2-Methoxyphenol
3-Methoxyphenol
4-Methoxyphenol

Method number:	PV2039
Target concentration:	5 mg/m^3 OSHA 1989 TWA PEL for 4-methoxyphenol. This has been vacated.
Procedure:	Samples are collected by drawing a known volume of air through an XAD-7 tube. Samples are desorbed with methanol and analyzed by gas chromatography with a flame ionization detector (GC-FID).
Air volume and sampling rate studied:	100 minutes at 0.2 Lpm (20 L)
Status of method:	Partially Validated method. This method has been only partially evaluated and is presented for information and trial use.

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1 General Discussion

1.1 Background

1.1.1 History of procedure

The OSHA Technical Center has received many requests for a sampling and analytical procedure for the isomers of methoxyphenol. OSHA promulgated an exposure standard for 4-methoxyphenol in January 1989, at a level of 5 mg/m^3. OSHA method 32 recommends collection of phenol and cresol on XAD-7 tubes and desorption with methanol (Ref. 5.1). This procedure was found to give good recoveries for the methoxyphenol isomers, in desorption, retention, and storage studies.

1.1.2 Potential workplace exposure (Ref. 5.2 and 5.3)

Methoxyphenols are used in the manufacture of antioxidants, and pharmaceuticals. 2-Methoxyphenol is used as an expectorant, and in synthetic flavors. 4-Methoxyphenol is used to manufacture plasticizers, dyestuffs, stabilizer for chlorinated hydrocarbons and ethyl cellulose, inhibitor for acrylic monomers and acrylonitriles, and as a UV inhibitor.

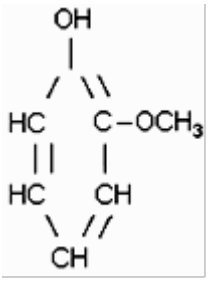
1.1.3 Toxic Effects (This section is for information purposes and should not be taken as the basis for OSHA policy.) (Ref. 5.2, 5.3, and 5.4)

Methoxyphenols are eye, skin, and mucous membrane irritants. Ingestion produces burning in the mouth and throat, followed by gastrointestinal distress, tremors, and collapse. 3-Methoxyphenol has also been reported to cause menstrual cycle changes or disorders.

1.1.4 Physical properties

2-Methoxyphenol (Ref. 5.2)

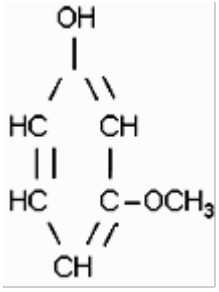
Structure:



CAS:	90-05-1
IMIS:	M168
RTECS:	56973; SL7525000
Synonyms:	Guaiacol; o-Methoxyphenol; Methyl catechol; Anastil; 1-Hydroxy-2-methoxybenzene; Pyrocatechol methyl ether; o-Hydroxyanisole; Pyroguaiac acid
Molecular weight:	124.15
Melting point:	28 °C
Boiling point:	205 °C
Flash point:	82.2 °C (180 °F) (open cup)
Odor:	sweet phenolic
Color:	white to pale yellow crystals
Molecular formula:	$C_7H_8O_2$

3-Methoxyphenol (Ref. 5.5)

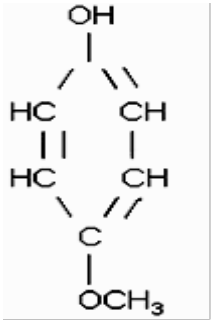
Structure:



CAS:	150-19-6
IMIS:	M169
RTECS:	56972; SL7524000
Synonyms:	Resorcinol monomethyl ether; m-Methoxyphenol; m-Hydroxyanisole
Molecular weight:	124.15
Density:	1.131
Melting point:	< -17 °C
Boiling point:	244 °C
Flash point:	82.2 °C (180 °F) (open cup)
Odor:	sweet phenolic
Color:	amber liquid
Molecular formula:	$C_7H_8O_2$

4-Methoxyphenol (Ref. 5.3.)

Structure:



CAS:	150-76-5
IMIS:	M329
RTECS:	56974; SL7700000
Synonyms:	p-Methoxyphenol; Hydroquinone monomethyl ether; p-Hydroxyanisole
Molecular weight:	124.15
Melting point:	52.5 °C
Boiling point:	243 °C
Flash point:	124 °C (257 °) (closed cup)
Odor:	sweet phenolic
Color:	white waxy solid
Molecular formula:	$C_7H_8O_2$

1.2 Limit defining parameters

1.2.1 The detection limit of the analytical procedure for each isomer of methoxyphenol is 1 µg. This is the smallest amount that could be detected under normal operating conditions.

1.2.2 The overall detection limit for each isomer of methoxyphenol is 0.05 mg/m^3. (All ppm amounts in this study are based on a 20 L air volume.)

1.3 Advantages

1.3.1 The sampling procedure is convenient.

1.3.2 The analytical method is reproducible and sensitive.

1.3.3 Reanalysis of samples is possible.

1.3.4 It may be possible to analyze other compounds at the same time.

1.3.5 Interferences may be avoided by proper selection of column and GC parameters.

1.4 Disadvantages

None known

2 Sampling procedure

2.1 Apparatus

2.1.1 A calibrated personal sampling pump, the flow of which can be determined within ±5% at the recommended flow.

2.1.2 XAD-7 tubes containing 15/50 mesh XAD-7 with a 100 mg adsorbing section with a 50 mg backup section separated by a silanized glass wool plug, with a silanized glass wool plug before and after the adsorbing sections. The ends are flame sealed and the glass tube containing the adsorbent is 8-cm x 8-mm o.d. x 6-mm i.d., SKC tubes, or equivalent.

2.2 Sampling technique

2.2.1 Open the ends of the XAD-7 tube immediately before sampling.

2.2.2 Connect the XAD-7 tube to the sampling pump with flexible tubing.

2.2.3 Place the tubes in a vertical position to minimize channeling, with the smaller section towards the pump.

2.2.4 Air being sampled should not pass through any hose or tubing before entering the XAD-7 tube.

2.2.5 Seal the XAD-7 tube with plastic caps immediately after sampling. Seal each sample lengthwise with Form OSHA-21 seal.

2.2.6 With each batch of samples, submit at least one blank tube from the same lot used for samples. This tube should be subjected to exactly the same handling as the samples (break ends, seal, & transport) except that no air is drawn through it.

2.2.7 Transport the samples (and corresponding paperwork) to the lab for analysis.

2.2.8 Bulks submitted for analysis must be shipped in a separate container from other samples.

2.3 Desorption efficiency

Six tubes were spiked at each loading of approximately 10 µg (0.5mg/m^3), 50 µg (2.5 mg/m^3), and 100 µg (5.0 mg/m^3) for each methoxyphenol. They were allowed to equilibrate overnight at room temperature. They were then opened, each section placed into a separate 2-mL vial, desorbed with 1 mL of the desorbing solution for 30 minutes with occasional shaking, and analyzed by GC-FID. The overall average was 99.7% for 2-methoxyphenol, 99.9% for 3-methoxyphenol, and 99.1% for 4-methoxyphenol. (Tables 1, 2, and 3)

Table 1
2-Methoxyphenol Desorption Efficiency

tube #	% recovered		
	10.1 µg	50.5 µg	101 µg
1	100	99.5	102
2	101	98.7	101
3	102	102	99.1
4	97.5	95.9	99.8
5	102	100	99.8
6	101	96.4	97.6
average	101	98.8	99.9

overall average = 99.7%
standard deviation = ±1.92

Table 2
3-Methoxyphenol Desorption Efficiency

tube #	% recovered		
	11 µg	55 µg	110 µg
1	100	97.6	101
2	98.6	97.9	101
3	97.4	98.7	100
4	103	98.4	102
5	102	101	102
6	99.2	96.9	101
average	100	98.4	101

overall average = 99.9%
standard deviation = ±1.85

Table 3
4-Methoxyphenol Desorption Efficiency

tube #	% recovered		
	10.2 µg	51.0 µg	102 µg
1	98.6	97.9	99.4
2	96.3	97.8	99.6
3	98.7	97.0	99.3
4	102	98.0	101
5	99.9	102	99.4
6	101	97.4	98.5
average	99.4	98.4	99.5

overall average = 99.1%
standard deviation = ±1.63

2.4 Retention efficiency

Six tubes were spiked with 101 µg (5.05 mg/m^3) 2-methoxyphenol, 110 µg (5.50 mg/m^3) 3-methoxyphenol, and 102 µg (5.10 mg/m^3) 4-methoxyphenol, allowed to equilibrate overnight, and then 20 liters humid air (91% RH) were pulled through them. They were then opened, desorbed, and analyzed by GC-FID. The retention efficiency averaged 99.8% for 2-methoxyphenol, 99.5% for 3-methoxyphenol, and 99.1% for 4-methoxyphenol. There was little or no methoxyphenol found on the backup portions of the tubes. (Tables 4, 5, and 6)

Table 4
2-Methoxyphenol Retention Efficiency
(101 µg spiked)

tube #	% recovered		total
	'A'	'B'	
1	98.9	0.7	99.6
2	98.1	0.0	98.1
3	100	0.0	100
4	99.1	0.0	99.1
5	102	0.0	102
6	100	0.0	100

average = 99.8%

Table 5
3-Methoxyphenol Retention Efficiency
(110 µg spiked)

tube #	% recovered		total
	'A'	'B'	
1	99.7	0.0	99.7
2	100	0.0	100
3	99.0	0.0	99.0
4	97.4	0.0	97.4
5	101	0.0	101
6	99.6	0.0	99.6

average = 99.5%

Table 6
4-Methoxyphenol Retention Efficiency
(102 µg spiked)

tube #	% recovered		total
	'A'	'B'	
1	98.1	0.0	98.1
2	98.2	0.0	98.2
3	101	0.0	101
4	98.3	0.0	98.3
5	100	0.0	100
6	98.8	0.0	98.8

average = 99.1%

2.5 Storage

Six tubes each were spiked with 101 µg (5.05 mg/m^3) 2-methoxyphenol, 110 µg (5.50 mg/m^3) 3-methoxyphenol, and 102 µg (5.10 mg/m^3) 4-methoxyphenol. They were stored at room temperature until opened and analyzed. The recoveries averaged 101% for 2-methoxyphenol, 100% for 3-methoxyphenol, and 99.7% for 4-methoxyphenol for the 14 days stored. (Tables 7, 8, and 9)

Table 7
2-Methoxyphenol Storage Study
(101 µg spiked)

day	% recovered
7	102
7	100
7	100
14	103
14	99.8
14	99.2
average	101

Table 8
3-Methoxyphenol Storage Study
(110 μg spiked)

day	% recovered
7	101
7	99.2
7	99.8
14	102
14	100
14	100
average	100

Table 9
4-Methoxyphenol Storage Study
(102 μg spiked)

day	% recovered
7	100
7	98.8
7	99.2
14	101
14	99.5
14	99.7
average	99.7

2.6 Precision

The precision was calculated using the area counts from six injections of each standard at concentrations of approximately 10, 50, 100, and 200 µg/mL of each methoxyphenol in the desorbing solution. The pooled coefficient of variation was 0.0226 for 2-methoxyphenol, 0.0180 for 3-methoxyphenol, and 0.0147 for 4-methoxyphenol. (Tables 10, 11, and 12)

Table 10
2-Methoxyphenol Precision Study

injection number	10.1 μg/mL	50.5 μg/mL	101 μg/mL	202 μg/mL
1	1605	8858	19242	40786
2	1691	8829	19596	40180
3	1567	8796	19406	39842
4	1543	8712	18530	40642
5	1553	8646	19569	40656
6	1609	8581	18602	39863
average	1595	8737	19158	40328
standard deviation -	±54.3	±109	±476	±422
CV -	0.0340	0.0125	0.0248	0.0105

pooled CV = 0.0226

Table 11
3-Methoxyphenol Precision Study

injection number	11.0 μg/mL	55.0 μg/mL	110 μg/mL	220 μg/mL
1	2011	9931	20670	42296
2	2024	9590	20444	42539
3	1933	9993	20071	42241
4	1873	9735	20468	42104
5	1966	9675	20586	42341
6	1968	9548	20126	42090
average	1963	9745	20394	42269
standard deviation -	±54.9	±181	±244	±167
CV -	0.0280	0.0186	0.0120	0.00395

pooled CV = 0.0180

Table 12
4-Methoxyphenol Precision Study

injection number	10.2 μg/mL	51.0 μg/mL	102 μg/mL	204 μg/mL
1	1982	10178	21314	42133
2	2032	10059	20806	43044
3	1983	10270	21214	42404
4	1968	10307	20503	42328
5	2043	10153	20814	42527
6	2061	10470	20609	42806
average	2012	10240	20877	42540
standard deviation -	±38.6	±143	±324	±333
CV -	0.0192	0.0140	0.0155	0.00783

pooled CV = 0.0147

Where:

$$CV\ \left(Coefficient\ of\ Variation\right) = \frac{\left(standard\ deviation\right)}{\left(average\right)}$$

$$Pooled\ CV = \sqrt{\frac{A1(CV1)^2 + A2(CV2)^2 + A3(CV3)^2 + A4(CV4)^2}{A1 + A2 + A3 + A4}}$$

A1, A2, A3, A4 = number of injections at each level
CV1, CV2, CV3, CV4 = Coefficients of variation at each level

2.7 Air volume and sampling rate studied

2.7.1 The air volume studied is 20 liters.

2.7.2 The sampling rate studied is 0.2 liters per minute.

2.8 Interferences

Suspected interferences should be listed on sample data sheets.

2.9 Safety precautions

2.9.1 Sampling equipment should be placed on an employee in a manner that does not interfere with work performance or safety.

2.9.2 Safety glasses should be worn at all times.

2.9.3 Follow all safety practices that apply to the workplace being sampled.

3 Analytical method

3.1 Apparatus

3.1.1 Gas chromatograph equipped with a flame ionization detector. A HP 5890 gas chromatograph was used in this study.

3.1.2 GC column capable of separating the analyte and an internal standard from any interference. The column used in this study was a 30-m x 0.32-mm i.d. with (0.25 µm d_f DB-225) capillary column. An alternate column is a 60-m x 0.32-mm i.d. with (1.0 µm d_f DB-1) capillary column.

3.1.3 An electronic integrator or some other suitable method of measuring peak areas.

3.1.4 Two milliliter vials with PTFE-lined caps.

3.1.5 A 1.0-µL syringe or other convenient size for sample injection.

3.1.6 Pipettes for dispensing the desorbing solution. The Glenco 1-mL dispenser was used in this method.

3.1.7 Volumetric flasks, 5-mL and other convenient sizes for preparing standards.

3.2 Reagents

3.2.1 Purified GC grade nitrogen, hydrogen, and air.

3.2.2 2-Methoxyphenol, Reagent grade

3.2.3 3-Methoxyphenol, Reagent grade

3.2.4 4-Methoxyphenol, Reagent grade

3.2.5 Methanol, HPLC grade

3.2.6 Dimethyl formamide, Reagent grade

3.2.7 Desorbing solution is methanol with 1 µL/mL dimethyl formamide used as internal standard.

3.3 Sample preparation

3.3.1 Sample tubes are opened and the front and back section of each tube are placed in separate 2-mL vials, and the front glass wool was included in the vial with the front section.

3.3.2 Each section is desorbed with 1 mL of the desorbing solution.

3.3.3 The vials are sealed immediately and allowed to desorb for 30 minutes with occasional shaking.

3.4 Standard preparation

3.4.1 Standards are prepared by diluting a known quantity of each isomer of methoxyphenol.

3.4.2 At least two separate stock standards should be made. Dilutions of the stock standards are prepared covering the concentrations in the samples. The analytical standards used in this study ranged from 1 to 110 µg/mL for each isomer of methoxyphenol in the desorbing solution.

3.5 Analysis

3.5.1 Gas chromatograph conditions for DB-225 capillary column.

Flow rates	**(mL/min)**	**Temperature**	**(°C)**
Nitrogen (makeup):	30	Injector:	240
Hydrogen (carrier):	1.5	Detector:	240
Hydrogen (detector):	30	Column:	(100 °C for 1 min then
Air:	450		increase 5°C/min to 140 °C)
Injection size	1 µL		
Elution times	4.554, 11.455, and 12.175 min		
Chromatogram	(See Figure 1)		

3.5.2 Gas chromatograph conditions for DB-1capillary column.

Flow rates	**(mL/min)**	**Temperature**	**(°C)**
Nitrogen (makeup):	30	Injector:	240
Hydrogen (carrier):	1.5	Detector:	240
Hydrogen (detector):	30	Column:	(80 °C for 0 min then
Air:	450		increase10 °C/min to 160°C)
Injection size	1 µL		
Elution time	12.180, 15.328, and 15.768 min		
Chromatogram	(See Figure 2)		

3.5.3 Peak areas are measured by an integrator or other suitable means.

3.6 Interferences (analytical)

3.6.1 Any compound having the general retention time of the analyte or the internal standard used is interference. Possible interferences should be listed on the sample data sheet. GC parameters should be adjusted if necessary so these interferences will pose no problems.

3.6.2 Retention time data on a single column is not considered proof of chemical identity. Samples over the target concentration should be confirmed by GC/Mass Spec or other suitable means.

3.7 Calculations

3.7.1 A curve with area counts versus concentration is prepared from the calibration standards.

3.7.2 The area counts for the samples are plotted on the calibration curve to obtain the concentration of methoxyphenol in solution.

3.7.3 To calculate the concentration of analyte in the air sample the following formulas are used:

$$mass\ of\ analyte,\ \mu g = \frac{(\mu g / mL)(desorption\ volume,\ mL)}{(desorption\ efficiency,\ decimal)}$$

$$moles\ of\ analyte = \frac{(mass\ of\ analyte,\ \mu g)(1\,g)}{(molecular\ weight)(10^6\ \mu g)}$$

$$volume\ of\ analyte = (moles\ of\ analyte)(molar\ volume)$$

$$ppm = \frac{(volume\ of\ analyte)(10^6)^*}{(air\ volume,\ L)}$$

* All units must cancel.

3.7.4 The above equations can be consolidated to form the following formula. To calculate the ppm of analyte in the sample based on a 20 liter air sample:

$$ppm = \frac{(\mu g / mL)(DV)(24.46)}{(L)(DE)(MW)}$$

Where:

µg/mL = concentration of analyte in sample
24.46 = Molar volume (liters/mole) at 25 °C and 760 mmHg
MW = Molecular weight (g/mole)
DV = Desorption volume, mL
20 L = 20 L Air volume
DE = Desorption efficiency, decimal

3.7.5 This calculation is done for each section of the sampling tube and the results added together.

3.8 Safety precautions

3.8.1 All handling of solvents should be done in a hood.

3.8.2 Avoid skin contact with all chemicals.

3.8.3 Wear safety glasses, gloves and a lab coat at all times.

4 Recommendations for further study

Collection study should be performed.

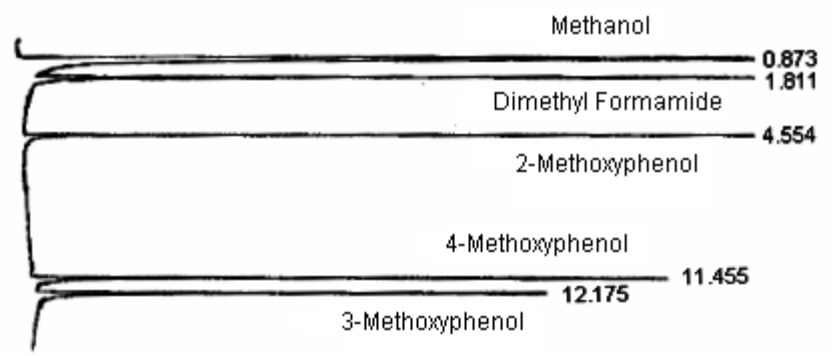


Figure 1. An analytical standard of 101 µg/mL 2-methoxyphenol, 110 µg/mL 3-methoxyphenol, and 102 µg/mL 4-methoxyphenol in methanol with 1 µL/mL dimethyl formamide internal standard, analyzed using a DB-225 capillary column.

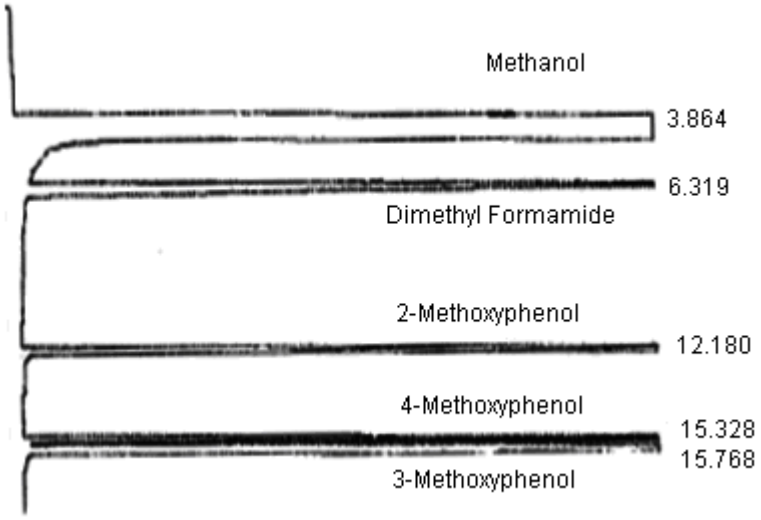


Figure 2. An analytical standard of 101 µg/mL 2-methoxyphenol,110 µg/mL 3-methoxyphenol, and 102 µg/mL 4-methoxyphenol in methanol with 1 µL/mL dimethyl formamide internal standard, analyzed using a DB-1 capillary column.

5 References

5.1 Cummins, K., Method 32, "Phenol and Cresol," Organic Methods Evaluation Branch, OSHA Salt Lake Technical Center, 1986.

5.2 Windholz, M., "The Merck Index," Eleventh Edition, Merck & Co., Rahway N.J., 1989, p. 715.

5.3 Sax, N., Lewis, R., "Hawley's Condensed Chemical Dictionary," Eleventh Edition, Van Nostrand Reinhold Co., New York, 1987, p. 620.

5.4 "Documentation of the Threshold Limit Values and Biological Exposure Indices," Fifth Edition, American Conference of Governmental Industrial Hygienists Inc., Cincinnati, OH, 1986, p. 367.

5.5 Weast, R.C., "Handbook of Chemistry and Physics," 67th Edition, CRC Press Inc., Boca Raton FL, 1986, p.C244.