CAswell # 526
526A

d-limonene 079701; linalool ?

Date Out EFB: 02 DEC 1983

To: William Miller
Product Manager 16
Registration Division (TS-767)

From: Samuel M. Creeger, Chief
Review Section No. 1
Exposure Assessment Branch
Hazard Evaluation Division (TS-769)

Attached please find the environmental fate review of:

Reg./File No.: 16-521

Chemical: d-Limonene and linalool

Type Product: ? Label not submitted

Product Name:

Company Name: Pet Chemicals

Submission Purpose: Request waiver from data requirements to support registration of technical product

ZBB Code: ?

ACTION CODE: 420

Date In: 11/4/83

EFB # 4061

Date Completed: 02 DEC 1983

TAIS (level II)	Days
61	1

Deferrals To:

_____ Ecological Effects Branch

_____ Residue Chemistry Branch

_____ Toxicology Branch

1. INTRODUCTION

1.1 The registrant, Pet Chemicals, Inc., is requesting a waiver from the data requirements for the registration of the technical grade of d-limonene and linalool. A label was not submitted, but it is assumed that the technical product(s) for which registration(s is (are) sought will be used for manufacturing purposes only and tha the technical product will not be used by the consumer. The PM agrees witht the above assumption.

2. CONCLUSIONS/RECOMMENDATIONS

2.1 Based on the above assumptions, hydrolysis studies will be needed on each active ingredient. Also, based on the submitted monograph of linalool showing it to be toxic to microbes, an activated sludge study should be done. (A monograph on d-limonene was not included with this submission).

2.2 Articles taken from the open literature may satisfy some data requirements.

2.3 The activated sludge study can be waived if the registrant can show that the manufacturing process will not result in contact between the active ingredients and an activated sludge (sewage) treatment plant. However, if the active ingredients are discharged directly into the aquatic environment, then additional data will be needed.

2.4 The final use products may require additional data to support their registration.

2.5 A Shaughnessy number must accompany the next submission of linalool so that the submission can be tracked in the EAB system. In addition, future submissions must include a label.

Samuel M. Creeger
December 2, 1983
Section #1/EAB
Hazard Evaluation Division

Monographs on Fragrance Raw Materials

A Collection of Monographs originally appearing in Food and Cosmetics Toxicology

An International Journal

Edited by

D. L. J. OPDYKE

Research Institute for Fragrance Materials, Inc., Englewood Cliffs, New Jersey 07632, USA

Published on behalf of the
RESEARCH INSTITUTE FOR FRAGRANCE MATERIALS
by
PERGAMON PRESS
OXFORD · NEW YORK · TORONTO · SYDNEY · PARIS · FRANKFURT

3

LINALOOL

Synonyms: 3,7-Dimethyl-1,6-octadien-3-ol; 2,6-dimethyl-octadien-2,7-ol-6.
Structure: $CH_3 \cdot C(CH_3):CH \cdot [CH_2]_2 \cdot (CH_3)C(OH) \cdot CH:CH_2$.
Description and physical properties: EOA Specs nos 48 & 226.
Occurrence: The optically active forms (*d*- and *l*-) and the optically inactive form occur natura in more than 200 oils from herbs, leaves, flowers and wood. The *l*-form is present in the larg amounts (80–85%) in the distillates from leaves of *Cinnamomum camphora* var. *orientalis* and *camphora* var. *occidentalis* and in the distillate from Cajenne rosewood. It has also been report in champaca, ylang-ylang, neroli, Mexican linaloe, bergamot, lavandin and others. A mixture *d*- and *l*-linalool has been reported in Brazil rosewood (85%). The *d*-form has been found in palm rosa, mace, sweet orange-flower distillate, petitgrain, coriander (60–70%), marjoram, *Orthodon linaloc ferum* (80%) and others. The inactive form has been reported in clary sage, jasmine, and *Nectanc elaiophora* (*Fenaroli's Handbook of Flavor Ingredients*, 1971).
Preparation: By fractionation of Bois de Rose oil or by chemical synthesis.
Uses: In public use before the 1900s. Use in fragrances in the USA amounts to approximately 200,(lb/yr.

Concentration in final product (%):

	Soap	*Detergent*	*Creams, lotions*	*Perfume*
Usual	0·04	0·004	0·02	0·5
Maximum	0·3	0·03	0·1	1·5

Analytical data: Gas chromatogram, RIFM no. 70–66; infra-red curve, RIFM no. 70–66.

Status

Linalool was given GRAS status by FEMA (1965) and is approved by the FDA for food u (GRAS). The Council of Europe (1974) listed linalool giving an ADI of 0.25 mg/kg. The *Fc Chemicals Codex* (1972) has a monograph on linalool and the Joint FAO/WHO Expert Commit on Food Additives (1967) has published a monograph and specifications for linalool giving a con tional ADI of 0–0.25 mg/kg.

Biological data

Acute toxicity. The acute ip LD_{50} of linalool was found to be 340 mg/kg for male albino m and 307 mg/kg for male albino rats (Atanassova-Shopova, Roussinov & Boycheva, 1973). In te using 75–800 mg/kg, animals rapidly developed an ataxic gait, obviously reduced spontaneous mo activity and depression while higher doses caused the assumption of a lateral position and develc ment of respiratory disturbances leading to death. Narcotic effects were obtained with a dose equiv ent to approximately half of the LD_{50}.

The acute oral LD_{50} of linalool for rats was found to be 2790 mg/kg, with ataxia soon af treatment and death within 4–18 hr (Jenner, Hagan, Taylor, Cook & Fitzhugh, 1964). The acu intramuscular LD_{50} for mice was found to be 8 g/kg (Northover & Verghese, 1962). The acu dermal LD_{50} in rabbits was reported as 5610 (3578–8374 mg/kg) Fogleman, 1970).

Subacute toxicity. The maximum tolerated dose (MTD) of linalool for mice was found to 0·125 g/kg, determined as the maximum single dose tolerated by all of a group of five mice giv six ip injections over a 2-wk period (Stoner, Shimkin, Kniazeff, Weisburger, Weisburger & Gc 1973). The effects of linalool on hepatic drug-metabolizing enzymes in the rat were studied Parke and co-workers. Pretreatment of rats for 3 days with 150 mg linalool/kg ip caused no increa in the activities of biphenyl 4-hydroxylase, glucuronyl transferase, or cytochrome *P*-450 in liv homogenates, but increased the activity of 4-nitrobenzoate reductase by 25–50% (Parke & Rahm 1969).

In a longer study, intragastric administration of 500 mg linalool/kg/day for up to 64 days indica that effects on liver proteins and drug-metabolizing enzymes developed slowly and might repres physiological adaptation to linalool. Thus linalool may be involved in the induction of drug-metal lizing enzymes in neonatal rats (from 4 wk old). Over the 64-day period, body weight was affected, while liver weight and relative liver weight were slightly increased after day 30. Microsom protein concentration was increased after day 14. Cytochrome concentrations were decreased day 7 but had increased by 50–70% by day 64. 4-Methylumbelliferone-glucuronyl transferase activ increased from 17% on day 3 to 150% by day 64, while alcohol-dehydrogenase activity was depres

Irritation. Linalool applied full strength to intact or abraded rabbit skin for 24 hr under occlusion was moderately irritating (Fogleman, 1970). Tested at 20% in petrolatum, it produced no irritation after a 48-hr closed-patch test on human subjects (Kligman, 1970). In other closed-patch tests on human skin, linalool caused no primary irritation in 28 normal subjects when applied as a 20% concentration in vaseline or ointment, in 30 normal subjects when applied at 2%, or in 84 subjects with dermatoses when tested in 0·4% concentration in ethanol or a cream base (Fujii, Furukawa & Suzuki, 1972).

In tests of acanthogenic activity, daily application of a 20% solution of linalool in absolute alcohol to guinea-pig skin for 8–10 days caused some epidermal thickening, with a mean acanthosis factor of 4·6 (solvent = 1) (Schaaf, 1961).

The effect of linalool and other alcohols on local capillary permeability was studied in rabbits by the intracutaneous injection of various concentrations dissolved in isopropyl myristate and the measurement of the resulting extravasal leakage of Evans blue injected iv. Tertiary alcohols showed lower responses than other types of alcohols, while responses were enhanced for unsaturated alcohols (Suzuki & Arai, 1966).

Sensitization. A maximization test (Kligman, 1966; Kligman & Epstein, 1975) was carried out on 25 volunteers. The material was tested at a concentration of 20% in petrolatum and produced no sensitization reactions (Kligman, 1970). In another maximization test (Kligman, 1966) on 25 volunteers the material was tested at a concentration of 8% in petrolatum and produced no sensitization reactions (Greif, 1967).

Metabolism. The metabolism of ^{14}C-labelled linalool in the rat was studied by Parke, Rahman & Walker (1974a). An intragastric dose of 500 mg linalool/kg body weight was largely (93%) excreted within 72 hr in the urine (55%), faeces (23%) and expired air (15%). The radioactivity remaining after 72 hr was located mainly in the liver (0·5%), gut (0·6%), skin (0·8%) and skeletal muscle (1·2%). Rapid urinary excretion indicated that linalool was rapidly absorbed from the gut, while delay in excretion in the expired air suggested that linalool might enter intermediary metabolism and also be metabolized by conjugation in the bile and urine. Ip administration of 20 mg linalool indicated that enterohepatic circulation occurred, resulting in a short-term metabolic load on the liver and delayed faecal excretion. The metabolism of large doses in the rat, with rapid excretion of linalool and its metabolites, suggests no long-term hazard from tissue accumulation on chronic exposure to concentrations normally encountered in foods, although enterohepatic circulation might prolong the metabolic load on the liver over a relatively short period.

A study of the effects of linalool and other terpenoids on hepatic drug-metabolizing enzymes suggested that these compounds induce the enzymes involved in their own metabolism. Linalool, which is metabolized by reduction and conjugation with glucuronic acid, increased the activity of 4-nitrobenzoate reductase but did not increase other enzymes studied (Parke & Rahman, 1969).

Linalool can be metabolized by micro-organisms. *l*-Linalool was partially oxidized by incubation with *Aspergillus niger* (Goto, 1967). The linalool content of grape essential oil decreased during must fermentation and wine formation (Rodopulo, Egorov, Bezzubov, Kormakova & Megrelidze, 1972). A strain of *Pseudomonas pseudomallei*, isolated from soil, metabolized linalool with the formation of camphor, 4-methyl-4-vinylbutyrolactone, 4-methyl-*trans*-3-hexenoic acid, and 2,6-dimethyl-6-hydroxy-*trans*-2,7-octadienoic acid (Mizutani, Hayashi, Ueda & Tatsumi, 1971).

Percutaneous absorption. Linalool was not absorbed within 2 hr on the intact shaved abdominal skin of the mouse (Meyer & Meyer, 1959). In an evaluation of skin penetrating agents, linalool as a 50% solution did not aid penetration of Rhodamine B into guinea-pig skin (Meyer, 1965).

Carcinogenicity. When mice received ip injections of the maximum tolerated dose (MTD) or 0·2 MTD (total dose 3·00 and 0·60 g/kg, respectively) 3 times/wk for 8 wk, 9–11 mice/group of 15 survived 24 wk, with no increase in primary lung-tumour induction compared with untreated controls (Stoner *et al.* 1973). Linalool as a 20% solution in acetone was reported to be a weak tumour-promoter on the skins of mice treated with the primary carcinogen, 9,10-dimethyl-1,2-benzanthracene (Roe & Field, 1965). Linalool and other terpenic compounds present in tobacco leaves or added during processing may be precursors of carcinogenic hydrocarbons formed during smoking by breakdown to isoprene, which is converted to an aromatic tar containing benzo[a]pyrene (Gil-Av & Shabtai, 1963).

Pharmacology. *l*-Linalool showed no sedative action in the mouse motility test when injected ip at a dose of 100 mg/kg (Binet, Binet, Miocque, Roux & Bernier, 1972), but Wagner & Sprinkmeyer (1973) reported that linalool depressed spontaneous motility of mice at doses of 31·6 and 100 mg/kg.

Linalool showed spasmolytic action against carbachol-, histamine- and barium chloride-induced contractions in isolated guinea-pig ileum, the ED_{50} being about 100–200 mg/litre (Wagner & Sprinkmeyer, 1973), and in the isolated rat duodenum, contractions caused by 0.05 μg acetylcholine/ml were inhibited by 50% by 10 μg *l*-linalool/ml (Binet *et al.* 1972). Linalool showed slight papavarine-like and very slight atropine-like antispasmodic action on small intestine isolated from the mouse (Imaseki & Kitabatake, 1962).

In studies carried out by Atanassova-Shopova *et al.* (1973), the ED_{50} for preventing tonic hyperextension of the hind limbs of rats from electric shock was found to be 135 mg/kg given ip. Linalool had a marked anticonvulsive and protective effect on pentylenetetrazol convulsions in mice at 150.

175 and 200 mg/kg and in rats at 200 and 300 mg/kg. It showed a slight antistrychnine effect in mice at high and toxic doses (300 mg/kg), reduced motor activity of mice at 100 mg/kg, and at 50 mg/kg slightly decreased the motor activity of amphetamine- or caffeine-stimulated mice. The TD_{50} (neurotoxic dose) of linalool for influencing motor co-ordination of mice in the Rota-rod test was found to be 178 mg/kg. Linalool at doses of 50 or 100 mg/kg prolonged the narcotic effects of hexobarbitone, alcohol and chloral hydrate.

The equilibrium and spontaneous or reflex activity of the goldfish, *Carassium auratus*, was disturbed by exposure to aquarium water containing a 0·1–3 ml/litre concentration of a suspension containing 1 ml linalool plus 9 ml of a 10% aqueous solution of Tween 80, and the agressiveness of the male fighting fish, *Betta splendens*, was only very slightly inhibited by exposure to aquarium water containing 0·3 ml of the same suspension of linalool/litre (Binet, 1972).

Linalool and other terpene alcohols were found to be useful in man as sedatives and spasmolytics when administered in doses of 0·01–1 g, the effects having been tested in mice, goldfish, and rats (Laboratoires Meram, 1966).

Linalool depressed frog-heart activity in doses above 0·2 mg/g (Lysenko, 1962). Vasodilation by direct action of linalool upon the blood vessels was demonstrated by Northover & Verghese (1962). An iv dose of 9·2 mg/kg was required to produce a 25% fall in systolic arterial blood pressure in the anaesthetized dog and a hypotensive response was also observed in the decerebrated and despinalized dog. A dose of 0·05 g in fluid perfusing the leg of an anaesthetized dog or the isolated ear of a rabbit produced a maximum increase of 120% or 90% respectively, in venous outflow over pre-injection values. Linalool dilated the small blood vessels of the exposed mesorchium of the anaesthetized mouse, lowering the threshold for electronic stimulation. Incubation of human, bovine and canine aortae in 0·15 M-linalool failed to stabilize the structure of the aortic wall proteins against hydrothermal shrinkage (Milch, 1965). Linalool inhibited incorporation of acetic acid or mevalonic acid into total or digitonin-precipitable nonsaponifiable lipids by rat-liver homogenates (Gey, Pletscher, Isler, Rüegg, Saucy & Würsch, 1960).

Micro-organisms. Linalool inhibited the *in vitro* growth of all three wood-destroying fungi studied by Maruzzella, Scrandis, Scrandis & Grabon (1960), and the vapour of linalool inhibited the growth of all four fungi tested by Maruzzella, Chiaramonte & Garofalo (1961). Linalool at 1:10.000 dilution showed moderate stimulatory action on the germination of uredospores of the wheat stem rust organism *Puccinia graminis* (French, 1961). Linalool strongly inhibited the rumen microbial activity of sheep and deer (Oh, Sakai, Jones & Longhurst, 1967) and at 1:500 dilution inhibited *in vitro* growth of *Escherichia coli* but not of three gram-positive bacteria, *Bacillus subtilis* and two strains of *Staphylococcus aureus* (Maruzzella & Bramnick, 1961). Münzing & Schels (1972) reported, however, that at 1:500 dilution it inhibited the growth of *Staph. aureus* and *Escherichia coli* but not of *Proteus vulgaris* and *Pseudomonas aeruginosa*, all found in contaminated cosmetics.

The relative bactericidal action of linalool was reported to be seven times that of phenol (Führer, 1972). It showed no antibacterial activity *in vitro* on tubercle bacilli, but enhanced the effectiveness of small (5 mg) daily doses of dihydrostreptomycin when given im in weekly doses of 10 mg to guinea-pigs infected with tuberculosis (Kato & Gözsy, 1958). It exhibited only weak therapeutic activity in experimental tuberculosis of guinea-pigs and slightly induced a local India-ink and trypan blue accumulation in rat skin, but did not stimulate the phagocytic activity of guinea-pig macrophages (Gözsy & Kato, 1958).

Linalool strongly inhibited the growth of all nine bacteria tested by Kellner & Kober (1956) and caused moderate to strong inhibition of the growth of most of 34 bacterial strains tested by Möse & Lukas (1957). In *in vitro* tests, it inhibited the production of spores and parasporal crystals by *Bacillus thuringiensis* (Morris, 1972).

In rabbits, linalool delayed the development of experimental gas gangrene, acted as a therapeutic agent and lowered mortality (Chuiko, Lavrushina & Pavlotskaya, 1957). The presence of linalool increased the bactericidal effectiveness of certain patented betaine compositions (Hofmann, 1971) and patented compositions containing linalool and a cetylpyridinium halide inhibit the growth of bacteria and fungi and may be used to disinfect skin and mucous surfaces, wounds and various articles and utensils (Gauvreau, 1971).

Viruses. Linalool in daily doses of 1 mg, given as a single oral dose or in the drinking-water, protected chicks against avian lymphomatosis virus strain ES4, and was proposed as an antineoplastic and antiviral agent for veterinary administration (Baranger, 1971).

Cytotoxicity. Linalool was found to be moderately cytotoxic to Chang, HeLa, and KB cells (Nachev, Zolotovich, Silvanovska & Stojcev, 1967). When tested against HeLa cells in monolayer culture, linalool was cytotoxic at 100 μg/litre, weakly active at 10 μg/litre, and inactive at 1 μg/litre (Nachev, Zolotovitch, Siljanowski & Stojcev, 1968).

Odour sensing. *d*-Linalool ($1–5 \times 10^{-4}$ M) stimulated $Na^+–K^+$ ATPase in rabbit olfactory preparations and in nerve-ending-particle fractions from rat olfactory endoturbinals, but caused approximately 20% inhibition of activity of this enzyme in rat brain. It was proposed that perturbation of this enzyme may be important in the initiation of odour sensing (Koch & Desaiah, 1974). Linalool decreased the 267 nm spectral absorption of rabbit olfactory epithelium preparations. The change was attributed to the formation of a complex involving stimulant and olfactory protein, rather than to enzyme activity (Ash, 1968; Ash & Skogen, 1970).

Insects. Linalool was found to be attractive to the honeybee, *Apis mellifera* (Waller, Loper & Berdel, 1973) and to larvae of the cotton leafworm, *Spodoptera littoralis* (Khalifa, Rizk, Salama & El-Sharaby, 1973), and the silkworm, *Bombyx mori* (Hamamura & Naito, 1961). It was found to be relatively ineffective as a repellent for the mosquito, *Aedes aegypti* (Burton, 1969). Linalool decreased the wing vibration response of male Mediterranean flour moths, *Ephestia kuehniella*, to sex pheromone from females over a 30-sec period, but increased the number of males attracted to the pheromone source (Traynier & Wright, 1973). Epoxidation of linalool produced a product with sex pheromone activity for the male codling moth, *Carpocapsa pomonella* (McDonough, George & Butt, 1969). Pure linalool possessed no juvenile-hormone activity against *Galleria mellonella* pupae, but a commercial sample of linalool showed slight activity (Schneiderman, Krishnakumaran, Kulkarni & Friedman, 1965).

Trematodes. Linalool applied to the tails of mice provided no protection against infestation with cercariae of *Schistosoma mansoni* (Gilbert, De Souza, Fascio, Kitagawa, Nascimento, Fortes, Seabra & Pellergrino, 1970).

Plants. The inhibiting effects of linalool on the growth of *Lepidium sativum* seedlings and the germination of *Raphanus sativus* seeds were studied by Garshtya & Koval'chuk (1972).

References

Ash, K. I. (1968). Chemical sensing: An approach to biological molecular mechanisms using difference spectroscopy. *Science, N.Y.* **162**, 452.

Ash, K. O. & Skogen, J. D. (1970). Chemosensing: Selectivity, sensitivity and additive effects on a stimulant-induced activity of olfactory preparations. *J. Neurochem.* **17**, 1143.

Atanassova-Shopova, S., Roussinov, K. S. & Boycheva, I. (1973). On certain central neurotropic effects of lavender essential oil. II. Studies on the effects of linalool and of terpinenol. *Izv. Inst. Fiziol., Sof.* **15**, 149.

Baranger, P. (1971). Nouveau procédé d'administration vétérinaire d'alcools terpéniques et alicycliques. French Patent Demande 2,062,871; Appln date 19 September 1969.

Binet, P. (1972). Action de quelques alcools terpéniques sur le système nerveux des poissons. *Annls pharm. fr.* **30**, 653.

Binet, L., Binet, P., Miocque, M., Roux, M. et Bernier, A. (1972). Recherches sur les propriétés pharmacodynamiques (action sédative et action spasmolytique) de quelques alcools terpéniques aliphatiques. *Annls pharm. fr.* **30**, 611.

Burton, D. J. (1969). Intrinsic mosquito repellency values of some chemical compounds. *Am. Perfumer Cosmet.* **84**, 41 & 44.

Chuiko, O. V., Lavrushina, T. T. & Pavlotskaya, Yu. G. (1957). Effect of some essential oils components on the development of experimental gas gangrene. *Trudy khar'kov. farmatsevt. Inst.* **1**, 300.

Council of Europe (1974). Natural Flavouring Substances. Their Sources, and Added Artificial Flavouring Substances. Partial Agreement in the Social and Public Health Field. List 1, no. 61, p. 136. Strasbourg.

Fenaroli's Handbook of Flavor Ingredients (1971). Edited by T. E. Furia and N. Bellanca, p. 484. Chemical Rubber Co., Cleveland, Ohio.

Flavoring Extract Manufacturers' Association (1965). Survey of flavoring ingredient usage levels. No. 2635. *Fd Technol., Champaign* **19** (2), part 2, 155.

Fogleman, R. W. (1970). Report to RIFM, 14 September.

Food Chemicals Codex (1972). 2nd ed. Prepared by the Committee on Specifications, Food Chemicals Codex, of the Committee on Food Protection, p. 458. National Academy of Sciences–National Research Council Publ. 1406. Washington, D.C.

French, R. C. (1961). Stimulation of uredospore germination in wheat stem rust by terpenes and related compounds. *Bot. Gaz.* **122**, 194.

Führer, H. (1972). Parfümölkompositionen mit baktericider Wirkung aus Reichstoffen und ätherischen Ölen. *Seifen-Öle-Fette-Wachse* **98**, 677.

Fujii, T., Furukawa, S. & Suzuki, S. (1972). Studies on compounded perfumes for toilet goods. On the non-irritative compounded perfumes for soaps. *Yukagaku* **21**, 904.

Garshtya, L. Ya. & Koval'chuk, Yu. G. (1972). Phytodynamic effect of solutions and vapors of some components of essential oils. Fiziol.-Biokhim. Osn. Vzaimodeistviya Rast. Fitotsenozakh, No. 3:21.

Gauvreau, C. (1971). Disinfection compositions. U.S. Patent 3,595,975; appln dates 21 October 1965 and 29 July 1969.

Gey, K. F., Pletscher, A., Isler, O., Rüegg, R., Saucy, C. & Würsch, J. (1960). On the effects of mono- and sesquiterpenes on the synthesis of cholesterol. On the question of intermediary products of cholesterol synthesis at the mono- and sesquiterpene level. *Int. Conf. biochem. Probl. Lipids, 5.* Vienna, 1958, p. 175.

Gil-Av, E. & Shabtai, J. (1963). Precursors of carcinogenic hydrocarbons in tobacco smoke. *Nature, Lond.* **197**, 1065.

Gilbert, B., De Souza, J. P., Fascio, M., Kitagawa, M., Nascimento, S. S. C., Fortes, C. C., Seabra, A. D. P. & Pellegrino, J. (1970). Esquistossomose: Protecao contra infeccao por terpenoides. *Anais Acad. bras. Cienc.* **42** (Suppl.), 397.

Goto, K. (1967). Biochemical degradation of geraniol by *Aspergillus niger*. *Obihiro Chikusandaigaku Gakijutsu Kenkyu Hokoku* **4**, 489.

Gözsy, B. & Kato, L. (1958). Reticulo-endothelial system stimulating compounds and their mechanism of action. *Can. J. Biochem. Physiol.* **36**, 319.

Greif, N. (1967). Cutaneous safety of fragrance material as measured by the maximization test. *Am. Perfumer Cosmet.* 82 (June). 54.

Hamamura, Y. & Naito, K.-I. (1961). Food selection by silkworm larvae, *Bombyx mori*. Citral, linalyl acetate, linalol, and terpinyl acetate as attractants of larvae. *Nature, Lond.* **190**, 879.

Hofmann, C. (1971). Bactericidal compositions containing (acylaminopropyl)-dimethylaminoacetic acid betaine. German Patent 2,020,349: Appln date 25 April 1970.

Imaseki, I. & Kitabatake, Y. (1962). Studies on effect of essential oils and their components on the isolated intestines of mice. *Yakugaku Zasshi* **82**, 1326.

Jenner, P. M., Hagan, E. C., Taylor, Jean M., Cook, E. L. & Fitzhugh, O. G. (1964). Food flavourings and compounds of related structure. I. Acute oral toxicity. *Fd Cosmet. Toxicol.* **2**, 327.

Joint FAO/WHO Expert Committee on Food Additives (1967). Toxicological Evaluation of Some Flavouring Substances and Non-nutritive Sweetening Agents. *F.A.O. Nutr. Mtg Rep. Ser. no.* 44A, Geneva, p. 52; WHO/Food/68.33.

Kato, L. & Gözsy, B. (1958). Treatment of experimental tuberculosis of the guinea pig with dihydrostreptomicine and simultaneously with substances acting on the host. *Archs int. Pharmacodyn. Ther.* **117**, 52.

Kellner, W. u. Kober, W. (1956). Möglichkeiten der Verwendung ätherischer Öle zur Raumdesinfektion. III. *Arzneimittel-Forsch.* **6**, 768.

Khalifa, A., Rizk, A., Salama, H. S. & El-Sharaby, A. F. (1973). Role of phagostimulants of cotton leaves in the feeding behavior of *Spodoptera littoralis*. *J. Insect Physiol.* **19**, 1501.

Kligman, A. M. (1966). The identification of contact allergens by human assay. III. The maximization test. A procedure for screening and rating contact sensitizers. *J. invest. Derm.* **47**, 393.

Kligman, A. M. (1970). Report to RIFM; 7 October.

Kligman, A. M. & Epstein, W. (1975). Updating the maximization test for identifying contact allergens. *Contact Dermatitis* **1**, 231.

Koch, R. B. & Desaiah, D. (1974). Preliminary studies on rat olfactory tissue: Effects of odorants on Na^+-K^+ ATPase activity. *Life Sci.* **15**, 1005.

Laboratoires Meram (1966). Nouveaux sedatifs et spasmolytiques. French Patent M4055; appln date 20 January 1964.

Lysenko, L. V. (1962). Pharmacological examination of geraniol, carvone, linalool, and thymol. *Trudy khar'kov. farmatsevt. Inst.* **2**, 176.

McDonough, L. M., George, D. A. & Butt, B. A. (1969). Artificial sex pheromones for the codling moth. *J. econ. Ent.* **62**, 243.

Maruzzella, J. C. & Bramnick, E. (1961). The antibacterial properties of perfumery chemicals. *Soap Perfum. Cosm.* **34**, 743.

Maruzzella, J. C., Chiaramonte, J. S. & Garofalo, M. M. (1961). Effects of vapors of aromatic chemicals on fungi. *J. pharm. Sci.* **50**, 665.

Maruzzella, J. C., Scrandis, D. A., Scrandis, J. B. & Grabon, F. (1960). Action of odoriferous organic chemicals and essential oils on wood-destroying fungi. *Pl. Dis. Reptr* **44**, 789.

Meyer, F. (1965). Penetrating agents. British Patent 1,001,949; German appln date 20 July 1961.

Meyer, Fr. & Meyer, E. (1959). Percutaneous absorption of essential oils and their constituents. *Arzneimittel-Forsch.* **9**, 516.

Milch, R. A. (1965). Hydrothermal shrinkage of metabolite-treated aortae. *J. Atheroscler. Res.* **5**, 215.

Mizutani, S., Hayashi, T., Ueda, H. & Tatsumi, C. (1971). Microbiological conversion of terpenes. IX. Conversion of linalool. *Nippon Nogei Kagaku Kaishi* **45**, 368.

Morris, O. N. (1972). Inhibitory effects of foliage extracts of some forest trees on commercial *Bacillus thuringiensis*. *Can. Ent.* **104**, 1357.

Möse, J. R. u. Lukas, G. (1957). Zur Wirksamkeit einiger ätherischer Öle und deren Inhaltsstoffe auf Bakterien. *Arzneimittel-Forsch.* **7**, 687.

Münzing, H.-P. u. Schels, H. (1972). Über die Möglichkeiten des Ersatzes von Konservierungsmitteln in kosmetischen Präparaten durch ätherische Öle. *J. Soc. cosmet. Chem.* **23**, 841.

Nachev, Kh., Zolotovich, G., Silyanovska, K. Stojcev, St. (1967). Cytotoxic effect of alcohols isolated from essential oils. *C.r. Acad. bulg. Sci.* **20**, 1081.

Nachev, Ch., Zolotovitch, G., Siljanowska, K. u. Stojcev, St. (1968). Untersuchungen über den cytotoxischen Effekt einiger ätherischer Öle und einzelner ihrer Bestandteile. I. Terpenkohlenwasserstoffe und -alkohole. *Parfüm. Kosmet.* **49**, 104.

Northover, B. J. & Verghese, J. (1962). The pharmacology of certain terpene alcohols and oxides. *J. scient. ind. Res.* **21C**, 342.

Oh, H. K., Sakai, T., Jones, M. B. & Longhurst, W. M. (1967). Effect of various essential oils isolated from Douglas fir needles upon sheep and deer rumen microbial activity. *Appl. Microbiol.* **15**, 777.

Parke, D. V. & Rahman, H. (1969). The effects of some terpenoids and other dietary anutrients on hepatic drug-metabolizing enzymes. *Biochem. J.* **113**, 12P.

Parke, D. V., Rahman, Kh. M. Q. & Walker, R. (1974a). The absorption, distribution and excretion of linalool in the rat. *Biochem. Soc. Trans. London* **2**, 612.

Parke, D. V., Rahman, Kh. M. Q. & Walker, R. (1974b). Effect of linalool on hepatic drug-metabolizing enzymes in the rat. *Biochem. Soc. Trans. London* **2**, 615.

Rodopulo, A. K., Egorov, I. A., Bezzubov, A. A., Kormakova, T. A. & Megrelidze, K. V. (1972). Essential oils from grape and wine of the main Azerbaidzhan varieties. *Prikl. Bioklim. Mikrobiol.* **8**, 52.

Roe, F. J. C. & Field, Winifred E. H. (1965). Chronic toxicity of essential oils and certain other products of natural origin. *Fd Cosmet. Toxicol.* **3**, 311.

Schaaf, F. (1961). Chemische Konstitution und Wirkung im Akanthosetest. *Dermatologica* **123**, 362.

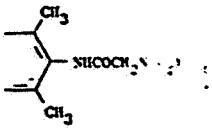
Schneiderman, H. A., Krishnakumaran, A., Kulkarni, V. G. & Friedman, L. (1965). Juvenile hormone activity of structurally unrelated compounds. *J. Insect Physiol.* **11**, 1641.

Stoner, G. D., Shimkin, M. B., Kniazeff, A. J., Weisburger, J. H., Weisburger, Elizabeth & Gori, G. B. (1973). Test for carcinogenicity of food additives and chemotherapeutic agents by the [illegible]

response in Strain A mice. *Cancer Res.* 33, 3069.
Suzuki, M. & Arai, H. (1966). The relation between the chemical structure of alcohols and their increasing effect on capillary permeability in skin. *Nippon Yakurigaku Zasshi* 62, 241.
Traynier, R. M. M. & Wright, R. H. (1973). Modification of responses to sex pheromone in the male Mediterranean flour moth, *Ephestia kuehniella*, by additional substances. *Entomologia exp. appl.* 16, 1.
Wagner, H. u. Sprinkmayer, L. (1973). Über die pharmakologische Wirkung von Melissengeist. *Dt. ApothZtg* 113, 1159.
Waller, G. D., Loper, G. M. & Berdel, R. L. (1973). Bioassay for determining honeybee responses to flower volatiles. *Environ. Entomol.* 2, 255.

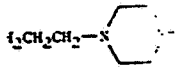
starch. $C_6H_{10}O_5$ ...
...%, O 49.34...
...) Ach., *Pure...*
Chem. Soc. 195...
J. Chem. 40, ...
...oluble in boiling w...

...*thylamino-2',6'*-...
...cetanilide; Xy...
...caina; Isicaine, ...
...sin; Xylocitin ...
...H 9.46%, N 11...
..., U.S. pat. 2,441,4...
...pat. 758,224 (19...
..., U.S. pat. 2,79...,241
...*shch. Khim.* 30, 1...
...*Local Anesthet...*
...eggstroms, Stock...
953).



...enzene or alcohol, ...
...-160°. Insoluble ...
...ene, chloroform, ...
...$_{14}H_{22}N_2O.HCl$, ...
...H_2O; crystals, ...
...hydrochloride ...
...on of dil HCl on ...
...g/kg.
...: Local anesthetic ...
...% to 4% soln. ...
...2% soln. *Side E...*

4-[4,4-Bis(*p*-fluoro...
...dide; 1-[4,4-di...
...ocarbonyl]methy...
...ium; Klinium. ...
H 7.18%, F 7.73...
Appl. 6,507,312 (19...
...*A.* 64, 12704g (19...



...-161°. Almost ...
...orm (>50°C), but ...
...solvents: Schaper ...
265 (1966).
...nental long-acting ...

F Yellowish. *C.I.* ...
p-[ethyl(*m*-sulfo...
...]-2,5-cyclohexa...
...hydroxide ...
...; mol wt 792.8...
...%, O 18.16%, S 12.1...

...powder. Soluble in water to a green ...yellowish-brown with HCl and then ... Addition of NaOH almost completely ...ing yielding a dull violet ppt.

...ner found in wood (25–30%). The struc... monomer is still not completely known. ...deryl alcohol, noted more than 50 years ... by the fact that it can be oxidized to ...enated to compds of the cyclohexyl... ...sulfite waste liquors from paper mills ... lignin. *Review:* F. F. Nord, W. J. ... *American* 199, no. 4, pp 104–113 (October ...sive monograph: F. E. Brauns, D. A. ...*istry of Lignin*, Supplement Volume cover... 1949–1958 (Academic Press, New York ...), 804 pages. Status report on research: ..., July 6, 1964, p 80 sqq. Concise mono... *The Chemistry of Lignin* (Marcel Dekker, ... 1967), 360 pp.
...d vanillin, syringic aldehyde. Extender for ... to strengthen rubber (esp for shoe soles), ...e, to stabilize asphalt emulsions, to pre... *Review:* "Lignin as a Raw Material for ... Pure Chemicals" L. A. Pearl, *J. Chem.* ... 1958).

... Acid. *Tetracosanoic acid.* $C_{23}H_{47}COOH$; ... $C_{24}H_{48}O_2$; C 78.19%, H 13.13%, O 8.68%. ...value 152.2. Obtained from beechwood tar ...ation of rotten oak wood: Sullivan, *Ind.* ... 1027 (1916). Most natural fats contain ...0.2–1%). The seed fat of the Indian tree ...*ainina* is said to contain 25%. A synthesis ... Hesse and Szmuszkovicz, *J. Am. Chem. Soc.* ...
... 84.5°. $n_D^{20°}$ 1.4287. Solubility in 91.53% ... 100 ml.
... $C_{16}H_{30}O_2$ platelets, mp 58–59.8°.

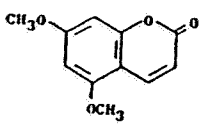
... The wood of *Guaiacum officinale* L., or ...*gophyllaceae*. *See also* Guaiac.

... &P. naphtha; varnish makers' and painters' ...d solvent naphtha; solvent naphtha; Benzo... Petroleum fractions of the same nature as ... petr benzin, but of higher density, higher ... and higher flash pt.
...ent naphtha meeting A.S.T.M. specifications ...mmable liquid. $d_{15.6}^{15.6}$ 0.850 to 0.870. Distilla... 760 mm: percentage recovered at 130° = not ... percentage recovered at 145° = not less than ... dry point) = not above 155°.
... benzin (high boiling petr ether) usually has a ... 150 and b_{760} 80–130°.
... *also* Mineral Spirits, Petroleum Benzin, ...

... Natural calcium carbonate; agricultural ...stone; lithographic stone; Sohnhofen stone. ...ally applied only to minerals consisting largely ... such as Portland stone, dolomite, marble, and ... used indiscriminately to designate technical and ... grades of calcium carbonate.

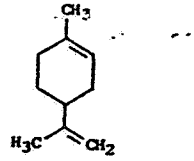
... **Saturated Solution.** Vlemingckx's soln or lotion; ...um oxysulfide. Made by boiling 16.5 parts ... lime with 25 parts sublimed sulfur and water ..., the resulting soln contg calcium polysulfide ...
... liquid.
... Topical antiseptic, scabicide. *Side Effects:* ... may occur.
... Has been used in boils, fistulas, mange.

... *5,7-Dimethoxycoumarin;* citropten. $C_{11}H_{10}O_4$; ... C 64.07%, H 4.89%, O 31.04%. From rind ...*rus lima* Lunan (*C. limetta* Auth.), *Rutaceae* ... Beck, *J. Chem. Soc.* 57, 323 (1890); from ...me oil: Caldwell, Jones, *ibid.* 1945, 570; from ...nley, Vannier, U.S. pat. 2,889,337 (1959 to ... Agriculture). Synthesis: Schmidt, *Arch.* ... (1904); Heyes, Robertson, *J. Chem. Soc.*



Needles from methanol, mp 147–148°. Absorption max in alcohol: 2220, 2470, 2505, 3240 Å (log ε 4.03, 3.84, 3.84, 4.18). Almost insol in boiling water, ether, petr ether; freely sol in alcohol, chloroform, acetone.

Limonene. *p-Mentha-1,8-diene;* cinene; cajeputene; kautschin. $C_{10}H_{16}$; mol wt 136.23. C 88.16%, H 11.84%. Occurs in various ethereal oils, particularly in oils of lemon, orange, caraway, dill and bergamot. Isoln of *d*-limonene from mandarin peel oil (*Citrus reticulata* Blanco, *Rutaceae*): Kugler, Kováts, *Helv. Chim. Acta* 46, 1480 (1963). *Review:* J. L. Simonsen, *The Terpenes* vol. I (2nd ed, University Press, Cambridge, 1947), pp 143–165.



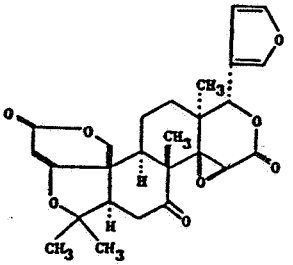
dl-Form. *Inactive limonene; dipentene.* Liquid. Pleasant lemon-like odor. bp_{762} 175.5–176.5°, $d_4^{20.4°}$ 0.8402. n_D 1.4744. Practically insol in water; miscible with alcohol. With dry HCl or HBr it forms monohalides, and with aq HCl or HBr, the dihalide.

d-Form. Liquid. bp_{762} 175.5–176°. d_4^{21} 0.8402. n_D^{21} 1.4743. $[\alpha]_D^{19.5}$ +123.8°.

l-Form. Liquid. bp_{762} 175.5–176.5°. $d_4^{20.6}$ 0.8407. n_D^{21} 1.474. $[\alpha]_D^{19.5}$ −101.3°.

USE: Solvent, manuf resins; wetting and dispersing agent. *Human Toxicity:* Skin irritant, sensitizer.

Limonin. $C_{26}H_{30}O_8$; mol wt 470.50. C 66.37%, H 6.43%, O 27.21%. Bitter principle of lemon and other *Rutaceae*. Isoln: Bernays, *Ann.* 40, 317 (1841). Structure and stereochemistry: Melera *et al.*, *Helv. Chim. Acta* 40, 1420 (1957); Arigoni *et al.*, *Experientia* 16, 41 (1960); Arnott *et al.*, *ibid.* 16, 49 (1960); Barton *et al.*, *J. Chem. Soc.* 1961, 255; Arnott *et al.*, *ibid.* 1961, 5197.



Bitter crystals from methylene chloride + isopropanol or acetic acid, mp 298°. $[\alpha]_D$ −128° (c = 1.21 in acetone). Absorption max: 207, 285 mμ (ε 7000; 38). Slightly sol in water, ether; sol in alcohol, glacial acetic acid.

Linalool. *3,7-Dimethyl-1,6-octadien-3-ol;* 2,6-dimethyl-2,7-octadien-6-ol; linalol. $(CH_3)_2C{=}CHCH_2CH_2C(CH_3)(OH)CH{=}CH_2$; mol wt 154.24. $C_{10}H_{18}O$; C 77.87%, H 11.76%, O 10.37%. Chief constituent of linaloe oil; also occurs in oils of Ceylon cinnamon, sassafras, orange flower, bergamot, *Artemisia balchanorum*, ylang ylang, etc.: Tiemann, *Ber.* 31, 808 (1898); Walbaum, Stephan, *ibid.* 33, 2305 (1900); Hesse, Zeitschel, *J. prakt. Chem.* 66, 493 (1902); Rafanova *et al.*, U.S.S.R. pat. 103,725 (1956); *C.A.* 51, 3656c (1957); Naves, *Helv. Chim. Acta* 42, 1692 (1959). Presence in essential oils: Naves, *Compt. Rend.* 251, 900 (1960). Absolute configuration: Prelog, Watanabe, *Ann.* 603, 1 (1957). Synthesis of *dl*-linalool: Ruzicka, Fornasir, *Helv. Chim. Acta* 2, 182 (1919). Surmatis, U.S. pat. 2,848,502 (1958 to Hoff-

manu-La Roche, Inc.); Naef, Pandit, *Tetrahedron Letters* 1966, 5097. *Review:* J. L. Simonsen, *The Terpenes* vol. I (2nd ed, University Press, Cambridge, 1947), pp 57 ff.

l-Form; *licareol.* Colorless liq. bp_{760} 198°; bp_{25} 98–98.3°, bp_{14} 86–87°, d^{20} 0.8622, n_D^{22} 1.4604, $[\alpha]_D^{20}$ −20.1°. Practically insol in water; miscible with alcohol, ether.

d-Form; *coriandrol.* bp_{760} 198–200°; bp_{26} 114–114.5°; $bp_{15.5}$ 93–94°; bp_{12} 86°, d_4^{20} 0.8733, n_D^{20} 1.4673, $[\alpha]_D^{20}$ +19.3°. Soluble in 10 vol 50% alc, 4 vol 60% alc.

dl-Form. bp_{720} 194–197°; bp_{14} 89–91°, d^{15} 0.865.

USE: In perfumery instead of bergamot or French lavender oil since it has an odor similar to these oils.

Linalyl Acetate. Bergamol. $CH_3COOC_{10}H_{17}$; mol wt 196.28. $C_{12}H_{20}O_2$; C 73.43%, H 10.27%, O 16.30%. Most valuable constituent of bergamot and lavender oils, also found in many other volatile oils.

Liquid; bergamot odor. d_4^{20} 0.895. bp 220°. n_D^{20} 1.4460. Insoluble in water; miscible with alcohol, ether.

USE: In perfumery.

Linamarin. Phaseolunatin. $C_{10}H_{17}NO_6$; mol wt 247.24. C 48.58%, H 6.93%, N 5.67%, O 38.83%. From the seed skins or embryos of flax: Jorissen, Hairs, *Bull. Acad. Roy. Sci. Belg.* [3] 21, 529 (1891); Andre *et al.*, *Compt. Rend.* 231, 590 (1950); Lüdtke, *Biochem. Z* 323, 428 (1953). Synthesis: Fischer, Anger, *Ber.* 52, 854 (1919). Biosynthesis in white clover: Butler, Butler, *Nature* 187, 780 (1960).

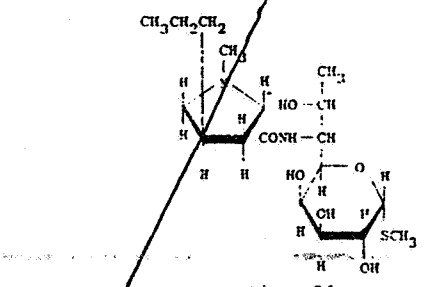
Bitter needles, mp 142–143°. $[\alpha]_D^{18}$ −29° (in water). Freely sol in water, cold alcohol, hot acetone; slightly sol in hot ethyl acetate, ether, benzene, chloroform; practically insol in petr ether. Evolves HCN with linseed meal but not with emulsin.

Tetraacetate, $C_{18}H_{25}NO_{10}$, needles from alcohol, mp 140–141°. $[\alpha]_D^{18}$ −10.8° (acetone). Soluble in acetone, ethyl acetate, chloroform, glacial acetic acid, benzene, warm methanol and ethanol; practically insol in petr ether.

Linarin. Acacetin-*d*-rutinoside; linariocitrin-glucoside; 5,7-dihydroxy-4′-methoxyflavone-D-glucosido(1→6)-L-rhamnoside; buddleoflavonoloside. $C_{28}H_{32}O_{14}$; mol wt 592.54. C 56.75%, H 5.44%, O 37.80%. From the flowers of *Linaria vulgaris* Mill., *Scrophulariaceae*: Merz, Wu, *Arch. Pharm.* 274, 126 (1936); from *Cirsium oleraceum* Scop., *Compositae*: Wagner *et al.*, *ibid.* 293, 1053 (1960). Structure: Baker *et al.*, *J. Chem. Soc.* 1951, 691. Synthesis: Zemplén, Bognár, *Ber.* 74, 1818 (1941).

Monohydrate, $C_{28}H_{32}O_{14}.H_2O$, needles from methanol, mp 268–270°. $[\alpha]_D^{26}$ −100° (0.07 g in 10 ml glacial acetic acid); $[\alpha]_D^{24}$ −87° (0.05 g in pyridine). Practically insol in water and the usual organic solvents. Soluble in nitrobenzene, phenol, aniline, pyridine, conc acids and alkalies. The water of crystn cannot be removed at 100° *in vacuo* over P_2O_5 (Merz); it may be removed at 138° in high vacuum (Zemplén). Hydrolysis gives 5,7-dihydroxy-4′-methoxyflavone, D-glucose, and L-rhamnose.

Lincomycin. *Methyl 6,8-dideoxy-6-(1-methyl-4-propyl-2-pyrrolidinecarboxamido)-1-thio-D-erythro-D-galacto-octopyranoside (α-form);* lincolnensin; Albiotic. $C_{18}H_{34}N_2O_6S$; mol wt 406.56. C 53.18%, H 8.43%, N 6.89%, O 23.61%, S 7.89%. Isoln and production by *Streptomyces lincolnensis* var. *lincolnensis:* Mason *et al.*, and Herr, Bergy, *Antimicrobial Agents & Chemotherapy* 1962, 555 and 560; Bergy, [illegible] and Bergy *et al.*, U.S. pats. 3,086,912 and 3,155,580 (both 1963 and 1964, both to Upjohn Co.). Structure: Hoeksema *et al.*, *J. Am. Chem. Soc.* 86, 4223 (1964).

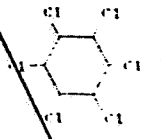


Free base, pK_a' 7.6. No ultraviolet absorption max (220–400 mμ). More stable in salt form. Soluble in methanol, ethanol, butanol, isopropanol, ethyl acetate, *n*-butyl acetate, amyl acetate, acetone, methyl ethyl ketone, isopropyl butyl ketone, methylene chloride, chloroform, ethylene dichloride. Somewhat sol in water. *See:* Bergy *et al.*, *loc. cit.*

Hydrochloride. $C_{18}H_{34}N_2O_6S.HCl.\frac{1}{2}H_2O$. *Frademicin, Lincocin, Mycivin.* Formerly obtained as needle-like crystals of low sp gr from aq soln by rapid addition of acetone at low temps; now obtained as crystals of higher sp gr, with [illegible] crystal structure and greater solubility in HCl, by slow addition of acetone: Neth. pat. Appl. 6,409,689 (1965 to Upjohn Co.); *C.A.* 63, 5458f (1965). mp 145–147°. $[\alpha]_D^{25}$ +137° (c = 1 in water). No ultraviolet absorption max (220–400 mμ). Freely sol in water, methanol, ethanol; sparingly sol in most organic solvents other than hydrocarbons.

MED USE: Antimicrobial. *Dose:* Oral 500 mg; i.m. [illegible] 600 mg. *Side Effects:* G.I. symptoms, pruritus, urticaria may occur.

Lindane. *1,2,3,4,5,6-Hexachlorocyclohexane;* HCH; Viton, *incorrect name:* benzene hexachloride; gamma benzene hexachloride [*not to be confused with hexachlorobenzene*]; Gammexane; Gexane; 666; Ben-Hex; BHC; Aplitaria; Aparasin; Streunex; Tri-6; Lorexane; Kwell; Jacutin. $C_6H_6Cl_6$; mol wt 290.85. C 24.78%, H 2.08%, Cl 73.14%. Eight well-described stereoisomers. The gamma isomer is the effective insecticide, hence the names Gammexane, Gexane, etc. The early technical mixture, prepd by the chlorination of benzene in the presence of light, contained about 12% of the γ-isomer and about 12% of the β-isomer; large amounts of the α-isomer were also present. Preps used for pharmaceutical or medicinal purposes now contain at least 99% pure γ-isomer as the active ingredient. The *cis-trans* relationships of the Cl substituents in the different isomers are: α = 1,2,4 3,5,6; β = 1,3,5 2,4,6; γ = 1,2,4 3,5,6; δ = 1,2,3,5 4,6; ε = 1,2,3,4,5,6; ζ = 1,2,3,4,5,6; η = 1,2,3,4 5,6; ι = 1,2,3,4,5,6. Prepn: Gunther, *Chemistry & Industry (London)* 1946, 399; U.S. pat. 2,218,148 (1940 to I.C.I.). Nomenclature and structure: Hornstein, *Science* 123, 206 (1955).



α-Isomer: crystals from alcohol. Persistent acrid odor. mp 158°. Vapor press. 0.06 mm Hg at 40°. Volatile with steam. Insoluble in water. Soluble in 22.8 parts chloroform at 15.25°; in 15.4 parts benzene at 18.25°.

β-Isomer: crystals from alcohol. mp 312°. Sublimes without melting. Not volatile with steam. Vapor press 0.17 mm Hg at 40°. Soluble in 775 parts chloroform at 20°; in 3[illegible] parts benzene at 17.25°.

γ-Isomer: crystals, mp 112.5°. Slight musty odor. Vapor press. 0.14 mm Hg at 40°. Soluble in 13.5 parts chloroform at 20°, in 1[illegible] parts abs alcohol, in 2 parts acetone, in 5.5 parts ether, in 3 parts benzene. Insoluble in water.

USE: Insecticide.