	Dimethylcarbonate	Methanol	Isopropanol	Acetonitrile
Boiling point (°C) <sup>a)</sup>	91	65	82	82
Density at 25 °C (g/mL)	1.06	0.792	0.785	0.787
Viscosity at 20 °C (mPa s)	0.67	0.54	2.0	0.35
Vapor pressure at 25 °C (mm Hg)	55	127	45	89
LogP <sup>b)</sup>	0.5	-0.5	0.3	0
H-bond donor count	0	1	1	0
H-bond acceptor count	3	1	1	1
Water miscibility (v/v%)	13%	miscible	miscible	miscible
Relative column back pressure <sup>c)</sup>	0.98	1.0	1.14	0.96
Carbon molarity	35	25	39	38
UV-cutoff (nm) <sup>d)</sup>	220	210	210	190
Chemical safety				

Table S1. Key properties of dimethylcarbonate and commonly used HPLC organic solvents

<sup>a)</sup> Data retrieved from <u>https://pubchem.ncbi.nlm.nih.gov</u> on 06.12.2020

<sup>b)</sup> Computed by XLogP3 3.0 (PubChem release 2019.06.18)

<sup>c)</sup> Column pressure ratio between 10% methanol in water and 10% organic solvent in water (determined inhouse).

<sup>d)</sup> UV-cutoff for DMC was determined in house and is based on the pure solvent (supplementary Fig. S6). The UV-cutoff for 10% DMC in water is <200 nm.



**Fig. S1** Investigating the strong elution behavior under dimethylcarbonate. Fig. A and B show an investigation of the presence of ionic interactions under dimethylcarbonate and methanol which may originate from minor impurities with the capacity of ion pair formation (e.g. long chain acids). This possibility is clearly ruled out as no retention for the doubly charged species calcium and sulfate was observed ( $t_0 = 0.35$  min). In the experiment illustrated in Fig. C the possibility of the modification of the chemical structure of one of the most heavily impacted tested analytes was investigated with a molecule selective detector (ESI-MS). The elution pattern is in agreement with the observations based on HPLC-ICPMS, which rules out this possibility.



**Fig. S2** Investigating peak tailing under dimethylcarbonate. Fig. A shows the pH dependency of peak tailing for trazodone under dimethylcarbonate. Fig. C shows similar tailing behavior for methanol when used at high concentrations that promote strong elutions similar to dimethylcarbonate (Fig. B).



**Fig. S3** A comparison between the elution strength of dimethylcarbonate and different concentrations of commonly used organic solvents in liquid chromatography at different concentrations. Detection was based on UV absorption at 254 nm. The employed flow rate for these experiments was 0.5 mL min<sup>-1</sup> ( $t_0$  = ca. 0.25 min) to save up analysis time. The other conditions are identical to those in the experimental section. Thb: theobromine; caff: caffeine; dith: dithiodibenzoic acid; acet: acetophenone.



**Fig. S4** Retention time stability under dimethylcarbonate. Stability was assessed at pH 5.0 (ammonium acetate buffer) and pH 3.0 (ammonium formate buffer). The graphs show the retention times for toluene sulfonamide (k = 3.7). The stability at pH 5.0 was also examined by storing the mobile phase for 5 days which yielded retention times within the range of 1.62-1.63).

## 0 hours

IF/BK Press: 1.95E+2 Pa Analyzer Press: 5.86E-04 Pa



8 hours 10% DMC, 0.3 mL/min

IF/BK Press: 1.98E+2 Pa Analyzer Press: 5.89E-04 Pa Reflected power: 2-5 W RF matching: 1.8



IF/BK Press: 1.96E+2 Pa Analyzer Press: 5.84E-04 Pa Reflected power: 2-5 W **RF matching:** 1.8



Fig. S5 Cone appearance following the exposure to dimethylcarbonate and isopropanol. The above photos show the appearance of the sampler and skimmer cone after a cleaning procedure involving ultrasonication in 1% nitric acid, after exposure to 10% DMC at 0.3 mL min<sup>-1</sup> for 8 hours, and after exposure to 15% isopropanol (which has a comparable elution strength to 10% DMC) preceding by a second cleaning procedure as described above. Although the appearance of the cones under DMC was slightly cleaner than that under isopropanol, the illustrated changes in analyzer pressure which can be an indication of carbon buildup and possible loss of sensitivity were insignificant in both cases.



Fig. S6 UV spectrum of pure dimethylcarbonate in the range from 220 to 300 nm.