Supporting Information

Organocatalytic Asymmetric Michael Addition of Aldehydes to β-Nitroacroleine Dimethyl Acetal

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1. General methods:

Melting points were determined in unsealed capillary tubes and are uncorrected. IR spectra were obtained on KBr pellets (solids) or CHCl$_3$ solution (oils). NMR spectra were recorded at 20-25°C, running at 250 or 300MHz for $^1$H and 62.8 or 75MHz for $^{13}$C in CDCl$_3$ solution and resonances are reported in ppm relative to tetramethylsilane unless otherwise stated. Mass spectra were recorded under electron impact at 70 eV. TLC was carried out with 0.2 mm. thick silica gel plates (Merck Kiesegel GF$_{254}$) and visualization was accomplished by UV light or by spraying with phosphomolybdic acid. Flash column chromatography on silica gel was performed with Merck Kiesegel 60 (230-400 mesh). All solvents used in reactions were purified according to standard procedures. Prolinol and the aldehydes employed as starting materials were used as purchased. β-Nitroacroleine dimethyl acetal was prepared using literature procedures.$^1$ Enantiomeric excesses and diastereomeric ratios were determined by chiral GC using a CP-Chirasil-Dex CB (25 m x 0.25 mm x 0.25 µm) column under conditions specified in each case and using a mass spectrometer working under electron impact at 70eV as detector. The racemic standards needed for the optimization of the conditions for the separation of both enantiomers were prepared using DL-proline as catalyst for each case.

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2.- Organocatalytic asymmetric Michael addition.

**General procedure:**

L-Prolinol (0.10 mmol) was placed in a 10.0 mL dram vial with a magnetic stirring bar. \( i\)-PrOH (2.0 mL) and the corresponding aldehyde (1.00 mmol) were added. After stirring for 5 min at r.t., \( \beta\)-nitroacroleine dimethyl acetal (1.00 mmol) was added at once. The reaction was stirred at this temperature until TLC analysis of aliquots indicated complete consumption of the nitroalkene, after which the crude reaction mixture was purified by flash column chromatography (hexanes:AcOEt 9:1) yielding pure \( \gamma\)-nitroaldehydes 17a-h.

**(2R,3R)-4,4-Dimethoxy-2-methyl-3-(nitromethyl)butanal (17a)**

\[
\text{NO}_2
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\( \gamma\)-Nitroaldehyde 17a (181 mg, 0.89 mmol) was prepared according to the general procedure starting from nitroalkene I (147 mg, 1.00 mmol) and propanal (72 \( \mu \)L, 1.00 mmol) and using L-prolinol (11 mg, 0.10 mmol) as catalyst. Yield: 89%.

\(^1\)H-NMR (\( \delta \), ppm, 250 MHz): (1.7/1 diastereoisomer ratio; *indicates minor diastereoisomer resonances) 1.17 (d, 3H, \( J=7.1 \) Hz), 2.62 (m, 2H), 3.11 (m, 2H), 3.36 (s, 3H), 3.37 (s, 3H), 3.39* (s, 3H), 4.50 (m, 3H), 9.60 (s, 1H). \(^{13}\)C-NMR (\( \delta \), ppm, 62.8 MHz): (1.7/1 diastereoisomer ratio; *indicates minor diastereoisomer resonances) 9.5; 10.8*; 41.0*; 41.2; 44.2*; 44.5; 54.4; 55.6*; 55.6*; 66.7; 73.0*; 73.6; 103.6; 104.5*; 201.6; 201.7. IR (\( \text{CHCl}_3 \)): 1554 (NO\(_2\)), 1723 (C=O). LRMS (EI) \( m/z \) (rel. Int.): 204 (M\(^+\)-1, 1), 174 (13), 142 (8), 127 (42), 113 (26) 99 (100), 84 (32), 75 (90). HRMS: Calcd. for [C\(_8\)H\(_{14}\)NO\(_5\)]\(^+\): 204.0872. Found: 204.0874.

For the e.e. determination, aldehyde 17a was converted into the corresponding propylene acetal by stirring a solution of 17a (181 mg, 0.89 mmol) in acetonitrile in the presence of PTSA (17 mg, 0.09 mmol) and propane-1,3-diol (192 \( \mu \)L, 2.67 mmol) during 24 h at r.t., according to Yamamoto’s procedure.\(^2\) \(^1\)H-NMR (\( \delta \), ppm, 250 MHz): (1.7/1 diastereoisomer ratio; *indicates minor diastereoisomer resonances) 0.91* (d, 3H, \( J=7.1 \) Hz), 1.02 (d, 3H, \( J=7.1 \) Hz), 1.31 (m, 2H), 2.01 (m, 2H), 2.72 (m, 1H), 3.14* (m, 1H), 3.32 (s, 6H), 3.70 (m, 2H), 4.09 (m, 2H), 4.45 (m, 4H). \(^{13}\)C-NMR (\( \delta \), ppm, 62.8 MHz): (1.7/1 diastereoisomer ratio; *indicates minor diastereoisomer resonances) 10.1*, 12.5, 25.3, 35.7*, 36.2, 38.9*, 41.8, 53.2, 54.1*, 55.0*, 55.4, 66.8, 73.2*, 73.8,

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103.1*, 103.4, 105.1. IR (CH₂Cl₂): 1553 (NO₂). LRMS (EI) m/z (rel. Int.): 263 (M⁺, 1), 185 (10), 169 (5), 141 (5), 114 (29), 99 (10), 87 (100), 75 (56).

e.e.: 80 %. (CP-Chirasil-Dex CB): Tₜᵢᵣᵢ = 250 °C, Tₑᵦᵣᵠ = 280 °C, Pₑ₂ᵢ = 7 psi, Tᵢ = 70 °C (2 min), Tₑᵠ = 100 °C (20 °C·min⁻¹; tₑᵠ = 30 min), Tᵢ = 135 °C (0.3 °C·min⁻¹): Retention times for the anti isomers: tᵣₑᵦᵣᵠ = 142.85 min (minor enantiomer); tᵣₑᵦᵣᵠ = 143.58 min (major enantiomer). Retention times for the syn isomers: tᵣₑᵦᵣᵠ = 146.77 (minor enantiomer); tᵣₑᵦᵣᵠ = 147.90 min (major enantiomer).

(2R,3R)-2-Ethyl-4,4-dimethoxy-3-(nitromethyl)butanal (17b)

γ-Nitroaldehyde 17b (164 mg, 0.75 mmol) was prepared according to the general procedure starting from nitroalkene 1 (147 mg, 1.00 mmol) and butanal (89 µL, 1.00 mmol) and using L-prolinol (11 mg, 0.10 mmol) as catalyst. e.e.: 80% (calculated on the corresponding acetate 18b). Yield: 75%.

¹H-NMR (δ, ppm, 250 MHz): (5/1 diastereoisomer ratio; *indicates minor diastereoisomer resonances) 0.95* (t, 3H, J=7.1 Hz), 1.02 (t, 3H, J=7.3 Hz), 1.49* (m, 1H), 1.79 (m, 2H), 2.38* (m, 1H), 2.53 (m, 1H), 2.82* (m, 1H), 3.00 (m, 1H), 3.35 (s, 3H), 3.36 (s, 3H), 4.35 (m, 2H), 4.60 (dd, 1H, J=13.7, 7.3 Hz), 9.54* (d, 1H, J=2.4 Hz), 9.63 (s, 1H). ¹³C-NMR (δ, ppm, 62.8 MHz): (5/1 diastereoisomer ratio; *indicates minor diastereoisomer resonances) 11.7*; 12.3; 19.4; 19.9*; 41.0; 41.3*; 51.2; 52.9*; 55.1; 55.2; 55.8*; 55.9*; 73.2; 104.3; 104.5*; 201.1; 202.6. IR (CH₂Cl₂): 1555 (NO₂), 1718 (C=O). LRMS (EI) m/z (rel. Int.): 218 (M⁺-1, 1), 141 (38), 127 (21), 113 (78), 97 (33), 81 (60), 75 (100). HRMS: Calcd. for [C₉H₁₆NO₅]+: 218.1028. Found: 218.1039.

(2R,3R)-2-Hexyl-4,4-dimethoxy-3-(nitromethyl)butanal (17c)

γ-Nitroaldehyde 17c (178 mg, 0.65 mmol) was prepared according to the general procedure starting from nitroalkene 1 (147 mg, 1.00 mmol) and octanal (156 µL, 1.00 mmol) and using L-prolinol (11 mg, 0.10 mmol) as catalyst. e.e.: 80% (calculated on the corresponding acetate 18c). Yield: 65%.

¹H-NMR (δ, ppm, 500 MHz): (1.7/1 diastereoisomer ratio; *indicates minor diastereoisomer resonances) 0.86 (m, 3H), 1.30 (m, 9H), 1.72 (m, 1H), 2.41* (m, 1H), 2.58 (m, 1H), 2.95 (m, 1H), 3.00* (m, 1H), 3.33 (s, 3H), 3.35* (s, 3H), 3.35 (s, 1H), 3.36 (s, 3H), 4.35 (m, 2H), 4.41* (dd, 1H, J=13.8, 6.0 Hz), 4.58 (m, 1H).
\(^{13}\text{C-NMR (δ, ppm, 125.7 MHz): (1.7/1 diastereoisomer ratio; *indicates minor diastereoisomer resonances) 13.1; 22.6; 27.1; 27.6; 27.3*; 27.9*; 29.8; 32.3; 43.1; 43.4*; 49.9; 51.2*; 56.7; 57.1; 73.4; 104.6; 104.7*; 202.9*; 203.4. IR (CH}_2\text{Cl}_2): 1555 (NO}_2), 1718 (C=O). LRMS (EI) \text{m/z (rel. Int.): 244 (M}^+\text{-31, 2), 197 (12), 183 (4), 169 (62), 137 (6), 125 (8), 101 (12), 95 (15), 75 (100) 55 (18). HRMS: Calcd. for [C}_{11}H_{18}NO_5]^+: 244.1185. Found: 244.1187."

\((2R,3R)-4,4\text{-dimethoxy-2-nonyl-3-(nitromethyl)butanal (17d)}\)

\[\text{γ-Nitroaldehyde 17d (199 mg, 0.63 mmol) was prepared according to the general procedure starting from nitroalkene I (147 mg, 1.00 mmol) and undecanal (206 µL, 1.00 mmol) and using L-prolinol (11 mg, 0.10 mmol) as catalyst. e.e.: 83% (calculated on the corresponding acetate 18d). Yield: 63%. ¹H-NMR (δ, ppm, 500 MHz): (9/1 diastereoisomer ratio; *indicates minor diastereoisomer resonances) 0.78 (t, 3H, J=7.3 Hz), 1.24 (m, 14H), 1.67 (m, 2H), 2.37* (m, 1H), 2.54 (m, 1H), 2.92* (m, 1H), 2.96 (m, 1H), 3.10 (s, 3H), 3.32 (s, 3H), 3.33* (s, 3H), 4.34 (m, 2H), 4.40* (dd, 1H, J=14.0, 6.2 Hz), 4.58 (dd, J=14.3, 7.3 Hz), 9.66* (s, 1H), 9.69 (s, 1H).¹³C-NMR (δ, ppm, 125.7 MHz): (9/1 diastereoisomer ratio; *indicates minor diastereoisomer resonances) 13.1, 22.9, 26.4, 27.2*, 27.6*, 28.0, 29.0, 29.1, 29.2, 29.3, 32.1, 42.5, 42.8*, 49.6, 49.8*, 55.1, 55.9*, 72.4, 103.8, 104.1*, 202.0*, 202.9. IR (CH}_2\text{Cl}_2): 1556 (NO}_2), 1722 (C=O). LRMS (EI) \text{m/z (rel. Int.): 317 (M}^+\text{, 1), 286 (M}^+\text{-31, 2), 255 (2), 239 (14), 225 (7), 211 (50), 195 (7), 179 (4), 135 (5), 125 (11), 95 (36), 81 (30), 75 (100), 55 (26). HRMS: Calcd. for [C}_{16}H_{31}NO_3]^+: 317.2202. Found: 317.2198."

\((2R,3R)-2\text{-Ethyl-4,4-dimethoxy-3-(nitromethyl)butanal (17e)}\)

\[\text{γ-Nitroaldehyde 17e (107 mg, 0.46 mmol) was prepared according to the general procedure starting from nitroalkene I (147 mg, 1.00 mmol) and 3-methylbutanal (107 µL, 1.00 mmol) and using L-prolinol (11 mg, 0.10 mmol) as catalyst. e.e.: 88% (calculated on the corresponding acetate 18e). Yield: 46%. ¹H-NMR (δ, ppm, 250 MHz): (9/1 diastereoisomer ratio; *indicates minor diastereoisomer resonances) 1.02 (d, 3H, J=7.1 Hz), 1.08 (d, 3H, J=7.0 Hz), 2.05 (m, 1H), 2.57 (m, 1H), 3.01 (m, 1H), 3.32 (s, 6H), 3.36* (s, 6H), 4.30 (d, 1H, J=5.4 Hz), 5.29 (s, 2H), 5.80 (s, 2H). \]
4.41 (dd, 1H, J=14.0, 4.5 Hz), 4.61 (dd, 1H, J=14.1, 6.2 Hz), 9.58* (s, 1H), 9.71 (s, 1H). 

$^{13}$C-NMR (δ, ppm, 125.7 MHz): (9/1 diastereoisomer ratio; indicates minor diastereoisomer resonances) 19.6*; 20.6*; 20.7; 20.9; 26.5*; 27.2; 40.2; 40.5*; 55.3; 55.4; 55.8*; 55.9*; 73.0; 73.5*; 104.7*; 105.3; 203.2*; 204.3. IR (CH$_2$Cl$_2$): 1558 (NO$_2$), 1719 (C=O). LRMS (EI) m/z (rel. Int.): 214(5), 131 (19), 129 (18), 115 (19), 105 (84), 91 (25), 77 (100), 51 (14). HRMS: Calcd. for [C$_{10}$H$_{19}$NO$_5$]+: 233.1263. Found: 233.1261.

(2S,3R)-4,4-Dimethoxy-3-(nitromethyl)-2-phenylbutanal (17f)

γ-Nitroaldehyde 17f (267 mg, 1.00 mmol) was prepared according to the general procedure starting from nitroalkene 1 (147 mg, 1.00 mmol) and phenylacetaldehyde (117 µL, 1.00 mmol) and using L-prolinol (11 mg, 0.10 mmol) as catalyst. e.e.: 40% (calculated on the corresponding acetate 18f). Yield: 99%. $^1$H-NMR (δ, ppm, 250 MHz): (1.3/1 diastereoisomer ratio; *indicates minor diastereoisomer resonances) 3.23* (s, 3H), 3.26* (s, 3H), 3.35 (m, 1H), 3.40 (s, 3H), 3.43 (s, 3H), 3.56* (m, 1H), 3.85 (m, 1H), 3.90* (d, 1H, J=4.3 Hz), 4.05 (dd, 1H, J=13.9, 4.0 Hz), 4.35 (m, 1H), 4.47 (d, J = 4.7 Hz), 4.72* (dd, J=13.9, 6.3 Hz), 7.30 (m, 5H), 9.61* (s, 1H), 9.69 (s, 1H). $^{13}$C-NMR (δ, ppm, 62.8 MHz): (1.3/1 diastereoisomer ratio; *indicates minor diastereoisomer resonances) 41.0; 41.2*; 55.3*; 55.4*; 55.8; 56.0; 56.7; 57.3*; 72.6*; 73.0; 104;0*; 104.8; 128.4*; 128.6; 129.4; 129.5*; 129.6; 132.1; 132.5*; 196.9; 198.4*. IR (CH$_2$Cl$_2$): 1554 (NO$_2$), 1720 (C=O). LRMS (EI) m/z (rel. Int.): 266 (M$^+$-1, 1), 192 (3), 172 (54), 157 (22), 144 (27), 129 (24), 115 (100), 102 (13), 89 (17), 75 (21), 63 (18). HRMS: Calcd. for [C$_{13}$H$_{16}$NO$_3$]+: 266.1028. Found: 266.1050.

(2R,3S)-2-Benzylxoy-4,4-dimethoxy-3-(nitromethyl)butanal (17g)

γ-Nitroaldehyde 17g (297 mg, 1.00 mmol) was prepared according to the general procedure starting from nitroalkene 1 (147 mg, 1.00 mmol) and benzyloxyacetaldehyde (150 mg, 1.00 mmol) and using L-prolinol (11 mg, 0.10 mmol) as catalyst. Yield: 99%. $^1$H-NMR (δ, ppm, 250 MHz): (1.5/1 diastereoisomer ratio; *indicates minor diastereoisomer resonances) 3.10 (m, 1H), 3.29* (s, 3H), 3.33 (s, 3H), 3.35* (s, 3H), 3.75* (d, 1H, J=2.0 Hz), 3.99 (d, 1H, J=4.3 Hz), 4.05 (dd, 1H, J=13.9, 4.0 Hz), 4.35 (m, 1H), 4.47 (d, J = 4.7 Hz), 4.72* (dd, J=13.9, 6.3 Hz), 7.30 (m, 5H), 9.61* (s, 1H), 9.69 (s, 1H). $^{13}$C-NMR (δ, ppm, 62.8 MHz): (1.5/1 diastereoisomer ratio; *indicates minor diastereoisomer resonances) 43.0; 43.2*; 55.3*; 55.4*; 55.8; 56.0; 56.7; 57.3*; 72.6*; 73.0; 104;0*; 104.8; 128.4*; 128.6; 129.4; 129.5*; 129.6; 132.1; 132.5*; 196.9; 198.4*. IR (CH$_2$Cl$_2$): 1554 (NO$_2$), 1720 (C=O). LRMS (EI) m/z (rel. Int.): 266 (M$^+$-1, 1), 192 (3), 172 (54), 157 (22), 144 (27), 129 (24), 115 (100), 102 (13), 89 (17), 75 (21), 63 (18). HRMS: Calcd. for [C$_{13}$H$_{16}$NO$_3$]+: 266.1028. Found: 266.1050.
4.51 (m, 5H), 7.31 (m, 5H), 9.53 (s, 1H), 9.55* (d, 1H, J=1.8 Hz). $^{13}$C-NMR (δ, ppm, 62.8 MHz): (1.5/1 diastereoisomer ratio; *indicates minor diastereoisomer resonances) 42.1*; 43.2; 53.8; 55.1; 71.3; 72.9*; 73.2; 80.4*; 80.6; 101.8; 103.1; 127.1; 127.5; 128.1; 136.2; 199.8*; 200.2. IR (CH$_2$Cl$_2$): 1555 (NO$_2$), 1732 (C=O). LRMS (EI) m/z (rel. Int.): 297 (M$^+$, 1), 267 (M$^+$-30, 1), 187 (2), 146 (2), 99 (12), 91 (100), 77 (3), 71 (14), 65 (8). HRMS: Calcd. for [C$_{12}$H$_{13}$NO$_6$]$^+$: 267.0743. Found: 267.0756.

(2R,3R,2'E)-4,4-Dimethoxy-3-(nitromethyl)-2-(oct-2-enyl)butanal (17h)

γ-Nitroaldehyde 17h (150 mg, 0.63 mmol) was prepared according to the general procedure starting from nitroalkene 1 (147 mg, 1.00 mmol) and E-4-decenal (183 µL, 1.00 mmol) and using L-prolinol (11 mg, 0.10 mmol) as catalyst. e.e.: 82% (calculated on the corresponding acetate 18h). Yield: 63%. $^1$H-NMR (δ, ppm, 500 MHz): (3/1 diastereoisomer ratio; *indicates minor diastereoisomer resonances) 0.78 (t, 3H, J=7.1 Hz), 1.23 (m, 6H), 1.92 (m, 2H), 2.12 (m, 1H), 2.23* (m, 1H), 2.41 (m, 1H), 2.49* (m, 1H), 2.65 (m, 1H), 3.00 (m, 1H), 3.30 (s, 3H), 3.31* (s, 3H), 3.32 (s, 3H), 3.33* (s, 3H), 4.37 (m, 2H), 4.44* (dd, 1H, J=14.0, 6.3 Hz), 4.59 (m, 1H), 5.34 (m, 1H), 5.54 (m, 1H), 9.69 (d, 1H, J=1.7 Hz), 9.71 (s, 1H). $^{13}$C-NMR (δ, ppm, 125.7 MHz): (3/1 diastereoisomer ratio; *indicates minor diastereoisomer resonances) 13.8; 22.5; 29.0; 29.5; 29.9*; 31.5; 32.3; 40.5; 40.8*; 49.0; 55.1; 56.0*; 56.1*; 72.1; 72.2*; 104.6; 125.2*; 125.8; 135.0*; 135.7; 202.5*; 203.0. IR (CH$_2$Cl$_2$): 1556 (NO$_2$), 1722 (C=O). LRMS (EI) m/z (rel. Int.): 270 (M$^+$-31, 2), 255 (2), 238 (5), 223 (7), 207 (6), 195 (17), 179 (9), 163 (27), 151 (12), 135 (12), 121 (20), 109 (28), 93 (30), 81 (72), 71 (100), 55 (41). HRMS: Calcd. for [C$_{12}$H$_{27}$NO$_5$]$^+$: 301.1889. Found: 301.1882.
3.- Reduction of the Michael adducts. Synthesis of acetates 18a-h.

General procedure:

NaBH₄ (10.0 mmol) was carefully added over a cooled (0°C) solution of the starting γ-nitro aldehyde (1.0 mmol) in MeOH (5 mL). The reaction was stirred for 30 min at r.t. and quenched with sat. NH₄Cl (3 mL). CH₂Cl₂ (2 mL) and water (2 mL) were added and the mixture was stirred for 30 min. The organic fraction was separated and the aqueous one was extracted with CH₂Cl₂ (5x15 mL). The combined organic fractions were dried over Na₂SO₄, filtered and the solvent was removed under reduced pressure. The obtained yellowish oil was dissolved in dry CH₂Cl₂ (2 mL) and DMAP (10 mg) and Ac₂O (1.0 mmol) were added at once. The mixture was stirred for 30 min after which the crude reaction mixture was directly purified by flash column chromatography (hexanes:AcOEt 9:1) yielding pure acetates 18a-h.

(2R,3R)-4,4-Dimethoxy-2-methyl-3-(nitromethyl)butyl acetate (18a)

Acetate 18a (144 mg, 0.60 mmol) was prepared according to the general procedure starting from γ-nitroaldehyde 17a (130 mg, 0.63 mmol), NaBH₄ (0.22 g, 6.00 mmol), DMAP (7 mg, 0.06 mmol) and Ac₂O (0.05 mL, 0.63 mmol). Yield: 95%. ¹H-NMR (δ, ppm, 250 MHz): (1.7/1 diastereoisomer ratio; *indicates minor diastereoisomer resonances) 0.92* (d, 3H, J=6.4 Hz), 1.02 (d, 3H, J=6.8 Hz), 2.05 (s, 3H), 2.08* (s, 3H), 2.75 (m, 1H), 3.36 (s, 6H), 3.37 (m, 1H), 4.06 (m, 2H), 4.32 (m, 2H), 4.48* (dd, 1H, J=14.0, 6.3 Hz), 4.57 (dd, 1H, J=13.9, 6.1 Hz). ¹³C-NMR (δ, ppm, 62.8 MHz): (1.7/1 diastereoisomer ratio; *indicates minor diastereoisomer resonances) 13.8*; 14.3 (CH₃CH); 21.7; 31.9*; 32.4; 41.8*; 42.3; 54.6*; 54.9; 55.3; 55.6*; 66.3; 72.8*; 73.2; 105.1; 105.2*; 171.2. IR (CH₂Cl₂): 1554 (NO₂), 1738 (C=O). LRMS (EI) m/z (rel. Int.): 171 (M+, 4), 126 (9), 110 (5), 97 (30), 75 (100), 67 (21). HRMS: Calcd. for [C₉H₁₆O₃]⁺: 171.1021. Found: 171.1009.
(2R,3R)-2-Ethyl-4,4-Dimethoxy-3-(nitromethyl)butyl acetate (18b)

Acetate 18b (157 mg, 0.60 mmol) was prepared according to the general procedure starting from γ-nitroaldehyde 17b (140 mg, 0.64 mmol), NaBH₄ (0.22 g, 6.00 mmol), DMAP (7 mg, 0.06 mmol) and Ac₂O (0.05 mL, 0.63 mmol). Yield: 90%. e.e.: 80 %. Calculated by chiral GC analysis of the crude reaction mixture (CP-Chirasil-Dex CB): Tₘᵢⱼ = 250 °C, Tₐₜₑᵗ = 280 °C, flow rate = 1.0 mL·min⁻¹, Tᵢ = 70 °C (2 min), Tᵢ = 100 °C (20 °C·min⁻¹; tᵢ = 30 min), Tᵢ = 200 °C (80 °C·min⁻¹): Retention times for the anti isomers: tᵣ = 61.17 min (minor enantiomer); tᵣ = 61.42 min (major enantiomer); Retention times for the syn isomers: tᵣ = 61.85 min (minor enantiomer); tᵣ = 62.23 min (major enantiomer (18b)).

¹H-NMR (δ, ppm, 500 MHz): (9/1 diastereoisomer ratio; *indicates minor diastereoisomer resonances) 0.86* (t, 3H, J=6.9 Hz) 0.90 (t, 3H, J=6.9 Hz), 1.32* (m, 2H), 1.39 (m, 2H), 1.87 (m, 1H), 2.05 (s, 3H), 2.86 (m, 1H), 3.34 (s, 3H), 3.35 (s, 3H), 4.08 (d, 2H), 4.32 (m, 2H), 4.50* (dd, 1H, J=12.7, 6.9 Hz), 4.52 (dd, 1H, J=12.9, 6.1 Hz). ¹³C-NMR (δ, ppm, 125.7 MHz): (9/1 diastereoisomer ratio; *indicates minor diastereoisomer resonances) 12.1; 21.9; 22.0*; 23.7; 38.2; 38.4*; 42.2; 54.6; 54.9*; 55.2; 55.9*; 64.5; 73.9; 104.8*; 105.2; 171.8. LRMS (EI) m/z (rel. Int.): 185 (M⁺-78, 2), 111 (21), 93 (4), 75 (100), 55 (4). HRMS: Calcd. for [C₁₀H₁₇O₃]⁺: 185.1178. Found: 185.1177.

(2R,3R)-2-Hexyl-4,4-Dimethoxy-3-(nitromethyl)butyl acetate (18c)

Acetate 18c (172 g, 0.54 mmol) was prepared according to the general procedure starting from γ-nitroaldehyde 17c (160 mg, 0.58 mmol), NaBH₄ (0.20 g, 5.40 mmol), DMAP (6 mg, 0.05 mmol) and Ac₂O (0.05 mL, 0.58 mmol). Yield: 93%. e.e.: 80 %. Calculated by chiral GC analysis of the crude reaction mixture (CP-Chirasil-Dex CB): Tₘᵢⱼ = 250 °C, Tₐₜₑᵗ = 280 °C, flow rate = 1.0 mL·min⁻¹, Tᵢ = 70 °C (3 min), Tᵢ = 100 °C (30 °C·min⁻¹; tᵢ = 30 min), Tᵢ = 210 °C (0.5 °C·min⁻¹): Retention times for the syn isomers: tᵣ = 134.44 min (major enantiomer (18c)); tᵣ = 135.42 min (minor enantiomer). Retention times for the anti isomers: tᵣ = 147.56 min (major enantiomer); tᵣ = 149.65 min (minor enantiomer). ¹H-NMR (δ, ppm, 500 MHz): (1.7/1 diastereoisomer ratio; *indicates minor diastereoisomer resonances) 0.90 (t, 3H, J=6.9 Hz), 1.31 (m, 10H), 1.91 (m, 1H), 2.05 (s, 3H), 2.79 (m, 1H), 3.30 (s, 6H), 4.10 (m, 2H), 4.32 (m, 2H), 4.52 (m, 1H). ¹³C-NMR (δ, ppm, 125.7 MHz): (1.7/1 diastereoisomer ratio; *indicates minor diastereoisomer resonances) 13.1; 21.6; 23.0; 27.8; 27.9*; 28.2*; 29.1; 29.3; 31.7; 36.3*; 36.4; 41.8*; 41.9; 54.0*; 54.2; 55.3*; 55.5; 64.6;
64.7; 73.2; 104.3*; 104.8; 201.2; 201.3*. IR (CH₂Cl₂): 1554 (NO₂), 1736 (C=O). LRMS (EI) m/z (rel. Int.): 241 (M⁺-78, 2), 181 (1), 167 (8), 123 (2), 109 (5), 95 (5), 83 (7), 75 (100), 67 (5). HRMS: Calcd. for [C₁₄H₂₅O₃]⁺: 241.1804. Found: 241.1807.

(2R,3R)-4,4-Dimethoxy-3-(nitromethyl)-2-nonylbutyl acetate (18d)

Acetate 18d (180 mg, 0.50 mmol) was prepared according to the general procedure starting from γ-nitroaldehyde 17d (166 mg, 0.52 mmol), NaBH₄ (0.19 g, 5.00 mmol), DMAP (6 mg, 0.05 mmol) and Ac₂O (0.05 mL, 0.58 mmol). Yield: 96%. e.e.: 81%. Calculated by chiral GC analysis of the crude reaction mixture (CP-Chirasil-Dex CB): T_inj = 250 °C, T_det = 280 °C, flow rate = 1.0 mL·min⁻¹, T₁ = 70 °C (3 min), T₁ = 100 °C (30 °C·min⁻¹; t₁ = 30 min). Retention times for the syn isomers: t_R = 180.88 min (major enantiomer (18d)); t_R = 181.45 min (minor enantiomer). Retention times for the anti isomers: t_R = 190.99 (major enantiomer); t_R = 191.81 min (minor enantiomer). ¹H-NMR (δ, ppm, 500 MHz): (>20/1 diastereoisomer ratio) 0.85 (t, 3H, J=6.5 Hz), 1.30 (m, 16H), 1.98 (m 1H), 2.76 (m, 1H), 3.35 (s, 3H), 3.36 (s, 3H), 4.05 (d, 2H, J=5.2 Hz), 4.32 (m, 2H), 4.49 (dd, 1H, J=13.8, 8.5 Hz). ¹³C-NMR (δ, ppm, 125.7 MHz): (>20/1 diastereoisomer ratio) 14.2, 22.9, 24.0, 29.4, 29.8, 30.0, 30.1, 30.2, 32.3, 37.2, 42.1, 54.1, 56.2, 64.2, 73.2, 104.8, 171.2. IR (CH₂Cl₂): 1555 (NO₂), 1736 (C=O). LRMS (EI) m/z (rel. Int.): 209 (M⁺-152, 4), 191 (1), 13 (3), 109 (7), 95 (8), 81 (6), 75 (100), 67 (5), 55 (7). HRMS: Calcd. for [C₁₄H₂₅O₃]⁺: 209.1905. Found: 209.1905.

(2R,3R)-4,4-Dimethoxy-3-(nitromethyl)-2-iso-propylbutyl acetate (18e)

Acetate 18e (83 mg, 0.34 mmol) was prepared according to the general procedure starting from γ-nitroaldehyde 17e (83 mg, 0.30 mmol), NaBH₄ (128 mg, 3.40 mmol), DMAP (4 mg, 0.03 mmol) and Ac₂O (0.03 mL, 0.30 mmol). Yield: 88%. e.e.: 88%. Calculated by chiral HPLC analysis of the crude reaction mixture (Chiralcel OJ, UV detector): Flow rate 0.85 mL·min⁻¹, hexanes/i-PrOH 97:3): Retention times for the anti isomers: 18.92 min (both enantiomers). Retention times for the syn isomers: t_R = 20.38 (major enantiomer (18e)); t_R = 28.82 min (minor enantiomer). ¹H-NMR (δ, ppm, 500 MHz): (6/1 diastereoisomer ratio, *indicates minor diastereoisomer resonances) 0.90* (d, 3H, J=6.9 Hz), 0.94 (d, 3H, J=6.6 Hz), 0.99* (d, 3H, J=6.9 Hz), 1.04 (d, 3H, J=6.7 Hz), 1.60* (m, 1H), 1.75 (m, 2H), 2.05 (s, 3H), 2.87* (m, 1H), 3.70* (m, 3H), 4.03 (d, 2H, J=6.9 Hz), 4.32 (m, 2H), 4.49 (dd, 1H, J=13.8, 8.5 Hz). ¹³C-NMR (δ, ppm, 125.7 MHz): (>10/1 diastereoisomer ratio) 14.2, 22.9, 30.0, 30.1, 30.2, 32.3, 37.2, 42.1, 54.1, 56.2, 64.2, 73.2, 104.8, 171.2. IR (CH₂Cl₂): 1555 (NO₂), 1736 (C=O).
2.97 (m, 1H), 3.33 (s, 3H), 3.35 (s, 3H), 3.37* (s, 3H), 4.14 (d, 1H, \( J = 3.5 \) Hz), 4.30 (m, 2H), 4.32* (dd, 1H, \( J = 6.9, 14.2 \) Hz), 4.43 (dd, 1H, \( J = 8.5, 14.2 \) Hz), 4.67* (dd, 1H, \( J = 5.8, 13.8 \) Hz).

\(^{13}\)C-NMR (\( \delta, \) ppm, 125.7 MHz): (6/1 diastereoisomer ratio, *indicates minor diastereoisomer resonances) 19.9*; 20.1; 21.1; 21.4; 22.1*; 27.6; 28.2*; 39.9; 40.3*; 42.3; 43.4*; 53.8; 55.0*; 55.3*; 55.7; 63.1; 63.6*; 74.3; 75.1*; 105.2*; 106.3; 171.1; 171.2*. IR (CH\(_2\)Cl\(_2\)): 1555 (NO\(_2\)), 1737 (C=O).

LRMS (EI) m/z (rel. Int.): 199 (M\(^+\) - 78, 1), 125 (16), 107 (6), 95 (5), 81 (6), 75 (100), 55 (5).

HRMS: Calcd. for [C\(_{11}\)H\(_{19}\)O\(_3\)]\(^+\): 199.1334. Found: 199.1326.

(2S,3R)-4,4-Dimethoxy-3-(nitromethyl)-2-phenylbutyl acetate (18f)

Acetate 18f (280 mg, 0.90 mmol) was prepared according to the general procedure starting from \( \gamma \)-nitroaldehyde 17f (250 mg, 0.93 mmol), NaBH\(_4\) (0.34 g, 9.00 mmol), DMAP (10 mg, 0.09 mmol) and Ac\(_2\)O (0.93 mmol).

Yield: 96%. e.e.: 40 %. Calculated by chiral GC analysis of the crude reaction mixture (CP-Chirasil-Dex CB): T\(_{ij} = 250 \) °C, T\(_{det} = 280 \) °C, flow rate = 1.0 mL·min\(^{-1}\), T\(_{i} = 70 \) °C (2 min), T\(_{i} = 100 \) °C (20 °C·min\(^{-1}\); t\(_{i} = 30 \) min), T\(_{f} = 210 \) °C (0.5 °C·min\(^{-1}\)).

Retention times for the anti isomers: t\(_{R} = 168.15 \) min (major enantiomer); t\(_{R} = 168.75 \) min (minor enantiomer). Retention times for the syn isomers: t\(_{R} = 169.47 \) min (minor enantiomer); t\(_{R} = 170.35 \) min (major enantiomer (18f)). \(^{1}H\)-NMR (\( \delta, \) ppm, 500 MHz): (2/1 diastereoisomer ratio, *indicates minor diastereoisomer resonances) 2.05 (s, 3H), 2.06* (s, 3H) 3.25 (m, 2H), 3.33* (s, 3H), 3.40* (s, 3H), 3.47 (s, 3H), 3.49 (s, 3H), 4.42 (m, 5H), 7.30 (m, 5H). \(^{13}\)C-NMR (\( \delta, \) ppm, 125.7 MHz): (2/1 diastereoisomer ratio, *indicates minor diastereoisomer resonances) 21.3; 40.6*; 41.0*; 41.4; 42.3; 53.8; 55.0*; 55.3*; 55.7; 65.0; 67.1*; 67.3*; 73.6; 102.3*; 103.1; 127.0; 127.3*; 128.0; 128.9; 148.1; 171.9. IR (CH\(_2\)Cl\(_2\)): 1554 (NO\(_2\)), 1741 (C=O).

LRMS (EI) m/z (rel. Int.): 173 (M\(^+\) - 138, 3), 159 (7), 131 (8), 129 (20), 115 (13), 91 (9), 75 (100). HRMS: Calcd. for [C\(_{12}\)H\(_{13}\)O\(_3\)]\(^+\): 173.0966. Found: 173.0985.

(2R,3S)-2-Benzylxoy-4,4-Dimethoxy-3-(nitromethyl)butyl acetate (18g)

Acetate 18g (204 mg, 0.60 mmol) was prepared according to the general procedure starting from \( \gamma \)-nitroaldehyde 17g (270 mg, 0.90 mmol), NaBH\(_4\) (0.22 g, 6.00 mmol), DMAP (10 mg, 0.09 mmol) and Ac\(_2\)O (0.90 mmol).

Yield: 66%. e.e.: n.d. We were not able to get baseline resolution for the racemic standard in all conditions tried both in HPLC (Chiracel OD, OJ and
OC and GC (CP-Chirasil-Dex CB) $^1$H-NMR ($\delta$, ppm, 250 MHz): (>20/1 diastereoisomer ratio) 2.05 (s, 3H), 2.72 (m, 1H), 3.32 (m, 1H), 3.32 (s, 3H), 3.39 (s, 3H), 3.92 (dd, 1H, $J$=3.2, 1.7 Hz), 4.11 (d, 1H, $J$=7.6 Hz), 4.19 (dd, 1H, $J$=5.1, 1.8 Hz), 4.52 (dd, 2H, $J$=14.0, 7.6 Hz), 4.78 (d, 1H, $J$=7.8 Hz), 6.29 (d, 1H, $J$=7.5 Hz). $^{13}$C-NMR ($\delta$, ppm, 62.8 MHz): (>20/1 diastereoisomer ratio) 21.2, 52.1, 52.6, 55.8, 71.6, 71.8, 79.0, 98.8, 101.7, 127.1, 127.6, 128.2, 137.7, 170.0. IR (CH$_2$Cl$_2$): 1554 (NO$_2$), 1742 (C=O). LRMS (EI) m/z (rel. Int.): 180 (1), 126 (30), 108 (19), 91 (100), 77 (21), 64 (23). HRMS: Calcd. for [C$_{16}$H$_{23}$O$_{5}$]$^+$: 296.1624. Found: 296.1618.

$(2R,3R,2'E)$-4,4-Dimethoxy-3-(nitromethyl)-2-(2-octenyl)butyl acetate (18h)

Acetate 18h (120 mg, 0.35 mmol) was prepared according to the general procedure starting from $\gamma$-nitroaldehyde 17d (120 mg, 0.39 mmol), NaBH$_4$ (0.13 g, 3.50 mmol), DMAP (5 mg, 0.04 mmol) and Ac$_2$O (0.03 mL, 0.39 mmol). Yield: 89%. e.e.: 82 %. Calculated by chiral GC analysis of the crude reaction mixture (CP-Chirasil-Dex CB): $T_{\text{ini}}$ = 250 °C, $T_{\text{det}}$ = 280 °C, flow rate = 1.0 mL·min$^{-1}$, $T_1$ = 70 °C (3 min), $T_1$ = 100 °C (30 °C·min$^{-1}$; $t_1$ = 30 min), $T_f$ = 210 °C (0.5 °C·min$^{-1}$): Retention times for the syn isomers: $t_R$ = 134.52 min (major enantiomer (18h)); $t_R$ = 135.52 min (minor enantiomer). Retention times for the anti isomers: $t_R$ = 147.89 (major enantiomer); $t_R$ = 149.71 min (minor enantiomer). $^1$H-NMR ($\delta$, ppm, 500 MHz): (>20/1 diastereoisomer ratio) 0.90 (t, 3H, $J$=6.7 Hz), 1.30 (m, 6H), 1.60 (m, 1H), 2.05 (m, 7H), 2.86 (m, 1H), 3.35 (s, 3H), 3.36 (s, 3H), 4.07 (m, 2H), 4.43 (m, 2H), 4.58 (m, 1H), 5.36 (m, 1H), 5.52 (m, 1H). $^{13}$C-NMR ($\delta$, ppm, 125.7 MHz): (>20/1 diastereoisomer ratio) 13.1; 22.9; 23.4; 29.5; 31.0; 32.2; 33.4; 37.0; 37.1*; 42.1; 54.6; 54.9*; 56.0; 56.1*; 66.2; 66.5*; 74.1; 74.6*; 104.7*; 105.5; 126.2*; 126.5; 135.2*; 135.5; 171.2. IR (CH$_2$Cl$_2$): 1555 (NO$_2$), 1739 (C=O). LRMS (EI) m/z (rel. Int.): 236 (M$^+$-109, 1), 207 (3), 196 (15), 163 (11), 136 (20), 121 (29), 107 (17), 93 (31), 79 (44), 75 (100), 67 (22). HRMS: Calcd. for [C$_{16}$H$_{23}$O$_{5}$]$^+$: 236.1776. Found: 236.1766.
4.- $^1$H- and $^{13}$C-NMR spectra of adducts 17a-h.

4.1.- $^1$H- and $^{13}$C-NMR spectra of $\gamma$-nitroaldehyde 17a.
4.2. $^{13}$C-NMR spectra of γ-nitroaldehyde 17a.
4.3.- $^1$H-NMR spectra of γ-nitroaldehyde 17b.
4.4.- $^{13}$C-NMR spectra of $\gamma$-nitroaldehyde 17b.
4.5.- $^1$H-NMR spectra of $\gamma$-nitroaldehyde 17c.
4.6.- $^{13}$C-NMR spectra of $\gamma$-nitroaldehyde 17c.
4.7. - $^1$H-NMR spectra of γ-nitroaldehyde 17d.
4.8. $^{13}$C-NMR spectra of γ-nitroaldehyde 17d.
4.9.- $^1$H-NMR spectra of $\gamma$-nitroaldehyde 17e.
4.10. $^{13}$C-NMR spectra of γ-nitroaldehyde 17e.
4.11. $^1$H-NMR spectra of $\gamma$-nitroaldehyde 17f.
4.12. $^{13}$C-NMR spectra of $\gamma$-nitroaldehyde 17f.
4.13. $^1$H-NMR spectra of $\gamma$-nitroaldehyde 17g.
4.14. $^{13}$C-NMR spectra of γ-nitroaldehyde 17g.
4.15. \(^1\)H-NMR spectra of \(\gamma\)-nitroaldehyde 17h.
4.16. $^{13}$C-NMR spectra of $\gamma$-nitroaldehyde 17h.
5.- $^1$H- and $^{13}$C-NMR spectra of acetates 18a-h

5.1.- $^1$H-NMR spectra of acetate 18a.
5.2.- $^{13}$C-NMR spectra of acetate **18a**.
5.3. $^1$H-NMR spectra of acetate 18b.
5.4. $^{13}$C-NMR spectra of acetate 18b.
5.5. - $^1$H-NMR spectra of acetate 18c.
5.6.- $^{13}$C-NMR spectra of acetate 18c.
5.7. \textsuperscript{1}H-NMR spectra of acetate 18d.
5.8. $^{13}$C-NMR spectra of acetate 18d.
5.9.- $^1$H-NMR spectra of acetate 18e.
5.10. $^{13}$C-NMR spectra of acetate 18e.
5.11. $^1$H-NMR spectra of acetate $^{18f}$.
5.12. $^{13}$C-NMR spectra of acetate 18f.
5.13. $^1$H-NMR spectra of acetate 18g.
5.14.  $^{13}$C-NMR spectra of acetate 18g.
5.15. $^1$H-NMR spectra of acetate 18h.
5.16. $^{13}$C-NMR spectra of acetate \textbf{18h}.