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Review

Derivatization reactions for the determination of amines by gas chromatography and their applications in environmental analysis

Hiroyuki Kataoka

Faculty of Pharmaceutical Sciences, Okayama University, Tsushima, Okayama 700, Japan

Abstract

The environmental analysis of amines is important to preserve human health because these compounds often have toxic effects. Gas chromatography (GC) of free amines is generally unsatisfactory owing to the adsorption and decomposition of the solutes on the column. Derivatization of amines is employed to reduce the polarity and to improve the GC properties. Derivatization reactions for the determination of amines by GC are reviewed with respect to reactivity, selectivity and sensitivity. Their applications to the determination of individual amines, ammonia and N-nitrosamines in various environmental samples are also described.

Keywords: Reviews; Derivatization, GC; Environmental analysis; Amines; Ammonia; Nitrosamines

Contents

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1. Introduction

1.1. Amines from environmental sources

As environmental issues and global environmental changes are generating an increasing amount of attention world-wide, the occurrence and determination of amines have received a great deal of attention in recent years. These amines occur in a number of ambient environments such as air, water, soil and foods, and are a source of serious social and hygienic problems [1].

Aliphatic and aromatic mono-, di- and polyamines are naturally occurring compounds formed as metabolic products in microorganisms, plants and animals, in which the principal routes of amine formation include the decarboxylation of amino acids, amination of carbonyl compounds and degradation of nitrogen-containing compounds [2–7]. These amines are also widely used as raw materials or at an intermediate stage in the manufacture of industrial chemicals, e.g., pesticides, medicines, dyestuffs, polymers, surfactants, cosmetics and corrosion inhibitors [1,8,9].

These amines are discharged into the atmosphere and water from anthropogenic sources such as cattle feeds and near livestock buildings [10–12], waste incineration [13], sewage treatment [13,14], automobile exhausts [15], cigarette smoke [16–18] and various industries [10,13,14, 19–21]. Presumably, a natural background level of amines also exists originating from animal wastes and microbiological activities [13].

Many amines have an unpleasant smell and are hazardous to health, i.e., as sensitizers and irritants to the skin, eye, mucous membranes and respiratory tract [21,22]. Some amines are also suspected to be allergenic [23] and mutagenic or carcinogenic [24] substances owing to their tendency for adsorption in tissues. Amines are not only toxic themselves but can also become toxic N-nitrosamines through chemical reactions with nitrosating agents such as nitrite or nitrate [25]. Recent developments in environmental carcinogenesis have demonstrated that N-nitrosamines are potentially carcinogenic substances that lead to a wide variety of tumours in many animals [25–27]. In general, the nitrosation of amines occurs in the human diet [25], the environment [28] and in vivo in the stomach or small intestine of experimental animals [29–32]. The reaction of nitrosating agents with primary amines produces short-lived alkylating species that react with other compounds in the matrix to generate products (mainly alcohols) devoid of toxic activity at the relevant concentrations. The nitrosation of secondary amines leads to the formation of stable N-nitrosamines while that of tertiary amines produces a range of labile N-nitroso products [33]. Although the reaction pathways are uncertain, it has also been demonstrated in model experiments that amines react with NO_x and OH radicals in air to form nitrosamines and nitramines [13,27,34].

1.2. Derivatization of amines for gas chromatography

Gas chromatography (GC) has been widely used for amine analysis because of its inherent advantages of simplicity, high resolving power, high sensitivity, short analysis time and low cost. In general, amines can be separated on strongly basic stationary phases as their free forms. The samples are analysed after addition of alkali, either by direct injection [35–42] or by the headspace technique [43–46], or they are extracted into an organic solvent before analysis [47,48]. Direct or headspace analyses of samples minimize sample preparation, thereby reducing sample contamination. Several packed columns deactivated with potassium hydroxide, trimethylchlorosilane or ammonia in the carrier gas have been used for the determination of free amines [36,42,49]. However, many of these techniques are limited to parts per million level determinations. Detection limits can be improved by concentrating the aqueous sample before measurement or by using a selective detector. For the former technique, steam distillation [50], vacuum distillation [51,52], treatments with absorber columns [53,54] or Sep-Pak cartridges [12] and membrane diffusion techniques [55–57] have

been investigated. For the last technique, nitrogen–phosphorus thermionic detection (NPD) [12,37,39,44,47,55,56,58,59], chemiluminescent detection (CLD) [43,52] and GC–mass spectrometry (GC–MS) [41,46] have been investigated. By using these methods, sub-nanogram detection limits have been achieved. However, the GC of free amines generally has some inherent problems related to the difficulty in handling low-molecular-mass amines because of their high water solubility and high volatility. Therefore, these amines are difficult to extract from water and are not easily chromatographed owing to their polarity. Furthermore, amines tend to be adsorbed and decomposed on the columns, and readily give tailed elution peaks, ghosting phenomena and low detector sensitivity [60–63]. The adsorption tendency in the analytical systems, i.e., in sample vessels, injection systems, glass-wool and GC columns, is in the order primary > secondary > tertiary amines, and it is generally more difficult to chromatograph aliphatic than aromatic amines [64].

Derivatization is a popular method for overcoming the above problems. Derivatization methods have been employed to reduce the polarity of the amino group and to improve GC properties. Derivatization reactions, often selective for amine type (primary, secondary, tertiary), have also been used to improve the detection and separation of these amines. Many derivatization reagents for GC analyses of amines by flame ionization detection (FID), electron-capture detection (ECD), flame photometric detection (FPD), NPD, CLD with a modified thermal energy analyser (TEA) and GC–MS with selected-ion monitoring (SIM) have been investigated. Acylation, silylation, dinitrophenylation and the formation of different condensation products (Schiff base) are common procedures. Furthermore, permethylation and the formation of carbamates, sulphonamides and phosphonamides have also been investigated. These derivatization reactions are described in detail in this paper. Chemical derivatizations of amines and their applications in GC have also been reviewed by Ma and Ladas [65], Knapp [66], Drozd [67] and Blau and Halket [68].

1.3. Objective and scope of the review

This review is concerned with the utilization of chemical derivatization and GC analysis for the determination of amines in environmental samples. The review consists of following two main parts. In the first part (Section 2), general aspects of the derivatization of amino groups for GC analysis are surveyed according to their reaction type. In the second part (Section 3), applications of the derivatization reactions in environmental analysis are considered according to the amine type. The review covers not only aliphatic and aromatic primary, secondary and tertiary amines but also ammonia and N-nitrosamines, which often occur in various environments as very toxic compounds. On the other hand, biogenic amines such as catecholamines, phenylethylamine and indolalkylamines, carcinogenic heterocyclic amines and other nitrogen-containing compounds are not covered.

2. Derivatization reactions

The GC of free amines, without special modification to the column, is unsatisfactory owing to the adsorption and decomposition of the solute, resulting in peak tailing and losses. Derivatization of amines may be employed not only to reduce the polarity but also to improve the volatility, selectivity, sensitivity and separation of these amines. The commonly used derivatization reactions for GC analysis of amines are listed in Table 1.

2.1. Acylation

Acylation is one of the most popular derivatization reactions for primary and secondary amines, and this is top of the list of available methods in Table 1. Acid anhydrides [16,17, 64,69–80], acyl chlorides [74,75,81–83], acylimidazoles [84,85] and acylamides [86,87] have been used as acylating reagents (Fig. 1). These reagents easily react with amino groups under mild reaction conditions. Many of them

Table 1
Derivatization reactions for gas chromatographic determination of amines

Reagent	Amine type[a]	Detection[b] (detection limit)	Ref.
Acylation			
Trifluoroacetic anhydride	P, S, A	I (4–5 ng), E (30 pg), M (1 ng)	[69–74,128]
Pentafluoropropionic anhydride	P, S	N (4–20 pg), E, M (1 ng)	[16,17,64,69–78]
Hexafluorobutyric anhydride	P, S	N (4–20 pg), E (0.1–6 pg), M (1 ng)	[69,73–77,79,80]
Chloro- or dichloroacetic anhydride	P	E (0.2–1.5 ng), M (1 ng)	[73, 74]
Trichloroacetyl chloride	P, S	E (0.2–2 ng)	[74]
Pentafluorobenzoyl chloride	P, S	N (0.1 ng), E (10 pg)	[74,81–83]
Heptafluorobutylimidazole	P, S	E (0.3–0.4 ng)	[84,85]
N-Methylbis(trifluoroacetamide)	P, S	I (80 ng), M (1 ng)	[54,86,87]
Silylation			
N,O-Bis(trimethylsilyl)trifluoroacetamide	P, S	M (4–20 pg)	[88]
N-Methyl-N-(*tert.*-butyldimethylsilyl)acetamide	P, S	M	[89]
Pentafluorophenyldimethylsilyl reagents	P, S	I (5 ng), E (5 pg)	[90]
Dinitrophenylation			
2,4-Dinitrofluorobenzene	P, S	I (1–2 ng), E (20 pg), M (0.3–4 ng)	[91–96]
2,4-Dinitrobenzenesulphonic acid	P, S, A	I (50–100ng)	[97–99]
Permethylation			
Formamide–sodium borohydride	P, S	N (0.1 ng)	[100, 101]
Schiff base formation			
Benzaldehyde	P	I (60 ng)	[61]
Furfural	P	I	[103]
2-Thiophenealdehyde	P	S	[104]
Pentafluorobenzaldehyde	P	E (20 pg), M (5 ng)	[105–108]
Dimethylformamide dimethyl acetal	P, A	S (25 pg)	[109,129]
Carbamate formation			
Diethylpyrocarbonate	P, A	I	[110]
Ethyl chloroformate	P, S, T	I, N (3–10 pg), M (1.5 pg)	[112–114,119]
Isobutyl chloroformate	P, S	I, N (3–20 pg), S (40 pg), M (2 pg)	[113,115,116]
Amyl chloroformate	P, S	I	[111]
2,2,2-Trifluoroethyl chloroformate	P, S	N (10 pg), M (10 pg)	[117]
Pentafluorobenzyl chloroformate	P, S, T	E (3 pg)	[120]
Sulphonamide formation			
Benzenesulphonyl chloride	P, S, A	S (6–25 pg), C (60 pg), M (5–30 pg)	[33,60,62,122–126,128,129]
p-Toluenesulphonyl chloride	S	I (10 ng), M (45 pg)	[63,127]
Phosphoamide formation			
Dimethylthiophosphinic chloride	P	N (0.5 pg)	[130]
Dimethylthiophosphoryl chloride	P, S	I, P	[131,134]
Diethylthiophosphoryl chloride	P, S, N	P (3–15 pg)	[18,132,133]

[a] P = primary amine; S = secondary amine; T = tertiary amine; A = ammonia; N = nitrosamine.
[b] I = FID; N = NPD; S = FPD (S mode); P = FPD (P mode); E = ECD; C = CLD; M = GC–MS–SIM.

also react with hydroxyl, phenol and thiol groups [65–68].

In the reactions of amines with acid anhydrides and acyl chlorides, it is usually necessary to remove excess reagent and by-product acid, because these compounds damage the GC column. These reagents are often used with bases such as pyridine, trimethylamine and triethylamine, which not only are excellent solvents but also act as catalysts to promote smooth reactions and as acceptors for by-product acids. On the other hand, the derivatives prepared with

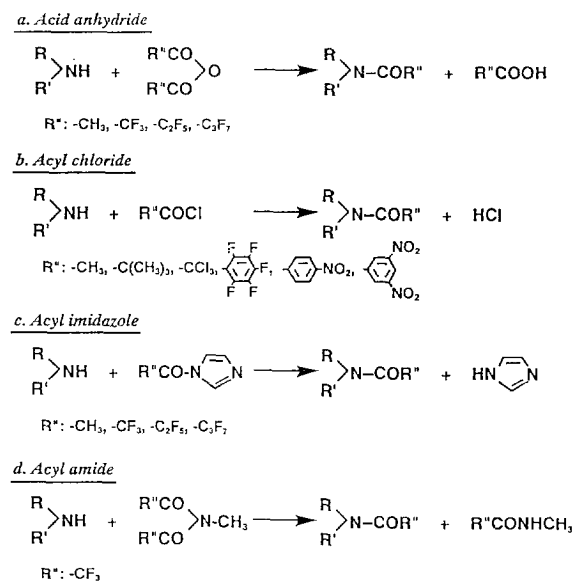

Fig. 1. Acylation of primary and secondary amines. R = alkyl or aryl; R′ = hydrogen, alkyl or aryl.

acylimidazoles can normally be analysed without removal of excess reagent and by-product imidazole. Acylimidazoles have been used in the derivatization of some drugs [84,85]. N-Methylbis(trifluoroacetamide) (MBTFA) is very volatile and by-product N-methyltrifluoroacetamide does not cause column damage. MBTFA can be useful for N-selective acylation after trimethylsilylation of hydroxyamino compounds [86].

Among these acylating reagents, fluorinated compounds are widely used to introduce electron-capturing properties. ECD gives a greatly enhanced response to halogenated derivatives, and the sensitivity of detection increases in the order F < Cl < Br < I. However, volatility and stability tend to decline in this order, so that fluoro derivatives are the most widely used in practice. Although fluorinated acyl derivatives are more volatile than the corresponding non-fluorinated acyl derivatives, there is generally little difference in retention times for trifluoroacetyl (TFA) versus pentafluoropropionyl (PFP) and heptafluorobutyryl (HFB) derivatives. The ECD response generally increases with increasing fluorine content. Mono-, di- and trichloroacetyl derivatives also possess higher ECD responses, but pentafluorobenzoyl (PFB) derivatives possess still higher ECD responses. The ECD responses for chloro and fluoro derivatives of anilines have been compared by Lee [73]. However, chloroacetyl and PFB derivatives tend to be less volatile than the smaller perfluoroacyl derivatives, and the reactions of lower aliphatic amines with PFB-CL give white, curdy precipitates, which may be the hydrochlorides of amines, so that these reactions are not quantitative [10]. Although derivatives containing a nitro group are also sensitive to ECD, they are generally much less volatile, and tend to give tailing chromatographic peaks, so that their use in GC analysis is limited. On the other hand, NPD, which is very specific to nitrogen and phosphorus compounds, has been widely used to detect picogram levels of amines. The detection limits of acyl derivatives depend essentially on the nitrogen content of the derivatives when using NPD. Although GC–MS-SIM is also specific and sensitive to each amine, the sensitivity of this detection method is generally lower than that of ECD and NPD (Table 1).

2.2. Silylation

The amino group is not very reactive to silylating reagents, and its conversion into a silyl derivative is difficult. By using stronger silylating reagents and catalysts, however, the silyl derivatives of amines can be prepared. N,O-Bis(trimethylsilyl)acetamide (BSA), N,O-bis(trimethylsilyl)trifluoroacetamide (BSTFA) [88], N-methyl-N-(*tert*-butyldimethylsilyl)trifluoroacetamide (MTBSTFA) [89] and pentafluorophenyldimethylsilyl (flophemesyl) reagents [90] have been used as silylating reagents (Fig. 2). These reagents react not only with amino groups but also hydroxyl and carboxyl groups under anhydrous reaction conditions. The ease of reaction with these reagents is generally in the order alcohols > phenols > carboxylic acids > amines > amides, and it is higher for primary than secondary amines. The addition of trimethylchlorosilane as a catalyst will generally ensure the effective derivatization of amino groups.

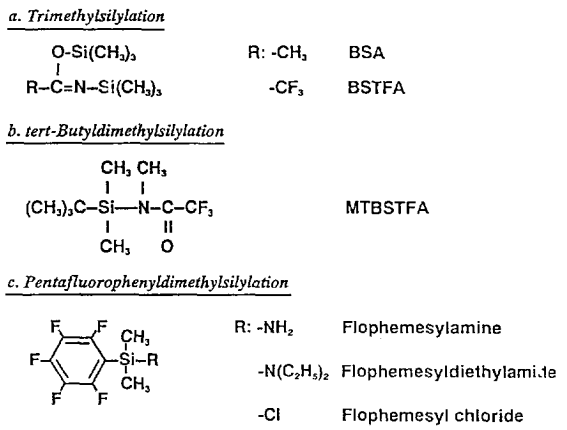

Fig. 2. Silylating reagents for primary and secondary amines.

In trimethylsilylation, BSTFA is a powerful reagent compared with BSA, and the by-product of the reagent is volatile, so that it does not interfere in analysis. However, the N-trimethylsilyl (TMS) derivatives produced by the reaction with these reagents are unstable to moisture. An additional problem in the silylation of amines arises from the possibility of replacing both protons in primary amines, resulting in the formation of mono- and di-TMS products. On the other hand, the N-*tert.*-butyldimethylsilyl (*t*-BDMS) derivatives produced by the reaction with MTBSTFA are about 10^4 times more stable to hydrolysis than the corresponding TMS derivatives, because the bulky *tert.*-butyl group of the *t*-BDMS derivative protects the silyl group from moisture. The sensitivity of *t*-BDMS derivatives is 10 and 100 times higher for mono-*t*-BDMS and di-*t*-BDMS derivatives, respectively, than that of TMS derivatives [89]. Flophemesyl reagents also react with alcohols, phenols, carboxylic acids and amines, and the flophemesyl derivatives are sensitive to ECD. The sequence of silyl donor power of reagents in pyridine solution is flophemesylamine > flophemesyl chloride > flophenesyldiethylamide.

2.3. Dinitrophenylation

Dinitrophenylation, which can be performed in aqueous media, is used for the derivatization of primary and secondary amines. 2,4-Dinitrofluorobenzene (DNFB) [91–96] and 2,4-dinitrobenzenesulphonic acid (DNBS) [97–99] have been used as dinitrophenylating reagents (Fig. 3). Dinitrophenyl (DNP) derivatives produced by reaction with these reagents are sensitive to ECD and they are particularly suitable for low-molecular-mass amines that have inconveniently short retention times. Although the reaction procedure with DNFB is simple, this reagent irritates the skin and occasionally causes allergenic dermatoses [60]. DNBS is water soluble and the resulting DNP derivatives of amines are soluble in organic solvents. Therefore, the derivatives can be easily separated from excess of reagent by solvent extraction after derivatization. Another important advantage of DNBS is its greater specificity for the amino group, whereas DNFB reacts with thiol, imidazole and hydroxyl groups along with amino groups. However, DNBS generally reacts more slowly than does DNFB, so that longer reaction times or more strongly alkaline conditions may be required to complete the reaction.

2.4. Permethylation

Permethylation, which converts primary and secondary amines into tertiary amines, can be performed in aqueous solution using formaldehyde–sodium borohydride and has been applied to the determination of polyamines [100,101]. Permethyl derivatives eliminate the polar NH groups but retain the troublesome adsorptive properties of tertiary amines.

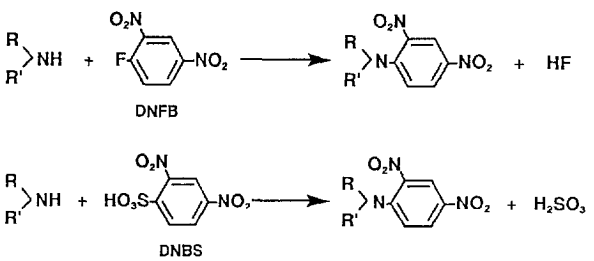

Fig. 3. Dinitrophenylation of primary and secondary amines. R = alkyl or aryl; R' = hydrogen, alkyl or aryl.

2.5. Schiff base formation

Schiff base-type reactions are employed to condense primary amines with a carbonyl compound (Fig. 4a). Acetone, 1,1,1-trifluoroacetone, methyl isobutyl ketone, cyclopentanone, cyclohexanone and cycloheptanone have been used for a series of long-chain and alicyclic monoamines, aliphatic diamines and aromatic amines [69,102]. Benzaldehyde [61], furfural [103], 2-thiophenealdehyde [104] and pentafluorobenzaldehyde (PFBA) [105–108] have also been used for low-molecular-mass amines. The condensation reactions with these reagents proceed rapidly in aqueous medium (usually an alcohol or acetic acid) at room temperature or on warming, and Schiff bases are obtainable in good yields. These carbonyl reagents are selective to primary amines, and the by-product water does not undergo secondary reactions in the reaction systems involved. However, excess reagents, which often disturb the amine analysis, have to be removed in a separate clean-up step. Selective and sensitive methods based on the formation of sulphur and fluorine-containing Schiff bases of primary amines have been developed for GC with FPD [104] and ECD [105], respectively. Although the sensitivity of FPD is much higher than that of FID for the derivatives of the C_1–C_4 amines, the sensitivities for the derivatives of the C_5–C_7 amines are similar [104].

Furthermore, dimethylformamide (DMF) dialkyl acetal forms a Schiff base-type derivative with primary amines [109] (Fig. 4b), but this reagent also reacts with carboxyl groups of fatty acids and amino acids to give the corresponding esters.

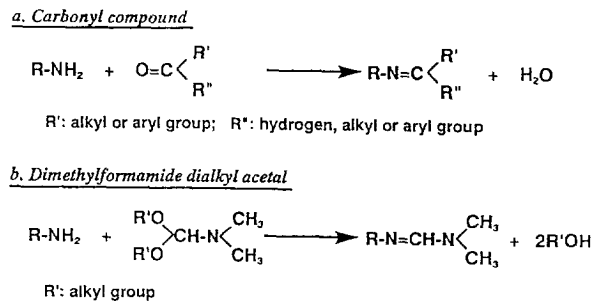

Fig. 4. Schiff base-type condensation reactions of primary and secondary amines.

2.6. Carbamate formation

Carbamate derivatives, generally made by Schotten–Buamann-type procedures, are useful for the determination of primary, secondary and tertiary amines. Diethyl pyrocarbonate (DEPC) [110] and alkyl chloroformates [111–118] have been used as reagents for this purpose (Fig. 5). The reaction of amines with these reagents can be easily performed in aqueous alkaline media and the resulting carbamate derivatives have good GC properties. Alkyl chloroformates react with phenol, thiol and imidazole groups along with amino groups. As shown in Table 1, the carbamate derivatives from primary and secondary amines are selectively and sensitively determined by GC–NPD [113,114,117], GC–FPD [115], GC–MS [113,116,117] and GC–ECD [120]. On the other hand, tertiary amines, which tend to give tailing peaks on chromatograms owing to their polar nature, can be also converted into carbamate derivatives with alkyl chloroformate after dealkylation [119,120]. Treatment with an alkyl chloroformate can dis-

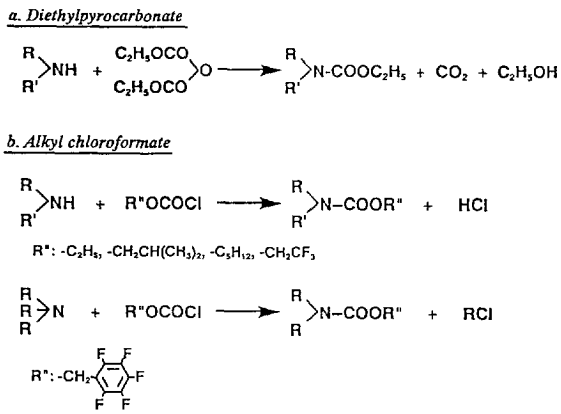

Fig. 5. Carbamate formation from primary, secondary and tertiary amines. R = alkyl or aryl; R′ = hydrogen, alkyl or aryl.

place the smallest of the alkyl groups to the nitrogen, particularly if it is a methyl group, to form a carbamate (Fig. 5b). This reaction proceeds in the presence of base catalyst sodium carbonate, but the yield is generally low. The carbamate derivatives obtained from tertiary amines by reaction with pentafluorobenzyl chloroformates are sensitively determined by GC–ECD [120].

2.7. Sulphonamide formation

As reported by Hinsberg [121], the reaction of amines with sulphonyl chloride is useful for the separation and identification of amine type, because sulphonamides derived from primary amines are soluble in alkaline solution and those from secondary amines are insoluble, and since tertiary amines do not react (Fig. 6). This reaction easily proceeds in aqueous alkaline media at room temperature. Benzenesulphonyl chloride (BSC) [33,60,63,122–126] and *p*-toluenesulphonyl chloride [63,127] have been used for the selective determination of low-molecular-mass primary and secondary amines. After benzenesulphonylation of amines, benzenesulphonyl (BS) derivatives of secondary amines are completely extracted into *n*-hexane in 50% potassium hydroxide–22.5% methanol solution, and remaining BS derivatives of primary amines in the aqueous layer are extracted into diethyl ether under acidic conditions [125]. These BS derivatives can be selectively and sensitively determined by GC–FPD [125,126]

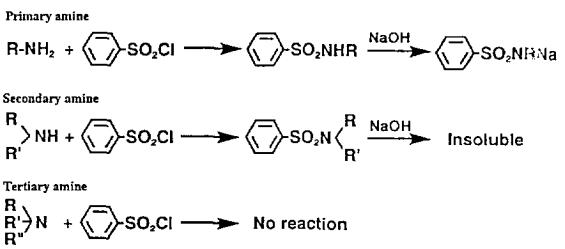

Fig. 6. Separation and identification of primary, secondary and tertiary amines by Hinsberg's method. R, R', R" = alkyl or aryl.

(Fig. 7), GC–NPD [127] and GC–CLD with modified TEA [33,62].

The BS derivatives of primary amines can also be determined by GC–ECD, these derivatives subsequently being converted into their N-TFA–N-BS derivatives by the reaction with trifluoroacetic anhydride (TFAA) [128]. This method is selective and sensitive to primary amines, because the BS derivatives of secondary amines do not react with TFAA.

Furthermore, ammonia is converted into its BS-dimethylaminomethylene derivative by a convenient procedure involving benzenesulphonylation with BSC and subsequent reaction with dimethylformamide dimethyl acetal, and is determined by GC–FPD [129]. This reaction is based on combination with both benzenesulphonylation (Fig. 6) and Schiff base-type condensation (Fig. 4b).

2.8. Phosphonamide formation

Primary aliphatic and aromatic amines react with dimethylthiophosphinic chloride in the presence of excess of triethylamine to give the corresponding N-dimethylthiophosphinic amides, which are determined by GC–NPD [130]. Although this method is highly sensitive, the preparation of the derivative requires a lengthy procedure and anhydrous conditions. On the other hand, the reaction of the amino group with dialkylthiophosphoryl chlorides can be performed rapidly in aqueous alkaline media [18, 131–134]. Although these reagents easily react with both primary and secondary amines, the N–P bond of the phosphorus amide is not as stable as the N–C and N–S bonds of the above derivatives. By using these reagents, a selective and sensitive method for the determination of aliphatic [18,132,133] and aromatic [134] amines by GC–FPD has been developed.

In particular, secondary amines can be selectively converted into their N-diethylthiophosphoryl (DETP) derivatives with diethyl chlorothiophosphate (DECTP) after treatment with *o*-phthaldialdehyde (OPA), because OPA react only with primary amino groups (Fig. 8). As shown in Fig. 9, primary amines are also deriva-

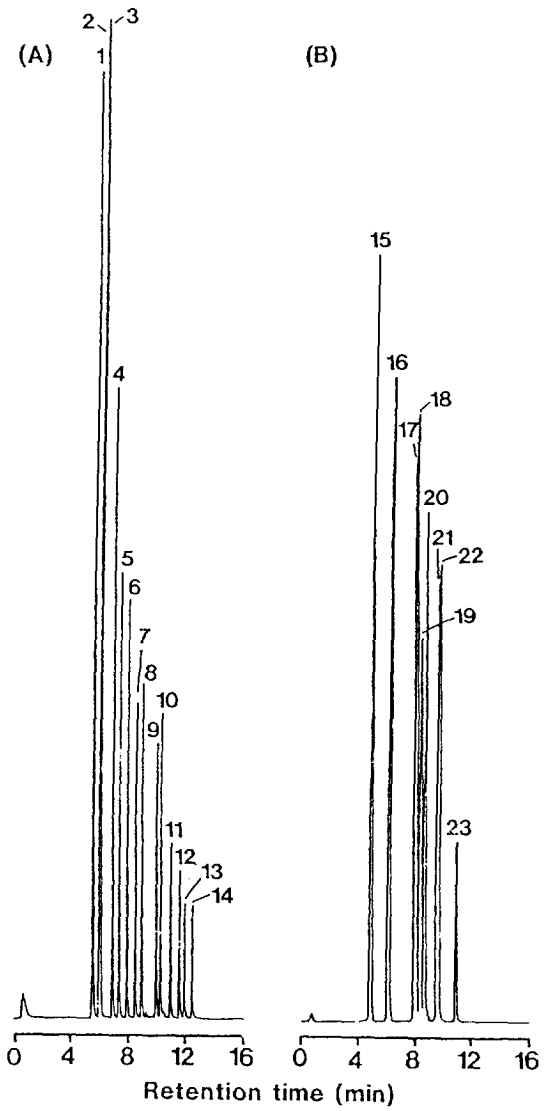

Fig. 7. Gas chromatograms obtained from benzenesulphonyl derivatives of (A) primary and (B) secondary amines. GC conditions: column, DB-1 (15 m × 0.53 mm I.D., 1.5 μm film thickness); column temperature, programmed at 10°C/min from 120 to 280°C; injection and detector temperatures, 290°C; nitrogen flow-rate, 10 ml/min; detector, flame photometric (S mode). Each peak represents 2 ng of amines. Peaks: 1 = methylamine; 2 = ethylamine; 3 = isopropylamine; 4 = *n*-propylamine; 5 = isobutylamine; 6 = *n*-butylamine; 7 = isoamylamine, 8 = *n*-amylamine; 9 = hexylamine; 10 = cyclohexylamine; 11 = heptylamine; 12 = benzylamine; 13 = octylamine; 14 = β-phenylethylamine; 15 = dimethylamine; 16 = diethylamine; 17 = dipropylamine; 18 = pyrrolidine; 19 = morpholine; 20 = piperidine; 21 = dibutylamine; 22 = hexamethyleneimine; 23 = N-methylbenzylamine.

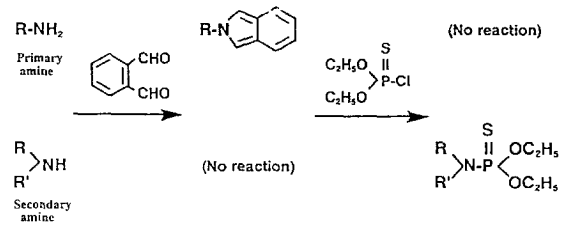

Fig. 8. Selective derivatization of primary and secondary amines with *o*-phthaldialdehyde and diethylthiophosphoryl chloride. R, R' = alkyl or aryl.

tized with DECTP without OPA pretreatment and detected by GC–FPD, but they are not detected at all with OPA pretreatment. On the other hand, secondary amines are detected irrespective of OPA pretreatment, because these amines do not react with OPA. Aromatic amines are detected as single and symmetrical peaks by capillary GC based on the preparation of N-dimethylthiophosphoryl derivatives of amines (Fig. 10). In these methods, excess reagents, which disturb the determination of low-molecular-mass amines, are removed by the reaction with cysteic acid before solvent extraction of the derivatives, because the dialkylthiophosphoryl derivative of cysteic acid is not extracted.

Furthermore, these reactions have been applied to the determination of N-nitrosamines, these amines being denitrosated with hydrobromic acid to produce the corresponding secondary amines and then derivatized with DECTP [18].

3. Applications in environmental analysis

Evidence for the potential health hazards of amines has been presented [21–24,135,136]. Amines from environmental sources can be toxic themselves or, more often, some of them can become toxic N-nitrosamines through chemical reactions with nitrite, nitrate, NO_x or OH radicals in the environment. It is therefore important to determine the concentration levels of these compounds in the environment. In this section, the GC of ammonia and N-nitrosamines, which

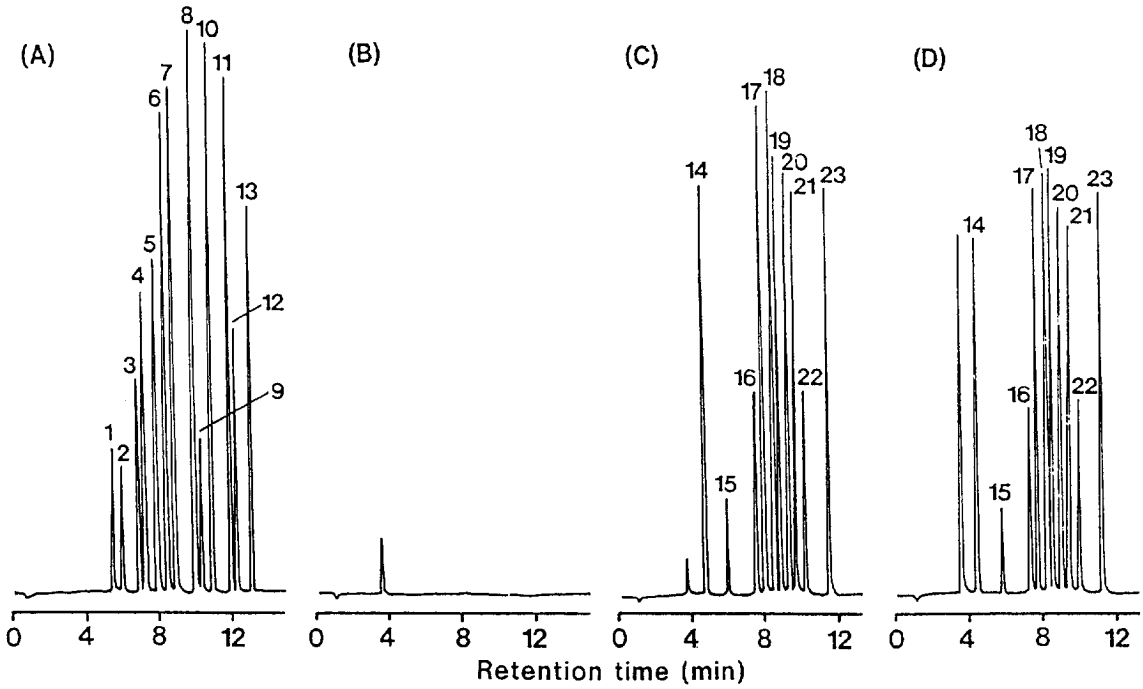

Fig. 9. Gas chromatograms obtained from N-diethylthiophosphoryl derivatives of primary and secondary amines. (A) Primary amines; (B) primary amines pretreated with OPA; (C) secondary amines; (D) secondary amines pretreated with OPA. GC conditions: column, DB-1701 (15 m × 0.53 mm I.D., 1.0 μm film thickness); column temperature, programmed at 10°C/min from 100 to 260°C; injection and detector temperatures, 280°C; nitrogen flow-rate, 10 ml/min; detector, flame photometer (P mode). Each peak represents 20 pmol of amines. Peaks: 1 = methylamine; 2 = ethylamine; 3 = propylamine; 4 = isobutylamine; 5 = *n*-butylamine; 6 = isoamylamine; 7 = *n*-amylamine; 8 = hexylamine; 9 = cyclohexylamine; 10 = heptylamine; 11 = octylamine; 12 = benzylamine; 13 = β-phenylethylamine; 14 = dimethylamine; 15 = diethylamine; 16 = dipropylamine; 17 = pyrrolidine; 18 = piperidine; 19 = morpholine; 20 = dibutylamine; 21 = hexamethyleneimine; 22 = N-methylcyclohexylamine; 23 = N-methylbenzylamine. Reproduced from Ref. [132].

often occur in various environments, are also described along with individual amine types.

3.1. Aliphatic primary and secondary amines

Low-molecular-mass aliphatic amines cause unpleasant odours due to the decay of foods and fish, and are hazardous to human health. These amines are also emitted from the living environment and various industries. Secondary amines such as dimethylamine and pyrrolidine are particularly important, because they are broadly distributed in various environments as precursors of carcinogenic N-nitrosamines.

Although GC determinations of aliphatic primary and secondary amines have been carried out in air [12,40,43,56], cigarette smoke [18], water [56,58,60,71,96,107] and soil [60], many of these methods have been used for free amines [12,40,42,43,46,55,56,58]. In particular, the trace determination of low-molecular-mass aliphatic amines in air has been performed with nitrogen-selective detection methods such as NPD, CLD and GC–MS by direct injection or the headspace technique. On the other hand, derivatization methods have also been used in water and soil samples [60,71,96,107], because these samples cannot be directly analysed.

Neurath et al. [71] reported the determination of 40 primary and secondary amines as their trifluoroacetamides in surface waters from rivers and swamps by GC–FID. High contents of C_1–C_3 aliphatic amines are found in these samples, but the contents of secondary amines are gener-

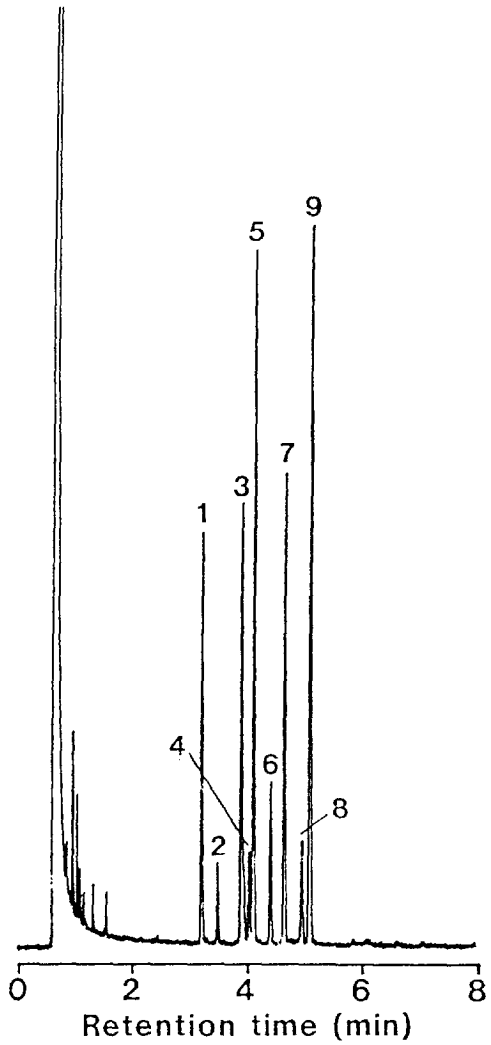

Fig. 10. Gas chromatogram obtained from N-dimethylthiophosphoryl derivatives of aromatic amines. GC conditions: column, DB-17 (15 m × 0.25 mm I.D., 0.25 μm film thickness); column temperature, programmed at 10°C/min from 180 to 220°C; injection and detector temperatures, 260°C; helium flow-rate, 1 ml/min; splitting ratio, 50:1; detector, flame ionization. Each peak represents 5 ng of amines. Peaks: 1 = aniline; 2 = *o*-toluidine; 3 = *m*-toluidine + *o*-ethylaniline; 4 = 2,5-dimethylaniline; 5 = *p*-toluidine; 6 = 2,4-dimethylaniline; 7 = *m*-ethylaniline; 8 = 2,3-dimethylaniline; 9 = *p*-ethylaniline.

ally below 15 ppb. Koga et al. [96] reported the determination of trace amoaunts of twelve aliphatic primary and secondary amines as their DNP derivatives in waters from sewage and rivers by GC–MS. By using this method, low-molecular-mass aliphatic amines in water samples can be determined in the range 1–3 ppb. Avery and Junk [107] reported the determination of trace amounts of seven aliphatic primary amines in tap and river waters and water from oil shale processing by GC–MS based on Schiff base formation with PFBA. This method is specific for primary amines and the detection limit is 10 ppb with no sample transfers or manipulations being necessary for sample volumes of 0.5 ml. Terashi et al. [60] reported the determination of eight primary and secondary amines in river water, sea water and sea sediment by GC–MS-SIM based on distillation of the sample under alkaline conditions and subsequent benzenesulphonylation. In this method, the detection limits of amines in water and sediment are 0.02–2 and 0.5–50 ppm, respectively. Kataoka et al. [18] reported the determination of secondary amines as their DETP derivatives in cigarette smoke by GC–FPD. This method is selective and sensitive to secondary amines, and the detection limits of amines are 0.05–0.2 pmol. By using this method, it was confirmed that dimethylamine, pyrrolidine, piperidine and morpholine occur in main- and sidestream smokes of cigarettes, and the contents of these amines in sidestream smoke are very high compared with those in mainstream smoke.

3.2. Aromatic primary and secondary amines

Aromatic amines such as aniline and its chlorinated analogues, phenylenediamine and diphenylamine are used in the manufacture of carbamate and urethane pesticides, dyestuffs, cosmetics and medicines. These amines are also employed in the rubber industry as antioxidants and antiozonants [138] and as components in epoxy and polyurethane polymers [139]. The toxicity of these amines to mammals and fish is well established [140,141]. Most of them are not only poisonous themselves but also may be converted into carcinogens such as N-nitroso compounds, naphthylamines, substituted phenylamines or benzidine analogues [142–144].

Although the GC determinations of aromatic

amines have been carried out in various environmental samples such as air [78], cigarette smoke [16,17,134] and waste water [59,134], most of these methods are based on the derivatization of amines with an acid anhydride. Skarping et al. [78] reported the determination of aniline and related aromatic amines in workplace air by GC–NPD. Air samples are collected in alkaline ethanol solutions and the amines are converted into the corresponding PFP amides by an extractive acylation procedure. The detection limit of this method is about 40–80 fmol. Pieraccini and co-workers [16,17] reported the determination of seventeen primary aromatic amines as their PFP amides in cigarette smoke and indoor air by GC–MS-SIM. Cigarette is smoked in a laboratory-made smoking machine and the amines in the main- and sidestream smokes are trapped in dilute hydrochloric acid. It was confirmed that sidestream smoke contains total levels of aromatic amines about 50–60 times higher than those of mainstream smoke, and some aromatic amines in ambient air such as offices and houses may be derived from considerable contamination of aromatic amines in sidestream smoke.

3.3. Tertiary amines

Low-molecular-mass aliphatic tertiary amines are important as industrial raw materials, and have an unpleasant smell and high toxicity. In particular, trimethylamine is found in a number of ambient environments [41,45,56,145,146], and is associated with the fish odour symdrome [147].

Determinations of aliphatic tertiary amines have been carried out in air [41,56], waters from industrial waste, sewage or rain [45,56,145,146] and river bottom sediments [45] by GC–FID, GC–NPD and GC–MS. However, most of these methods have been applied to free amines, and no method using derivatization for environmental analysis has been reported.

3.4. Ammonia

Ammonia arises mainly from natural sources by decomposition of organic matter containing nitrogen and from manufacturing process for industrial chemicals [148]. Ammonia is the principal atmospheric base responsible for aerosol formation and the neutralization of atmospheric acidity [149]. Therefore, the determination of ammonia in the atmosphere is important in studies of smog and acid rain formation. Ammonia is an irritant to the skin, respiratory tract and mucous membranes. Higher ammonia levels are therefore becoming a hygienic problem in indoor environments where industrial operations such as refrigeration or fertilizer manufacture are carried out. The short-term exposure limit for occupational exposure to ammonia is a time-weighted average of 35 ppm over a 15-min period, and yet the lower limit of human perception is 53 ppm [150]. Water pollution by ammonia often has a toxic influence on aquatic species.

Although GC determinations of ammonia have been carried out in air [40,43] and water [58,71,129] samples, many of these methods have been used for free ammonia by direct injection or the headspace technique. However, most of these methods give peak tailing owing to the polarity of ammonia. Neurath et al. [71] reported the simultaneous determination of ammonia and primary and secondary amines in surface waters from rivers and swamps. Ammonia is determined as trifluoroacetamide by GC–FID and its contents in these samples are in the range 30–700 ppm. On the other hand, Kataoka et al. [129] reported the determination of ammonia in river, lake, sea, sewage and pool water samples. Since the benzenesulphonamide derived from ammonia by benzenesulphonylation overlaps the BS derivative of methylamine on the chromatogram [126], it is additionally converted into its dimethylaminomethylene derivative with DMF dimethyl acetal, and then determined by GC–FPD. By using this method, ammonia in environmental samples can be selectively and sensitively analysed as a single and symmetrical peak, and the detection limit is about 25 pg.

3.5. N-Nitrosamines

It is well known that N-nitrosamaines are potent mutagenic and carcinogenic compounds

in human and laboratory animals, and are widely distributed in various human environments. N-Nitrosamines are found in foodstuffs [25,151–155], drinking water [156] and various environmental sources [29,157], such as rubber products [158–165], drug formulations [166,167], herbicide formulations [168], tobacco and tobacco smoke [18,28,169–175] and indoor [176] and outdoor [177,178] environments. The occurrence of N-nitrosamines in baby bottle rubber nipples and pacifiers is of special concern because traces of these amines may migrate into infant saliva during sucking, and then be ingested. The N-nitrosamines in environmental tobacco smoke, to which both smokers and non-smokers are exposed, have received a great deal of attention as a source of indoor pollutions. The toixicity of N-nitrosamines can be manifested even at a low level (μg/kg). Therefore, a sensitive method for the determination of these amines is essential.

GC determinations of N-nitrosamines in environmental samples have been carried out in rubber nipples and pacifiers [162–164] and cigarette smoke samples [18,28,169–175]. In most of them, N-nitrosamines are directly determined as the free forms by GC–TEA, based on the detection of chemiluminescence emitted from a reaction between released NO radicals and ozone after thermal cleavage of the N–NO bond in N-nitroso compounds. Although GC–TEA is sensitive and specific for N-nitroso compounds, it is very expensive. Kataoka et al. [18] reported the determination of seven N-nitrosamines by GC–FPD. The method is based on denitrosation with hydrobromic acid to produce the corresponding secondary amines and subsequent diethylthiophosphorylation of secondary amines. By using this method, it was confirmed that N-nitrosodimethylamine, N-nitrosopyrrolidine and N-nitrosopiperidine occur in main- and sidestream smoke of cigarettes.

4. Conclusions

Monitoring amines in various environments is important to preserve human health because these compounds often have toxic effects. The GC determination of free amines is generally unsatisfactory owing to the adsorption and decomposition of the solute on the column, resulting in peak tailing and losses. Therefore, a wide variety of derivatization reactions, surveyed in this review, have been employed to reduce the polarity, to improve the GC separation of compounds and to increase both the selectivity and sensitivity of GC detection. Some potential problems with derivatization procedures include the formation of unwanted derivatives, the presence of unchanged derivatization reagents and a requirement for non-aqueous reaction conditions. Amines in environmental samples and industrial process streams are usually found in aqueous solutions except for air samples, and are often at trace levels. Therefore, it is desirable that these amines can be derivatized in aqueous solution and be sensitively detected. Of the derivatization reactions presented in this review, acylation and silylation usuallay require anhydrous reaction conditions because the derivatization reagents are very sensitive to moisture and are hydrolysed. On the other hand, dinitrophenylation, permethylation and the formation of Schiff bases, carbamates, sulphonamides and phosphonamides can be generally performed in aqueous solution. For obtaining high sensitivity and selectivity, nitrogen-selective detection (NPD), nitrosamine-specific detection (TEA) and GC–MS have been used. In addition, the conversions of amines into fluorinated derivative to introduce an ECD response and into sulphur and phosphorus derivatives to introduce an FPD response have been devised for these purposes. Although the utility of derivatization in amine determinations by GC is clear, its application to environmental analysis is not so well known. Therefore, it is hoped that this review will be useful for further applications of derivatization in the GC determination of environmental amines.

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