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Supporting Information

69451 Weinheim, Germany

A Chiral Primary Amine-Thiourea Catalyst for the Highly Enantioselective Direct Conjugate Addition of α,α-Disubstituted Aldehydes to Nitroalkenes

Mathieu P. Lalonde, Yonggang Chen, and Eric N. Jacobsen

General Information: All reactions were performed under a nitrogen atmosphere in oven-dried round-bottomed flasks fitted with rubber septa or yellow polyethylene stoppers. Liquid reagents were transferred with stainless steel syringes. Flash Chromatography was performed with EM Science silica gel 60 (230-400 mesh).

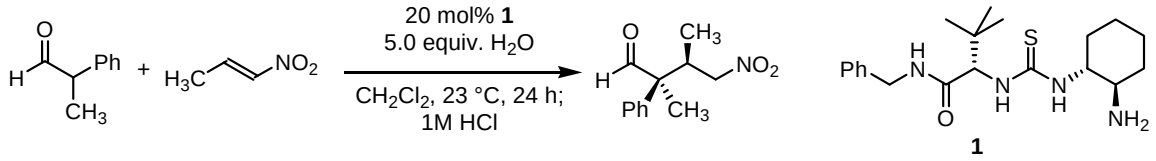
Materials: Dichloromethane was distilled from CaH_2 at 760 Torr. Commercially available aldehydes were purified by distillation from anhydrous calcium sulfate and/or column chromatography prior to use. Commercially available nitroalkenes were used as received. *trans*-β-nitrostyrene, *trans*-4-methoxy-β-nitrostyrene, *trans*-2-(2-nitrovinyl)thiophene, *trans*-2-(2-nitrovinyl)furan, *trans*-4-bromo-β-nitrostyrene, *trans*-β-nitro-2-(trifluoromethyl)styrene, 2-phenylpropionaldehyde, 2-methylpentanal, 2,6-dimethyl-5-heptenal, 2-methyl-3-(3,4-methylenedioxyphenyl)propanal were purchased from Aldrich. 3-(2-nitroethenyl)pyridine was purchased from TCI America. 4-fluoro-β-nitrostyrene was purchased from Fluka. (*R*)-3,3-dimethyl-2-butylamine was purchased from Lancaster. (*E*)-1-nitroprop-1-ene,[1] (*E*)-1-nitrohex-1-ene,[1] (*E*)-3-(benzyloxy)-1-nitroprop-1-ene,[1] *trans*-3,3,3-trifluoro-1-nitroprop-1-ene,[2] 3-(*tert*-butyldimethylsilyloxy)-2-methylpropanal,[3] 2-(4-methoxybenzyloxy)propanal,[4] thiourea catalysts[5] **1**-**2** were prepared according to previously published procedures.

Instrumentation: Proton nuclear magnetic resonance (^{1}H NMR) spectra and carbon nuclear magnetic resonance (^{13}C NMR) spectra were recorded on a Varian Mercury-400 (400 MHz) NMR spectrometer. Chemical shifts for protons are reported in parts per million downfield from tetramethylsilane and are referenced to the solvent residual peak ($CHCl_3$: δ 7.26). Chemical shifts for carbon are reported in parts per million downfield from tetramethylsilane and are referenced to the carbon resonances of the solvent ($CDCl_3$: δ 77.0). Data are represented as follows: chemical shift, integration, multiplicity (br = broad, s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet), and coupling constants in Hertz (Hz). Infrared (IR) spectra were obtained using a Mattson Galaxy Series FTIR 3000 spectrophotometer referenced to a polystyrene standard. Data are represented as follows: frequency of absorption (cm^{-1}), intensity of absorption (s = strong, m = medium, w = weak). Optical rotations were measured using a 2.0 mL cell

[1] D. Lucet, S. Sabelle, O. Kostelitz, T. Le Gall, C. Mioskowski, *Eur. J. Org. Chem.* **1999**, 2583-2591.
[2] M. Molteni, A. Volonterio, M. Zanda, *Org. Lett.* **2003**, *5*, 3887-3890.
[3] S.-I. Kiyooka, K. A. Shahid, F. Goto, M. Okazaki, Y. Shuto, *J. Org. Chem.* **2003**, *68*, 7967-7978.
[4] W. Yu, Y. Zhang, Z. Jin, *Org. Lett.* **2001**, *3*, 1447-1450. Procedure was followed using racemic ethyl lactate.
[5] A. G. Wenzel, E. N. Jacobsen, *J. Am. Chem. Soc.* **2002**, *124*, 12964-12965.

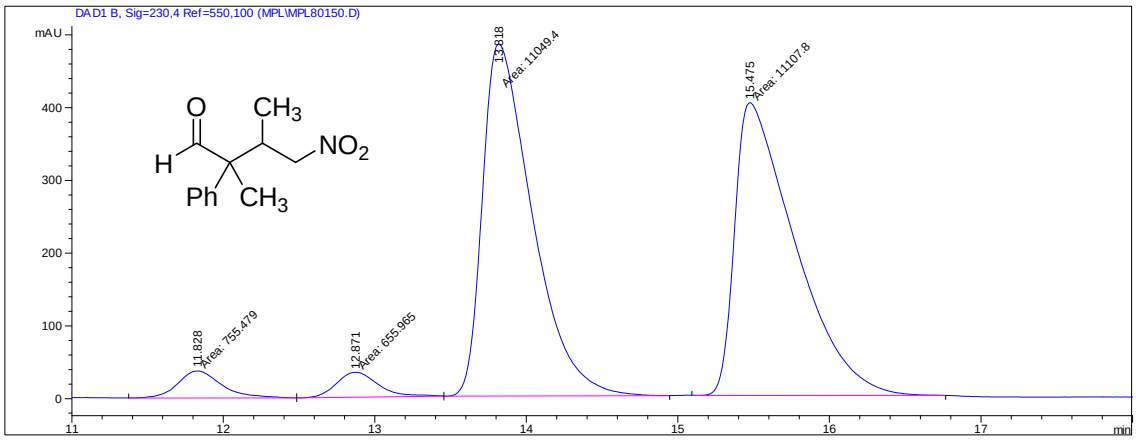
with a 1.0 dm path length on a Jasco DIP 370 digital polarimeter. Melting points were measured on a Mel-Temp apparatus, and are uncorrected. The mass spectroscopic data were obtained at the Harvard University mass spectrometry facility. Chiral HPLC analysis was performed on a Hewlett Packard 1050 Series instrument. Chiral SFC analysis was performed on a Berger instrument.

General Procedure for the Addition of α,α-Disubstituted Aldehydes to Nitroalkenes.



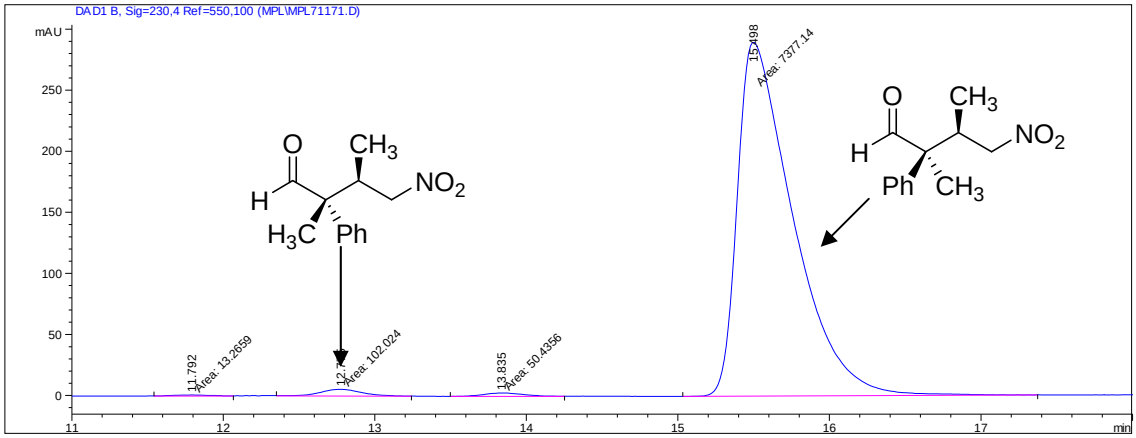
(2*S*,3*R*)-2,3-dimethyl-4-nitro-2-phenylbutanal (**6**): Under a positive pressure of nitrogen at room temperature, thiourea catalyst **1** (75.3 mg, 0.20 mmol, 20 mol%) was loaded into an oven-dried 25 mL round-bottomed flask, equipped with a magnetic stir bar, rubber septum, and nitrogen inlet. The catalyst was dissolved in dichloromethane (6.7 mL). Water (90.1 μL, 5.0 mmol, 5.0 equiv.) and 2-phenylpropionaldehyde (265.4 μL, 2.0 mmol, 2.0 equiv.) were subsequently added via syringe. The resulting clear colorless solution was stirred for approximately two minutes. 1-nitropropene (87.1 mg, 1.0 mmol, 1.0 equiv.) was added via syringe resulting in a light yellow solution. The rubber septum was quickly replaced with a yellow polyethylene stopper (to prevent dichloromethane evaporation) and the reaction mixture was stirred for 24 hours at room temperature. Aqueous hydrochloric acid solution (1M, 7 mL) was added to the reaction flask and the resulting biphasic mixture was stirred vigorously for 5 minutes at room temperature. The biphasic mixture was transferred to a separatory funnel and additional portions of dichloromethane (30 mL) and 1M HCl (30 mL) were added. The phases were separated and the aqueous layer was washed with dichloromethane (30 mL). The organic layers were combined and washed with saturated aqueous sodium bicarbonate solution (30 mL), saturated aqueous sodium chloride solution (30 mL), dried over anhydrous sodium sulfate, filtered, and concentrated *in vacuo*. The resulting yellow residue was purified by chromatography on silica (8% diethyl ether/hexanes), providing the title compound as a colorless to light yellow liquid in 91% yield (201.1 mg) with a 23:1 diastereomeric ratio and 99% enantiomeric excess (major diastereomer) as determined by HPLC (Chiralpak AD-H, 2.0% isopropanol/Hexanes, 1.0 mL/min, 230 nm; t_r(minor enantiomer, minor diastereomer) = 11.83 min, t_r(major enantiomer, minor diastereomer) = 12.87 min, t_r(minor enantiomer, major diastereomer) = 13.82 min, t_r(major enantiomer, major diastereomer) = 15.48 min). $[\alpha]^{25}_D$ = +88.6 (c = 0.0200 g/2.0 mL, chloroform). ^{1}H NMR (400 MHz, $CDCl_3$): δ 9.47 (1H, s), 7.42 (2H, t, J = 7.3 Hz), 7.34 (1H, t, J = 7.3 Hz), 7.24 (2H, d, J = 7.3 Hz), 4.57 (1H, dd, J = 3.3, 12.0 Hz), 4.19 (1H, dd, J = 10.6, 12.0 Hz), 3.17 (1H, m), 1.48 (3H, s), 0.81 (3H, d, J = 7.0 Hz). ^{13}C (100 MHz, $CDCl_3$): δ 200.6, 137.4, 129.4, 128.2, 127.4, 78.8, 55.9, 37.1, 14.6, 13.2. IR (neat): 3060 (w), 2981 (m), 2819 (w), 2719 (w), 1722 (s), 1533 (s), 1496 (m), 1446 (m), 1377 (s), 763 (m), 702 (m). HRMS (ESI): expected for $[C_{12}H_{15}NO_3+NH_4]^+$: 239.1396, found: 239.1402.

Racemic 2,3-dimethyl-4-nitro-2-phenylbutanal



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area [%]
1	11.828	MM	0.3336	744.17249	37.17384	3.1239
2	12.871	MM	0.3334	700.51599	35.01959	2.9407
3	13.818	MM	0.3825	1.11430e4	485.54669	46.7766
4	15.475	MM	0.4643	1.12340e4	403.25229	47.1588
Totals:				2.38216e4	960.99240	

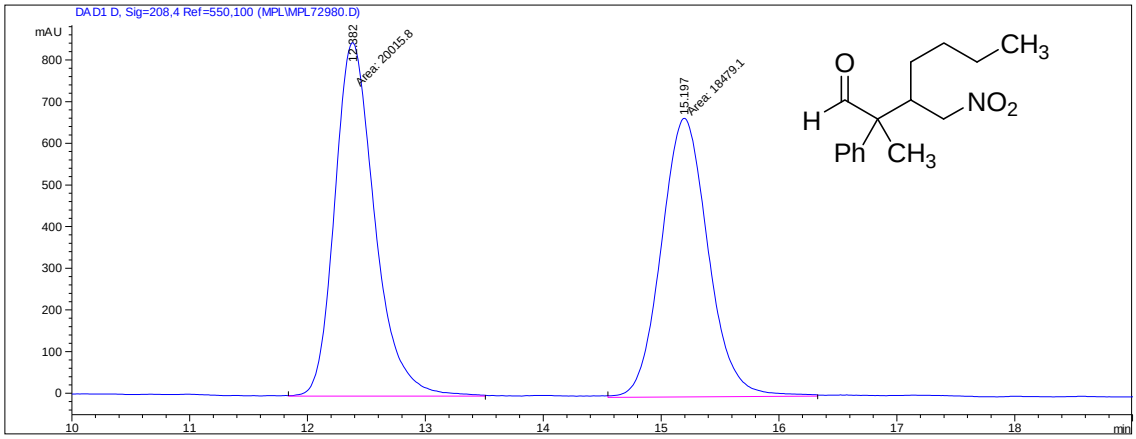
Enantioenriched (2*S*,3*R*)-2,3-dimethyl-4-nitro-2-phenylbutanal



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area [%]
1	11.792	MM	0.2958	14.55923	8.20360e-1	0.1922
2	12.775	MM	0.3166	105.39117	5.54822	1.3912
3	13.835	MM	0.3109	50.89827	2.72861	0.6719
4	15.498	MM	0.4254	7404.60938	290.08578	97.7447
Totals:				7575.45805	299.18297	

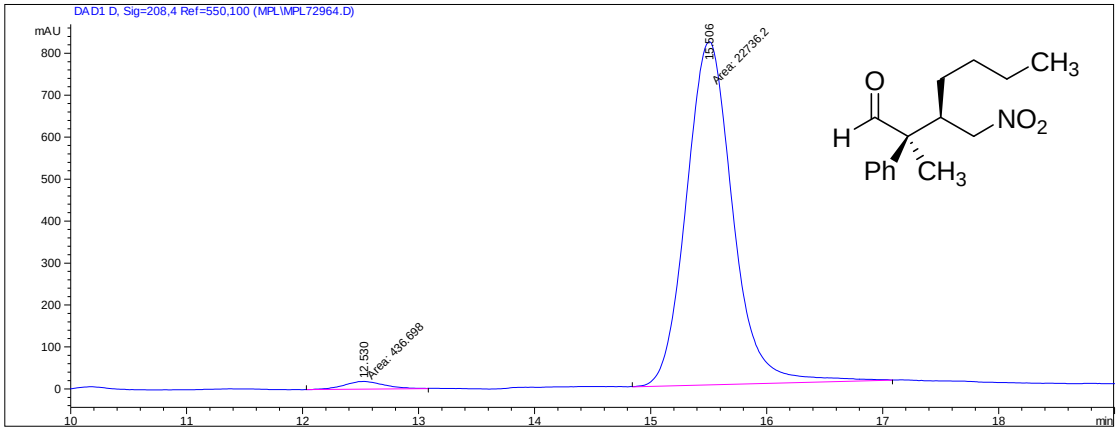
(2*S*,3*R*)-2-methyl-3-(nitromethyl)-2-phenylheptanal (**5**): General procedure, chromatography on silica (5% diethyl ether/hexanes), colorless to light yellow liquid, 54% yield (143.8 mg), 28:1 dr as determined by HPLC (Econosphere CN 5U + Chiralcel OD-H, 5.0% isopropanol/hexanes, 1.0 mL/min, 208nm; t_r(major enantiomer, minor diastereomer) = 13.80 min, t_r(minor enantiomer, minor diastereomer) = 15.04, t_r(minor enantiomer, major diastereomer) = 16.53 min, t_r(major enantiomer, major diastereomer) = 18.87), 96% ee (major diastereomer) as determined by HPLC (Chiralcel OD-H, 5.0% isopropanol/hexanes, 1.0 mL/min, 208 nm; t_r(minor enantiomer, major diastereomer) = 12.38 min, t_r(major enantiomer, major diastereomer) = 15.20 min). $[\alpha]^{25}_D$ = +59.8 (c = 0.0200 g/2.0 mL, chloroform). ^{1}H NMR (400 MHz, $CDCl_3$): δ 9.49 (1H, s), 7.41 (2H, t, J = 7.3 Hz), 7.33 (1H, t, J = 7.3 Hz), 7.29 (2H, d, J = 7.3 Hz), 4.48 (1H, dd, J = 4.2, 13.5 Hz), 4.28 (1H, dd, J = 7.3, 13.5 Hz), 3.12 (1H, m), 1.47 (3H, s), 1.47-0.98 (6H, m), 0.72 (3H, t, J = 7.0 Hz). ^{13}C (100 MHz, $CDCl_3$): δ 200.9, 137.6, 129.3, 128.1, 127.5, 77.7, 57.0, 41.9, 29.9, 29.2, 22.6, 15.2, 13.8. IR (neat): 2958 (m), 2933 (m), 2864 (m), 2716 (w), 1722 (s), 1553 (s), 1447 (m), 1380 (m), 762(m), 702 (m). HRMS (ESI): expected for $[C_{15}H_{21}NO_3+NH_4]^+$: 281.1865, found: 281.1877.

Racemic 2-methyl-3-(nitromethyl)-2-phenylheptanal



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area [%]
1	12.382	MM	0.3899	1.98279e4	847.53461	51.8699
2	15.197	MM	0.4595	1.83983e4	667.27185	48.1301
Totals:				3.82262e4	1514.80646	

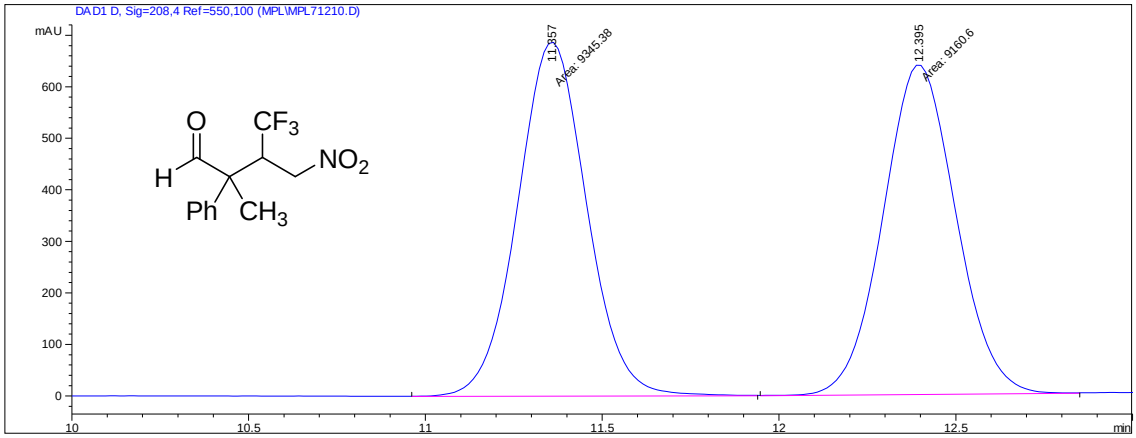
Enantioenriched (2*S*,3*R*)-2-methyl-3-(nitromethyl)-2-phenylheptanal



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area [%]
1	12.530	MM	0.4030	448.04437	18.52734	1.9355
2	15.506	MM	0.4625	2.27005e4	818.05493	98.0645
Totals:				2.31485e4	836.58227	

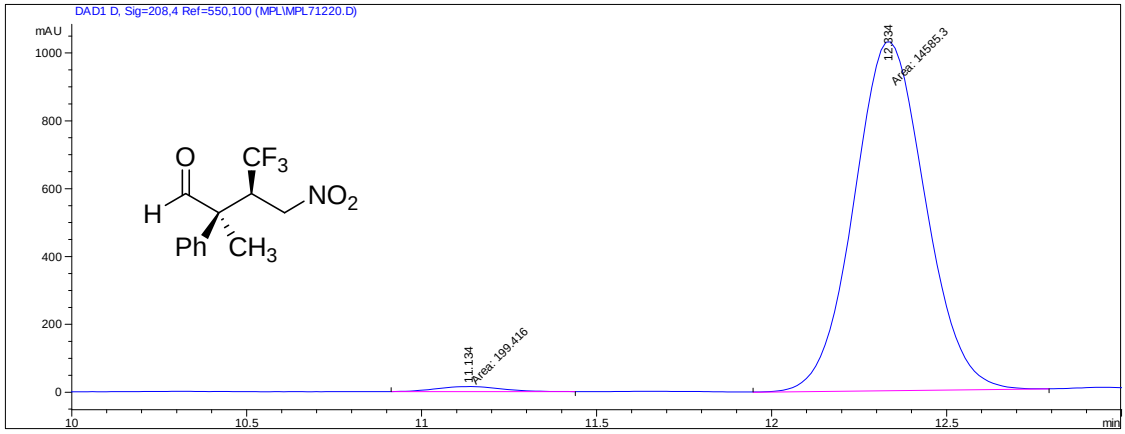
(2*S*,3*R*)-4,4,4-trifluoro-2-methyl-3-(nitromethyl)-2-phenylbutanal (**7**): General procedure, chromatography on silica (10% diethyl ether/hexanes), colorless to light yellow liquid, 34% yield (92.6 mg), >50:1 dr (the presence of another diastereomer could not be detected by either ^{1}H NMR, SFC, or HPLC), 97% ee (major diastereomer) as determined by HPLC (Chiralpak AD-H, 2.0% isopropanol/hexanes, 1.0 mL/min, 208 nm; t_r(minor enantiomer, major diastereomer) = 11.36 min, t_r(major enantiomer, major diastereomer) = 12.40 min). $[\alpha]^{25}_{D}$ = +140.1 (c = 0.0210 g/2.0 mL, chloroform). ^{1}H NMR (400 MHz, $CDCl_3$): δ 9.28 (1H, s), 7.45 (2H, t, J = 7.3 Hz), 7.38 (1H, t, J = 7.3 Hz), 7.28 (2H, t, J = 7.3 Hz), 4.72 (1H, dd, J = 8.1, 15.4 Hz), 4.48 (1H, dd, J = 2.2, 15.4 Hz), 4.20 (1H, m), 1.71 (3H, s). ^{13}C (100 MHz, $CDCl_3$): δ 197.8, 135.1, 129.5, 128.9, 127.2, 126.1 (1C, q, J = 282.5 Hz), 124.7, 71.5, 46.7 (1C, q, J = 25.6 Hz), 16.1. IR (neat): 3062 (m), 3032 (m), 2981 (m), 2828 (m), 2722(m), 1721 (s), 1567 (s), 1497 (m), 1448 (m), 1380 (s), 1249 (s), 1178 (s), 1100 (s), 1001 (m), 763 (m), 701 (s), 543 (m). LRMS (ESI): 296.3 (100%) $[C_{12}H_{12}F_3NO_3+Na]^+$.

Racemic 4,4,4-trifluoro-2-methyl-3-(nitromethyl)-2-phenylbutanal



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area [%]
1	11.357	PV	0.2112	9325.99316	687.88574	50.1677
2	12.395	MM	0.2403	9263.65332	642.42816	49.8323
Totals:				1.85896e4	1330.31390	

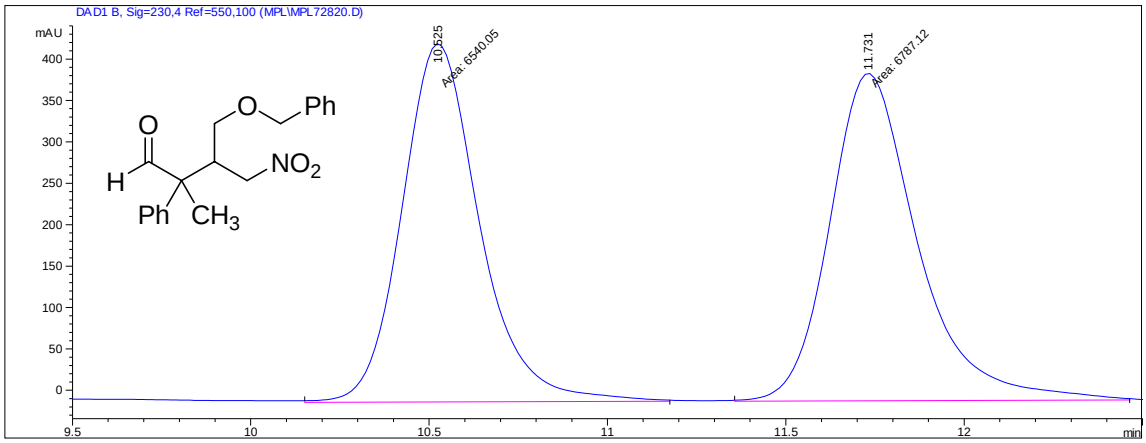
Enantioenriched (2*S*,3*R*)-4,4,4-trifluoro-2-methyl-3-(nitromethyl)-2-phenylbutanal



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area [%]
1	11.134	MM	0.2359	229.92702	16.24365	1.5519
2	12.334	MM	0.2357	1.45856e4	1031.53821	98.4481
Totals:				1.48155e4	1047.78186	

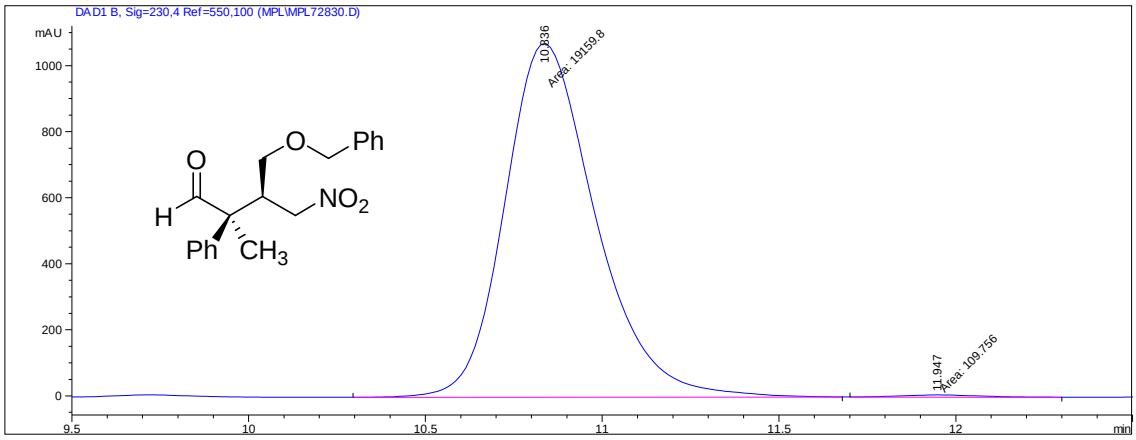
(2*S*,3*R*)-4-(benzyloxy)-2-methyl-3-(nitromethyl)-2-phenylbutanal (**8**): General procedure, chromatography on silica (20% diethyl ether/hexanes), colorless to light yellow liquid, 87% yield (284.3 mg), >50:1 dr (the presence of another diastereomer could not be detected by either ^{1}H NMR, SFC, or HPLC), 99% ee (major diastereomer) as determined by HPLC (Chiralpak AD-H, 5% isopropanol/hexanes, 1.0 mL/min, 230 nm; t_r(major enantiomer, major diastereomer) = 10.53 min, t_r(minor enantiomer, major diastereomer) = 11.73 min). $[\alpha]^{25}_{D}$ = +92.2 (c = 0.0240 g/2.0 mL, chloroform). ^{1}H NMR (400 MHz, $CDCl_3$): δ 9.41 (1H, s), 7.43-7.21 (10H, m), 4.70 (1H, dd, J = 9.5, 13.0 Hz), 4.50 (1H, dd, J = 3.3, 13.0 Hz), 4.36 (1H, d, J = 11.9 Hz), 4.27 (1H, d, J = 11.9 Hz), 3.34 (2H, m), 3.17 (1H, dd, J = 4.0, 9.5 Hz), 1.57 (3H, s). ^{13}C (100 MHz, $CDCl_3$): δ 200.0, 137.5, 137.2, 129.2, 128.3, 128.1, 127.7, 127.5, 127.2, 67.5, 55.1, 42.0, 16.3. IR (neat): 3062 (m), 3030 (m), 2863 (m), 2814 (m), 2717 (m), 1722 (s), 1555 (s), 1496 (m), 1454 (m), 1379 (m), 1104 (m), 740 (m), 700(m). HRMS (ESI): expected for $[C_{19}H_{21}NO_4+NH_4-]^+$: 345.1814, found: 345.1817.

Racemic 4-(benzyloxy)-2-methyl-3-(nitromethyl)-2-phenylbutanal



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area [%]
1	10.525	MM	0.2523	6561.72607	433.44318	48.9134
2	11.731	MM	0.2881	6853.26660	396.42261	51.0866
Totals:				1.34150e4	829.86578	

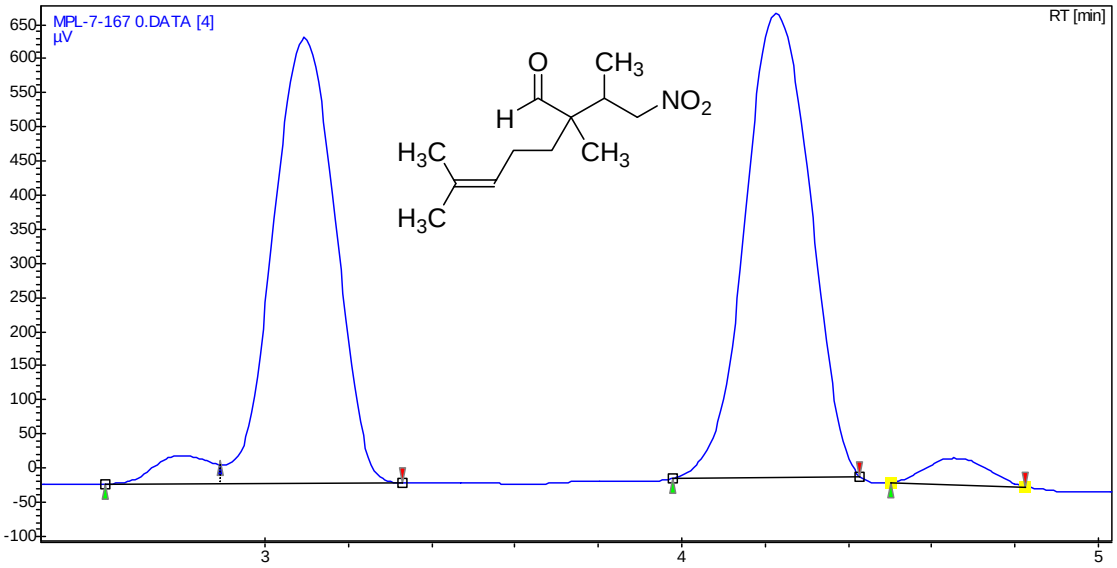
Enantioenriched (2*S*, 3*R*)-4-(benzyloxy)-2-methyl-3-(nitromethyl)-2-phenylbutanal



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area [%]
1	10.836	MM	0.2982	1.91983e4	1072.96790	99.3543
2	11.947	MM	0.2888	124.76044	7.19885	0.6457
Totals:				1.93230e4	1080.16675	

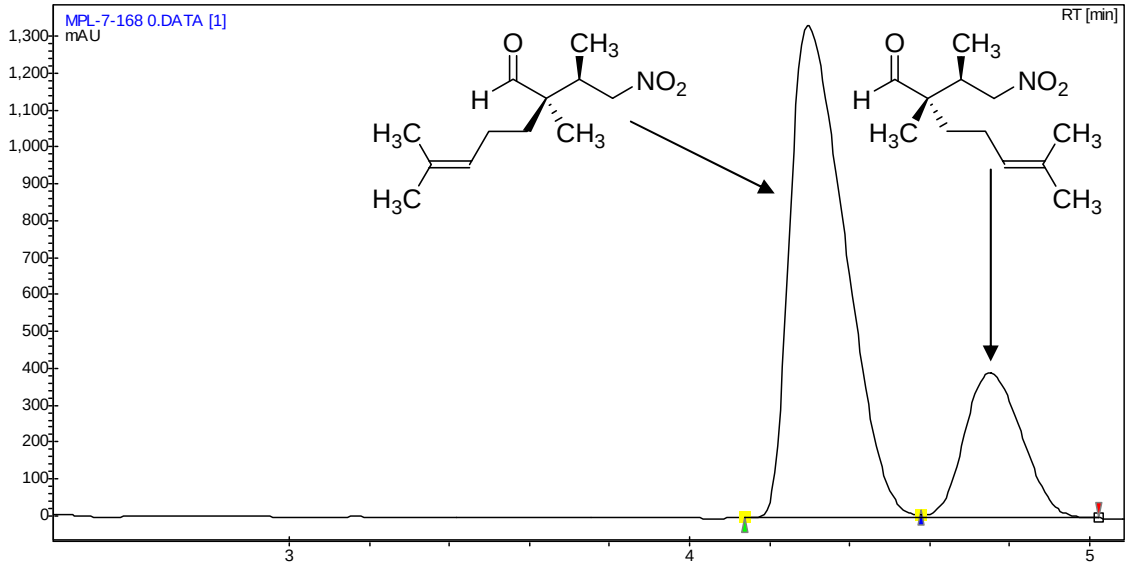
(*R*)-2,6-dimethyl-2-((*R*)-1-nitropropan-2-yl)hept-5-enal + (*S*)-2,6-dimethyl-2-((*R*)-1-nitropropan-2-yl)hept-5-enal (**9**): General procedure, chromatography on silica (8% diethyl ether/hexanes) diastereomers could not be separated, colorless to light yellow liquid, 61% yield, 3.3:1 dr, 99% ee (major diastereomer) as determined by SFC (Chiralcel OD-H, 2.0% methanol/CO_2, 2.0 mL/min, 208 nm, 30 °C; t_r(minor enantiomer, minor diastereomer) = 2.80 min, t_r(minor enantiomer, major diastereomer) = 3.09 min, t_r(major enantiomer, major diastereomer) = 4.23 min, t_r(major enantiomer, minor diastereomer) = 4.66 min). $[\alpha]^{25}_D$ = +28.3 (c = 0.0135 g/2.0 mL, chloroform). ^{1}H NMR (400 MHz, $CDCl_3$): Signals corresponding to the major diastereomer δ 9.47 (1H, s), 5.02 (1H, tt, J = 1.5, 7.0 Hz), 4.39 (1H, dd, J = 3.3, 12.1 Hz), 4.13 (1H, dd, J = 10.6, 12.1 Hz), 2.73 (1H, m), 1.88 (2H, q, J = 7.7 Hz), 1.67 (3H, s), 1.65-1.49 (2H, m), 1.57 (3H, s), 1.04 (3H, d, J = 6.6 Hz), 1.03 (3H, s). Peaks corresponding to the minor diastereomer δ 9.46 (1H, s), 5.02 (1H, tt, J = 1.5, 7.0 Hz), 4.49 (1H, dd, J = 3.7, 12.1 Hz), 4.16 (1H, dd, J = 10.6, 12.1 Hz), 2.73 (1H, m), 1.88 (2H, q, J = 7.7 Hz), 1.67 (3H, s), 1.65-1.49 (2H, m), 1.57 (3H, s), 1.05 (3H, s), 0.99 (3H, d, J = 6.6 Hz). ^{13}C (100 MHz, $CDCl_3$): Signals corresponding to the major diastereomer δ 204.6, 133.1, 122.8, 78.7, 50.7, 34.8, 34.6, 25.6, 22.3, 17.7, 14.9, 12.2. Signals corresponding to the minor diastereomer δ 204.1, 133.1, 122.8, 78.2, 50.7, 36.0, 34.2, 29.7, 25.6, 22.4, 14.8, 13.4. IR (neat): 2973 (s), 2924 (s), 2858 (m), 2713 (w), 1726 (s), 1554 (s), 1436 (m), 1378 (s), 1231 (w), 1119 (w), 902 (w). HRMS (ESI): expected for $[C_{12}H_{21}NO_3+H]^+$: 228.1599, found: 228.1596.

Racemic 2,6-dimethyl-2-(1-nitropropan-2-yl)hept-5-enal



#	Time [Min]	Height [µV]	Area [µV.Min]	Area [%]
1	2.80	40.8	6.5	2.592
4	3.09	652.6	112.9	45.185
3	4.23	679.8	123.9	49.563
2	4.66	38.4	6.6	2.660
Total		1411.6	250.0	100.000

Enantioenriched (*R*)-2,6-dimethyl-2-((*R*)-1-nitropropan-2-yl)hept-5-enal + (*S*)-2,6-dimethyl-2-((*R*)-1-nitropropan-2-yl)hept-5-enal



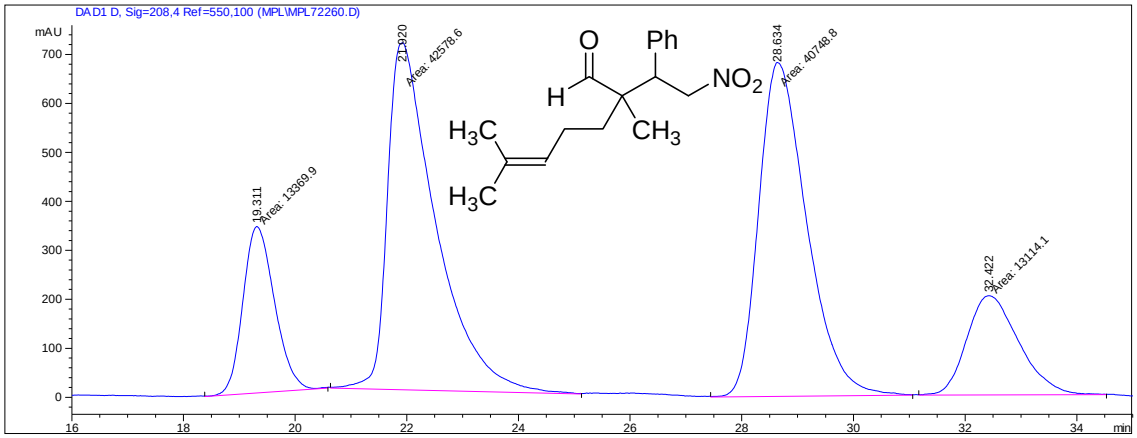
#	Time [Min]	Height [mAU]	Area [mAU*min]	Area [%]
1	4.29	1336.73	212.96	76.532
2	4.75	391.84	65.30	23.468
Total			278.26	100.000

(*R*)-2,6-dimethyl-2-((*R*)-2-nitro-1-phenylethyl)hept-5-enal (**10**): General procedure, diastereomeric products separable by chromatography on silica (10% diethyl ether/hexanes), colorless to light yellow liquid, 82% yield (238.7 mg), 3.9:1 dr, 99% ee (major diastereomer), 97% ee (minor diastereomer) as determined by HPLC (Chiralcel OD-H, 5.0% isopropanol/hexanes, 1.0 mL/min, 208 nm; t_r(major enantiomer, major diastereomer) = 21.92 min, t_r(minor enantiomer, major diastereomer) = 28.63 min). $[\alpha]^{25}_D$ = +55.9 (c = 0.0210 g/2.0 mL, chloroform). ^{1}H NMR (400 MHz, $CDCl_3$): δ 9.52 (1H, s), 7.34-7.18 (5H, m), 4.90 (1H, t, J = 7.0 Hz), 4.81 (1H, dd, J = 11.3, 12.8 Hz), 4.60 (1H, dd, J = 3.8, 12.8 Hz), 3.58 (1H, dd, J = 3.8, 11.3 Hz), 1.84 (2H, q, J = 8.1 Hz), 1.61 (3H, s), 1.55 (1H, m), 1.50 (3H, s), 1.20 (1H, m), 1.10 (3H, s). ^{13}C (100 MHz, $CDCl_3$): δ 205.0, 135.2, 133.0, 129.2, 128.7, 128.2, 122.8, 76.7, 51.5, 47.6, 35.5, 25.6, 22.4, 17.7, 15.7. IR (neat): 3033 (m), 2972 (m), 2920 (m), 2856 (m), 2724 (m), 1723 (s), 1556 (s), 1455 (m), 1378 (s), 750 (m), 705 (s). HRMS (ESI): expected for $[C_{17}H_{23}NO_3+NH_4]^+$: 307.2022, found: 307.2030.

(*S*)-2,6-dimethyl-2-((*R*)-2-nitro-1-phenylethyl)hept-5-enal: 99% ee (minor diastereomer) as determined by HPLC (Chiralcel OD-H, 5.0% ispropanol/hexanes, 1.0 mL/min, 208 nm; t_r(major enantiomer, minor diastereomer) = 19.31 min, t_r(minor

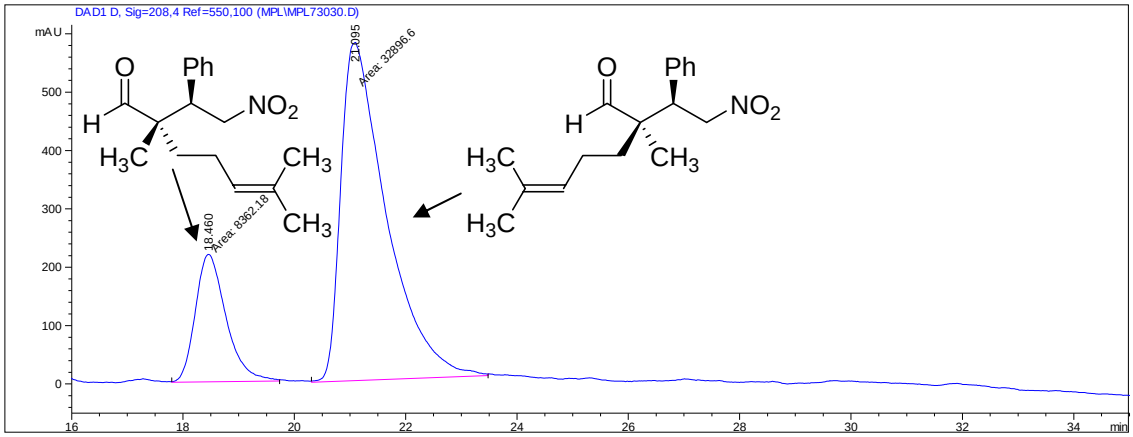
enantiomer, minor diastereomer) = 32.42 min). $[\alpha]^{25}_{D}$ = –1.3 (c = 0.0580 g/2.0 mL, chloroform). ^{1}H NMR (400 MHz, $CDCl_3$): δ 9.53 (1H, s), 7.34-7.15 (5H, m), 4.99 (1H, t, J = 7.1 Hz), 4.84 (1H, dd, J = 11.3, 13.2 Hz), 4.76 (1H, dd, J = 4.4, 13.2 Hz), 3.76 (1H, dd, J = 4.4, 11.3 Hz), 1.97 (1H, m), 1.88 (1H, m), 1.68 (1H, m), 1.66 (3H, s), 1.56 (3H, s), 1.52 (1H, m), 1.13 (3H, s). ^{13}C (100 MHz, $CDCl_3$): δ 204.8, 135.2, 133.0, 129.1, 128.8, 128.2, 122.9, 76.3, 50.9, 49.4, 34.4, 25.6, 22.6, 17.7, 17.2. IR (neat): 3033 (m), 2969 (m), 2922 (m), 2854 (m), 2722 (m), 1724 (s), 1556 (s), 1455 (m), 1379 (s), 750 (m), 704 (s). HRMS (ESI): expected for $[C_{17}H_{23}NO_3+NH_4]^+$: 307.2022, found: 307.2007.

Racemic 2,6-dimethyl-2-(2-nitro-1-phenylethyl)hept-5-enal



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area [%]
1	19.311	MM	0.6552	1.33646e4	339.94751	12.2017
2	21.920	MM	0.9991	4.24427e4	708.04962	38.7498
3	28.634	MM	0.9932	4.06252e4	681.74896	37.0904
4	32.422	MM	1.0794	1.30977e4	202.23651	11.9581
Totals:				1.09530e5	1931.98260	

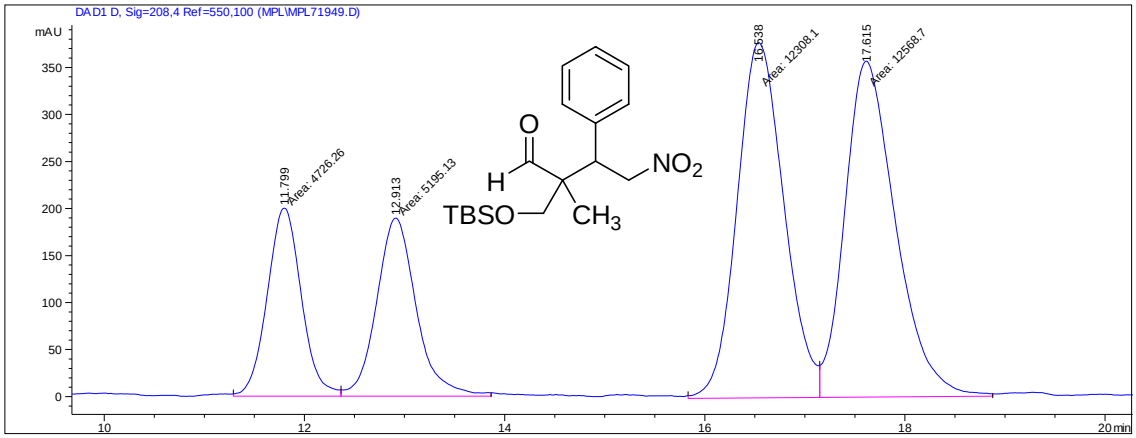
Enantioenriched (*R*)-2,6-dimethyl-2-((*R*)-2-nitro-1-phenylethyl)hept-5-enal + (*S*)-2,6-dimethyl-2-((*R*)-2-nitro-1-phenylethyl)hept-5-enal



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area [%]
1	18.460	MM	0.6623	8759.28125	220.44008	20.2295
2	21.095	MM	0.9880	3.45403e4	582.65924	79.7705
Totals:				4.32996e4	803.09932	

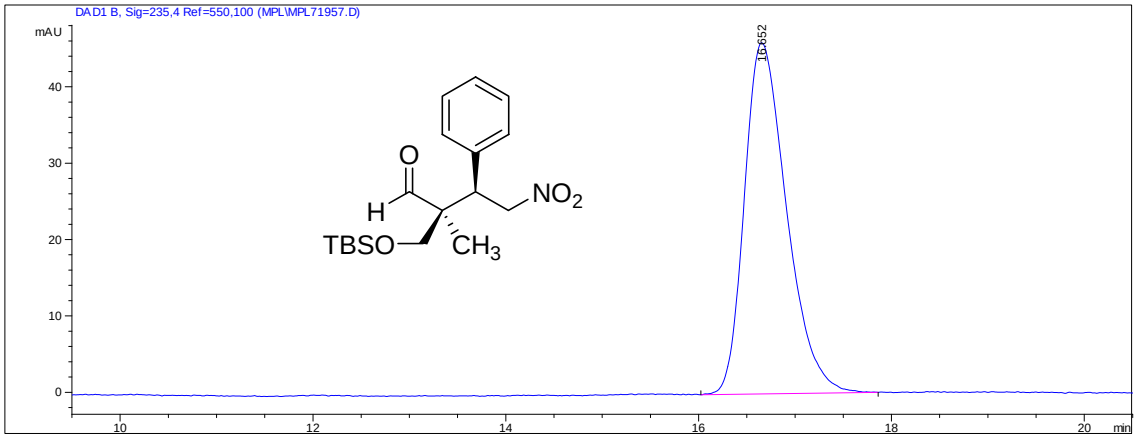
(2*S*,3*R*)-2-((*tert*-butyldimethylsilyloxy)methyl)-2-methyl-4-nitro-3-phenylbutanal (**11**): General procedure, diastereomeric products separable by chromatography on silica (8% diethyl ether/hexanes), colorless to light yellow oil, 87% yield (306.3 mg), 6.3:1 dr (determined using the HPLC conditions below and the crude product mixture), 99% ee (major diastereomer) as determined by HPLC (Chiralcel OD-H, 0.5% isopropanol/hexanes, 1.0 mL/min, 208 nm; t_r(major enantiomer, major diastereomer) = 16.54 min, t_r(minor enantiomer, major diastereomer) = 17.62 min). $[\alpha]^{25}_D$ = +18.9 (c = 0.0203 g/2.0 mL, chloroform). ^{1}H NMR (400 MHz, $CDCl_3$): δ 9.61 (1H, s), 7.32-7.24 (5H, m), 4.90 (1H, dd, J = 11.3, 13.2 Hz), 4.80 (1H, dd, J = 4.0, 13.2 Hz), 4.13 (1H, dd, J = 4.0, 11.3 Hz), 3.49 (1H, d, J = 10.2 Hz), 3.34 (1H, d, J = 10.2 Hz), 1.04 (3H, s), 0.90 (9H, s), 0.01 (6H, s). ^{13}C (100 MHz, $CDCl_3$): δ 204.0, 135.2, 129.1, 128.6, 128.1, 76.4, 53.1, 44.4, 25.7, 18.1, 13.7, –5.7, –5.8. IR (neat): 3066 (m), 3035 (m), 2955, (s), 2930 (s), 2897 (m), 2858 (s), 2712 (m), 1730 (s), 1556 (s), 1472 (m), 1378 (m), 1259 (m), 1099 (s), 834 (s), 779 (s), 731 (s). HRMS (ESI): expected for $[C_{18}H_{29}NO_4Si+NH_4]^+$: 369.2210, found: 369.2216.

Racemic 2-((*tert*-butyldimethylsilyloxy)methyl)-2-methyl-4-nitro-3-phenylbutanal



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area [%]
1	11.799	MF	0.3911	4669.92187	199.00484	13.5112
2	12.913	FM	0.4519	5106.52588	188.35178	14.7743
3	16.538	MF	0.5418	1.22711e4	377.48682	35.5030
4	17.615	FM	0.5850	1.25159e4	356.55698	36.2115
Totals:				3.45635e4	1121.40041	

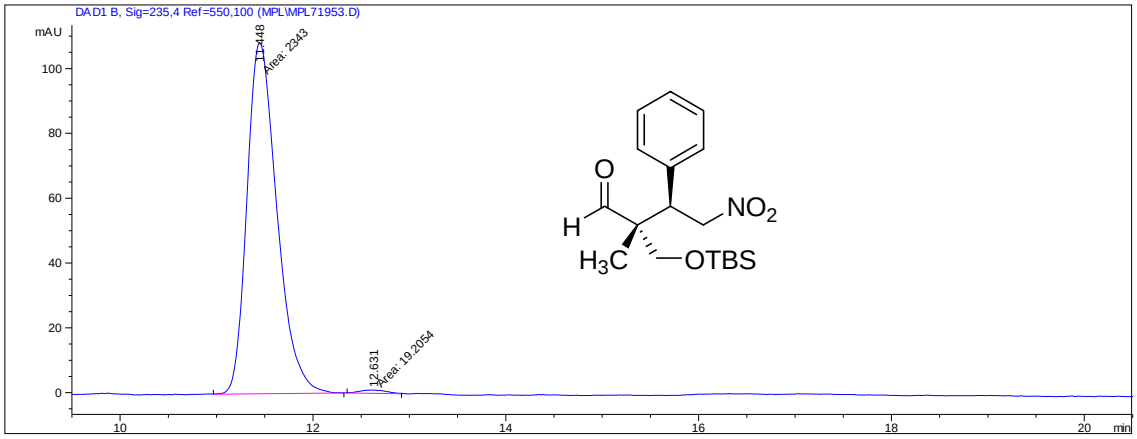
Enantioenriched (2*S*,3*R*)-2-((*tert*-butyldimethylsilyloxy)methyl)-2-methyl-4-nitro-3-phenylbutanal



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area [%]
1	16.652	PV	0.4497	1397.35815	45.98453	100.0000
Totals:				1397.35815	45.98453	

(2*R*,3*R*)-2-((*tert*-butyldimethylsilyloxy)methyl)-2-methyl-4-nitro-3-phenylbutanal: white solid, m.p. = 79-80 °C, 96% ee (minor diastereomer) as determined by HPLC (Chiralcel OD-H, 0.5% isopropanol/hexanes, 1.0 mL/min, 235 nm; t_r(major enantiomer, minor diastereomer) = 11.80 min, t_r(minor enantiomer, minor diastereomer) = 12.91 min). $[\alpha]^{25}_D$ = –24.5 (c = 0.0103 g/2.0 mL, chloroform). ^{1}H NMR (400 MHz, $CDCl_3$): δ 9.61 (1H, s), 7.35-7.23 (5H, m), 5.08 (1H, dd, J = 11.7, 13.5 Hz), 4.83 (1H, dd, J = 3.3, 13.5 Hz), 4.01 (1H, dd, J = 3.3, 11.7 Hz), 3.74 (1H, d, J = 11.0 Hz), 3.65 (1H, d, J = 11.0 Hz), 0.94 (9H, s), 0.82 (3H, s), 0.14 (3H, s), 0.10 (3H, s). ^{13}C (100 MHz, $CDCl_3$): δ 203.5, 135.6, 129.3, 128.7, 128.0, 77.0, 64.7, 53.5, 46.7, 25.8, 18.1, 17.0, –5.6, –5.7. IR (thin film): 3066 (m), 3035 (m), 2956 (s), 2930 (s), 2897 (m), 2858 (s), 2715 (m), 1726 (s), 1555 (s), 1472 (m), 1378 (m), 1259 (m), 1090 (s), 838 (s), 779 (s), 705 (s). HRMS (ESI): expected for $[C_{18}H_{29}NO_4Si+NH_4]^+$: 369.2210, found: 369.2209.

Enantioenriched (2*R*,3*R*)-2-((*tert*-butyldimethylsilyloxy)methyl)-2-methyl-4-nitro-3-phenylbutanal

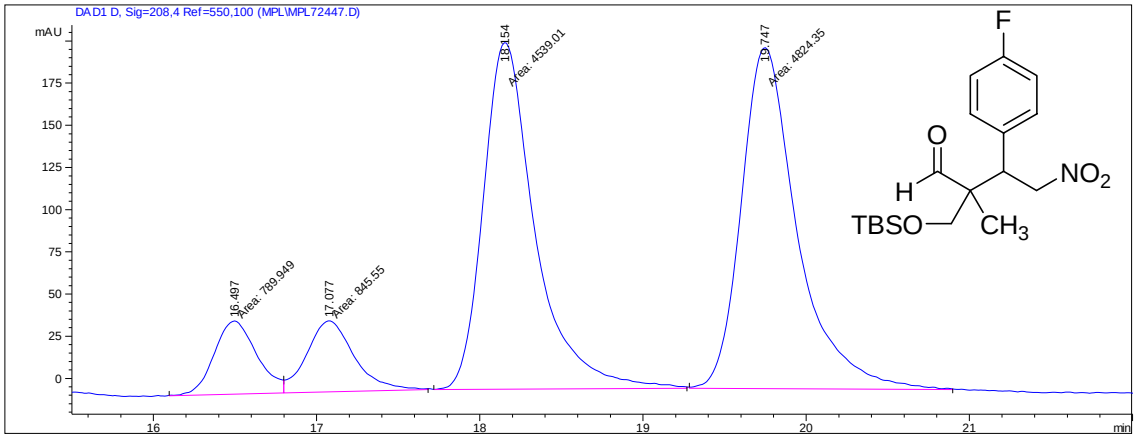


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area [%]
1	11.448	MM	0.3598	2340.93750	108.44026	99.1828
2	12.631	MM	0.3190	19.28873	1.00766	0.8172
Totals:				2360.22623	109.44792	

(2*S*,3*R*)-2-((*tert*-butyldimethylsilyloxy)methyl)-3-(4-fluorophenyl)-2-methyl-4-nitrobutanal (**12**): General procedure, diastereomeric products separable by chromatography on silica (15% diethyl ether/hexanes), white solid, m.p.(major diastereomer) = 59-61 °C, 86% yield (318.6 mg), 6.6:1 dr (determined using the HPLC conditions below and the crude product mixture), 99% ee (major diastereomer) as

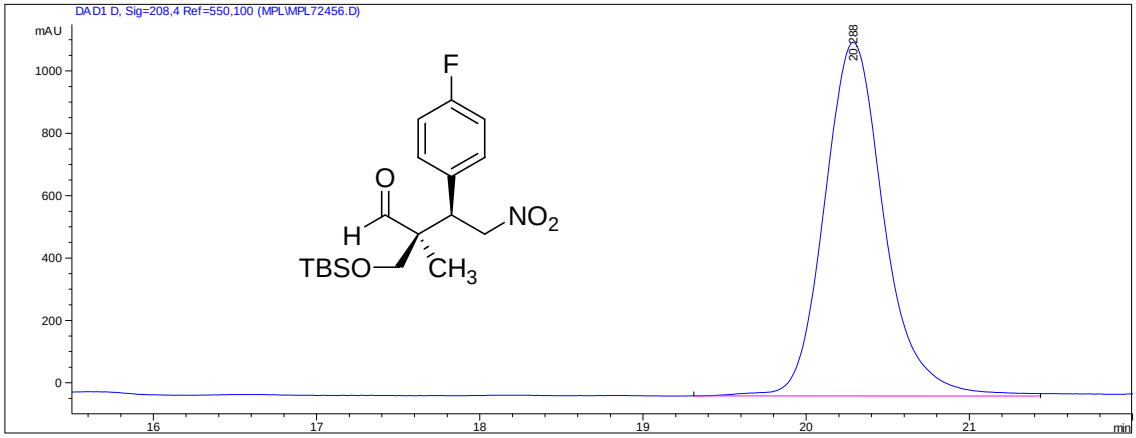
determined by HPLC (Econosphere CN 5U + Chiralpak AD-H, 0.5% isopropanol/hexanes, 1.0 mL/min, 208 nm; t_r(minor enantiomer, major diastereomer) = 18.15 min, t_r(major enantiomer, major diastereomer) = 19.75 min). $[\alpha]^{25}_D$ = +15.9 (c = 0.0202 g/2.0 mL, chloroform). ^{1}H NMR (400 MHz, $CDCl_3$): δ 9.58 (1H, s), 7.24 (2H, dd, J = 5.3, 8.8 Hz), 7.00 (2H, t, J = 8.8 Hz), 4.84 (2H, m), 4.12 (1H, dd, J = 4.9, 10.6 Hz), 3.52 (1H, d, J = 10.2 Hz), 3.30 (1H, d, J = 10.2 Hz), 1.02 (3H, s), 0.90 (9H, s), 0.02 (6H, s). ^{13}C (100 MHz, $CDCl_3$): δ 203.6, 162.3 (1C, d, J = 247.2 Hz), 131.1 (1C, d, J = 3.8 Hz), 130.7 (1C, d, J = 7.6 Hz), 115.5 (1C, d, J = 21.4 Hz), 76.5, 65.8, 53.3, 43.8, 25.7, 18.1, 13.6, –5.7, –5.8. IR (thin film): 2955 (s), 2930 (s), 2858 (s), 2712 (m), 1727 (s), 1607 (m), 1556 (s), 1512 (s), 1472 (m), 1378 (m), 1254 (m), 1229 (m), 1163 (m), 1104 (s), 840 (s), 779 (s). HRMS (ESI): expected for $[C_{18}H_{28}FNO_4Si]^+$: 369.1772, found: 369.1786.

Racemic 2-((*tert*-butyldimethylsilyloxy)methyl)-3-(4-fluorophenyl)-2-methyl-4-nitrobutanal



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area [%]
1	16.497	MF	0.3072	801.61078	43.49492	7.3643
2	17.077	FM	0.3290	831.22321	42.10474	7.6363
3	18.154	MM	0.3652	4499.10645	205.32422	41.3325
4	19.747	MM	0.3931	4753.20898	201.53207	43.6669
Totals:				1.08851e4	492.45595	

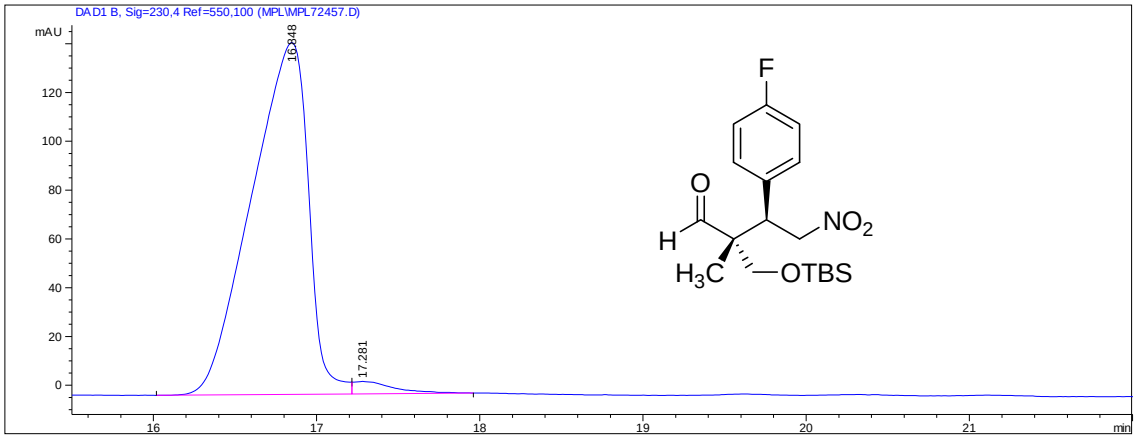
Enantioenriched (2*S*,3*R*)-2-((*tert*-butyldimethylsilyloxy)methyl)-3-(4-fluorophenyl)-2-methyl-4-nitrobutanal



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area [%]
1	20.288	MM	0.4161	2.81835e4	1128.84021	100.0000
Totals:				2.81835e4	1128.84021	

(2*R*,3*R*)-2-((*tert*-butyldimethylsilyloxy)methyl)-3-(4-fluorophenyl)-2-methyl-4-nitrobutanal: Colorless to light yellow liquid, 94% ee (minor diastereomer) as determined by HPLC (Econosphere CN 5U + Chiralpak AD-H, 0.5% isopropanol/hexanes, 1.0 mL/min, 208 nm; t_r(major enantiomer, minor diastereomer) = 16.50 min, t_r(minor enantiomer, minor diastereomer) = 17.08 min). $[\alpha]^{25}_D$ = –22.5 (c = 0.0296 g/2.0 mL, chloroform). ^{1}H NMR (400 MHz, $CDCl_3$): δ 9.59 (1H, s), 7.22 (2H, dd, J = 5.3, 8.8 Hz), 7.03 (2H, t, J = 8.8 Hz), 5.03 (1H, dd, J = 11.7, 13.5 Hz), 4.82 (1H, dd, J = 3.7, 13.5 Hz), 4.01 (1H, dd, J = 3.7, 11.7 Hz), 3.74 (1H, d, J = 11.2 Hz), 3.61 (1H, d, 11.2 Hz), 0.93 (9H, s), 0.82 (3H, s), 0.14 (3H, s), 0.10 (3H, s). ^{13}C (100 MHz, $CDCl_3$): δ 203.2, 162.4 (1C, d, J = 248.0 Hz), 131.3 (1C, d, J = 3.1 Hz), 130.9 (1C, d, J = 8.4 Hz), 115.7 (1C, d, J = 21.4 Hz), 77.0, 64.6, 53.5, 46.1, 25.8, 18.1, 16.9, –5.6, –5.7. IR (neat): 2955 (s), 2930 (s), 2858 (s), 2715 (m), 1729 (s), 1607 (m), 1555 (s), 1512 (s), 1378 (m), 1100 (s), 838 (s). HRMS (ESI): expected for $[C_{18}H_{28}FNO_4Si+H]^+$: 370.1850, found: 370.1859.

Enantioenriched (2*R*,3*R*)-2-((*tert*-butyldimethylsilyloxy)methyl)-3-(4-fluorophenyl)-2-methyl-4-nitrobutanal

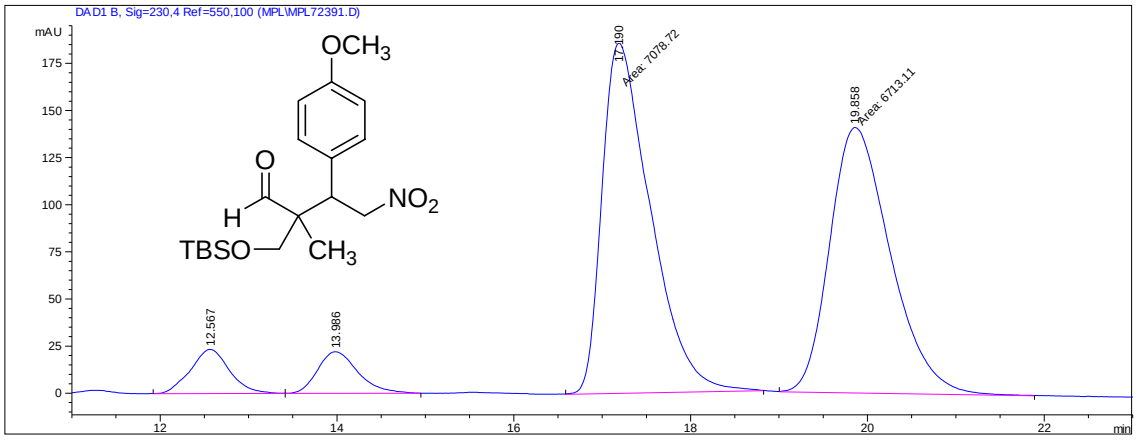


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area [%]
1	16.848	MF	0.4034	3495.52808	144.41087	97.2581
2	17.281	FM	0.3138	98.54705	5.23440	2.7419
Totals:				3594.07513	149.64527	

(2*S*,3*R*)-2-((*tert*-butyldimethylsilyloxy)methyl)-3-(4-methoxyphenyl)-2-methyl-4-nitrobutanal + (2*R*,3*R*)-2-((*tert*-butyldimethylsilyloxy)methyl)-3-(4-methoxyphenyl)-2-methyl-4-nitrobutanal (**13**): General procedure, chromatography on silica (15% diethyl ether/hexanes) diastereomers could not be separated, colorless to light yellow oil, 85% yield (325.4 mg), 7.1:1 dr, 99% ee (major diastereomer), 95% ee (minor diastereomer) as determined by HPLC (Chiralcel OD-H, 1.0% ethanol/hexanes, 1.0 mL/min, 230 nm; t_r(minor enantiomer, minor diastereomer) = 12.57 min, t_r(major enantiomer, minor diastereomer) = 13.99 min, t_r(minor enantiomer, major diastereomer) = 17.19 min, t_r(major enantiomer, major diastereomer) = 19.86 min). $[\alpha]^{25}_D$ = +9.0 (c = 0.0212g /2.0 mL, chloroform). ^{1}H NMR (400 MHz, $CDCl_3$): Signals corresponding to the major diastereomer δ 9.60 (1H, s), 7.16 (2H, d, J = 8.8 Hz), 6.83 (2H, d, J = 8.8 Hz), 4.85 (1H, dd, J = 11.7, 13.2 Hz), 4.76 (1H, dd, J = 4.2, 13.2 Hz), 4.06 (1H, dd, J = 4.2, 11.7 Hz), 3.77 (3H, s), 3.48 (1H, d, J = 10.4 Hz), 3.36 (1H, d, J = 10.4 Hz), 1.03 (3H, s), 0.90 (9H, s), 0.02 (3H, s), 0.01 (3H, s). Signals corresponding to the minor diastereomer δ 9.60 (1H, s), 7.12 (2H, d, J = 8.8 Hz), 6.85 (2H, d, J = 8.8 Hz), 5.02 (1H, dd, J = 11.7, 13.2 Hz), 4.82 (1H, dd, J = 3.7, 13.2 Hz), 3.95 (1H, dd, J = 3.7, 11.7 Hz), 3.77 (3H, s), 3.72 (1H, d, J = 11.0 Hz), 3.63 (1H, d, J = 11.0 Hz), 0.93 (9H, s), 0.81 (3H, s), 0.13 (3H, s), 0.09 (3H, s). ^{13}C (100 MHz, $CDCl_3$): Signals corresponding to the major diastereomer δ 204.2, 159.2, 130.1, 127.0, 113.9, 76.5, 65.8, 55.1, 53.4, 43.8, 25.7, 18.1, 13.6, –5.7, –5.8. Signals corresponding to the minor diastereomer δ 203.7, 130.3, 127.2, 114.0, 77.1, 64.7, 55.0, 53.6, 46.0, 25.6, 18.1, 16.8, –5.6, –5.7. IR (neat): 2956 (s), 2931 (s), 2857 (s), 2711 (m), 1727 (s), 1612 (m), 1559 (s), 1515 (s), 1471 (m), 1378 (m), 1253 (s), 1097 (s),

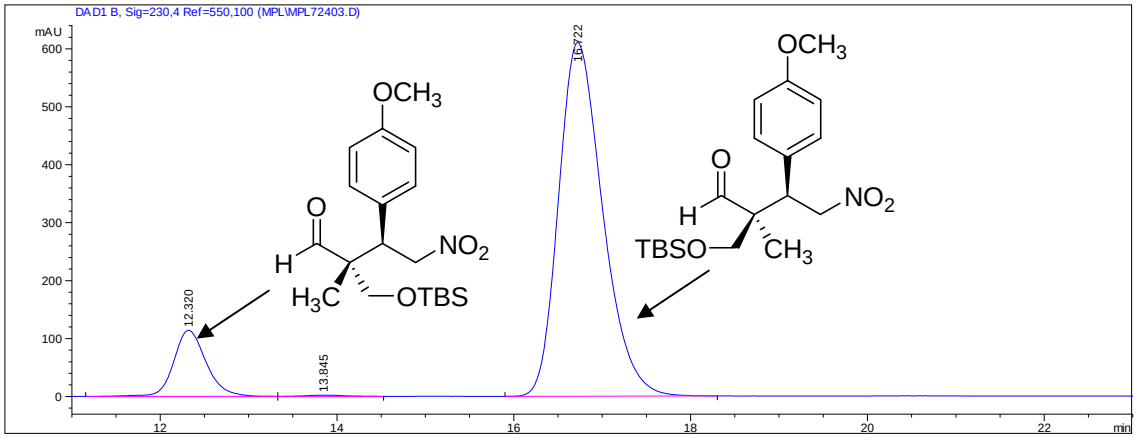
1036 (m), 838 (s), 779 (m). HRMS (ESI): expected for $[C_{19}H_{31}NO_5Si+NH_4]^+$: 399.2315, found: 399.2311.

Racemic 2-((*tert*-butyldimethylsilyloxy)methyl)-3-(4-methoxyphenyl)-2-methyl-4-nitrobutanal



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area [%]
1	12.567	VV	0.4630	723.73651	23.43773	4.7555
2	13.986	VV	0.4589	703.28253	22.13266	4.6211
3	17.190	MM	0.6346	7078.71680	185.90570	46.5128
4	19.858	MM	0.7937	6713.10840	140.97058	44.1105
Totals:				1.52188e4	372.44667	

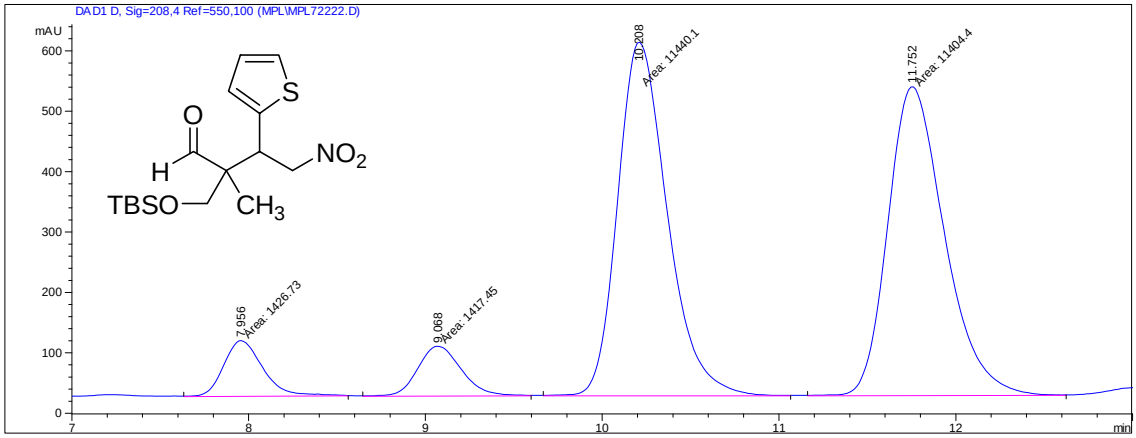
Enantioenriched (2*S*,3*R*)-2-((*tert*-butyldimethylsilyloxy)methyl)-3-(4-methoxyphenyl)-2-methyl-4-nitrobutanal + (2*R*,3*R*)-2-((*tert*-butyldimethylsilyloxy)methyl)-3-(4-methoxyphenyl)-2-methyl-4-nitrobutanal



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area [%]
1	12.320	VV	0.3901	2920.71484	114.09811	12.1030
2	13.845	VV	0.3947	66.05161	2.04576	0.2737
3	16.722	PV	0.5300	2.11454e4	610.57416	87.6233
Totals:				2.41322e4	726.71802	

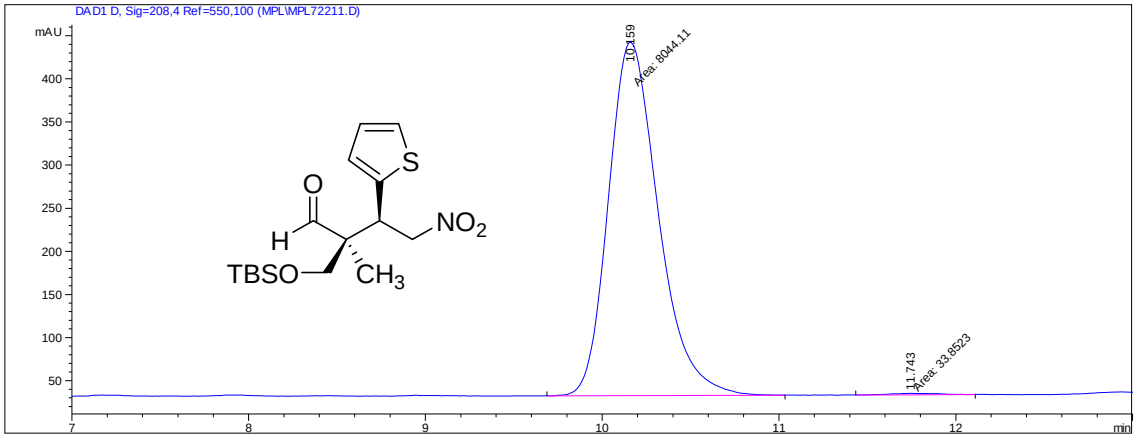
(2*S*,3*R*)-2-((*tert*-butyldimethylsilyloxy)methyl)-2-methyl-4-nitro-3-(thiophen-2-yl)butanal (**14**): General procedure, diastereomeric products separable by chromatography on silica (10% diethyl ether/hexanes), colorless to light yellow oil, 85% yield (304.9 mg), 6.6:1 dr (determined using the HPLC conditions below and the crude product mixture), 99% ee (major diastereomer) as determined by HPLC (Chiralcel OD-H, 1.0% ethanol/hexanes, 1.0 mL/min, 208 nm; t_r(major enantiomer, major diastereomer) = 10.21 min, t_r(minor enantiomer, major diastereomer) = 11.75 min). $[\alpha]^{25}_D$ = +20.4 (c = 0.0101 g/2.0 mL, chloroform). ^{1}H NMR (400 MHz, $CDCl_3$): δ 9.61 (1H, s), 7.24 (1H, dd, J = 1.1, 5.1 Hz), 6.96 (1H, dd, J = 3.5, 5.1 Hz), 6.95 (1H, dd, J = 1.1, 3.5 Hz), 4.80 (1H, dd, J = 4.4, 13.2 Hz), 4.75 (1H, dd, J = 10.6, 13.2 Hz), 4.46 (1H, dd, J = 4.4, 10.6 Hz), 3.59 (1H, d, J = 10.6 Hz), 3.45 (1H, d, 10.6 Hz), 1.11 (3H, s), 0.89 (9H, s), 0.02 (6H, s). ^{13}C (100 MHz, $CDCl_3$): δ 203.4, 137.7, 127.8, 126.8, 125.4, 77.8, 65.8, 53.4, 40.2, 25.7, 18.1, 13.6, –5.7, –5.8. IR (neat): 2956 (m), 2930 (m), 2857 (m), 2711 (w), 1728 (m), 1556 (s), 1437 (m), 1378 (m), 1253 (m), 1098 (m), 839 (s), 779 (m), 702 (m). HRMS (ESI): expected for $[C_{16}H_{27}NO_4SSi+NH_4]^+$: 375.1774, found: 375.1764.

Racemic 2-((*tert*-butyldimethylsilyloxy)methyl)-2-methyl-4-nitro-3-(thiophen-2-yl)butanal



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area [%]
1	7.956	MM	0.2574	1426.73389	92.36478	5.5540
2	9.068	MM	0.2859	1417.45203	82.62922	5.5178
3	10.208	MM	0.3254	1.14401e4	585.99036	44.5336
4	11.752	MM	0.3713	1.14044e4	511.94601	44.3946
Totals:				2.56886e4	1272.93037	

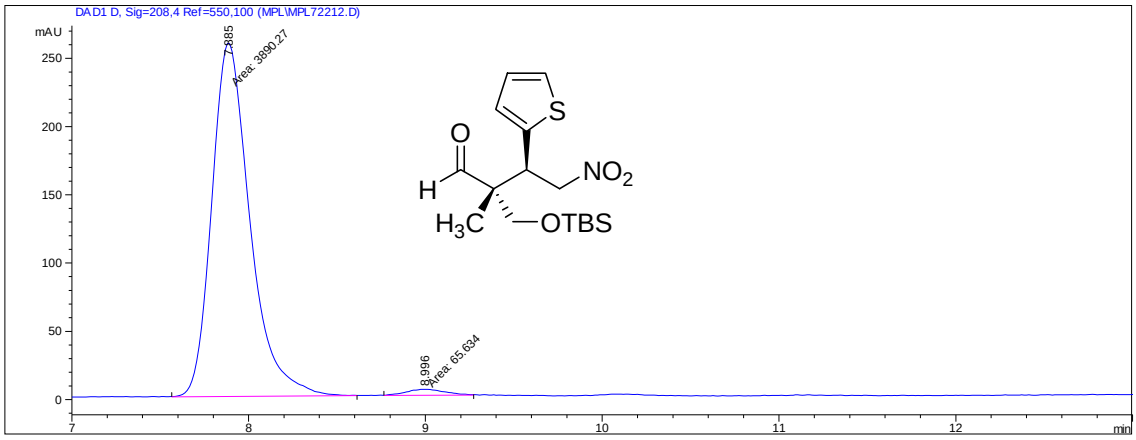
Enantioenriched (2*S*,3*R*)-2-((*tert*-butyldimethylsilyloxy)methyl)-2-methyl-4-nitro-3-(thiophen-2-yl)butanal



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area [%]
1	10.159	MM	0.3267	8044.11377	410.32178	99.5809
2	11.743	MM	0.3171	33.85229	1.77910	0.4191
Totals:				8077.96606	412.10087	

(2*R*,3*R*)-2-((*tert*-butyldimethylsilyloxy)methyl)-2-methyl-4-nitro-3-(thiophen-2-yl)butanal: 95% ee (minor diastereomer) as determined by HPLC (Chiralcel OD-H, 5.0% isopropanol/hexanes, 1.0 mL/min, 208 nm; t_r(major enantiomer, minor diastereomer) = 7.74 min, t_r(minor enantiomer, minor diastereomer) = 8.98 min). $[\alpha]^{25}_D$ = –2.3 (c = 0.0173 g/2.0 mL, chloroform). ^{1}H NMR (400 MHz, $CDCl_3$): δ 9.61 (1H, s), 7.25 (1H, dd, J = 1.1, 5.1 Hz), 6.96 (1H, dd, J = 3.5, 5.1 Hz), 6.93 (1H, dd, J = 1.1, 3.5 Hz), 4.89 (1H, dd, J = 11.3, 13.5 Hz), 4.80 (1H, dd, J = 3.7, 13.5 Hz), 4.40 (1H, dd, J = 3.7, 11.3 Hz), 3.84 (1H, d, J = 11.0 Hz), 3.79 (1H, d, J = 11.0 Hz), 0.92 (9H, s), 0.91 (3H, s), 0.14 (3H, s), 0.10 (3H, s). ^{13}C (100 MHz, $CDCl_3$): δ 202.9, 138.2, 127.9, 126.9, 125.5, 78.5, 64.8, 53.6, 42.2, 25.8, 18.1, 16.9, –5.6, –5.7. IR (neat): 2956 (s), 2930 (s), 2858 (s), 2715 (m), 1728 (s), 1555 (s), 1472 (m), 1378 (m), 1254 (m), 1094 (s), 838 (s), 780 (s), 702 (s). HRMS (ESI): expected for $[C_{16}H_{27}NO_4SSi+NH_4]^+$: 375.1774, found: 375.1769.

Enantioenriched (2*R*,3*R*)-2-((*tert*-butyldimethylsilyloxy)methyl)-2-methyl-4-nitro-3-(thiophen-2-yl)butanal

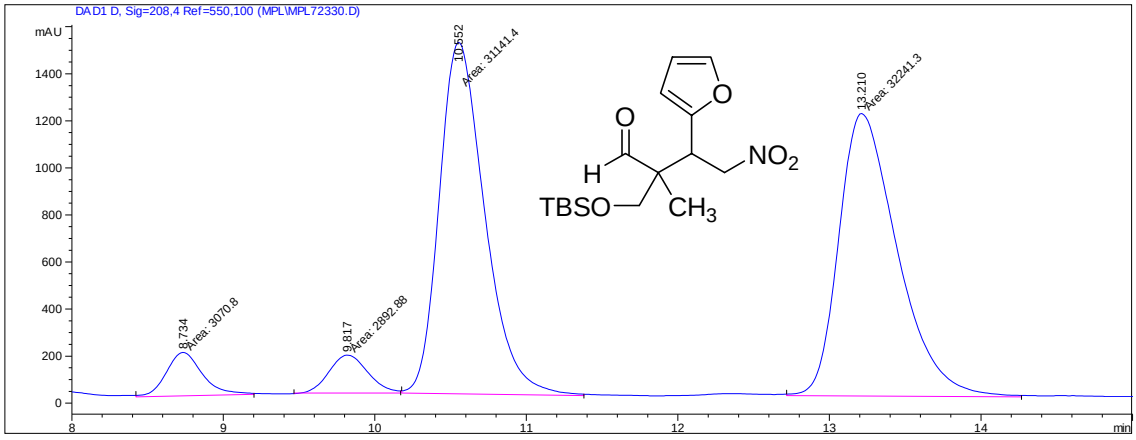


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area [%]
1	7.885	MM	0.2498	3890.26636	259.57452	98.3409
2	8.996	MM	0.2531	65.63396	4.32216	1.6591
Totals:				3955.90032	263.89668	

(2*S*,3*R*)-2-((*tert*-butyldimethylsilyloxy)methyl)-2-methyl-4-nitro-3-(furan-2-yl)butanal + (2*R*,3*R*)-2-((*tert*-butyldimethylsilyloxy)methyl)-2-methyl-4-nitro-3-(furan-2-yl)butanal (**15**): General procedure, chromatography on silica (10% diethyl ether/hexanes) diastereomers could not be separated, colorless to light yellow oil, 79% yield (271.7 mg), 5.4:1 dr, 99% ee (major diastereomer), 95% ee (minor diastereomer) as determined by HPLC (Chiralcel OD-H, 1.0% isopropanol/hexanes, 1.0 mL/min, 208 nm; t_r(major enantiomer, minor diastereomer) = 8.73 min, t_r(minor enantiomer, minor

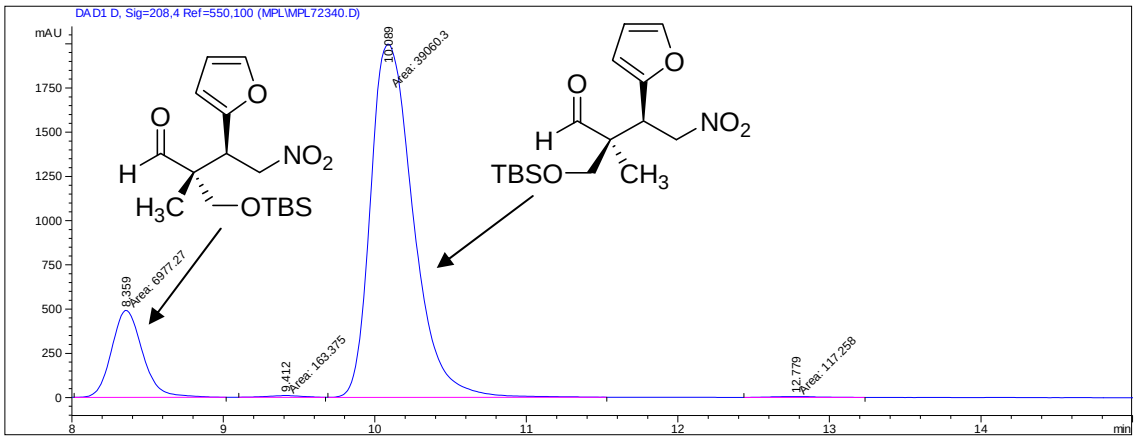
diastereomer) = 9.82 min, t_r(major enantiomer, major diastereomer) = 10.55 min, t_r(minor enantiomer, major diastereomer) = 13.21 min). $[\alpha]^{25}_D$ = +3.0 (c = 0.0209 g/2.0 mL, chloroform). ^{1}H NMR (400 MHz, $CDCl_3$): Signals corresponding to the major diastereomer δ 9.58 (1H, s), 7.35 (1H, dd, J = 0.7, 1.8 Hz), 6.30 (1H, dd, J = 1.8, 3.3 Hz), 6.22 (1H, dd, J = 0.7, 1.8 Hz), 4.80 (1H, dd, J = 11.3, 13.2 Hz), 4.68 (1H, dd, J = 3.7, 13.2 Hz), 4.21 (1H, dd, J = 3.7, 11.3 Hz), 3.54 (1H, d, J = 10.6 Hz), 3.42 (1H, d, J = 10.6 Hz), 1.09 (3H, s), 0.87 (9H, s), 0.00 (6H, s). Signals corresponding to the minor diastereomer δ 9.57 (1H, s), 7.35 (1H, dd, J = 0.7, 1.8 Hz), 6.30 (1H, dd, J = 1.8, 3.3 Hz), 6.20 (1H, dd, J = 0.7, 1.8 Hz), 4.89 (1H, dd, J = 11.3, 13.2 Hz), 4.73 (1H, dd, J = 3.7, 13.2 Hz), 4.18 (1H, dd, J = 3.7, 11.3 Hz), 3.78 (1H, d, J = 10.6 Hz), 3.75 (1H, d, J = 10.6 Hz), 0.90 (9H, s), 0.89 (3H, s), 0.10 (3H, s), 0.07 (3H, s). ^{13}C (100 MHz, $CDCl_3$): Signals corresponding to the major diastereomer δ 203.3, 149.7, 142.6, 110.4, 109.8, 74.9, 53.2, 38.5, 25.7, 18.0, 13.9, –5.8, –5.9. Signals corresponding to the minor diastereomer δ 202.8, 150.1, 142.7, 110.4, 109.6, 75.3, 65.2, 53.4, 40.1, 25.7, 18.1, 16.3, –5.7, –5.8. IR (neat): 2958 (s), 2931 (s), 2886 (m), 2858 (s), 2713 (m), 1733 (s), 1557 (s), 1472 (m), 1376 (m), 1254 (m), 1101 (s), 1015 (m), 840 (s), 779 (s), 737 (m). HRMS (ESI): expected for $[C_{16}H_{27}NO_5Si+NH_4]^+$: 359.2002, found: 359.1987.

Racemic 2-((*tert*-butyldimethylsilyloxy)methyl)-2-methyl-4-nitro-3-(furan-2-yl)butanal



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area [%]
1	8.734	MM	0.2887	3220.02832	185.88496	4.5858
2	9.817	MM	0.3198	3283.60132	171.10840	4.6763
3	10.552	MM	0.3522	3.18460e4	1507.09766	45.3534
4	13.210	MM	0.4432	3.18679e4	1198.31396	45.3845
Totals:				7.02176e4	3062.40498	

Enantioenriched (2*S*,3*R*)-2-((*tert*-butyldimethylsilyloxy)methyl)-2-methyl-4-nitro-3-(furan-2-yl)butanal + (2*R*,3*R*)-2-((*tert*-butyldimethylsilyloxy)methyl)-2-methyl-4-nitro-3-(furan-2-yl)butanal

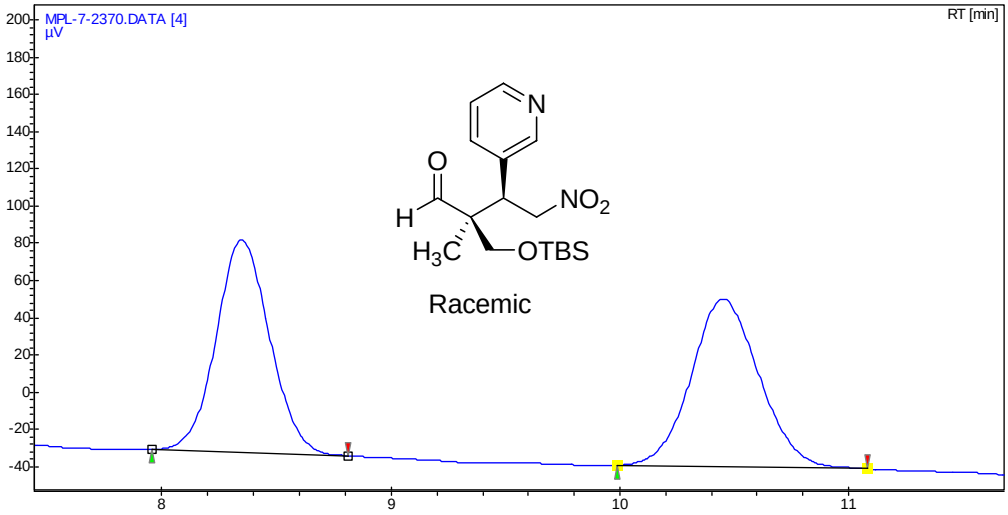


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area [%]
1	8.359	MM	0.2374	7019.18848	492.82800	15.1191
2	9.412	MM	0.2874	173.29816	10.04999	0.3733
3	10.089	MM	0.3259	3.90897e4	1999.21619	84.1981
4	12.779	MM	0.4413	143.67551	5.42637	0.3095
Totals:				4.64258e4	2507.52056	

(2*S*,3*R*)-2-((*tert*-butyldimethylsilyloxy)methyl)-2-methyl-4-nitro-3-(pyridin-3-yl)butanal + (2*R*,3*R*)-2-((*tert*-butyldimethylsilyloxy)methyl)-2-methyl-4-nitro-3-(pyridin-3-yl)butanal (**16**): Under a positive pressure of nitrogen at room temperature, thiourea catalyst **1** (75.3 mg, 0.20 mmol, 20 mol%) was loaded into an oven-dried 25 mL round-bottomed flask, equipped with a magnetic stir bar, rubber septum, and nitrogen inlet. The catalyst was dissolved in dichloromethane (6.7 mL). Water (90.1 μL, 5.0 mmol, 5.0 equiv.) and 3-(*tert*-butyldimethylsilyloxy)-2-methylpropanal (404.8 μg, 2.0 mmol, 2.0 equiv.) were subsequently added via syringe. The resulting clear colorless solution was stirred for approximately two minutes. Solid 3-(2-nitroethenyl)pyridine (150.1 mg, 1.0 mmol, 1.0 equiv.) was added in one portion resulting in a dark yellow solution. The rubber septum was quickly replaced with a yellow polyethylene stopper (to prevent dichloromethane evaporation) and the reaction mixture was stirred for 24 hours at room temperature. Aqueous hydrochloric acid solution (1M, 7 mL) was added to the reaction flask and the resulting biphasic mixture was stirred vigorously for 5 minutes at room temperature. The acidic solution was neutralized by the portion wise addition of solid sodium bicarbonate. The biphasic mixture was transferred to a separatory funnel and additional portions of dichloromethane (30 mL) and saturated aqueous sodium bicarbonate (30 mL) were added. The phases were separated and the aqueous layer was washed with dichloromethane (30 mL). The organic layers were combined and washed with saturated aqueous sodium chloride solution (30 mL), dried over anhydrous sodium

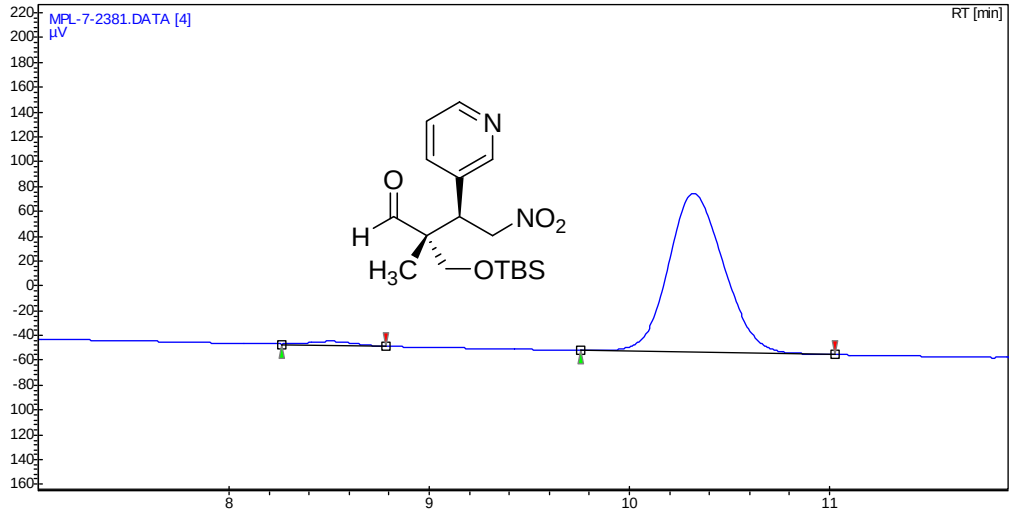
sulfate, filtered, and concentrated *in vacuo*. Chromatography on silica (1.0% methanol/dichloromethane) diastereomers could not be separated, colorless to light yellow oil, 94% yield (332.3 mg), 5.6:1 dr as determined by SFC (Chiralcel OD-H, 2.0% methanol/CO_2, 2.0 mL/min, 208 nm, 30 °C; t_r(minor enantiomer, minor diastereomer) = 8.39 min, t_r(major enantiomer, minor diastereomer) = 10.49 min, t_r(major enantiomer, major diastereomer) = 13.11 min, t_r(minor enantiomer, major diastereomer) = 14.03 min), 99% ee (major diastereomer) as determined by HPLC (Chiralcel OD-H 2.5% ethanol/hexanes, 1.0 mL/min, 208 nm; t_r(minor enantiomer, major diastereomer) = 30.27 min, t_r(minor enantiomer, major diastereomer) = 34.50 min), 96% ee (minor diastereomer) as determined by SFC (Chiralcel OD-H, 2.0% methanol/CO_2, 2.0 mL/min, 208 nm, 30 °C; t_r(minor enantiomer, minor diastereomer) = 8.39 min, t_r(major enantiomer, minor diastereomer) = 10.49 min). $[\alpha]^{25}_D$ = +7.3 (c = 0.0200 g/2.0 mL, chloroform). ^{1}H NMR (400 MHz, $CDCl_3$): Signals corresponding to the major diastereomer δ 9.54 (1H, s), 8.53 (2H, m), 7.62 (1H, dt, J = 1.8, 8.1 Hz), 7.25 (1H, ddd, J = 0.7, 4.0, 8.1 Hz), 4.88 (2H, d, J = 7.7 Hz), 4.16 (1H, t, J = 7.7 Hz), 3.56 (1H, d, J = 10.6 Hz), 3.25 (1H, d, J = 10.6 Hz), 1.02 (3H, s), 0.88 (9H, s), 0.00 (6H, s). Signals corresponding to the minor diastereomer δ 9.56 (1H, s), 8.53 (1H, m), 8.48 (1H, dd, J = 1.5, 4.8 Hz), 7.59 (1H, dt, J = 1.8, 8.1 Hz), 7.27 (1H, ddd, J = 0.7, 4.0, 8.1 Hz), 5.06 (1H, dd, J = 11.7, 13.9 Hz), 4.85 (1H, dd, J = 3.3, 13.9 Hz), 4.02 (1H, dd, J = 3.3, 11.7 Hz), 3.77 (1H, d, J = 11.7 Hz), 3.58 (1H, d, J = 11.7 Hz), 0.92 (9H, s), 0.80 (3H, s), 0.12 (3H, s), 0.09 (3H, s). ^{13}C (100 MHz, $CDCl_3$): Signals corresponding to the major diastereomer δ 202.9, 150.6, 149.4, 136.4, 131.4, 123.4, 75.9, 65.6, 53.4, 42.0, 25.7, 18.1, 13.5, –5.7, -5.9. Signals corresponding to the minor diastereomer δ 202.5, 150.6, 149.4, 136.5, 131.6, 123.5, 76.4, 64.4, 53.5, 44.3, 25.8, 18.0, 16.9, –5.7, –5.9. IR (neat): 3034 (m), 2955 (s), 2931 (s), 2713 (m), 1728 (s), 1556 (s), 1471 (m), 1429 (m), 1377 (s), 1255 (s), 1097 (s), 839 (s), 780 (s), 714 (s). HRMS (ESI): expected for $[C_{17}H_{28}N_2O_4Si+H]^+$: 353.1896, found: 353.1900.

Racemic 2-((*tert*-butyldimethylsilyloxy)methyl)-2-methyl-4-nitro-3-(pyridin-3-yl)butanal (minor diastereomer)



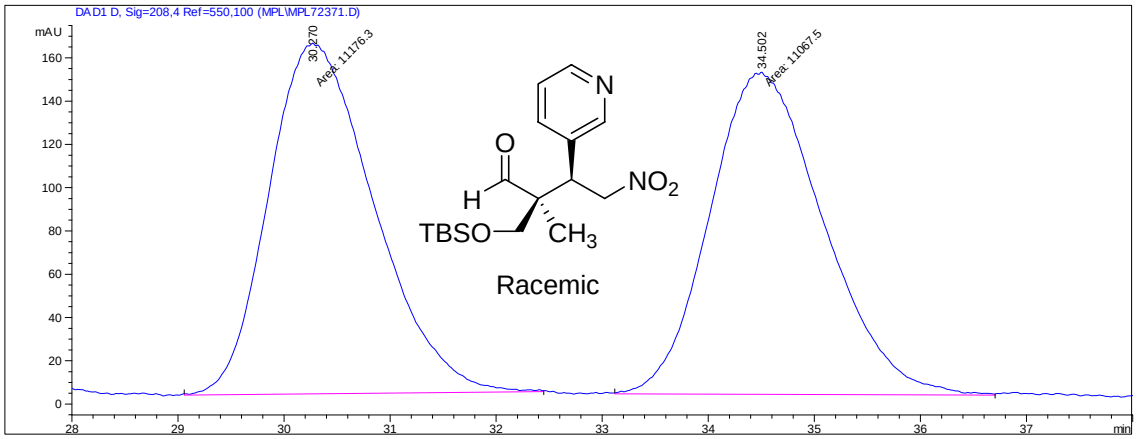
#	Time [Min]	Height [µV]	Area [µV.Min]	Area [%]
1	8.35	114.2	31.0	49.885
2	10.45	90.2	31.1	50.115
Total		204.4	62.1	100.000

Enantioenriched (2*R*,3*R*)-2-((*tert*-butyldimethylsilyloxy)methyl)-2-methyl-4-nitro-3-(pyridin-3-yl)butanal



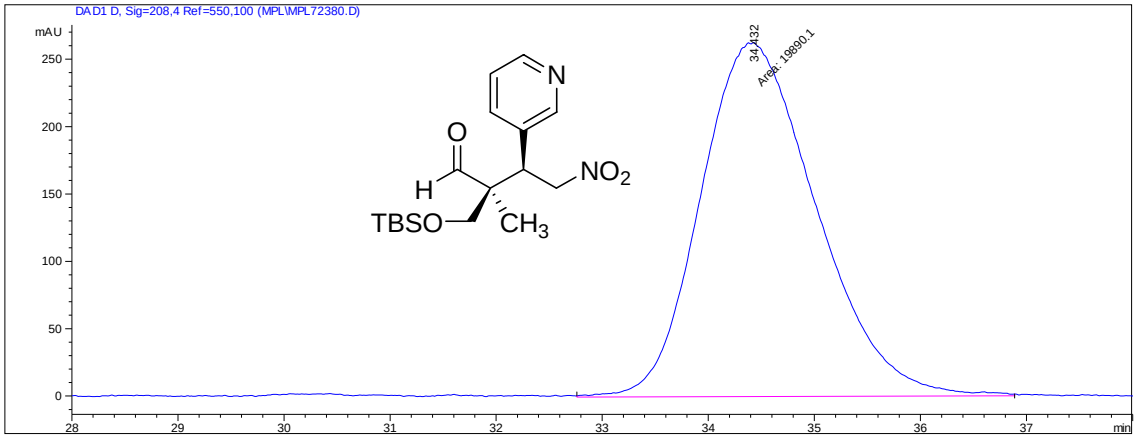
#	Time [Min]	Height [µV]	Area [µV.Min]	Area [%]
1	8.52	3.1	0.8	1.832
2	10.33	128.1	40.9	98.168
Total		131.2	41.7	100.000

Racemic 2-((*tert*-butyldimethylsilyloxy)methyl)-2-methyl-4-nitro-3-(pyridin-3-yl)butanal (major diastereomer)



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area [%]
1	30.270	MM	1.1486	1.11763e4	162.17905	50.2446
2	34.502	MM	1.2375	1.10675e4	149.05533	49.7554
Totals:				2.22438e4	311.23438	

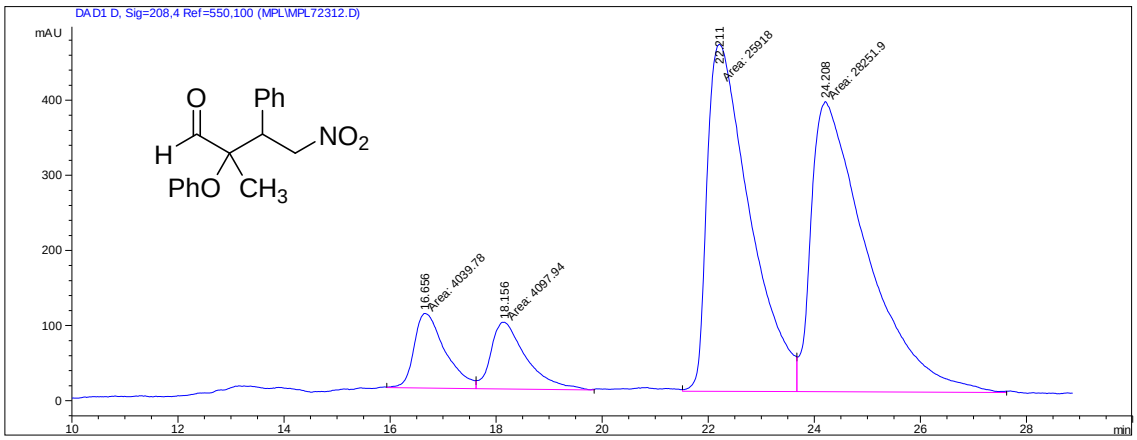
Enantioenriched (2*S*,3*R*)-2-((*tert*-butyldimethylsilyloxy)methyl)-2-methyl-4-nitro-3-(pyridin-3-yl)butanal



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area [%]
1	34.432	MM	1.2618	1.98901e4	262.72925	100.0000
Totals:				1.98901e4	262.72925	

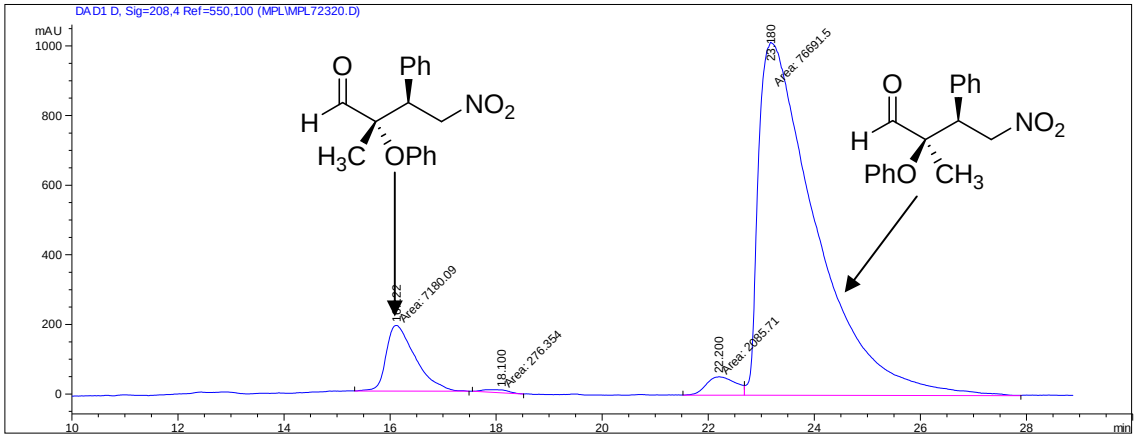
(2*R*,3*S*)-2-methyl-4-nitro-2-phenoxy-3-phenylbutanal + (2*S*,3*S*)-2-methyl-4-nitro-2-phenoxy-3-phenylbutanal (**17**): General procedure, chromatography on silica (15% diethyl ether/hexanes) diastereomers could not be separated, colorless to light yellow oil, 78% yield (233.5 mg), 10.4:1 dr, 92% ee (minor diastereomer), 94% ee (major diastereomer) as determined by HPLC ((*R*,*R*)-Whelk-01, 5.0% isopropanol/hexanes, 1.0 mL/min, 208 nm; t_r(major enantiomer, minor diastereomer) = 16.66 min, t_r(minor enantiomer, minor diastereomer) = 18.16 min, t_r(minor enantiomer, major diastereomer) = 22.21 min, t_r(major enantiomer, major diastereomer) = 24.21 min). $[\alpha]^{25}_D$ = –61.0 (c = 0.0212 g/2.0 mL, chloroform). ^{1}H NMR (400 MHz, $CDCl_3$): Signals corresponding to the major diastereomer δ 10.02 (1H, s), 7.42-7.33 (5H, m), 7.27 (2H, m), 7.10 (1H, m), 6.88 (2H, m), 5.07 (1H, dd, J = 9.9, 13.5 Hz), 5.00 (1H, dd, J = 5.1, 13.5 Hz), 4.05 (1H, dd, J = 5.1, 9.9 Hz), 1.14 (3H, s). Signals corresponding to the minor diastereomer δ 9.59 (1H, s), 7.42-7.33 (5H, m), 7.28 (2H, m), 7.09 (1H, m), 6.84 (2H, m), 5.14 (1H, dd, J = 5.1, 13.2 Hz), 5.08 (1H, dd, J = 9.9, 13.2 Hz), 3.91 (1H, dd, J = 5.1, 9.9 Hz), 1.50 (3H, s). ^{13}C (100 MHz, $CDCl_3$): Signals corresponding to the major diastereomer δ 201.7, 154.0, 134.1, 129.5, 129.4, 128.8, 128.6, 124.0, 121.3, 86.5, 75.6, 49.5, 17.0. Signals corresponding to the minor diastereomer δ 203.2, 154.2, 133.7, 129.7, 129.5, 128.9, 128.3, 123.5, 119.7, 85.2, 76.0, 51.9, 18.1. IR (neat): 3065 (m), 3036 (m), 3008 (m), 2921 (m), 2817 (m), 2714 (m), 1736 (s), 1590 (s), 1554 (s), 1492 (s), 1455 (m), 1379 (s), 1219 (s), 1109 (m), 916 (m), 786 (m), 759 (m), 702 (s). HRMS (ESI): expected for $[C_{17}H_{17}NO_4+NH_4]^+$: 317.1501, found: 317.1516.

Racemic 2-methyl-4-nitro-2-phenoxy-3-phenylbutanal



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area [%]
1	16.656	MM	0.6981	4215.40381	100.64341	6.8115
2	18.156	MM	0.7712	4133.89746	89.33551	6.6798
3	22.221	MM	0.9340	2.58337e4	461.00085	41.7439
4	24.208	MM	1.1999	2.77032e4	384.81418	44.7648
Totals:				6.18862e4	1035.79395	

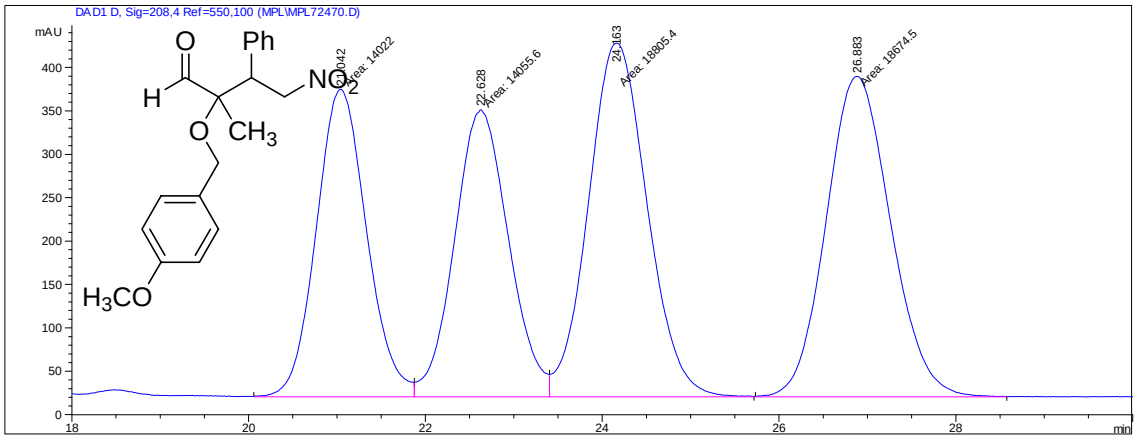
Enantioenriched (2*R*,3*S*)-2-methyl-4-nitro-2-phenoxy-3-phenylbutanal + (2*S*,3*S*)-2-methyl-4-nitro-2-phenoxy-3-phenylbutanal



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area [%]
1	16.122	MM	0.6415	7309.00879	189.89044	8.4384
2	18.100	MM	0.5758	316.11319	9.14928	0.3650
3	22.200	MM	0.6886	2297.62646	55.61406	2.6526
4	23.180	MM	1.2611	7.66937e4	1013.59253	88.5440
Totals:				8.66164e4	1268.24632	

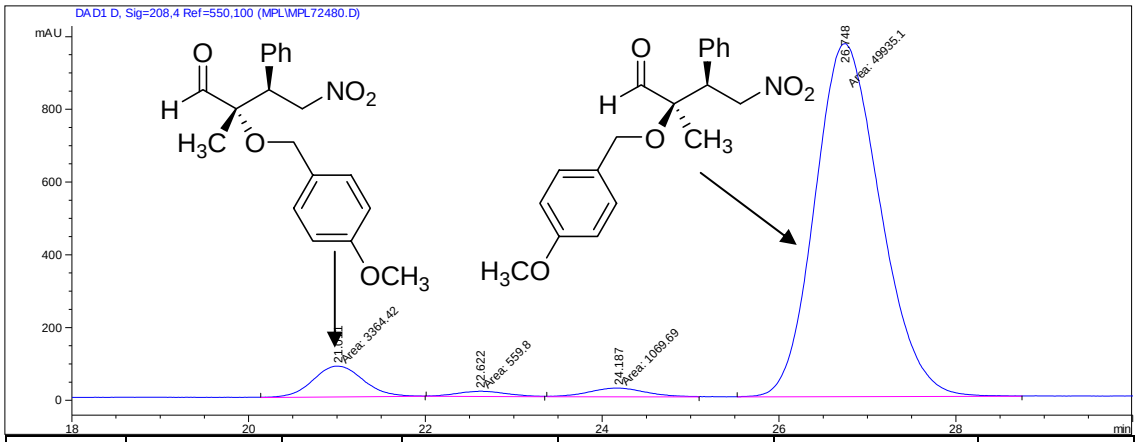
(2*R*,3*S*)-2-(4-methoxybenzyloxy)-2-methyl-4-nitro-3-phenylbutanal (**18**): General procedure, chromatography on silica (20% diethyl ether/hexanes), colorless to light yellow liquid, 78% yield (267.9 mg), 13:1 dr, 71% ee (minor diastereomer), 96% ee (major diastereomer) as determined by HPLC (Chiralcel OD-H, 5.0% ethanol/hexanes, 1.0 mL/min, 208 nm; t_r(minor diastereomer) = 21.04 min, t_r(minor diastereomer) = 22.63 min, t_r(minor enantiomer, major diastereomer) = 24.16 min, t_r(major enantiomer, major diastereomer) = 26.88 min). $[\alpha]^{25}_D$ = –88.0 (c = 0.0202 g/2.0 mL, chloroform). ^{1}H NMR (400 MHz, $CDCl_3$): δ 9.76 (1H, s), 7.3 (2H, m), 6.93 (2H, m), 4.89 (1H, dd, J = 10.2, 13.5 Hz), 4.80 (1H, dd, J = 4.8, 13.5 Hz), 4.42 (2H, s), 3.87 (1H, dd, J = 4.8, 10.2 Hz), 3.83 (3H, s), 1.24 (3H, s). ^{13}C (100 MHz, $CDCl_3$): δ 202.3, 159.4, 134.4, 129.5, 129.4, 129.2, 128.7, 128.4, 113.9, 83.6, 75.8, 66.6, 55.2, 49.1, 16.1. IR (neat): 3064 (m), 3039 (m), 3003 (m), 2950 (m), 2834 (m), 1731 (s), 1601 (m), 1562 (s), 1512 (s), 1445 (m), 1385 (s), 1307 (m), 1247 (s), 1169 (s), 1130 (s), 1064 (m), 1032 (s), 822 (s), 757 (m), 709 (s). HRMS (ESI): expected for $[C_{19}H_{21}NO_5+NH_4]^+$: 361.1763, found: 361.1752.

Racemic 2-(4-methoxybenzyloxy)-2-methyl-4-nitro-3-phenylbutanal



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area [%]
1	21.042	MF	0.6592	1.40220e4	354.53027	21.3889
2	22.628	MF	0.7078	1.40556e4	330.96271	21.4401
3	24.163	FM	0.7691	1.88054e4	407.52982	28.6853
4	26.883	MM	0.8430	1.86745e4	369.20105	28.4857
Totals:				6.55575e4	1462.22385	

Enantioenriched (2*R*,3*S*)-2-(4-methoxybenzyloxy)-2-methyl-4-nitro-3-phenylbutanal

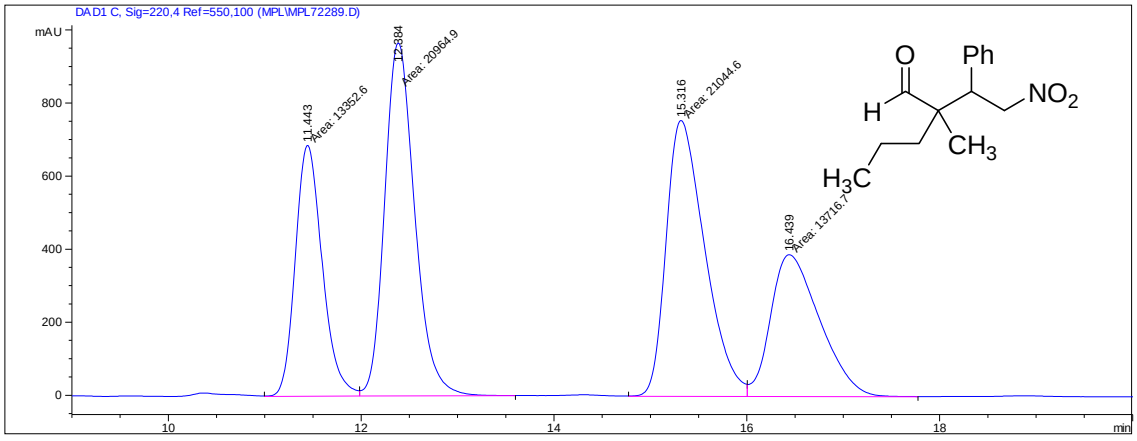


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area [%]
1	21.011	MM	0.6594	3364.41528	85.04200	6.1250
2	22.622	MM	0.6496	559.79999	14.36372	1.0191
3	24.187	MM	0.7454	1069.68701	23.91820	1.9474
4	26.748	MM	0.8569	4.99351e4	971.18719	90.9084
Totals:				5.49290e4	1094.51112	

(*R*)-2-methyl-2-((*R*)-2-nitro-1-phenylethyl)pentanal + (*S*)-2-methyl-2-((*R*)-2-nitro-1-

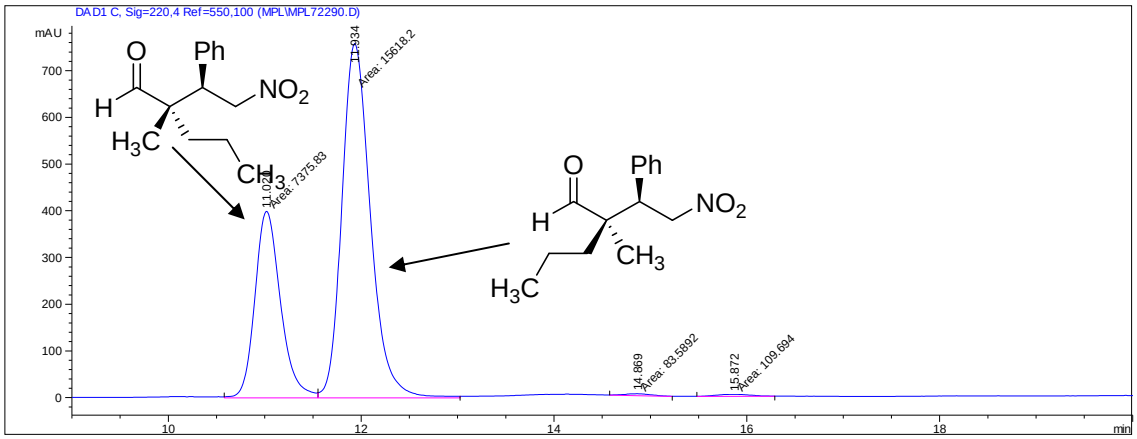
phenylethyl)pentanal (**19**): General procedure, chromatography on silica (10% diethyl ether/hexanes) diastereomers could not be separated, colorless to light yellow oil, 98% yield (244.7 mg), 2.1:1 dr, 99% ee (major diastereomer), 97% ee (minor diastereomer) as determined by HPLC (Chiralcel OD-H, 5.0% ethanol/hexane, 1.0 mL/min, 220 nm; t_r(major enantiomer, minor diastereomer) = 11.44 min, t_r(major enantiomer, major diastereomer) = 12.38 min, t_r(minor enantiomer, major diastereomer) = 15.32 min, t_r(minor enantiomer, minor diastereomer) = 16.44 min). $[\alpha]^{25}_D$ = +19.1 (c = 0.0200 g/2.0 mL, chloroform). ^{1}H NMR (400 MHz, $CDCl_3$): Signals corresponding to the major diastereomer δ 9.52 (1H, s), 7.30 (5H, m), 4.83 (1H, dd, J = 11.3, 13.2 Hz), 4.62 (1H, dd, J = 4.0, 13.2 Hz), 3.79 (1H, dd, J = 4.0, 11.3 Hz), 1.46 (1H, m), δ 1.32 (1H, m), 1.20 (2H, m), 1.10 (3H, s), 0.82 (3H, t, J = 7.3 Hz). Signals to the major diastereomer δ 9.50 (1H, s), 7.18 (5H, m), 4.85 (1H, dd, J = 11.3, 13.2 Hz), 4.75 (1H, dd, J = 4.4, 13.2 Hz), 3.77 (1H, dd, J = 4.4 11.3 Hz), 1.62 (1H, m), 1.46 (1H, m), 1.20 (2H, m), 1.08 (3H, s), 0.89 (3H, t, J = 7.3 Hz). ^{13}C (100 MHz, $CDCl_3$): Signals corresponding to the major diastereomer δ 205.3, 135.2, 129.1, 128.6, 128.0, 76.6, 51.6, 47.5, 37.5, 17.0, 15.7, 14.4. Signals corresponding to the minor diastereomer δ 204.9,135.2, 129.0, 128.6, 128.1, 76.2, 51.0, 49.1, 36.4, 17.2, 17.0, 14.5. IR (neat): 3032 (m), 2962 (s), 2935 (s), 2875 (s), 2720 (m), 1723 (s), 1556 (s), 1497 (m), 1455 (s), 1436 (m), 1379 (s), 1203 (m), 1090 (m), 913 (m), 751 (m), 705 (s). HRMS (ESI): expected for $[C_{14}H_{19}NO_3+NH_4]^+$: 267.1709, found: 267.1711.

Racemic 2-methyl-2-(2-nitro-1-phenylethyl)pentanal



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area [%]
1	11.443	MF	0.3237	1.33526e4	687.59418	19.3295
2	12.384	FM	0.3612	2.09649e4	967.24445	30.3492
3	15.316	MF	0.4643	2.10446e4	755.43335	30.4646
4	16.439	FM	0.5888	1.37167e4	388.26694	19.8566
Totals:				6.90788e4	2798.53891	

Enantioenriched (*R*)-2-methyl-2-((*R*)-2-nitro-1-phenylethyl)pentanal + (*S*)-2-methyl-2-((*R*)-2-nitro-1-phenylethyl)pentanal

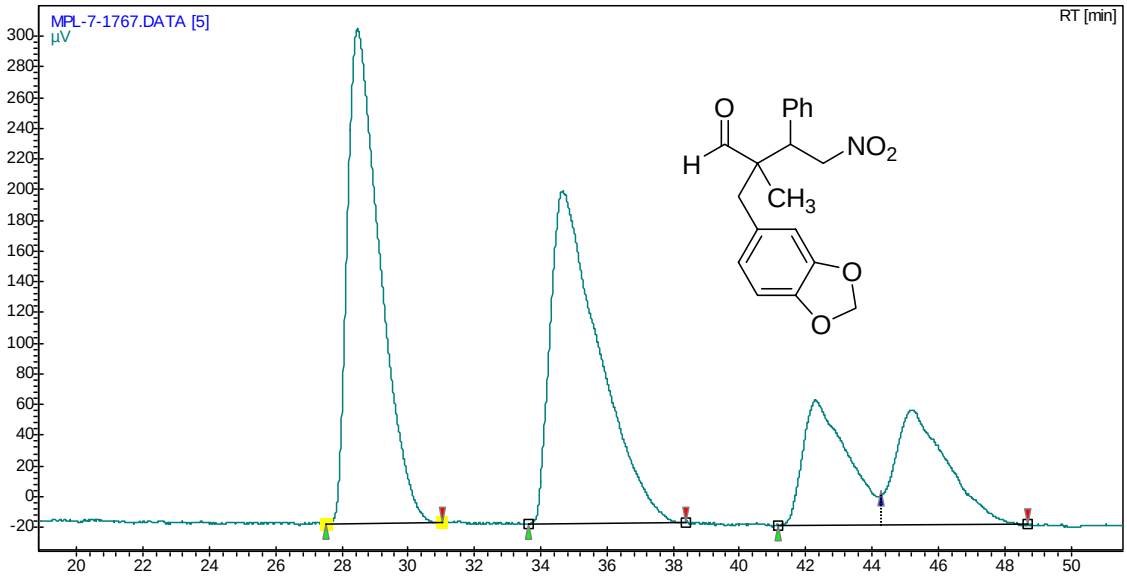


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area [%]
1	11.020	MF	0.3073	7375.82764	687.59418	31.8098
2	11.934	FM	0.3429	1.56182e4	967.24445	67.3567
3	14.869	MM	0.3403	83.58918	755.43335	0.3605
4	15.872	MM	0.4016	109.69353	388.26694	0.4731
Totals:				2.31873e4	2798.53891	

(2*R*,3*R*)-2-(benzo[*d*][1,3]dioxol-5-ylmethyl)-2-methyl-4-nitro-3-phenylbutanal + (2*S*,3*R*)-2-(benzo[*d*][1,3]dioxol-5-ylmethyl)-2-methyl-4-nitro-3-phenylbutanal (**20**): General procedure, chromatography on silica (20% diethyl ether/hexanes) diastereomers could not be separated, white solid, m.p. = 136 °C, 82% yield (278.8 mg), 3.1:1 dr, 99% ee (major diastereomer), 99% ee (minor diastereomer) as determined by SFC (Chiralcel OD-H, 3.0% methanol/CO_2, 3.0 mL/min, 208 nm, 30 °C; t_r(major enantiomer, major diastereomer) = 28.47 min, t_r(minor enantiomer, major diastereomer) = 34.67 min, t_r(major enantiomer, minor diastereomer) = 42.29 min, t_r(minor enantiomer, minor diastereomer) = 45.25 min). $[\alpha]^{25}_D$ = +25.3 (c = 0.0212 g/2.0 mL, chloroform). ^{1}H NMR (400 MHz, $CDCl_3$): Signals corresponding to the major diastereomer δ 9.62 (1H, s), 7.34 (3H, m), 7.22 (2H, m), 6.68 (1H, d, J = 7.7 Hz), 6.43 (2H, m), 5.91 (2H, s), 4.90 (1H, dd, J = 11.7, 13.2 Hz), 4.64 (1H, dd, J = 4.0, 13.2 Hz), 3.82 (1H, dd, J = 4.0, 11.7 Hz), 3.01 (1H, d, J = 13.7 Hz), 2.32 (1H, d, J = 13.7 Hz), 1.06 (3H, s). Signals corresponding to the minor diastereomer δ 9.59 (1H, s), 7.34 (3H, m), 7.22 (2H, m), 6.69 (1H, d, J = 7.7 Hz), 6.49 (2H, m), 5.91 (2H, s), 4.82 (2H, m), 3.83 (1H, m), 3.04 (1H, d, J = 13.5 Hz), 2.67 (1H, d, J = 13.5 Hz), 1.25 (3H, s). ^{13}C (100 MHz, $CDCl_3$): Signals corresponding to the major diastereomer δ 205.8, 147.6, 135.1, 129.3, 128.8,128.6, 128.3, 123.3, 110.4, 108.2, 101.0, 76.7, 52.3, 48.7, 42.1, 17.8. Signals corresponding to the minor diastereomer δ 204.6, 146.6, 135.0, 129.2, 129.2, 129.0, 128.9, 128.4, 123.4, 110.5, 108.2, 101.0, 76.2, 51.8, 49.5, 40.3, 17.8. IR (neat): 3031 (w), 2982 (w), 2919 (w), 2778 (w), 2724 (w), 1723

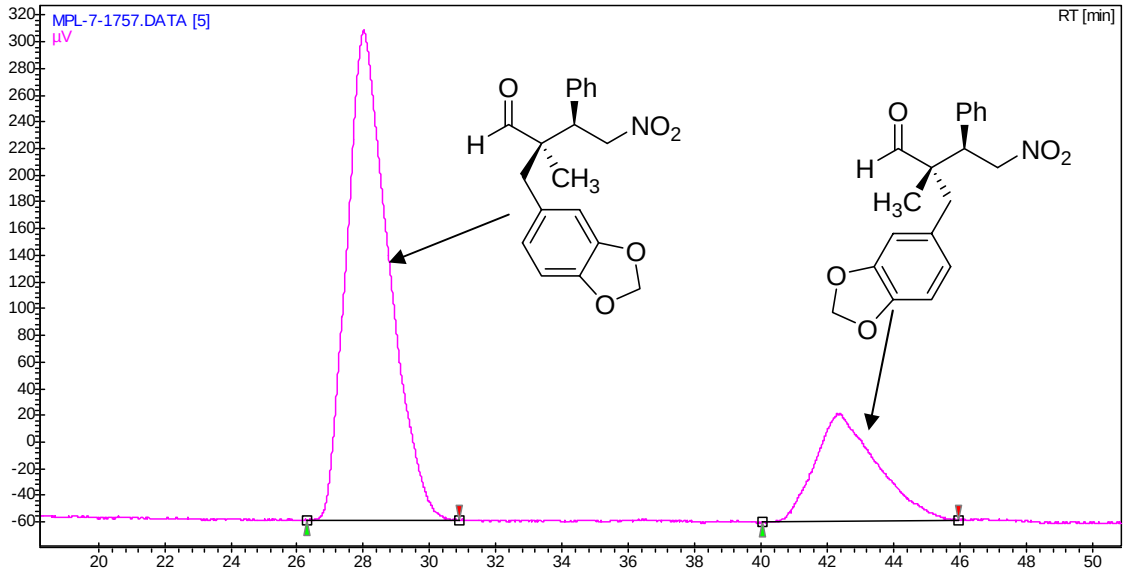
(m), 1555 (s), 1490 (s), 1455 (m), 1379 (m), 1252 (s), 1039 (s), 929 (m), 752 (m), 705 (m). HRMS (ESI): expected for $[C_{19}H_{19}NO_5+NH_4]^+$: 359.1607, found: 359.1592.

Racemic 2-(benzo[*d*][1,3]dioxol-5-ylmethyl)-2-methyl-4-nitro-3-phenylbutanal



#	Time [Min]	Height [µV]	Area [µV.Min]	Area [%]
1	28.47	321.9	367.9	36.752
2	34.67	216.5	368.1	36.774
3	42.29	81.4	128.7	12.858
4	45.25	75.0	136.3	13.616
Total		694.8	1001.0	100.000

(2*R*,3*R*)-2-(benzo[*d*][1,3]dioxol-5-ylmethyl)-2-methyl-4-nitro-3-phenylbutanal + (2*S*,3*R*)-2-(benzo[*d*][1,3]dioxol-5-ylmethyl)-2-methyl-4-nitro-3-phenylbutanal

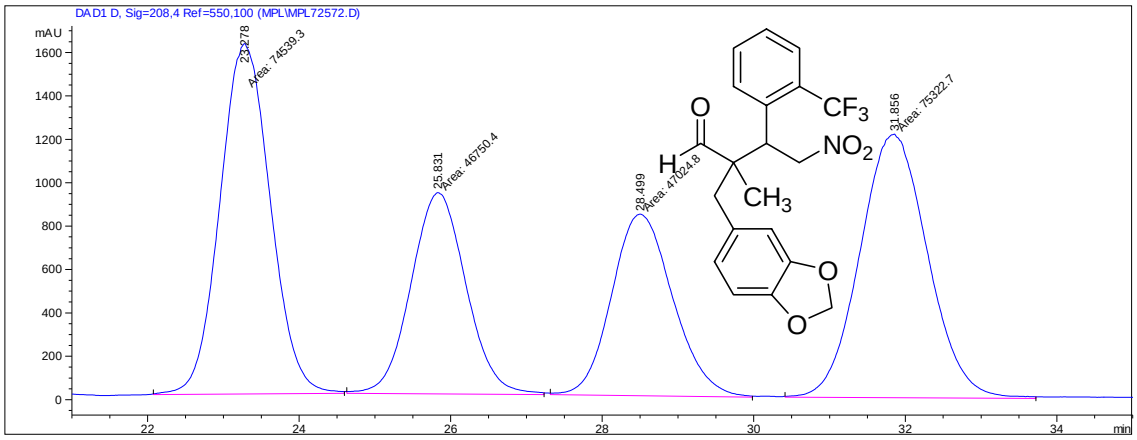


#	Time [Min]	Height [µV]	Area [µV.Min]	Area [%]
1	28.01	367.0	539.0	75.748
2	42.39	80.3	172.6	24.252
Total		447.2	711.5	100.000

(2*R*,3*R*)-2-(benzo[*d*][1,3]dioxol-5-ylmethyl)-2-methyl-4-nitro-3-(2-(trifluoromethyl)phenyl)butanal + (2*R*,3*R*)-2-(benzo[*d*][1,3]dioxol-5-ylmethyl)-2-methyl-4-nitro-3-(2-(trifluoromethyl)phenyl)butanal (**21**): General procedure, chromatography on silica (20% diethyl ether/hexanes) diastereomers could not be separated, white solid, m.p. = 128-130 °C, 63% yield (258.6 mg), 4.7:1 dr, 98% ee (major diastereomer), 93% ee (minor diastereomer) as determined by HPLC (Chiralcel OD-H, 10.0% ethanol/hexane, 1.0 mL/min, 208 nm; t_r(major enantiomer, major diastereomer) = 23.28 min, t_r(minor enantiomer, minor diastereomer) = 25.83 min, t_r(major enantiomer, minor diastereomer) = 28.50 min, t_r(minor enantiomer, major diastereomer) = 31.86 min). $[\alpha]^{25}_D$ = –10.8 (c = 0.0202 g/2.0 mL, chloroform). ^{1}H NMR (400 MHz, $CDCl_3$): Signals corresponding to the major diastereomer δ 9.62 (1H, s), 7.72-7.36 (4H, m), 6.72 (1H, m), 6.54 (2H, m), 5.92 (2H, s), 4.93 (1H, dd, J = 10.2, 11.7 Hz), 4.83 (1H, dd, J = 3.7, 11.7 Hz), 4.24 (1H, dd, J = 3.7, 10.2 Hz), 3.07 (1H, d, J = 13.7 Hz), 2.49 (1H, d, J = 13.9 Hz), 1.00 (3H, s). Signals corresponding to the minor diastereomer δ 9.52 (1H, s), 7.72-7.36 (4H, m), 6.71 (1H, m), 6.54 (2H, m), 4.80 (1H, dd, J = 4.4, 12.1), 4.75 (1H, dd, J = 9.9, 12.1 Hz), 4.28 (1H, dd, J = 4.4, 9.9 Hz), 2.91 (1H, d, J = 13.9 Hz), 2.77 (1H, d, J = 13.9 Hz), 1.18 (3H, s). ^{13}C (100 MHz, $CDCl_3$): Signals corresponding to the major diastereomer δ 205.3, 147.6, 146.7, 135.9, 132.4, 130.2 (1C, q, J = 29.0 Hz), 129.2, 128.2, 128.1, 127.3 (1C, q, J =6.1 Hz), 124.0 (1C, q, J = 274.7 Hz), 123.6, 110.5, 108.2,

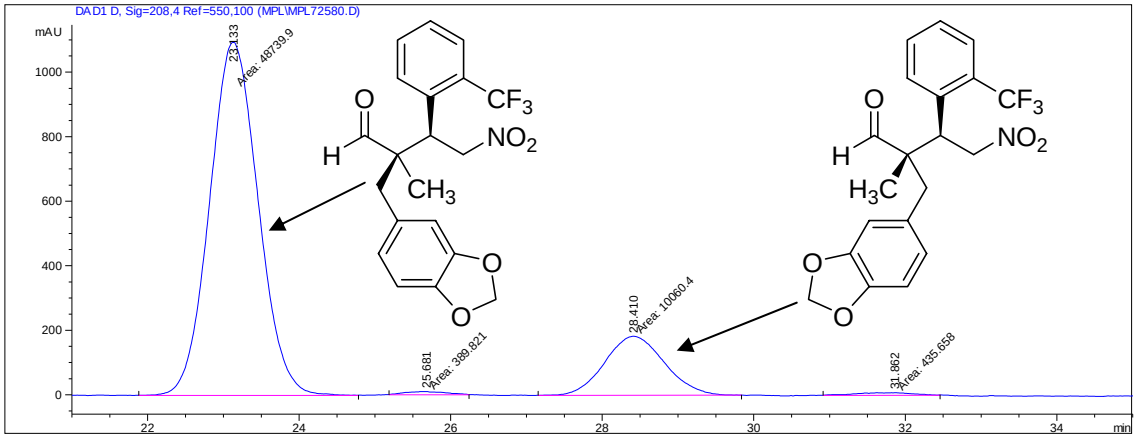
101.0, 78.2, 53.0, 43.6, 41.5, 17.2. Signals corresponding to the minor diastereomer δ 203.8, 147.7, 146.7, 153.2, 132.5, 130.2 (1C, q, J = 29.0 Hz), 128.9, 128.5, 128.4, 127.0 (1C, q, J = 6.1 Hz), 124.0 (1C, q, J = 274.7 Hz), 123.5, 110.5, 108.2, 101.0, 77.6, 52.2, 44.0, 41.3, 17.8. IR (neat): 3078 (w), 2991 (w), 2904 (w), 2779 (w), 2730 (w), 1725 (m), 1491 (s), 1454 (m), 1379 (m), 1310 (s), 1253 (s), 1163 (m), 1122 (s), 1037 (s), 929 (m), 772 (m), 733 (m). HRMS (ESI): expected for $[C_{20}H_{18}F_3NO_5+NH_4]^+$: 427.1481, found: 427.1501.

Racemic2-(benzo[*d*][1,3]dioxol-5-ylmethyl)-2-methyl-4-nitro-3-(2-(trifluoromethyl) phenyl)butanal



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area [%]
1	23.278	MM	0.7687	7.45393e4	1616.07373	30.5944
2	25.831	MM	0.8398	4.67504e4	927.86145	19.1885
3	28.499	MM	0.9367	4.70248e4	836.73743	19.3012
4	31.856	MM	1.0328	7.53227e4	1215.49036	30.9159
Totals:				2.43637e5	4596.16296	

(2*R*,3*R*)-2-(benzo[*d*][1,3]dioxol-5-ylmethyl)-2-methyl-4-nitro-3-(2-(trifluoromethyl) phenyl)butanal + (2*R*,3*R*)-2-(benzo[*d*][1,3]dioxol-5-ylmethyl)-2-methyl-4-nitro-3-(2-(trifluoromethyl)phenyl)butanal

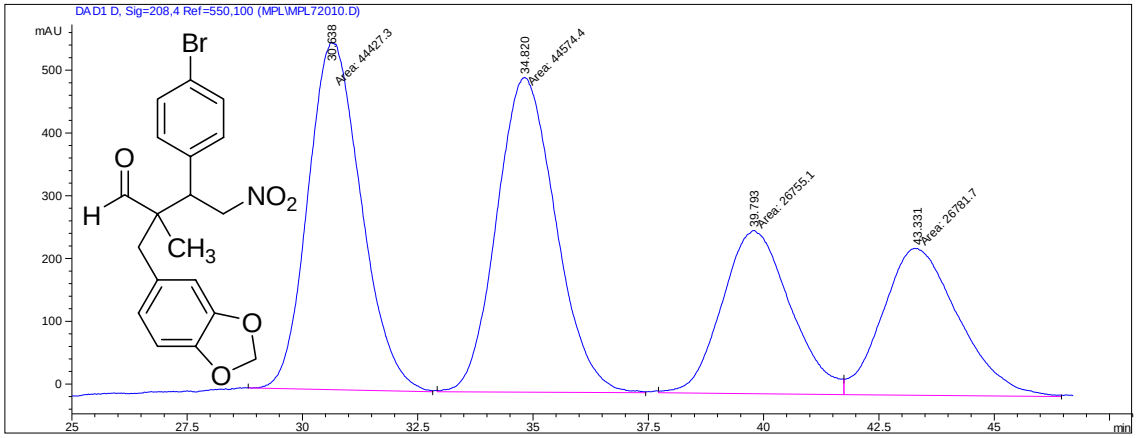


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area [%]
1	23.133	MM	0.7421	4.87399e4	1094.68542	81.7431
2	25.681	MM	0.6496	389.82111	10.00170	0.6538
3	28.410	MM	0.9139	1.00604e4	183.47906	16.8725
4	31.862	MM	0.8988	435.65826	8.07817	0.7307
Totals:				5.96258e4	1296.24436	

(2*R*,3*R*)-2-(benzo[*d*][1,3]dioxol-5-ylmethyl)-3-(4-bromophenyl)-2-methyl-4-nitrobutanal + (2*R*,3*R*)-2-(benzo[*d*][1,3]dioxol-5-ylmethyl)-3-(4-bromophenyl)-2-methyl-4-nitrobutanal (**22**): General procedure, chromatography on silica (20% diethyl ether/hexanes) diastereomers could not be separated, white solid, m.p. = 166-168 °C, 81% yield (340.3 mg), 3.8:1 dr, 99% ee (major diastereomer), 99% ee (minor diastereomer) as determined by HPLC (Chiralcel OD-H, 25.0% isopropanol/hexanes, 1.0 mL/min, 208 nm; t_r(major enantiomer, major diastereomer) = 30.64 min, t_r(minor enantiomer, major diastereomer) = 34.82 min, t_r(major enantiomer, minor diastereomer) = 39.79 min, t_r(minor enantiomer, minor diastereomer) = 43.33 min). $[\alpha]^{25}_D$ = +15.9 (c = 0.0201 g/2.0 mL, chloroform). ^{1}H NMR (400 MHz, $CDCl_3$): Signals corresponding to the major diastereomer δ 9.57 (1H, s), 7.47 (2H, d, J = 8.4 Hz), 7.08 (2H, d, J = 8.4 Hz), 6.67 (1H, d, J = 7.7 Hz), 6.44-6.41 (2H, m), 5.91 (2H, s), 4.85 (1H, dd, J = 11.7, 13.2 Hz), 4.63 (1H, dd, J = 4.0, 13.2 Hz), 3.76 (1H, dd, J = 4.0, 11.7 Hz), 2.95 (1H, d, J = 13.9 Hz), 2.33 (1H, d, J = 13.9 Hz), 1.03 (3H, s). Signals corresponding to the minor diastereomer δ 9.52 (1H, s), 7.47 (2H, d, J = 8.4 Hz), 7.08 (2H, d, J = 8.4 Hz), 6.68 (1H, d, J = 7.7 Hz), 6.49-6.44 (2H, m), 5.91 (2H, s), 4.78 (2H, m), 3.78 (1H, m), 2.99 (1H, d, J = 13.5 Hz), 2.62 (1H, d, 13.5 Hz), 1.05 (3H, s). ^{13}C (100 MHz, $CDCl_3$): Signals corresponding to the

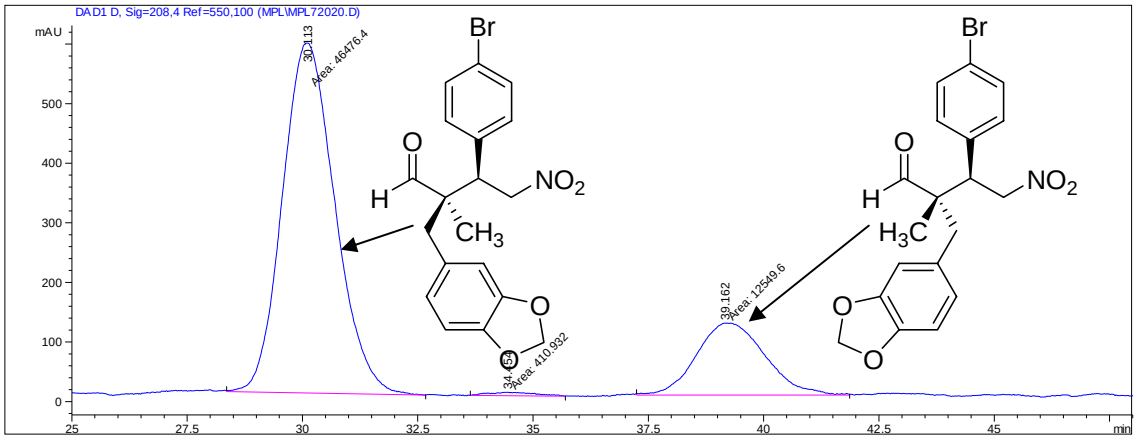
major enantiomer δ 205.5, 147.7, 146.7, 134.3, 132.0, 130.9, 123.4, 122.5, 110.4, 108.2, 101.1, 76.4, 52.1, 48.2, 42.1, 16.2. Signals corresponding to the minor diastereomer δ 204.3, 147.6, 146.7, 134.1, 132.1, 130.8, 128.6, 128.2, 127.6, 110.4, 108.2, 101.1, 75.9, 51.7, 48.8, 40.3, 17.9. IR (neat): 3026 (w), 2980 (w), 2917 (w), 2778 (w), 2725 (w), 1723 (m), 1555 (s), 1490 (s), 1443 (m), 1378 (m), 1251 (m), 1039 (m), 1011 (m), 929 (m), 814 (m), 757 (m). HRMS (ESI): expected for $[C_{19}H_{18}BrNO_5+NH_4]^+$: 437.0712, 439.0692, found: 437.0721, 439.0699.

Racemic 2-(benzo[*d*][1,3]dioxol-5-ylmethyl)-3-(4-bromophenyl)-2-methyl-4-nitrobutanal



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area [%]
1	30.638	MM	1.3348	4.43107e4	553.27155	12.2017
2	34.820	MM	1.4722	4.42024e4	500.41241	38.7498
3	39.793	MF	1.7061	2.64750e4	258.63345	37.0904
4	43.331	FM	1.8820	2.62786e4	232.71701	11.9581
Totals:				1.41267e5	1545.03442	

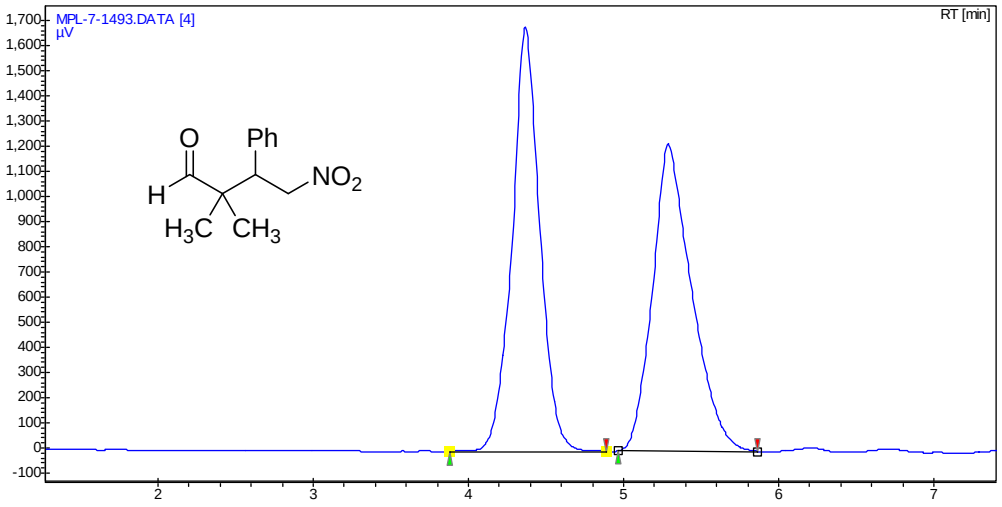
Enantioenriched (2*R*,3*R*)-2-(benzo[*d*][1,3]dioxol-5-ylmethyl)-3-(4-bromophenyl)-2-methyl-4-nitrobutanal + (2*R*,3*R*)-2-(benzo[*d*][1,3]dioxol-5-ylmethyl)-3-(4-bromophenyl)-2-methyl-4-nitrobutanal



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area [%]
1	30.113	MM	1.3197	4.64822e4	587.03113	78.7708
2	34.454	MM	1.0085	288.76703	4.77232	0.4894
3	39.162	MM	1.7001	1.22385e4	119.98075	20.7399
Totals:				5.90095e4	711.78420	

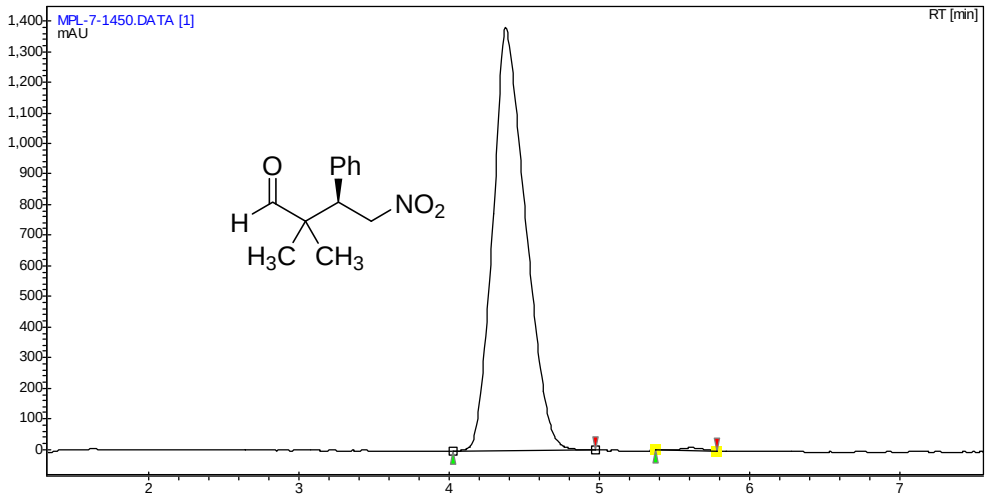
(*R*)-2,2-dimethyl-4-nitro-3-phenylbutanal: General procedure, chromatography on silica (15% diethyl ether/hexanes), colorless to light yellow liquid, 89% yield (197.6 mg), 99% ee as determined by SFC (Chiralcel OD-H, 3.0% methanol/CO_2, 3.0 mL/min, 208 nm, 30 ºC; t_r(major enantiomer) = 4.37 min, t_r(minor enantiomer) = 5.29 min). $[\alpha]^{25}_D$ = +8.7 (c = 0.0163 g/2.0 mL, chloroform). ^{1}H NMR (400 MHz, $CDCl_3$): δ 9.53 (1H, s), 7.31 (3H, m), 7.13 (2H, m), 4.85 (1H, dd, J = 11.3, 13.2 Hz), 4.69 (1H, dd, J = 4.4, 13.2 Hz), 3.78 (1H, dd, J = 4.4, 11.3 Hz), 1.31 (3H, s), 1.00 (3H, s). ^{13}C (100 MHz, $CDCl_3$): δ 204.2, 135.3, 129.0, 128.7, 128.1, 76.3, 48.4, 48.2, 21.6, 18.8. IR (neat): 3033 (w), 2974 (m), 2933 (w), 2819 (w), 2721 (w), 1725 (s), 1555 (s), 1496 (m), 1455 (m), 1379 (m), 882 (m), 750 (m), 705 (m). HRMS (ESI): expected for $[C_{12}H_{15}NO_3+NH_4]^+$: 239.1396, found: 239.1401.

Racemic 2,2-dimethyl-4-nitro-3-phenylbutanal



#	Time [Min]	Height [µV]	Area [µV.Min]	Area [%]
1	4.37	1687.3	350.3	49.591
2	5.29	1222.5	356.1	50.409
Total		2909.9	706.3	100.000

Enantioenriched (*R*)-2,2-dimethyl-4-nitro-3-phenylbutanal

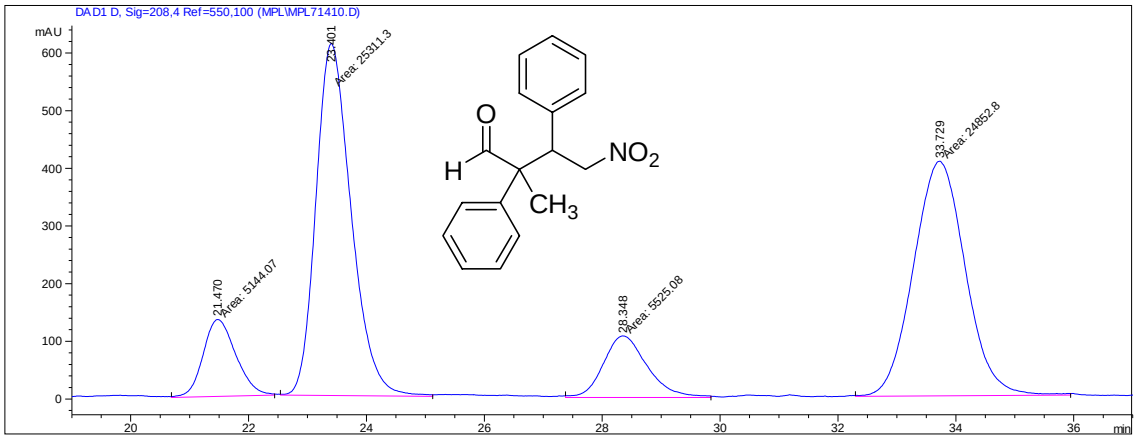


#	Time [Min]	Height [mAU]	Area [mAU*min]	Area [%]
1	4.37	1381.47	349.28	99.490
2	5.61	9.74	1.79	0.510
Total			351.07	100.000

(2*S*,3*R*)-2-methyl-4-nitro-2,3-diphenylbutanal: General procedure, diastereomeric products separable by chromatography on silica (15% diethyl ether/hexanes), white solid, m.p. = 76-78 °C, 94% yield (267.7 mg), 11.9 : 1 dr, 97% ee (major diastereomer) as determined by HPLC (Chiralcel OD-H, 5.0% isopropanol/hexanes, 1.0 mL/min, 208 nm; t_r(minor enantiomer, major diastereomer) = 22.77 min), t_r(major enantiomer, major diastereomer) = 31.97 min). $[\alpha]^{25}_D$ = +170.9 (c = 0.0227 g/2.0 mL, chloroform). ^{1}H NMR (400 MHz, $CDCl_3$): δ 9.56 (1H, s), 7.24 (3H, m), 7.14 (3H, m), 7.06 (2H, m), 6.94 (2H, m), 5.03 (1H, dd, J = 11.7, 13.2 Hz), 4.86 (1H, dd, J = 4.0, 13.2 Hz), 4.20 (1H, dd, J =4.0, 11.7 Hz), 1.53 (3H, s). ^{13}C (100 MHz, $CDCl_3$): δ 201.0, 137.3, 135.4, 129.3, 129.0, 128.2, 128.1, 127.7, 127.3, 76.2, 56.6, 49.6, 16.8. IR (thin film): 3062 (m), 3032 (m), 2977 (m), 2923 (m), 2822 (m), 2719 (m), 1957 (w), 1885 (w), 1809 (w), 1721 (s), 1562 (s), 1495 (m), 1454 (m), 1377 (s), 1216 (m), 1096 (m), 1030 (m), 918 (m), 858 (m), 759 (s), 700 (s). HRMS (CI): expected for $[C_{17}H_{17}NO_3+NH_4]^+$: 301.1552, found: 301.1549.

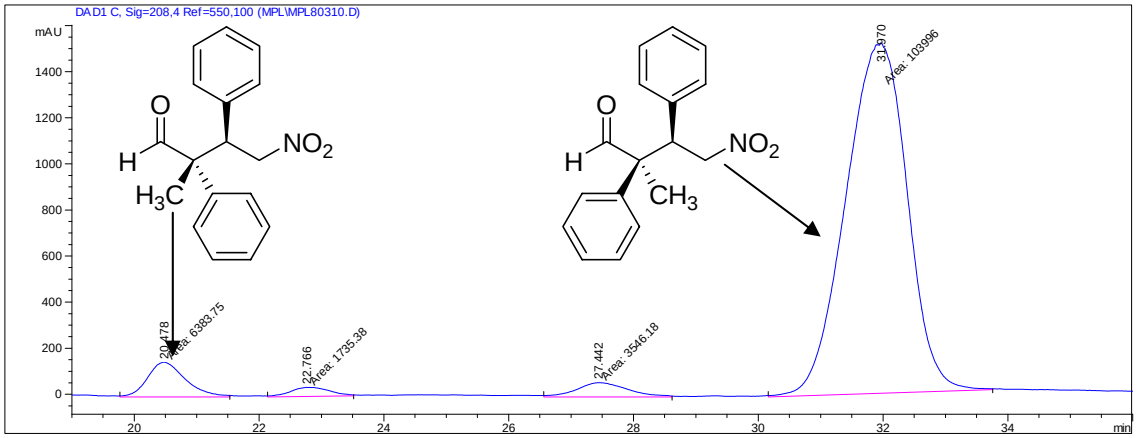
(2*R*,3*R*)-2-methyl-4-nitro-2,3-diphenylbutanal: colorless to light yellow oil, 32 % ee (minor diastereomer) as determined by HPLC (Chiralcel OD-H, 5.0% isopropanol/hexanes, 1.0 mL/min, 208 nm; t_r(major enantiomer, minor diastereomer) = 20.48 min, t_r(minor enantiomer, minor diastereomer) = 27.44 min. $[\alpha]^{25}_D$ = –16.4 (c = 0.0078 g/2.0 mL, chloroform). ^{1}H NMR (400 MHz, $CDCl_3$): δ 9.57 (1H, s), 7.43 (3H, m), 7.25 (3H, m), 7.11 (2H, m), 6.97 (2H, m), 4.68 (1H, dd, J = 3.7, 12.8 Hz), 4.51 (1H, dd, J = 11.7, 12.8 Hz), 4.37 (1H, dd, J =3.7, 11.7 Hz), 1.39 (3H, s). ^{13}C (100 MHz, $CDCl_3$): δ 200.0, 135.6, 135.0, 129.6, 129.1, 128.5, 128.3, 128.1, 128.0, 76.5, 56.2, 47.8, 17.8. IR (neat): 3063 (m), 3033 (m), 2975 (m), 2921 (m), 2820 (m), 2719 (m), 1960 (w), 1889 (w), 1811 (w), 1724 (s), 1552 (s), 1497 (m), 1454 (m), 1378 (s), 1205 (m), 1093 (m), 906 (m), 702 (s). HRMS (ESI): expected for $[C_{17}H_{17}NO_3+NH_4]^+$: 301.1552, found: 301.1560.

Racemic 2-methyl-4-nitro-2,3-diphenylbutanal



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area [%]
1	21.470	MM	0.6502	5218.46484	133.76399	8.6173
2	23.401	MM	0.6855	2.50737e4	609.59735	41.4042
3	28.348	MM	0.8327	5227.61572	104.63694	8.6324
4	33.729	MM	1.0242	2.50385e4	407.46124	41.3461
Totals:				6.05582e4	1255.45953	

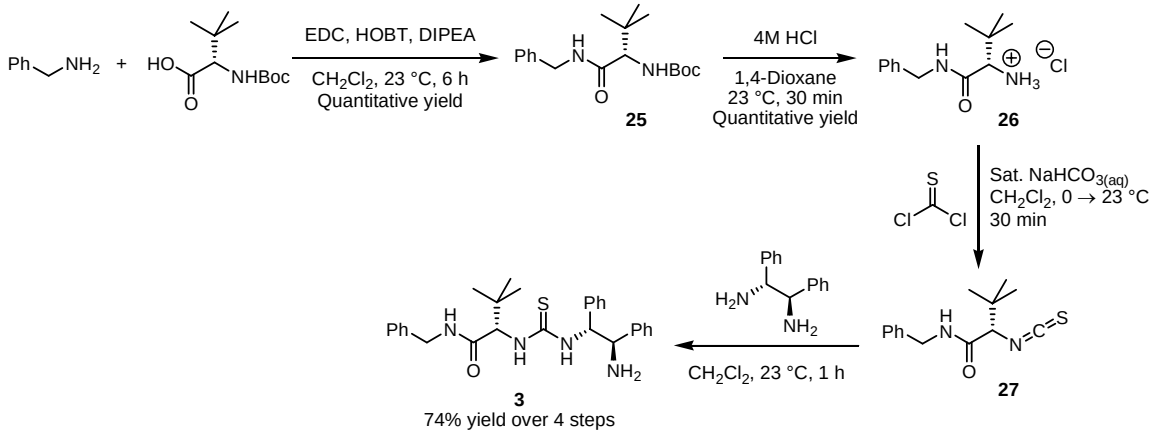
Enantioenriched (2*S*,3*R*)-2-methyl-4-nitro-2,3-diphenylbutanal + (2*R*,3*R*)-2-methyl-4-nitro-2,3-diphenylbutanal



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area [%]
1	20.478	MM	0.6718	5880.19775	145.87737	5.1001
2	22.766	MM	0.6898	1475.95178	35.65924	1.2801
3	27.442	MM	0.8372	2833.51196	56.40998	2.4576
4	31.970	MM	1.1491	1.05107e5	1524.43115	91.1622

Totals:				1.15297e5	1762.37774	

General Procedure for the Synthesis of Primary Amine-Thiourea Catalysts.



(*S*)-2-(3-((1*R*,2*R*)-2-amino-1,2-diphenylethyl)thioureido)-*N*-benzyl-3,3-dimethylbutanamide (3): *N*-Boc-L-*tert*-leucine (1.00 g, 4.32 mmol, 1.00 equiv.), 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride (912.5 mg, 4.76 mmol, 1.10 equiv.) and 1-hydroxybenzotriazole hydrate (643.2 mg, 4.76 mmol, 1.10 equiv.) were loaded into an oven-dried round-bottomed flask equipped with a magnetic stir bar, rubber septum, and nitrogen inlet. The solids were dissolved in dichloromethane (21.6 mL) and the resulting clear colorless solution was stirred (~500 rpm) at room temperature. Benzylamine (520 μL, 4.76 mmol, 1.10 equiv.) and *N*,*N*-diisopropylethylamine (829 μL, 4.76 mmol, 1.10 equiv.) were sequentially added and the reaction mixture was stirred at room temperature for 6 hours. The reaction mixture was poured into a separatory funnel containing a 1M HCl solution (20.0 mL). The phases were separated and the aqueous phase was extracted with dichloromethane (20.0 mL). The organic phases were combined, washed sequentially with saturated aqueous sodium bicarbonate and brine, dried over sodium sulfate, filtered, and concentrated under reduced pressure to provide amide **25** as a white solid in quantitative yield. A magnetic stir bar and 4M HCl in 1,4-dioxane (9.7 mL, 38.9 mmol, 9.0 equiv.) were added to a round-bottomed flask containing **25** and the reaction mixture was stirred for 30 minutes at room temperature. The magnetic stir bar was removed, the solvent was evaporated under reduced pressure, and the resulting residue was dried *in vacuo* to provide **26** in quantitative yield as a white foamy solid. A magnetic stir bar, dichloromethane (43.2 mL), and saturated aqueous sodium bicarbonate (43.2 mL) were added to a flask containing **26** and the resulting clear colorless solution was cooled to 0 °C with an ice bath. Thiophosgene (346 μL, 4.54 mmol, 1.05 equiv.) was added via syringe and the resulting light orange biphasic mixture was stirred vigorously at 0 °C for 10 minutes, warmed to room temperature, and stirred at room temperature for 20 minutes. The biphasic mixture was poured into a separatory funnel and the phases were separated. The aqueous phase was extracted with dichloromethane (40.0 mL) and the organic phases were combined, washed with brine, dried over sodium sulfate, filtered, and concentrated under reduced pressure. The resulting yellow residue was dissolved in dichloromethane (43.2 mL), (*R*,*R*)-1,2-diphenylethylenediamine (318.4 mg, 6.48 mmol, 1.50 equiv.) was added in one portion,

and the yellow reaction mixture was stirred at room temperature for 1.0 hour. The solvent was evaporated and the resulting yellow residue was purified by chromatography on silica (3.0% methanol/dichloromethane). The title compound was obtained as a white foamy solid, m.p. = 102 °C, in 74% yield (1.520 g) over four steps, $[\alpha]^{25}_{D}$ = 27.9 (c = 0.0216 g/2.0 mL, chloroform). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.58 (1H, br s), 7.31-7.15 (15H, m), 6.82 (1H, br s), 6.31 (1H, br s), 5.00 (1H, br s), 4.68 (1H, br s), 4.37 (1H, dd, J = 5.9, 14.6 Hz), 4.24-4.20 (2H, m), 1.84 (2H, br s), 0.95 (9H, s). ^{13}C (100 MHz, $CDCl_3$): δ 182.8, 170.6, 141.6, 139.3, 137.7, 128.6, 128.5, 128.3, 127.7, 127.4, 127.2, 126.8, 66.3, 64.7, 60.7, 43.3, 34.7, 26.9. IR (thin film): 3294 (s), 3062 (m), 3031 (m), 2964 (m), 2872 (m), 1951 (w), 1878 (w), 1808 (w), 1645 (s), 1531 (s), 1454 (m), 1357 (m), 1233 (m), 1070 (m), 1029 (m), 755 (s), 699 (s), 667 (m), 593(m). LRMS (ESI): 475.2 (100%) $[C_{28}H_{34}N_4OS+H]^+$.

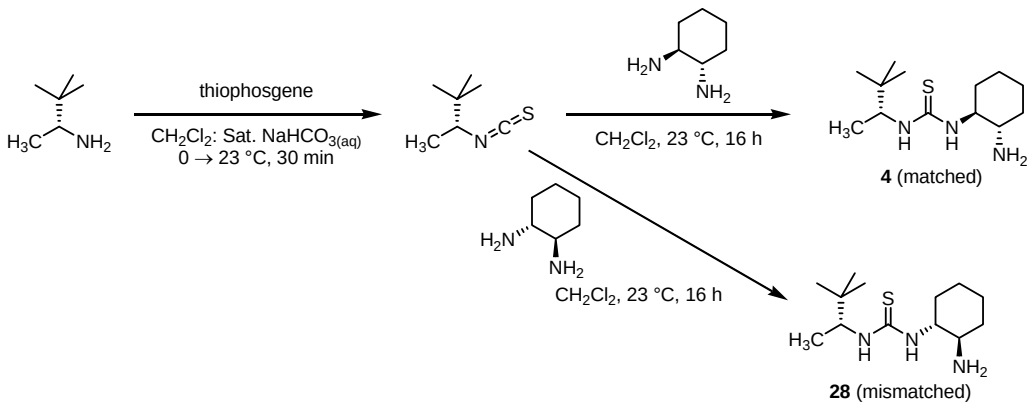
(*S*)-2-(3-((1*R*,2*R*)-2-amino-1,2-diphenylethyl)thioureido)-*N*-benzyl-3-methylbutanamide (23): General procedure, chromatography on silica (3.0% methanol/dichloromethane), white foamy solid, m.p. = 169 °C, 68% yield (1.353 g) over four steps, $[\alpha]^{25}_{D}$ = 18.7 (c = 0.0211 g/2.0 mL, chloroform). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.71 (1H, br s), 7.28-7.17 (16H, m), 6.52 (1H, br s), 5.21 (1H, br s), 4.73 (1H, br s), 4.42 (1H, dd, J = 5.9, 14.6 Hz), 4.29-4.24 (2H, m), 2.20 (1H, m), 1.82 (1H, br s), 0.92-0.86 (6H, m). ^{13}C (100 MHz, $CDCl_3$): δ 182.8, 171.8, 141.7, 139.6, 137.6, 128.5, 128.3, 127.4, 127.3, 126.9, 126.7, 64.2, 60.6, 43.3, 30.6, 19.1, 18.5. IR (thin film): 3292 (s), 3063 (m), 3030 (m), 2963 (m), 2930 (m), 2873 (m), 1955 (w), 1888 (w), 1810 (w), 1651 (s), 1537 (s), 1453 (m), 1356 (m), 1259 (m), 1073 (m), 1029 (m), 755 (s), 698 (s), 605 (m). LRMS (ESI): 461.2 (100%) $[C_{27}H_{32}N_4OS+H]^+$.

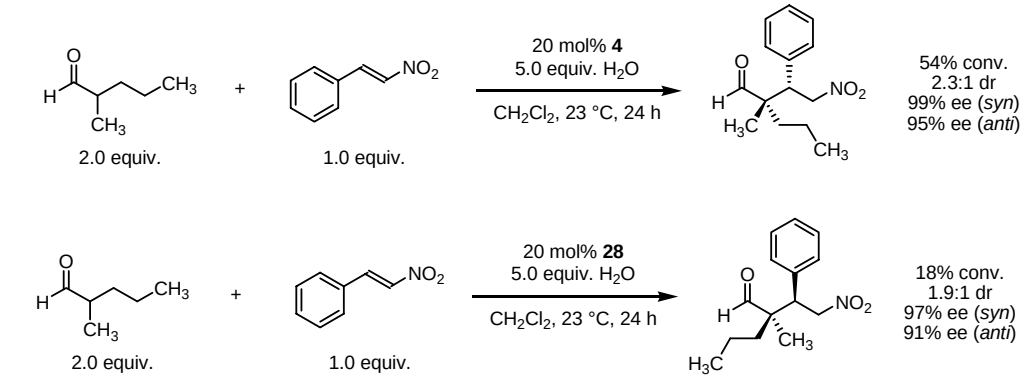
(*S*)-2-(3-((1*S*,2*S*)-2-amino-1,2-diphenylethyl)thioureido)-*N*-benzyl-3-methylbutanamide (24): General procedure, chromatography on silica (3.0% methanol/dichloromethane), white foamy solid, m.p. = 87-88 °C, 69% yield (1.373 g) over four steps, $[\alpha]^{25}_{D}$ = –51.5 (c = 0.0201 g/2.0 mL, chloroform). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.67 (1H, br s), 7.34-7.19 (16H, m), 6.62 (1H, br s), 4.68 (1H, br s), 4.45 (1H, dd, J = 5.9, 14.6 Hz), 4.32 (1H, dd, J = 5.9, 14.6 Hz), 4.24 (1H, br s), 2.04 (1H, br s), 1.51 (2H, br s), 0.76 (3H, br s), 0.65 (3H, br s). ^{13}C (100 MHz, $CDCl_3$): δ 182.3, 171.9, 141.8, 139.6, 137.6, 128.6, 128.5, 128.2, 127.3, 127.2, 126.8, 126.6, 64.0, 63.5, 60.3, 43.2, 30.8, 19.0, 18.2. IR (thin film): 3291 (s), 3063 (m), 3030 (m), 2962 (m), 2931 (m), 2874 (m), 1952 (w), 1879 (w), 1810 (w), 1651 (s), 1536 (s), 1453 (m), 1358 (m), 1265 (m), 736 (m), 699 (s), 598 (m). LRMS (ESI): 461.2 (100%) $[C_{27}H_{32}N_4OS+H]^+$.

1-((1*S*,2*S*)-2-aminocyclohexyl)-3-((*R*)-3,3-dimethylbutan-2-yl)thiourea (4): Saturated aqueous sodium bicarbonate (25.0 mL) and dichloromethane (25.0 mL) were loaded into a 200 mL round-bottomed flask equipped with a magnetic stir bar. (*R*)-3,3-dimethyl-2-butylamine (250.0 mg, 2.47 mmol, 1.0 equiv.) was added via syringe and the biphasic mixture was cooled to 0 °C with an ice bath. Thiophosgene (198.0 μL, 2.59 mmol, 1.05 equiv.) was added and the biphasic mixture was stirred vigorously for 10.0 minutes at 0 °C, warmed to room temperature, and stirred for an additional 20.0 minutes. The biphasic mixture was poured into a separatory funnel and the organic phase was separated. The aqueous layer was washed with dichloromethane (25.0 mL), the organic phases were

combined, washed with brine, dried over sodium sulfate, filtered, and concentrated. The yellow residue was dissolved in dichloromethane and a magnetic stir bar was added to the solution. (*S*,*S*)-1,2-diaminocyclohexane (564.0 mg, 4.94 mmol, 2.0 equiv.) was added in one portion and the solution was stirred at room temperature for 16 hours. The solvent was evaporated and the yellow residue was purified by chromatography on silica (2.0% CH_3OH, 1.0% Et_3N, 97% CH_2Cl_2). The title compound was obtained as a white solid (m.p. = 113-115 °C) in 92% yield (587.3 mg), $[\alpha]^{25}_D$ = –133.0 (c = 0.0200 g/2.0 mL, chloroform). ^{1}H NMR (400 MHz, $CDCl_3$): δ 6.12 (1H, br s), 4.15 (2H, br s), 3.23 (1H, br s), 2.09 (2H, br m), 1.96 (1H, br m), 1.83 (1H, br m), 1.71 (2H, br m), 1.22 (4H, br m), 1.10 (3H, d, J = 6.6 Hz), 0.92 (9H, s). ^{13}C (100 MHz, $CDCl_3$): δ 182.5, 61.9, 59.3, 56.2, 34.5, 34.3, 32.1, 26.5, 24.8, 24.6, 15.3. IR (thin film): 3259 (m), 3058 (m), 2962 (s), 2935 (s), 2859 (m), 2209 (w), 1541 (s), 1365 (m), 1240 (m), 1200 (m), 1087 (m), 915 (m), 732 (s). LRMS (CI): 223.4 (100%) $[C_{13}H_{27}N_3S - H_2S]^+$.

1-((1*R*,2*R*)-2-aminocyclohexyl)-3-((*R*)-3,3-dimethylbutan-2-yl)thiourea (28): Procedure identical to that utilized for the synthesis of **4** with the exception that (*R*,*R*)-1,2-diaminocyclohexane is used instead of (*S*,*S*)-1,2-diaminocyclohexane. Chromatography on silica (2.0% CH_3OH, 1.0% Et_3N, 97% CH_2Cl_2), white solid (m.p. = 174-175 °C), 91% yield (578.7 mg). $[\alpha]^{25}_D$ = +79.5 (c = 0.0201 g/2.0 mL, chloroform). ^{1}H NMR (400 MHz, $CDCl_3$): δ 6.39 (1H, br s), 4.24 (2H, br s), 3.24 (1H, br s), 2.53 (2H, m), 1.97 (1H, br m), 1.81 (1H, br m), 1.66 (4H, br m), 1.18 (4H, br m), 1.06 (3H, d, J = 6.6 Hz), 0.90 (9H, s). ^{13}C (100 MHz, $CDCl_3$): δ 182.0, 61.8, 59.0, 55.9, 34.6, 34.4, 32.1, 26.4, 24.7, 24.6, 16.1. IR (thin film): 3260 (m), 3057 (m), 2963 (s), 2934 (s), 2859 (m), 2210 (w), 1542 (s), 1448 (m), 1365 (m), 1241 (m), 1201 (m), 1085 (m), 914 (m), 732 (s). LRMS (CI): 223.4 (100%) $[C_{13}H_{27}N_3S - H_2S]^+$.





General Procedure for the Synthesis of Racemic Samples.

2,3-dimethyl-4-nitro-2-phenylbutanal: 2-Phenylpropionaldehyde (332 μL, 2.5 mmol, 10.0 equiv.) is loaded into a 1/2 dram vial equipped with a magnetic stir bar. Thiocarbanilide (11.4 mg, 0.05 mmol, 20 mol%), pyrrolidine (4.2 μL, 0.05 mmol, 20 mol%), and 1-nitroprop-1-ene (87.1 mg, 0.25 mmol, 1.0 equiv.) are sequentially added. The vial is capped, and the yellow mixture is stirred at room temperature for 24 hours. The resulting orange mixture is loaded directly onto a silica gel column (8% diethyl ether/hexanes), providing the title compound as a colorless to light yellow liquid in 92% yield (51.0 mg) with a 20:1 diastereomeric ratio as measured by SFC (Chiralcel OD-H, 2.0% methanol/CO_2, 2.0 mL/min, 208 nm, 30 °C; t_r(minor diastereomer) = 6.73 min, t_r(minor diastereomer) = 6.73 min, t_r(major diastereomer) = 7.44 min), t_r(major diastereomer) = 8.25 min).

Probing Catalyst Deactivation

Incubation of catalyst and aldehyde for 12 hours prior to nitroalkene addition had no observable detrimental effect on product yield. Interestingly, aldol addition or condensation products were not observed or isolated upon stirring catalyst and aldehyde for 12 hours. Alternatively, incubation of catalyst and nitroalkene for 12 hours prior to aldehyde addition resulted in lower product yield. Primary amine-catalyzed nitroalkene polymerization, rather than catalyst deactivation, was identified as the origin of lower product yield under these circumstances. The excess of aldehyde required under optimized conditions may prevent nitroalkene decomposition or polymerization by ensuring that the catalyst rests in the imine state.

Careful monitoring of the reaction of 2-phenylpriopionaldehyde with 1-nitrohex-1-ene catalyzed by **1** (20 mol%) revealed that substrate conversion ceased after 24 hours, and that both starting materials could be recovered alongside product. These observations suggested catalyst deactivation either by decomposition or poisoning pathways. Addition of a second 20 mol% aliquot of catalyst to a stalled reaction mixture, followed by further stirring for 24 hours, led to complete conversion and generation of **5** in 92% isolated yield, indicating that *build-up of catalyst poisons was not responsible for the deactivation*. Similar yields were obtained in the presence, or absence, of a full equivalent of added 5, thus *ruling out product inhibition*.

It was therefore postulated that decomposition of an intermediate along the catalytic cycle was responsible for catalyst deactivation. A zwitterionic intermediate is often invoked in the numerous studies concerning the mechanism of conjugate addition of enamines to nitroalkenes.[6] This intermediate may undergo hydrolysis to a nitroaldehyde, or collapse to a 1,2-oxazine-N-oxide or cyclobutane. 1,2-Oxazine-N-oxides resulting from the addition of aldehyde-derived enamines to nitroalkenes have been shown to hydrolyze readily upon exposure to atmospheric moisture.[6l] Conversely, cyclobutanes resulting from the addition of aldehyde-derived enamines to nitroalkenes only undergo hydrolysis when treated with aqueous acid (such as 1 M HCl).[6i,l]

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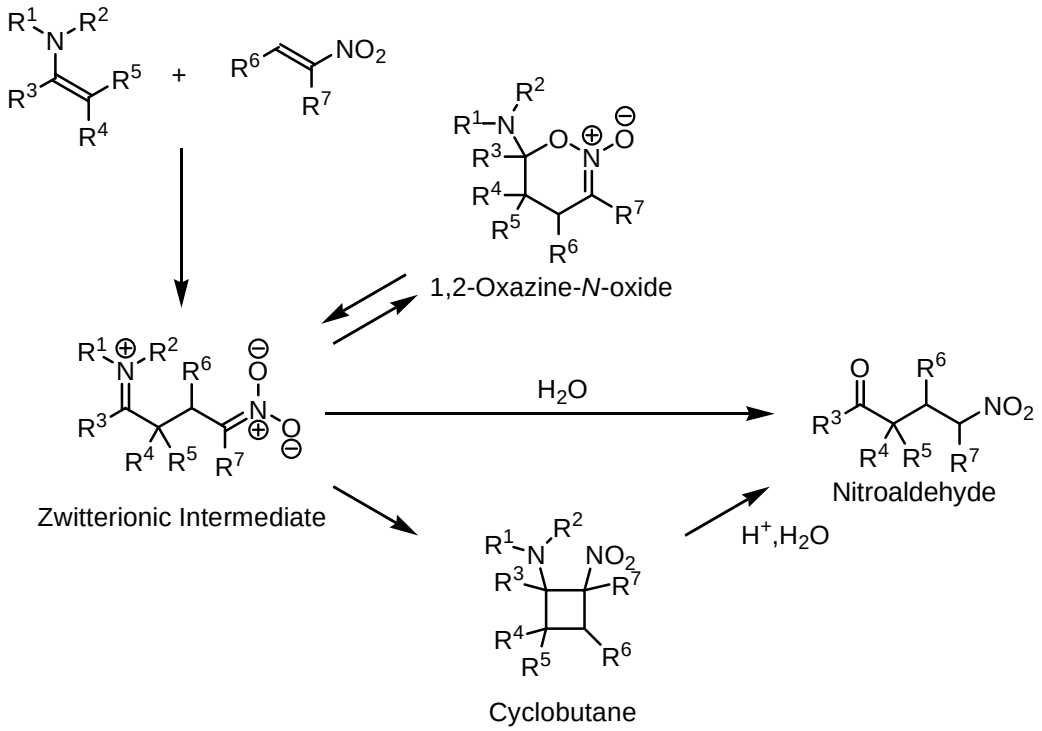
[6] a) K. C. Brannock, A. Bell, R. D. Burpitt, C. A. Kelly, *J. Org. Chem.* **1964**, *29*, 801-812; b) M. E. Kuehne, L. Foley, *J. Org. Chem.* **1965**, *30*, 4280-4284; c) A. Risaliti, S. Fatutta, M. Forchiassin, E. Valentin, *Tetrahedron Lett.* **1966**, *7*, 1821-1825; d) A. Risaliti, M. Forchiassin, E. Valentin, *Tetrahedron Lett.* **1966**, *7*, 6331-6335; e) A. T. Nielsen, T. G. Archibald, *Tetrahedron* **1970**, *26*, 3475-3485; f) D. Seebach, J. Golinski, *Helv. Chim. Acta* **1981**, *64*, 1413-1423; g) S. J. Blarer, W. B. Schweizer, D. Seebach, *Helv. Chim. Acta* **1982**, *65*, 1637-1654; h) S. J. Blarer, D. Seebach, *Chem. Ber.* **1983**, *116*, 3086-3096; i) D. Seebach, A. K. Beck, J. Golinski, J. N. Hay, T. Laube, *Helv. Chim. Acta* **1985**, *68*, 162-172; j) F. Felluga, P. Nitti, G. Pitacco, E. Valentin, *Tetrahedron* **1989**, *45*, 2099-2108; k) F. Felluga, P. Nitti, G. Pitacco, E. Valentin, *Tetrahedron* **1989**, *45*, 5667-5678; l) F. Felluga, P. Nitti, G. Pitacco, E. Valentin, *J. Chem. Soc., Perkin Trans. 1* **1992**, 2331-2335.



The beneficial role of water is most likely due to acceleration of imine hydrolysis and/or 1,2-oxazine-N-oxide decomposition. However, a cyclobutane intermediate is unlikely to undergo hydrolysis under the non-acidic reaction conditions, and its formation could therefore lead to catalyst deactivation. If cyclobutane formation is responsible for catalyst deactivation, the acidic workup (1M HCl) would release an amount of product roughly equivalent to the catalyst loading. Indeed, replacing the HCl workup with a simple aqueous workup in the addition of 2-phenylpropionaldehyde to 1-nitrohex-1-ene reduced the isolated yield of product from 54% to 39%. This corresponds closely to the catalyst loading (20 mol%). In addition, the only byproduct that could be isolated from the reaction that was not treated with 1M HCl possessed mass spectral characteristics consistent with the expected cyclobutane intermediate (HRMS-ESI $(M+H)^+$ Calcd: 622.3785; Found: 622.3786). NMR analysis of this byproduct was precluded by extensive peak broadening due to hydrogen bonding. Zwitterionic, imine, and 1,2-oxazine-*N*-oxide intermediates are most likely unstable under the aqueous reaction conditions or silica gel chromatography. Hence, the results above lend credence to the hypothesis that catalyst deactivation occurs through irreversible cyclobutane formation. Unfortunately, no acidic additives could be identified that were both capable of cyclobutane hydrolysis and compatible with the catalytic conditions.

Structural Data for compound 22:

Experimental Section:

X-Ray quality crystals were obtained via slow evaporation of a dichloromethane

solution of **22**. A colorless block crystal with dimensions 0.20 x 0.16 x 0.12 mm was mounted on a glass fiber using a very small amount of paratone oil.

Data were collected using a Bruker SMART CCD (charge coupled device) based diffractometer equipped with an Oxford Cryostream low-temperature apparatus operating at 193 K. Data were measured using omega scans of 0.3 ° per frame for 30 seconds, such that a hemisphere was collected. A total of 1271 frames were collected with a maximum resolution of 0.76 Å. The first 50 frames were recollected at the end of data collection to monitor for decay. Cell parameters were retrieved using SMART[1] software and refined using SAINT on all observed reflections. Data reduction was performed using the SAINT software[2] which corrects for Lp and decay. Absorption corrections were applied using SADABS[6] multiscan technique, supplied by George Sheldrick. The structures are solved by the direct method using the SHELXS-97[3] program and refined by least squares method on F^2, SHELXL-97,[4] incorporated in SHELXTL-PC V 6.10.[5]

The structure was solved in the space group $P2_12_12_1$ (# 19) by analysis of systematic absences. All non-hydrogen atoms are refined anisotropically. Hydrogens were calculated by geometrical methods and refined as a riding model. The Flack[7] parameter is used to determine chirality of the crystal studied, the value should be near zero, a value of one is the other enantiomer and a value of 0.5 is racemic. The Flack parameter was refined to 0.028(7), confirming the absolute stereochemistry. The crystal used for the diffraction study showed no decomposition during data collection. All drawing are done at 50% ellipsoids.

Acknowledgement. The CCD based x-ray diffractometer at Harvard University was purchased through NIH grant (1S10RR11937-01).

References

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2. SAINT V 6.22 (NT) *Software for the CCD Detector System* Bruker Analytical X-ray Systems, Madison, WI (2001).

3. Sheldrick, G. M. SHELXS-90, *Program for the Solution of Crystal Structure*, University of Göttingen, Germany, 1990.

4. Sheldrick, G. M. SHELXL-97, *Program for the Refinement of Crystal Structure,* University of Göttingen, Germany, 1997.

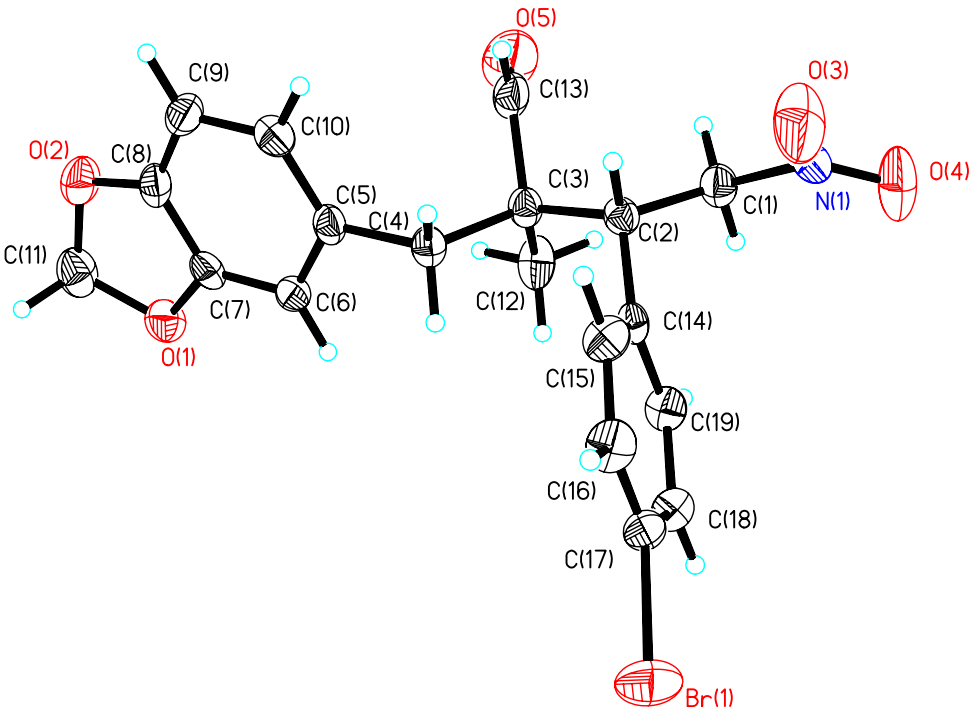
5. SHELXTL 6.1 (PC-Version), *Program library for Structure Solution and Molecular Graphics*; Bruker Analytical X-ray Systems, Madison, WI (2000).

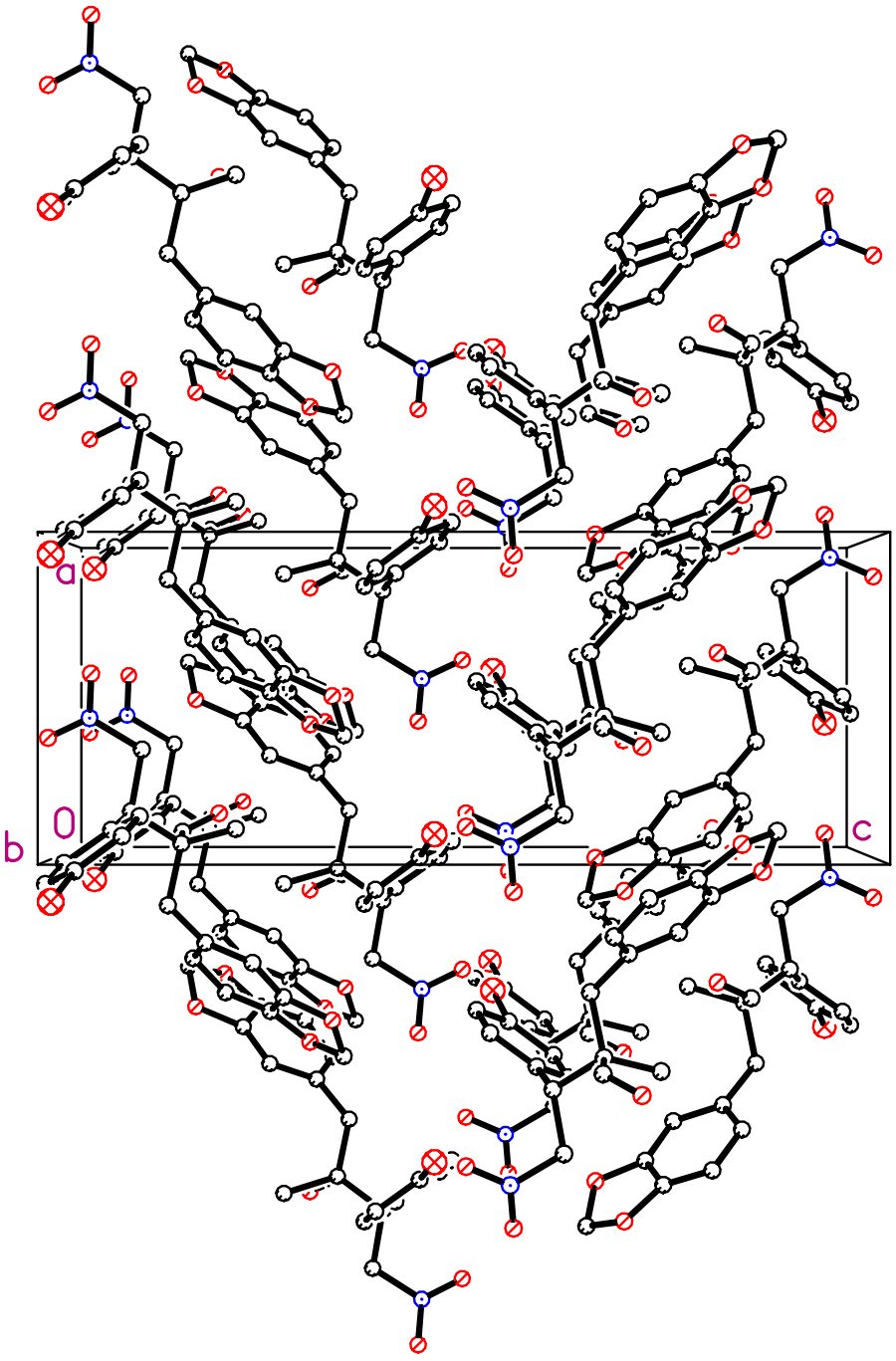
6. SADABS. Program for absorption corrections using Siemens CCD based on the method of Robert Blessing; Blessing, R.H. *Acta Cryst. A51* **1995**, 33-38.

7. Flack, H. D.. Acta Cryst. A39, **1983**, 876-881.

[a] Obtained with graphite monochromated Mo Kα (λ = 0.71073 Å) radiation.
[b] $R1 = \sum||F_o| - |F_c||/\sum|F_o|$. [c] $wR_2 = \{\sum[w(F_o^2 - F_c^2)^2/\{\sum[w(F_o^2)^2]\}^{1/2}$.

The following are 50% thermal ellipsoidal drawings of the molecule in the asymmetric cell with various amount of labeling.


O(5)
C(13)
O(3)
C(9)
C(10)
O(2)
C(8)
C(5)
C(3)
C(1)
N(1)
O(4)
C(4)
C(2)
C(11)
C(12)
C(7)
C(6)
C(14)
O(1)
C(15)
C(19)
C(16)
C(18)
C(17)
Br(1)



This is a drawing of the packing along the b-axis.

Table 1. Crystal data and structure refinement for **22**.

Identification code	enj72t	
Empirical formula	C19 H18 Br N O5	
Formula weight	420.25	
Temperature	193(2) K	
Wavelength	0.71073 Å	
Crystal system	Orthorhombic	
Space group	P2(1)2(1)2(1)	
Unit cell dimensions	a = 8.0316(9) Å	α= 90°.
	b = 10.9639(12) Å	β= 90°.
	c = 20.583(2) Å	γ = 90°.
Volume	1812.5(3) $Å^3$	
Z	4	
Density (calculated)	1.540 Mg/m^3	
Absorption coefficient	2.298 mm^{-1}	
F(000)	856	
Crystal size	0.20 x 0.16 x 0.12 mm^3	
Theta range for data collection	1.98 to 27.88°.	
Index ranges	-10<=h<=10, -14<=k<=14, -27<=l<=15	
Reflections collected	11673	
Independent reflections	4263 [R(int) = 0.0267]	
Completeness to theta = 27.88°	99.6 %	
Absorption correction	Empirical	
Max. and min. transmission	0.7700 and 0.6565	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	4263 / 0 / 236	
Goodness-of-fit on F^2	0.980	
Final R indices [I>2sigma(I)]	R1 = 0.0334, wR2 = 0.0631	
R indices (all data)	R1 = 0.0483, wR2 = 0.0668	
Absolute structure parameter	0.028(7)	
Largest diff. peak and hole	0.401 and -0.338 $e.Å^{-3}$	

Table 2. Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters ($Å^2$x 10^3) for **22**. U(eq) is defined as one third of the trace of the orthogonalized U^{ij} tensor.

	x	y	z	U(eq)
Br(1)	9149(1)	13687(1)	354(1)	51(1)
O(1)	5057(2)	7624(2)	3411(1)	37(1)
O(2)	4164(2)	5699(2)	3104(1)	40(1)
O(3)	13783(3)	8242(2)	23(1)	79(1)
O(4)	15743(2)	9030(2)	576(1)	58(1)
O(5)	11371(3)	5921(2)	1993(1)	67(1)
N(1)	14389(2)	8550(2)	534(1)	35(1)
C(1)	13426(3)	8362(2)	1153(1)	30(1)
C(2)	11540(3)	8468(2)	1025(1)	24(1)
C(3)	10533(2)	7905(2)	1605(1)	26(1)
C(4)	8645(2)	8132(2)	1453(1)	26(1)
C(5)	7439(3)	7444(2)	1877(1)	26(1)
C(6)	6865(3)	7975(2)	2461(1)	27(1)
C(7)	5743(3)	7315(2)	2816(1)	27(1)
C(8)	5188(3)	6176(2)	2629(1)	30(1)
C(9)	5715(3)	5638(2)	2065(1)	33(1)
C(10)	6855(3)	6309(2)	1690(1)	31(1)
C(11)	3838(3)	6688(2)	3536(1)	42(1)
C(12)	11002(3)	8407(2)	2272(1)	40(1)
C(13)	10830(3)	6539(2)	1569(1)	37(1)
C(14)	11034(3)	9760(2)	852(1)	24(1)
C(15)	10048(3)	9967(2)	308(1)	31(1)
C(16)	9489(3)	11135(2)	150(1)	35(1)
C(17)	9941(3)	12089(2)	539(1)	30(1)
C(18)	10956(3)	11922(2)	1076(1)	31(1)
C(19)	11485(3)	10757(2)	1226(1)	29(1)

Table 3. Bond lengths [Å] and angles [°] for **22**.

Br(1)-C(17)	1.902(2)	O(1)-C(7)	1.383(3)
O(1)-C(11)	1.443(3)	O(2)-C(8)	1.381(3)
O(2)-C(11)	1.427(3)	O(3)-N(1)	1.208(3)
O(4)-N(1)	1.211(3)	O(5)-C(13)	1.187(3)
N(1)-C(1)	1.504(3)	C(1)-C(2)	1.542(3)
C(1)-H(1A)	0.9900	C(1)-H(1B)	0.9900
C(2)-C(14)	1.517(3)	C(2)-C(3)	1.568(3)
C(2)-H(2)	1.0000	C(3)-C(13)	1.518(3)
C(3)-C(12)	1.527(3)	C(3)-C(4)	1.568(3)
C(4)-C(5)	1.507(3)	C(4)-H(4A)	0.9900
C(4)-H(4B)	0.9900	C(5)-C(10)	1.384(3)
C(5)-C(6)	1.412(3)	C(6)-C(7)	1.368(3)
C(6)-H(6)	0.9500	C(7)-C(8)	1.381(3)
C(8)-C(9)	1.370(3)	C(9)-C(10)	1.405(3)
C(9)-H(9)	0.9500	C(10)-H(10)	0.9500
C(11)-H(11A)	0.9900	C(11)-H(11B)	0.9900
C(12)-H(12A)	0.9800	C(12)-H(12B)	0.9800
C(12)-H(12C)	0.9800	C(13)-H(13)	0.9500
C(14)-C(19)	1.385(3)	C(14)-C(15)	1.390(3)
C(15)-C(16)	1.395(3)	C(15)-H(15)	0.9500
C(16)-C(17)	1.365(3)	C(16)-H(16)	0.9500
C(17)-C(18)	1.385(3)	C(18)-C(19)	1.382(3)
C(18)-H(18)	0.9500	C(19)-H(19)	0.9500

C(7)-O(1)-C(11)	104.75(19)	C(8)-O(2)-C(11)	105.25(18)
O(3)-N(1)-O(4)	123.1(2)	O(3)-N(1)-C(1)	119.5(2)
O(4)-N(1)-C(1)	117.5(2)	N(1)-C(1)-C(2)	110.51(19)
N(1)-C(1)-H(1A)	109.5	C(2)-C(1)-H(1A)	109.5
N(1)-C(1)-H(1B)	109.5	C(2)-C(1)-H(1B)	109.5
H(1A)-C(1)-H(1B)	108.1	C(14)-C(2)-C(1)	111.97(18)
C(14)-C(2)-C(3)	114.08(17)	C(1)-C(2)-C(3)	110.30(18)
C(14)-C(2)-H(2)	106.7	C(1)-C(2)-H(2)	106.7
C(3)-C(2)-H(2)	106.7	C(13)-C(3)-C(12)	111.1(2)
C(13)-C(3)-C(4)	107.38(18)	C(12)-C(3)-C(4)	111.12(19)

C(13)-C(3)-C(2)	105.66(18)	C(12)-C(3)-C(2)	114.59(18)
C(4)-C(3)-C(2)	106.55(17)	C(5)-C(4)-C(3)	115.30(18)
C(5)-C(4)-H(4A)	108.4	C(3)-C(4)-H(4A)	108.4
C(5)-C(4)-H(4B)	108.4	C(3)-C(4)-H(4B)	108.4
H(4A)-C(4)-H(4B)	107.5	C(10)-C(5)-C(6)	119.8(2)
C(10)-C(5)-C(4)	120.5(2)	C(6)-C(5)-C(4)	119.7(2)
C(7)-C(6)-C(5)	116.8(2)	C(7)-C(6)-H(6)	121.6
C(5)-C(6)-H(6)	121.6	C(6)-C(7)-C(8)	122.8(2)
C(6)-C(7)-O(1)	127.3(2)	C(8)-C(7)-O(1)	109.88(19)
C(9)-C(8)-C(7)	121.8(2)	C(9)-C(8)-O(2)	128.4(2)
C(7)-C(8)-O(2)	109.7(2)	C(8)-C(9)-C(10)	116.1(2)
C(8)-C(9)-H(9)	121.9	C(10)-C(9)-H(9)	121.9
C(5)-C(10)-C(9)	122.7(2)	C(5)-C(10)-H(10)	118.7
C(9)-C(10)-H(10)	118.7	O(2)-C(11)-O(1)	107.71(19)
O(2)-C(11)-H(11A)	110.2	O(1)-C(11)-H(11A)	110.2
O(2)-C(11)-H(11B)	110.2	O(1)-C(11)-H(11B)	110.2
H(11A)-C(11)-H(11B)	108.5	C(3)-C(12)-H(12A)	109.5
C(3)-C(12)-H(12B)	109.5	H(12A)-C(12)-H(12B)	109.5
C(3)-C(12)-H(12C)	109.5	H(12A)-C(12)-H(12C)	109.5
H(12B)-C(12)-H(12C)	109.5	O(5)-C(13)-C(3)	125.8(3)
O(5)-C(13)-H(13)	117.1	C(3)-C(13)-H(13)	117.1
C(19)-C(14)-C(15)	117.9(2)	C(19)-C(14)-C(2)	122.4(2)
C(15)-C(14)-C(2)	119.66(19)	C(14)-C(15)-C(16)	121.3(2)
C(14)-C(15)-H(15)	119.3	C(16)-C(15)-H(15)	119.3
C(17)-C(16)-C(15)	118.8(2)	C(17)-C(16)-H(16)	120.6
C(15)-C(16)-H(16)	120.6	C(16)-C(17)-C(18)	121.5(2)
C(16)-C(17)-Br(1)	119.97(18)	C(18)-C(17)-Br(1)	118.53(17)
C(19)-C(18)-C(17)	118.8(2)	C(19)-C(18)-H(18)	120.6
C(17)-C(18)-H(18)	120.6	C(18)-C(19)-C(14)	121.6(2)
C(18)-C(19)-H(19)	119.2	C(14)-C(19)-H(19)	119.2

Symmetry transformations used to generate equivalent atoms:

Table 4. Anisotropic displacement parameters ($Å^2 x\ 10^3$) for **22**. The anisotropic displacement factor exponent takes the form: $-2\pi^2[\ h^2\ a^{*2}U^{11} + ...\ + 2\ h\ k\ a^*\ b^*\ U^{12}\ ]$

	U^{11}	U^{22}	U^{33}	U^{23}	U^{13}	U^{12}
Br(1)	65(1)	33(1)	54(1)	11(1)	-5(1)	11(1)
O(1)	38(1)	39(1)	36(1)	3(1)	13(1)	1(1)
O(2)	37(1)	42(1)	41(1)	9(1)	7(1)	-9(1)
O(3)	71(2)	117(2)	50(1)	-45(1)	27(1)	-44(2)
O(4)	28(1)	86(2)	59(1)	24(1)	3(1)	-9(1)
O(5)	56(1)	51(1)	93(2)	30(1)	-10(1)	3(1)
N(1)	28(1)	32(1)	45(1)	-2(1)	9(1)	4(1)
C(1)	26(1)	32(1)	32(1)	5(1)	2(1)	0(1)
C(2)	21(1)	27(1)	24(1)	-2(1)	-1(1)	0(1)
C(3)	20(1)	29(1)	28(1)	5(1)	-1(1)	1(1)
C(4)	21(1)	30(1)	28(1)	3(1)	0(1)	-1(1)
C(5)	18(1)	29(1)	31(1)	5(1)	-1(1)	2(1)
C(6)	22(1)	24(1)	34(1)	2(1)	-1(1)	2(1)
C(7)	22(1)	31(1)	29(1)	4(1)	2(1)	8(1)
C(8)	20(1)	33(1)	38(1)	11(1)	-1(1)	-1(1)
C(9)	29(1)	29(1)	41(1)	1(1)	-3(1)	-6(1)
C(10)	27(1)	34(1)	32(1)	-2(1)	1(1)	4(1)
C(11)	36(1)	50(2)	41(2)	13(1)	8(1)	1(1)
C(12)	31(1)	55(2)	32(1)	5(1)	2(1)	-10(1)
C(13)	22(1)	31(1)	56(2)	13(1)	-1(1)	0(1)
C(14)	20(1)	29(1)	23(1)	3(1)	6(1)	-2(1)
C(15)	34(1)	32(1)	27(1)	-1(1)	-5(1)	-4(1)
C(16)	36(1)	40(1)	29(1)	9(1)	-7(1)	0(1)
C(17)	31(1)	24(1)	35(1)	10(1)	4(1)	2(1)
C(18)	33(1)	29(1)	31(1)	0(1)	-1(1)	-3(1)
C(19)	27(1)	34(1)	26(1)	3(1)	-5(1)	-1(1)

Table 5. Hydrogen coordinates (x 10^4) and isotropic displacement parameters ($Å^2$x 10^3) for **22**.

	x	y	z	U(eq)
H(1A)	13766	8980	1477	36
H(1B)	13680	7545	1332	36
H(2)	11296	7952	635	29
H(4A)	8416	9015	1498	32
H(4B)	8433	7907	995	32
H(6)	7240	8755	2600	32
H(9)	5331	4856	1934	40
H(10)	7241	5970	1293	37
H(11A)	3920	6409	3993	51
H(11B)	2702	7009	3463	51
H(12A)	10361	7981	2608	59
H(12B)	10752	9281	2289	59
H(12C)	12194	8280	2348	59
H(13)	10560	6144	1172	44
H(15)	9748	9300	37	37
H(16)	8807	11265	-220	42
H(18)	11282	12597	1336	37
H(19)	12176	10636	1595	35

Table 6. Torsion angles [°] for **22**.

O(3)-N(1)-C(1)-C(2)	-31.4(3)
O(4)-N(1)-C(1)-C(2)	147.4(2)
N(1)-C(1)-C(2)-C(14)	-68.3(2)
N(1)-C(1)-C(2)-C(3)	163.48(17)
C(14)-C(2)-C(3)-C(13)	163.34(19)
C(1)-C(2)-C(3)-C(13)	-69.6(2)
C(14)-C(2)-C(3)-C(12)	-74.0(2)
C(1)-C(2)-C(3)-C(12)	53.0(2)
C(14)-C(2)-C(3)-C(4)	49.3(2)
C(1)-C(2)-C(3)-C(4)	176.35(18)
C(13)-C(3)-C(4)-C(5)	55.2(3)
C(12)-C(3)-C(4)-C(5)	-66.5(2)
C(2)-C(3)-C(4)-C(5)	168.03(18)
C(3)-C(4)-C(5)-C(10)	-91.7(3)
C(3)-C(4)-C(5)-C(6)	90.0(2)
C(10)-C(5)-C(6)-C(7)	0.3(3)
C(4)-C(5)-C(6)-C(7)	178.59(19)
C(5)-C(6)-C(7)-C(8)	0.6(3)
C(5)-C(6)-C(7)-O(1)	177.5(2)
C(11)-O(1)-C(7)-C(6)	174.3(2)
C(11)-O(1)-C(7)-C(8)	-8.6(2)
C(6)-C(7)-C(8)-C(9)	-0.9(4)
O(1)-C(7)-C(8)-C(9)	-178.3(2)
C(6)-C(7)-C(8)-O(2)	175.7(2)
O(1)-C(7)-C(8)-O(2)	-1.7(2)
C(11)-O(2)-C(8)-C(9)	-172.4(2)
C(11)-O(2)-C(8)-C(7)	11.3(2)
C(7)-C(8)-C(9)-C(10)	0.3(3)
O(2)-C(8)-C(9)-C(10)	-175.6(2)
C(6)-C(5)-C(10)-C(9)	-0.9(3)
C(4)-C(5)-C(10)-C(9)	-179.2(2)
C(8)-C(9)-C(10)-C(5)	0.6(3)
C(8)-O(2)-C(11)-O(1)	-16.5(2)
C(7)-O(1)-C(11)-O(2)	15.4(2)

C(12)-C(3)-C(13)-O(5)	-0.7(3)
C(4)-C(3)-C(13)-O(5)	-122.5(3)
C(2)-C(3)-C(13)-O(5)	124.1(3)
C(1)-C(2)-C(14)-C(19)	-51.0(3)
C(3)-C(2)-C(14)-C(19)	75.2(3)
C(1)-C(2)-C(14)-C(15)	130.6(2)
C(3)-C(2)-C(14)-C(15)	-103.2(2)
C(19)-C(14)-C(15)-C(16)	-1.7(3)
C(2)-C(14)-C(15)-C(16)	176.8(2)
C(14)-C(15)-C(16)-C(17)	0.7(4)
C(15)-C(16)-C(17)-C(18)	1.0(4)
C(15)-C(16)-C(17)-Br(1)	-178.14(18)
C(16)-C(17)-C(18)-C(19)	-1.5(4)
Br(1)-C(17)-C(18)-C(19)	177.65(18)
C(17)-C(18)-C(19)-C(14)	0.4(4)
C(15)-C(14)-C(19)-C(18)	1.2(3)
C(2)-C(14)-C(19)-C(18)	-177.3(2)

Symmetry transformations used to generate equivalent atoms: