Butyl butyrate
Isobutyl isobutyrate

Method no.:	PV2090
Target Concentration:	100 ppm (590 mg/m^3)
Procedure:	Samples are collected by drawing a known volume of air through a charcoal tube. Samples are desorbed with 1:99 dimethyl formamide:carbon disulfide and analyzed by gas chromatography with a flame ionization detector (GC-FID).
Air volume and sampling rate studied:	50 minutes at 0.2 Lpm (10 liters)
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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Mary E. Eide

Organic Service Branch I
OSHA Salt Lake Technical Center
Salt Lake City UT-84115

1 General Discussion

1.1 Background

1.1.1 History of procedure

Butyl butyrate and isobutyl isobutyrate have been proposed as a replacement for the cellosolves in the manufacturing of circuit boards. Sampling for butyl butyrate and isobutyl isobutyrate using charcoal tubes had good retention and storage efficiencies. Desorption of both butyl butyrate and isobutyl isobutyrate with carbon disulfide showed no constant desorption ranging from 91.5% to 97.6% for loadings of 0.592 to 11.85 mg butyl butyrate and 91.8% to 98.9% for loadings of 0.59 to 11.8 mg isobutyl isobutyrate. The butyl butyrate and isobutyl isobutyrate desorption efficiency using 1:99 dimethyl formamide:carbon disulfide was constant and averaged 101% for butyl butyrate and 100% for isobutyl isobutyrate.

1.1.2 Potential workplace exposure (Ref. 5.1)

Butyl butyrate is used in the manufacture of circuit boards, and in the flavoring and fragrance industries.

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)

Butyl butyrate and isobutyl isobutyrate are moderate eye, mucous membrane, and respiratory irritants. An exposure of 5000 ppm for 6 hours killed two out of three rats exposed, but there were no exposure symptoms when rats were exposed to 500 ppm for 6 hours. Isobutyl isobutyrate exposure of 5000 ppm for 6 hours killed half the rats exposed.

1.1.4 Physical properties:

Butyl butyrate (Ref. 5.1):

Compound:	$CH_3(CH_2)_2COO(CH_2)_3CH_3$
CAS:	109-21-7
IMIS:	SLC1
Synonyms:	butyl butanoate; butanoic acid butyl ester; butyric acid butyl ester; n-butyl n-butyrate; n-butyl butyrate
Molecular weight:	144.24
Density:	0.8721
Freezing point:	- 91.5 °C
Boiling point:	166 °C
Flash point:	53.5 °C (128 °F) (open cup)
Color:	clear liquid
Molecular formula:	$C_8H_{16}O_2$
RTECS:	ES8120000
DOT:	UN 2528

Isobutyl isobutyrate (Ref. 5.3):

Compound:	$(CH_3)_2CHCOOCH_2CH(CH_3)_2$
CAS:	97-85-8
IMIS:	1537
Synonyms:	2-Methylpropyl isobutyrate; 2-Methylpropyl 2-methylpropanoate; Isobutyric acid, isobutyl ester; 2-Methylpropyl 2-methypropionate
Molecular weight:	144.24
Density:	0.875
Freezing point:	- 81 °C
Boiling point:	147 °C
Flash point:	37 °C (99 °F) (open cup)
Color:	clear liquid
Molecular formula:	$C_8H_{16}O_2$
RTECS:	44147; NQ5250000
DOT:	UN 2528

1.2 Limit defining parameters

1.2.1 The detection limit of the analytical procedure for both compounds is 5 ng with a 1-µL injection or 5 µg/mL. This is the smallest amount that could be detected under normal operating conditions.

1.2.2 The overall detection limit for both compounds is based on a 10-liter 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 with the sample tube attached.

2.1.2 Charcoal tubes, lot 120, containing 100-mg adsorbing section with a 50-mg backup section separated by a 2-mm portion of urethane foam, with a silanized glass wool plug before the adsorbing section and a 3-mm plug of urethane foam at the back of the backup section. The ends are flame sealed and the glass tube containing the adsorbent is 7-cm x 6-mm o.d. and 4-mm i.d., SKC tubes or equivalent.

2.2 Sampling technique

2.2.1 Open the ends of the charcoal tube immediately before sampling.

2.2.2 Connect the charcoal 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 charcoal tube.

2.2.5 Seal the charcoal tube with plastic caps immediately after sampling. Seal each sample lengthwise with a 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 mailing container from the samples.

2.3 Desorption efficiency

2.3.1 Six tubes were spiked at each loading of 0.52 mg (10.0 ppm), 2.96 mg (50.1 ppm), 5.92 mg (100 ppm), and 11.9 mg (201 ppm) butyl butyrate, and 0.59 mg (10.0 ppm), 2.95 mg (50.0 ppm), 5.9 mg (100 ppm), and 11.8 mg (200 ppm) isobutyl Isobutyrate. They were sealed and allowed to equilibrate overnight at room temperature. They were then opened, each section placed into a separate 2-mL vial, desorbed with 1 mL carbon disulfide for 30 minutes with occasional shaking, and analyzed by GC-FID. Desorption for butyl butyrate was non-constant ranging from 91.5% to 97.6%. Desorption for isobutyl isobutyrate was also non-constant ranging from 91.8% to 98.9%. (See Tables 2.3.1.1 and 2.3.1.2)

Table 2.3.1.1
Butyl Butyrate
Carbon Disulfide Desorption Efficiency

tube #	% recovered			
	0.592 mg	2.96 mg	5.92 mg	11.8 mg
1	92.6	97.4	96.5	97.7
2	90.7	93.8	95.3	98.7
3	94.6	97.3	96.4	97.4
4	90.3	94.4	96.3	97.3
5	91.0	96.2	95.9	97.0
6	89.6	96.1	96.0	97.5
average	91.5	95.9	96.1	97.6

Table 2.3.1.2
Isobutyl Isobutyrate
Carbon Disulfide Desorption Efficiency

tube #	% recovered			
	0.59 mg	2.95 mg	5.9 mg	11.8 mg
1	91.3	96.1	97.8	99.5
2	91.4	97.3	97.6	99.1
3	91.5	97.8	97.1	98.7
4	91.2	95.3	96.4	98.9
5	94.0	96.9	97.0	98.9
6	91.3	96.5	97.4	98.0
average	91.8	96.7	97.2	98.9

2.3.2 Six tubes were spiked at each loading of 0.592 mg (10.0 ppm), 2.96 mg (50.1 ppm), 5.92 mg (100 ppm), and 11.8 mg (201 ppm) butyl butyrate, and 0.19 mg (10.0 ppm), 2.95 mg (50.0 ppm), 5.9 mg (100 ppm), and 11.8 mg (200 ppm) isobutyl isobutyrate. They were sealed and allowed to equilibrate overnight at room temperature. They were then opened, each section placed into a separate 2-mL vial, desorbed with 1 mL, 1:99 dimethyl formamide:carbon disulfide, for 30 minutes with occasional shaking, and were analyzed by GC-FID. The desorption efficiency averaged 101% for butyl butyrate and 100% for isobutyl isobutyrate. (Tables 2.3.2.1 and 2.3.2.2)

Table 2.3.2.1
Butyl Butyrate
(1/99) DMF/Carbon Disulfide Efficiency

tube #	% recovered			
	0.592 mg	2.96 mg	5.92 mg	11.8 mg
1	97.4	101	102	102
2	100	100	102	102
3	100	101	102	102
4	97.5	102	102	103
5	100	102	102	102
6	101	101	101	102
average	99.3	101	102	102

overall average = 101%
standard deviation = ±1.41

Table 2.3.2.2
Isobutyl Isobutyrate
(1/99) DMF/Carbon Disulfide Efficiency

tube #	% recovered			
	0.59 mg	2.95 mg	5.9 mg	11.8 mg
1	101	102	100	101
2	101	101	100	101
3	100	100	99.7	101
4	99.2	101	100	100
5	100	99.2	100	101
6	100	99.9	100	100
average	100	100	99.9	101

Overall average = 100%
Standard deviation = ±0.763

2.4 Retention efficiency

Six tubes were spiked with 5.92 mg (100 ppm) butyl butyrate and 5.9 mg (100 ppm) isobutyl isobutyrate, allowed to equilibrate overnight, and had 10 liters of humid air (90% RH) pulled through them. They were opened, desorbed, and analyzed by GC-FID. The retention efficiency averaged 101% for butyl butyrate and 99.6% isobutyl isobutyrate. There was no butyl butyrate or isobutyl isobutyrate found on the backup portions of the tubes. (Tables 2.4.1 and 2.4.2)

Table 2.4.1
Butyl Butyrate Retention Efficiency

tube #	% recovered		
	'A'	'B'	total
1	101	0.0	101
2	101	0.0	101
3	101	0.0	101
4	102	0.0	102
5	101	0.0	101
6	101	0.0	101

average = 101%

Table 2.4.2
Isobutyl Isobutyrate
Retention Efficiency

tube #	% recovered		
	'A'	'B'	total
1	98.5	0.0	98.5
2	99.0	0.0	99.0
3	99.5	0.0	99.5
4	99.8	0.0	99.8
5	99.7	0.0	99.7
6	101	0.0	101

average = 99.6%

2.5 Storage

Tubes were spiked with 5.92 mg (100 ppm) butyl butyrate (BUBU) and 5.9 mg (100 ppm) isobutyl isobutyrate (IBUIBU), and stored at room temperature until opened and analyzed. The recoveries averaged 100% for the 14 days stored for both compounds. (Table 2.5)

Table 2.5
Storage Study

day	% BUBU recovered	% IBUIBU recovered
7	99.2	100
7	101	101
7	99.5	101
14	101	101
14	100	100
14	101	99.1
average	100	100

2.6 Precision

The precision was calculated using the area counts from six injections of each standard at concentrations of 0.592, 2.96, 5.92, and 11.8 mg/mL butyl butyrate acid 0.59, 2.95, 5.9, and 11.8 mg/mL isobutyl isobutyrate in the desorbing solution. The pooled coefficient of variation for butyl butyrate was 0.000499 and for isobutyl isobutyrate was 0.00473. (Tables 2.6.1 and 2.6.2)

Table 2.6.1
Butyl Butyrate Precision Study

injection number	0.592 mg/mL	2.96 mg/mL	5.92 mg/mL	11.8 mg/mL
1	197949	971557	1970639	3690291
2	197906	971669	1971073	3961489
3	197924	971238	1972333	3962383
4	197635	970749	1971981	3961327
5	197791	970969	1970218	3961751
6	197627	970573	1970264	3960444
average	197805	971126	1971085	3961280
standard deviation	±146	±440	±893	±795
CV	0.000738	0.000453	0.000453	0.000201

pooled CV = 0.00499

Table 2.6.2
Isobutyl Isobutyrate Precision Study

injection number	0.59 mg/mL	2.95 mg/mL	5.9 mg/mL	11.8 mg/mL
1	211436	987164	1938231	3933722
2	213291	999762	1934835	3922986
3	211528	987648	1931985	3920749
4	214111	998123	1937375	3914866
5	212498	996116	1923764	3914166
6				
average	212393	995694	1933979	3922677
standard deviation	±1117	±7118	±5292	±6952
CV	0.000526	0.00718	0.00274	0.00177

pooled CV = 0.00473

where:

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

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

A(1), A(2), A(3), A(4) = number of Injections at each level
CV1, CV2, CV3, CV4 = Coefficients at each level

2.7 Air volume and sampling rate studied

2.7.1 The air volume studied was 10 liters.

2.7.2 The sampling rate studied was 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 in designated areas.

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 HP5890 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 15-m x 0.32-mm i.d. with an (O.25-µm d_f DB-WAX) capillary column. Other columns that can be used are a 60-m x 0.32-mm i.d. (O.25-µm d_f DB-WAX) capillary column, or a 60-m x 0.32-mm i.d. with a (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-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 Butyl butyrate, Reagent grade

3.2.3 Isobutyl isobutyrate, Reagent grade

3.2.4 Dimethyl formamide, Reagent grade

3.2.5 Carbon disulfide, Reagent grade

3.2.6 n-Hexylbenzene Reagent grade, internal standard

3.2.7 The desorbing solution is prepared by adding 250 mL n-hexylbenzene to 1 liter of a 1:99 dimethyl formamide:carbon disulfide solution to obtain a concentration of 0.25 µL/mL n-hexylbenzene in the solution. The n-hexylbenzene is used as the 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.

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 At least two separate standards are prepared by diluting a known quantity of butyl butyrate and isobutyl isobutyrate with the desorbing solution.

3.4.2 A third analytical standard should be prepared at a higher concentration to check the linearity of the detector. For this study two standard at 1 µL/mL (0.871 mg/mL butyl butyrate and 0.855 mg/mL isobutyl isobutyrate), one standard at 4 µL/mL (3.48 mg/mL butyl butyrate and 3.42 mg/mL isobutyl isobutyrate), one standard at 8 µL/mL (6.97 mg/mL butyl butyrate and 6.84 mg/mL isobutyl isobutyrate), and one standard at 14 µL/mL (12.2 mg/mL butyl butyrate and 11.97 mg/mL isobutyl isobutyrate) were used.

3.5 Analysis

3.5.1 Gas chromatograph conditions for 15-m x 0.32-mm i.d. (O.25-µm d_f DB-WAX) capillary column.

Flow rates (mL/min.)		**Temperature (°C)**	
Nitrogen (make-up):	30	Injector:	180
Hydrogen (carrier):	2	Detector:	220
Hydrogen (detector):	30	Column:	60^0 then 10°/min to 130
Air:	350		

Injection size: 1µL
Chromatogram: See Figure 1

3.5.2 Gas chromatograph conditions for 60-m x 0.32-mm i.d. with a (1.0-µm d_f DB-1) capillary column.

Flow rates (mL/min.)		**Temperature (°C)**	
Nitrogen (make-up):	30	Injector:	180
Hydrogen (carrier):	2	Detector:	220
Hydrogen (detector):	60	Column:	50^0 then 10°/min to 180^0
Air:	420		

Injection size: 1 µL
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 The instrument is calibrated with a standard of 0.871 mg/mL (1 µL/mL) butyl butyrate and 0.855 mg/mL (1 µL/mL) isobutyl isobutyrate in the desorbing solution. The linearity of the calibration is checked with a standard of 3.48 mg/mL (4 µL/mL) butyl butyrate and 3.42 mg/mL(4 µL/mL) isobutyl isobutyrate in the desorbing solution.

3.7.2 If the calibration is non-linear, two more standards must be analyzed so a calibration curve can be plotted and sample values obtained.

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

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

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

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

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

* All units must cancel.

3.7.4 The above equations can be consolidated to form the following equation. To calculate the ppm of analyte in the sample based on a 10-liter sample:

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

µg/mL = Concentration of analyte in sample or standard
24.46 = Molar Volume (Liters/mole) at 25 °C and 760 mm Hg.
MW = Molecular Weight (g/mole)
DV = Desorption Volume, mL
10 L = 10-Liter air sample
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 studies need to be performed.

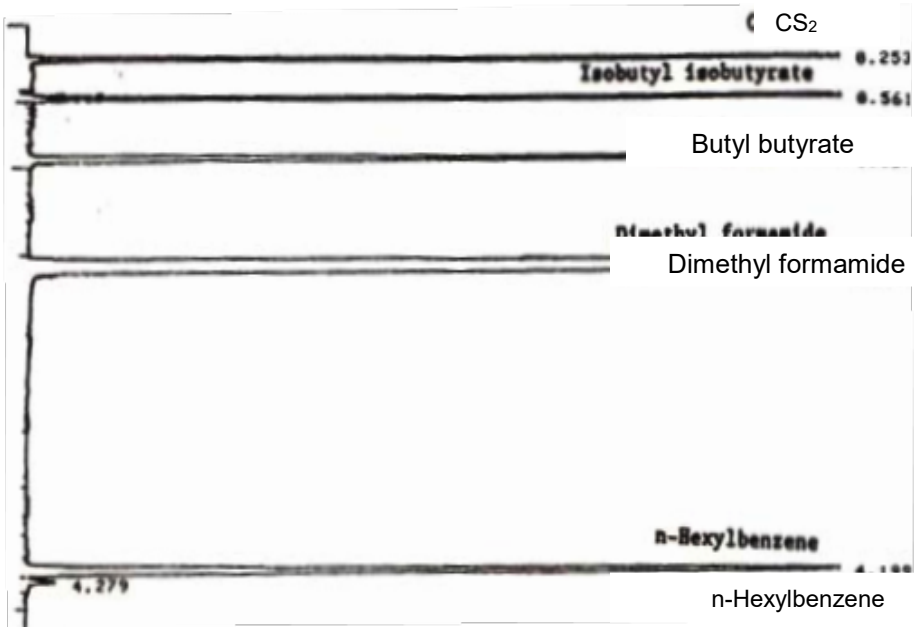

Figure 1.
An analytical standard containing 871 µg/mL butyl butyrate and 855 µg/mL isobutyl isobutyrate in 1:99 dimethyl formamide:carbon disulfide, with 0.25 µL/mL n-hexylbenzene internal standard, analyzed on a 15-meter DB-WAX capillary column.

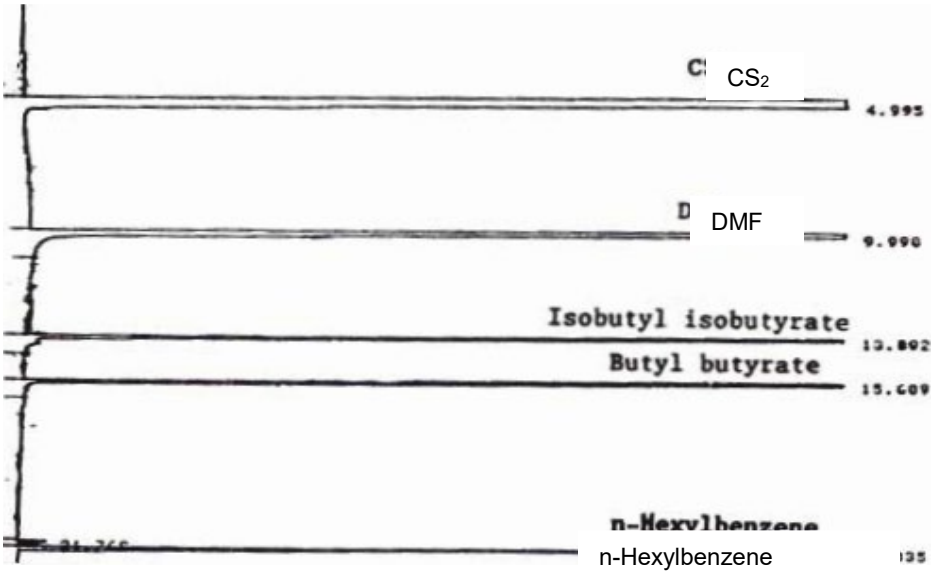

Figure 2.

An analytical standard containing 871 µg/mL butyl butyrate and 855 µg/mL isobutyl isobutyrate in 1:99 dimethyl formamide:carbon disulfide, with 0.25 µL/mL n-hexylbenzene internal standard, analyzed on a 60-meter DB-1 capillary column.

5 References

5.1 Windholz, M., "The Merck Index," Eleventh Edition, Merck Co., Rahway N.J., 1989, p. 239.

5.2 Clayton, G.D.t Clayton, F.E., "Patty's Industrial Hygiene and Toxicology," Third Edition, Volume 2A, John Wiley & Sons, New York N.Y., 1981, p. 2286.

5.3 Sax, N., Lewis, R., "Hawley's Condensed Chemical Dictionary," Eleventh Edition, Van Nostrand Reinhold Co., New York, 1987, p. 654.