TC NES SUBGROUP ON IDENTIFICATION OF PBT AND VPVB SUBSTANCES

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

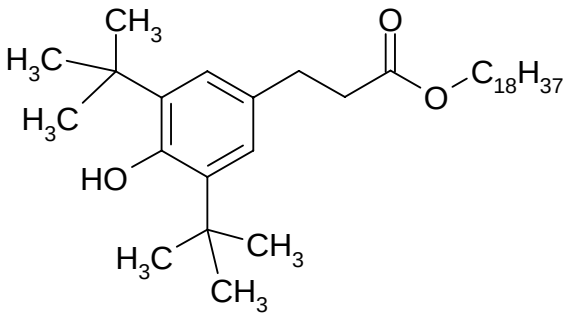
Substance name: Octadecyl 3-(3,5-di-tert-butyl-4-hydroxyphenyl)propionate

EC number: 218-216-0

CAS number: 2082-79-3

Molecular formula: C35H62O3

Structural formula:



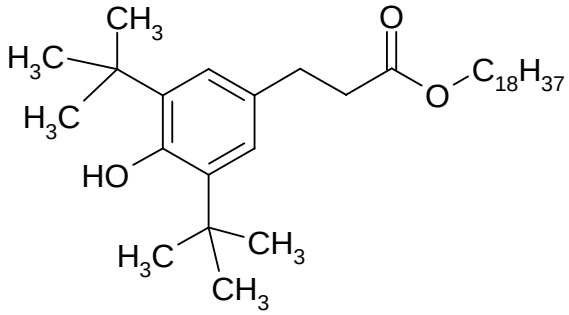
Summary of the evaluation:

Octadecyl 3-(3,5-di-tert-butyl-4-hydroxyphenyl)propionate is not considered as a PBT substance. It does not fulfil the P/vP screening criteria due to a fast primary degradation and the fact that the main metabolites do not meet the B or P criterion. The main degradation products are metilox acid (CAS no. 20170-32-5) and 1-octadecanol (CAS no. 112-92-5). Metilox acid does not meet the B criterion and 1-octadecanol does not meet the P/vP screening criteria. Assessment of ecotoxicity was not completed.

JUSTIFICATION

1 IDENTIFICATION OF THE SUBSTANCE AND PHYSICAL AND CHEMICAL PROPERTIES

Name: Octadecyl 3-(3,5-di-tert-butyl-4-hydroxyphenyl)propionate
EC Number: 218-216-0



CAS Number: 2082-79-3
IUPAC Name:
Molecular Formula: $C_{35}H_{62}O_3$
Structural Formula:

Smiles: O=C(OCCCCCCCCCCCCCCCCCC)CCc(cc(c(O)c1C(C)(C)C)C(C)(C)C)c1

Molecular Weight: 530.88
Synonyms: 3,5-di-tert-butyl-4-hydroxyphenylpropionic acid octadecyl ester
Benzenepropanoic acid, 3,5-bis(1,1-dimethylethyl)-4-hydroxy-,octadecyl ester. For a complete list of synonyms, see European Commission (2000).

1.1 Purity/Impurities/Additives

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1.2 Physico-Chemical properties

Table 1 Summary of physico-chemical properties..

REACH ref Annex, §	Property	Value	Comments
VII, 7.1	Physical state at 20 C and 101.3 Kpa	solid	European Commission (2000)
VII, 7.2	Melting / freezing point	49 °C 50-55 °C	Great Lakes Chemical, Italia, Milan (data not evaluated) Ciba Geigy AG (1989) (data not evaluated)
VII, 7.3	Boiling point	-	
VII, 7.5	Vapour pressure	2.67×10^{-7} Pa at 20 °C	Great Lakes Chemical, Italia, Milan (data not evaluated)

VII, 7.7	Water solubility	2.85 µg l^{-1} at 20 °C (distilled water)	RCC Ltd. (2006a). OECD 105; column elution method (HPLC-MS)
		6.088 × 10^{-9} mg l^{-1} at 25 °C	Estimate (WSKOW v1.41)
		<0.1 g l^{-1} at 20 °C	Great Lakes Chemical, Italia, Milan (data not evaluated)
		<0.2 mg l^{-1} at 20 °C	Great Lakes Chemical, Italia, Milan (data not evaluated)
VII, 7.8	Partition coefficient n-octanol/water (log value)	13.41	Estimate (KOWWIN v1.67)
		>6	Great Lakes Chemical, Italia, Milan, (1994) (data not evaluated)
		>6	Estimate; Ciba Specialty Chemicals Inc. (1988)(data not evaluated)
	Dissociation constant	-	

2 MANUFACTURE AND USES

Nine producers/importers have provided data under Regulation 93/793/EEC.

The substance is used as a stabilizer in polymers industry in closed systems and in non-dispersive use. Other use-category listed: antioxidant. The substance is used in quantities between 10 000 – 50 000 tonnes per year (European Commission, 2000).

3 CLASSIFICATION AND LABELLING

The substance is not classified under Directive 67/548/EEC.

4 ENVIRONMENTAL FATE PROPERTIES

4.1 Degradation (P)

4.1.1 Abiotic degradation

RCC Ltd. (2006a) carried out a water solubility test according to OECD 105 and observed relatively high concentrations of benzenepropanoic acid, 3,5-bis(1,1-dimethylethyl)-4-hydroxy- ("Metilox acid"; CAS no. 20170-32-5), up to ca. 80 µg l^{-1}, in a preliminary water solubility test conducted as simplified flask method in distilled water. The origin of metilox acid could not be identified. Metilox acid could have been formed during the flask test (hydrolysis), or it could have been already present in the test material as impurity which showed up due to its much higher solubility in water. When the final water solubility test with column elution method (HPLC-MS) was carried out (with significantly lower amount of test substance than in the preliminary test), no metilox acid was observed. This showed that hydrolysis was not interfering during water solubility testing, i.e. probably no significant abiotic hydrolysis occurred in the first test, but the metilox acid was present as impurity.

A hydrolysis study could not be conducted as no analytical method could be developed which would be sensitive enough for the purpose (CiBa, 2006).

Indirect photochemical degradation in the atmosphere is considered to be very slow based on the estimated half-life of 40.8 days for the reaction with OH-radicals using AOP v1.91 (24 h day^{-1}; $5*10^5$ OH^- cm^{-3}).

4.1.2 Biotic degradation

Based on the studies below, octadecyl 3-(3,5-di-tert-butyl-4-hydroxyphenyl)propionate seems to be hydrolysed in a biotic process to benzenepropanoic acid, 3,5-bis(1,1-dimethylethyl)-4-hydroxy- ("Metilox acid"; see Figure 4.1) and 1-octadecanol (see Figure 4.2).

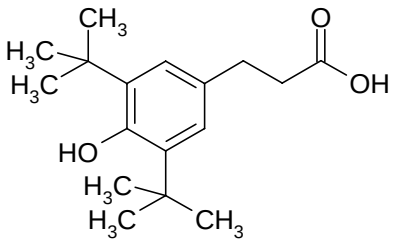

Figure 4.1 Main metabolite Metilox acid
CAS RN 20170-32-5

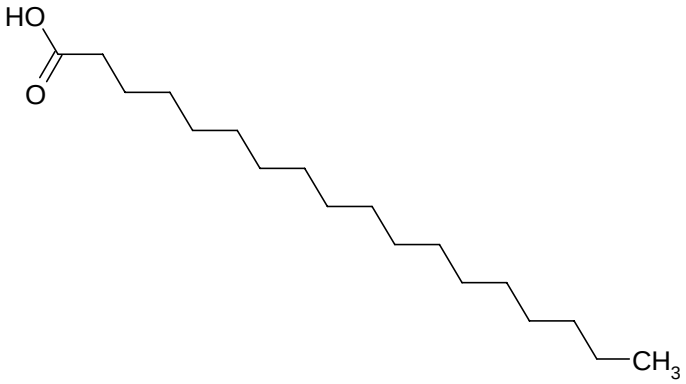

Figure 4.2 Main metabolite 1-Octadecanol
CAS RN 112-92-5

Following screening biodegradation data are provided by European Commission (2000). Octadecyl 3-(3,5-di-tert-butyl-4-hydroxyphenyl)propionate reached a mineralisation of 32 % in 29 days in an OECD 301B–test (CO_2-evolution) according to CiBa Specialty Chemicals Inc. Basel. Another OECD 301B-study showed mineralisation of 6 % in 28 days (Great Lakes Chemical, Italia). CiBa, (1991) reports, that up to 47 % of the substance was degraded in 35 days in an OECD 302B –test. It is noted, that the study reports were not available to the Rapporteur for evaluation.

METI (1996) has also reported on a ready biodegradability test (OECD 301C). With 100 mg l^{-1} test concentration, 21-39 % mineralization was observed after 28 days (measured as BOD) and metilox acid was observed to be formed. Primary degradation was based on metilox acid formation 62-93 % of the parent substance concentration. 1-Octadecanol was not detected suggesting that it was further degraded. It is noted, that the study report was not available to the Rapporteur for evaluation.

RCC Ltd. (2006b) reports on a 3-day ready biodegradation test with octadecyl 3-(3,5-di-tert-butyl-4-hydroxyphenyl)propionate in test concentrations of 0.1 mg l^{-1} (run in duplicate) and 400 µg l^{-1} (one vial run), sludge concentration of 30 mg SS l^{-1} and temperature of 20-24 ºC. Degradation was followed by analysis of the degradation product metilox acid. In the lower exposure vials, 37.8 % and 52.5 % of the parent compound degraded to metilox acid and in the higher exposure vial 35.6 % degraded. No degradation was observed in the abiotic controls.

A ready biodegradation test according to OECD 301A (DOC die away) has been conducted by RCC Ltd. (2006c). A test concentration of 0.1 mg l^{-1} and predominantly domestic sludge (final conc. 30 mg SS l^{-1}) were used and degradation was measured by means of monitoring the concentration of the parent compound and the anticipated degradation product metilox acid (see Figure 4.1) with LC-MS (LOQ = 0.003 mg l^{-1} for the parent compound, LOQ = 0.001 mg l^{-1} for metilox acid). Only the inoculum and procedure controls were followed by means of DOC. Acetone was used as solvent. Removal of the parent compound was 85 % in 10 days. Metilox acid was detected in the same samples analysed for the parent compound, whereas the concentrations

increased from 0.005 mg l^{-1} on day 1 to mean concentrations between 0.024 mg l^{-1} and 0.037 mg l^{-1} on days 2 to 10 (see Figure 4.3).

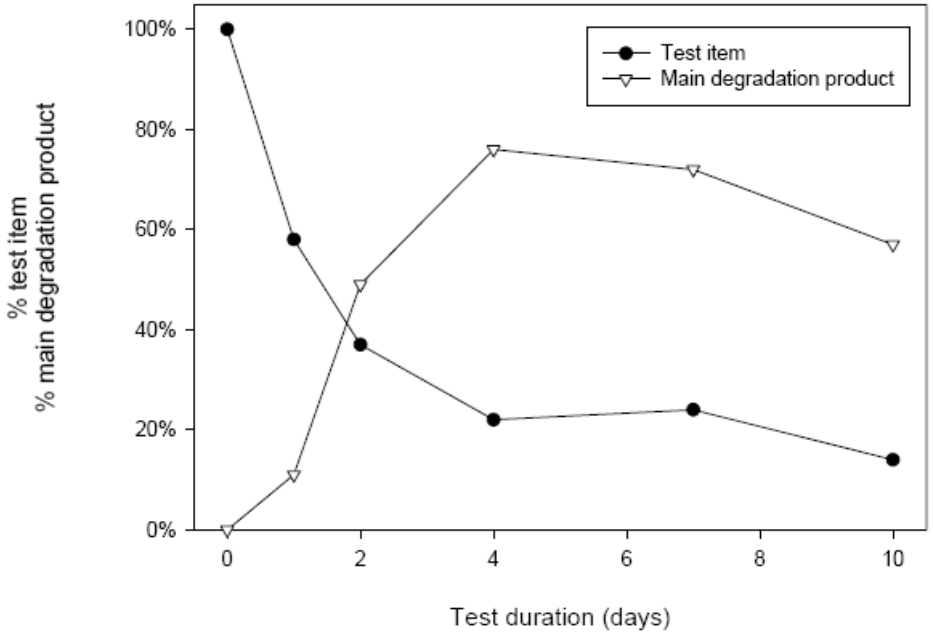

Figure 4.3. Primary degradation of the test item and formation of the main degradation product in the test flasks “test item” (RCC Ltd., 2006c).

In the abiotic control, the concentration of the test item decreased by 47 % over the incubation period of 10 days. However, no quantifiable concentrations of metilox acid were found. Loss of the parent compound could therefore probably be attributed to sorption to the glass walls.

Biodegradability of the main degradation product metilox acid was tested by CiBa-Geigy (1989) in an OECD 301B–test. At test concentrations of 10.27 and 20.33 mg l^{-1}, 7% and 3%, respectively, mineralized within 28 days based on carbon dioxide formation. The substance was emulsified with nonylphenol polyethoxylate in order to achieve a better distribution in the medium. Based on the result, metilox acid is considered not readily biodegradable. It is noted, that the study report was not available to the Rapporteur for evaluation.

BIOWIN v4.02 provides for metilox acid the following predictions: BIOWIN2 = 0.094; BIOWIN3 = 2.51; BIOWIN6 = 0.081. Based on BIOWIN v4.02 predictions metilox acid would be not readily biodegradable.

No experimental data are available on the biodegradability of 1-octadecanol. BIOWIN v4.02 provides for 1-octadecanol following predictions: BIOWIN2 = 0.894; BIOWIN3 = 3.06; BIOWIN6 = 0.954. Based on BIOWIN v4.02 results 1-octadecanol would be readily biodegradable.

4.1.3 Other information [1]

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

4.1.4 Summary and discussion of persistence

According to the available biodegradation screening tests, octadecyl 3-(3,5-di-tert-butyl-4-hydroxyphenyl)propionate is not readily biodegradable. However, fast primary degradation has been observed. The identified primary degradation product is benzenepropanoic acid, 3,5-bis(1,1-dimethylethyl)-4-hydroxy- ("metilox acid"; CAS no. 20170-32-5). The other hydrolysis product is assumed to be accordingly 1-octadecanol (CAS 112-92-5). The rate of primary degradation seems to vary depending on the test conditions. Metilox acid is based on the available result from an OECD 301B -test not readily biodegradable. 1-Octadecanol is assumed to be not persistent based on BIOWIN–predictions.

4.2 Environmental distribution

4.2.1 Adsorption

4.2.2 Volatilisation

4.2.3 Long-range environmental transport

4.3 Bioaccumulation (B)

4.4 Screening data

The very high (calculated) logKow of 13.41 indicates reduced uptake potential.

For the primary degradation product metilox acid, a logKow of 4.77 is predicted by KOWWIN v1.67. For 1-octadecanol, a logKow of 7.72 was predicted by KOWWIN v1.67.

4.4.1 Measured bioaccumulation data

A Japanese flow-through bioconcentration test with *Cyprinus carpio* is available for octadecyl 3-(3,5-di-tert-butyl-4-hydroxyphenyl)propionate (NITE, 1997). The test duration was 6 weeks and nominal test concentrations 0.5 and 0.05 mg l^{-1}. CITI (2003) has provided additional information on the test. The test was run according to OECD 305C at 25 ± 2 ºC and a dispersant (HCO-20) was used at concentrations of 5000 and 500 µg l^{-1} for each exposure level, respectively. Measured exposure concentrations (HPLC used for analysis) were as follows:

Level	2w	3w	4w	6w
1 (µg l^{-1})	482	477	479	486
2 (µg l^{-1})	46.7	46.6	47.2	47.3

BCFs reported for each sampling occasion based on measured concentrations were:

Level	2w	3w	4w	6w

1	<1.2 <1.2	<1.2 <1.2	8.4 <1.2	2.4 3.7
2	<12 <12	<12 <12	<12 <12	<12 <12

With the known solubility of the substance (2.85 µg l^{-1}), the old Japanese bioaccumulation study can be reassessed. In this study the bioaccumulation was determined at 0.05 mg/l and 0.5 mg/l. The resulting BCFs were <12 and <1.2-8.4 respectively. Assuming that in both cases the fish were exposed to saturated aqueous solution, the BCF values can be recalculated as <210 l/kg in the lower concentration and <210-1470 in the higher concentration.

Gakushuin University (1986) carried out a bioconcentration study with 3-(3-tert.-butyl-4-hydroxy-5-methyl-phenyl)-propionic acid in accordance to OECD 305C. The substance is closely related to metilox acid. At the end of an 8-week exposure period, the BCF at a test concentration of 0.5 mg l^{-1} was <0.4, and at a test concentration of 0.05 mg l^{-1} the BCF was <4.3.

Gakushuin University (1988) performed also a bioconcentration test with a hindered phenol derivative reaction mass. In this study, a bioconcentration factor was also determined for metilox acid that occurred in the test water as a metabolite. This bioconcentration factor was based on the metilox acid concentration in test water and should be considered worst-case as metilox acid was additionally formed from parent substance in fish body. The bioconcentration factor was determined to be 94-108 at high exposure concentration (1 mg l^{-1} of parent) and 373-532 at the lower exposure concentration (0.1 mg l^{-1} of parent).

4.4.2 Other supporting information[2]

4.4.3 Summary and discussion of bioaccumulation

Based on a re-evaluation of an OECD 305C bioconcentration study with fish, octadecyl 3-(3,5-di-tert-butyl-4-hydroxyphenyl)propionate has a BCF of < 210-1470 and hence a moderate to high bioaccumulation potential. Additionally, due to the fast primary degradation, bioaccumulation of the substance is not likely to occur in the environment. The main primary degradation product metilox acid has, based on experimental data, a BCF of 532 or lower and it has hence low to moderate bioaccumulation potential. The second primary degradation product, 1-octadecanol, has a high bioaccumulation potential based on its estimated logKow (7.72), but is not likely to be bioaccumulated in the environment due to its ready biodegradability.

5 HUMAN HEALTH HAZARD ASSESSMENT

Studies on toxicity to laboratory mammals are available for metilox acid. However, only the available toxicokinetic study is summarised here.

In a metabolism study of RCC (1990) groups of 5 male rats were administered a single dose of 1 and 10 mg/kg body weight of ^{14}C-labelled compound by gavage. Over a period of 168 hours faeces

[2]For example, measured concentrations in biota

and urine was analysed for radioactivity. In addition, tissues and organs were analysed for residual radioactivity after necropsy.

Absorption was rapid at both dose levels, and maximum plasma levels were reached already after one hour. Urinary excretion was 46 and 43 % for low and high dose animals, respectively, after 168 hours, and excretion via faeces was 49 and 55 %, for low and high dose animals. Peak plasma levels were about 15 times higher at the high dose, indicating that the system was not saturated with a dose of 10 mg/kg bw.

Elimination half-times ranged from 3.0 to 10.4 hours. The occurrence of a second maximum concentration in the plasma indicates, that the substance went through an additional cycle of enterohepatic circulation. Residual activity in tissues/organs was low. Rapid absorption of considerable amounts and rapid elimination within the 7-day experimental period (>90% of absorbed material excreted within 48 hours) indicates that no accumulation in any part of the animals took place.

6 ENVIRONMENTAL HAZARD ASSESSMENT

6.1 Aquatic compartment (including sediment)

6.1.1 Toxicity test results

6.1.1.1 Fish

Acute toxicity

Long-term toxicity

6.1.1.2 Aquatic invertebrates

Acute toxicity

Long-term toxicity

6.1.1.3 Algae and aquatic plants

6.1.2 Sediment organisms

No data available.

6.1.3 Other aquatic organisms

Data not evaluated for this report.

6.2 Terrestrial compartment

No data available.

6.3 Atmospheric compartment

No data available.

7 PBT AND vPvB

7.1 PBT, vPvB assessment

Persistence: Octadecyl 3-(3,5-di-tert-butyl-4-hydroxyphenyl)propionate does not meet the P/vP criteria based on screening data. According to several biodegradation screening tests, the substance is subject to a fast primary biodegradation with metilox acid (CAS no. 20170-32-5) and 1-octadecanol (CAS no. 112-92-5) as biodegradation products. Of these, the first one is not readily biodegradable and hence fulfils the P/vP screening criteria. 1-Octadecanol is, based on BIOWIN–predictions, not persistent.

Bioaccumulation: The substance does not fulfil the B criterion. Results of a standard flow-through test with fish are available for the substance. The re-evaluated BCF is < 210-1470. The primary degradation product metilox acid has a BCF of 532 or lower based on two old studies. Furthermore, metilox acid was not bioaccumulated in a toxicokinetic study with rats. It is considered, that there is enough evidence to conclude, that the substance does not fulfil the B criterion. The primary degradation product 1-octadecanol has based on its predicted logKow (7.72) a high bioaccumulation potential, but due to its ready biodegradability, it is not likely to be bioaccumulated in the environment and hence no further testing is not considered necessary.

Toxicity: Data not reviewed for this report.

Summary: Octadecyl 3-(3,5-di-tert-butyl-4-hydroxyphenyl)propionate does not fulfil the P/vP screening criteria data due to its fast primary degradation. It neither meets the B criterion. The main degradation products are metilox acid (CAS no. 20170-32-5) and 1-octadecanol (CAS no. 112-92-5). Metilox acid does not meet the B criterion and 1-octadecanol does not meet the P/vP screening criteria. Assessment of ecotoxicity was not completed. It is concluded, that octadecyl 3-(3,5-di-tert-butyl-4-hydroxyphenyl)propionate is not considered as a PBT substance.

INFORMATION ON USE AND EXPOSURE

Not relevant as the substance is not identified as a PBT.

OTHER INFORMATION

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

European Commission, 2000. IUCLID Dataset, Octadecyl 3-(3,5-di-tert-butyl-4-hydroxyphenyl)propionate, CAS 2082-79-3, 18.2.2000.

Other sources:

CiBa, 2006. A letter from Severin Müller to Eric Verbrueggen on, March 27, 2006.

CiBa, 2005. Letter to Dr. Jack de Bruijn ("2082-79-3_Interim_Oct05.doc").

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CiBa, 1991. Inherent biodegradability in the combined Zahn-Wellens/Carbondioxid evolution test of TK 10044 (OECD-guideline no. 302B / EEC guideline 84/449, C.5). CIBA-GEIGY Ltd., Product Safety, Ecotoxicology, Basle, Switzerland. Project-no. 918132. December 10, 1991.

Ciba-Geigy Ltd. (1989). Biodegradability of TK 10797 in the Modified Sturm Test, OECD-guideline no. 301 B, Ciba-Geigy Ltd., Ecotoxicology, Basle, Switzerland, Project No.: 884588, April 26, 1989. As cited in CiBa, 1999.

CITI, 2003. Additional information on the METI –tests provided to ECB on 7.10.2003.

Gakushuin University, 1988. Bioconcentration study with CG31-1017 in Carp. Gakushuin University, Japan. Report No. G4.9821.C94.CP, September 30, 1998. As cited in CiBa, 2006.

Gakushuin University, 1986. Bioconcentration study with 3-(3-tert.-butyl-4-hydroxy-5-methyl-phenyl)-propionic acid. Gakushuin University, Japan. December 3, 1986. As cited in CiBa, 2006.

METI, 1996. IUCLID Data on the METI study on Ready biodegradability (OECD 301 C Modified MITI (I) Test) as reported under the OECD HPV program by the Japanese authorities; as cited in CiBa, 2006.

NITE, 1997. Biodegradation and Bioconcentration of Existing Chemical Substance under the Chemical Substances Control Law. National Institute of Technology and Evaluation. Web database: http://www.safe.nite.go.jp/data/hazkizon/pk_e_kizon_data_result.home_data. Published Date for the substance data of CAS no. 2082-79-3: 1997/12/26.

RCC Ltd., 2006a. Determination of the water solubility of CAS RN: 2082-79-3. RCC Study Number A04803, October 31, 2006.

RCC Ltd., 2006b. Interim report, biodegradation of Benzenepropanoic acid, 3,5-bis(1,1-dimethylethyl)-4-hydroxy-, octadecyl ester (CAS 2082-79-3) over three days. March, 20, 2006.

RCC Ltd., 2006c. Benzenepropanoic acid, 3,5-bis(1,1-dimethylethyl)-4-hydroxy-, octadecyl ester: primary biodegradability in a ready biodegradability test according to OECD 301. RCC Study Number: A37811, November 03, 2006.

RCC, 1990. TK 10797: Absorption, Distribution and Excretion after Single Oral Administration to the Rat. RCC Umweltchemie AG, Itingen, Switzerland. Project-no. 894422. August 29, 1990.