Supplementary material

Methylone and pentylone – structure analysis of new psychoactive substances

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Table S1 Boltzmann populations of five stable conformers of (*R*)-methylone hydrochloride calculated at several levels of theory.

level of DFT theory	Boltzmann populations [%]				
	I	**II**	**III**	**IV**	**V**
B3LYP/6-311++G(d,p)	85	7	3	3	2
B3PW91/6-311++G(d,p)	83	6	4	5	2
B3PW91/ aug-cc-pVDZ	24	46	1	21	8
CAM-B3LYP/6-311++G(d,p)	81	7	4	5	3
CAM-B3LYP/aug-cc-pVDZ	63	14	2	19	2
wB97XD/6-311++G(d,p)	88	4	2	3	3
wB97XD/aug-cc-pVDZ	61	2	2	1	34
wB97XD/TZVP	89	4	2	2	3

Table S2 Boltzmann populations of nine stable conformers of (*R*)-pentylone hydrochloride calculated at several levels of theory.

level of DFT theory	Boltzmann populations [%]								
	I	**II**	**III**	**IV**	**V**	**VI**	**VII**	**VIII**	**IX**
B3LYP/6-311++G(d,p)	33	26	19	12	4	2	2	1	1
B3PW91/ 6-311++G(d,p)	30	23	18	16	4	3	3	2	1
B3PW91/ aug-cc-pVDZ	62	1	2	33	2	0	0	0	0
CAM-B3LYP/ 6-311++G(d,p)	18	8	11	27	26	4	3	1	2
CAM-B3LYP/ aug-cc-pVDZ	9	6	53	10	10	9	1	1	1
wB97XD/ 6-311++G(d,p)	3	7	5	14	61	4	3	1	2
wB97XD/aug-cc-pVDZ	47	8	3	8	27	1	5	1	0
wB97XD/TZVP	4	8	6	23	45	5	5	2	2

The development of preparative enantioseparation method

Since there has already been data on chiral separation of butylone available, we decided to test this method also for the resolution of methylone and pentylone first in the analytical mode (Fig. S1). While the mobile phase consisting of heptane/propan-2-ol (95/5, v/v) with 0.1% DEA as a basic buffer provided very nice resolution of pentylone enantiomers (R_S > 2), it failed for methylone.

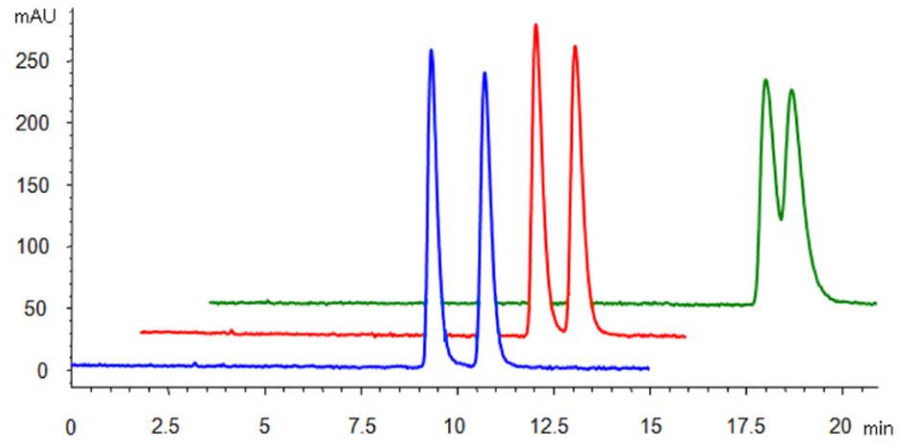

Fig. S1 Overlaid chromatograms of pentylone (blue), butylone (red) and methylone (green). Chiral stationary phase: Chiralart Amylose-SA (250×4.6 mm I.D., 5 μm), mobile phase heptane/IPA (95/5, v/v), 0.1% DEA, flow rate of 1 ml min^{-1}, laboratory temperature (23 °C). Detection wavelength of 254 nm was used.

We assumed that this behaviour can be explained by higher polarity of methylone, which can also be documented by higher retention times of this drug. Therefore, we increased the amount of IPA in the mobile phase and, consequently, switched to a hexane/EtOH mobile phase. In the analytical mode, we found that hexane/EtOH (95/5, v/v), 0.1% DEA mobile phase provides very good resolution of methylone enantiomers, however, at the cost of long retention times. Therefore, the amount of EtOH was gradually increased to 20% in the mobile phase, which led to acceptable length of separation method with good resolution under preparative mode separation (Fig. S2).

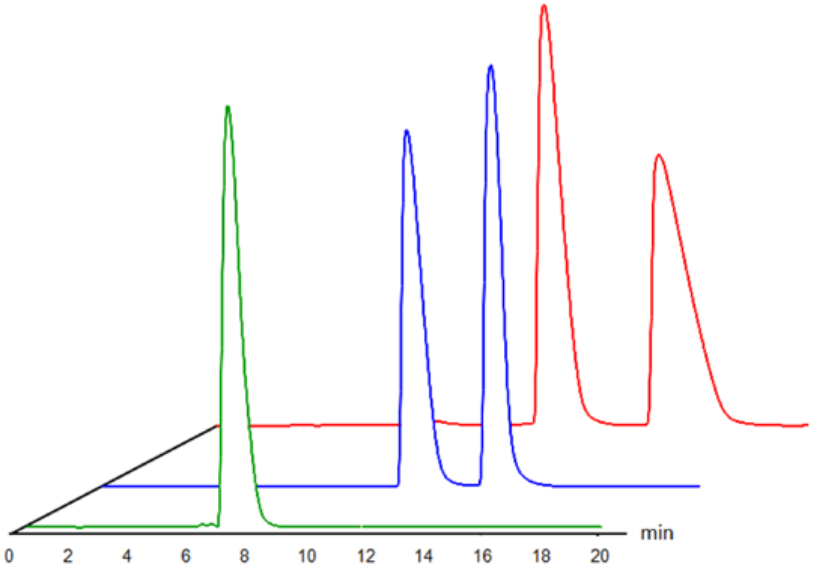

Fig. S2 Overlaid chromatograms of pentylone (green), butylone (blue), and methylone (red) under preparative enantioseparation conditions; chiral stationary phase: Chiralpak IA (250×20 mm I.D., 5 μm), mobile phase hexane/EtOH (4/1, v/v), 0.1% DEA, flow rate of 15 ml min^{-1}, laboratory temperature (23 °C). Detection wavelength of 254 nm was used.

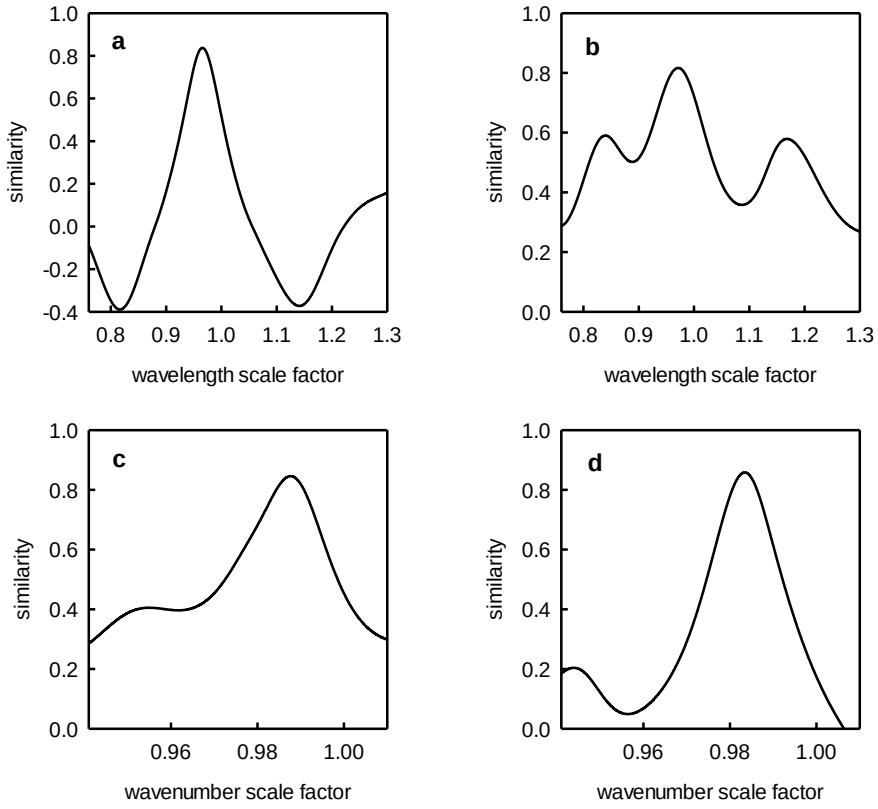

Fig. S3 Similarity plots for the calculated (B3LYP/6-311++G(d,p)) and experimental ECD (a), UV (b), IR (c) and VCD (d) spectra of (*R*)-methylone hydrochloride. The scale factors reveal the maximum similarity available among the experimental and calculated spectra.

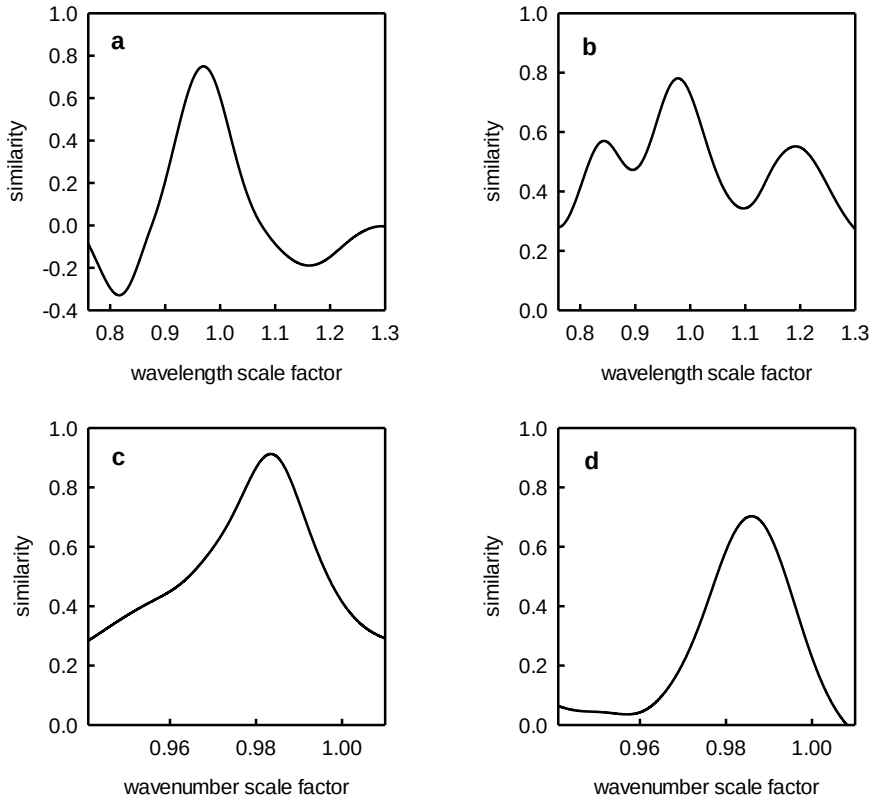

Fig. S4 Similarity plots for the calculated (B3LYP/6-311++G(d,p) or B3PW91/6-311++G(d,p)) and experimental ECD (a), UV (b), IR (c) and VCD (d) spectra of (*R*)-pentylone hydrochloride. The scale factors reveal the maximum similarity available among the experimental and calculated spectra.