TC NES SUBGROUP ON IDENTIFICATION OF PBT AND VPVB SUBSTANCES

RESULTS OF THE EVALUATION OF THE PBT/VPVB PROPERTIES OF:

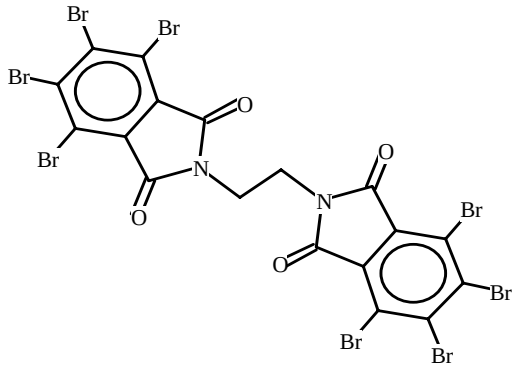
Substance name: N,N'-ethylenebis(3,4,5,6-tetrabromophthalimide)

EC number: 251-118-6

CAS number: 32588-76-4

Molecular formula: C18H4Br8N2O4

Structural formula:



Summary of the evaluation:

N,N'-ethylenebis(3,4,5,6-tetrabromophthalimide) is not considered as a PBT substance. N,N'-ethylenebis(3,4,5,6-tetrabromophthalimide) meets the P/vP criteria based on screening data. The substance does not meet the B criterion based on indicators of limited bioaccumulation potential. It neither meets the T criterion in mammals.

JUSTIFICATION

1 IDENTIFICATION OF THE SUBSTANCE AND PHYSICAL AND CHEMICAL PROPERTIES

Name: N,N'-ethylenebis(3,4,5,6-tetrabromophthalimide)
EC Number: 251-118-6
CAS Number: 32588-76-4
IUPAC Name:
Molecular Formula: C18H4Br8N2O4
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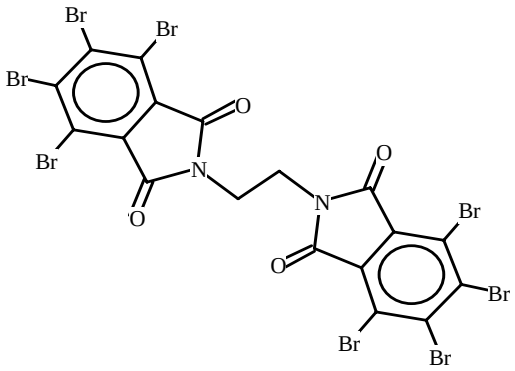

Molecular Weight: 951.5
Synonyms: Bis(tetrabromophthalimido)ethane; BT93; 1H-Isoindole-1,3(2H)-dione,2,2'—(1,2-ethanediyl)bis(4,5,6,7-tetrabromo-); Ethylene-bistetrabromophthalimide; EBTP (abbreviation)

1.1 PURITY/IMPURITIES/ADDITIVES

No information available.

1.2 PHYSICO-CHEMICAL PROPERTIES

Table 1 Summary of physico-chemical properties. For details and references, see European Commission (2000) and Albemarle Corporation (2004)

REACH ref Annex, §	Property	Value	Comments
VII, 7.1	Physical state at 20 C and 101.3 KPa	solid	
VII, /.2	Melting / freezing point	> 445ºC 450-455ºC	Ethyl Corporation Data (1982) Albermale Corp.
VII, 7.3	Boiling point	-	
VII, 7.5	Vapour pressure	2.5×10^{-22} mmHg (= 3.3×10^{-20} Pa) at 25ºC	MPBPWIN v1.41
VII, 7.7	Water solubility	< 1.63 mg l-1 at 25ºC < 0.01% w/w at 25ºC 3×10^{-9} mg l^{-1} at 25ºC	MITI (1992) ; WS determined for the BCF-test with fish (data not evaluated) Albemarle Corp. (2004)(data not evaluated) WSKOW v1.41
VII, 7.8	Partition coefficient n-octanol/water (log value)	9.8	KOWWIN v1.67 Kow not possible to measure due to the lack of solubility
	Dissociation constant		

2 MANUFACTURE AND USES

Three companies have provided information on the substance under Regulation 93/793/EEC. EBTP is according to Albemarle Corporation (2004) used as an additive flame retardant in various plastics types.

3 CLASSIFICATION AND LABELLING

The substance is not classified in the Annex I of Directive 67/548/EEC.

4 ENVIRONMENTAL FATE PROPERTIES

4.1 DEGRADATION (P)

4.1.1 Abiotic degradation

Indirect photochemical degradation in the atmosphere is fast based on a half-life of approximately 10 hours estimated by AopWin v1.91 (24-hour day^{-1}; $5*10^5$ OH^- cm^{-3}).

4.1.2 Biotic degradation

Biodegradability of the substance was tested according to OECD 301C using 100 mg l^{-1} test substance. The substance was observed to be not readily biodegradable (CITI, 1981). It is noted that the test report was not available to the Rapporteur for evaluation.

BIOWIN v4.02 predictions also indicate that the substance is recalcitrant. BIOWIN2=0.000, BIOWIN 3 = 0.009 and BIOWIN 6 = 0.000.

EBTP is expected to partition to sediment and soil, where anaerobic dehalogenation may be for some halogenated compounds a relevant route of degradation. Reductive dehalogenation of aromatic halogenated substances has been investigated in several studies (Bedard et al. 1998; Bedard and Quensen 1995; Gerecke et al. 2006; Gerecke et al., 2005; Morris et al. 1993; Morris et al., 1992; Schaefer and Flaggs 2001; Schaeffer and Siddiqui 2001; all as cited in Albemarle Corp., 2006). Based on the results, it seems unlikely, that a reductive dehalogenation of a molecule such as EBPT containing more than 6 bromine atoms would occur in sediment or soil. If debromination would occur, it would probably be limited to sediment containing primers which have not yet been identified and the process would be very slow. If a sequential debromination did occur, the complete debromination would lead to the ethylene bisphthalimide molecule (see figure below), which is not expected to be problematic in this context (e.g. logKow of 2.68 predicted by KOWWIN v1.67).

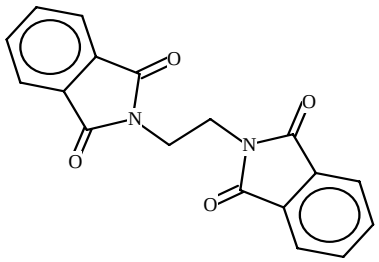

Figure 4.1 Ethylene bisphthalimide.

According to industry, under aerobic conditions, the most probable degradation route would be cleavage of the ethylene bridge with a formation of either carboxylic acids or an imide. Neither of these is expected to be readily biodegradable, but their bioaccumulation potential and toxicity is anticipated to be low (Albermale Corporation, 2006).

4.1.3 Other information [1]

4.1.4 Summary and discussion of persistence

4.2 ENVIRONMENTAL DISTRIBUTION

Data not reviewed for this report.

4.2.1 Adsorption

EBTBP is expected to bind to organic carbon based on its estimated log Koc of 8 x 10^5 (PCKOC v1.66) and to be immobile in soil.

4.2.2 Volatilisation

EBTBP is expected to volatilise to any significant extent based on its measured vapour pressure, 2.27 x 10^{-4} Pa at 20°C, and its estimated Henry's law constant is 3.64 x 10^{-21}atm-m^3/m or 1.49 x 10^{-19} (unitless) (HENRYWIN v3.10). EBTBP is not expected to volatilise from wet and dry soil or from water. Its volatilisation half-life from water, based on its Henry's law constant, is 5.66 x 10^{+13} years (river) and 6.17 x 10^{+14} years (lake). EBTBP is expected to exist solely in the particulate phase in the ambient atmosphere (AOPWIN v1.01) and be removed from air via wet and dry deposition.

4.2.3 Long-range environmental transport

EBTBP is not expected to undergo long-range transport due to its large molecular weight and size and its high binding to carbon. EBTBP will exist in air bound to particulates. EBTBP will tend to settle out from air at a short distance from its point of release and be removed from the atmosphere via wet and dry deposition.

[1] For example, half life from field studies or monitoring data

4.3 BIOACCUMULATION (B)

4.3.1 Screening data[2]

EBTBP's estimated logKow is 9.79 (KOWWIN v1.67). A valid measure of its logKow or water solubility could not be determined due to the insufficient solubility in either organic solvents or water.

EBTBP's solubility in octanol was measured using a nonspecific method in response to questions under its PBT assessment. Using measurements of total bromine content via X-ray fluorescence spectroscopy , EBTBP's solubility in octanol was found to be 0.54 or 0.6 mg/l (Albemarle Corporation, 2005).

BCFWINv2.15 estimates a BCF of 9.5 based on the logKow of 9.8.

The measured octanol solubility of the substance is 0.45-0.6 mg l^{-1} (). The molecular diameter ($D_{max\ aver}$) is 1.1-1.68 nm for the most stable conformers and 0.55-2 nm for the least stable conformers (Comber et al., 2005).

Comber et al. (2005) discussed properties indicating low potential for bioaccumulation: "a chemical may be considered as not B if it has:

- a maximum molecular length of 43 A
- a maximum cross-sectional diameter of 17.4 A plus a molecular weight of 700-1,000
- a measured octanol solubility (mg/l) of < 0.002*MW"

EBTBP's molecular weight is > 700. Its solubility in octanol, 0.4 or 0.6 mg/l, is < 0.002 times its molecular weight (0.002 * 951.47 = 1.9 mg/l). EBTBP has the potential to exist as 10 different conformers, whose maximum length, also known as the maximum cross-sectional diameter, range from 16.8 to 20 A coupled with a molecular weight > 700.

These factors indicate EBTBP has little potential to bioaccumulate.

4.3.2 Measured bioaccumulation data[3]

CITI (1982) has reported on a bioconcentration test with *Cyprinus carpio* according to the MITI flow-through method using nominal test concentrations of 2 mg l^{-1} and 0.2 mg l^{-1}. BCFs < 3.3 were determined in the experiment. As the water solubility may be considerably lower than the concentrations tested, the results cannot be used for the evaluation of the bioaccumulation potential.

4.3.3 Other supporting information[4]

The available studies on mammalian toxicity and substance distribution have been discussed in Section 5.

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2 For example, log K_{ow} values, predicted BCFs

3 For example, fish bioconcentration factor

4For example, measured concentrations in biota

4.3.4 Summary and discussion of bioaccumulation

See section 7.

4.4 SECONDARY POISONING

Data not reviewed for this report.

5 HUMAN HEALTH HAZARD ASSESSMENT

A 14-day distribution study was conducted with 5 (+2 control) female Sprague Dawley rats by Cannon Laboratories, Inc. (1978). ^{14}C-labelled EBTP was dosed at a level of approximately 0.67 mg kg^{-1} d^{-1} by gavage in corn oil for 14 consecutive days. Two animals were sacrificed 24 hours after the last dose and the remaining animals 7, 14 and 30 days after the last dosing. Of the total 14–day dose ^{14}C-activity, 65% was collected in the faeces during the dosing period. Approximately 15% of the total 14-day dose was detected in the urine during the dosing period. ^{14}C-activity at the end of dosing was in tissues analysed 0.39 ppm (liver), 0.32 (kidney), 0.08 (muscle), 0.075 (fat) and 0.032 ppm (brain). Levels in liver and kidney dropped by approximately 50% during the first 7 days of depuration. According to the study summary, the level of ^{14}C-activity continued to fall in liver, kidney, muscle and brain (fat not mentioned) and was below 0.05 ppm at day 30 of exposure withdrawal.

It is noted, that no information is available, whether the dose was completely dissolved in the carrier or not. Based on the measured octanol solubility (0.45-0.6 mg l^{-1}) it is likely, that a relevant part of the dose remained undissolved and hence was not available for uptake. Consequently, the actual absorption efficiency could not be determined. The only reliable output of this study on the basis of the study summary is, that the concentration in tissues dropped to approximately 50% of the level at the end of the exposure period and continued to drop also after than (except in fat tissue, which is not mentioned).

This study however, together with the intrinsic properties of the test substance (molecular weight and size) indicates that the test substance is probably only poorly absorbed through the gastrointestinal tract when absorbed with food.

In the following toxicity studies, the administration of the test substance was carried out using different method and carrier, such as corn oil or methylcellulose. With this respect, the studies comply with accepted guidelines. However, it should be underlined that in view of the low solubility of the test substance in water and in organic matrices, it can not be certified that the test substance was fully bioavailable in the gastrointestinal tracts.

Considering that no effects were observed at the highest tested dose, they are reported below either showing that the substance is poorly absorbed or of low toxicity.

EBTBP has been tested in acute and repeated dose studies in rats and rabbits. It was not acutely toxic by oral, dermal and inhalation routes and was not irritating to the skin or eyes.

A developmental 20-day toxicity test with 25 mated Sprague Dawley rats was conducted by Springborn Life Sciences (1988a). EBTP was administered by gavage in corn oil at doses of 0, 100, 500 and 1,000 mg kg^{-1} d^{-1} on gestation days 6-15. Several variables of maternal and fetal toxicity were measured and no effects were observed at the highest level tested. The maternal and fetal NOEL was 1,000mg/kg/day.

It is noted, that no information is provided on whether the test substance was dissolved to the carrier, which is unlikely based on the measured low octanol solubility. A significant part of the test substance may not have been available for uptake from the gastrointestinal tract due to the very low lipid solubility of the substance.

Springborn Life Sciences (1988b) reported also on a developmental 29-day toxicity test with 20 mated New Zealand White rabbits. EBTP was administered by gavage in methyl cellulose at doses of 0 and 1,000 mg kg^{-1} d^{-1} on gestation days 7-19. Several variables of maternal and fetal toxicity were measured and no effects were observed at the dose level tested. The maternal and fetal NOEL was 1,000mg/kg/day.

Similar to the study with rats cited above, it is noted, that no information is provided on whether the test substance was (or can be assumed to be) actually dissolved to the carrier. Also the summaries of the two subchronic '(28-day and 90-day) repeated dose toxicity tests in Albemarle Corporation (2004) cannot exclude the very likely non-availability of the test substance for uptake.

6 ENVIRONMENTAL HAZARD ASSESSMENT

6.1 AQUATIC COMPARTMENT (INCLUDING SEDIMENT)

6.1.1 Toxicity test results

6.1.1.1 Fish

Acute toxicity

CITI (1982) reported on a 48-hour LC_{50} of > 500 mg l^{-1} with *Oryzias latipes*. The test was a range-finding test in semi-static conditions conducted to find the suitable test concentration for the bioconcentration test (see Section 4.3.2). It is noted, that the reported LC_{50} is far beyond the expected water solubility and no information is available on the other test concentrations. The reliability of the test could not be evaluated, as the test report was not available to the Rapporteur.

Long-term toxicity

6.1.1.2 Aquatic invertebrates

Acute toxicity

No data available.

Long-term toxicity

No data available.

6.1.1.3 Algae and aquatic plants

No data available.

6.1.2 Sediment organisms

No data available.

6.1.3 Other aquatic organisms

No data available.

6.2 TERRESTRIAL COMPARTMENT

No data available.

6.3 ATMOSPHERIC COMPARTMENT

No data available.

7 PBT AND VPVB

7.1 PBT, VPVB ASSESSMENT

Persistence: N,N'-ethylenebis(3,4,5,6-tetrabromophthalimide) (EBTP) is not readily biodegradable based on an available standard MITI-test. According to the BIOWIN-predictions, the substance is persistent. Anaerobic degradation via dehalogenation is based on available literature unlikely for this substance. It is concluded that the substance meets the P/vP criteria according to screening data.

Bioaccumulation: Several factors, as described by Comber et al. (2005) indicate that EBTBP has low potential for bioaccumulation. Its molecular weight, 959.2, is > 700. Its measured solubility in octanol, 0.45-0.6 mg/l, is < 0.002*MW or 1.9. EBTBP's estimated fish bioconcentration factor, 9.3, is similar to the measured value derived from a study conducted at concentrations higher than its water solubility. Repeated dose study in two mammalian species provides NOEL's of 1,000 mg/kg/day. A repeated dose excretion and distribution study in rats did not indicate accumulation of the radiolabelled compound. Thus, EBTBP is not considered bioaccumulative or toxic in mammals.

Toxicity: No long-term data on ecotoxicity are available for the substance. ECOSAR (v0.99h) predicts that EBTBP will not be chronically toxic to aquatic organisms due to a lack of solubility.

Summary

N,N'-ethylenebis (3,4,5,6-tetrabromophthalimide) meets the P/vP criteria based on screening data. Overall, the substance does not meet the B criterion based on indicators of low bioaccumulation potential. The substance does not meet the T criteria in mammals. It is concluded that the N,N'-ethylenebis(3,4,5,6-tetrabromophthalimide) is not considered as a PBT substance.

INFORMATION ON USE AND EXPOSURE

OTHER INFORMATION

The information and references used in this report were mainly taken from the following sources:

Albemarle Corporation (2004) HPV Data Summary and Test Plan for 1H-Isoindole-1,3(2H)-dione, 2,2'-(1,2-ethaanediyl)bis(4,5,6,7-tetrabromo-) (a.k.a Ethylene bis tetrabromophthalimide), CAS No. 32588-76-4. Feburary 4, 2004.

European Commission (2000) IUCLID Dataset, N,N'-ethylenebis(3,4,5,6-tetrabromophthalimide); CAS-No.: 32588-76-4, 18.2.2000.

Other sources:

Albemarle Corporation (2006) Ethylene bis tetrabromphthalimide: Potential for Degradation via Loss of Bromine Atoms. M.L. Hardy, DVM, PhD, February 15, 2006. A review submitted to the Rapporteur France.

Albemarle Corporation (2005) Memorandum sent to the Rapporteur.

Comber et al. (2005) Discussion paper for the TC NESsubgroup on PBT.