Supporting Information

Polyethylene glycol (PEG) as a Reusable Solvent Medium for Asymmetric Organocatalytic Michael Addition. Application on the Synthesis of Bioactive Compounds

Karla S. Feu, Alexander F. de la Torre, Sandrina Silva, Marco A. F de Moraes Junior, Arlene G. Corrêa and Márcio Weber Paixão*

Department of Chemistry, Federal University of São Carlos (UFSCar), São Carlos, SP, Brazil.
CEP:13565-905. Tel: +55 55 3351 8215

Corresponding Author*: E-mail: mwpaixao@ufscar.br

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1. General Information:

^{1}H and ^{13}C NMR spectra were recorded on a Bruker ARX-400 (400 and 100 MHz respectively). All NMR spectra were obtained with $CDCl_3$.

HPLC chromatograms of Michael adduct were obtained on a Shimadzu apparatus, LC-20AT Pump, SPD-M20A UV-Vis Detector, CBM-20A System Controller, using a Chiralcel OD-H (4,6 mmØ x 250 mmL, particle size 5 μm), Chiralpak AD-H (4,6 mmØ x 250 mmL, particle size 5 μm), Chiralcel AS-H (4,6 mmØ x 250 mmL, particle size 5 μm) and Chiralpak IC (2,1 mmØ x 150 mmL, particle size 5 μm).

Optical rotations were measured with a Schmidt + Haensch Polartronic H Polarimeter, at 589 nm, 23 °C. Using a 1 mL cell with a 1 dm path length and reported as follows: $[\alpha]_D^{23}$(c in g per mL of solvent).All the compounds synthesized in the manuscript are known componds. Their relative and absolute configurations of the products were determined by comparison with the known ^{1}H and ^{13}C NMR, chiral HPLC analysis, and optical rotation values.

Column chromatography was performed using Merck Silica Gel (230-400 mesh). Thin layer chromatography (TLC) was performed using Merck Silica Gel GF254, 0.25 mm thickness. For visualization, TLC plates were either placed under ultraviolet light, or stained with KMnO4 solution.

2. General procedure for Michael Addition:

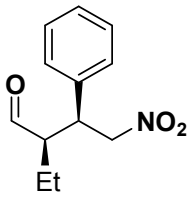
The aldehyde (0.6 mmol), nitroolefin (0.3 mmol) and the benzoic acid (0.015 mmol) were added to a solution of the catalyst (0.015 mmol) in PEG-400 (0.5 mL). The reaction mixture was stirred for 19 h and then was direct purified by flash column chromatography on silica gel using n-hexane/EtOAc as the eluent. The enantiomeric excess was determined by chiral-stationary-phase HPLC analysis through comparison with the authentic racemic material. Assignment of the stereoisomers was performed by comparison with literature data.

3- General procedure for PEG-400 recyclability experiments

After complete the reaction time, 0.25 mL of water was added to the PEG mixture (an emulsion appears) and the mixture PEG-aqueous solution were extracted sequentially with 1 mL of Ether for three times until light yellow color in PEG-aqueous solution disappear. The organic phase was then dried over anhydrous Na_2SO_4 and concentrated under reduced pressure. The resulting crude product was purified by flash column chromatography on silica gel using n-hexane/EtOAc as eluent. The PEG-aqueous solutions was concentrated under reduced pressure until the water was removed and the result PEG recovered was dried in high vacuum pump and further add the Michael reagents and run a new reaction in the solvent recycled.

4- Characterization of conjugate addition products

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

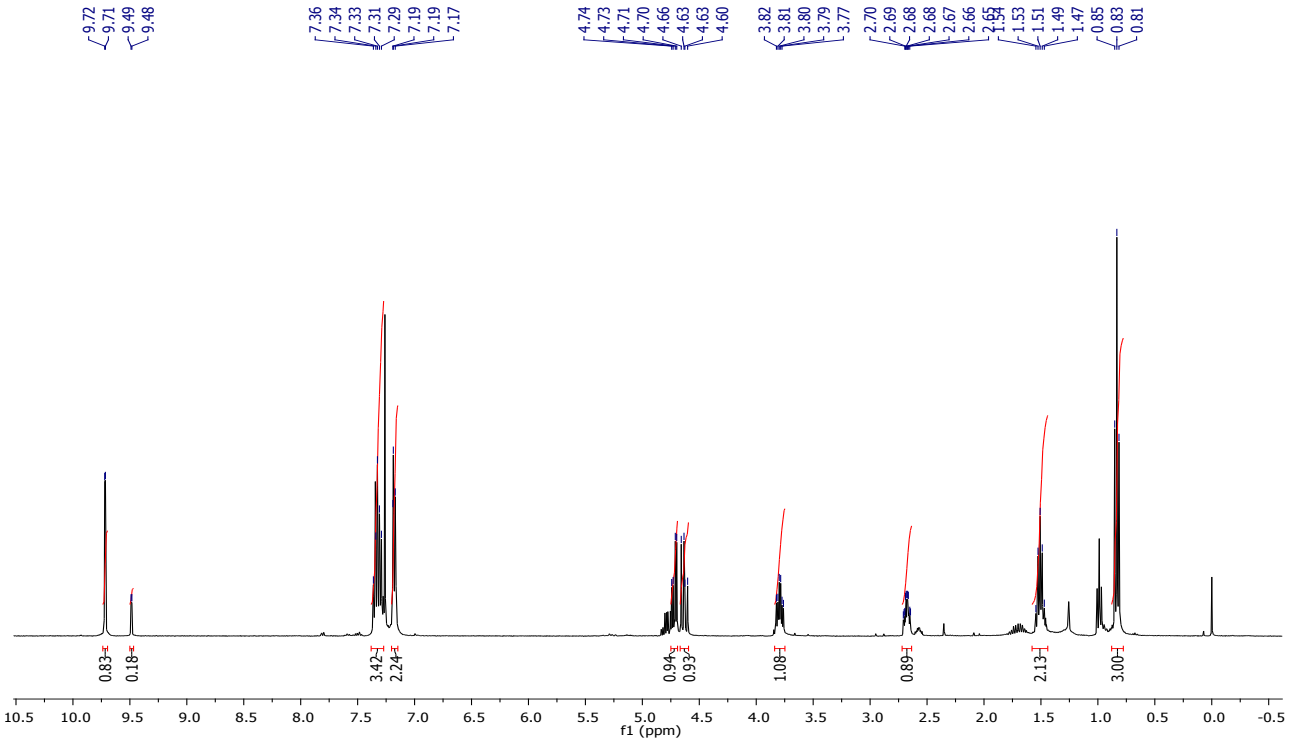


Analytical data for major diastereoisomer were in agreement with the published data.

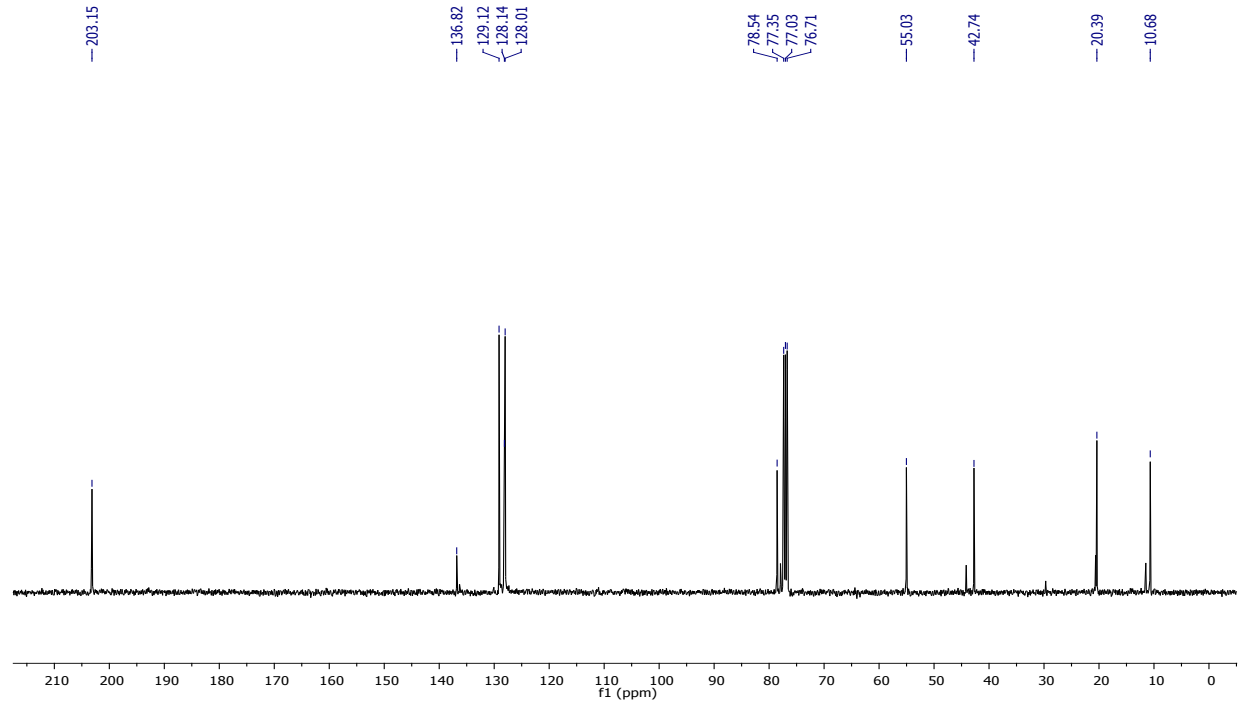
^{1}H NMR (400 MHz,$CDCl_3$, 25°C) δ = 9.72, 9.49 (2xd, *J* = 2.6 Hz, 1H; CHO), 7.36- 7.29 (m, 3H; Ph), 7.19- 7.17 (m, 2H; Ph), 4.72 (dd, *J* = 5.0 Hz, 12.7 Hz, 1H; CH_2NO_2), 4.63 (dd, *J* = 9.6 Hz, 12.7 Hz, 1H, CH_2NO_2), 3.79 (td, *J* = 5.0 Hz, 9.8 Hz, 1H; CHPh), 2.71- 2.65 (m, 1H; CHCHO), 1.54- 1.47 (m, 2H; CH_2CH_3), 0.83 (t, *J* = 0.83 Hz, 3H, CH_3) ppm; **^{13}C NMR** (100 MHz, $CDCl_3$, 25°C) δ = 203.2, 136.8, 129.1, 128.1, 128.0, 78.5, 55.0, 42.7, 20.4, 10.7 ppm.

$[\alpha]_D^{25}$ = +25.21 (*c* 0.0046 g. mL^{-1}, MeOH); lit = **$[\alpha]_D^{20}$** = +32.3 (*c* 1.6, $CHCl_3$)

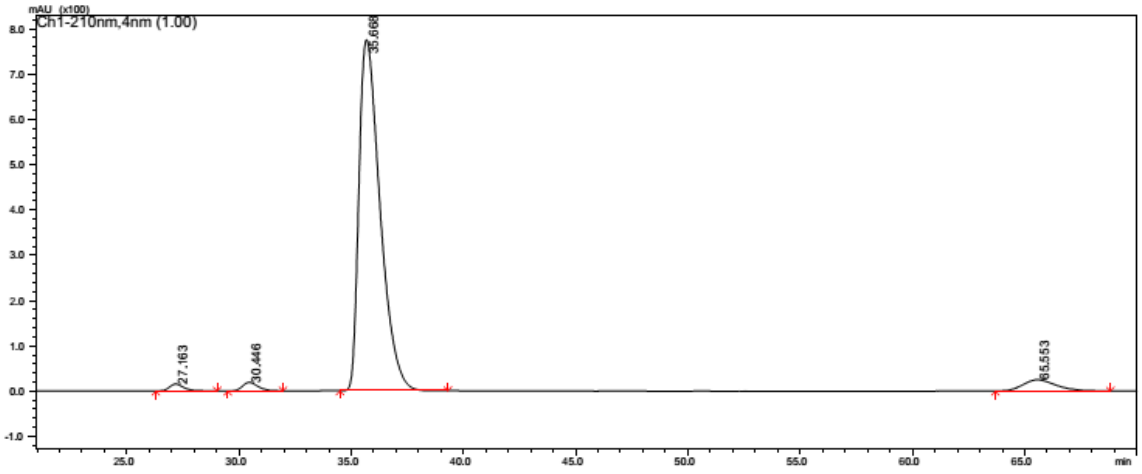
^{1}H NMR



^{13}C NMR



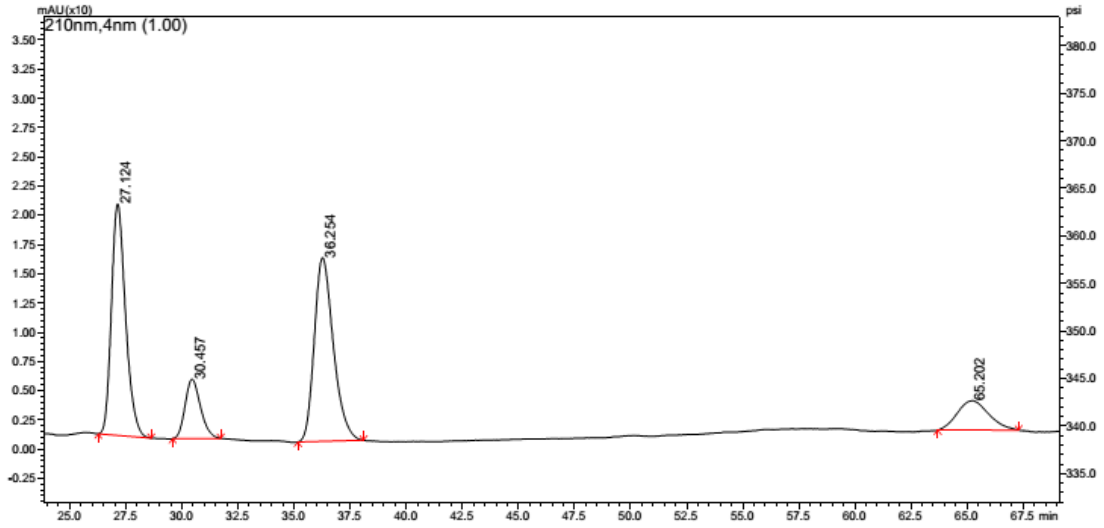
HPLC: Chiracel OD-H column (n-hexane/i-PrOH 91:09, 25ºC) at 0.9 mL/min (97% ee)



PeakTable

PDA Ch1 210nm 4nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	27.163	712943	15604	1.295	1.866
2	30.446	943621	19257	1.715	2.303
3	35.668	50772270	776262	92.254	92.847
4	65.553	2606421	24945	4.736	2.984
Total		55035255	836068	100.000	100.000

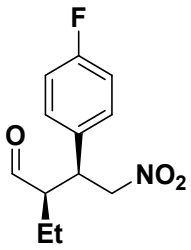


PeakTable

PDA Ch1 210nm 4nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	27.124	867445	19800	37.957	45.951
2	30.457	242098	5070	10.593	11.767
3	36.254	931040	15712	40.739	36.463
4	65.202	244769	2508	10.710	5.819
Total		2285353	43090	100.000	100.000

(2R,3S)-2-ethyl-3-(4-fluorophenyl)-4-nitrobutanal- (10a)

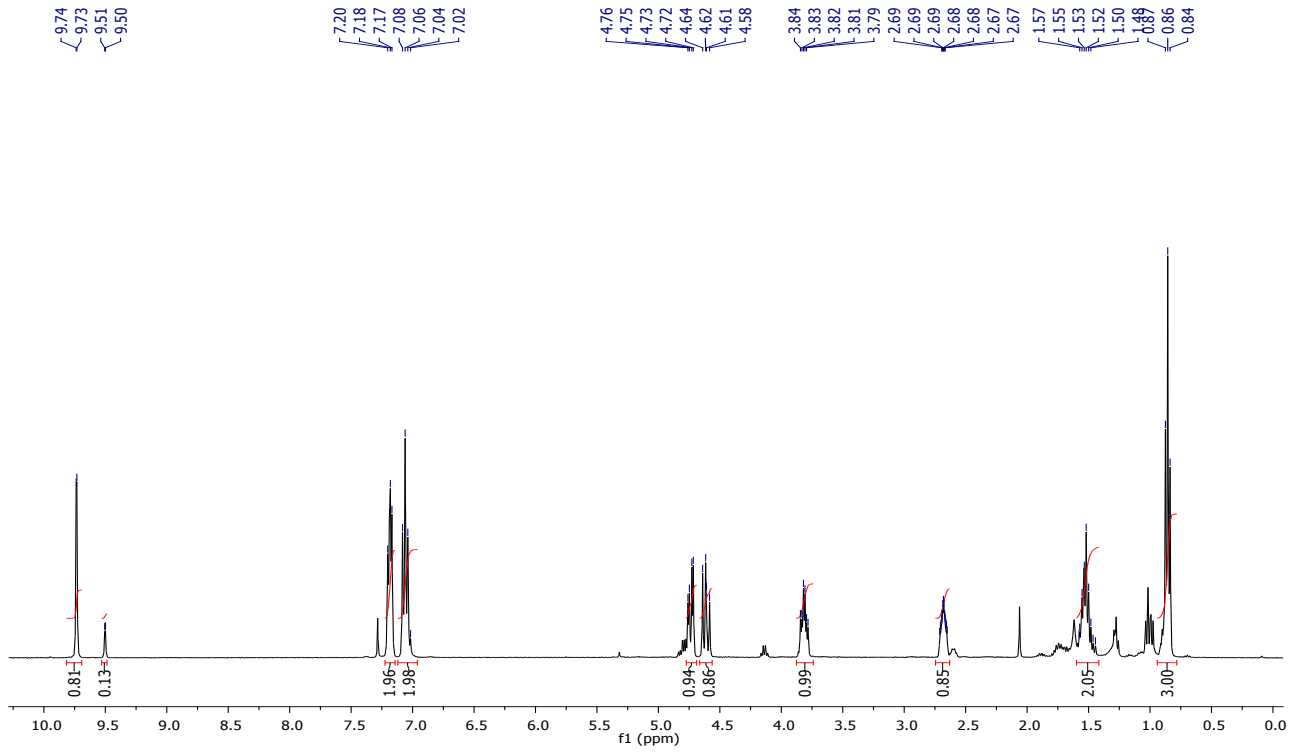


Analytical data for major diastereoisomer were in agreement with the published data

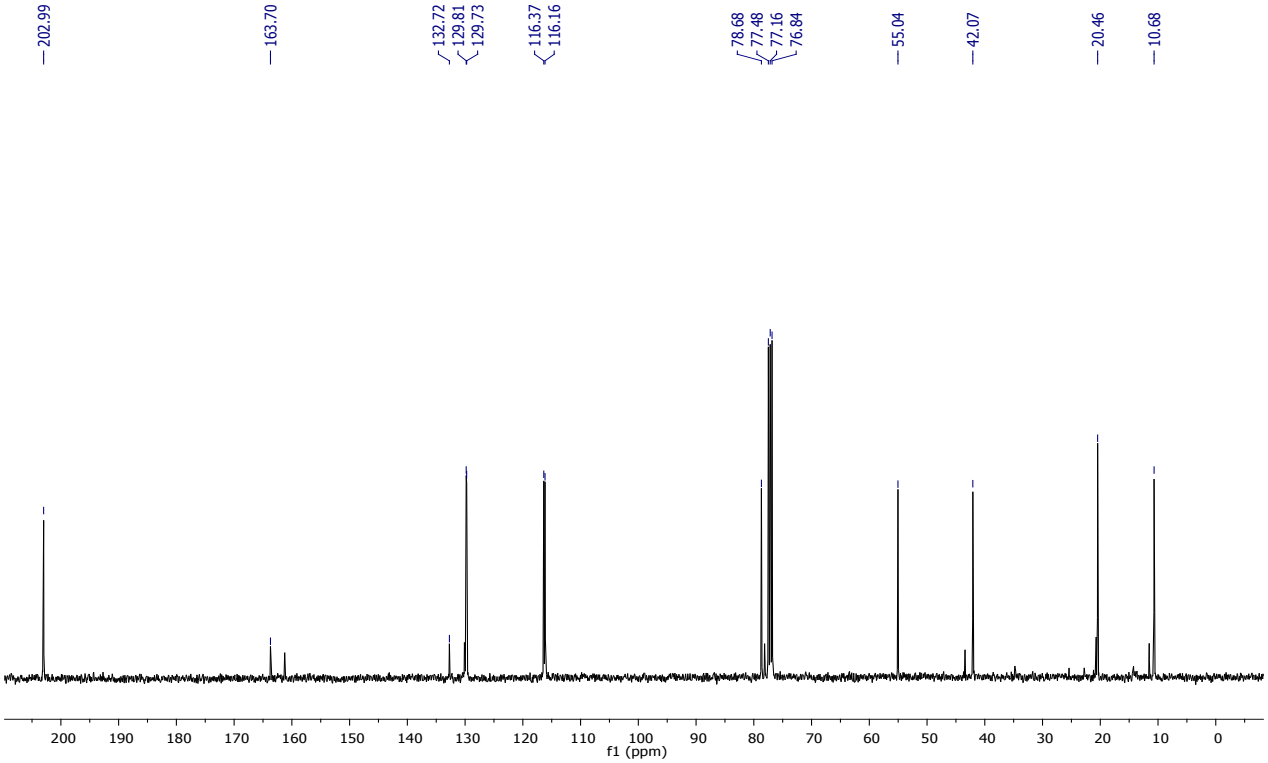
^{1}H NMR (400 MHz,$CDCl_3$, 25°C) δ = 9.74-9.51 (2xd, *J* = 2.4 Hz, 1H; CHO), 7.20- 7.17 (m, 2H; Ph), 7.08- 7.02 (m, 2H; Ph), 4.74 (dd, *J* = 4.8 Hz, 12.7 Hz, 1H; CH_2NO_2), 4.61 (dd, *J* = 9.9 Hz, 12.7 Hz, 1H; CH_2NO_2), 3.84- 3.78 (m, 1H; CHPh), 2.71- 2.65 (m, 1H; CHCHO), 1.58–1.44 (m, 2H; CH_2CH_3), 0.86 (t, *J* = 7.5 Hz, 3H; CH_3) ppm; **^{13}C NMR** (100 MHz, CDCl3, 25°C) δ = 203.0, 163.7, 132.7, 129.8, 129.7, 116.4, 116.2, 78.7, 55.0, 42.7, 20.4, 10.7ppm.

[α] $_D^{25}$ = +9.75 (*c* 0.0041 g. mL^{-1}, MeOH); lit. = **[α] $_D^{20}$** = +12.9 (*c* 0.7, $CHCl_3$);

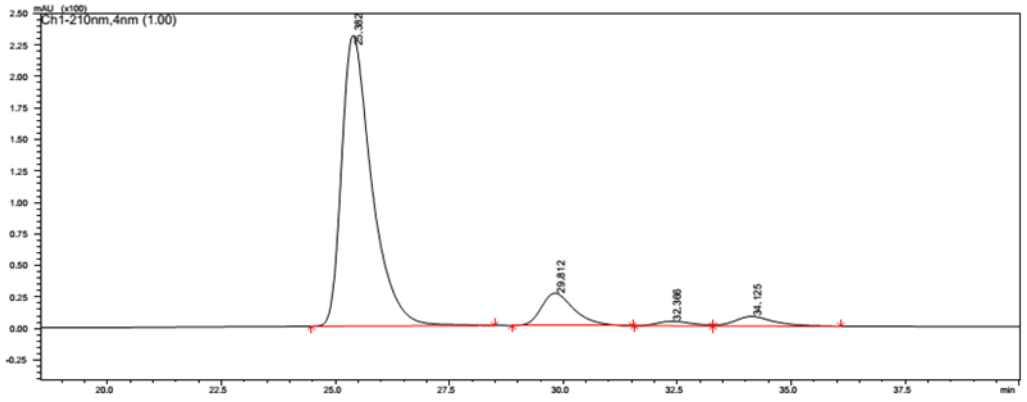
^{1}H NMR



^{13}C NMR



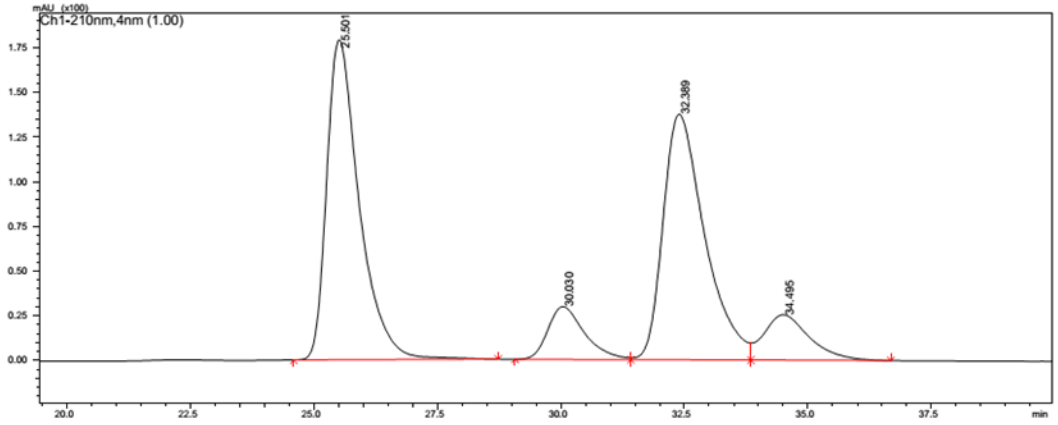
HPLC: Chiracel OD-H column (n-hexane/i-PrOH 95:05, 25ºC) at 1 mL/min (96% ee)



PeakTable

PDA Ch1 210nm 4nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	25.382	10571892	230508	84.542	86.175
2	29.812	1289444	25764	10.312	9.632
3	32.366	189253	3620	1.513	1.353
4	34.125	454313	7595	3.633	2.839
Total		12504901	267488	100.000	100.000

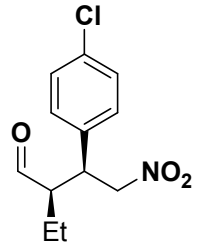


PeakTable

PDA Ch1 210nm 4nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	25.501	8204258	179078	42.238	48.219
2	30.030	1520218	29493	7.827	7.941
3	32.389	8069247	137384	41.543	36.992
4	34.495	1630250	25432	8.393	6.848
Total		19423975	371387	100.000	100.000

(2R,3S)-3-(4-chlorophenyl)-2-ethyl-4-nitrobutanal- (10b)

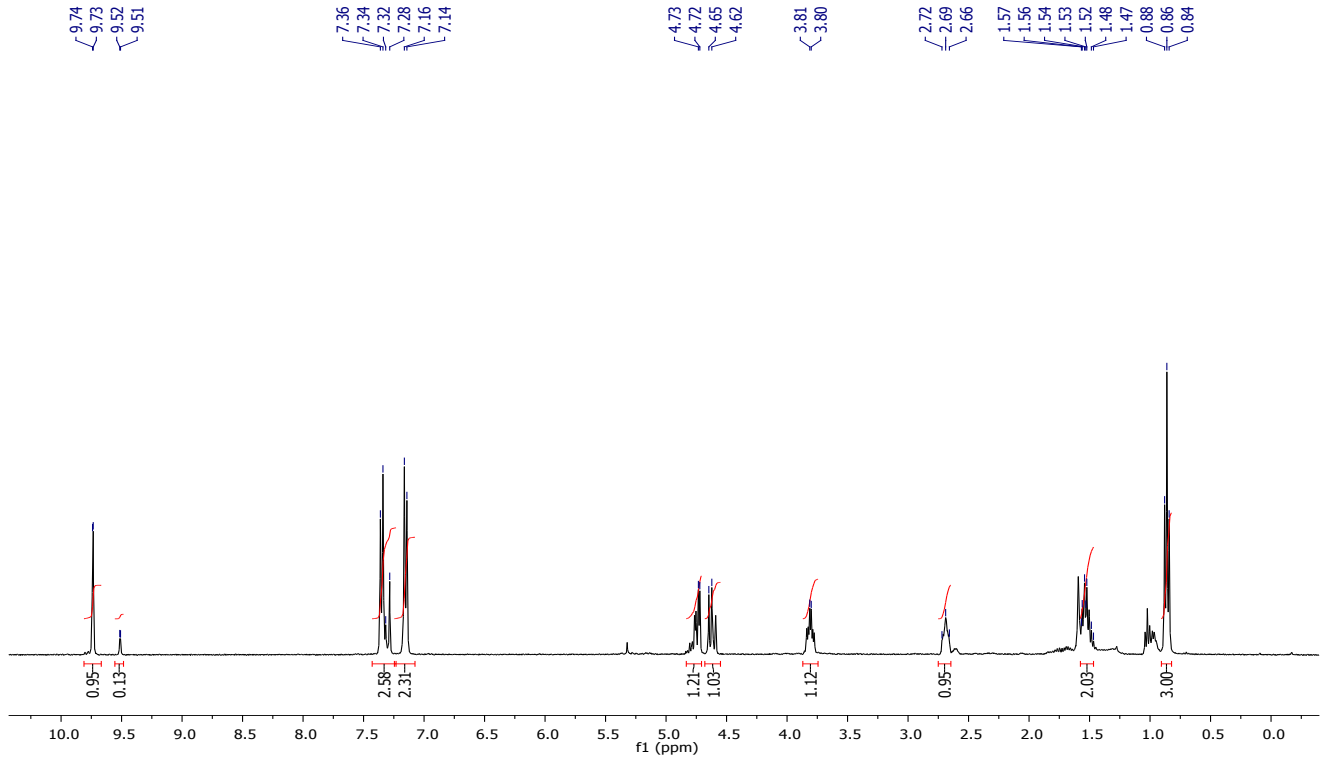


Analytical data for major diastereoisomer were in agreement with the published data.

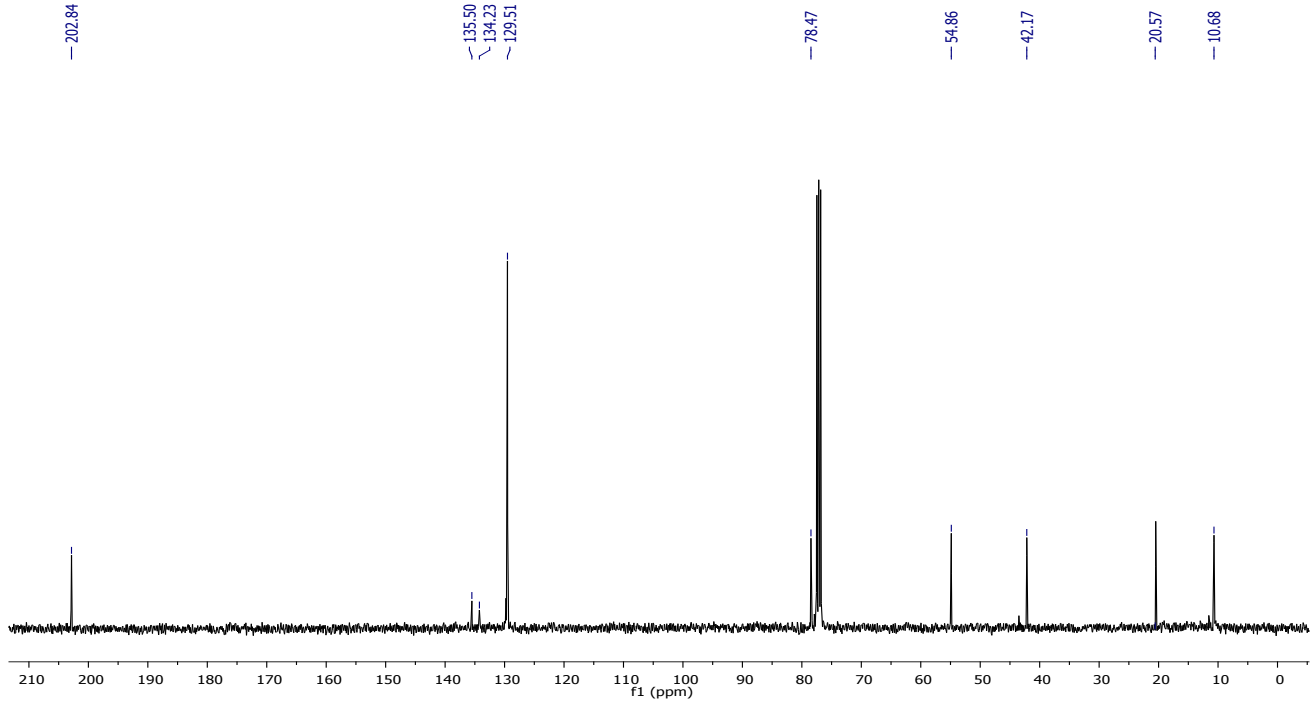
^{1}H NMR (400 MHz,$CDCl_3$, 25°C) δ = 9.74, 9.51 (2xd, *J* = 2.8 Hz, 1H; CHO), 7.36-7.28 (m, 2H; Ph), 7.16-7.14 (m, 2H; Ph), 4.73 (dd, *J* = 4.8 Hz, 12.8 Hz, 1H; CH_2NO_2), 4.63 (dd, *J* = 9.9 Hz, 12.8 Hz, 1H; CH_2NO_2), 3.80 (dt, *J* = 4.8 Hz, 10.0 Hz, 1H; CHPh), 2.72- 2.66 (m, 1H; CHCHO), 1.57- 1.47 (m, 2H; CH_2CH_3), 0.86 (t, *J* = 7.5 Hz, 3H; CH_3) ppm; **^{13}C NMR** (100 MHz, $CDCl_3$, 25°C) δ = 202.8, 135.5, 134.2, 129.8, 129.5, 54.8, 42.2, 20.5, 10.7 ppm.

[α] $_D^{25}$ = +7.5 (*c* 0.0020 g. mL^{-1}, MeOH); lit. = **[α]** $_D^{20}$ = +28.6 (*c* 1.1, $CHCl_3$)

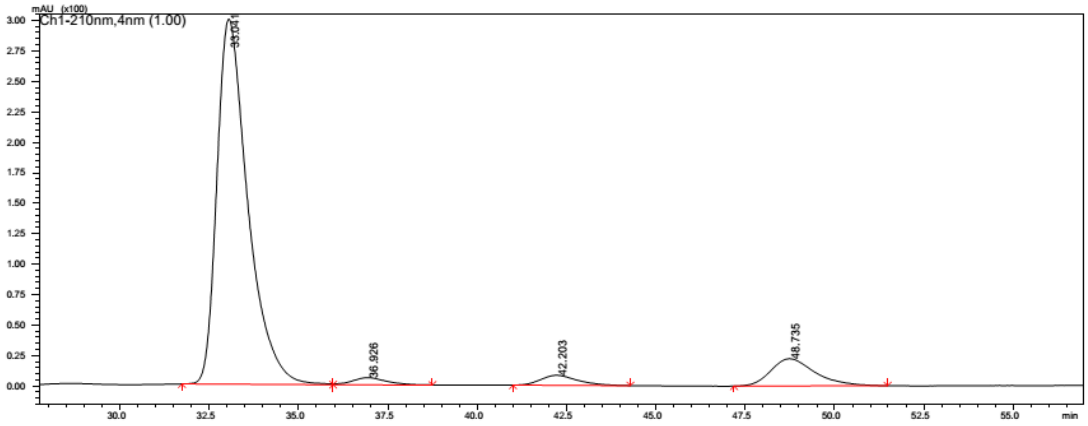
^{1}H NMR



^{13}C NMR



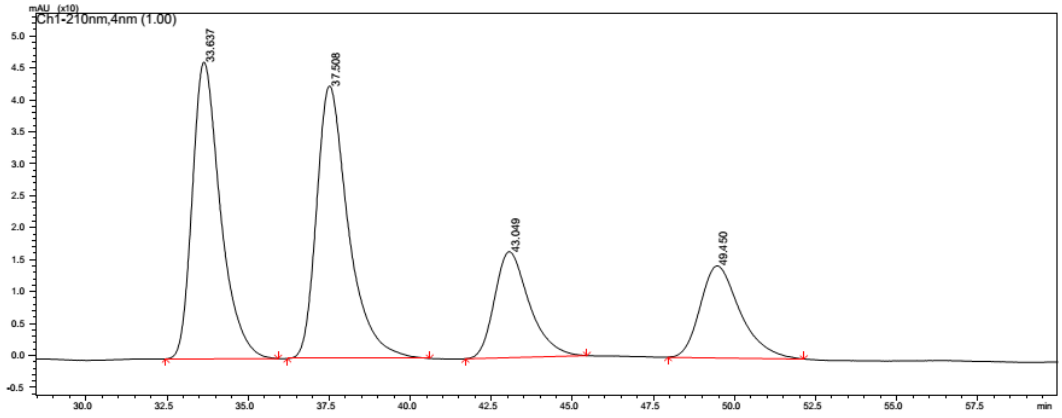
HPLC: Chiracel OD-H column (n-hexane/i-PrOH 95:5, 25ºC) at 1 mL/min (96% ee)



PeakTable

PDA Ch1 210nm 4nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	33.041	18052281	299606	86.237	89.199
2	36.926	378705	5873	1.809	1.749
3	42.203	590311	8143	2.820	2.424
4	48.735	1912108	22265	9.134	6.629
Total		20933405	335886	100.000	100.000

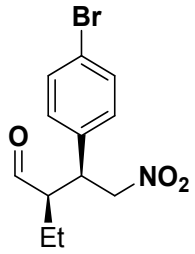


PeakTable

PDA Ch1 210nm 4nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	33.637	2800026	46439	34.224	38.680
2	37.508	2907345	42657	35.535	35.529
3	43.049	1236687	16551	15.115	13.786
4	49.450	1237525	14414	15.126	12.005
Total		8181582	120061	100.000	100.000

(2R,3S)-3-(4-bromophenyl)-2-ethyl-4-nitrobutanal – (10c)

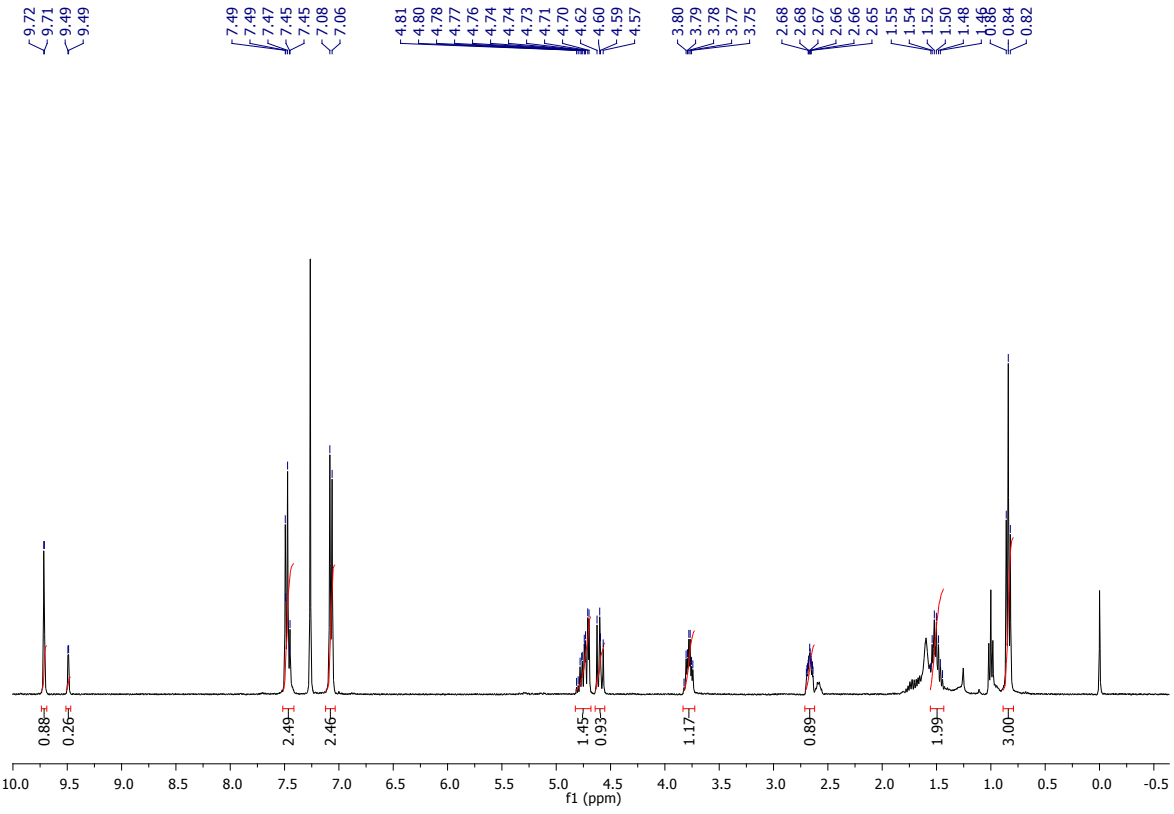


Analytical data for major diastereoisomer were in agreement with the published data.

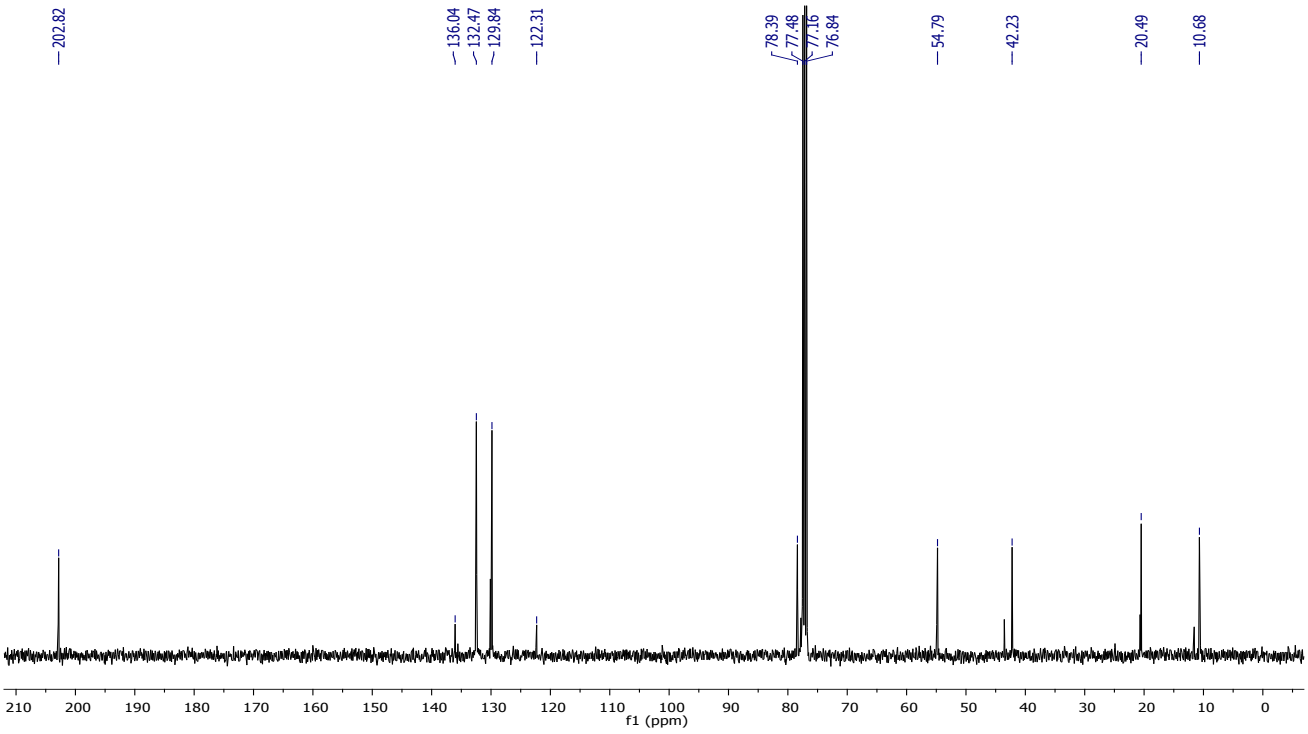
^{1}H NMR (400 MHz,$CDCl_3$, 25°C) δ =9.79, 9.49 (2xd, *J* = 2.3 Hz, 1H, CHO), 7.49- 7.45 (m, 2H, Ph), 7.07 (d, *J* = 8.3 Hz, 2H, Ph), 4.81-4.70 (m, 1H, CH_2NO_2), 4.62- 4.57 (m, 1H, CH_2NO_2), 3.80- 3.74 (m, 1H, CHPh), 2.70- 2.64 (m, 1H, CHCHO), 1.55- 1.44 (m, 2H, CH_2CH_3), 0.84 (t, *J* = 7.5 Hz, 3H, CH_3) ppm; **^{13}C NMR** (100 MHz, $CDCl_3$, 25°C) δ = 202.8, 136.0, 132.5, 129.8, 122.3, 78.4, 54.8, 42.2, 20.5, 10.7 ppm.

$[\alpha]_D^{25}$ = +0.61 (*c* 0.0065 g. mL^{-1}, MeOH); lit. = **$[\alpha]_D^{20}$**= +27.3 (*c* 1.3, $CHCl_3$);

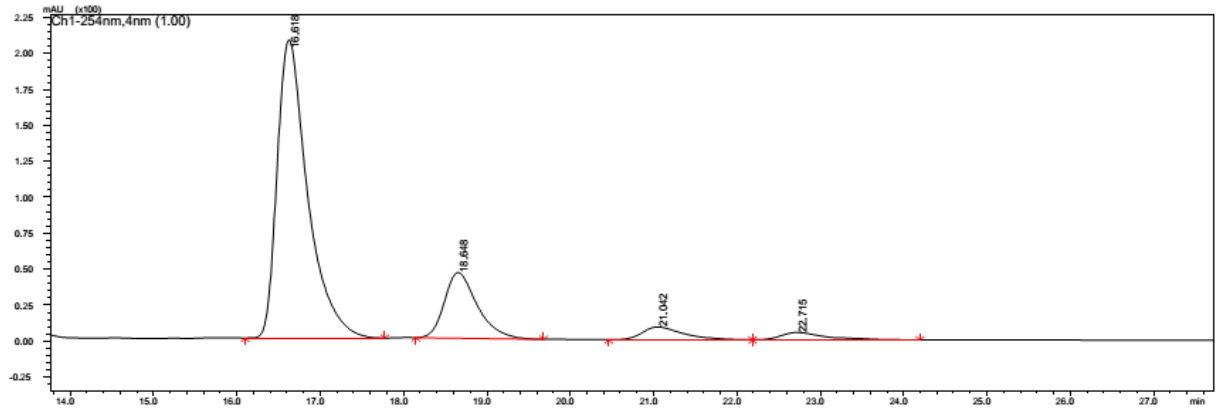
^{1}H NMR



^{13}C NMR



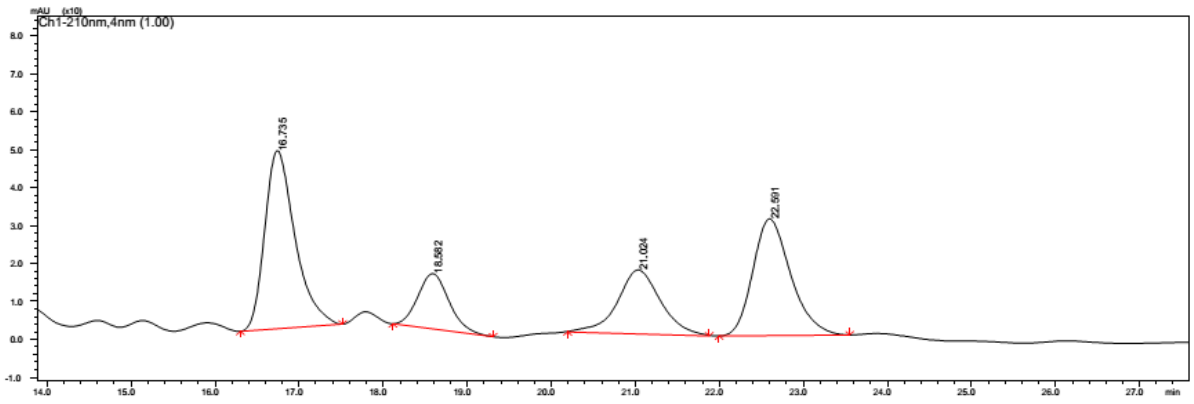
HPLC: Chiracel AD-H column (n-hexane/i-PrOH 95:05, 25ºC) at 0.8 mL/min (93% ee)



PeakTable

PDA Ch1 254nm 4nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	16.618	5290575	207418	74.982	77.585
2	18.648	1253711	45652	17.769	17.076
3	21.042	312597	9045	4.430	3.383
4	22.715	198871	5227	2.819	1.955
Total		7055754	267341	100.000	100.000

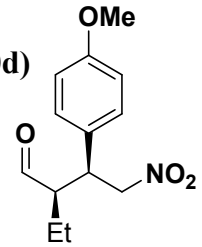


PeakTable

PDA Ch1 210nm 4nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	16.735	1181332	46993	37.799	43.045
2	18.582	377420	14605	12.076	13.378
3	21.024	602704	16844	19.285	15.429
4	22.591	963847	30730	30.840	28.148
Total		3125303	109172	100.000	100.000

(2R,3S)-2-ethyl-3-(4-methoxyphenyl)-4-nitrobutanal- (10d)

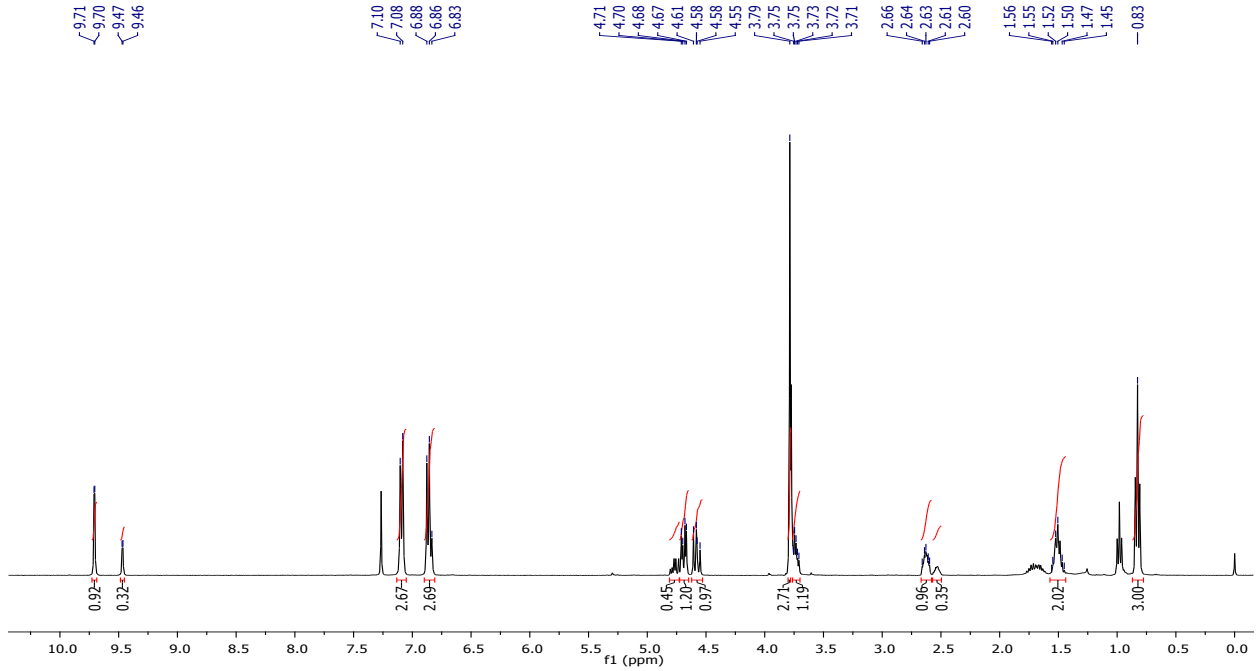


Analytical data for major diastereoisomer were in agreement with the published data.

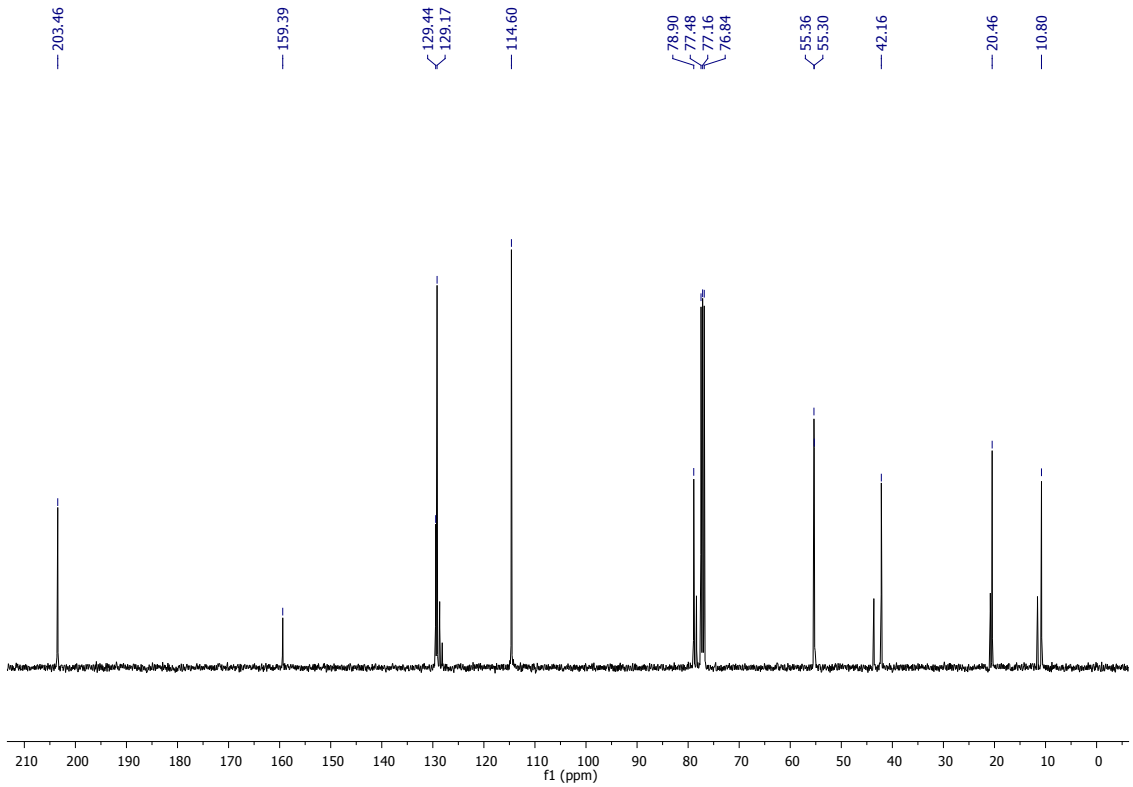
^{1}H NMR (400 MHz,$CDCl_3$, 25°C) δ = 9.71, 9.47 (2xd, *J* = 2.6 Hz, 1H, CHO), 7.09 (d, *J* = 8.6 Hz, 2H, Ph), 6.88- 6.83 (m, 2H, Ph), 4.69 (dd, *J* = 4.9 Hz, 12.5 Hz, 1H, CH_2NO_2), 4.61- 4.55 (m, 1H, CH_2NO_2), 3.79 (s, 3H, OMe), 3.75- 3.71 (m, 1H, CHPh), 2.66-2.60 (m, 1H, CHCHO), 1.56-1.45 (m, 2H, CH_2CH_3), 0.83 (t, *J* = 7.5 Hz, 3H, CH_3) ppm; **^{13}C NMR** (100 MHz, $CDCl_3$, 25°C) δ = 203.5, 159.4, 129.4, 129.2, 114.6, 78.9, 55.4, 55.3, 42.2, 20.5, 10.8 ppm.

$[\alpha]_D^{25}$ = +2.29 (*c* 0.0061 g. mL^{-1}, MeOH); lit. = **$[\alpha]_D^{20}$** = +15.1 (*c* 0.7, $CHCl_3$)

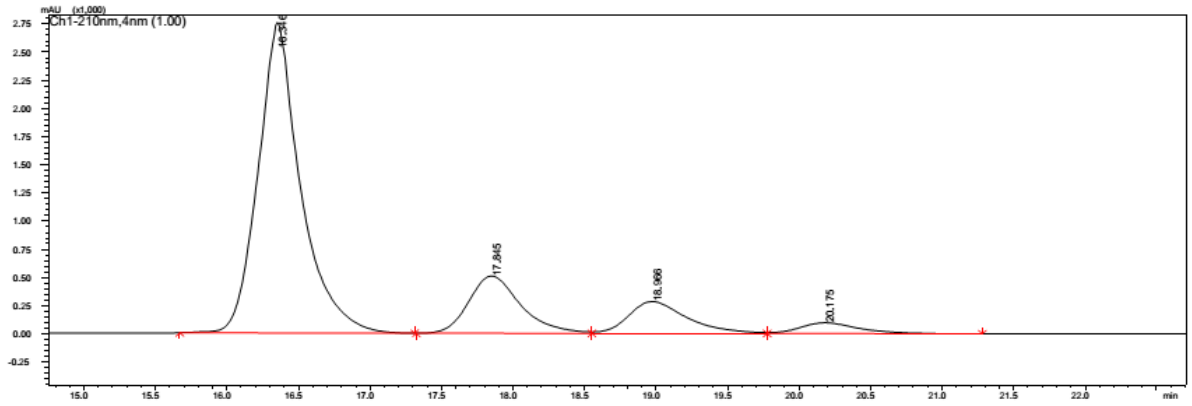
^{1}H NMR



^{13}C NMR



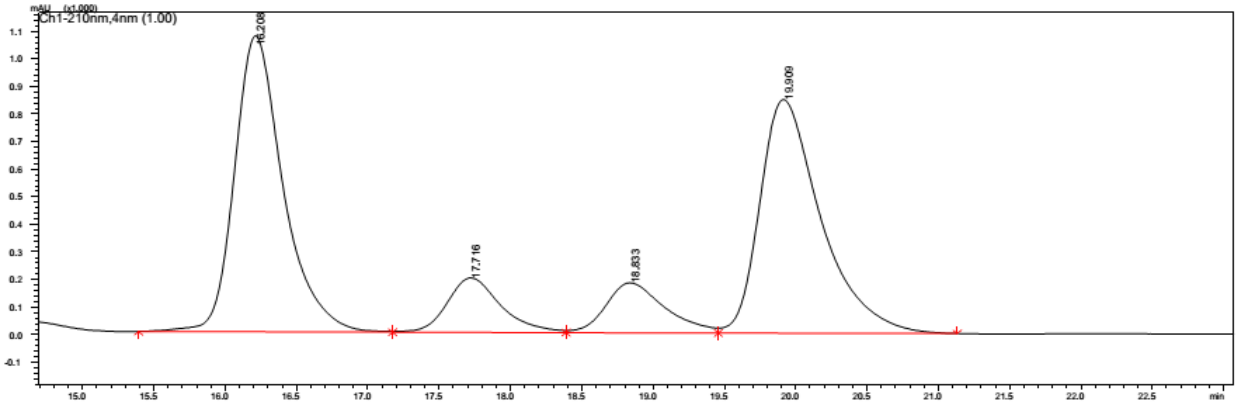
HPLC: Chiracel AD-H column (n-hexane/i-PrOH 95:05, 25ºC) at 0.8 mL/min (91% ee)



PeakTable

PDA Ch1 210nm 4nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	16.346	56792073	2755759	70.590	75.632
2	17.845	12846339	508628	15.968	13.959
3	18.966	8068180	283133	10.028	7.771
4	20.175	2746272	96107	3.414	2.638
Total		80452864	3643626	100.000	100.000

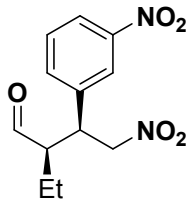


PeakTable

PDA Ch1 210nm 4nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	16.208	25562652	1074881	41.739	46.707
2	17.716	5176706	197838	8.453	8.597
3	18.833	5204060	181030	8.497	7.866
4	19.909	25301159	847583	41.312	36.830
Total		61244577	2301332	100.000	100.000

(2R,3S)-2-ethyl-4-nitro-3-(3-nitrophenyl)butanal-(10e)

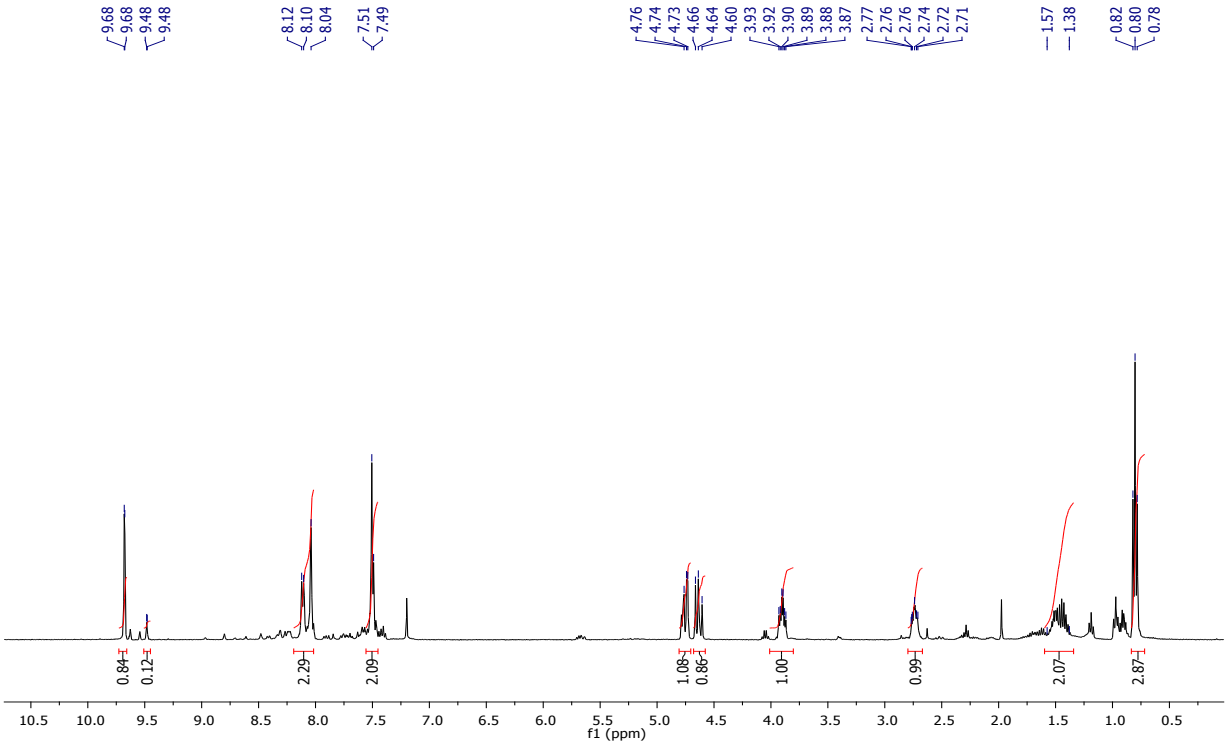


Analytical data for major diastereoisomer were in agreement with the published data

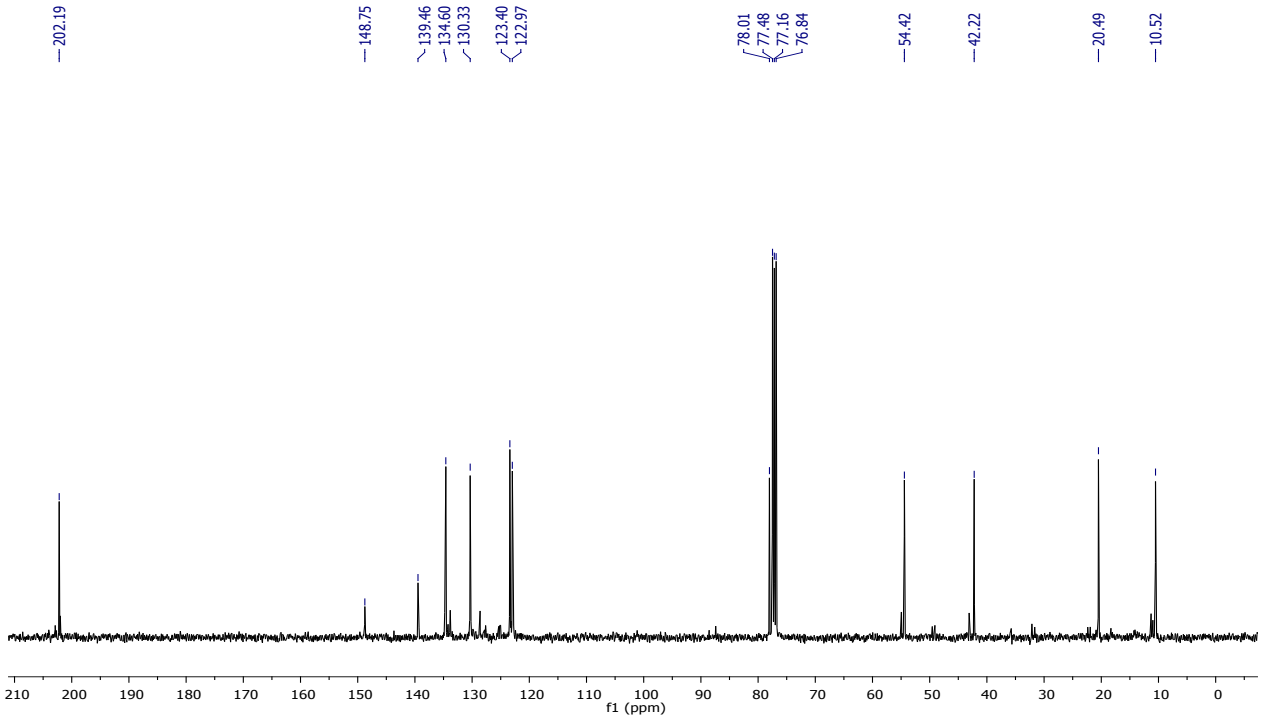
^{1}H NMR (400 MHz,$CDCl_3$, 25°C) δ = 9.68, 9.48 (2xd, *J* = 2.8 Hz, 1H; CHO), 8.12-8.04 (m, 2H; Ph), 7.56-7.47 (m, 2H; Ph), 4.74 (dd, *J* = 4.8 Hz, 12.8 Hz, 1H; CH_2NO_2), 4.63 (dd, *J* = 9.9 Hz, 12.8 Hz, 1H; CH_2NO_2), 3.89 (dt, *J* = 4.8 Hz, 10.0 Hz, 1H; CHPh), 2.77-2.71 (m, 1H; CHCHO), 1.57-1.38 (m, 2H; CH_2CH_3), 0.80 (t, *J* = 7.5 Hz, 3H; CH_3) ppm; **^{13}C NMR** (100 MHz, $CDCl_3$, 25°C) δ = 202.2, 148.8, 139.5, 134.6, 130.3, 123.4, 123.0, 78.0, 54.4, 42.2, 20.5, 10.5 ppm,

$[\alpha]_D^{25}$ = -1.90 (*c* 0.0042 g. mL^{-1}, MeOH); lit. = **$[\alpha]_D^{20}$** = +17.8 (*c* 0.45, $CHCl_3$)

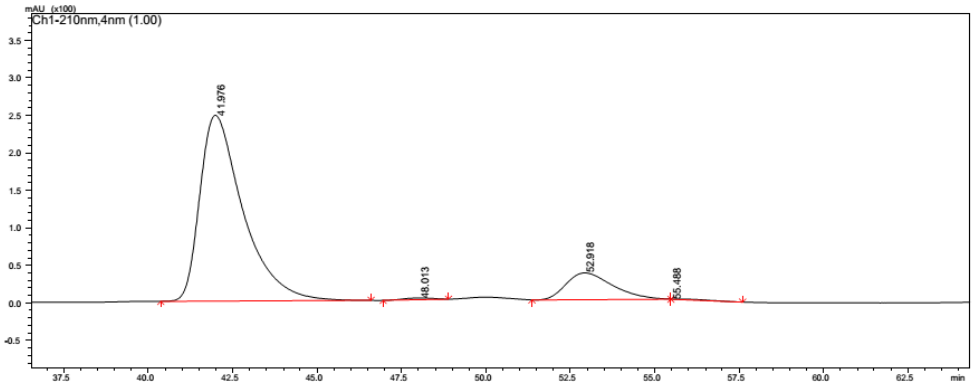
^{1}H NMR



^{13}C NMR



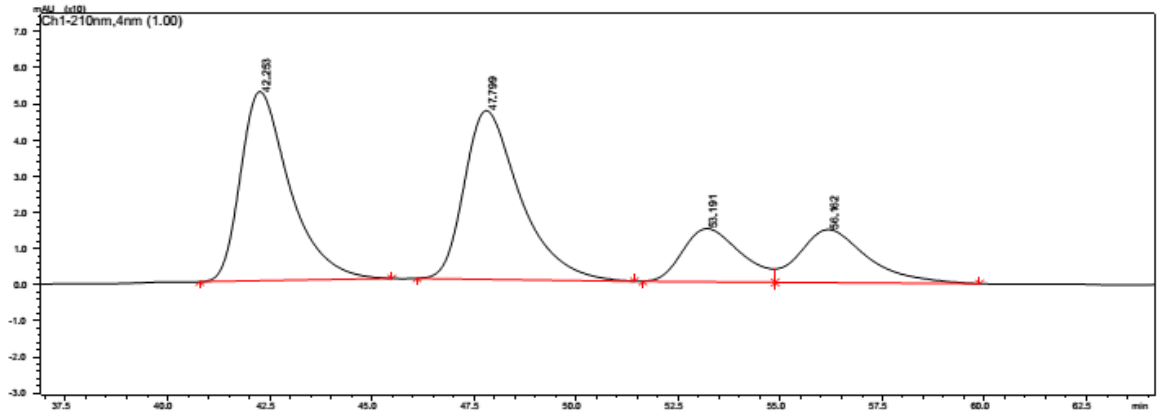
HPLC: Chiracel OD-H column (n-hexane/i-PrOH 90:10, 25ºC) at 1 mL/min (99% ee)



PeakTable

PDA Ch1 210nm 4nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	41.976	22013627	247499	85.838	86.634
2	48.013	130876	2282	0.510	0.799
3	52.918	3431372	35738	13.380	12.510
4	55.488	69770	164	0.272	0.057
Total		25645644	285683	100.000	100.000

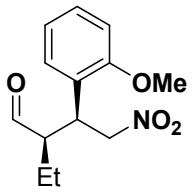


PeakTable

PDA Ch1 210nm 4nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	42.253	4399573	52337	36.607	40.761
2	47.799	4460646	46658	37.116	36.338
3	53.191	1460219	14706	12.150	11.453
4	56.162	1697791	14700	14.127	11.449
Total		12018229	128401	100.000	100.000

(2R,3S)-2-ethyl-3-(2-methoxyphenyl)-4-nitrobutanal- (10f)

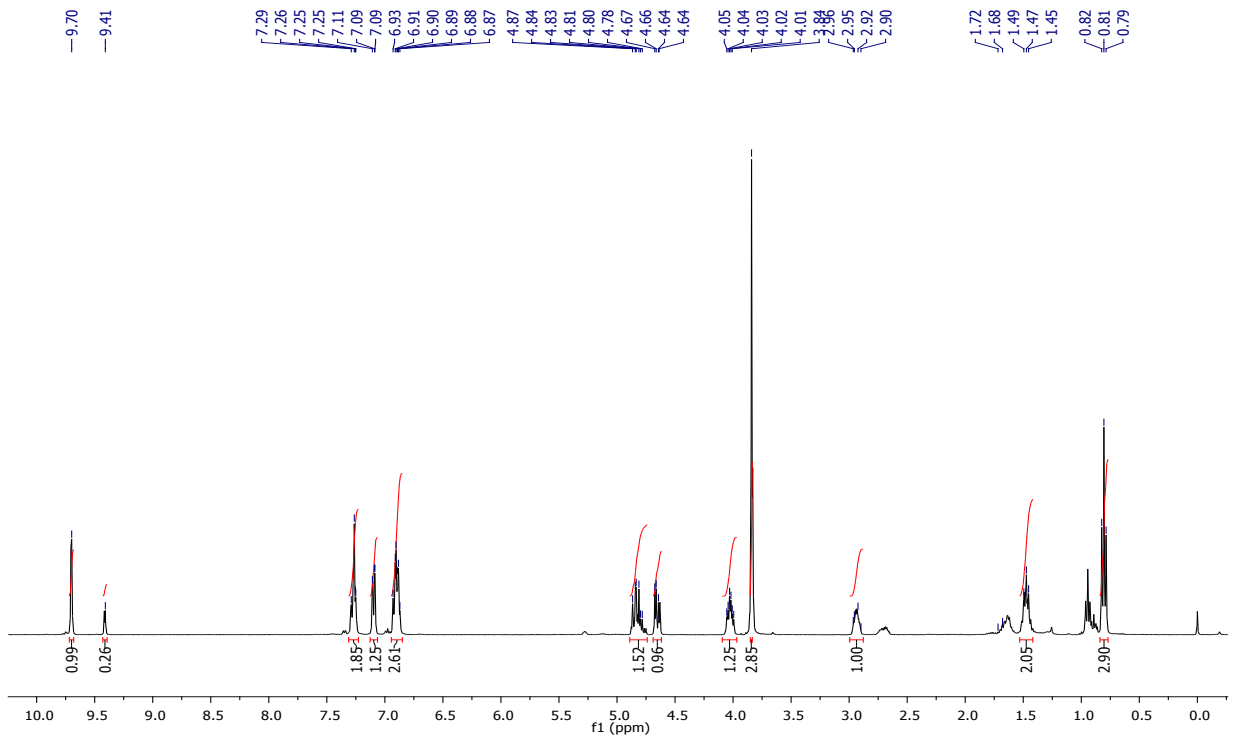


Analytical data for major diastereoisomer were in agreement with the published data.

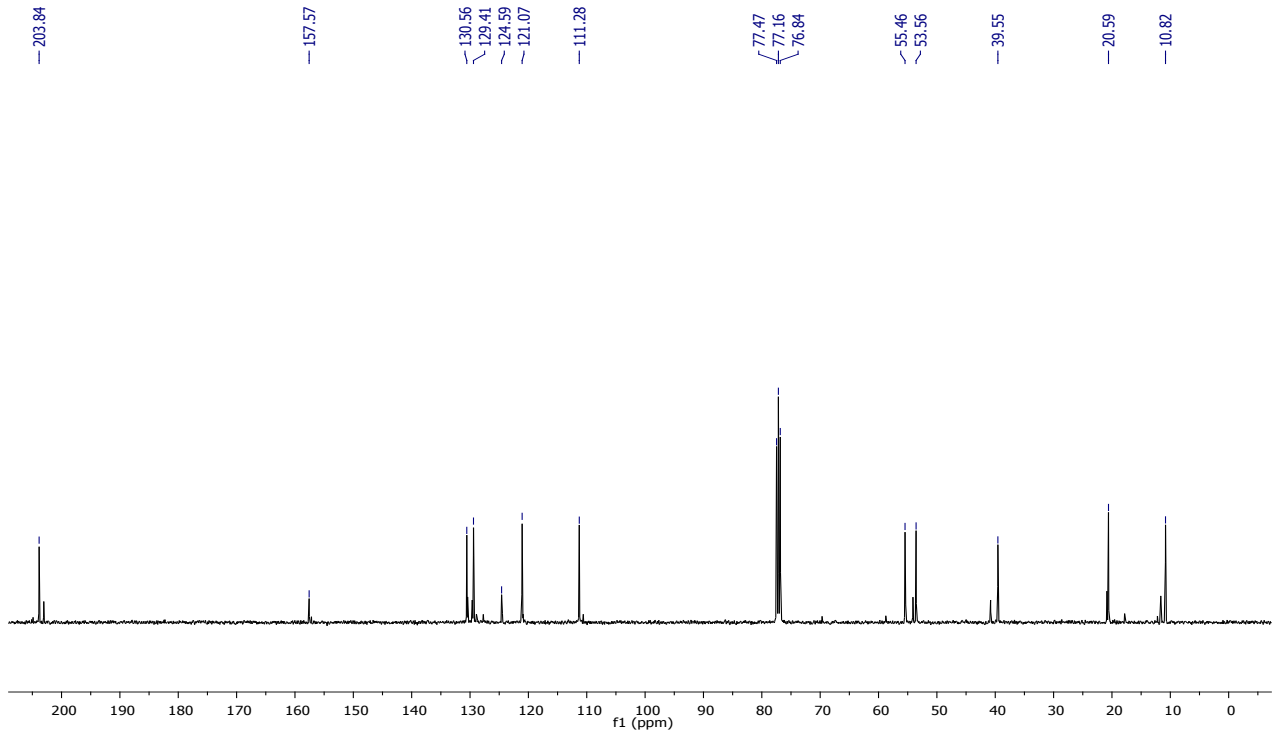
^{1}H NMR (400 MHz,$CDCl_3$, 25°C) δ = 9.70, 9.41 (2xd, *J* = 2.6 Hz, 1H, CHO), 7.29-7.25 (m, 1H, Ph), 7.11-7.09 (m, 1H, Ph), 6.93-6.87 (m, 2H, Ph), 4.87- 4.78 (m, 1H, CH_2NO_2), 4.67-4.64 (m, 1H, CH_2NO_2), 4.05- 3.99 (m, 1H, CHPh), 3.84 (s, 3H, OCH_3Ph), 2.96-2.90 (m, 1H, CHCHO), 1.49-1.45 (m, 2H, CH_2CH_3), 0.81 (t, *J* = 7.5 Hz, CH_3) ppm; **^{13}C NMR** (100 MHz, $CDCl_3$, 25°C) δ = 203.8, 157.6, 130.6, 129.4, 124.6, 121.1, 111.3, 55.5, 53.6, 39.5, 20.6, 10.9 ppm.

$[\alpha]_D^{25}$ = +11.72 (*c* 0.00435 g. mL^{-1}, MeOH)

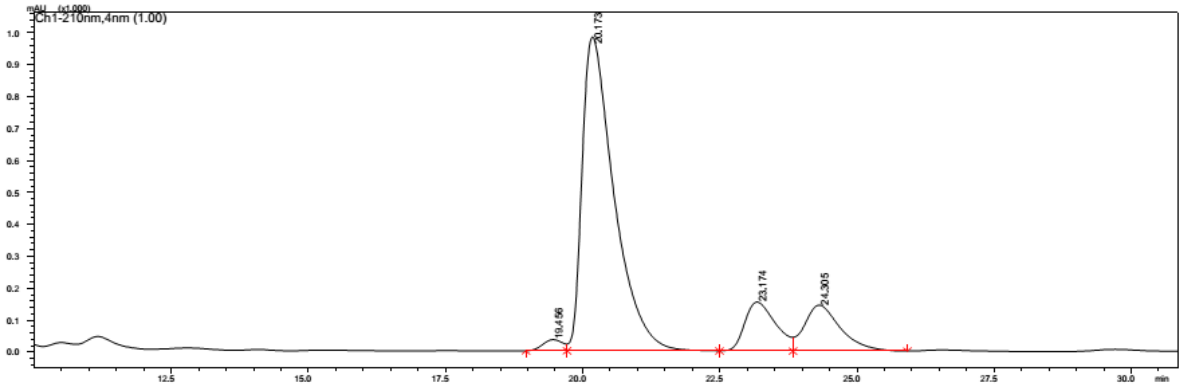
^{1}H NMR



^{13}C NMR



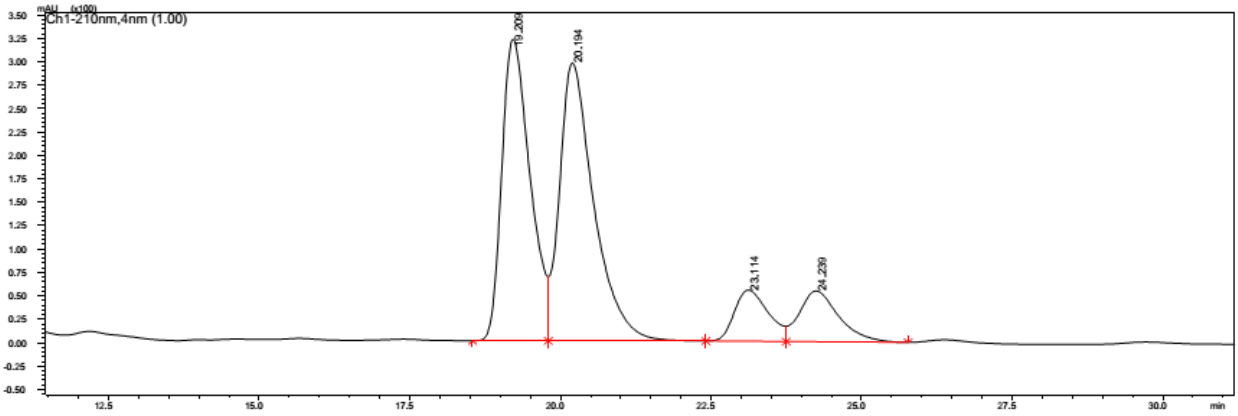
HPLC: Chiracel OD-H column (n-hexane/i-PrOH 95:05, 25ºC) at 1 mL/min (96% ee)



PeakTable

PDA Ch1 210nm 4nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	19.456	885406	34777	1.660	2.645
2	20.173	39884513	983325	74.761	74.776
3	23.174	6006592	153201	11.259	11.650
4	24.305	6572705	143724	12.320	10.929
Total		53349216	1315026	100.000	100.000

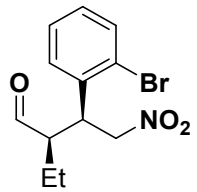


PeakTable

PDA Ch1 210nm 4nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	19.209	10533469	322156	39.152	44.236
2	20.194	11748218	296954	43.667	40.776
3	23.114	2146171	54823	7.977	7.528
4	24.239	2476109	54332	9.204	7.460
Total		26903965	728264	100.000	100.000

(2R,3S)-3-(2-bromophenyl)-2-ethyl-4-nitrobutanal – (10g)

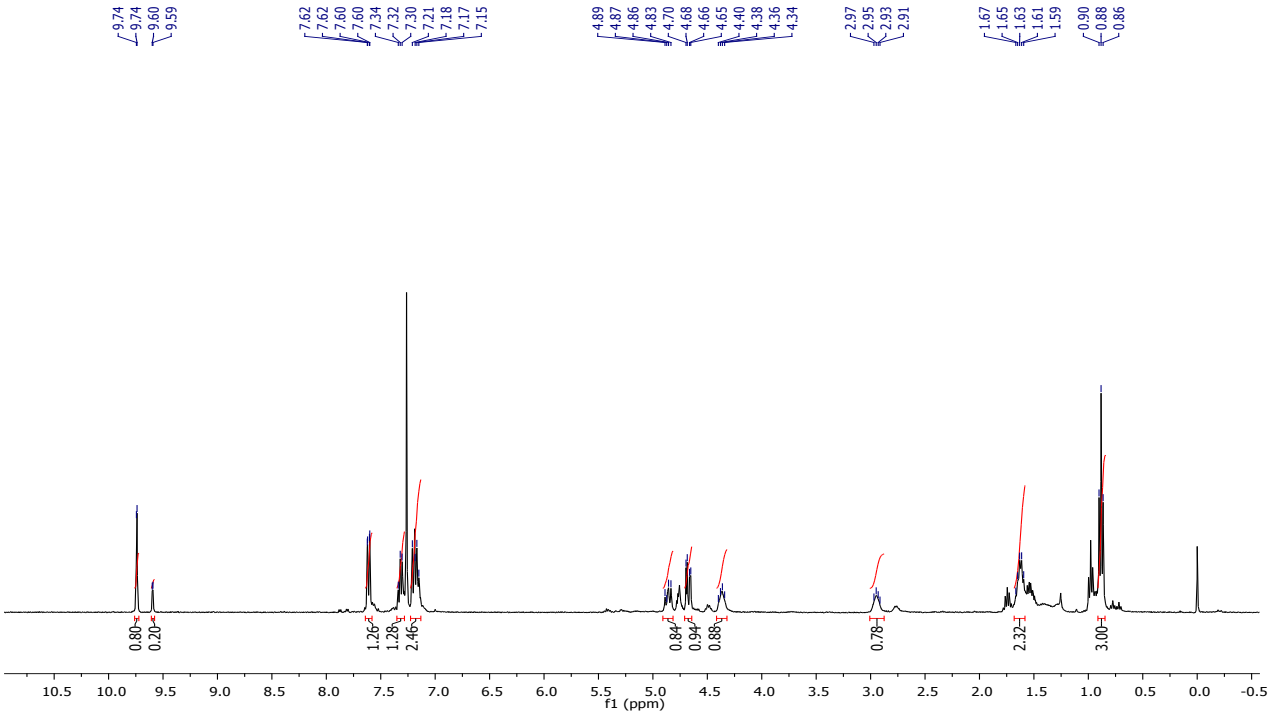


Analytical data for major diastereoisomer were in agreement with the published data.

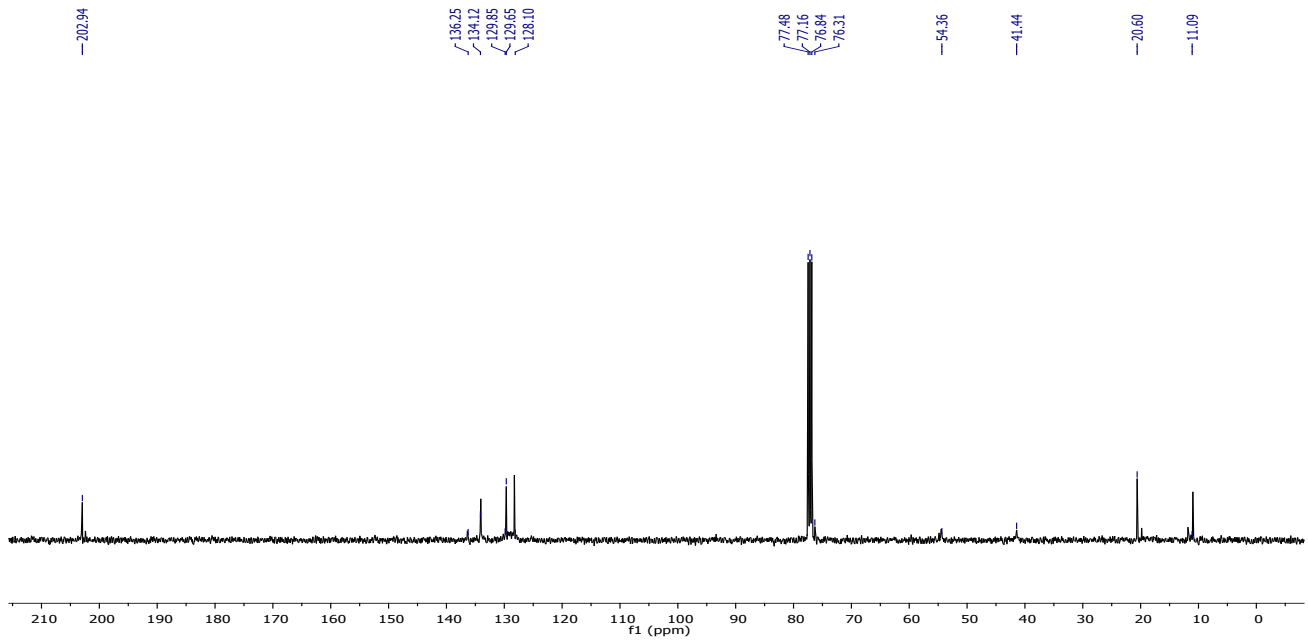
^{1}H NMR (400 MHz,$CDCl_3$, 25°C) δ = 9.74, 9.60 (2xd, *J* = 2.4 Hz, 1H, CHO), 7.61 (dd, *J* = 1.1 Hz, 8 Hz, 1H, Ph), 7.34- 7.30 (m, 1H, Ph), 7.21-7.15 (m, 2H, Ph), 4.89- 4.83 (m, 1H,CH_2NO_2), 4.67 (dd, *J* = 4.6 Hz, 13 Hz, 1H, CH_2NO_2), 4.40- 4.31 (m, 1H, CHPh), 2.97- 2.91 (m, 1H, CHCHO), 1.67- 1.59 (m, 2H, CH_2CH_3), 0.88 (t, *J* = 0.9 Hz, 3H, CH_3) ppm; **^{13}C NMR** (100 MHz, $CDCl_3$, 25°C) δ = 202.9, 136.2, 134.1, 129.8, 129.6, 128.1, 76.3, 54.4, 41.4, 20.6, 11.1 ppm.

$[\alpha]_D^{25}$ = +2.98 (*c* 0.0057 g. mL^{-1}, MeOH)

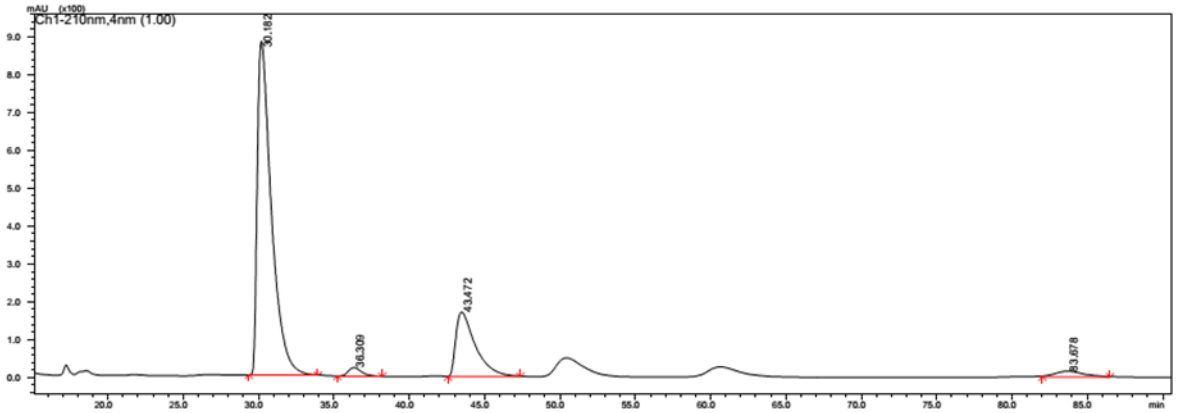
^{1}H NMR



^{13}C NMR



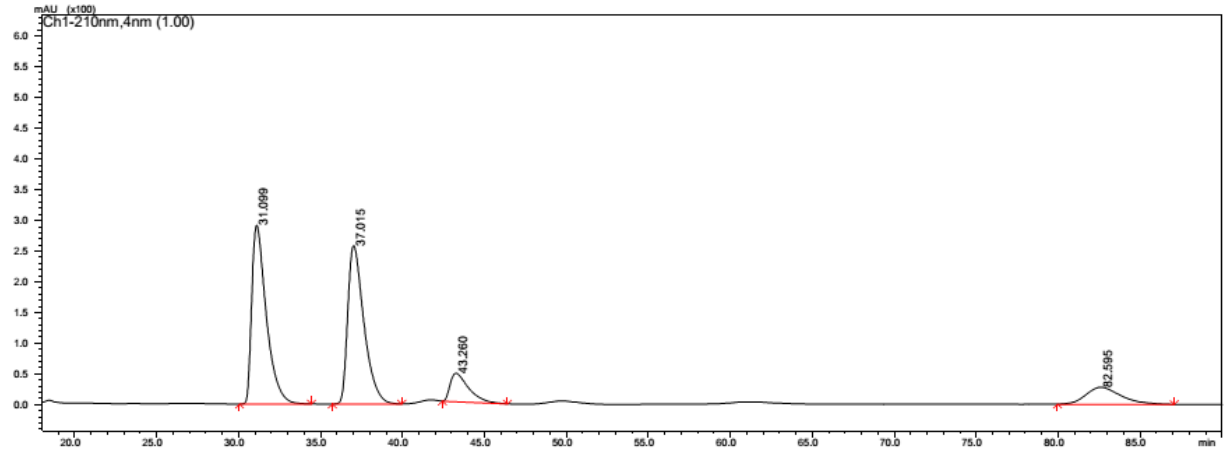
HPLC: Chiracel OD-H column (n-hexane/i-PrOH 95:05, 25ºC) at 1 mL/min (95% ee)



PeakTable

PDA Ch1 210nm 4nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	30.182	57553572	880816	75.266	80.868
2	36.309	1432781	22787	1.874	2.092
3	43.472	15485752	170553	20.252	15.659
4	83.678	1994695	15045	2.609	1.381
Total		76466801	1089201	100.000	100.000

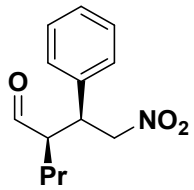


PeakTable

PDA Ch1 210nm 4nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	31.099	18029233	291323	41.452	46.736
2	37.015	17746888	258153	40.803	41.415
3	43.260	3634125	46419	8.356	7.447
4	82.595	4083517	27444	9.389	4.403
Total		43493762	623340	100.000	100.000

(R)-2-((S)-2-nitro-1-phenylethyl)pentanal- (10h)

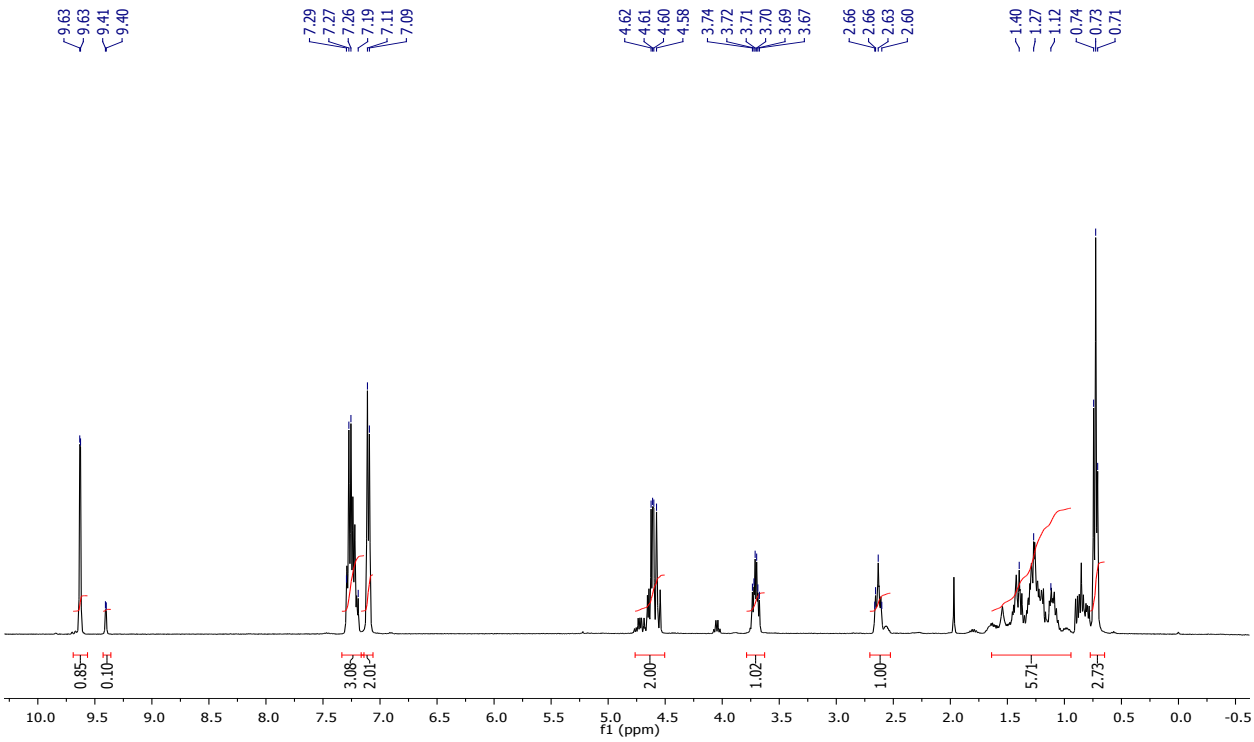


Analytical data for major diastereoisomer were in agreement with the published data

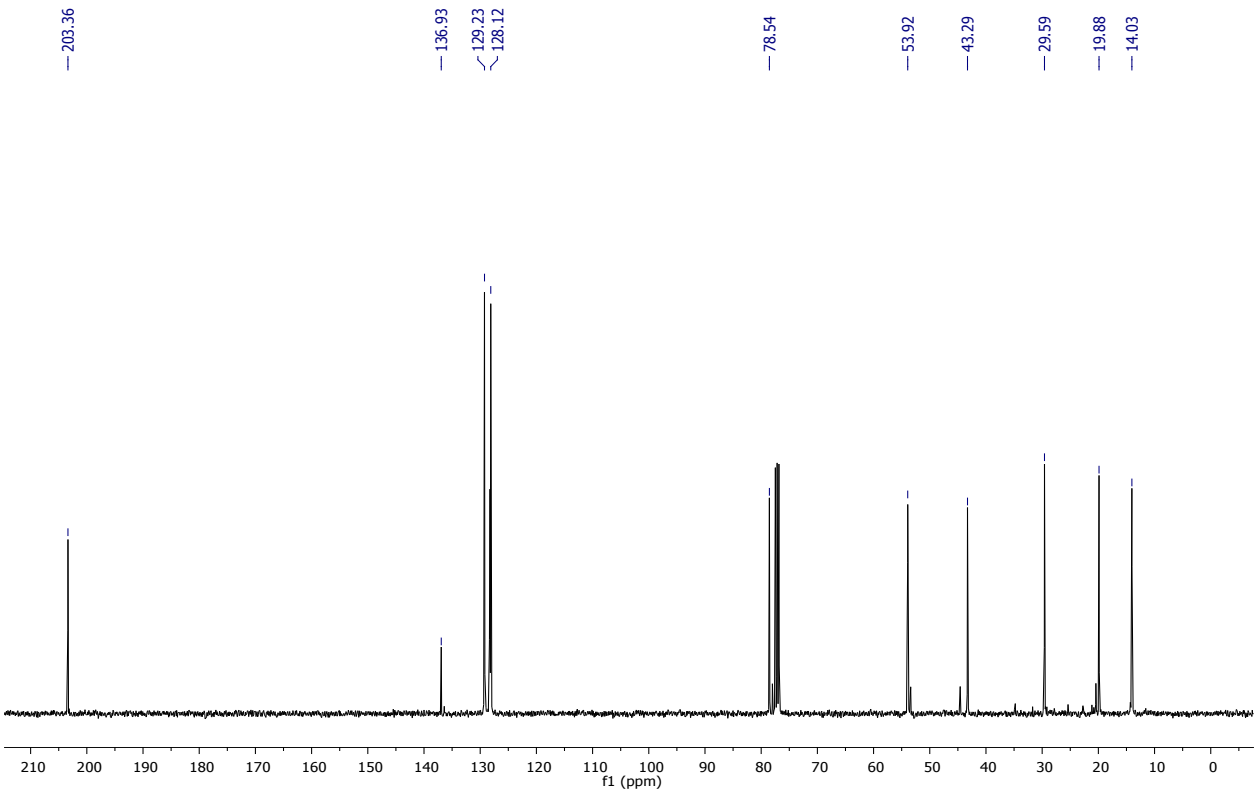
^{1}H NMR (400 MHz,CDCl3, 25°C) δ = 9.63, 9.40 (2xd, *J* = 2.4 Hz, 1H; CHO), 7.29-7.19 (m, 3H; Ph), 7.11- 7.09 (m, 2H; Ph), 4.60 (dd, *J* = 7.4 Hz, 11.7 Hz, 2H; CH_2NO_2), 3.71 (dt, *J* = 4.8 Hz, 10.0 Hz, 1H; CHPh), 2.66-2.60 (m, 1H; CHCHO), 1.58–1.06 (m, 6H; 3xCH_2), 0.73 (t, *J* = 7.5 Hz, 3H; CH_3) ppm;**^{13}C NMR** (100 MHz, $CDCl_3$, 25°C) δ = 203.4, 136.9, 129.2, 128.12, 78.6, 53.9, 43.4, 29.6, 19.8, 14.0 ppm.

[α] $_D^{25}$ = +23.94 (*c* 0.005075 g. mL^{-1}, MeOH); lit.= **[α]** $_D^{25}$ = -24.04 (*c* 8.9, $CHCl_3$)- for the opposite isomer, (2S,3R).

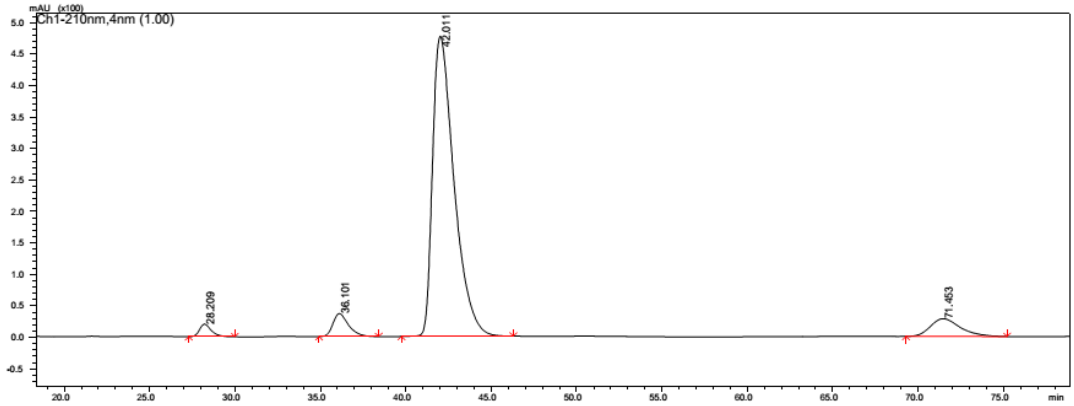
^{1}H NMR



^{13}C NMR



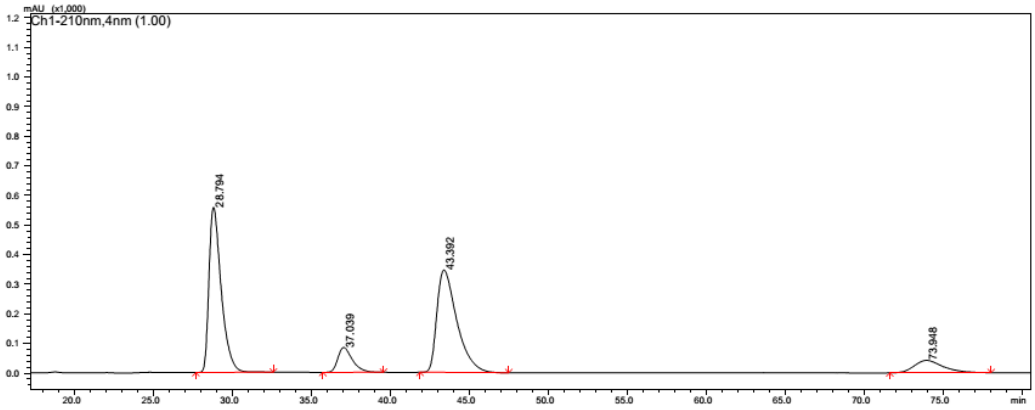
HPLC: Chiracel OD-H column (n-hexane/i-PrOH 95:05, 25ºC) at 1 mL/min (96% ee)



PeakTable

PDA Ch1 210nm 4nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	28.209	959547	19811	1.979	3.530
2	36.101	2313933	36406	4.773	6.488
3	42.011	41771751	476791	86.164	84.968
4	71.453	3434066	28134	7.084	5.014
Total		48479297	561142	100.000	100.000

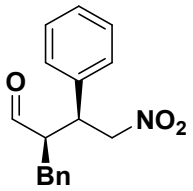


PeakTable

PDA Ch1 210nm 4nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	28.794	30160554	558032	42.287	54.233
2	37.039	5418411	83953	7.597	8.159
3	43.392	30467988	345598	42.718	33.587
4	73.948	5276000	41371	7.397	4.021
Total		71322953	1028955	100.000	100.000

(2R,3S)-2-benzyl-4-nitro-3-phenylbutanal-(10i)

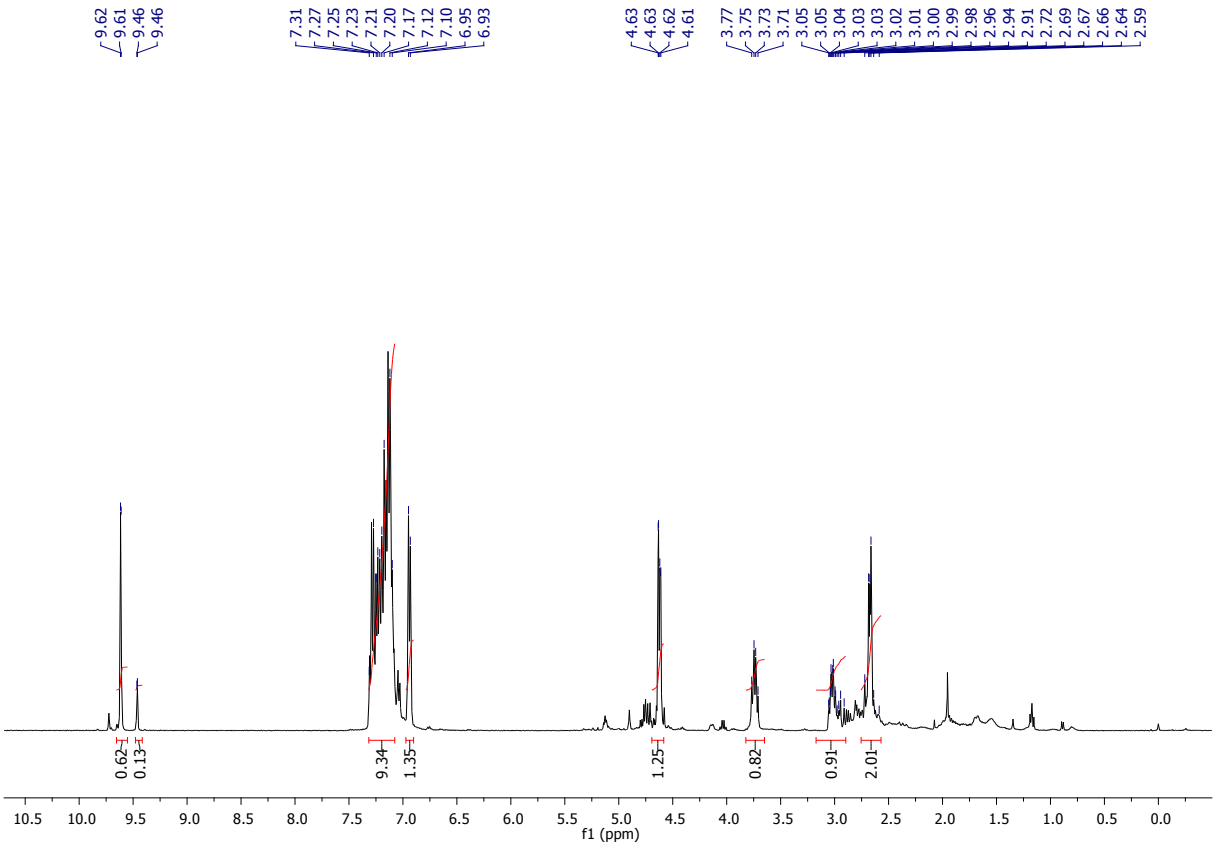


Analytical data for major diastereoisomer were in agreement with the published data

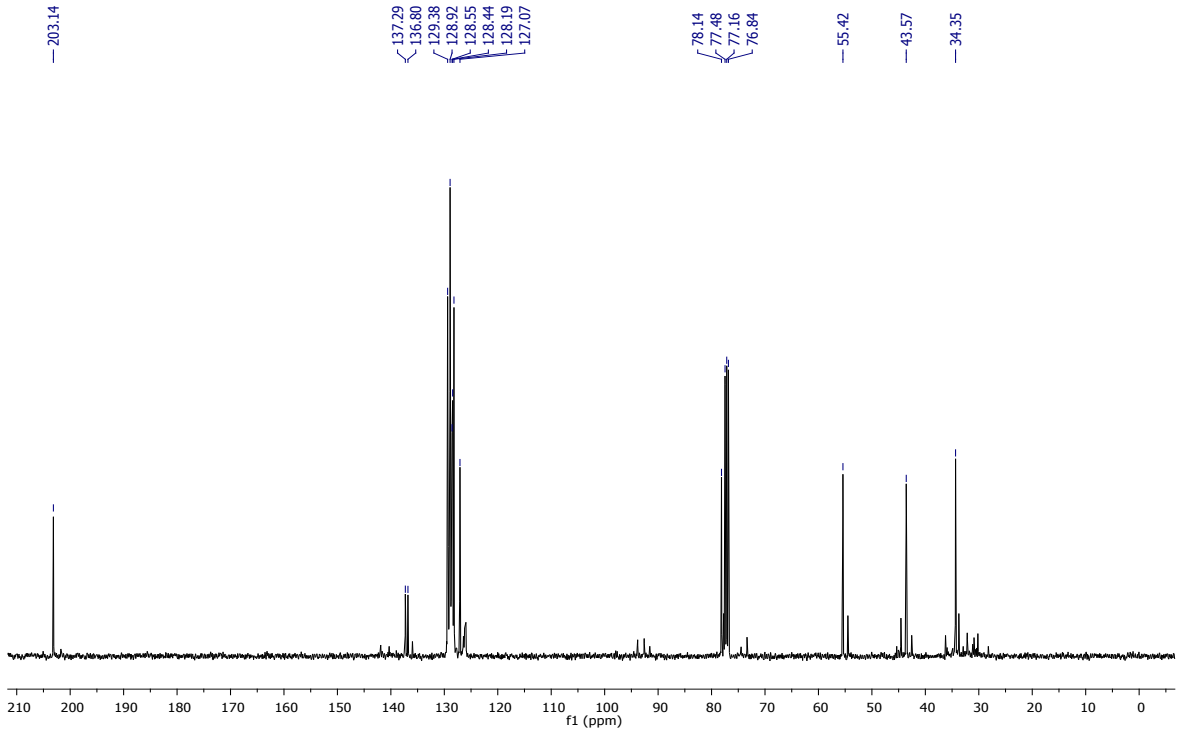
^{1}H NMR (400 MHz,$CDCl_3$, 25°C) δ = 9.61, 9.46 (2xd, *J* = 2.3 Hz, 1H; CHO), 7.31-7.10 (m, 9H; Ph), 6.93-6.95 (m, 1H; Ph), 4.62 (dd, *J* = 2.6 Hz, 7.3 Hz, 2H; CH_2NO_2), 3.77- 3.71 (m, 1H; CHPh), 3.05- 2.91 (m, 1H); 2.79-2.59 (m, 2H) ppm; **^{13}C NMR** (100 MHz, $CDCl_3$, 25°C) δ = 203.1, 137.3, 136.8, 129.4, 128.9, 128.6, 128.4, 128.2, 127.1, 78.4, 55.4, 43.6, 34.4 ppm.

$[\alpha]_D^{25}$ = -8.80 (*c* 0.0042 g. mL^{-1}, MeOH)

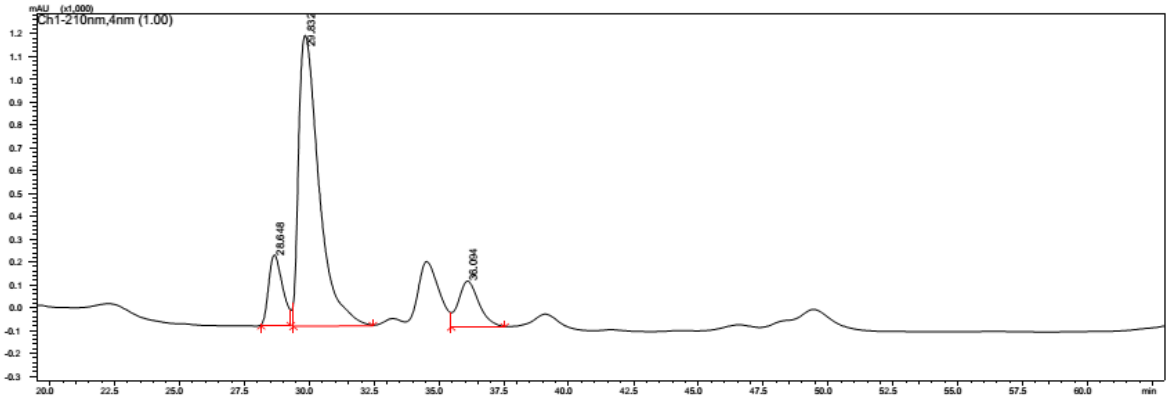
^{1}H NMR


9.62
9.61
9.46
9.46
7.31
7.27
7.25
7.23
7.21
7.20
7.17
7.12
7.10
6.95
6.93
4.63
4.63
4.62
4.61
3.77
3.75
3.73
3.71
3.05
3.05
3.04
3.03
3.03
3.02
3.01
3.00
2.99
2.98
2.96
2.94
2.91
2.72
2.69
2.67
2.66
2.64
2.59
0.62
0.13
9.34
1.35
1.25
0.82
0.91
2.01
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

^{13}C NMR



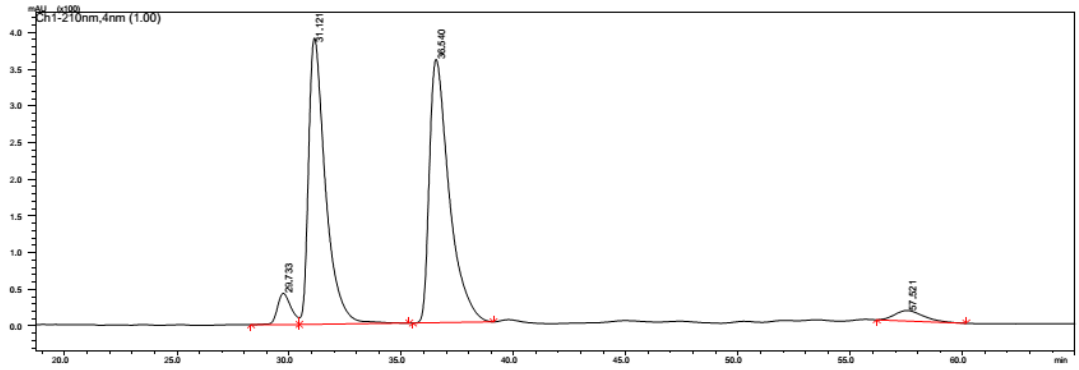
HPLC: Chiracel AD-H column (n-hexane/i-PrOH 99:01, 25ºC) at 1 mL/min (72% ee)



PeakTable

PDA Ch1 210nm 4nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	28.648	11558683	309610	12.532	17.355
2	29.832	69522947	1273340	75.380	71.378
3	36.094	11148613	200988	12.088	11.267
Total		92230243	1783939	100.000	100.000

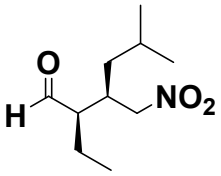


PeakTable

PDA Ch1 210nm 4nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	29.733	1786881	42339	3.920	5.259
2	31.121	20463196	389848	44.893	48.427
3	36.540	22079447	358784	48.438	44.569
4	57.521	1253110	14044	2.749	1.745
Total		45582633	805016	100.000	100.000

(2R,3R)-2-ethyl-5-methyl-3-(nitromethyl)hexanal- (10j)

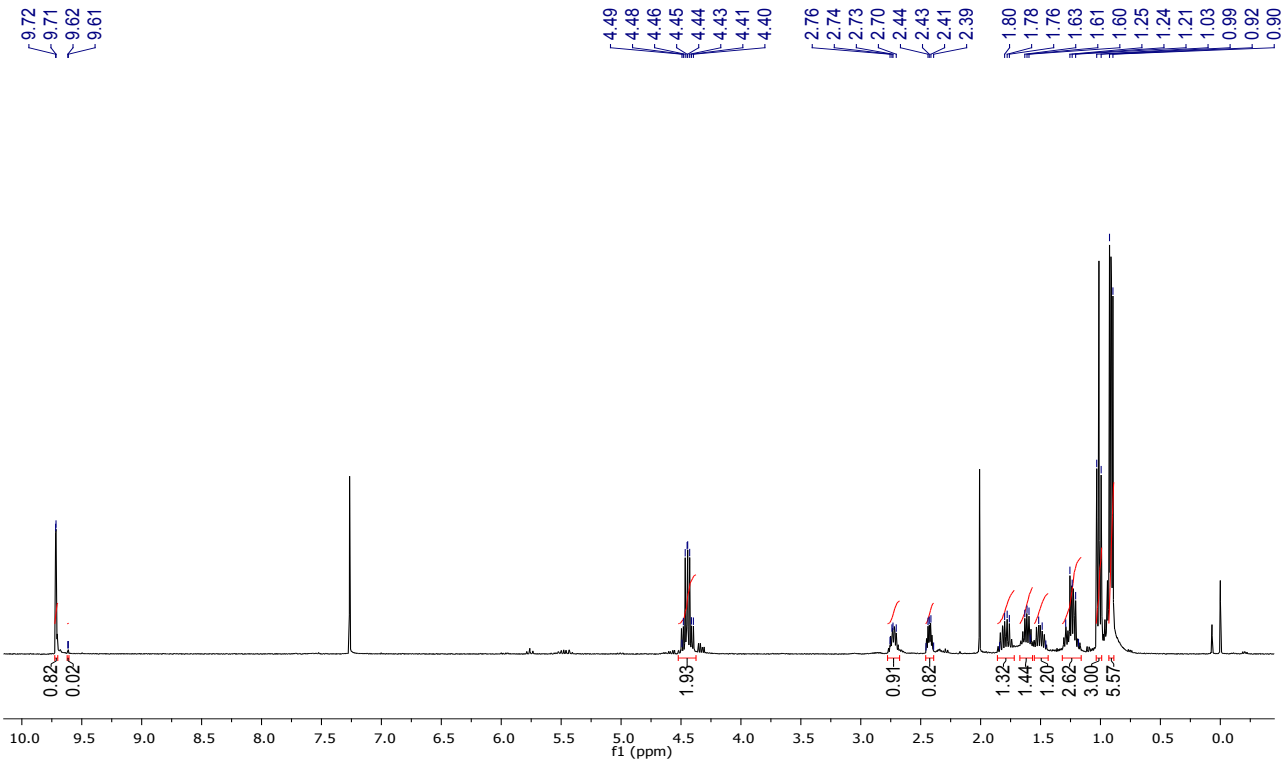


Analytical data for major diastereoisomer were in agreement with the published data

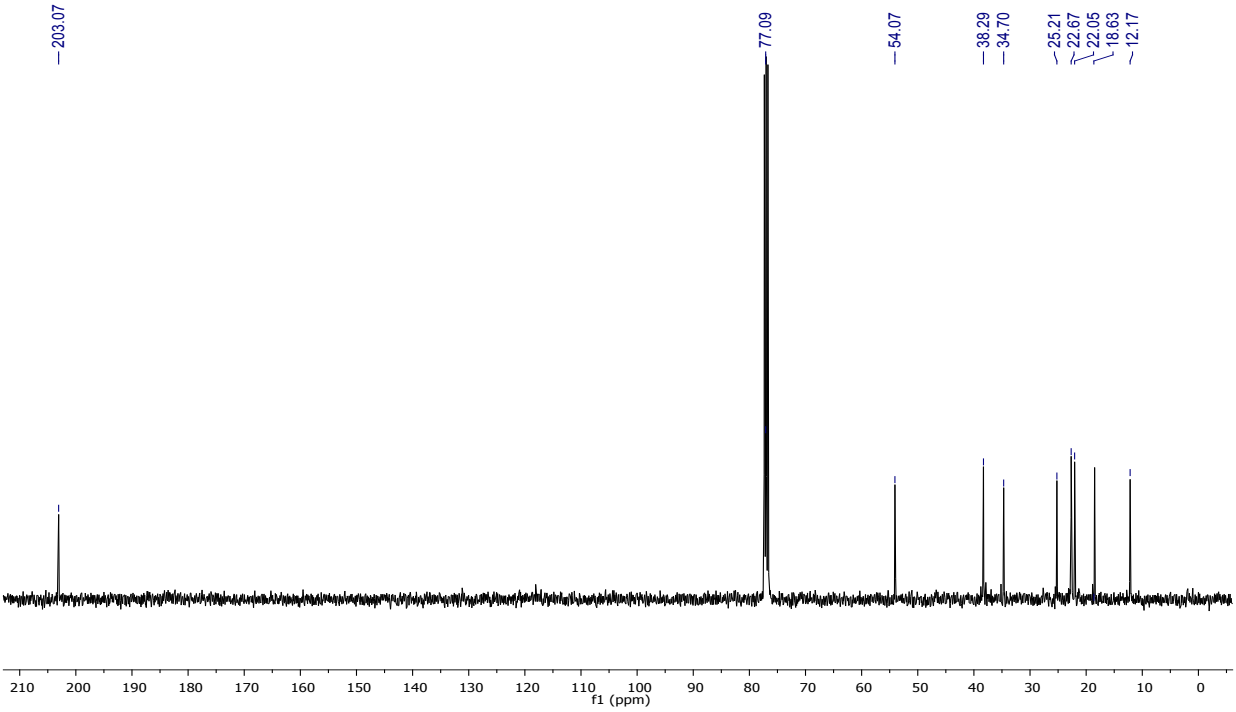
^{1}H NMR (400 MHz,$CDCl_3$, 25°C) δ = ppm; **^{13}C NMR** (100 MHz, $CDCl_3$, 25°C) δ = 9.72, 9.61 (2xd, *J* = 1.8 Hz, 1H; CHO), 4.49- 4.40 (m, 2H, CH_2NO_2), 2.76- 2.70 (m, 1H; CH_2CH_3), 2.46- 2.33 (m, 1H, CH_2CH_3), 1.84- 1.76 (m, 1H, CHCHO), 1.63- 1.52 (m, 1H, $CH(CH_3)_2$), 1.52- 1.46 (m, 1H, $CHCH_2CH(CH_3)_2$), 1.29- 1.18 (m, 2H, $CH_2CH(CH_3)_2$), 1.03- 0.99 (m, 3H, CH_3), 0.92- 0.90 (m, 3H, CH_3) ppm; **^{13}C NMR** (100 MHz, $CDCl_3$, 25°C) δ = 203.1, 77.1, 54.1, 38.3, 34.7, 25.2, 22.7, 22.1, 18.6, 12.2 ppm.

$[\alpha]_D^{25}$ = -9.37 (*c* 0.0061 g. mL^{-1}, MeOH)

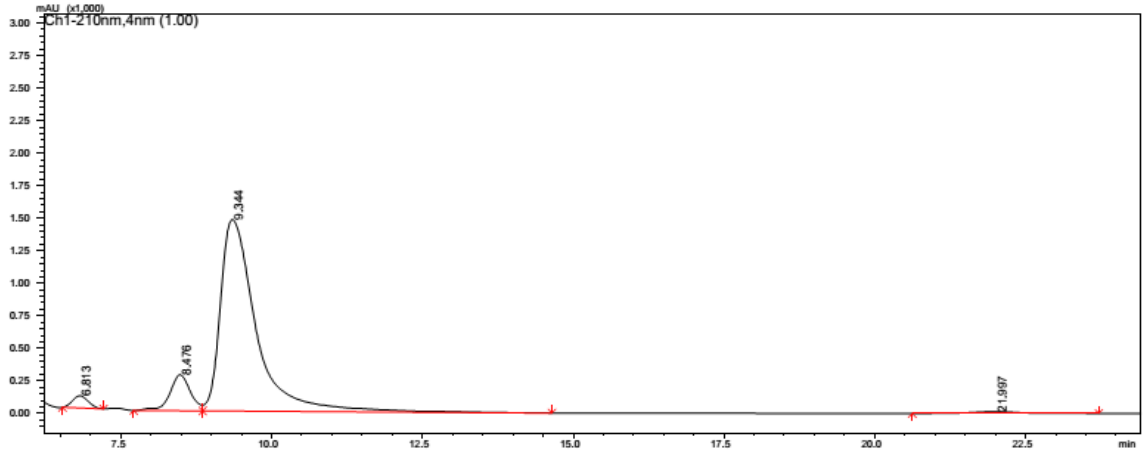
^{1}H NMR



^{13}C NMR



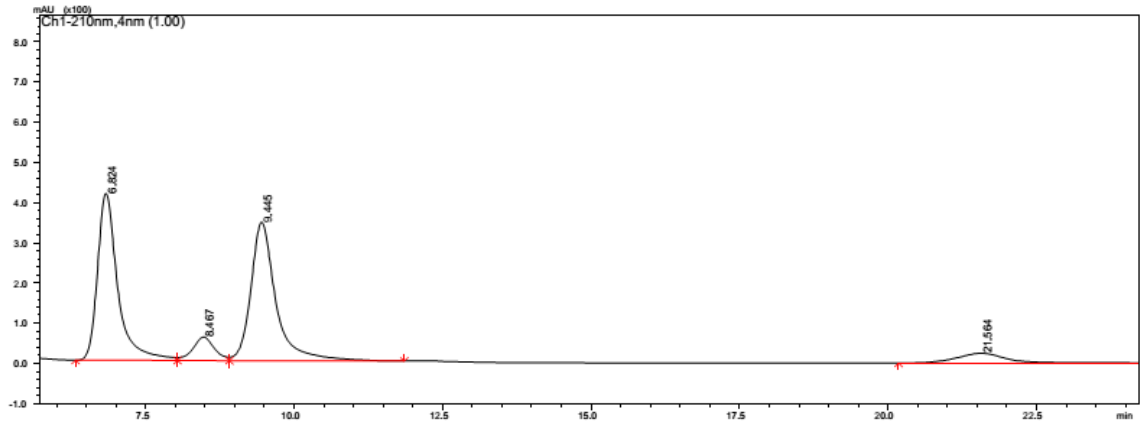
HPLC: Chiracel IC column (n-hexane/i-PrOH 90:10, 25ºC) at 0.2 mL/min (95% ee)



PeakTable

PDA Ch1 210nm 4nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	6.813	1699149	93660	2.438	5.050
2	8.476	6562659	276559	9.417	14.913
3	9.344	60731553	1471959	87.142	79.372
4	21.997	698936	12337	1.003	0.665
Total		69692296	1854515	100.000	100.000

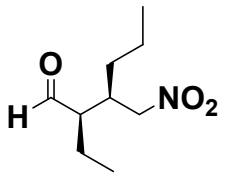


PeakTable

PDA Ch1 210nm 4nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	6.824	9875113	415746	43.075	49.280
2	8.467	1472253	58532	6.422	6.938
3	9.445	10167574	344987	44.351	40.893
4	21.564	1410484	24372	6.152	2.889
Total		22925424	843638	100.000	100.000

(2R,3R)-2-ethyl-3-(nitromethyl)hexanal –(10k)

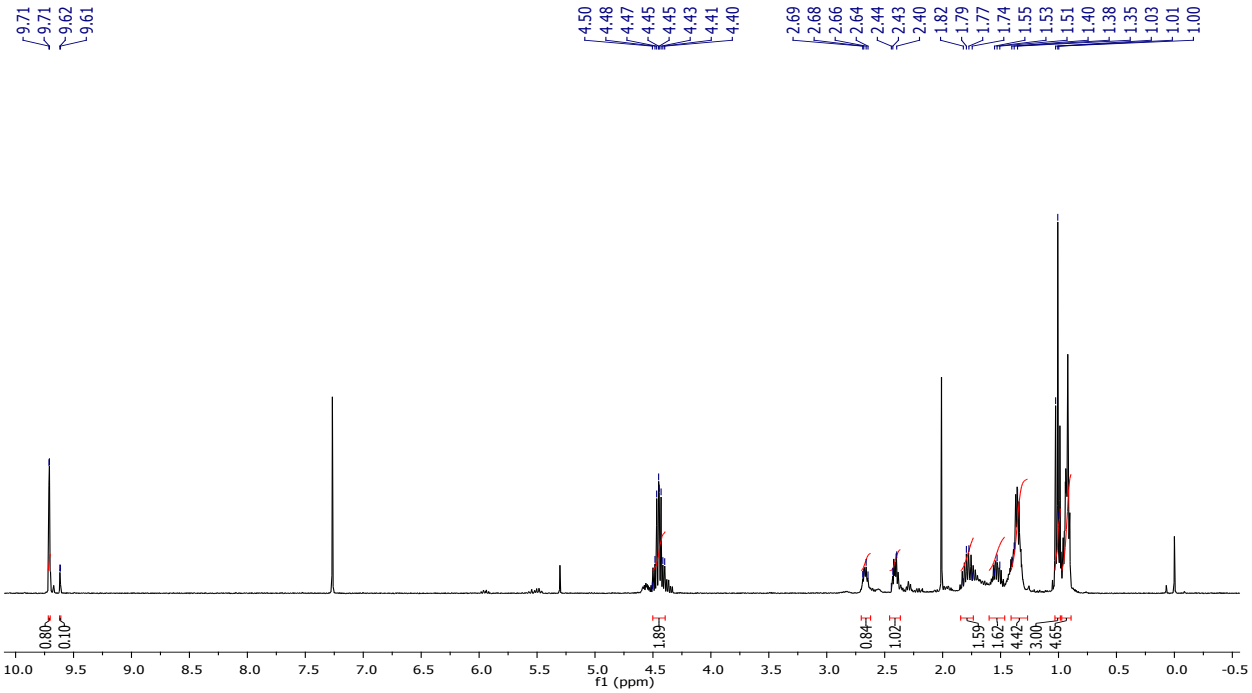


Analytical data for major diastereoisomer were in agreement with the published data

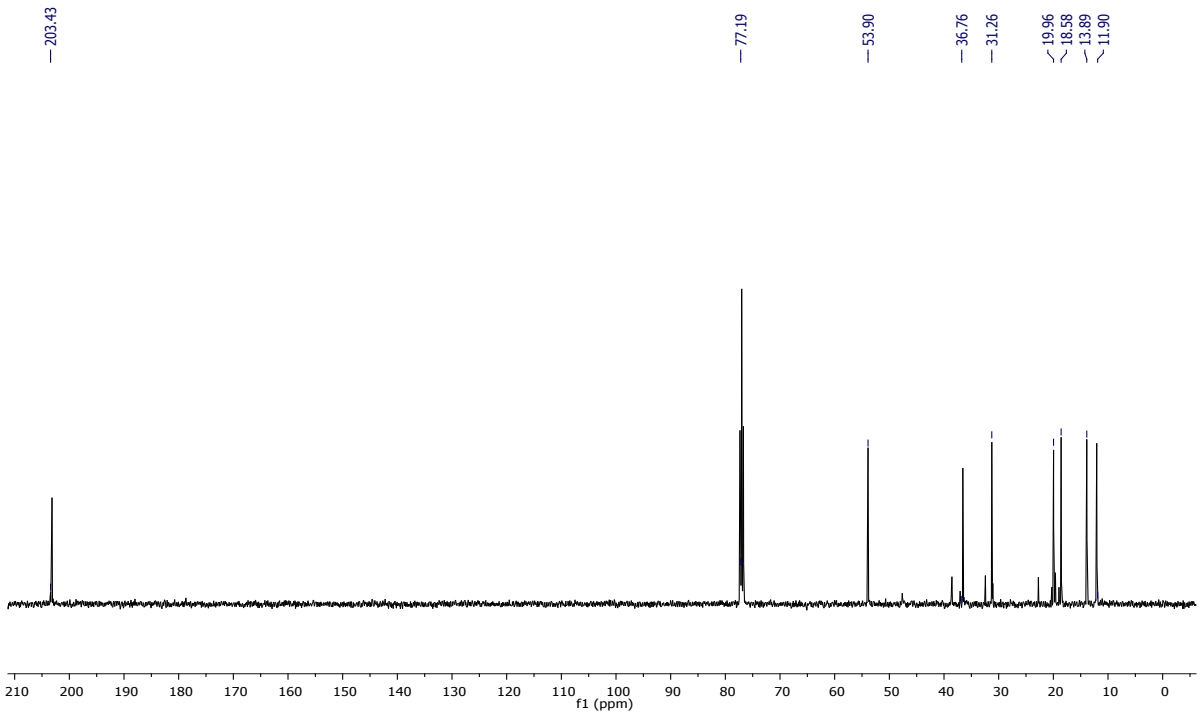
^{1}H NMR (400 MHz,$CDCl_3$, 25°C) δ = 9.71, 9.62 (2xd, *J* = 1.7 Hz, 1H; CHO), 4.45 (qd, *J* = 6.6 Hz, 12.5 Hz, 2H, CH_2NO_2), 2.69- 2.64 (m, 1H; CH_2CH_3), 2.44- 2.40 (m, 1H, CH_2CH_3), 1.82- 1.74 (m, 1H, CHCHO), 1.55- 1.51 (m, 1H, $CH(CH_2)_2CH_3$), 1.40- 1.35 (m, 4H, $(CH_2)_2CH_3$), 1.03- 1.00 (m, 3H, CH_3), 0.95- 0.90 (m, 3H, CH_3) ppm; **^{13}C NMR** (100 MHz, $CDCl_3$, 25°C) δ = 200.4, 77.2, 53.9, 36.8, 31.3, 19.9, 18.6, 13.8, 11.9ppm.

$[\alpha]_D^{23}$ = -2.5 (*c* 0.00326 g. mL^{-1}, MeOH)

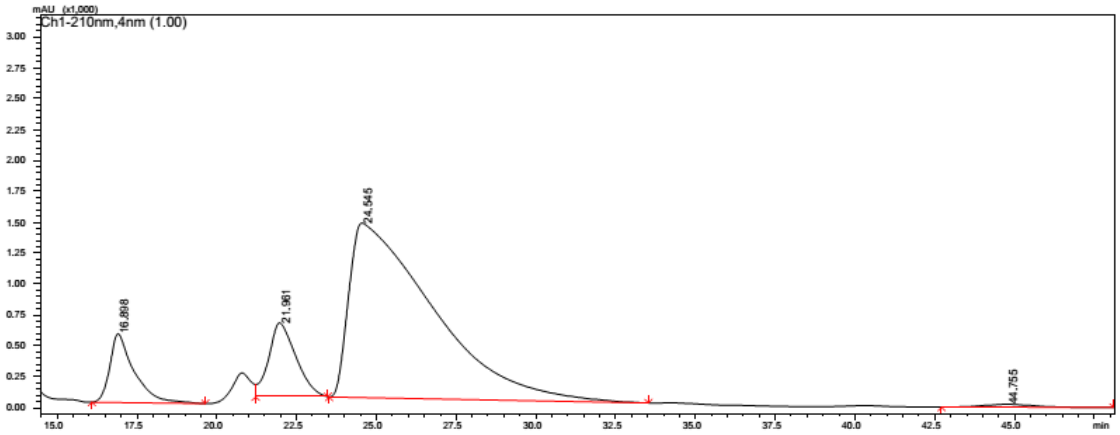
^{1}H NMR



^{13}C NMR



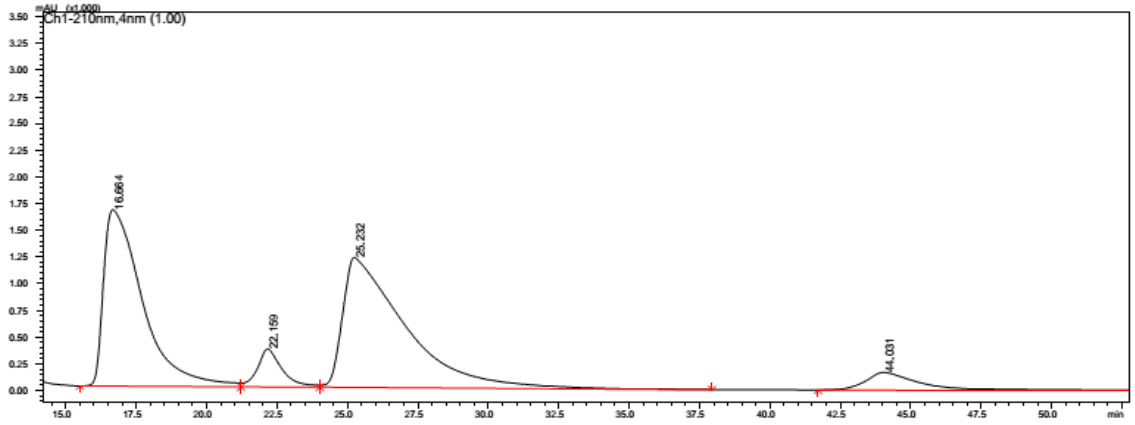
HPLC: Chiracel IC column (n-hexane/i-PrOH 99:01, 25ºC) at 0.2 mL/min (80% ee)



PeakTable

PDA Ch1 210nm 4nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	16.898	29136538	555221	8.961	21.466
2	21.961	35454136	596745	10.904	23.072
3	24.545	258037892	1410406	79.360	54.530
4	44.755	2518747	24103	0.775	0.932
Total		325147314	2586476	100.000	100.000

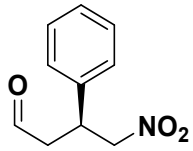


PeakTable

PDA Ch1 210nm 4nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	16.664	158471883	1650229	40.737	48.692
2	22.159	21596703	356055	5.552	10.506
3	25.232	187427692	1217595	48.180	35.927
4	44.031	21520373	165227	5.532	4.875
Total		389016650	3389106	100.000	100.000

(S)-4-nitro-3-phenylbutanal-(10 l)

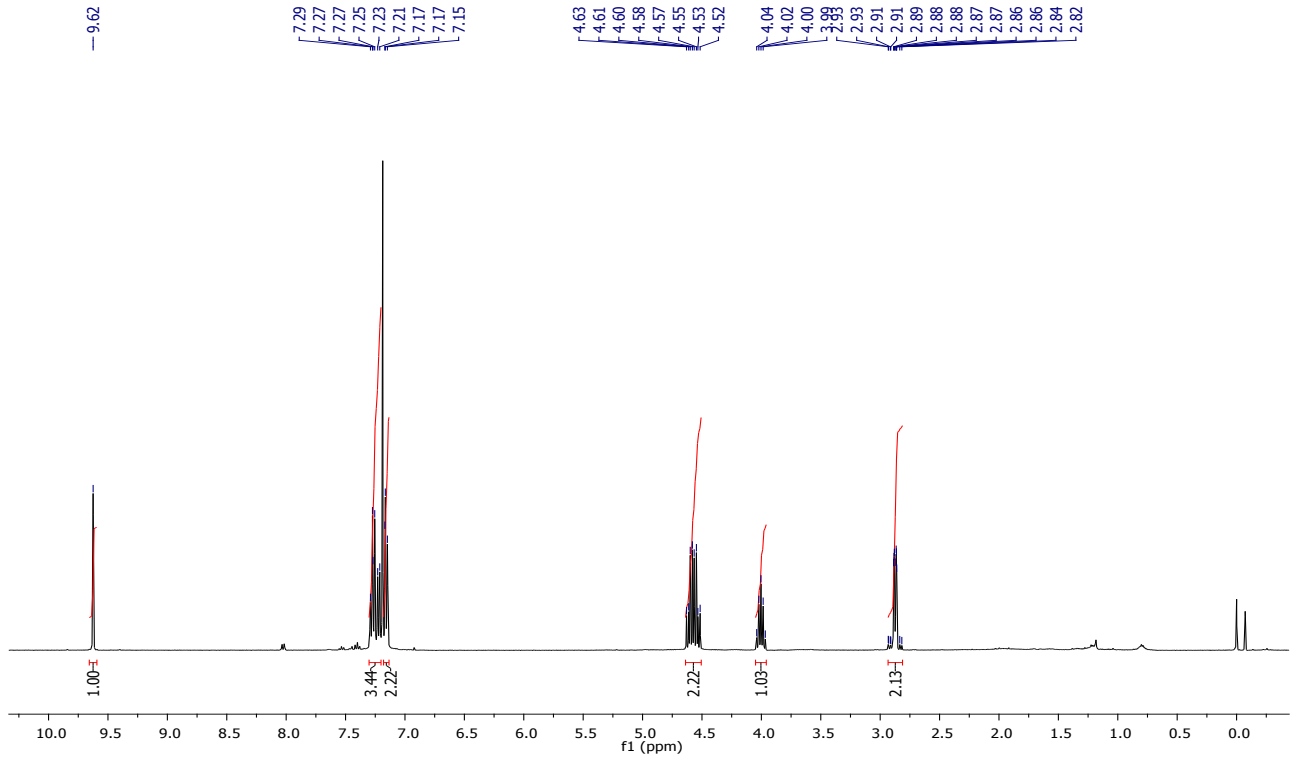


Analytical data for major diastereoisomer were in agreement with the published data.

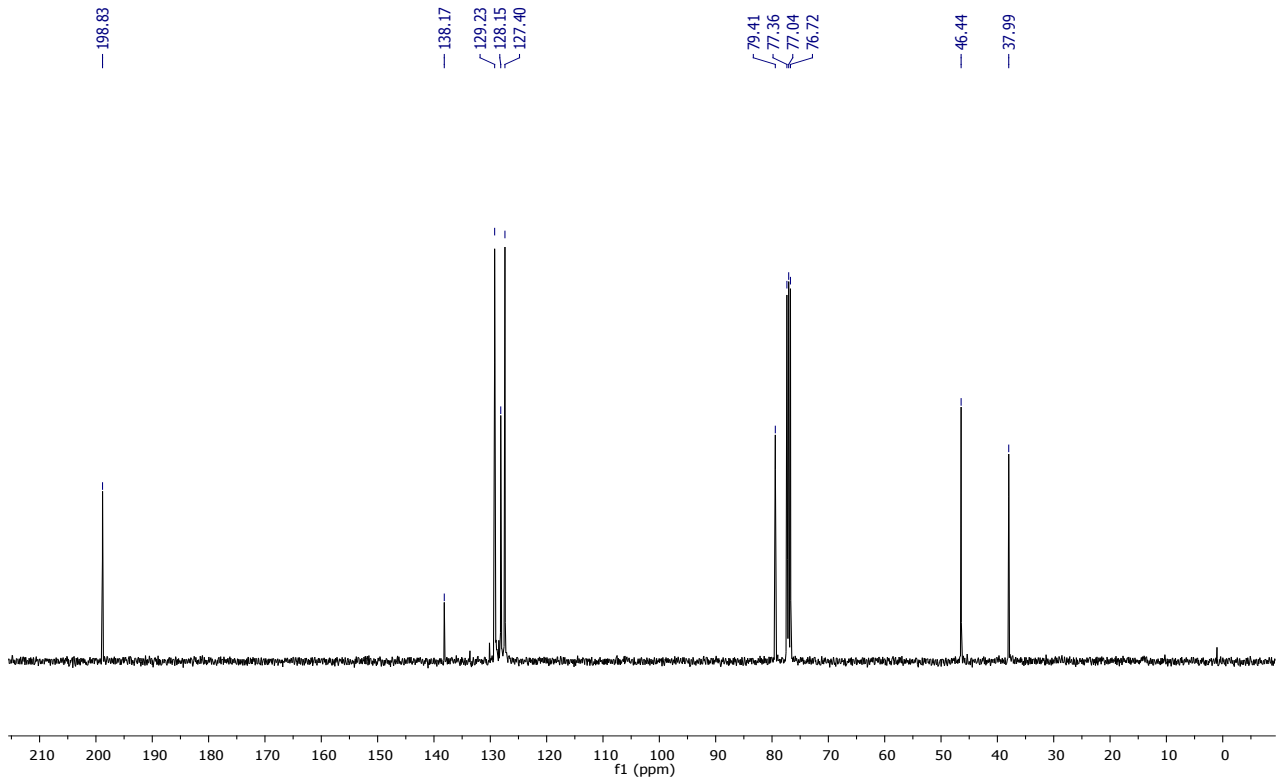
^{1}H NMR (400 MHz, $CDCl_3$, 25°C) δ = 9.62 (s, 1H; CHO), 7.29- 7.21 (m, 3H; Ph), 7.17-7.15 (m, 2H; Ph), 4.57 (qd, *J* = 7.4 Hz, 12.5 Hz; 2H,CH_2NO_2), 4.0 (p, *J* = 7.2 Hz, 1H; CHPh), 2.93-2.82 (m, 2H; CH_2CHO) ppm; **^{13}C NMR** (100 MHz, $CDCl_3$, 25°C) δ = 198.8, 138.2, 129.2, 128.1, 127.4, 79.4, 46.4, 37.9 ppm.

$[\alpha]_D^{25}$ = -0.85 (*c* 0.0047 g. mL^{-1}, MeOH); lit. = **$[\alpha]_D^{24}$** = -8.3 (*c* 1.0, $CHCl_3$)

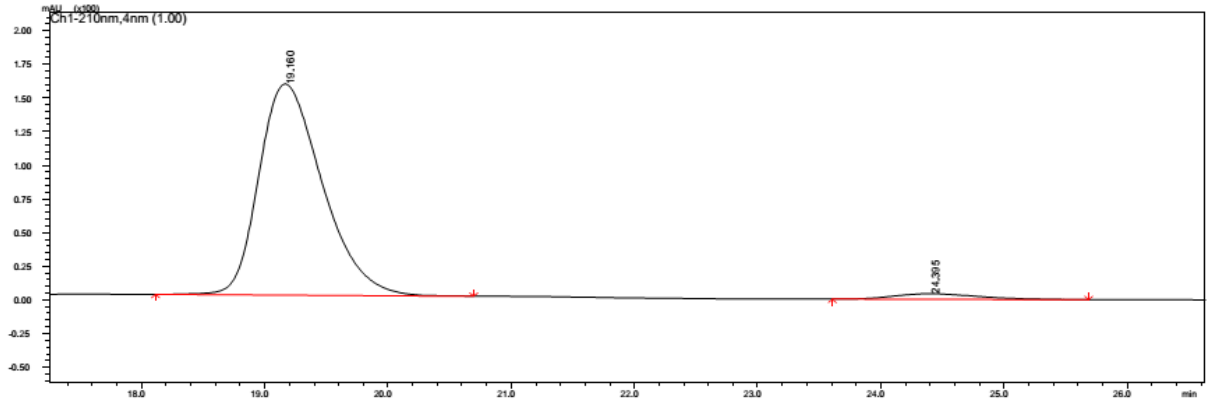
^{1}H NMR



^{13}C NMR



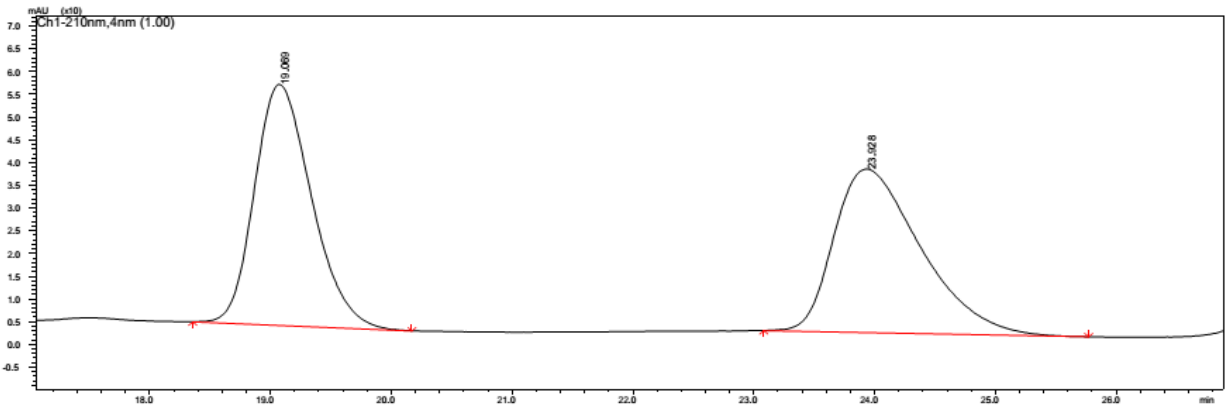
HPLC: Chiracel AS-H column (n-hexane/i-PrOH 70:30, 25ºC) at 1 mL/min (93% ee)



PeakTable

PDA Ch1 210nm 4nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	19.160	5618996	156741	96.598	97.349
2	24.395	197904	4268	3.402	2.651
Total		5816900	161009	100.000	100.000

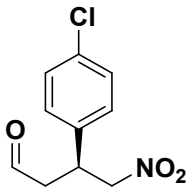


PeakTable

PDA Ch1 210nm 4nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	19.069	1740855	53014	49.243	59.568
2	23.928	1794404	35983	50.757	40.432
Total		3535259	88996	100.000	100.000

(S)-3-(4-chlorophenyl)-4-nitrobutanal-(10m)

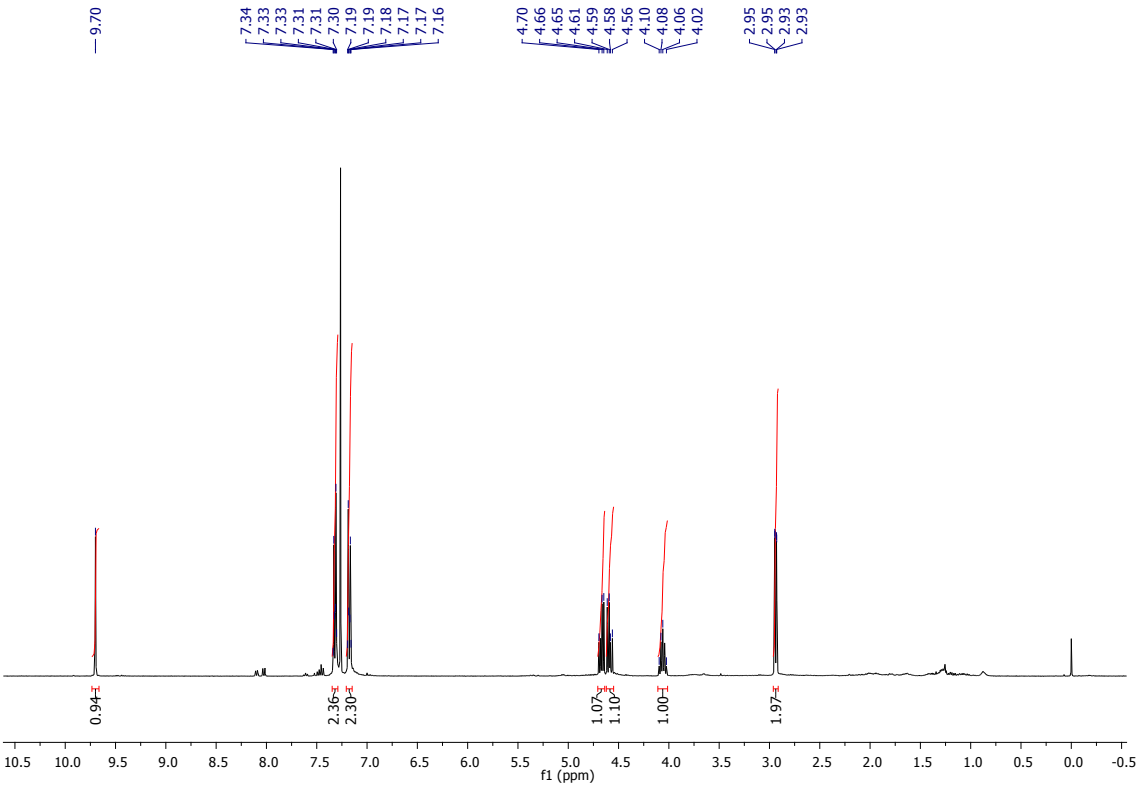


Analytical data for major diastereoisomer were in agreement with the published data.

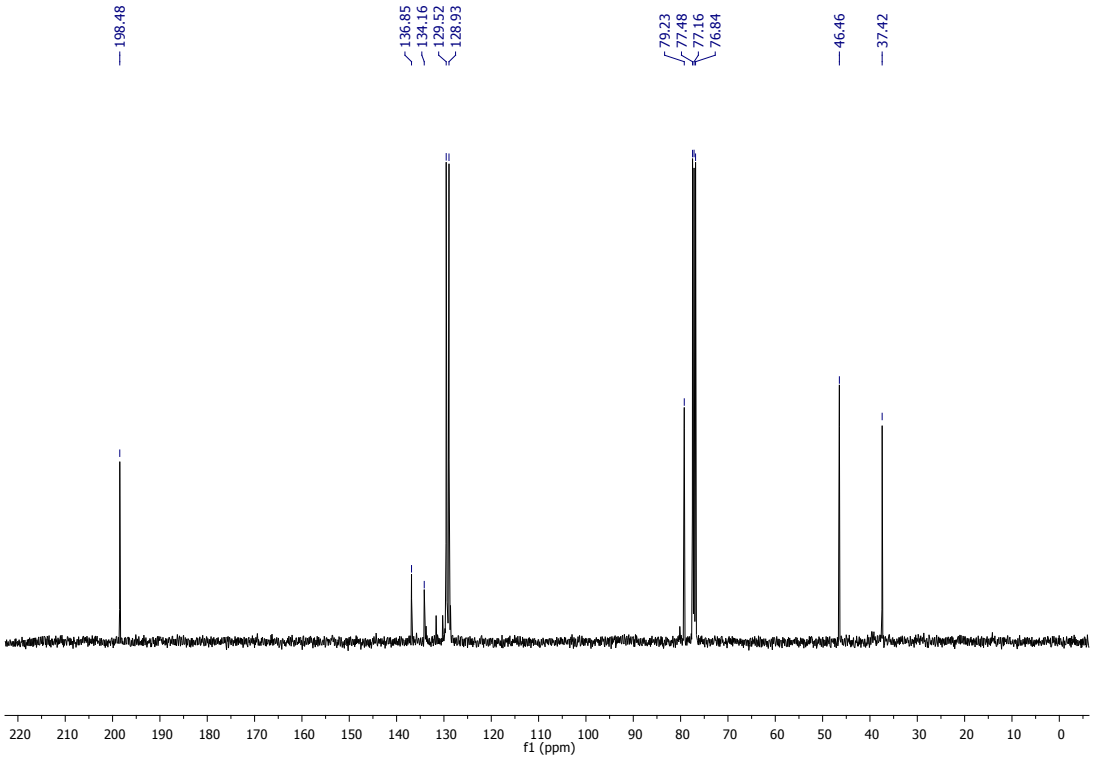
^{1} H NMR (400 MHz,$CDCl_3$, 25°C) δ = 9.70 (s, 1H; CHO), 7.34-7.30 (m, 2H; Ph), 7.19-7.16 (m, 2H; Ph), 4.70-4.65 (m, 1H; CH_2NO_2), 4.59 (dd, *J* = 7.9 Hz, 12.6 Hz, 1H; CH_2NO_2), 4.10-4.02 (m, 1H; CHPh), 2.94 (dd, *J* = 0.7 Hz, 7.1 Hz, 2H; CH_2CHO) ppm; **^{13}C NMR** (100 MHz, $CDCl_3$, 25°C) δ = 198.5, 136.8, 134.2, 129.5, 128.9, 79.2, 46.4, 37.4 ppm.

$[\alpha]_D^{25}$ = -8.67 (*c* 0.0128 g. mL^{-1}, MeOH); lit. = **$[\alpha]_D^{24}$** = -20.5 (*c* 1, $CHCl_3$)

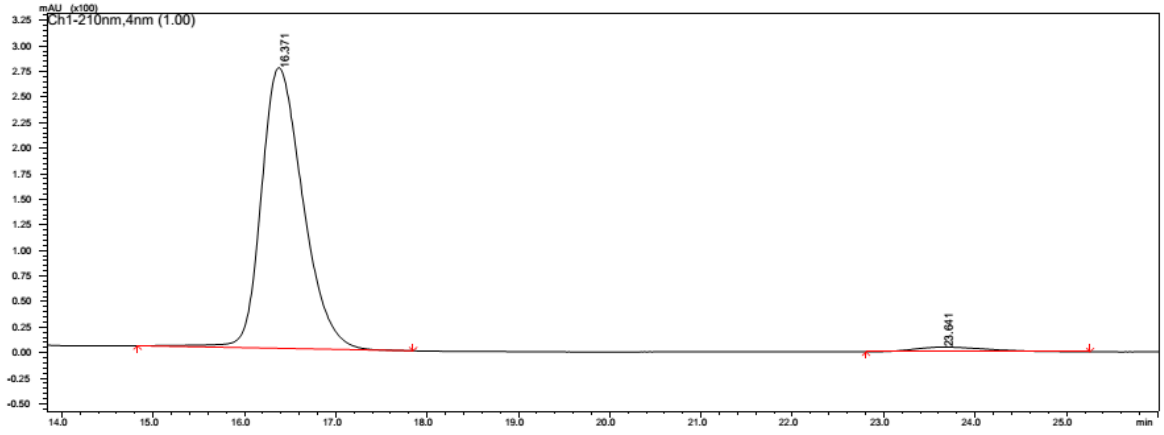
^{1}H NMR



^{13}C NMR



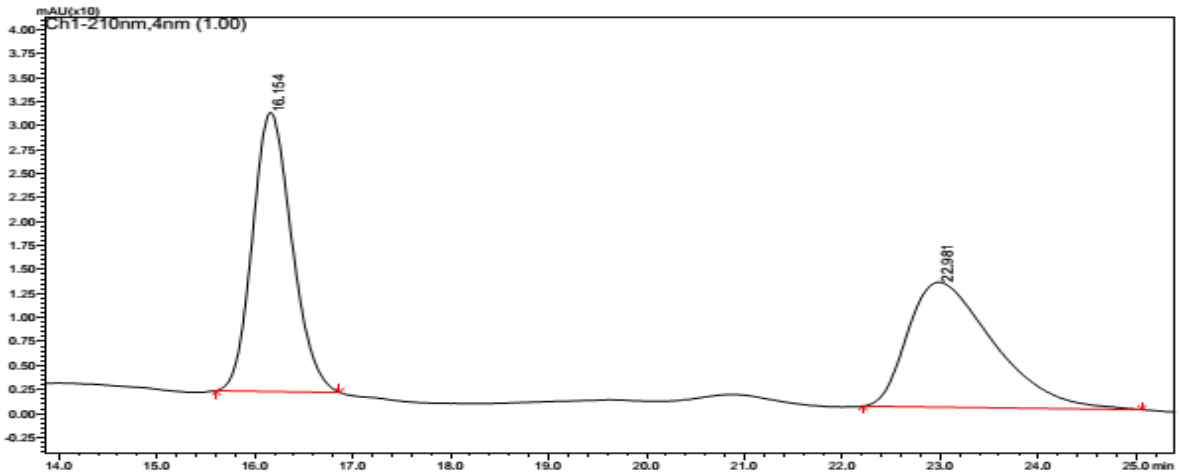
HPLC: Chiracel AS-H column (n-hexane/i-PrOH 70:30, 25ºC) at 1 mL/min (94% ee)



PeakTable

PDA Ch1 210nm 4nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	16.371	8686859	274364	97.106	98.409
2	23.641	258934	4435	2.894	1.591
Total		8945793	278799	100.000	100.000

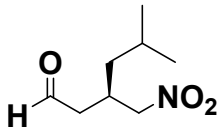


PeakTable

PDA Ch1 210nm 4nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	16.154	813477	29075	50.673	69.081
2	22.981	791878	13013	49.327	30.919
Total		1605354	42089	100.000	100.000

(R)-5-methyl-3-(nitromethyl)hexanal- (10 n)

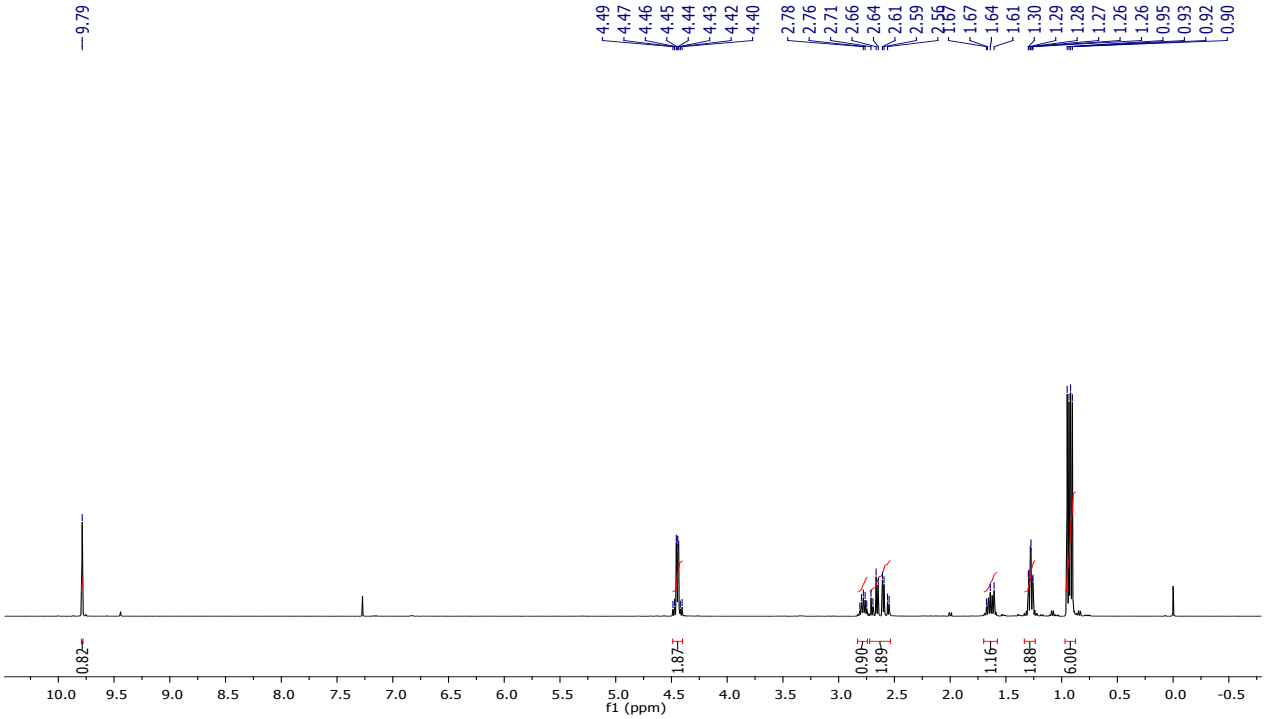


Analytical data for major diastereoisomer were in agreement with the published data

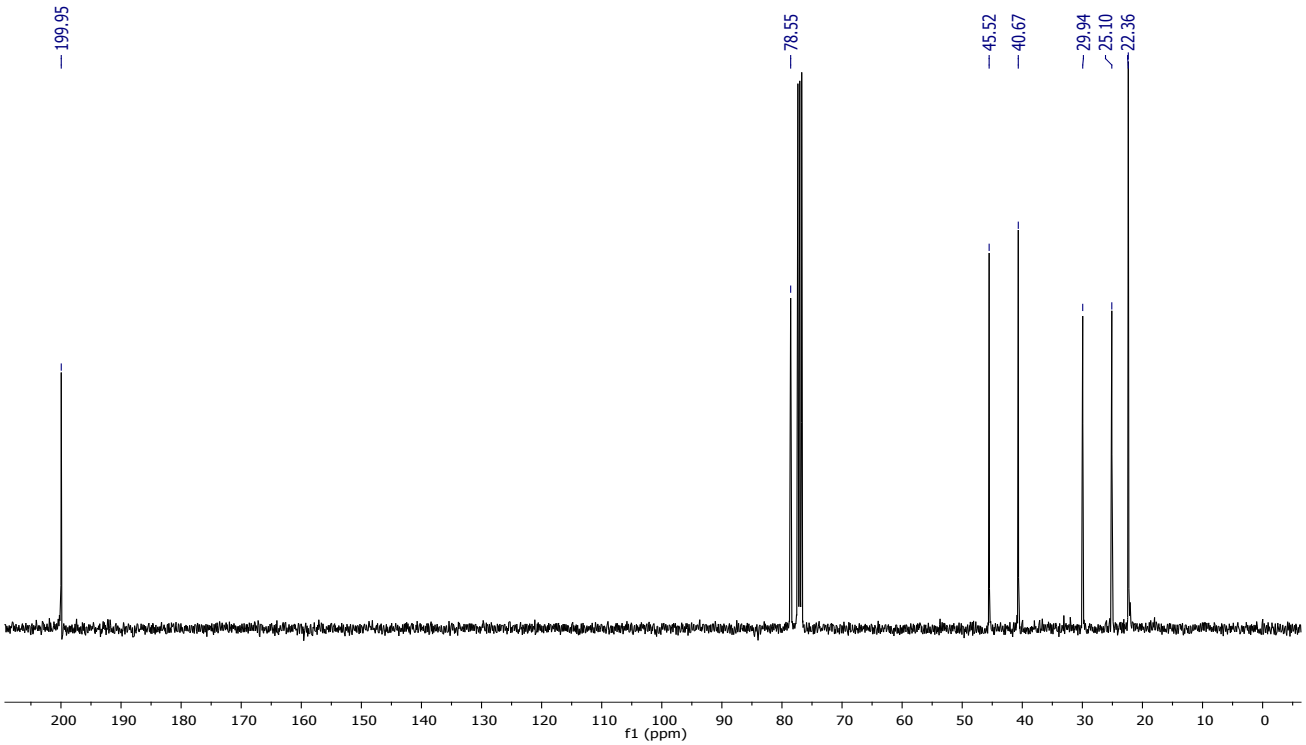
^{1}H NMR (400 MHz,$CDCl_3$, 25°C) δ = 9.79 (s, 1H, CHO), 4.49- 4.40 (m, 2H, CH_2NO_2), 2.81-2.75 (m, 1H, $CHCH_2CH(CH_3)_2$, 2.63 (ddd, *J* = 6.2 Hz, 18.4 Hz, 24.1 Hz, 2H, CH_2CHO), 1.67-1.61 (m, 1H, $CH(CH_3)_2$), 1.28 (td, *J* = 2.3 Hz, 7.2 Hz, 2H, $CH_2CH(CH_3)_2$) 0.93 (dd, *J* = 6.5 Hz, 12.2 Hz, 6H, $(CH_3)_2$) ppm; **^{13}C NMR** (100 MHz, $CDCl_3$, 25°C) δ = 199.9, 78.5, 45.5, 40.7, 29.9, 25.1, 22.3 ppm.

$[\alpha]_D^{25}$ = -15.38 (*c* 0.0195 g. mL^{-1}, MeOH); lit.= **$[\alpha]_D^{25}$** = -5.2 (*c* 0.85, $CHCl_3$)

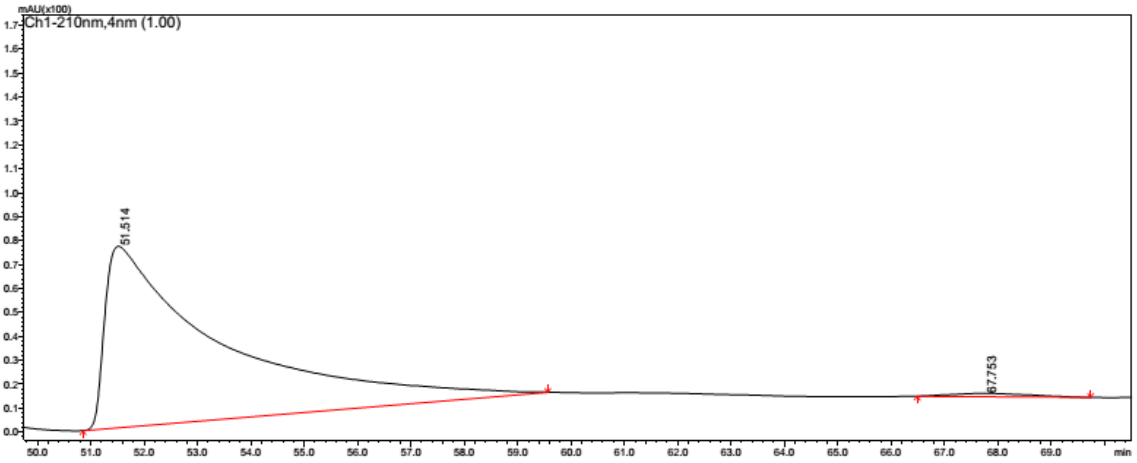
^{1}H NMR



^{13}C NMR



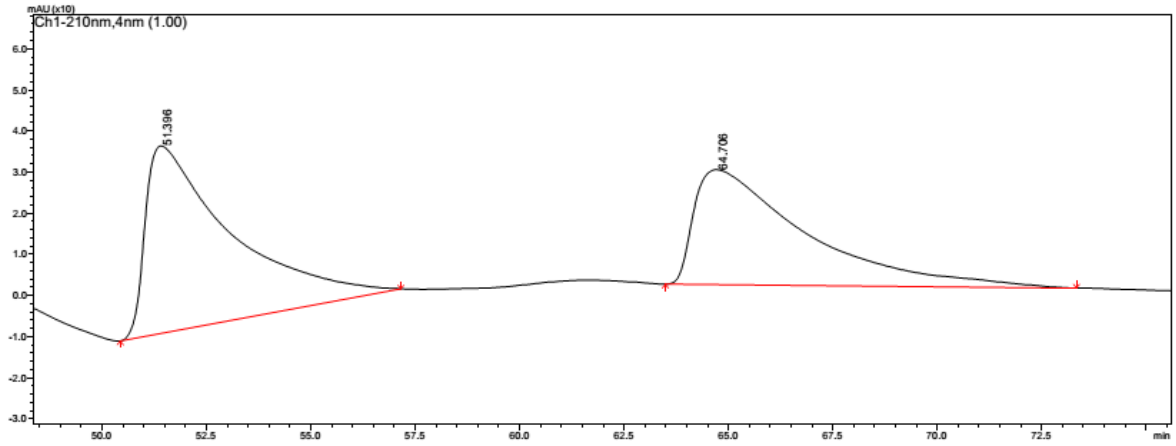
HPLC: Chiracel AS-H column (n-hexane/i-PrOH 99:01, 25ºC) at 0.2 mL/min (80% ee)



PeakTable

PDA Ch1 210nm 4nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	51.514	11400161	75811	98.791	98.209
2	67.753	139557	1383	1.209	1.791
Total		11539718	77194	100.000	100.000



PeakTable

PDA Ch1 210nm 4nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	51.396	6484054	45592	55.699	62.007
2	64.706	5157098	27936	44.301	37.993
Total		11641152	73528	100.000	100.000

5-References:

For NMR- data see:

a) Y.-Q. Cheng, Z. Bian, Y.-B. He, F.-S. Han, C.-Q. Kang, Z.-L. Ning, L.-X. Gao. *Tetrahedron Asymm.* **2009**, *20*, 1753-1758.

b) M. Wiesner, J. D. Revell, H. Wennemers. *Angew. Chem. Int. Ed.*, **2008**, 47, 1871−1874.

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d) M. T. Barros, A. M. F. Phillips. *Eur. J. Org. Chem*., **2007,** 178-185.

e) J. Watts, L. Luu, V. McKee, E. Carey, F. Kelleher. *Adv. Synth. Catal.,* **2012**, 354, 1035-1042.

For Specific rotation see:

a) Y.-Q. Cheng, Z. Bian, Y.-B. He, F.-S. Han, C.-Q. Kang, Z.-L. Ning, L.-X. Gao. *Tetrahedron Asymm.* **2009**, *20*, 1753-1758.

f) K. Xu, S. Zhang, Y. Hu, Z. Zha, Z. Wang. *Chem. Eur. J.* **2013**, *19*, 3573 – 3578.

g) A. Alexakis, O. Andrey. *Org. Lett*., **2002**, *4*, 21, 3611-3614.

h) O. V. Maltsev, A. S. Kucherenko, I. P. Beletskaya, V. A. Tartakovsky, S. G. Zlotin. *Eur. J. Org. Chem*. **2010**, 2927-2933.

i) E. M. Geertsema, Y. Miao, P. G. Tepper, P. de Haan, E. Zandvoort, G. J. Poelarends. *Chem. Eur. J.* **2013**, 19, 14407-14410.