sec 

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**DSS COSY**

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**Solvent:** CDCl3  
**Additional parameters:**  
**Temperature:** 25°C  
**Date:** 2010-08-15  
**HD:** 1.38 ppm 
**FT size:** 128K  
**Total time:** 0.56 sec 

**Chemical Shifts:**

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Pulse Sequence: s2pal
Solvent: CDCl3
 Ambient temperature
 Mercury-300B 'H

Pulse: delay 1.600 scc
Pulse 75.1 degrees
 Acq. time 1.000 scc

Maximum 180° pulse

16 repetitions


Total time 0 min, 53 sec

O
H

CO2Et
5a

O
H

CO2Et
5a
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### Diagram

- **6b**
- Racemic Sample

**Chart 1**

**Chart 2**

**Chart 3**
Pulse sequence: zgpol
Solvent: CDCl3
Ambient temperature
File: Acenaphthenone.htm
Mercury-300DS "Mercury500"

B1= 1.962424 MHz, delay 1.000 sec
Pulse 39.1 degrees
Acq. time 1.998 sec
Width 500.5 Hz
If repetitions
Resolution: Ax. 299.860000 sec
Data processing
FT size 32768
Total time 0 min. 53 sec