

Simultaneous Analysis of Endocrine Disruptors, 4-Alkylphenol and Bisphenol A, Contained in Synthetic Resin Products Used for Drug Containers and Household Utensils

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The chemical structures of individual isomers present in a mixture of 4-nonylphenol have recently been clarified, and differences in estrogen activity due to differences in the structure have been reported. Considering the importance of investigations of the chemical structure of 4-nonylphenol contained in commonly used synthetic resin products, we investigated an analytical method of individual isomers of 4-nonylphenol using positive chemical ionization-gas chromatography/mass spectrometry (PCI-GC/MS). Furthermore, we established a highly sensitive simultaneous analysis method using PCI-GC/MS [selected ion monitoring (SIM)], in which 4-alkylphenol and bisphenol A were extracted using a simple dissolution method without pretreatment such as solid-phase extraction and derivatized by trimethylsilylation.

Key words — alkyphenol, bisphenol A, positive chemical ionization-GC/MS, chemical endocrine disruptor, drug container, household utensil

INTRODUCTION

4-Alkylphenols are used as an additive for commonly used synthetic resin products. Among 4-alkylphenols, 4-nonylphenol is widely used as a nonionic surfactant and an antioxidant in detergents, herbicides, insecticides, and synthetic resin products. Bisphenol A is widely used in tableware as a material in polycarbonate resin and is possibly ingested by humans through food and water. Since products containing these compounds are disposed of in landfills or by incineration, environmental pollution, particularly adverse influences on humans and other organisms, with endocrine disruptors has been suggested.^{1,2)}

Among 4-alkylphenols, 4-octylphenol, 4-nonylphenol with C₈ and C₉ alkyl chains, and bisphenol A

have been specified as compounds with endocrine-disruptive action in fish and shellfish by the Ministry of the Environment of Japan.³⁾ Moreover, endocrine disruption in mammals (rats and mice) and estrogen-like activity in cultured cells and yeast have been reported.^{1,2)}

Recently, it has been also reported that relatively pure 4-nonylphenol compounds purified from a 4-nonylphenol mixture using high-performance liquid chromatography (HPLC) and synthesized 4-nonylphenol were tested for estrogen activity, and that the activity varied due to differences in structure.⁴⁾ Generally, 4-alkylphenols with a tertiary carbon at the benzyl site has stronger estrogen activity than those with a primary or secondary carbon. In the analytical methods for 4-alkylphenol and bisphenol A in synthetic resin products currently reported, samples are eluted with an organic solvent and analyzed using HPLC⁵⁾ and GC/MS.^{6,7)} In those reports, 4-nonylphenol compounds were analyzed as a mixture. However, analysis of individual compounds is important to determine variations in ac-

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Table 1. Experimental Parameters for Measurements

GC	Column: EQUITY TM -5 Supelco (Bellefonte, PA, U.S.A.) 0.25 mm i.d. × 30 m, df: 0.25 μm Temperature: 50°C (5 min) → 10°C/min → 280°C (5 min) Injection volume: 1 μl Injector: 200°C, splitless Carrier gas: helium Flow: 33 cm/sec
MS	Ionization: EI, PCI Ionization energy: 70 eV Ion source temperature: 180°C Reagent gas: isobutane (99.999%)

tivity among isomers. Thus we directly or indirectly prepared TMS derivatives of 4-alkylphenols with known structures and newly synthesized 4-nonylphenols and analyzed these compounds using electron-impact ionization (EI)- and positive chemical ionization (PCI)-GC/MS. We clarified that the primary, secondary, and tertiary positions of benzyl carbon in 4-alkylphenols can be differentiated based on the cleavage patterns of the mass spectra.

Using this method, reference 4-*t*-butylphenol, 4-*n*-pentylphenol, 4-*n*-hexylphenol, 4-*n*-heptylphenol, 4-*t*-octylphenol[4-(1,1,3,3-tetramethylbutyl)phenol], 4-*n*-octylphenol, 4-nonylphenol mixture, 4-*n*-nonylphenol, and bisphenol A were analyzed using PCI-GC/MS [selected ion monitoring (SIM)], and differentiation of the position of the benzyl carbon and simultaneous analysis of these compounds were possible. Then we applied simultaneous analysis of 4-alkylphenols to synthetic resin products used in containers for commercial drugs and household utensils and obtained good results.

MATERIALS AND METHODS

Samples — Twenty-four samples of synthetic resin products (containers of drugs and household utensils) sold in department stores and specialty stores for household goods in August 2004 were used.

Reagents — For 4-*t*-butylphenol (**1**), 4-*n*-pentylphenol (**2**), 4-*n*-hexylphenol (**3**), 4-*n*-heptylphenol (**4**), 4-*t*-octylphenol[4-(1,1,3,3-tetramethylbutyl)phenol] (**5**), 4-*n*-octylphenol (**6**), and 4-nonylphenol mixture (**7**), reagents for environmental analytical use were purchased from Kanto Kagaku

Co. 4-*n*-Nonylphenol (**8**) for the residual pesticide test and 4-dodecylphenol (**9**) were also purchased from Kanto Kagaku Co. For bisphenol A (**10**), 4-(1-methyloctyl)phenol (0.1 mg/ml) in hexane (**13**), and 4-(1-methyloctyl)phenol-*d*₅ (0.1 mg/ml) in hexane (**12**), standard environmental residual compounds were purchased from Hayashi Pure Chemicals Ind., Ltd. 4-(1,1,5-Trimethylhexyl)phenol (**11**) and 4-(1,1-dimethylheptyl)phenol (**14**) were synthesized, and the structures were confirmed by mass spectra, nuclear magnetic resonance spectra, and infrared absorption spectra. Phenanthrene-*d*₁₀ for environmental analysis was purchased from Kanto Kagaku Co. bis(Trimethylsilyl)trifluoroacetamide (BSTFA) for gas chromatography was purchased from Kanto Kagaku Co. *n*-Heptane for the phthalate ester test was purchased from Kanto Kagaku Co. Dichloromethane for the residual pesticide test was purchased from Kanto Kagaku Co. Nitrogen gas with 99.999% purity was used. For the reaction gas, isobutane with 99.999% purity was used.

Instruments — The GC used was Model HP6890 from Agilent Co., and the MS used was the Platform model from Micromass Co. The analytical conditions for GC/MS are shown in Table 1.

Dissolution Test — The dissolution test was performed referring to the Standard Methods of Analysis for Hygienic Chemists,⁸⁾ and *n*-heptane was used as the dissolution solvent. The sample was cut into 2 × 5 cm, and the surface was washed with pure water and air-dried. The sample was then immersed in 20 ml of *n*-heptane in a glass vial and kept at 25°C for 1 hr. The sample was removed, and the *n*-heptane eluate was transferred to an eggplant-shaped flask, concentrated using a rotary evaporator, and dried under nitrogen gas flow. The residue was dis-

Table 2. Monitor Ions of TMS 4-Alkylphenol, Bisphenol A, and Internal Standard (PCI)

Compound	M.W.	R.T. min	Base peak fragment ion	Major fragment ion
(1) 4- <i>t</i> -Butylphenol	222	16.26	223	207
(2) 4- <i>n</i> -Pentylphenol	236	18.42	237	179 (279)
(3) 4- <i>n</i> -Hexylphenol	250	19.59	251	179 (293)
(4) 4- <i>n</i> -Heptylphenol	264	20.72	265	179 (307)
(5) 4- <i>t</i> -Octylphenol	278	19.87	279	207
(6) 4- <i>n</i> -Octylphenol	278	21.81	279	179 (321)
(7) 4-Nonylphenol	292	20.60–21.70	293	—
(8) 4- <i>n</i> -Nonylphenol	292	22.84	293	179
(10) Bisphenol A	228	25.65	207	373
Phenanthrene- <i>d</i> ₁₀ (IS)	188	21.56	189	—

Figures in parentheses are the adduct ion (m/z) with CI gas of isobutane.

solved in 1 ml of dichloromethane and combined with 0.4 ml of TMS derivatization reagent, and the volume was accurately adjusted to 2 ml with dichloromethane. The solution was vigorously shaken, kept at room temperature for 1 hr, and then used as the test solution.

Preparation of Blank Test Solution — A blank test solution was prepared following the same procedure described above except for the test sample.

Preparation of Standard Solution — For the mixture of 7 alkylphenol compounds (4-*t*-butylphenol, 4-*n*-pentylphenol, 4-*n*-hexylphenol, 4-*n*-heptylphenol, 4-*t*-octylphenol[4-(1,1,3,3-tetramethylbutyl)phenol], 4-*n*-octylphenol, and 4-nonylphenol), a standard stock solution (in dichloromethane) containing 0.1 mg/ml of each of the compounds was prepared. For the other compounds, 1 mg/ml of standard stock solution (in dichloromethane) was prepared. Standard solutions at the specified concentrations were prepared by dilution of these stock solutions. The internal standard solution (phenanthrene-*d*₁₀) was prepared in the same manner as the standard stock solutions and standard solutions.

Measurement — The quantitative ions of the compounds measured using PCI-GC/MS are shown in Table 2.

Calibration Curve — The standard solution was prepared as follows: 100 mg each of 4-alkylphenol and bisphenol A standards were added to dichloromethane to make a 1 mg/ml standard stock solution that was further diluted with dichloromethane to create several different concentrations of standard solutions.

The standard solution (1 μ l) was injected into the PCI-GC/MS (SIM) system, and a calibration curve

was prepared from the peak areas of the compound using the internal standard method.

Measurement of Samples — The test and blank test solutions (1 μ l each) were injected into the PCI-GC/MS and measured.

Quantification and Calculation — The test solution was injected into the PCI-GC/MS system, and the concentration of the compound was calculated from the peak area ratio of the compound and the internal standard based on the calibration curve.

RESULTS AND DISCUSSION

Separation of 4-Alkylphenol and Bisphenol A

The total ion chromatograms of 4-alkylphenol and bisphenol A and their TMS derivatives are shown in Fig. 1. The retention times of the TMS derivatives were prolonged, compared with those of the nonderivatized forms, and separated as sharp peaks with no tailing. The retention time increased with an increase in the number of carbons in the alkyl group. The total ion chromatograms of 4-nonylphenol with known structure and its TMS derivative are shown in Fig. 2. Generally, when the number of carbons is the same, the boiling point decreases as branches increase. Wheeler *et al.* reported that the retention time of 4-nonylphenol with many branches was shorter than that with fewer branches in an analysis using a nonpolar column.⁹⁾ Since a slightly polar column was used in our study, the retention time was shorter when the compound had a benzyl carbon at the secondary position than that with a tertiary carbon in some cases, confirming a difference in the retention time due to the polarity of the column.

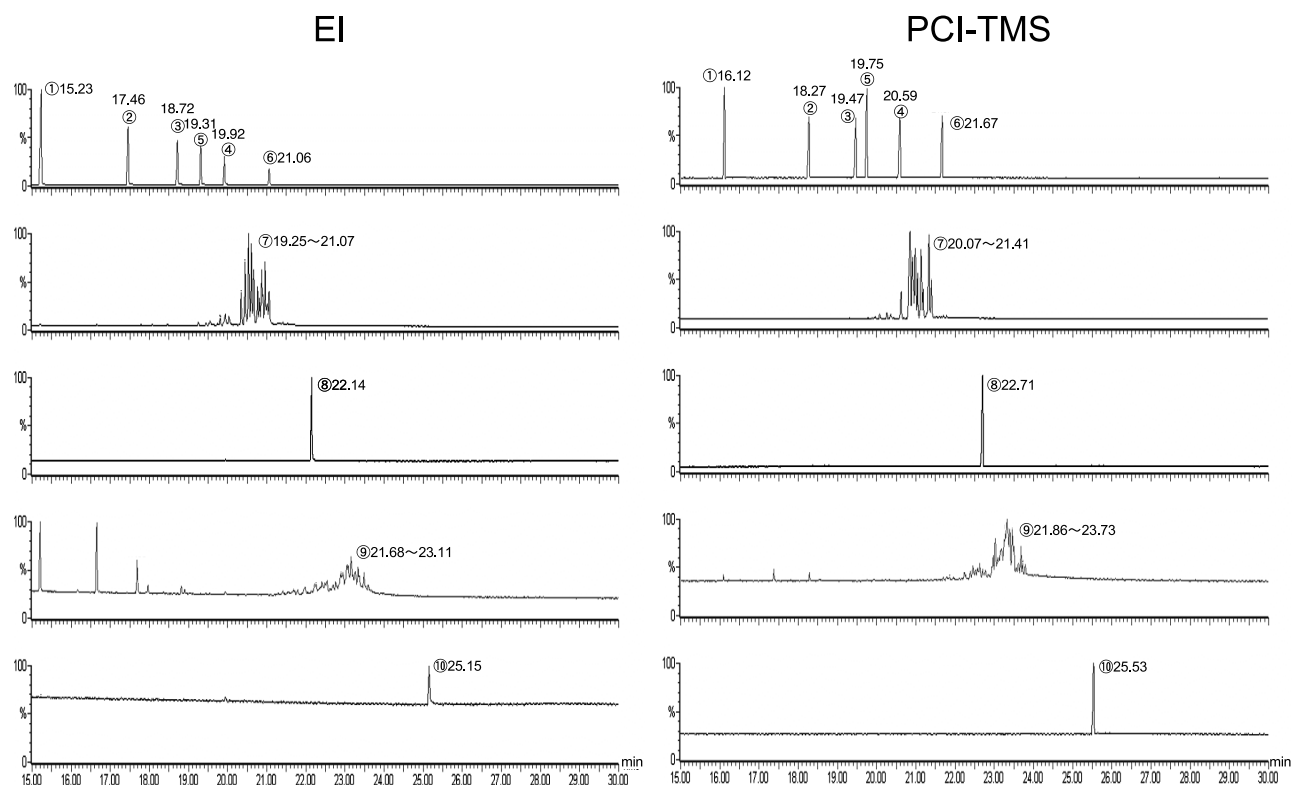


Fig. 1. Total Ion Chromatograms of 4-Alkylphenol and Bisphenol A and their TMS Derivatives

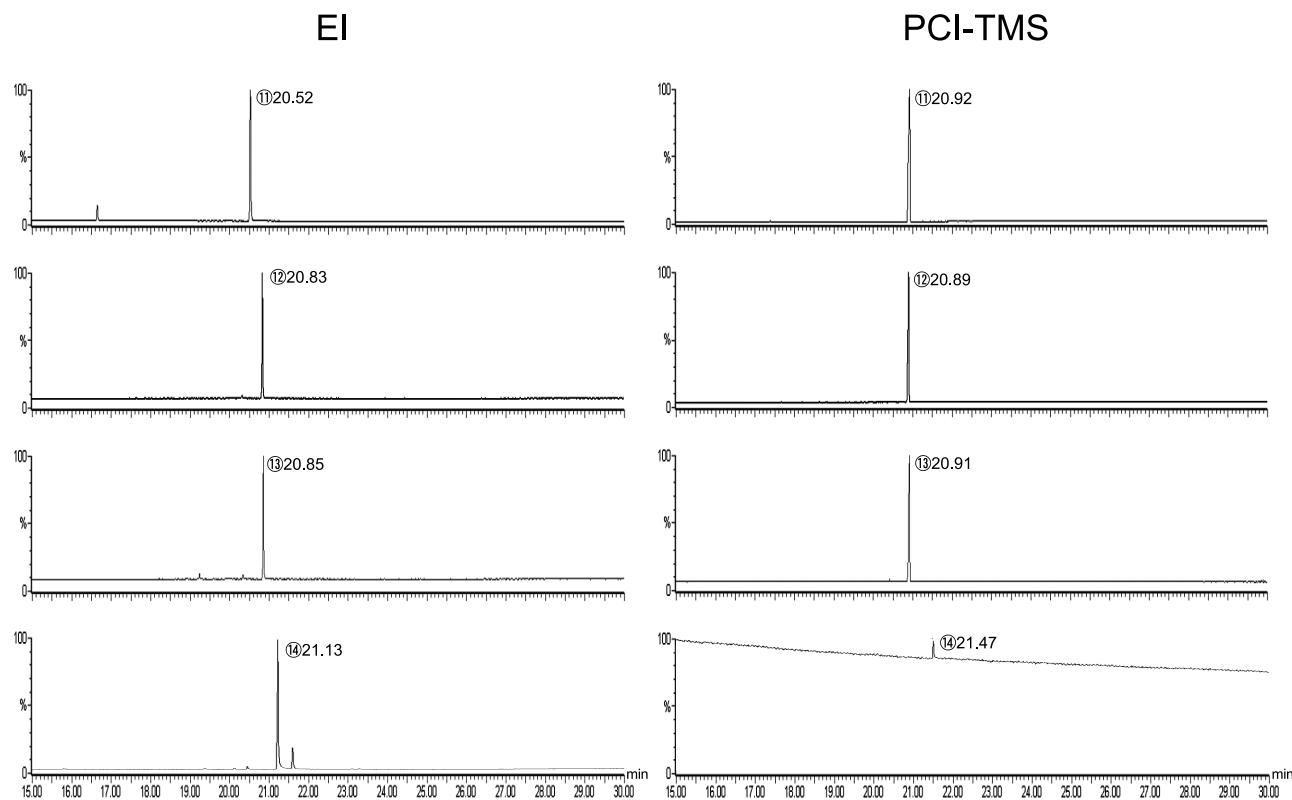


Fig. 2. Total Ion Chromatograms of 4-Nonylphenol with Known Structure and its TMS Derivative

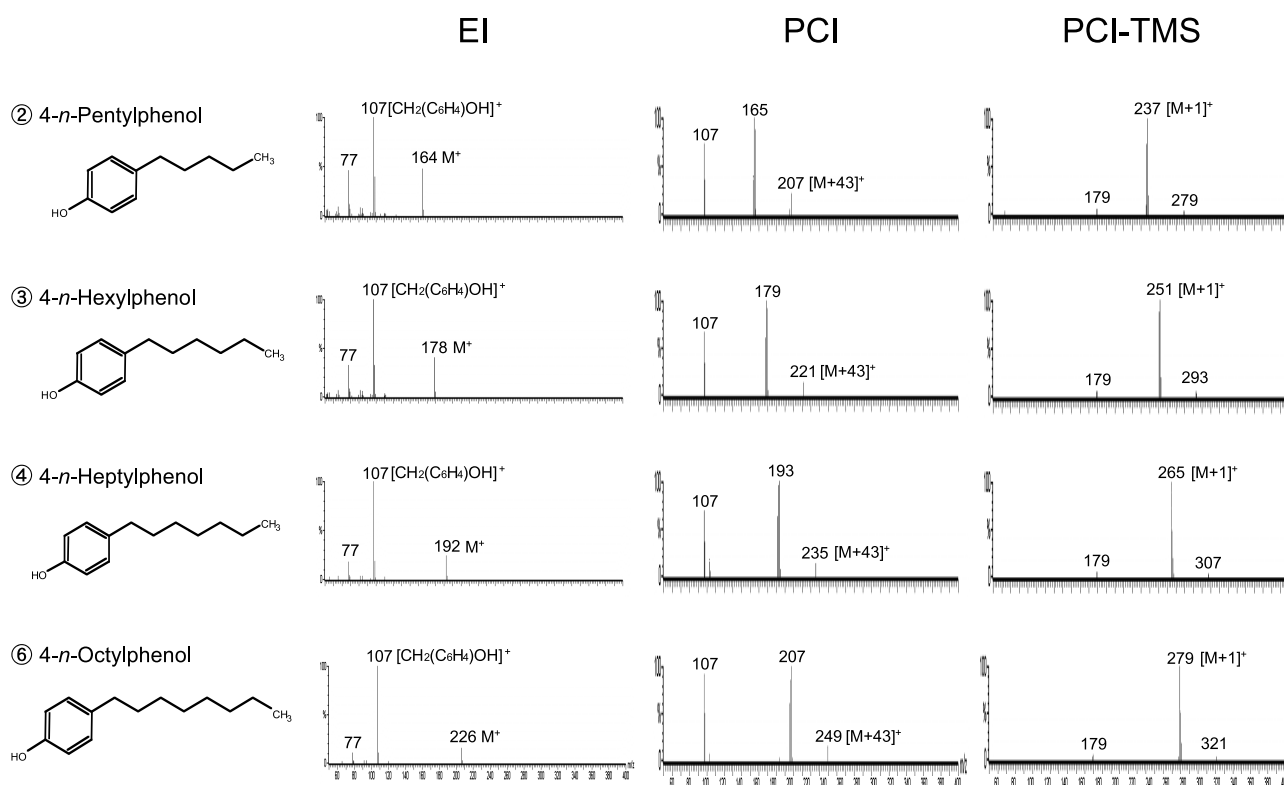


Fig. 3. Mass Spectra of 4-*n*-Alkylphenols and TMS Derivatives in EI- and PCI-GC/MS

Comparison of EI- and PCI-GC/MS Mass Spectra of 4-*n*-Alkylphenol

The mass spectra of 4-*n*-alkylphenols (2, 3, 4, 6) and TMS derivatives in EI- and PCI-GC/MS are shown in Fig. 3. On EI-GC/MS, m/z 107 [CH₂(C₆H₄)OH]⁺ was detected as the base fragment ion, and molecular ion M⁺ was detected in each compound. In contrast, +1[M + 1]⁺ produced by proton transfer was detected as a base peak in all of the compounds using PCI-GC/MS, and a fragment ion of m/z 107 [CH₂(C₆H₄)OH]⁺ was detected as in EI-GC/MS. Unlike EI-GC/MS, a fragment ion with a mass number increased by 42, [M + 43]⁺, derived from the reaction gas isobutane, was detected in [M + 1]⁺ by PCI-GC/MS. Compared with EI-GC/MS, the molecular ion peak was the base peak in PCI-GC/MS.

In the mass spectra of TMS derivatives of 4-*n*-alkylphenols, [M + 1]⁺ was detected as the base peak in all of the TMS derivatives, and m/z 179 [CH₂(C₆H₄)OTMS]⁺ and [M + 43]⁺ were detected as specific fragment ions.

Comparison of EI- and PCI-GC/MS Mass Spectra of 4-*t*-Alkylphenol and Bisphenol A

The EI- and PCI-GC/MS mass spectra of 4-*t*-

alkylphenols (1, 5) and bisphenol A (10) and their TMS derivatives are shown in Fig. 4. In the EI-GC/MS mass spectra, m/z 135 [C(CH₃)₂(C₆H₄)OH]⁺ and M⁺ were detected as base fragment ions of 4-*t*-alkylphenol. In bisphenol A, m/z 213 [HO(C₆H₄)C(CH₃)₂(C₆H₄)OH]⁺ and M⁺ were detected as base fragment ions.

There was less fragmentation in the measurement using PCI-GC/MS than in that using EI-GC/MS, and m/z 135 [C(CH₃)₂(C₆H₄)OH]⁺ and [M + 1]⁺ were detected as fragment ions in all of the compounds. However, the fragment ion of [M + 43]⁺ detected in 4-*n*-alkylphenol was not detected, showing a marked difference from the mass spectra of 4-*n*-alkylphenol. In addition, m/z 113 of the octyl group, which was undetectable using EI-GC/MS, was detected as a base fragment ion in 4-*t*-octylphenol.

In the PCI-GC/MS mass spectra of the TMS derivatives of 4-*t*-alkylphenols and bisphenol A, [M + 1]⁺ and m/z 207 [(CH₃)₂C(C₆H₄)OTMS]⁺ of each compound were detected as fragment ions. In addition, an octyl group-derived m/z 113 was detected in 4-*t*-octylphenol.

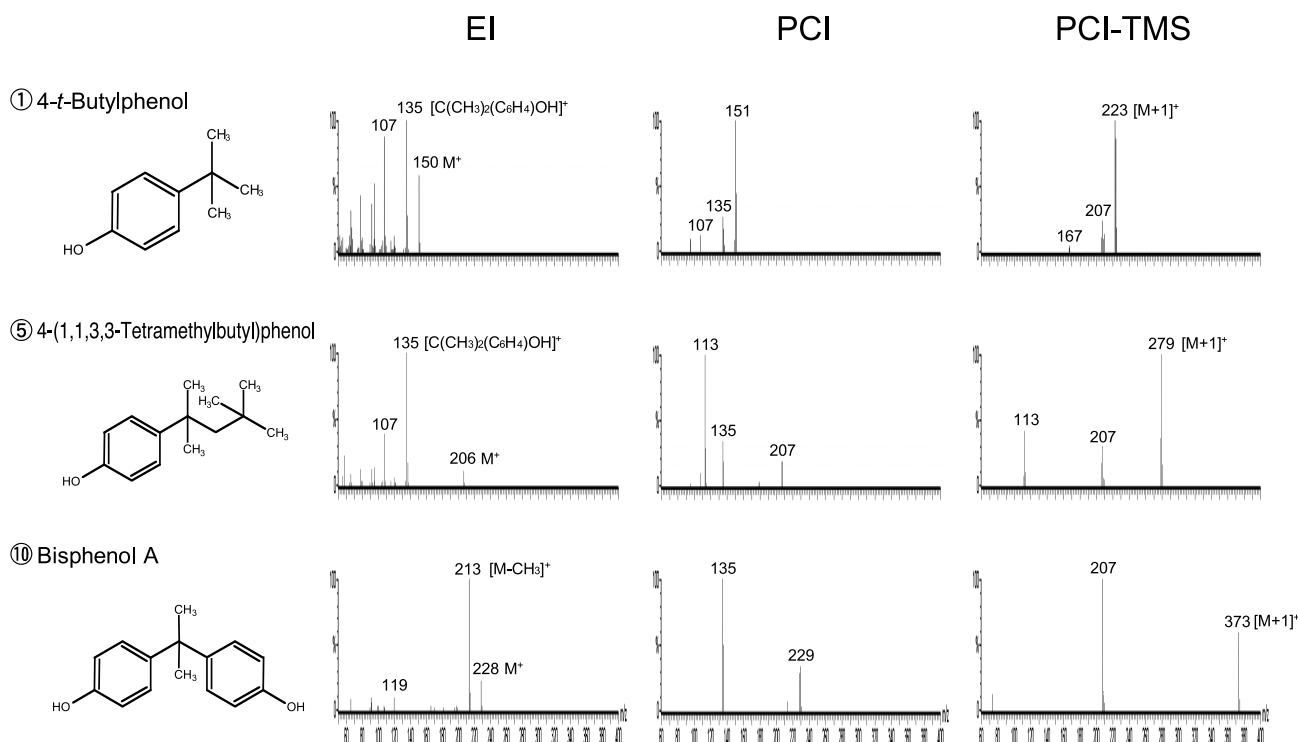


Fig. 4. Mass Spectra of 4-*t*-Alkylphenols and Bisphenol A and their TMS Derivatives in EI- and PCI-GC/MS

Chemical Structures and Mass Spectra of 4-Nonylphenol

4-Nonylphenol is a mixture of various isomers. To investigate the structure of 4-nonylphenol mainly contained in commercial resin products, it is necessary to measure 4-nonylphenol with known structure using GC/MS for comparison with the compound in commercial products. Thus the EI- and PCI-GC/MS mass spectra of the standard 4-*n*-nonylphenol, 4-(1-methyloctyl)phenol, 4-(1,1,5-trimethylhexyl)phenol, and 4-(1,1-dimethylheptyl)phenol and their TMS derivatives were compared.

As shown in Fig. 5, m/z 121 and 126 were detected as base fragment ions in the EI-GC/MS mass spectra of 4-(1-methyloctyl)phenol and its deuterium-labeled form, indicating that cleavage occurred between the benzyl carbon and the linear carbon chain. When the benzyl carbon was located at the primary position (**8**), m/z 107 was detected as a base fragment ion, and when located at the secondary (**12**, **13**) and tertiary (**11**, **14**) positions, m/z 121 and 135 were detected due to one and two additional methyl groups, respectively.

In PCI-GC/MS, in addition to m/z 107, 121, and 135 detected with EI-GC/MS, respectively, m/z 221 of [M + 1]⁺ and m/z 263 of [M + 43]⁺ were detected as fragment ions when the benzyl carbon was lo-

cated at the primary position, and m/z 221 (m/z 226 for the deuterium-labeled form) of [M + 1]⁺ and m/z 277 (m/z 282 for the deuterium-labeled form) of [M + 56]⁺ were detected when located at the secondary position, showing that the base fragment ions of primary and secondary 4-nonylphenol were [M + 1]⁺. As for the tertiary position, m/z 127 of the nonyl group was detected as the base fragment ion, showing clear differences due to the position of the benzyl carbon.

In PCI-GC/MS of the TMS derivatives, [M + 1]⁺ of each TMS derivative was detected as the base fragment ion. When the benzyl carbon was located at the primary position, the mass number was increased by 72 from m/z 107 to 179 due to TMS derivatization. When the benzyl carbon was located at the secondary position, the mass number was increased by 72 from m/z 121 (m/z 126 for the deuterium-labeled form) to m/z 193 (m/z 198 for the deuterium-labeled form). As for the tertiary position, an increase in the mass number by 72 from m/z 135 to 207 and 127 of the nonyl group was detected.

The chemical structure of the commercial 4-nonylphenol mixture was investigated using EI- and PCI-GC/MS. As shown in Fig. 6, the retention time of the synthesized 4-(1,1,5-trimethylhexyl)phenol was 20.52 min. In the mass spectrum of the peak of

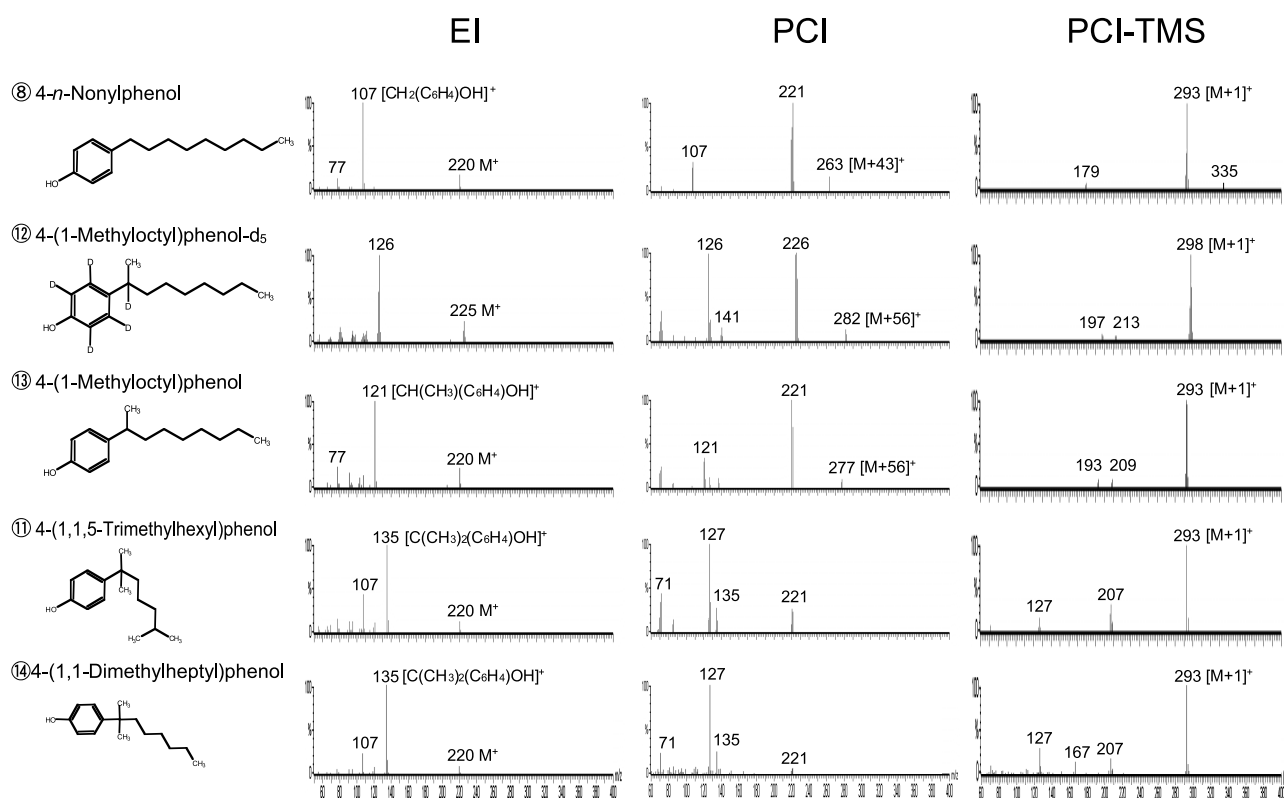


Fig. 5. Mass Spectra of 4-Nonylphenols and TMS Derivatives in EI- and PCI-GC/MS

the commercial 4-nonylphenol mixture corresponding to the peak at 20.52 min (Fig. 6B), fragment ions were detected at m/z 149 and 191 in addition to the fragment ions (m/z 107, 121, and 135) derived from 4-(1,1,5-trimethylhexyl)phenol. In PCI-GC/MS, a new fragment ion was detected at m/z 191, which was not noted in the mass spectrum of 4-(1,1,5-trimethylhexyl)phenol (Fig. 6C). Since PCI-GC/MS detected m/z 127 derived from the nonyl group as a base fragment ion, the benzyl carbon was assumed to be located at the tertiary position.

The mass spectra of the TMS derivative are shown in Fig. 7. In EI-GC/MS, in addition to the fragment ion derived from 4-(1,1,5-trimethylhexyl)phenol (Fig. 7A), fragment ions were detected at m/z 179, 193, 221, and 263 in the mass spectrum of the peak of the commercial 4-nonylphenol mixture, corresponding to the retention time of 4-(1,1,5-trimethylhexyl)phenol (20.89 min) (Fig. 7B), suggesting that the peak of the 4-nonylphenol mixture corresponding to the peak of 4-(1,1,5-trimethylhexyl)phenol (20.89 min) was a mixture of 4-(1,1,5-trimethylhexyl)phenol and 4-(1,4-dimethyl-1-ethylpentyl)phenol. This compound is considered to have the third highest activity.¹⁰⁾

Total investigation of the cleavage patterns in the EI- and PCI-GC/MS mass spectra allowed predictions that the single peak on the chromatogram was a mixture, which may be useful for an investigation of the relationship between the degree of activity and chemical structure.

Calibration Curves

The calibration curves prepared based on PCI-GC/MS (SIM) measurement of the TMS derivatives of 4-*t*-butylphenol, 4-*n*-pentylphenol, 4-*n*-hexylphenol, 4-*n*-heptylphenol, 4-*t*-octylphenol[4-(1,1,3,3-tetramethylbutyl)phenol], 4-*n*-octylphenol, 4-*n*-nonylphenol, 4-nonylphenol, and bisphenol A are shown in Fig. 8. Good correlation coefficients of $R^2 = 0.9973$ – 0.9999 were obtained for 4-nonylphenol, bisphenol A, and the other compounds within the ranges of 50–50000, 50–5000, and 5–5000 ng/ml, respectively. The lower detection limits were obtained from the General Test Methods section in the 14th revision of the *Japanese Pharmacopoeia*,¹¹⁾ and the value was 5 ng/ml for 4-nonylphenol and bisphenol A, and 0.5 ng/ml for the other compounds.

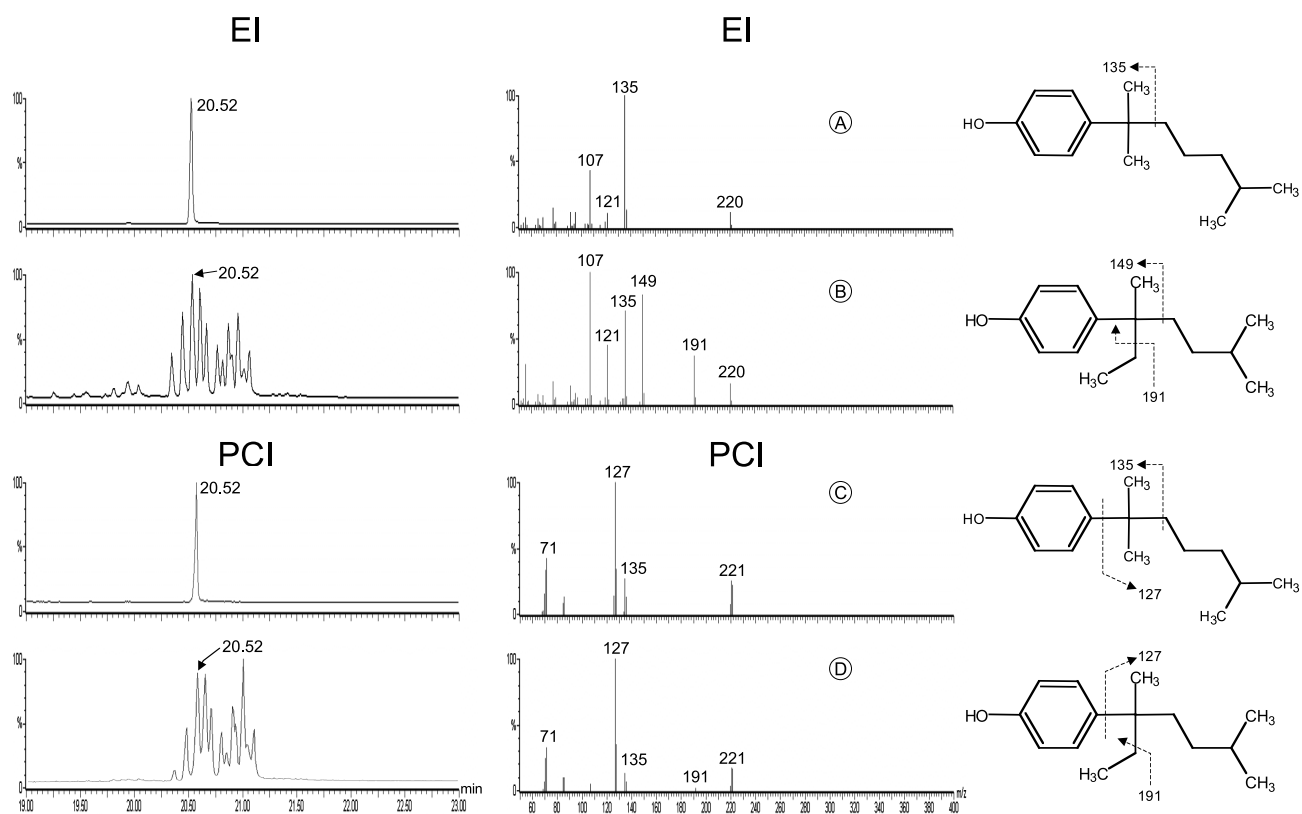


Fig. 6. Mass Spectra of Commercial 4-Nonylphenol Mixture and 4-(1,1,5-Trimethylhexyl)phenol in EI- and PCI-GC/MS

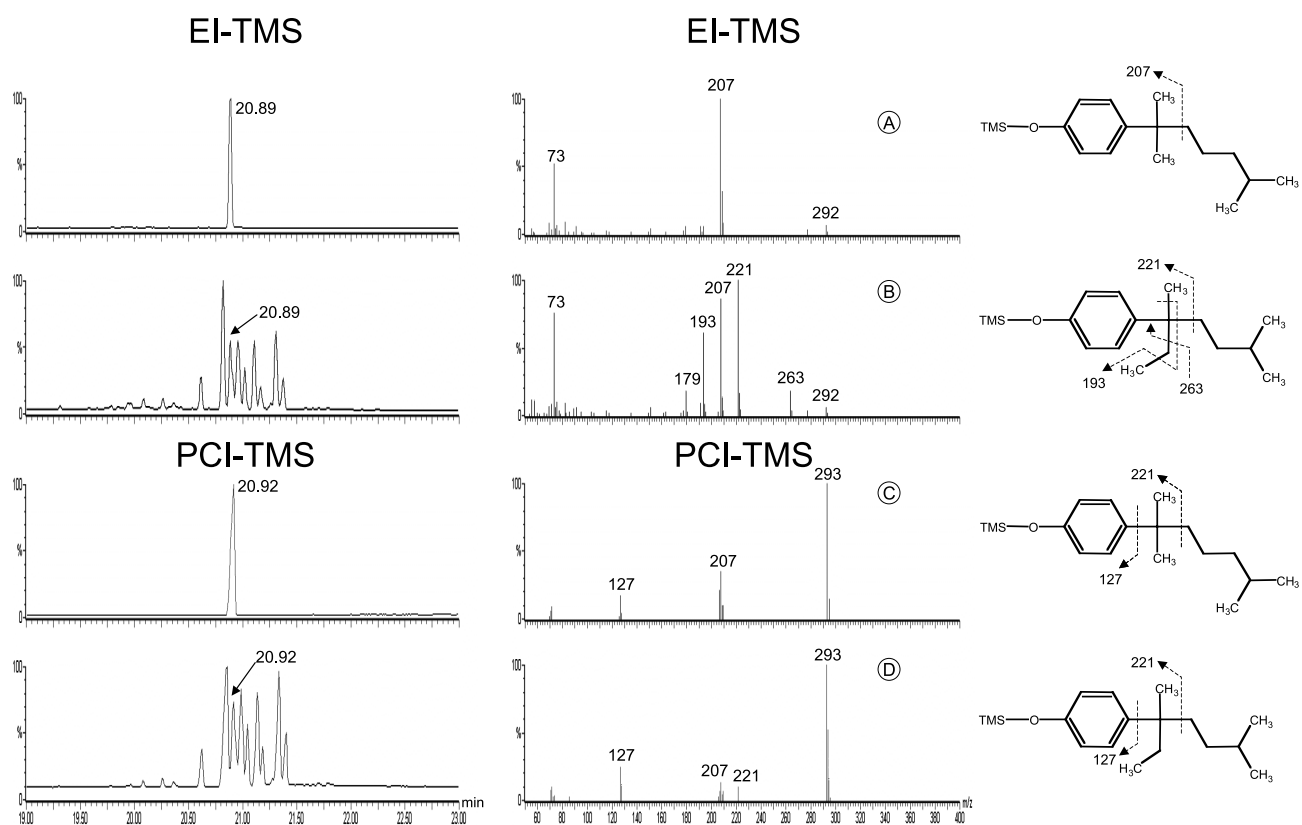


Fig. 7. Mass Spectra of the TMS Derivative in EI- and PCI-GC/MS

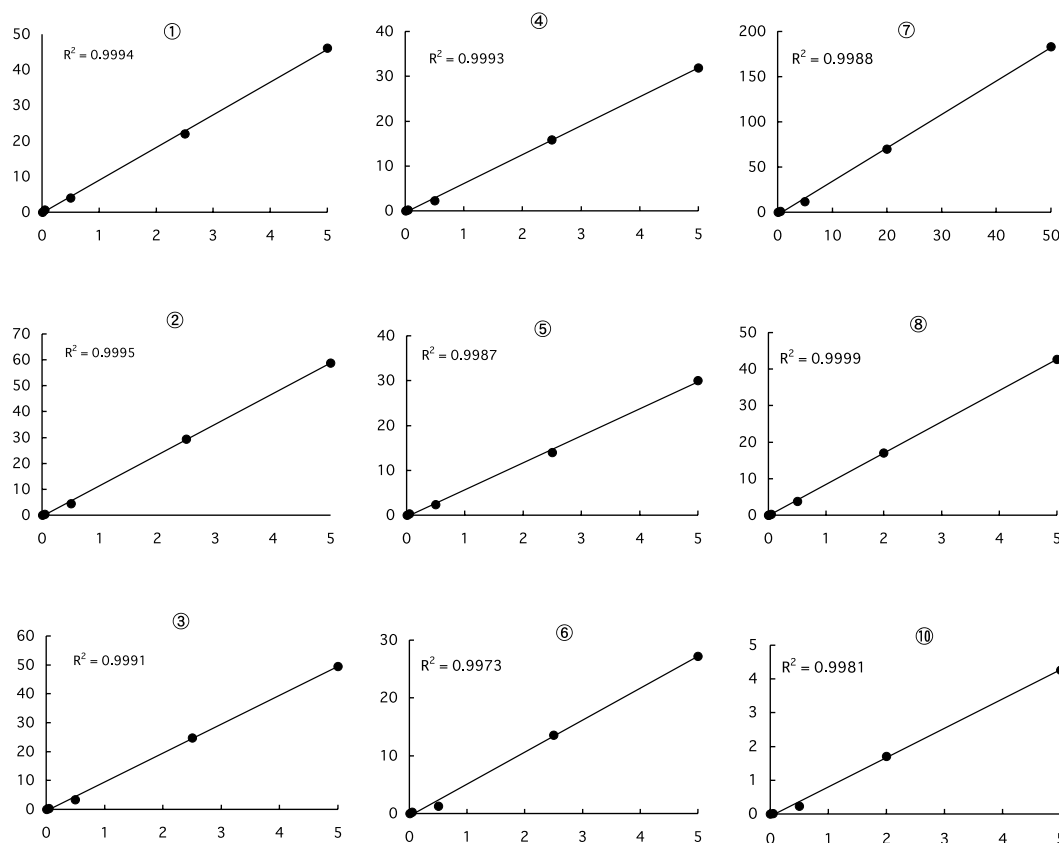


Fig. 8. Calibration Curves of 4-Alkylphenols and Bisphenol A
Vertical line: area ratio; transverse: concentration (ng/ml).

Repeatability and Additive Recovery

For investigation of the repeatability of each compound, the analysis was repeated six times using 50 ng/ml solutions of 4-*t*-butylphenol, 4-*n*-pentylphenol, 4-*n*-hexylphenol, 4-*n*-heptylphenol, 4-*t*-octylphenol[4-(1,1,3,3-tetramethylbutyl)phenol], 4-*n*-octylphenol, and 4-*n*-nonylphenol and 500 ng/ml solutions of 4-nonylphenol and bisphenol A, and the relative standard deviation was 1.1–8.0%. In the additive recovery test, a 2 × 5 cm sample was prepared from a vinyl chloride glove, from which no 4-alkylphenol was dissolved, and the surface was washed with pure water and air-dried. Each compound was added to the sample and adjusted to the concentration specified for the repeatability test, and the dissolution test described in Dissolution Test was performed. The recovery rate was 86–122%, and the repeatability as relative standard deviation was 3.6–10.2%.

Simultaneous Analysis of 4-Alkylphenols and Bisphenol A Contained in Containers of Drugs and Household Utensils

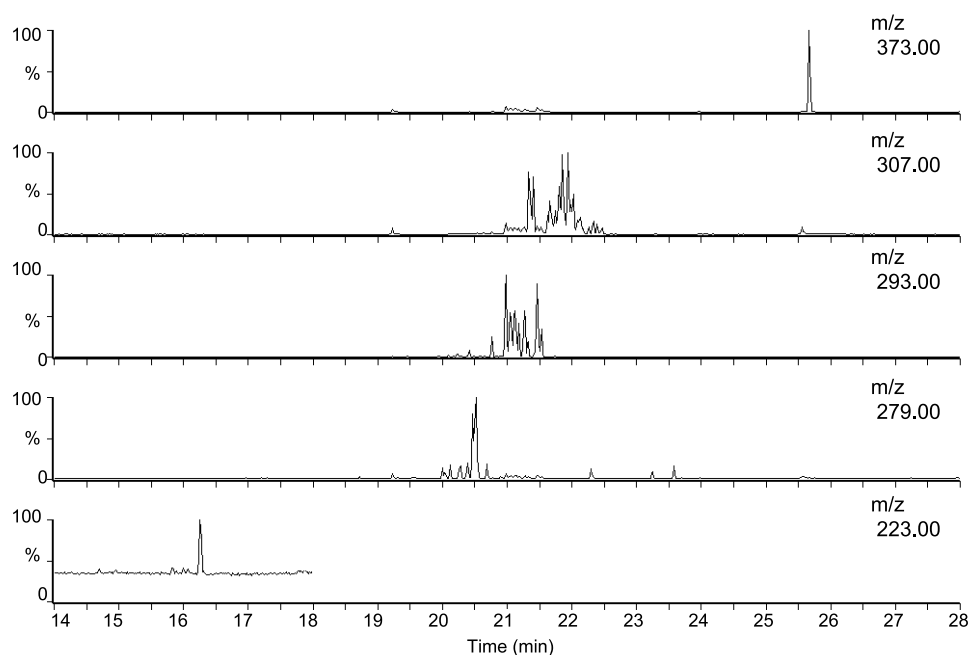
Since there are many structural isomers of 4-alkylphenols containing numerous carbons in the alkyl chain, quantification based on mass chromatographic fragment ions similar to multiple peaks in the chromatogram is a problem. To analyze the peak with high sensitivity, it is necessary to detect common fragment ions of the structural isomers that represent the difference in the number of carbons in the alkyl chain. The simultaneous analysis using PCI-GC/MS with isobutane detects $[M + 1]^+$ as a base fragment ion in all of the TMS-derivatized 4-alkylphenols, allowing highly sensitive analysis, compared with the current analysis using EI-GC/MS.

The results of the measurement of 4-*t*-butylphenol, 4-*n*-pentylphenol, 4-*n*-hexylphenol, 4-*n*-heptylphenol, 4-*t*-octylphenol[4-(1,1,3,3-tetramethylbutyl)phenol], 4-*n*-octylphenol, 4-*n*-nonylphenol, 4-nonylphenol, and bisphenol A in 24 samples of containers of drugs (*e.g.*, eyedrop containers) and household utensils (*e.g.*, card case, vi-

Table 3. 4-Nonylphenol and Bisphenol A Released from Containers of Drugs and Household Utensils

Sample	Material	Sample weight (g)	4-Nonylphenol		Bisphenol A		
			$\mu\text{g/g}$	$\mu\text{g/cm}^2$	$\mu\text{g/g}$	$\mu\text{g/cm}^2$	
1	Nasal spray container	—	1.51	N.D.	N.D.	N.D.	N.D.
2	Eyedrop container	—	0.30	N.D.	N.D.	N.D.	N.D.
3	Eyedrop container	—	0.32	N.D.	N.D.	N.D.	N.D.
4	Eyedrop container	—	0.20	N.D.	N.D.	N.D.	N.D.
5	Eyedrop container	—	0.24	N.D.	N.D.	N.D.	N.D.
6	Eyedrop container	—	0.21	N.D.	N.D.	N.D.	N.D.
7	Bankbook case	PVC	0.39	12	0.5	15	0.6
8	Card case	—	0.50	N.D.	N.D.	0.8	0.04
9	Vinyl bag	PVC	0.35	499	17	29	1.0
10	Toy	PVC	2.23	37	8.3	N.D.	N.D.
11	Toy	PVC	2.01	1.0	0.2	N.D.	N.D.
12	Toy	PVC	0.37	13	0.5	43	1.6
13	Hose	PVC	2.71	N.D.	N.D.	N.D.	N.D.
14	Glove	PVC	0.30	N.D.	N.D.	N.D.	N.D.
15	Glove	PVC	0.15	N.D.	N.D.	N.D.	N.D.
16	Air frame	PVC	0.19	7.8	0.1	16	0.3
17	Air frame	PVC	0.23	10	0.2	41	1.0
18	Foot pillow	PVC	0.30	38	1.1	1.3	0.04
19	Keyring	—	0.52	N.D.	N.D.	N.D.	N.D.
20	Wristband	—	1.85	N.D.	N.D.	N.D.	N.D.
21	Ice tray	—	2.42	134	32	N.D.	N.D.
22	Hanging	—	0.88	54	4.8	8.6	0.8
23	Drinking glass	—	1.78	N.D.	N.D.	N.D.	N.D.
24	Coaster	PVC	1.45	30	4.3	N.D.	N.D.

PVC: Polyvinyl chloride; —: not indicated; N.D.: not detected.

**Fig. 9.** PCI Mass Fragmentogram of Sample No. 9

nyl bag, and air frame) using PCI-GC/MS are shown in Table 3. None of the compounds were detected in six samples of drug containers. In 18 samples of household utensils, 0.1–32 $\mu\text{g}/\text{cm}^2$ 4-nonylphenol and 0.04–1.6 $\mu\text{g}/\text{cm}^2$ bisphenol A were detected, and a trace amount of 4-*t*-octylphenol[4-(1,1,3,3-tetramethylbutyl)phenol] was detected in samples 8, 9, and 11. Since $[\text{M} + 1]^+$ was detectable as a base fragment ion, 4-dodecylphenol assumed to have a C_{10} alkyl chain was detected in sample 9 (Fig. 9).

In conclusion, we established a highly sensitive simultaneous analytical method for 4-alkylphenol and bisphenol A using PCI-GC/MS (SIM). The established method has both sensitivity and repeatability and can be used to analyze synthetic resin products used as containers for drugs and household utensils. Most samples in which 4-nonylphenol was detected contained a tertiary benzyl carbon, and a few samples contained a primary or secondary carbon.

The PCI-GC/MS analysis of 4-alkylphenol is capable of clarifying the characteristics of the benzyl carbon based on the cleavage pattern of the mass spectrum. Furthermore, TMS derivatization produces $\text{M} + 1$ as a base fragment ion, which allows estimation of the number of carbons in the alkyl chain of 4-alkylphenol. Comprehensive investigation of the cleavage patterns in the EI- and PCI-GC/MS mass spectra of 4-alkylphenols and their TMS derivatives allowed predictions that a single peak on the chromatogram was a mixture, which may be useful for investigations of the relationship between the degree of activity and chemical structure.

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