Supporting Information

Highly Enantioselective Conjugate Addition of Aldehydes to Nitroolefins Catalyzed by Chiral Bifunctional Sulfamides

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A) General Information

Experimental Methods

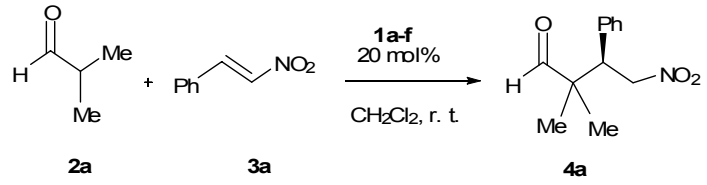
^{1}H NMR and ^{13}C NMR spectra were recorded on Varian Mercury 300 spectrometer or Varian INOVA500NB spectrometer. Chemical shifts of protons are reported in parts per million downfield from tetramethylsilane and are referenced to residual protium in the NMR solvent ($CHCl_3$: δ 7.26). Chemical shifts of carbon are referenced to the carbon resonances of the solvent ($CHCl_3$: δ 77.0 and CH_3OH: δ 46.0). Peaks are labeled as singlet (s), doublet (d), triplet (t), quartet (q) and multiplet (m). Optical

rotations were measured on a Perkin Elmer digital polarimeter. Melting points were measured on a WRS-2A melting point apparatus and are uncorrected. The mass spectroscopic data were obtained at the Thermo DSQⅡ and Agilent 6120 mass spectrometer. The high resolution mass spectroscopic data were obtained at the Thermo MAT 95XP mass spectrometer. Infrared (IR) spectra were recorded on a Bruker Tensor 37 spectrophotometer. Data are represented as follows: frequency of absorption (cm^{-1}), intensity of absorption (vs = very strong, s = strong, m = medium, w = weak). Enantiomeric excesses were determined by HPLC using a Daicel Chiralcel AD-H, OD-H, column and eluting with a hexane/*i*PrOH solution.

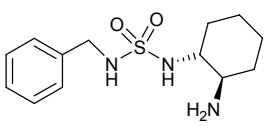
Materials.

Flash chromatography was performed over silica gel (230-400 mesh), purchased from Qingdao Haiyang Chemical Co., Ltd. Commercial reagents were used as received. Toluene was distilled over sodium and dichloromethane was distilled over calcium hydride. The other solvents were used as received in analytical grade.

B) Catalyst optimization

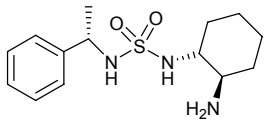


2a **3a** **4a**



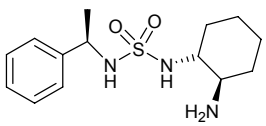
1a

160 h, 74% Yield, 94%ee



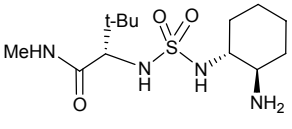
1b

160 h, 52% Yield, 94%ee



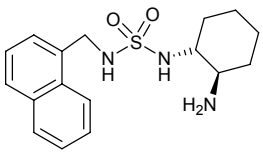
1c

160 h, 50% Yield, 94% ee



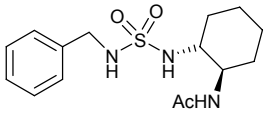
1d

160 h, 62% Yield, 93%ee



1e

160 h, 38% Yield, 77%ee



1f

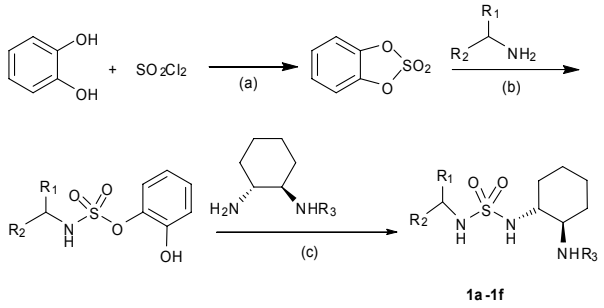
240 h, no reaction

C) Effects of reaction solvents

Entry	Solvent	T (h)	Yield (%)	ee (%)
1	CH_2Cl_2	72	73	94
2	$CHCl_3$	108	61	98
3	^{i}-PrOH	100	71	93
4	THF	168	51	97
5	Et_2O	91	46	98
6	Hexane	168	69	97
7	Toluene	156	38	97

[a] The reactions were carried out with 20 mol% **1a** at room temperature.

D) General procedure for the preparation of sulfamides 1a-1f[1-2]



Reaction conditions: (a) pyridine, hexane, ice-bath, 1d; (b) Et_3N, CH_2Cl_2; (c) dioxane, reflux, 2.5 h.

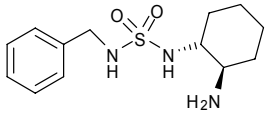
A 100-mL round bottomed flask was charged with catechol (2.2 g, 0.02 mmol), pyridine (3.2 g, 0.04 mmol) and hexane (20 mL). A solution of sulfuryl chloride (2.7 g, 0.02 mol) in 5 mL of hexane was then added dropwise over 1 h at -5 ℃. The reaction mixture was stirred at 0 ℃ overnight and at ambient temperature for another 12 h. The upper layer of the reaction mixture was decanted. The lower layer was diluted with 50 mL water and extracted with ethyl ether (4 × 30 mL). The combined organic layer was washed with 2% NaOH (3 × 30 mL) and dried over sodium sulfate. After the evaporation of solvent under vacuum, catechol sulfate was obtained as a colorless oil (1.3 g, 38% yield), which was used in next step without further purification.

To a solution of benzylamine (1.17 g, 10.0 mmol), triethylamine (1.2 g, 12.0 mmol), DMF (20 mL) and anhydrous dichloromethane (10 mL) under an ice-bath,

was added dropwise a solution of catechol sulfate (1.72 g, 10.0 mmol) in dichloromethane (20 mL). The reaction mixture was stirred for 24 h at room temperature and then diluted with dichloromethane (30 mL). The reaction solution was washed with 1 M hydrochloric acid (2 × 20 ml), brine (2 × 20 ml) and dried over Na_2SO_4. After the evaporation of solvent under vacuum, the crude product was purified by flash chromatography over silica gel (EtOAc/petroleum ether = 1/1) to give 2-Hydroxyphenyl N-Benzylsulfamate as a white solid (2.79 g, 100% yield).

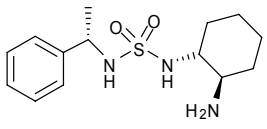
A solution of 2-hydroxyphenyl N-benzylsulfamate (279 mg, 1.0 mmol) and (*R*, *R*) -cyclohexane-1, 2-diamine (114 mg, 1.0 mmol) in dry dioxane (30 mL) was refluxed for 2.5 h. After dioxane was removed under vacuum, the residue was dissolved in ethyl acetate (50 mL). The solution was washed with water (1 × 20 mL), 2% NaOH (3 × 20 ml), brine (1 × 20 mL) and dried over Na_2SO_4. After evaporation of the solvent under vacuum, the crude product was purified by flash chromatography over silica gel (MeOH / EtOAc = 1/10) to give N-benzyl-N'-(2-aminocyclohexyl) sulfamide (**1a**) as a white solid (139 mg, 49% yield).

***1S, 2S*-N-benzyl-N'-(2-aminocyclohexyl) sulfamide (1a)**



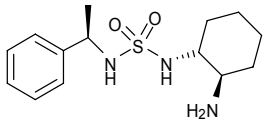
M.p.: 148-149 ℃; $[\alpha]_{24}^{589}$ = - 8.0 (c 2.0, CH_3OH); **^{1}H NMR** (300 MHz, CD_3OD) δ: 7.39-7.25 (m, 5H, Ar-H), 4.17 (d, ^3J(H,H) = 9.1 Hz, 2H, CH_2), 2.81-2.80 (m, 1H, CH), 2.41-2.33 (m, 1H, CH), 2.09-2.06 (m, 2H, CH_2), 1.73-1.71 (m, 2H, CH_2), 1.30-1.22 (m, 4H, $2CH_2$); **^{13}C NMR** (75 MHz, CD_3OD) δ: 136.6, 126.7, 126.1, 112.5, 58.1, 53.1, 45.1, 32.0, 31.2, 23.8, 23.2; **IR** (thin film) ν/cm^{-1}: 3369 (m), 3291 (m), 3033 (m), 2860 (m), 1610 (w), 1454 (m), 1306 (s), 1144 (s), 910 (m); **MS** (FAB$^+$): 284, 154, 149, 136, 115, 107, 91; **HRMS** (FAB$^+$) calcd. for $C_{13}H_{22}O_2N_3S_1$ (M + H$^+$): 284.1427, found: 284.1425.

N-(*S*-1-phenylethyl)-N'-(2-aminocyclohexyl) sulfamide (1b)



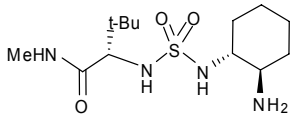
White solid (114 mg, 38.4% yield). **M.p.**: 115-118℃, $[\alpha]_{24}^{589}$ = - 32.2 (c 2.3, CH_3OH); **^{1}H NMR** (300 MHz, CD_3OD) δ: 7.38-7.22 (m, 5H, Ar-H), 4.48 (d, ^3J(H,H) = 6.9 Hz, 1H, CH), 2.67-2.64 (m, 1H, CH), 2.28-2.27 (m, 1H, CH), 1.90-1.60 (m, 4H, $2CH_2$), 1.49 (d, ^3J(H,H) = 6.9 Hz, 3H, CH_3), 1.25-1.01 (m, 4H, $2CH_2$); **^{13}C NMR** (75 MHz, CD_3OD) δ: 144.6, 128.4, 127.0, 126.1, 59.8, 54.8, 53.6, 33.6, 32.6, 25.3, 24.8, 24.1; **IR** (thin film) ν/cm^{-1}: 3369 (s), 3268 (s), 3062 (w), 2921 (m), 2858 (m), 1601 (w), 1451 (vs), 1314 (vs), 1156 (vs), 1100 (s), 758 (m); **MS** (FAB^+): 298, 280, 149, 136, 115, 105, 57; **HRMS** (FAB^+) calcd. for $C_{14}H_{24}O_2N_3S_1$ ($M + H^+$): 298.1584, found: 298.1558.

N-(*R*-1-phenylethyl)-N'-(2-aminocyclohexyl) sulfamide (1c)



White solid (90.0 mg, 30.3% yield). **M.p.**: 110-111 ℃; $[\alpha]_{29}^{589}$ = + 8.0 (c 2.5, CH_3OH); **^{1}H NMR** (400 MHz, CD_3OD) δ: 7.29-7.11 (m, 5H, Ar-H), 4.41-4.39 (q, ^3J(H,H) = 6.8 Hz, 1H, CH), 2.62-2.56 (m, 1H, CH), 2.20-2.13 (m, 1H, CH), 2.00-1.98 (m, 1H, CH_2), 1.80-1.77 (m, 1H, CH_2), 1.60-1.57 (m, 2H, CH_2), 1.38-1.36 (d, ^3J(H,H) = 6.8 Hz, 3H, CH_3), 1.15-0.97 (m, 4H, $2CH_2$); **^{13}C NMR**: (100 MHz, CD_3OD) δ: 146.0, 129.6, 128.2, 127.4, 61.3, 55.8, 54.7, 35.0, 34.1, 26.5, 26.0, 25.0; **IR** (thin film) ν/cm^{-1}: 3415 (vs), 3236 (m), 3063 (w), 2932 (m), 2858 (m), 1638 (m), 1618 (m), 1449 (m), 1308 (s), 1150 (s), 1105 (m), 627 (m); **MS** (EI): 297, 282, 113, 106, 96, 79; **HRMS** (EI) calcd. for $C_{14}H_{23}O_2N_3S_1$ (M^+): 297.1505, found: 297.1501.

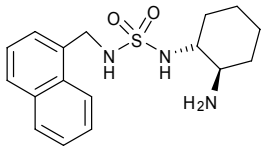
***1S,2S*-N-[3,3-dimethyl-1-(methylamino)-1-oxo-butan-2-yl]-N'-(2-aminocyclohexyl) sulfamide (1d)**[3]



White solid (167 mg, 52.1% yield). **M.p.**: 101-105 ℃;

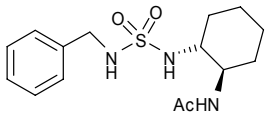
$[\alpha]_{29}^{589}$ = + 19.0 (c 1.0, CH_3OH); **^{1}H NMR** (300 MHz, CD_3OD) δ: 3.53 (d, ^3J(H,H) = 1.2 Hz, 1H, CH), 2.95-2.87 (m, 1H, CH), 2.72 (dd, ^3J(H,H) = 3.6 Hz, ^3J(H,H) = 0.9 Hz, 3H, CH_3), 2.67-2.59 (m, 1H, CH), 2.03-1.98 (m, 2H, CH_2), 1.75-1.73 (m, 2H, CH_2), 1.29-1.21 (m, 4H, $2CH_2$), 0.97 (d, ^4J(H,H) = 0.9 Hz, 6H, $2CH_3$), 0.95 (d, ^4J(H,H) = 0.9Hz, 3H, CH_3); **^{13}C NMR** (125 MHz, CD_3OD) δ: 170.9, 63.2, 54.4, 53.2, 32.3, 30.4, 29.1, 24.2, 24.1, 23.1, 23.0, 22.1; **IR** (thin film) ν/cm^{-1}: 3276 (br), 2940 (s), 2869 (s), 1654 (s), 1450 (m), 1367 (w), 1311 (m), 1155 (s), 1105 (m), 1036 (m), 755 (m); **MS** (FAB$^+$): 321, 207, 165, 145, 115, 95, 69, 55; **HRMS** (FAB$^+$) calcd. for $C_{13}H_{29}O_3N_4S_1$ (M + H$^+$): 321.1955, found: 321.1969.

***1S, 2S*-N-(naphthalen-1-ylmethyl)-N'-(2-aminocyclohexyl) sulfamide (1e)**



White solid (154 mg, 46.2% yield). **M.p.**: 150-152 ℃, $[\alpha]_{24}^{589}$ = - 5.5 (c 2.0, CH_3OH); **^{1}H NMR** (300 MHz, CD_3OD) δ: 8.19-7.41 (m, 7H, Ar-H), 4.64 (d, ^3J(H,H) = 14.1 Hz, 2H, CH_2), 2.84-2.81 (m, 1H, CH), 2.44-2.36 (m, 1H, CH), 2.05-1.91 (m, 2H, CH_2), 1.69-1.68 (m, 2H, CH_2), 1.29-1.15 (m, 4H, $2CH_2$); **^{13}C NMR** (75 MHz, CD_3OD) δ: 132.4, 131.6, 129.9, 127.0, 126.9, 126.7, 124.7, 124.6, 124.1, 121.9, 57.8, 53.2, 43.2, 31.8, 31.2, 23.7, 23.1; **IR** (thin film) ν/cm^{-1}: 3037 (w), 2931 (m), 2858 (m), 2360 (m), 1599 (w), 1489 (m), 1454 (m), 1306 (s), 1141 (s), 1038 (m), 773 (s); **MS** (FAB$^+$): 334, 307, 279, 219, 205, 149, 136, 115, 107, 77, 57; **HRMS** (FAB$^+$) calcd. for $C_{17}H_{24}O_2N_3S_1$ (M + H$^+$): 334.1584, found: 334.1580.

***1S, 2S*-N-benzyl-N'-(2-acetamidocyclohexyl) sulfamide (1f)**



White solid (235 mg, 72.3% yield). **M.p.**: 181-182 ℃; $[\alpha]_{24}^{589}$ = + 40.9 (c 2.2, CH_3OH); **^{1}H NMR** (300 MHz, CD_3OD) δ: 7.34-7.20 (m, 5H, Ar-H), 4.12 (d, ^3J(H,H) = 2.4 Hz, 2H, CH_2), 3.61-3.53 (m, 1H, CH), 3.06-3.98 (m, 1H, CH), 2.11-2.08 (m, 2H, CH_2), 1.93 (s, 3H, CH_3), 1.73-1.71 (m, 2H, CH_2), 1.31-1.29

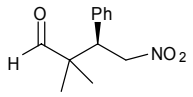
(m, 4H, $2CH_2$); **^{13}C NMR** (75 MHz, CD_3OD) δ: 170.6, 136.5, 126.7, 126.1, 125.6, 55.6, 51.4, 45.1, 31.9, 30.7, 23.3, 23.0, 20.3; **IR** (thin film) ν/cm^{-1}: 3368 (s), 3259 (s), 3165 (m), 2941 (s), 2856 (s), 1638 (vs), 1556 (s), 1465 (m), 1323 (vs), 1087 (s), 1053 (m), 732 (m); **MS** (FAB^+): 326, 279, 149, 136, 120, 91, 77, 57; **HRMS** (FAB^+) calcd. for $C_{15}H_{24}O_3N_3S_1$ ($M + H^+$): 326.1533, found: 326.1531.

E) General procedure for the conjugate addition of aldehydes to nitroolefins.

Representative method A: *trans*-β-Nitrostyrene (45 mg, 0.3 mmol), **1a** (17.0 mg, 0.06 mmol), 4-Dimethylaminopyridine (7.3 mg, 0.06 mmol), isobutyraldehyde (100 μL, 1.1 mmol) and chloroform (0.4 mL) in a 5-mL flask was stirred at room temperature for 3 hr. After evaporation of solvent under vacuum, the residue was separated by flash chromatography over silica gel (Petroleum ether / EtOAc = 10/1) to give 2, 2-dimethyl-4-nitro-3-phenyl-butanal as a colorless oil.

Representative method B: *trans*-β-Nitrostyrene (45 mg, 0.3 mmol), **1a** (17.0 mg, 0.06 mmol), imidazole (4.1 mg, 0.06 mmol), isobutyraldehyde (100 μL, 1.1 mmol) and dichloromethane (0.5 mL) in a 5-mL flask was stirred at room temperature. The reaction was monitored by TLC until *trans*-β-Nitrostyrene was completely consumed. After evaporation of solvent under vacuum, the residue was separated by flash chromatography over silica gel (Petroleum ether / EtOAc = 10/1) to give 2, 2-dimethyl-4-nitro-3-phenyl-butanal as a colorless oil.

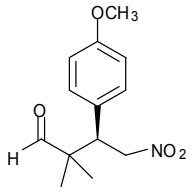
(*R*)-2, 2-dimethyl-4-nitro-3-phenyl-butanal (4a)



The title compound was prepared from *trans*-β-nitrostyrene[4] and isobutyraldehyde according to Method A. The enantiomeric excess was determined by HPLC with Chiralpak AD-H column at 208 nm (hexane / ^{i}-PrOH = 98/2, 0.5 mL/min). t_{major} = 24.0 min, t_{minor} = 25.0 min); $[\alpha]_{24}^{589}$ = + 3.0 (c 1.0, $CHCl_3$); **^{1}H NMR** (300 MHz, $CDCl_3$) δ: 9.51 (s, 1H, CHO), 7.31-7.24 (m, 5H, Ar-H), 4.85 (dd,

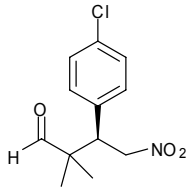
^2J(H,H) = 12.9 Hz, ^3J(H,H) = 11.1 Hz, 1H, CH_2), 4.68 (dd, ^2J(H,H) = 12.9 Hz, ^3J(H,H) = 4.2 Hz, 1H, CH_2), 3.78 (dd, ^3J(H,H) = 11.1 Hz, ^3J(H,H) = 4.2 Hz, 1H, CH), 1.14 (s, 3H, CH_3), 1.01 (s, 3H, CH_3); **^{13}C NMR** (75 MHz, $CDCl_3$) δ: 204.0, 135.2, 129.0, 128.6, 128.0, 76.3, 48.5, 48.2, 21.7, 19.0; **IR** (thin film) ν/cm^{-1}: 2925 (w), 1726 (m), 1638 (m), 1556 (s), 1456 (w), 1380 (m), 705 (m); **MS** (EI): 221, 187, 170, 159, 145, 117, 105, 91, 77, 72.

(*R*)-3-(4-methoxyphenyl)-2,2-dimethyl-4-nitrobutanal (4b)



The title compound was prepared from *trans*-1-methoxy-4-(2-nitro-vinyl) benzene [4] and isobutyraldehyde according to Method A. The enantiomeric excess was determined by HPLC with Chiralpak OD-H column at 208 nm (hexane / $^{i-}$PrOH = 75/25, 0.8 mL/min; t_{major} = 14.4 min, t_{minor} = 19.5 min); $[\alpha]_{29}^{589}$ = - 5.0 (c 1.0, $CHCl_3$); **^{1}H NMR** (300 MHz, $CDCl_3$) δ: 9.51 (s, 1H, CHO), 7.11 (d, ^3J(H,H) = 8.7 Hz, 2H, 3,5-Ar-H), 6.84 (d, ^3J(H,H) = 8.7 Hz, 2H, 2,6-Ar-H), 4.81 (dd, ^2J(H,H) = 12.6 Hz, ^3J(H,H) = 11.4 Hz, 1H, CH_2), 4.66 (dd, ^2J(H,H) = 12.6 Hz, ^3J(H,H) = 4.2 Hz, 1H, CH_2), 3.79 (s, 3H, OCH_3), 3.74 (dd, ^3J(H,H) = 11.4 Hz, ^3J(H,H) = 4.5 Hz, 1H, CH), 1.13 (s, 3H, CH_3), 1.01 (s, 3H, CH_3); **^{13}C NMR** (125 MHz, $CDCl_3$) δ: 204.3, 159.3, 130.1, 127.1, 114.1, 76.5, 55.2, 48.3, 47.9, 21.5, 18.9; **IR** (thin film) ν/cm^{-1}: 2927 (w), 1725 (m), 1611 (w), 1556 (vs), 1514 (s), 1465 (w), 1380 (m), 1252 (m), 1033 (w), 836 (w); **MS** (EI): 251, 180, 135, 134, 121, 119, 91; **HRMS** (EI) calcd. for $C_{13}H_{17}O_4N_1$ (M^+): 251.1152, found: 251.1150.

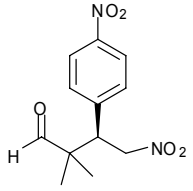
(*R*)-3-(4-chlorophenyl)-2,2-dimethyl-4-nitrobutanal (4c)



The title compound was prepared from *trans*-1-chloro-4-(2-nitrovinyl) benzene[4] and isobutyraldehyde according to Method A. The enantiomeric excess

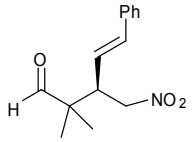
was determined by HPLC with Chiralpak OD-H column at 208 nm (hexane / ^{i}-PrOH = 75/25, 0.8 mL/min; t_{major} = 13.2 min, t_{minor} = 19.2 min); $[\alpha]_{24}^{589}$ = + 3.0 (c 1.0, $CHCl_3$); **^{1}H NMR** (300 MHz, $CDCl_3$) δ: 9.48 (s, 1H, CHO), 7.32 (t, ^3J(H,H) = 2.4 Hz, 1H, 2-Ar-H), 7.29 (t, ^3J(H,H) = 2.4 Hz, 1H, 6-Ar-H), 7.15 (t, ^3J(H,H) = 2.4 Hz, 1H, 3-Ar-H), 7.12 (t, ^3J(H,H) = 2.4 Hz, 1H, 5-Ar-H), 4.82 (dd, ^2J(H,H) = 13.2 Hz, ^3J(H,H) = 11.4 Hz, 1H, CH_2), 4.68 (dd, ^2J(H,H) = 13.2 Hz, ^3J(H,H) = 4.2 Hz, 1H, CH_2), 3.77 (dd, ^3J(H,H) = 11.4 Hz, ^3J(H,H) = 4.2 Hz, 1H, CH), 1.13 (s, 3H, CH_3), 1.01 (s, 3H, CH_3); **^{13}C NMR** (75 MHz, $CDCl_3$) δ: 203.5, 134.0, 133.9, 130.3, 128.8, 76.1, 48.2, 48.0, 21.8, 19.0; **IR** (thin film) ν/cm^{-1}: 2926 (w), 1728 (m), 1556 (s), 1494 (w), 1378 (m), 1094 (w), 835 (w); **MS** (EI): 255, 193, 184, 140, 138, 125, 103, 77, 72; **HRMS** (EI) calcd. for $C_{12}H_{14}O_3N_1Cl$ (M^+): 255.0657, found: 255.0658.

(*R*)-2,2-dimethyl-4-nitro-3-(4-nitrophenyl)-butanal (4d)



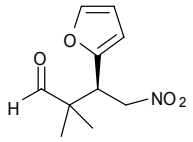
The title compound was prepared from *trans*-1-nitro-4-(2-nitrovinyl) benzene[4] and isobutyraldehyde according to Method A. The enantiomeric excess was determined by HPLC with Chiralpak OD-H column at 208 nm (hexane / ^{i}-PrOH = 80/20, 0.8 mL/min; t_{major} = 25.6 min, t_{minor} = 38.2 min); $[\alpha]_{24}^{589}$ = + 8.0 (c 1.0, $CHCl_3$); **^{1}H NMR** (300 MHz, $CDCl_3$) δ: 9.48 (s, 1H, CHO), 8.21 (d, ^3J(H,H) = 8.7 Hz, 2H, 3, 5-Ar-H), 7.42 (d, ^3J(H,H) = 8.7 Hz, 2H, 2, 6-Ar-H), 4.90 (t, $^{2,3}J$(H,H) = 13.5 Hz, 1H, CH_2), 4.77 (dd, ^2J(H,H) = 13.5 Hz, ^3J(H,H) = 3.9 Hz, 1H, CH_2), 3.94 (dd, ^3J(H,H) = 13.5 Hz, ^3J(H,H) = 3.9 Hz, 1H, CH), 1.17 (s, 3H, CH_3), 1.06 (s, 3H, CH_3); **^{13}C NMR** (75 MHz, $CDCl_3$) δ: 203.3, 147.8, 143.5, 130.4, 124.1, 76.1, 48.6, 48.3, 22.3, 19.4; **IR** (thin film) ν/cm^{-1}: 2923 (w), 1725 (m), 1604 (w), 1556 (s), 1522 (s), 1377 (w), 1348 (s), 858 (m), 703 (w); **MS** (EI): 267$(M+1)^+$, 220, 204, 190, 177, 164, 149, 129, 115, 103, 91, 77; **HRMS** (EI) calcd. for $C_{12}H_{15}O_5N_2$ $(M+1)^+$: 267.0975, found: 267.0973.

(*R*)-*E*-2,2-dimethyl-3-(nitromethyl)-5-phenylpent-4-enal (4e)



The title compound was prepared from (1E, 2E)-4-nitrobuta-1,3-dienyl benzene[4] and isobutyraldehyde according to Method A. The enantiomeric excess was determined by HPLC with Chiralpak OD-H column at 208 nm (hexane / $^{i-}$PrOH = 80/20, 0.8 mL/min; t_{major} = 15.4 min, t_{minor} = 16.5 min); $[\alpha]_{24}^{589}$ = - 2.0 (c 1.0, $CHCl_3$); **^{1}H NMR** (400 MHz, $CDCl_3$) δ: 9.52 (s, 1H, CHO), 7.35-7.26 (m, 5H, Ar-H), 6.53 (d, ^3J(H,H) = 15.6 Hz, 1H, =CH), 6.02 (dd, ^3J(H,H) = 10.2 Hz, ^3J(H,H) = 15.6 Hz, 1H, =CH), 4.52 (dd, ^3J(H,H) = 4.0 Hz, ^2J(H,H) = 12.0 Hz, 1H, CH_2), 4.45 (dd, ^3J(H,H) = 4.0 Hz, ^2J(H,H) = 12.0 Hz, 1H, CH_2), 3.28 (dt, ^3J(H,H) = 4.0 Hz, ^3J(H,H) = 10.2 Hz, 1H, CH), 1.17 (s, 3H, CH_3), 1.16 (s, 3H, CH_3); **^{13}C NMR** (100 MHz, $CDCl_3$) δ: 203.8, 136.3, 136.0, 128.6, 128.2, 126.6, 122.9, 47.8, 47.2, 21.0, 19.1; **IR** (thin film) ν/cm^{-1}: 2974 (w), 1723 (m), 1554 (s), 1450 (w), 1380 (m), 972 (m), 887 (w), 749 (m); **MS** (EI): 247, 200, 157, 129, 115, 104, 91, 77; **HRMS** (EI) calcd. for $C_{14}H_{17}O_3N_1$ $(M)^+$: 247.1203, found: 247.1206.

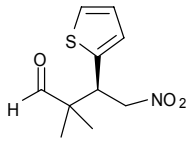
(*R*)-3-(furan-2-yl)-2,2-dimethyl-4-nitrobutanal (4f)



The title compound was prepared from *trans*-2-(2-nitrovinyl) furan[4] and isobutanal according to Method A. The enantiomeric excess was determined by HPLC with Chiralpak OD-H column at 208 nm (hexane / $^{i-}$PrOH = 75/25, 0.8 mL/min; t_{major} = 9.7 min, t_{minor} = 13.9 min); $[\alpha]_{29}^{589}$ = - 19.0 (c 1.0, $CHCl_3$); **^{1}H NMR** (300 MHz, $CDCl_3$) δ: 9.50 (s, 1H, CHO), 7.36 (s, 1H, Ar-H), 6.30 (s, 1H, Ar-H), 6.21 (d, ^3J(H,H) = 3.0 Hz, 1H, Ar-H), 4.75 (dd, ^2J(H,H) = 12.6 Hz, ^3J(H,H) = 11.1 Hz, 1H, CH_2), 4.57 (dd, ^2J(H,H) = 12.6 Hz, ^3J(H,H) = 3.6 Hz, 1H, CH_2), 3.92 (dd, ^3J(H,H) = 11.1 Hz, ^3J(H,H) = 3.6 Hz, 1H, CH), 1.18 (s, 3H, CH_3), 1.05 (s, 3H, CH_3); **^{13}C NMR** (75 MHz, $CDCl_3$) δ: 203.7, 149.9, 142.9, 110.7, 109.9, 75.2, 48.5, 42.5, 21.5, 19.4; **IR** (thin film) ν/cm^{-1}: 2925 (w), 1728 (m), 1557 (s), 1376 (m), 1148 (m), 740

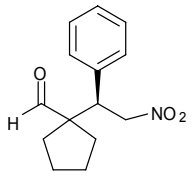
(m); **MS** (EI): 211, 181, 164, 149, 121, 94, 81.

(*R*)-2,2-dimethyl-4-nitro-3-(thiophen-2-yl) butanal (4g)



The title compound was prepared from *trans*-2-(2-nitrovinyl) thiophene[4] and isobutanal according to Method A. The enantiomeric excess was determined by HPLC with Chiralpak OD-H column at 208 nm (hexane / $^{i-}$PrOH = 75/25, 0.8 mL/min; t_{major} = 12.3 min, t_{minor} = 18.7 min); $[\alpha]_{29}^{589}$ = + 11.0 (c 1.0, $CHCl_3$); **^{1}H NMR** (300 MHz, $CDCl_3$) δ: 9.52 (s, 1H, CHO), 7.23-7.22 (m, 1H, 5-Ar-H), 6.95 (dd, ^3J(H,H) = 5.1 Hz, ^3J(H,H) = 3.6 Hz, 1H, 4-Ar-H), 6.91 (dd, ^3J(H,H) = 3.6 Hz, ^4J(H,H) = 0.9 Hz, 1H, 3-Ar-H), 4.76-4.62 (m, 2H, CH_2), 4.14 (dd, ^3J(H,H) = 10.5 Hz, ^3J(H,H) = 4.5 Hz, 1H, CH), 1.22 (s, 3H, CH_3), 1.08 (s, 3H, CH_3); **^{13}C NMR** (75 MHz, $CDCl_3$) δ: 203.8, 138.0, 128.1, 127.2, 125.7, 78.1, 48.7, 44.3, 21.9, 19.2; **IR** (thin film) ν/cm^{-1}: 2925 (w), 1725 (m), 1557 (s), 1433 (w), 1378 (m), 882 (w), 704 (m); **MS** (EI): 227, 207, 180, 165, 156, 110, 97, 84.

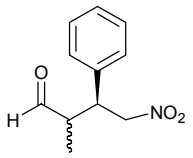
(*R*)-1-(2-nitro-1-phenyl) cyclopentanecarbaldehyde (4h)



The title compound was prepared from *trans*-ß-nitrostyrene and cyclopentanecarbaldehyde according to method B. The enantiomeric excess and diastereomeric ratio were determined by HPLC with Chiralpak AS-H column at 208 nm (hexane / $^{i-}$PrOH = 75/25, 0.8 mL/min; t_{major} = 12.3 min, t_{minor} = 16.3 min); $[\alpha]_{24}^{589}$ = - 13.0 (c 1.0, $CHCl_3$); **^{1}H NMR** (300 MHz, $CDCl_3$) δ: 9.52 (s, 1H, CHO), 7.36-7.22 (m, 5H, Ar-H), 4.99 (dd, ^2J(H,H) = 13.2 Hz, ^3J(H,H) = 11.4 Hz, 1H, CH_2), 4.72 (dd, ^2J(H,H) = 13.2 Hz, ^3J(H,H) = 3.6 Hz, 1H, CH_2), 3.72 (dd, ^3J(H,H) = 11.4 Hz, ^3J(H,H) = 3.6 Hz, 1H, CH), 2.09-1.88 (m, 2H, CH_2), 1.69-1.54 (m, 6H, $3CH_2$); **^{13}C NMR** (75 MHz, $CDCl_3$) δ: 204.3, 136.3, 128.7, 128.0, 77.3, 60.2, 49.2, 32.5, 31.4,

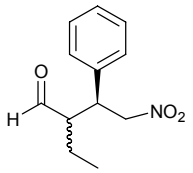
24.8, 24.6; **IR** (thin film) ν/cm^{-1}: 2957 (w), 2361 (w) , 1781 (w), 1710 (s), 1554 (m), 1455 (w), 1229 (w), 702 (m); **MS** (EI): 247, 199, 171, 129, 115, 105, 104, 91, 67.

(*2R/2S, 3R*)-2-methyl-4-nitro-3-phenylbutanal (4i)



The title compound was prepared from *trans*-ß-nitrostyrene and propionaldehyde according to method B. The enantiomeric excess and diastereomeric ratio were determined by HPLC with Chiralpak OD-H column at 208 nm (hexane / ^{i}-PrOH = 80/20, 0.8 mL/min; t_{major} = 16.9 min, t_{min} = 21.1 min); $[\alpha]_{29}^{589}$ = + 19.0 (c 1.0, $CHCl_3$); **^{1}H NMR** (300 MHz, $CDCl_3$) Signals corresponding to the major Diastereomer δ: 9.69 (s, 1H, CHO), 7.32-7.13 (m, 5H, Ar-H), 4.82-4.63 (m, 2H, CH_2), 3.86-3.76 (m, 1H, CH), 2.81-2.74 (m, 1H, CH), 1.21 (d, ^3J(H,H) = 7.2 Hz, 3H, CH_3); Signals corresponding to the minor Diastereomer δ: 9.51 (s, 1H, CHO), 7.32-7.13 (m, 5H, Ar-H), 4.82-4.63 (m, 2H, CH_2), 3.86-3.76 (m, 1H, CH), 2.81-2.74 (m, 1H, CH), 1.00 (d, ^3J(H,H) = 7.2 Hz, 3H, CH_3); **^{13}C NMR** (125 MHz, $CDCl_3$) δ: 202.3, 136.6, 130.9, 129.0, 128.0, 78.1, 48.7, 44.0, 12.0; **IR** (thin film) ν/cm^{-1}: 3032 (w), 2973 (w), 2929 (w), 1724 (m), 1603 (w), 1555 (s), 1456 (m), 1377 (m), 702 (m); **MS** (EI): 207, 160, 145, 131, 117, 104, 91, 77.

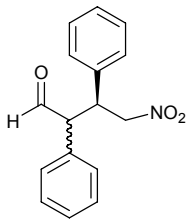
(*2R/2S, 3R*)-2-ethyl-4-nitro-3-phenylbutanal (4j)



The title compound was prepared from *trans*-ß-nitrostyrene and butyraldehyde according to method B. The enantiomeric excess and diastereomeric ratio were determined by HPLC with Chiralpak OD-H column at 208 nm (hexane / ^{i}-PrOH = 80/20, 0.8 mL/min; t_{minor} = 15.3 min, t_{major} = 17.2 min); $[\alpha]_{29}^{589}$ = + 7.0 (c 1.0, $CHCl_3$); **^{1}H NMR** (300 MHz, $CDCl_3$) Signals corresponding to the major Diastereomer δ: 9.70 (d, 1H, ^3J(H,H) = 2.4 Hz, CHO), 7.33-7.14 (m, 5H, Ar-H),

4.79-4.58 (m, 2H, CH_2), 3.82-3.77 (m, 1H, CH), 2.69-2.66 (m, 1H, CH), 0.86-0.81 (t, ^3J(H,H) = 7.5 Hz, 3H, CH_3); Signals corresponding to the minor Diastereomer δ: 9.46(d, 1H, ^3J(H,H) = 2.4 Hz, CHO), 7.33-7.14 (m, 5H, Ar-H), 4.79-4.58 (m, 2H, CH_2), 3.82-3.77 (m, 1H, CH), 2.61-2.53 (m, 1H, CH), 1.02-0.97 (t, ^3J(H,H) = 7.5 Hz, 3H, CH_3); **^{13}C NMR** (75 MHz, $CDCl_3$) Signals corresponding to the major Diastereomer δ: 202.8, 136.7, 128.9, 128.1, 127.8, 78.5, 42.7 29.7, 20.4, 10.7; Signals corresponding to the minor Diastereomer δ: 202.9, 136.7, 128.9, 128.1, 127.9, 77.8, 44.1, 29.7, 20.6, 11.5; **IR** (thin film) ν/cm^{-1}: 2956 (w), 2926 (m), 2360 (w), 1718 (m), 1555 (s), 1496 (m), 1379 (m), 701 (m); **MS** (EI): 221, 175, 145, 131, 117, 105, 104, 91, 77.

(*2R/2S, 3R*)-4-nitro-2,3-diphenylbutanal (4k)



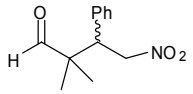
The title compound was prepared from *trans*-ß-nitrostyrene and 2-phenylacetylaldehyde according to method B. The enantiomeric excess and diastereomeric ratio were determined by HPLC with Chiralpak OD-H column at 208 nm (hexane / ^{i}PrOH = 90/10, 0.8 mL/min; t_{major} = 26.3 min, t_{minor} = 29.6 min); $[\alpha]_{29}^{589}$ = - 62.0 (c 1.0, $CHCl_3$); **^{1}H NMR** (300 MHz, $CDCl_3$) Signals corresponding to the major Diastereomer δ: 9.53 (d, ^3J(H,H) = 1.6 Hz, 1H, CHO), 7.55-7.24 (m, 10H, Ar-H), 4.49-4.40 (m, 2H, CH_2), 4.37-4.29 (m, 1H, CH), 4.08-4.05 (m, 1H, CH); **^{13}C NMR** (75 MHz, $CDCl_3$) δ: 196.6, 136.9, 132.2, 129.6, 129.2, 128.9, 128.4, 128.1, 128.0, 61.6, 44.4, 29.7; **IR** (thin film) ν/cm^{-1}: 3030 (w), 2925 (s), 2854 (m), 2360 (w), 1715 (m), 1553 (s), 1455 (m), 1380 (m), 757 (m), 700 (s); **MS** (EI): 269, 223, 193, 178, 120, 104, 91, 77.

F) Preparation of racemic samples[5]

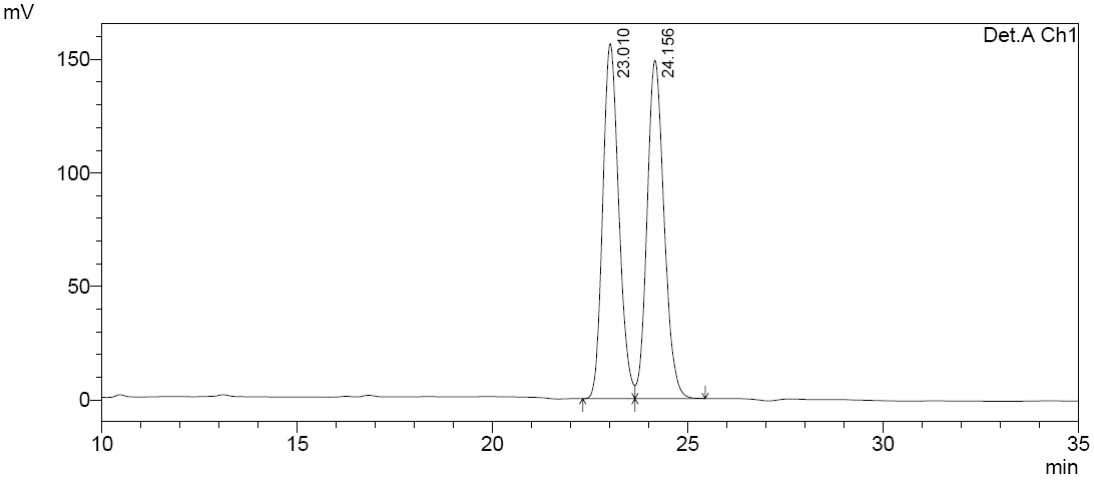
Racemic samples of the conjugate addition products were prepared using piperazine

or racemic organocatalyst **1a**, which was synthesized from racemic cyclohexane-1, 2-diamine and 2-hydroxyphenyl N-Benzylsulfamate.

G) **HPLC Chromatograms of conjugate addition products**

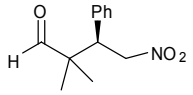


racemic-4a Chiralpak AD-H, 98:2 hexane:iPrOH, 0.5mL/min, λ = 208nm

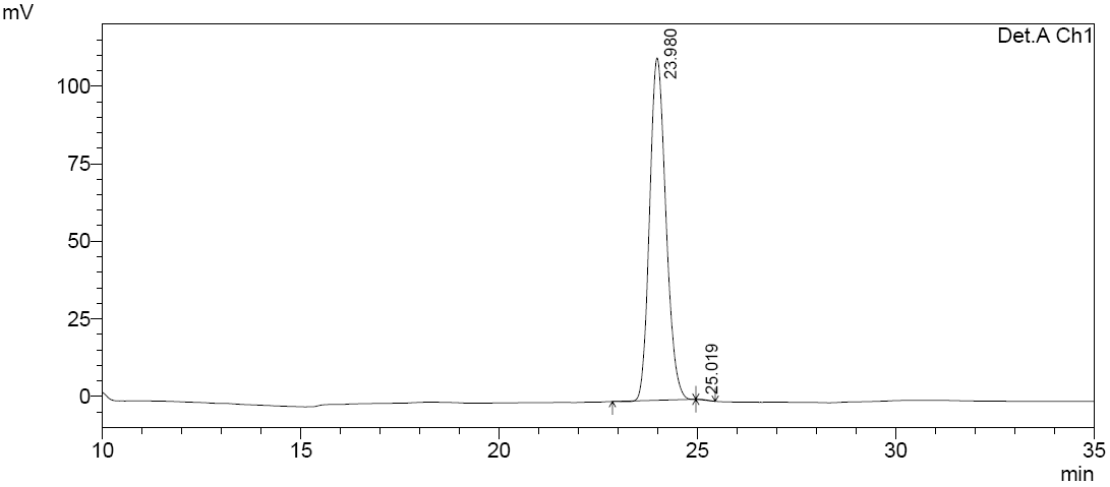


Detector A Ch1 208nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	23.010	4458148	156272	49.748	51.202
2	24.156	4503381	148936	50.252	48.798
Total		8961528	305208	100.000	100.000

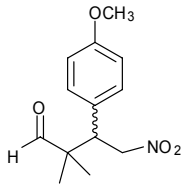


4a

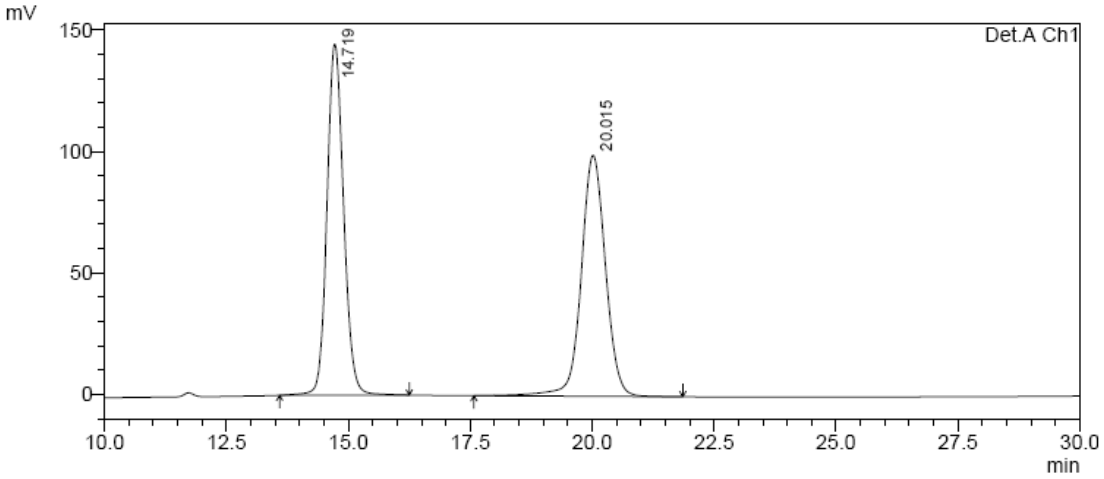


Detector A Ch1 208nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	23.980	3154115	110373	99.923	99.902
2	25.019	2444	108	0.077	0.098
Total		3156559	110481	100.000	100.000

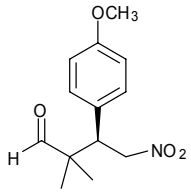


racemic-4b Chiralpak OD-H, 75:25 hexane:iPrOH, 0.8mL/min, λ = 208nm

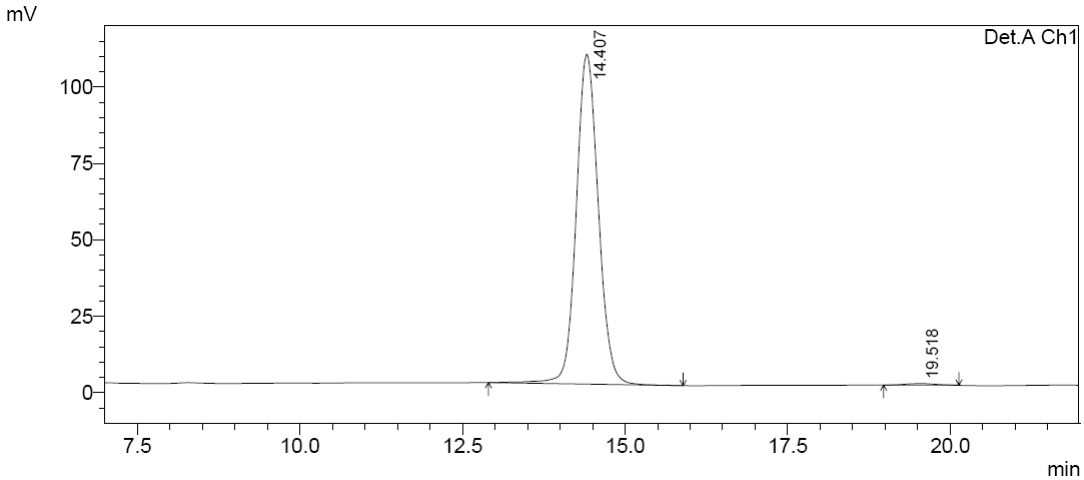


Detector A Ch1 208nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	14.719	3437454	144585	50.031	59.314
2	20.015	3433202	99175	49.969	40.686
Total		6870656	243760	100.000	100.000

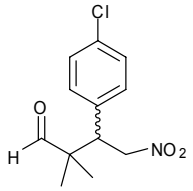


4b

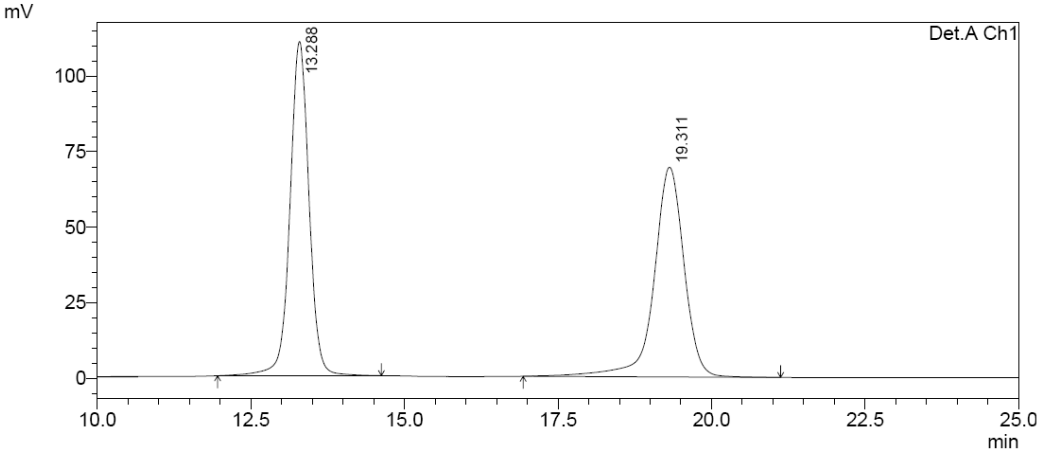


Detector A Ch1 208nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	14.407	2555755	107863	99.423	99.547
2	19.518	14824	490	0.577	0.453
Total		2570579	108353	100.000	100.000

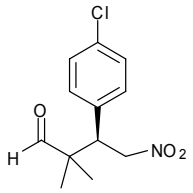


racemic-4c Chiralpak OD-H, 75:25 hexane:iPrOH, 0.8mL/min, λ = 208nm

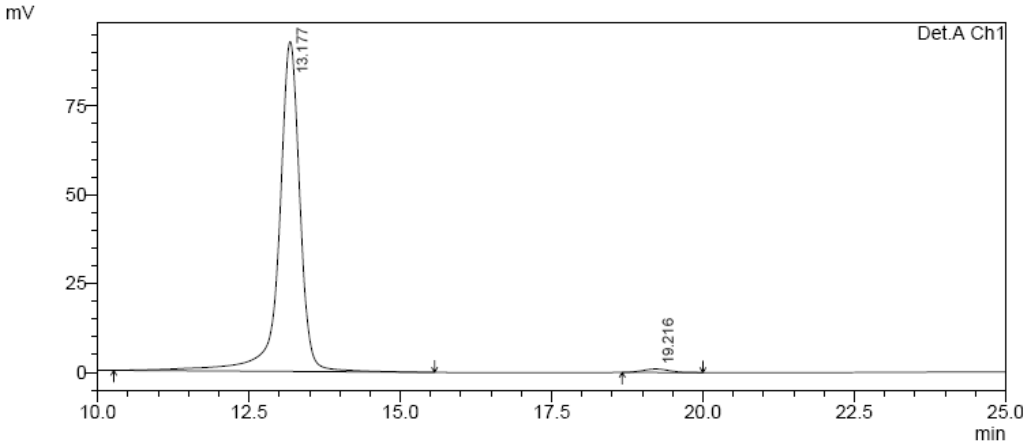


Detector A Ch1 208nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	13.288	2394213	110741	50.214	61.450
2	19.311	2373762	69473	49.786	38.550
Total		4767975	180214	100.000	100.000

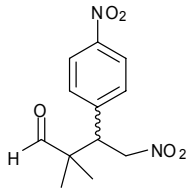


4c

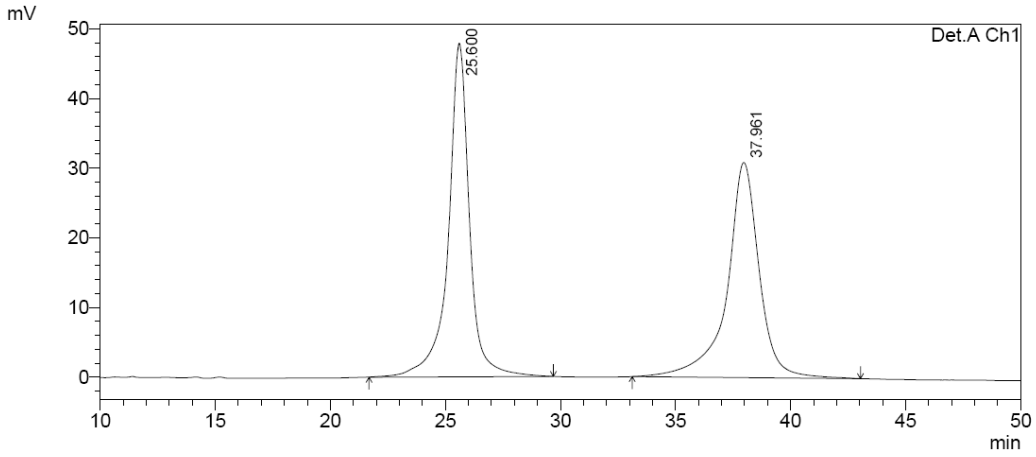


Detector A Ch1 208nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	13.177	2234518	92870	98.701	98.951
2	19.216	29414	984	1.299	1.049
Total		2263932	93854	100.000	100.000

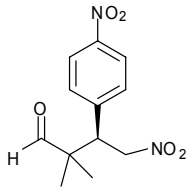


racemic-4d Chiralpak OD-H, 75:25 hexane:iPrOH, 0.8mL/min, λ = 208nm

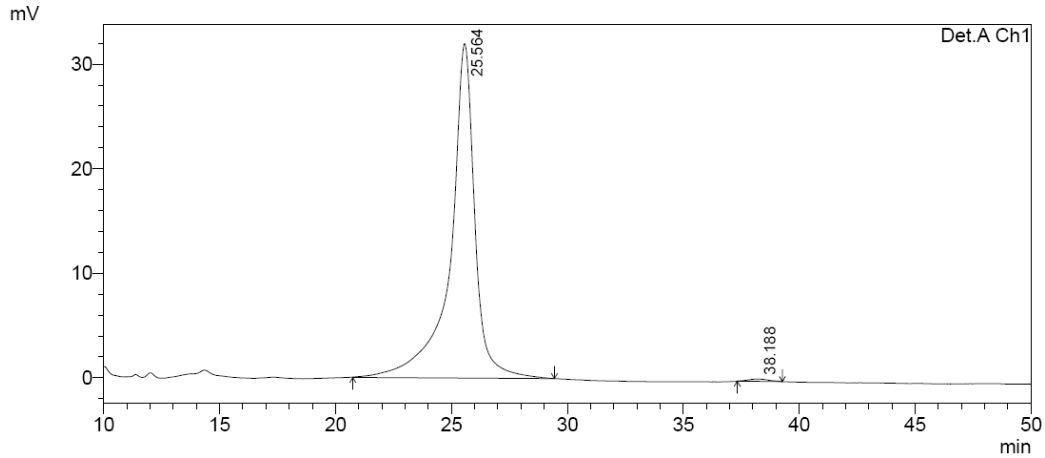


Detector A Ch1 208nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	25.600	3067504	47876	50.497	60.805
2	37.961	3007157	30862	49.503	39.195
Total		6074661	78738	100.000	100.000

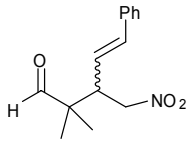


4d

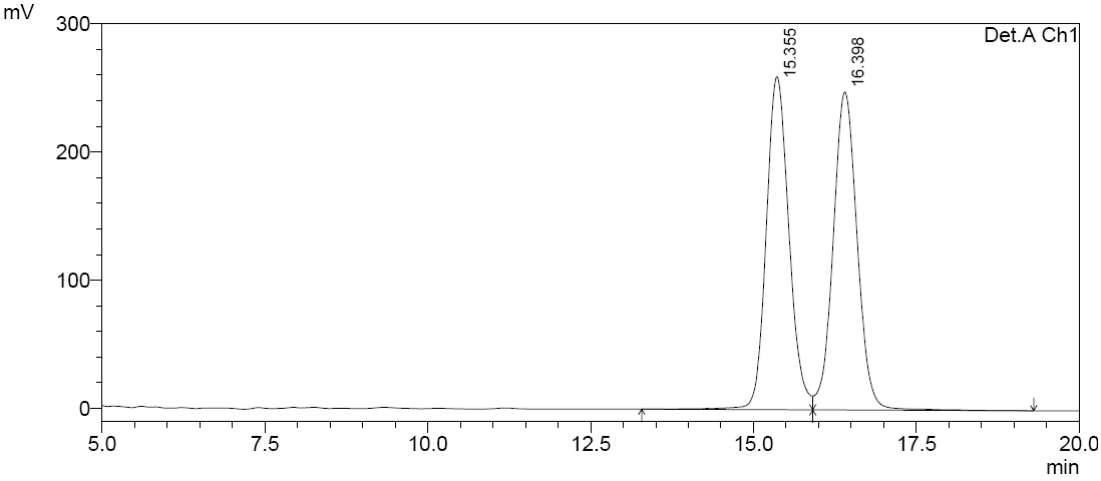


Detector A Ch1 208nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	25.564	2356601	32000	99.433	99.317
2	38.188	13431	220	0.567	0.683
Total		2370031	32220	100.000	100.000

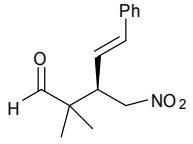


racemic-4e Chiralpak OD-H, 80:20 hexane:iPrOH, 0.8mL/min, λ = 208nm

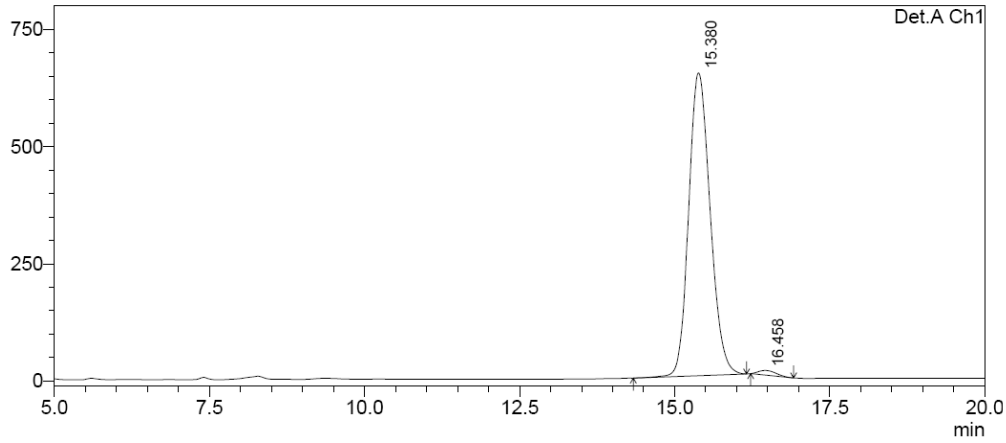


Detector A Ch1 208nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	15.355	6308891	259736	49.754	51.151
2	16.398	6371382	248043	50.246	48.849
Total		12680273	507779	100.000	100.000

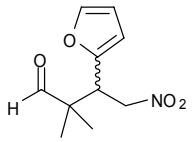


4e

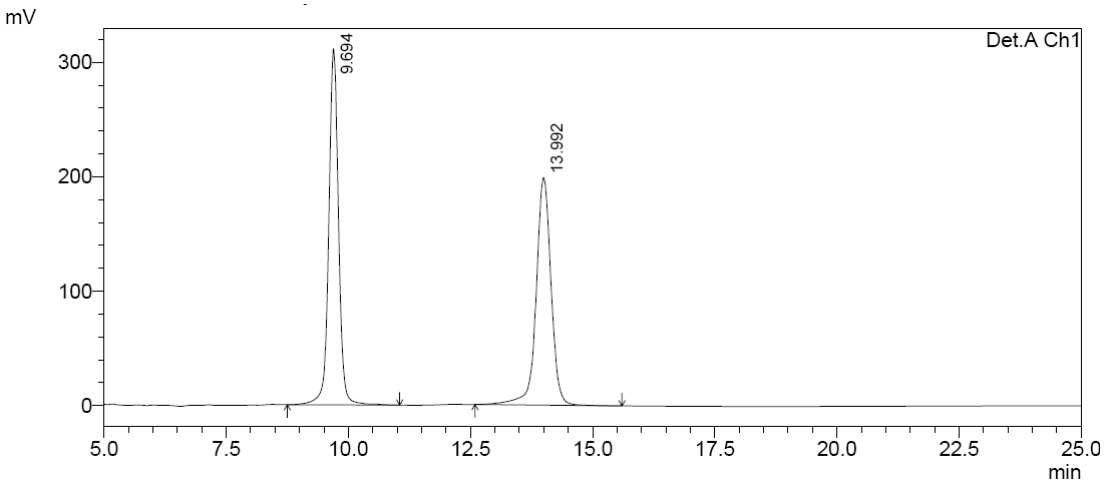


Detector A Ch1 208nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	15.380	15552051	645677	98.758	98.499
2	16.458	195616	9837	1.242	1.501
Total		15747667	655514	100.000	100.000

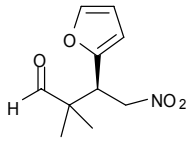


racemic-4f Chiralpak OD-H, 75:25 hexane:iPrOH, 0.8mL/min, λ = 208nm

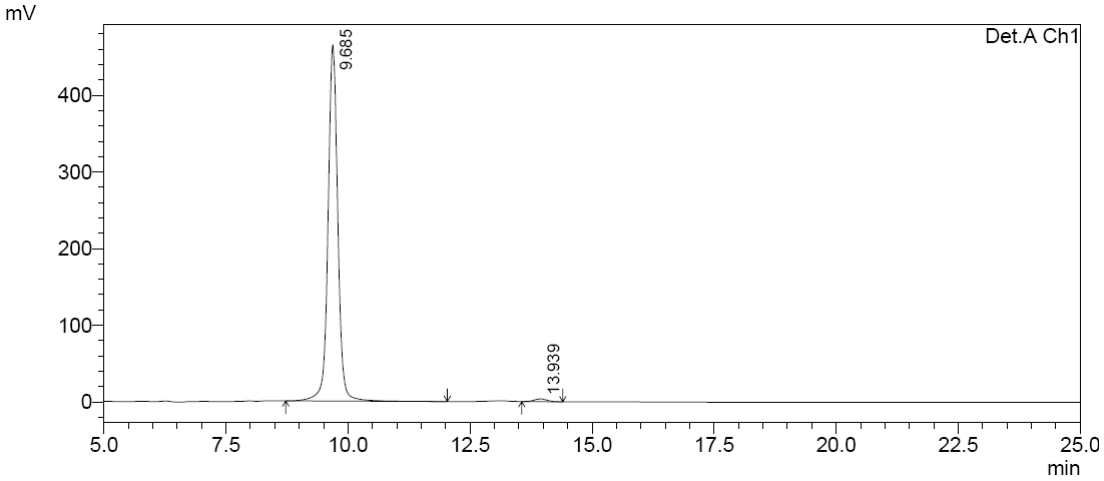


Detector A Ch1 208nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	9.694	4339008	311451	50.639	61.026
2	13.992	4229467	198904	49.361	38.974
Total		8568475	510355	100.000	100.000

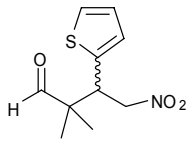


4f

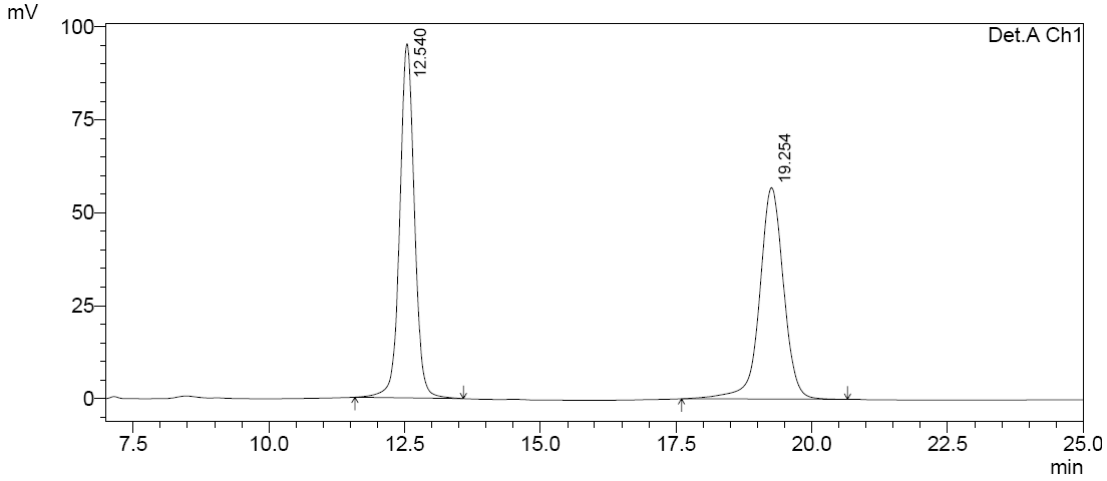


Detector A Ch1 208nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	9.685	6470337	465090	98.992	99.245
2	13.939	65904	3536	1.008	0.755
Total		6536241	468626	100.000	100.000

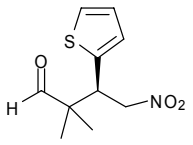


racemic-4g Chiralpak OD-H, 75:25 hexane:iPrOH, 0.8mL/min, λ = 208nm

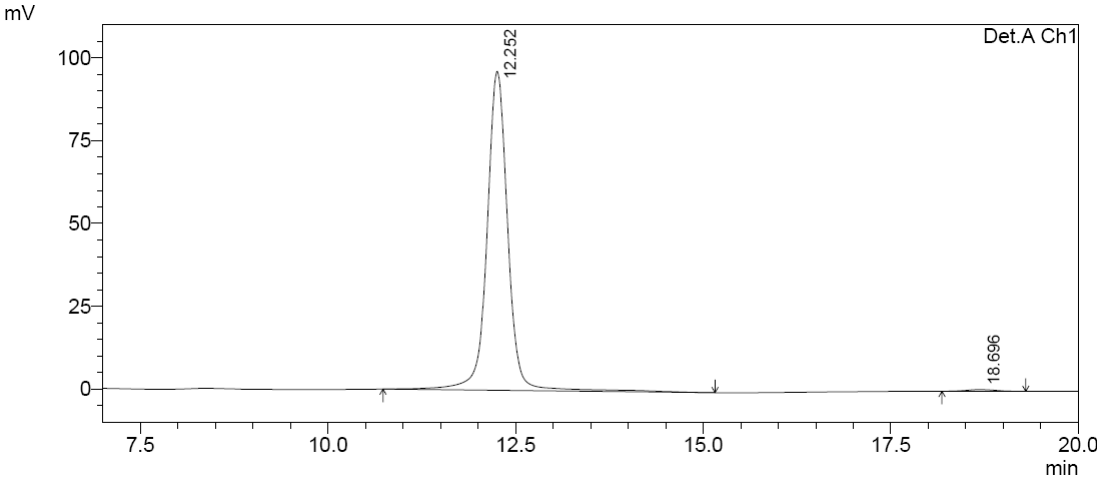


Detector A Ch1 208nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	12.540	1794474	95265	50.621	62.622
2	19.254	1750464	56863	49.379	37.378
Total		3544937	152128	100.000	100.000

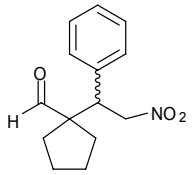


4g

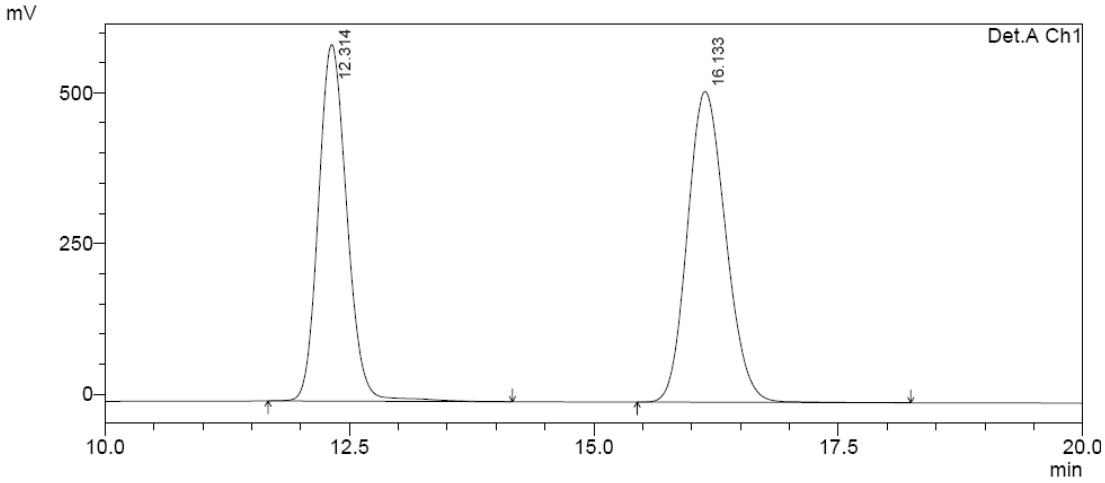


Detector A Ch1 208nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	12.252	1876566	96311	99.250	99.450
2	18.696	14178	533	0.750	0.550
Total		1890744	96843	100.000	100.000

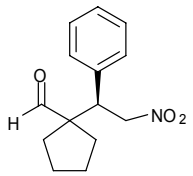


racemic-4h Chiralpak AS-H, 75:25 hexane:iPrOH, 0.8mL/min, λ = 208nm

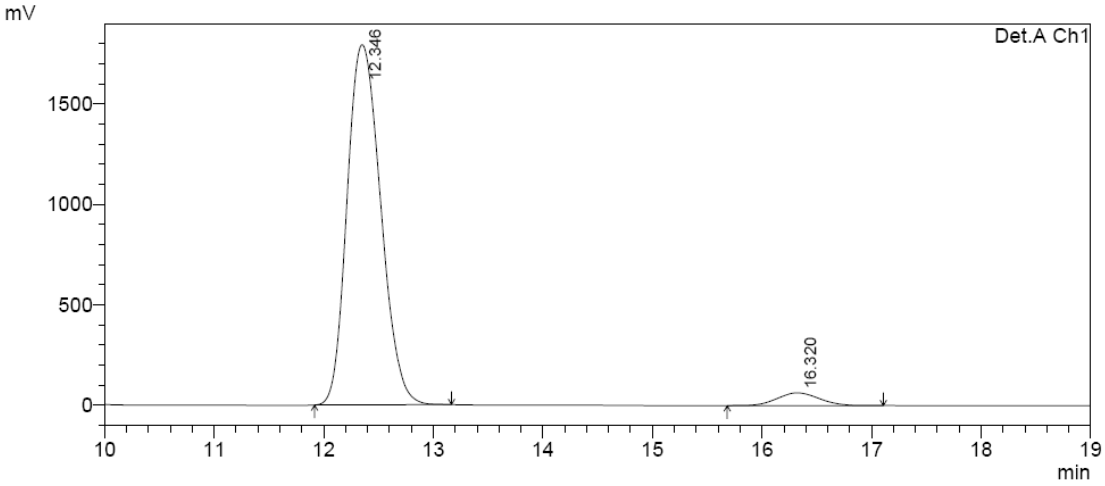


Detector A Ch1 208nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	12.314	11974427	591657	46.112	53.442
2	16.133	13993624	515440	53.888	46.558
Total		25968051	1107096	100.000	100.000

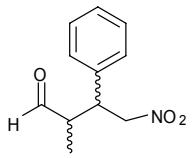


4h

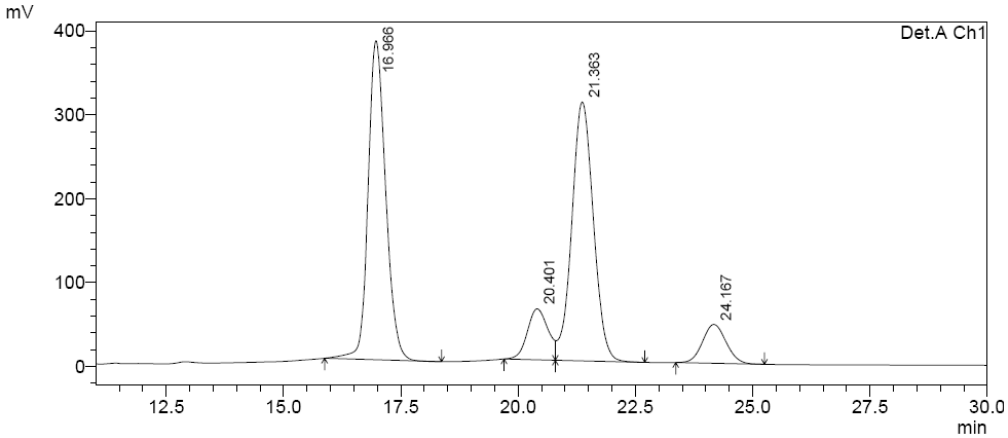


Detector A Ch1 208nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	12.346	38270739	1795146	95.727	96.574
2	16.320	1708465	63692	4.273	3.426
Total		39979204	1858838	100.000	100.000

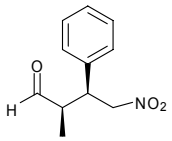


racemic-4i Chiralpak OD-H, 80:20 hexane:iPrOH, 0.8mL/min, λ = 208nm

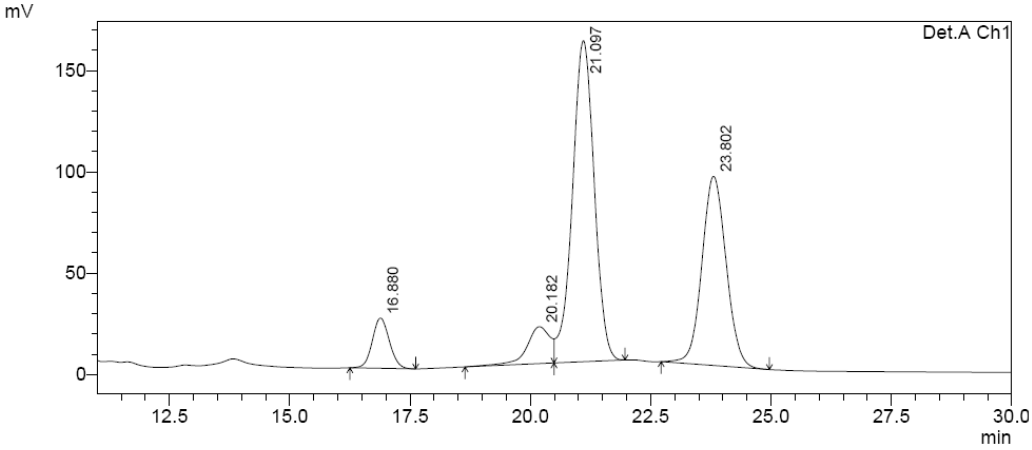


Detector A Ch1 208nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	16.966	9912877	380497	42.565	47.782
2	20.401	1858532	60756	7.980	7.630
3	21.363	9894925	308713	42.488	38.768
4	24.167	1622406	46350	6.966	5.821
Total		23288741	796315	100.000	100.000

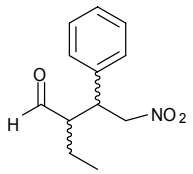


4i

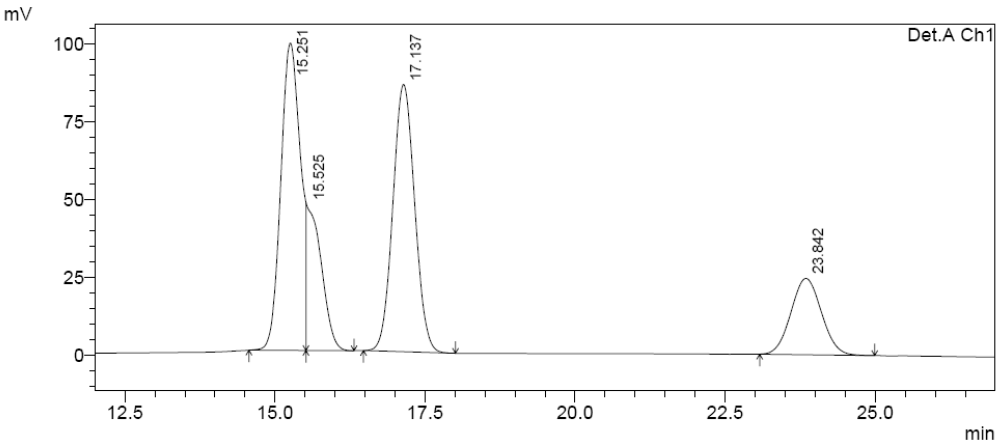


Detector A Ch1 208nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	16.880	610354	24753	6.415	8.391
2	20.182	610590	18244	6.417	6.185
3	21.097	5016458	158599	52.724	53.766
4	23.802	3277134	93383	34.443	31.658
Total		9514536	294979	100.000	100.000

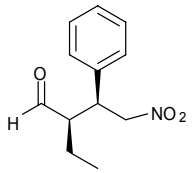


racemic-4j Chiralpak OD-H, 80:20 hexane:iPrOH, 0.8mL/min, λ = 208nm

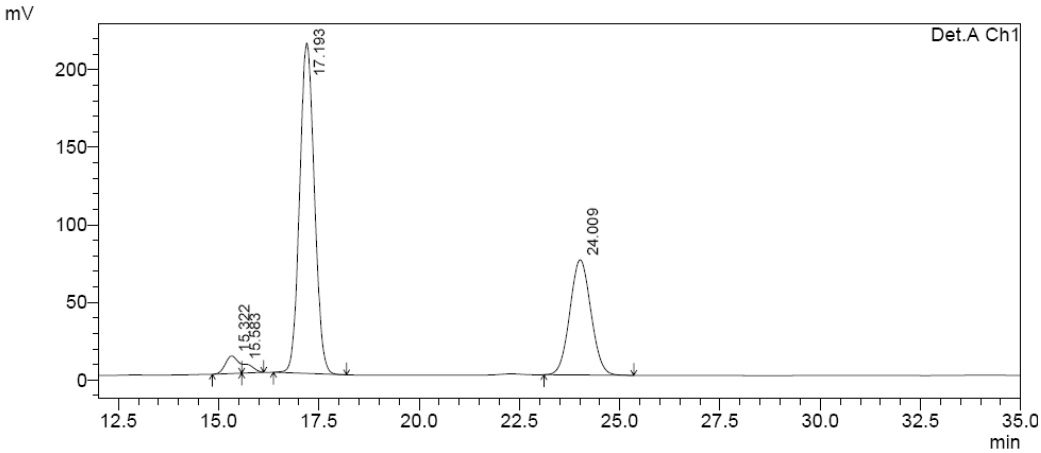


Detector A Ch1 208nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	15.251	2240862	98813	36.803	38.564
2	15.525	805275	46943	13.225	18.321
3	17.137	2173390	85944	35.695	33.542
4	23.842	869284	24529	14.277	9.573
Total		6088811	256230	100.000	100.000

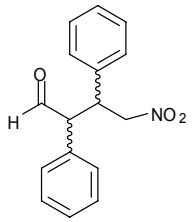


4j

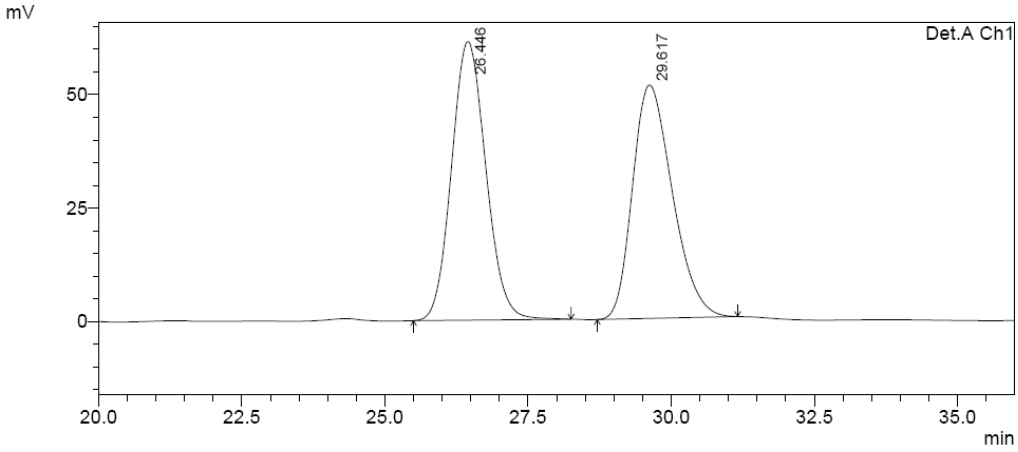


Detector A Ch1 208nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	15.322	255072	11348	2.988	3.728
2	15.583	106649	5822	1.249	1.913
3	17.193	5458791	213024	63.938	69.984
4	24.009	2717063	74197	31.825	24.376
Total		8537575	304391	100.000	100.000

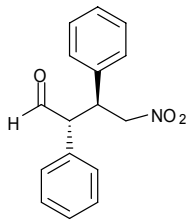


racemic-4k Chiralpak OD-H, 90:10 hexane:iPrOH, 0.8mL/min, λ = 208nm

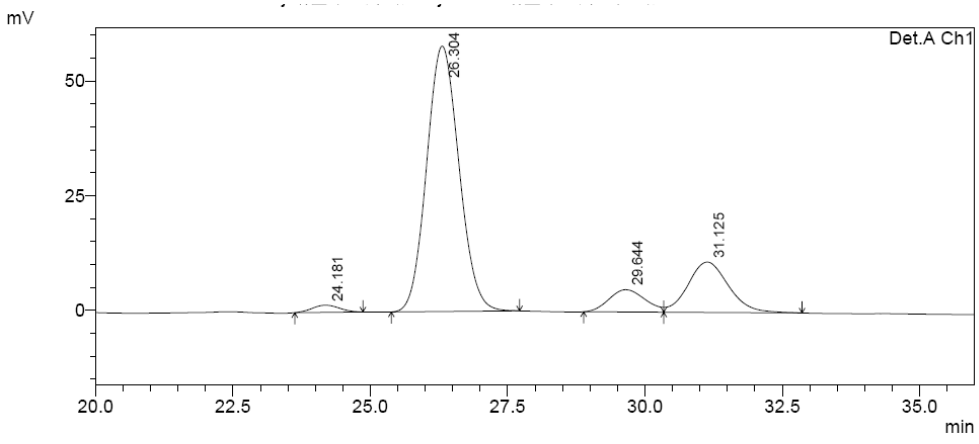


Detector A Ch1 208nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	26.446	2564181	61419	50.726	54.421
2	29.617	2490737	51440	49.274	45.579
Total		5054918	112858	100.000	100.000



4k



Detector A Ch1 208nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	24.181	54322	1573	1.691	2.090
2	26.304	2369970	57851	73.793	76.849
3	29.644	222278	4869	6.921	6.468
4	31.125	565086	10986	17.595	14.593
Total		3211656	75279	100.000	100.000

H) References and Notes

[1] G. E. Dubois, R. A. Stephenson, *J. Org. Chem.* **1980**, *45*, 5371-5373.
[2] G. E. DuBois, *J. Org. Chem.* **1980**, *45,* 5373-5375.
[3] For the synthesis of 2-amino-3,3,N-trimethyl-butyramide hydrochloride, see: D. E. Fuerst and E. N. Jacobsen, *J. Am. Chem. Soc.* **2005**, *127*, 8964-8965.
[4] For the synthesis of nitroolefins, see: David E. Worrall*, Org. Syn.* **1929**, *9,* 66.
[5] Racemic **4i** was synthesized using piperazine as catalyst; other racemic conjugation products were prepared using racemic **1a**.