Electronic Supplementary Material (ESI) for RSC Advances.

Supporting information

A comprehensive examination of the self-disproportionation of enantiomers (SDE) of chiral amides via achiral, laboratory-routine, gravity-driven column chromatography

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CONTENTS

Materials and methods.
Hexane and ethyl acetate (EtOAc) were purchased from OPPAC, S.A. (Spain) and used without further purification. Silica gel for chromatography, sizes 40–63 μm (230–400 mesh) and 60–200 μm (70–230 mesh) were purchased from Rocc and Acros, respectively. Aluminum oxide (neutral, Grade I) was purchased from Acros. Amides **1**–**9** are known compounds and were prepared by acylation of their amine precursors. Both enantiomeric samples of each amine were used, and the corresponding amides were mixed in the desired ratio in order to obtain the required samples for the SDE experiments. Gas chromatographic analysis was performed on a Thermo Scientific-Trace 1300 instrument using a Hydrodex β-6TBDM chiral column (25 m × 0.25 mm i.d.).

General procedure for the SDE experiments.
A sample of the corresponding optically enriched amide was eluted on a chromatographic column using the stationary phase and eluent indicated on each case. The column flow rate was targeted to 10 mL/3–6 mins and a number of fractions were collected (10 mL each). Analysis of each fraction was performed by gas chromatography.

Table S1. Chromatography of amide **1** with 72.3% ee on silica gel (50 mg of compound **1** per 6.3 g of silica gel, 60 Å pore size, 40–63 μm particle size) on a column 20 mm in diameter and length 45 mm. Eluent: hexane/EtOAc, 5:3.

Fraction	Volume (mL)	% weight	ee (%)
1	10	0.09	89.0
2	20	1.42	92.5
3	30	9.76	90.4
4	40	6.35	84.7
5	50	15.98	77.0
6	60	7.61	70.5
7	70	15.25	66.0
8	80	14.40	62.3
9	90	11.27	59.8
10	100	8.89	56.3
11	110	2.29	53.2
12	120	3.47	54.7
13	130	1.35	49.1
14	140	1.86	46.3

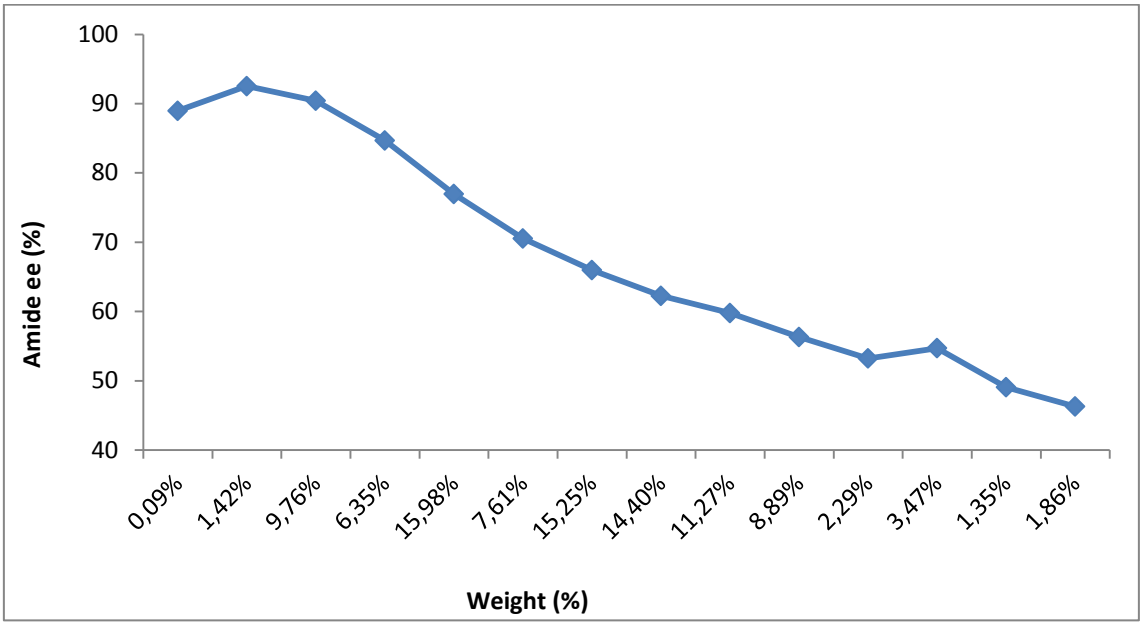

Figure S1. Graphical representation of Table S1 (% ee of each fraction vs the weight percent of each fraction).

Table S2. Chromatography of amide **1** with 72.3% ee on silica gel (50 mg of compound **1** per 6.3 g of silica gel, 60 Å pore size, 40–63 μm particle size) on a column 20 mm in diameter and length 45 mm. Eluent: hexane/EtOAc, 5:4.

Fraction	Volume (mL)	% weight	ee (%)
1	10	5.16	92.1
2	20	12.87	92.0
3	30	24.35	82.3
4	40	21.26	72.3
5	50	6.87	66.0
6	60	13.48	60.9
7	70	8.50	57.1
8	80	4.89	53.4
9	90	0.99	51.2
10	100	1.63	51.1

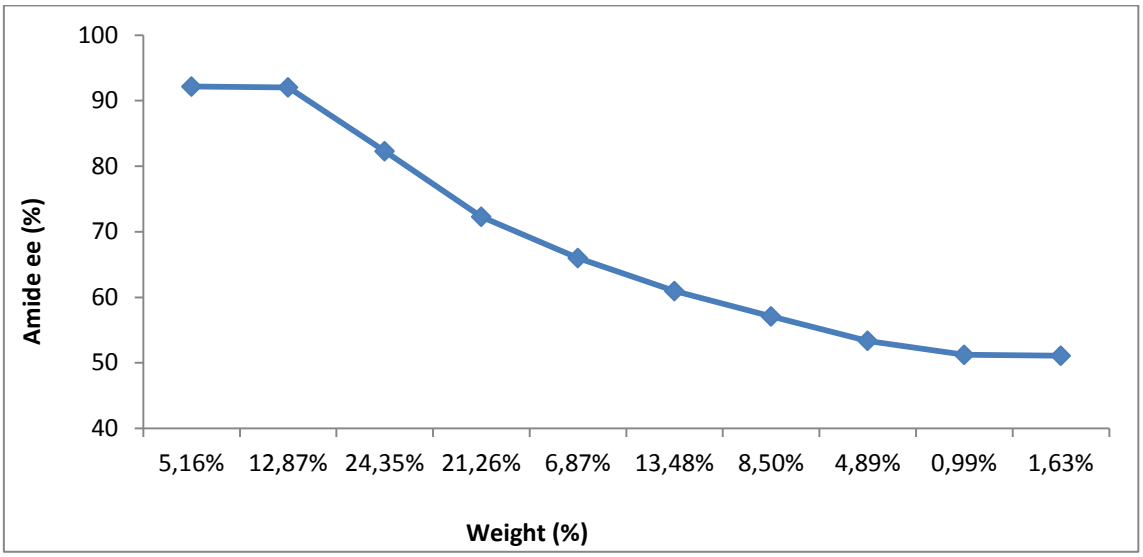

Figure S2. Graphical representation of Table S2 (% ee of each fraction vs the weight percent of each fraction).

Table S3. Chromatography of amide **1** with 72.3% ee on silica gel (50 mg of compound **1** per 6.3 g of silica gel, 60 Å pore size, 40–63 μm particle size) on a column 20 mm in diameter and length 45 mm. Eluent: hexane/EtOAc, 5:5.

Fraction	Volume (mL)	% weight	ee (%)
1	10	0.18	92.8
2	20	13.54	88.8
3	30	33.27	83.4
4	40	28.96	72.7
5	50	7.85	64.5
6	60	13.02	58.4
7	70	3.17	53.0

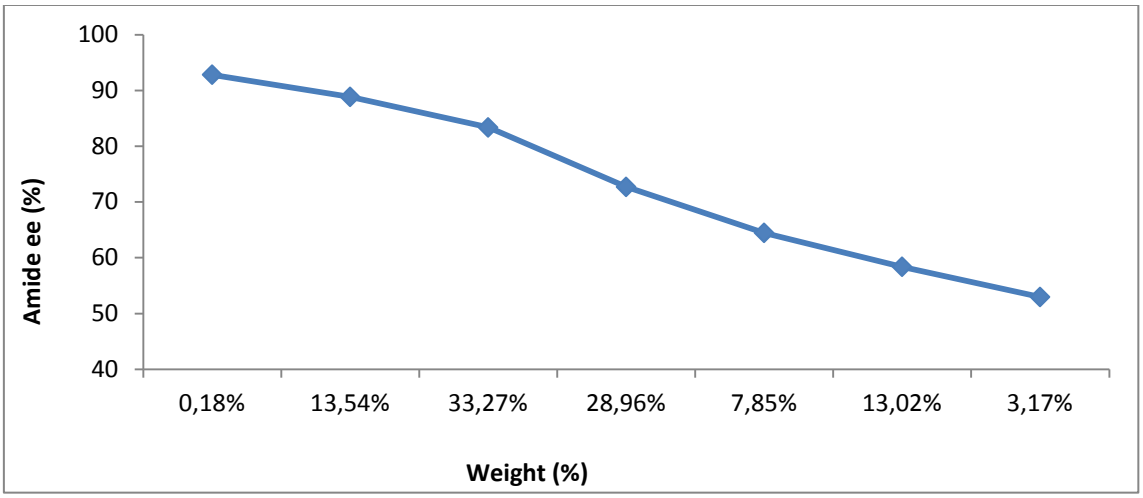

Figure S3. Graphical representation of Table S3 (% ee of each fraction vs the weight percent of each fraction).

Table S4. Chromatography of amide **1** with 72.3% ee on silica gel (50 mg of compound **1** per 6.3 g of silica gel, 60 Å pore size, 40–63 μm particle size) on a column 20 mm in diameter and length 45 mm. Eluent: hexane/EtOAc, 5:6.

Fraction	Volume (mL)	% weight	ee (%)
1	10	0.19	96.6
2	20	19.50	87.8
3	30	49.91	77.6
4	40	11.60	68.5
5	50	10.68	62.5
6	60	3.37	57.4
7	70	4.75	54.4

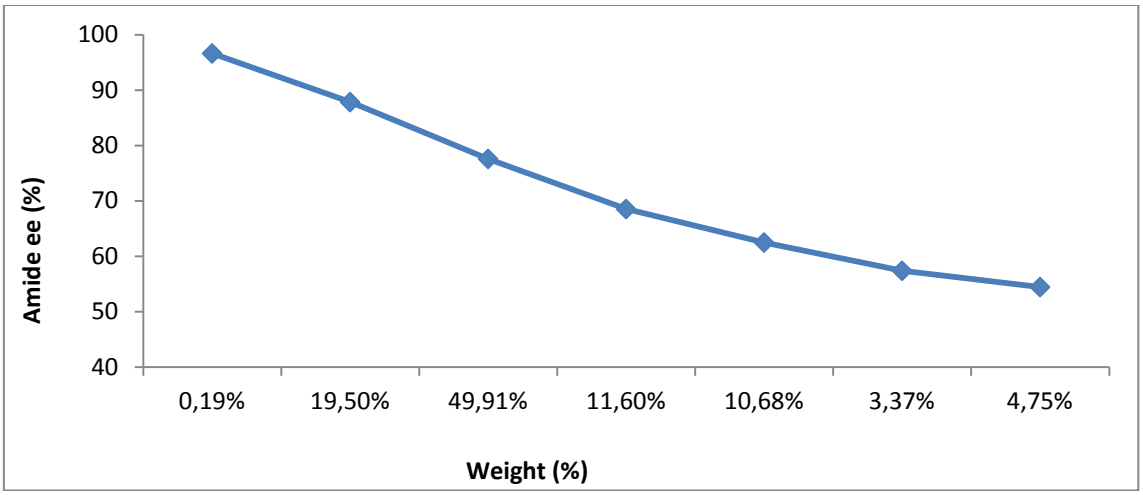

Figure S4. Graphical representation of Table S4 (% ee of each fraction vs the weight percent of each fraction).

Table S5. Chromatography of amide **1** with 72.3% ee on silica gel (100 mg of compound **1** per 6.3 g of silica gel, 60 Å pore size, 40–63 μm particle size) on a column 20 mm in diameter and length 45 mm. Eluent: hexane/EtOAc, 5:5.

Fraction	Volume (mL)	% weight	ee (%)
1	10	2.45	89.8
2	20	23.36	82.5
3	30	32.26	74.1
4	40	12.81	68.3
5	50	9.94	61.7
6	60	3.16	61.1
7	70	7.80	56.3
8	80	4.87	53.3
9	90	3.35	50.4

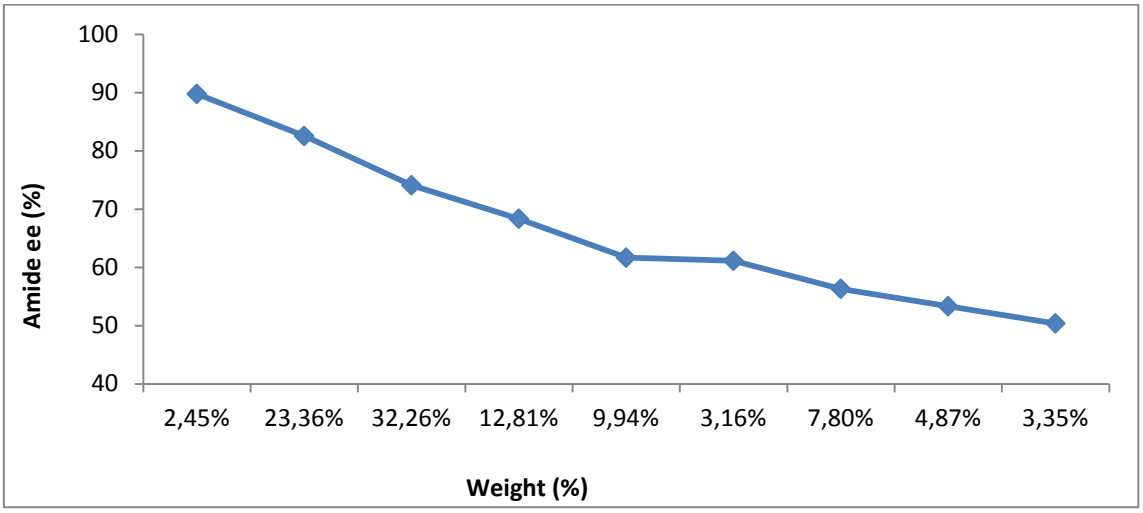

Figure S5. Graphical representation of Table S5 (% ee of each fraction vs the weight percent of each fraction).

Table S6. Chromatography of amide **1** with 72.3% ee on silica gel (50 mg of compound **1** per 12.6 g of silica gel, 60 Å pore size, 40–63 μm particle size) on a column 20 mm in diameter and length 90 mm. Eluent: hexane/EtOAc, 5:5.

Fraction	Volume (mL)	% weight	ee (%)
1	10	9.31	94.1
2	20	10.16	87.9
3	30	7.57	84.6
4	40	19.18	78.4
5	50	8.53	72.7
6	60	18.17	67.9
7	70	4.85	64.5
8	80	7.80	61.8
9	90	9.64	58.3
10	100	4.78	56.3

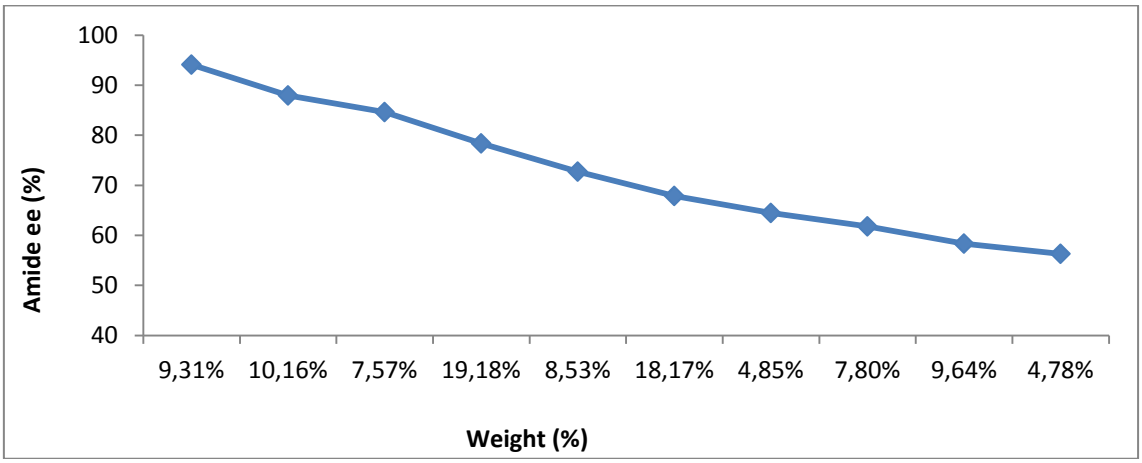

Figure S6. Graphical representation of Table S6 (% ee of each fraction vs the weight percent of each fraction).

Table S7. Chromatography of amide **1** with 72.3% ee on silica gel (50 mg of compound **1** per 6.3 g of silica gel, 60 Å pore size, 60-200 μm particle size) on a column 20 mm in diameter and length 45 mm. Eluent: hexane/EtOAc, 5:5.

Fraction	Volume (mL)	% weight	ee (%)
1	10	4.25	87.7
2	20	27.38	82.0
3	30	20.72	74.0
4	40	20.02	68.3
5	50	6.56	63.8
6	60	8.34	61.1
7	70	6.91	57.0
8	80	3.66	55.3
9	90	2.15	53.7

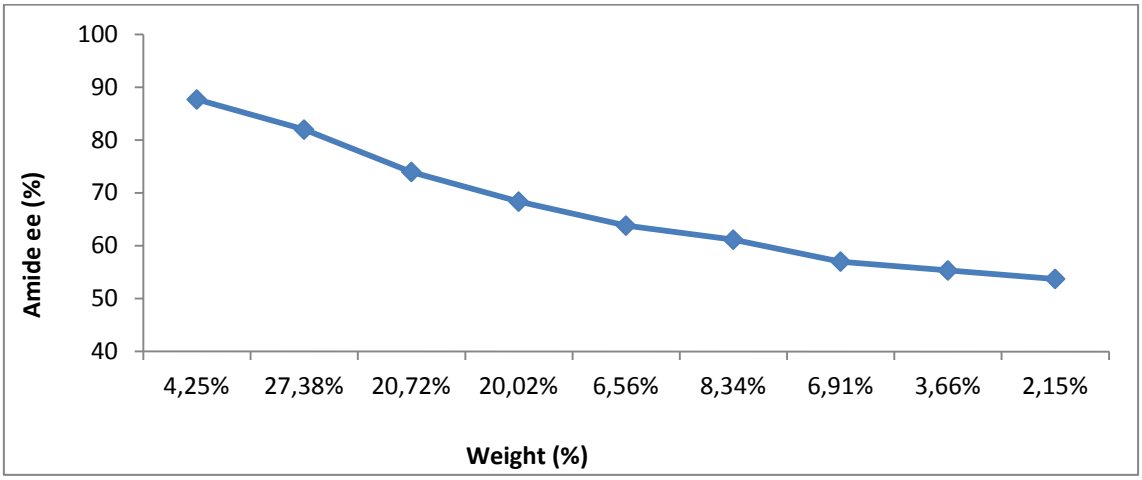

Figure S7. Graphical representation of Table S7 (% ee of each fraction vs the weight percent of each fraction).

Table S8. Chromatography of amide **1** with 72.3% ee on aluminium oxide (50 mg of compound **1** per 12.5 g of Al_2O_3, neutral, grade I) on a column 20 mm in diameter and length 45 mm. Eluent: hexane/EtOAc, 5:5.

Fraction	Volume (mL)	% weight	ee (%)
1	10	0.25	75.1
2	20	19.59	78.2
3	30	26.39	73.8
4	40	28.80	70.6
5	50	6.14	68.6
6	60	9.10	66.8
7	70	6.07	65.5
8	80	3.67	64.1

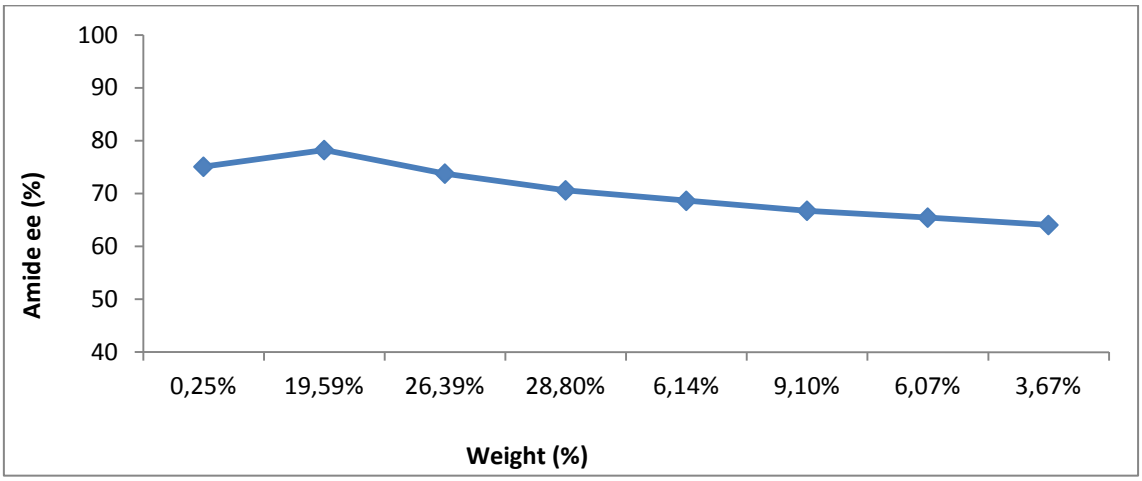

Figure S8. Graphical representation of Table S8 (% ee of each fraction vs the weight percent of each fraction).

Table S9. Chromatography of amide **1** with 89.9% ee on silica gel (50 mg of compound **1** per 6.3 g of silica gel, 60 Å pore size, 40–63 μm particle size) on a column 20 mm in diameter and length 45 mm. Eluent: hexane/EtOAc, 5:5.

Fraction	Volume (mL)	% weight	ee (%)
1	10	5.87	97.8
2	20	16.61	96.1
3	30	15.92	91.5
4	40	26.56	89.9
5	50	7.56	86.5
6	60	12.82	83.6
7	70	10.18	81.6
8	80	4.49	79.7

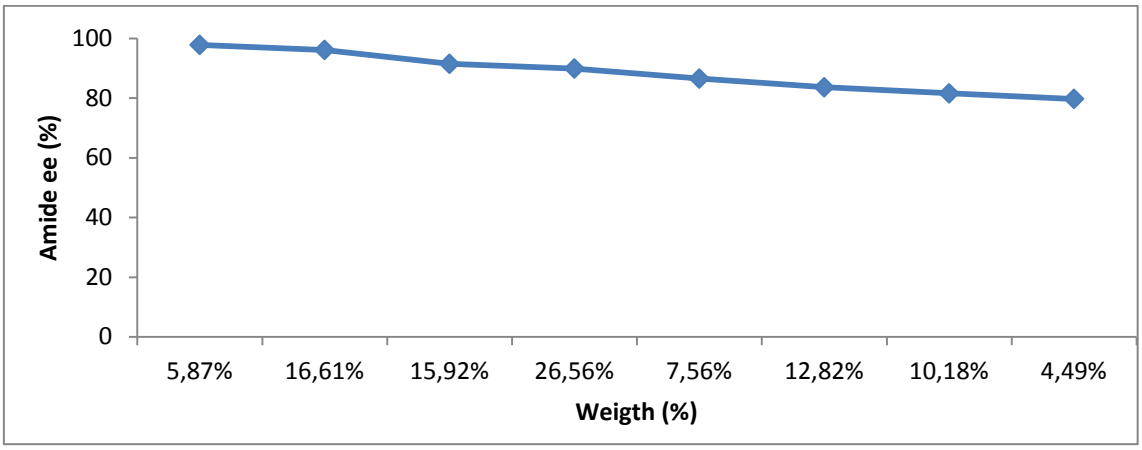

Figure S9. Graphical representation of Table S9 (% ee of each fraction vs the weight percent of each fraction).

Table S10. Chromatography of amide **1** with 78.1% ee on silica gel (50 mg of compound **1** per 6.3 g of silica gel, 60 Å pore size, 40–63 μm particle size) on a column 20 mm in diameter and length 45 mm. Eluent: hexane/EtOAc, 5:5.

Fraction	Volume (mL)	% weight	ee (%)
1	10	10.90	93.2
2	20	39.89	88.8
3	30	17.00	82.1
4	40	16.54	76.5
5	50	4.23	71.4
6	60	7.15	66.5
7	70	4.28	65.8

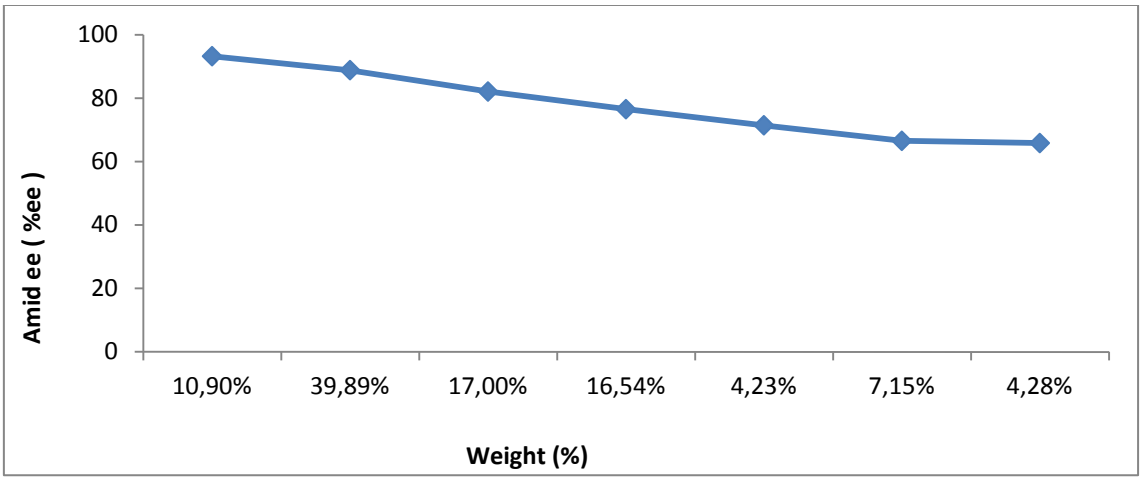

Figure S10. Graphical representation of Table S10 (% ee of each fraction vs the weight percent of each fraction).

Table S11. Chromatography of amide **1** with 59.3% ee on silica gel (50 mg of compound **1** per 6.3 g of silica gel, 60 Å pore size, 40–63 μm particle size) on a column 20 mm in diameter and length 45 mm. Eluent: hexane/EtOAc, 5:5.

Fraction	Volume (mL)	% weight	ee (%)
1	10	0.18	81.7
2	20	26.66	75.9
3	30	32.79	66.6
4	40	17.11	60.7
5	50	12.79	56.9
6	60	8.45	52.9
7	70	2.01	52.4

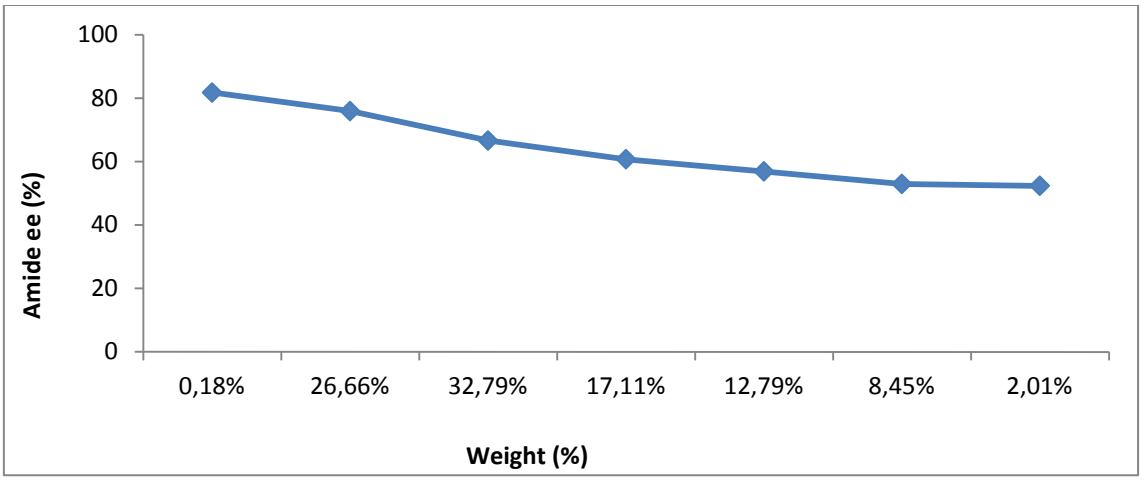

Figure S11. Graphical representation of Table S11 (% ee of each fraction vs the weight percent of each fraction).

Table S12. Chromatography of amide **1** with 53.7% ee on silica gel (50 mg of compound **1** per 6.3 g of silica gel, 60 Å pore size, 40–63 μm particle size) on a column 20 mm in diameter and length 45 mm. Eluent: hexane/EtOAc, 5:5.

Fraction	Volume (mL)	% weight	ee (%)
1	10	0.23	84.4
2	20	10.75	82.7
3	30	17.76	75.9
4	40	19.78	66.0
5	50	18.55	60.3
6	60	14.80	55.7
7	70	12.13	51.2
8	80	6.00	47.7

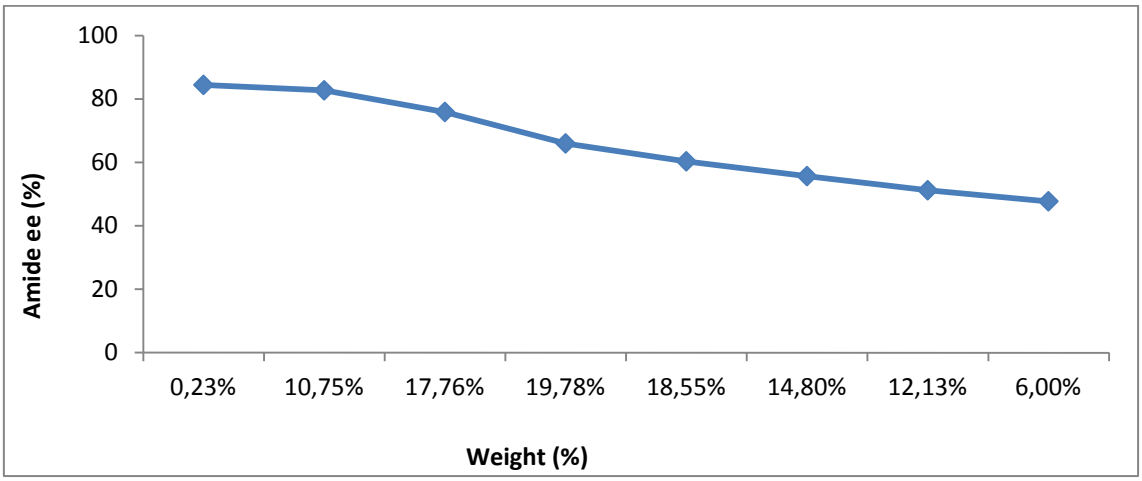

Figure S12. Graphical representation of Table S12 (% ee of each fraction vs the weight percent of each fraction).

Table S13. Chromatography of amide **1** with 44.8% ee on silica gel (50 mg of compound **1** per 6.3 g of silica gel, 60 Å pore size, 40–63 μm particle size) on a column 20 mm in diameter and length 45 mm. Eluent: hexane/EtOAc, 5:5.

Fraction	Volume (mL)	% weight	ee (%)
1	10	19.63	61.4
2	20	19.39	52.0
3	30	25.44	43.9
4	40	12.25	39.0
5	50	6.64	35.3
6	60	9.33	32.6
7	70	7.33	31.8

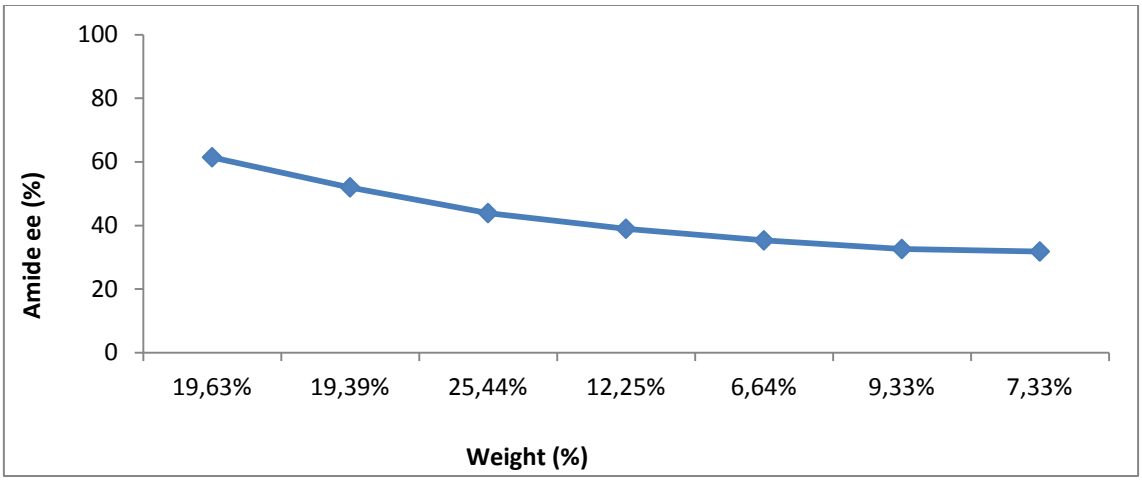

Figure S13. Graphical representation of Table S13 (% ee of each fraction vs the weight percent of each fraction).

Table S14. Chromatography of amide **1** with 30.5% ee on silica gel (50 mg of compound **1** per 6.3 g of silica gel, 60 Å pore size, 40–63 μm particle size) on a column 20 mm in diameter and length 45 mm. Eluent: hexane/EtOAc, 5:5.

Fraction	Volume (mL)	% weight	ee (%)
1	10	5.89	45.5
2	20	21.18	37.3
3	30	27.44	32.5
4	40	19.38	28.8
5	50	11.27	26.7
6	60	7.64	24.2
7	70	4.64	22.8
8	80	2.56	22.0

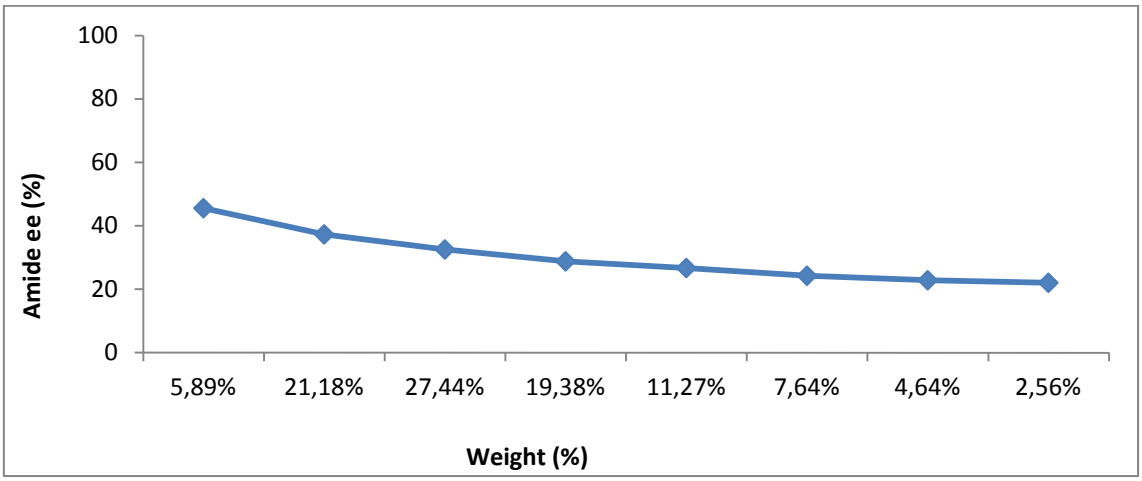

Figure S14. Graphical representation of Table S14 (% ee of each fraction vs the weight percent of each fraction).

Table S15. Chromatography of amide **1** with 21.9% ee on silica gel (50 mg of compound **1** per 6.3 g of silica gel, 60 Å pore size, 40–63 μm particle size) on a column 20 mm in diameter and length 45 mm. Eluent: hexane/EtOAc, 5:5.

Fraction	Volume (mL)	% weight	ee (%)
1	10	0.29	37.1
2	20	25.49	27.0
3	30	36.29	21.8
4	40	29.02	19.3
5	50	3.92	17.2
6	60	3.85	17.1
7	70	1.15	17.9

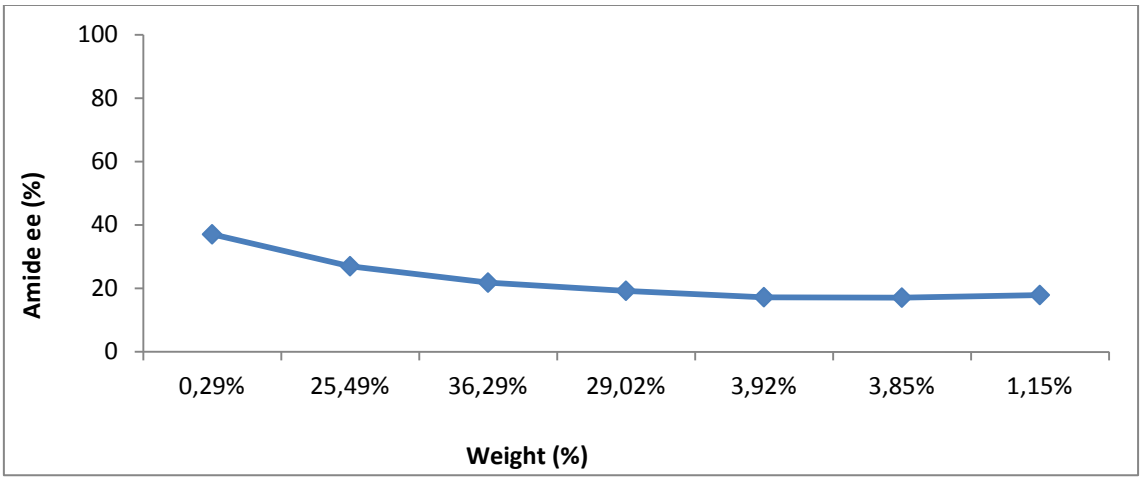

Figure S15. Graphical representation of Table S15 (% ee of each fraction vs the weight percent of each fraction).

Table S16. Chromatography of amide **1** with 12.1% ee on silica gel (50 mg of compound **1** per 6.3 g of silica gel, 60 Å pore size, 40–63 μm particle size) on a column 20 mm in diameter and length 45 mm. Eluent: hexane/EtOAc, 5:5.

Fraction	Volume (mL)	% weight	ee (%)
1	10	1.32	17.7
2	20	28.60	16.0
3	30	29.77	12.3
4	40	23.93	11.0
5	50	4.77	10.1
6	60	7.07	9.0
7	70	3.23	8.8
8	80	1.31	9.0

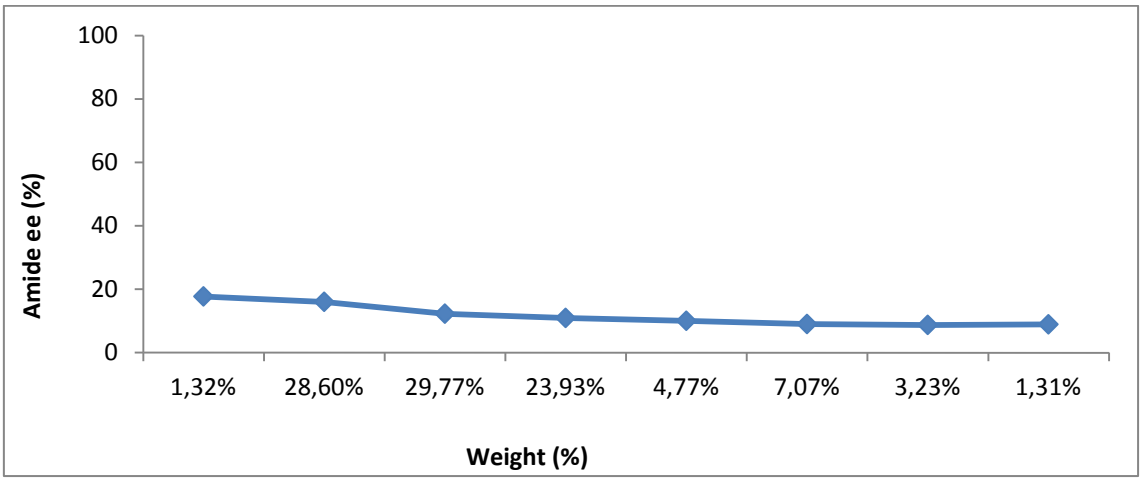

Figure S16. Graphical representation of Table S16 (% ee of each fraction vs the weight percent of each fraction).

Table S17. Chromatography of amide **2** with 69.6% ee on silica gel (50 mg of compound **1** per 6.3 g of silica gel, 60 Å pore size, 40–63 μm particle size) on a column 20 mm in diameter and length 45 mm. Eluent: hexane/EtOAc, 8:1.

Fraction	Volume (mL)	% weight	ee (%)
1	10	4.32	75.6
2	20	42.85	73.2
3	30	30.29	70.4
4	40	14.23	69.5
5	50	6.47	70.8
6	60	1.37	70.2
7	70	0.46	69.3

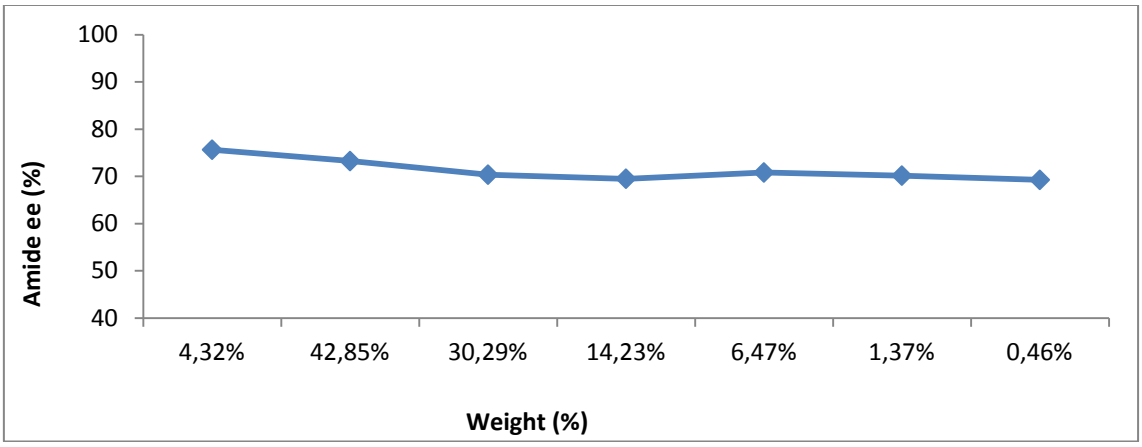

Figure S17. Graphical representation of Table S17 (% *ee* of each fraction *vs* the weight percent of each fraction).

Table S18. Chromatography of amide **3** with 68.7% ee on silica gel (50 mg of compound **1** per 6.3 g of silica gel, 60 Å pore size, 40–63 μm particle size) on a column 20 mm in diameter and length 45 mm. Eluent: hexane/EtOAc, 30:1.

Fraction	Volume (mL)	% weight	ee (%)
1	10	0.53	78.9
2	20	14.51	75.4
3	30	28.17	72.0
4	40	27.67	69.5
5	50	17.06	69.7
6	60	8.20	68.3
7	70	2.93	68.0
8	80	0.93	68.6

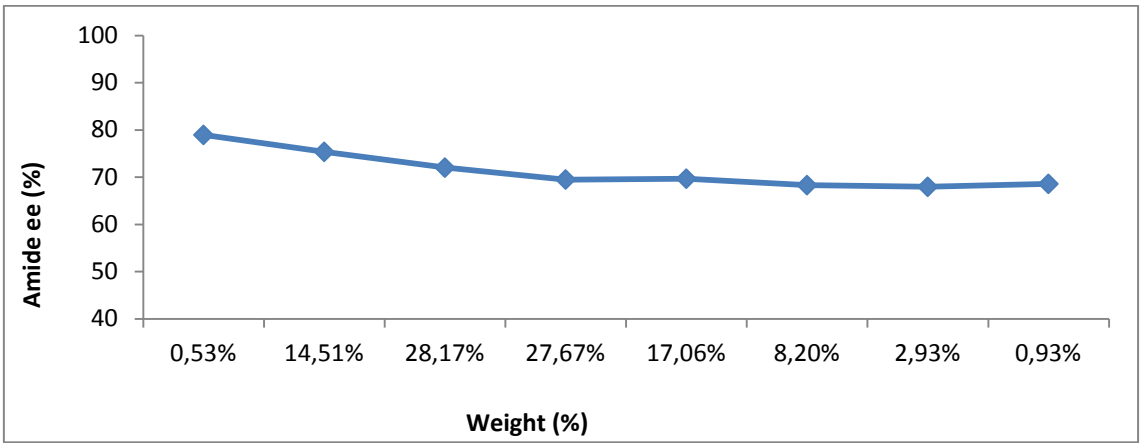

Figure S18. Graphical representation of Table S18 (% ee of each fraction vs the weight percent of each fraction).

Table S19. Chromatography of amide **4** with 69.9% ee on silica gel (50 mg of compound **1** per 6.3 g of silica gel, 60 Å pore size, 40–63 μm particle size) on a column 20 mm in diameter and length 45 mm. Eluent: hexane/EtOAc, 5:3.

Fraction	Volume (mL)	% weight	ee (%)
1	10	5.33	83.9
2	20	15.67	78.3
3	30	18.39	75.1
4	40	14.57	70.4
5	50	14.75	65.5
6	60	10.62	61.3
7	70	10.35	59.1
8	80	6.02	55.6
9	90	2.85	53.3
10	100	1.46	52.7

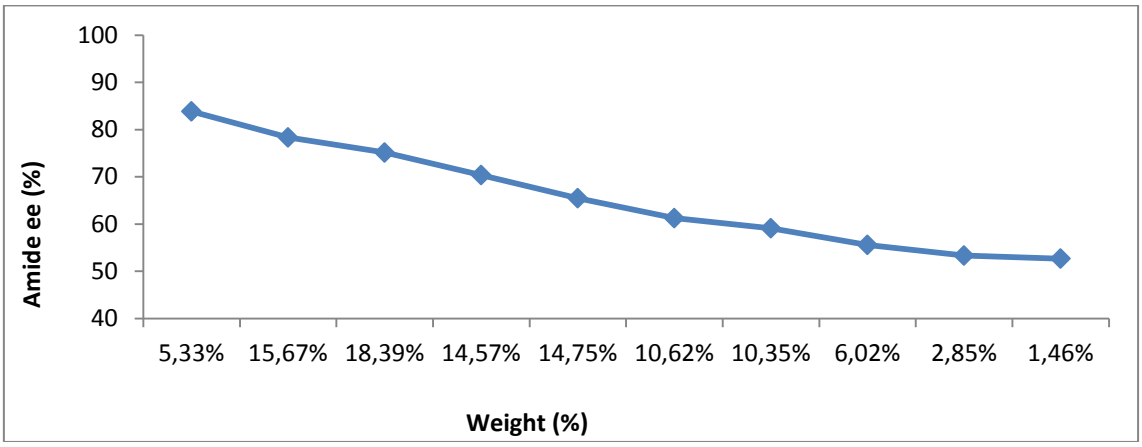

Figure S19. Graphical representation of Table S19 (% ee of each fraction vs the weight percent of each fraction).

Table S20. Chromatography of amide **5** with 72.0% ee on silica gel (50 mg of compound **1** per 6.3 g of silica gel, 60 Å pore size, 40–63 μm particle size) on a column 20 mm in diameter and length 45 mm. Eluent: hexane/EtOAc, 5:5.

Fraction	Volume (mL)	% weight	ee (%)
1	10	2.09	88.2
2	20	21.10	81.9
3	30	19.42	77.3
4	40	17.78	70.3
5	50	16.44	66.6
6	60	8.59	63.5
7	70	7.63	61.2
8	80	4.27	60.8
9	90	2.68	59.3

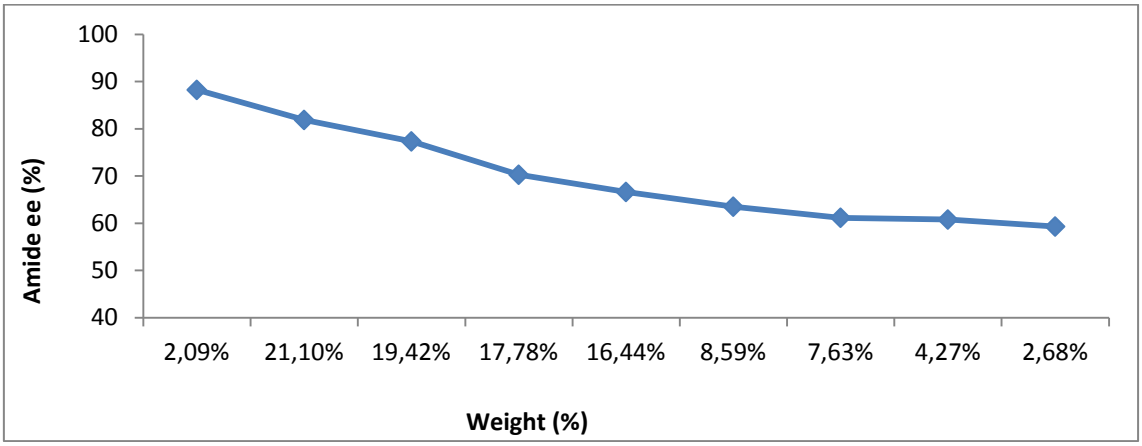

Figure S20. Graphical representation of Table S20 (% ee of each fraction vs the weight percent of each fraction).

Table S21. Chromatography of amide **6** with 72.5% ee on silica gel (50 mg of compound **1** per 6.3 g of silica gel, 60 Å pore size, 40–63 μm particle size) on a column 20 mm in diameter and length 45 mm. Eluent: hexane/EtOAc, 5:5.

Fraction	Volume (mL)	% weight	ee (%)
1	10	15.10	85.4
2	20	28.48	76.9
3	30	21.43	71.3
4	40	13.98	67.9
5	50	9.40	65.2
6	60	5.97	62.8
7	70	3.55	61.2
8	80	2.08	60.7

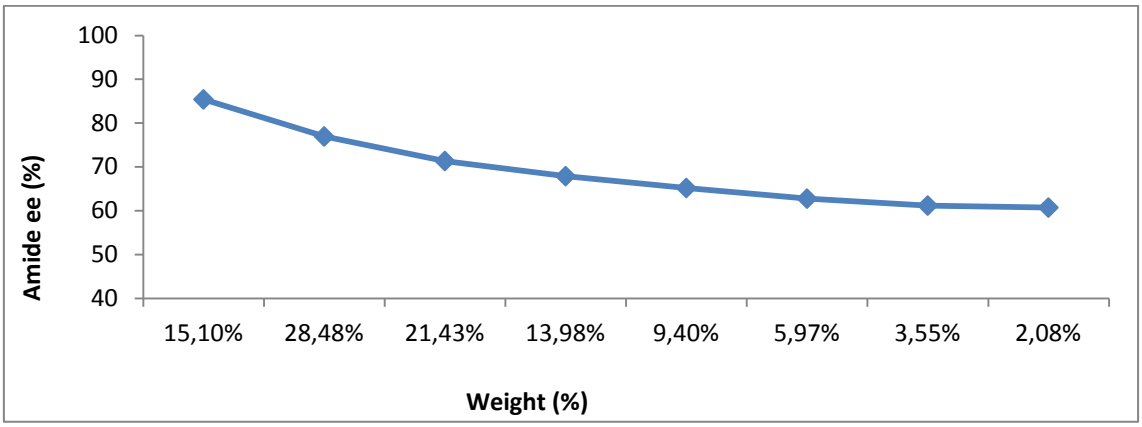

Figure S21. Graphical representation of Table S21 (% ee of each fraction vs the weight percent of each fraction).

Table S22. Chromatography of amide **7** with 70.2% ee on silica gel (50 mg of compound **1** per 6.3 g of silica gel, 60 Å pore size, 40–63 μm particle size) on a column 20 mm in diameter and length 45 mm. Eluent: hexane/EtOAc, 5:3.

Fraction	Volume (mL)	% weight	ee (%)
1	10	12.36	81.9
2	20	12.69	76.2
3	30	11.62	71.1
4	40	19.16	67.6
5	50	13.62	65.3
6	60	9.59	63.0
7	70	6.15	61.3
8	80	8.34	59.2
9	90	4.53	59.4
10	100	1.94	57.4

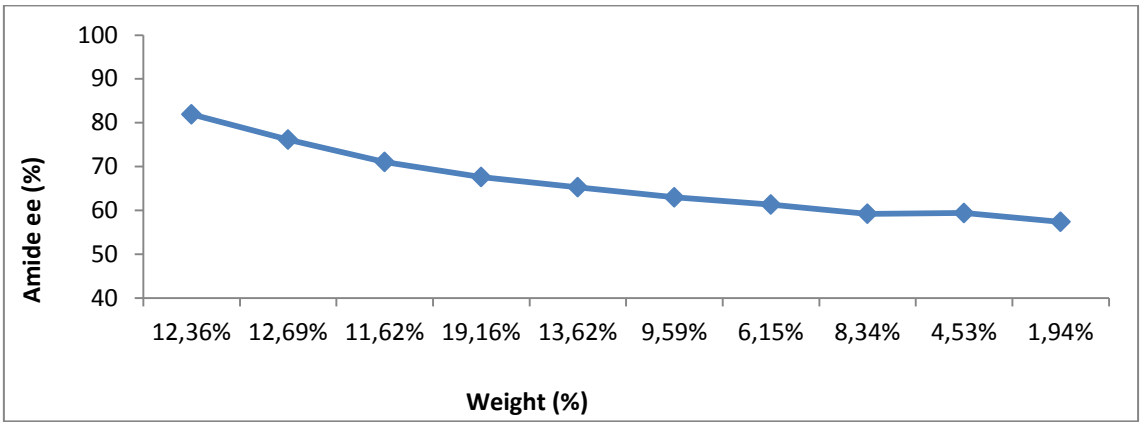

Figure S22. Graphical representation of Table S22 (% ee of each fraction vs the weight percent of each fraction).

Table S23. Chromatography of amide **8** with 72.9% ee on silica gel (50 mg of compound **1** per 6.3 g of silica gel, 60 Å pore size, 40–63 μm particle size) on a column 20 mm in diameter and length 45 mm. Eluent: hexane/EtOAc, 5:3.

Fraction	Volume (mL)	% weight	ee (%)
1	10	0.93	83.0
2	20	16.90	80.6
3	30	24.00	74.9
4	40	22.50	73.0
5	50	13.26	69.9
6	60	10.65	71.3
7	70	5.82	71.7
8	80	3.16	68.3
9	90	1.87	66.9
10	100	0.90	65.4

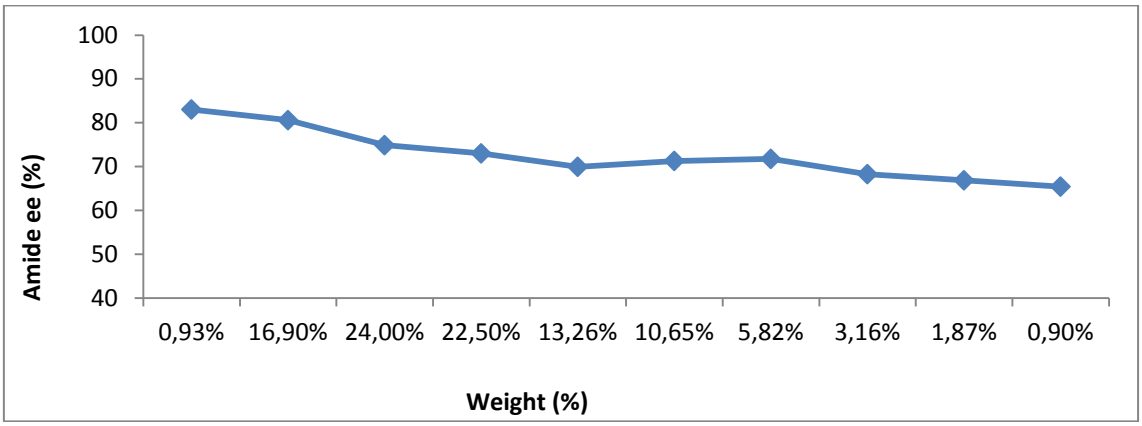

Figure S23. Graphical representation of Table S23 (% ee of each fraction vs the weight percent of each fraction).

Table S24. Chromatography of amide **9** with 75.0% ee on silica gel (50 mg of compound **1** per 6.3 g of silica gel, 60 Å pore size, 40–63 μm particle size) on a column 20 mm in diameter and length 45 mm. Eluent: hexane/EtOAc, 5:3.

Fraction	Volume (mL)	% weight	ee (%)
1	10	2.36	87.0
2	20	19.13	83.9
3	30	22.75	78.1
4	40	22.96	73.7
5	50	14.06	70.9
6	60	10.10	68.4
7	70	5.67	66.7
8	80	2.97	65.2

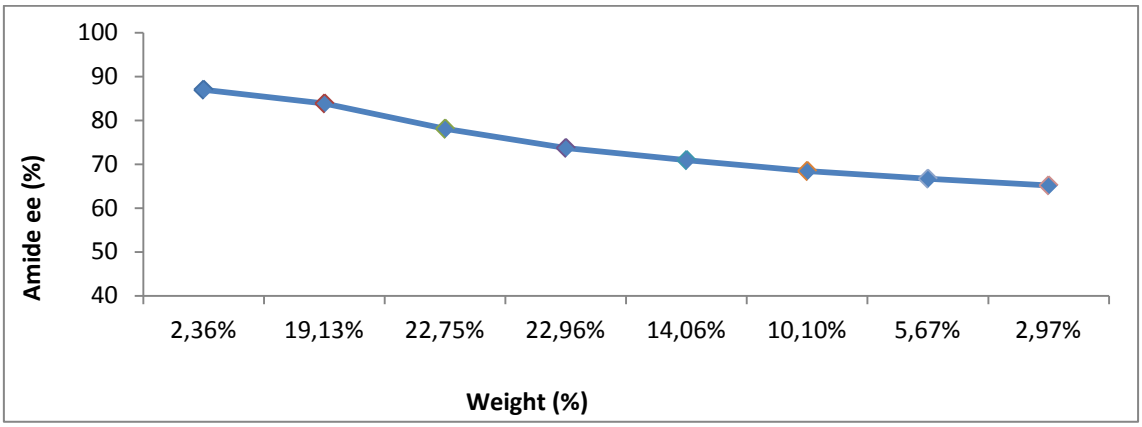

Figure S24. Graphical representation of Table S24 (% ee of each fraction vs the weight percent of each fraction).