BPB Reports

Report

Comparison of Helium-Alternative Carrier Gases for Gas Chromatography/Mass Spectrometry of Standard Test Methods for Indoor Air Quality Guidelines in Japan

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Received June 14, 2022; Accepted July 4, 2022

Helium is the most frequently used carrier gas for GC/MS, which is the official standardized test method in Japan to assess chemical substances in indoor air. However, recent global challenges in the supply chain for helium have led to a need to validate GC/MS using alternative carrier gases. In this study, we examined the applicability of hydrogen and nitrogen as helium-alternative carrier gases in the standardized GC/MS analytical test method for volatile organic compounds (VOC) and phthalate esters in indoor air. Comparison of the signal-to-noise ratios of standard solutions showed that detection sensitivities of hydrogen and nitrogen analysis were enough for the standard test method, although these gases, especially nitrogen, were less sensitive than helium. Measurements using these alternative carrier gases showed good linearity and could quantify around 1/100th of Japanese guideline values for indoor air concentrations. Therefore, hydrogen and nitrogen gases can be applied to the standard GC/MS analysis test method for VOC and phthalate esters in indoor air as alternative carrier gases to helium.

Key words indoor air, helium, alternative carrier gas, volatile organic compounds, phthalate esters

INTRODUCTION

Chemical substances in indoor air are widely analyzed by GC/MS, and helium is the carrier gas most frequently used. Although helium is easy to handle and has a high analytical performance because it is inert and non-flammable, Japan imports its entire supply of helium, and this is becoming difficult due to recent global supply chain issues.[1–4)]

Hydrogen and nitrogen are helium-alternative carrier gases that are attracting attention because of their stable supply in contrast to noble gases such as helium. Studies on GC/MS analysis with hydrogen and nitrogen have been reported,[5–8)] and many instrument companies have developed GC/MS analytical equipment that can use both as carrier gases in recent years. Thus, GC/MS analyses with hydrogen and nitrogen are becoming possible with a degree of safety and high performance.

Previously, we developed a standardized test method of GC/MS for chemical substances in indoor air and promoted national and international standardization of the test method. Additionally, the Committee on Sick House Syndrome: Indoor Air Pollution (CIAP) has set and revised the guideline values for indoor air concentration in Japan to prevent health deterioration caused by indoor air pollution.[9)] However, the current standardized method to assess chemicals in indoor air has specified the carrier gas as helium, which has an unstable supply. Therefore, validation of GC/MS with carrier gases that can be supplied stably has become urgently required in the face of restrictions on the use of helium.

In this study, we examined the applicability of hydrogen and nitrogen as helium-alternative carrier gases for GC/MS for chemicals in indoor air, including volatile organic compounds (VOC) such as toluene and semi-volatile organic compounds (SVOC) such as phthalate esters.

MATERIALS AND METHODS

Chemicals Standard solutions were purchased from Tokyo Chemical Industry Co. (Tokyo, Japan), Fujifilm Wako Pure Chemicals Co. (Osaka, Japan), and Kanto Chemical Co. (Tokyo, Japan). Toluene-d_8 (Fujifilm Wako Pure Chemicals Co., Osaka, Japan) for VOC and di-*n*-butyl phthalate-d_4 (DnBP-d_4), di-2-ethylhexyl phthalate-d_4 (DEHP-d_4) for SVOC were used as internal standard substances. Methanol (MeOH), testing after 5,000-fold concentrated for pesticide residue and poly chlorinated biphenyl analysis, was purchased from Fujifilm Wako Pure Chemicals Co. (Osaka, Japan) and Kanto Chemical Co. (Tokyo, Japan).

Instruments GC/MS analysis was performed using the Agilent 5977B GC/MSD series with the PAL3 RSI Autosampler system (Agilent Technologies, Inc., CA, USA). The NM Plus 160 Hydrogen Generator (Airtech Co., Kanagawa, Japan) was used to supply hydrogen as the carrier gas.

Analytical Methods The analytical conditions of GC were determined in accordance with the "Manual for Measuring Indoor Air Chemical Substances" set by CIAP,[10)] and were modified for each alternative carrier gas with reference to EZGC Method Translator and Flow Calculator (Restek Corporation, PA, USA).

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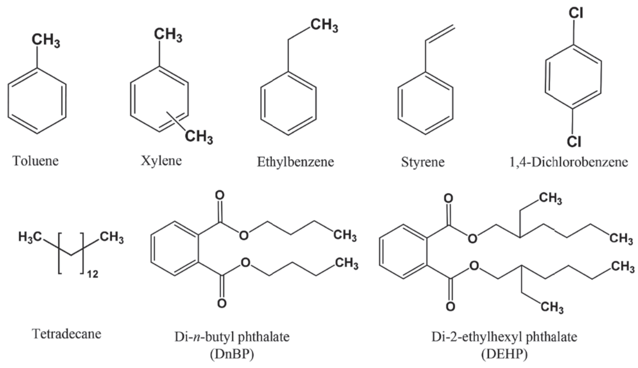

Fig. 1. Structures of the Target Chemicals

Table 1. Target and Qualifier Ions

Chemicals	Target Ion	Qualifier Ion
Toluene	91	65, 92
Xylene	91	105, 106
Styrene	104	78, 103
Ethylbenzene	91	51, 106
1,4-Dichlorobenzene	146	111, 148
Tetradecane	57	43, 71
Toluene-d_8	98	70, 100
DnBP	149	223
DEHP	149	167
DnBP-d_4	153	227
DEHP-d_4	153	171

Table 2. Measurement Conditions
(A) VOC

Carrier gases	He	H_2	N_2
Sampling conditions			
Expected air volume	144 L (0.1 L/min, 24 h)		
Expected extraction volume	1 mL		
Analytical conditions			
Column	Rtx®-1 (0.32 mm i.d. × 60 m, 1 μm)	Rtx®-1MS (0.25 mmi.d. × 60 m, 1 μm)	
Time	45 min	52.5 min	105 min
Gradient mode	40°C→(5°C/min)→250°C	40°C→(4°C/min)→250°C	40°C→(2°C/min)→250°C
Inlet temperature	280°C		
Source temperature	230°C		
Quad temperature	150°C		
Linear velocity (cm/sec)	36.5	36.5	18.9
flow (mL/min)	2	0.92	0.5
Inlet pressure (kPa)	12.3	5.4	6
Split ratio	20:1		10:1
Acquisition type	SIM/Scan		
Range (*m/z*)	35–450		
Injection volume	1.0 μL		

(B) Phthalate esters

Carrier gases	He	H_2	N_2
Sampling conditions			
Expected air volume	4,320 L (3 L/min, 24 h)		
Expected extraction volume	5 mL		
Analytical conditions			
Column	DB-1 (0.25 mm i.d. × 15 m, 0.10 μm)	DB-1MS (0.18 mm i.d. × 20 m, 0.18 μm)	
Time	30 min	18 min	35 min
Gradient mode	80°C (2 min)→(8°C/min)→ 210°C (5 min)→(20°C/min)→ 250°C (5 min)	80°C (1 min)→(26°C/min)→ 210°C (3 min)→40°C/min→ 250°C (8 min)	80°C (2 min)→(13°C/min)→ 210°C (5 min)→(20°C/min)→ 250°C (16 min)
Inlet temperature	250°C		
Source temperature	230°C		
Quad temperature	150°C		
Linear velocity (cm/sec)	67.6	57.8	28.5
flow (mL/min)	1.67	0.74	0.36
Inlet pressure (kPa)	50		
Split ratio	Splitless		
Acquisition type	SIM/Scan		
Range (*m/z*)	35–450		
Injection volume	1.0 μL		

The targeted chemicals were toluene, xylene, styrene, ethylbenzene, 1,4-dichlorobenzene, tetradecane as VOC and di-*n*-butyl phthalate (DnBP), and di-2-ethylhexyl phthalate (DEHP) for SVOC (Fig. 1). These target and qualifier ions are shown in Table 1. These chemicals were measured using Selected Ion Monitoring (SIM) modes and were quantified based on internal standard methods using toluene-d_8 for VOC and DnBP-d_4 and DEHP-d_4 for phthalate esters. The concentration range of the calibration curve was 0.5–100 ng. *m*-, *p*-Xylenes, parts of the three isomers of xylene, were quantified as overlapping peaks. The chromatograms were processed with PRISM 9 (GraphPad Software, CA, USA). The limits of detection (LOD) and those of quantification (LOQ) were calculated as 3-fold, 10-fold the standard deviation of five analyses of the lowest concentration samples (0.1 ng), respectively, and were further divided by the expected sampling volume according to the standard test method specified by the CIAP, MHLW.[10] The details of the measurement conditions are shown in Table 2.

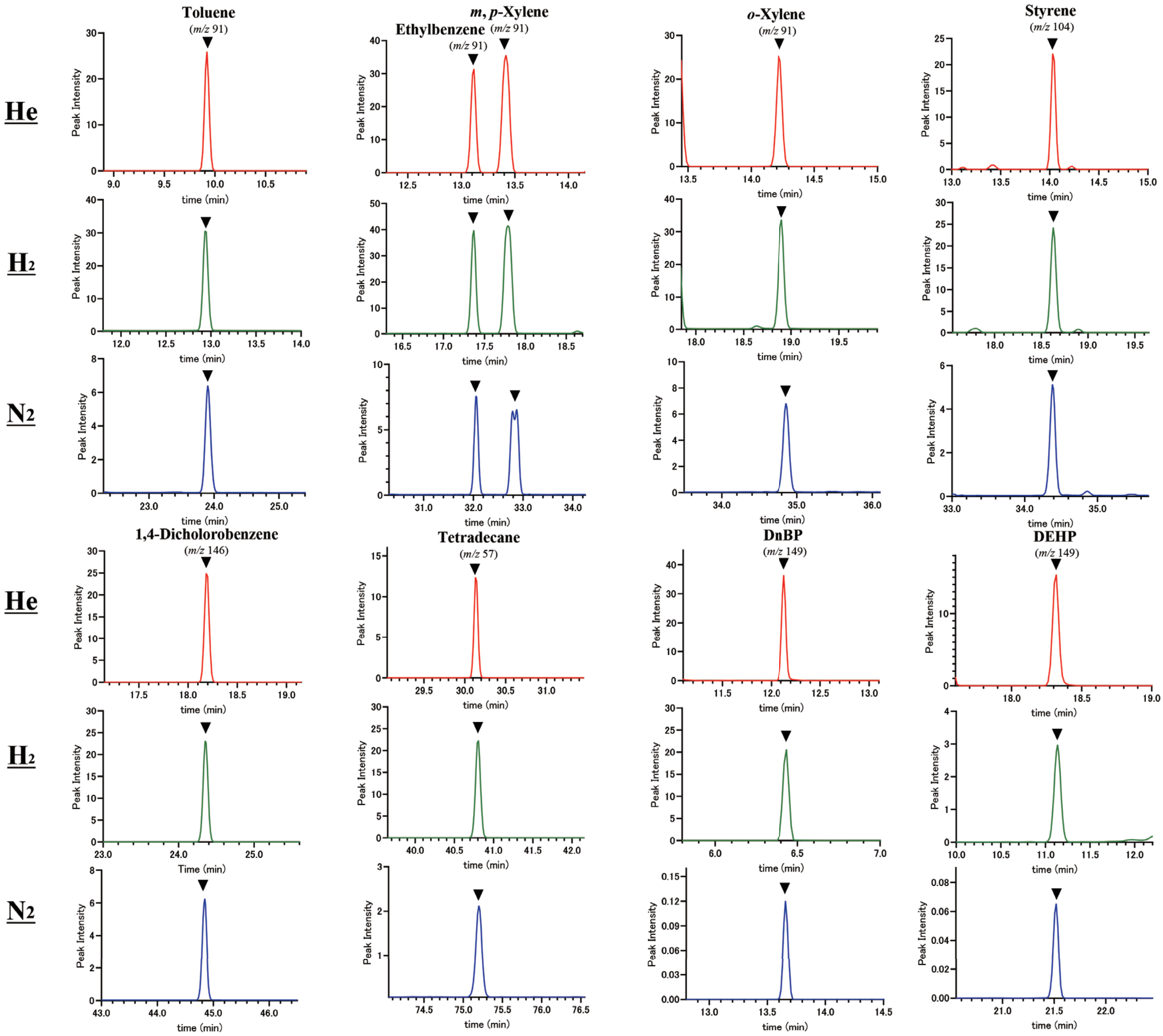

Fig. 2. SIM Chromatograms of the Target Chemicals for Each Carrier Gas

RESULTS AND DISCUSSION

The SIM chromatograms of the standard solutions for the targeted chemicals showed that the peaks had good separation for qualitative and quantitative analysis for all tested carrier gases (Fig. 2). The signal-to-noise (S/N) ratios of the measurements with 100 ng of the targeted chemicals are shown in Table 3. The S/N ratio was the highest for helium, followed by hydrogen, which was 55%–93% lower than that of helium, and nitrogen, which was 93%–98% lower than that of helium. The reason for the extremely low sensitivity of nitrogen is suspected to be the lower vacuum pressure.

The coefficients of determination (R^2) of the calibration curves are shown in Table 4. Most of the chemicals showed good linearities, even the least sensitive nitrogen carrier gas with an R^2 of 0.9917–0.9998 in the concentration range of 0.1–100 μg/mL for VOC and 0.1–5 μg/mL for phthalate esters. However, as the R^2 of tetradecane was below 0.99, the concentration range was changed to 0.1–20 μg/mL to give an R^2 of 0.9948.

A comparison of the LOD, LOQ, and guideline values for indoor air concentrations is shown in Table 5. The LOQ of all chemicals was less than 1/100th of guideline values, except for xylene with helium carrier gas and for toluene, xylene, and tetradecane with nitrogen. However, the LOQ of xylene with helium was 2.40 μg/m^3, and that of toluene, xylene, and tetradecane with nitrogen were 3.40 μg/m^3, 7.20 μg/m^3, and 5.90 μg/m^3, respectively, revealing that these LOQs were close to 1/100th of the guideline values. Therefore, measurements using any of these carrier gases can quantify around 1/100th of the guideline values for the indoor air concentrations of all tested chemicals.

Herein, we found that the analysis results using hydrogen as a carrier gas were comparable to those of helium, suggesting that hydrogen is a promising alternative to helium in the standard GC/MS test method for chemicals in indoor air. Meanwhile, nitrogen was clearly less sensitive than helium, and it might be difficult to conduct non-targeted analyses at the current level of an analytical equipment. However, target

Table 3. S/N Ratios of the Targeted Chemicals

Chemicals	S/N ratio*		
	He	H_2	N_2
Toluene	20,544	1,392	1,416
Ethylbenzene	32,635	2,660	1,714
m,*p*-Xylene	37,030	2,850	1,472
o-Xylene	29,770	2,465	1,447
Styrene	31,055	5,384	1,115
1,4-Dichlorobenzene	68,362	6,289	1,287
Tetradecane	29,086	11,650	520
DnBP	48,249	9,500	1,087
DEHP	12,193	5,429	589

*100 µg/mL, 1 µL inj.

Table 4. Coefficients of Determination for the Targeted Chemicals

Chemicals	R^2		
	He	H_2	N_2
Toluene	1.0000	1.0000	0.9998
Ethylbenzene	0.9997	0.9984	0.9989
m,p-Xylene	0.9996	0.9986	0.9923
o-Xylene	0.9995	0.9978	0.9917
Styrene	0.9986	0.9976	0.9980
1,4-Dichlorobenzene	0.9989	0.9979	0.9992
Tetradecane	0.9978	0.9994	*0.9948
DnBP#	0.9999	0.9904	0.9988
DEHP#	0.9999	0.9998	0.9986

0.1–100 µg/mL in MeOH, 1 µL inj.
*0.1–20 µg/mL in MeOH, 1 µL inj.
#0.1–5 µg/mL in MeOH, 1 µL inj.

Table 5. Comparison of LOD, LOQ, and the Guideline Values for Indoor Air Concentration

Chemicals	LOD# (µg/m³)			LOQ# (µg/m³)			Guideline values[9] (µg/m³)
	He	H_2	N_2	He	H_2	N_2	
Toluene*	0.064	0.034	1.02	0.21	0.11	3.40	260
Ethylbenzene*	0.20	0.15	0.70	0.65	0.49	2.30	3,800
Xylene*	0.72	0.27	2.17	2.40	0.90	7.20	200
Styrene*	0.53	0.14	0.37	1.80	0.47	1.20	220
1,4-Dichlorobenzene*	0.70	0.17	0.46	2.30	0.56	1.50	240
Tetradecane*	0.29	0.20	1.80	0.96	0.66	5.90	330
DnBP§	0.0014	0.012	0.018	0.0047	0.039	0.059	17
DEHP§	0.0024	0.0030	0.018	0.0080	0.010	0.059	100

0.1 ng injection at five times repeatedly
* Divided by 144 L specified collection volume for VOC in indoor air
§ Divided by 4,320 L specified collection volume for phthalate esters in indoor air

analysis using SIM measurements showed the good linearity. Moreover, around 1/100th of guideline values for indoor air concentrations were quantifiable. Therefore, nitrogen can be also applied to the standardized GC/MS test method for chemicals in indoor air, which is a targeted analysis.

In conclusion, in this study, we examined the applicability of hydrogen and nitrogen as helium-alternative carrier gases for the standard GC/MS test for indoor air quality. Comparison of the S/N ratios of the standard solutions showed that detection sensitivities of hydrogen and nitrogen analysis were enough for standard test method, although these gases, especially nitrogen, were less sensitive than helium. Measurements using all of these carrier gases showed good linearity, and around 1/100th of guideline values could be quantified in indoor air concentrations. Therefore, hydrogen and nitrogen gases can be applied to the GC/MS analysis of standard test methods for indoor air quality guidelines in Japan as helium-alternative carrier gases.

Acknowledgments This work was financially supported by the Grant-in-Aid for Research on Risk of Chemical Substances (H30-chemical/designation-002) provided by the Ministry of Health, Labour, and Welfare, Japan. We would like to thank Enago (Crimson Interactive Pvt. Ltd.) for English language editing.

Conflict of interest The authors declare no conflict of interest.

REFERENCES

1) Nuttall WJ, Clarke RH, Glowacki BA. Stop squandering helium. *Nature*, **485**, 573–575 (2012).
2) Izumi Oe. Outlook for the supply and demand of helium. *Rev High Press Sci. Technol.*, **22**, 185–190 (2012).
3) Reisch M. Helium shortage looms. *C EN Glob Enterp*, **95**, 112017 (2017).
4) Bettenhausen C. Membranes open up new sources of helium. *C EN Glob Enterp.*, **99**, 21 (2021).
5) Kikuchi H, Sakai T, Okura T, Nemoto S, Akiyama H. Evaluation of simultaneous LC-MS/MS method for quantifying residual pesticides in agricultural products as a measure against the helium shortage. *Jpn. J. Food Chem. Saf.*, **27**, 184–189 (2020).
6) Abe Y, Yamaguchi M, Ohno H, Kataoka Y, Mutsuga M, Sato K. Validation of the testing method for the determination of dibutyltin compounds in food utensils, containers, and packaging products made from polyvinyl chloride using gas chromatograph-mass spectrometry with nitrogen as a carrier gas. *Jpn. J. Food Chem.*, **28**, 16–22 (2021).
7) Lin Y-P, Lee Y-L, Hung C-Y, Chang C-F, Chen Y. Detection of adulterated drugs in traditional Chinese medicine and dietary supplements using hydrogen as a carrier gas. *PLoS One*, **13**, e0205371 (2018).
8) Saito-Shida S, Nagata M, Nemoto S, Akiyama H. Multi-residue determination of pesticides in green tea by gas chromatography-tandem mass spectrometry with atmospheric pressure chemical ionisation using nitrogen as the carrier gas. *Food Addit. Contam. Part A*, **38**, 125–135 (2021).
9) Azuma K, Jinno H, Tanaka-Kagawa T, Sakai S. Risk assessment concepts and approaches for indoor air chemicals in Japan. *Int. J. Hyg. Environ. Health*, **225**, 113470 (2020).
10) MHLW. Manual for Measuring Chemical Substances in Indoor Air. Committee on Sick House Syndrome: Indoor Air Pollution, Ministry of Health, Labour and Welfare, Japan (in Japanese). Attachment 3. https://www.mhlw.go.jp/houdou/0107/h0724-1c.html, Accessed on, 27 April, 2022.