

Supporting Information

A chiral switch: balancing between equilibrium and non-equilibrium states

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General remarks:

Chiral HPLC analyses were performed using an Agilent Technologies Infinity 1260 HPLC system equipped with a Chiralpak IA (250 x 4.6 mm, 5 μ m) column; eluent: *n*-heptane/isopropanol: 95/5 (v/v); flow rate: 0.7 mL/min; UV-light detector: 220 nm). Glass beads (borosilicate, diam. 2 mm) were purchased from Sigma-Aldrich. 20 mL vials used (WHEATON® 180 low potassium borosilicate glass) were purchased from VWR International. Compounds **1**, **2** and **3** were obtained in course of the previous research.^{1,2}

Experimental Section:

Note, the procedure below is representative for all Chiral Switches performed.

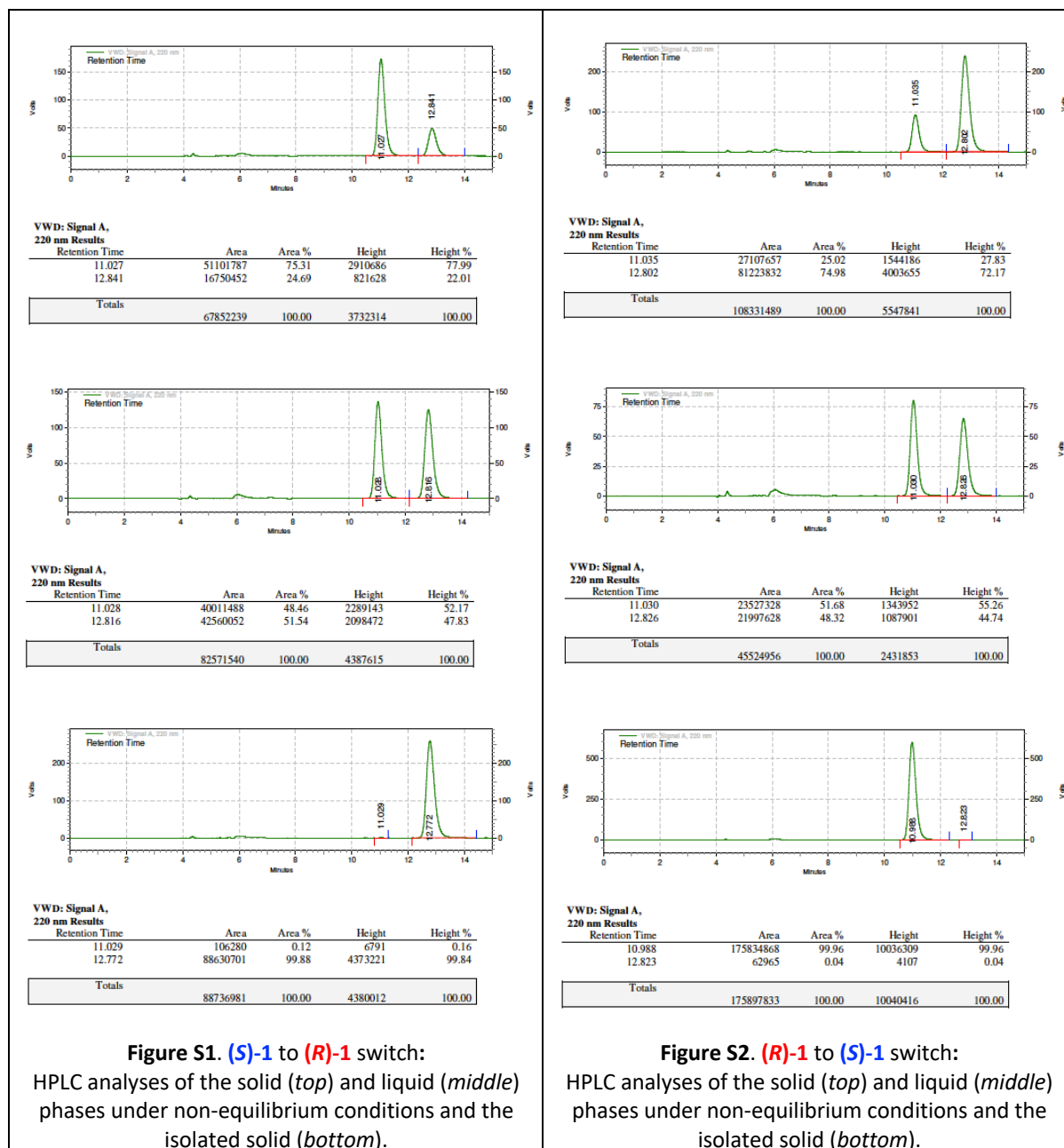
A screw cap 20 mL vial was charged with 2 mm glass beads (10 g), racemic conglomerate, pure enantiomer (either *R* or *S*) and solvent (12 mL). The vial was placed in an ultrasonic bath, equipped with a thermostat, and sonicated for 2 hours at 20 °C. Then, the slurry was rapidly (within *ca.* 30 seconds) filtered through a P4 filter providing an enantiomerically enriched liquid phase. The isolated liquid phase (10 mL) was added into a 20 mL vial charged with the corresponding racemate (1.0 g) and glass beads (10 g). The resulting mixture was sonicated at 20 °C for 1 hour followed by addition of the racemization catalyst (1,8-diazabicyclo[5.4.0]undec-7-ene (DBU)). The resulting slurry was sonicated at 20°C for 24 hours. The suspension was replaced into a P4 filter, using a Pasteur's pipet to separate the suspension and glass beads, and filtered. The isolated solid was rinsed with the corresponding solvent (2 x 3.0 mL) and dried to afford the desired material.

Table S1. Summary of the Chiral Switch experiments

Starting solid material			Solvent used	non-equilibrium		DBU added, μ L	Chiral Switch outcome (ee, %); (m, g)
Racemate (m, g)	Enantiomer (m, g)	ee*, %		solid phase ee, %	liquid phase ee, %		
(RS)-1 (0.65 g)	(S)-1 (0.5 g)	(S)-1 (43.5%)	MeCN	(S)-1 (50.6%)	(R)-1 (3.1%)	180 μ L	(R)-1 (99.8%) 0.87 g
(RS)-1 (0.65 g)	(R)-1 (0.5 g)	(R)-1 (43.5%)	MeCN	(R)-1 (50.0%)	(S)-1 (3.4%)	180 μ L	(S)-1 (99.9%) 0.85 g
(RS)-2 (0.6 g)	(S)-2 (0.6 g)	(S)-2 (50.0%)	MeOH	(S)-2 (61.7%)	(R)-2 (0.2%)	180 μ L	(R)-2 (99.3%) 0.81 g
(RS)-2 (0.6 g)	(R)-2 (0.6 g)	(R)-2 (50.0%)	MeOH	(R)-2 (60.9%)	(S)-2 (0.8%)	180 μ L	(S)-2 (98.7%) 0.79 g
(RS)-3 (0.6 g)	(S)-3 (0.6 g)	(S)-3 (50.0%)	MeCN	(S)-3 (52.6%)	(R)-3 (2.3%)	150 μ L	(R)-3 (99.5%) 0.86 g
(RS)-3 (0.6 g)	(R)-3 (0.6 g)	(R)-3 (50.0%)	MeCN	(R)-3 (51.9%)	(S)-3 (1.9%)	150 μ L	(S)-3 (99.1%) 0.82 g

* calculated based on the weighed amounts of racemates and enantiomerically pure materials used.

Chiral HPLC analyses:



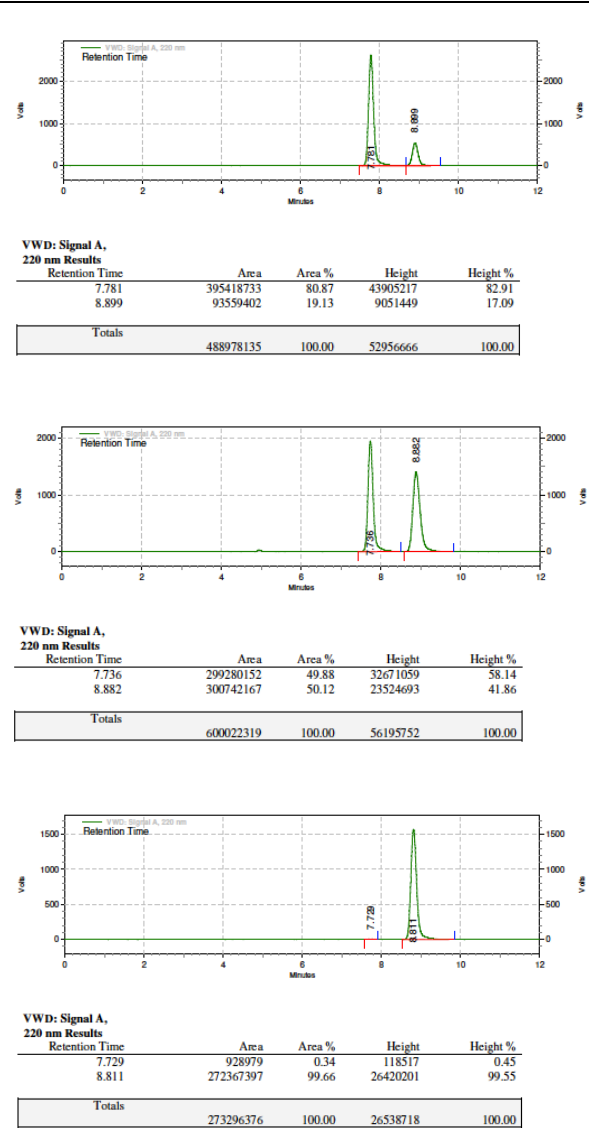


Figure S3. (S)-2 to (R)-2 switch:
HPLC analyses of the solid (*top*) and liquid (*middle*) phases under non-equilibrium conditions and the isolated solid (*bottom*).

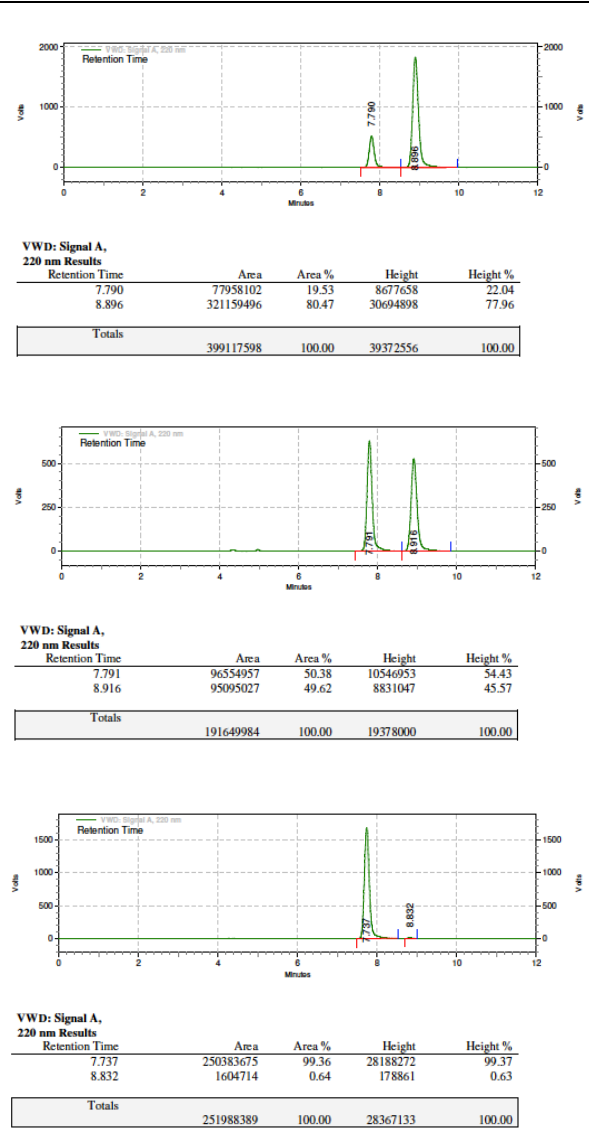
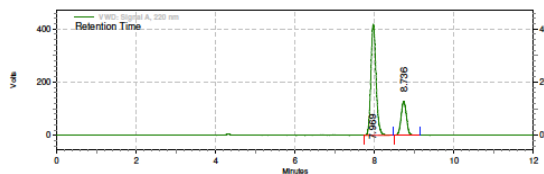
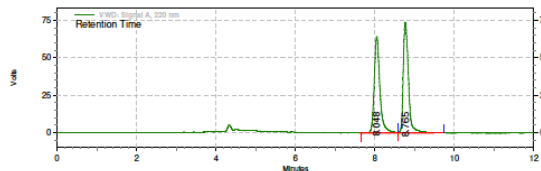


Figure S4. (R)-2 to (S)-2 switch:
HPLC analyses of the solid (*top*) and liquid (*middle*) phases under non-equilibrium conditions and the isolated solid (*bottom*).



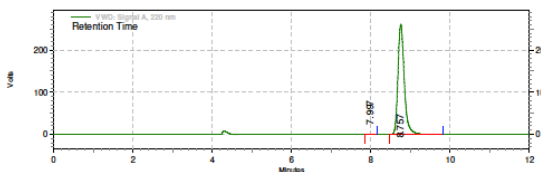
VWD: Signal A,
220 nm Results

Retention Time	Area	Area %	Height	Height %
7.969	63432970	76.30	7008860	76.81
8.736	19706155	23.70	2115832	23.19
Totals	83139125	100.00	9124692	100.00



VWD: Signal A,
220 nm Results

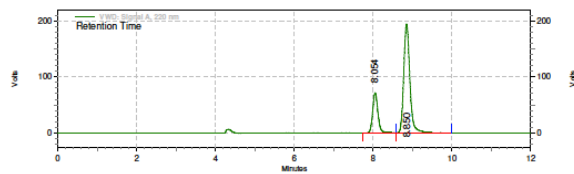
Retention Time	Area	Area %	Height	Height %
8.048	10613690	48.86	1077857	46.52
8.765	11107326	51.14	1239290	53.48
Totals	21721016	100.00	2317147	100.00



VWD: Signal A,
220 nm Results

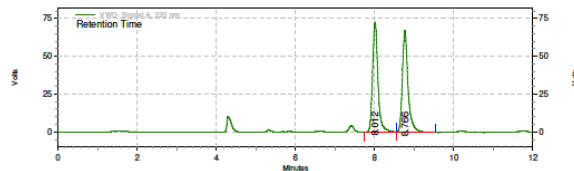
Retention Time	Area	Area %	Height	Height %
7.997	111373	0.23	13012	0.30
8.757	48463650	99.77	4389851	99.70
Totals	48575023	100.00	4402863	100.00

Figure S5. (S)-3 to (R)-3 switch:
HPLC analyses of the solid (*top*) and liquid (*middle*)
phases under non-equilibrium conditions and the
isolated solid (*bottom*).



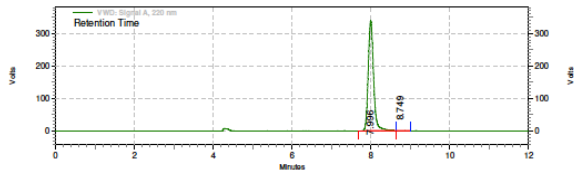
VWD: Signal A,
220 nm Results

Retention Time	Area	Area %	Height	Height %
8.054	11209535	24.07	1197733	26.87
8.850	35359230	75.93	3259180	73.13
Totals	46568765	100.00	4456913	100.00



VWD: Signal A,
220 nm Results

Retention Time	Area	Area %	Height	Height %
8.012	11659814	50.97	1220728	51.93
8.766	11214231	49.03	1130179	48.07
Totals	22874045	100.00	2350907	100.00



VWD: Signal A,
220 nm Results

Retention Time	Area	Area %	Height	Height %
7.996	54082820	99.57	5690353	99.68
8.749	231575	0.43	18278	0.32
Totals	54314395	100.00	5708631	100.00

Figure S6. (R)-3 to (S)-3 switch:
HPLC analyses of the solid (*top*) and liquid (*middle*)
phases under non-equilibrium conditions and the
isolated solid (*bottom*).

References:

- 1 M. van der Meijden, M. Leeman, E. Gelens, W. L. Noorduin, H. Meekes, W. J. P. van Enkevort, B. Kaptein, E. Vlieg and R. M. Kellogg, *Org. Process Res. Dev.*, 2009, **13**, 1195–1198.
- 2 I. Baglai, M. Leeman, K. Wurst, B. Kaptein, R. M. Kellogg and W. L. Noorduin, *Chem. Commun.*, 2018, **54**, 10832–10834.