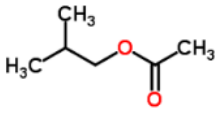
Substance name: isobutyl acetate

CAS: 110-19-0 MW: 116.16 gm/mole

Synonyms: acetic acid, 2-methylpropyl ester; acetic acid, isobutyl ester
Molecular formula: $C_6H_{12}O_2$ Structural formula:



ppm to mg/m^3 conversion factors at 20 ºC and 760 mm/Hg: 1 ppm = 4.83 mg/m^3
Physical characteristics at room temp:

- boiling point 237 ºF
- melting point -107 ºF
- vapor pressure 14 mmHg
- solubility 7 gm/l
- density 0.87 gm/cm^3
- Log P_{ow} 1.60

Special physical characteristics if any:

- colorless with fruity odor

Flammability and other hazards:

- flash point 63 ºF (closed cup); 95 ºF (open cup)

Uses/applications:

- It is usually found in as a component in paints and in the production of paper coatings.

Major commercial form(s):

- Estimated uses: nitrocellulose-based lacquers 63%, exports 27%, ink solvent 5%, adhesives solvent 2%, and other solvent uses 3%. As a lacquer solvent it is used in wooden furniture and auto top-coat applications. Other uses may include solvent in the production of airplane dopes, extraction solvent in the manufacture of penicillin, synthetic flavoring ingredient used in producing banana, pear, pineapple and berry flavors, solvent for fats, waxes, camphor, gums, resins, lacquer stains, ester-soluble dyes and cellulose esters. In commercial grade it has been used in the manufacturing of vinyl resins, and preservation of foodstuffs. Other reported uses include photographic film manufacturing, in nail polish removers, other products for manicure, and as a flavoring agent in the cosmetics industry. It occurs naturally in bananas and other related fruits, and it is created during fermentation processes.

Odor Thresholds:

- Detection: 0.31 ppm; Recognition: 0.68 ppm (AIHA 1997).

Metabolism:

- All butyl acetates are absorbed by the lung, the gastrointestinal tract and to a smaller extent through the skin. Once absorbed, isobutyl acetate is hydrolysed by unspecific esterases to acetic acid and isobutanol, then further oxidized to isobutyric acid (Greim 1999). The human blood/air partition coefficient for isobutyl acetate is 578, which is similar to that of the *n*-butyl acetate isomer (660) (Kaneko *et al* 1994). Small amounts of isobutyl acetate are excreted unchanged or conjugated as glucuronide (WHO 1987). Dahl *et al* (1987) measured the hydrolysis rates of all four butyl acetate isomers using esterases from a rat S9-mix. Steric factors at the site of hydrolysis such as degree of branching clearly contributed to the velocity of the reaction: *n*-butyl acetate: 77 ± 3 nmol/mg protein, isobutyl acetate: 67 ± 3 nmol/mg protein, isobutyl acetate: 62 ± 3 nmol/mg protein and *tert*-butyl acetate: 42 ± 2 nmol/mg protein. For comparison purposes, the partition coefficients for isobutyl acetate in rats for several tissues (liver: 5.06, kidney: 4.08, brain: 2.65, muscle: 2.12 and fat: 21.3) and the blood/air partition coefficient (880).

Organizational sources and recommendations:

Source and date	Findings/Recommendations	Basis/source/ref(s)	Discussion and Assessment
Cal/OSHA Title 8	PEL 150 ppm**;** STEL 200 ppm		
NIOSH REL (1992)	TWA 150 ppm; STEL 200 ppm		
ACGIH TLV (2015)	TWA 50 ppm; STEL 150 ppm	Eye and upper respiratory tract irritation.	
MAK (current)	TWA 100 ppm		
Washington State OSHA	TWA 150 ppm; STEL 200 ppm		

Peer-reviewed journal articles and other studies:

Oral

Oral LD50 values for rats and rabbits are 13,400 mg/kg (Smyth *et al* 1962) and 4,763 mg/kg (Munch, 1972), respectively.

Skin

The dermal LD50 in rabbits is ≥ 20 ml/kg (17,400 mg/kg) indicating only minor skin penetration ability (Smyth *et al* 1962). Uncovered application of 0.01 ml undiluted isobutyl acetate for 24 hours to the shaved skin of rabbits did not cause irritation (Smyth *et al* 1962), while occlusive application of pure isobutyl acetate caused moderate irritation of the intact or abraded skin of rabbits after 24 hours (unpublished results, Opdyke 1978).

Ocular

Instillation of up to 0.5 ml undiluted isobutyl acetate into the rabbit eye resulted in moderate inflammation (Smyth *et al* 1962).

Respiratory

Inhalation exposure of rats to 8,000 ppm for 4 hours caused death in 4 of 6 animals, while after exposure to 16,000 ppm all rats (6/6) died (Smyth *et al* 1962). In a repeat-dose study using Swiss-OF1 mice, the concentration causing a 50% depression of the respiratory rate due to sensory irritation of the respiratory tract of isobutyl acetate was 818 ppm, and the RD50 of isobutanol was 1,819 ppm (Alarie *et al* 1998).

Sensitization

Negative results on sensitization of isobutyl acetate were obtained in a 48-hour closed patch test and in a maximization test on 28 human volunteers with 2% isobutyl acetate in petroleum (Opdyke 1978). Some epicutaneous tests for isobutanol were reported positive, however, the effect was probably attributed to a cross reaction with ethanol (Greim 1999). Isobutyl acetate did not show any sensitizing potential in a maximization test performed on guinea pigs according to OECD guideline 406 (Huels AG report 1187 1988).

Genotoxicity

Testing the genotoxicity of isobutyl acetate in *Salmonella typhimurium* (TA98, TA100, TA153, TA1537, TA1538) with or without metabolic activation resulted in no mutagenic potential up to the highest concentrations tested: 5 mg/plate (Bayer 1997). In V79 hamster cells, no chromosomal aberrations were caused with up to 2,500 µg/ml. At this concentration, the mitotic index was already at 50% (BAU 1996).

Other Studies

The ACGIH TLV for acetates reported the acute irritancy of isobutyl acetate to be less than n-butyl acetate, however, the data supporting this was unpublished. Another author reported less irritation for those acetates with lower boiling points (von Oettingen, 1960). This aligns with nasal irritation data published for many different organic molecules of differing boiling point: higher boiling point equals higher irritation.

HEAC Health-based Assessment and Recommendation

n-Butyl acetate, sec-butyl acetate and isobutyl acetate have structural similarities and a common metabolic pathway. The main critical effect is irritation, which is common to all three acetates. And all three form similar metabolites which have been studied for adverse effects. These common toxicological properties have been used to justify the same OEL for all three compounds by numerous standard-setting bodies (ACGIH TLV, SCOEL, etc.). Therefore, the n-butyl acetate data was used to establish a recommended PEL and STEL. The critical effect, irritation in humans, is based upon the LOAEC of 150 ppm in the study by Iregren et al 1993. Due to the exposure duration of 4 hours, a safety factor of 3 is justified for deriving a recommended OEL. An OEL of 50 ppm is proposed for all three butyl acetates to protect workers against systemic and local toxic effects during an 8-hour exposure.

A STEL of 150 ppm is recommended to avoid possible irritating effects reported in case and human exposure studies. IsoButyl acetate was not sensitizing to the skin after dermal exposure of either humans or animals, nor is the permeability through human skin high enough to warrant a 'skin' notation.

Usage information: EPA Inventory Update Reporting (IUR), other sources

Measurement information

OSHA Method 1009 (fully validated) uses a charcoal tube (or organic vapor monitor), a flowrate of 0.05 lpm, a volume range of 0.75 to 12 liters, and a GC-FID analytical method with an estimated reliable quantitation limit of 38.9 parts per billion (.0389 ppm).

NIOSH Method 1450 uses a charcoal tube (or organic vapor monitor), a GC-FID, and provides an estimated detection limit of 0.9 ug per sample. The range studied was 14-440 ug per sample. With a maximum 10L sample this would yield 0.29 to 9.26 ppm range.

Based on this information, there are no anticipated concerns with analytical feasibility to 50 ppm.

References

ACGIH. (2001). *Threshold Limit Value n-Butyl Acetate.* Cincinnati: ACGIH.

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McLain, V. (2008). Final Report of the Addendum to the Safety Assessment of n-Butyl Alcohol as Used in Cosmetics. *Int J Toxicol*, 53-69.

Park, H. (2011). Quantitative Exposure Assessment of Various Chemical Substances in a Wafer Fabrication Industry Facility. *Saf Health Work*, 39-51.

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