Electronic Supplementary Material (ESI) for ChemComm.

Developing An Atroposelective Dynamic Kinetic Resolution of MRTX1719 by Resolving Incompatible Chemical Operations

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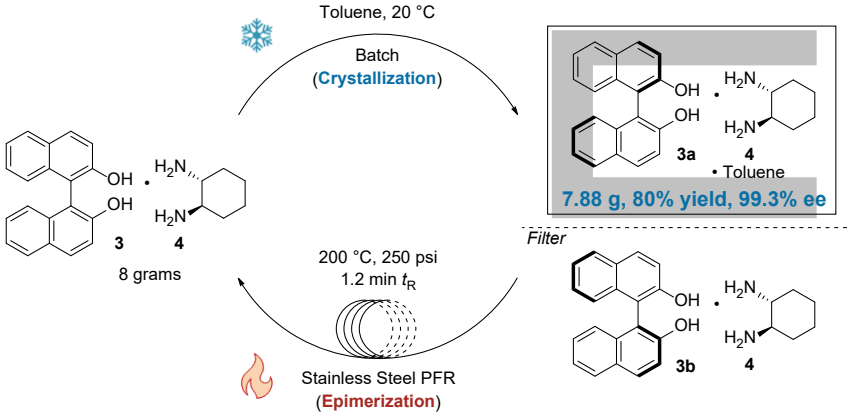
Continuous Resolution of R-BINOL:



Scheme S1:

1,1'-Bi-2-napthol (5.71 g, 19.9 mmol, 1.00 equiv.) was added to an Erlenmeyer flask equipped with a magnetic stir-bar. 80 mL of toluene was added to the flask. The flask was then heated to 80 °C on a hot-plate, while stirring. (1*R*, 2*R*)-diaminocyclohexane (2.28 g, 19.9 mmol, 1.00 equiv.) was added to the hot BINOL, and the slurry quickly transitioned to a homogeneous phase. After becoming homogeneous, crystals began to form, heating was turned off, and the mixture was allowed to cool to room temperature and age for 1 hr. A sample of the supernatant was collected for HPLC analysis. A 20 µm stainless steel HPLC filter from IDEX was immersed in the toluene. It was connected to an Eldex Optos Model 3 metering pump by 1/8" O.D. PFA tubing (1/16" I.D.). The pump was connected to a stainless steel plug flow reactor (3.5 mL, 1/8" O.D, 0.09" I.D.) by PFA tubing (1/8" O.D., 1/16" I.D.). Swagelok 1/8" compression fittings were used to securely connect the tubing. The outlet of the plug flow reactor (PFR) was connected to a 250 psi spring-loaded back pressure regulator from IDEX. The stream flowed out of the bpr and back into the Erlenmeyer crystallization flask. The plug-flow reactor was immersed in mineral oil heated to 200 °C, and prior to pumping the BINOL solution through the stainless steel filter and PFR, the recycle loop was pre-filled with pure toluene to facilitate start-up of the recycle procedure. The pump driving the recycle loop was operated at a rate of 3 mL/min, and the recycle was run continuously for 30 hr. After this time, the solids in the flask were filtered. The solids were washed with 5 mL of toluene and left on the filter until dry. 7.88 g of white solid was obtained. The complex was a 1:1:1 mixture of BINOL, diamine and toluene (MW 492 g/mol). Sample was submitted for 1H qNMR analysis to attain the assay weight percent. Spectrum matched that reported in the literature. It was 99.6% of the 81.0% assay wt. percent of the BINOL/diaminocyclohexane complex corresponding to 99.6 assay wt% of the 1:1:1 complex of BINOL, diamine, and toluene. The assay adjusted isolated yield is 80%. Sample was taken for chiral HPLC analysis. The sample showed 99.65% of R-BINOL and 0.35% of S-BINOL (99.3% ee).

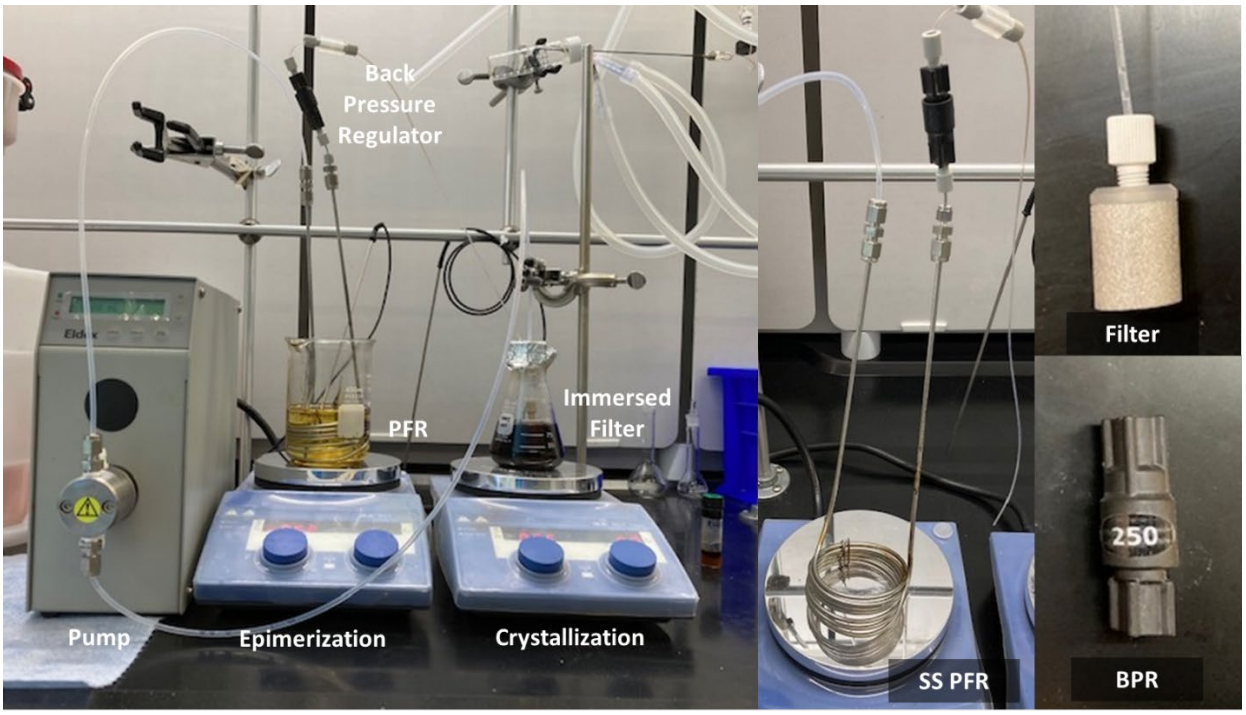


Figure S1: Reaction Setup for Resolution of BINOL.

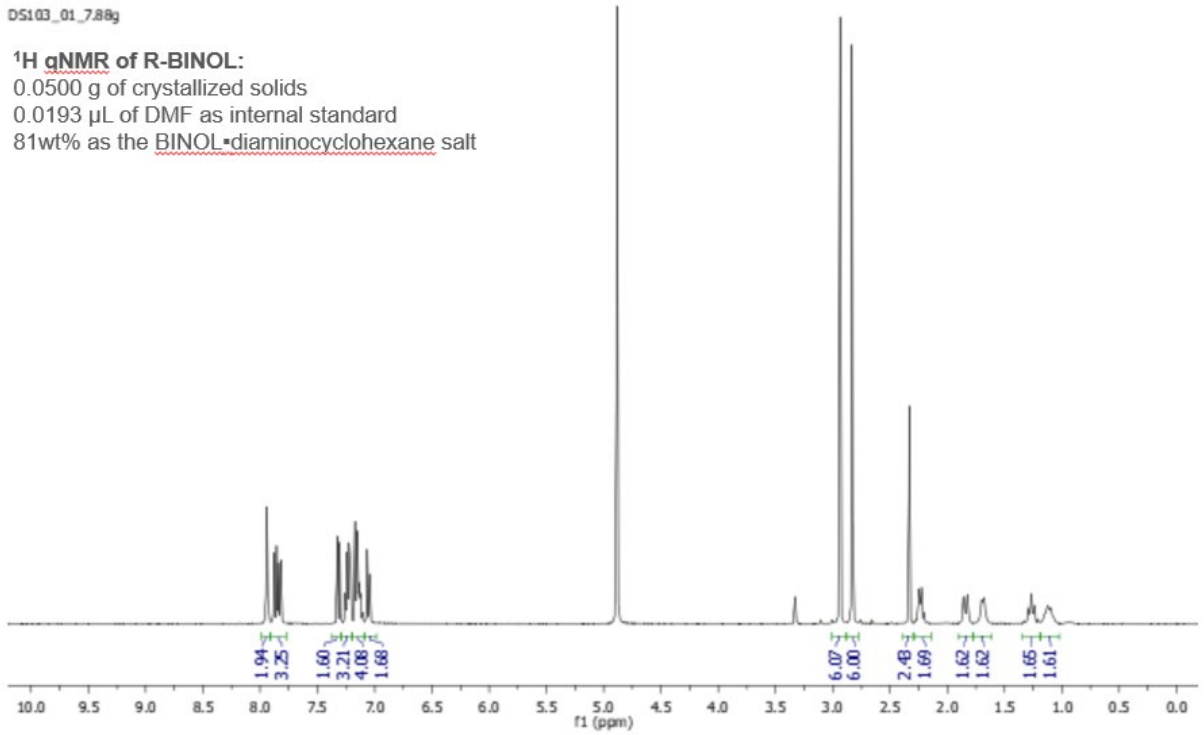
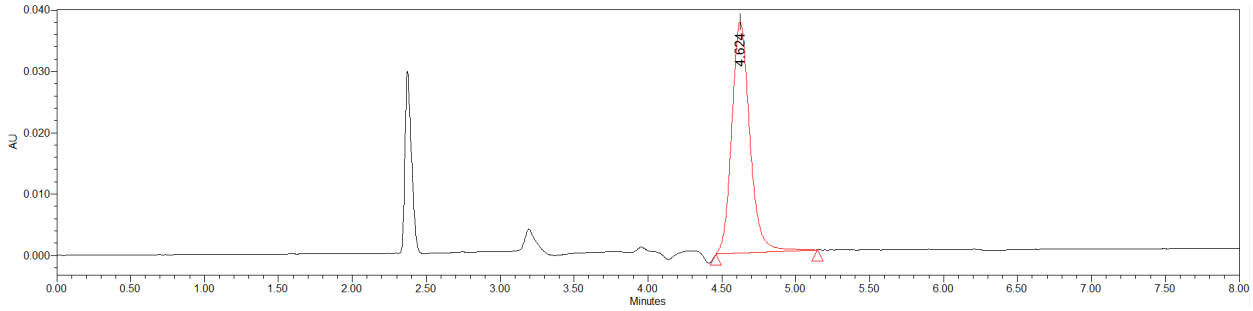


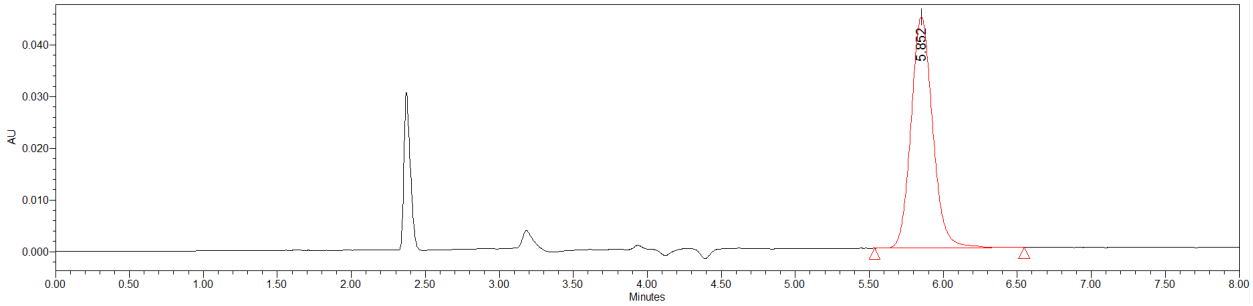
Table S1: HPLC conditions for BINOL. Spectra of R and S isomers of BINOL

Column	Chiralpak IC, 5 μm, 4.6 x 250 mm (Daicel Chiral Technologies, Part No. 83325)
Wavelength	265 nm
Column Temperature	40 °C
Column Flow	1.3 mL/min
Acquisition Time	8 min
Isocratic Elution	Hexane:2-Propanol 90:10 (v/v)
Injection Volume	5 μL
Retention Times	~4.5 min (*R*-BINOL), ~6.0 min (*S*-BINOL)

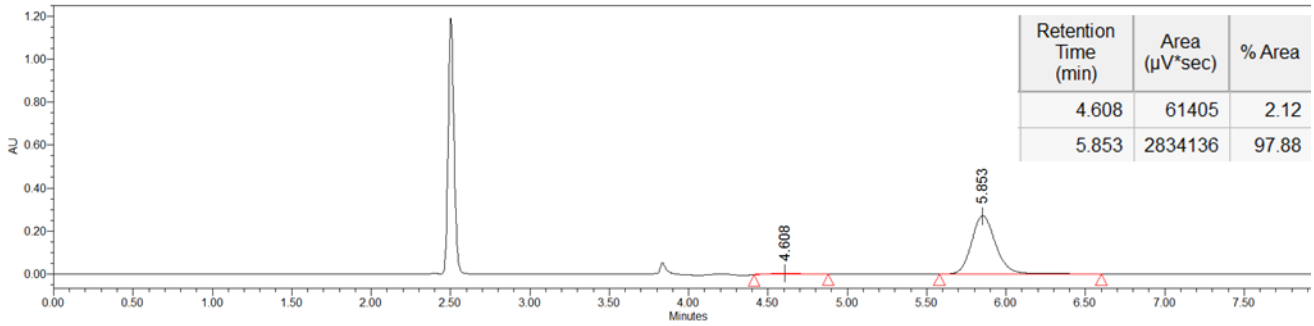
HPLC Chromatogram of R-BINOL:



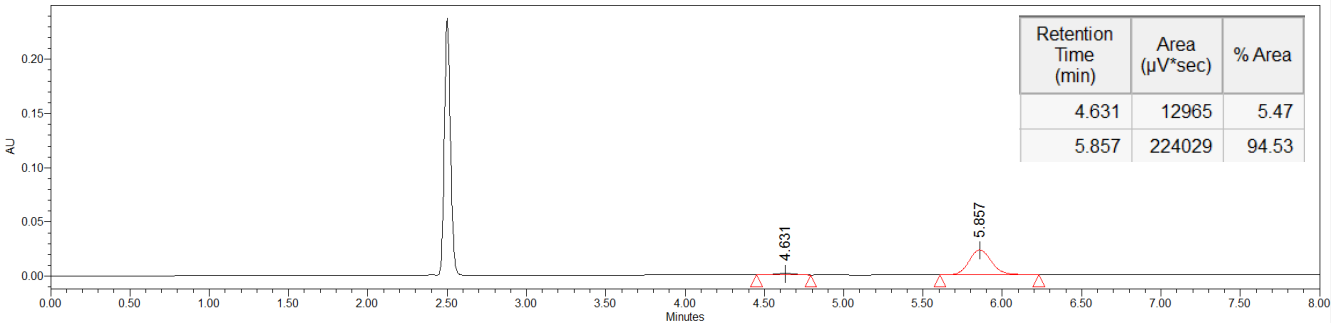
HPLC Chromatogram of S-BINOL:



HPLC Chromatogram of Supernatant after 1 hr of aging:

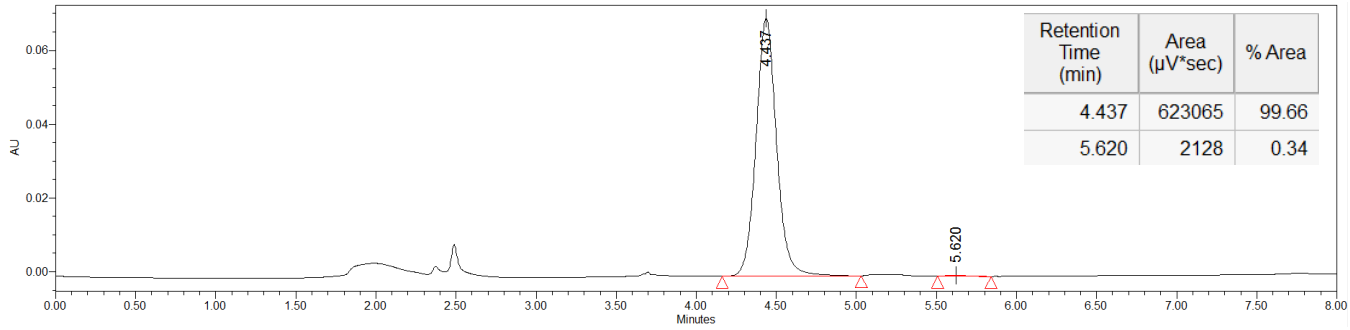


HPLC Chromatogram of Eluent from Flash Epimerization at t = 0:



Retention Time (min)	Area (µV*sec)	% Area
4.631	12965	5.47
5.857	224029	94.53

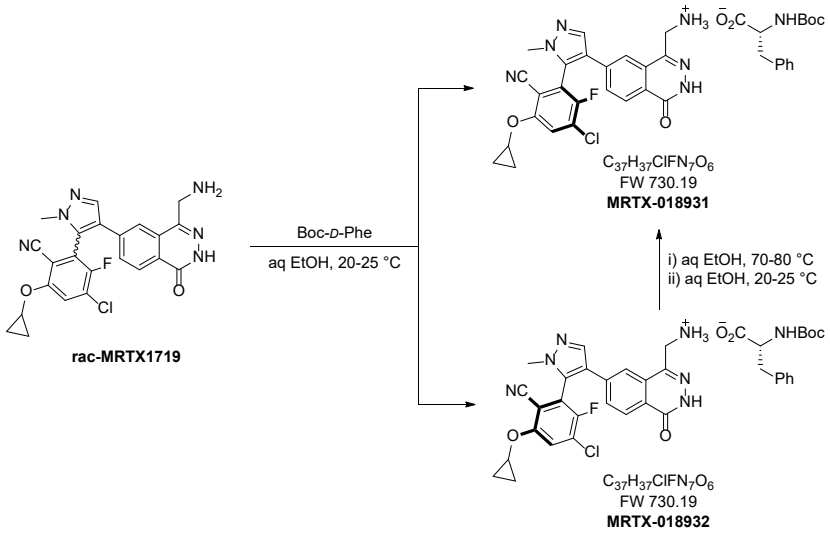
HPLC of crystallized R-BINOL:



Retention Time (min)	Area (µV*sec)	% Area
4.437	623065	99.66
5.620	2128	0.34

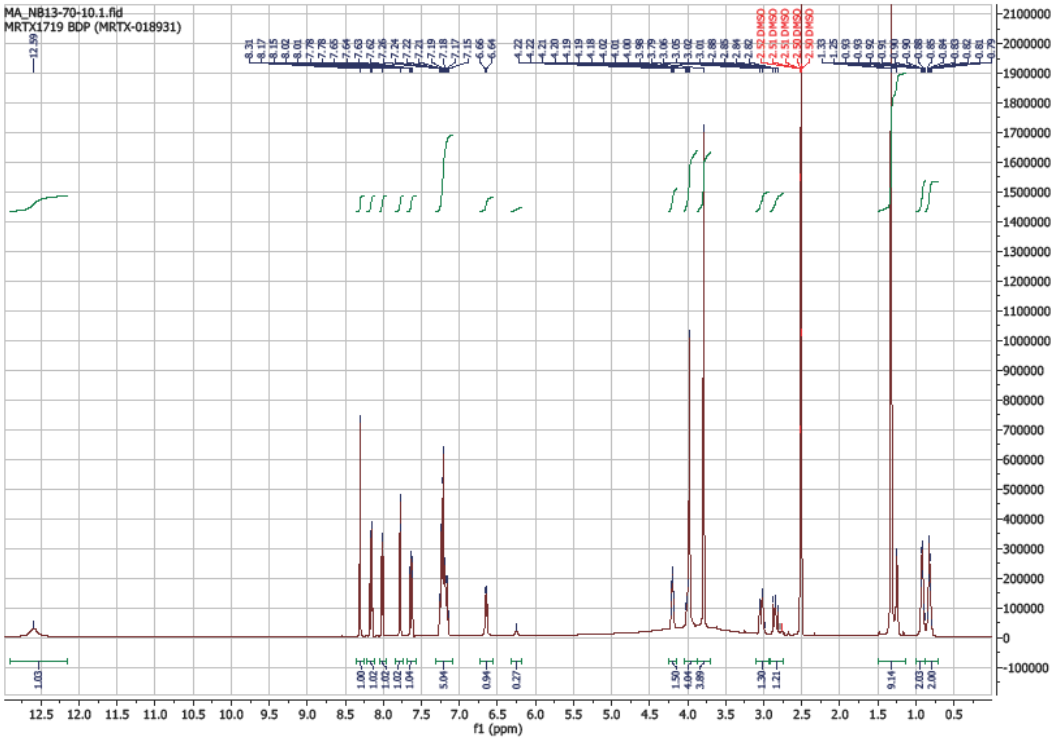
Batch Resolution of MRTX1719:

Description of Batch crystallization.

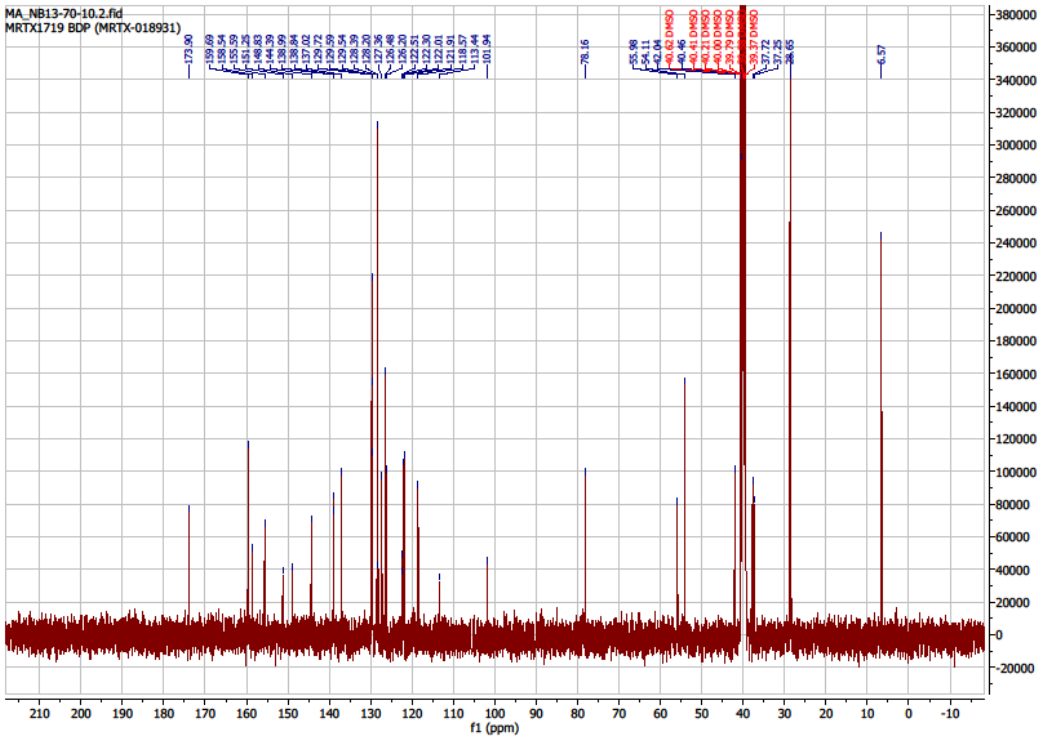


rac-MRTX1719 (1.0 equiv) and Boc-D-Phe (1.1 equiv) were allowed to dissolve in EtOH:water (90:10 v/v, 12 V) at room temperature. The resulting supersaturated mixture was seeded with 0.5% w/w of MRTX-018931 (MRTX1719 Boc-D-Phe salt) and equilibrated at ~22 °C until selective crystallization of MRTX1719 Boc-D-Phe salt (MRTX-018931) was complete while the supernatant became enriched in the undesired enantiomer salt (MRTX-018932). The crystalline solids were separated by filtration and additional reslurry in aqueous EtOH (85:15 v/v, 10 V) was performed to effect additional chiral upgrade (target: ⩾95.5% enantiomeric excess [e.e.] by chiral HPLC). The mother liquors consisting of a mixture of MRTX-018932 and MRTX-018932 in aqueous EtOH were thermally racemized (target: <20% enantiomeric excess [e.e.] by chiral HPLC) at 70-80 °C for 24-48 h. Additional crop of MRTX1719 Boc-D-Phe salt (MRTX-018931) was obtained by repeating the aging and reslurry as described above (target: ⩾ 95.5% enantiomeric excess [e.e.] by chiral HPLC). Drying of the resulting crystalline solids at ~45°C afforded MRTX-018931 as off white solids in combined 60% yield (first crop: 37% yield; second crop: 23% yield).

MRTX-018931 – ^{1}H NMR (d_6-DMSO)



MRTX-018931 – ^{13}C NMR (d_6-DMSO)



MRTX-018931 – ^{19}F NMR (d_6-DMSO)

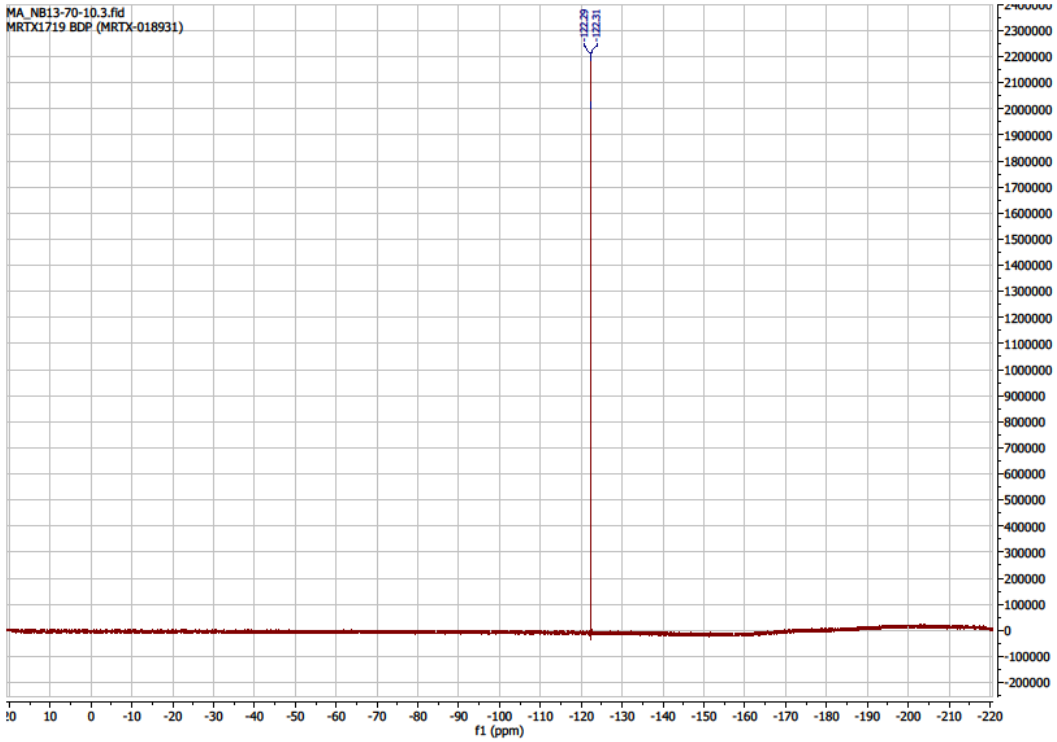


Table S2: HPLC conditions for 1719.

Column	Chiralpak IC, 5 μm, 4.6 x 250 mm (Daicel Chiral Technologies, Part No. 83325)
Wavelength	265 nm
Column Temperature	40 °C
Column Flow	1.3 mL/min
Acquisition Time	8 min
Isocratic Elution	Ethanol (0.1% Ethanolamine):Heptane 90:10 (v/v)
Injection Volume	10 μL
Retention Times	~9.7 min (MRTX1719), ~7.4 min (MRTX1273)

Continuous Resolution of MRTX1719:

Racemic MRTX1719 (92.4 wt%, 10.82 g, 21.5 mmol) was suspended in ethanol and water mixture (EtOH:water 98:2 v/v, 100 mL) in 100 mL EasyMax reactor. Solid Boc-D-phenylalanine (6.25 g, 23.6 mmol, 1.1 equiv) was added and the resulting thick slurry was agitated at 600 rpm using overhead stirrer at room temperature. Within 10 min nearly all the solids went into solution affording a thin yellowish suspension. Thus obtained supersaturated solution of MRTX-018931 was seeded with crystalline MRTX-018931 (78 mg, 0.0050 equiv) and allowed to equilibrate with efficient agitation at room temperature. After ~16 h thick slurry of crystals was obtained. Analysis of the supernatant by chiral LC showed 91.5% of MRTX1273 and 8.5% of MRTX1719 (83% e.e.) with MRTX-018932 at 39.7 mg/mL (equilibrium solubility of ~40 mg/mL) and MRTX-018931 at 3.7 mg/mL (equilibrium solubility of ~4 mg/mL). Having confirmed the mixture is close to equilibrium $_{SPACE}$DKR process was initiated. A 20 µm stainless steel HPLC filter from IDEX was immersed in the crystallization vessel (100 mL EasyMax reactor) containing thick slurry of MRTX-018931 in ethanol water mixture. It was connected to a Syrris Asia Syringe Pump by 1/16" O.D. PFA tubing (0.03" I.D.). The pump was connected to a plug flow reactor made from PFA tubing (1.5 mL, 1/16" O.D, 0.03" I.D.). The outlet of the plug flow reactor (PFR) was connected to a 250 psi spring-loaded back pressure regulator from IDEX. The stream flowed out of the bpr and back into the crystallization vessel. The plug-flow reactor was immersed in mineral oil heated to 160 °C. The pump driving the recycle loop was operated at a rate of 0.75 mL/min, and the recycle was run continuously for 14.5 h. Intermittent HPLC sampling was conducted. After 14.5 h the productive phase of $_{SPACE}$DKR was completed as indicated by nearly identical supernatant concentration of MRTX-018932 and MRTX-018931 (5.4 mg/mL and 4.3 mg/mL, respectively). The slurry from the crystallizer was filtered. The filtercake was thoroughly deliquored and air-dried to afford technical MRTX-018931 as off-white powder in 87% yield (14.43 g, 94.2 wt%, 90% d.r., 98.0% LC). Additional reslurry in aq EtOH (EtOH:water 95:5 v/v, 10 V) for 6 h with temperature cycling (20-40 °C) upgraded the chiral and achiral purity (96.6 d.r., 98.5% LC) at the cost of 5% product loss to the liquors.

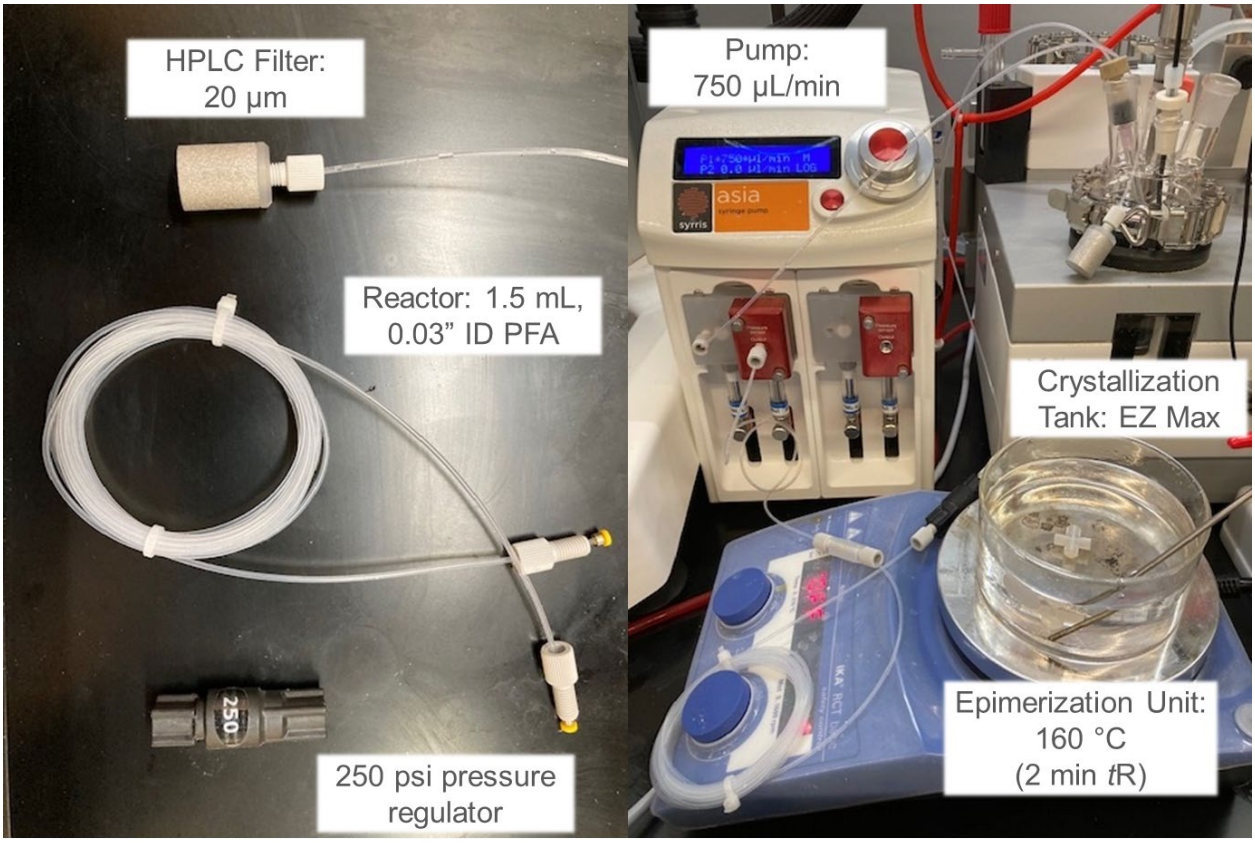


Figure S2: Reaction setup for Resolution of MRTX1719.

Racemic MRTX1719 input (achiral LC)

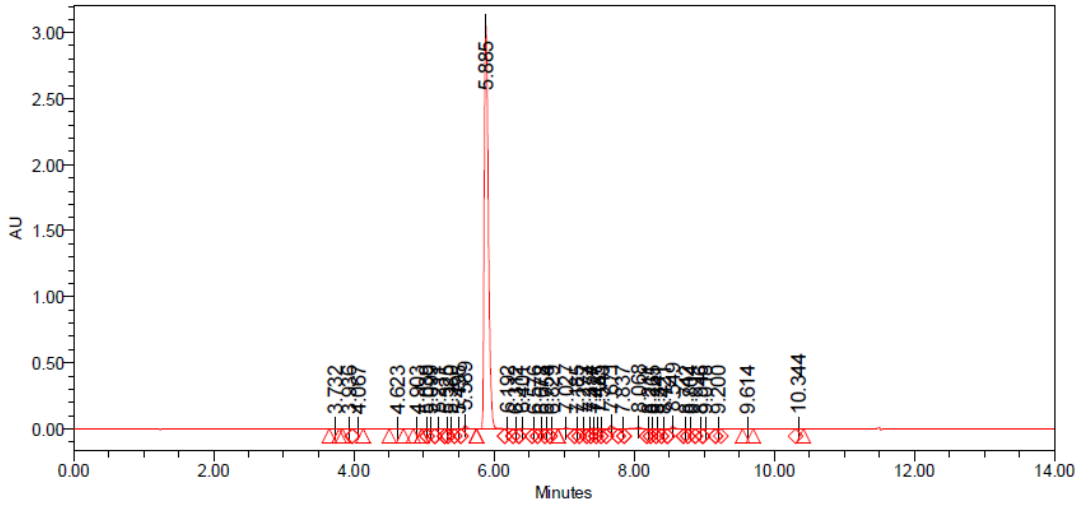
Empower 3 SOFTWARE

1719

SAMPLE INFORMATION

Sample Name:	NB51-40-0 slurry,100xdil	Acquired By:	AchmatowiczM
Sample Type:	Unknown	Sample Set Name:	MA_Agilent5_05032022a
Vial:	1:D,4	Acq. Method Set:	MRTX1719_AgilentLC5_14min
Injection #:	1	Processing Method:	1719_14min
Injection Volume:	5.00 ul	Channel Name:	DAD.0.0
Run Time:	14.0 Minutes	Proc. Chnl. Descr.:	DAD: Signal A, 265 nm/Bw:4 nm
Date Acquired:	5/3/2022 4:31:18 PM PDT		
Date Processed:	6/13/2022 2:18:17 PM PDT		

Auto-Scaled Chromatogram



Peak Results

	Name	RT	Area	Height	Amount	% Area
1		3.732	1152	315		0.01
2		3.936	879	209		0.01
3		4.067	4030	1218		0.03
4		4.623	1662	448		0.01
5		4.903	806	295		0.01
6		5.039	1128	522		0.01
7		5.099	6946	1992		0.05
8		5.211	9096	2835		0.07
9		5.325	677	248		0.01
10		5.380	1169	304		0.01

Peak Results

	Name	RT	Area	Height	Amount	% Area
11		5.495	4876	1430		0.04
12		5.589	79773	26248		0.63
13		5.885	12276237	3051328		96.39
14		6.192	10781	2466		0.08
15		6.312	5839	1677		0.05
16		6.401	14155	3499		0.11
17		6.576	942	241		0.01
18		6.678	3509	992		0.03
19		6.754	1989	600		0.02
20		6.829	1496	430		0.01
21		7.027	23324	6726		0.18
22		7.185	758	276		0.01
23		7.277	3586	949		0.03
24		7.374	4542	2197		0.04
25		7.427	11932	3225		0.09
26		7.485	9143	2765		0.07
27		7.543	4461	1604		0.04
28		7.671	84118	21155		0.66
29		7.837	3979	934		0.03
30		8.068	76454	11148		0.60
31		8.211	2948	1034		0.02
32		8.265	4246	1358		0.03
33		8.341	3513	1067		0.03
34		8.421	2135	575		0.02
35		8.549	59394	18276		0.47
36		8.742	758	266		0.01
37		8.804	1597	367		0.01
38		8.946	2589	713		0.02
39		9.018	7313	1609		0.06
40		9.200	509	188		0.00
41		9.614	870	236		0.01
42		10.344	752	250		0.01

Processed Channel: DAD: Signal A, 265 nm/Bw:4 nm

	Processed Channel	Retention Time (min)	Area	% Area	Height
1	DAD: Signal A, 265 nm/Bw:4 nm	3.732	1152	0.01	315
2	DAD: Signal A, 265 nm/Bw:4 nm	3.936	879	0.01	209
3	DAD: Signal A, 265 nm/Bw:4 nm	4.067	4030	0.03	1218
4	DAD: Signal A, 265 nm/Bw:4 nm	4.623	1662	0.01	448
5	DAD: Signal A, 265 nm/Bw:4 nm	4.903	806	0.01	295
6	DAD: Signal A, 265 nm/Bw:4 nm	5.039	1128	0.01	522

Processed Channel: DAD: Signal A, 265 nm/Bw:4 nm

	Processed Channel	Retention Time (min)	Area	% Area	Height
7	DAD: Signal A, 265 nm/Bw:4 nm	5.099	6946	0.05	1992
8	DAD: Signal A, 265 nm/Bw:4 nm	5.211	9096	0.07	2835
9	DAD: Signal A, 265 nm/Bw:4 nm	5.325	677	0.01	248
10	DAD: Signal A, 265 nm/Bw:4 nm	5.380	1169	0.01	304
11	DAD: Signal A, 265 nm/Bw:4 nm	5.495	4876	0.04	1430
12	DAD: Signal A, 265 nm/Bw:4 nm	5.589	79773	0.63	26248
13	DAD: Signal A, 265 nm/Bw:4 nm	5.885	12276237	96.39	3051328
14	DAD: Signal A, 265 nm/Bw:4 nm	6.192	10781	0.08	2466
15	DAD: Signal A, 265 nm/Bw:4 nm	6.312	5839	0.05	1677
16	DAD: Signal A, 265 nm/Bw:4 nm	6.401	14155	0.11	3499
17	DAD: Signal A, 265 nm/Bw:4 nm	6.576	942	0.01	241
18	DAD: Signal A, 265 nm/Bw:4 nm	6.678	3509	0.03	992
19	DAD: Signal A, 265 nm/Bw:4 nm	6.754	1989	0.02	600
20	DAD: Signal A, 265 nm/Bw:4 nm	6.829	1496	0.01	430
21	DAD: Signal A, 265 nm/Bw:4 nm	7.027	23324	0.18	6726
22	DAD: Signal A, 265 nm/Bw:4 nm	7.185	758	0.01	276
23	DAD: Signal A, 265 nm/Bw:4 nm	7.277	3586	0.03	949
24	DAD: Signal A, 265 nm/Bw:4 nm	7.374	4542	0.04	2197
25	DAD: Signal A, 265 nm/Bw:4 nm	7.427	11932	0.09	3225
26	DAD: Signal A, 265 nm/Bw:4 nm	7.485	9143	0.07	2765
27	DAD: Signal A, 265 nm/Bw:4 nm	7.543	4461	0.04	1604
28	DAD: Signal A, 265 nm/Bw:4 nm	7.671	84118	0.66	21155
29	DAD: Signal A, 265 nm/Bw:4 nm	7.837	3979	0.03	934
30	DAD: Signal A, 265 nm/Bw:4 nm	8.068	76454	0.60	11148
31	DAD: Signal A, 265 nm/Bw:4 nm	8.211	2948	0.02	1034
32	DAD: Signal A, 265 nm/Bw:4 nm	8.265	4246	0.03	1358
33	DAD: Signal A, 265 nm/Bw:4 nm	8.341	3513	0.03	1067
34	DAD: Signal A, 265 nm/Bw:4 nm	8.421	2135	0.02	575
35	DAD: Signal A, 265 nm/Bw:4 nm	8.549	59394	0.47	18276
36	DAD: Signal A, 265 nm/Bw:4 nm	8.742	758	0.01	266
37	DAD: Signal A, 265 nm/Bw:4 nm	8.804	1597	0.01	367
38	DAD: Signal A, 265 nm/Bw:4 nm	8.946	2589	0.02	713
39	DAD: Signal A, 265 nm/Bw:4 nm	9.018	7313	0.06	1609
40	DAD: Signal A, 265 nm/Bw:4 nm	9.200	509	0.00	188
41	DAD: Signal A, 265 nm/Bw:4 nm	9.614	870	0.01	236
42	DAD: Signal A, 265 nm/Bw:4 nm	10.344	752	0.01	250

Racemic MRTX1719 input (chiral LC)

Empower 3 SOFTWARE

1719

SAMPLE INFORMATION

Sample Name:	NB51-40-0 slurry,100xdil	Acquired By:	AchmatowiczM
Sample Type:	Unknown	Sample Set Name:	MA_Agilent1_04272022f
Vial:	1:F,2	Acq. Method Set:	HPLC000305_Chiral
Injection #:	1	Processing Method:	1719 chiral purity v2
Injection Volume:	5.00 ul	Channel Name:	MWD.0.0
Run Time:	15.0 Minutes	Proc. Chnl. Descr.:	MWD: Signal A, 265 nm/Bw:4 nm
Date Acquired:	4/27/2022 4:28:50 PM PDT		
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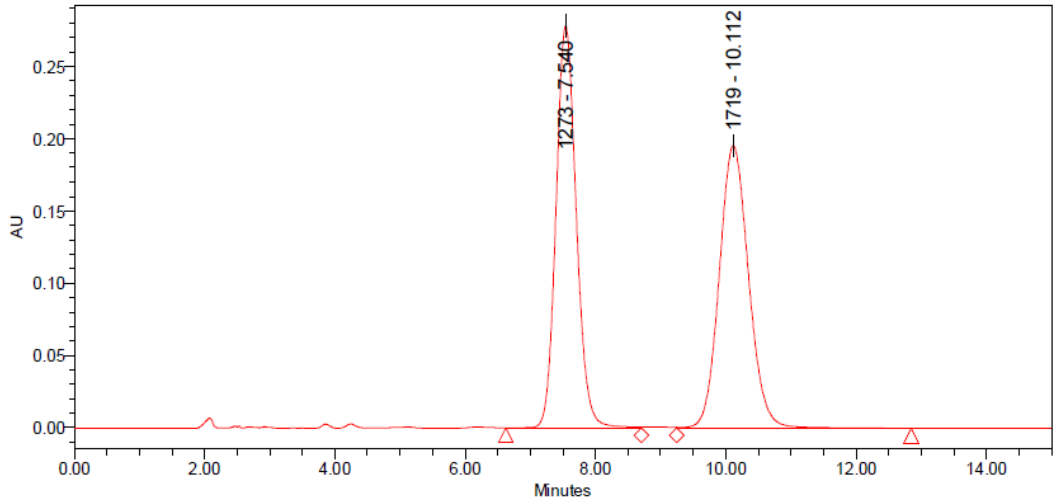
Auto-Scaled Chromatogram



Peak Results

	Name	RT	Area	Height	Amount	% Area
1	1273	7.540	6018362	278342		49.56
2	1719	10.112	6125260	195401		50.44

Processed Channel: MWD: Signal A, 265 nm/Bw:4 nm

	Peak Name	Processed Channel	Retention Time (min)	Area	% Area	Height
1	1273	MWD: Signal A, 265 nm/Bw:4 nm	7.540	6018362	49.56	278342
2	1719	MWD: Signal A, 265 nm/Bw:4 nm	10.112	6125260	50.44	195401

Supernatant at the end of SPACEDKR (achiral LC)

Empower 3 SOFTWARE

1719

SAMPLE INFORMATION

Sample Name:	NB51-40-6ML 28h,100xdil	Acquired By:	AchmatowiczM
Sample Type:	Unknown	Sample Set Name:	MA_Agilent5_05032022a
Vial:	1:E,1	Acq. Method Set:	MRTX1719_AgilentLC5_14min
Injection #:	1	Processing Method:	1719_14min
Injection Volume:	5.00 ul	Channel Name:	DAD.0.0
Run Time:	14.0 Minutes	Proc. Chnl. Descr.:	DAD: Signal A, 265 nm/Bw:4 nm
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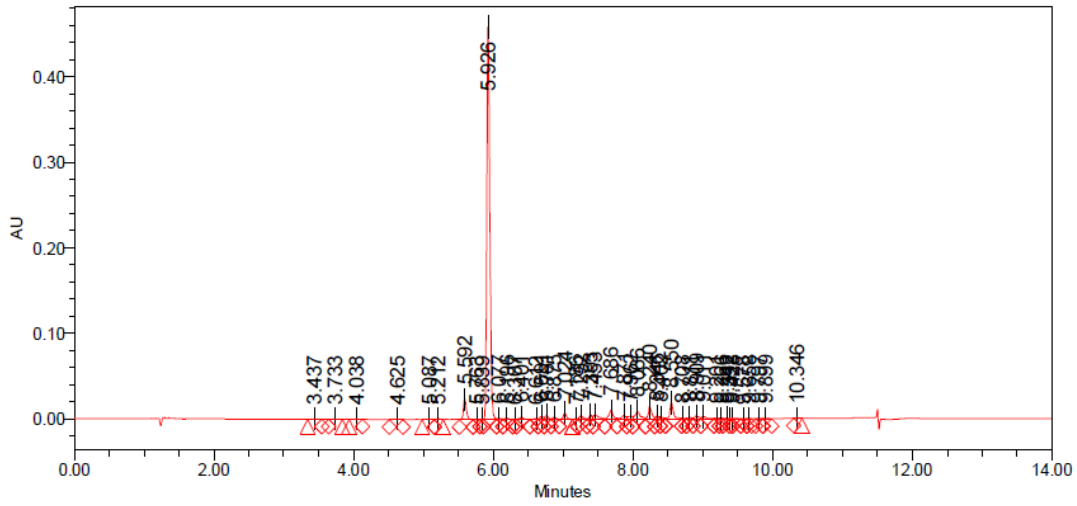
Auto-Scaled Chromatogram



Peak Results

	Name	RT	Area	Height	Amount	% Area
1		3.437	875	249		0.05
2		3.733	1734	395		0.09
3		4.038	1640	329		0.08
4		4.625	1550	390		0.08
5		5.087	3144	533		0.16
6		5.212	2596	865		0.13
7		5.592	70336	23648		3.63
8		5.763	1104	327		0.06
9		5.839	630	252		0.03
10		5.926	1407178	460152		72.65

Peak Results

	Name	RT	Area	Height	Amount	% Area
11		6.077	4066	1055		0.21
12		6.196	5397	1258		0.28
13		6.307	960	333		0.05
14		6.401	9193	2411		0.47
15		6.612	2908	853		0.15
16		6.691	10225	3470		0.53
17		6.761	14164	4265		0.73
18		6.875	7975	2423		0.41
19		7.024	22511	6904		1.16
20		7.186	1735	729		0.09
21		7.252	14752	4027		0.76
22		7.393	14170	4966		0.73
23		7.453	26590	4656		1.37
24		7.686	41967	10113		2.17
25		7.871	18441	4400		0.95
26		7.962	14967	3381		0.77
27		8.066	45988	8545		2.37
28		8.240	48300	14029		2.49
29		8.346	12463	3779		0.64
30		8.402	7009	1927		0.36
31		8.550	68911	18897		3.56
32		8.708	3840	987		0.20
33		8.811	6956	1775		0.36
34		8.909	13878	3454		0.72
35		9.011	13715	2490		0.71
36		9.201	2139	571		0.11
37		9.266	1342	508		0.07
38		9.342	4344	937		0.22
39		9.392	1008	487		0.05
40		9.428	2000	419		0.10
41		9.578	721	164		0.04
42		9.658	631	188		0.03
43		9.797	970	247		0.05
44		9.899	999	206		0.05
45		10.346	853	270		0.04

Processed Channel: DAD: Signal A, 265 nm/Bw:4 nm

	Processed Channel	Retention Time (min)	Area	% Area	Height
1	DAD: Signal A, 265 nm/Bw:4 nm	3.437	875	0.05	249
2	DAD: Signal A, 265 nm/Bw:4 nm	3.733	1734	0.09	395
3	DAD: Signal A, 265 nm/Bw:4 nm	4.038	1640	0.08	329

Processed Channel: DAD: Signal A, 265 nm/Bw:4 nm

	Processed Channel	Retention Time (min)	Area	% Area	Height
4	DAD: Signal A, 265 nm/Bw:4 nm	4.625	1550	0.08	390
5	DAD: Signal A, 265 nm/Bw:4 nm	5.087	3144	0.16	533
6	DAD: Signal A, 265 nm/Bw:4 nm	5.212	2596	0.13	865
7	DAD: Signal A, 265 nm/Bw:4 nm	5.592	70336	3.63	23648
8	DAD: Signal A, 265 nm/Bw:4 nm	5.763	1104	0.06	327
9	DAD: Signal A, 265 nm/Bw:4 nm	5.839	630	0.03	252
10	DAD: Signal A, 265 nm/Bw:4 nm	5.926	1407178	72.65	460152
11	DAD: Signal A, 265 nm/Bw:4 nm	6.077	4066	0.21	1055
12	DAD: Signal A, 265 nm/Bw:4 nm	6.196	5397	0.28	1258
13	DAD: Signal A, 265 nm/Bw:4 nm	6.307	960	0.05	333
14	DAD: Signal A, 265 nm/Bw:4 nm	6.401	9193	0.47	2411
15	DAD: Signal A, 265 nm/Bw:4 nm	6.612	2908	0.15	853
16	DAD: Signal A, 265 nm/Bw:4 nm	6.691	10225	0.53	3470
17	DAD: Signal A, 265 nm/Bw:4 nm	6.761	14164	0.73	4265
18	DAD: Signal A, 265 nm/Bw:4 nm	6.875	7975	0.41	2423
19	DAD: Signal A, 265 nm/Bw:4 nm	7.024	22511	1.16	6904
20	DAD: Signal A, 265 nm/Bw:4 nm	7.186	1735	0.09	729
21	DAD: Signal A, 265 nm/Bw:4 nm	7.252	14752	0.76	4027
22	DAD: Signal A, 265 nm/Bw:4 nm	7.393	14170	0.73	4966
23	DAD: Signal A, 265 nm/Bw:4 nm	7.453	26590	1.37	4656
24	DAD: Signal A, 265 nm/Bw:4 nm	7.686	41967	2.17	10113
25	DAD: Signal A, 265 nm/Bw:4 nm	7.871	18441	0.95	4400
26	DAD: Signal A, 265 nm/Bw:4 nm	7.962	14967	0.77	3381
27	DAD: Signal A, 265 nm/Bw:4 nm	8.066	45988	2.37	8545
28	DAD: Signal A, 265 nm/Bw:4 nm	8.240	48300	2.49	14029
29	DAD: Signal A, 265 nm/Bw:4 nm	8.346	12463	0.64	3779
30	DAD: Signal A, 265 nm/Bw:4 nm	8.402	7009	0.36	1927
31	DAD: Signal A, 265 nm/Bw:4 nm	8.550	68911	3.56	18897
32	DAD: Signal A, 265 nm/Bw:4 nm	8.708	3840	0.20	987
33	DAD: Signal A, 265 nm/Bw:4 nm	8.811	6956	0.36	1775
34	DAD: Signal A, 265 nm/Bw:4 nm	8.909	13878	0.72	3454
35	DAD: Signal A, 265 nm/Bw:4 nm	9.011	13715	0.71	2490
36	DAD: Signal A, 265 nm/Bw:4 nm	9.201	2139	0.11	571
37	DAD: Signal A, 265 nm/Bw:4 nm	9.266	1342	0.07	508
38	DAD: Signal A, 265 nm/Bw:4 nm	9.342	4344	0.22	937
39	DAD: Signal A, 265 nm/Bw:4 nm	9.392	1008	0.05	487
40	DAD: Signal A, 265 nm/Bw:4 nm	9.428	2000	0.10	419
41	DAD: Signal A, 265 nm/Bw:4 nm	9.578	721	0.04	164
42	DAD: Signal A, 265 nm/Bw:4 nm	9.658	631	0.03	188
43	DAD: Signal A, 265 nm/Bw:4 nm	9.797	970	0.05	247

Processed Channel: DAD: Signal A, 265 nm/Bw:4 nm

	Processed Channel	Retention Time (min)	Area	% Area	Height
44	DAD: Signal A, 265 nm/Bw:4 nm	9.899	999	0.05	206
45	DAD: Signal A, 265 nm/Bw:4 nm	10.346	853	0.04	270

Supernatant at the end of SPACEDKR (chiral LC)

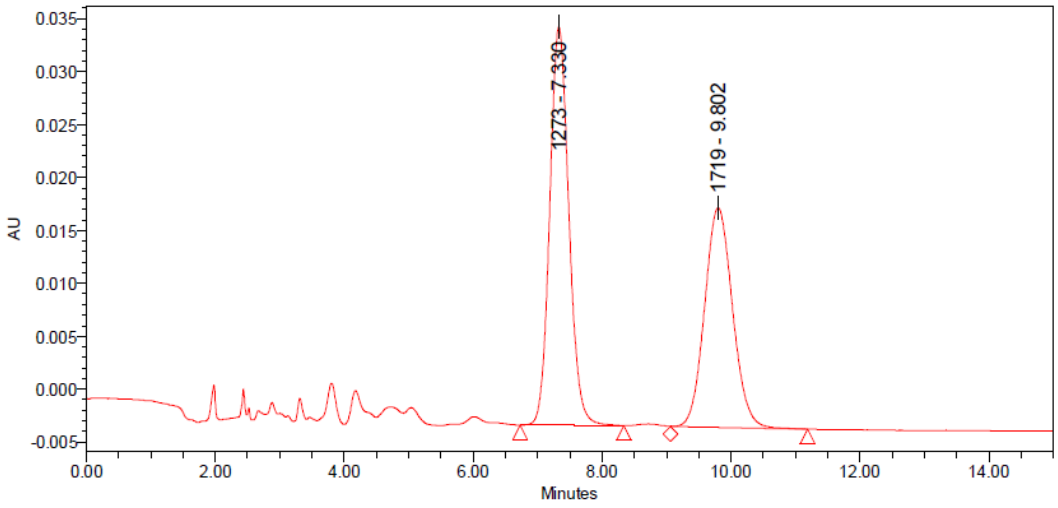
Empower 3 SOFTWARE

1719

SAMPLE INFORMATION

Sample Name:	NB51-40-6ML 28h,100xdil	Acquired By:	AchmatowiczM
Sample Type:	Unknown	Sample Set Name:	MA_Agilent1_04292022c
Vial:	1:B,7	Acq. Method Set:	HPLC000305_Chiral
Injection #:	1	Processing Method:	1719 chiral purity v2
Injection Volume:	5.00 ul	Channel Name:	MWD.0.0
Run Time:	15.0 Minutes	Proc. Chnl. Descr.:	MWD: Signal A, 265 nm/Bw:4 nm
Date Acquired:	4/29/2022 2:33:32 PM PDT		
Date Processed:	6/13/2022 2:42:59 PM PDT		

Auto-Scaled Chromatogram



Peak Results

	Name	RT	Area	Height	Amount	% Area
1	1273	7.330	774227	37645		55.30
2	1719	9.802	625918	20752		44.70

Processed Channel: MWD: Signal A, 265 nm/Bw:4 nm

	Peak Name	Processed Channel	Retention Time (min)	Area	% Area	Height
1	1273	MWD: Signal A, 265 nm/Bw:4 nm	7.330	774227	55.30	37645
2	1719	MWD: Signal A, 265 nm/Bw:4 nm	9.802	625918	44.70	20752

Technical-grade MRTX1719 (achiral LC)

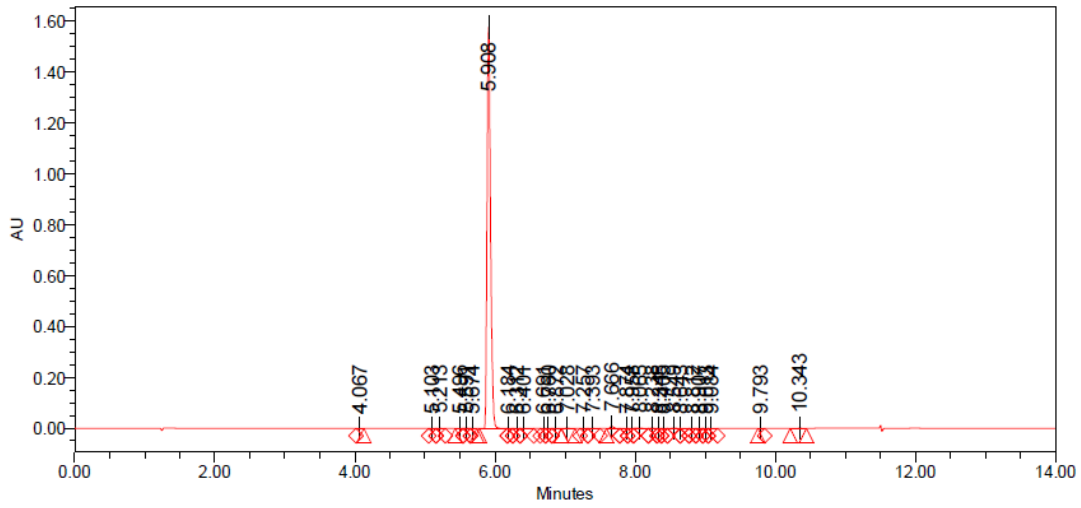
Empower 3 SOFTWARE

1719

SAMPLE INFORMATION

Sample Name:	NB51-40-11 solid,0.618uncorr	Acquired By:	AchmatowiczM
Sample Type:	Unknown	Sample Set Name:	MA_Agilent5_05032022a
Vial:	1:E,6	Acq. Method Set:	MRTX1719_AgilentLC5_14min
Injection #:	1	Processing Method:	1719_14min
Injection Volume:	5.00 ul	Channel Name:	DAD.0.0
Run Time:	14.0 Minutes	Proc. Chnl. Descr.:	DAD: Signal A, 265 nm/Bw:4 nm
Date Acquired:	5/3/2022 7:17:16 PM PDT		
Date Processed:	6/13/2022 2:15:19 PM PDT		

Auto-Scaled Chromatogram



Peak Results

	Name	RT	Area	Height	Amount	% Area
1		4.067	996	371		0.02
2		5.103	2455	823		0.04
3		5.213	4107	1413		0.07
4		5.496	2193	679		0.04
5		5.591	7552	2598		0.13
6		5.674	929	341		0.02
7		5.908	5489456	1578857		98.01
8		6.184	1114	342		0.02
9		6.312	1906	568		0.03
10		6.401	3499	798		0.06

Peak Results

	Name	RT	Area	Height	Amount	% Area
11		6.691	1330	465		0.02
12		6.760	1950	623		0.03
13		6.872	1050	283		0.02
14		7.028	7279	2365		0.13
15		7.257	1973	514		0.04
16		7.393	6026	1227		0.11
17		7.666	25141	7541		0.45
18		7.874	1929	597		0.03
19		7.958	4135	1005		0.07
20		8.065	13026	1836		0.23
21		8.238	5934	1674		0.11
22		8.345	1410	459		0.03
23		8.405	1178	325		0.02
24		8.549	8271	2119		0.15
25		8.643	870	235		0.02
26		8.812	695	218		0.01
27		8.907	857	277		0.02
28		9.013	763	259		0.01
29		9.084	1546	398		0.03
30		9.793	576	209		0.01
31		10.343	871	244		0.02

Processed Channel: DAD: Signal A, 265 nm/Bw:4 nm

	Processed Channel	Retention Time (min)	Area	% Area	Height
1	DAD: Signal A, 265 nm/Bw:4 nm	4.067	996	0.02	371
2	DAD: Signal A, 265 nm/Bw:4 nm	5.103	2455	0.04	823
3	DAD: Signal A, 265 nm/Bw:4 nm	5.213	4107	0.07	1413
4	DAD: Signal A, 265 nm/Bw:4 nm	5.496	2193	0.04	679
5	DAD: Signal A, 265 nm/Bw:4 nm	5.591	7552	0.13	2598
6	DAD: Signal A, 265 nm/Bw:4 nm	5.674	929	0.02	341
7	DAD: Signal A, 265 nm/Bw:4 nm	5.908	5489456	98.01	1578857
8	DAD: Signal A, 265 nm/Bw:4 nm	6.184	1114	0.02	342
9	DAD: Signal A, 265 nm/Bw:4 nm	6.312	1906	0.03	568
10	DAD: Signal A, 265 nm/Bw:4 nm	6.401	3499	0.06	798
11	DAD: Signal A, 265 nm/Bw:4 nm	6.691	1330	0.02	465
12	DAD: Signal A, 265 nm/Bw:4 nm	6.760	1950	0.03	623
13	DAD: Signal A, 265 nm/Bw:4 nm	6.872	1050	0.02	283
14	DAD: Signal A, 265 nm/Bw:4 nm	7.028	7279	0.13	2365
15	DAD: Signal A, 265 nm/Bw:4 nm	7.257	1973	0.04	514
16	DAD: Signal A, 265 nm/Bw:4 nm	7.393	6026	0.11	1227
17	DAD: Signal A, 265 nm/Bw:4 nm	7.666	25141	0.45	7541

Processed Channel: DAD: Signal A, 265 nm/Bw:4 nm

	Processed Channel	Retention Time (min)	Area	% Area	Height
18	DAD: Signal A, 265 nm/Bw:4 nm	7.874	1929	0.03	597
19	DAD: Signal A, 265 nm/Bw:4 nm	7.958	4135	0.07	1005
20	DAD: Signal A, 265 nm/Bw:4 nm	8.065	13026	0.23	1836
21	DAD: Signal A, 265 nm/Bw:4 nm	8.238	5934	0.11	1674
22	DAD: Signal A, 265 nm/Bw:4 nm	8.345	1410	0.03	459
23	DAD: Signal A, 265 nm/Bw:4 nm	8.405	1178	0.02	325
24	DAD: Signal A, 265 nm/Bw:4 nm	8.549	8271	0.15	2119
25	DAD: Signal A, 265 nm/Bw:4 nm	8.643	870	0.02	235
26	DAD: Signal A, 265 nm/Bw:4 nm	8.812	695	0.01	218
27	DAD: Signal A, 265 nm/Bw:4 nm	8.907	857	0.02	277
28	DAD: Signal A, 265 nm/Bw:4 nm	9.013	763	0.01	259
29	DAD: Signal A, 265 nm/Bw:4 nm	9.084	1546	0.03	398
30	DAD: Signal A, 265 nm/Bw:4 nm	9.793	576	0.01	209
31	DAD: Signal A, 265 nm/Bw:4 nm	10.343	871	0.02	244

Technical-grade MRTX1719 (chiral LC)

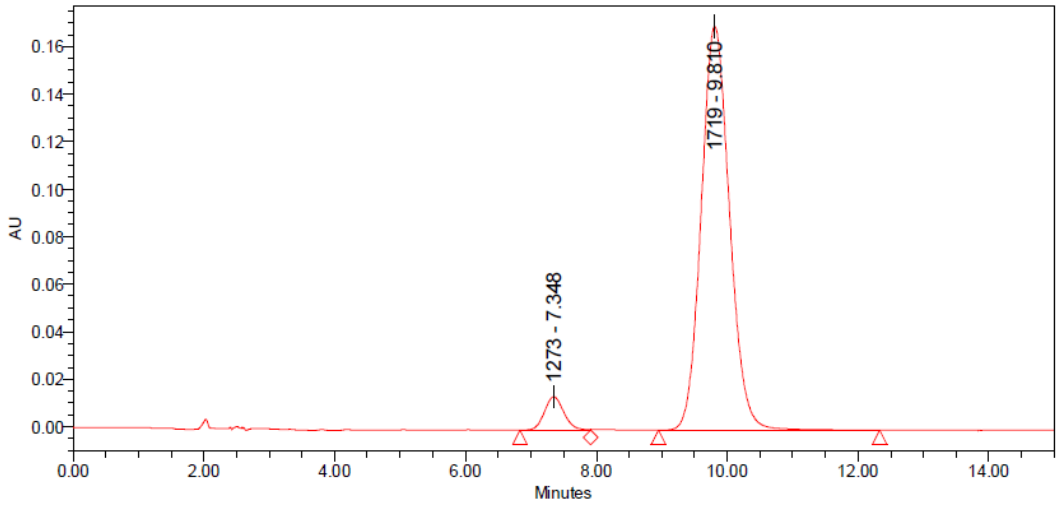
Empower 3 SOFTWARE

1719

SAMPLE INFORMATION

Sample Name:	NB51-40-11 solid, 0.618 uncorr	Acquired By:	AchmatowiczM
Sample Type:	Unknown	Sample Set Name:	MA_Agilent1_05022022b
Vial:	1:D,1	Acq. Method Set:	HPLC000305_Chiral
Injection #:	1	Processing Method:	1719 chiral purity v2
Injection Volume:	5.00 ul	Channel Name:	MWD.0.0
Run Time:	15.0 Minutes	Proc. Chnl. Descr.:	MWD: Signal A, 265 nm/Bw:4 nm
Date Acquired:	5/2/2022 1:00:49 PM PDT		
Date Processed:	6/13/2022 2:40:57 PM PDT		

Auto-Scaled Chromatogram



Peak Results

	Name	RT	Area	Height	Amount	% Area
1	1273	7.348	289067	13980		5.35
2	1719	9.810	5115239	169823		94.65

Processed Channel: MWD: Signal A, 265 nm/Bw:4 nm

	Peak Name	Processed Channel	Retention Time (min)	Area	% Area	Height
1	1273	MWD: Signal A, 265 nm/Bw:4 nm	7.348	289067	5.35	13980
2	1719	MWD: Signal A, 265 nm/Bw:4 nm	9.810	5115239	94.65	169823

Upraded MRTX1719 (achiral LC)

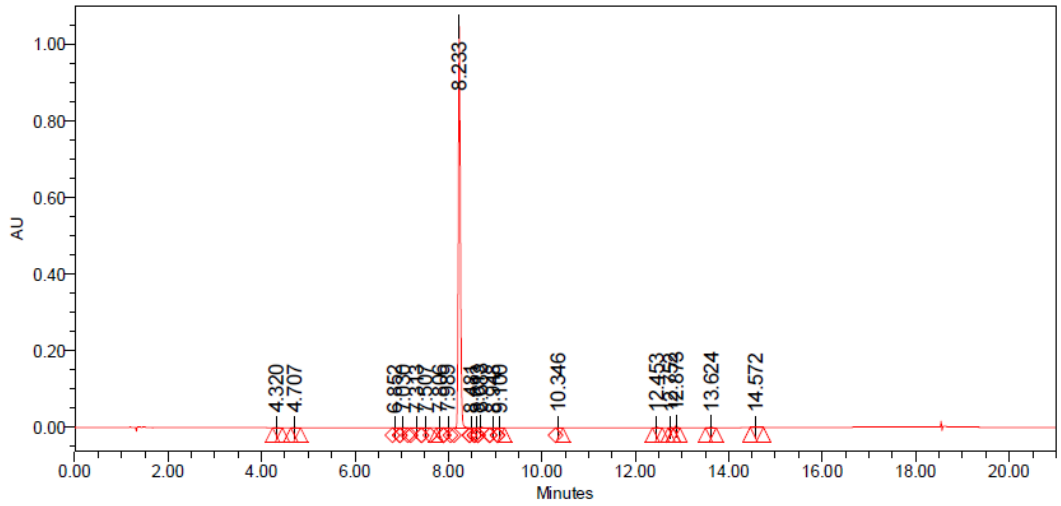
Empower 3 SOFTWARE

1719

SAMPLE INFORMATION

Sample Name:	NB51-40-210S solid,20-40Cx4	Acquired By:	AchmatowiczM
Sample Type:	Unknown	Sample Set Name:	MA_Agilent5_05182022a
Vial:	1:B,3	Acq. Method Set:	AgilentLC5_MRTX1719_Purity
Injection #:	1	Processing Method:	1719_14min
Injection Volume:	5.00 ul	Channel Name:	DAD.0.0
Run Time:	21.0 Minutes	Proc. Chnl. Descr.:	DAD: Signal A, 265 nm/Bw:4 nm
Date Acquired:	5/18/2022 12:50:46 PM PDT		
Date Processed:	6/13/2022 2:27:05 PM PDT		

Auto-Scaled Chromatogram



Peak Results

	Name	RT	Area	Height	Amount	% Area
1		4.320	1077	251		0.03
2		4.707	1758	410		0.05
3		6.852	1304	386		0.04
4		7.030	2226	681		0.07
5		7.313	1236	256		0.04
6		7.507	1277	307		0.04
7		7.806	856	238		0.03
8		7.989	1928	513		0.06
9		8.233	3231703	1046318		98.00
10		8.481	2030	478		0.06

Peak Results

	Name	RT	Area	Height	Amount	% Area
11		8.613	1367	428		0.04
12		8.688	10844	2661		0.33
13		8.948	1296	280		0.04
14		9.100	773	179		0.02
15		10.346	2426	753		0.07
16		12.453	6742	2284		0.20
17		12.752	4638	1760		0.14
18		12.873	12624	4178		0.38
19		13.624	8347	2741		0.25
20		14.572	3349	893		0.10

Processed Channel: DAD: Signal A, 265 nm/Bw:4 nm

	Processed Channel	Retention Time (min)	Area	% Area	Height
1	DAD: Signal A, 265 nm/Bw:4 nm	4.320	1077	0.03	251
2	DAD: Signal A, 265 nm/Bw:4 nm	4.707	1758	0.05	410
3	DAD: Signal A, 265 nm/Bw:4 nm	6.852	1304	0.04	386
4	DAD: Signal A, 265 nm/Bw:4 nm	7.030	2226	0.07	681
5	DAD: Signal A, 265 nm/Bw:4 nm	7.313	1236	0.04	256
6	DAD: Signal A, 265 nm/Bw:4 nm	7.507	1277	0.04	307
7	DAD: Signal A, 265 nm/Bw:4 nm	7.806	856	0.03	238
8	DAD: Signal A, 265 nm/Bw:4 nm	7.989	1928	0.06	513
9	DAD: Signal A, 265 nm/Bw:4 nm	8.233	3231703	98.00	1046318
10	DAD: Signal A, 265 nm/Bw:4 nm	8.481	2030	0.06	478
11	DAD: Signal A, 265 nm/Bw:4 nm	8.613	1367	0.04	428
12	DAD: Signal A, 265 nm/Bw:4 nm	8.688	10844	0.33	2661
13	DAD: Signal A, 265 nm/Bw:4 nm	8.948	1296	0.04	280
14	DAD: Signal A, 265 nm/Bw:4 nm	9.100	773	0.02	179
15	DAD: Signal A, 265 nm/Bw:4 nm	10.346	2426	0.07	753
16	DAD: Signal A, 265 nm/Bw:4 nm	12.453	6742	0.20	2284
17	DAD: Signal A, 265 nm/Bw:4 nm	12.752	4638	0.14	1760
18	DAD: Signal A, 265 nm/Bw:4 nm	12.873	12624	0.38	4178
19	DAD: Signal A, 265 nm/Bw:4 nm	13.624	8347	0.25	2741
20	DAD: Signal A, 265 nm/Bw:4 nm	14.572	3349	0.10	893

Upraded MRTX1719 (chiral LC)

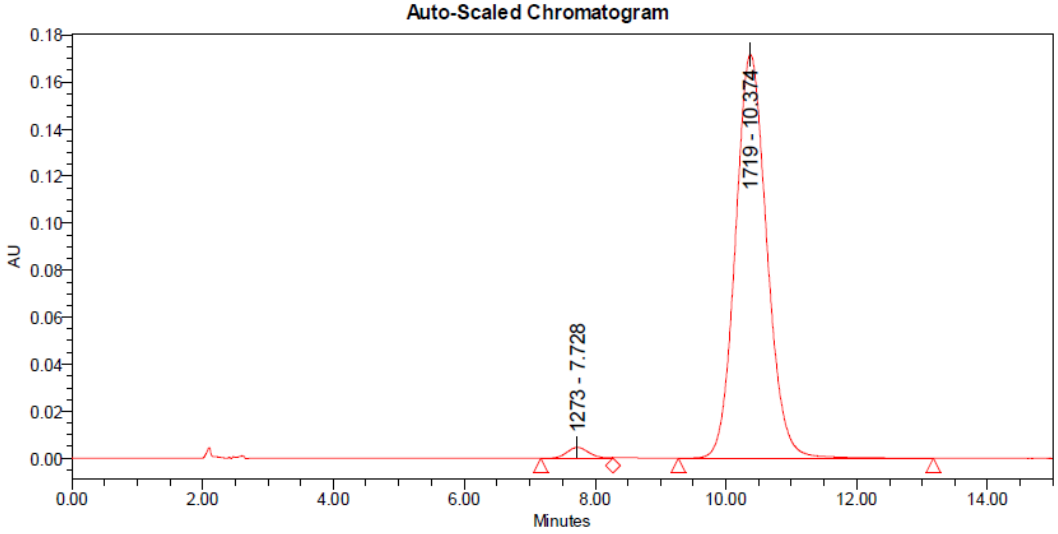
Empower 3 SOFTWARE

1719

SAMPLE INFORMATION

Sample Name:	NB51-40-220 0.626mg/mL uncorr	Acquired By:	AchmatowiczM
Sample Type:	Unknown	Sample Set Name:	MA_Agilent1_05242022a
Vial:	1:A,3	Acq. Method Set:	HPLC000305_Chiral
Injection #:	1	Processing Method:	1719 chiral purity
Injection Volume:	5.00 ul	Channel Name:	MWD.0.0
Run Time:	15.0 Minutes	Proc. Chnl. Descr.:	MWD: Signal A, 265 nm/Bw:4 nm
Date Acquired:	5/24/2022 10:29:00 AM PDT		
Date Processed:	6/13/2022 2:25:32 PM PDT		

Auto-Scaled Chromatogram



Peak Results

	Name	RT	Area	Height	Amount	% Area
1	1273	7.728	107806	4611		1.85
2	1719	10.374	5722739	171762		98.15

Processed Channel: MWD: Signal A, 265 nm/Bw:4 nm

	Peak Name	Processed Channel	Retention Time (min)	Area	% Area	Height
1	1273	MWD: Signal A, 265 nm/Bw:4 nm	7.728	107806	1.85	4611
2	1719	MWD: Signal A, 265 nm/Bw:4 nm	10.374	5722739	98.15	171762