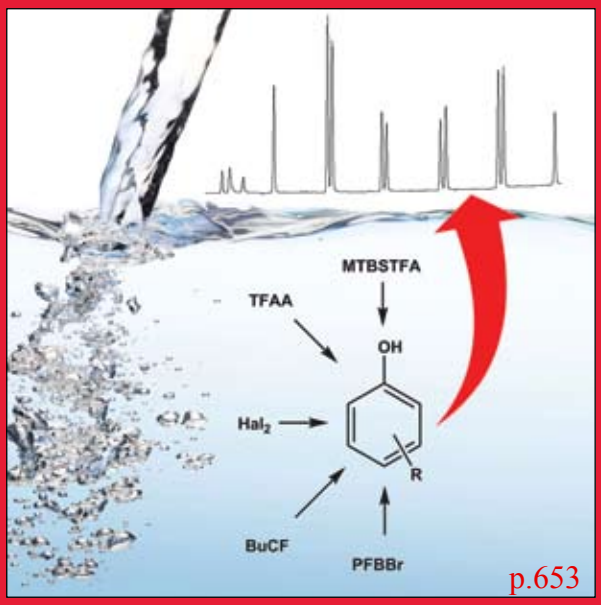
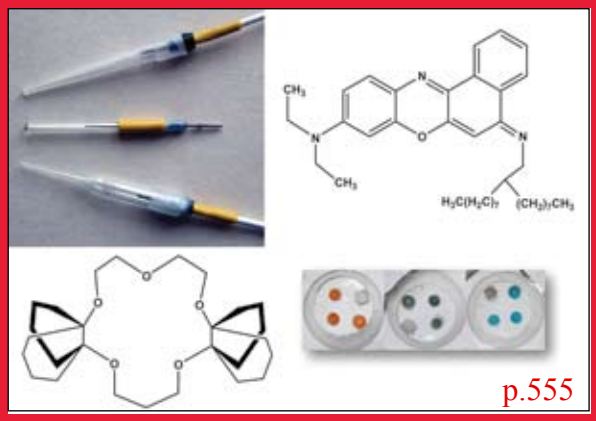
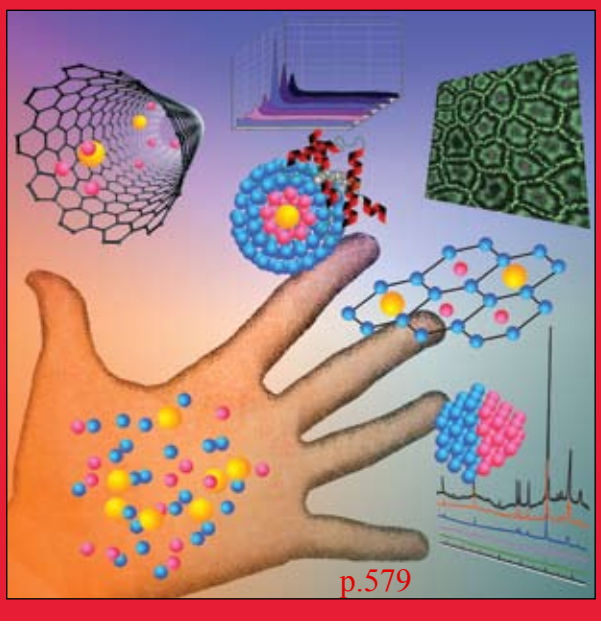
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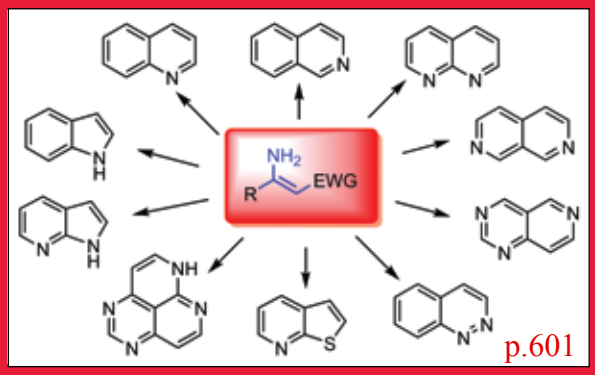
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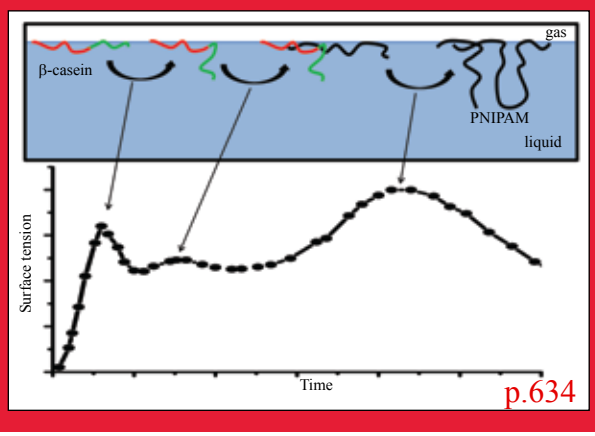
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Derivatization in gas chromatographic determination of phenol and aniline traces in aqueous media

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Substituted anilines and phenols are the most common hydrophilic organic environmental toxicants. The principles of gas chromatographic determination of trace amounts of these compounds in aqueous media at concentrations $\leqslant 0.1$ μg litre^{-1} based on synthesis of their derivatives (derivatization) directly in the aqueous phase are considered. Conversion of relatively hydrophilic analytes into more hydrophobic derivatives makes it possible to achieve such low detection limits and optimize the protocols of extractive preconcentration and selective chromatographic detection. Among the known reactions, this condition is best met by electrophilic halogenation of compounds at the aromatic moiety.
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I. Introduction

The urgency of research in the field of analytical chemistry of hydrophilic organic environmental toxicants, many of them being substituted phenols and anilines, is due to the fact that the content of several dozens of such compounds is currently regulated in potable water and reservoirs for fishery purposes.[1–3] Their distribution and accumulation in biosphere objects are promoted by wide industrial use, good solubility in water and low vapour pressure.[4] The content of these compounds should be monitored in the wastewater of woodworking and pharmaceutical plants, organic synthesis and petrochemical industry where phenols and anilines are target or intermediate products.[5–8] Chlorinated phenols (more rarely, anilines) are formed in drinking water during its chlorination and, which is especially dangerous, are the direct precursors of polychlorinated dibenzo-*p*-dioxins.[9–12] In nature, phenols and anilines can be formed upon hydrolytic or biochemical destruction of organic substances located in the soil, as well as widely used antiseptics and pesticides, such as chlorhexidine, triclosan, linuron, and aminocarb.[13–19]

The need for creating highly sensitive and selective methods for determining phenol and aniline traces is due to their high toxicity. The threshold limit values (TLV) for these compounds in water are 0.1 – 100 μg litre^{-1}. The necessity of the selective determination of these compounds, rather than the determination of their overall content, is associated with significant differences in toxicity (and, hence, in TLV) of phenol and aniline isomers.[1, 2, 20] This condition dictates the use of precisely chromatographic methods, primarily capillary gas chromatography, which provides the desired selectivity of isomer separation. The limits of direct chromatographic determination of such analytes, even with the use of modern methods of precon-

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centration, high-performance capillary columns and selective detection, as a rule, do not exceed 0.1–1 μg litre^{-1} (Refs 21–24). A major cause of these limitations should be believed to be the presence of hydroxyl (phenols) and amino (anilines) groups with so-called active hydrogen atoms, which impart noticeable polarity to these compounds. For illustration, let us compare polarity characteristics, such as dielectric permeability (ε), dipole moment (μ) and solubility in water (S), of the simplest unsubstituted phenol, aniline and hydrocarbon (toluene) with close molecular weights (Table 1).

Table 1. Polarity characteristics of phenol, aniline and toluene.

Compound	ε	μ/D	S/g per 100 g
Toluene	2.38	0.36 ± 0.04	0.055 ± 0.004
Aniline	7.0 ± 0.3	1.52 ± 0.03	3.5 ± 0.1
Phenol	9.7 ± 0.5	1.4 ± 0.2	8.4 ± 0.2

The μ values for phenol and aniline are close to that for ethanol (1.69 ± 0.01 D). Such properties of polar compounds reduce the efficiency of their extraction from aqueous solutions with nonpolar organic solvents and can be responsible for peak broadening and asymmetry during chromatographic separation. At the same time, the presence of functional groups containing active hydrogen atoms makes possible the synthesis of derivatives of target analytes (derivatization, chemical modification) during sample preparation to improve their chromatographic characteristics.

This review deals with basic methods of obtaining phenol and aniline derivatives and their subsequent gas chromatographic (GC) analysis considered in the studies published mainly after 2000. Depending on the nature of analytical tasks, derivatization of target analytes can be carried out in organic solvents after their extraction from aqueous samples or directly in aqueous media followed by extractive preconcentration. The first approach reflects traditional principles of sample preparation for determination of trace amounts of organic compounds in aqueous media. The second approach has been successfully implemented relatively recently in the 1990s (some attempts were made earlier). Derivatization before extraction allows one to improve not only the chromatographic parameters of analytes but also the extraction characteristics.

II. Specific features of derivatization reactions

Synthesis of derivatives for chromatographic analysis (derivatization) is a special type of organic reactions involving compounds with known functional groups or a specific structure of the molecular carbon skeleton.[25] The fundamental distinction of transformations that can be classified with derivatization reactions is that there is no need to determine the structure of the products. The reaction itself in combination with the structures of initial analytes (which should be known *a priori*) is considered as a proof of the structure of the resulting derivatives.

Basic requirements to the derivatization reactions are as follows:[26–30]

— Experimental operations should be as simple as possible; reagents are most often added directly to samples; mixtures can be heated for several hours in sealed ampoules; reaction mixtures are usually analyzed without additional treatment.

— Most transformations used for derivatization involve active hydrogen atoms of functional groups and, hence, are reversible reactions; many of the derivatives are unstable to hydrolysis; therefore, the reaction mixtures should be protected from contact with water traces; the products of reactions involving skeleton carbon atoms are, as a rule, considerably more stable.

— The number of derivatization stages should be minimal (no more than 1–2); in any case, reactions should be carried out successively without replacement of the reaction medium (single-pot synthesis); for derivatization of trace amounts of compounds, large excesses of modifying agents are usually used, which is caused by the absence of *a priori* information on the qualitative and quantitative compositions of analyte samples and by the necessity to ensure high derivatization reaction rates;[23,25] the excess of the reagents should not interfere with the detection of the forming derivatives or should be readily removed after the end of the reaction.

— The conversion of the initial analytes into the products should be maximal (nearly quantitative) and reproducible; otherwise, the detection limits can be significantly increased, which can complicate the quantitative analysis.

— The reaction mixtures after derivatization should be homogeneous; otherwise, the distribution of the products between the layers of heterophase systems can be indefinite, which can necessitate the analysis of both phases and the measurement of their volumes.

— The chemical nature of the products should be known: their number and structure should unambiguously correspond to those of the initial analytes; optimally, the transformations should correspond to the scheme $1 \to 1$ (one initial analyte $\to$ one derivative); examples of the $1 \to 2$ are known; however, all cases of $1 \to N$ ($N \geqslant 3$) should be excluded; in other words, the selectivity of transformations should be maximal.

As a rule, derivatives for gas chromatographic analysis are obtained to solve the following analytical problems:[23,25,26,31,32]

— transformation of nonvolatile, thermally unstable or highly reactive compounds into more stable derivatives;

— reduction of detection limits through the introduction of so-called electrophoric functional groups, which makes possible the use of selective element-specific detectors;

— improvement of metrological characteristics of analytical determinations owing to the decrease in losses related to irreversible adsorption of polar compounds onto different parts of chromatographic equipment, as well as to the decrease of asymmetry of the chromatographic peaks of derivatives;

— 'shift' of chromatographic peaks of target components from the regions 'overloaded' with signals of other compounds into less 'populated' regions of chromatograms.

For chromatography/mass spectrometry and high-performance liquid chromatography (HPLC), the set of problems solved by means of derivatization is different and includes, in addition to the above problems, the increase in the signal intensity of molecular ions, enhancement of fragmentation specificity, determination of the number of active hydrogen atoms *etc*.[25] It is worth noting that the possibilities of HPLC to vary chromatographic character-

istics of analytes without their transformation into derivatives are wider than those of gas chromatography: not only can sorbents be selected, but also the eluent composition can be changed by introducing different additives.[23]

It should be noted that optimization of sample preparation procedures, especially if they include liquid–liquid extraction of analytes from aqueous solutions, has been considered among the main goals of derivatization rather rarely. According to common recommendations, derivatization is carried out in organic solvents free of water traces, *i.e.*, after analyte extraction from aqueous samples, which can be accompanied by considerable losses of hydrophilic analytes. In similar cases, it is advisable to change the sequence of operations, namely, to obtain hydrophobic derivatives of hydrophilic analytes directly in aqueous solutions for optimization of the extraction stage aimed at increasing the degree of extraction and minimizing the extractant volumes. This 'design' of analytical procedures excludes the use of reactions involving functional groups that lead to products often unstable in the presence of water, and it becomes necessary to use irreversible reactions involving carbon atoms of analyte molecules.

III. Synthesis of functionalized derivatives of phenols and anilines

Derivatives of compounds with functional groups containing active hydrogen atoms are usually formed in reversible processes involving elimination of water or other low-molecular-weight products. As a rule, such derivatives are unstable in the presence of water and are readily hydrolyzed. Among the known reactions used for derivatization of phenols and anilines, silylation (synthesis of trialkylsilyl ethers), acylation and alkylation are most popular.[21, 23, 25, 27–31]

III.1. Silylation

Silylation (Scheme 1) is a universal method of deactivation of polar functional groups of organic compounds, e.g., phenols.[28, 33]

Scheme 1

$$ArOH \xrightarrow{XSiMe_3} ArOSiMe_3$$

where X is a structural fragment bearing the trimethylsilyl functionality.

In analytical practice, trialkylsilyl derivatives, and among them — trimethyl- and *tert*-butyldimethylsilyl derivatives, are most abundant. The following reagents are used for their synthesis: bis(trimethylsilyl)acetamide (BSA), *N*,*O*-bis(trimethylsilyl)trifluoroacetamide (BSTFA), *N*-methyl-*N*-(trimethylsilyl)acetamide (MSA), *N*-methyl-*N*-(trimethylsilyl)trifluoroacetamide (MSTFA) and *N*-*tert*-butyldimethylsilyl-*N*-methyltrifluoroacetamide (MTBSTFA). Pyridine is used as a solvent, and trimethylchlorosilane and/or *N*-(trimethylsilyl)imidazole are used as catalysts. The reactivity of phenol hydroxyl groups toward the above silylating reagents is rather high, and they form trimethylsilyl and *tert*-butyldimethylsilyl ethers in nearly quantitative yield.[34–40]

The detection selectivity for the derivatives with the use of element-specific detectors is enhanced when silylating agents containing different heteroatoms are employed.[32] For example, the introduction of halogen-containing groups $C_6F_5SiMe_2$ or $ClCH_2SiMe_2$ allows one to determine phenols with the use of an electron-capture detector (ECD) at their concentrations in samples about 0.02–0.05 μg litre^{-1}; however, such derivatives are characterized by lower volatility and hydrolytic stability as compared with classical silyl derivatives that do not contain extra heteroatoms.[41, 42]

The reaction has the following specific features: [28, 32]

— strict requirements for the inertness of gas chromatography equipment, including the obligatory presence of the liner (glass or quartz insert) in the injector and the use of silica capillary columns; note that this condition is met by most of modern devices;

— for some reagents, heat, ultrasonic or microwave treatment of reaction mixtures is recommended for promoting the reaction and increasing the yield of reaction products;

— low stability of reagents and most of the resulting derivatives to the presence of even trace amounts of water;

— some silylating reagents react not only with compounds containing functional groups with active hydrogen atoms but also with analytes of another chemical nature (for example, MSA and MSTFA form adducts with aromatic aldehydes).[43]

tert-Butyldimethylsilyl derivatives, as well as MTBSTFA used for their synthesis, are most stable to hydrolysis.[33]

For silylation of primary amines, BSTFA[44] and MTBSTFA[45, 46] are used. However, as compared with phenols, the activity of aromatic amines in silylation reactions is considerably lower;[47] therefore, such derivatives are rather rarely used for analytical purposes. If the aromatic moiety of anilines contains electron-withrawing substituents, trimethylsilyl derivatives are formed in low yields,[45] and their synthesis requires severe conditions (elevated temperatures and longer reaction time).

Another problem of amine silylation is the possibility of substitution of silyl groups for both hydrogen atoms to give a mixture of mono- and bis(trialkylsilyl) derivatives,[47] *i.e.*, the decrease in selectivity of derivatization. The use of MTBSTFA is advisable to avoid this detrimental effect, since bis(*tert*-butylmethylsilyl)anilines almost do not form because of steric hindrances induced by bulky groups containing quaternary carbon and silicon atoms.

III.2. Acylation

In addition to silylation, acylation (Scheme 2) is widely used for derivatization and subsequent gas chromatographic analysis of polar organic compounds (for example, phenols) containing functional groups with active hydrogen atoms.[23, 27, 29, 32]

Scheme 2

$$ArOH \xrightarrow{YC(O)R} ArOC(O)R$$

Here, Y bears the acyl functionality. The acyl derivatives are characterized by the higher hydrolytic stability than the corresponding silyl derivatives, other conditions being the same.

It has been mentioned above that the use of silylating agents for functionalization at the polar OH and NH_2 groups is possible only in organic solvents, although derivatization in an aqueous phase (prior to analyte extraction) is preferable. If the resulting derivatives are more hydrophobic, then changing the sequence of extraction and derivati-

zation reactions makes it possible to reduce the overall number of stages of the analytical cycle and simplify the procedure as a whole owing to the exclusion of salting-out, multiple extraction, and concentration of extracts through removal of the extractant, and thus minimize errors caused by these stages. In addition, the increased extraction efficiency makes it possible to reduce the required amounts of organic solvents, and water-soluble reagents should not interfere with subsequent stages of synthesis.

Acylation of phenol compounds directly in water is accomplished with acetic anhydride (AA) in the presence of potassium or sodium carbonates[48–66] or hydrogen carbonates.[67,68] The challenge of using these salts is in that the acylation is accompanied by a vigorous release of CO_2, and this can lead to analyte loss. For this reasons, acylation of phenols is often carried out with sodium hydrogen phosphates (phosphates)[69–72] or sodium hydroxide.[73–75]

For selective detection of phenol compounds with the use of an ECD, they are recommended to be converted into chloroacetates.[76,77] The sensitivity of determination of monochloroacetates (monochloroacetic anhydride as a reagent) with the use of ECD is ~50 times as high as that of the corresponding acetates.[76] Perfluoroacylating agents are also used for analysis of phenols with ECD.[78] Phenols are often determined as trifluoroacetates,[45,79–81] pentafluoropropionates[82–85] and heptafluorobutyrates.[86–88] Perfluoroacylation is usually carried out in aprotic organic solvents with trifluoroacetic (TFAA), pentafluoropropionic (PFPA), and heptafluorobutyric (HFBA) anhydrides or pentafluorobenzoyl chloride (PFBCl). Pyridine or triethylamine is used as an acceptor of byproducts (free perfluorocarboxylic acids or halohydrocarbons). However, as the number of carbon atoms in perfluoroacyl moieties increases, the stability of the resulting esters decreases and the background ECD current increases because of formation of a large number of byproducts.

Among the fluorinated phenols, pentafluorobenzoates are most stable to hydrolysis; they can be obtained both in organic solvents[89,90] and in heterogeneous systems where one of the phases is an alkaline buffer solution.[91,92] A disadvantage of pentafluorobenzoates is a noticeable increase in the retention parameters of these derivatives, which increases the duration of chromatographic analysis.

Anilines can be acylated only in the form of bases ($ArNH_2$) rather than salts ($ArNH_3^+X^-$); this necessitates control of the pH of reaction mixtures or the use of only the most reactive agents — TFAA,[93–95] PFPA,[93,96,97] HFBA,[93,98,99] PFBCl[97] and benzoyl chloride.[100]

Acylation of anilines aimed at enhancing the degree of extraction from aqueous media can be combined with the stage of solid-phase extraction. Several variants of combination of these processes are possible:[94,97,100]

— anilines are adsorbed by sorbent fibres saturated with a reagent;

— derivatives are obtained after the sorption of anilines onto the sorbent;

— adsorbed anilines are eluted from the sorbent with a mixture of solvents containing an acylating reagent.

To enhance the sensitivity of determination of derivatives by means of an ECD or negative ion chemical ionization gas chromatography–mass spectrometry (GC/MS), acid anhydrides and acyl halides containing fluorine or chlorine atoms are used.[93,101] The sensitivity of selective detection (ECD) for structural analogues increases in the order

$$F < Cl < Br < I \quad (1)$$

so that anilides of mono-, di- and trichloroactic acids are detected better than anilides of C_2-C_4 perfluorocarboxylic acids.[32] However, using such reagents necessitates removal of their excess and byproducts (corresponding halocarboxylic acids) since these compounds can interfere with the chromatographic analysis of reaction mixtures.

Recently, phenol derivatives have been synthesized directly in aqueous media with the use of alkyl chloroformates.[102,103] The simplest homologues of this series are commonly used: methyl,[104] ethyl,[105–107] n-butyl (BuCF)[108] or isobutyl chloroformates (Scheme 3).

Scheme 3

$$ArOH \xrightarrow{ClC(O)OBu^n} ArOCO_2Bu^n$$

To improve the volatility of the products and sensitivity of their determination with a selective ECD or by chemical ionization mass spectrometry (CI-MS), fluorinated alkyl and aryl chloroformates are used.[109–111] Among the weaknesses of these reagents are their tendency for hydrolysis and limited solubility in water; with increasing the number of carbon atoms in a molecule, their hybrophobicity naturally increases. Hence, for derivatization in aqueous solutions, large molar excesses of alkyl chloroformates are required, and their solubility is improved by adding water-soluble organic compounds (ethanol, acetone or acetonitrile) and a catalyst (pyridine).

Aromatic amines react with a chloroformate excess in an alkaline medium at room temperature for a few minutes to form the corresponding carbamates in nearly quantitative yield[112–114] (Scheme 4).

Scheme 4

$$ArNH_2 \xrightarrow{ClC(O)OBu^n} ArNHCO_2Bu^n$$

Isobutyl chloroformate[112,113] and 2,2,2-trichloroethyl chloroformate[114] are used as reagents. To prevent the hydrolysis of the resulting derivatives, derivatization of anilines is carried out simultaneously with their extractive preconcentration with organic solvents.

III.3. Alkylation

Methyl ethers synthesized by methylation (Scheme 5) are the most stable phenol derivatives.[23,24] Classical reagents for their synthesis are methyl iodide,[115] diazomethane[116] and dimethyl sulfate (DMS).[117,118]

Scheme 5

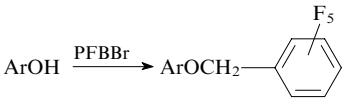
$$ArOH \xrightarrow{DMS} ArOMe$$

Alkylation under phase-transfer catalysis conditions (catalysts are crown ethers or quaternary ammonium salts) lead to nearly quantitative conversion of phenols (~85%–90%). The detection limits of methyl ethers of phenols are ~1.5–3 times as low as those of the initial compounds, which is due to an increase in their volatility (lower retention parameters) and higher symmetry of chromatographic peaks. A disadvantage of methylation is the occurrence of side reactions (electrophilic substitution in the aromatic rings of phenols), and the by products, as a rule,

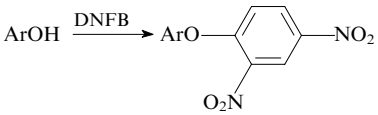
interfere with chromatographic determination of target products.

To enhance the sensitivity in selective detection (ECD) of phenol compounds, pentafluorobenzyl bromide (PFBBr)[88,119–124] and 2,4-dinitro-1-fluorobenzene (DNFB)[125–127] have been suggested as reagents. The derivatives obtained by the reaction of phenol compounds with PFBBr and DNFB are shown in Schemes 6 and 7, respectively.

Scheme 6



Scheme 7



Pentafluorobenzyl ethers can be obtained in the two-phase system methylene chloride–aqueous NaOH (the phase-transfer catalyst is tetra-n-butylammonium hydrogen sulfate). This method ensures detection limits within 0.05–10 μg litre^{-1}; however, it has the following essential limitations:

— long reaction duration (1–2 h) with the semi-quantitative yield of the derivatives (30%–80%);

— fluorinated byproducts are resposible for the increase in the ECD background current and interfere with determination of the target ethers;

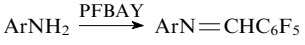
— chromatographic retention parameters of pentafluorobenzyl phenol ethers are considerably larger (by some estimates, by a factor of 5–10) than the retention parameters of the corresponding trimethylsilyl derivatives.

To obtain 2,4-dinitrophenyl ethers, water samples (a buffer solution with pH ~11.5) are treated with 2,4-dinitro-1-fluorobenzene (50 °C, 40 min). The resulting ether are extracted with hexane, and the extracts are studied by gas chromatography (ECD). However, the relative sensitivity of ECD to 2,4-dinitrophenyl ethers is comparable with the sensitivity to pentafluorobenzyl ethers, while their relative retention times are 3–5 times as large as those of the latter.[125]

III.4.Other types of reactions

To determine primary amines (including aromatic) directly in aqueous solutions, it is recommended to convert them into N-substituted imines (Schiff bases) (Scheme 8) by the reaction with aldehydes.[47,128] The use of pentafluorobenzaldehyde (PFBAY) in combination with selective detection (ECD) provides detection limits for N-substituted imines at the level 0.04–0.09 μg litre^{-1}.[129]

Scheme 8



The same detection limits are achieved when aniline amino groups are replaced by iodine atoms.[130–133] The reaction occurs in two stages (Scheme 9): first, diazotization with sodium nitrite in the presence of hydroiodic acid is carried out (20 °C, 20 min), and then, the diazo group is substituted by iodine through the Sandmeyer reaction (100 °C, 5 min).

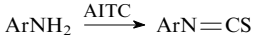
Scheme 9



This reaction is specific only for primary aromatic amines. Among side reactions, substitution of a hydroxyl group for the diazo group to give phenols should be noted. If water contains high levels of chlorides and bromides, chloro- and bromobenzenes can form in significant amounts.[134]

It has been suggested to substitute an isothiocyanate fragment NCS for the amino group in primary aromatic amines through their reaction with allyl isothiocyanates (AITC)[135,136] (Scheme 10).

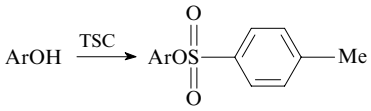
Scheme 10



At the first stage, the reactants react in water (50 °C, 20 min) to give allylthiocarbamoyl derivatives ArNHC(S)NHAll. After sorptive preconcentration, extracts are introduced into a chromatograph evaporator where they are pyrolyzed at 250 °C to give aryl isothiocyanates. A flame photometric detector can be used for selective detection of aryl isothiocyanates.

For derivatization of phenol compounds, their tosylation with *p*-tolyenesulfonyl chloride (TSC) (Scheme 11) is recommended.[137]

Scheme 11

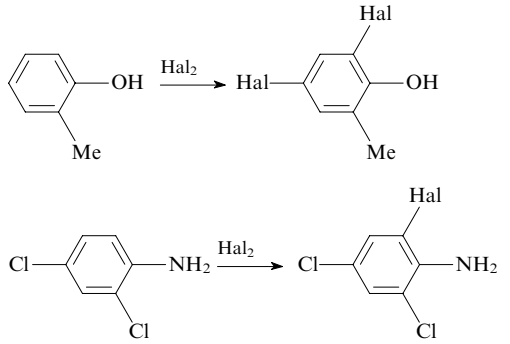


The reaction proceeds at room temperature in an alkaline medium (phosphate buffer) for 30–40 min. Since this reagent is nearly insoluble in water, the derivatives are obtained in the presence of water-soluble organic compounds or simultaneously with extraction (TSC is introduced into the extractant). A flame photometric detector can also be used for selective detection of phenol tosylation products.

IV. Synthesis of phenol and aniline derivatives by substitution in the aromatic moiety

Phenol and aniline derivatives suitable for gas chromatographic determination can be obtained not only through functionalization of the OH and NH_2 groups but also through electrophilic substitution for hydrogen atoms of the aromatic ring (Scheme 12). Such reactions involving C–X bond formation (X is a heteroatom) can be classified as oxidation reactions and, as distinct from the above reactions, are irreversible. Both functional groups exhibit a pronounced +M-effect (the increase in mobility of hydrogen atoms in the *ortho* and *para* positions of the aromatic ring); this is responsible for the high rate of electrophilic substitution reactions, including halogenation, only in the 2-, 4- and 6-positions.

Scheme 12



Hal = Cl, Br, I

Such reactions of phenols and anilines proceed especially easily in the presence of water, which catalyzes the process by polarizing halogen molecules and generating electrophilic species,[138] *i.e.*, acts as a Lewis acid. The interfering effect of other organic compounds should be minimal since mainly phenol, aniline and their homologues will react with halogens under such conditions.[139] After the end of reaction, a halogen excess can be easily removed by adding an inorganic reducing agent. The resulting derivatives are stable in water and organic solvents.

In addition, some advantages of halogenation of phenols and anilines in aqueous solutions are worth of noting.

1. The introduction of halogen atoms into a molecule considerably increases the hydrophobicity of analytes and, as a result, leads to their efficient extraction from an aqueous matrix into the organic phase. The hydrophobic effect of halogens is different and increases along series (1).[140, 141]

The increase in the hydrophobicity of halogenated phenol and aniline derivatives can be illustrated by the increase in the logarithms of their partition constant ($\log P$) in the standard solvent system n-octanol–water. The data in Table 2 show that the partition constant of 2,4,6-triiodophenol in this system is ~ 250 times as large as that of phenol, while for 2,4,6-tribromoaniline, the partition constant is more than 3000 times higher than that of the unsubstituted aniline.

2. The introduction of halogen atoms into molecules enables highly sensitive determination of analytes with a halogen-sensitive ECD; for halogenated compounds of the same type, the sensitivity increases in the same sequence (1).[30, 32, 142]

3. With an increase in the number of halogen atoms in analyte molecules, their extraction characteristics and ECD sensitivities are equalized so that the mono-, di- and trichlorinated phenols and anilines can be determined simultaneously.[143–145]

4. Halogenation does not involve the functional groups of phenols and anilines, which makes possible their additional derivatization in organic solvents (after extraction) by a wide range of reagents.[23]

5. The synthesis of two (or more) analytical forms halogenated at functional groups (from the same extract) provides additional information for their identification based on the differences in chromatographic properties of these derivatives (retention values, ECD sensitivity).[146, 147]

6. The use of molecular chlorine or bromine as the halogenation agent simplifies the interpretation of the mass spectra of the derivatives. These halogens are unique two-isotope elements, and molecules containing atoms of such elements give rise to characteristic multiplets of peaks of halogenated ions in mass spectra.[148] The intensity ratio of signals in the multiplets makes it possible to determine the number of chlorine and bromine atoms in a molecule, which essentially contributes to the identification reliability. It should be noted that, in detection of halogenated compounds, a negative chemical ionization mass spectrometer has the sensitivity similar to the ECD sensitivity.

Despite the above advantages of the halogenation reaction for determination of trace amounts of phenols and anilines, this derivatization method has remained uncharacterized until recently.

Molecular bromine has been proposed for derivatization of anilines[149–153] and phenols.[154, 155] Organic media — acetic acid,[149–152] isooctane,[153] diethyl ether[154] and ethanol[155] — have been recommended for this reaction. The choice of such conditions is presumably dictated by the high activity of bromine in water: its redox potential in acid and neutral media can be as high as 0.9–1.1 V.[156] However, transfer of the target analytes to organic phases requires their preliminary multistage extraction from aqueous media (preconcentration by the liquid and/or solid-phase extraction), which deteriorates their conversion and sharply increases the complexity of preparation.

We have shown that brominated anilines and substituted anilines (chloro-, nitro- and methylanilines) can be obtained in the aqueous phase provided that the oxidative activity of bromine is reduced.[143, 144, 157] Systems for bromination in the presence of reagents reversibly binding bromine into products with a lower oxidative activity have been described. In particular, in the presence of bromide ions[144] and amino acids,[143, 157] the redox potential of bromine decreases to 0.7–0.8 V, which enhances the conversion of the initial analytes into brominated derivatives and their stability in aqueous solutions.

Advantages of halogenation in aqueous solutions can be illustrated by the following example. Determination of chlorinated anilines in water by GC-ECD has been reported.[143, 150] When chloroanilines are brominated in water, there are only two stages before their GC determination: bromination itself and microextraction of brominated derivatives.[143] In the second case, sample preparation consisting of the five stages is required before gas chromatographic determination:[150]

— solid-phase extraction,
— back extraction,
— extract evaporation/solvent change,
— bromination in acetic acid,

Table 2. Logarithms of partition ratios of halogenated phenols and anilines in the n-octanol–water system.[140, 141]

Initial compound	$\log P$	Halogenated derivatives	$\log P$
Phenol	1.47 ± 0.01	4-iodophenol	2.92 ± 0.01
		2,4-diiodophenol	3.6 ± 0.4 [a]
		2,4,6-triiodophenol	3.9 ± 0.5 [a]
Aniline	0.92 ± 0.05	4-bromoaniline	2.12 ± 0.12
		2,4-dibromoaniline	3.3 ± 0.4 [a]
		2,4,6-tribromoaniline	4.4 ± 0.5 [a]

[a] The values estimated with the use of the ACD software.

— liquid extraction of the products after neutralization of the acid.

Despite such a complicated procedure, the detection limit for chloroanilines is no lower than 1 μg litre^{-1}, while for their bromination directly in water this limit is 0.002–0.007 μg litre^{-1}. It is evident that differences between the detection limits are caused by aniline losses at the first three stages of the analytical cycle. In addition, the bromination of anilines in acetic acid is a slower reaction — it lasts for 15 min at a bromine concentration of 0.1 mol litre^{-1} against 2 min at a bromine concentration in water of 0.0005 mol litre^{-1}.

Molecular iodine was also used to synthesize halogenated aromatic amines in aqueous solutions (phosphate buffer, pH 6–7).[158] However, as distinct from bromination, exhaustive iodination was achieved for none of the charac-

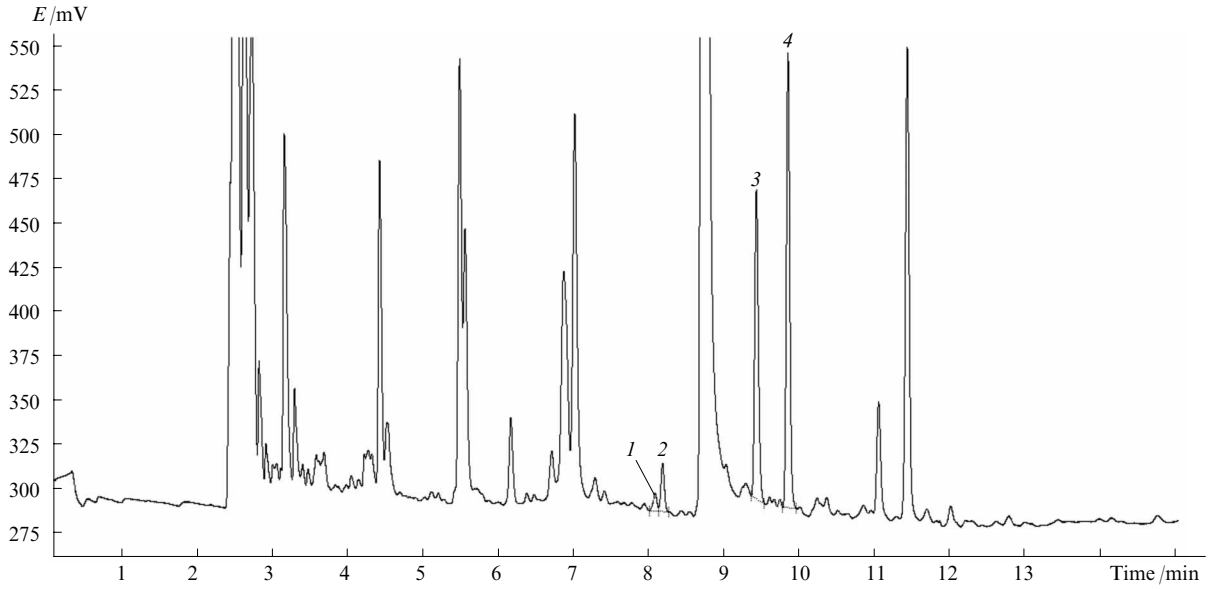


Figure 1. Chromatogram illustrating the quantification of chloroanilines in potable water as their brominated derivatives.[143] (*1*) 4-Chloroaniline (0.03 ± 0.01 μg litre^{-1}), (*2*) 2-chloroaniline (0.04 ± 0.01 μg litre^{-1}), (*3*) 4,6-dibromo-1,2-dimethoxybenzene (internal standard), (*4*) aniline (0.07 ± 0.03 μg litre^{-1}). *E* is GC detector voltage.

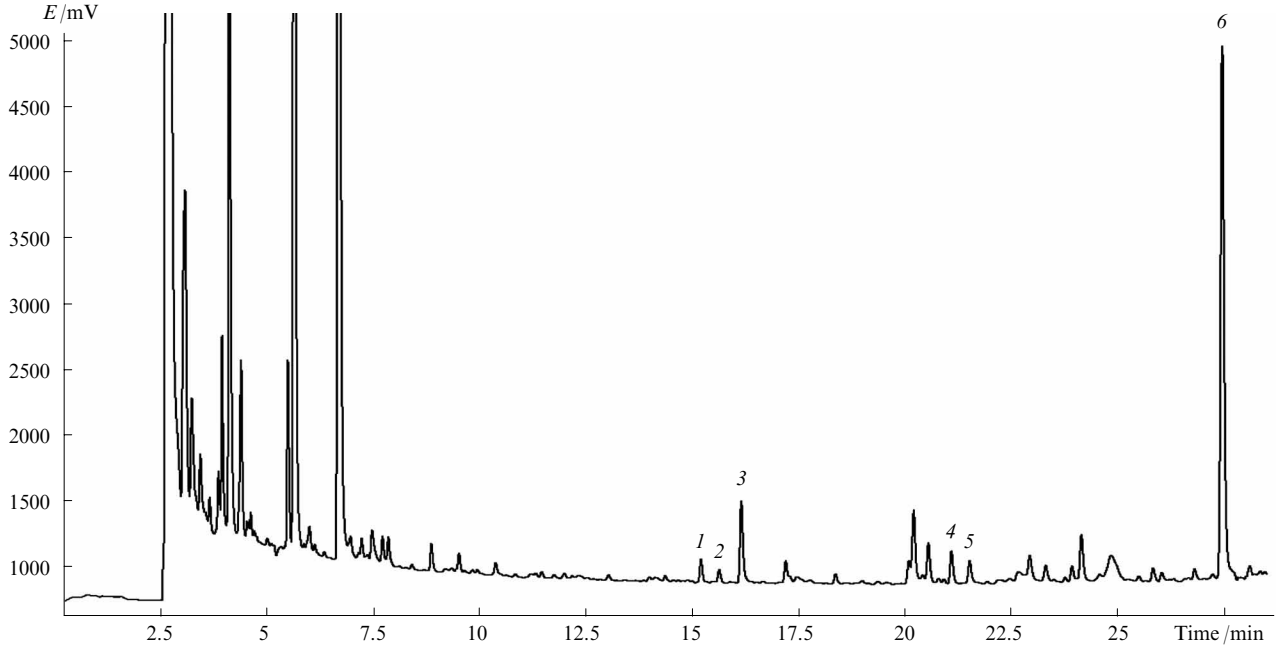


Figure 2. Chromatogram illustrating the quantification of chlorophenols in potable water as acetates of their iodinated derivatives.[145] (*1*) 2,4-Dichlorophenol (0.047 ± 0.007 μg litre^{-1}), (*2*) 2,6-dichlorophenol (0.039 ± 0.007 μg litre^{-1}), (*3*) 4,6-dibromo-1,2-dimethoxybenzene (internal standard), (*4*) 4-chlorophenol (0.037 ± 0.007 μg litre^{-1}), (*5*) 2-chlorophenol (0.042 ± 0.006 μg litre^{-1}), (*6*) phenol (0.29 ± 0.04 μg litre^{-1}).

terized anilines because of the lower electrophilicity of molecular iodine.[138, 139] When iodination is incomplete, quantification limits of the analytes significantly increase, and their identification is complicated because of the appearance of a large number of incomplete conversion byproducts (isomeric mono- and diiodinated derivatives).

It has also been recommended[159] to carry out the bromination of methylphenols in an aqueous phase; however, brominated derivatives have been obtained only for phenol and monomethylphenols. More reactive di- and trimethylphenols are completely oxidized under these conditions. We have demonstrated that conversion of chlorophenols,[145] as well as mono-, di- and trimethylphenols,[147, 160] into the iodinated derivatives by the reaction with molecular iodine in an alkaline buffer solution (pH 9.5–10) provides good results. As compared with analogous brominated compounds, the degree of extraction of iodinated phenols is essentially higher, while the limits of their selective detection with ECD are lower. In addition, as compared with aqueous solutions of bromine, aqueous solutions of iodine are characterized by lower redox potentials (0.5–0.6 V), lower toxicity, higher availability and better stability in storage.[156] The use of iodination in combination with acylation (second stage of derivatization) makes it possible to decrease the quantification limits of phenol compounds in water to 5–10 μg litre^{-1}.

Quantification of chloroanilines as brominated derivatives and determination of chlorophenols as iodinated derivatives in water are illustrated in Figs 1 and 2, respectively.

V. Combination of derivatization with extractive preconcentration

The use of gas chromatography for analysis of aqueous media implies the exchange of the water matrix for a less polar organic solvent. At the extraction stage, researchers intend to achieve selective extraction and maximal degree of concentration of target analytes, which determine the detection limits of all analytical procedures; to this end, liquid or solid-phase extraction is commonly used.[24, 161–163]

In recent years, the efficiency of extractive preconcentration has been increased by increasing the phase ratio (r) to the values exceeding 1000.[31, 164, 165] In addition, minimal amounts of resulting extracts are used as completely as possible in chromatographic analysis — up to 100% (for common extraction of $<1\%$); this makes it possible to reduce the consumption of toxic organic solvents.

In this context, the following variants of have been suggested for concentrating organic compounds from aqueous media:

— solid-phase microextraction from the gas phase,[166]

Table 3. Characteristics of modern methods of gas chromatographic determination of phenols and anilines in aqueous media.

Analytes	Reagent for derivatization [a]	Extraction method	Detection limit /ng litre^{-1}	Ref.
Methyl- and chlorophenols	AA	solid-phase microextraction from the gas phase	5–8	68
Chlorophenols	AA	liquid microextraction	100–200	74
Alkyl- and chlorophenols	AA	stir bar sorptive extraction	0.5–5	66
Bromo- and chlorophenols	DMS	solid-phase microextraction from the gas phase	1–3	117
Alkyl- and chlorophenols	BSTFA [b]	liquid microextraction	5–15	172
Chlorophenols	AA	stir bar sorptive extraction dispersive liquid–liquid microextraction	1–20 10–2000	59 57
Phenol, methyl- and chlorophenols	AA	liquid microextraction	5–680	49
Bromo-, methyl- and chlorophenols	AA	solid-phase microextraction from the gas phase, solid-phase microextraction from aqueoues samples	2–46	173
Phenol and chlorophenols	AA	solid-phase microextraction from the gas phase	20–50	174
Phenol, methyl- and chlorophenols	AA	stir bar sorptive extraction	100–400	60
Methyl-, nitro- and chlrophenols	BSA [c]	liquid microextraction in a single drop of solvent	4–61	175
Methyl-, nitro- and chlorophenols	TSC	the same	200–280	137
Aniline and chloroanilines	PFBAY	dispersive liquid–liquid microextraction	40–90	129
Aniline, nitro- and chloroanilines	$NaNO_2$/HI	solid-phase microextraction	2–38	129
Aniline, methyl- and chloroanilines	AITC	solid-phase microextraction from the gas phase	6–180	136
Aniline, methyl- and chloroanilines	BuCF	dispersive liquid–liquid microextraction	1000–3000	176
Aniline, methyl- and chloroanilines	CS_2/Zn(II)	solid-phase microextraction from gas phase	25–240	177

[a] Derivatization is carried out before the extraction (sorption) stage or simultaneously with it. [b] Derivatization is carried out after extraction in the chromatograph injector. [c] Derivatization is carried out in a microsyringe after extraction.

— solid-phase microextraction from the aqueous phase,[167]

— liquid microextraction,[168]

— dispersive liquid–liquid microextraction,[169]

— liquid micriexraction in a single drop of a solvent,[170]

— stir bar sorptive extraction.[171]

Characteristics of some popular methods of determination of phenols and anilines in aqueous media combining the use of the above reagents and modern extractive preconcentration techniques are summarized in Table 3.

Although almost all of the methods ensure the required detection limits of toxicants (0.005–0.05 μg litre^{-1}), it is expedient to note some of their inherent disadvantages:

— the use of evaporation of organic extracts for additional preconcentration of analytes distorts the information on the qualitative and quantitative compositions of analytes;[49, 74, 131, 172, 173]

— all of the above methods involve multistep analytical procedures and require special equipment: devices for solid-phase and liquid microextraction, temperature-programmed evaporators, centrifuges, magnetic stirrers, *etc.*;[49, 57, 59, 60, 66, 68, 74, 131, 172, 174]

— for extraction at high phase ratios, it is necessary to introduce salting-out additives into aqueous samples (30 mass %–55 mass %), apply high temperatures (up to 100 °C) and carry out long-term extraction (up to 1.5 h);[49, 60, 172, 173, 175]

— the use of some reagents for derivatization leads to formation of byproducts (in some cases, even traces of water should be excluded), and the derivatization takes long time (up to 2 h) at high temperature (up to 100 °C);[68, 131, 136, 137, 172, 176, 177]

— in some cases of solid-phase microextraction, there are observed the destruction of derivatives on the sorbent surface during thermodesorption,[68] dependence of sorption characteristics on the presence of the salting-out agent and the excess of modifying reagents,[59, 137] memory effects and unsatisfactory reproducibility of results even when identical sorbents are used;[31]

— in the case of preconcentration using liquid microextraction in a single drop of a solvent, equilibrium concentrations of distributed components are often not achieved, and the stability of the organic extractant drop strongly depends on the stirring rate of the aqueous solution.[31, 137]

VI. Conclusion

Good solubility in water, low vapour pressure and wide commercial use of phenols and anilines contribute to their distribution and accumulation in bioshpere objects. It should be taken into account that the products of conversion of initial environmental toxicants can be extremely hazardous. For example, contact of phenols and anilines with chlorine in any technological processes leads to the formation of highly toxic chlorinated products.

The necessity of selective determination of phenols and anilines in water at the level of 0.1–100 μg litre^{-1} is dictated by considerable differences in toxicity of isomers of these compounds. Such detection limits can be achieved only by means of chromatographic methods. However, direct gas chromatographic determinations do not provide detection limits at the level of $< 0.1-1$ μg litre^{-1} mainly because of low degrees of extraction of relatively hydrophilic analytes from aqueous media. This is a reason why it seems rational and effective for improving analytical properties of these analytes to convert them into more hydrophobic derivatives.

Of most interest for determination of phenols and anilines are methods of synthesis of derivatives directly in aqueous solutions rather than in organic solvents after extractive preconcentration. Derivatization of phenols and anilines before their extraction results in lower detection limits, since it simultaneously improves both the extraction and chromatographic properties of these compounds. However, most of reagents used in chromatography are readily hydrolyzed; they can be used only in organic phases. Among such reagents are all silylating agents, halocarboxylic acid anhydrides, *etc*. To synthesize derivatives directly in the aqueous phase, only some acylating and alkylating agents are used; however, in such cases, it is recommended to combine derivatization with sorption or extraction (because the derivatives are rather unstable to hydrolysis). In this context, the stage of extractive preconcentration turns out to be a key one in the set of analytical procedures, and it is not accidental that numerous studies have been dedicated to increasing its efficiency (first of all, by increasing the degree of extraction and decreasing the extractant volumes).

An optimal approach to determination of traces of hydrophilic organic compounds in aqueous media consists in creation of conditions for extraction of their maximal amounts into organic solvents where they are subjected to additional derivatization. We believe that this approach can be realized through the irreversible electrophilic substitution reaction leading to halogenation of phenols and anilines. This reaction meets general requirements for methods of derivative synthesis; however, despite obvious advantages, almost no relevant studies have been carried out until recently. It is evident that further development of this method will make it possible to extend it to other classes of organic compounds.

References

1. *SanPiN 2.1.4.1074-01. Pit'evaya Voda. Gigienicheskie Trebovaniya k Kachestvu Vody Tsentralizovannykh Sistem Pit'evogo Vodosnabzheniya. Kontrol' Kachestva* (SanPiN 2.1.4.1074-01. Drinking Water. Hygienic Requirements for Water Quality of Centralized Drinking Water Supply Systems. Quality Control) (Moscow: Goskomsanepidnadzor Rossii, 2001)
2. *Perechen' Rybokhozyaistvennykh Normativov* (List of Fishery Regulations) (Moscow: VNIRO, 1999)
3. L I Kozubova, S V Morozov *Organicheskie Zagryazniteli Pit'evoi Vody* (Organic Pollutants of Drinking Water) (Novosibirsk: Siberian Brunch of the Russian Academy of Sciences, 1993)
4. *Handbook of Physical-Chemical Properties and Environmental Fate for Organic Chemicals* (Ed. D Mackay) (Boca Raton, FL: CRC Press, 2006)
5. E S Elin *Fenol'nye Soedineniya v Biosfere* (Phenolic Compounds in the Biosphere) (Novosibirsk: Siberian Brunch of the Russian Academy of Sciences, 2001)
6. G D Kharlampovich, Yu V Churkin *Fenoly* (Phenols) (Moscow: Khimiya, 1974)
7. M A Chekalin, B V Passet, B A Ioffe *Tekhnologiya Organicheskikh Krasitelei i Promezhutochnykh Produktov* (Technology of Organic Dyes and Intermediates) (Moscow: Khimiya, 1980)

8. N N Mel'nikov *Pestitsidy: Khimiya, Tekhnologiya, Primenenie* (Pesticides: Chemistry, Technology and Application) (Moscow: Khimiya, 1987)
9. G V Slavinskaya *Khim. Tekhnol. Wody* **13** 1013 (1991) [a]
10. L A Fedorov, B F Myasoedov *Russ. Chem. Rev.* **59** 1063 (1990)
11. A D Kunzevich, V F Golovkov, V R Rembovskii *Russ. Chem. Rev.* **65** 27 (1996)
12. L I Kozubova, V N Kobrina *Khimicheskie Metody Podgotovki Vody* (Chemical Methods of Water Treatment) (Novosibirsk: Siberian Brunch of the Russian Academy of Sciences, 1996)
13. N Epperlein, B Kramhöller, K Speer *Dtsch. Lebensm.-Rundsch.* **102** 53 (2006)
14. H T Rasmussen, N Omelczenko, S K Friedman, B P McPherson *J. Chromatogr., A* **719** 434 (1996)
15. B Kettner, B Kramhöller, K Speer, N Epperlein *Dtsch. Lebensm.- Rundsch.* **103** 4 (2007)
16. H Below, N Lehan, A Kramer *Microchim. Acta* **146** 129 (2004)
17. R Roehrs, M Roehrs, S L O Machado, R Zanella *CLEAN-Soil Air Water* **40** 958 (2012)
18. S Giacomazzi, N Cochet *Chemosphere* **56** 1021 (2004)
19. K Murugesan, Y-Y Chang, Y-M Kim, J-R Jeon, E-J Kim *Water Res.* **44** 298 (2010)
20. V Aruoja, M Sihtmäe, H-C Dubourguier, A Kahru *Chemosphere* **84** 1310 (2011)
21. A Fekete, A K Malik, A Kumar, P Schmitt-Kopplin *Crit. Rev. Anal. Chem.* **40** 102 (2010)
22. T V Vorob'eva, A V Terletskaya, N F Kushchevskaya *Khim. Tekhnol. Vody* **29** 370 (2007) [a]
23. P I Dem'yanov *Zh. Anal. Khim.* **47** 1942 (1992) [b]
24. M C Quintana, L Ramos *Trends Anal. Chem.* **27** 418 (2008)
25. I G Zenkevich, in *Encyclopedia of Chromatography* (Ed. J Cazes) (Boca Raton, FL: CRC Press, 2010) p. 562
26. M Rompa, E Kremer, B Zygmunt *Anal. Bioanal. Chem.* **377** 590 (2003)
27. R J Wells *J. Chromatogr., A* **843** 1 (1999)
28. C F Poole *J. Chromatogr., A* **1296** 2 (2013)
29. A M C Ferreira, M E F Laespada, J L P Pavón, B M Cordero *J. Chromatogr. A* **1296** 70 (2013)
30. *Handbook of Derivatives for Chromatography* (Eds K Blau, J M Halket) (New York: Wiley, 1993)
31. M A Farajzadeh, N Nouri, P Khorramy *Trends Anal. Chem.* **55** 14 (2014)
32. C F Poole *J. Chromatogr., A* **1296** 15 (2013)
33. C Schummer, O Delhomme, B Appenzeller, R Wennig, M Millet *Talanta* **77** 1473 (2009)
34. T Heberer, H-J Stan *Anal. Chim. Acta* **341** 21 (1997)
35. M Helaleh, S Fujii, T Korenaga *Talanta* **54** 1039 (2001)
36. L Ask Reitzel, A Ledin *J. Chromatogr., A* **972** 175 (2002)
37. F Jaber, C Schummer, J Chami, P Mirabel, M Millet *Anal. Bioanal. Chem.* **387** 2527 (2007)
38. M Kawaguchi, N Sakui, N Okanouchi, R Ito, K Saito *J. Chromatogr., A* **1062** 23 (2005)
39. J B Quintana, R Rodil, S Muniategui-Lorenzo, P López-Mahía, D Prada-Rodríguez *J. Chromatogr., A* **1174** 27 (2007)
40. P M Hoai, S Tsunoi, M Ike, Y Kuratani, K Kudou *J. Chromatogr., A* **1020** 161 (2003)
41. C F Poole, W-F Sye, S Singhawangcha, F Hsu, A Zlatkis *J. Chromatogr., A* **199** 123 (1980)
42. C F Poole, S Singhawangcha, L-E C Hu, W-F Sye, R Brazell *J. Chromatogr. A* **187** 331 (1980)
43. J L Little *J. Chromatogr., A* **844** 1 (1999)
44. G Bioque, J Abián, O Bulbena, J Roselló-Catafau, E Gelpí *J. Chromatogr., B* **615** 191 (1993)
45. K Schoene, H-J Bruckert, J Steinhanses, A König *Fresenius' J. Anal. Chem.* **348** 364 (1994)
46. S Casal, E Mendes, J Fernandes, M B P Oliveira, M Ferreira *J. Chromatogr., A* **1040** 105 (2004)
47. H Kataoka *J. Chromatogr. Library* **70** 364 (2005)
48. R Morales, M Cruz Ortiz, L A Sarabia *Anal. Chim. Acta* **754** 20 (2012)
49. H Faraji, M S Tehrani, S W Husain *J. Chromatogr., A* **1216** 8569 (2009)
50. D Budziak, E Martendal, E Carasek *Anal. Chim. Acta* **598** 254 (2007)
51. F Galán-Cano, R Lucena, S Cárdenas, M Valcárcel *J. Chromatogr., A* **1229** 48 (2012)
52. P De Morais, T Stoichev, M C P Basto, P N Carvalho, M T S D Vasconcelos *Anal. Bioanal. Chem.* **399** 2531 (2011)
53. X Wang, C-P Diao, R-S Zhao *J. Sep. Sci.* **32** 154 (2009)
54. M Kawaguchi, K Inoue, M Yoshimura, R Ito, N Sakui *J. Chromatogr., B* **805** 41 (2004)
55. J I Cacho, N Campillo, P Viñas, M Hernández-Córdoba *J. Chromatogr., A* **1247** 146 (2012)
56. B L L Tan, D W Hawker, J F Müller, L A Tremblay, H F Chapman *Water Res.* **42** 404 (2008)
57. N Fattahi, Y Assadi, M R M Hosseini *J. Chromatogr., A* **1157** 23 (2007)
58. J Olejniczak, J Staniewski *Anal. Chim. Acta* **588** 64 (2007)
59. M Kawaguchi, Y Ishii, N Sakui, N Okanouchi, R Ito *Anal. Chim. Acta* **533** 57 (2005)
60. L Montero, S Conradi, H Weiss *J. Chromatogr., A* **1071** 163 (2005)
61. M Kawaguchi, N Sakui, N Okanouchi, R Ito, K Saito *J. Chromatogr., B* **820** 49 (2005)
62. S C Cunha, J O Fernandes *Talanta* **83** 117 (2010)
63. K Bielicka-Daszkiewicz, M Dkbicka, A Voelkel *J. Chromatogr., A* **1052** 233 (2004)
64. S Nakamura, S Daishima *J. Chromatogr., A* **1038** 291 (2004)
65. R-S Zhao, C-G Cheng, J-P Yuan, T Jiang, X Wang *Anal. Bioanal. Chem.* **387** 687 (2007)
66. M Kawaguchi, K Inoue, M Yoshimura *J. Chromatogr., A* **1041** 19 (2004)
67. M Llompart, M Lourido, P Landín, C García-Jares, R Cela *J. Chromatogr., A* **963** 137 (2002)
68. J L Pérez Pavón, A M Casas Ferreira, M E Fernández Laespada, B M Cordero *J. Chromatogr., A* **1216** 1192 (2009)
69. J Regueiro, M Llompart, E Psillakis, J C Garcia-Monteagudo, C Garcia-Jares *Talanta* **79** 1387 (2009)
70. J Regueiro, E Becerril, C Garcia-Jares, M Llompart *J. Chromatogr., A* **1216** 4693 (2009)
71. E Priego-López, M D Luque de Castro *Chromatographia* **57** 513 (2003)
72. A Prichodko, E Janenaite, V Smitiene, V Vickackaite *Acta Chromatogr.* **24** 589 (2012)
73. M Kawaguchi, R Ito, N Okanouchi, K Saito, H Nakazawa *J. Chromatogr., B* **870** 98 (2008)
74. R Ito, M Kawaguchi, H Honda *J. Chromatogr., B* **872** 63 (2008)
75. M Kawaguchi, R Ito, N Endo, N Okanouchi, N Sakui *J. Chromatogr., A* **1110** 1 (2006)
76. R J Argauer *Anal. Chem.* **40** 122 (1968)
77. Y A Andreev, M S Chernov'yants *J. Anal. Chem.* **65** 1021 (2010) [*Zh. Anal. Khim.* **65** 1046 (2010)]
78. V E Kirichenko, K I Pashkevich *Analitika Kontrol* (1) 16 (1998)
79. J B Green, S K-T Yu, R P Vrana *J. High Res. Chromatogr.* **17** 439 (1994)
80. S Dilli, K Robards *J. Chromatogr., A* **133** 363 (1977)
81. A T Shulgin *Anal. Chem.* **36** 920 (1964)
82. H-B Lee, T E Peart, M L Svoboda *J. Chromatogr., A* **1094** 122 (2005)
83. A Azzouz, E Ballesteros *J. Chromatogr., A* **1360** 248 (2014)
84. E Watson, S Wilk, J Roboz *Anal. Biochem.* **59** 441 (1974)
85. N Migowska, M Caban, P Stepnowski, J Kumirska *Sci. Total Environ.* **441** 77 (2012)
86. L L Lamparski, T J Nestrick *J. Chromatogr., A* **156** 143 (1978)

87. G Bengtsson *J. Chromatogr. Sci.* **23** 397 (1985)
88. O Lerch, P Zinn *J. Chromatogr., A* **991** 77 (2003)
89. M J Bartels, K A Brzak, G A Bormett *J. Chromatogr., B* **703** 97 (1997)
90. J Yang, H Li, Y Ran, K Chan *Chemosphere* **107** 439 (2014)
91. S Boitsov, S Meier, J Klungsøyr, A Svardal *J. Chromatogr., A* **1059** 131 (2004)
92. S Meier, J Klungsøyr, S Boitsov, T Eide, A Svardal *J. Chromatogr., A* **1062** 255 (2005)
93. H-B Lee *J. Chromatogr., A* **457** 267 (1988)
94. C Brede, I Skjevrak, H Herikstad *J. Chromatogr., A* **983** 35 (2003)
95. J S Thomson, J B Green, T B McWilliams, S K-T Yu *J. High Res. Chromatogr.* **17** 415 (1994)
96. G Skarping, L Renman, C Sangö, L Mathiasson, M Dalene *J. Chromatogr., A* **346** 191 (1985)
97. C Kutzer, B Branner, W Zwickenpflug, E Richter *J. Chromatogr. Sci.* **35** 1 (1997)
98. M Longo, A Cavallaro *J. Chromatogr., A* **753** 91 (1996)
99. J Forehand, G Dooly, S Moldoveanu *J. Chromatogr., A* **898** 111 (2000)
100. S Mishra, V Singh, A Jain, K K Verma *Analyst* **126** 1663 (2001)
101. D E Bradway, T Shafik *J. Chromatogr. Sci.* **15** 322 (1977)
102. P Hušek *J. Chromatogr., B* **717** 57 (1998)
103. P Hušek, P Šimek *Curr. Pharm. Anal.* **2** 23 (2006)
104. S Luo, L Fang, X Wang, H Liu, G Ouyang *J. Chromatogr., A* **1217** 6762 (2010)
105. M-J Paik, Y Choi, K-R Kim *Anal. Chim. Acta* **560** 218 (2006)
106. Y C Fiamegos, C D Stalikas *Anal. Chim. Acta* **597** 32 (2007)
107. M K R Mudiam, R Jain, V K Dua, A K Singh, V P Sharma *Anal. Bioanal. Chem.* **401** 1695 (2011)
108. T Henriksen, B Svensmark, B Lindhardt, R K Juhler *Chemosphere* **44** 1531 (2001)
109. M Vincenti, F Fasano, M C Valsania, P Guarda, S D Richardson *Anal. Bioanal. Chem.* **397** 43 (2010)
110. M Vincenti, S Biazzi, N Ghiglione, M C Valsania, S D Richardson *J. Am. Soc. Mass Spectrom.* **16** 803 (2005)
111. V Maurino, C Minero, E Pelizzetti, S Angelino, M Vincenti *J. Am. Soc. Mass Spectrom.* **10** 1328 (1999)
112. M Akyüz, S Ata *J. Chromatogr. A* **1129** 88 (2006)
113. K R Kim, M J Paik, J H Kim, S W Dong, D H Jeong *J. Pharm. Biomed. Anal.* **15** 1309 (1997)
114. A Dasgupta *J. Chromatogr. B* **716** 354 (1998)
115. N N Sirotkina, M N Marunyak, V S Dobrov *Gigien. Sanitariya* (9) 65 (1985)
116. A Krämer, J Angerer *Fresenius' J. Anal. Chem.* **351** 327 (1995)
117. A Diaz, F Ventura, M T Galceran *Anal. Bioanal. Chem.* **386** 293 (2006)
118. A Diaz, F Ventura, M T Galceran *Anal. Chem.* **74** 3869 (2002)
119. S Nakamura, M Takino, S Daishima *Analyst* **126** 835 (2001)
120. Z Kuklenyik, J Ekong, C D Cutchins, L L Needham, A M Calafat *Anal. Chem.* **75** 6820 (2003)
121. R-C Duca, G Salquebre, E Hardy, B M R Appenzeller *J. Chromatogr., B* **955 – 956** 98 (2014)
122. Y Liu, B Wen, X Shan *Talanta* **69** 1254 (2006)
123. Y Yoshimura, J W Brock, T Makino, H Nakazawa *Anal. Chim. Acta* **458** 331 (2002)
124. J-L Zhao, G-G Ying, L Wang, J-F Yang, X-B Yang *Sci. Total Environ.* **407** 962 (2009)
125. J N Seiber, D G Crosby, H Fouda, C J Soderquist *J. Chromatogr., A* **73** 89 (1972)
126. I C Cohen, J Norcup, J H A Ruzicka, B B Wheals *J. Chromatogr., A* **44** 251 (1969)
127. M Lehtonen *J. Chromatogr., A* **202** 413 (1980)
128. A Llop, E Pocurull, F Borrull *J. Chromatogr., A* **1217** 575 (2010)
129. J Chiang *Talanta* **75** 70 (2008)
130. R Haas, T C Schmidt, K Steinbach, E V Löw *Fresenius' J. Anal. Chem.* **359** 497 (1997)
131. T Zimmermann, W J Ensinger, T C Schmidt *Anal. Chem.* **76** 1028 (2004)
132. T C Schmidt, M Less, R Haas, E V Löw, K Steinbach *J. Chromatogr., A* **810** 161 (1998)
133. X Lamani, S Horst, T Zimmermann,T C Schmidt *Anal. Bioanal. Chem.* **407** 241 (2015)
134. J March *Advanced Organic Chemistry. Reactions: Mechanisms and Structure* (New York: Wiley, 2001)
135. V Singh, M Gupta, A Jain, K K Vermas *J. Chromatogr., A* **1010** 243 (2003)
136. N Sharma, A Jain, K K Verma *Anal. Methods* **3** 970 (2011)
137. Y C Fiamegos, A-P Kefala, C D Stalikas *J. Chromatogr., A* **1190** 44 (2008)
138. A E Agronomov *Izbrannye Glavy Organicheskoi Khimii* (Selected Chapters of Organic Chemistry) (Moscow: Khimiya, 1990)
139. H Becker, W Berger, G Domschke *et al. Organicum* (Berlin: VEB Deutscher Verlag der Wissenschaften, 1976)
140. P T Sukhanov, Ya I Korenman *Kontsentrirovanie i Opredelenie Fenolov* (Preconcentration and Determination of Phenols) (Voronezh: State Technology Academy, 2005)
141. I M Korenman *Ekstraktsiya Organicheskikh Veshchestv* (Extraction of Organic Compounds) (Gorkii: Gorkii State University, 1973)
142. A Zlatkis, C F Poole *Journal Chromatography Library: Electron Capture* (New York: Elsevier, 1981)
143. I V Gruzdev, M V Alferova, B M Kondratenok, I G Zenkevich *J. Anal. Chem* **66** 955 (2011) [*Zh. Anal. Khim.* **66** 1073 (2011)]
144. I V Gruzdev, M V Alferova, B M Kondratenok *Izv. Komi NTs UrO RAN* **4** 16 (2010)
145. I V Gruzdev, B M Kondratenok *Zavod. Lab.* **78** 14 (2012)
146. I V Gruzdev, M V Filippova, I G Zenkevich, B M Kondratenok *Russ. J. Appl. Chem.* **84** 1748 (2011) [*Zh. Prikl. Khim.* **84** 1656 (2011)]
147. I V Gruzdev, I M Kuzivanov, I G Zenkevich, B M Kondratenok *Russ. J. Appl. Chem.* **85** 1355 (2012) [*Zh. Prikl. Khim.* **85** 1440 (2012)]
148. V G Zaikin, A V Varlamov, A I Mikaya, N S Prostakov *Osnovy Mass-Spektrometrii Organicheskikh Soedinenii* (Fundamentals of Mass-Spectrometry of Organic Compounds) (Moscow: Nauka, 2001)
149. T C Schmidt, R Haas, K Steinbach, E V Löw *Fresenius' J. Anal. Chem.* **357** 909 (1997)
150. T C Schmidt, R Haas, E Löw, K Steinbach *Chromatographia* **48** 436 (1998)
151. T C Schmidt, M Leß, R Haas, E V Löw, K Steinbach *Int. J. Environ. Anal. Chem.* **74** 25 (1999)
152. A E Dados, C D Stalikas, G A Pilidis *Chromatographia* **59** 335 (2004)
153. R C C Wegman, G A L De Korte *Int. J. Environ. Anal. Chem.* **9** 1 (1981)
154. L I Kosychenko, L E Izoriya, L V Stupchenko *Gigien. Sanitariya* **6** 71 (1990)
155. Y Hoshika, G Muto *J. Chromatogr., A* **179** 105 (1979)
156. V I Ksenzenko, D S Stasinevich *Khimiya i Tekhnologiya Broma, Ioda i ikh Soedinenii* (Chemistry and Technology of Bromine, Iodine and Their Compounds) (Moscow: Khimiya, 1995)
157. I V Gruzdev, B M Kondratenok *Zavod. Lab.* **75** 12 (2009)
158. K Reddy-Noone, A Jain, K Verma *Talanta* **73** 684 (2007)
159. Y I Korenman, I V Gruzdev, B M Kondratenok *J. Anal. Chem.* **56** 166 (2001) [*Zh. Anal. Khim.* **56** 188 (2001)]
160. I V Gruzdev, I M Kuzivanov, I G Zenkevich, B M Kondratenok *J. Anal. Chem.* **68** 161 (2013) [*Zh. Anal. Khim.* **68** 175 (2013)]
161. E Matisová, S Skrabáková *J. Chromatogr., A* **707** 145 (1995)

162. C Molins-Legua, P Campins-Falcu *Anal. Chim. Acta* **546** 206 (2005)
163. P D Morais, T Stoichev, M C P Basto, M T S D Vasconcelos *Talanta* **89** 1 (2012)
164. S Koning, H-G Janssen, U A T Brinkman *Chromatographia* **69** 33 (2009)
165. A Spietelun, L Marcinkowski, M de la Guardia, J Namieśnik *J. Chromatogr., A* **1321** 1 (2013)
166. D A Lambropoulou, I K Konstantinou, T A Albanis *J. Chromatogr., A* **1152** 70 (2007)
167. G Ouyang, J Pawliszyn *Anal. Bioanal. Chem.* **386** 1059 (2006)
168. J B Quintana, I Rodríguez *Anal. Bioanal. Chem.* **384** 1447 (2006)
169. M Rezaee, Y Yamini, M Faraji *J. Chromatogr., A* **1217** 2342 (2010)
170. L Xu, C Basheer, H K Lee *J. Chromatogr., A* **1152** 184 (2007)
171. F David, P Sandra *J. Chromatogr., A* **1152** 54 (2007)
172. C Basheer, H K Lee *J. Chromatogr., A* **1057** 163 (2004)
173. H Bagheri, E Babanezhad, F Khalilian *Anal. Chim. Acta* **616** 49 (2008)
174. M A Farajzadeh, N Nouri *Talanta* **99** 1004 (2012)
175. M Polo, M Llompart, C Garcia-Jares, G Gomez-Noya, M-H Bollain *J. Chromatogr., A* **1124** 11 (2006)
176. M Saraji, M Bakhshi *J. Chromatogr., A* **1098** 30 (2005)
177. A Jain, K Reddy-Noone, A K K V Pillai *Anal. Chim. Acta* **801** 48 (2013)

[a] — *J. Water Chem. Technol. (Engl. Transl.)*
[b] — *J. Anal. Chem. (Engl. Transl.)*