Determination of ketones and C_4 – C_5 alcohols in solvent mixtures

Method number	5
Application	Air analysis
Analytical principle	Gas chromatography-mass spectrometry (GC-MS) (silica gel / ternary mixture)
Completed in	April 2013

Summary

Selected ketones and C_4–C_5 alcohols can be determined in the workplace air using this analytical method. A defined volume of air is drawn through a silica gel tube by a suitable pump for the sampling procedure. After completion of sampling the substances are desorbed with a ternary mixture consisting of dichloromethane, methanol and water. The sample solution is analysed by means of gas chromatography-mass spectrometry (GC-MS). The quantitative evaluation is based on calibration functions obtained by means of multiple-point calibrations using toluene D_8 as internal standard (IS).

Characteristics of the method

Precision:	Standard deviation (rel.):	s = 0.70 to 4.1%
	Expanded uncertainty:	U = 16 to 18%
	in the concentration range from 2.2 up to 1 340 mg/m^3 (depending on the substance) and for n = 6 determinations	
Limit of quantification:	0.060 to 0.75 mg/m^3 depending on the substance for an air sample volume of 7.5 L, 5 mL of desorption solution and an injection volume of 1 µL	
Recovery:	83 to 101%	
Sampling recommendations:	Air sample volume:	7.5 L
	Flow rate:	30 mL/min

Authors: *W. Krämer, W. Schneider*

Determination of ketones and C_4 – C_5 alcohols in solvent mixtures

Method number	5
Application	Air analysis
Analytical principle	Gas chromatography-mass spectrometry (GC-MS) (silica gel / ternary mixture)
Completed in	April 2013

Contents

1 General principles

Selected ketones and C_4–C_5 alcohols can be determined in the workplace air using this analytical method. A defined volume of air is drawn through a silica gel tube by a suitable pump for the sampling procedure, whereby the substances to be investigated are adsorbed onto silica gel. After completion of sampling the substances are desorbed with a ternary mixture consisting of dichloromethane, methanol and water. The sample solution is analysed by means of gas chromatography-mass spectrometry (GC-MS). The quantitative evaluation is based on calibration functions obtained by means of multiple-point calibrations using toluene D_8 as internal standard.

2 Equipment, chemicals and solutions

2.1 Equipment

- Silica gel tubes, collection layer of 520 mg, control layer of 260 mg (e.g. SKC, item No. 226-15 from Analyt-MFC, 79379 Müllheim, Germany)
- Pump, suitable for a flow rate of 30 mL/min (e.g. LFS-113DC model, from Gilian Inc, USA)
- Gas chromatograph with a mass selective detector (GC-MSD), autosampler, split/splitless injector and evaluation system
- Capillary column e.g. HP-5MS: 30 m, film thickness 1.0 µm, internal diameter 0.25 mm (e.g. from Agilent, 76337 Waldbronn, Germany)
- Flow meter
- Headspace vials with septum and aluminium screw cap, nominal volume 10 mL
- Volumetric flasks, nominal volumes 1, 5, 10, 20, 50 and 1 000 mL
- Microlitre syringes, 50 and 100 µL
- Adjustable volume piston pipette

2.2 Chemicals

The substances to be determined should have the highest possible purity.

- 1-Butanol, purity (GC) ≥ 99%
- 2-Butanol, purity (GC) ≥ 99.5%
- 2-Methyl-1-propanol, purity (GC) ≥ 99.5%
- 1-Pentanol, purity (GC) ≥ 99%
- Butanone, purity (GC) ≥ 99%
- Cyclohexanone, purity (GC) ≥ 99.8%
- Cyclopentanone, purity (GC) ≥ 99%
- 2-Hexanone, purity (GC) 98%

- 4-Methylpentan-2-one, purity (GC) ≥ 99.5%
- 3-Pentanone, purity (GC) ≥ 99%
- Toluene D_8, purity (GC) ≥ 99% (internal standard)
- *n*-Pentane (Spectranal)
- Dichloromethane, p.a.
- Methanol, p.a.
- Demineralised water
- Helium 5.0 (carrier gas)

2.3 Solutions

Desorption solution: Ternary mixture: $CH_2Cl_2/MeOH/H_2O$ (65/33/2)

330 mL of methanol and 20 mL of demineralised water are placed into a 1 000 mL volumetric flask. Then 20 µL of toluene-D_8 (internal standard) are added, the volumetric flask is filled to the mark with dichloromethane and shaken.

Calibration standards are necessary for obtaining the required calibration functions. These should cover at least the concentration range of one tenth to twice the respective Occupational Exposure Limits (for minimum ranges see [1]). If this is not possible for reasons of linearity, then calibration is carried out in the linear range and the sample is subsequently diluted accordingly.

Stock solution

Several millilitres of desorption solution are placed into a 20 mL volumetric flask. Then approx. 60 mg of each of the substances to be investigated (for exact masses see Table 1), weighed exactly to the nearest 0.1 mg, are transferred into the volumetric flask. The flask is filled to the mark with desorption solution and shaken.

Calibration solutions

Nine calibration solutions are prepared from the stock solution. For calibration solutions Nos. 2 to 9 pipettes are used to add the volumes of stock solution listed in Table 2 to 5 mL volumetric flasks into which several millilitres of the desorption solution have already been placed. Calibration solution 1 is prepared by diluting calibration solution 2 by a factor of 10; this is equivalent to 0.5 µL of the calibration stock solution. The volumetric flasks are then filled to the mark with desorption solution and shaken.

2.4 Validation solutions

The following validation solutions were prepared for the purpose of determining the characteristics of the method.

Table 1 Preparation of the stock solution

Substance	Purity	Mass [mg/20 mL]	Concentration [mg/mL]
1-Butanol	0.99	60.2	2.98
2-Butanol	1.00	59.7	2.99
2-Methyl-1-propanol	1.00	57.8	2.89
1-Pentanol	0.99	58.9	2.92
Butanone	0.99	60.6	3.00
Cyclohexanone	1.00	68.9	3.44
Cyclopentanone	0.99	72.1	3.57
2-Hexanone	0.98	62.5	3.06
4-Methylheptan-2-one	1.00	60.6	3.03
3-Pentanone	0.99	62.0	3.07

Table 2 Dosing scheme for the preparation of the calibration solutions and corresponding air concentrations*

Calibration solution	No.	1	2	3	4	5	6	7	8	9
Volume of	[µL]	0.5	5	10	25	50	100	200	300	400
1-Butanol	mg/L	0.30	2.98	5.96	14.9	29.8	59.6	119	179	238
	_[mg/m^3]*_	_0.20_	_1.99_	_3.97_	_9.93_	_19.9_	_39.7_	_79.5_	_119_	_159_
2-Butanol	mg/L	0.30	2.99	5.97	14.9	29.9	59.7	119	179	239
	_[mg/m^3]*_	_0.20_	_1.99_	_3.98_	_9.95_	_19.9_	_39.8_	_79.6_	_119_	_159_
2-Methyl-1-propanol	mg/L	0.29	2.89	5.78	14.4	28.9	57.8	116	173	231
	_[mg/m^3]*_	_0.19_	_1.93_	_3.85_	_9.63_	_19.3_	_38.5_	_77.0_	_116_	_154_
1-Pentanol	mg/L	0.29	2.92	5.83	14.6	29.2	58.3	117	175	233
	_[mg/m^3]*_	_0.19_	_1.94_	_3.89_	_9.72_	_19.4_	_38.9_	_77.7_	_117_	_155_
Butanone	mg/L	0.30	3.00	6.00	15.0	30.0	60.0	120	180	239
	_[mg/m^3]*_	_0.20_	_2.00_	_4.00_	_10.0_	_20.0_	_40.0_	_80.0_	_120_	_160_
Cyclohexanone	mg/L	0.34	3.44	6.89	17.2	34.5	68.9	138	207	276
	_[mg/m^3]*_	_0.23_	_2.30_	_4.59_	_11.5_	_23.0_	_45.9_	_91.9_	_138_	_184_
Cyclopentanone	mg/L	0.36	3.57	7.14	17.9	35.7	71.4	143	214	286
	_[mg/m^3]*_	_0.24_	_2.38_	_4.76_	_11.9_	_23.8_	_47.6_	_95.2_	_143_	_190_
2-Hexanone	mg/L	0.31	3.06	6.13	15.3	30.6	61.3	123	184	245
	_[mg/m^3]*_	_0.21_	_2.04_	_4.08_	_10.2_	_20.4_	_40.8_	_81.7_	_123_	_163_
4-Methylheptan-2-one	mg/L	0.30	3.03	6.06	15.2	30.3	60.6	121	182	243
	_[mg/m^3]*_	_0.20_	_2.02_	_4.04_	_10.1_	_20.2_	_40.4_	_80.8_	_121_	_162_
3-Pentanone	mg/L	0.31	3.07	6.13	15.3	30.7	61.3	123	184	245
	_[mg/m^3]*_	_0.21_	_2.04_	_4.09_	_10.2_	_20.4_	_40.9_	_81.8_	_123_	_164_

* The stated concentrations in mg/m^3 are valid for an air sample volume of 7.5 L and desorption volume of 5 mL.

Validation Solution 1

The alcohols and ketones listed in Table 3, weighed exactly to the nearest 0.1 mg, are placed into a 20 mL volumetric flask and the flask is then filled to the mark with n-pentane.

Table 3 Concentrations of the alcohols and ketones in the validation solutions

Substance	Purity	Mass [mg/20 mL]	Validation solution 1 [mg/mL]	Validation solution 2 [mg/mL]
1-Butanol	0.99	942.3	46.6	4.66
2-Butanol	1.00	345.0	17.3	1.73
2-Methyl-1-propanol	1.00	929.9	46.5	4.65
1-Pentanol	0.99	971.2	48.1	4.81
Butanone	0.99	1649	81.6	8.16
Cyclohexanone	1.00	140.0	7.00	0.70
Cyclopentanone	0.99	2097	104	10.4
2-Hexanone	0.98	66.0	3.23	0.32
4-Methylheptan-2-one	1.00	116.7	5.84	0.58
3-Pentanone	0.99	2030	100	10.0

Validation Solution 2

0.5 mL of validation solution 1 is placed into a 5 mL volumetric flask, then the flask is filled to the mark with n-pentane.

3 Sampling and sample preparation

3.1 Sampling

A silica gel tube is opened and connected to a suitable pump for sampling. A volumetric flow of 30 mL/min is set. At a sampling period of 4 hours this is equivalent to an air sample volume of max. 7.5 L. The pump and the tube are either worn by a person during working hours or stationary sampling is carried out. After sampling, the flow rate must be checked for constancy. If the deviation from the set flow rate is greater than ± 5%, it is advisable to reject the measurements. The silica gel tube is tightly sealed with caps that are supplied with it and unambiguously labelled. The important parameters for the determination of the concentration in air (sample volume, temperature, air pressure, relative humidity) are documented in the sampling record.

3.2 Sample preparation

As part of the sample preparation the entire contents of the loaded silica gel tube are transferred into a 10 mL headspace vial, 5 mL of desorption solution are added, the vials are sealed and shaken. Desorption of the analytes occurs while the sample is standing for 24 hours (overnight) at room temperature.

4 Operating conditions for gas chromatography

Apparatus:	Agilent 7890 A gas chromatograph with MPS2 autosampler, split/splitless injector, and an Agilent 5975 series mass selective detector (MSD)	
Column:	Fused silica capillary:	HP-5MS
	Stationary phase:	95% methylsiloxane, 5% phenylsiloxane
	Length:	30 m
	Internal diameter (ID):	0.25 mm
	Film thickness:	1.0 μm
Split ratio:	10:1	
Injection volume:	1 μL	
Column flow:	1.75 mL/min	
Injector temperature:	250 °C	
Temperature program:	2 min at 50 °C, increase by 10 °C/min to 100 °C, increase by 45 °C/min to 250 °C, 3 min run time: 13 min	
Transfer line:	280 °C	
Detector:	Mass spectrometer (MSD)	
Ionisation mode:	Electron impact ionisation EI (70 eV)	
Measurement mode:	Scan/SIM (for evaluation masses see Table 4)	
Mass range:	27 to 150 amu	
Carrier gas:	Helium 5.0	

5 Analytical determination

For the purpose of analytical determination of the samples 1 μL of the sample solution is injected into the gas chromatograph in each case and analysed under the conditions stated in Section 4. If the measured concentrations are above the calibration range, then a suitable dilution of the sample solution must be prepared and this must be analysed again. The substances are identified by comparison of the retention times and mass spectra of the peaks in the chromatogram.

6 Calibration

The internal standard method is used for calibration. 1 µL each of the calibration solutions described in Section 2.4 is injected into the gas chromatograph by means of an autosampler. The evaluation masses listed in Table 4 are used for the quantification and identification of the substances. The ratios of the resulting peak areas of the alcohols or ketones with respect to that of the internal standard (Toluene-D_8) are plotted versus the concentration ratios of the substances with respect to the internal standard contained in the corresponding calibration solutions to obtain the calibration functions.

Table 4 Evaluation masses for the quantitative determination

Substance	Quantification m/z in amu	Identification m/z in amu
1-Butanol	56	41, 43, 31
2-Butanol	45	59, 31
2-Methyl-1-propanol	43	41, 31, 74
1-Pentanol	42	55, 70, 31
Butanone	72	39, 57
Cyclohexanone	98	42, 55, 69
Cyclopentanone	55	84, 41, 56
2-Hexanone	43	58, 100, 85
4-Methylheptan-2-one	43	58, 85, 100
3-Pentanone	57	86, 42
Toluene-D_8 (internal standard)	98	100, 70, 42

7 Calculation of the analytical result

For this purpose the peak areas of the alcohols or ketones as well as that of the internal standard are determined, the respective quotient is calculated and the corresponding value for the mass X in the sample (in µg) is read off from the calibration curve. The corresponding mass concentration (ρ) is calculated according to Equation (1) as follows:

$$\rho = \frac{X}{V \times \eta} \tag{1}$$

Equation (2) enables calculation of the value at 20 °C and 1013 hPa:

$$\rho_0 = \rho \times \frac{273 + t_a}{293} \times \frac{1013}{p_a} \tag{2}$$

where:

ρ	is the mass concentration of an alcohol or ketone in mg/m^3
ρ_0	is the mass concentration of the alcohol or ketone in mg/m^3 at 20 °C and 1013 hPa
X	is the mass of the alcohol or ketone in the analytical sample in µg
V	is the air sample volume in litres
η	is the recovery
t_a	is the temperature during sampling in °C
p_a	is the air pressure during sampling in hPa

8 Reliability of the method

The characteristics of the method were calculated as stipulated in EN 482 [1] and DIN 1076 [2].

8.1 Precision and expanded uncertainty

In order to determine the precision in the minimum measurement range (from 0.1 to twice the Occupational Exposure Limits) the characteristics of the method were determined at three different concentrations of the selected substances. The following volumes of validation solution 1 and 2 were injected onto a plug of quartz wool of the respective silica gel tube:

- 50 µL of validation solution 2 for the lowest concentration
- 50 µL and 100 µL of validation solution 1 for both of the highest concentrations

Then air with a relative humidity of 51% and a temperature of 23 °C was drawn through the tubes at a flow rate of approx. 30 mL/min for a period of 250 min. Six determinations were carried out in the course of the tests in each case. Sample preparation and analytical determination proceeded according to the Sections 3.2, 4 and 5. The resulting relative standard deviations are shown in Table 5.

The expanded uncertainties were estimated, taking all relevant influencing factors into consideration, as stipulated in EN 482 [1] and EN 1076 [2]. The expanded uncertainties are between 16 and 18% for the listed substances. The individual results are shown in Table 5.

8.2 Recovery

The recoveries for the alcohols or ketones were determined by comparison with reference solutions. For this purpose the volumes stated in Section 8.1 of the

Table 5 Relative standard deviations and expanded uncertainties for $n = 6$ determinations

Substance	Concentration [mg/m^3]	Standard deviation (rel.) [%]	Expanded uncertainty U [%]
1-Butanol	31.1	3.3	17
	311	2.0	16
	622	0.80	16
2-Butanol	11.5	3.2	17
	115	2.5	16
	230	0.80	16
Butanone	54.4	3.1	17
	544	2.2	16
	1088	1.0	16
Cyclohexanone	4.7	3.2	17
	46.7	2.4	16
	93.3	1.4	16
Cyclopentanone	69.2	3.3	17
	692	2.1	16
	1284	0.90	16
2-Hexanone	2.2	4.1	18
	21.6	2.1	16
	43.1	0.70	16
2-Methyl-1-propanol	31.0	3.1	17
	310	2.3	16
	620	1.0	16
4-Methylheptan-2-one	3.9	2.8	16
	38.9	2.5	16
	77.8	0.80	16
1-Pentanol	32.1	4.1	18
	321	3.4	17
	641	1.5	16
3-Pentanone	67.0	3.1	17
	670	2.2	16
	1340	1.1	16

respective validation solutions were added directly to 5 mL of the desorption solution. The results can be found in Table 6.

8.3 Limit of quantification

The limits of quantification of the investigated alcohols or ketones were calculated from the measurement of the signal-to-noise ratio. The calculations were based on a signal-to-noise ratio of 10. The limits of quantification are listed in Table 6.

Table 6 Mean recoveries and limits of quantification for n = 6 determinations

Substance	Mean recovery [%]	Limit of quantification absolute [ng]	Limit of quantification relative [mg/m^3]
1-Butanol	95	0.33	0.22
2-Butanol	95	0.44	0.29
2-Methyl-1-propanol	95	1.1	0.75
1-Pentanol	91	0.47	0.31
Butanone	102	0.87	0.58
Cyclohexanone	83	0.21	0.14
Cyclopentanone	96	0.32	0.21
2-Hexanone	100	0.12	0.080
4-Methylheptan-2-one	101	0.30	0.20
3-Pentanone	99	0.090	0.060

8.4 Storage stability

Tests on storage stability of the silica gel tubes loaded with alcohols or ketones were carried out at concentrations of the respective Occupational Exposure Limits. For this purpose the loaded silica gel tubes were stored over a period of 14 days at room temperature. After a storage period of 7 and 14 days six silica gel tubes each were analysed. No significant losses could be detected during the investigation period of two weeks.

8.5 Capacity of the adsorbent

Two silica gel tubes connected in series were used to determine the capacity of the sample tubes. The breakthrough rates of the alcohols or ketones were determined at concentrations of twice the respective Occupational Exposure Limits in a duplicate determination. During this test the breakthrough rates were around < 0.2%.

8.6 Blank values

In order to ensure that the desorption solution used and the silica gel contain no interfering impurities, the contents of an untreated adsorption tube is prepared and analysed at regular intervals as described in the Sections 3.2, 4 and 5.

References

1 EN 482 (2012) Workplace atmospheres – General requirements for the performance of procedures for the measurement of chemical agents. Beuth Verlag, Berlin, Germany

2 EN 1076 (2010) Workplace exposure – Procedures for measuring gases and vapours using pumped samplers – Requirements and test methods. Beuth Verlag, Berlin, Germany

Authors: *W. Krämer, W. Schneider*