Electronic Supplementary Material (ESI) for Analytical Methods.

Regression Plots for Mix of 16 Controlled Synthetic Cathinones

Table S1 Retention time measurements for chromatographic columns employed in this study for the mixture of 16 synthetic cathinones.

Compound	Acquity UPLC BEH C8 1.7 µm 2.1 x 100 mm RT (minutes)	Acquity UPLC BEH C18 1.7 µm 2.1 x 100 mm RT (minutes)	Acquity UPLC BEH Phenyl 1.7 µm 2.1 x 100 mm RT (minutes)	Acquity UPLC HSS T3 1.8 µm 2.1 x 100 mm RT (minutes)	Acquity UPLC HSS PFP 1.8 µm 2.1 x 100 mm (RPC) RT (minutes)
Cathinone	2.05	1.84	1.72	1.91	2.23
Methcathinone	2.37	2.13	2.01	2.22	2.53
Mephedrone	4.49	3.95	3.60	3.94	3.39
Buphedrone	3.83	3.27	3.02	3.34	3.08
4-Fluoromethcathinone	2.89	2.64	2.51	2.74	2.93
3-Fluoromethcathinone	2.80	2.54	2.40	2.67	2.93
Pentedrone	5.76	4.96	4.54	4.88	4.10
4-Methylethcathinone	5.14	4.58	4.22	4.55	4.00
Methylone	2.80	2.46	2.40	2.67	2.78
4-MePPP	5.59	5.06	4.92	5.09	4.78
α-PBP	4.72	4.08	4.10	4.22	4.27
Butylone	4.29	3.65	3.60	3.77	3.39
α-PVP	6.47	5.87	5.68	5.87	5.73
Pentylone	6.09	5.37	5.10	5.32	4.47
MDPV	6.80	6.31	6.26	6.34	6.18
Naphyrone	10.32	10.67	10.03	10.26	10.18

Table S1 cont. Retention time measurements for chromatographic columns used in this study for the mixture of 16 synthetic cathinones.

Compound	Acquity UPLC HSS PFP 1.8 µm 2.1 x 50 mm (HILIC)[a] RT (minutes)	Acquity UPLC HSS PFP 1.8µm 2.1 x 100 mm (HILIC)[a] RT (minutes)	Acquity UPLC BEH HILIC 1.7 µm 2.1 x 50 mm RT (minutes)	Acquity UPLC BEH C8 1.7 µm 2.1 x 50mm high pH MeOH[b] RT (minutes)
Cathinone	1.66	2.92	1.92	0.88
Methcathinone	2.15	4.00	1.92	1.18
Mephedrone	2.33	4.27	1.82	1.79
Buphedrone	1.91	3.59	1.55	1.67
4-Fluoromethcathinone	2.01	3.77	1.82	1.35
3-Fluoromethcathinone	1.85	3.50	1.68	1.41
Pentedrone	1.70	3.37	1.55	2.44
4-Methylethcathinone	2.23	4.18	1.55	2.44
Methylone	2.15	4.00	1.92	1.18
4-MePPP	3.31	5.95	1.68	3.40
α-PBP	2.86	5.37	1.55	3.32
Butylone	1.91	3.59	1.60	1.67
α-PVP	2.63	5.09	1.31	4.08
Pentylone	1.70	3.37	1.31	2.44
MDPV	2.63	5.09	1.31	4.04
Naphyrone	3.31	6.26	1.19	5.20

[a] All column combinations were originally investigated using the PFP HILIC 5 cm column. The PFP HILIC 10 cm column was then used for the final multi-dimensional separations in order to increase the peak capacity of the second dimension.

[b] High pH methanol was used as the organic modifier due to solubility concerns encountered with high pH acetonitrile.

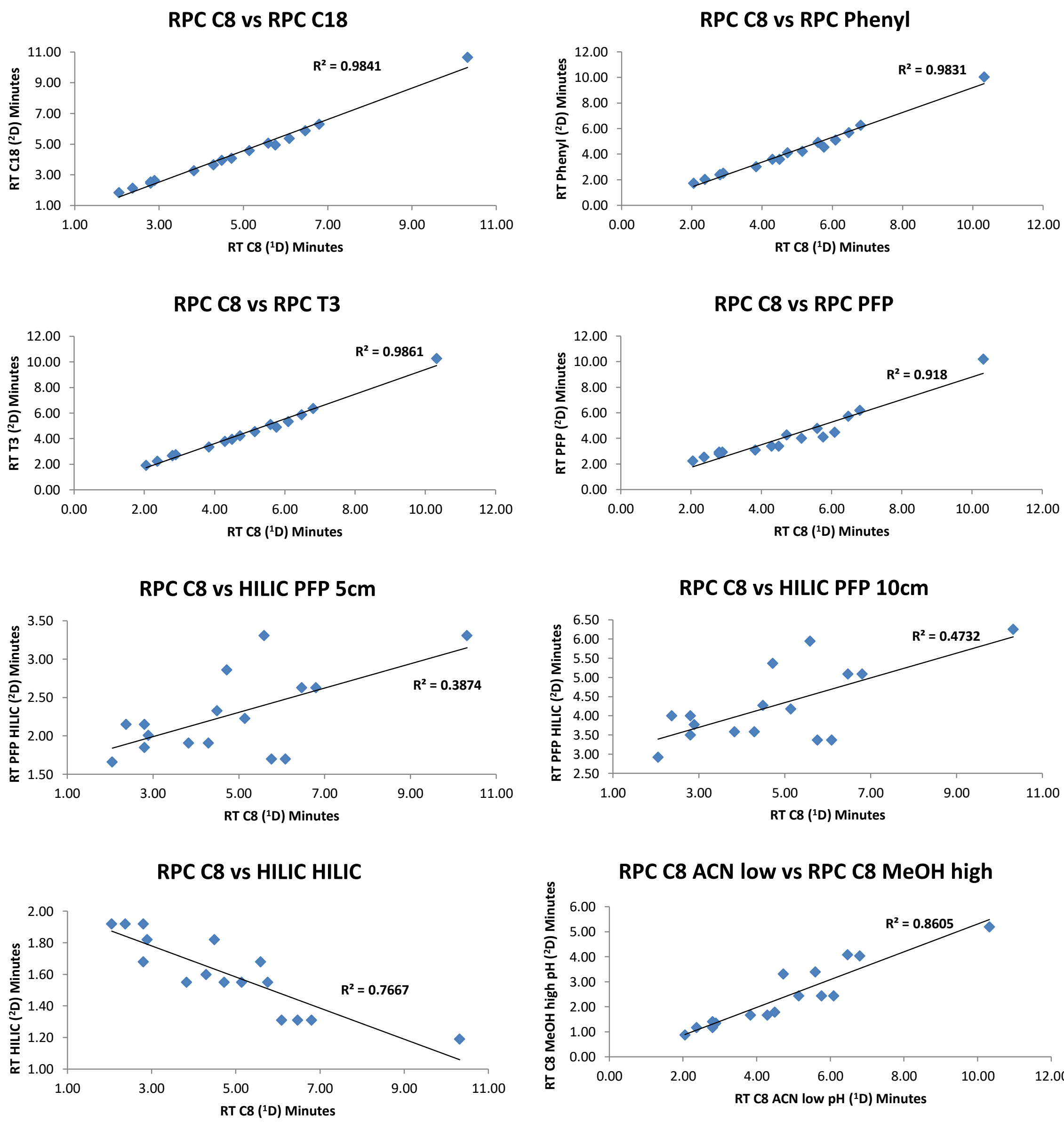

Fig. S1 Regression plots for mixture of 16 synthetic cathinones using retention time data shown in Table S1. The plots show column combinations utilizing the BEH C8 column as the first dimension column (^{1}D) and various second dimension columns (^{2}D). Combinations were first evaluated using the PFP HILIC 5 cm column. The PFP HILIC 10 cm column was used in the final multi-dimensional separations to increase peak capacity. The BEH C8 column was used in order to examine the effects of high pH elution in the second dimension. High pH methanol was used instead of high pH acetonitrile due to solubility concerns.

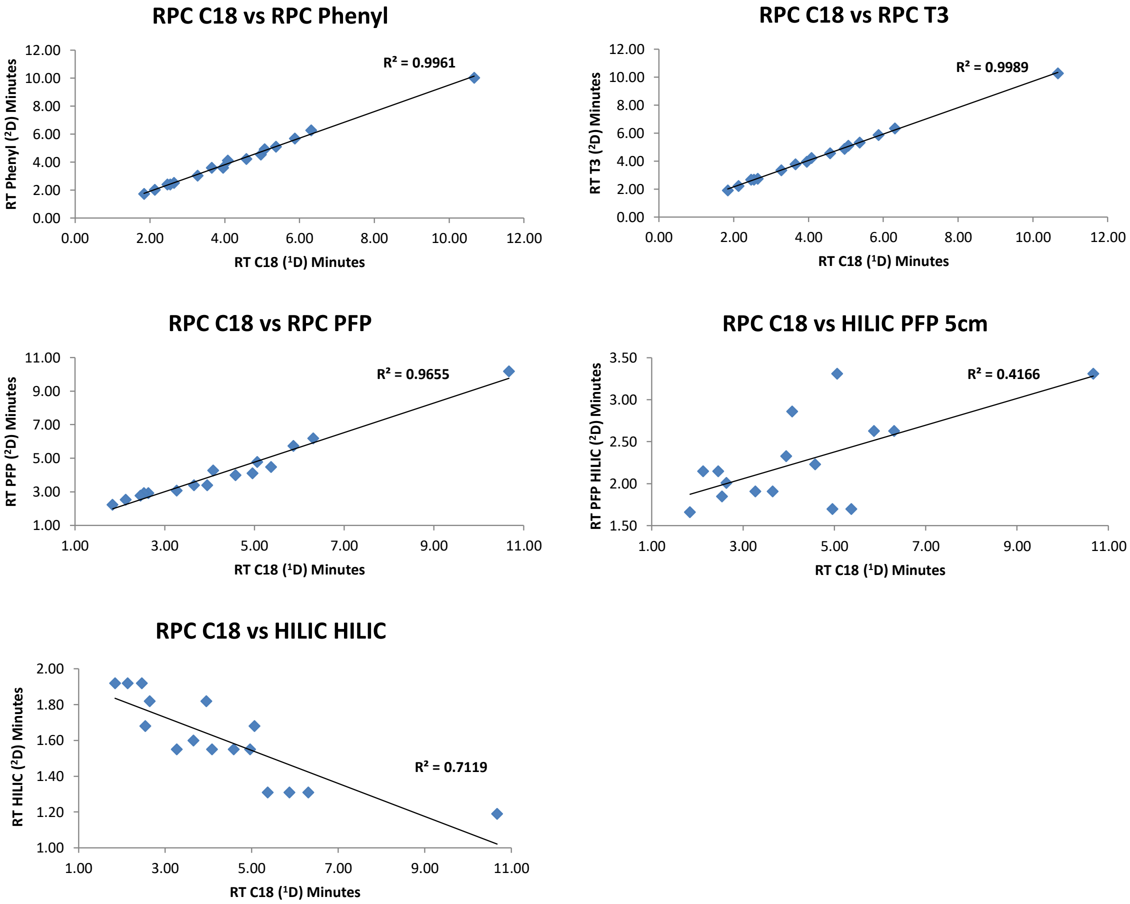

Fig. S2 Regression plots for mixture of 16 synthetic cathinones using retention time data shown in Table S1. The plots show column combinations utilizing the BEH C18 column as the first dimension column (^{1}D) and various second dimension columns (^{2}D). Plots of inverse combinations are not shown as they produce the same R2 values. Combinations with the PFP HILIC 10 cm and high pH methanol are not shown as these were investigated as alternatives to the PFP HILIC 5 cm column once it was determined that the BEH C8 and PFP HILIC 5 cm columns were the best combination.

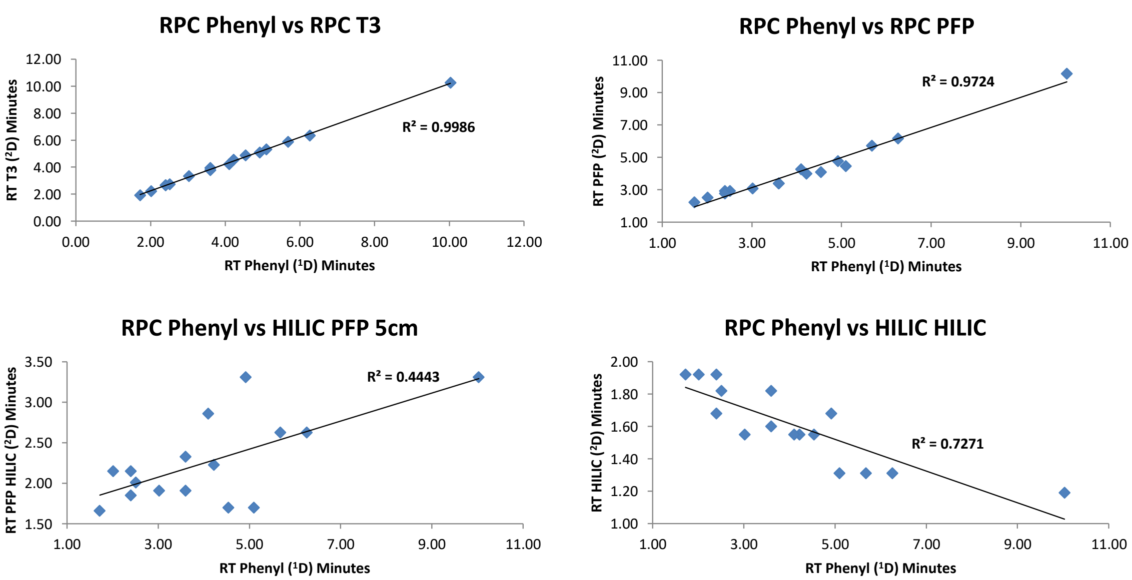

Fig. S3 Regression plots for mixture of 16 synthetic cathinones using retention time data shown in Table S1. The plots show column combinations utilizing the Phenyl column as the first dimension column (^{1}D) and various second dimension columns (^{2}D). Plots of inverse combinations are not shown as they produce the same R2 values. Combinations with the PFP HILIC 10 cm and high pH methanol are not shown as these were investigated as alternatives to the PFP HILIC 5 cm column once it was determined that the BEH C8 and PFP HILIC 5 cm columns were the best combination.

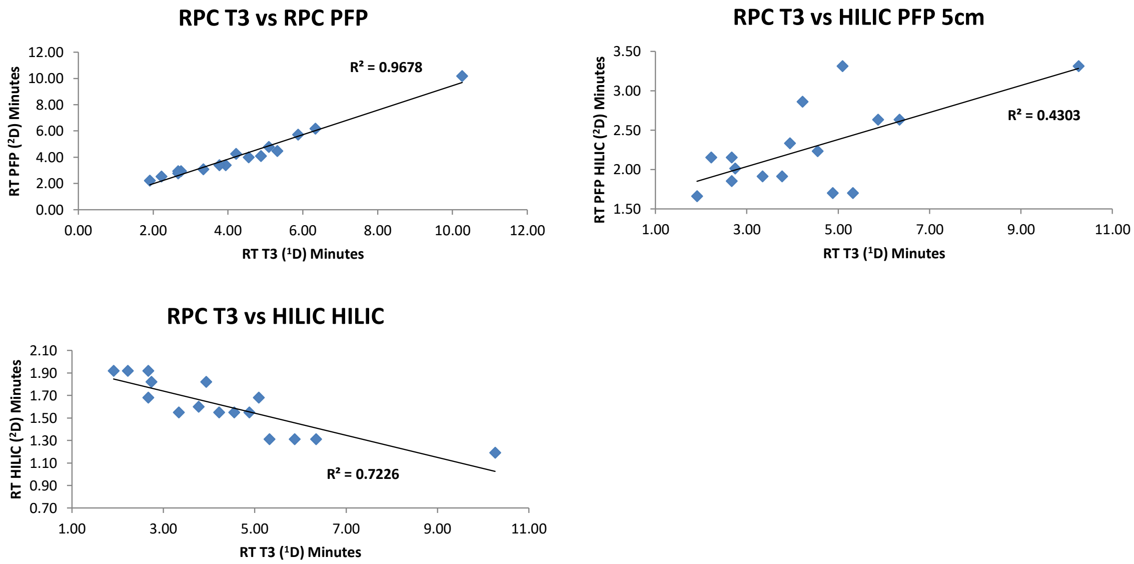

Fig. S4 Regression plots for mixture of 16 synthetic cathinones using retention time data shown in Table S1. The plots show column combinations utilizing the T3 column as the first dimension column (^{1}D) and various second dimension columns (^{2}D). Plots of inverse combinations are not shown as they produce the same R2 values. Combinations with the PFP HILIC 10 cm and high pH methanol are not shown as these were investigated as alternatives to the PFP HILIC 5 cm column once it was determined that the BEH C8 and PFP HILIC 5 cm columns were the best combination.

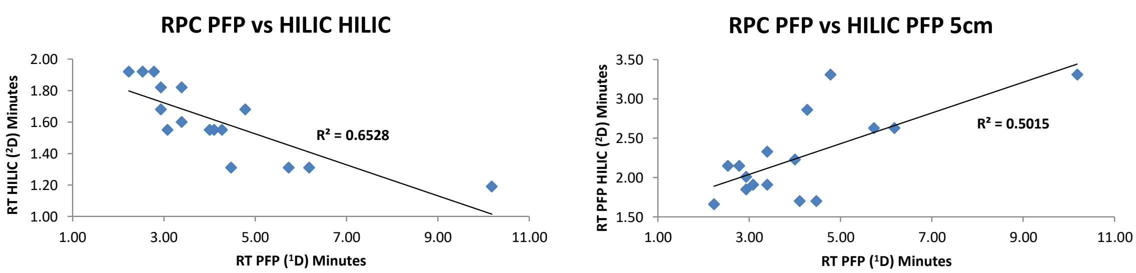

Fig. S5 Regression plots for mixture of 16 synthetic cathinones using retention time data shown in Table S1. The plots show column combinations utilizing the RPC PFP column as the first dimension column (^{1}D) and various second dimension columns (^{2}D). Plots of inverse combinations are not shown as they produce the same R2 values. Combinations with the PFP HILIC 10 cm and high pH methanol are not shown as these were investigated as alternatives to the PFP HILIC 5 cm column once it was determined that the BEH C8 and PFP HILIC 5 cm columns were the best combination.

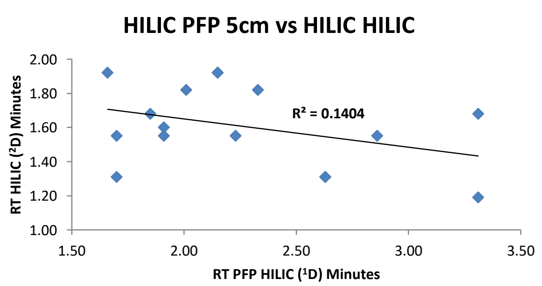

Fig. S6 Regression plots for mixture of 16 synthetic cathinones using retention time data shown in Table S1. The plots show column combinations utilizing the PFP HILIC 5cm column as the first dimension (^{1}D) and the HILIC column as the second dimension (^{2}D). Plots of inverse combinations are not shown as they produce the same R2 values. Combinations with the PFP HILIC 10 cm and high pH methanol are not shown as these were investigated as alternatives to the PFP HILIC 5 cm column once it was determined that the BEH C8 and PFP HILIC 5 cm columns were the best combination.

Regression Plots for Mix of Pentedrone Positional Isomers

Table S2 Retention time measurements for chromatographic columns employed in this study for the mixture of pentedrone positional isomers.

Compound	Acquity UPLC BEH C8 1.7 µm 2.1 x 100 mm RT (minutes)	Acquity UPLC BEH C18 1.7 µm 2.1 x 100 mm RT (minutes)	Acquity UPLC BEH Phenyl 1.7 µm 2.1 x 100 mm RT (minutes)	Acquity UPLC HSS T3 1.8 µm 2.1 x 100 mm RT (minutes)	Acquity UPLC HSS PFP 1.8 µm 2.1 x 100 mm (RPC) RT (minutes)
Pentedrone	6.17	4.94	3.95	4.84	4.13
4-Methylethcathinone	5.61	4.56	4.25	4.52	3.98
2,3-Dimethylmethcathinone	6.46	5.45	4.74	5.26	4.13
2,4-Dimethylmethcathinone	6.83	5.92	5.10	5.67	4.54
3,4-Dimethylmethcathinone	6.71	5.79	4.96	5.55	4.40
2-Ethylmethcathinone	6.75	5.71	4.96	5.55	4.54
4-Methylbuphedrone	6.35	5.32	4.55	5.14	4.13

Table S2 cont. Retention time measurements for chromatographic columns used in this study for the mixture of pentedrone positional isomers.

Compound	Acquity UPLC HSS PFP 1.8 µm 2.1 x 50 mm (HILIC)[a] RT (minutes)	Acquity UPLC HSS PFP 1.8µm 2.1 x 100 mm (HILIC)[a] RT (minutes)	Acquity UPLC BEH HILIC 1.7 µm 2.1 x 50 mm RT (minutes)	Acquity UPLC BEH C8 1.7 µm 2.1 x 50mm high pH MeOH[b] RT (minutes)
Pentedrone	1.73	3.47	1.33	2.44
4-Methylethcathinone	2.28	4.34	1.53	2.44
2,3-Dimethylmethcathinone	2.21	4.23	1.62	2.26
2,4-Dimethylmethcathinone	2.47	4.64	1.66	2.57
3,4-Dimethylmethcathinone	2.47	4.64	1.66	2.44
2-Ethylmethcathinone	2.07	4.03	1.53	2.50
4-Methylbuphedrone	2.07	4.03	1.53	2.41

[a] All column combinations were originally investigated using the PFP HILIC 5 cm column. The PFP HILIC 10 cm column was then used for the final multi-dimensional separations in order to increase the peak capacity of the second dimension.

[b] High pH methanol was used as the organic modifier due to solubility concerns encountered with high pH acetonitrile.

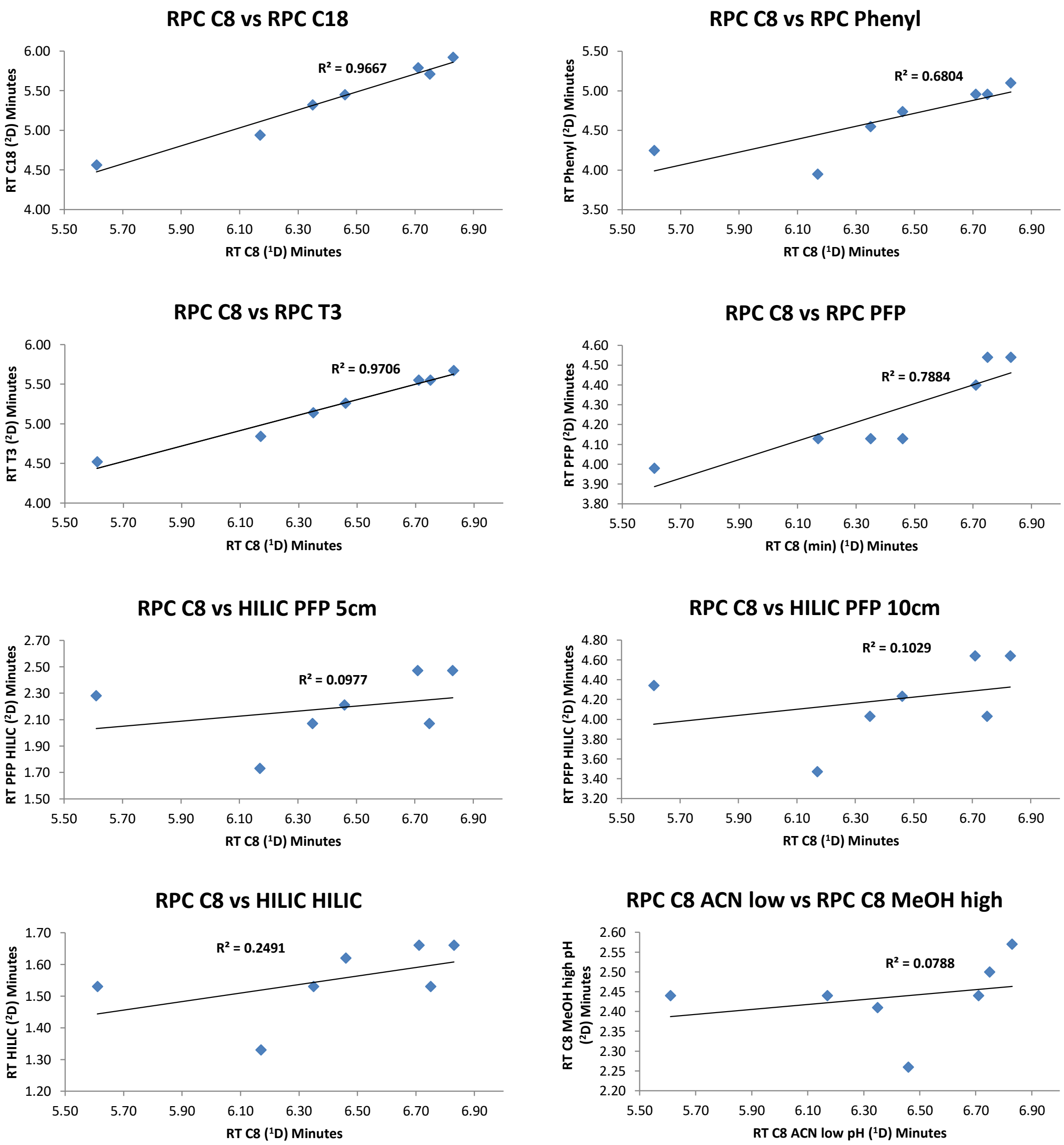

Fig. S7 Regression plots for mixture of pentedrone positional isomers using retention time data shown in Table S2. The plots show column combinations utilizing the BEH C8 column as the first dimension column (^{1}D) and various second dimension columns (^{2}D). Combinations were first evaluated using the PFP HILIC 5 cm column. The PFP HILIC 10 cm column was used in the final multi-dimensional separations to increase peak capacity. The BEH C8 column was used in order to examine the effects of high pH elution in the second dimension. High pH methanol was used instead of high pH acetonitrile due to solubility concerns.

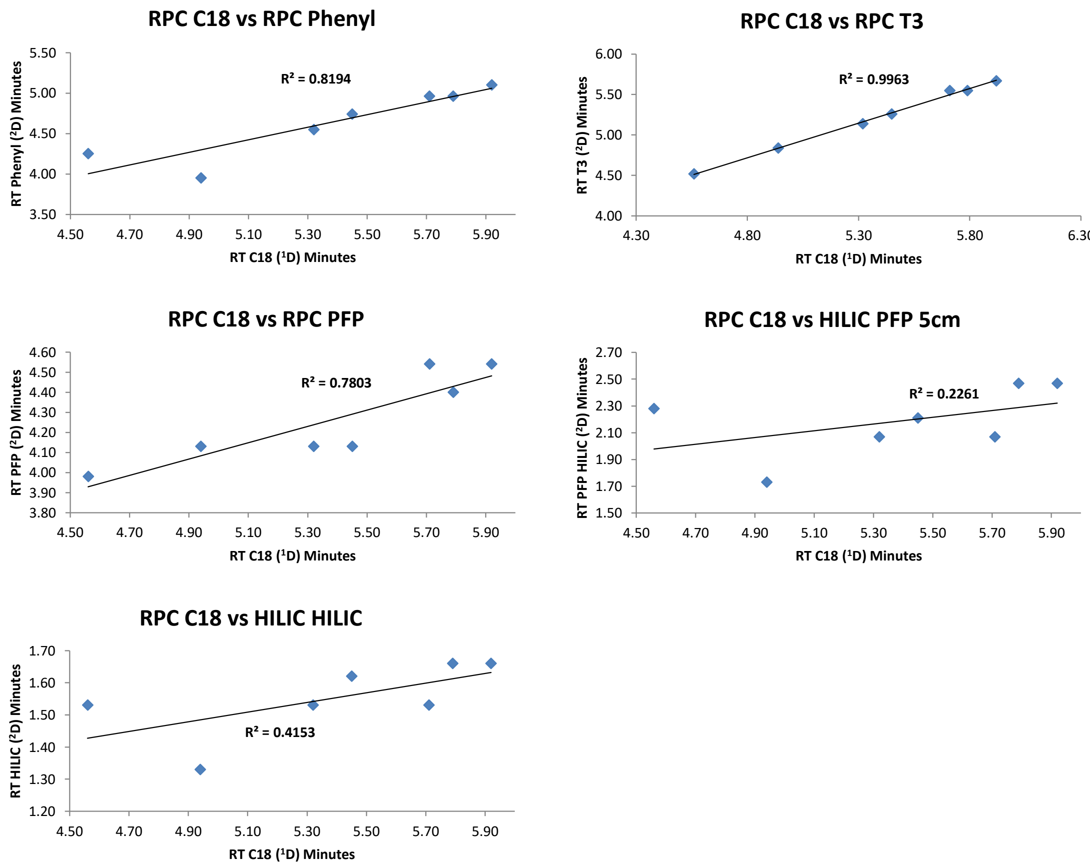

Fig. S8 Regression plots for mixture of pentedrone positional isomers using retention time data shown in Table S2. The plots show column combinations utilizing the BEH C18 column as the first dimension column (^{1}D) and various second dimension columns (^{2}D). Plots of inverse combinations are not shown as they produce the same R2 values. Combinations with the PFP HILIC 10 cm and high pH methanol are not shown as these were investigated as alternatives to the PFP HILIC 5 cm column once it was determined that the BEH C8 and PFP HILIC 5 cm columns were the best combination.

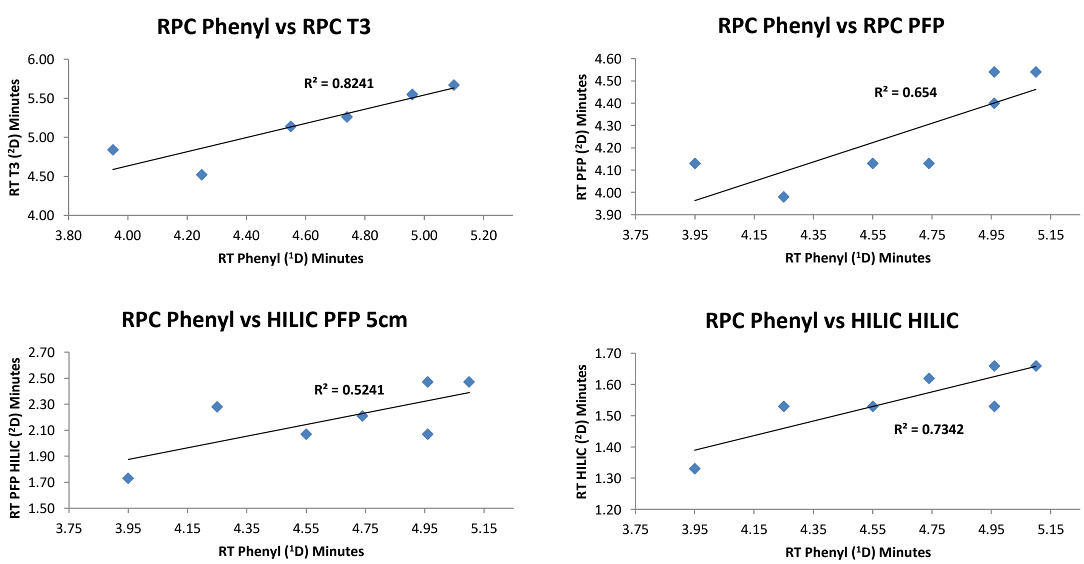

Fig. S9 Regression plots for mixture of pentedrone positional isomers using retention time data shown in Table S2. The plots show column combinations utilizing the Phenyl column as the first dimension column (^{1}D) and various second dimension columns (^{2}D). Plots of inverse combinations are not shown as they produce the same R2 values. Combinations with the PFP HILIC 10 cm and high pH methanol are not shown as these were investigated as alternatives to the PFP HILIC 5 cm column once it was determined that the BEH C8 and PFP HILIC 5 cm columns were the best combination.

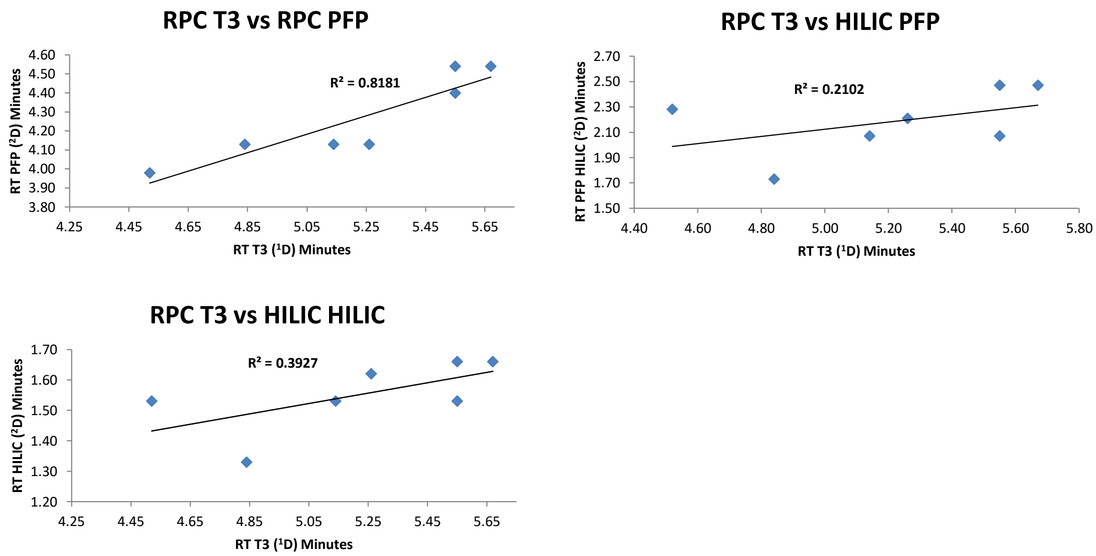

Fig. S10 Regression plots for mixture of pentedrone positional isomers using retention time data shown in Table S2. The plots show column combinations utilizing the T3 column as the first dimension column (^{1}D) and various second dimension columns (^{2}D). Plots of inverse combinations are not shown as they produce the same R2 values. Combinations with the PFP HILIC 10 cm and high pH methanol are not shown as these were investigated as alternatives to the PFP HILIC 5 cm column once it was determined that the BEH C8 and PFP HILIC 5 cm columns were the best combination.

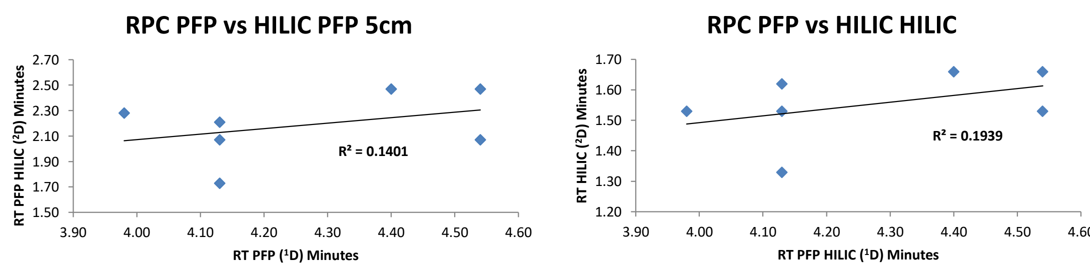

Fig. S11 Regression plots for mixture of pentedrone positional isomers using retention time data shown in Table S2. The plots show column combinations utilizing the RPC PFP column as the first dimension column (^{1}D) and various second dimension columns (^{2}D). Plots of inverse combinations are not shown as they produce the same R2 values. Combinations with the PFP HILIC 10 cm and high pH methanol are not shown as these were investigated as alternatives to the PFP HILIC 5 cm column once it was determined that the BEH C8 and PFP HILIC 5 cm columns were the best combination.

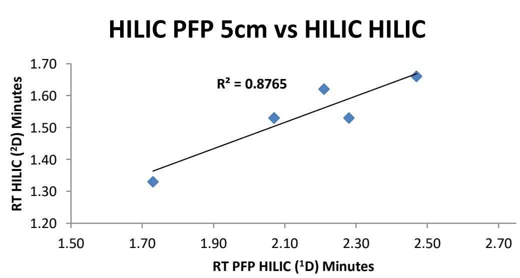

Fig. S12 Regression plots for mixture of pentedrone positional isomers using retention time data shown in Table S2. The plots show column combinations utilizing the PFP HILIC 5cm column as the first dimension (^{1}D) and the HILIC column as the second dimension (^{2}D). Plots of inverse combinations are not shown as they produce the same R2 values. Combinations with the PFP HILIC 10 cm and high pH methanol are not shown as these were investigated as alternatives to the PFP HILIC 5 cm column once it was determined that the BEH C8 and PFP HILIC 5 cm columns were the best combination.

Regression Tables of the S^2 of the Column Combinations*

*selectivity was determined using the following formula $S^2 = 1 - R^2$; See equation 1 in manuscript.

Table S3 Selectivity factors for previously plotted column combinations for the mixture of 16 synthetic cathinones. The rows of the table represent the first dimension column (^{1}D) and the columns represent the second dimension column (^{2}D).

	C8 low pH ACN	C18	Phenyl	T3	PFP (RPC)	PFP (HILIC) 5cm[a]	HILIC
C8 low pH ACN	0.0000	0.0159	0.0169	0.0139	0.0011	0.6126	0.2333
C18	0.0159	0.0000	0.0039	0.0011	0.0345	0.5834	0.2881
Phenyl	0.0169	0.0039	0.0000	0.0014	0.0276	0.5557	0.2729
T3	0.0139	0.0011	0.0014	0.0000	0.0322	0.5697	0.2774
PFP (RPC)	0.0011	0.0345	0.0276	0.0322	0.0000	0.7485	0.6553
PFP (HILIC) 5cm	0.6126	0.5834	0.5557	0.5697	0.7485	0.0000	0.8960
HILIC	0.2333	0.2881	0.2729	0.2774	0.6553	0.8960	0.0000

[a] All column combinations were initially performed using the PFP (HILIC) 5cm column.

Table S3 cont. Selectivity factors for column combinations for the mixture of 16 synthetic cathinones.

	C8 low pH ACN	PFP (HILIC) 10cm[a]	C8 high pH MeOH[b]
C8 low pH ACN	0.0000	0.5268	0.1395
PFP (HILIC) 10cm	0.5268	0.0000	N/A[c]
C8 high pH MeOH	0.1395	N/A[c]	0.0000

[a] All column combinations were initially performed using the PFP (HILIC) 5cm column. The PFP (HILIC) 10cm column was used for the final multi-dimensional separations to increase the peak capacity of the second dimension.

[b] High pH methanol was used as the organic modifier due to solubility concerns encountered with high pH acetonitrile.

[c] Not applicable as the the PFP (HILIC) 10cm and high pH methanol were used to further optimize multi-dimensional separations with the C8 low pH ACN column as the first dimension.

Table S4 Selectivity factors for previously plotted column combinations for the mixture of pentedrone positional isomers. The rows of the table represent the first dimension column (^{1}D) and the columns represent the second dimension column (^{2}D).

	C8 low pH ACN	C18	Phenyl	T3	PFP (RPC)	PFP (HILIC) 5cm[a]	HILIC
C8 low pH ACN	0.0000	0.0333	0.3196	0.0294	0.2116	0.9023	0.7509
C18	0.0333	0.0000	0.1806	0.0037	0.2197	0.7739	0.5847
Phenyl	0.3196	0.1806	0.0000	0.1759	0.3460	0.4759	0.2658
T3	0.0294	0.0037	0.1759	0.0000	0.1819	0.7898	0.6073
PFP (RPC)	0.2116	0.2197	0.3460	0.1819	0.0000	0.8599	0.8061
PFP (HILIC) 5cm	0.9023	0.7739	0.4759	0.7898	0.8599	0.0000	0.2317
HILIC	0.7509	0.5847	0.2658	0.6073	0.8061	0.2317	0.0000

[a] All column combinations were initially performed using the PFP (HILIC) 5cm column.

Table S4 cont. Selectivity factors for column combinations for the mixture of pentedrone positional isomers.

	C8 low pH ACN	PFP (HILIC) 10cm[a]	C8 high pH MeOH[b]
C8 low pH ACN	0.0000	0.8971	0.9212
PFP (HILIC) 10cm	0.8971	0.0000	N/A[c]
C8 high pH MeOH	0.9212	N/A[c]	0.0000

[a] All column combinations were initially performed using the PFP (HILIC) 5cm column. The PFP (HILIC) 10cm column was used for the final multi-dimensional separations to increase the peak capacity of the second dimension.

[b] High pH methanol was used as the organic modifier due to solubility concerns encountered with high pH acetonitrile.

[c] Not applicable as the the PFP (HILIC) 10cm and high pH methanol were used to further optimize multi-dimensional separations with the C8 low pH ACN column as the first dimension.

One-Dimensional Peak Capacities (n_c)*

* calculated using the following formula $n_c = (t_f - t_i)/w_{avg}$; See equation 2 in manuscript.

Table S5 One-dimensional peak capacities (n_c) of chromatographic columns for the mixture of 16 synthetic cathinones and pentedrone positional isomers. Peak capacities are the same when the column is used as the first (peak capacity ^1n_c) or second (peak capacity ^2n_c) separation dimension.

	C8 low pH ACN	C18	Phenyl	T3	PFP (RPC)	PFP (HILIC) 5cm	HILIC	PFP (HILIC) 10cm	C8 High pH MeOH
Synthetic Cathinones	50.75	67.54	63.81	51.04	41.54	18.47	8.66	23.88	49.75
Pentedrone Isomers	8.96	11.94	13.06	8.48	4.90	8.77	5.67	10.75	6.31

Theoretical Multi-Dimensional Peak Capacities $^{2D}[n_c]_{theory}$*

* calculated using the following formula $^{2D}[n_c]_{theory} = {}^1n_c \times {}^2n_c$; See equation 3 in manuscript.

Table S6 Theoretical multi-dimensional peak capacities for the mixture of 16 synthetic cathinones. The rows of the table represent the first dimension column with peak capacity ^1n_c and the columns represent the second dimension column with peak capacity ^2n_c.

	C8 low pH ACN	C18	Phenyl	T3	PFP (RPC)	PFP (HILIC) 5cm[a]	HILIC
C8 low pH ACN	2575.18	3427.27	3237.91	2590.33	2108.12	937.29	439.30
C18	3427.27	2575.18	4309.28	3447.43	2805.65	1247.42	584.65
Phenyl	3237.91	4309.28	4071.20	3256.96	2650.65	1178.51	552.35
T3	2590.33	3447.43	3256.96	2605.57	2120.52	942.80	441.88
PFP (RPC)	2108.12	2805.65	2650.65	2120.52	1725.76	767.29	359.62
PFP (HILIC) 5cm	937.29	1247.42	1178.51	942.80	767.29	341.15	159.89
HILIC	439.30	584.65	552.35	441.88	359.62	159.89	74.94

[a] All column combinations were initially performed using the PFP (HILIC) 5cm column.

Table S6 cont. Theoretical multi-dimensional peak capacities for the mixture of 16 synthetic cathinones.

	C8 low pH ACN	PFP (HILIC) 10cm	C8 high pH MeOH
C8 low pH ACN	2575.18	1211.85	2524.69
PFP (HILIC) 10cm	1211.85	570.28	N/A[a]
C8 high pH MeOH	2524.69	N/A[a]	2475.19

[a] Not applicable as the the PFP (HILIC) 10cm and high pH methanol were used to further optimize multi-dimensional separations with the C8 low pH ACN column as the first dimension.

Table S7 Theoretical multi-dimensional peak capacities for the mixture of pentedrone positional isomers. The rows of the table represent the first dimension column with peak capacity ^1n_c and the first columns represent the second dimension column with peak capacity ^2n_c.

	C8 low pH ACN	C18	Phenyl	T3	PFP (RPC)	PFP (HILIC) 5cm[a]	HILIC
C8 low pH ACN	80.20	106.93	116.95	75.92	43.84	78.53	50.79
C18	106.93	142.57	155.94	101.23	58.45	104.70	67.72
Phenyl	116.95	155.94	170.56	110.72	63.93	114.52	74.07
T3	75.92	101.23	110.72	71.87	41.50	74.34	48.08
PFP (RPC)	43.84	58.45	63.93	41.50	23.97	42.93	27.77
PFP (HILIC) 5cm	78.53	104.70	114.52	74.34	42.93	76.89	49.73
HILIC	50.79	67.72	74.07	48.08	27.77	49.73	115.48

[a] All column combinations were initially performed using the PFP (HILIC) 5cm column.

Table S7 cont. Theoretical multi-dimensional peak capacities for the mixture of pentedrone positional isomers.

	C8 low pH ACN	PFP (HILIC) 10cm	C8 high pH MeOH
C8 low pH ACN	80.20	96.24	56.55
PFP (HILIC) 10cm	96.24	115.48	N/A[a]
C8 high pH MeOH	56.55	N/A[a]	39.87

[a] Not applicable as the the PFP (HILIC) 10cm and high pH methanol were used to further optimize multi-dimensional separations with the C8 low pH ACN column as the first dimension.

Assignment-Gain Factor*

* calculated using the following formula $[1 + S^2 ({}^2n_c - 1)]$; See equation 5 in manuscript.

Table S8 Gain factors of column combinations for the mixture of 16 synthetic cathinones. The rows of the table represent the first dimension column (^1D) and the columns represent the second dimension column (^2D).

	C8 low pH ACN	C18	Phenyl	T3	PFP (RPC)	PFP (HILIC) 5cm[a]	HILIC
C8 low pH ACN	1.00	2.06	2.06	1.70	1.04	11.70	2.79
C18	1.79	1.00	1.24	1.06	2.40	11.19	3.21
Phenyl	1.84	1.26	1.00	1.07	2.12	10.71	3.09
T3	1.69	1.07	1.09	1.00	2.31	10.95	3.12
PFP (RPC)	1.05	3.30	2.73	2.61	1.00	14.08	6.02
PFP (HILIC) 5cm	31.47	39.82	35.90	29.51	31.35	1.00	7.86
HILIC	12.61	20.17	18.14	14.88	27.57	16.65	1.00

[a] All column combinations were initially performed using the PFP (HILIC) 5cm column.

Table S8 cont. Gain factors of column combinations for the mixture of 16 synthetic cathinones.

	C8 low pH ACN	PFP (HILIC) 10cm	C8 high pH MeOH
C8 low pH ACN	1.00	13.05	7.80
PFP (HILIC) 10cm	27.21	1.00	N/A[a]
C8 high pH MeOH	7.94	N/A[a]	1.00

[a] Not applicable as the the PFP (HILIC) 10cm and high pH methanol were used to further optimize multi-dimensional separations with the C8 low pH ACN column as the first dimension.

Table S9 Gain factors of column combinations for the mixture of pentedrone positional isomers. The rows of the table represent the first dimension column (^1D) and the columns represent the second dimension column (^2D).

	C8 low pH ACN	C18	Phenyl	T3	PFP (RPC)	PFP (HILIC) 5cm[a]	HILIC
C8 low pH ACN	1.00	1.36	4.85	1.22	1.82	8.01	4.51
C18	1.26	1.00	3.18	1.03	1.86	7.01	3.73
Phenyl	3.54	2.98	1.00	2.32	2.35	4.70	2.24
T3	1.23	1.04	3.12	1.00	1.71	7.14	3.84
PFP (RPC)	2.68	3.40	5.17	2.36	1.00	7.68	4.77
PFP (HILIC) 5cm	8.18	9.47	6.74	6.91	4.35	1.00	2.08
HILIC	6.97	7.40	4.21	5.54	4.14	2.80	1.00

[a] All column combinations were initially performed using the PFP (HILIC) 5cm column.

Table S9 cont. Gain factors of column combinations for the mixture of pentedrone positional isomers

	C8 low pH ACN	PFP (HILIC) 10cm	C8 high pH MeOH
C8 low pH ACN	1.00	9.74	5.90
PFP (HILIC) 10cm	8.14	1.00	N/A[a]
C8 high pH MeOH	8.33	N/A[a]	1.00

[a] Not applicable as the the PFP (HILIC) 10cm and high pH methanol were used to further optimize multi-dimensional separations with the C8 low pH ACN column as the first dimension.

Actual Multi-Dimensional Peak Capacities $^{2D}[n_c]_{actual}$*

* calculated using the following formula $^{2D}[n_c]_{actual} = {}^{1}n_c\,[1 + S^2\,({}^{2}n_c - 1)]$; See equation 5 in manuscript.

Table S10 Actual multi-dimensional peak capacities for the mixture of 16 synthetic cathinones. The rows of the table represent the first dimension column with peak capacity $^{1}n_c$ and the columns represent the second dimension column with peak capacity $^{2}n_c$.

	C8 low pH ACN	C18	Phenyl	T3	PFP (RPC)	PFP (HILIC) 5cm[a]	HILIC
C8 low pH ACN	50.75	104.43	104.61	86.05	53.01	593.84	141.39
C18	120.96	67.54	84.08	71.26	162.00	755.88	216.52
Phenyl	117.45	80.36	63.81	68.28	135.20	683.24	197.13
T3	86.34	54.78	55.53	51.04	117.68	559.08	159.46
PFP (RPC)	43.82	136.90	113.55	108.49	41.54	584.76	249.99
PFP (HILIC) 5cm	581.34	735.44	663.10	545.06	578.96	18.47	145.18
HILIC	109.12	174.60	157.03	128.83	238.65	144.16	8.66

[a] All column combinations were initially performed using the PFP (HILIC) 5cm column.

Table S10 cont. Actual multi-dimensional peak capacities for the mixture of 16 synthetic cathinones.

	C8 low pH ACN	PFP (HILIC) 10cm	C8 high pH MeOH
C8 low pH ACN	50.75	662.42	395.86
PFP (HILIC) 10cm	649.70	23.88	N/A[a]
C8 high pH MeOH	395.01	N/A[a]	49.75

[a] Not applicable as the the PFP (HILIC) 10cm and high pH methanol were used to further optimize multi-dimensional separations with the C8 low pH ACN column as the first dimension.

Table S11 Actual multi-dimensional peak capacities for the mixture of pentedrone positional isomers. The rows of the table represent the first dimension column (^{1}D) and the columns represent the second dimension column (^{2}D).

	C8 low pH ACN	C18	Phenyl	T3	PFP (RPC)	PFP (HILIC) 5cm[a]	HILIC
C8 low pH ACN	8.96	12.22	43.47	10.92	16.34	71.73	40.37
C18	15.10	11.94	37.95	12.27	22.16	83.73	44.56
Phenyl	46.26	38.86	13.06	30.24	30.66	61.34	29.28
T3	10.46	8.82	26.46	8.48	14.48	60.49	32.53
PFP (RPC)	13.14	16.66	25.32	11.55	4.90	37.60	23.33
PFP (HILIC) 5cm	71.71	83.01	59.09	60.55	38.14	8.77	18.26
HILIC	39.55	41.95	23.85	31.43	23.48	15.88	5.67

[a] All column combinations were initially performed using the PFP (HILIC) 5cm column.

Table S11 cont. Actual multi-dimensional peak capacities for the mixture of pentedrone positional isomers.

	C8 low pH ACN	PFP (HILIC) 10cm	C8 high pH MeOH
C8 low pH ACN	8.96	87.25	52.80
PFP (HILIC) 10cm	87.44	10.75	N/A[a]
C8 high pH MeOH	52.59	N/A[a]	6.31

[a] Not applicable as the the PFP (HILIC) 10cm and high pH methanol were used to further optimize multi-dimensional separations with the C8 low pH ACN column as the first dimension.