THE MERCK INDEX

TENTH EDITION

THE MERCK INDEX

AN ENCYCLOPEDIA OF
CHEMICALS, DRUGS, AND BIOLOGICALS

TENTH EDITION

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EDITOR'S PREFACE

The Merck Index has now been published for 94 years. Written and edited by several generations of Merck chemists, this one-volume encyclopedia of chemicals, drugs, and biological substances has established itself as an internationally recognized reference work, a source of authoritative information and a valued laboratory and teaching companion.

With a circulation of 200,000 copies for the previous edition, The Merck Index is probably the most widely used chemical/biomedical encyclopedia in the world. Lively correspondence with readers indicates an extremely varied audience including chemists, biochemists, biologists, environmentalists, human and animal health specialists, journal and book editors, medical writers, patent and trademark attorneys, market analysts and innumerable other professionals.

This new edition of The Merck Index is the result of our efforts to collect, to distill and to make accessible to an interdisciplinary and international readership the considerable new knowledge that has accumulated in the seven years since the publication of the Ninth Edition. The most important editorial concern and challenge was to effectively report major developments at the forefront of the life sciences and to reflect the complex and inextricable interdependence of chemistry, biology and medicine. Therefore, without abandoning the original purpose of covering organic and inorganic chemicals, and drugs marketed worldwide, The Merck Index has been broadened in scope to incorporate more information on biochemistry, pharmacology, toxicology and metabolism and to treat a range of topics related to agriculture and the environment. The selection of entries for this edition was especially difficult because of the abundance of important new compounds and the prevailing space limitations. The monographs on compounds or on groups of compounds had to be concise, but references to reviews and to the original literature have been provided to aid those who want to pursue any particular aspect of a subject.

Preparation of this edition has reinforced our belief that updating The Merck Index at intervals of seven to eight years does not respond to today's need for instant information. Therefore, a computer-searchable online version of the monograph section is in preparation. When completed, the database will not only provide a continuous flow of information, but will also yield immediate answers to questions that would be time-consuming, difficult or even impossible to answer from the printed version.

Support for publishing this new edition was again generously provided by Merck & Co., Inc. It is another example of the company's steadfast commitment to serve the scientific community at large. The editorial staff has made every effort to present precise, reliable and up-to-date information and we sincerely hope that the Tenth Edition of The Merck Index will continue the successful tradition of its predecessors.

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The successful publication of the Tenth Edition of The Merck Index required an extraordinary group effort. The editorial staff would like to acknowledge the skills and assistance of all whose support made the realization of this edition possible. In particular, we are indebted to the technical assistants for their dedication and invaluable editorial and administrative contributions: to Jo Ann Gallipeau for diligently drawing all the structures and coordinating their processing and for providing guidance in all aspects of computer input, and to Elizabeth V. Gannon and Michelina Nunez for their untiring efforts and patient cooperation throughout the years. Special gratitude is due to members of the Automation and Control Department of Merck & Co., Inc., who generously gave their knowledge and time and guided us through the intricacies of computer systems: to Theodore Coleman, Dr. Arthur Rosenberg, and Robert J. Cimato for project management and coordination; to Maurice L. Leslie, Jerome M. Starr, and Joel Flamholz for computer program design, modification, and implementation; to Benjamin J. Hickey, James J. Polashock, John M. Flanagan, and George Murchake for computer hardware support; to Arlene Daniels and Linda Davies for laboratory assistance.

We also wish to express our appreciation to Dr. Ludmila Birladeanu for updating the Organic Name Reactions section and for making suggestions for including and excluding monographs; to former Assistant Editors Margaret Noether Fertig and Lorraine Y. Stroumtsos for helping with the transition from the Ninth to the Tenth Edition; to John Reminger of the Research Photolab for providing photographs of all structures; and to Gary Zelko of the Publications Department for his enthusiastic support and cooperation.

It is not possible to name all our Merck colleagues and other individuals who have reviewed critical monographs and who have taken the trouble to write notes and letters proposing corrections, additions, and deletions. Our gratitude to them is expressed by having included most of their suggestions in this new edition.

Finally, special thanks are due to Dr. Horace D. Brown for his personal interest, trust, and encouragement.

EXPLANATORY NOTES

The monograph section of the Tenth Edition of The Merck Index comprises descriptions of more than 10,000 chemicals, drugs, and biologicals of current interest and importance. The entries are not a list of Merck products. Since the last edition, over 4000 monographs have been revised and updated, almost 1000 new monographs have been added, more than 500 have been deleted and approximately 100 have been combined with other monographs. (*Note:* A list of monographs that appear in the Ninth Edition but not in the Tenth can be found on page CI-316.) Entries are limited to single substances, except for a small number of natural mixtures such as pseudomonic acids, cyclosporins, periplanones, etc.; drugs that are mixtures are generally excluded. Although the information contained in the monographs is from the published literature, the number of references or the length of a particular entry is not necessarily related to the importance of a compound but may simply be an indication of the current amount of available information.

The organization of monographs is essentially the same as that of previous editions. The illustration shows the format of a typical entry; the type of information included in the monographs is described below.

Monograph Number. Sequential accession numbers are assigned to monographs to assist in location of entries from the Cross Index of Names and from the Formula Index, which are referenced to these numbers rather than to monograph titles or to page numbers. (*Note:* Monograph numbers in the Tenth Edition do not necessarily correspond to Ninth Edition numbers.)

Title: Titles, arranged in alphabetical order, are usually generic (USAN, WHO, or INN), trivial, or simple chemical names. Trademarks (designated by ®) are used for a small number of entry titles.

Chemical Abstracts Name(s). The first synonym in ***boldface italic*** is the uninverted form of the name corresponding to that used by Chemical Abstracts Service (CAS) during the ninth and/or subsequent Collective Index Periods (CIPs). The second synonym in ***boldface italic*** is the uninverted form of the eighth (or earlier) CIP name. For this edition of The Merck Index, there is a separate section of CAS names/registry numbers associated with alphabetically arranged monograph titles, beginning on page REG-1. In that section, each CAS name is presented in its inverted form (as in the CAS Index Guides), followed by stereochemical descriptors and registry number. This arrangement will aid in locating the compound of interest in both hard copy and on-line Chemical Abstracts and can thus serve as an entry point to further literature searching.

Alternate Name(s). Other chemical names identifying the entry, trivial names, experimental drug codes, and trademarks are in lightface roman. Trademarks are indicated by first letter capitalization; absence of capitalization, however, does not exclude the possibility that a name

Title

Chemical Abstracts name *(boldface italic)*

Monograph number

Molecular formula

Drug code number

Percentage composition

Literature references

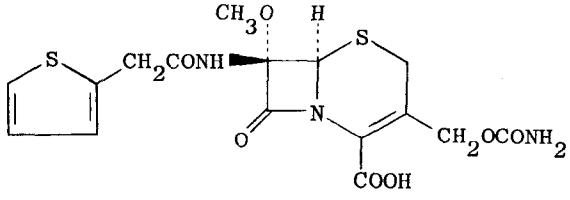
Structure

Physical data for title compound

Derivative of title compound

Therapeutic category (in humans)

1910. Cefoxitin. ***3-[[(Aminocarbonyl)oxy]methyl]-7-methoxy-8-oxo-7-[(2-thienylacetyl)amino]-5-thia-1-azabicyclo[4.2.0]oct-2-ene-2-carboxylic acid;*** 3-(hydroxymethyl)-7-methoxy-8-oxo-7-[2-(2-thienyl)acetamido]-5-thia-1-azabicyclo[4.2.0]oct-2-ene-2-carboxylic acid carbamate (ester); 3-carbamoyloxymethyl-7α-methoxy-7-[2-(2-thienyl)acetamido]-3-cephem-4-carboxylic acid; MK-306. $C_{16}H_{17}N_3O_7S_2$; mol wt 427.46. C 44.96%, H 4.01%, N 9.83%, O 26.20%, S 15.00%. Semi-synthetic derivative of cephamycin C, *q.v.*, possessing high resistance to β-lactamase inactivation. Synthesis: Christensen *et al.*, **Ger.** pats. **2,129,675, 2,203,653** corresp to **U.S.** pat **4,297,488** (1971, 1972, 1981 all to Merck & Co.); Karady *et al.*, *J. Am. Chem. Soc.* **94,** 1410 (1972); Ratcliffe, Christensen, *Tetrahedron Letters* **1973,** 4653. Biological evaluation: Wallick, Hendlin, *Antimicrob. Ag. Chemother.* **5,** 25 (1974); Miller *et al.*, *ibid.* 33; Onishi *et al.*, *ibid.* 38; Hamilton, Miller *et al.*, *J. Antibiot.* **27,** 42 (1974). Mode of action: Onishi *et al.*, *Ann. N.Y. Acad. Sci.* **235,** 406 (1974). Comprehensive reviews: *J. Antimicrob. Chemother.* **4,** Suppl. B, 1–256 (1978); R. N. Brogden *et al.*, *Drugs* **17,** 1–37 (1979); E. O. Stapley, K. R. Brown, in *Pharmacological and Biochemical Properties of Drug Substances* **vol. 3,** M. E. Goldberg, Ed. (Am. Pharm. Assoc., Washington, DC, 1981) pp 262–290. Comprehensive description: G. S. Brenner in *Analytical Profiles of Drug Substances* **vol. 11,** K. Florey, Ed. (Academic Press, New York, 1982) pp 169–195.



Crystals, mp 149–150° (dec). pKa 2.2. Very sol in acetone; sol in aq $NaHCO_3$; very slightly sol in water. Practically insol in ether and chloroform.

Sodium salt, $C_{16}H_{16}N_3NaO_7S_2$, ***Mefoxin, Mefoxitin, Merxin, Cenomycin.*** White crystals with characteristic odor. $[\alpha]^{25}_{589\,nm}$ + 210° (c = 1 in methanol). Very sol in water; sol in methanol; sparingly sol in ethanol and acetone. Insol in aromatic and aliphatic hydrocarbons. LD_{50} in mice, rats, dogs (g/kg): 5.10, 8.98, > 10.0 i.v., S. Takayama *et al.*, *Chemotherapy (Tokyo)* **26,** Suppl. 1, 150 (1978).

THERAP CAT: Antibacterial.

Trademarks (capitalized) and/or generic names of derivatives *(boldface italic)*

Physical data for derivative

Toxicity data

Molecular weight

Patent and chemical information

Biological, pharmacological, etc. information

Review articles

may be a proprietary name or the subject of proprietary rights. *Note:* Names appearing elsewhere in the monograph in ***boldface italic*** also appear in the Cross Index of Names.

Molecular Formula, Molecular Weight, % Composition. Elements in the molecular formula are listed according to the Hill convention (C, H, then other elements in alphabetical order). This information and molecular weight are provided for all compounds having a specific known structure.

Literature References. This section contains a concise reference history of the compound. Frequently, a brief description or capsule statement is provided, although in some monographs, particularly those on biologically active substances, a lengthier description is given. References to isolation, preparation, patent information, and structural studies are cited and a special effort has been made in this edition to provide more extensive information on pharmacological, clinical, toxicological, and toxicity studies. Review articles, where available, are usually cited at the end of the references, but when a review covers a family of compounds it is generally given only in the monograph for the parent element or compound. Literature references are cited in the conventional manner; journal abbreviations (with the few exceptions listed in the table of Abbreviations, p. xii) correspond to those in Chemical Abstracts Service Source Index (CASSI).

Structure. Structural displays, depicting modern stereochemical representations wherever possible, are contained in almost 6000 monographs. Standard conventions of heavy and dotted lines to show bonds directed above or below the plane of the paper are used where appropriate. In addition, more than 2000 monographs contain line formulas showing molecular arrangements. In polypeptide representations, all optically active amino acid residues are assumed to be L unless specified otherwise.

Physical Data. Data are presented as found within references cited in the monograph. Whenever possible, the color of a substance is stated, but the absence of color (white, colorless) is often omitted. Temperatures are given in degrees Celsius (centigrade) unless otherwise noted. When solubilities are determined at room temperature (about 25°C), the temperature is generally omitted. When optical rotations are measured in water, the solvent is usually not specified. For ultraviolet absorption measurements, the solvent is provided within parentheses.

As in the previous edition, an effort has been made to provide toxicity data (e.g. LD_{50}, LC_{50}, etc.) and to include the source of this information. *Caution* and/or *Human Toxicity* statements are also provided for a number of substances. Specific caution statements are given for drugs and compounds on the U.S. Government's Schedules of Controlled Substances, for additives controlled by the Food and Drug Administration, and for compounds listed as suspected or confirmed carcinogens in the *Second Annual Report on Carcinogens* issued in 1981 by the U.S.

Department of Health and Human Services. *Note:* Absence of toxicity data does not imply that toxic effects do not exist.

Derivatives. Data for derivatives are presented in the same format as the parent compound. A derivative molecular formula is listed in the Formula Index only if there is a chemical name, generic name, or trademark associated with it.

Use. Descriptions of specific uses that are not medical or veterinary therapeutic applications are summarized here.

Therapeutic Category and Therapeutic Category (Veterinary). Wherever possible, the editors have adhered to the categories of activity proposed by the USAN Council in describing therapeutic indications of drugs. However, there are minor differences in the wording of some categories, e.g. β-adrenergic blocker, rather than anti-adrenergic (β-receptor). In cases where no USAN classification was available, the editors chose the therapeutic category that most closely described the indication claimed by the manufacturer.

Indexes. More than 55,000 synonyms, including titles, CAS names, alternate names, trademarks, and derivatives are contained in the Cross Index of Names, and over 10,000 entries appear in the Formula Index. Each entry directs the reader to the monograph number in which the compound of interest is described. The effort to match trademarks with company ownership, begun in the Ninth Edition, has been greatly expanded for this edition. In the Cross Index of Names, an abbreviated form of the company name appears in brackets following the trademark. (Due to reorganizations or mergers, some company names changed after the initial matching process was completed, and it was not always possible to make the appropriate corrections.) A list of company addresses appears in an updated and expanded Company Register that begins on page MISC-7.

Although The Merck Index has a strong medical character, it is not intended as an official therapeutic guide. Inclusion of a drug in this book is not an endorsement but merely a statement of the fact that such an entity exists. THERAPEUTIC CATEGORY and THERAPEUTIC CATEGORY (VETERINARY) paragraphs are intended only as summary statements of major pharmacological properties or indications for the individual drugs. For additional information on uses, dosage, side effects and adverse reactions, readers should consult pertinent scientific and professional publications and product circulars published by the respective manufacturers.

Great care has been taken to assure the accuracy of the information contained in The Merck Index. However, the Editorial Staff and the Publisher cannot be responsible for errors in publication or for any consequences arising from use of the information published in The Merck Index. Accordingly, reference to original sources is encouraged as is reporting of errors and omissions in order to assure that appropriate changes may be made in the next edition.

ABBREVIATIONS

A . . . . . absorbance (extinction)
Å . . . . . Angstrom unit(s)
abs . . . . . absolute; absorption
abs config . . . . absolute configuration
abstr . . . . . abstract
Ac . . . . . acetyl CH_3CO—; ethyl acetate AcOEt; acetic acid AcOH; acetic anhydride Ac_2O
acac . . . . . acetylacetonate
acc . . . . . according
A.C.S. . . . . American Chemical Society
add . . . . . adding
addn . . . . . addition
AEC . . . . . (United States) Atomic Energy Commission
alc, alcoh . . . . . alcohol(ic); ethanol; ethyl alcohol
alk . . . . . alkali(ne)
$[\alpha]_D^{25}$ . . . . . specific optical rotation at 25°C for D (sodium) line; absence of brackets indicates optical rotation of a liquid in a 1 decimeter cell—neat.
a_M . . . . . molar absorptivity (concentration in g-moles/l)
ammon . . . . . ammonia
amorph . . . . . amorphous
amps . . . . . ampules
amt(s) . . . . . amount(s)
anhydr . . . . . anhydrous
Ann. . . . . . *Justus Liebig's Annalen der Chemie*
anti- . . . . . anti (stereomeric opposite of *syn-*)
APhA . . . . . American Pharmaceutical Association
approx . . . . . approximate(ly)
aq . . . . . aqueous
Ar . . . . . aryl
A.R. . . . . analytical reagent
Archiv Exp. Pathol. Pharmakol. . . *Naunyn Schmiedebergs Archiv für Experimentelle Pathologie und Pharmakologie*
ArCO— . . . . . aromatic acyl radical
assoc . . . . . association
assocd . . . . . associated
A.S.T.M. . . . . American Society for Testing Materials
asym- . . . . . asymmetrical, unsymmetrical
at. . . . . atomic
atm, atmos . . . . . atmosphere(s), atmospheric
at. no. . . . . atomic number
at. wt . . . . . atomic weight
B . . . . . base. Example: if the formula of an alkaloid is $C_{21}H_{23}NO_5$ the abbreviated formula for the hydrochloride may be written B.HCl instead of $C_{21}H_{23}NO_5$.HCl.
B. . . . . . *Bacillus*, used only in genus and species names
BAN . . . . . British Approved Name
Bé . . . . . Baumé (a specific gravity scale)
Beilstein . . . . . *Beilsteins Handbuch der Organischen Chemie*, a comprehensive German encyclopedia of organic chemistry (Springer)
Belg. pat. . . . . Belgian patent
Ber. . . . . . *Chemische Berichte* (Berichte der Deutschen Chemischen Gesellschaft)
biol . . . . . biological
B.I.O.S. . . . . British Intelligence Objectives Subcommittee
B.O.D. . . . . biochemical oxygen demand
boil . . . . . boiling
bp . . . . . boiling point; boils; boils at; boiling at (always followed by a figure denoting temperature; the pressure, if different from one atm, is indicated by a subscript. Example: bp_{70} 48° means *boils at 48°C if the pressure is 70 mm Hg*).
B.P. . . . . . *British Pharmacopeia*
B.P.C. . . . . . *British Pharmaceutical Codex*
Brit. pat. . . . . British patent
Btu . . . . . British thermal units
Bu . . . . . butyl (*normal*-butyl)
Bz . . . . . benzoyl C_6H_5CO—; BzH benzaldehyde; BzOH benzoic acid
c . . . . . concentration by volume (after optical rotations only). Example: $[\alpha]_D^{25}$ + 14° (c = 2.5 in abs alcohol), meaning 2.5 g of the substance dissolved in 100 ml abs alcohol; when no solvent is given, the solvent is water.
C . . . . . Centigrade degrees
C_p . . . . . heat capacity (constant pressure)
ca. . . . . (*circa*) about
C.A. . . . . . *Chemical Abstracts*
cal . . . . . calorie(s)
calc . . . . . calculate
calcd . . . . . calculated
Can. pat. . . . . Canadian patent
cc . . . . . cubic centimeter(s) (milliliter)
cf. . . . . . (*confer*) compare
chem . . . . . chemical
Chem. Commun. . . *J. Chem. Soc., Chem. Commun.*
Ci . . . . . curie
C.I. . . . . *Colour Index* (British)
cis- . . . . . stereochemical opposite of *trans-*
cm . . . . . centimeter(s)
CNS . . . . . central nervous system
coll. vol. . . . . collective volume
compd . . . . . compound
compn . . . . . composition
conc, concd, concentr . . . . . concentrated
concn . . . . . concentration
config . . . . . configuration
constit . . . . . constituent
contd . . . . . continued
contg . . . . . containing
cor(r) . . . . . corrected
corresp . . . . . corresponding, corresponds
cp . . . . . centipoise
C.P. . . . . chemically pure
cpd . . . . . compound
crit press. . . . . critical pressure
crit temp . . . . critical temperature
cryst . . . . . crystalline or crystals
crystn . . . . . crystallization
CTFA . . . . . The Cosmetic, Toiletry and Fragrance Assoc.
d . . . . . density; specific gravity (d_4^{19} specific gravity at 19° referred to water at 4°).
d- . . . . . *dextro*(rotatory), refers to optical rotation, indicating that a soln of the substance is capable of turning the plane of polarized light to the right.
D- . . . . . *dextro* (in configurational sense only). Used before carbohydrates and amino acids to show that the groups at the significant asymmetric carbon atom are placed at the right. In carbohydrate nomenclature the configuration of the highest numbered asymmetric carbon atom determines the prefix that is used. Carbohydrate nomencla-

ture is based upon the glyceric aldehydes, the dextrorotatory isomer being by convention designated D-*glyceric aldehyde*. In the amino acid field, it is the configuration of the lowest numbered asymmetric carbon atom, i.e., the α-carbon atom, that determines the prefix, as in D-alanine.

dec, decomp . . . . decompose(s)
decompn . . . . decomposition
deg . . . . . degree
deliquesc . . . . deliquescent
delta (Δ) . . . . double bond
deriv . . . . . derivative
determn . . . . . determination
diff . . . . . difference
dil . . . . . dilute
dild . . . . . diluted
diln . . . . . dilution
distln . . . . . distillation
dl-, DL- . . . . . racemic; optically inactive by external compensation as contrasted with *meso-*.
dm . . . . . decimeter(s)
DMF . . . . . dimethylformamide
DMSO . . . . . dimethylsulfoxide
dp(DP) . . . . . degree of polymerization (number of monomeric units in the polymer)
D.R.P. . . . . . (*Deutsches Reichs-Patent*) German patent
dyn . . . . . dynes
(*E*)- . . . . . *entgegen* (German for opposite). Geometric stereodescriptor used for substances having achiral elements resulting from double bonds where the groups of highest priority are on the opposite sides of the vertical reference plane; equivalent to *trans* in simple cases.
$E^{1\%}_{1cm}$ . . . . . the absorbance of a solution containing one gram per 100 ml contained in a cell having an absorption path of one centimeter.
EC . . . . . electron capture
E_M . . . . . molar extinction coefficient (conc. in g-moles/l)
ECG . . . . . electrocardiogram
E.C. No. . . . . Enzyme Commission Number
ed. . . . . edition
Ed(s) . . . . . editor(s)
EEG . . . . . electroencephalogram
e.g. . . . . (*exempli gratia*) for example
eidem . . . . . the same (authors), plural of *idem*
EKG . . . . . electrocardiogram
emf . . . . . electromotive force
en . . . . . ethylenediamine (in formulas)
EPA . . . . . Environmental Protection Agency
epsilon (ε) . . . . molar extinction coefficient (conc. in g-moles/l); dielectric constant
eq . . . . . equation
equilib . . . . . equilibrium
equiv . . . . . equivalent
esp . . . . . especially
esu . . . . . electrostatic units of electrical charge; the amount of electrical charge which in a vacuum will repel a like charge at a distance of one centimeter with a force of one dyne
Et . . . . . ethyl C_2H_5—; ethyl alcohol EtOH
eta (η) . . . . . viscosity
et al. . . . . . (*et alii*) and others
etc. . . . . *et cetera*
Et_2O . . . . . ether
Eur. pat. Appl. . . . European patent application
ev . . . . . electron volt
evac . . . . . evacuated
evapn . . . . . evaporation
exptl(ly) . . . . . experimental(ly)
ext . . . . . extract
extd . . . . . extracted
extern . . . . . externally
F . . . . . Fahrenheit degrees; also Fourneau
F.D.A. . . . . Food and Drug Administration (U.S.A.)
FD & C . . . . . Food, Drug and Cosmetic (Act)—U.S.A.
ff . . . . . following
FFC . . . . . free from chlorine
FIAT . . . . . Field Information Agency, Technical (U.S. reports)
Fortschr. Chem. Org. Naturst. . . . . *Fortschritte der Chemie Organischer Naturstoffe* (Progress in the Chemistry of Organic Natural Products, Springer-Verlag)
fp . . . . . freezing point
Frdl. . . . . . *P. Friedländer Fortschritte der Teerfarbenfabrikation*, a collection of patents (Springer)
FT . . . . . Fourier transform
g . . . . . gram(s)
gal . . . . . gallon(s)
gamma (γ) . . . . microgram(s)
GC . . . . . gas chromatography
gem- . . . . . geminate (two substituents on the same atom)
geol . . . . . geological
Ger. pat. . . . . . German patent
G.I. . . . . gastrointestinal
g/l . . . . . grams per liter
GLC . . . . . gas-liquid chromatography
Gmelin's . . . . *Gmelin's Handbuch der Anorganischen Chemie*, a comprehensive German encyclopedia of inorganic chemistry (Verlag Chemie)
gov't . . . . . government
G.U. . . . . genitourinary
habit. . . . . habitat
Houben . . . . . a German collection of medicinal patents
Houben Weyl. . . . *Houben-Weyl Methoden der Organischen Chemie*, a German collection of preparative methods in organic chemistry (Thieme)
HPLC . . . . . high performance liquid chromatography
hr . . . . . hour
i- . . . . . optically inactive by internal compensation as *i*-inositol; archaic for *meso-*
IACR . . . . . International Association of Cancer Registries
IARC . . . . . International Agency for Research on Cancer
IARC Monographs . . *IARC Monographs on the Evaluation of Carcinogenic Risk of Chemicals to Man*
ibid. . . . . . (*ibidem*) at the same place
I.C.C. . . . . Interstate Commerce Commission
idem . . . . . the same (author); plural: *eidem*, the same (authors)
i.e. . . . . (*id est*) that is
i.g. . . . . intragastric
I.G. Farben . . . *Interessengemeinschaft der Farbenindustrie, Aktiengesellschaft*—the German dye trust
i.m. . . . . intramuscular
incl . . . . . including
incompat . . . . incompatibility
INN . . . . . International Nonproprietary Name
inorg . . . . . inorganic
insol . . . . . insoluble
intern . . . . . internal

Intl . . . . . International
i.p. . . . . intraperitoneal
IR . . . . . infrared
ISO . . . . . Internal Organization for Standardization
isoln . . . . . isolation
I.U. . . . . international unit
I.U.C. . . . . International Union of Chemistry
I.U.P.A.C. . . . International Union of Pure and Applied Chemistry
i.v. . . . . intravenous
Japan. Kokai . . . Japanese patent (unexamined)
Japan. pat. . . . . Japanese patent
kcal . . . . . kilocalorie(s)
kg . . . . . kilogram(s)
l . . . . . liter
l- . . . . . *levo*(rotatory), the opposite of *d*, which see.
L- . . . . . *levo* (in configurational sense only), the opposite of D, which see.
lb . . . . . pound(s)
LC . . . . . Lethal Concentration; LC_{50}, a concentration which is lethal to 50% of the animals tested; liquid chromatography
LD . . . . . Lethal Dose; LD_{50}, a dose which is lethal to 50% of the animals tested
ln . . . . . logarithm (natural)
loc. cit. . . . . . (*loco citato*) in the place cited
log . . . . . logarithm (common)
l.o.i. . . . . limit of impurities
m . . . . . meter; given after mass number signifies metastable isomer
m- . . . . . *meta*
M . . . . . molar (concentration)
MAC . . . . . maximum allowable concentration
mass spec . . . . mass spectrometry
max . . . . . maximum, maxima
M.C.A. . . . . Manufacturing Chemists Association (U.S.A.)
mcg . . . . . microgram
mCi . . . . . millicurie
M_D . . . . . molecular rotation $\frac{[\alpha]_D \times \text{mol wt}}{100}$
Me . . . . . methyl CH_3—; methyl alcohol MeOH; acetone Me_2CO
Mellor's . . . . . *Mellor's Comprehensive Treatise on Inorganic and Theoretical Chemistry* (Longmans)
mEq . . . . . milli-equivalent ($\frac{1}{1000}$ of an equivalent)
MeV . . . . . million electron volts
manuf } mfr } . . . . . manufacture
mfg . . . . . manufacturing
mg . . . . . milligram
μCi . . . . . microcurie
μg . . . . . microgram
microcryst . . . . microcrystalline
min . . . . . minimum; also minute(s)
misc . . . . . miscible
mixt . . . . . mixture
ml . . . . . milliliter (cubic centimeter)
MLD . . . . . minimum lethal dose
mm . . . . . millimeter
mμ . . . . . millimicron(s)
mol wt . . . . . molecular weight
Monatsh. . . . . . *Monatshefte für Chemie*
mp . . . . . melting point; melts, melting at, when followed by a figure denoting temperature
ms- . . . . . *meso-* (internally compensated)
n . . . . . index of refraction (n_D^{20} for 20° and sodium light); normal, as *n*-propyl
N . . . . . normal (equivalents per liter, as applied to concentration); nitrogen (as in *N*-methylpyridine)
NBS . . . . . National Bureau of Standards
NCTC . . . . . *National Collection of Type Cultures*
Neth. pat. **Appl.** . . . . Netherlands patent application
N.F. . . . . . *National Formulary*
ng . . . . . nanogram (10^{-9} grams)
NIOSH . . . . . National Institute for Occupational Safety and Health
nm . . . . . nanometers
NMR . . . . . nuclear magnetic resonance
N.N.D. . . . . . *New and Nonofficial Drugs* (Lippincott, 1959–1964)
N.N.R. . . . . . *New and Nonofficial Remedies* (Lippincott, 1933–1958)
no. . . . . number
nor- . . . . . (*Nitrogen ohne Radikal*) a prefix indicating a parent compound (no longer limited to nitrogenous compounds)
NRDC . . . . . National Research Development Corporation
NSC . . . . . National Service Center
o- . . . . . *ortho*
O . . . . . denoting attachment to oxygen, as in *O*-acetylhydroxylamine
op. cit. . . . . . (*opere citato*) in the work cited
org . . . . . organic
OSHA . . . . . Occupational Safety and Health Act
oz . . . . . ounce(s)
P *or* p . . . . . concentration by weight (after optical rotations only)
p, pp . . . . . page(s)
p- . . . . . *para*
passim . . . . . here and there, scattered
pat. . . . . patent
PB report . . . . Publication Board Report (United States Department of Commerce, Scientific and Industrial Reports)
petr } petrol } . . . . . petroleum
pH . . . . . acid-base scale; log of reciprocal of hydrogen ion concn.
physiol . . . . . physiological
pK . . . . . $\log \frac{1}{K}$
potass . . . . . potassium
ppm . . . . . parts per million
ppt or precip . . . precipitate
pptd . . . . . precipitated
pptg . . . . . precipitating
Pr . . . . . propyl (normal)
prepd . . . . . prepared
prepn . . . . . preparation
press. . . . . pressure
psi (ψ) . . . . . pseudo
pt . . . . . point
q.q.v. . . . . . (*quae vide*) which see, plural
q.v. . . . . . (*quod vide*) which see
r . . . . . "roentgen" unit of radiation. That quantity of x or gamma radiation which produces one esu of charge in one cubic centimeter of air under standard conditions, i.e., the associated corpuscular emission per 0.001293 g of air (1 cc at 0° and 760 mm) produces, in air, ions carrying one esu.
R . . . . . alkyl, univalent hydrocarbon radical (or hydrogen)
(R)- . . . . . *rectus* (right). Absolute term describing the spatial arrangement about an asymmetric carbon when the observed order of decreasing priority of the groups is clockwise.
RCO— . . . . . aliphatic acyl radical
recryst(n) . . . . recrystallize, recrystallization
ref . . . . . reference
rep [REP] . . . . "roentgen equivalent physical" means a dose of ionizing radia-

tion capable of producing energy absorption of 93 ergs per gram of tissue.

resp . . . . . respectively

R_f or R_F . . . . . (in paper chromatography) ratio of movement of the band to the front of the solvent

RTECS . . . . . *Registry of Toxic Effects of Chemical Substances*

S . . . . . denoting attachment to sulfur as *S*-methylcysteine; *Streptomyces*, used only in genus and species names

(S)- . . . . . *sinister* (left) (opposite of *(R)*).

S.A.E. . . . . Society of Automotive Engineers.

sapon } . . . . saponification
saponif }

satd . . . . . saturated

s.c. . . . . subcutaneous

S.D. . . . . Sprague Dawley

sec . . . . . second(s)

sec- . . . . . secondary

sepn . . . . . separation

SI . . . . . International System of Units

sod. . . . . sodium

sol; soly . . . . . soluble; solubility

solidif . . . . . solidifies, solidification

soln . . . . . solution

sp. . . . . species; specific

spec . . . . . spectroscopy

sp gr . . . . . specific gravity

spp. . . . . species (plural)

sq . . . . . square

sqq. . . . . . *(sequentia)* and following

S.T.P. . . . . standard temperature and pressure

subl . . . . . sublimes

suppl . . . . . supplement

sym- . . . . . symmetrical

syn- . . . . . stereochemical opposite of *anti*

$T_{\frac{1}{2}}$ . . . . . half-life

tabl . . . . . tablet(s)

TB, tb. . . . . tuberculosis

tech . . . . . technical

temp . . . . . temperature

tert- . . . . . tertiary

TLC . . . . . thin-layer chromatography

THF . . . . . tetrahydrofuran

trans- . . . . . stereochemical opposite of *cis-*

U.K. . . . . United Kingdom

uncor(r). . . . . uncorrected

uns- . . . . . unsymmetrical, asymmetrical

U.S.A.E.C. . . . United States Atomic Energy Commission

USAN . . . . . United States Adopted Names

U.S.D. . . . . . *United States Dispensatory*

U.S.D.A. . . . . United States Department of Agriculture

U.S.P. . . . . . *United States Pharmacopeia*

U.S. pat. . . . . United States patent

uv . . . . . ultraviolet

v . . . . . volt(s)

v- . . . . . vicinal (adjacent)

var. . . . . variety

viz. . . . . . *(videlicet)* that is to say: namely

vol. . . . . volume

vs . . . . . versus

v/v . . . . . % "volume in volume" expresses the number of milliliters of an active constituent in 100 milliliters of solution.

WHO . . . . . World Health Organization

wks . . . . . weeks

wt . . . . . weight

w/v . . . . . percent "weight in volume" expresses the number of grams of an active constituent in 100 milliliters of solution, and is used regardless of whether water or another liquid is the solvent.

w/w . . . . . percent "weight in weight" expresses the number of grams of an active constituent in 100 grams of solution or mixture.

yr(s) . . . . . year(s)

(Z)- . . . . . *zusammen* (German for together). Opposite of *(E)-*. Equivalent to *cis-* in simple cases.

Z. Physiol. Chem. . *Hoppe-Seyler's Zeitschrift für Physiologische Chemie*

$\sim$ . . . . . approximately

$\simeq$ . . . . . approximately equal

$>$ . . . . . greater than

$<$ . . . . . less than

TABLE OF CONTENTS

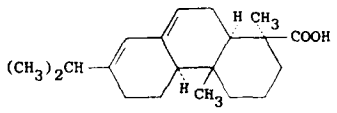
MONOGRAPHS

THE MERCK INDEX

OF CHEMICALS, DRUGS, AND BIOLOGICALS

A

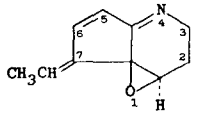
1. Abietic Acid. ***1,2,3,4,4a,4b,5,6,10,10a-Decahydro-1,4a-dimethyl-7-(1-methylethyl)-1-phenanthrenecarboxylic acid; 13-isopropylpodocarpa-7,13-dien-15-oic acid;*** sylvic acid. $C_{20}H_{30}O_2$; mol wt 302.44. C 79.42%, H 9.99%, O 10.58%. A widely available organic acid, prepared by isomerization of rosin: Harris, Sanderson, *Org. Syn.*, **coll. vol. IV**, 1 (1963); Fieser, Fieser, *The Chemisty of Natural Products Related to Phenanthrene* (New York, 3rd ed., 1949). Synthesis from dehydroabietic acid: Stork, Schulenberg, *J. Am. Chem. Soc.* **78,** 250 (1956); Burgstahler, Worden, *ibid.* **83,** 2587 (1961); E. Wenkert *et al., ibid.* **86,** 2038 (1964). Chromatographic study: A. G. Douglas, T. G. Powell, *J. Chromatog.* **43,** 241 (1969).



Monoclinic plates from alcohol + water, mp 172-175°. $[\alpha]_D^{24}$ −106° (c = 1 in abs alc). uv max: 235, 241.5, 250 nm (ε 19500, 22000, 14300). Insol in water; sol in alc, benzene, chloroform, ether, acetone, carbon disulfide, dil NaOH soln. Commercial abietic acid made by heating rosin alone or with acids may be glassy or partly crystalline, usually of yellow color and melting as low as 85°.

USE: Manufacture of esters (ester gums), e.g., methyl ester (Abalyn, *see also* methyl abietate), vinyl and glyceryl esters for use in lacquers and varnishes. Manufacture of "metal resinates", soaps, plastics and paper sizes. Assists growth of lactic and butyric acid bacteria.

2. Abikoviromycin. ***7-Ethylidene-1a,2,3,7-tetrahydrocyclopent[b]oxireno[c]pyridine;*** 4,4a-epoxy-5-ethylidene-2,3,4,4a-tetrahydro-5*H*-1-pyridine; abicoviromycin; latumcidin. $C_{10}H_{11}NO$; mol wt 161.20. C 74.51%, H 6.88%, N 8.69%, O 9.93%. Antiviral substance produced by *Streptomyces abikoensis* and *Streptomyces rubescens.* Chromatographic isoln from broth cultures: Umezawa *et al., Japan. Med. J.* **4,** 331 (1951); *C.A.* **46,** 7167 (1952); Umezawa, **Japan.** pat. **6200('54)** (to Nippon). Identity with latumcidin: Sakagami *et al., J. Antibiot.* **11A,** 231 (1958). Structure: Gurevich *et al., Tetrahedron Letters* **1968,** 2209. Stereochemistry: Kono *et al., J. Antibiot.* **23,** 572 (1970); Gurevich *et al., Khim. Prir. Soedin.* **7,** 104 (1971), *C.A.* **75,** 5752e (1971). Crystal and molecular structure of the selenate: Y. Kono *et al., Acta Crystallog.* Sect. B, **27,** 2341 (1971).



Highly unstable and polymerizes promptly on isolation even at −50°; however, it can be handled in dilute solutions and in the form of its salts. uv max (neutral ethanol or 0.1*N* KOH): 218, 244, 289 nm (log ε 3.83, 3.99, 3.94); (0.1*N* HCl) 236, 341 nm (log ε 3.99, 4.05).

3. Abrin. Agglutinin; toxalbumin. A toxic lectin and hemagglutinin obtained from seeds of ***jequirity, Abrus precatorius*** L., ***Leguminosae,*** a common vine of tropical countries, also found in central and southern Florida. Isoln and purification: J. Y. Lin *et al., J. Formosan Med. Assoc.* **68,** 518 (1969), *C.A.* **72,** 98695 (1970); *eidem, Toxicon* **9,** 97 (1971). The high toxicity of abrin was originally believed to result from its hemagglutinating activity, but subsequent studies have shown that separate proteins are responsible for the toxicity and agglutination: S. Olsnes, A. Pihl, *Eur. J. Biochem.* **35,** 179 (1973). Abrin has been shown to be more toxic to tumor cells than to normal cells; it provides therapeutic protection vs Ehrlich ascites tumor and fibrosarcoma in mice, vs Yoshida sarcoma in rats and has demonstrated an inhibitory effect in nude mice bearing solid human cancers, *cf.* V. V. S. Reddy, M. Sirsi, *Cancer Res.* **29,** 1447 (1969); J. Y. Lin *et al., Nature* **227,** 292 (1970); O. Fodstad *et al., Cancer Res.* **37,** 4559 (1977). Five proteins have been purified from the seeds of *A. precatorius:* ***abrins A, B, C, D*** and ***Abrus agglutinin.*** A through D are toxic lectins; *Abrus* agglutinin is non-toxic to animal cells and a potent hemagglutinator. All five are glycoproteins but not metaloproteins. Abrins A through D are monovalent and have mol wts of 63,000-67,000; they are composed of two polypeptide chains joined by a disulfide bond. The smaller of these chains (A-chain) is an enzyme that inhibits protein synthesis and causes cell death; the larger B-chain contains a higher amount of sugar than the A. *Abrus* agglutinin is a bivalent tetramer of 134,900 daltons. Purification of abrins A and C: C. H. Wei *et al., J. Biol. Chem.* **249,** 3061 (1974). Crystallographic study: C. H. Wei, J. R. Einstein, *ibid.* 2985. Improved purification, properties, crystallography of *Abrus* agglutinin: C. H. Wei *et al., ibid.* **250,** 4790 (1975). Physical studies: M. S. Herrmann, W. D. Behnke, *Biochim. Biophys. Acta* **621,** 43 (1980). Physical and biological properties of abrin A: *eidem, ibid.* **667,** 397 (1981). Isoln and purification of all five proteins: J. Y. Lin *et al., Toxicon* **19,** 41 (1981). Immunoelectron microscopy studies of abrin toxic action on tumor cells: C. T. Lin *et al., J. Ultrastruc. Res.* **73,** 310 (1980). Studies on toxicity and binding kinetics: M. Witten *et al., Exp. Cell Biol.* **49,** 306 (1981); C. E. Bennett *et al., ibid.* 319. *See also* Ricin, Lectins.

Yellowish-white powder. Sol in solns of sodium chloride, usually with turbidity. The toxic portion is heat-stable to incubation at 60° for 30 min; at 80°, most of the toxicity is lost in 30 min. LD_{50} i.p. in mice: 0.020 mg/kg, J. Y. Lin *et al., J. Formosan Med. Assoc.* **68,** 322 (1969), *C.A.* **71,** 121926 (1969).

Caution: Seeds of *A. precatorius* are extremely toxic; one seed, if thoroughly masticated, can cause fatal poisoning, *cf.* J. M. Kingsbury, *Poisonous Plants of the United States and Canada* (Prentice-Hall, New Jersey, 1964) p 303; K. Genest *et al., Arzneimittel-Forsch.* **21,** 888 (1971).

Note: Do not confuse with abrine, *q.v.*

USE: Exptly in cancer research.

4. Abrine. ***N-Methyl-L-tryptophan;*** α-methylamino-β-(3-indole)propionic acid. $C_{12}H_{14}N_2O_2$; mol wt 218.25. C 66.03%, H 6.47%, N 12.84%, O 14.66%. Not to be confused