5	CAS No.: 103-50-4	Substance: Dibenzyl ether

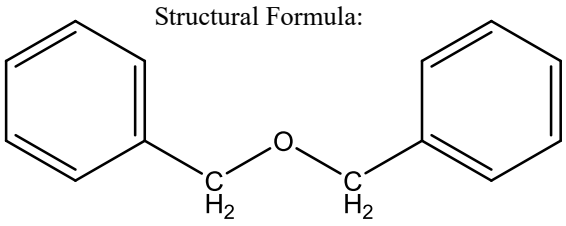
Chemical Substances Control Law Reference No.: 3-1082

PRTR Law Cabinet Order No.: 2-49

Molecular Formula: $C_{14}H_{14}O$

Molecular Weight: 198.26

Structural Formula:



1. General information

The aqueous solubility of this substance is 40 mg/1,000 g (35°C), the partition coefficient (1-octanol/water) (log K_{ow}) is 3.31, and the vapor pressure is 1.03×10^{-3} mmHg (=0.137 Pa) (25°C). The biodegradability (aerobic degradation) is characterized by a BOD degradation rate of 0%, and bioaccumulation is thought to be nonexistent or low. Moreover, the substance is stable towards hydrolysis (experimental temperature 50°C, pH: 4, 7, 9).

The main uses of this substance are as a dyestuff carrier and fragrance solvent. The production and import quantity in fiscal 2015 was less than 1,000 t.

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2. Exposure assessment

Because this substance is not classified as a Class 1 Designated Chemical Substance under the PRTR Law, release and transfer quantities could not be obtained. Predictions of proportions distributed to individual media by using a Mackay-type level III fugacity model indicated that if equal quantities were released to the atmosphere, water bodies, and soil, the proportion distributed to soil would be largest.

The maximum expected concentration of exposure to humans via inhalation, based on ambient atmospheric data, was around 0.00056 μg/m^3.

The maximum expected oral exposure was estimated to be generally 0.00026 μg/kg/day based on calculations from data for public freshwater bodies. Further, the oral exposure calculated from public freshwater data for a limited area (0.3 μg/L) was 0.012 μg/kg/day. In addition, the maximum expected oral exposure was estimated to be around 0.017 μg/kg/day based on calculations from past data for public freshwater bodies. The risk of exposure to this substance by intake from an environmental medium via food is considered slight, given its perceived low or nonexistent bioaccumulation.

The predicted environmental concentration (PEC), which indicates exposure to aquatic organisms, is generally 0.0064 μg/L for public freshwater bodies and generally less than 0.0019 μg/L for seawater. Further, an environmental survey of public freshwater bodies covering a limited area reported a maximum value of 0.3 μg/L. In addition, a maximum value of 0.43 μg/L was reported for public freshwater bodies in past data.

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3. Initial assessment of health risk

No information was available on acute symptoms in humans. Somnolence, dyspnea, ataxia and reduced food intake were observed in rats and mice exposed to this substance by ingestion.

As sufficient information on the carcinogenicity of the substance was not available, the initial assessment was conducted on the basis of information on its non-carcinogenic effects.

The NOAEL for oral exposure of 196 mg/kg/day (based on increased weight of the liver), determined from medium-term toxicity tests in rats, was divided by a factor of 10 to account for extrapolation to chronic exposure. The

calculated value of 20 mg/kg/day was deemed to be the lowest reliable dose and was identified as the 'non-toxic level*' of the substance for oral exposure. The 'non-toxic level*' for inhalation exposure could not be identified.

With regard to oral exposure, assuming the substance is absorbed via public freshwater bodies, the predicted maximum exposure level would be 0.00026 μg/kg/day, approximately. The MOE (Margin of Exposure) would be 7,700,000, when calculated from the predicted maximum exposure level and the 'non-toxic level*'of 20 mg/kg/day, and subsequently divided by a factor of 10 to account for extrapolation from animals to humans.

In addition, based on the concentration in public freshwater bodies reported in a restricted area, the estimated maximum exposure level was 0.012 μg/kg/day, and the MOE calculated from this level would be 170,000. Based on the concentration in public freshwater bodies in 2006, the estimated maximum exposure level was 0.017 μg/kg/day, approximately, and the MOE calculated from this level would be 120,000. Since exposure to the substance in environmental media via food is presumed to be limited, including this concentration value in the calculation would not change the MOE significantly. Therefore, no further work would be required at present to assess the health risk of the substance via oral exposure.

With regard to inhalation exposure, owing to the lack of identified 'non-toxic level*', the health risk could not be assessed. Assuming that 100% of the ingested substance is absorbed, the 'non-toxic level*' for inhalation exposure, derived from the conversion of the 'non-toxic level*' for oral exposure, would be 67 mg/m^3. The MOE would be 12,000,000, when calculated from the predicted maximum exposure concentration of 0.00056 μg/m^3, approximately, and the converted 'non-toxic level*' for inhalation exposure, and subsequently divided by a factor of 10 to account for extrapolation from animals to humans. Therefore, collection of further information would not be required to assess the health risk of this substance via inhalation in ambient air.

Toxicity				Exposure assessment		Result of risk assessment			Judgment
Exposure Path	Criteria for risk assessment	Animal	Criteria for diagnoses (endpoint)	Exposure medium	Predicted maximum exposure dose and concentration				
Oral	'Non-toxic level*' 20 mg/kg/day	Rats	Increased weight of the liver	Drinking water	— μg/kg/day	MOE	—	×	○
				Public Freshwater bodies	0.00026 μg/kg/day	MOE	7,700,000	○	
Inhalation	'Non-toxic level*' — mg/m^3	—	—	Ambient air	0.00056 μg/m^3	MOE	—	×	(○)
				Indoor air	— μg/m^3	MOE	—	×	×

Non-toxic level *

- When a LOAEL is available, it is divided by 10 to obtain a NOAEL-equivalent level.
- When an adverse effect level for the short-term exposure is available, it is divided by 10 to obtain a level equivalent to an adverse effect level for the long-term exposure.

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4. Initial assessment of ecological risk

With regard to acute toxicity, the following reliable data were obtained: a 72-h EC_{50} of 4,070 μg/L for growth inhibition in the green alga *Pseudokirchneriella subcapitata*, a 48-h EC_{50} of 770 μg/L for immobilization in the crustacean *Daphnia magna*, and a 96-h LC_{50} of 6,800 μg/L for the fish species *Oryzias latipes* (medaka). Accordingly, based on these acute toxicity values and an assessment factor of 100, a predicted no effect concentration (PNEC) of 7.7 μg/L was obtained.

With regard to chronic toxicity, the following reliable data were obtained: a 72-h NOEC of 320 μg/L for growth inhibition in the green alga *P. subcapitata* and a 21-d NOEC of 98 μg/L for reproductive inhibition in the crustacean *D. magna*. Accordingly, based on these chronic toxicity values and an assessment factor of 100, a PNEC of 0.98 μg/L was obtained.

The value of 0.98 μg/L obtained from the chronic toxicity to the crustacean was used as the PNEC for this substance.

The PEC/PNEC ratio is 0.007 for freshwater bodies and less than 0.002 for seawater; accordingly, further work is considered unnecessary at this time. Further, an environmental survey of a limited area reported a maximum concentration of 0.3 μg/L, and the ratio of this value to PNEC is 0.3. However, an environmental survey carried out the following fiscal year did not detect the substance. Furthermore, while no data has been reported within the past 10 years, there is an older report of a maximum concentration of around 0.43 μg/L for freshwater bodies (2006). Because the ratio of this concentration to PNEC is 0.4, further collection of data regarding these freshwater bodies is considered necessary.

Hazard assessment (basis for PNEC)			Assessment coefficient	Predicted no effect concentration PNEC (μg/L)	Exposure assessment		PEC/ PNEC ratio	Judgment based on PEC/PNEC ratio	Assessment result
Species	Acute/ chronic	Endpoint			Water body	Predicted environmental concentration PEC (μg/L)			
Crustacean *Daphnia magna*	Chronic	NOEC Reproductive inhibition	100	0.98	Freshwater	0.0064	0.007	○	○
					Seawater	<0.0019	<0.002		

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5. Conclusions

	Conclusions		Judgment
Health risk	Oral exposure	No need for further work.	○
	Inhalation exposure	Although risk to human health could not be confirmed, collection of further information would not be required.	(○)
Ecological risk	No need of further work at present.		○

［Risk judgments］ ○: No need for further work ▲: Requiring information collection

■: Candidates for further work ×: Impossibility of risk characterization

（○）: Although risk to human health could not be confirmed, collection of further information would not be required.

（▲）: Further information collection would be required for risk characterization.