Supporting Information

Direct asymmetric organocatalytic Michael reactions of α,α -disubstituted aldehydes with β -nitrostyrenes for the synthesis of quaternary carbon containing products

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General. Chemicals and solvents were either purchased from commercial suppliers or purified by standard techniques. For thin-layer chromatography (TLC), silica gel plates Merck 60 F₂₅₄ were used and compounds were visualized by irradiation with UV light and/or by treatment with a solution of phosphomolybdic acid in ethanol followed by heating. Flash column chromatography was performed using silica gel Merck 60 (particle size 0.040-0.063 mm). ¹H NMR and ¹³C NMR spectra were recorded on Valian Inova-399 and Mercury-300. Chemical shifts are given in δ relative to tetramethylsilane (TMS), the coupling constants J are given in Hz. The spectra were recorded in CDCl₃ as solvent at RT, TMS served as internal standard (δ = 0 ppm) for ¹H NMR, and CDCl₃ was used as internal standard (δ = 77.0) for ¹³C NMR. High-resolution mass spectra were recorded on an Ion Spec Fourier Transform Mass Spectrometer using dihydrobenzoic acid (DHB) as the matrix. HPLC was carried out using a Hitachi organizer consisting of a D-7000 Interface, an L-7200 Autosampler, an L-7400 UV Detector, and an L-7100 Intelligent Pump.

The direct Michael reaction of α,α -dialkylaldehyde **13** with β -nitrostyrene **14** (Table 2, entry 14):

A catalyst stock solution (1.0 M in 2-propanol) was prepared as a mixture of (*S*)-(+)-1-(2-pyrrolidinylmethyl)pyrrolidine (0.5 mmol) and trifluoroacetic acid (0.5 mmol) in 2-propanol (0.5 mL, HPLC grade) before use. β -nitrostyrene **14** (0.5 mmol) was dissolved in 2-propanol (0.85 mL) and isobutyraldehyde **13a** (1.0 mmol) was added. To the mixture the catalyst stock solution (1.0M in 2-propanol, 0.15 mL, 0.15 mmol) was added at 4 °C. After stirring for 48 h at 4 °C, the reaction mixture was directly purified by column chromatography (silica gel 10 g, hexanes/ethyl acetate = 90/10) to afford the Michael product **15a** (87% yield, 80% ee).

2,2-Dimethyl-4-nitro-3-phenylbutyraldehyde (15a): Reg. No.: 93086-29-4 (racemate); $R_f = 0.48$ (hexane:AcOEt = 70:30); ^1H NMR (CDCl_3 , 400 MHz) $\delta = 0.99$ (s, 3H, $-\text{CH}_3$), 1.12 (s, 3H, $-\text{CH}_3$), 3.78 (dd, $J = 3.1, 8.4$ Hz, 1H, $-\text{CHPh}$), 4.69 (dd, $J = 3.1, 9.9$ Hz, 1H, $-\text{CH}_2\text{NO}_2$), 4.85 (dd, $J = 8.4, 9.9$ Hz, 1H, $-\text{CH}_2\text{NO}_2$), 7.10-7.25 (m, 2H), 7.26-7.40 (m, 3H), 9.52 (s, 1H, $-\text{CHO}$); ^{13}C NMR (CDCl_3 , 75 MHz) $\delta = 19.1, 21.9, 48.3, 48.4, 76.1, 127.4, 128.0, 128.4, 134.7, 203.0$; ESI-MS 244 (MNa^+); GC/MS 221 (M^+); HPLC (Daicel CHIRALPAK AS-H, hexane/2-PrOH = 90:10, flow rate 1.0 mL/min, $\lambda = 254$ nm) $t_R = 12.00$ (minor), 12.73 (major) min.

1-(2-Nitro-1-phenylethyl)cyclopentanecarbaldehyde (15b): $R_f = 0.60$ (hexane:AcOEt = 70:30); ^1H NMR (CDCl_3 , 300 MHz) $\delta = 1.35$ -1.75 (m, 6H, 3X- CH_2), 1.76-2.15 (m, 2H, $-\text{CH}_2$), 3.70 (dd, $J = 3.9, 11.3$ Hz, 1H, $-\text{CHPh}$), 4.69 (dd, $J = 3.9, 13.2$ Hz, 1H, $-\text{CH}_2\text{NO}_2$), 4.96 (dd, $J = 11.3, 13.2$ Hz, 1H, $-\text{CH}_2\text{NO}_2$), 7.14-7.25 (m, 2H), 7.25-7.36 (m, 3H), 9.48 (s, 1H, $-\text{CHO}$); ^{13}C NMR (CDCl_3 , 75 MHz) $\delta = 24.6, 24.8, 31.4, 32.5, 49.2, 60.2, 77.3, 128.0, 128.7, 136.3, 204.3$; ESI-MS 246 ($[\text{M}-\text{H}]^-$); HPLC (Daicel CHIRALCEL OD-H, hexane/2-PrOH = 80:20, flow rate 1.0 mL/min, $\lambda = 254$ nm) $t_R = 10.13$ (major), 14.16 (minor) min.

1-(2-Nitro-1-phenylethyl)cyclohexanecarbaldehyde (15c): $R_f = 0.60$ (hexane:AcOEt = 70:30); ^1H NMR (CDCl_3 , 300 MHz) $\delta = 0.96$ -1.75 (m, 8H, 4X- CH_2), 1.75-2.14 (m, 2H, $-\text{CH}_2$), 3.54 (dd, $J = 4.8$, 10.8 Hz, 1H, $-\text{CHPh}$), 4.73 (dd, $J = 4.8$, 13.2 Hz, 1H, $-\text{CH}_2\text{NO}_2$), 4.80 (dd, $J = 10.8$, 13.2 Hz, 1H, $-\text{CH}_2\text{NO}_2$), 7.08-7.18 (m, 2H), 7.24-7.34 (m, 3H), 9.53 (s, 1H, $-\text{CHO}$); ^{13}C NMR (CDCl_3 , 75 MHz) $\delta = 22.4$, 22.5, 24.9, 29.4, 30.8, 50.2, 51.1, 75.9, 127.9, 128.4, 128.9, 134.8, 207.0; ESI-MS 284 (MNa^+), 260 ($[\text{M}-\text{H}]^-$); HPLC (Daicel CHIRALCEL OD-H, hexane/2-PrOH = 80:20, flow rate 1.0 mL/min, $\lambda = 254$ nm) $t_R = 9.06$ (major), 21.21 (minor) min.

2-Ethyl-2-methyl-4-nitro-3-phenylbutyraldehyde (15d): $R_f = 0.56$ (hexane:AcOEt = 70:30); ^1H NMR (CDCl_3 , 300 MHz, diastereomer mixtures) $\delta = 0.78$ (syn) and 0.86 (anti) (t, $J = 7.5$ and 7.5 Hz, 3H, $-\text{CH}_2\text{CH}_3$), 1.07 (anti) and 1.08 (syn) (s, 3H, $-\text{CH}_3$), 1.16-1.80 (m, 2H, $-\text{CH}_2\text{CH}_3$), 3.77 (anti) and 3.80 (syn) (dd, $J = 4.5$, 11.2 and 4.0, 11.4 Hz, 1H, $-\text{CHPh}$), 4.61 (syn) and 4.75 (anti) (dd, $J = 4.0$, 13.0 and 4.5, 13.1 Hz, 1H, $-\text{CH}_2\text{NO}_2$), 4.84 (syn) and 4.85 (anti) (dd, $J = 11.4$, 13.0 and 11.2, 13.1 Hz, 1H, $-\text{CH}_2\text{NO}_2$), 7.12-7.24 (m, 2H), 7.24-7.34 (m, 3H), 9.49 (anti) and 9.51 (syn) (s, 1H, $-\text{CHO}$); ESI-MS 234 ($[\text{M}-\text{H}]^-$); HPLC (Daicel CHIRALCEL OD-H, hexane/2-PrOH = 90:10, flow rate 1.0 mL/min, $\lambda = 254$ nm) $t_R = 12.38$ (anti, major), 14.91 (syn, major), 16.94 (anti, minor), 22.16 (syn, minor) min.

2-Methyl-2-(2-nitro-1-phenylethyl)pentanal (15e): $R_f = 0.60$ (hexane:AcOEt = 70:30); ^1H NMR

(CDCl₃, 300 MHz, diastereomer mixtures) δ = 0.83 (syn) and 0.89 (anti) (t, J = 7.0 and 7.2 Hz, 3H, -CH₂CH₃), 1.08 (anti) and 1.09 (syn) (s, 3H, -CH₃), 1.10-1.70 (m, 4H, 2X-CH₂), 3.77 (anti) and 3.79 (syn) (dd, J = 4.5, 11.2 and 4.1, 11.4 Hz, 1H, -CHPh), 4.62 (syn) and 4.75 (anti) (dd, J = 3.9, 13.0 and 4.5, 13.1 Hz, 1H, -CH₂NO₂), 4.83 (syn) and 4.85 (anti) (dd, J = 11.4, 13.0 and 11.2, 13.1 Hz, 1H, -CH₂NO₂), 7.12-7.24 (m, 2H), 7.24-7.36 (m, 3H), 9.50 (anti) and 9.52 (syn) (s, 1H, -CHO); ESI-MS 272 (MNa⁺), 248 ([M-H]⁻); HPLC (Daicel CHIRALCEL OJ-H, hexane/2-PrOH = 90:10, flow rate 1.0 mL/min, λ = 254 nm) t_R = 24.09 (syn, minor), 26.04 (anti, major), 30.11 (anti, minor), 34.80 (syn, major) min.

2-Methyl-2-(2-nitro-1-phenylethyl)undecanal (15f): R_f = 0.40 (hexane:AcOEt = 90:10); ¹H NMR (CDCl₃, 300 MHz, diastereomer mixtures) δ = 0.87 (syn) (t, J = 6.8 Hz, 3H, -CH₂CH₃), 1.10 (anti) and 1.11 (syn) (s, 3H, -CH₃), 1.08-1.75 (m, 16H, 8X-CH₂), 3.79 (syn) (dd, J = 4.0, 11.4 Hz, 1H, -CHPh), 4.62 (syn) and 4.75 (anti) (dd, J = 4.0, 13.0 and 4.5, 13.0 Hz, 1H, -CH₂NO₂), 4.83 (syn) and 4.85 (anti) (dd, J = 11.4, 13.0 and 11.2, 13.0 Hz, 1H, -CH₂NO₂), 7.12-7.23 (m, 2H), 7.23-7.38 (m, 3H), 9.51 (anti) and 9.53 (syn) (s, 1H, -CHO); ESI-MS 356 (MNa⁺), 332 ([M-H]⁻); HPLC (Daicel CHIRALCEL OD-H, hexane/2-PrOH = 95:5, flow rate 1.0 mL/min, λ = 254 nm) t_R = 10.02 (anti, major), 10.94 (anti, minor), 12.15 (syn, major), 15.79 (syn, minor) min.

2,6-Dimethyl-2-(2-nitro-1-phenylethyl)hept-5-enal (15g): $R_f = 0.36$ (hexane:AcOEt = 90:10); ^1H NMR (CDCl_3 , 300 MHz, diastereomer mixtures) $\delta = 1.12$ (anti) and 1.13 (syn) (s, 3H, $-\text{CH}_3$), 1.20-1.35 (m, 1H, $-\text{CH}_2\text{CH}_2\text{CH}=\text{}$), 1.50-1.70 (m, 1H, $-\text{CH}_2\text{CH}_2\text{CH}=\text{}$), 1.52 (s, 3H, $-\text{CH}_3$), 1.63 (s, 3H, $-\text{CH}_3$), 1.78-1.94 (m, 2H, $-\text{CH}_2\text{CH}=\text{}$), 3.79 (syn) (dd, $J = 4.0, 11.4$ Hz, 1H, $-\text{CHPh}$), 4.62 (syn) and 4.76 (anti) (dd, $J = 4.0, 13.0$ and 4.6, 13.1 Hz, 1H, $-\text{CH}_2\text{NO}_2$), 4.83 (syn) and 4.85 (anti) (dd, $J = 11.4, 13.0$ and 11.0, 12.9 Hz, 1H, $-\text{CH}_2\text{NO}_2$), 4.87-5.06 (m, 1H, $-\text{C}=\text{CH}-$), 7.12-7.24 (m, 2H), 7.24-7.37 (m, 3H), 9.53 (anti) and 9.54 (syn) (s, 1H, $-\text{CHO}$); ESI-MS 312 (MNa^+), 288 ($[\text{M}-\text{H}]^-$); HPLC (Daicel CHIRALCEL OD-H, hexane/2-PrOH = 99:1, flow rate 1.5 mL/min, $\lambda = 254$ nm) $t_R = 20.07$ (anti, major), 24.25 (syn, major), 29.18 (syn, minor), 34.16 (anti, minor) min.

2-Methyl-4-nitro-2,3-diphenylbutyraldehyde (15h): Reg. No.: 144632-52-0 (racemate); $R_f = 0.24$ (hexane:AcOEt = 90:10); ^1H NMR (CDCl_3 , 300 MHz, diastereomer mixtures) $\delta = 1.38$ (anti) and 1.50 (syn) (s, 3H, $-\text{CH}_3$), 4.20 (syn) and 4.36 (anti) (dd, $J = 3.9, 11.5$ and 3.8, 11.8 Hz, 1H, $-\text{CHPh}$), 4.85 (syn) and 4.50 (anti) (dd, $J = 3.9, 13.1$ and 11.8, 12.6 Hz, 1H, $-\text{CH}_2\text{NO}_2$), 5.01 (syn) and 4.67 (anti) (dd, $J = 11.5, 13.1$ and 3.8, 12.6 Hz, 1H, $-\text{CH}_2\text{NO}_2$), 6.86-7.02 (m, 2H), 7.02-7.16 (m, 4H), 7.20-7.50 (m, 4H), 9.54 (syn) and 9.56 (anti) (s, 1H, $-\text{CHO}$); MALDI-FTMS Calcd for $\text{C}_{17}\text{H}_{17}\text{NO}_3$ (MNa^+): 306.1101, found: 306.1107; ESI-MS 282 ($[\text{M}-\text{H}]^-$); HPLC (Daicel CHIRALPAK AS-H, hexane/2-PrOH = 95:5, flow rate 1.0 mL/min, $\lambda = 254$ nm) $t_R = 17.73$ (syn, minor), 19.15 (syn, major), 20.09 (anti, major), 23.65 (anti, minor) min.

2-(4-Isopropylbenzyl)-2-methyl-4-nitro-3-phenylbutyraldehyde (15i): $R_f = 0.36$ (hexane:AcOEt = 70:30); ^1H NMR (CDCl_3 , 300 MHz, diastereomer mixtures) $\delta = 1.04$ (syn) and 1.09 (anti) (s, 3H, - CH_3), 1.20 (d, $J = 6.9$ Hz, 6H, 2X-CH_3), 2.38 (syn) and 2.72 (anti) (d, $J = 13.7$ and 13.6 Hz, 1H, - CH_2Ar), 3.03 (syn) and 3.06 (anti) (d, $J = 13.7$ and 13.6 Hz, 1H, - CH_2Ar), 2.68 - 2.94 (m, 1H, - $\text{CH}(\text{CH}_3)_2$), 3.83 (syn) (dd, $J = 3.8, 11.5$ Hz, 1H, - CHPh), 4.66 (syn) (dd, $J = 3.8, 13.1$ Hz, 1H, - CH_2NO_2), 4.91 (syn) (dd, $J = 11.5, 13.1$ Hz, 1H, - CH_2NO_2), 6.84 - 7.00 (m, 2H), 7.04 - 7.16 (m, 2H), 7.18 - 7.24 (m, 2H), 7.26 - 7.45 (m, 3H), 9.59 (anti) and 9.62 (syn) (s, 1H, -CHO); MALDI-FTMS Calcd for $\text{C}_{21}\text{H}_{25}\text{NO}_3$ (MNa^+): 362.1727, found: 362.1740; HPLC (Daicel CHIRALCEL OJ-H, hexane/2-PrOH = 95:5, flow rate 1.0 mL/min, $\lambda = 254$ nm) $t_R = 48.25$ (syn, major), 67.96 (syn, minor), 78.75 (anti, minor), 85.04 (anti, major) min.

2-(4-*tert*-Butylbenzyl)-2-methyl-4-nitro-3-phenylbutyraldehyde (15j): $R_f = 0.40$ (hexane:AcOEt = 70:30); ^1H NMR (CDCl_3 , 300 MHz, diastereomer mixtures) $\delta = 1.04$ (syn) and 1.10 (anti) (s, 3H, - CH_3), 1.27 (syn) and 1.28 (anti) (s, 9H, 3X-CH_3), 2.38 (syn) and 2.72 (anti) (d, $J = 13.7$ and 13.6 Hz, 1H, - CH_2Ar), 3.03 (syn) and 3.06 (anti) (d, $J = 13.7$ and 13.6 Hz, 1H, - CH_2Ar), 3.84 (syn) (dd, $J = 3.8, 11.5$ Hz, 1H, - CHPh), 4.67 (syn) (dd, $J = 3.8, 13.1$ Hz, 1H, - CH_2NO_2), 4.91 (syn) (dd, $J = 11.5, 13.1$ Hz, 1H, - CH_2NO_2), 6.86 - 7.02 (m, 2H), 7.16 - 7.46 (m, 7H), 9.59 (anti) and 9.62 (syn) (s, 1H, -CHO); MALDI-FTMS Calcd for $\text{C}_{22}\text{H}_{27}\text{NO}_3$ (MNa^+): 376.1883, found: 376.1896; HPLC (Daicel CHIRALCEL OD-H, hexane/2-PrOH = 90:10, flow rate 1.0 mL/min, $\lambda = 254$ nm) $t_R = 14.05$ (anti, major), 16.22 (syn, major), 18.02 (syn, minor), 20.49 (anti, minor) min.

2-Benzo[1,3]dioxol-5-ylmethyl-2-methyl-4-nitro-3-phenylbutyraldehyde (15k): $R_f = 0.38$ (hexane:AcOEt = 70:30); ^1H NMR (CDCl_3 , 300 MHz, diastereomer mixtures) $\delta = 1.04$ (syn) and 1.05 (anti) (s, 3H, $-\text{CH}_3$), 2.31 (syn) and 2.66 (anti) (d, $J = 13.8$ and 13.5 Hz, 1H, $-\text{CH}_2\text{Ar}$), 3.00 (syn) and 3.03 (anti) (d, $J = 13.8$ and 13.5 Hz, 1H, $-\text{CH}_2\text{Ar}$), 3.82 (syn) (dd, $J = 3.8$, 11.5 Hz, 1H, $-\text{CHPh}$), 4.64 (syn) (dd, $J = 3.8$, 13.1 Hz, 1H, $-\text{CH}_2\text{NO}_2$), 4.89 (syn) (dd, $J = 11.5$, 13.1 Hz, 1H, $-\text{CH}_2\text{NO}_2$), 5.88 (syn) and 5.89 (anti) (s, 2H, $-\text{OCH}_2\text{O}-$), 6.36 - 6.80 (m, 3H), 7.16 - 7.26 (m, 2H), 7.26 - 7.48 (m, 3H), 9.57 (anti) and 9.61 (syn) (s, 1H, $-\text{CHO}$); MALDI-FTMS Calcd for $\text{C}_{19}\text{H}_{19}\text{NO}_5$ (MNa^+): 364.1155, found: 364.1161; ESI-MS 364 (MNa^+), 340 ($[\text{M}-\text{H}]^-$); HPLC (Daicel CHIRALPAK AS-H, hexane/2-PrOH = 80:20, flow rate 1.0 mL/min, $\lambda = 254$ nm) $t_R = 21.01$ (syn, major), 23.64 (anti, major), 27.14 (syn, minor), 36.91 (anti, minor) min.

***N*-(2,4-Dinitrophenyl)-*N'*-(2-ethyl-2-methyl-4-nitro-3-phenylbutylidene)hydrazine (16):** ^1H NMR (CDCl_3 , 300 MHz, diastereomer mixtures) $\delta = 0.86$ (t, $J = 7.5$ Hz, 3H, $-\text{CH}_2\text{CH}_3$), 1.23 (s, 3H, $-\text{CH}_3$), 1.18 - 1.75 (m, 2H, $-\text{CH}_2$), 3.81 (dd, $J = 5.5$, 9.4 Hz, 1H, $-\text{CHPh}$), 4.74 - 4.90 (m, 2H, $-\text{CH}_2\text{NO}_2$), 7.18 - 7.25 (m, 2H), 7.30 - 7.42 (m, 3H), 7.95 (d, $J = 9.5$ Hz, 1H), 8.37 (dd, $J = 2.6$, 9.5 Hz, 1H), 9.16 (d, $J = 2.6$ Hz, 1H), 11.1 (s, 1H, $-\text{CH}=\text{N}-$); MALDI-FTMS Calcd for $\text{C}_{19}\text{H}_{21}\text{N}_5\text{O}_6$ (MH^+): 416.1565, found: 416.1565.

Table 1. Crystal data and structure refinement for 16.

Empirical formula	$C_{19}H_{21}N_5O_6$
Formula weight	415.41
Temperature	296(2) K
Wavelength	0.71073 Å
Crystal system	Triclinic
Space group	$P\bar{1}$ (No. 2, C_i^1)
Unit cell dimensions	$a = 8.2921(17)$ Å $\alpha = 64.65(3)^\circ$ $b = 11.639(2)$ Å $\beta = 88.22(3)^\circ$ $c = 12.066(2)$ Å $\gamma = 74.29(3)^\circ$
Volume, Z	$1008.2(4)$ Å ³ , 2
Density (calculated)	1.368 Mg/m ³
Absorption coefficient	0.104 mm ⁻¹
F(000)	436
Crystal size	$0.28 \times 0.22 \times 0.17$ mm
θ range for data collection	2.02 to 25.00°
Limiting indices	$-9 \leq h \leq 9$, $-13 \leq k \leq 13$, $-14 \leq l \leq 14$
Reflections collected	7293
Independent reflections	3525 ($R_{int} = 0.0360$)
Completeness to $\theta = 25.00^\circ$	99.6 %
Absorption correction	Empirical
Max. and min. transmission	0.9825 and 0.9714
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	3525 / 0 / 273
Goodness-of-fit on F^2	0.989
Final R indices [$I > 2\sigma(I)$]	$R1 = 0.0740$, $wR2 = 0.1795$
R indices (all data)	$R1 = 0.1614$, $wR2 = 0.2328$
Largest diff. peak and hole	0.455 and -0.226 eÅ ⁻³

$R1 = (\sum \ F_o\ - \ F_c\) / \sum \ F_o\ , \quad wR2 = \sum w(F_o^2 - F_c^2)^2 / \sum w[(F_o^2)^2]^{1/2}, \quad S = [\sum w(F_o^2 - F_c^2)^2 / (n-p)]^{1/2}$	