

Simultaneous determination of tetrabutylammonium and tributylamine in wastewater by IC/LC-MS

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Goal

To develop a robust, fast, selective, and sensitive chromatographic method to determine tributylamine and tetrabutylammonium in industrial wastewater

Introduction

Trialkyl amines (TAMs) and quaternary ammonium compounds (QACs) are known as environmental contaminants, with negative impacts on aquatic biota. QACs, in particular, are resistant toward biological degradation, which mandates their trace determination. The analytical speciation of TAMs and QACs relies heavily on gas chromatography (GC) and high-performance liquid chromatography (HPLC). Existing approaches describe separate workflows for TAMs and QACs.



TAMs are used as specific organic markers to trace their transport and impact on marine habitats. Valls et al. characterize TAMs as ubiquitous contaminants in the aquatic environment.¹ They have been found as impurities in QACs designed as fabric softeners in laundry detergents and other household products. QACs resist the biological treatment of wastewaters and are found at higher concentrations in urban sewage sludges.² TAMs have been identified in water and air, and to determine low concentrations of individual species in environmental samples GC and HPLC methods are used. The specific and sensitive determination of TAMs with HPLC often requires pre-column derivatization techniques to introduce chromophores or fluorophores and to increase retention on reversed-phase columns. For GC methods, derivatizations

are useful to improve separation efficiency by suppressing unwanted interactions of the amines with the stationary phase.³⁻⁶ As the sample matrix impacts the separation, recovery, and sensitivity, most of the known approaches describe additional sample preparation steps like liquid/liquid extraction, evaporation, solid-phase extraction (SPE) with different sorbent selectivity,⁷ and in some cases even steam distillation.⁸ Recent developments in ion chromatography (IC) show that the combination with mass spectrometric detection (MS) improves detection selectivity for low molecular weight amines.^{9,10}

QACs constitute a class of cationic surfactants with at least one hydrophobic hydrocarbon chain linked to a positively charged nitrogen atom. Because of their germicidal properties, QACs are used extensively in detergents, emulsifiers, fabric softeners, disinfectants, and floating agents. Their large-scale application predictably leads to their release into the environment, and they are detected ubiquitously in surface water, sediment, sewage effluent, municipal sludge, and soil, with the highest concentrations found in wastewaters of hospitals and laundries. QACs, as hydrophobic cationic surface-active compounds, are more toxic than anionic and nonionic compounds, causing adverse ecological effects even at low concentrations.^{11,12}

In most cases, QACs cannot be derivatized so that HPLC applications use direct detection schemes. UV-detection can be applied in the case of chromophores, e.g., for the determination of alkyl benzyl QACs. In other cases, the use of MS-detection is described.^{11,13} GC can be used for the determination of non-volatile QACs, after pyrolyzing the sample in the injector before the injection. At temperatures between 250 °C and 350 °C, QACs undergo a Hofmann degradation¹⁴ or a decomposition reaction similar to Stevens rearrangement¹⁵ forming TAMs. The volatile reaction products are then analyzed by GC-FID, GC-NPD, or GC-MS/MS.^{12,16,17} In the case of QACs with four identical alkyl groups, only one reaction product results.¹⁸ However, the pyrolytic rearrangements are temperature-dependent, not always specific or quantitative, and depending on the sample matrix.¹⁹

To the best of our knowledge, no chromatographic approach has been reported for the simultaneous determination of TAMs and QACs. For a recent environmental project, our group was challenged to analyze tributylamine and tetrabutylammonium ions in industrial wastewater samples. As tributylamine is the Hofmann dealkylation product of tetrabutylammonium, the use of GC was not advisable. Due to the lack of chromophores and

no applicable derivatization technique for the quaternary amine, a direct, specific, and selective detection was needed. The weak retention of non-derivatized, short-chained TAMs on conventional reversed-phase columns and the complex matrix composition of the industrial wastewaters added to the challenge.

This study describes the development and evaluation of a novel automated chromatographic method for the direct and simultaneous determination of tributylamine and tetrabutylammonium in environmental samples. This approach has the potential to serve as a comprehensive tool for the simultaneous determination of other TAMs and QACs.

Experimental

Equipment and consumables

- Thermo Scientific™ Dionex™ ICS-6000 DP Pump module (P/N 22181-60007)*
- Thermo Scientific™ Dionex™ ICS-6000 DC Detector/Chromatography module (P/N 22181-60043) with conductivity detector and cell (P/N 079829)
- Thermo Scientific™ Dionex™ AS-AP Autosampler (P/N 079656) with 250 µL sample syringe (P/N 074306) and 1.2 mL buffer line (P/N 074989)
- Thermo Scientific™ ISQ™ EC Single Quadrupole Mass Spectrometer (P/N ISQEC0001C)
- PEAK® Scientific Genius NM32LA Nitrogen Generator (P/N 1R77606-1230 (230 V))
- Thermo Scientific™ Dionex™ IonPac™ NS1-5µm Analytical Column (4 × 150 mm, P/N 039568) with guard column Dionex IonPac NG1 (4 × 35 mm, P/N 039567)
- Thermo Scientific™ Dionex™ CERS 500e Cation Electrolytically Regenerated Suppressor for External Water Mode (2 mm, P/N 302664)
- ISMATEC® Peristaltic Pump, Reglo Digital MS-2/12-160 (P/N 300122) with consumables kit (P/N 64911) and Tygon Tubing 1.5 mm ID (P/N SC0065)
- Dionex AS-AP Autosampler Vials: 1.5 mL polypropylene vials with caps and septa (P/N 079812)
- Thermo Scientific™ Chromeleon™ Chromatography Data System (CDS) version 7.2

* These methods can also be run on a Thermo Scientific™ Dionex™ Integriion™ HPIC system

Conditions

Parameter	Value
IC system	Dionex ICS-6000
MS detector	ISQ EC single quadrupole mass spectrometer
Columns	Dionex IonPac NS1-5 μ m (4 \times 150 mm) with Dionex IonPac NG1 (4 \times 35 mm)
Eluents	IC experiments: 2 mM heptafluorobutyric acid (HFBA) in a mixture of water and acetonitrile (volume fraction ϕ = 50%); isocratic conditions LC-MS experiments: 2 mM formic acid (FA) in a mixture of water (ϕ = 44%) and acetonitrile (ϕ = 56%); isocratic conditions
Flow rate	0.5 mL/min IC 1.0 mL/min LC-MS
Injection volume	10 μ L (push seq. full)
Temperature	30 $^{\circ}$ C (column compartment) 20 $^{\circ}$ C (detector compartment)
Backpressure	~1200 psi IC ~2400 psi LC-MS (100 psi = 0.6894 MPa)
Suppressed conductivity detection (MPIC)	Thermo Scientific™ Dionex™ CERS 500e Cation Electrolytically Regenerated Suppressor (2 mm), regeneration current = 7 mA, external water flow rate (1 mL/min) delivered by a peristaltic pump. Remark: The recommended volume fraction of organic solvent in the mobile phase should not exceed 40% ²⁰ if electrolytic regeneration of the suppressor is used.
Background conductance (MPIC)	<1 μ S/cm
Run time	>25 min for IC 9 min for LC-MS
Mass spectrometric detection	
Ionization interface	Heated electrospray ionization (HESI), positive mode
Gas control	Sheath gas pressure: 70 psi Aux gas pressure: 8.7 psi Sweep gas pressure: 0.5 psi
Source voltage	(+) 3000 V
Vaporizer temperature	459 $^{\circ}$ C
Ion transfer tube temperature	300 $^{\circ}$ C
Selected ion monitoring (SIM) scan	SIM for tributylamine [M+1] ⁺ m/z 186.4 (Scan width 1.00 amu / CID 0 V) SIM for tetrabutylammonium [M] ⁺ m/z 242.5 (Scan width 1.00 amu / CID 0 V)
Full scan	m/z 90–260 (Scan time 0.111 s / CID 0 V) Tube lens voltage: 50 V

Preparation of solutions and reagents

Mobile phases

The mobile phases used for the IC experiments were composed of heptafluorobutyric acid (ACROS Organics™, 99%), acetonitrile (Honeywell Riedel-de Haen™ CHROMASOLV™ Plus, for HPLC, \geq 99.9%) and deionized (DI) water (class 1, >18 M Ω -cm, TOC <5 μ g/L). The DI water was also used for the continuous electrochemical regeneration of the suppressor (see Conditions).

The eluents for the LC-MS application consisted of DI water (Fisher Chemicals, Optima™ LC/MS Grade), acetonitrile (Fisher Chemicals, UHPLC-MS Optima), and formic acid for mass spectrometry (Honeywell Fluka).

Standard solutions

Standard solutions were prepared by diluting a 40% TBAOH solution (Merck) and by dissolving tributyl ammonium pyrophosphate (\geq 99%, Merck KGaA, P8533) in DI water. The tetrabutylammonium check standards were prepared by dissolving tetrabutylammonium bromide (\geq 99%, Merck KGaA, 193119) in DI water. Aqueous standard solutions containing tetrabutylammonium and tributylamine were prepared separately. The LC-MS standards contained tributylamine between 0.02 mg/L and 2.3 mg/L, and tetrabutylammonium between 0.05 mg/L and 4.7 mg/L.

Sample handling and preparation

The liquid, yellowish to brownish wastewater samples of distinct odors were taken over a period of 12 weeks from different sampling sites. They were kept at 4 $^{\circ}$ C to 6 $^{\circ}$ C in the dark until measurement. Only the aliquots needed for the experiments were removed and diluted with DI water, while the primary sample was returned to the refrigerator as quickly as possible to minimize a potential loss of the volatile tributylamine.

Results and discussion

MPIC separation of tributylamine and tetrabutylammonium in industrial wastewater

Initial experiments focused on the use of suppressed conductivity as a direct detection mode using mobile phase ion chromatography (MPIC).^{21,22} The separation of tributylamine and tetrabutylammonium was achieved under acid eluent conditions with HFBA as the ion-pairing reagent and isocratic elution. Detection was carried out using suppressed conductivity detection with electrolytic regeneration of the suppressor in the external water mode. To prevent unwanted cation exchange interactions of amines and ammonium components, as known for silica-based stationary phases, the polymeric-based Dionex IonPac NS1 column was chosen. Figure 1 shows the chromatogram of a combined tributylamine and tetrabutylammonium standard solution. The components are well separated, eluted as symmetric peaks, and suppressed conductivity detection would allow their detection and quantification in the single-digit mg/L-concentration range.

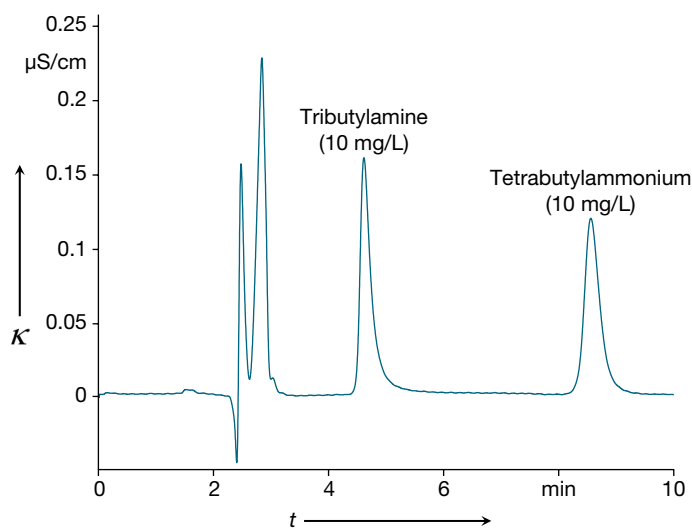


Figure 1. Chromatogram of a standard solution of tributylamine and tetrabutylammonium ($\rho = 10$ mg/L, each) using MPIC. For experimental information, see Conditions.

A chromatogram of industrial wastewater obtained under the same conditions (Figure 2), however, showed a sizeable interfering peak at the beginning of the chromatogram caused by other cationic sample species present at high concentrations. This peak overlapped with tributylamine, tetrabutylammonium eluted on its signal tail, and the signal took about 25 min to reach the starting baseline level.

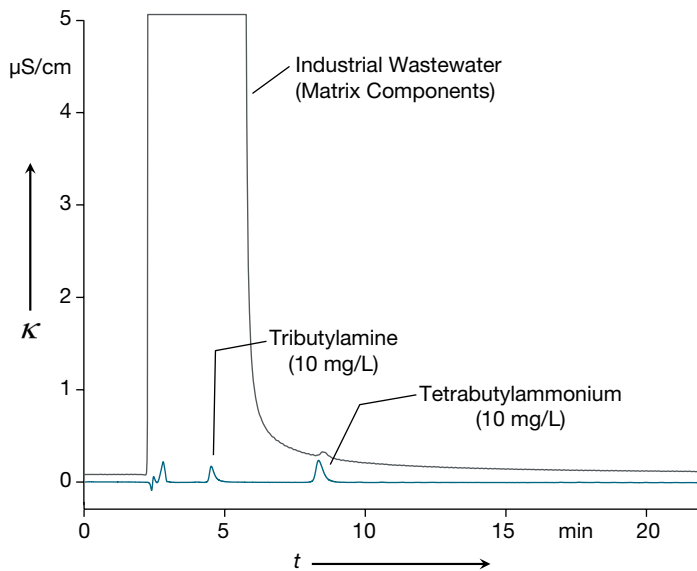


Figure 2. Overlay of two chromatograms. An industrial wastewater sample after dilution (1 to 10), and a standard chromatogram of tributylamine and tetrabutylammonium ($\rho = 10$ mg/L, each) using MPIC. For experimental information, see Conditions.

Modifications of the experimental conditions, e.g., more sample dilution or gradient elution with acetonitrile, did not improve the chromatographic resolution and prevented higher sample throughput due to longer injection cycle times and increased manual labor.

LC-MS detection of tributylamine and tetrabutylammonium in industrial wastewater

To overcome the limitations of the MPIC approach, a single-quadrupole MS-detector was added to the experimental setup. The conditions were adapted using volatile formic acid (FA) in the eluent instead of HFBA. The suppressor was removed, and the column effluent directed to the HESI interface of the ISQ EC mass spectrometer. Lewis *et al.* described that ionization efficiency for low molecular weight amines improved with an acidic effluent entering the HESI interface.⁹

The conductivity detector, though not used for the following experiments, should be kept in the instrument configuration, as it can help in case of troubleshooting incidents. The volume fraction of acetonitrile was slightly increased compared to the afore-mentioned conditions, and the flow rate was set to 1.0 mL/min.

An overlay of representative SIM-chromatograms of standard solutions is shown in Figure 3. The mass spectra of tributylamine and tetrabutylammonium are displayed in Figure 4 and Figure 5, respectively. Despite the high temperatures used for vaporization and in the ion transfer tube (see Conditions), no in-source Hofmann elimination was observed for tetrabutylammonium. It would show as a signal in the tributylamine channel at the retention time (RT) of tetrabutylammonium.

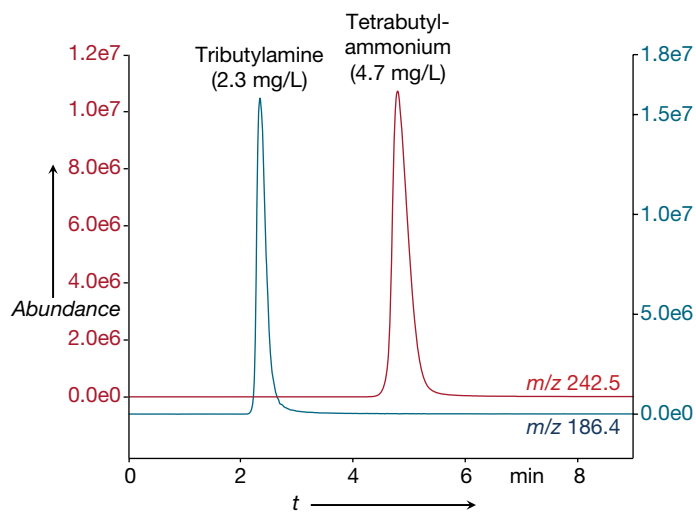


Figure 3. Overlay of LC-MS chromatograms (SIM-channels) of tributylamine and tetrabutylammonium standard solutions. For experimental information, see Conditions.

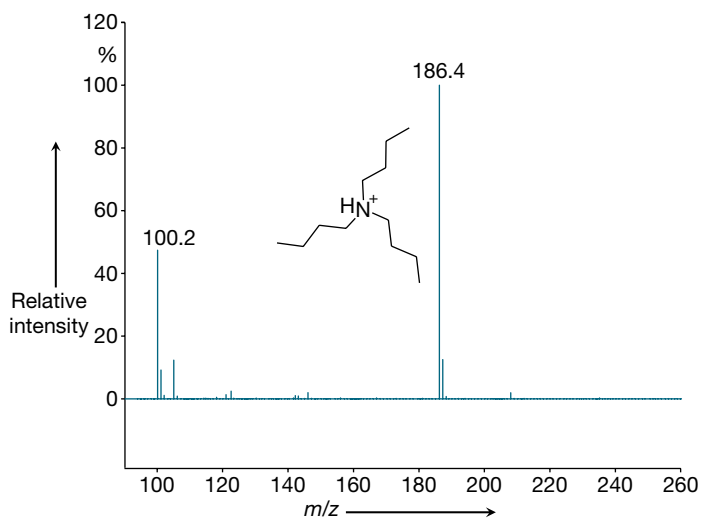


Figure 4. Mass spectrum of tributylamine showing the cationized molecule $[M+1]^+$ at m/z 186.4

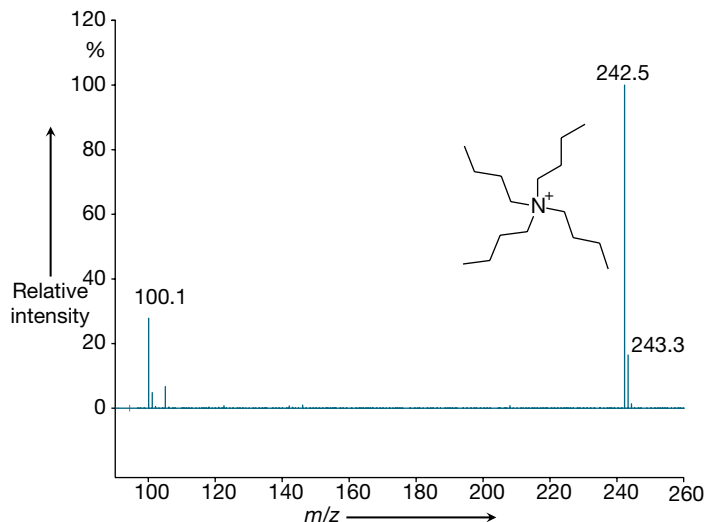


Figure 5. Mass spectrum of tetrabutylammonium showing the cation at $[M]^+$; m/z 242.5

In contrast to the GC-method described by Lopez *et al.*, no internal standard is needed, facilitating a simplified quantification using the external standard calibration approach.¹⁸

A representative overlay of the SIM-channels for tributylamine and tetrabutylammonium of diluted industrial wastewater is shown in Figure 6. The selective MS-detection allows the interference-free detection of both components at low concentrations.

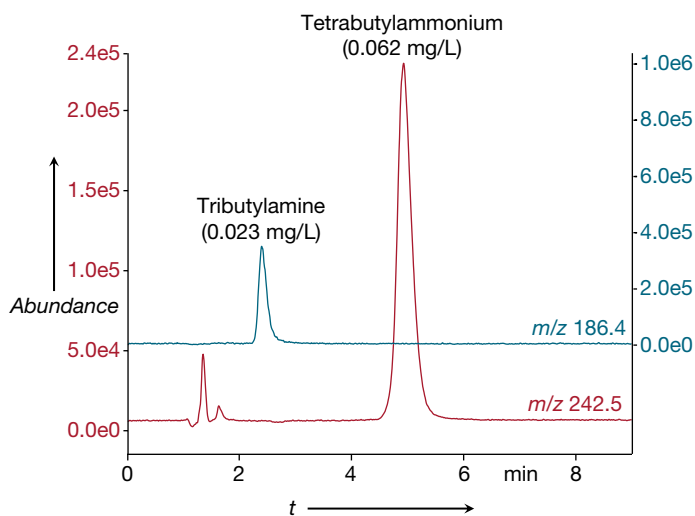


Figure 6. Overlay of SIM-channels of diluted industrial wastewater (1 to 20) spiked with tributylamine (0.023 mg/L); the labeled concentrations are for the diluted sample. The tetrabutylammonium concentration in the original sample was 1.24 mg/L. For experimental information, see Conditions.

External calibrations were conducted using five concentration levels in the range of 0.02 mg/L to 2.3 mg/L for tributylamine and between 0.04 mg/L and 4.7 mg/L for tetrabutylammonium with duplicate or triplicate injections per level. All calculations used the least-squares method and included the origin, as it is permissible for blank-free analytical procedures.²³ Best correlations resulted in a second-order polynomial fit (Table 1). The analytical numbers of merit were calculated according to ISO 8466-2.²⁴

Intra-day reproducibility for the lowest tetrabutylammonium calibration standard (0.05 mg/L) was determined to be <0.5% for the RT and <2.5% for the amount (Table 2).

Inter-day reproducibility of the method was evaluated by injecting a tetrabutylammonium check standard solution (0.4 mg/L). Retention time RSD was below 0.5%, and RSD for the amount was lower than 2.2% (Table 3). Comparing inter-day and intra-day reproducibility data shows no significant performance difference, despite the difference in analyte concentration.

Table 1. LC-MS calibration details

Component	Coefficient of determination (r ²)	Relative standard deviation (RSD) of calibration	LOD (mg/L)	LOQ (mg/L)
Tributylamine	>0.999	3.5	0.023	0.075
Tetrabutylammonium	>0.999	2.9	0.10	0.32

The calculations, based on a second-order polynomial, were performed according to ISO 8466-2; confidence level: 95%; tolerated deviation at LOD: 33.3%.

Table 2. Intra-day reproducibility data for the lowest tetrabutylammonium calibration standard (0.05 mg/L, SIM, m/z 242.5)

Injection	Tetrabutylammonium			
	Retention time (RT) (min)	Amount (mg/L)	Area (counts*min)	Height (counts)
1	4.90	0.041	49808	159905
2	4.90	0.040	49611	156183
3	4.93	0.040	49019	153844
4	4.93	0.040	48825	154696
5	4.92	0.040	48827	154890
6	4.87	0.041	49690	158339
7	4.91	0.041	49803	159152
8	4.92	0.043	52045	165036
9	4.87	0.042	51341	163232
10	4.89	0.041	50303	158518
11	4.91	0.040	49458	157055
Maximum	4.93	0.043	52045	165036
Average	4.91	0.041	49885	158259
Minimum	4.87	0.040	48825	153844
Standard deviation (SD)	0.02	0.001	1013	3514
RSD	0.4	2.4	2.0	2.2

Table 3. Inter-day reproducibility for a tetrabutylammonium check standard (0.41 mg/L, SIM, *m/z* 242.5)

	Tetrabutylammonium			
	RT (min)	Amount (mg/L)	Area (counts*min)	Height (counts)
	4.85	0.391	501948	1553325
	4.86	0.387	496137	1545560
	4.85	0.386	495553	1510096
	4.87	0.387	496587	1534690
	4.89	0.395	505840	1562909
	4.89	0.401	513202	1585867
	4.86	0.398	509754	1595135
	4.89	0.377	484092	1519075
	4.92	0.376	482748	1506871
	4.89	0.389	499083	1566021
Maximum	4.92	0.401	513202	1595135
Average	4.88	0.389	498495	1547955
Minimum	4.85	0.376	482748	1506871
SD	0.02	0.008	9903	30512
RSD	0.5	2.1	2.0	2.0

The corresponding precisions for tributylamine were in a similar range with values of better than 0.9% for the RT across all standards and spiked samples. Peak area reproducibility was better than 2.6% obtained from repetitive injections of a check standard solution (0.11 mg/L; n = 5).

The inter-day stabilities of the RTs for tetrabutylammonium measured in wastewater samples from different sampling sites were better than 1.2% (n = 71). The tetrabutylammonium amounts of the same sample type were determined with precisions better than 2.5%. The wastewater samples did not contain tributylamine.

Despite the stable retention times under isocratic conditions, we included a column rinsing step at the end of each sequence by increasing the acetonitrile concentration to 90% for 20 min, followed by a 20 min equilibration at the analytical conditions.

Table 4. Reproducibility data for a representative wastewater sample; dilution 1 to 20; the sample did not contain tributylamine.

Injection	Tetrabutylammonium	
	RT (min)	Amount (mg/L)
1	4.85	0.065
2	4.92	0.063
3	4.85	0.064
4	4.87	0.063
5	4.92	0.061
6	4.87	0.062
7	4.89	0.062
8	4.86	0.062
9	4.85	0.063
10	4.84	0.062
11	4.88	0.067
12	4.90	0.065
13	4.93	0.064
14	4.87	0.064
15	4.87	0.063
Maximum	4.93	0.067
Average	4.88	0.063
Minimum	4.84	0.061
SD	0.03	0.001
RSD	0.5	2.1

Conclusion

A robust and easy to use IC/LC-MS application and workflow were developed to allow the separation and detection of tributylamine and tetrabutylammonium in complex industrial wastewaters. The volatile eluent consisting of acetonitrile, water, and a small amount of formic acid supported the ionization of the amine. Due to the polymer-based non-functionalized column, symmetric peaks were obtained without any further eluent additives. LODs and LOQs for both analytes were in the sub mg/L-range, attesting to the high sensitivity of the single quadrupole MS detection. High throughput was achieved with injection cycle times of 9 min. Sample preparation was limited to a simple dilution of the wastewater samples with DI water. This approach and workflow have the potential to be applied to other TAMs and QACs in environmental samples.

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