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Review

Sample preparation in alkaline media

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Abstract

The use of tetramethylammonium hydroxide, tertiary amines and strongly alkaline reagents for sample treatment involving extraction and digestion procedures is discussed in this review. The preparation of slurries is also discussed. Based on literature data, alkaline media offer a good alternative for sample preparation involving an appreciable group of analytes in different types of samples. These reagents are also successfully employed in tailored speciation procedures wherein there is a critical dependence on maintenance of chemical forms. The effects of these reagents on measurements performed using spectroanalytical techniques are discussed. Several undesirable effects on transport and atomization processes necessitate use of the method of standard additions to obtain accurate results. It is also evident that alkaline media can improve the performance of techniques such as inductively coupled plasma mass spectrometry and accessories, such as autosamplers coupled to graphite furnace atomic absorption spectrometers.

Keywords: Sample preparation; Alkaline medium; Tetramethylammonium hydroxide; Tertiary amine; Strong base

Contents

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1. Introduction

Sample preparation is one critical step of an analytical procedure, and despite all recent advances it still requires further development to reach the same high standards of all instrumental techniques required for accurate determination of analytes [1–4].

Advances in sample preparation over the last few decades have been propelled by the advance of microwave-assisted procedures, as detailed in landmark books [5–7] and reviews [8–13].

Almost all of the old and new sample preparation procedures are based on the use of concentrated acids for promoting aggressive attack, especially under high temperatures and high pressures when conducted using closed, pressurized reaction vessels.

A close look at the literature, however, reveals that the use of alkaline reagents has also led to the development of suitable sample preparation procedures, involving digestions, extractions, or formation of slurries before determinations using spectroanalytical techniques.

This review will discuss the literature dealing with the use of tetramethylammonium hydroxide (TMAH), water-soluble tertiary amines (CFA-C), and strong bases for sample preparation. The discussion emphasizes analytes, samples and effects on measurement conditions. It will become evident that the employment of an alkaline medium is a good alternative to some analytical tasks and provides fast and simple sample preparation approaches.

2. Procedures based on tetramethylammonium hydroxide (TMAH)

2.1. General background

Depending on the analysis goals, specific information about structural composition of molecules is important and may be obtained by degradative methods that form other individual subunits. In 1989, Challinor proposed the use of a modified pyrolysis method based on the use of tetramethylammonium hydroxide (TMAH) [14]. The aim of TMAH pretreatment was to avoid thermal decarboxylation and dehydroxylation reactions and to improve gas chromatographic separation by converting carboxylic acids and phenols into more volatile methyl derivatives.

Tetramethylammonium hydroxide is an alkaline (pH 13.4–14.7) solution with the chemical formula $(CH_3)_4NOH$. It is commercially available as 25% m/v in water, 25% m/v in methanol, or 10% m/v in water solutions. Several chemical companies market it, e.g., Carlo Erba (Italy), Fluka (Switzerland), Merck (Germany), Riedel-de-Haën (Germany), Sigma-Aldrich (USA) and Tama Chemicals (Japan). Some of these TMAH brands can suffer contamination, yielding high blank levels, which inhibit ultra trace analysis, but some companies can supply ultra pure TMAH. The reagent is a colorless liquid with a strong amine odor, completely soluble in water and stable at room temperature. Little information about its toxicity is available, but vapors of this reagent cause irritation to the nose, throat and respiratory system. Its absorption through the skin may lead to adverse effects [15]. On the other hand, treatment of wastewater containing TMAH consists of a combination of two decomposition processes: pyrolyzing TMAH to TMA (tetramethylammonium) and decomposing TMA to N_2, H_2O, and CO_2 by means of a selective oxidation catalyst for nitrogenous compounds [16].

Strongly basic TMAH causes hydrolytic scission and methylation of ester, amide and some ether bonds at temperatures around 250–300 °C, allowing the classification of TMAH applications into two different categories: TMAH thermochemolysis (carried out at temperatures low enough to adequately characterize certain C–O linked biomacromolecules) and TMAH pyrolysis (temperatures of about 500–600 °C are necessary to degrade the more resistant C–C bond structural backbone) [17].

According to these characteristics, TMAH has been widely used for studies involving chemical species such as humic substances [17,18], lignin [19], fatty acids [20–22], anisotropic etching properties [23], etc. The use of quaternary ammonium hydroxides, such as Soluene [24] and Lumatom [25], was previously described for the dissolution of biological materials as an alternative to conventional digestion for the determination of metallic ions by atomic spectrometry.

2.2. Digestion, extraction and dilution procedures

Although some atomic spectrometric techniques allow the direct determination of inorganic species without sample treatment, it is usually necessary to dissolve the sample prior to analysis.

As early as 1973, use of TMAH was proposed for digestion of animal tissues [26]. Murthy et al. used an aqueous TMAH solution for digestion of rat liver, kidney homogenates and homogeneous rat hair samples. The results obtained for determinations of Cd, Cu, Pb, and Zn agreed with those obtained by a conventional acid digestion using concentrated nitric acid or nitric–perchloric acids. The use of reference solutions prepared in 5% v/v HNO_3 was not suitable due to changes in the aspiration rate of the digestates arising from the viscosity and surface tension effects caused by TMAH [26].

In the same decade, Julshamn and Andersen [27] used TMAH in toluene for digesting human muscle biopsies for determination of Al, Cd, Cu, and Mn by GFAAS. All metals but Al were successfully determined. This same technique was employed for determination of Se in human spermatozoa and prostasomes digested with 25% m/v TMAH in methanol [28]. The authors emphasized that the results obtained using TMAH digestion agreed well with a conventional digestion procedure using concentrated nitric acid and did not require either heating or strong acids and was suitable for small biological samples.

Tetramethylammonium hydroxide in the presence of ethylenediaminetetraacetic acid (EDTA) was used by Uchida et al. in 1992 for the digestion of botanical samples [29]. In 1994, Hayashibe et al. [30] proposed the use of TMAH for the on-line

decomposition of proteins prior to the spectrophotometric determination of zinc in human serum samples.

Special attention has been given to methods of sample preparation using reagents that involve procedures with minimal handling and time consumption, thus reducing sample loss or possible contamination [31–33]. Many studies have been reported based on different applications of TMAH [21,22,29,31–87].

Martín-Hernández et al. [21] used TMAH as a catalyst to obtain methyl esters, but the reduction of the analysis time was counter-balanced by problems with the pyrolysis of excess TMAH. On the other hand, Juárez et al. [22] obtained good results for the determination of free fatty acids by gas chromatography after the extraction of lipids with diethyl ether and treatment with TMAH. The solubilization of biological materials that contain fats may be carried out with a solution of TMAH [20–22]. This procedure has been used prior to determination of different analytes by ICP OES, ICP-MS and GFAAS.

Some examples are presented in Table 1 involving the use of TMAH for different kinds of samples. Methods for speciation studies are also reported [34–40,69–72,82–84], mainly involving arsenic, lead, mercury, and tin in various samples.

Extraction procedures employing TMAH involve, in general, a complete or partial dissolution of the sample with TMAH. This step is usually carried out with heating and/or magnetic [29,32–34,37,54] or ultrasonic [33,40,41] stirring. For this purpose, different proportions of sample/TMAH have been used. Room temperature [41,42,54,55] and temperatures from 60 to 120 °C have been applied to the sample/TMAH mixture using a water bath [41,42], microwave-assisted heating with closed [29,36,37,39,46–49] or open vessels [32,34,40] and electrothermal vaporization (ETV) [31,35], in which the TMAH is used to prepare a slurry of the sample. In addition, different approaches related to the heating time have been undertaken, as summarized in Table 1. Procedures employing other reagents in extraction steps [29], mainly for speciation purposes [34–37,39,40,54–56,69–72,82–84] have also been described.

For the analysis of botanical samples, a mixture of TMAH and EDTA was used to prepare a suspension of the sample, in which 12 elements were determined by ICP OES [29], FAAS and GFAAS [49]. In other cases, for the determination of organotin compounds [34,56], a derivatization of butyl- and triphenyl-tin was carried out in the same medium containing TMAH. Another example is the work of Willie et al. [35] in which a mixture of reagents containing iodoacetic acid, sodium thiosulfite, and acetic acid was added to a previously prepared slurry for determination of inorganic mercury by ETV-ICP-MS.

Tan et al. described high-pressure homogenization as a rapid, sample treatment procedure to generate slurries of biological tissues for the determination of Cd, Cu and Pb [57] by GFAAS. The strategy consisted of macerating (20,000 rpm, 60 s) the sample matrix in a medium of tetramethylammonium hydroxide-ethanol and subjecting the blended mixture to four passes through a flat valve homogenizer (34.58 MPa). The final solutions did not contain visible suspended solids and were stable for at least 6 days. However, the homogenization process introduced metallic contaminants into the sample. The combination of high-pressure homogenization and alkaline medium was also evaluated by Tan et al. [73] and Chen and Marshall [81]. These studies investigated the determination of Cr, Cu, Fe, Mn, Ni, and Se [73] and Se [81] in biological materials by GFAAS. In general, slurries obtained in TMAH media are sufficiently homogeneous to yield satisfactory results when the sample particle size is relatively homogeneous and larger particles are absent [51].

On the other hand, a sample can be simply diluted, as demonstrated by Matusiewicz and Golik [33], Stürup and Büchert [50] and Tao et al. [51]. The former study introduced a sample suspension, which was homogenized by sonication, into a microwave induced plasma optical emission spectrometer for analysis.

As already mentioned, most spectroanalytical techniques are based on the introduction of liquid samples. This has led to the development of different methods for sample treatment. In some cases, however, it is important to evaluate the effect of the reagents themselves on the spectrometric measurements.

The use of chemical modifiers is well established for GFAAS analysis. Nevertheless, when TMAH is used for sample treatment a modifier compatible with the alkaline medium should be selected. Tsalev et al. [59] used V and V+Pd as chemical modifiers for the determination of several inorganic ions in conjunction with different sample treatments (TMAH, HNO_3, $HNO_3/HClO_4$ and Triton X-100). They observed that the vanadate modifier was compatible with the alkaline sample solutions but, in the presence of the mixed chemical modifier, precipitation may occur. This problem was not observed for palladium-tungsten and alkaline solubilization with tetraethylammonium hydroxide (TEAH) [60].

According to Ribeiro et al. [45], the use of an acidic solution of Pd as a chemical modifier may result in formation of a precipitate with the alkaline TMAH solution, requiring specific and long pipeting time and temperature programs. Nevertheless, this limitation was not observed when a mixture of Pd and phosphate was used. In addition, TMAH is not aggressive to the graphite tube, and more than 1000 atomization cycles were performed for the determination of cadmium. However, for the same determination, Silva et al. [61] recommended the use of Rh as chemical modifier, which allowed low detection limits, considering the low blanks values obtained, and no evidence of problems concerning precipitation in the presence of the alkaline reagent.

A problem found with the determination of aluminum in human serum by GFAAS is related to the accumulation of carbonaceous residues inside the graphite tube, which affects repeatability and sensitivity and interferes with the background correction. To overcome this problem, Almeida and Lima [62] used TMAH as a chemical modifier. A 15-μl aliquot of sample was introduced into the graphite tube together with 5 μl of 1 mol L^{-1} TMAH using the sequence: (1) pipeting TMAH, (2) pipeting sample (or standard), (3) injection into the graphite tube. TMAH promotes the in situ decomposition of proteins and prevents the build-up of carbonaceous residue.

Table 1
Applications of tetramethylammonium hydroxide for sample preparation

Sample type	Analytes	Procedure	Technique [a]	Remarks	Ref.
Rat liver, kidney homogenates, and homogeneous rat hair	Cd, Cu, and Zn	Biological samples were digested using aqueous TMAH.	FAAS	Reference solutions prepared in 5% v v^{-1} HNO_3 were not suitable for calibration due to viscosity and surface tension effects on the aspiration rate. The developed procedure was faster and safer than a conventional acid digestion procedure.	[26]
Pepperbush, chlorella, hair, mussel, tea leaves, Sargasso, rice flour, and bovine liver	P, Zn, Ni, Al, Fe, Mn, Mg, Ca, Cu, Sr, Na, and K	A mass of 50 mg of dried sample (at 85 °C for 4 h) was introduced into a vial containing a stirring bar and 1 ml of 25% m v^{-1} TMAH and 0.2 mol l^{-1} EDTA. The mixture was agitated for 10 min and the vial was then closed. The vial was placed in a PTFE vessel (containing 2 ml of water) inserted in a stainless-steel jacket. The vessel was heated for 4 h in a thermostated oven at 120 °C. The resulting solution was diluted with 2 ml of water, the pH was adjusted to 8–9 with 3 mol l^{-1} HCl and diluted with water to 5 ml. This solution was centrifuged for 3 min and the supernatant was analyzed by ICP OES.	ICP OES	TMAH was used with EDTA. The accuracy for each element was different from sample to sample, mainly for Al and Fe.	[29]
Animal tissues, orchard leaves, and whole egg powder	As, Se, Te, Ag, Cr, Cu, V, Ni, Mn, Co, Cd, Pb, Sb, Sn, and Bi	*Animal tissue and whole egg powder:* Use of 2 µl of 25% m v^{-1} TMAH per milligram of sample. *Plant leaves:* Use of 2 ml of 25% m v^{-1} TMAH per milligram of sample and heating (90 °C) for 2 h.	ETV-ICP-MS	Good accuracy was obtained for four certified reference materials, although Cr and Cd could not be determined in the bovine muscle sample.	[31]
Powdered coffee and milk	Ca, Fe, K, Mg, Na, P, Se, Cu, Mn, Sn, and Zn	*Soluble coffee samples*: 350 mg of sample was mixed with 500 µl of 25% m v^{-1} TMAH and the solution was heated (80 °C) for 10 min in a block digester, with constant stirring. *Powdered milk samples*: 350 mg of sample was diluted with 1000 µl of water followed by addition of 1000 µl of 25% m v^{-1} TMAH. The resulting solution was heated at 80 °C for 20 min (whole milk) or 30 min (skimmed milk) in a block digester, with constant stirring. For both coffee and milk samples, the resulting solutions were diluted to 25 ml with water.	ICP OES	LODs for analysis of milk were generally better those for analysis of coffee.	[32]
Lobster hepatopancreas, bovine liver, and milk powder	Na, K, Ca, Mg, Cu, Fe, Sr, and Zn	250 mg of the samples studied was mixed with 2–4 ml of 25% m v^{-1} TMAH and, after 2 min, 2 ml of water was added. The resulting suspensions were treated by sonication (40 W) for 2–4 min. After sonication, the samples were diluted to 10 ml with water.	MIP-OES	Calibration against aqueous solutions did not lead to accurate results. The use of standard addition technique is recommended.	[33]
Fish tissue	Sn (triphenyltin and butyltin compounds)	A 5 ml portion of the TMAH solution was added to a 0.1 g tissue sample in an extraction vessel. The mixture was stirred magnetically for 4 h at 60 °C, then 20 ml of a buffer pH 5, 1.3 ml of acetic acid, 1 ml of $NaBEt_4$ solution and 1 ml of hexane containing the internal standard were added and the mixture was extracted for 5 min.	GC-AED	The results for tributyltin were better than those for triphenyltin (which is unstable). The procedure with TMAH was faster than acid digestion.	[34]
Dogfish (muscle and liver) and lobster (hepatopancreas)	Hg (inorganic and total)	A 0.25 g sample was mixed with 4 ml of TMAH. After reacting for approximately 5 min, the solution was diluted in water to a volume of 25 ml.	ETV-ICP-MS	No chemical modifiers were required.	[35]

Hair	Gd and Gd-DTPA	Use of 25% m v^{-1} TMAH in a microwave-assisted at 60 °C for 6 h. Before analysis, the solutions were adjusted to pH 7.4.	SEC-ICP-MS	TMAH induced partial degradation of Gd-DTPA to Gd^{3+}.	[36]
Potatoes and mussels	Triphenyltin	A 0.5 g mass of freeze-dried sample was placed in a 40-ml vial with a Teflon stirring bar and 5 ml of TMAH solution. The mixture was heated at 60 °C for 1 h. After cooling, 30 ml of ammonium buffer (pH 8) was added. In the next step, 500 μl of $NaBEt_4$ solution (1% m v^{-1}) was added and the vial was placed in a thermostatically controlled bath at 85 °C for 15 min.	SPME-CGC-ICP-MS	Use of a suitable internal standard was essential for obtaining accurate results.	[37]
Fish tissue	Mono-, di- and tributyltin	A mass of 0.1–0.2 g of lyophilized tissue was mixed with 5 ml of 25% m v^{-1} TMAH solution and placed in an extraction tube exposed to microwave radiation for 3 min. The solution was diluted with 15 ml of water and the pH was adjusted to 5 by addition of acetic acid. Volumes of 1 ml of $NaBEt_4$ solution and 1 ml of hexane containing the internal standard (tetrabutyltin) were added. The mixture was shaken for 5 min and submitted to microwave radiation for 2 min. The organic phase was subjected to clean-up before analysis.	Capillary GC-QFAAS	Microwave-assisted digestion reduced significantly the time required for the dissolution of samples without affecting Sn–C bonds.	[40]
Aquatic plant, dogfish muscle, and dogfish hepatopancreas	Cu, Cd, Ni, Pb, Mn, and Cr	A mass of 250 mg of sample was mixed with 4 ml of 25% m v^{-1} TMAH. The solubilization occurred at room temperature for 18 h, or alternatively by heating in an ultrasonic bath for 45 min. Following the reaction, the mixture was diluted to 25 ml with water.	GFAAS	Samples prepared with TMAH can be stored for up to 3 years at room temperature without any change in analyte concentration.	[41]
Bovine and human blood	Total Hg	A volume of 300 μl of sample was diluted 1 + 1 v v^{-1} with 10% m v^{-1} TMAH solution, incubated for 1 h at room temperature and then diluted 1 + 4 v v^{-1} with 2% v v^{-1} HCl.	FI-CV-AAS	Hg losses were not observed even 24 h after blood sample preparation combined with storage at 4 °C.	[42]
Milk powder, bovine liver, and muscle	Cd, Pb, Ni, Cr, Cu, and Ag	Sample masses between 0.1 and 0.26 mg were mixed with appropriate volumes of 25% m v^{-1} TMAH. The mixture was heated in a water bath (60–70 °C) for 1 h and left to stand for 30 min. Then the volume was made up to 10 ml with water.	GFAAS	The LODs obtained for Cr, Ni, Ag, Pb, and Cd were worse than those obtained with an acid digestion procedure because of the matrix effects and impurities in the TMAH solution.	[43]
Dogfish muscle	As, Cd, Pb, and Se	A mass of 300 mg of sample was mixed with 1.2 ml of TMAH in a screw-capped vessel and heated to 60 °C in a water bath for 10 min. Then the mixture was made up to a volume of 25 ml with water.	GFAAS	After dissolution, As and Se were determined using Pd and Mg nitrates as chemical modifier added in solution. For Cd and Pb, best results were obtained with a mixture of 250 μg of each of Ir and Rh as permanent modifiers.	[44]
Human hair	As, Cd, Ni, and Pb	A mass of 125 mg of sample was mixed with 500 μl of 25% m v^{-1} TMAH in a closed vessel and left at room temperature for 2 h with conventional shaking. Alternatively, the sample/TMAH mixture was completely solubilized for 10 min after heating in a water bath at 60–70 °C.	GFAAS	When TMAH was added to the calibration solution, and this pipetted into the tubes, no linearity was obtained in the analytical calibration curves.	[45]
Liver, muscle, milk, flour, and fish	Br and I	A mass of 0.5 g of sample (dry mass) was mixed with 5% v v^{-1} TMAH in a polyethylene bottle. The closed vessel was heated for 3 h at 80 °C in a drying oven, then diluted to 30 ml with water and filtered through a 0.45 μm membrane filter.	MIP-MS	The proposed method presented satisfactory accuracy although the standard deviations were considered slightly high.	[46]

(continued on next page)

Table 1 (*continued*)

Sample type	Analytes	Procedure	Technique[a]	Remarks	Ref.
Milk powder, egg powder, animal tissues, and hay powder	I	Appropriate amounts of each sample were mixed with 1 ml of 25% m v^{-1} TMAH and dried in an oven at 90 °C. After 3 h, the sample was diluted with water to 25 ml and filtered using a 0.45 μm membrane filter.	ICP-MS	Iodine associated with larger particles was not extracted with TMAH.	[47]
Milk powder and bovine liver	I	A mass of 0.5 g of a $^{129}IO_3^-$ spike solution was added to sample amounts between 0.1 and 0.8 g, in a Teflon–PFA vessel. To this mixture were added 4.5 ml of water and 1 ml of TMAH and the resulting solution was heated to 90 °C for 3 h. After, the solution was diluted with water to 25 ml.	ICP-IDMS	The TMAH extraction method was slower than the $HClO_4/HNO_3$ extraction method.	[48]
Bovine liver, apple leaves, pepperbush, chlorella, mussel, and tea leaves	Mn, Ca, K, Mg, Na, Zn, and Fe; Al, Cu, Ni, Zn, and Pb	A mass of 0.1 g of dried sample was added to a PTFE vessel containing a stirring bar and 2 ml each of 25% m v^{-1} TMAH and 0.200 mol l^{-1} ammoniacal EDTA solution. After 10 min of mixing, 1 ml of water was added to the vessel, which was closed and the mixture was digested in a microwave oven (30 min). The digestate was diluted to 10 ml with water and the mixture was stirred for 5 min. Then it was centrifuged for 5 min and the supernatant was analyzed.	FAAS GFAAS	TMAH was used with EDTA. Microwave digestion reduced TMAH-EDTA digestion time.	[49]
Milk and milk powder	Cu and I	*Milk powder*: 0.2 g of the sample was dissolved in 50 ml of KOH/TMAH solution*. *Raw milk*: 0.5 ml of milk was diluted with 9.5 ml TMAH/KOH solution*. (*) 20 ml of a 25% m v^{-1} TMAH solution was mixed with 50 ml 1 mol l^{-1} KOH and diluted to 1 l with water.	FI-ICP-MS	The KOH/TMAH mixture as a dilution agent improved the precision of the analysis for both iodine and copper in comparison to the results obtained using only KOH or ammonia solution.	[50]
Dogfish muscle, dogfish liver, and lobster hepatopancreas	Inorganic Hg	A mass of 0.25 g of sample was mixed with 4 ml of TMAH. After 5 min, water was added to bring the volume to 25 ml. The samples were ready to be analyzed in 30 min.	FI-CV-AAS	No difference was found in the final results for samples prepared 30 min or 3 months prior to determination.	[51]
Water	As V, total inorganic arsenic, and total arsenic	A 100 ml volume of a sample (containing lower than 0.4 μg l^{-1} of the analyte) was mixed with 8 ml of molybdate solution and set aside for 5 min. After, 2 ml of a tetraphenylphosphonium bromide solution was added to the mixture, which was set aside for 2 min and then passed through a membrane filter (MF). The MF was washed with water and placed into a beaker containing 0.4 ml of 12.5% m v^{-1} TMAH solution. The mixture was heated at 100 °C for 1 min and then diluted with both 1.2 ml of 0.02 mol l^{-1} zirconyl nitrate solution and 2 ml of water.	GFAAS	TMAH solution completely dissolved the mixed cellulose ester membrane filter, generating a solution of low viscosity.	[52]
Dogfish flesh, dogfish liver, and lobster hepatopancreas	Total Hg	A mass of 0.25 g of sample was mixed with 4 ml of 4% v v^{-1} TMAH. After 5 min, water was added to bring the volume to 25 ml. The samples were ready to be analyzed in 30 min and the sample of dogfish flesh was diluted 4 times prior to analysis.	FI-CV-AAS	Due to the simplicity of slurry preparation and the fully automated measurement of Hg, a large batch of samples can be rapidly processed.	[53]

Fish tissue	Hg(II) and methyl mercury	Fish samples were dissolved using a focused microwave system model Microdigest 301 (PROLABO). Procedure 1: 0.2 g of sample was weighed into the extraction container and 5 ml of TMAH was added. The mixture was treated for 20 min at 20 W microwave power. After that it was neutralized with 1.3 ml of 99% v v^{-1} acetic acid, buffered with 20 ml of sodium acetate buffer, pH 5, and was allowed to cool down to room temperature in a water bath. Then 1 ml of $NaBEt_4$ solution and 1 ml of hexane were added and the mixture was shaken for 7 min. To enable phase separation it was centrifuged for 2 min, water was added to lift the liquid level to the neck of the bottle and it was centrifuged for another 3 min. After that the organic phase was transferred into a small polyethylene container and stored in a cool, dark place until the analysis. Procedure 2: 0.2 g of sample was digested in the same way as in Procedure 1. The solution was washed out of the digestion vessel into a 50 ml volumetric flask with several portions of water and was made up to volume with water. A volume of 100 or 200 μl of this solution was added to 10 ml of sodium acetate buffer pH 4 in a purge vessel which was then attached to the purge-and-trap injector with a pre-cooled trap. A volume of 500 μl of $NaBH_4$ solution was injected with a syringe in the side arm of the vessel and the purging step was started immediately. After completion of the purging process, the trap was heated rapidly and trapped analytes were released onto the column of the gas chromatograph.	CG-MIP AES	Both studied procedures are suitable for the determination of different mercury species in fish samples.	[69]
Grass and tree leaves	alkyllead	Procedure 1: A mass of 1–5 g of samples was swirled overnight in 10–20 ml of a 25% m v^{-1} aqueous solution of TMAH. After dilution to about 400 ml, the mixture was filtered through a paper and the filter rinsed with a further 100 ml of water. Extraction of the ionic alkyllead species from the filtrate and the subsequent derivatization and GC-AAS measurement. Procedure 2: This procedure included some additional steps to avoid filtration and extraction losses. Before weighing, a portion of grass or leaves was first pulverized in liquid nitrogen by crushing in a mortar. This resulted in a powder that was sufficiently fine to allow the filtration step after the leaching treatment to be omitted. For the latter purpose, 30 ml of the TMAH solution was transferred into a beaker containing 1 g of the sample and swirled for 2 h on magnetic stirrer.	GC-AAS	Procedure 2 allows a sensitive speciation of ionic alkyllead compounds in grass and tree leaves.	[70]

(continued on next page)

Table 1 (*continued*)

Sample type	Analytes	Procedure	Technique [a]	Remarks	Ref.
Fish tissue and sediment	Dialkyl lead, trialkyl lead, and Pb	Fish tissue: A mass of 2 g of the homogenized sample was digested in 5 ml of TMAH solution in a water bath at 60 °C for 1–2 h until the tissue had completely dissolved to a pale yellow solution. After cooling, the solution was neutralized with 50% v v^{-1} hydrochloric acid to pH 6–8. The mixture was extracted with 3 ml of benzene for 2 h in a mechanical shaker after addition of 2 g of NaCl and 3 ml of NaDDTC. After centrifugation of the mixture, 1 ml of the benzene was transferred to a glass-stoppered vial and butylated with 0.2 ml of *n*-BuMgCl with occasional mixing ca. 10 min. The mixture was washed with 2 ml of H_2SO_4 (0.5 mol l^{-1}) to destroy the excess Grignard reagent. The organic layer was separated in a capped vial and dried with anhydrous Na_2SO_4. Suitable aliquots (10–20 μl) were analyzed by GC-AAS. Sediment: Dried (1–2 g) or wet (5 g) of sample was extracted in a capped vial with 3 ml of benzene after addition of 10 ml of water, 6 g of sodium chloride, 1 g of potassium iodide, 2 g of sodium benzoate, 3 ml of NaDDTC, and 2 g of course glass beads (20–40 mesh) for 2 h in a mechanical shaker. After centrifugation of the mixture, a measured aliquot (1 ml) of the benzene was taken for butylation as it was described for fish samples.	GC-AAS	The methods were useful in studying the degradation of tetraalkyllead and the pathways of alkyllead in the environment.	[71]
Mouse tissue	$CH_3^{200}Hg^+$, $C_2H_5^{199}Hg^+$, and $^{201}Hg^{2+}$	In a 10 ml glass centrifuge tube with a plastic cap, thawed mouse tissue, 6–149 mg was mixed with 50–200 μl of each $CH_3^{200}Hg^+$, $C_2H_5^{199}Hg^+$, and $^{201}Hg^{2+}$ diluted aqueous standards (11–580 ng ml^{-1}) and 2 ml of TMAH. The resulting mixture was agitated until the solution was homogeneous (ca. 3.5 h). This solution was adjusted to pH ca. 9 with the borate buffer and dropwise addition of 4 mol l^{-1} HCl (ca. 0.3 ml). To the solution, 1 ml of DDTC and 1 ml of saturated NaCl solution were added. After vigorous shaking, 2.5 ml of toluene was added. The tube was agitated for 5–10 min, and after 5 min centrifuging at 5800 rpm, the organic phase was transferred to a new centrifuge tube standing on ice, 0.3 ml butylmagnesium chloride was added, and the tube was allowed to stand for 5 min reaction at room temperature. The Grignard reagent was quenched with 0.5 ml of 0.6 mol l^{-1}. After centrifugation, the toluene phase was transferred to a 2 ml screw-capped GC glass vial.	GC-ICP-MS	Up to 9% of the $C_2H_5Hg^+$ was decomposed to Hg^{2+} during the sample preparation, and it is therefore crucial to use a species-specific internal standard.	[72]

Soft organ tissue (liver and kidney), biological CRM and botanical origin and animal feeds	Cr, Cu, Fe, Mn, Ni, and Se	Frozen fresh organ tissue, (2 g) or certified reference material or dried, ground plant material (0.1 g) was blended, at high speed with 20 ml of ethanol–water (1 + 9 v v^{-1}) containing 0.25% m m^{-1} TMAH and the resulting mixture was subjected to homogenization at 38.9 MPa. After four treatments with the homogenizer, the resulting solution was analyzed by ETAAS.	GFAAS	The results indicated that high-pressure homogenization is capable of generating emulsions/dispersions of soft organ tissues, dried animal feeds and botanical CRMs. Estimates of Se in biological CRMs were consistently lower than their certified values.	[73]
Biological samples	Hg	A mass of 0.25 g of sub-samples of reference material biological tissues was weighed into 50 ml pre-cleaned screw-capped poly(propylene) bottles and 4 ml of TMAH was added. Following the reaction of the tissue with the TMAH for ca. 5 min, high purity water was added to bring the volume to 25 ml. The organically bound mercury was cleaved and converted to inorganic mercury by on-line addition of $KMnO_4$.	FI-CVAAS	FI-CVAAS with on-line decomposition of organomercury is a fast and reliable method for the routine analysis of total mercury in solid biological samples.	[74]
Biological materials	iodine	Serum sample was diluted only 1:10 v v^{-1} using 2.5% v v^{-1} TMAH solution. Solid materials were weighed (20–25 mg) and transferred onto the Pt-wire in a Schöninger combustion cell. A volume of 5 ml NaOH (0.1 mol l^{-1}) was used as absorbing solution.	ICP-MS	The results obtained for human serum were in good agreement with other published values. The results for solid samples show a good agreement with the certified values, exception for the milk powder BCR 150.	[75]
Seaweed samples	Iodide and total iodine	Microwave-assisted alkaline digestion of 0.20 g of sample was performed using a 7.5 ml of TMAH and irradiating samples at 670 W for two 5.5 min steps in closed test tubes. After cooling, the alkaline digests were transferred to centrifuge tubes and centrifuged at 6000 rpm for 10 min. The pellets were separated and the digests were made up to 10 or 25 ml and were kept into polyethylene vials at 4 °C before measuring. Microwave-assisted distillation was carried out using 4 ml of alkaline digest and 3 ml of a 2.2 mol l^{-1} hydrochloric acid and 0.05% m v^{-1} sodium nitride solution, with a microwave power at 670 W for two 90 s steps. The distillate (iodine vapor) was bubbled in 10 ml of a 500 μg ml^{-1} hydroxylamine hydrochloride solution (accepting solution) and stored in polyethylene vials at 4 °C before measuring.	Catalytic spectrophotometry	The method was based on the catalytic effect of iodide on the oxidation of As(III) by Ce(IV) in H_2SO_4/HCl medium (Sandell–Kolthoff reaction). Both methods were precise, accurate and with adequate analytical recoveries.	[76]
Milk powder, cod muscle, oyster tissue, diet soya, milk pap, egg powder, hay powder, pig kidney	I	A mass of 200–500 mg of sample was weighed into a bottle and mixed with 5 ml of water and 1 ml of 25% m v^{-1} TMAH. The bottle was sealed and placed in a drying oven at 90 °C for 3 h. After, the sample was cooled down and the volume was made up with water to 25 ml. Before analysis, the solution was centrifuged and filtered through a membrane filter in order to separate undissolved particles.	ICP-MS	Results were in good agreement with certified values.	[77]

(continued on next page)

Table 1 (*continued*)

Sample type	Analytes	Procedure	Technique [a]	Remarks	Ref.
Orchard leaves, pine needles, peach leaves, apple leaves	Pb	A mass of 1 g of dried sample was ground in an agate mortar and mixed with 0.5 g of diammonium hydrogenphosphate. 10 mg of this mixture was weighed in a small cuvette which was positioned on a tungsten boat furnace atomizer where 50 μl of 25% m v^{-1} TMAH was added. The cuvette was heated at 150 °C for 50 s, 300 °C for 30 s, 1000 °C for 90 s and finally the temperature was elevated to 2500 °C; the analyte vapor was transported to the plasma by the carrier gas stream.	ETV-ICP OES	The chemical sample fusion with diammonium hydrogenphosphate and TMAH, during electrothermal heating, allowed the use of aqueous reference solutions for calibration.	[78]
Mussel, rice flour, bovine liver, apple leaves, oyster tissue, peach leaves	Pb	A mass of 1 g of dried sample was ground in an agate mortar and mixed with 1 g of diammonium hydrogenphosphate. 1 mg of this mixture was weighed in a small cuvette which was positioned on a tungsten boat furnace atomizer and 35 μl of 25% m v^{-1} TMAH was added. The cuvette was heated at 130 °C for 30 s, 200 °C for 20 s, 850 °C for 40 s and 2500 °C for 4 s (vaporization).	ETV-ICP-MS	The chemical sample fusion with diammonium hydrogenphosphate and TMAH, during electrothermal heating, allowed calibration with aqueous reference solutions.	[79]
Silicon dioxide–ascorbic acid mixture, siloxane–ascorbic acid mixture, pork liver, bovine liver, bovine muscle	Si	A mass of 50–100 mg of sample was mixed with 2 ml of 25% m m^{-1} TMAH and 2.5 ml of water. The mixture was pre-treated for 30 min in an ultrasonic bath and for digestion, the microwave power was set at 600 W for 10 min followed by 30 min at 800 W. A load pressure of 40.105 Pa was used throughout. After cooling, digests were diluted to 20 ml.	ICP OES	Good accuracy was obtained employing calibration with digested reference solutions.	[80]
Whole egg powder, dogfish muscle, dogfish liver, wheat flour, rapeseed sample	Se	A mass of 0.2 g of sample was added to 10 ml of 5% v v^{-1} ethanol–0.03 mol l^{-1} TRIS containing 20 ml of protease. The suspension was sonicated at low power for 15 min and then processed three times through the flat valve homogenizer capable of developing 137.9 MPa. The slurries, in a 50 ml Erlenmeyer flask were digested for up to 4 h at 60 °C with gentle agitation every 15 min. Alternatively, the solid sample was suspended in 90% v v^{-1} water–ethanol containing 0.25% m v^{-1} TMAH. The suspension was sonicated at low power up to 15 min and then processed as above.	GFAAS	Multiple passes through the homogenizing valve generated quasi-stable slurries that could be sampled reliably for Se even several days of storage at 4 °C post-preparation.	[81]
Tuna fish, dogfish mussel	Total Hg, inorganic Hg, MeHg	A mass of 0.1–0.2 g of sample and 5 ml of 25% m v^{-1} TMAH was placed in a reaction vessel and exposed to	GC-AED	No losses of either MeHg or inorganic Hg occurred during the sample digestion process.	[82]

		microwave radiation (45 W for 2.5 min). After digestion, the sample was diluted with 15 ml of water and the pH was adjusted to 4 using acetic acid and a sodium acetate–acetic acid buffer. Then, 1 ml of 1% m v^{-1} $NaBEt_4$ and 2 ml of hexane were added and the mixture was shaken for 5 min. The addition of $NaBEt_4$ was repeated twice. The mixture was centrifuged for 2 min at 2000 rpm and an aliquot of the supernatant was injected onto the GC column.		The use of both external calibration and the standard addition technique produced accurate results.	
Dogfish muscle, dogfish liver, oyster tissue, pike	Inorganic Hg, MeHg	In a 10 ml glass centrifuge tube 50–300 mg of dried sample was mixed with 100 μl of each of the $Me^{198}Hg$ and ^{201}Hg diluted aqueous standards and 2–5 ml of 20% m m^{-1} TMAH. The mixture was sonicated for 1–2 h. Then, 0.5 ml of the digest was transferred to a new centrifuge tube and the pH was adjusted to 4 with 0.2 ml of 4.4 mol l^{-1} acetic acid or 0.2 mol l^{-1} citric acid. This mixture was centrifuged (5 min at 3700 rpm), filtered through a 0.45 μm syringe filter and analyzed in triplicate by HPLC-ICP-MS.	HPLC-ICPMS	Depending on the matrix, up to 11.5% of Hg was methylated and up to 6.26% MeHg was demethylated.	[83]
Fish (tuna, swordfish, sardine)	Total Hg, inorganic Hg, MeHg, Me_2Hg, EtHg	Four extraction procedures were investigated for Hg speciation in fish samples: HCl leaching, alkaline-methanolic extraction with TMAH and with KOH, and sodium dodecyl sulfate (SDS) extraction.	FI-CV-GCAFS	Accurate results (for total Hg) were obtained only with HCl leaching. The methods involving alkaline digestion produced lower recoveries and artifact formation of Me_2Hg occurred when TMAH was used.	[84]
Bovine liver (a), dog fish muscle (b)	Ag, Cd, Hg, Pb, and Tl	A mass of 100 mg of sample "a" or 1000 mg of sample "b" was mixed with 25% m v^{-1} TMAH (0.2 and 0.9 ml, respectively). The mixture was heated in a water bath (100 °C for 30 min) and let to stand for 24 h. The volume was made up to 5 ml for sample "a" and to 15 ml for sample "b". Ir was used as chemical modifier for the analytes Pb and Hg, while Pd was used for Cd and Tl. The volume of sample solution delivered to the graphite tube was 20 μl for sample "a" and 10 μl for "b". The pyrolysis temperatures were: 200 °C for Hg, 600 °C for Tl and Cd and 800 °C for Ag and Pb. The vaporization temperatures were: 1000 °C for Hg and 2000 °C for the others.	ETV-ICP-MS	The LODs for bovine liver sample, dissolved with TMAH, were higher than the ones obtained with an acid digestion procedure.	[85]

[a] ETV ICP-MS—electrothermal vaporization inductively coupled plasma mass spectrometry. ETV-ICP OES—electrothermal vaporization inductively coupled plasma optical emission spectrometry. ICP OES—inductively coupled plasma optical emission spectrometry. MIP-OES—microwave induced plasma optical emission spectrometry. GC-AED—gas chromatography with atomic emission detection. MIP-MS—microwave induced plasma mass spectrometry. FI-ICP-MS—flow injection inductively coupled plasma mass spectrometry. SEC-ICP-MS—size exclusion chromatography and inductively coupled plasma mass spectrometry. SPME-CGC-ICP-MS—headspace solid-phase microextraction-capillary gas chromatography-inductively coupled plasma mass spectrometry. ICP-MS—inductively coupled plasma mass spectrometry. FAAS—flame atomic absorption spectrometry. GFAAS—graphite furnace atomic absorption spectrometry. GC-AAS—gas chromatography with atomic absorption spectrometric detection. FI-CV-AAS—flow injection cold vapor atomic absorption spectrometry. CG-MIP-AES—gas chromatography-microwave induced plasma atomic emission spectrometry. HPLC-ICP-MS—high performance liquid chromatography-inductively coupled plasma mass spectrometry. FI-CV-GC-AFS—flow injection-cold vapor-gas chromatography-atomic fluorescence spectrometry.

The determination of cobalt in biological samples by solid sampling GFAAS and the performance of alkaline treatment was compared with TMAH using two different instruments: a conventional line-source atomic absorption spectrometer and a high-resolution continuum source spectrometer. For the solid sampling procedure, subsamples of 0.2–1.0 mg mass with particle size ≤50 μm were weighed directly on the SS-platform and introduced into the graphite furnace. For procedures using TMAH, 2 ml of a 25% m/v alkaline reagent solution were added to about 250 mg of sample and the volume was completed to 15 ml with de-ionized water. As a consequence of dilution and partial destruction of the matrix, no molecular absorption was observed with the alkaline procedures, and the analyte was released more quickly to the vapor phase during the atomization step [63].

Other difficulties related to the use of TMAH are associated with high blank values and the analysis time [32]. Initially, only diluted TMAH was available, but pure and relatively concentrated TMAH reagent become commercially available in the middle of the 1990s. Following this, it was noted that analytical blanks from TMAH solutions did not affect the concentration values of the analytes [49]. In order to reduce the time necessary for sample treatment, Zhou et al. used a microwave-digestion system with a closed PTFE vessel for the solubilization of biological samples with TMAH and ammoniacal solution of EDTA prior to the determination by FAAS or GFAAS. Considering the ability of EDTA to form stable complexes with many elements, its addition improved recoveries in the supernatant of the digestate. Under these conditions, the digestion time was reduced from 4 h to 30 min, with complete recovery of the analytes [49]. Similarly, after the dissolution of samples in a 25% m/v TMAH solution, processed in a low-power focused microwave, Szpunar et al. [40] reduced by 20-fold the time required for the dissolution of biomaterials without affecting Sn–C bonds.

The reduction of dissolution time using TMAH is particularly appropriate for speciation studies of different inorganic species. For speciation and quantification of organotin compounds (especially tributyltin and triphenyltin), which must be extracted from the solid samples, Simon et al. [56] evaluated six extraction solutions, including TMAH. Both the reagent concentration and the extraction time depended on the sample type. For 0.5 g of aquatic plants, algae or beans, 15 ml of 25% m/v TMAH solution was used at 60 °C in combination with 1 h of ultrasonic or magnetic stirring. This treatment, however, did not perform well as a consequence of emulsion formation that interfered with the analytical process during the chromatographic separation. A similar study was carried out by Santos et al. [64] for determination of mercury using cold vapor generation and axial inductively coupled plasma optical emission spectrometry. Five different slurry preparation procedures were evaluated after grinding the solid samples to a particle size of ≤53 μm, including the use of TMAH; 13–30 mg of sample was weighed and placed in a 15 ml volumetric flask, 1500 μl of de-ionized water and 150 μl 25% m/v TMAH were added. The mixture was placed in an ultrasonic bath for 30 min and then the volume was made up with water leading to a 0.25% m/v final concentration of the alkaline reagent. This procedure resulted in very low recoveries (12–81%), probably because part of the mercury remained occluded in the solid particles and was not available to react with $NaBH_4$. Furthermore, the reaction of the slurry in the TMAH medium with HCl and $NaBH_4$ produced a precipitate in the phase separator that could also retain the analyte.

Better results were obtained by Ceulemans et al. [34] and Szpunar et al. [40] who used TMAH for the solubilization of marine biomaterials to determine tin compounds by GC-AED after derivatization with sodium tetraethylborate.

A procedure based on a soluble membrane filter (MF) technique for solid phase extraction of inorganic species, wherein the analyte is converted to hydrophobic species and retained on a MF by filtration was described [52]. The collected material was dissolved in a small volume of organic solvent or sulfuric acid together with the MF. This procedure was simple, rapid and versatile, but resulted in an extremely high viscosity solution. To overcome this limitation, the authors proposed dissolution of a mixed cellulose ester MF with a small volume of TMAH. This solubilization technique was used for preconcentration of arsenic from water; an arsenomolybdate complex collected on the MF was dissolved prior to its determination by GFAAS. The addition of peroxodisulfate without and with heating allowed the determination of As(V), total inorganic arsenic, and total arsenic (organic + inorganic), respectively. The use of zirconyl nitrate as a chemical modifier gave good analytical results.

Tetramethylammonium hydroxide is nonetheless not suitable for all samples. Although high extraction efficiencies were reported for the determination of methionine (Met) and selenomethionine (SeMet) by ICPMS and GC-MIP-OES [65,66], the application of TMAH for the solubilization of yeast proved to be inadequate when compared with other extraction methods [38]. The very poor results found were attributed to the degradation of Met and SeMet during the sample treatment with 10 ml of the alkaline reagent for 4 h at 60 °C.

Other analytical problems have been reported, depending on the analytes [29,31] and the matrix [29], especially when analyte concentration levels are close to the limits of detection (LOD) [32,50].

Stürup and Büchert [50] determined I and Cu with poor repeatability and reproducibility and attributed this to the low concentrations of the analytes, which were very close to the LOD. In other work, Pozebon et al. [31] noted that the preparation of slurries with TMAH was not adequate for determination of ^{63}Cu and ^{62}Ni by ETV-ICP-MS, because the background equivalent mass (BEM) increased as the concentration of TMAH increased, degrading the sensitivity. In other speciation studies, the use of TMAH was not feasible [67,68]. Ackley et al. observed that TMAH solutions shifted the peak retention times for arsenic species when injected onto a C_{18} column and this shift also occurred in subsequent analyses [67]. Sanz et al. also discarded the use of TMAH for the determination of As species because TMAH converted As (III) to As (V) during the extraction process [68].

Another aspect that could be considered as a limitation related to TMAH applications is the frequent use of the standard additions technique instead of external calibration for analyte quantification [26,31,33]. Pozebon et al. [31] obtained better results for some analytes such as Cd, Sb, Pb and Mn, depending on the sample and Matusiewicz and Golik obtained accurate results for biological materials only when the standard additions technique was used [33]. This limitation is caused either by transport interferences or by effects on atomization.

Accurate determinations of inorganic mercury and methylmercury by HG-CT-GC-GFAAS were reported following solubilization of biological samples using microwave-assisted extraction with TMAH [39]. Considering the higher extraction efficiency and lower solution volatility compared with other extractants, TMAH allowed the development of a simple, accurate and rapid method. Its use was recommended for the solubilization of biological tissues, since it dissolved the sample completely without decomposition of methylmercury [39,54].

Total inorganic mercury was determined by cold vapor atomic absorption spectrometry (CV-AAS) after a 5-min solubilization of 0.25 g of biological samples using 4 ml TMAH. This approach was less prone to contamination and analyte losses and the digestates are stable for a long period of time. No difference was found in the final results for samples prepared 30 min or 3 months before the final determination [51]. Alternatively, organically bound mercury was cleaved and converted to inorganic mercury by on-line addition of $KMnO_4$, and the total inorganic mercury (originally present or formed during the alkaline solubilization) was reduced to elemental mercury using $NaBH_4$ and determined by FI-CVAAS [53].

Barbosa et al. [42] compared the performance obtained for the determination of total mercury in blood by FI-CV-AAS using TMAH solution at room temperature and with on-line microwave-assisted heating. Samples were diluted in two steps to avoid protein precipitation. The incubation time in the first step was optimized and good recoveries were obtained after 1 h. The analytical performance parameters for TMAH procedure proved to be equivalent to or better than the microwave-assisted digestion.

Silva et al. [41] used TMAH for treatment of animal and botanic samples for the determination of Cu, Cd, Ni, Pb, Mn, and Cr by GFAAS. The reaction between the TMAH solution and the biological materials occurred at room temperature, but heating at 40–60 °C in an ultrasonic bath for 45 min was also recommended to increase the solubilization rate. The use of Mg $(NO_3)_2$–Pd or $Mg(NO_3)_2$–$NH_4H_2PO_4$ as chemical modifiers enhanced the pyrolysis temperature for all the elements except Mn. The procedure was simple, fast, accurate and reproducible. In comparison to microwave-assisted digestion, this procedure was not limited by the sample mass that could be treated. The authors did not observe any precipitation as a result of hydrolysis during the treatment with TMAH.

Since the digestion with TMAH occurs at relatively low temperatures, this may be particularly advantageous when the goal of the analysis is the determination of volatile elements, such as I, Br, As, Cd, Hg, and Sb. Fecher and Nagengast [46] used TMAH for the solubilization of biological materials and some foods to determine Br and I by MIP-MS. Similarly, Stürup and Büchert [50] employed TMAH and determined I and Cu in milk by FI-ICP-MS using KOH as an auxiliary reagent. For the analysis of powdered and raw milk, the sample solution was stable for at least 3 days. However, attempts to determine Al, As, Cr, Ni, Cd, Se, and Pb were not successful because either the elements were insoluble in the alkaline solution, or memory or polyatomic interferences arose during the ICP-MS analysis.

For such situations, lower memory effects and fewer polyatomic interferences can be obtained with ICP-MS when employing TMAH instead of nitric acid [31,47]. In addition, TMAH based procedures are adequate for the preparation of samples when elements such as Sb and Sn, which are not compatible with nitric acid, are to be determined [31]. It should also be mentioned that after preparation of organic samples with TMAH the residue has a high concentration of organic compounds and this may cause systematic errors with ICP OES and ICP-MS. On the other hand, TMAH is very useful for preconditioning of the spray chamber.

An additional advantage was reported by Ribeiro et al. [32], who compared the limits of detection for a number of elements in powdered coffee and milk samples prepared using either acid or TMAH digestion. For both samples, lower blank values for Ca, Cu, Fe, K, Mg, Mn, Na, P, Se, Sn, and Zn were realized when TMAH was used, resulting in better LODs.

In addition to the works described in this review, a general overview about the use of TMAH can also be found in book chapters [86,87].

3. Procedures based on water-soluble tertiary amines

3.1. Background

The use of water-soluble tertiary amines for sample preparation originated with the work of Tatro et al. who undertook the dissolution of zeolites and coal ash [88] as well as zeolite fluid cracking catalysts and clays [89], using hydrofluoric acid based solutions. The solution of water-soluble tertiary amines was added after the dissolution to deactivate the free fluoride and to stabilize the analytes in solution. Hydrofluoric acid is usually used for wet acid-digestion of samples containing Si compounds, but excess HF should be complexed to obtain a final solution compatible with ICP quartzware. Frequently, this process is achieved by adding boric acid, but this acid did not completely avoid the hydrofluoric acid attack on the ICP quartz torch and caused an increment in background signals that deteriorated limits of detection. Tatro [89] also emphasized that adding the water-soluble amines avoided the formation of fluoride precipitates.

Based on these reports, Peru and Collins [90] developed a cold digestion method for analysis of zeolites. After dissolving the zeolite samples at room temperature using a mixture containing hydrofluoric acid, hydrochloric acid plus nitric acid, a solution of water-soluble tertiary amines was added to neutralize the acids and to complex excess fluoride ions by forming HBF_4, permitting easy introduction of the final solution into an ICP OES.

Table 2
Applications of water-soluble tertiary-amines (CFA-C) for sample preparation

Sample type	Analytes	Procedure	Technique [a]	Remarks	Ref.
Food and coral soil	Si	Food samples: 1 g of sample was digested using 5 ml HNO_3, 2 ml H_2O_2, and 5 ml HF in a closed microwave vessel. After cooling, 12 ml of 4% m v^{-1} H_3BO_3 was added and sample solution was diluted to 25 ml. Two 3 ml aliquots of sample solution, 2 ml of 250 mg l^{-1} Sc, and 2 ml of CFA-C were transferred into 15 ml tubes and diluted to 10 ml. Coral soil samples: 0.5 g of sample was digested using 4 ml HNO_3, 1 ml H_2O_2, and 1 ml HF in a closed microwave vessel. After cooling, 25 ml of 4% m v^{-1} H_3BO_3 was added and sample solution was diluted to 50 ml. Two 5 ml aliquots of sample solution, 2 ml of 250 Sc mg l^{-1}, and 2 ml of CFA-C (to one aliquot) were transferred into 15 ml tubes and diluted to 10 ml.	ICP OES	CFA-C solution stabilizes the Si emission signal and reduces drift and bias.	[92]
Biological materials	38 elements	A mass of 1 g of sample was fused using 0.5 ml of HF + 2 ml H_2O_2 and 5 ml 4% m v^{-1} of H_3BO_3 and diluted to 50 ml. To 10 ml and 20 ml aliquots, 5 ml of a 1 ng ml^{-1} Ge, In, and Re standard solution and 5 ml CFA-C reagent were added and pH adjusted to 7–8 and diluted to 50 ml. A mass of 1 g of sample was digested in microwave oven with 5 ml HNO_3, 0.5 ml HF, and 2 ml H_2O_2. After, 5 ml 4% m v^{-1} H_3BO_3 and 5 ml of CFA-C were added the pH was adjusted to 7–8.	ICP-MS	CFA-C shifts the maximum of the metal ion signal towards lower aerosol gas flow rates, and decreases interferences in ICP-MS.	[93]
Orchard leaves, total diet, non-fat milk powders, bovine liver, and oyster tissue	Se and As	Microwave sample dissolution: 0.5–1 g of sample was digested with 5 ml of HNO_3 and diluted to 25 ml. High pressure sample preparation (HPA): 0.2 g of sample was digested with 2 ml of HNO_3 and heated at 230 °C. Dry ashing: 5 g of sample was dry ashed using a solution 20% m v^{-1} $Mg(NO_3)_2{\cdot}6H_2O$ and MgO. After these procedures, aliquots of 2 or 5 ml are taken, 2 ml of 200 ng ml^{-1} Ge and 2 ml of CFA-C solution (1 + 1 v v^{-1}) are added, and the mixture is diluted to 10 ml.	ICP-MS	Addition of CFA-C resulted in an element-specific enhancement of As and Se ICP-MS signals; whereas, the $ArCl^+$ interferences were significantly reduced.	[94]
Bovine liver, oyster tissue, apple leaves, corn bran, whole egg powder, total diet, and rice	Al, Ca, Cu, Fe, Mg, Mn, Na, K, and Zn (ICP OES) As, Ba, Ca, Cu,	0.2 g of sample + 0.5 ml of 20 mg l^{-1} Sc (ICP OES) or 0.5 mg l^{-1} Y (ICP-MS) was dispersed in 9.5 ml 10% v v^{-1} CFA-C solution and agitated for 30 min with a magnetic stirrer. After, the samples were centrifuged for 5 min and the supernatant analyzed by ICP OES; extracts were diluted 10-fold before ICP-MS measurements.	ICP OES ICP-MS	Good recoveries, except for Al and Fe, in all samples and for Ca in spinach and apple leaves.	[95]
Flour	Pb, Mn, Mo, Rb, Se, Cr, and Zn (ICPMS)				
Non-fat milk powder, whole milk powder, skimmed milk, and milk fat	Ca, K, Mg, Na, and Zn (ICP OES) Al, Ba, Cu, I, Mn, Mo, Pb, Rb, Se, Sr, and Zn (ICP-MS)	ICP OES: A 0.1 g of non-fat milk powder (or 1.0 ml of liquid milk) was dissolved in 10.0 ml (or 9.0 ml) of 10% v v^{-1} CFA-C solution at pH 8. ICP-MS: A 0.2 g of non-fat milk powder (or 2.5 ml of liquid milk) was dissolved in 49.5 ml (or 47.0 ml) of 5% v v^{-1} CFA-C solution at pH 8. A 0.5 ml aliquot of 2.5 mg l^{-1} Y was added.	ICP OES ICP-MS	CFA-C dissociated casein micelles and stabilized cations in the liquid phase. Analysis by ICP OES did not need internal reference element. ICP-MS: all elements investigated agreed with certified values except for Se.	[96]
Nutritional and biological samples	I, Mn, Co, Ni, Cu, Zn, Rb, Cd, and Pb	Sample preparation was carried in a Trace-O-Mat combustion chamber. Mass of sample: 0.2–0.5 g. The combustion products were collected in 2 ml of 5% v v^{-1} CFA-C or 0.05 mol l^{-1} solution of NaOH and diluted to 25 ml.	ICP-MS	Lower LODs and LOQs were obtained with CFA-C solution. CFA-C solution permits the simultaneous determination of iodine and other trace metals.	[97]

Mixed diet, milk powder, infant formula, and baby food	I, Mn, Co, Ni, Cu, Zn, As, Se, Sr, Rb, Mo, Cd, Ba, and Pb	The sample preparation was carried in a Trace-O-Mat and Schöniger combustion. After the combustion, the products were collected in 2 ml 5% v v^{-1} CFA-C solution and 10 ml 5% v v^{-1} CFA-C solution, respectively. The total preparation time was around 45 min. For the extraction method, samples were weighed into a 50 ml volumetric flask before dilution with approximately 40 ml of 5% v v^{-1} CFA-C solution. After, the samples were sonicated for 30 min.	ICP-MS	Lower LODs were obtained. Extraction is ideal for many samples. Aluminum, Ti, Fe, and Zn were not stable in CFA-C solution.	[98]
Infant formulas and milk powder	Ca, Cu, Fe, Mg, Mn, Na, P, and Zn	Samples were prepared in an aqueous solution of CFA-C (10% v v^{-1}) adjusted to pH 8.	ICP OES	The use of CFA-C avoided the occurrence of significant inter-element interferences.	[99]
Coconut water and coconut milk	Se	1 ml of sample was transferred to a 5 ml volumetric flask and 50 μl of 10 mg l^{-1} Se solution added; the volume was made up with 10% v v^{-1} CFA-C solution. This sample was further diluted before measurements.	GFAAS	CFA-C improves the repeatability of analytical signals.	[100]
Hair	Cd, Cu, and Pb	Hair samples were washed with water and acetone and oven-dried at 60 °C. After, 1–2 g of sample was ground in a cryogenic mill. Masses of 10–50 mg of powdered samples were suspended to 10 ml with 0.1% v v^{-1} CFAC solution	GFAAS	The lowest RSDs were obtained using CFA-C. The action of the automatic sampler was improved and the formation of carbon residues in the graphite tube was avoided.	[101]
Tea samples	Al, Ca, Mg, and Mn	Extraction solution: 1% and 10% v v^{-1} HCl and HNO_3, and 5% v v^{-1} CFA-C. 0.2, 0.5, or 1.0 g of sample was suspended in 20 ml extraction solution. The extractions were carried out using conventional heating for 5 min. After cooling, the suspensions were filtered and the extracts transferred to a 50 ml volumetric flask and the volumes were made up with water.	FAAS ICP OES	5% v v^{-1} CFA-C solution was efficient for extraction of Ca, Mg, and Mn. The Al extraction was lower than 10% in CFA-C solution.	[102]
Milk powder	I, Cu, K, Mg, Na, P, S, and Zn	Samples were prepared using a combustion procedure in a commercial stainless steel oxygen bomb. The analytes were collected in 10 ml CFA-C (10 % v v^{-1}) solution or 5 ml 0.1 v v^{-1} HNO_3 solution.	ICP OES	For iodine determination CFA-C was better than HNO_3 solution, but HNO_3 was better for the remaining elements.	[103]
Bovine milk	Fe and Se	Se: 1 ml liquid milk sample was diluted to 5 ml with 10% v v^{-1} CFA-C solution Fe: 0.5 ml of liquid milk (non-fortified) sample was diluted to 10 ml with 10% v v^{-1} CFA-C solution.	GFAAS	CFA-C had a favorable effect on the automatic sampler and consequently on repeatability.	[104]
Bovine milk and fruit juices	Cu and Zn	Commercial milk and fruit juice samples were diluted 1:1 v v^{-1} with 10% v v^{-1} CFA-C.	TS-FFAAS	Improvement of LOD.	[105]
Milk	Cr	Four media were investigated: 5 ml of milk + 5 ml of water; 9.9 ml of milk + 0.1 ml of CFA-C; 9.5 ml of milk + 0.5 ml of CFA-C; and milk + chemical modifier.	GFAAS	CFA-C improves the repeatability of analytical signals.	[106]
Fish muscle tissue	Ca, Cu, Fe, Mg, and Zn	An aliquot of 0.2 g of dried sample was transferred to a 10-ml volumetric flask and 300 μl of 30% m m^{-1} H_2O_2 and 1 ml of CFA-C with EDTA were added. After resting overnight, 2 ml of water was added and the suspension was sonicated for 25 min. The volume was made up with 50% v v^{-1} HCl and the resulting extract was centrifuged at 3500 rpm for 5 min.	ICP OES	This procedure allowed the quantitative extraction of metals.	[109]

[a] ICP OES—inductively coupled plasma optical emission spectrometry. ICP-MS—inductively coupled plasma mass spectrometry. GFAAS—graphite furnace atomic absorption spectrometry. FAAS—flame atomic absorption atomic spectrometry. TS-FFAAS—thermospray flame furnace atomic absorption spectrometry.

The preliminary literature is unclear about the composition of this proprietary commercial reagent, and it is difficult to hypothesize how this chemical approach might have originated. Perhaps this idea came from the chemical behavior of silicates in solution, since all the above cited work [88–90] dealt with the determination of Si in poorly dissolved samples. Silicates are hydrolyzable in water, generating H_2SiO_3, a gelatinous precipitate. This same precipitate is also formed in concentrated acids and is converted to a SiO_2 powder under heating [91]. Silicates can be kept in solution in alkaline media. A solution containing water-soluble tertiary amines could present enough basicity to neutralize residual acids and avoid grave effects caused by hydrofluoric acids, including leaching of quartz parts and formation of precipitates. The complexing action on fluoride is not clear, however, the formation of hexafluorosilicates (SiF_6^{2-}) could be an operative process that also helps to keep Si in solution. All but Ba and K hexafluorosilicates salts are soluble in water [91].

Krushevska et al. introduced a new sample preparation procedure incorporating addition of tertiary amines after microwave digestion to dissolve fluorides and neutralize free fluorides; they verified that CFA-C improved the analysis [92–94]. The acronym CFA-C is a brand name that stands for coal fly-ash type C and the reagent is produced by Spectrasol (Warwick, NY, USA). This proprietary commercial mixture contains triethanolamine and triethylenetetramine [98].

Afterwards, the use of CFA-C gradually increased as a reagent for sample preparation that also served to improve instrumental performance. These characteristics will be discussed in the following sections.

Compared to TMAH the water-soluble tertiary amines do not cause hydrolysis of cations, and solutions can be kept without formation of precipitates. The stability of water-soluble tertiary amine solutions containing Al, Ca, Fe, and Mn at pH 8 was tested, and no losses were observed after 3 months of successive measurements by ICP OES [95]. The commercial reagent also did not present elevated levels of contamination, except for easily contaminated elements such as Fe and Zn.

Various methods incorporating CFA-C solution for sample preparation are summarized in Table 2. In general, these methods use CFA-C to dissolve and neutralize free fluorides, and for extraction, dilution and digestion of samples.

3.2. Extraction, dilution and digestion procedures

Following preliminary investigations, the application of the commercial reagent now named CFA-C was extended to include extraction, dilution, and digestion procedures.

The first application of CFA-C as an extraction reagent involved the determination of Al, Ca, Cu, Fe, Mg, Mn, Na, K, and Zn by ICP OES and As, Ba, Ca, Cu, Pb, Mn, Mo, Rb, Se, Sr, and Zn by ICP-MS in biological standard reference materials (apple leaves, bovine liver, corn bran, oyster tissue, rice flour, spinach leaves, total diet, wheat flour, and whole egg powder). All extractions were carried out using 10% v/v CFA-C solution at room temperature for 30 min. The final pH was adjusted to 8 with nitric acid to avoid deterioration of the quartz torch at higher pHs [95]. The procedure was simple and could be adopted for screening purposes in nutritional studies involving huge numbers of samples.

This extraction procedure was extended by Gélinas et al. using agitation of samples in an ultrasonic bath for 30 min [98]. In addition to extending its field of application to other elements, such as Cd, Co, and Ni, the procedure was fully suitable for the extraction of iodine in mixed diet, milk powder and infant formula samples. Total iodine was also determined using two oxygen combustion methods, Trace-O-Mat and Schöniger combustion, with CFA-C as the absorbing solution. All measurements were made by ICP-MS without the memory effects frequently observed when acid solutions containing iodine are nebulized [106]. The determination of total iodine in nutritional and biological samples was studied in detail in other work using the Trace-O-Mat instrument based on its collection with 5% v/v CFA-C solution [97]. The combustion of samples within an oxygen stream and the collection of the combustion products in CFA-C permitted the simultaneous determination of total iodine and other trace metals of biological and toxicological importance, including Cd, Co, Cu, Mn, Ni, Pb, Rb, and Zn with an acceptable level of accuracy (±20%). According to the authors, the tertiary amine solution also improved the quality of the results obtained for iodine because of a significant enhancement in the sensitivity of elements having high first ionization potential and a stabilization of the dissolved iodine in the liquid phase. Consequently, it eliminated memory effects observed when iodine was nebulized in acid solution without affecting the determination of most of the other major and trace elements [97].

Costa et al. evaluated the efficiency of extraction of Al, Ca, Mg, and Mn in tea leaves using CFA-C and FAAS and ICP OES detection [102]. A 5% v/v CFA-C solution was efficient for the extraction of Ca, Mg, and Mn in all teas, except *Cymbopogan citrates* (non-fermented), in which the extraction was lower than 40% for Mn. Extraction of Al was lower than 10% in the CFA-C medium for all tea samples.

Recently, ultrasound assisted extraction of metals with CFA-C in the presence of H_2O_2 was used for improving metal solubilization in fish samples, and quantitative extraction of Ca, Cu, Mg, and Zn was obtained [109].

The utility of CFA-C as a dilution medium was demonstrated for milk samples by developing a simple dilute-and-shoot procedure [96]. After diluting milk samples having different fat contents, Ca, K, Mg, Na, P, and Zn were determined by ICP OES and Al, Ba, Cu, I, Mn, Mo, Pb, Rb, Se, Sr, and Zn were determined by ICP-MS. All diluted samples contained 10% v/v CFA-C solution and the pH was adjusted to 8 to avoid fast degradation of the quartz torch. Both ICPs were operated using conventional concentric nebulizers. This represented an advance considering previously unsuccessful performance when trying to directly nebulize milk samples since particle size effects negatively affected nebulization and atomization processes [107]. The CFA-C reagent could apparently promote the total or partial dissociation of casein micelles, since the dispersions containing non-fat milk were clear and colorless. This hypothesis was tested and confirmed by Hua et al. [99].

These authors demonstrated the advantages of this direct protocol, such as sample throughput and analytical accuracy.

These extraction and dilution procedures, developed after 1997, expanded the applications of CFA-C reagent and presented new alternatives to classical sample preparation in acidic media. It seems clear that for some analytes, e.g. I, and for some samples, e.g. milk, the use of water-soluble tertiary amines as a reagent presents a useful analytical strategy. Similar effects probably could be obtained using TMAH. However, this reagent could not generate stable analytical solutions.

3.3. Effects on spectrometric measurements

The beneficial effects arising from use of CFA-C on ICP measurements emphasized by Gélinas et al. [97] were previously demonstrated for Si during its determination in food and coral soil samples [92], for the semi-quantitative multi-element analysis of biological materials [93], and for measurements of As and Se [94].

The determination of Si in foods and coral soils by ICP OES was achieved after acid-digestion including hydrofluoric acid followed by the addition of either boric acid or CFA-C to complex free fluoride [92]. When complexed fluoride was present in an acid solution containing Si, the Si concentration was found to increase with time and eventually reached a plateau. When tertiary amines were added, the concentration response was constant and close to a Si solution containing only nitric acid. The addition of CFA-C stabilized the Si emission signal and reduced drift and bias. As a result of this effect, when HF is complexed with only boric acid, the Si values were higher than those obtained using a fusion procedure. On the other hand, when the amine mixture was added the measured Si concentrations are in agreement with fusion results at the 95% confidence level [92].

Krushevska et al. showed that tertiary amines were operative in dissolving insoluble fluorides and to neutralize fluorides in a semiquantitative procedure for analysis of biological materials by ICP-MS [93]. Most elements of nutritional interest and rare-earth elements were determined using this procedure. All measurements were carried out with solutions containing 10% v v^{-1} tertiary amines. Higher concentrations tested (12 and 20% v v^{-1}) caused carbon deposition on the sampler cone and increased carbon and nitrogen polyatomic ion interferences [93].

In this same year, use of water-soluble tertiary amines was shown to enhance signals and decrease polyatomic chloride interferences in the determination of As and Se in biological samples by ICP-MS [94]. The effects of the amines were more pronounced than the introduction of N_2 to the outer gas flow of the plasma.

An additional experimental study showed that CFA-C also reduced memory effects when determining Th in urine by ICP-MS [110]. The reagent was also used for performance evaluation of an axially viewed ICP OES for analysis of milk emulsions. Accurate results for a complex sample introduced into two ICPs without a previous digestion were obtained using both instruments with different interfaces [111].

The effects caused by CFA-C in graphite furnace atomic absorption spectrometry have also been evaluated. Aleixo and Nóbrega proposed a procedure for determination of Fe and Se in bovine milk by GFAAS without need for a tedious step for sample preparation when using CFA-C as a diluting medium [104]. All diluted samples contained 10% v v^{-1} CFA-C solution. The reagent was effective in overcoming problems such as the accumulation of fat compounds in the autosampler cups, irregular drop formation, accumulation of carbonaceous residues inside the atomizer and elevated background signals. All these undesirable effects are observed when direct analysis of milk samples is performed without any dilution. Aleixo and Nóbrega suggested that dilution with CFA-C would have a favorable effect on the action of the autosampler and consequently on repeatability.

Chromium was determined in milk samples using CFA-C without loss or contamination by GFAAS [108]. Milk samples were introduced into the furnace with CFA-C to avoid blockage of the autosampler and sample foaming.

A new strategy using CFA-C for determination of Cd, Cu, and Pb in hair slurries was developed by Kamogawa et al. [101]. Hair samples were ground in a cryogenic mill and dispersed in 0.1% v v^{-1} CFA-C solution. Results generated in the CFA-C medium were compared with those from use of two other media: 0.1% v v^{-1} Triton X-100 and 0.14 mol l^{-1} HNO_3. In HNO_3, the RSDs were higher than 25% and transfer of the slurries was difficult owing to their strong adherence to the capillar of the autosampler. This effect was completely eliminated using CFA-C or Triton X-100. The best stabilization and RSDs of the results for hair slurries were obtained using a CFA-C solution. The combination of cryogenic grinding and CFAC solution was effective for the determination of Cd, Cu, and Pb.

CFA-C was recently used for direct analysis in thermospray flame furnace atomic absorption spectrometry (TS-FFAAS) [105] and FAAS [102]. Nascentes et al. [105] employed TS-FFAAS for determination of Cu in bovine milk samples using 10% v v^{-1} CFA-C solution as diluent for which it prevented rapid accumulation of carbon residues in the capillary tip without requiring excessive dilution of the samples.

4. Procedures based on strongly alkaline reagents

4.1. Background

The use of strongly alkaline reagents in sample preparation has been recommended to promote digestion and extraction of several analytes in diverse samples. The use of this medium for both purposes is discussed below.

Several aspects should be considered when considering microwave-assisted alkaline digestion [112]. (a) The control of temperature in the microwave heated closed vessel system resulting from the high boiling point of alkali bases is critical; it should be noted that high temperatures can be reached even at low pressures, however, the boiling point is dependent on the concentration of the base. (b) When H_2O_2 is used, higher pressures will be reached owing to the release of gases during

oxidation reactions. It is important to cap the vessel immediately after the addition of H_2O_2 for samples to fully react at higher pressures. (c) A partial digestion of the sample with a base and completion of the digestion with an acid has proved to be more successful than attempts involving an acid followed by a base. This is most likely due to the ease of acidifying diluted bases with concentrated acids. (d) One may observe a precipitate after completing the digestion process, once a sample has cooled. In successful digestions, this precipitate is probably caused by salts coming out of solution as a consequence of the mixing of acids and bases.

Other applications of alkaline media include extraction of elements that are stable in such a medium, such as metals that form stable complexes with EDTA [113], As [114,115], and Cr [117–120].

The solubilization of metals depends on the pH. For example the ultrasonic-assisted solubilization of Ca, Mg, Mn, and Zn in cinnamon samples at different pHs was studied by Filgueiras et al. [113]. Generally, recoveries for Ca, Mg, Zn, and Mn were greater at low pHs, indicating that acid is necessary to obtain good recovery of the metal. However, metal solubilization can be promoted by adding a strong complexing agent, such as EDTA, to the alkaline medium. The authors have shown that for efficient formation of complexes with EDTA, a pH higher than 10 should be employed.

Alkaline media were also investigated for the determination of arsenic. Arsenic is an important element present in high concentrations in marine biota. It can be found in many forms: arsenobetaine is the predominant and non-toxic species in fish, bivalves and crustaceans, while the more toxic inorganic species, arsenite (As(III)) and arsenate (As(V)), usually constitute a minor amount for analysis of total content [114,115]. Analytical approaches reported in the literature for the determination of inorganic arsenic have included specific extraction of inorganic species followed by their determination as As in the extracts. Alkaline solvents were selected to facilitate the dissolution of arsenous acid, which has a pK_a value of 9.2 [115].

Chromium is another element that can be extracted using an alkaline medium. Chromium and its compounds are widely used by the metallurgical industry and, consequently, the steel and alloy industries are dominant sources of anthropogenic chromium emission into the environment. The main oxidation states of chromium are Cr(VI) and Cr(III). The redox speciation of chromium has attracted a great deal of interest in view of the toxic properties of Cr(VI) as compared with the essentiality of Cr(III) [117–120]. Several factors control the interconversion of Cr(III) and Cr(VI) species [121]. The formal reduction potential (E_h) of Cr(VI)/Cr(III) in solution changes from −0.04 (pH 13) to 0.52 (pH 7.4) and then to 1.07 in an acid medium (pH 2). Chromium (III) is thermodynamically stable under low E_h and low pH, while high E_h and high pH favor the existence of Cr (VI), hence, alkaline conditions are used to stabilize Cr(VI). Studies have also shown that the oxidation of Cr(III) to Cr(VI) is highly dependent on its chemical forms: Cr_2O_3 and aged Cr $(OH)_3$ are resistant to oxidation while Cr^{3+} and freshly precipitated $Cr(OH)_3$ are relatively easy to oxidize [118,119].

Alkaline procedures for extracting Cr(VI) from soluble, adsorbed and precipitated forms of Cr compounds in several samples must satisfy three criteria: the extracting solution must solubilize all forms of Cr(VI), the conditions of extraction must not induce reduction of native Cr(VI) to Cr(III), and the method must not cause oxidation of native Cr(III) to Cr(VI) [120].

Various methods incorporating strong bases for sample preparation are shown in Table 3.

4.2. Digestion and extraction procedures using strong bases

To the best of our knowledge, only one paper was published in the literature dealing with the digestion of refractory samples using strong bases. Zehr et al. [112] proposed an alternative method for digestion of inorganic samples using bases with microwave-assisted procedures. They compared microwave base/acid digestion and fusion methods. Microwave-assisted alkaline digestion of samples of barium aluminate ($BaAl_2O_4$), cobalt oxide (CoO), molybdenum oxides (MoO_2 and MoO_3), thorium oxide (ThO_2), and/or tungsten oxides (WO_2, W_2O_5, W_4O_{11}, and WO_3) were investigated using open vessels. Both LiOH solution and H_2O_2 were added to complete the dissolution of samples. This mixture was then acidified using HNO_3 and HF with gentle mixing. The microwave-assisted alkaline digestion yielded good spike recovery of 94%. Overall sample digestion time was much greater with the fusion method than with the microwave-assisted digestion methods.

Recently, Costa [135] proposed a procedure for the digestion of alumina powders, and their impurities (Ca, Fe, Na, Si, and Ti) were determined by ICP OES. An effective microwave-assisted digestion of samples using an alkaline reactant (25% m/v KOH solution and H_2O_2) was accomplished in the closed vessel. The total time for sample digestion for Al_2O_3 did not exceed 30 min. Good agreement between results obtained using acid digestion and alkaline digestion was obtained.

The use of NaOH as an extractant was evaluated by Wuilloud et al. [133] for determination of Bi, Co, Cu, Fe, I, Mo, Ni, Se, and Zn in mushroom samples by size exclusion chromatography coupled to ICP-MS. Low and high molecular weight compounds were extracted using 0.05 mol l^{-1} NaOH solution and vortex agitation. Recoveries of 46–97% were achieved. The alkaline medium increased the solubilization of compounds through deprotonation. The 0.05-mol l^{-1} HCl solution extracted only low molecular weight compounds owing to the lower solubility of protonated species, and water (60 °C) extracted only organoelemental species. Extraction efficiencies were also element-dependent; for example, Zn, Cu, Ni, Co and Fe have shown better extraction in alkaline media, whereas Bi, I, Mo and Se show no significant differences using different media (water or 0.05 mol l^{-1} HCl solution) [133].

The use of alkaline media for metal solubilization was studied by Filgueiras et al. [113], who verified that EDTA promoted the solubilization of Zn, Mn, Mg, Ca, Cd, Fe, and Pb at pH 10. The determination of these metals in food samples by FAAS and GFAAS was investigated using an ultrasonic-assisted solubilization method. Microwave-assisted acid digestion in closed vessels was used for comparison. Differences

Table 3
Applications of strong bases for sample preparation

Sample type	Analytes	Procedure	Technique[a]	Remarks	Ref.
Mo scrap and Mo oxides/W oxides/Co oxides	As, Al, Mo, Si (Mo scrap) Mo and W (Mo oxides/W oxides/Co oxides)	Mo scrap—Step 1: 50 ml of 10% m v^{-1} $LiOH{\cdot}H_2O$ (3.4 atm for 30 min); Step 2: 50 ml of HCl (3.4 atm for 30 min); Step 3: 25 ml HF cold was added and transferred to tube. The tube was capped and placed in a hot water bath until the sample dissolved to avoid loss of Si. Mo oxides/W oxides/Co oxides—Step 1: 10 ml of 10% m v^{-1} $LiOH{\cdot}H_2O$/2 ml of 30% m m^{-1} H_2O_2 (3.4 atm for 15 min); Step 2: 10 ml of HNO_3/10 ml of HF (3.4 atm for 15 min). Sample masses ranged from 0.1 to 0.5 g/microwave vessel.	FAAS	Microwave-assisted digestion combining bases and acids resulted in good recoveries.	[112]
ThO_2/W/W oxide and $W/BaAl_2O_4$/Ni	W, Th, and Ni	ThO_2/W/W oxide—Step 1: 10 ml of 10% m v^{-1} $LiOH{\cdot}H_2O$/2 ml of 30% m m^{-1} H_2O_2 (3.4 atm for 15 min); Step 2: 10 ml of HNO_3/10 ml of HF (3.4 atm for 15 min). $W/BaAl_2O_2$/Ni—Step 1: 10 ml of 10% m v^{-1} $LiOH{\cdot}H_2O$/2 ml of 30% m m^{-1} H_2O_2 (3.4 atm for 15 min); Step 2: 10 ml of HNO_3/10 ml of HF (3.4 atm for 15 min).	FAAS	Microwave-assisted digestion combining bases and acids resulted in good recoveries.	[112]
W/oxide scrap and WO_3/CoO	Cd, V, Co, K, Na, and V	W/oxide scrap—Step 1: 10 ml of 10% m v^{-1} $LiOH{\cdot}H_2O$/2 ml of 30% m m^{-1} H_2O_2 (3.4 atm for 15 min); Step 2: 10 ml of HNO_3/10 ml of HF (3.4 atm for 15 min). WO_3/CoO—Step 1: 10 ml of 10% m v^{-1} $LiOH{\cdot}H_2O$/2 ml of 30% m m^{-1} H_2O_2 (3.4 atm for 15 min); Step 2: 1 ml of H_3PO_4/10 ml of HCl/5 ml of HNO_3/10 ml of HF (3.4 atm for 15 min).	FAAS	Microwave-assisted digestion combining bases and acids resulted in good recoveries.	[112]
W_2O_5/W_4O_{11} and WO_3	K and Na	WO_5—6.6 ml of 10% m v^{-1} $LiOH{\cdot}_2O$/0.6 ml of H_2O_2 (in open vessel, microwave heat to boiling). W_2O_5/W_4O_{11} —6.6 ml of 10% m v^{-1} $LiOH{\cdot}_2O$ (in open vessel, microwave heat to boiling).	FAAS	Microwave-assisted digestion combining bases and acids resulted in good recoveries.	[112]
Plants	Ca, Fe, Mg, Mn, and Zn	A 0.1-g sample mass (particle size <50 μm) was weighed into polypropylene centrifuge tubes (50 ml) and 5 ml of extraction solution was added. The sample was sonicated at room temperature for 3 min. Buffer solutions: pH 1, pH 2, and pH 6: 3.4 g of dihydrogen sodium dihydrogen phosphate + 200 ml of water + HCl. pH 3: 4.2 g citric acid + 200 ml of water + NaOH. pH 4 and 5: 2.0 g of sodium acetate + 250 ml of water + HCl. pH 9: 2.0 g of ammonium chloride + 250 ml of water + NaOH solution pH 10: 2.1 g sodium carbonate + 200 ml of water + NaOH. pH 11: 3.4 g sodium hydrogen phosphate + 200 ml of water + NaOH. EDTA was used in alkaline medium (NaOH) for metal solubilization.	FAAS/GFAAS	Determination of metals in the extracts can be performed by FAAS and GFAAS with good accuracy and precision.	[113]
Soils	As(III), As(V), DMA, and MMA.	Extractants: deionized water; 5% v v^{-1} glacial acetic acid solution; 1 mol l^{-1} phosphoric acid solution; 10 mmol l^{-1} citrate buffer with 0.1 mol l^{-1} NaOH to obtain pH 3; 10 mmol l^{-1} ammonium dihydrogen phosphate with NH_4OH to obtain pH 5.8; degassed Coke® (pH ~3); and household vinegar. A 20-g mass of soil (particle size <250 μm) was placed in each of six 400 ml beakers to which were added 150 ml of deionized water. To one of the beakers, 0.4 ml of 1000 mg l^{-1} As (III) was added dropwise with continuous stirring. The remaining beakers received the other arsenic species [DMA, MMA, and As(V)] and a soil with a mixture of four arsenic species was prepared. Another beaker contained reagent blank soil. These six beakers containing the soils were dried in an oven at 70 °C for 1 week. 0.2 g of soil was weighed into a 15 ml centrifuge tube. To each tube, 5 ml of given extractant was added and the mixture sonicated for 20 min. After, the mixture was centrifuged for 15 min and the supernatant was used for determination of arsenic.	HPLC-ICPMS	The highest extraction efficiency was obtained when NaOH was used.	[114]

(continued on next page)

Table 3 (*continued*)

Sample type	Analytes	Procedure	Technique [a]	Remarks	Ref.
Fish samples	As	Procedure A—A mass of 1 g of thawed fresh or acetone-extracted fish flesh was placed in a quartz vial of the Multiwave system and 10 ml of an alkaline alcohol mixture (2 ml of 3 mol l^{-1} NaOH, 3 ml of water, and 5 ml of ethanol) were added. The samples were placed in an oven, which was adjusted to turn off the microwave power at a mixture temperature of 90 °C—equal to the approximate boiling point of the mixture. After cooling, the dissolved sample was diluted with water to a total mass of 11 g. The samples were filtered through a 0.45 μm disposable syringe filter and passed through a 0.8 μm SepPak cartridge for removal of lipophilic material. Approximately the first 2 ml of the filtrate was discarded and the remaining filtrate was collected for speciation analysis. Procedure B—A mass of 1 g of mackerel sample was extracted by adding 5 ml of acetone using gentle mechanical shaking for 1 h to remove fat. The acetone fraction was decanted and the residue in the sample was evaporated overnight at room temperature. Following this procedure, the defatted samples were submitted to procedure A.	HPLC-ICPMS	This method allows the quantitative determination of inorganic arsenic (As(III) and As(V)) in fish samples as As(V).	[115]
Dietetic foods	Br	A mass of 0.1 g of sample was mixed with 0.5 mol l^{-1} NaOH (0.5 ml) in a PTFE closed vessel and microwave-assisted heated at 100–200 W for 2 min. After cooling down, 100–200 ml 30% m m^{-1} H_2O_2 was added and the same heating step was repeated.	IC-UV	Recoveries of bromide ranged from 87 to 119%. Samples containing fats and oils were saponified as digestion proceeded. Particles of saponified components separated from the mixture and floated onto the surface of the solution.	[116]
Plastic and metallic materials from vehicles	Cr(VI) and Cr(III)	Three different Cr(VI) extraction procedures were evaluated: 20 ml of water was added to 1.5 g of sample in an open glass vessel; this mixture was boiled for 5 min, the sample was removed from the solution rinsed with water and diluted to 25 ml. Two additional procedures were optimized to extract the coatings of the screws. These experiments were carried out using 10 ml of water and ammonium/ammonia buffer solution at pH 8.9 (0.05 mol l^{-1} $(NH_4)_2SO_4$–0.05 mol l^{-1} NH_4OH) for 1.5 g of sample in a closed glass vessel followed by sonication in a bath and the optimal time was determined. After, the supernatant was diluted to 25 ml. This procedure was evaluated using four different corrosion-preventive coatings.	HPLC-ICPMS	Extraction in alkaline medium for Cr(VI) was compared with that described in the E ISO 3613 standard. For 2 of them, good results were obtained with the NH_4^+/NH_3 buffer solution at pH 8.9 associated with sonication, but caused Cr(VI) degradation for 2 others coatings.	[117]
Ambient air	Cr(VI)	The procedure involves a 24 h sampling of air into a 100 ml KOH (0.02 mol l^{-1}). The sample pH was adjusted to 8 with 2% v v^{-1} nitric acid and eluted through a silica gel column. The pH of the eluted solution was adjusted to 2.9 with 2% v v^{-1} nitric acid. APDC (5% m/v, 2 ml) was added and shaken for 15 min at room temperature. After, 5 ml of chloroform was added and shaken again for 15 min. The solution was then transferred to a 250 ml separating funnel to allow phase separation for 10 min and the chloroform phase was collected. The remaining aqueous phase was re-extracted and the extracts were combined, evaporated to dryness, dissolved in HNO_3 (20% v v^{-1}, 1 ml) and diluted to 5 ml.	DRC-ICP-MS	This procedure is applicable to determination of Cr(VI) in air. Studies have verified no conversion of Cr(VI) to Cr(III), and an average of 13% conversion of Cr(III) to Cr(VI).	[118]
Chromite ore processing residue, fly ash, and SRM 1645 (river sediment)	Cr(VI)	1 g of sample waste + 0.74 g of Na_2CO_3 (99.6%) and deionized water were added to the vessel so that the total volume of the liquid in each vessel was 25 ml. 5 ml of 2.5 mol l^{-1} NaOH, a proper amount of isoCr(III), i.e., sample doped with ^{50}Cr(III), and a proper amount of ^{53}Cr(VI) were added to the vessel. The amounts of the isotopic spikes depend on the levels of Cr(VI) and Cr(III) in the sample. The vessels are then heated at 93 °C for 1 h or at 150 °C for 10 min (microwave oven-open vessel). After extraction, the extracts are filtered using a 0.2 μm Nylon syringe filters. The filtrates were acidified between pH 1 and 2 with HNO_3.	ID-ICP-MS	This method was developed to correct for interconversion of chromium species.	[119]

Soils, sludges, sediments, and similar waste materials	Cr	The sample was digested using 0.28 mol l^{-1} Na_2CO_3/0.5 mol l^{-1} NaOH solution and heated at 90–95 °C for 60 min to dissolve the Cr(VI) and stabilize it against reduction to Cr(III).	IC-ICP-MS, HPLC-ICPMS, and colorimetry	Under the alkaline conditions of the extraction, minimal reduction of Cr(VI) or oxidation of native Cr(III) occurs. The Cr(VI) reaction with diphenylcarbazide is the most common and reliable method for analysis of Cr(VI) solubilized in the alkaline digestate.	[120]
Infant formulas	Iodide	0.2 g of sample was placed in a porcelain cup and 1 g of Na_2CO_3, 1 ml of 6 mol l^{-1} NaOH solution and 10 ml of MeOH were added. The cup was allowed to dry in a heater at 110 °C for 2 h. After, the cup was placed in a cold muffle furnace for 3 h, the temperature was slowly increased to 500 °C. After cooling in a desiccator, the cup was then placed in a sand bath and the ash was redissolved in 10 ml of ultrapure water. The solution obtained was filtered and diluted to 25 ml. A 2 ml aliquot of this solution was added to 2 ml of $AgNO_3$ solution in order to precipitate iodide as AgI. The precipitated was separated by filtration and redissolved in 4 ml of a 1 mg l^{-1} NaCN solution and silver was then determined in the resulting solution.	GFAAS	The iodide was determined indirectly by atomic absorption spectrometry with acceptable accuracy, precision, and sensitivity.	[122]
Freeze-dried poplar leaves, pine shoots, and spruce shoots	As and Sb	Six extraction media (acetic acid, EDTA, TMAH, NaOH, MeOH/H_2O, and acetonitrile/H_2O) were tested. Freeze-dried samples: 1 mg of samples + 9 ml of extraction medium were put into 15 ml graduated polyethylene tubes. Fresh samples: 5 g of sample and 30 ml of extractant were added to 50 ml polyethylene tubes. The sealed tubes were placed on a rotary mixer and soluble fraction of the powders was extracted for 24 h at room temperature. After centrifugation of the mixtures at 2000×*g* for 2 min, 4 ml of supernatant was pipetted into the digestion vessels and subsequently mineralized with HNO_3, H_2SO_4, $HClO_4$, and HF and diluted to 10 ml.	FI-HG-AAS	High extraction efficiency was obtained with NaOH. Extraction efficiencies were generally low and lower for Sb than for As.	[123]
Solid matrices	Cr(III) and Cr(VI)	2.5 g of sample was placed into a 250 ml digestion glass vessel and spiked with an aliquot of enriched $^{50}Cr^{3+}$ and $^{53}Cr^{6+}$, and 50 ml of 0.5 mol l^{-1} NaOH/2.8 mol l^{-1} Na_2CO_3 solution were added. Also, ~61 mg of $Mg(NO_3)_2$ was added plus 0.5 ml of 1.0 mol l^{-1} K_2HPO_4/KH_2PO_4 buffer (pH 7). The sample was covered with a watch glass and heated at 90–95 °C for 60 min with continuous stirring. It was then quantitatively transferred, after gradually cooling to room temperature, to the filtration apparatus (PTFE filter). The filtrate and rinses of the digestion vessel were collected in a 100 ml volumetric flask and diluted with Milli-Q water.	IC-ICP-MS	This method was suitable for analysis of hexavalent chromium in solid matrices.	[124]
Fish and sediment	$^{200}Hg^{2+}$, MMHg, $CH_3^{200}Hg^+$	Three extraction techniques were evaluated: distillation, acid extraction (5 ml of HCl 6 mol l^{-1} or a mixture of 5 ml of H_2SO_4 1 mol l^{-1}/KBr 1.5 mol l^{-1} and 1 ml of $CuSO_4$ 1 mol l^{-1} and shaken for 1 h.), and alkaline extraction (5 ml of methanolic KOH solution 25% m v^{-1} or 5 ml of a solution containing Bu_4NBr 0.25 mol l^{-1} and 4 mol l^{-1} KOH solution). A volume of 5 ml HCl (6 mol l^{-1}) was added to the alkaline solutions. All solutions were then extracted with 5 ml of toluene. 4 ml of the toluene solution was back extracted into 10 ml of water by evaporating the solvent in a rotatory evaporator (5 min at 60 °C). For preservation purposes, 100 µl of HCl (1 mol l^{-1}) was added.	GC-ICP-MS	The two alkaline leaching conditions both generated artifacts of MMHg. KOH/MeOH methylated 0.0060% of the added tracer. The compound Bu_4NBr/KOH showed a higher conversion rate of 0.03%. Only leaching using a H_2SO_2/KBr/$CuSO_4$ mixture did not cause any artifacts.	[125]
Solid matrices	Cr(III) and Cr(VI)	A 10 mg mass of the test sample was weighed (to the nearest 0.01 mg) in a PTFE vessel and 10 ml of a 0.25% m v^{-1} NaOH–0.40% m v^{-1} Na_2CO_3 solution was added to leach soluble chromium species (Cr(VI) and any soluble Cr(III) compounds) at 70 °C for 30 s in an ultrasonic bath. The residue was filtered and the	ID-ICP-MS	Recoveries of both chromium species were close to 100%.	[126]

(continued on next page)

Table 3 (*continued*)

Sample type	Analytes	Procedure	Technique [a]	Remarks	Ref.
Solid matrices	Cr(III) and Cr(VI)	alkaline solution was made up to 100 ml. The filter containing the residue (insoluble Cr(III) compounds and Cr metal) was transferred to a 20 ml platinum crucible, charred at a low heat and ignited slowly to 1000 °C. After cooling, the contents were fused with 0.5 g $NaHSO_4$, and the melt extracted with 2 ml of 12 mol l^{-1} HCl. After 14 ml of a 3% m v^{-1} NaOH–4% m v^{-1} Na_2CO_3 solution was added; pH was then lowered to 1–4 by adding 0.5 ml of 12 mol l^{-1} HCl solution and the solution was diluted to 100 ml.			
Nuts	Mg, Fe, Co, Mo, Ag, Hg, and Pb	Three different extractants, 0.05 mol l^{-1} NaOH, 0.05 mol l^{-1} HCl, and hot water at 60 °C were evaluated. A sample mass of 0.5 g was weighed into a plastic tube and 10 ml of the extractant was added. The tubes were agitated in a vortex for 30 min and centrifuged for 10 min at 3500 rpm. The supernatant was collected and then filtered through a 0.45 μm PVDF filter.	SEC-ICP-MS	The highest extraction efficiency was obtained with NaOH.	[127]
Chromate-containing certified filter samples	Cr(VI)	Sample + 10 ml of 0.05 mol l^{-1} $(NH_4)_2SO_4$/0.05 mol l^{-1} NH_4OH (pH 8) or 0.05 mol l^{-1} Na_2CO_3/0.05 mol l^{-1} NaOH (insoluble chromate and total Cr) were added to 15 ml plastic centrifuge tubes, followed by sonication in an ultrasonic bath.	IC-UV	Recoveries around 100% demonstrated that ultrasonic extraction is an effective technique for the quantitative dissolution of chromium species from industrial hygiene samples.	[128]
Soils	Cr(VI)	A mass of 2.5 g of sample was weighed into 45 250 ml beakers and the beakers were divided into 5 groups of 9. Each group was further divided into 3 groups of 3. To a group of 9, the spiking treatments were applied in triplicate: (a) Cr_2O_3—37 ml of a suspension containing 6.6 mmol l^{-1} Cr_2O_3, equivalent to adding 10 g of Cr (III)/kg of soil. (b) K_2CrO_4—1.25 ml of 38.5 mmol l^{-1} Cr(VI) solution, equivalent to 1.0 g of Cr(VI) kg^{-1} of soil. (c) Control: no Cr spike was added. After, 50 ml of extracting solution was added. Extraction solutions: distilled water (pH 5.7); phosphate buffer (pH 5.0 5 mmol l^{-1} K_2HPO_4, pH 7.0); carbonate-hydroxide solution (0.28 mol l^{-1} Na_2CO_3/0.55 mol l^{-1} NaOH, pH ~ 11.8) with (80–90 °C for 30–45 min on a hot plate) and without heating; and hydroxide solution (0.15 mol l^{-1} NaOH, pH 13) with 30–45 min sonication. After, all samples were diluted to 120 ml.	Spectrophotometry UV–VIS	The heated carbonate-hydroxide solution was the most effective medium for extraction of Cr(VI).	[129]
Coal fly ash and paint chips	Cr(VI)	10 ml of 0.05 mol l^{-1} $(NH_4)_2SO_4$–0.05 mol l^{-1} NH_3 (pH 8) buffer solution was added to the sample followed by ultrasonication in an ultrasonic bath for 30 min at 40 °C. The supernatant (10 ml) was transferred to a column filled with an anionic resin and was eluated using a buffer solution containing 0.05 mol l^{-1} $(NH_4)_2SO_4$–0.1 mol l^{-1} NH_3 (pH 8). After separation, the eluate was acidified with 2 drops of 37% v v^{-1} HCl solution followed by mixing with 2 ml of 0.02 mol l^{-1} diphenylcarbazide complexing reagent.	FIA-UV/VIS	The method was suitable for determination of Cr(VI) down to low ppb (μg l^{-1}) levels and was shown to extract Cr(VI) efficiently from real samples.	[131]
Welding fumes	Cr(VI)	Samples of welding fumes were collected during regular welding on polycarbonate membrane filters of 8 μm and 0.4 μm pore size. The filter was covered with 10 ml of an alkaline buffer (2% m v^{-1} NaOH–3% m v^{-1} Na_2CO_3) and subjected to agitation in a filter paper. HCO_3^-/H_2CO_3 buffer (pH 6.4) was used as a washing solution. The final pH of extracts was 12.	FPLC-GFAAS	Good repeatability for measurements of alkaline extracts was obtained for Cr(VI). Low detection limit was attained.	[132]
Fungi porcini mushroom	Bi, Co, Cu, Fe, I, Mo, Se, and Zn	Three different extraction media were investigated: 0.05 mol l^{-1} NaOH, 0.05 mol l^{-1} HCl, and hot water at 60 °C. 0.1 g of sample and 12 ml of extracting solution were stirred (vortex) for 30 min at room temperature and centrifuged at 3000 rpm for 10 min.	SEC-ICP-MS	Most of the elements (Bi, Cu, Zn, Fe, Co, and Ni) were found to be associated with a high weight molecular fraction, which was most effectively extracted with the NaOH solution.	[133]

Sewage sludge and landfill samples	Sb	Water, methanol–water (1 + 1 v v^{-1}) or 0.1 mol l^{-1} KOH were used as extractors. The mixtures were filtered through a 0.45-μm filter before measurements.	ICP-MS and ESI-MS	The KOH extraction solution was the most effective.	[134]
Alumina	Ca, Fe, Na, Si, and Ti	A mass of sample (0.1 g) was digested in a microwave oven (ETHOS, Milestone) in a closed vessel using 5 ml of 25% m v^{-1} KOH solution + 1 ml of H_2O_2. After, the vessels were heated using the following program: Step 1: 5 min, 500 W, and 180 °C; Step 2: 15 min, 700 W, and 240 °C, Step 3: 5 min, 500 W, and 240 °C and ventilation Step 4: 5 min, 0 W.	ICP OES	Good recoveries were obtained.	[135]
Sediment	CH_3Hg^+	A mass of 2 g of spiked sediment was extracted by 5 ml KOH/CH_3OH (25% m v^{-1}) in ultrasonic bath (45 min). After cooling, 5 ml of H_2SO_4 (4 mol l^{-1}, saturated $CuSO_4$), 5 ml of mol l^{-1} KBr, and 4 ml of toluene were carefully added and the sample was manually shaken for about 3 min. After centrifugation (2200 rpm for 10 min), the supernatant organic phase was collected. The solvent extraction was repeated three times by 2 ml of toluene. The collected organic extract (10 ml) was subjected twice to a back-extraction by 1 ml cysteine solution (1% m v^{-1}). The two cysteine solutions (1 + 1 ml) were collected in the same vial and extracted by a mixture of benzene (0.5 ml), $CuSO_4$ saturated solution (0.5 ml), and 5 mol l^{-1} KBr (1 ml). After manual shaking, an adequate volume of B1 solution was added, as internal injection standard. Finally, the organic phase was separated from the aqueous phase and 2 μl was injected in the gas chromatography.	GC-EDC	The method was reliable when using CRM materials and was characterized by satisfactory accuracy and reproducibility, short time of analysis, and ease of execution.	[136]
Fish sample	CH_3Hg^+	A mass of 30–80 mg of sample was transferred into a 30 ml PTFE bottle and 10 ml of 25% m v^{-1} KOH/methanol solution was added, and the sample was shaken in an ultrasonic bath for 2 h so that all the tissue was dissolved. The sample was then diluted with 10 ml of methanol and stored in the dark until analysis.	GC-AAS	The method demonstrates accuracy, precision, and reproducibility when standard reference materials were analyzed.	[137]
Biological tissues	CH_3Hg^+	A mass of 0.15 g of sample was transferred into a glass tube and 6 ml of 25% m v^{-1} KOH/methanol solution was added and the tubes were capped. The slurry was homogenized by magnetic agitation and submitted to microwave irradiation for 30–180 s at 48–132 W. The digestate was allowed to cool down to laboratory temperature. The alkaline extract was mechanically shaken in a glass separating funnel for 10 min with 6 ml of dichloromethane and 4.5 ml of concentrated hydrochloric acid. An aliquot of dichloromethane was transferred into another tube and the slurry was again treated with 6 ml of dichloromethane for 10 min. The dichloromethane layers were combined and organomercurials were solvent exchanged into 35 ml of ultra-pure water by evaporation of the organic solvent with a current of nitrogen.	HPLC-UVPCO-CV-AFS	The method has shown good agreement with certified values of the sample.	[138]
Methanolic NaOH	MeHg and EtHg	A volume of 5 ml of 4.5 mol l^{-1} methanolic NaOH solution was added to 500 μl of a solution containing MeHgCl and EtHgCl in a microwave vial. Microwave radiation was applied varying the time (from 2 to 10 min) and the power (from 20 to 160 W). Then, a volume of 50 μl of the digestate was mixed with 5 ml of 1 mol l^{-1} sodium acetate buffer (pH 5). After, headspace SPME extraction was carried out by adding 500 μl of 1% m v^{-1} $NaBPh_4$ to the solution under magnetic stirring.	SPME-GCAFS	Blank problems occurred due to the inorganic Hg contents of the buffer solution and the methanolic NaOH medium. MeHg appeared to be much more tolerant towards microwave energy than EtHg.	[139]
Urine	Iodine	To 1 ml of urine, introduced in a combustion test tube, it was added 1 ml of 0.35 mol l^{-1} $ZnSO_4$ solution, 2 ml of 2 mol l^{-1} NaOH solution and 70 mg of KCl. This mixture was dried at 115 °C overnight. After that the samples were heated in a furnace following the temperature program: 200 °C for 30 min, 500 °C for 30 min, 600 °C for 1 h. Then the residue in the cooled test tube was suspended in 6 ml of deionized water and the tubes were centrifuged for 10 min at 1800 rpm and 2 ml of the clear supernatant was used for the analysis.	Spectrophotometry UV–VIS	The alkaline ashing was more laborious and time-consuming compared with wet mineralization procedures.	[140]

(continued on next page)

Table 3 (*continued*)

Sample type	Analytes	Procedure	Technique [a]	Remarks	Ref.
Dogfish muscle, river water	MeHg	Fish extract: A mass of 100–200 mg sample was mixed with 10–20 ml of 25% m v^{-1} methanolic KOH solution and the mixture was shaken in an ultrasonic bath for 3 h. A volume of 100 µl and 20 µl of fish extract was used for headspace SPME or aqueous-phase SPME sampling, respectively. For analysis of river water 17 ml of sample was used. Before the SPME, sampling an aqueous-phase derivatization of ionic mercury species was made with $NaBEt_4$ in a sample vial.	GC-MS	Accurate determinations of MeHg and labile Hg from fish and water samples could be achieved using an in situ aqueous derivatization followed by SPME and GC-MS detection.	[141]
Egg, yeast, animal feeds, soil, bovine serum	Se	A mass of 0.2 g of sample was mixed with 1.0 g of NaOH and an appropriate amount of $NaNO_3$ in a graphite crucible, then heated to fusion for 30 min. The fusion cake was dissolved with water and 2.5 g of thiourea was added; after mixing thoroughly, the solution was allowed to stand for 15 min. An amount of $NaBH_4$ was added and the volume was made up to 50 ml with water. This solution was reacted with HCl solution in a continuous generation mode and the generated H_2Se was carried by an argon flow to the plasma.	HG-ICP OES	High concentrations of interfering elements (Fe, Cu and Mn) could be eliminated using the alkaline fusion-alkaline hydride generation.	[142]
Fish	MeHg	A mass of 0.25 g of sample with an appropriate amount of enriched $Me^{198}Hg$ spike and 20 ml of 25% m v^{-1} methanolic KOH solution were shaken for 5 h. For SPME headspace sampling, 100 µl of digest was transferred to a 50 ml glass vial for quantification. After, 20 ml of 1 mol l^{-1} sodium acetate buffer solution and 1 ml of 1% m v^{-1} $NaBPr_4$ were added, the vial was capped and the SPME needle was inserted through the septum and headspace sampling was performed for 10 min, under vigorous stirring. The collected analyte was then desorbed onto the GC column.	SMPE-GC-ICP-MS	A significant improvement in the accuracy of monomethylmercury determination was achieved using isotope dilution.	[143]
Solid waste material, packaging materials	Cr(VI)	A mass of 2.5 g of sample was placed into a 250-ml digestion glass vessel and spiked with an aliquot of enriched isotopes ^{50}Cr(III) and ^{53}Cr(VI). After, 50 ml of a digestion solution (0.5 mol l^{-1} NaOH and 0.28 mol l^{-1} Na_2CO_3) and 0.5 ml of a 1 mol l^{-1} K_2HPO_4/KH_2PO_4 buffer (pH 7) were added. The mixture was covered with a watch glass and heated at 90–95 °C for 60 min with continuous stirring. The digest was transferred (after cooling down to room temperature) to the filtration apparatus (polytetrafluoroethylene filter). The filtrate was collected in a 100 ml volumetric flask, diluted with water and injected on the AS 10 column for the ICP-MS analysis.	IC-ICP-MS	The use of alkaline digestion guaranteed a minimum species interconversion during sample preparation.	[144]
Milky products, milk powder	Iodine	KOH (2 ml, 2 mol l^{-1} in ethanol) and $Ca(NO_3)_2$ (2 ml, 0.4 mol l^{-1} in ethanol) were mixed with 2 ml of milk sample (or 200 mg of milk powder). The mixture was dried in a drying oven and then heated in a muffle furnace (2 h at 240 °C, 1 h at	VG-ICP OES	Different fat contents in milk samples (from 0.5% to 12% m v^{-1}) had no evident effect on the accuracy or precision.	[145]

Milky products, milk powder	Iodine	340 °C, 1 h at 440 °C and 4 h at 640 °C). The sample ash was transferred to a beaker and Na_2S (1.25 ml, 1 mol l^{-1}) and HCl (1.5 ml, 5 mol l^{-1}) were added. Carbon dioxide was eliminated by gentle boiling of the mixture and the resulting solution was diluted to 25 ml with water.			
Fish	MeHg, EtHg	A mass of 0.2 g of sample was mixed with 2 ml of water and shaken. Then 2 ml of 6 mol l^{-1} KOH was added; the mixture was shaken overnight, an isolation solution was added (2 ml 6 mol l^{-1} HCl, 4 ml of acidic KBr/$CuSO_4$, 5 ml CH_2Cl_2) and then shaken for 2 h. The resulted mixture was centrifuged and 2 ml of CH_2Cl_2 phase was removed and to this sample solution 1 ml of 0.01 mol l^{-1} $Na_2S_2O_3$ was added and then shaken for 45 min. This new mixture was centrifuged, 0.4 ml of the aqueous phase was removed and mixed with 0.3 ml of acidic KBr/$CuSO_4$ and 0.15 ml CH_2Cl_2. It was shaken for 15 min, mixed for 15 s in a Vortex Genie mixer and 0.1 ml of the CH_2Cl_2 phase was removed and introduced in the GC-AFS system.	GC-AFS	The alkaline digestion followed by solvent extraction produced a more uniform sample solution than the one obtained with an acidic digestion and solvent extraction procedure.	[146]

[a] ICP OES—inductively coupled plasma optical emission spectrometry. ICP-MS—inductively coupled plasma mass spectrometry. GFAAS—graphite furnace atomic absorption spectrometry. FAAS—flame atomic absorption atomic spectrometry. HPLC-ICP-MS—high-performance liquid chromatography and inductively coupled plasma mass spectrometry. DRC-ICP-MS—dynamic reaction cell and inductively coupled plasma mass spectrometry. SEC-ICP-MS—size exclusion chromatography and inductively coupled plasma mass spectrometry. FI-HG-AAS—flow injection hydride generation atomic absorption spectrometry. SAE-SPE—strong anion-exchange solid-phase extraction. ID-ICP-MS—isotope dilution and Inductively coupled plasma mass spectrometry. IC-ICP-MS—ion chromatography and Inductively coupled plasma mass spectrometry. GC-ICP-MS—gas chromatography and inductively coupled plasma mass spectrometry. IC-UV—ion chromatography with ultraviolet detection. FIA-UV/VIS—flow injection analysis with ultraviolet–visible detection. FPLC-ETAAS—fast protein liquid chromatography-electrothermal atomic absorption spectrometry. ESI-MS—electrospray-ionization mass spectrometry. GC-EDC—gas chromatography with electron capture detector. HPLC-UV-PCO-CV-AFS—high performance liquid chromatography and ultraviolet post column oxidation and cold vapor atomic fluorescence spectrometry. SPME-GC-AFS—solid phase microextraction and Gas chromatography with atomic fluorescence detection. GC-MS—gas chromatography-mass spectrometry. SPME-GC-ICP-MS—solid phase microextraction with gas chromatography and inductively coupled plasma mass spectrometry. VG-ICP OES—vapor generation inductively coupled plasma optical emission spectrometry.

between the average concentrations obtained with the two methods for food plants were usually within ±15% of each other. On the other hand, good agreement was obtained between the certified and found concentration values for tea leaves, aquatic moss and lichen.

Kannamkumarath et al. [127] studied the effect of extraction media on the elemental speciation of nuts. Three different media were used for the extraction of several nut fractions: NaOH (50 mmol l^{-1}), HCl (50 mmol l^{-1}) and hot water (60 °C). The extractions were performed for 30 min with constant agitation. Size exclusion chromatography and ICP-MS were used for the separation and identification of various chemical species containing Mg, Fe, Co, Mo, Ag, Hg, and Pb. Recoveries for elements using the NaOH medium were 28–105%; these values were higher than those obtained using the other extraction media, except for Mg. Recovery of Mg was 8–11% in the alkaline medium and 82–84% in the hydrochloric acid medium.

The extraction and quantification of Cr(VI) were studied in soils using an alkaline medium followed by ion chromatography with ultraviolet detection after post-column reaction with diphenylcarbazide [129]. The authors compared the efficiency of extraction using several extractants: distilled water (pH 5.7), phosphate buffer (5 mmol l^{-1} K_2HPO_4/5 mmol l^{-1} KH_2PO_4, pH 7.0), carbonate–hydroxide extractant (0.28 mol l^{-1} Na_2CO_3/0.5 mol l^{-1} NaOH, pH ~11.8) with and without heating, and sodium hydroxide solution (0.1 mol l^{-1}, pH 13) with sonication. The carbonate-hydroxide solution with heating at 90–95 °C led to maximum dissolution of all forms of Cr(VI) while minimizing method-induced oxidation and reduction, for example more than 90% of a soluble K_2CrO_4 spike was recovered using this medium. Water and phosphate buffer extracted 71% and 79% of the Cr(VI), respectively, indicating that 29% of the Cr(VI) in the sample was insoluble, or 8% was interconverted. The non-heated hydroxide solution and NaOH with sonication extraction removed slightly greater quantities of Cr(VI) than did water and phosphate buffer, indicating that heating enhanced dissolution of insoluble Cr(VI) and that sonication with NaOH was not as efficient as the heating with the carbonate-hydroxide solution [129]. Pettine and Capri studied the effect of the humic matter also extracted in soils when using an alkaline medium on the spectrophotometric determination of Cr(VI) by the diphenylcarbazide method [130].

Speciation of Cr in steelmaking solid wastes samples was studied by Coedo et al. [126]. Chromium (VI) and Cr(III) were separated and determined by isotope dilution ICP-MS. The sample dissolution and preparation method was developed using mixtures of CrO_3 (Cr(VI)) and Cr_2O_3 (Cr(III)). A solution containing 0.25% m v^{-1} NaOH–0.40% m v^{-1} Na_2CO_3 was used for leaching of soluble chromium species (Cr(VI)) and any soluble Cr(III) compounds. Digestion of the residue (insoluble Cr(III) compounds and Cr metal) by fusion with $NaHSO_4$ and extraction of the melt with HCl was then undertaken. This sample pre-treatment procedure did not modify the oxidation state of the Cr in the original sample. The method allows differentiation of Cr(VI), soluble Cr(III) as the negatively charged $Cr(OH)^-$ complex, and insoluble Cr(III) (coming from Cr_2O_3 and Cr metal). Recoveries of both chromium species (Cr (VI) and Cr(III)) were close to 100% [126].

Kahakachchi et al. [114] proposed a procedure for extraction of arsenic species [As(III), As(V), dimethylarsenic acid (DMA), and monomethylarsonic acid (MMA)] from spiked soils by high-performance liquid chromatography with detection by ICP-MS. The authors showed that the highest extraction efficiency was obtained when NaOH was used. The extractants studied for sample preparation were capable of recovering different amounts of arsenic from the soils. Using a high pH extractant, 0.1 mol l^{-1} NaOH, 46% As(III), 53% DMA, 100% MMA and 84% As(V) were extracted. Under acidic conditions, with citrate buffer at pH 3, 3.3% As(III), 88% DMA, 64% MMA, and 53% As(V) were extracted. The efficiency of extraction was improved using an ultrasonic probe. After 20 min of sonication, the efficiency was increased to 88% As(V), 85% DMA, and 98% MMA.

Inorganic arsenic in fish samples was determined by high-performance liquid chromatography (HPLC) coupled to ICP-MS. Microwave-assisted digestion was achieved using sodium hydroxide in ethanol (2 ml of 3 mol l^{-1} NaOH + 3 ml of water + 5 ml of ethanol) which dissolved the sample and quantitatively oxidized arsenite (As(III)) to arsenate (As(V)). Quantitative recovery of As(V) was obtained. Quantitative oxidation of As (III) to As(V) was also demonstrated. In contrast to As(III), the other arsenic species of interest, As(V), MMA and arsenobetaine, remained stable during this treatment [115]. Microwave-assisted digestion using sodium hydroxide was also performed for food samples for determining bromide [116].

Krachler and Emons [123] verified the efficiency of extraction of As and Sb in fresh and freeze-dried plants by studying several extraction media. The concentration of As and Sb in the extractants was determined by hydride generation AAS using a flow system. Extraction efficiencies were generally lower for Sb (10–19%) than for As (22–36%).

In a subsequent study, Sb was extracted from environmental samples and determined by HPLC-ICP-MS and electrospray-ionization mass spectrometry. The efficiency of extraction with KOH for Sb(V) was 86%, but no trimethylantimony was detected in any extraction [134].

Alkaline leaching conditions were evaluated for the extraction of monomethylmercury (MMHg) in sediments. Methanolic KOH solution and a solution containing Bu_2NBr and KOH were tested. Both extractants generated artifacts of MMHg (from Hg^{2+}) [125]. There are many alkaline digestion procedures proposed for speciation analysis [135–139,141–144,146], however the formation of artifacts must be carefully evaluated [147].

5. Conclusions

Tetramethylammonium hydroxide-based procedures provide an alternative to conventional acid digestion for biological materials, since satisfactory accuracy, precision and instrument performance have been reported in the majority of such studies.

In addition to this good performance, treatment with TMAH proved to be an advantageous approach to prepare samples for

the determination of elements that are not compatible with nitric acid, which is frequently used in conventional sample digestion.

A reduction in sample preparation time and the long-term stability of the digests are two of the greatest advantages of this reagent.

The use of TMAH allows complete or partial dissolution, depending on the sample, and the extraction may be carried out at elevated or at room temperature.

TMAH may also be used for applications involving measurements by GFAAS since the solution resulting from the solubilization process shows adequate physical and chemical properties, but attention must be given to the selection of a modifier which is compatible with the alkaline medium.

Although a number of advantages arise when undertaking sample preparation with TMAH, it may not be considered a universal reagent. On the other hand, the majority of studies focus only on its performance, and the mechanism of action has not been mentioned.

By contrast, the use of water-soluble tertiary amines for sample preparation has also resulted in some significant positive effects:

1. neutralization of acids and deactivation of free fluoride in digests;
2. extraction of elements from biological materials at room temperature;
3. collection of the combustion products following oxidation of food samples;
4. dilute-and-shoot procedures for the analysis of milk;
5. elimination of memory effects, as demonstrated for Th by ICP-MS and for Si by ICP OES;
6. elimination of polyatomic ion interferences and enhancement in sensitivity during measurements of As and Se by ICP-MS.

The chemical basis for all of these effects has not yet been established, owing to the unknown composition of the tertiary reagents. However, it seems that there is room for use of alkaline reagents in sample preparation. Perhaps similar effects could probably be attained by adding a complexing agent, e.g., EDTA, to a commercial amine, e.g., TMAH.

Alternative strategies, involving use of alkaline media in combination with microwave-assisted procedures in open or closed vessels still need further evaluation. However, it appears that strongly alkaline reagents can be used successfully in microwave-assisted digestion and extraction procedures. This approach can promote the digestion of materials containing oxides and the total sample digestion time is generally not increased. The efficiency of microwave-assisted decomposition of samples using an alkaline reagent can be characterized by several aspects:

1. high temperatures can be reached even at low pressures; however, the boiling point is dependent on the concentration of the base;
2. the use of H_2O_2 promotes higher pressures during the digestion;
3. one may note a precipitate once a sample has cooled, after completing the digestion process.

The following advantages of use of an alkaline medium during extraction procedures can be emphasized:

1. they do not modify the oxidation state of the analyte;
2. they can be utilized for speciation of several elements and compounds;
3. they offer a simple preparation method for subsequent analysis;
4. extraction of elements can be enhanced by applying either microwave radiation or elevated temperature.

Taking into account all the aforementioned aspects, it may be concluded that alkaline digestion or extraction procedures can be properly employed in tailored procedures for the determination of a large number of analytes in a variety of samples.

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(54) **DISSOLUTION OF CELLULOSE IN MIXED SOLVENT SYSTEMS**

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See application file for complete search history.

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(57) **ABSTRACT**

A method for dissolving cellulose in which the cellulose based raw material is admixed with a mixture of a dipolar aprotic intercrystalline swelling agent and an ionic liquid at a temperature of 25° C. to 180° C. for a time sufficient to dissolve the cellulose based raw material. The molar ratio of dipolar aprotic intercrystalline swelling agent to ionic liquid is 0.05 to 1.5 moles of dipolar aprotic intercrystalline swelling agent to 1 mole of ionic liquid. Dipolar aprotic intercrystalline swelling agents do not include imidazole based agents or amine based agents.

11 Claims, No Drawings

DISSOLUTION OF CELLULOSE IN MIXED SOLVENT SYSTEMS

This application claims priority from Provisional Application 60/976,221 filed Sep. 28, 2007.

FIELD

This application relates to the dissolution of cellulose in a mixture of dipolar aprotic intercrystalline swelling agents and ionic liquids. Further, it relates to the dissolution of cellulose in a mixture of protic intercrystalline swelling agents and ionic liquids.

DESCRIPTION

As the current world demand for cellulose increases, there is an increasing demand for low cost raw materials which can be used in commercial processes that use these raw materials. Additionally, there is a need to develop new processes which use these raw materials and which are simpler, have less of an environmental impact and do not have some of the shortcomings of the current processes.

Solvents for the dissolution of cellulose and other constituents in trees and other woody and non-woody plants are increasingly important in order to maximize the utilization of the components in their entirety. Increased use of textiles, fibers, films, membranes and other products dictate the need for new solvent systems which can help meet demands in these areas. Manufacturing facilities with these solvent systems must be have low capital costs and must meet environmental and regulatory laws.

Currently rayon and lyocell are commercially available cellulose fibers. Rayon is made in the viscose process. In the process, cellulose is first steeped in a mercerizing strength caustic soda solution to form an alkali cellulose. This is reacted with carbon disulfide to form cellulose xanthate which is then dissolved in dilute caustic soda solution. After filtration and deaeration the xanthate solution is extruded from submerged spinnerets into a regenerating bath of sulfuric acid, sodium sulfate, zinc sulfate, and glucose to form continuous filaments. The resulting viscose rayon is presently used in textiles and has been used in such applications as tires and drive belts.

Cellulose is also soluble in a solution of ammonia copper oxide. This property forms the basis for production of cuprammonium rayon. The cellulose solution is forced through submerged spinnerets into a solution of 5% caustic soda or dilute sulfuric acid to form the fibers, which are then decoppered and washed. Cuprammonium rayon can be available in fibers of very low deniers and is used almost exclusively in nonwoven wipe application.

The foregoing processes for preparing rayon both require that the cellulose be chemically derivatized or complexed in order to render it soluble and therefore capable of being spun into fibers. In the viscose process, the cellulose is derivatized, while in the cuprammonium rayon process, the cellulose is complexed. In either process, the derivatized or complexed cellulose must be regenerated and the reagents that were used to solubilize it must be removed. The derivatization and regeneration steps in the production of rayon significantly add to the cost of this form of cellulose fiber and also possess environmental issues in the use of zinc in coagulation baths and in the handling of carbon disulfide. Consequently, in recent years attempts have been made to identify solvents that are capable of dissolving underivatized cellulose to form a dope of underivatized cellulose from which fibers can be spun.

One class of organic solvents useful for dissolving cellulose are the amine-N oxides, in particular the tertiary amine-N oxides. Lyocell is made by dissolving cellulose in a mixture of N-methylmorpholine-N-oxide (NMMO) and water and extruding the solution into regenerating bath, usually water.

Lyocell is a generic term for a fiber composed of cellulose precipitated from an organic solution in which no substitution of hydroxyl groups takes place and no chemical intermediates are formed. Several manufacturers presently produce lyocell fibers, principally for use in the textile industry. For example, Lenzing, Ltd. presently manufactures and sells a lyocell fiber called Tencel® fiber.

Currently available lyocell fibers and high performance rayon fibers are produced from high quality wood pulps that have been extensively processed to remove non-cellulose components, especially hemicellulose. These highly processed pulps are referred to as dissolving grade or high a (or high alpha) pulps, where the term a (or alpha) refers to the percentage of cellulose remaining after extraction with 17.5% caustic. Alpha cellulose can be determined by TAPPI 203. Thus, a high alpha pulp contains a high percentage of cellulose, and a correspondingly low percentage of other components, especially hemicellulose. The processing required to generate a high alpha pulp significantly adds to the cost of rayon and lyocell fibers and products manufactured therefrom. Typically, the cellulose for these high alpha pulps comes from both hardwoods and softwoods; softwoods generally have longer fibers than hardwoods.

A wide variety of cellulose based raw materials can be used in the present application. Chemical pulp fibers used in the present application are derived primarily from wood pulp. Other sources such as from kenaf and straw pulp may also be used. Suitable wood pulp fibers for use with the application can be obtained from well-known chemical processes such as the kraft and sulfite processes, with or without subsequent bleaching. Softwoods and hardwoods can be used. Details of the selection of wood pulp fibers are well known to those skilled in the art. For example, suitable cellulosic fibers (chemical pulp fibers) produced from southern pine that are useable in the present application are available from a number of companies including Weyerhaeuser Company under the designations C-Pine, Chinook, CF416, FR416, and NB416. A Prince Albert Softwood and Grande Prairie Softwood, manufactured by Weyerhaeuser are examples of northern softwoods that can be used. Mechanically and chemimechanically treated fibers such as chemithermomechanical pulp fibers (CTMP), bleached chemithermomechanical pulp fibers (BCTMP), thermomechanical pulp fibers (TMP), refiner groundwood pulp fibers and groundwood pulp fibers can also be used. Examples of these pulps are TMP (thermomechanical pulp) made by Bowater, Greenville, S.C., a TMP (thermomechanical pulp) made by Weyerhaeuser, Federal Way, Wash., made by passing wood chips through three stages of dual refiners, and a CTMP (chemithermomechanical pulp) obtained from NORPAC, Longview, Wash., sold as a CTMP NORPAC Newsprint Grade with a brightness from 53 to 75.

Ionic liquids such as 1-ethyl-3-methylimidizolium acetate (EMIMAc) and 1-butyl-3-methyl imidazoliumchloride (BMIMCl) are known to dissolve cellulose. It has now been found that the solubility of cellulose is increased in mixtures of dipolar aprotic intercrystalline swelling agents and ionic liquids. Similar effects are noted when cellulose is dissolved in a mixture of a protic solvent and an ionic liquid.

Dipolar aprotic intercrystalline swelling agents include but are not limited to dimethyl sulfoxide (DMSO), dimethyl acetamide (DMAc), N-methylmorpholine oxide, formamide, pyridine, acetone, dioxane, N-methyl pyrolidine (NMP), piperylene sulfone and hexamethylphosphoramide (HMPA). These dipolar aprotic intercrystalline swelling agents, by themselves, do not dissolve cellulose. In general, it is thought that liquids which produce a significant amount of swelling are those that are capable of forming hydrogen bonded complexes with the cellulose molecule. Dipolar aprotic intercrystalline swelling agents do not include imidazole based agents or amine based agents.

Protic solvents include but are not limited to water, low molecular alcohols such as methyl, ethyl, propyl, butyl and amyl alcohol, ethylene glycol, acetic acid, methylamine, di- and triethylamine and butylamine and mixtures thereof.

As defined herein, ionic liquids are ionic compounds which are liquid below 100° C. A few ionic liquids for cellulose have melting points below room temperatures, some even below 0° C. The compounds are liquid over a wide temperature range from the melting point to the decomposition temperature of the ionic liquid. Ionic liquids have cations or anions associated with the molecule. Examples of the cation moiety of ionic liquids are cations from the group consisting of cyclic and acyclic cations. Cyclic cations include pyridinium, imidazolium, and imidazole and acyclic cations include alkyl quaternary ammonium and alkyl quaternary phosphorous cations. Counter anions of the cation moiety are selected from the group consisting of halogen, pseudohalogen and carboxylate. Carboxylates include acetate, citrate, malate, maleate, formate, and oxylate and halogens include chloride, bromide, zinc chloride/choline chloride, 3-methyl-N-butyl-pyridinium chloride and benzyldimethyl (tetradecyl) ammonium chloride. Substituent groups, (i.e. R groups), on the cations can be C_1, C_2, C_3, and C_4; these can be saturated or unsaturated. Examples of compounds which are ionic liquids include, but are not limited to, 1-ethyl-3-methyl imidazolium chloride, 1-ethyl-3-methyl imidazolium acetate, 1-butyl-3-methyl imidazolium chloride, 1-allyl-3-methyl imidazolium chloride, zinc chloride/choline chloride, 3-methyl-N-butyl-pyridinium chloride, benzyldimethyl(tetradecyl) ammonium chloride and 1-methylimidazolehydrochloride. The 1-ethyl-3-methyl imidazolium acetate used in this work was obtained from Sigma Aldrich, Milwaukee.

In one embodiment cellulose is dissolved in a mixture of a dipolar aprotic agent and an ionic liquid. Mixtures of the dipolar aprotic agent and the ionic liquid dissolve cellulose over a wide temperature range. In one embodiment cellulose is dissolved in the range of 25° C. to 180° C. In another embodiment cellulose is dissolved over the range of 80° C. to 120° C. In yet another embodiment cellulose is dissolved over a temperature range of from 100° C. to 110° C. Dissolution of cellulose can be conducted with or without stirring. The latter accelerates dissolution of cellulose. Table 1 shows the dissolution of cellulose (10% weight add on of Peach® on total weight of mixture of dipolar aprotic agent and ionic liquid) in a mixture of dipolar aprotic agents and ionic liquids at 105° C.; Table 2 shows the dissolution of cellulose (10% weight Peach® add on) in a mixture of dipolar aprotic agents and ionic liquids at 105° C. with stirring. For purposes of this application, cellulose is considered dissolved when the solution is visually examined and is cloudy or clear. The dissolution of cellulose is further confirmed by casting the cellulose dope on a glass slide to form a film and regenerating the film in water. In the tables, molar ratio refers to the ratio of the dipolar aprotic agent to the ionic liquid. For example a molar ratio of 10.27 for the mixture of DMSO and EMIMAc (1-ethyl-3-methyl imidazolium acetate) means that 10.27 moles of DMSO and one mole of EMIMAc dissolve cellulose at 105° C. in one hour.

Cellulose is dissolved over a wide range of molar ratios of the dipolar aprotic solvent to the ionic liquid. For ionic liquids that are liquids, the calculated amount of dipolar aprotic solvent was added to the ionic liquid, mixed and a fixed quantity of cellulose was added. For ionic liquids that are solids, the ionic liquid was heated to melt the solid, the calculated amount of a dipolar aprotic solvent was added to the ionic liquid, mixed and a fixed quantity of cellulose was added. Heating was conducted in a sealed vial at 105° C. for samples that were not stirred and at 105° C. with occasional stirring with a spatula after opening the heated sealed vial. In some cases dissolution was conducted as low as 25° C. if the solvent mixture is a solution at room temperature.

In some embodiments the molar ratio Of dipolar aprotic intercrystalline swelling agent to ionic liquid may be from 0.5 to 25 moles of dipolar aprotic intercrystalline swelling agent to 1 mole of ionic liquid. In some embodiments the molar ratio of dipolar aprotic intercrystalline swelling agent to ionic liquid may be from 0.5 to 15 moles of dipolar aprotic intercrystalline swelling agent to 1 mole of ionic liquid. In some embodiments the molar ratio of dipolar aprotic intercrystalline swelling agent to ionic liquid may be from 0.5 to 2 moles of dipolar aprotic intercrystalline swelling agent to 1 mole of ionic liquid. In one embodiment a molar ratio of 10.27 for the mixture of DMSO and EMIMAc (1-ethyl-3-methyl imidazolium acetate) dissolves cellulose in one hour at 105° C. In another embodiment a molar ratio of 1.25 for the mixture of DMSO and EMIMCl (1-ethyl-3-methyl imidazolium chloride) dissolves cellulose at 105° C. in 20 hours. In one embodiment a molar ratio of 0.8 for the mixture of DMSO and EMIMCl (1-ethyl-3-methyl imidazolium chloride) dissolves cellulose in 45 minutes at 105° C. with stirring. In another embodiment a molar ratio of 1.7 for the mixture of DMAc and BMIMCl (1-butyl-3-methyl imidazolium chloride) dissolves cellulose at 105° C. in 30 minutes with stirring.

In some embodiments the time of dissolution for mixtures of dipolar aprotic agents and ionic liquids may be 5 minutes to 24 hours. In some embodiments the time of dissolution for mixtures of dipolar aprotic agents and ionic liquids may be 5 minutes to 1 hours.

Mixtures of the dipolar aprotic agents and ionic liquids have a surprising effect on viscosity and exhibit Newtonian flow characteristics. Viscosity was determined at a different shear rates with a rotational rheometer from Bohlin (Viscometry Mode at room temperature) Table 4, 5 and 6 show the effect on viscosity (Pas, pascal seconds) at different shear rates ($second^{-1}$) of cellulose dissolved in a mixture dipolar aprotic intercrystalline swelling agents and ionic liquids. The tables show that with increasing shear rate the viscosity decreases. This is particularly beneficial where throughput in manufacturing is important since more weight per unit time can be achieved through the spinning head.

In another embodiment cellulose is dissolved in a mixture of a protic solvent and an ionic liquid. Protic solvents include but are not limited to water, low molecular alcohols such as methyl, ethyl, propyl, butyl and amyl alcohol, ethylene glycol, acetic acid, quaternary ammonium hydroxide, quaternary ammonium cations, methylamine, di- and triethylamine and butylamine and mixtures thereof. For ionic liquids that are liquids, the calculated amount of protic agent was added to the ionic liquid, mixed and a fixed quantity of cellulose was added. For ionic liquids that are solids, the ionic liquid was heated to melt the solid, the calculated amount of protic solvent was added to the ionic liquid, mixed and a fixed quantity of cellulose was added. Heating was conducted in a sealed vial at 105° C. for samples that were not stirred and at 105° C. with stirring. In some cases dissolution was conducted as low as 25° C. if the ionic liquid and the protic agent are liquid at room temperature.

Mixtures of the protic agent and the ionic liquid dissolve cellulose over a wide temperature range. In one embodiment cellulose is dissolved in the range of 25° C. to 180° C. In another embodiment cellulose is dissolved over the range of 80° C. to 120° C. In yet another embodiment cellulose is dissolved over a temperature range of from 100° C. to 110° C. Dissolution of cellulose can be conducted with or without stirring. The latter accelerates dissolution of cellulose. Table 3 shows the dissolution of cellulose in a mixture of protic solvents and ionic liquids at 105° C. For purposes of this application, cellulose is considered dissolved when the solution is visually examined and the solution is cloudy or clear. In the table, molar ratio refers to the ratio of the protic solvent to the ionic liquid. For example a molar ratio of 0.13 for the mixture of acetic and EMIMCl (1-ethyl-3-methyl imidazolium chloride) means that 0.13 moles of acetic acid and one

mole of EMIMCl dissolve cellulose at 105° C. in two hours 105° C. The molar ratio of protic intercrystalline swelling agent to ionic liquid may be from 0.05 to 1.5 moles of dipolar aprotic intercrystalline swelling agent to 1 mole of ionic liquid.

In some embodiments the dissolution time for a mixture of protic agents and ionic liquids may be 5 minutes to 24 hours. In some embodiments the dissolution time for a mixture of protic agents and ionic liquids may be 5 minutes to 5 hours. In some embodiments the dissolution time for a mixture of protic agents and ionic liquids may be 5 minutes to 2 hours. In some embodiments the dissolution time for a mixture of protic agents and ionic liquids may be 5 minutes to 1 hour.

Cellulose dissolved in the protic agent and the ionic liquid or the dipolar aprotic agent and the ionic liquid can be regenerated by precipitating the cellulose in a liquid in which it is immiscible such as water, alcohol, mixtures thereof, a mixture of a protic agent and an ionic liquid, or with a high ratio of a protic or dipolar aprotic agent to the ionic liquid. Preferably the liquid non-solvent is miscible with water but other non-solvents such methanol, ethanol, acetonitrile, an ether such as furan or dioxane or a ketone can be used. The advantage of water is that the process avoids the use of a volatile organic compound and regeneration does not require the use of volatile organic solvents. Thus the ionic liquid can be dried and reused after regeneration. In one embodiment water is used as the non-solvent for regeneration of the cellulose. Mixtures of from 0% by weight non-solvent/solvent to about 50% by weight non-solvent/solvent can be used for regenerating the cellulose from the ionic liquid solution. For example, up to a 50% by weight water and 50% by weight 1-ethyl-3-methyl imidazolium acetate can be used in the regeneration process.

In the following tables the numbers in parenthesis are the grams of material. For example in Table 1 DMSO (8.25) means 8.25 grams of DMSO.

In table 3, two molar ratios are given for BTMAH. There is water in BTMAH. The first molar ratio is for moles of water to a mole of ionic liquid. The second is the molar ratio of water to BTMAH. BTMAH is Benzyltrimethylammonium hydroxide, 40% in water.

TABLE 1

Cellulose Dissolution In Ionic Liquids With Dipolar aprotic Agents At 105° C.

Dipolar aprotic Agent (g)	Ionic Liquid, (g)	Molar Ratio	Solubility, 1 Hr.	2 Hr.	20 Hr.
DMSO (8.25)	EMIMAc (1.75)	10.27	yes		
DMSO (8.5)	EMIMAc (1.5)	12.35	no	dissolved in 5 hr.	
DMSO (9)	EMIMAc (1)	21	no	cloudy	
DMSO (4)	EMIMCl (6)	1.25	cloudy		
DMSO (5)	EMIMCl (5)	1.88	incomplete		
DMSO (8)	EMIMCl (2)	7.51	incomplete		
DMSO (4)	BMIMCl (6)	1.49	yes		
DMSO (4.5)	BMIMCl (5.5)	1.83	yes		
DMSO (5)	BMIMCl (5)	2.24	incomplete	incomplete	incomplete
DMSO (8)	BMIMCl (2)	8.94	no	no	

TABLE 2

Cellulose Dissolution in Ionic Liquids With Dipolar aprotic Agents At 105° C. With Stirring

Additive	Ionic Liquid	Molar ratio	Solubility, 15 min.	Solubility, 30 min.	Solubility, 45 min.
DMSO (3)	EMIMCl (7)	0.8	yes		
DMSO (4)	EMIMCl (6)	1.25	cloudy	cloudy	yes
DMSO (5)	EMIMCl (5)	1.88	incomplete	incomplete	incomplete
DMAc (3.5)	EMIMCl (6.5)	0.91	cloudy	cloudy	yes
DMAc (4)	EMIMCl (6)	1.12	no	mostly	mostly
DMF (3.5)	EMIMCl (6.5)	1.08	mostly	yes	yes
DMF (4)	EMIMCl (6)	1.34	no	no	mostly
NMP (4)	EMIMCl (6)	0.99	Yes	yes	
NMP (5)	EMIMCl (5)	1.48	mostly	yes	
NMP (4.5)	EMIMCl (5.5)	1.81	no	no	no
DMSO (4.5)	BMIMCl (5.5)	1.83	Yes	yes	yes
DMSO (5)	BMIMCl (5)	2.24	incomplete	incomplete	incomplete
DMAc (3.5)	BMIMCl (6.5)	1.7	mostly	yes	
DMAc (4)	BMIMCl (6)	1.34	no	no	yes
DMAc (4.5)	BMIMCl (5.5)	1.64	no	no	incomplete
DMF (3.5)	BMIMCl (6.5)		no	no	yes
DMF (4)	BMIMCl (6)		no	no	incomplete
NMP (3)	BMIMCl (7)	0.76	yes		

TABLE 2-continued

Cellulose Dissolution in Ionic Liquids With Dipolar aprotic Agents At 105° C. With Stirring

Additive	Ionic Liquid	Molar ratio	Solubility, 15 min.	Solubility, 30 min.	Solubility, 45 min.
NMP (4)	BMIMCl (6)	1.17	no	yes	yes
NMP (4.5)	BMIMCl (5.5)	1.44	no	yes	yes
NMP (5)	BMIMCl (5)	1.76	incomplete	incomplete	incomplete

TABLE 3

Cellulose Dissolution in Ionic Liquids With Protic Agents At 105° C.

Protic Additive	Ionic Liquid	Molar Ratio*	1 Hr.	2 Hr.	20 Hr.
Water (0)	EMIMCl (10)		yes	yes	yes
Water (0.5)	EMIMCl (9.5)	0.43	no	yes	yes
Water (0.75)	EMIMCl (9.25)	0.66	no	no	no
Acetic Acid (1)	EMIMAc (9)	0.32	yes	yes	yes
Acetic Acid (1.5)	EMIMAc (8.5)	0.51	yes	yes	yes
Acetic Acid (2)	EMIMAc (8)	0.72	no	No, 6 hr.	not at 6 hr.
Acetic Acid (0.5)	EMIMCl (9.5)	0.13	No-	yes	yes
Acetic Acid (1)	EMIMCl (9)	0.27	no	no	incomplete
BTMAH(1)	EMIMAc (9)	0.61/0.05*	yes		
BTMAH(1.5)	EMIMAc (8.5)	0.87/0.07*	no	yes	
BTMAH(1.75)	EMIMAc (8.25)	1/.09*	no	4 hr.	
BTMAH(2)	EMIMAc (8)	1.38/0.11*	incomplete	incomplete	incomplete
Acetic Acid (0.5)	EMIMCl (9.5)	0.13	no	yes	
Acetic Acid (1)	EMIMCl (9)	0.27	no	no	50%
Water (0.25)	BMIMCl (9.75)	0.25	cloudy	cloudy	cloudy
Water (0.5)	BMIMCl (9.5)	0.51	incomplete	incomplete	incomplete
Acetic Acid (0.25)	BMIMCl (9.75)	0.07	Yes (a)	Yes (b)	Yes (c)
Acetic Acid (0.5)	BMIMCl (9.5)	0.15	no (a)	Yes (b)	Yes (c)
Acetic Acid (0.75)	BMIMCl (9.25)	0.24	cloudy	cloudy	cloudy
Acetic Acid (1.0)	BMIMCl (9.0)	0.32	No (a)	No (b)	No (c)

(a) solubility in 90 min.
(b) solubility in 150 min.
(c) solubility in 22 hr.
*water/BTMAH

TABLE 4

Effect Of Shear Rate on Solution Viscosity

Shear Rate	2% Peach ® pulp in EMIMAc Viscosity	2% Peach ® pulp in EMIMAc + DMSO 1/9 Viscosity
0.15	18.44	0.27
0.27	18.28	0.28
0.48	17.75	0.32
0.86	16.91	0.31
1.54	16.00	0.31

TABLE 4-continued

Effect Of Shear Rate on Solution Viscosity

Shear Rate	2% Peach ® pulp in EMIMAc Viscosity	2% Peach ® pulp in EMIMAc + DMSO 1/9 Viscosity
2.75	15.17	0.32
4.93	14.29	0.32
8.82	13.36	0.32
15.80	12.45	0.32
28.30	11.25	0.31

TABLE 4-continued

Effect Of Shear Rate on Solution Viscosity

Shear Rate	2% Peach ® pulp in EMIMAc Viscosity	2% Peach ® pulp in EMIMAc + DMSO 1/9 Viscosity
50.69	9.81	0.31
90.78	8.23	0.30
162.56	6.62	0.29
291.11	5.10	0.27
521.40	3.83	0.24

TABLE 5

Effect Of Shear Rate on Solution Viscosity

Shear Rate	1% Peach ® pulp in BMIMCl Viscosity	1% Peach ® pulp in BMIMCl/NMP 7/3 Viscosity	1% Peach ® pulp in BMIMCl/DMSO 7/3 Viscosity	1% Peach ® pulp in BMIMCl/DMAc 7/3 Viscosity	1% Peach ® pulp in BMIMCl/DMF 7/3 Viscosity
0.15	11.07	7.31	5.78	3.93	2.78
0.27	11.37	7.30	5.72	3.88	2.77
0.48	11.57	7.16	5.62	3.84	2.75
0.86	11.77	6.95	5.54	3.78	2.73
1.54	11.86	6.62	5.38	3.69	2.69
2.75	11.74	6.27	5.16	3.56	2.63
4.93	11.69	5.89	4.90	3.42	2.55
8.82	11.37	5.47	4.54	3.24	2.43
15.80	11.20	4.96	4.14	2.98	2.27
28.30	11.23	4.39	3.68	2.70	2.08
50.69	11.26	3.80	3.26	2.41	1.88
90.78	11.24	3.21	2.85	2.11	1.65
162.56	11.10	2.66	2.42	1.80	1.42
291.11	10.70	2.18	2.01	1.51	1.20
521.40	9.34	1.75	1.64	1.25	0.99

TABLE 6

Effect Of Shear Rate on Solution Viscosity

Shear Rate	1% Peach ® pulp in EMIMCl Viscosity	1% Peach ® pulp in EMIMCl/NMP 7/3 Viscosity	1% Peach ® pulp in EMIMCl/DMSO 7/3 Viscosity	1% Peach ® pulp in EMIMCl/DMF 7/3 Viscosity
0.15	21.27	4.11	4.23	1.48
0.27	21.44	4.05	4.17	1.52
0.48	21.36	3.95	4.06	1.50
0.86	21.22	3.83	3.97	1.46
1.54	20.75	3.68	3.87	1.42
2.75	19.84	3.55	3.75	1.37
4.93	18.98	3.41	3.58	1.33
8.82	17.93	3.23	3.39	1.27
15.80	16.92	3.01	3.12	1.21
28.30	16.13	2.72	2.81	1.14
50.69	15.49	2.41	2.48	1.05
90.78	14.75	2.12	2.15	0.95
162.56	13.73	1.81	1.84	0.84
291.11	12.05	1.52	1.53	0.73
521.40	9.62	1.26	1.26	0.63

EXAMPLE 1

A dope for forming films was made by dissolving a Kraft pulp, Peach® pulp having an average degree of polymerization of about 760 and a hemicellulose content of about 12% (6.7% xylan, 5.2% mannan) in 1-ethyl-3-methylimidazolium acetate/water or benzyltrimethyl ammonium hydroxide (BTMAH) mixture at 105° C. with stirring. The solid concentration in the dope was about 13.2% by weight. The dope was cast on a glass plate to make film, which is regenerated in water, washed, air dried for analysis. X-ray diffraction indicated that samples treated with IL containing 10% H2O still has cellulose I structure while other films have cellulose II structure (regenerated form). X-ray diffraction measurements of fiber samples were recorded on a Shimadadzu X-ray diffractometer using Ni— filtered, CuKα radiation, a voltage of 40 k V and a current of 40 mA. The scanning rate employed was 5 degrees per min over a 5 degree to 40 degree 20 (diffraction angle) range. The crystallinity index was determined by Segal's formula (Segal L C, Martin A E, Conrad C M. 1959 *Textile Res J.* 29: 786-794). The % Crystallinity Index was calculated as $((I_{020}-I_{am})/I_{020})\times 100$, where I_{020}=intensity at Lowest 2θ value near 18 degrees. The properties of the film are given below.

Solution		Cellulose Pulp		Film Properties		
Cellulose Wt %	cosolvent	R10 %	R18 %	Xylan %	Mannan %	Crystallinity index
13.2	10% H2O	83	87	4.22	4.26	0.67
13.2	5% H2O	83	87	5.66	4.88	0.57
13.2	10% BTMAH	83	87	5.53	4.75	0.58

EXAMPLE 2

A dope for forming films was made by dissolving cellulose acetate, (6.6 g) and 6.6 g of a Kraft pulp, Peach® having an average degree of polymerization of about 760 and a hemicellulose content of about 12% (6.7% xylan, 5.2% mannan) in 1-ethyl-3-methylimidazolium acetate/DMSO mixture (43.4 g/43.4 g) at 105° C. with stirring. The solid concentration in the dope was about 13.2% by weight. The dope was cast on a glass plate to make film, which is regenerated in water, washed, air dried for analysis. Cellulose acetate lowers the film crystallinity.

As used in this application one method for measuring the degraded shorter molecular weight components in the pulp is

by the R_{18} and R_{10} content as described in TAPPI 235. R_{10} represents the residual undissolved material that is left extraction of the pulp with 10 percent by weight caustic and R_{18} represents the residual amount of undissolved material left after extraction of the pulp with an 18% caustic solution. Generally, in a 10% caustic solution, hemicellulose and chemically degraded short chain cellulose are dissolved and removed in solution. In contrast, generally only hemicellulose is dissolved and removed in an 18% caustic solution. Thus, the difference between the R_{10} value and the R_{18} value, ($\Delta R=R_{18}-R_{10}$), represents the amount of chemically degraded short chained cellulose that is present in the pulp sample. Hemicellulose is measured as the sum of the xylan and mannan content and was determined by the method described below for sugar analysis. As defined herein degree of polymerization (abbreviated as D.P.) refers to the number of anhydro-D-glucose units in the cellulose chain. D.P. was determined by ASTM Test 1795-96.

The properties of the film are given below.

Solution		Pulp Properties		Film Properties			
Cellulose Wt %	DP	R10 %	R18 %	Xylan %	Mannan %	Insoluble %	Crystallinity index
6.6	760	83	87	1.70	1.68	0.4	0.51

EXAMPLE 3

A dope for forming filaments was made by dissolving a wood chip in 1-ethyl-3-methylimidazolium acetate (EMIMAc) or its mixture with DMSO mixture at 105° C. with stirring. The chip concentration in the dope was about 13% by weight. The dope was cast on a glass plate to make film, which is regenerated in water, washed, air dried for x-ray analysis. Wood chips, approximately 1.3 g dissolved in a mixture of 5 g of EMIMAc/5 g DMSO had the lowest crystallinity (0.27), while those treated with EMIMAc had a crystallinity index of 0.35 and the untreated chip has a crystallinity index of 0.60. This would suggest that relative to the crystallinity index of the chip, the mixed solvent system of EMIMAc/DMSO has a higher impact on the crystallinity region than does the EMIMAc alone.

Sugar Analysis

This method is applicable for the preparation and analysis of pulp and wood samples for the determination of the amounts of the following pulp sugars: fucose, arabinose, galactose, rhamnose, glucose, xylose and mannose using high performance anion exchange chromatography and pulsed amperometric detection (HPAEC/PAD).

Summary of Method

Polymers of pulp sugars are converted to monomers by hydrolysis using sulfuric acid. Samples are ground, weighed, hydrolyzed, diluted to 200-mL final volume, filtered, diluted again (1.0 mL+8.0 mL H_2O) in preparation for analysis by HPAEC/PAD.

Sampling, Sample Handling and Preservation

Wet samples are air-dried or oven-dried at 25±5° C.

Equipment Required

Autoclave, Market Forge, Model #STM-E, Serial #C-1808

100×10 mL Polyvials, septa, caps, Dionex Cat #55058

Gyrotory Water-Bath Shaker, Model G76 or some equivalent.

Balance capable of weighing to ±0.01 mg, such as Mettler HL52 Analytical Balance.

Intermediate Thomas-Wiley Laboratory Mill, 40 mesh screen.

NAC 1506 vacuum oven or equivalent.

0.45-μ GHP filters, Gelman type A/E, (4.7-cm glass fiber filter discs, without organic binder)

Heavy-walled test tubes with pouring lip, 2.5×20 cm.

Comply SteriGage Steam Chemical Integrator

GP 50 Dionex metal-free gradient pump with four solvent inlets

Dionex ED 40 pulsed amperometric detector with gold working electrode and solid state reference electrode

Dionex autosampler AS 50 with a thermal compartment containing the columns, the ED 40 cell and the injector loop

Dionex PC10 Pneumatic Solvent Addition apparatus with 1-L plastic bottle

3 2-L Dionex polyethylene solvent bottles with solvent outlet and helium gas inlet caps

CarboPac PA1 (Dionex P/N 035391) ion-exchange column, 4 mm×250 mm

CarboPac PA1 guard column (Dionex P/N 043096), 4 mm×50 mm

Millipore solvent filtration apparatus with Type HA 0.45 u filters or equivalent

Reagents Required

All references to H_2O is Millipore H_2O

72% Sulfuric Acid Solution (H2SO4)—Transfer 183 mL of water into a 2-L Erlenmeyer flask. Pack the flask in ice in a Rubbermaid tub in a hood and allow the flask to cool. Slowly and cautiously pour, with swirling, 470 mL of 96.6% H_2SO_4 into the flask. Allow solution to cool. Carefully transfer into the bottle holding 5-mL dispenser. Set dispenser for 1 mL.

J T Baker 50% sodium hydroxide solution, Cat. No. Baker 3727-01, [1310-73-2]

Dionex sodium acetate, anhydrous (82.0±0.5 grams/1 L H_2O), Cat. No. 59326, [127-09-3].

Standards

Internal Standards

Fucose is used for the kraft and dissolving pulp samples. 2-Deoxy-D-glucose is used for the wood pulp samples.

Fucose, internal standard. 12.00±0.005 g of Fucose, Sigma Cat. No. F 2252, [2438-80-4], is dissolved in 200.0 mL H_2O giving a concentration of 60.00±0.005 mg/mL. This standard is stored in the refrigerator.

2-Deoxy-D-glucose, internal standard. 12.00±0.005 g of 2-Deoxy-D-glucose, Fluka Cat. No. 32948 g [101-77-9] is dissolved in 200.0 mL H_2O giving a concentration of 60.00±0005 mg/mL. This standard is stored in the refrigerator.

Kraft Pulp Stock Standard Solution

Kraft Pulp Sugar Standard Concentrations

Sugar	Manufacturer	Purity	g/200 mL
Arabinose	Sigma	99%	0.070
Galactose	Sigma	99%	0.060
Glucose	Sigma	99%	4.800
Xylose	Sigma	99%	0.640
Mannose	Sigma	99%	0.560

Kraft Pulp Working Solution

Weigh each sugar separately to 4 significant digits and transfer to the same 200-mL volumetric flask. Dissolve sugars in a small amount of water. Take to volume with water, mix well, and transfer contents to two clean, 4-oz. amber bottles. Label and store in the refrigerator. Make working standards as in the following table.

Pulp Sugar Standard Concentrations for Kraft Pulps

Fucose Sugar	mg/mL	mL/200 mL 0.70 ug/mL	mL/200 mL 1.40 ug/mL	mL/200 mL 2.10 ug/mL	mL/200 mL 2.80 ug/mL	mL/200 mL 3.50 ug/mL
Fucose	60.00	300.00	300.00	300.00	300.00	300.00
Arabinose	0.36	1.2	2.5	3.8	5.00	6.508
Galactose	0.30	1.1	2.2	3.30	4.40	5.555
Glucose	24.0	84	168.0	252.0	336.0	420.7
Xylose	3.20	11	22.0	33.80	45.00	56.05
Mannose	2.80	9.80	19.0	29.0	39.0	49.07

Dissolving Pulp Stock Standard Solution

Dissolving Pulp Sugar Standard Concentrations

Sugar	Manufacturer	Purity	g/100 mL
Glucose	Sigma	99%	6.40
Xylose	Sigma	99%	0.120
Mannose	Sigma	99%	0.080

Dissolving Pulp Working Solution

Weigh each sugar separately to 4 significant digits and transfer to the same 200-mL volumetric flask. Dissolve sugars in a small amount of water. Take to volume with water, mix well, and transfer contents to two clean, 4-oz. amber bottles. Label and store in the refrigerator. Make working standards as in the following table.

Pulp Sugar Standard Concentrations for Dissolving Pulps

Fucose Sugar	mg/mL	mL/200 mL 0.70 ug/mL	mL/200 mL 1.40 ug/mL	mL/200 mL 2.10 ug/mL	mL/200 mL 2.80 ug/mL	mL/200 mL 3.50 ug/mL
Fucose	60.00	300.00	300.00	300.00	300.00	300.00
Glucose	64.64	226.24	452.48	678.72	904.96	1131.20
Xylose	1.266	4.43	8.86	13.29	17.72	22.16
Mannose	0.8070	2.82	5.65	8.47	11.30	14.12

Wood Pulp Stock Standard Solution

Wood Pulp Sugar Standard Concentrations

Sugar	Manufacturer	Purity	g/200 mL
Fucose	Sigma	99%	12.00
Rhamnose	Sigma	99%	0.0701

Dispense 1 mL of the fucose solution into a 200-mL flask and bring to final volume. Final concentration will be 0.3 mg/mL.

Wood Pulp Working Solution

Use the Kraft Pulp Stock solution and the fucose and rhamnose stock solutions. Make working standards as in the following table.

Pulp Sugar Standard Concentrations for Kraft Pulps

2-Deoxy-D-glucose Sugar	mg/mL	mL/200 mL 0.70 ug/mL	mL/200 mL 1.40 ug/mL	mL/200 mL 2.10 ug/mL	mL/200 mL 2.80 ug/mL	mL/200 mL 3.50 ug/mL
2-DG	60.00	300.00	300.00	300.00	300.00	300.00
Fucose	0.300	1.05	2.10	3.15	4.20	6.50
Arabinose	0.36	1.2	2.5	3.8	5.00	6.508
Galactose	0.30	1.1	2.2	3.30	4.40	5.555
Rhamnose	0.3500	1.225	2.450	3.675	4.900	6.125

-continued

2-Deoxy-D-glucose Sugar	mg/mL	mL/200 mL 0.70 ug/mL	mL/200 mL 1.40 ug/mL	mL/200 mL 2.10 ug/mL	mL/200 mL 2.80 ug/mL	mL/200 mL 3.50 ug/mL
Glucose	24.00	84	168.0	252.0	336.0	420.7
Xylose	3.20	11	22.0	33.80	45.00	56.05
Mannose	2.80	9.80	19.0	29.0	39.0	49.07

Procedure

Sample Preparation

Grind 0.2±05 g sample with Wiley Mill 40 Mesh screen size. Transfer 200 mg of sample into 40-mL Teflon container and cap. Dry overnight in the vacuum oven at 50° C. Add 1.0 mL 72% H_2SO_4 to test tube with the Brinkman dispenser. Stir and crush with the rounded end of a glass or Teflon stirring rod for one minute. Turn on heat for Gyrotory Water-Bath Shaker. The settings are as follows:

Heat: High

Control Thermostat: 7° C.

Safety thermostat: 25° C.

Speed: Off

Shaker: Off

Place the test tube rack in gyrotory water-bath shaker. Stir each sample 3 times, once between 20-40 min, again between 40-60 min, and again between 60-80 min. Remove the sample after 90 min. Dispense 1.00 mL of internal standard (Fucose) into Kraft samples.

Tightly cover samples and standard flasks with aluminum foil to be sure that the foil does not come off in the autoclave.

Place a Comply SteriGage Steam Chemical Integrator on the rack in the autoclave. Autoclave for 60 minutes at a pressure of 14-16 psi (95-105 kPa) and temperature >260° F. (127° C.).

Remove the samples from the autoclave. Cool the samples. Transfer samples to the 200-mL volumetric flasks. Add 2-deoxy-D-glucose to wood samples. Bring the flask to final volume with water.

For Kraft and Dissolving Pulp Samples:

Filter an aliquot of the sample through GHP 0.45μ filter into a 16-mL amber vial.

For Wood Pulp Samples:

Allow particulates to settle. Draw off approximately 10 mL of sample from the top, trying not to disturb particles and filter the aliquot of the sample through GHP 0.45μ filter into a 16-mL amber vial. Transfer the label from the volumetric flask to the vial. Add 1.00 mL aliquot of the filtered sample with to 8.0 mL of water in the Dionex vial. Samples are run on the Dionex AS/500 system. See Chromatography procedure below.

Chromatography Procedure

Solvent Preparation

Solvent A is distilled and deionized water (18 meg-ohm), sparged with helium while stirring for a minimum of 20 minutes, before installing under a blanket of helium, which is to be maintained regardless of whether the system is on or off.

Solvent B is 400 mM NaOH. Fill Solvent B bottle to mark with water and sparge with helium while stirring for 20 minutes. Add appropriate amount of 50% NaOH.

(50.0 g NaOH/100 g solution)*(1 mol NaOH/40.0 g NaOH)*(1.53 g solution/1 mL solution)*(1000 mL solution/1 L solution)=19.1 M NaOH in the container of 50/50 w/w NaOH.

0.400 M NaOH*(1000 mL H_2O/19.1 M NaOH)=20.8 mL NaOH

Round 20.8 mL Down for Convenience:

19.1 M*(20.0 mL×mL)=0.400 M NaOH

x mL=956 mL

Solvent D is 200 mM sodium acetate. Using 18 meg-ohm water, add approximately 450 mL deionized water to the Dionex sodium acetate container. Replace the top and shake until the contents are completely dissolved. Transfer the sodium acetate solution to a 1-L volumetric flask. Rinse the 500-mL sodium acetate container with approximately 100 mL water, transferring the rinse water into the volumetric flask. Repeat rinse twice. After the rinse, fill the contents of the volumetric flask to the 1-L mark with water. Thoroughly mix the eluent solution. Measure 360±10 mL into a 2-L graduated cylinder. Bring to 1800±10 mL. Filter this into a 2000-mL sidearm flask using the Millipore filtration apparatus with a 0.45 pm, Type HA membrane. Add this to the solvent D bottle and sparge with helium while stirring for 20 minutes.

The postcolumn addition solvent is 300 mM NaOH. This is added postcolumn to enable the detection of sugars as anions at pH>12.3. Transfer 15±0.5 mL of 50% NaOH to a graduated cylinder and bring to 960±10 mL in water.

(50.0 g NaOH/100 g Solution)*(1 mol NaOH/40.0 g NaOH)*(1.53 g Solution/1 mL Solution) (1000 mL Solution/1 L solution)=19.1 M NaOH in the container of 50/50 w/w NaOH.

0.300 M NaOH*(1000 ml H2O/19.1 M NaOH)=15.7 mL NaOH

Round 15.7 mL Down:

19.1M*(15.0 mL/x mL)=0.300 M NaOH

x mL=956 mL

(Round 956 mL to 960 mL. As the pH value in the area of 0.300 M NaOH is steady, an exact 956 mL of water is not necessary.)

Set up the AS 50 schedule.

Injection volume is 5 uL for all samples, injection type is "Full", cut volume is 10 uL, syringe speed is 3, all samples and standards are of Sample Type "Sample". Weight and Int. Std. values are all set equal to 1.

Run the Five Standards at the Beginning of the Run in the Following Order:

STANDARD A1 DATE

STANDARD B1 DATE

STANDARD C1 DATE

STANDARD D1 DATE

STANDARD E1 DATE

After the last sample is run, run the mid-level standard again as a continuing calibration verification

Run the control sample at any sample spot between the beginning and ending standard runs.

Run the samples.

Calculations

Calculations for Weight Percent of the Pulp Sugars

$$\text{Normalized area for sugar} = \frac{(\text{Area sugar}) * (\mu g/mL \text{ fucose})}{(\text{Area Fucose})}$$

$$IS \text{ Corrected sugar amount}(\mu g/mL = \frac{\left(\begin{matrix}(\text{Normalized area for sugar}) - \\ (\text{intercept})\end{matrix}\right)}{(\text{slope})}$$

$$\text{Monomer Sugar Weight \%} = \frac{IS - \text{Corrected sugar amt}(\mu g/mL)}{\text{Sample wt.(mg)}} * 20$$

Example for Arabinose:

$$\text{Monomer Sugar Weight \%} = \frac{0.15 \ \mu g/mL \text{ arabinose}}{70.71 \text{ mg arabinose}} * 20 = 0.043\%$$

$$\text{Polymer Weight \%} = (\text{Weight \% of Sample sugar}) * (0.88)$$

Example for Arabinan:

$$\text{Polymer Sugar Weight \%} = (0.043 \text{ wt \%}) * (0.88) = 0.038$$
$$\text{Weight}$$

Note: Xylose and arabinose amounts are corrected by 88% and fucose, galactose, rhamnose, glucose, and mannose are corrected by 90%.

Report results as percent sugars on an oven-dried basis.

The embodiments of this invention, including the examples, are exemplary of numerous embodiments that may be made of this invention. It is contemplated that numerous other configurations of the process may be used and the equipment used in the process may be selected from numerous sources other than those specifically disclosed. In short, it is the applicant's intention that the scope of the patent issuing herefrom will be limited only by the scope of the appended claims

The invention claimed is:

1. A method for dissolving cellulose comprising admixing a cellulose based raw material with a mixture of dimethyl sulfoxide and 1-ethyl-3-methyl imidazolium acetate at a temperature of 25° C. to 180° C. for a time sufficient to dissolve the cellulose based raw material, wherein the molar ratio of the dimethyl sulfoxide to 1-ethyl-3-methyl imidazolium acetate is in the range of 0.5 to 25 moles of dimethyl sulfoxide to 1 mole of 1-ethyl-3-methyl imidazolium acetate.

2. The method of claim **1** wherein the cellulose based raw material is wood chips, wood pulp, kenaf or straw.

3. The method of claim **2** wherein the wood pulp is chemical wood pulp, kraft wood pulp, sulfite wood pulp, mechanical wood pulp, thermomechanical wood pulp, or chemithermomechanical wood pulp.

4. The method of claim **1** wherein the temperature range is 80° C. to 120° C.

5. The method of claim **1** wherein the temperature range is 100° C. to 110° C.

6. The method of claim **1** wherein the molar ratio is 0.5 to 15 moles of dimethyl sulfoxide to 1 mole of 1-ethyl-3-methyl-imidazolium acetate.

7. The method of claim **1** wherein the time is 5 minutes to 24 hours.

8. The method of claim **1** wherein the time is 5 minutes to 1 hour.

9. The method of claim **1** further comprising regenerating the dissolved cellulose.

10. The method of claim **1** wherein the molar ratio is 5 to 25 moles of dimethyl sulfoxide to 1 mole of 1-ethyl-3-methyl imidazolium acetate.

11. The method of claim **1** wherein the molar ratio is 5 to 15 moles of dimethyl sulfoxide to 1 mole of 1-ethyl-3-methyl imidazolium acetate.

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(54) **METAL SAFE STABILIZED STRIPPER FOR REMOVING CURED POLYMERIC LAYERS AND NEGATIVE TONE ACRYLIC PHOTORESISTS**

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(57) **ABSTRACT**

A stabilized stripping composition is provided for removing fully cured polymeric organic substances from an inorganic substrate, including polyimide and liquid crystal polymer (LCP). The stripping composition comprises about 3 to about 15 percent of benzyltrimethylammonium hydroxide (BTMAH), about 50 to about 87.5 weight percent of n-methylpyrrolidone as a solvent with ethylene glycol ranging from 15 to about 45 weight percent and a stabilizer. The stripping composition preferable also contains a suitable corrosion inhibitor and a non-ionic surfactant. Also provided is a method for stripping thick negative-tone photoresists, e.g. acrylic, styrenic, maleic anhydride, and similar, from inorganic substrates by contacting the polymeric organic substance with the organic stripping BTMAH composition for a period of time sufficient to dissolve and remove said polymeric substances.

METAL SAFE STABILIZED STRIPPER FOR REMOVING CURED POLYMERIC LAYERS AND NEGATIVE TONE ACRYLIC PHOTORESISTS

BACKGROUND OF THE INVENTION

[0001] This invention relates to metal safe stripping compositions for use in dissolving, i.e. removing, various polymer layers such as polyimide, liquid crystal polymer (LCP) and thick negative-tone acrylic photoresists. More particularly, the invention describes a blend of chemistries to yield a product which performs at elevated temperatures with limited degradation or loss of the active constituents, providing substantially improved stability and allowing for broad processing conditions with accelerated removal and cleaning.

[0002] During the manufacture of semiconductors and semiconductor microcircuits, various polymers may be used for their insulative and chemical resistance properties. These materials, including polyimide and liquid crystal polymer (LCP), are substantially cured to a full cross-link condition to exhibit dense and glass-like qualities allowing them to be incorporated into, or to comprise, the substrate. Through the action of chemicals in both wet (solution) and dry (plasma) forms, further processing is carried out on the substrate, e.g. silicon, silicon dioxide, aluminum, copper, or the cured polymer, etc., to include etch (removal) and deposition (addition). Upon completion, part or all of the exposed polyimide or LCP may need to be stripped (removed).

[0003] In some cases, the microcircuit is coated with a polymeric organic substance, such as a thick film negative-tone acrylic photoresist to form a resist mask after undergoing a photolithography process. Typically, the acrylic resist is formed over inorganic substrates, however, the resist may also be in contact with cured polymer layers such as polyimide and LCP. Although resists are used where etching or deposition is needed, a thick film resist is commonly used when deposition of thick layers of metal, e.g. copper, is needed. Following the metal deposition and after subsequent rinsing or conditioning, it is necessary that the thick resist mask and any residue be removed to leave behind the thick deposited pattern of metallization.

[0004] A common method used in removing cured polymer or resist mask from the substrate is by direct contact with an organic stripper. The chemistry of the stripper is such that it penetrates the material surface and may undergo a reaction to sever cross-linked portions and facilitate the swelling, dissolution, and lifting from the surface of the underlying substrate. The protected area of the substrate is then revealed. The substrate protected area is typically inorganic, e.g. silicon, its native oxide, a hybrid compound semiconductor, such as gallium arsenide, and may include sensitive metallic microcircuity, such as, aluminum or copper; or the underlying area may be organic, e.g. cured polymer to include polyimide or LCP.

[0005] Where a thick resist must be removed from underlying cured polymer and potentially in contact with metallization, selectivity towards the resist over the polymer and metal must be achieved. In certain cases, the underlying cured polymer must be removed using the same approach, yet with a more aggressive stripper or conditions. Prior stripping compositions have usually been less than satisfactory or have the distinct disadvantage of unacceptable toxicity and/or presenting pollution problems from the disposal of such compounds as phenol, cresol, sulfonic acid, and chlorinated hydrocarbons. Other prior art of stripping compositions for removing polymeric organic substances, for example, comprise aqueous sulfuric acid containing a significant amount of fluoride ion to reduce metallic dulling and corrosion, as exemplified in U.S. Pat. No. 3,932,130. When operated at elevated temperatures, some photoresist strippers require the presence of fluoride ion stabilizers to prevent metallic corrosion, especially towards aluminum and copper.

[0006] There is a need, accordingly, for improved stripping compositions which will remove the thick acrylic resist from cured polymer, and in some cases, to remove the cured polymer. In either application safety towards other underlying and adjacent substances, such as, the substrate and metallic circuitry, in preventing corroding, gouging, dissolving, dulling, or otherwise marring these surfaces is a requirement. Also the efficiency and selectivity of the stripper is extremely desirable.

[0007] It is an object of this invention to provide organic stripping compositions which operate effectively while avoiding the prior mentioned toxic substances and at moderate or high temperatures, to clean effectively and quickly, cured polymer and thick film negative tone photoresist from metallized or inorganic substrates. It is another object of this invention to provide organic stripping compositions which are highly effective for removing thick film negative tone photoresists, particularly those comprising acrylic, styrene, novolak, and related polymers, which in the presence of certain cross-linking photoinitiators, will cure to a hard and highly chemically resistant framework. In the removal process of cured polymer and resist, selectivity must be achieved on the material to be removed over the unwanted etch or damage to the substrate or corrosion and dulling of metallic circuitry present as adjacent structures.

SUMMARY OF THE INVENTION

[0008] In accordance with this invention, a blend of chemistries is provided to remove cured polymer, such as polyimide and liquid crystal polymer (LCP), and fully-cured thick film negative tone acrylic photoresist. Polymers and resists of this kind will undergo a curing profile either through thermal, chemical, or photoinitiation means and form a dense, hard, and highly chemically resistant framework. Polyimide and LCP are used to isolate conductive portions of the circuit and may be used as a flexible substrate alternative to rigid glass fiber circuit boards. Photoresists are used to produce patterns (masks) which become the basis for depositing microcircuits in semiconductor manufacturing.

[0009] In the past, these chemically resistant layers have been difficult or impossible to fully remove, usually resulting in a time consuming and expensive process. The present invention affords a means to remove the resist mask from the circuit and to rework the insulative polymer. Upon exposure to the system of the invention at given conditions, the cured polymer or resist will begin to breakdown and dissolve, allowing the by-products to be rinsed away with water. Removal rates will vary depending upon polymer type, extent of cure, thickness, and processing (removal) conditions. Heat and agitation will generally accelerate removal and may help to achieve selectivity in removing a resist over

a polyimide or LCP. Increased heat is required to remove cured polyimide or LCP. The composition of the invention also includes a stabilizer and an inhibitor for metal corrosion.

DETAILED DESCRIPTION OF THE INVENTION

[0010] The present invention provides a novel metal-safe and stabilized formulated chemical composition which quickly and effectively removes cured polymer and thick-film photoresist from a range of substrates, and involves methods of using same.

[0011] The invention employs a high molecular weight and heat stable quaternary ammonium hydroxide (QAH) and, more specifically, benzyl trimethylammonium hydroxide (BTMAH), to maintain a strong alkaline environment to cleave the cross-linked polymer of the kind which is typical of a cured negative tone acrylic photoresist, polyimide, liquid crystal polymer, and other similar materials and allow the solvent of the system invention to penetrate, dissolve, and lift reacted material so that it can be rinsed away. The solvent system is composed of a glycol to assist in stabilizing the BTMAH and a cyclic ketone that is ideal for polymer dissolution. Additives also include a stabilizer to terminate internal reactions between BTMAH and the ketone, a blend of triazole-based corrosion inhibitors to protect free copper and aluminum, and a surfactant used to penetrate small geometries and aid in rinsing. Although the QAH compounds are chosen for alkaline saponifying and emulsification of polymers, the BTMAH offers added heat stability and bath life, enabling the product to be used at elevated temperatures for tenacious polymer coatings. When the BTMAH is combined with the selected solvents and suitable additives, the chemical system becomes an excellent medium for processing microelectronic parts where performance must be maintained for extended periods of time with high loading capacity and where safety and integrity of the substrate and adjacent metal devices must be carefully preserved.

[0012] While the novel composition of the invention is described for use in microelectronic applications to remove cured negative-tone acrylic photoresist, the product has also been proven useful for removal of other cured polymer such as polyimide and liquid crystal polymer (LCP), common surface dielectric (insulator) coatings used in microelectronic manufacturing. The invention also appears to be an excellent choice to remove a variety of other tenacious residue originating from fully cured polymer and photoresist while not affecting the integrity of adjacent materials. Examples include negative-tone acrylic and novolak which have been hard baked (i.e. exposed to high temperatures). The performance and selectivity of the compositions are key characters to specialty products used for high tech applications. Environmentally, the invention is a desirable replacement for toxic or hazardous products (i.e., phenols, sulfuric acid, etc.) used for the same applications.

[0013] The BTMAH stripping compositions of the invention function by maintaining a strong alkaline environment whereby the solvent penetrates and dissolves cross-linked polymer and cured negative-tone acrylic and novolak photoresists. The solvent system is composed of a glycol, e.g., ethylene glycol (EG), to stabilize the BTMAH and cyclic ketone that effects the polymer dissolution. Advantageous additives contained within the stripping composition may include a stabilizer which functions to stop degradative reactions between the BTMAH and the ketone, triazole-based corrosion inhibitors to protect copper and aluminum and a suitable surfactant to aid in penetrating small geometries and in rinsing.

[0014] Like most caustics, QAH compounds are chosen for alkaline saponifying and emulsification of polymers, however, QAH has improved solubility in organic systems over common metal hydroxides. Further, out of the series of QAH compounds available, the BTMAH offers added heat stability and bath life, enabling the product to be used in elevated temperatures for prolonged periods. Heat is commonly used when having to penetrate, dissolve, and lift tenacious polymer coatings. When BTMAH is combined with the selected solvents and additives, the chemical system of the invention affords an excellent vehicle for processing microelectronic parts where reliable performance must be maintained and safety to the substrate and adjacent metal devices is required.

[0015] A typical composition in accordance with the invention comprises the (BTMAH) benzyltrimethylammonium hydroxide, a solvent system and stabilizer, and preferable, includes also, a corrosion inhibitor and a non-ionic surfactant.

[0016] The BTMAH content may vary from about 3 to about 15 weight percent and preferably comprise about 4 to about 8 weight percent of the stripper. BTMAH is an organic solid and is commonly made available in lower alcohols, e.g. methanol, or water. In the invention, the BTMAH is prepared in a stock solution of ethylene glycol (EG). Stock concentrations of BTMAH in EG can run near 50% by weight as BTMAH. To ensure this stock solution of a strong caustic (BTMAH) and EG is stable over time, a stabilizer is added. The preferred stabilizer is paraformaldehyde (PF). The concentration of PF in the final solution (invention mixture) ranges from 300 to 10,000 ppm (1%) and is preferred to be approximately 500 to 1000 ppm.

[0017] The solvent system comprises a cyclic ketone e.g., N-methylpyrrolidone (NMP), Dimethylpiperidone (DMPD), etc. The ketone solvent is employed in amounts from 50 to about 87.5 weight percent and preferably in proportions of about 60 to about 75 weight percent. Other common photoresist solvent families such as amides, aldehydes and certain ketones not mentioned here such as acetone and methylethylketone (MEK) are not stable with BTMAH. Due to the alkaline nature of BTMAH, these solvents tend to react with BTMAH via Hoffman Degradation (amides) and Reductive Amination (aldehydes and certain ketones) to reduce the hydroxide to trimethylamine, neutralize the system, cause a color change i.e. slight yellow to dark brown, which may adversely affect performance. For this reason, certain solvents are avoided to come into contact with BTMAH and therefore are not considered for these compositions.

[0018] In addition to the selected cyclic ketones deemed to be stable with BTMAH, suitable glycol is added to further stabilize the system during processing and to act as a cosolvent. A glycol that may be employed with the BTMAH includes, for example, EG. It has been determined that low molecular weight species appear to be more stable with

BTMAH due to their lack of color change. Therefore, even though alternatives to EG exist such as propylene glycol (PG), glycerin, or other polyhydric alcohols, such may not be desirable due to their ability to discolor upon exposure to BTMAH. The actual color intensity observed will depend upon the glycol chosen and the relative concentrations present with respect to BTMAH. Concentrations of the chosen glycol in the invention vary from 15-45% by weight and is preferably between about 20-30% by weight.

[0019] Water may also be added to facilitate selective removal of one polymer over another. This selectivity is needed when two polymers appear to be both soluble in the invention. Addition of water will discriminate one polymer's solubility over another to the extent that selective removal is accomplished. In such removal cases, water makes up approximately 10% by weight of the mix.

[0020] To afford protection for transition metals such as copper and aluminum, a suitable corrosion inhibitor such as BTA (benzyltriazole), TTA (tolytriazole), MBTA (mercaptobenzyltriazole), or combinations thereof, may be incorporated into the stripper composition. Alternatives to these inhibitors include pyrogallol (neutral form of gallic acid) and pyrocatachol (catachol). A preferred corrosion inhibitor for copper and similar soft metal substrates includes a combination of the triazoles, e.g. BTA, TTA, MBTA, and the like, to give a synergistic effect on the desired metal to protect. The combined triazole system comprises a concentration of approximately 0.5 to 5% by weight and is preferably a concentration of from about 1.0 to about 4.0 percent by weight.

[0021] When substantial amounts of transition metal is present as part of the polymer residue and must be complexed during the removal process, a suitable chelating agent such as EDTA (ethylenediaminetetraacetic acid) is preferably also included. The basified and solubilized form of this chelating agent is added to combine these trace metals present in the matrix of the target polymer to be removed. Alternative chelates include the basified versions of DTPA (dietyhylenetriaminepentaacetic acid); NTA (nitrilotriacetic acid), and 2,4-pentanedione. Each of these products is preferably converted to an alkaline form before using in the stripper matrix, otherwise, the "weak acid" tends to react with the product.

[0022] Suitable surfactant includes a non-ionic alkoxylated linear alcohol such as the tradename Polytergent (Pluronic) SL92, available from BASF Corporation. The surfactant functions to reduce surface tension, emulsify dissolved polymer, and aid in water rinsing. The surfactant preferably has a high cloud point (i.e. >60° C.) to allow for heated processing and rinsing. A non-ionic environment is required for non-reaction towards dissolved metals and maximum solubility in non-aqueous chemistries and water. Low foaming capacity allows for product use in various automated equipment. Alternative surfactants include nonyl-phenols and non-ethoxylates with a HLB (hydrophilic/lipophilic balance) ranging from 7-15. Less than about 2 weight percent of the non-ionic surfactant and preferable an amount of about 0.1 to about 1.4 weight percent is sufficient.

[0023] For dissolution and removal of LCP, polyimide, and thick film acrylic resists, the temperature employed for suitable performance is important. Generally, in any polymer removal application, an elevated temperature above about 70° C. is preferred. Although some systems will vary, it is preferred that the dissolution and removal of full-cure LCP and polyimide be conducted at a temperature in the range of about 120° C. to about 130° C. for at least about 20 minutes. Thick film acrylic resists which have been fully-cured and exposed to temperatures of 200° C. are dissolved and removed in most cases within about 5 minutes using a processing temperature of about 80° to 90° C. In all removal applications deionized water is recommended for rinsing.

[0024] The stripping compositions quickly and effectively remove organic polymers from metallized and metallic surfaces without attacking the metal surface, and without using various toxic or intrusive metal corrosion inhibitors. Although the invention has been shown to be safe for aluminum it has been shown to be extremely suitable with copper. When measured on electrodeposited copper on silicon substrates, it was found that the stripping composition removed less than 0.1 Å/min copper at selected temperatures and time.

[0025] The present invention also resides in providing a method of removing a cured thick-film organic polymeric material from an inorganic substrate which comprises contacting the polymeric organic substance with the BTMAH stripping composition for a period of time sufficient to remove the polymeric substances. The solvent system comprises: a) a glycol to stabilize the BTMAH and cyclic ketone for polymer dissolution; b) a stablizer to effectively terminate the internal reaction between the BTMAH and the ketone; c) a corrosion inhibitor, such as triazole based inhibitors to protect metallized areas, such as, free copper and aluminum; and d) a surfactant to penetrate small geometries and act as an aid in rinsing.

[0026] The photoresists which are removed by the stripping solutions of this invention generally comprise acrylic, styrenic, maleic anhydride, and related monomers and copolymers used to produce negative tone photosensitive thick films. These photoresists are processed to apply thick films which can be on the order of >50 microns. They are available in commerce as a dry-film photoresist, e.g. Riston, a product of E.I. duPont deNemours and Co. or Laminar, a product of Shipley Company, L.L.C.. These dry film resists are available as a film of the photosensitive polymer of defined thickness sandwiched between two peel-away plastic coverings, e.g. Mylar® polyester and polyethylene. The resist may also be available as a liquid-base spin-on variety. In this case, the resist is applied by conventional means by delivering a specific volume of the polymer to a substrate and followed by rotating the base to cause the liquid polymer to coat the surface by drawing it from the center to the edge in a uniform manner through centrifugal force resulting from a high rate of spinning.

[0027] Whether the photoresist is a dry film or liquid spin-on variety, it is applied to an inorganic substrate, e.g. aluminum, copper, silicon, silicon dioxide or silicon dioxide metallized with aluminum and where portions thereof are masked. The masked substrate is then exposed to ultra violet (UV) light, e.g. a 120 volt 650 watt quartz lamp for 1-15 seconds at a distance of $1.524\text{-}3\text{-}3.048\times10^{-1}$ m, to harden the exposed photoresist. For negative photoresists, the portion of the photoresist which is not exposed, i.e., masked from the light, is then removed by a mild solvent which does not dissolve the exposed photoresist. Thus, a pattern, e.g., a

portion of an electrical circuit pattern, is left on the exposed substrate. In preparation of further processing, the remaining photoresist pattern is then baked for further hardening, typically to temperatures approaching 200° C. The portion of the substrate which is not covered by the photoresist is treated by etching (removal) or deposition (addition). In most cases where negative tone resist is used (i.e. a negative slope or close to 90 degree is formed), metal is deposited (added). The hardened photoresist must be removed to leave behind the metal traces and before the substrate can be further processed or used.

[0028] In employing the stripping solutions of this invention, the substrate covered with the baked photoresist is brought into contact with the stripping solution at a temperature of ≧70° C.; additional heating will improve performance and loading capacity. Times required for stripping the photoresist vary to quite an extent depending on the specific polymer used in the photoresist, the photoresist curing prefacing conditions, temperature of the stripper, and agitation of the medium, varying from no agitation (static) to a maximum agitated solution resulting from ultrasonic cavitation action. Generally, the time involved will be less than 10 minutes and during optimized performance conditions, may be measured in seconds, while some photoresist, depending on the baked temperature, may require times of more than 10 minutes and up to 30 to 60 minutes, where lower processing temperatures of the invention stripper are employed on highly polymerized and metallized surfaces. It will be appreciated that many photoresists are completely dissolved from the substrate while others may be loosened, and floated off, and then subsequently dissolved in the stripping composition. Examples of the kind of photoresists which may be stripped by the composition of the present invention are shown in Table I:

TABLE I

TYPE NEGATIVE	TRADEMARKS	SOURCE
Acrylic	THB-Series to include: THB-130N, THB-150N	JSR Micro, Inc.
Acrylic	RISTON Dry Film	E.I. duPont deNemours and Co.
Acrylic	LAMINAR Dry Film	Shipley Company, L.L.C.
Novolak	NFR-Series to include: NFR-015, NFR-016D2	JSR Micro, Inc.

[0029] It is to be understood that other negative photoresists having a broad range of molecular weights, as well as the positive-series type, can be effectively removed by the stripping composites of the present invention.

[0030] After the photoresist has been stripped from the substrate, the substrate may then be rinsed in water, or in an alcohol such as isopropanol or other hydrophilic and compatible solvents, e.g. NMP, DMPD, EG, or mixtures thereof; other compatible rinsing solvents well known to one of ordinary skill in the art may also be used.

[0031] While the stripping compositions and method of the present invention operate in baths at temperatures above 70° C., other temperatures and apparatus are considered within the scope of this invention. For example, when the stripping compositions of the present invention are used in a spray tool apparatus maintained at a temperature or about 80° C., the time required for the stripping solution to completely remove negative tone acrylic photoresists, that are of moderate cure (i.e. 150° C.), the time would be of the order of approximately one-third that of the stripping time required at 70° C. temperature in a static bath. In another embodiment, ultrasonic energy is applied to produce removal rates that are dramatically improved by factors of 3 or 4 at specific temperatures. And in yet another embodiment of the present invention, the stripping composition may operate at a temperature greater than 120° C. to remove the LCP and polyimide polymer substances resulting in the organic matter to be fully dissolved in 10-20 min

[0032] Examples of the kind of polyimide and LCP which may be stripped by the composition of the present invention are shown in Table II below:

TABLE II

POLYMER	TRADEMARKS	SOURCE
Polyimide	Kapton	E.I. DuPont de Nemours
Polyimide	PI - Series & HD - Series	HD Microsystems L.L.C. (Hitachi - DuPont)
LCP	Vectra & Vectron	Ticona
LCP	Zenite	E.I. DuPont de Nemours

[0033] The compositions of the kind contemplated by the invention and the method of making is illustrated by the examples which follow. It is understood, however, that the invention is not meant to be limited to the details described therein. In the examples, the percentages provided are percent (%) by weight unless otherwise stated.

General Procedure

[0034] In preparing the stripping compositions of the invention, a preferred order of addition is employed. As stated earlier in this document, the invention includes BTMAH which has been shown to be incompatible with certain organic materials at certain concentrations and conditions. Therefore, it is important to maintain a diluted state when the BTMAH is added to the other components and that the stabilizer, PF, be added as early as possible, and preferably is present in the original BTMAH mixture concentrate. With dilution in mind for the BTMAH stability, it is generally planned to add the BTMAH ingredient last. Therefore, all of the solvents and additives are measured in the desired proportion and introduced into a suitable mixing vessel and thoroughly mixed by stirring. Suitable alternative means may be used to effectively intermix the components such as by concurrent introduction of streams of the respective components, or other suitable known means that fully intersperse the components. Once all of the solvents and additives are mixed, the BTMAH may be added and stirred by the method deemed most feasible. Once the stripping composition is completely mixed, it is deemed stable, with no detectable separation of components and has excellent shelf life when stored at standard warehouse conditions. In the example stripping composition of a kind contemplated by the invention, and comprising 4-8 weight percent BTMAH with PF stabilizer, 60-75 weight percent NMP, 20-30 weight percent EG, surfactant and corrosion inhibitor was employed.

[0035] The photoresist compositions comprise commercially available organic photosensitizer alkaline soluble

resin formulations which include (a) a suitable sensitizer such as diazo ketone compounds, e.g., naphthaquione-1,2-diazo sulfonic acid esters, (b) a novolak resin and (c) a suitable solvent such as xylene. Photoresists of this kind are generally described, for example, on page 67 in the work done by D. J. Elliot in Integrated Fabrication Technology, McGraw-Hill Book Company, 1982.

[0036] Equipment and Materials: Equipment, common ware, and materials that are available in an industrial chemistry laboratory were used to screen test a variety of specimens. These included a range of substrate coupons, UV and thermal curing items, identification scopes with a high resolution system having digital imaging, and various ultrasonic cleaning equipment having frequencies of 40, 80 and 170 kHz. Analytical equipment includes physical property and chemical characterization tools from simple pH meters and flash point testers to UV/VIS scanning, GC, and ICP-MS. Where necessary, product purification was used to include distillation (vacuum, up to 10 plates), filtration, and desiccation.

[0037] Procedure: Negative-tone acrylic photoresist (THB-130N, JSR Micro, Inc.) was applied to silicon substrates and treated to the following conditions: a) soft baked at 90-100° C. for 2 hrs, b) selected coupons from (a) are exposed to UV (360 nm) @ 2 W intensity for 5 min, and c) selected coupons from (b) are then post baked at 200° C. for 20 min. The noted coupons are labeled as (a), (b), and (c), with those in the (c) category to be the most rigorous, e.g. full cured. All stripping processes were carried out in small glass vessels, held at 70-80° C., and utilizing static conditions (i.e. no agitation). Observations were done with the aid of an optical microscope (50-400×). In a separate experiment, full cured resist (i.e. JSR THB-130N) is collected in its solid form, e.g. scraped from a polyester substrate, and entered into bath life studies where the presence of an active species is measured vs resist loading.

[0038] Results: Complete removal of the negative type resist was demonstrated using the BTMAH product of the invention vs other stripper blends. Performance was shown to be dependent upon temperature and time. However, for a temperature of 70-80° C., results for scenarios (a), (b), and (c) were deemed to be <5 min, approximately 7 min, and <30min, respectively. No other stripper blend was found to perform as well as the noted invention.

[0039] Bath life (stability) was determined on the invention stripper vs the negative tone acrylic resist (JSR THB-130N). The BTMAH invention was noted to have excess of active species present even as the loading capacity exceeded 5% by weight of the resist solid. The bath life was determined for a concentration range between 0.5-5%, where the 5% value was deemed to be still active. The value of 5% is well beyond the normal processing limit of photoresist stripping.

[0040] Although the invention has been described in terms of specific tests and embodiments, one skilled in the art can substitute other tests and embodiments and these are meant to be included herein. The invention is only to be limited by the scope of the appended claims.

What is claimed is:

1. A stripping composition for removing polymeric organic substances from an inorganic substrate, the stripping composition comprising about 4 to about 8 weight percent BTMAH, from about 60 to about 75 weight percent NMP and from about 20 to about 30 weight percent of a glycol, and an effective amount of a stabilizer additive.

2. The composition of claim 1 wherein the glycol is ethylene glycol.

3. The composition of claim 1 wherein the stabilizer is paraformaldelhyde.

4. The composition of claim 2 wherein the stabilizer is paraformaldelhyde.

5. The composition of claim 1 in which the stripper composition contains up to about 5 weight percent of a corrosion inhibitor.

6. The composition of claim 1 wherein the stripping composition incorporates up to about 5 weight percent of a corrosion inhibitor and a non-ionic surfactant in amounts not to exceed about 2 weight percent.

7. The composition of claim 4 wherein the stripping composition incorporates up to about 5 weight percent of a corrosion inhibitor and a non-ionic surfactant in an amount not to exceed 2 weight percent.

8. The composition of claim 3 in which the BTMAH is about 4 to about 8 weight percent, of the NMP is from about 60 to 75 weight percent and the ethylene glycol comprises about 20 to 30 weight percent.

9. The composition of claim 8 wherein the triazole corrosion inhibitor is from about 1 to 4 weight percent and the nonionic surfactant is about 0.1 to 1.4 weight percent.

10. In a method for removing relatively thick film layers of a cured polymeric organic substance from an inorganic substrate the improvement characterized in that a stripping composition comprising about 4 to about 8 weight percent BTMAH, from about 60 to about 75 weight percent NMP and from about 20 to about 30 weight percent of a glycol, and an effective amount of a stabilzer additive is applied to a cured polymeric organic layer to be removed from inorganic substrate, maintaining the stripping composition in contact with said cured polymeric layer for a period of time sufficient to disengage said polymeric layer, and flushing said disengaged layer from the inorganic substrate.

11. The method of claim 10 wherein the stripping composition glycol is ethylene glycol.

12. The method of claim 10 wherein the stripping composition contains a paraformaldehyde stabilizer.

13. The method of claim 10 in which the stripper composition contains up to about 5 weight percent of a corrosion inhibitor.

14. The method of claim 10 wherein the stripping composition incorporates up to about 5 weight percent of a corrosion inhibitor and a non-ionic surfactant in amounts not to exceed about 2 weight percent.

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