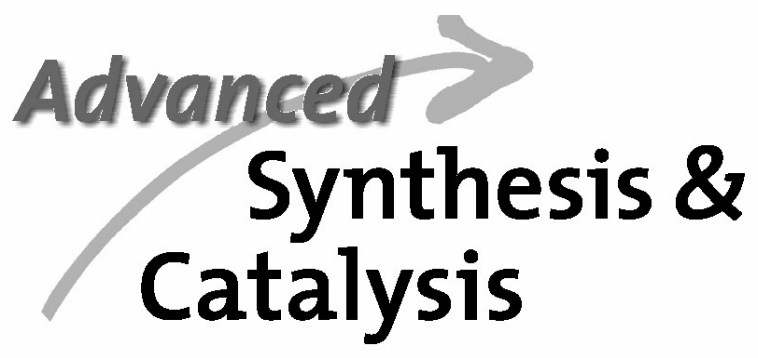

Supporting Information

Supporting Information

Direct Asymmetric Dynamic Kinetic Resolution by Combined Lipase-Catalysis and Nitroaldol (Henry) Reaction

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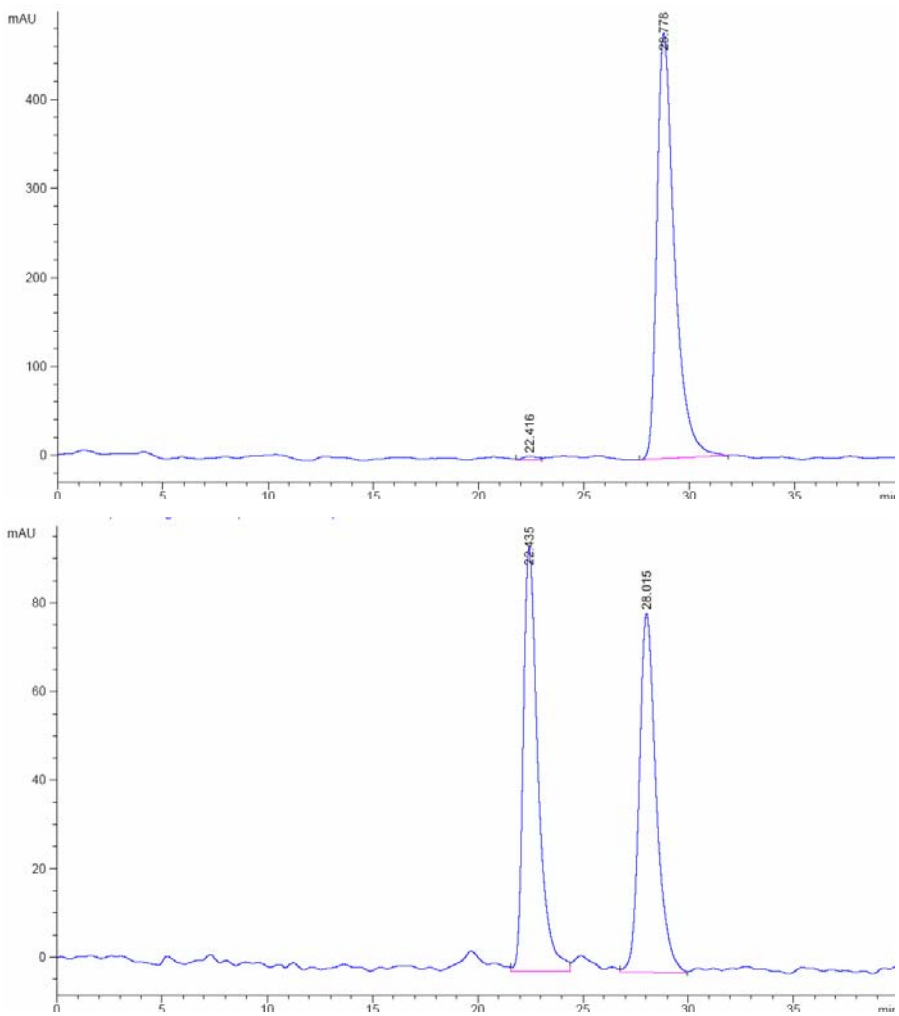
EXPERIMENTAL

General. Reagents were purchased from Sigma-Aldrich and Lancaster and used as received. Lipases were from Sigma-Aldrich; *Candida antarctica* Lipase B (Sigma L4777), lipases from *Candida rugosa* (Sigma L1754, Fluka 62316), Amano lipase PS from *Pseudomonas cepacia* (Aldrich 534641), Amano lipase PS-C I from *Pseudomonas cepacia* (Aldrich 534897), Amano lipase PS-C II from *Pseudomonas cepacia* (Aldrich 534889), and Amano lipase from *Pseudomonas fluorescens* (Aldrich 534730). ^{1}H and ^{13}C NMR data were recorded on a Bruker Avance 400 spectrometer at 400 (100) MHz and/or a Bruker Avance DMX 500 at 500 (125) MHz respectively. Chemical shifts are reported as δ values (ppm) with $CDCl_3$ (^{1}H NMR δ 7.26, ^{13}C NMR δ 77.0) as an internal standard. *J* values are given in Hertz (Hz). Analytical high performance liquid chromatography (HPLC) with chiral stationary phase was performed on HP-Agilent 1110 Series controller, using Daicel Chiralpak OD (4.6×250 mm, 20 μm) and OD-H (4.6×250 mm, 5 μm) columns. Solvents for HPLC use were of spectrometric grade. Melting points were analyzed by a Stuart Scientific melting point apparatus SMP3. Thin layer chromatography (TLC) was performed on precoated Polygram® SIL G/UV_{254} silica plates (0.20 mm, Macherey-Nagel), visualized with UV-detection. Flash column chromatography was performed on silica gel 60, 0.040-0.063 mm (SDS). High resolution mass spectrometry was performed by Instrument station Lund University, Sweden. Optical rotations were determined using Perkin Elmer Polarimeter 343 at the sodium D-line (589 nm).

General procedure for dynamic kinetic resolution. In a typical experiment, a reaction mixture of 4-nitrobenzaldehyde (**4a**) (18.88 mg, 0.125 mmol), 2-nitropropane (**3**) (44.5 mg, 0.5 mmol), triethylamine (25.28 mg, 0.25 mmol), and 5 equivalents of *p*-chlorophenyl acetate (106.25 mg) in dry toluene (0.25 mL) were added to a sealed-cap vial (1.75 mL) containing *Pseudomonas cepacia* (PS-C I, immobilized on ceramic, Sigma-Aldrich, EC 3.1.1.3, 90 mg) together with ground molecular sieve 4 Å (20 mg). The reaction mixture was flushed with argon and stirred at 40 ^{o}C. After 2 days the reaction was cooled to room temperature, filtered and washed with CH_2Cl_2 (3 × 5 mL). The solvent were removed *in vacuo* and the crude product was purified by column chromatography (Hexane:CH_2Cl_2 (1:4) to pure CH_2Cl_2) yielding 32 mg of **2a** (90%) as a white amorphous in 99% ee.

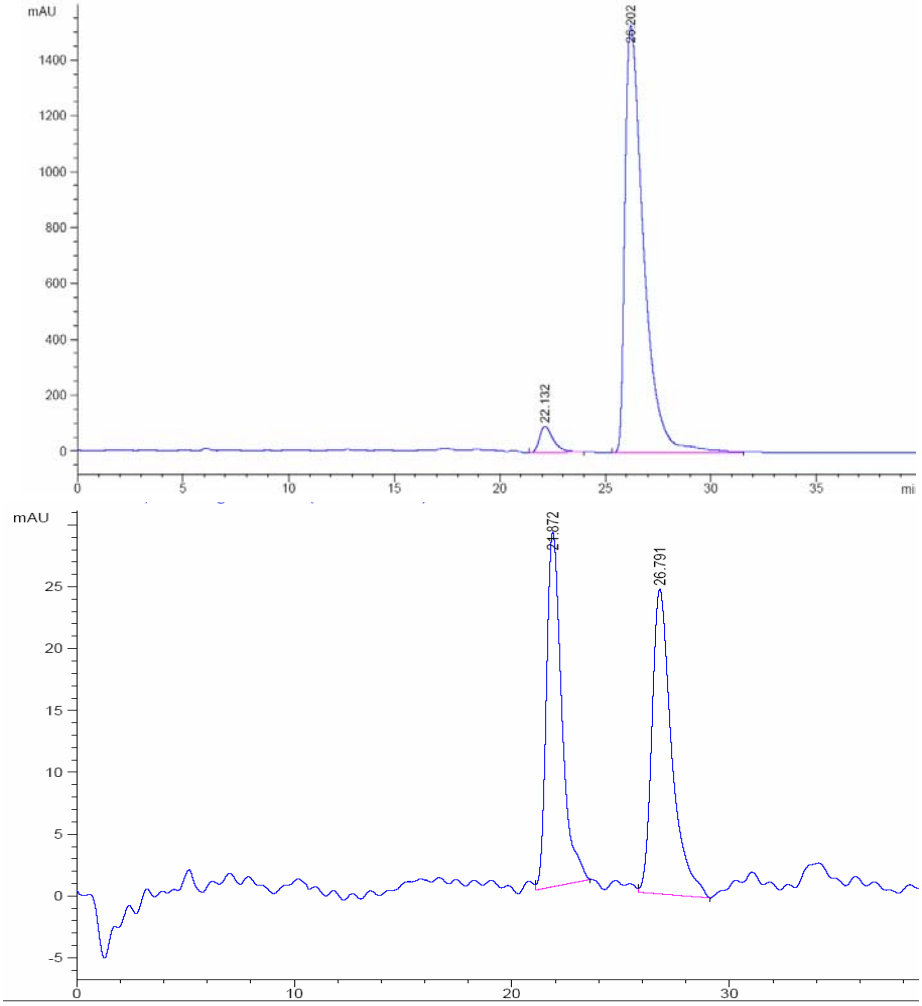
2-methyl-2-nitro-1-(4-nitrophenyl)propyl acetate (**2a**). Yield 90%. Enantiomeric ratio (99:1), determined by HPLC analysis (Chiralpak OD 95:5 Hex:^{i}PrOH, 0.8 ml/min; t_R 22.4 min; t_R 28.7 min. Colorless amorph, $[\alpha]^{20}_D$ = -5.1 (*c* = 0.52, $CHCl_3$); ^{1}H NMR ($CDCl_3$) δ = 1.52 (3H, s), 1.65 (3H, s), 2.12 (3H, s), 6.37 (1H, s), 7.52 (2H, d, *J* = 8.8 Hz), 8.24 (2H,d, *J* = 8.8 Hz); ^{13}C NMR ($CDCl_3$) δ = 20.4, 20.7, 23.9, 77.5, 89.5, 123.7, 128.5, 142.1, 148.3, 168.8; HRMS (ESI-TOF): 300.1205 ($[M+NH_4]^+$, $C_{12}H_{18}N_3O_6$; calc. 300.1196).

Peak	Processed Channel	Retention time (min)	Area	%Area	Height
1	@210nm	22.416	195	0.70	3.99
2	@210nm	28.778	277807	99.30	478.08



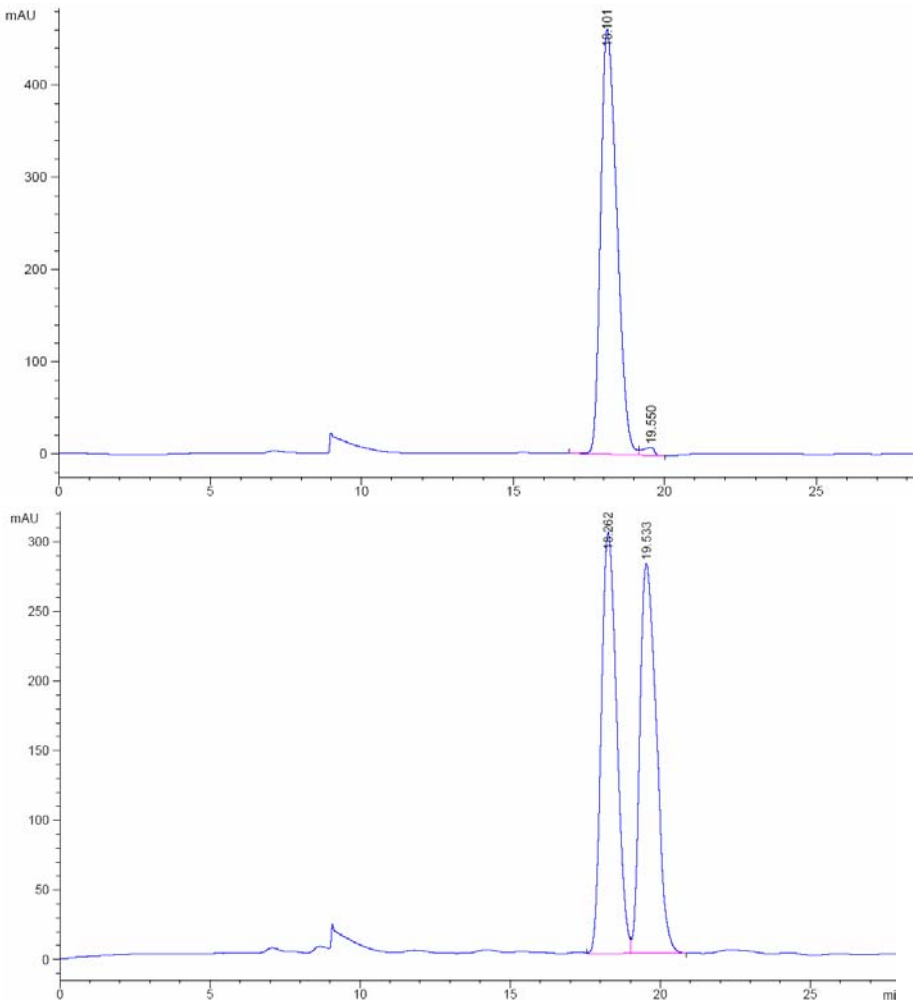
1-(4-cyanophenyl)-2-methyl-2-nitropropyl acetate (**2b**). The general procedure was followed. Yield 89%. Enantiomeric ratio (96:4), determined by HPLC analysis (Chiralpak OD 95:5 Hex:^{i}PrOH, 0.8 ml/min; t_R 22 min; t_R 26 min. Colorless amorphous, $[\alpha]^{20}_D$ = +6.6 (*c* = 1.0, $CHCl_3$); ^{1}H NMR ($CDCl_3$) δ = 1.49 (3H, s), 1.62 (3H, s), 2.10 (3H, s), 6.31 (1H, s), 7.44 (2H, d, *J* = 8.4 Hz), 7.67 (2H,d, *J* = 8.4 Hz); ^{13}C NMR ($CDCl_3$) δ = 20.3, 20.6, 23.9, 77.6, 89.6, 113.1, 118.0, 128.3, 132.3, 140.2, 168.7; HRMS (ESI-TOF): 263.1021 ($[M+H]^+$, $C_{13}H_{15}N_2O_4$; calc. 263.1032).

Peak	Processed Channel	Retention time (min)	Area	%Area	Height
1	@210nm	22.132	4235	4.33	93.70
2	@210nm	28.202	936445	95.67	1526.05



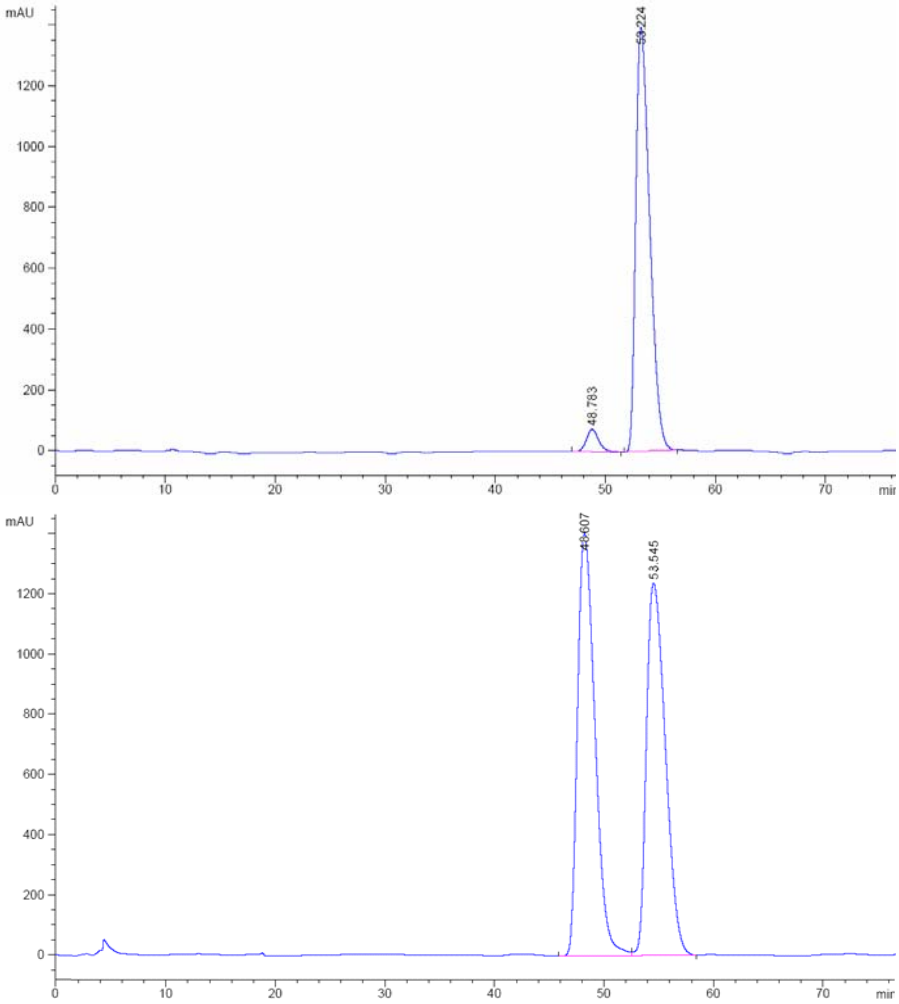
2-methyl-2-nitro-1-(4-(trifluoromethyl)phenyl)propyl acetate (**2c**). The general procedure was followed. Yield 89%. Enantiomeric ratio (99:1), determined by HPLC analysis (Chiralpak OD-H 99:1 Hex:^{i}PrOH, 0.6 ml/min; t_R 18 min; t_R 19.5 min. Colorless solid. m.p. 108–110°C, $[\alpha]^{20}_D$ = -8.2 (*c* = 0.5, $CHCl_3$); ^{1}H NMR ($CDCl_3$) δ = 1.50 (3H, s), 1.64 (3H, s), 2.10 (3H, s), 6.35 (1H, s), 7.46 (2H, d, *J* = 8.0 Hz), 7.64 (2H, d, *J* = 8.0 Hz; ^{13}C NMR ($CDCl_3$) δ = 20.1, 20.7, 24.1, 77.8, 89.7, 122.4, 125.5, 128.0, 131.1, 131.4, 139.1, 168.8; HRMS (ESI-TOF): 323.1212 ($[M+NH_4]^+$, $C_{13}H_{18}F_3N_2O_4$; calc. 323.1219).

Peak	Processed Channel	Retention time (min)	Area	%Area	Height
1	@210nm	18.101	172030	98.66	460.70
2	@210nm	19.550	233	1.34	8.45



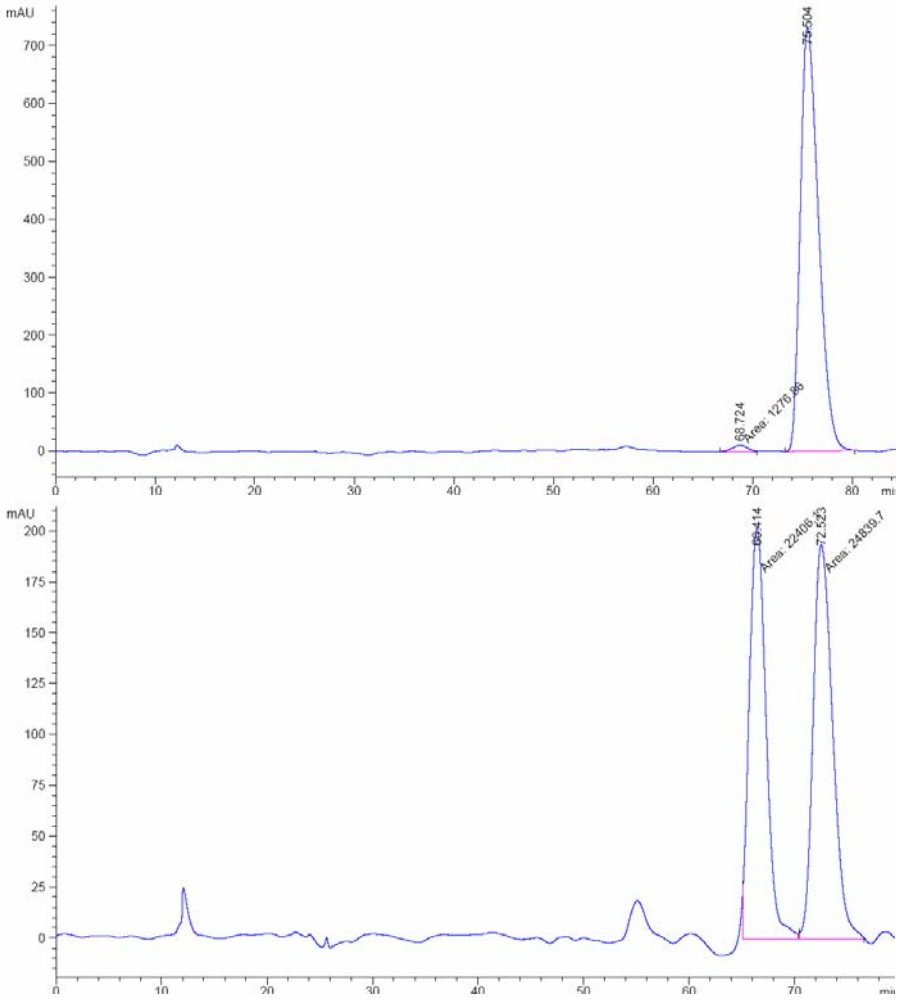
2-methyl-2-nitro-1-(3-nitrophenyl)propyl acetate (**2d**). The general procedure was followed. Yield 90%. Enantiomeric ratio (96:4), determined by HPLC analysis (Chiralpak OD-H 98:2 Hex:^{i}PrOH, 0.5 ml/min; t_R 49 min; t_R 53 min. Colorless amorphous, $[\alpha]^{20}_D$ = -11.3 (*c* = 1.0, $CHCl_3$); ^{1}H NMR ($CDCl_3$) δ = 1.52 (3H, s), 1.66 (3H, s), 2.13 (3H, s), 6.39 (1H, s), 7.57, 7.59 (1H,dd, *J* = 7.8, 8.0 Hz), 7.66 (1H,d, *J* = 7.8 Hz), 8.20 (1H, brs), 8.24 (1H, brd, *J* = 8.0 Hz); ^{13}C NMR ($CDCl_3$) δ = 20.3, 20.7, 23.8, 77.8, 89.6, 122.3, 124.1, 129.7, 133.7, 137.3, 148.3, 168.8; HRMS (ESI-TOF): 300.1183 ($[M+NH_4]^+$, $C_{12}H_{18}N_3O_6$; calc. 300.1196).

Peak	Processed Channel	Retention time (min)	Area	%Area	Height
1	@210nm	48.783	5644	4.40	73.08
2	@210nm	53.224	122526	95.60	1394.19



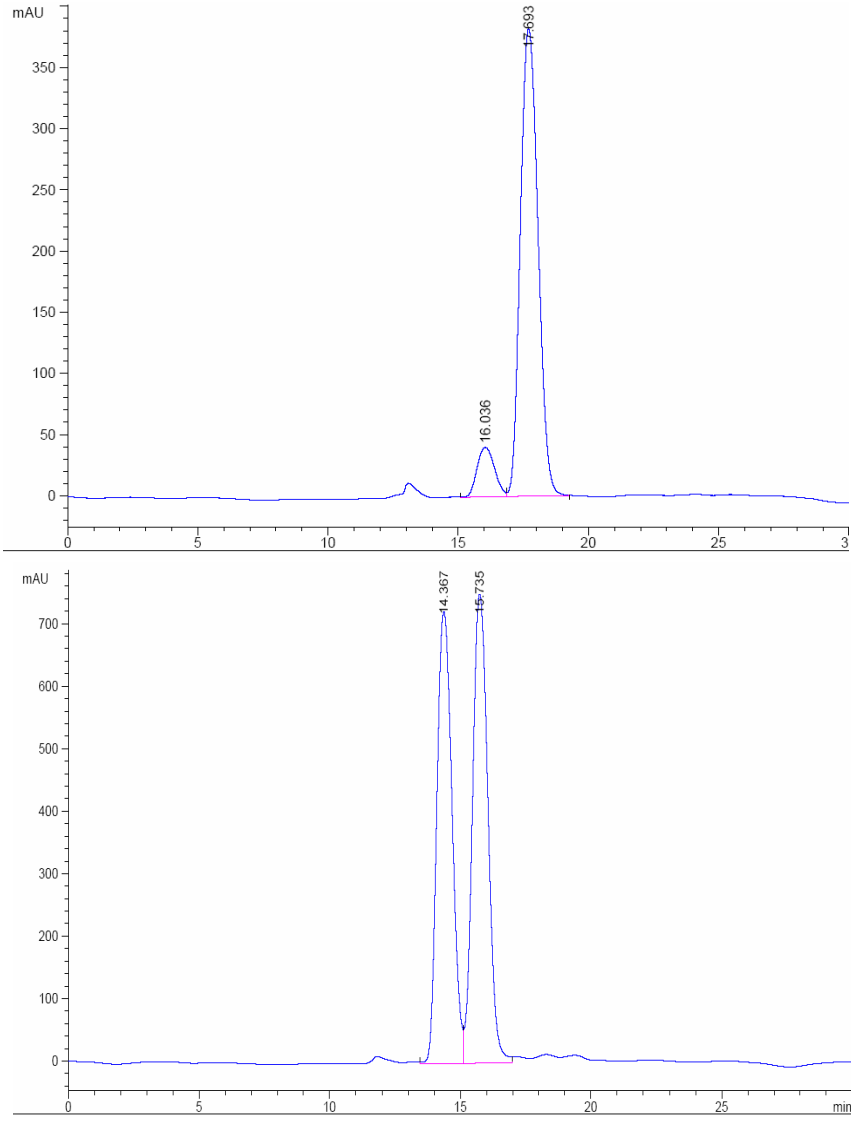
1-(3-cyanophenyl)-2-methyl-2-nitropropyl acetate (**2e**). The general procedure was followed. Yield 92%. Enantiomeric ratio (99:1), determined by HPLC analysis (Chiralpak OD-H 98:2 Hex:^{i}PrOH, 0.5 ml/min; t_R 68.7 min; t_R 75.5 min. Colorless amorphous, $[\alpha]^{20}_D$ = -2.2 (*c* = 1.0, $CHCl_3$); ^{1}H NMR ($CDCl_3$) δ = 1.50 (3H, s), 1.63 (3H, s), 2.11 (3H, s), 6.31 (1H, s), 7.49, 7.51 (1H, dd, *J* = 7.52, 7.8 Hz), 7.56 (1H,brd, *J* = 7.52 Hz), 7.62 (1H, brs), 7.66 (1H, brd, *J* = 7.8 Hz); ^{13}C NMR ($CDCl_3$) δ = 20.3, 20.7, 23.8, 77.8, 89.6, 113.0, 118.1, 129.4, 130.9, 132.0, 132.6, 136.8, 168.7; HRMS (ESI-TOF): 263.1030 ($[M+H]^+$, $C_{13}H_{15}N_2O_4$; calc. 263.1032).

Peak	Processed Channel	Retention time (min)	Area	%Area	Height
1	@210nm	68.724	1276	1.35	11.59
2	@210nm	75.504	933715	98.65	731.69



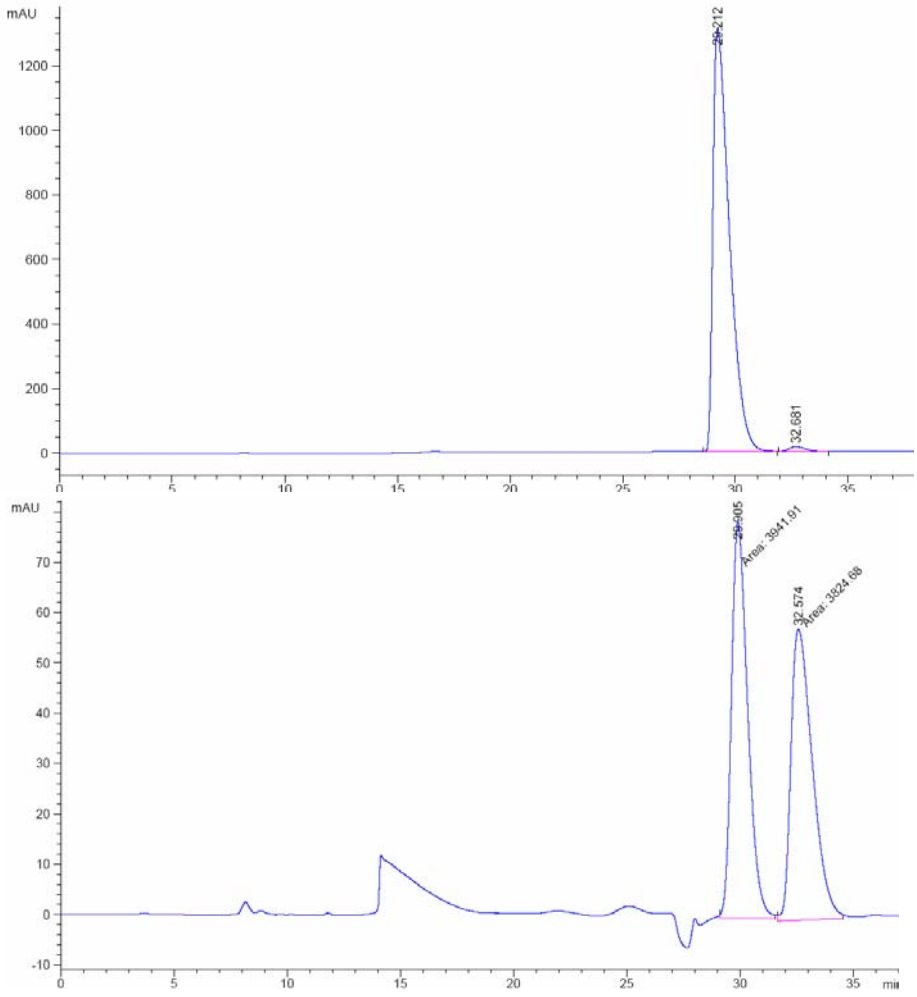
1-(3,5-bis(trifluoromethyl)phenyl)-2-methyl-2-nitropropyl acetate (**2f**). The general procedure was followed. Yield 80%. Enantiomeric ratio (90:10), determined by HPLC analysis (Chiralpak OD-H 98:2 Hex:^{i}PrOH, 0.5 ml/min; t_R 16 min; t_R 17.6 min. Colorless amorphous, $[\alpha]^{20}_D$ = -8.8 (*c* = 0.8, $CHCl_3$); ^{1}H NMR ($CDCl_3$) δ = 1.52 (3H, s), 1.64 (3H, s), 2.14 (3H, s), 6.41 (1H, s), 7.78 (2H,s,), 7.90 (1H,s); ^{13}C NMR ($CDCl_3$) δ = 20.3, 20.7, 23.8, 77.1, 89.4, 119.6, 121.8, 123.2, 123.9, 126.1, 127.7, 132.1, 137.9, 168.7; HRMS (ESI-TOF): 391.1086 ($[M+NH_4]^+$, $C_{14}H_{17}F_6N_2O_4$; calc. 391.1093).

Peak	Processed Channel	Retention time (min)	Area	%Area	Height
1	@210nm	16.036	1908	9.57	40.69
2	@210nm	17.693	180256	90.43	382.10



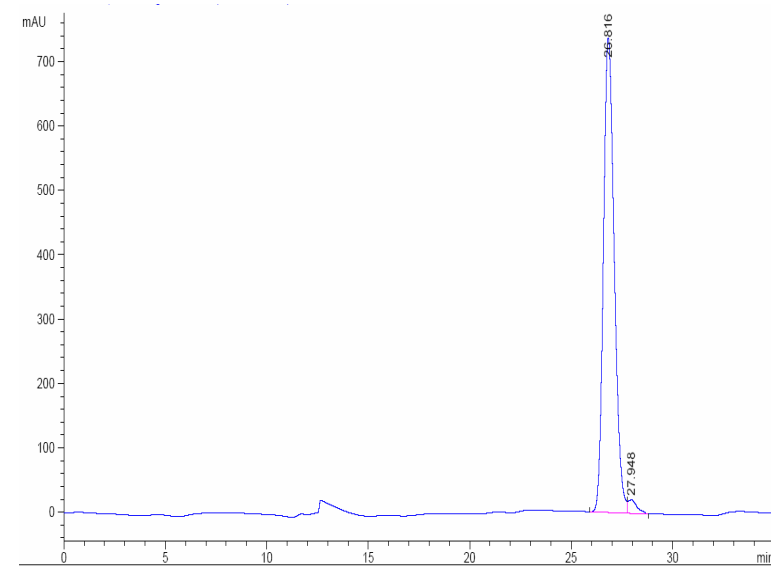
1-(4-fluorophenyl)-2-methyl-2-nitropropyl acetate (**2g**). The general procedure was followed. Yield 85%. Enantiomeric ratio (99:1), determined by HPLC analysis (Chiralpak OD-H 99.5:0.5 Hex:^{i}PrOH, 0.6 ml/min; t_R 29.2 min; t_R 32.7 min. Colorless amorphous, $[\alpha]^{20}_D$ = -8.9 (*c* = 0.7, $CHCl_3$); ^{1}H NMR ($CDCl_3$) δ = 1.48 (3H, s), 1.62 (3H, s), 2.08 (3H, s), 6.29 (1H, s), 7.06 (2H, brt, *J* = 8.3 Hz), 7.31 (2H,brt, *J* = 8.3 Hz); ^{13}C NMR ($CDCl_3$) δ = 19.9, 20.8, 24.1, 77.8, 90.0, 115.6, 129.2, 129.4, 130.9, 161.7, 164.2, 168.8; HRMS (ESI-TOF): 256.0990 ($[M+H]^+$, $C_{12}H_{15}FNO_4$; calc. 256.0985).

Peak	Processed Channel	Retention time (min)	Area	%Area	Height
1	@210nm	29.212	667802	98.79	1313.00
2	@210nm	32.681	816	1.21	15.47



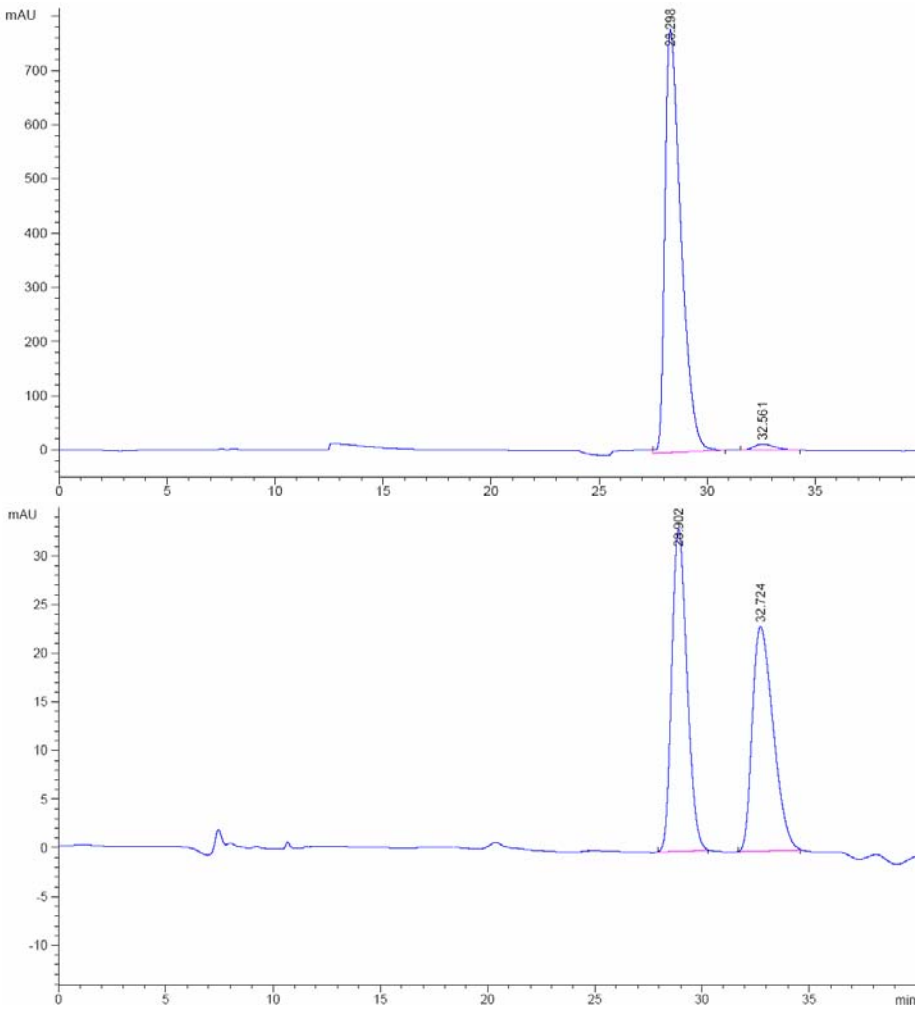
1-(4-chlorophenyl)-2-methyl-2-nitropropyl acetate (**2h**). The general procedure was followed. Yield 83%. Enantiomeric ratio (98:2), determined by HPLC analysis (Chiralpak OD-H 99:1 hex:^{i}PrOH, 0.6 ml/min; t_R 26.8 min; t_R 27.9 min. Colorless amorphous, $[\alpha]^{20}_D$ = +7.0 (*c* = 0.7, $CHCl_3$); ^{1}H NMR ($CDCl_3$) δ = 1.48 (3H, s), 1.62 (3H, s), 2.08 (3H, s), 6.28 (1H, s), 7.26 (2H, d, *J* = 8.3 Hz), 7.34 (2H,d, *J* = 8.3 Hz); ^{13}C NMR ($CDCl_3$) δ = 19.9, 20.7, 24.1, 77.8, 89.9, 128.8, 128.9, 133.6, 135.1, 168.8; HRMS (ESI-TOF): 271.0608 ($[M]^+$, $C_{12}H_{14}ClNO_4$; calc. 271.0611).

Peak	Processed Channel	Retention time (min)	Area	%Area	Height
1	@210nm	26.816	273158	97.68	739.79
2	@210nm	27.948	648	2.32	21.06



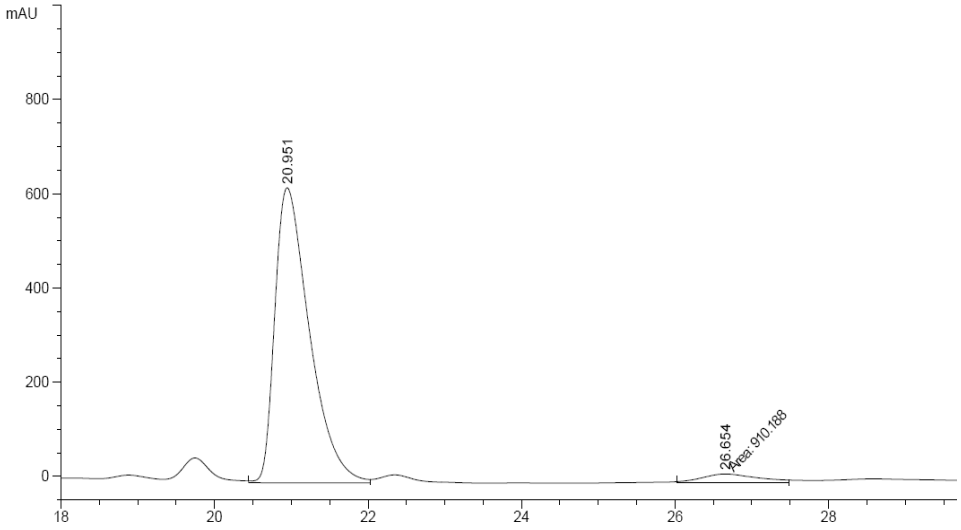
1-(4-chlorophenyl)-2-methyl-2-nitropropyl acetate (**2i**). The general procedure was followed. Yield 81%. Enantiomeric ratio (98:2), determined by HPLC analysis (Chiralpak OD-H 99.5:0.5 Hex:^{i}PrOH, 0.6 ml/min; t_R 28.3 min; t_R 32.6 min. Colorless amorphous, $[\alpha]^{20}_D$ = +11.6 (*c* = 1.0, $CHCl_3$); ^{1}H NMR ($CDCl_3$) δ = 1.48 (3H, s), 1.61 (3H, s), 2.08 (3H, s), 6.28 (1H, s), 7.20 (2H, d, *J* = 8.3 Hz), 7.50 (2H,d, *J* = 8.3 Hz); ^{13}C NMR ($CDCl_3$) δ = 19.9, 20.7, 24.1, 77.9, 89.9, 123.3, 129.2, 131.7, 134.1, 168.8; HRMS (ESI-TOF): 315.0112 ($[M]^+$, $C_{12}H_{14}BrNO_4$; calc. 315.0106).

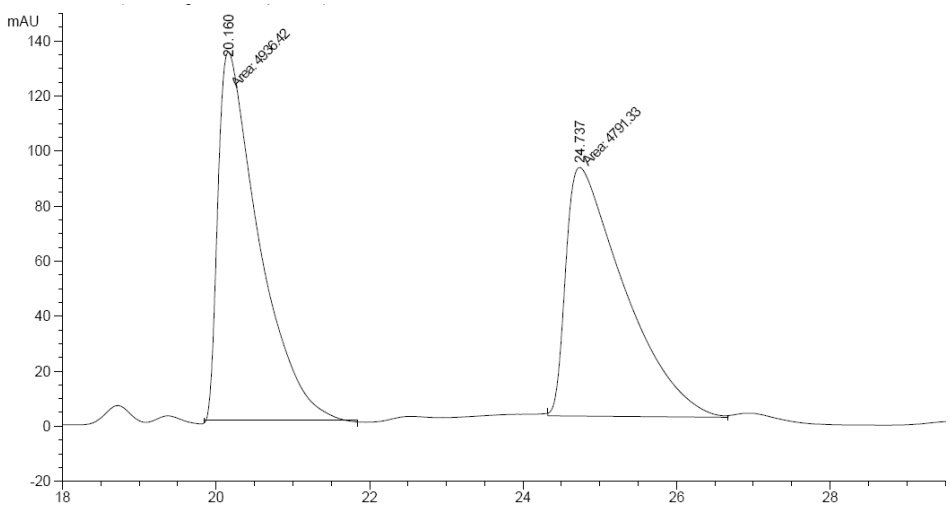
Peak	Processed Channel	Retention time (min)	Area	%Area	Height
1	@210nm	28.298	403541	98.18	780.23
2	@210nm	32.561	749	1.82	11.30



2-methyl-2-nitro-1-phenylpropyl acetate (2j). The general procedure was followed. Yield 79%. Enantiomeric ratio (96:4), determined by HPLC analysis (Chiralpak OD-H 99:1 Hex:^{i}PrOH, 0.5 ml/min; t_R 20.9 min; t_R 26.6 min. Colorless oil; ^{1}H NMR ($CDCl_3$) δ = 1.49 (3H, s), 1.63 (3H, s), 2.08 (3H, s), 6.32 (1H, s), 7.35 (5H, m); ^{13}C NMR ($CDCl_3$) δ = 19.8, 20.8, 24.4, 78.5, 90.2, 127.6, 128.5, 129.0, 135.1, 168.9.

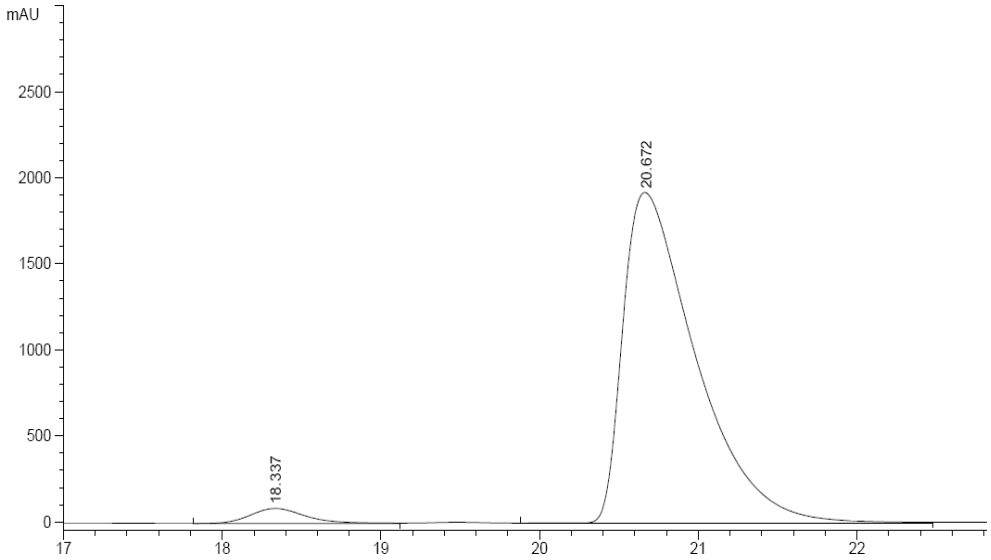
Peak	Processed Channel	Retention time (min)	Area	%Area	Height
1	@210nm	20.951	196470	95.57	625.83
2	@210nm	26.654	910	4.42	18.00

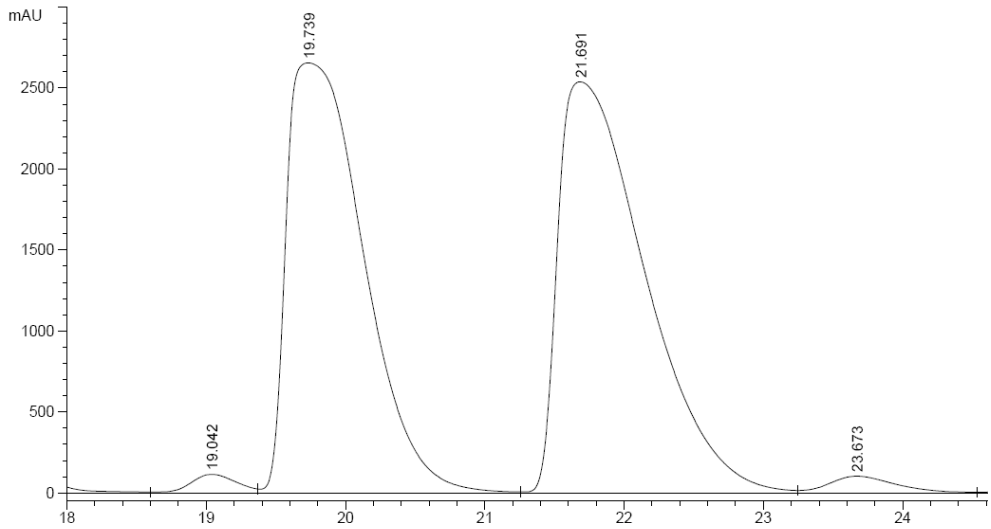




2-methyl-2-nitro-1-p-tolylpropyl acetate (2k). The general procedure was followed. Yield 35%. Enantiomeric ratio (97:3), determined by HPLC analysis (Chiralpak OD-H 99:1 Hex:^{i}PrOH, 0.4 ml/min; t_R 18.3 min; t_R 20.6 min. Colorless oil; ^{1}H NMR ($CDCl_3$) δ = 1.47 (3H, s), 1.63 (3H, s), 2.06 (3H, s), 2.34 (3H, s), 6.28 1H, s), 7.16 (2H, d, *J* = 8.0 Hz), 7.21 (2H, d, *J* = 8.0 Hz); ^{13}C NMR ($CDCl_3$) δ = 19.8, 20.8, 21.1, 24.4, 78.5, 90.2, 127.5, 129.1, 132.1, 138.9, 168.9.

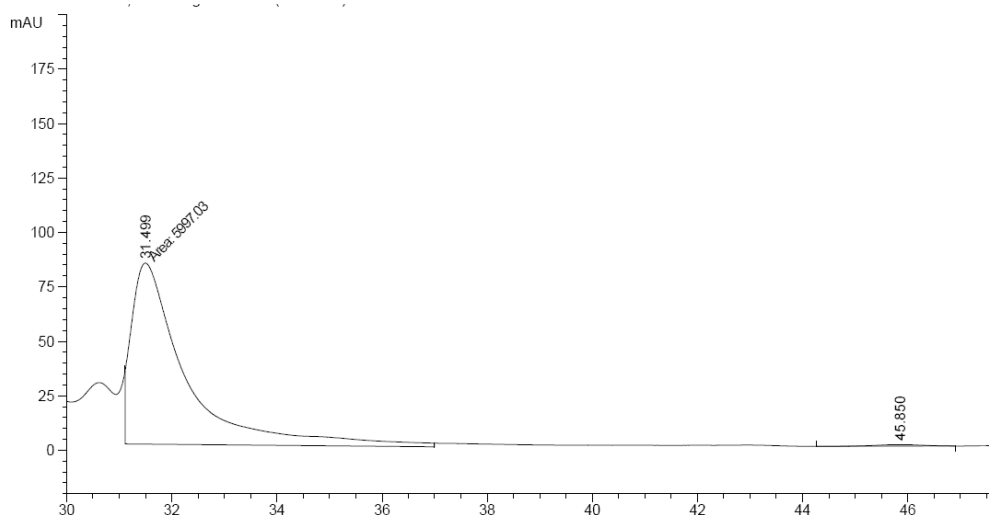
Peak	Processed Channel	Retention time (min)	Area	%Area	Height
1	@210nm	18.337	2208	3.45	780.23
2	@210nm	20.672	618691	96.55	11.30

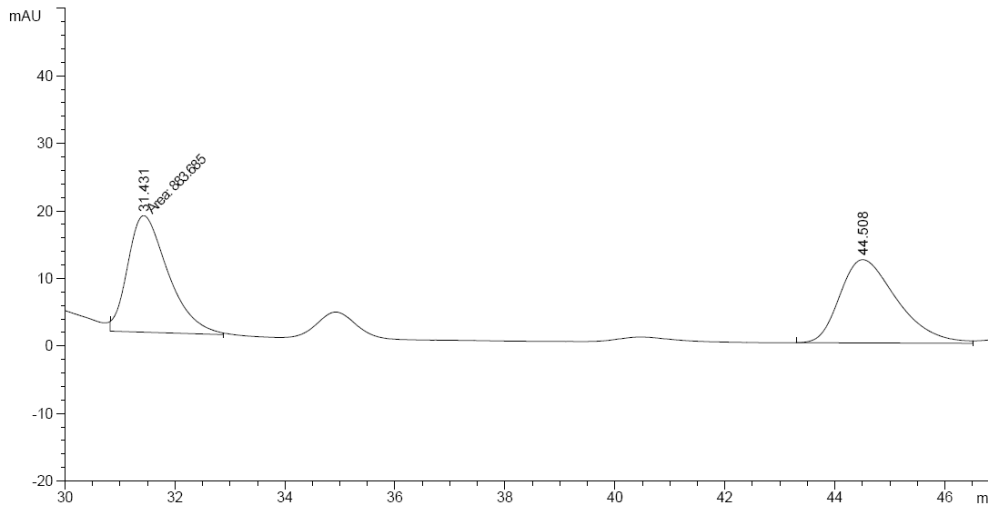




1-(4-methoxyphenyl)-2-methyl-2-nitropropyl acetate (2l). The general procedure was followed. Yield 28%. Enantiomeric ratio (99:1), determined by HPLC analysis (Chiralpak OD-H 99:1 Hex:^{i}PrOH, 0.5 ml/min; t_R 30.9 min; t_R 44.5 min. Colorless oil**;** ^{1}H NMR ($CDCl_3$) δ = 1.46 (3H, s), 1.62 (3H, s), 2.06 (3H, s), 3.79 (3H, s), 6.26 (1H, s), 6.87 (2H, d, *J* = 8.5 Hz), 7.24 (2H, d, *J* = 8.5 Hz); ^{13}C NMR ($CDCl_3$) δ = 19.8, 20.8, 24.3, 55.3, 78.2, 90.3, 113.8, 128.8, 132.0, 160.0, 168.9.

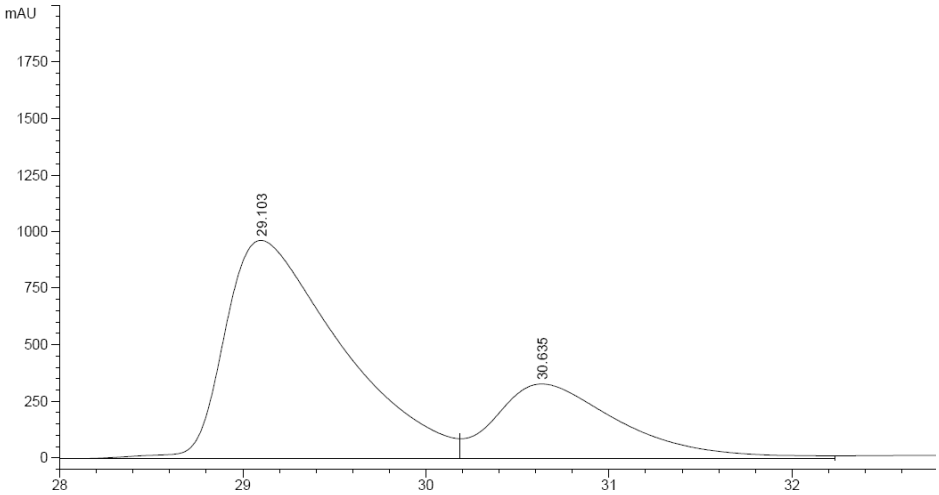
Peak	Processed Channel	Retention time (min)	Area	%Area	Height
1	@210nm	31.499	5997	99.29	83.18
2	@210nm	45.85	42	0.71	0.68

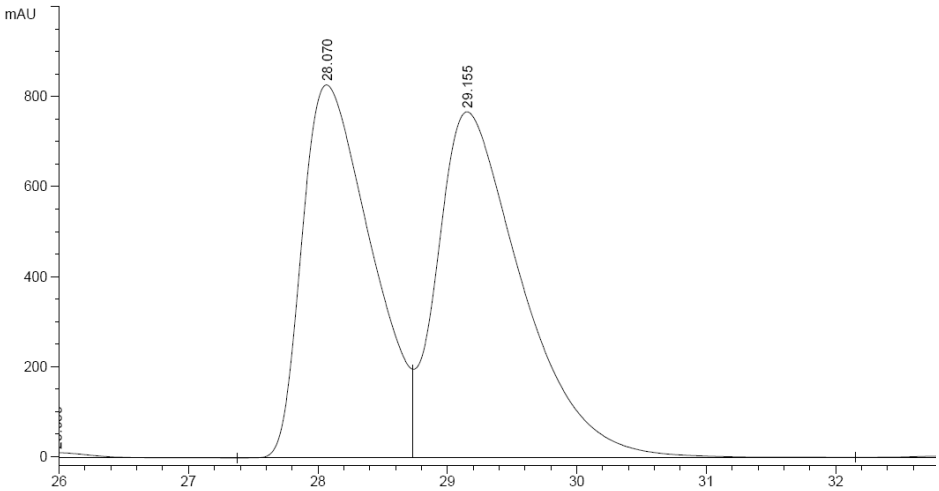




2-methyl-2-nitro-1-(thiophen-2-yl)propyl acetate (2m). The general procedure was followed. Yield 68%. Enantiomeric ratio (73:27), determined by HPLC analysis (Chiralpak OD-H 99:1 Hex:^{i}PrOH, 0.4 ml/min; t_R 29.1 min; t_R 30.6 min. Colorless oil; ^{1}H NMR ($CDCl_3$) δ = 1.54 (3H, s), 1.74 (3H, s), 2.07 (3H, s), 6.65 (1H, s), 6.99, 7.01 (1H, dd, *J* = 3.6, 5.2 Hz), 7.09 (1H, brd, *J* = 3.6), 7.31, 7.32 (1H, dd, *J* = 1.2, 5.2 Hz); ^{13}C NMR ($CDCl_3$) δ = 20.2, 20.7, 24.1, 24.4, 74.8, 90.1, 126.3, 126.8, 128.0, 137.1, 168.8.

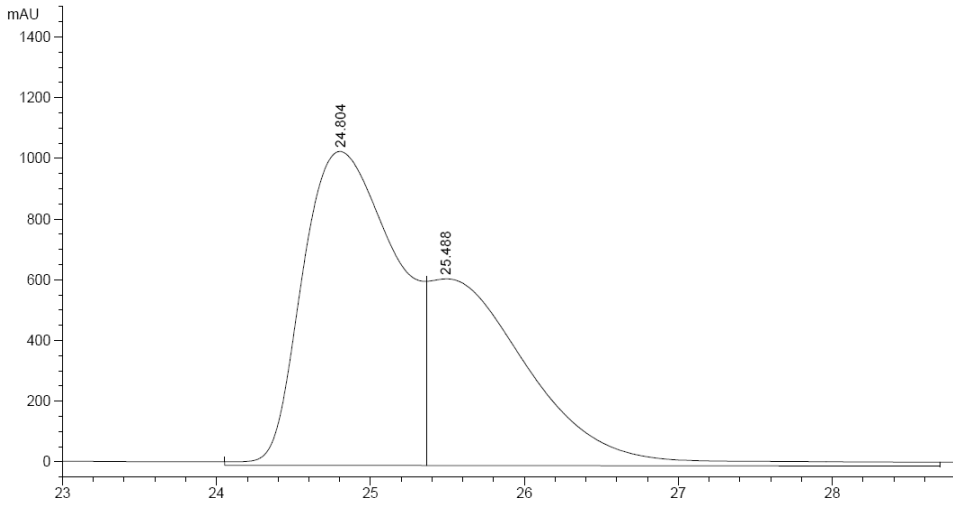
Peak	Processed Channel	Retention time (min)	Area	%Area	Height
1	@210nm	29.103	426839	72.99	966.02
2	@210nm	30.635	157928	27.00	331.47

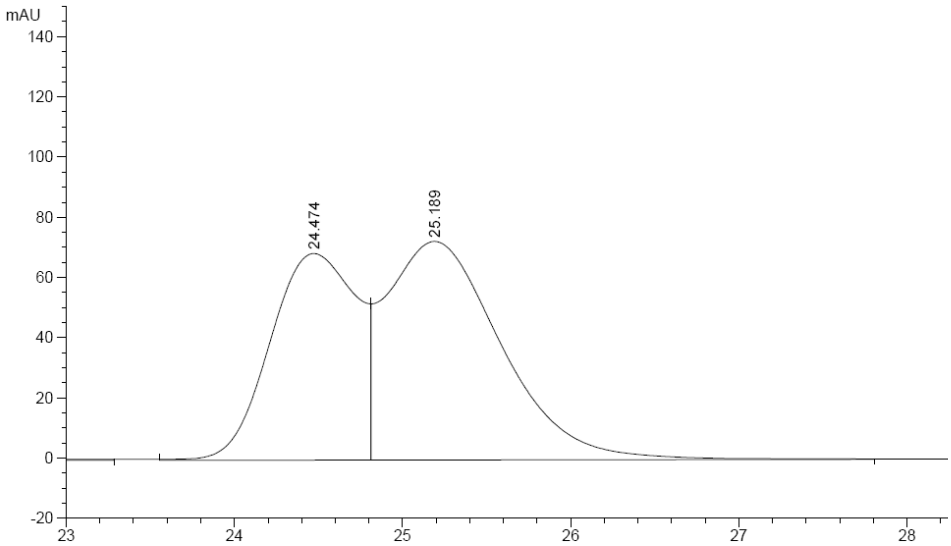




2-methyl-2-nitrohexan-3-yl acetate (2n). The general procedure was followed. Yield 71%. Enantiomeric ratio (61:39), determined by HPLC analysis (Chiralpak OJ 99:1 hex:^{i}PrOH, 0.4 ml/min; t_R 24.8 min; t_R 25.4 min. Colorless oil; ^{1}H NMR ($CDCl_3$) δ = 0.925 (3H, t, *J* = 7.2 Hz), 1.33 (2H, m), 1.48 (2H, m), 1.56 (3H, s), 1.59 (3H, s), 2.06 (3H, s), 5.46, 5.48 (1H, dd, *J* = 4, 9.2 Hz); ^{13}C NMR ($CDCl_3$) δ = 13.7, 19.2, 20.7, 21.7, 22.9, 32.0, 75.7, 89.9, 169.9.

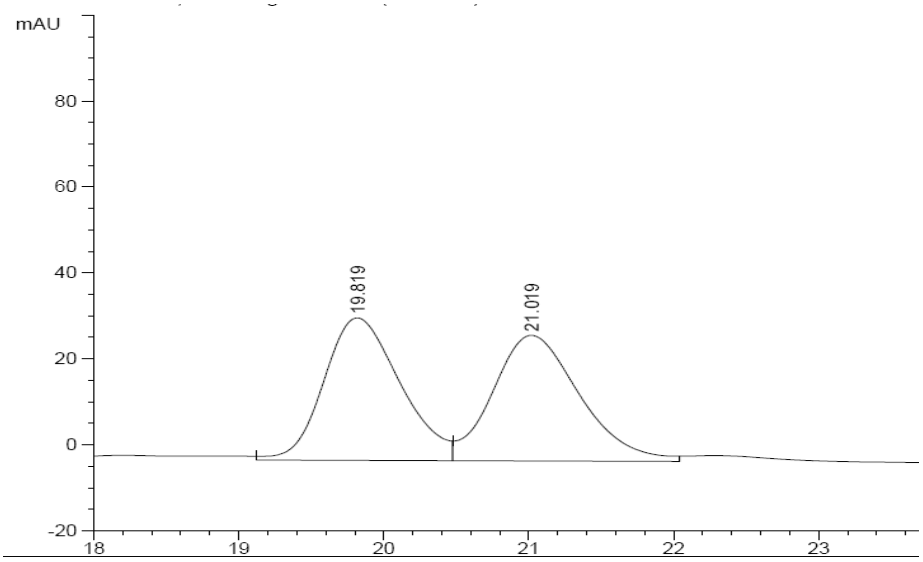
Peak	Processed Channel	Retention time (min)	Area	%Area	Height
1	@210nm	24.804	443433	60.83	1033.33
2	@210nm	25.488	285531	39.17	615.22

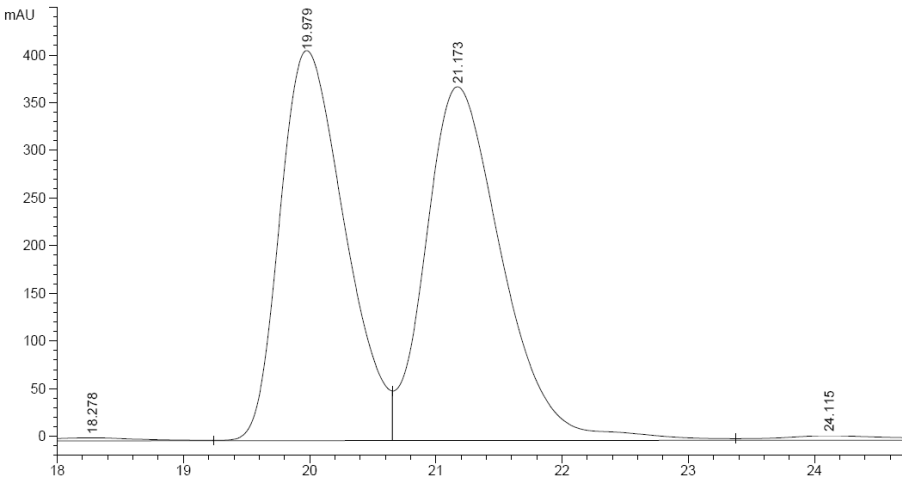




2,5-dimethyl-2-nitrohexan-3-yl acetate (2o). The general procedure was followed. Yield 60%. Enantiomeric ratio (50:50), determined by HPLC analysis (Chiralpak OJ 99:1 hex:^{i}PrOH, 0.3 ml/min; t_R 19.8 min; t_R 21.0 min. Colorless oil; ^{1}H NMR ($CDCl_3$) δ = 0.88 (3H, d, *J* = 6.5 Hz), 0.91 (3H, d, *J* = 6.5 Hz), 1.15 (1H, m), 1.49 (2H, m), 1.52 (3H, s), 1.54 (3H, s), 2.03 (3H, s), 5.48, 5.50 (1H, dd, *J* = 2, 10.5 Hz); ^{13}C NMR ($CDCl_3$) δ = 20.6, 21.2, 21.8, 22.6, 23.6, 24.5, 38.9, 74.2, 89.9, 169.8.

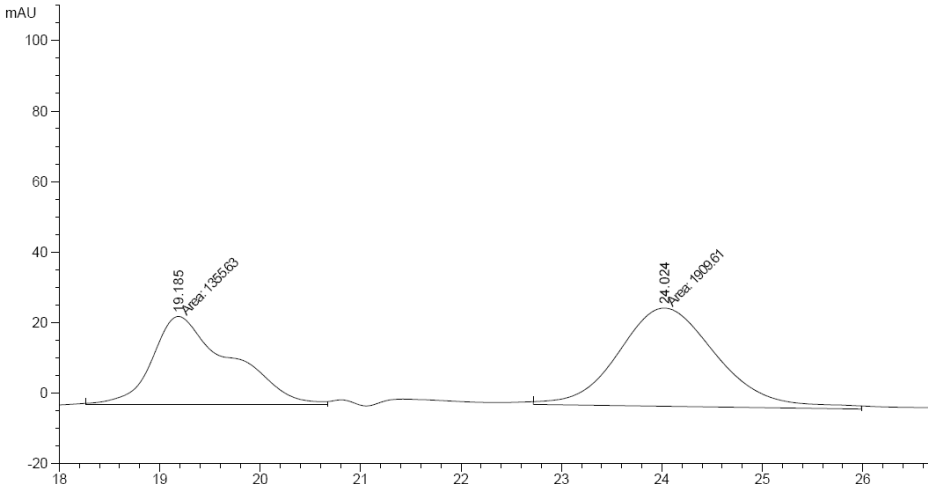
Peak	Processed Channel	Retention time (min)	Area	%Area	Height
1	@210nm	19.819	1214	49.89	33.14
2	@210nm	21.019	1219	50.11	29.25

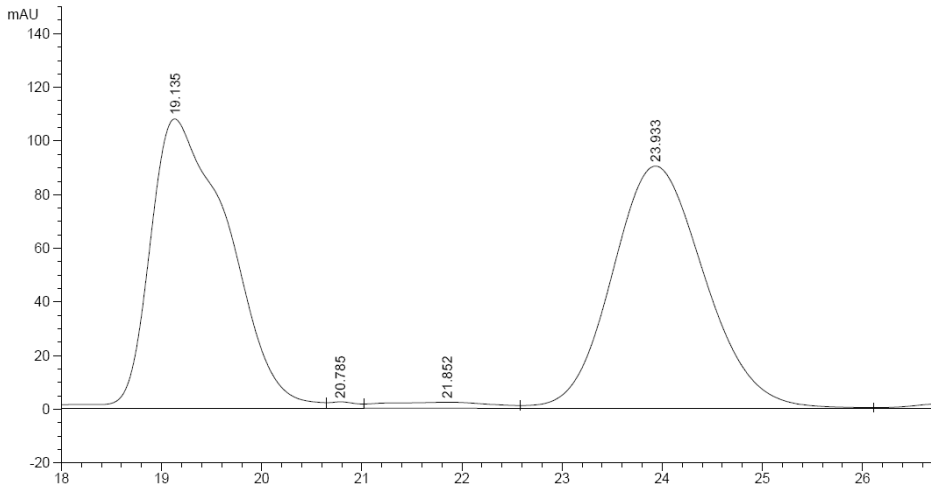




2-methyl-2-nitrodecan-3-yl acetate (2p). The general procedure was followed. Yield 62%. Enantiomeric ratio (58:42), determined by HPLC analysis (Chiralpak OJ 99:1 hex:^{i}PrOH, 0.4 ml/min; t_R 19.1 min; t_R 24.0 min. Colorless oil; ^{1}H NMR ($CDCl_3$) δ = 0.89 (3H, d, *J* = 7.0 Hz), 1.30 (10H, m), 1.51 (2H, m), 1.58 (3H, s), 1.60 (3H, s), 2.08 (3H, s), 5.46, 5.47 (1H, dd, *J* = 5, 8 Hz); ^{13}C NMR ($CDCl_3$) δ = 14.0, 20.7, 21,8, 22.6, 22.9, 25.9, 29.0, 29.2, 29.9, 31.7, 76.0, 89.9, 169.9.

Peak	Processed Channel	Retention time (min)	Area	%Area	Height
1	@210nm	19.185	1355	41.52	24.98
2	@210nm	24.024	1909	58.48	27.88





General procedure studies of nitroaldol reaction thermodynamics.

The reactions were performed by mixing benzaldehyde (0.25 mmol), 2-nitropropane (1 equivalent), and base (1 equivalent) in $CDCl_3$ (0.55 ml). The reactions were followed by ^1H NMR at room temperature (298K). Results were obtained by comparing the integrals of the signals of the benzaldehyde-nitroaldol adduct at each time till equilibrium.

General procedure for the synthesis of nitroaldol adduct 1a. In a typical experiment, 4-nitrobenzaldehyde (**4a**) (75.5 mg, 0.5 mmol) was dissolved in $CHCl_3$ (1 mL) followed by adding 2-nitropropane (**3**) (178 mg, 2 mmol) and triethylamine (101 mg, 1 mmol). The reaction was stirred at room temperature (298K) for 3 h. The reaction was quenched with diluted HCl (1 mL), extracted with CH_2Cl_2 (3 × 2 mL) and the combined organic layer washed with brine (2 × 1 mL). The organic layer was dried with $MgSO_4$ and the solvent evaporated. The crude product, nitroaldol adduct **1a** was purified by column chromatography (Hexane:CH_2Cl_2 (1:4) to pure CH_2Cl_2, 102 mg, 85 %).

2-methyl-2-nitro-1-(4-nitrophenyl)propan-1-ol (1a). Colorless amorph; ^1H NMR ($CDCl_3$) δ = 1.81 (3H, s), 1.91 (3H, s), 2.13 (3H, s), 5.78 (1H, s), 7.91 (2H, d, *J* = 8.5 Hz), 8.57 (2H, d, *J* = 8.5 Hz); ^{13}C NMR ($CDCl_3$) δ = 19.4, 23.9, 91.7, 123.4, 128.5, 145.2, 148.1.

General procedure to synthesis of racemic mixtures of compounds 2a-i. In a typical experiment, 3-nitrobenzaldehyde (**4d**) (37.75 mg, 0.25 mmol) was dissolved in $CHCl_3$ (0.5 ml) followed by addition of 2-nitropropane (**3**) (111.25 mg, 1.25 mmol) and triethylamine (75.75 mg, 0.75 mmol), and stirred at room temperature for 3 h. The reaction was acidified with diluted HCl, extracted with CH_2Cl_2 (3 × 2 mL) and the combined organic layer washed with brine (2 × 1 mL). The organic layer was dried with $MgSO_4$ and the solvent evaporated. The crude mixture was dissolved in dry pyridine (1 ml) followed by addition of 5 equivalents of acetic anhydride (127.5 mg, 1.25 mmol). The reaction mixture was stirred at room temperature for 6 h, followed by the same work-up as above, providing the corresponding crude racemic mixture of compound **2d**. The crude mixture was purified by column chromatography (CH_2Cl_2/Hexane (7:3 (*v*/*v*)) to yield compound **2d** (60 mg, 85%).

General procedure for the synthesis of *p*-chlorophenyl acetate.[1] In a typical experiment, acetyl chloride (5.5 mmol) was added dropwise to a solution of 4-chlorophenol (0.643 g, 5.0

mmol), triethylamine (1.52 g, 15 mmol), and DMAP (12 mg, 0.1 mmol) in CH_2Cl_2 (10 mL). The reaction mixture was stirred at room temperature overnight. The solution was washed with diluted HCl (3 × 8 mL), and the combined aqueous phases were re-extracted with ether (3 × 8 mL). The combined organic phases were washed with saturated $NaHCO_3$ (aq, 5 mL), and brine (4 mL) and dried over $MgSO_4$. The solvent was concentrated in vacuo, and the crude mixture was purified on silica (CH_2Cl_2/hexane, 7:3 (v/v)).

***p*-chlorophenyl acetate** Colorless oil; ^{1}H NMR ($CDCl_3$) δ = 2.29 (s, 3H), 7.03 (d, 2H, *J* = 8.8 Hz), 7.34 (d, 2H, *J* = 8.8 Hz).

General procedure for the synthesis of 1-ethoxyvinyl acetate.[2] Ethoxy acetylene (686 mg, 9.8 mmol) and Bennet's ruthenium complex ($[RuCl_2(p\text{-cymene})]_2$) (20 mg, 0.03 mmol) were dissolved in diisopropyl ether (40 mL). The mixture was cooled to 0 ^{o}C and a solution of freshly distilled acetic acid (360 mg, 6 mmol) in diisopropyl ether (30 mL) was added dropwise. The reaction was allowed to warm up to room temperature and was stirred overnight. After concentration the residue was distilled under vacuum (80 ^{o}C, 0.4 mbar) to obtain the desired product as a colourless oil in a yield of 429 mg (55%). ^{1}H NMR ($CDCl_3$) δ = 1.33 (t, 3H, *J* = 7.02 Hz), 2.16 (s, 3H), 3.76 (d, 1H, *J* = 3.7 Hz), 3.82 (d, 1H, *J* = 3.7 Hz), 3.86 (q, 2H, *J* = 7.02 Hz).

General procedure for preparation of MTPA Ester Derivatives of 7a and 7a′.[3] A reaction mixture consisting of **1a** (4 mg, 99%ee), generated from kinetic resolution by enzyme-lipase PS-C I, pyridine (0.5 mL), and (*R*)-(-)-α-methoxy-α-trifluoromethylphenylacetyl chloride (20 mg) was left standing at room temperature for 40 h. The mixture was acidified with dilute HCl, then extracted with EtOAc (3 × 1 mL) and subsequently washed with brine. The EtOAc layer was dried, yielding the (*S*)-(-)-MTPA ester of **7a** (2 mg). Preparation of the (*R*)-(+)-MTPA ester of **7a′** from (*S*)-(+)-α-methoxy-α-trifluoromethylphenylacetyl chloride was performed in the same manner as that of the (*S*)-(-)-MTPA ester derivative.

(*S*)-(-)-MTPA ester (**7a**) Colorless oil: ^{1}H NMR ($CDCl_3$) δ = 1.47 (3H, s), 1.60 (3H, s), 3.41 (3H, s, OMe), 6.65 (1H, s), 7.38 (3H, m, aromatic protons of MTPA), 7.40 (2H, m, aromatic protons of MTPA), 7.44 (2H, d, *J* = 8.5 Hz), 8.23 (2H, d, *J* = 8.5 Hz).

(*R*)-(+)-MTPA ester (**7a′**) Colorless oil: ^{1}H NMR ($CDCl_3$) δ = 1.48 (3H, s), 1.55 (3H, s), 3.45 (3H, s, OMe), 6.57 (1H, s), 7.28 (2H, d, *J* = 7 Hz), 7.37 (3H, m, aromatic protons of MTPA), 7.42 (2H, m, aromatic protons of MTPA)**,** 8.16 (2H, d, *J* = 7 Hz).

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3. Seephonkai P; Isaka M; Kittakoop P; Boonudomlap U; Thebtaranonth Y. *J. Antibiot.* **2004**, *57*, 10-16.