Preface to the fourth edition

The third edition of this book was a great success. Within less than 18 months it was more or less sold out, the printed version as well as the electronic one. So the publishers plagued the authors to prepare the next edition. Again, our "junior authors", Prof. Dr. Bernhard Kutscher and Dr. Dietmar Reichert, were doing an excellent job in elaborating the manuscript of about 100 new drug monographs. Furthermore we took the chance to carry out numerous additions and corrections. As a consequence of this extension it was no longer possible to stay with a "one volume edition" and we now have the fourth edition with two volumes.

This fourth edition contains 2267 active pharmaceutical ingredients ("API's") including those which were launched only recently. No fundamental changes were made in comparison to the third edition, which means that the preface, the acknowledgements and the introduction to the third edition are also still valid for the new edition.

We are very grateful to the many readers who kindly provided us with proposals for corrections. Again, the authors are deeply indebted to Dr. Hans-Georg Scharnow and his excellent team from the FIZ CHEMIE BERLIN, for their contributions to the preparation process of this book. We also would like to thank Dr. Elisabeth Hillen and Dr. Guido Herrmann from the Georg Thieme Verlag for the good cooperation. Finally the authors are very grateful to the colleagues of the experienced "ASTA Medica team", who were already mentioned in the "Acknowledgements" to the third edition. In the meantime Dr. Knut Eis joined this team.

Frankfurt a. M., Autumn 2000 Axel Kleemann
Jürgen Engel

Preface to the third edition

For many years, the second edition of "Pharmazeutische Wirkstoffe" has been out of print and colleagues and friends have asked and plagued us to publish a new edition. Everyone who has ever prepared a similar reference book knows how much energy and enthusiasm has to be put into such a task besides the "daily job" in industry. After some hesitation we finally decided to prepare the new edition, in English. Two fortunate circumstances made things a lot easier.

Firstly, Mr. Willi Plein brought us into contact with Dr. H.-G. Scharnow of the FIZ CHEMIE BERLIN[1], who was interested in preparing the new edition as an electronic version by making use of their specialised know-how and self-developed software. With this technology we were able to transform greater parts of the second edition, especially the formula drawings, into the new electronic version – thereby establishing an innovative method of book production, making future new editions much easier to prepare, and also enabling the publisher to offer a CD-ROM version. The FIZ CHEMIE team was successful in attracting the BMBF[2] for this interesting project and luckily received generous financial support.

Secondly, we persuaded the young colleagues Prof. Dr. Bernhard Kutscher and Dr. Dietmar Reichert to take responsibility as "junior authors" for this book. About a quarter of the workload for this volume was done by them and furthermore they have the capability and talent to contribute to future editions – if hopefully necessary.

The purpose and object of this book are to establish a link between INN's[3], structure, synthesis and production processes, patent (and literature) situation, medical use and trade names of important pharmaceuticals.

This volume contains a collection of 2171 active pharmaceutical ingredients, which are listed alphabetically according to their INN's. Often there are still other Generic Names in use, for example BAN[4], DCF[5], USAN[6], which are added in brackets under the INN's and are listed in the index. In addition to the foregoing editions, we have added the molecular formulas and molecular weights as well as the CAS Registry Numbers[7] and – where available – the ATC Code Numbers[8], the EINECS numbers[9], and data for acute toxicology as well as pharmaceutical dosage forms. In the last section of each monograph, the trade names in the six most important markets are listed. The trade names were taken from the relevant reference books on pharmaceutical specialities[10] [11] [12].

Within the 16 years since the second edition, respectively 11 years since the supplement volumes were published, many changes have occurred. Companies disappeared or were acquired and the trade names of many products were changed. Some products were withdrawn from the market, either as mono drugs or combinations. In such cases, we added "w f m" behind the trade name, when we felt that we should not eliminate

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1) FIZ CHEMIE BERLIN, Fachinformationszentrum Chemie GmbH, Franklinstraße 11, D-10587 Berlin
2) Bundesministerium für Bildung, Wissenschaft, Forschung und Technologie, Bonn
3) INN = International Nonproprietary Names; synonymous with "Generic Names"
4) BAN = British Approved Name
5) DCF = Dénomination Commune Française
6) USAN = United States Adopted Name
7) CAS = Chemical Abstracts Service
8) ATC = Anatomic Therapeutic Chemical (Classification of Drugs)
   a) ATC Index, WHO Collaborating Center for Drug Statistics Methodology, Oslo 1997
   b) European Drug Index, N. F. Miller, R. P. Dessing, 4th ed., Deutscher Apotheker Verlag Stuttgart 1997
9) EINECS = European Inventory of Existing Chemical Substances
10) "WDI, World Drug Index" – database, Derwent Information, 1998
11) "MDDR"-database, Drug Data Report, Prous Science, MDL, San Leandro, 1998
12) Speciality lists for
    D: "Rote Liste 2000", Hrsg. Bundesverband der Pharmazeutischen Industrie e.V., Frankfurt/M.
    "List of Pharmaceutical Substances", 10. edition, ABDATA Pharma-Daten-Service, Eschborn, March 1997
    F: "Dictionnaire VIDAL 1998" OUP, Paris
    GB: "MIMS" (Monthly Index of Medical Specialities), Haymarket Publishing Services Ltd., London 1998
    I: "L'Informatore Farmaceutico", 58. edit., Organizzazione Editoriale Medico Farmaceutico srl, Milano 1998
    J: a) "Japta List" 1987, Japanese Drug Directory, 3rd ed., Tokyo 1987
    b) Drugs in Japan/Ethical Drugs 1970, 10, ed. by Japan Pharmaceutical Information Center, Tokyo, Japan
    USA: "PDR, Physicians Desk Reference", 52. edition, 1998; Medical Economics Comp., Montvale, N. J.

the monograph or its former trade name because the drug is still in use in other countries or in numerous combinations – even if not listed here – or is of historical interest. The given trade names are normally representing the mono drug product. In some cases, we listed the year of market introduction behind the name of the company.

It was the intention of the authors to present the synthesis routes in broad details. In many cases, we describe different synthesis routes, especially for the economically most important drugs – but also when we are not completely sure which particular route is applied technically. The practicability of such a reference book is to a great extent dependent on clearly arranged and in-depth indexes. The reader will find appropriate and comprehensive indexes for

1. Trade Names
2. Intermediates
3. Enzymes, Microorganisms, Plants, Animal Tissues
4. Substance classes.

As many abbreviations are used in this book, a separate "list of abbreviations" has been added, see front and back endpapers. Concerning abbreviations for chemicals and reagents we adhered to the "Standard List of Abbreviations", published in J. Org. Chem., Vol. **68**, No. 1, 1998, p. 19A.

We have had many discussions regarding the inclusion of the newer biopharmaceuticals ("Pharmaproteins") which are produced by recombinant DNA methods (e.g., Interferons, human Insulin, Erythropoietin etc.). After several trials, we dropped this plan because we could not find a concept consistent with the original character of the book, which predominantly contains synthetic drugs as well as some antibiotics made by conventional fermentation and some plant ingredients that are produced by extraction. A borderline case exists with many synthethic peptides. It is often practically impossible to find out the applied technical synthesis process among the manifold routes described in the literature. So, we more or less stayed with the peptide drugs that were already included in the 2nd edition and supplement volume.

The book is designed to serve the needs of not only the specialists in drug synthesis but also of a broad usergroup in the chemical, intermediates and pharmaceutical industry, pharmacists, universities and other research institutes. So, it is important for everybody who has to deal with pharmaceuticals or their raw materials and intermediates and would like to have a quick survey. For the analytical chemist, knowledge about the synthesis route of an active ingredient is essential in order to recognize contaminations with intermediates or possible byproducts. Often, also the allergologist has a need for information regarding the synthesis of a drug in order to localize allergic byproducts or intermediates. The synthetic chemist will be provided with stimulating suggestions for his work.

We hope that this book will prove to be a standard reference for everyone who is interested in pharmaceuticals.

Frankfurt a. M., Autumn 1998 Axel Kleemann
Jürgen Engel

Acknowledgements

Preparing a reference book of this kind is by no means feasible without the contributions of numerous dedicated colleagues who bring in their special expertise and knowledge.

The authors are deeply indebted to Dr. Hans-Georg Scharnow, Ingo Adamczyk, Gerhard Fabian, Martin Holberg, Gudrun Lippmann, Ulrich Quandt, Karin Raatsch and Dr. Katrin Seemeyer from FIZ CHEMIE BERLIN, for providing their computer know-how and software expertise. This FIZ CHEMIE team has taken a decisive part in the preparation of the book, also in reminding the authors regularly of their obligation to deliver the manuscripts on time. It was always a reliable, fruitful and pleasant cooperation. We also wish to extend our gratefulness to the BMBF (Bundesministerium für Bildung, Wissenschaft, Forschung und Technologie) for generous support of this project.

It is the authors special desire to express their gratitude to the many co-workers of the Chemical Research Department of ASTA Medica AG, who willingly agreed to assist and support the process of manuscript preparation and correction. For their assistance in patent and literature searching, we wish to thank Dr. Ilona Fleischhauer, Dieter Heiliger, Christa Krehmer, Thomas Kynast, Horst Mai, Dr. Ulf Niemeyer, Wolfgang Paul, Horst Rauer, Jürgen Schael and Norbert Schulmeyer. Important contributions in the search for and correction of trade names have been made by Dr. Thomas Arnold, Dr. Gerhard Nößner, Dr. Klaus Paulini and Dr. Heinz Weinberger and the trade name searching process was greatly supported by Dr. Patricia Charpentier, Dr. Stefan Eils, Anja Heddrich, Dr. Gilbert Müller, Sandra Nemetz, Sven-Oliver Schmidt, Anita Storch and Silvia Werner.

Important advice concerning the pharmaceutical specialities on the Japanese market was provided by our Japanese colleague Nobuo Kumagai, whom we wish to thank sincerely.

A word of thanks has also to be addressed to Dr. Elisabeth Hillen and Dr. Rolf Hoppe from the Georg Thieme Verlag for the always good cooperation and acceptance of many special suggestions concerning the production of this book and its CD-ROM version.

Finally, we would like to express our gratitude to the many readers and users of the foregoing editions who took the time to provide us with comments, corrections and suggestions.

The authors

Introduction

This reference book describes the production/isolation processes of 2267 active pharmaceutical substances (including the syntheses of their intermediates) that are or have been marketed. In order to illustrate what particular information can be drawn from the book a typical monograph is depicted below and labelled. It is self-explanatory.

The frequently-used abbreviations are explained in a separate list, q.v. see front and back endpapers.

With respect to the names of reagents and intermediates in the course of the syntheses the authors tried to use the names found in the catalogues of the commercial providers of fine chemicals, e.g. Sigma-Aldrich, otherwise the Chemical Abstracts Names are given.

In addition to the respective patents and publications in journals several standard reference books for Pharmaceuticals and Fine Chemicals were used and sometimes also cited. The most important sources are given here:

The Merck Index, 12 ed., Merck & Co., Inc.; NJ 1996
abbrev.: Merck Index

- Z. Budesinsky and M. Protiva, Synthetische Arzneimittel, Akademie-Verlag, Berlin 1961
  abbrev.: Budesinsky-Protiva
- G. Ehrhart, H. Ruschig, Arzneimittel, vols. 1–5, Verlag Chemie, Weinheim 1972
  abbrev.: Ehrhart-Ruschig
- Index Nominum, international drug directory, ed. by Swiss Pharmaceutical Society, 1992/93
- A. Kleemann, E. Lindner, J. Engel, Arzneimittel-Fortschritte 1972–1985, VCH Verlagsgesellschaft mbH, Weinheim 1987
- D. Lednicer, L. A. Mitscher, The Organic Chemistry of Drug Synthesis, vols. 1–6, John Wiley & Sons, New York 1977–1999
- Ullmanns Encyclopädie der technischen Chemie, 3. and 4. edition, Verlag Chemie Weinheim;
- Ullmann's Encyclopedia of Industrial Chemistry, 5. ed., vols. A1–A28, B1–B8, VCH Verlagsgesellschft mbH, Weinheim 1985–1997
  abbrev.: Ullmanns Encycl. Techn. Chem.
- Ullmann's Encyclopedia of Industrial Chemistry, 6. ed., on CD-ROM, 1999 and 2000
  M. Negwer, Organic-chemical drugs and their synonyms, Akademie-Verlag, Berlin 1994
  USP Dictionary of USAN and International Drug Names, US Pharmacopeia, Rockville, MD 1998

The acute toxicity data were in most cases taken from different data banks or other secondary sources, so no guarantee can be given for validity.

For information regarding pharmaceutical dosage forms see preface, footnote 12.

Alphabetical List of Drug Monographs

G

H

T

U

Molecular formula

ATC Code Number

INN

CAS Registry Number

Medical Use, Therapeutic category

other Generic Names (Synonyms)

Simvastatin
(MK-733; Synvinolin)

ATC: C10AA01
Use: antihyperlipidemic cholesterol synthesis inhibitor, HMG-CoA-reductase inhibitor

EINECS Number (where given if available)

RN: 79902-63-9 MF: $C_{25}H_{38}O_5$ MW: 418.57 EINECS: n/a

Acute Toxicity

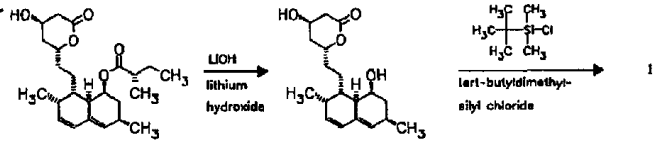
LD_{50}: 3 g/kg (M, p.o.);
4438 mg/kg (R, p.o.);
>5 g/kg (dog, p.o.)

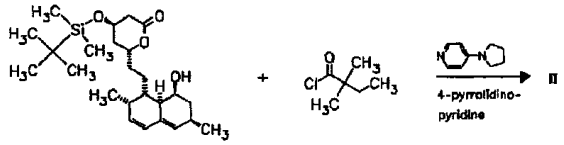
Chemical Abstracts name

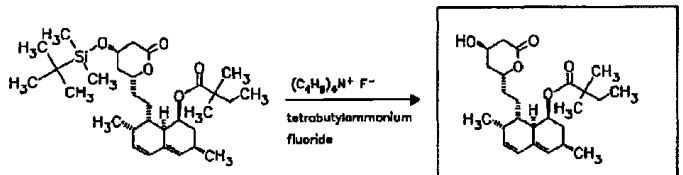
CN: [1*S*-[1α,3α,7β,8β(2*S**,4*S**),8aβ]]-2,2-dimethylbutanoic acid 1,2,3,7,8,8a-hexahydro-3,7-dimethyl-8-[2-(tetrahydro-4-hydroxy-6-oxo-2*H*-pyran-2-yl)ethyl]-1-naphthalenyl ester

Molecular weight

Synthesis Scheme







Structure of Title INN

Issue date for US patent

Reference(s):
US 4 444 784 (Merck & Co.; 24.4.1984; prior. 5.8.1980, 4.2.1980).
US 4 450 171 (Merck & Co.; 22.5.1984; prior. 14.6.1982, 18.12.1980, 5.8.1980, 4.2.1980).
Hoffmann, W.F. et al.: J. Med. Chem. (JMCMAR) **29**, 849 (1986).

Application and Priority dates

Literature and Patent references

alternative synthesis:
US 5 159 104 (Merck & Co.; 27.10.1992; appl. 1.5.1992).
GB 2 255 974 (Merck & Co.; 25.11.1992; US-prior. 24.5.1991).
WO 9 812 188 (Brantford; 5.9.1997; CA-prior. 19.9.1996).
US 5 763 653 (Ranbaxy; 9.6.1998; appl. 13.3.1997).
US 5 763 646 (Ranbaxy; 9.6.1998; appl. 13.3.1997).
US 5 393 893 (Apotex; 28.2.1995; appl. 8.11.1993).
EP 33 538 (Merck & Co.; appl. 2.2.1981; USA-prior. 4.2.1980, 5.8.1980).

Pharma-ceutical dosage forms

controlled-release formulation:
EP 302 693 (Merck & Co.; appl. 1.8.1988; USA-prior. 3.8.1987, 31.8.1987).

Formulation(s): f.c. tabl. 5 mg, 10 mg, 20 mg, 40 mg; tabl. 5 mg, 10 mg, 20 mg, 40 mg

Trade Names in important markets

Trade Name(s):

D: Denan (Boehringer Ing.; 1990)
Zocor (Dieckmann; 1990)

F: Lodalès (Sanofi Winthrop)
Zocor (MSD-Chibret; 1989)

GB: Zocor (Merck Sharp & Dohme)

I: Liponorm (Gentili)
Medipo (Mediolanum)
Sinvacor (Merck Sharp & Dohme)
Sivastin (Sigma-Tau)
Zocor (Neopharmed)

J: Lipovas (Banyu)

USA: Zocor (Merck)

Marketing Company

Year of introduction

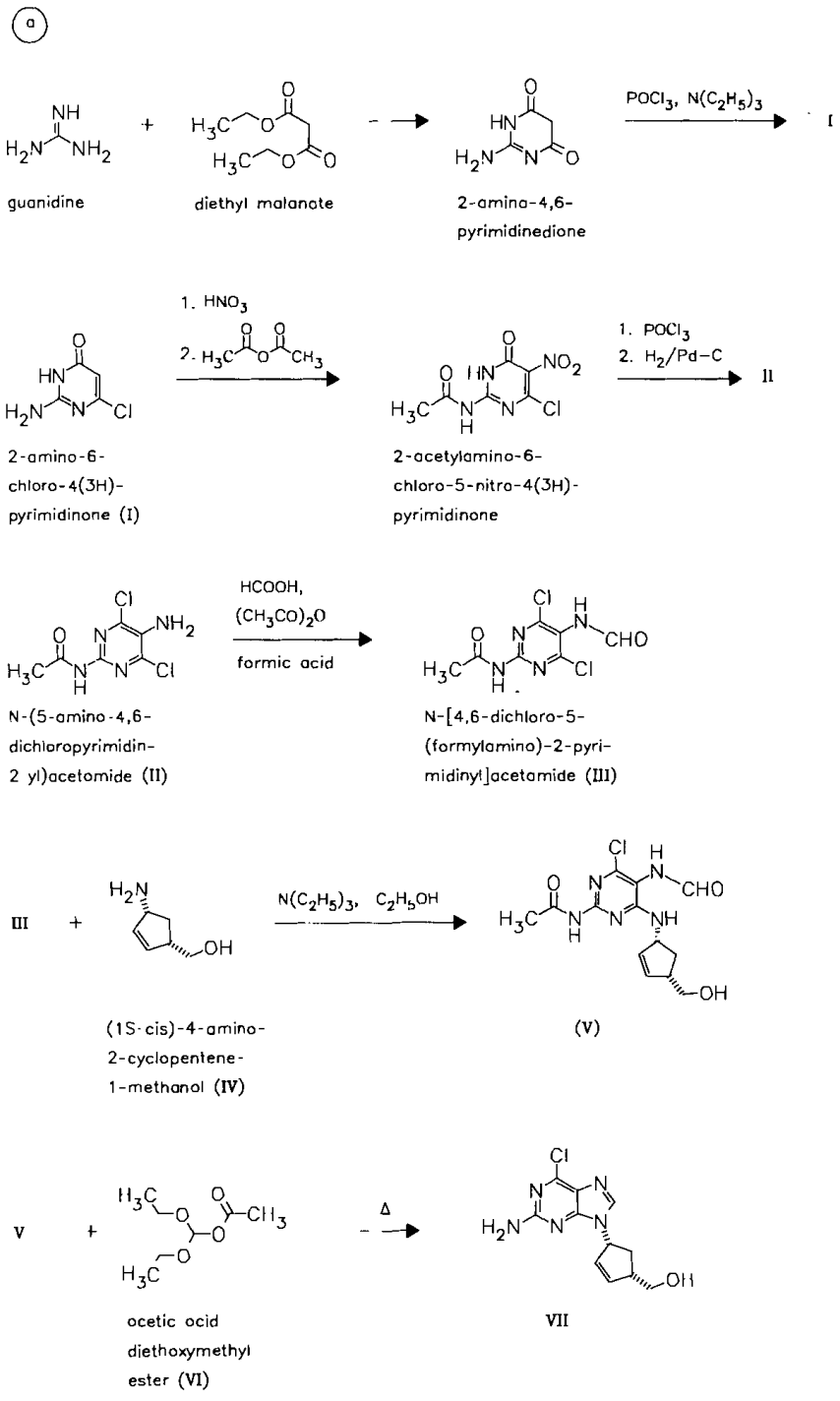
Abacavir

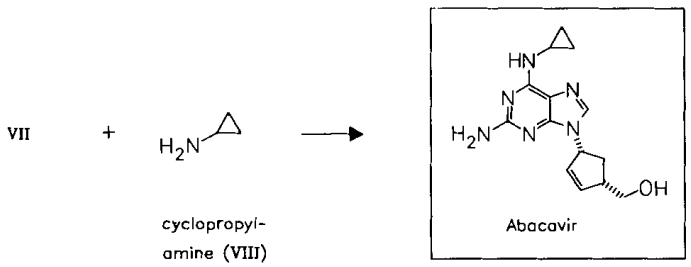
(1592U89)

ATC: J05AF06
Use: antiviral, anti HIV, reverse transcriptase inhibitor

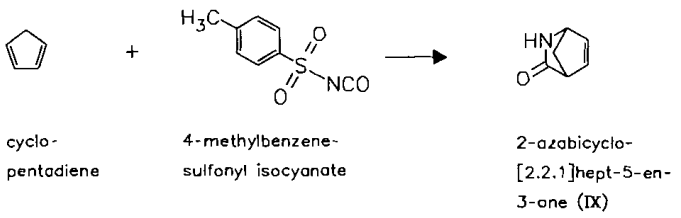
RN: 136470-78-5 MF: $C_{14}H_{18}N_6O$ MW: 286.34
CN: (1*S*,4*R*)-4-[2-Amino-6-(cyclopropylamino)-9*H*-purin-9-yl]-2-cyclopentene-1-methanol

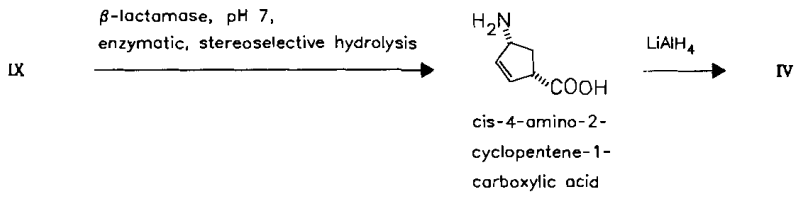
succinate
RN: 168146-84-7 MF: $C_{14}H_{18}N_6O \cdot C_4H_6O$ MW: 356.43
sulfate
RN: 188062-50-2 MF: $C_{14}H_{18}N_6O \cdot 1/2H_2SO_4$ MW: 670.76



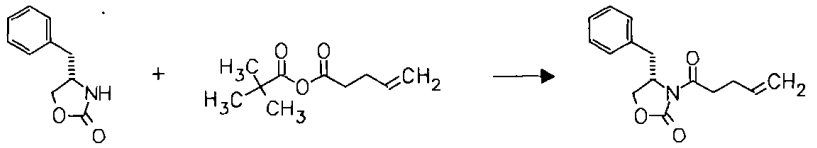


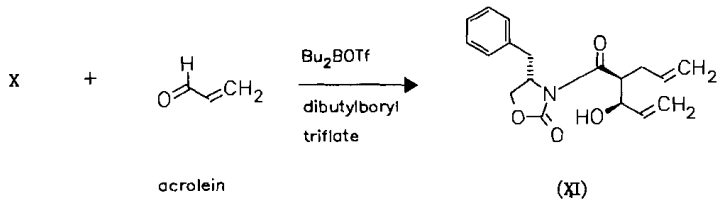
(aa) synthesis of (1S-cis)-4-amino-2-cyclopentene-1-methanol (IV)

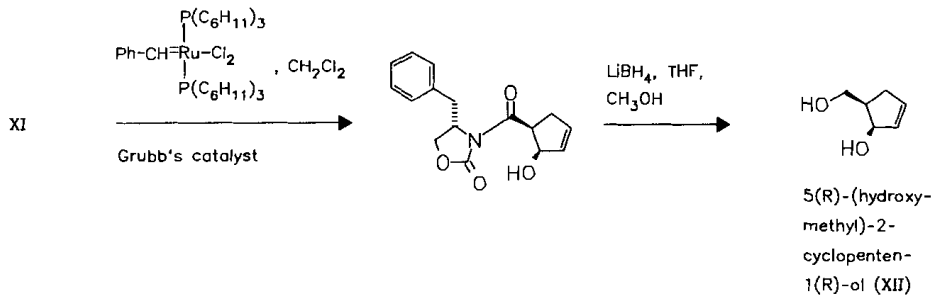


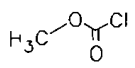


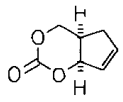
(b)

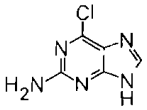






XII +  methyl chloroformate

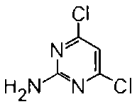
TEA, DMAP, CH_2Cl_2 →  (XIII)

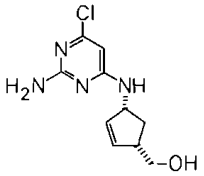
XIII +  2-amino-6-chloropurine (cf. famciclovir)

NaH, THF, DMSO, $Pd(PPh_3)_4$ → tetrakis(triphenylphosphine)palladium

VII → VIII → Abacavir

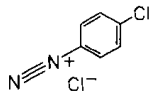
(c)

 + rac-IV

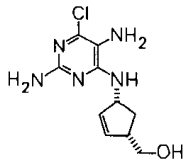
TEA, 1-butanol → 

2-amino-4,6-dichloropyrimidine

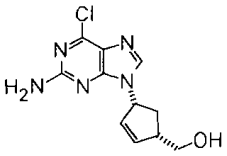
(±)-cis-4-[(2 amino-4-chloro-6-pyrimidinyl)-amino]-2-cyclopentene-1-methanol (XIV)

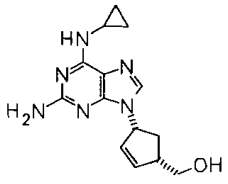
XIV + 

4-chlorobenzenediazonium chloride

1. Ac-ONa, CH_3COOH
2. Zn, CH_3COOH, C_2H_5OH → 

(±)-cis-4-[(2,5-diamino-4-chloro-6-pyrimidinyl)-amino]-2-cyclopentene-1-methanol (XV)

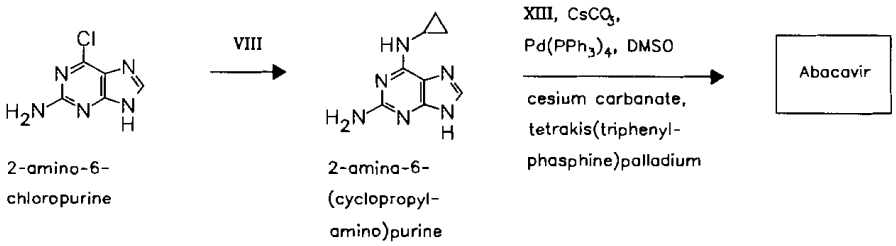
XV + VI → Δ → 

VIII, C_2H_5OH → 

(XVI)

XVI → 1. $POCl_3$ 2. stereoselective enzymatic hydrolysis with alkaline phosphatase → Abacavir

(d)



Reference(s):

a EP 434 450 (Wellcome Found.; 26.6.1991; appl. 21.12.1990; USA-prior. 22.12.1989).
Crimmins, M.T. et al.: J. Org. Chem. (JOCEAH) **61** 4192 (1996).
aa EP 424 064 (Enzymatix; appl. 24.4.1991; GB-prior. 16.10.1989).
b Olivo, H.F. et al.: J. Chem. Soc., Perkin Trans. 1 (JCPRB4) **1998**, 391.
c US 5 034 394 (Welcome Found.; 23.7.1991; appl. 22.12.1989; GB-prior. 27.6.1988).
d WO 9 924 431 (Glaxo; appl. 12.11.1998; WO-prior. 12.11.1997).

alternative syntheses:
EP 878 548 (Lonza; appl. 13.5.1998; CH-prior. 13.5.1997).

condensation of pyrimidines *with* cyclopentylamine IV:
Vince, R.; Hua, M.: J. Med. Chem. (JMCMAR) **33** (1), 17 (1990).
EP 349 242 (Wellcome Found.; appl. 26.6.1989; GB-prior. 27.6.1988).
EP 366 385 (Wellcome Found.; appl. 23.10.1989; GB-prior. 24.10.1988).
Grumam, A. et al.: Tetrahedron Lett. (TELEAY) **36** (42), 7767 (1995).
JP 1 022 853 (Asahi Glass Co.; appl. 17.7.1987).

alternative preparation of 4-amino-2-cyclopentene-1-methanol:
EP 926 131 (Lonza; appl. 24.11.1998; CH-prior. 27.11.1997).
WO 9 745 529 (Lonza; appl. 30.5.1997; CH-prior. 30.5.1996).

abacavir succinate *as antiviral agent:*
WO 9 606 844 (Wellcome; 7.3.1996; appl. 25.8.1995; GB-prior. 26.8.1994).

synergistic combinations for treatment of HIV infection:
WO 9 630 025 (Wellcome; 3.10.1996; appl. 28.3.1996; GB-prior. 30.3.1995).

Formulation(s): oral sol. 20 mg/ml; tabl. 300 mg (as sulfate)

Trade Name(s):
D: Ziagen (Glaxo Wellcome; 1999) USA: Ziagen (Glaxo Wellcome)

Abciximab

(7E3; C7E3; C7E3 Fab; C7E3-F(ab')2)

ATC: B01AC13
Use: platelet antiaggregation inhibitor, antianginal, GPIIb/IIIa-receptor antagonist

RN: 143653-53-6 MF: unspecified MW: unspecified
CN: immunoglobulin G (human-mouse monoclonal c7E3 clone p7E3V_Hh$C\gamma_4$ Fab fragment antihuman glycoprotein IIb/IIIa receptor), disulfide with human-mouse monoclonal c7E3 clone p7E3V_KhC_K light chain

Reference(s):
Gold, H.K. et al.: Circulation Suppl. (CISUAQ) **80**(4) (1989), Abst. 1063.

Formulation(s): vial 10 mg/5 ml

Trade Name(s):

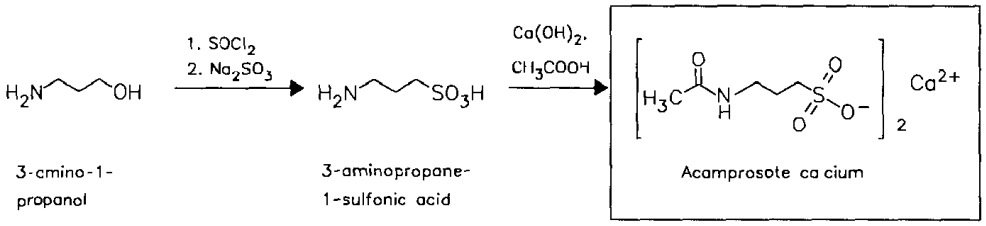
D:	ReoPro (Lilly)	GB:	Reopro (Lilly)
F:	ReoPro (Lilly)	USA:	ReoPro (Lilly)

Acamprosate calcium

ATC: V03AA
Use: alcohol deterrent

RN: 77337-73-6 MF: $C_{10}H_{20}CaN_2O_8S_2$ MW: 400.49 EINECS: 278-665-3
LD_{50}: >10 g/kg (M, p.o.)
CN: 3-(acetylamino)-1-propanesulfonic acid calcium salt (2:1)

free acid
RN: 77337-76-9 MF: $C_5H_{11}NO_4S$ MW: 181.21 EINECS: 278-667-4



Reference(s):
DE 3 019 350 (Lab. Meram; appl. 21.5.1980; F-prior. 23.5.1979).

synthesis of 3-aminopropane-1-sulfonic acid:
JP 46 002 012 (Kowa; appl. 19.1.1971).
Fujii, A. et al.: J. Med. Chem. (JMCMAR) **18**, 502 (1975).
WO 8 400 958 (Mitsui; appl. 15.3.1984; J-prior. 7.9.1982, 19.7.1983, 8.9.1982).

Formulation(s): tabl. 333 mg

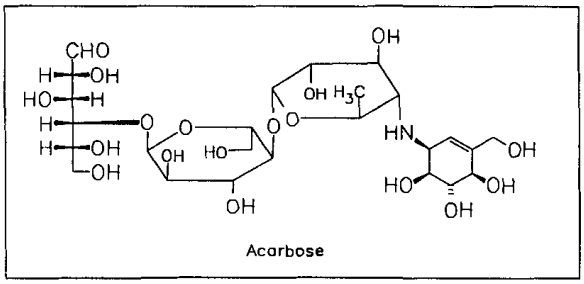
Trade Name(s):

D:	Campral (Lipha)	F:	Aotal (Meram)	GB:	Campral (Lipha)

Acarbose
(Bay-g-5421)

ATC: A10BF01
Use: antidiabetic, α-glucosidase inhibitor, hypoglycemic

RN: 56180-94-0 MF: $C_{25}H_{43}NO_{18}$ MW: 645.61 EINECS: 260-030-7
LD_{50}: >500.000 SIE/kg (M, i.v.); >1000.000 SIE/kg (M, p.o.);
478.000 SIE/kg (R, i.v.); >1000.000 SIE/kg (R, p.o.)
65.000 SIE = 1 g (SIE = saccharase inhibitory units)
CN: [1*S*-(1α,4α,5β,6α)]-*O*-4,6-dideoxy-4-[[4,5,6-trihydroxy-3-(hydroxymethyl)-2-cyclohexen-1-yl]amino]-α-D-glucopyranosyl(1→4)-*O*-α-D-glucopyranosyl-(1→4)-D-glucose



Acarbose

Fermentation of *Actinoplanes* SE50/110.

Reference(s):
US 4 062 950 (Bayer; 13.12.1977; D-prior. 22.9.1973).
DOS 2 347 782 (Bayer; appl. 21.9.1973).
Schmidt, D.D. et al.: Naturwissenschaften (NATWAY) **64**, 535 (1977).

total synthesis:
Ogawa, S.; Shibata, Y.: Chem. Commun. (CCOMA8) **1988**, 605.

review:
Tschesche, H. in Arzneimittel, Fortschritte 1972-1985 (Ed. A. Kleemann, E. Lindner, J. Engel), p. 87, VCH Verlagsgesellschaft, Weinheim 1987.

Formulation(s): tabl. 50 mg, 100 mg

Trade Name(s):

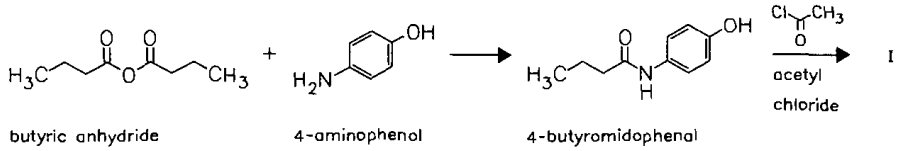
D:	Glucobay (Bayer; 1990)	GB:	Glucobay (Bayer)	USA:	Precose (Bayer)
F:	Glucor (Bayer)	J:	Glucobay (Bayer)		

Acebutolol

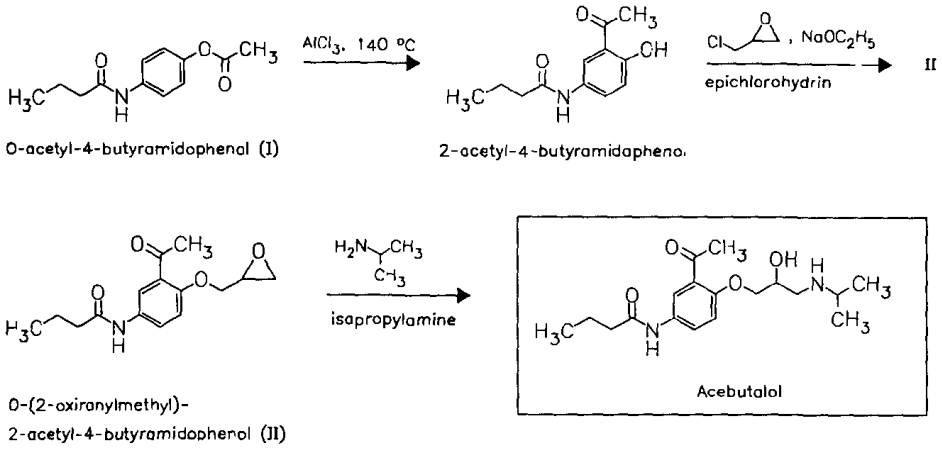
ATC: C07AB04; C07BB04
Use: β-adrenergic receptor blocker

RN: 37517-30-9 MF: $C_{18}H_{28}N_2O_4$ MW: 336.43 EINECS: 253-539-0
LD_{50}: 75.2 mg/kg (M, i.v.);
4 mg/kg (dog, i.v.)
CN: (±)-*N*-[3-acetyl-4-[2-hydroxy-3-[(1-methylethyl)amino]propoxy]phenyl]butanamide

(*R*)-base
RN: 68107-81-3 MF: $C_{18}H_{28}N_2O_4$ MW: 336.43
(*S*)-base
RN: 68107-82-4 MF: $C_{18}H_{28}N_2O_4$ MW: 336.43
(*RS*)-monohydrochloride
RN: 34381-68-5 MF: $C_{18}H_{28}N_2O_4 \cdot HCl$ MW: 372.89 EINECS: 251-980-3
LD_{50}: 185 mg/kg (M, i.p.); 53 mg/kg (M, i.v.); 4050 mg/kg (M, p.o.); 291 mg/kg (M, s.c.); 222 mg/kg (R, i.p.); 103 mg/kg (R, i.v.); 6620 mg/kg (R, p.o.); 1310 mg/kg (R, s.c.); 41 mg/kg (rabbit, i.v.); 296 mg/kg (rabbit, p.o.)



butyric anhydride 4-aminophenol 4-butyromidophenol



Reference(s):
GB 1 247 384 (May & Baker; appl. 22.12.1967).
DAS 1 815 808 (May & Baker; appl. 19.12.1968; GB-prior. 22.12.1967, 14.5.1968, 2.8.1968).
US 3 726 919 (May & Baker; appl. 19.12.1968; GB-prior. 22.12.1967, 14.5.1968, 2.8.1968).
US 3 857 952 (May & Baker; appl. 3.8.1972).

preparation of 4-butyramidophenol:
Kuhn; Koehler; Koehler: Hoppe-Seyler's Z. Physiol. Chem. (HSZPAZ) **247**, 197, 216 (1937).
Verma, K.K.; Tyagi, P.: Anal. Chem. (ANCHAM) **56** (12), 2157 (1984).
US 2 824 838 (Esso Research & Eng. Co.; 25.2.1958; appl. 13.1.1955).

Formulation(s): amp. 25 mg; tabl. 200 mg, 400 mg (as hydrochloride)

Trade Name(s):

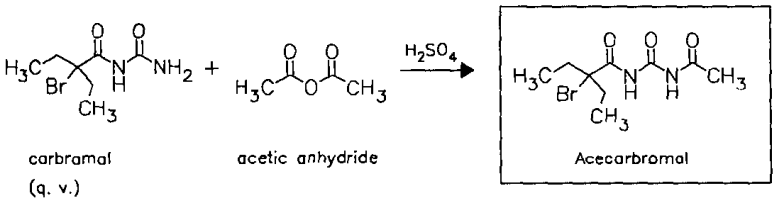
D:	Prent (Bayer; 1977)		Sectral (Rhône-Poulenc Rorer; 1975)	J:	Acetanol (Rhodia; 1984)
	Sali-Prent (Bayer; 1982)-comb.	I:	Accor (SPA)		Sectral (Kanebo; 1981)
	Tredalat (Bayer)-comb.		Alol (SIT)	USA:	Sectral (Wyeth-Ayerst; 1985)
F:	Sectral (Specia; 1976)		Prent (Bayropharm; 1981)		
GB:	Secadrex (Rhône-Poulenc Rorer; 1982)-comb.		Sectral (Rhône-Poulenc Rorer; 1980)		

Acecarbromal

(Acetylcarbromal; Acetcarbromal)

ATC: N05CM
Use: sedative, hypnotic

RN: 77-66-7 MF: $C_9H_{15}BrN_2O_3$ MW: 279.13 EINECS: 201-047-1
LD_{50}: 1600 mg/kg (M, p.o.)
CN: *N*-[(acetylamino)carbonyl]-2-bromo-2-ethylbutanamide



Reference(s):
DRP 225 710 (Bayer; 1910).

alternative syntheses:
DRP 286 760 (Bayer; 1913).
DRP 327 129 (Bayer; 1917).

Formulation(s): drg. 100 mg

Trade Name(s):

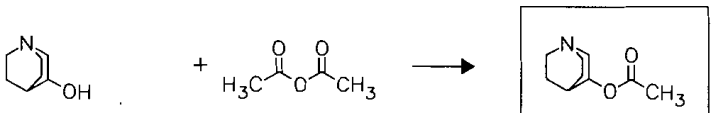
D:	Abasin (Bayer); wfm	USA:	Carbased (Mallard); wfm
	Afrodor (Farco-Pharma)		Sedamyl (Riker); wfm

Aceclidine

ATC: S01EB08; S01EB58
Use: antiglaucoma, miotic

RN: 827-61-2 MF: $C_9H_{15}NO_2$ MW: 169.22 EINECS: 212-574-1
LD_{50}: 78 mg/kg (M, i.p.); 36 mg/kg (M, i.v.); 165 mg/kg (M, p.o.); 102 mg/kg (M, s.c.); 45 mg/kg (R, i.v.); 225 mg/kg (R, s.c.)
CN: 1-azabicyclo[2.2.2]octan-3-ol acetate (ester)

hydrochloride
RN: 6109-70-2 MF: $C_9H_{15}NO_2 \cdot HCl$ MW: 205.69 EINECS: 228-071-5
LD_{50}: 27 mg/kg (M, i.v.); 165 mg/kg (M, p.o.); 45 mg/kg (R, i.v.)
salicylate (1:1)
RN: 6821-59-6 MF: $C_9H_{15}NO_2 \cdot C_7H_6O_3$ MW: 307.35
LD_{50}: 113 mg/kg (M, s.c.)



3-hydroxy-quinuclidine (cf. clidinium bromide synthesis)

acetic anhydride

Aceclidine

Reference(s):
US 2 648 667 (Roche; 1953; prior. 1951).
Grob, C.A. et al.: Helv. Chim. Acta (HCACAV) **40**, 2170 (1957).

Formulation(s): eye drops 200 mg (as hydrochloride), 20 mg

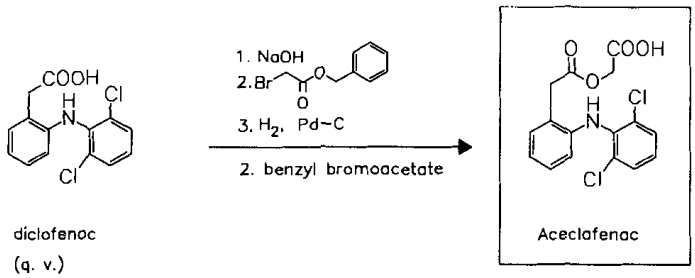
Trade Name(s):

D:	Glaucotat (Chibret)		Glaucostat (Merck Sharp &
F:	Glaucadrine (Merck Sharp		Dohme-Chibret)
	& Dohme-Chibret)-comb.	I:	Glaunorm (Farmigea)

Aceclofenac

ATC: M01AB16
Use: non-steroidal anti-inflammatory, analgesic, antipyretic, prostaglandin synthesis inhibitor

RN: 89796-99-6 MF: $C_{16}H_{13}Cl_2NO_4$ MW: 354.19
LD_{50}: 121 mg/kg (M, p.o.)
CN: 2-[(2,6-dichlorophenyl)amino]benzeneacetic acid carboxymethyl ester



diclofenac
(q. v.)

Aceclofenac

Reference(s):
EP 119 932 (Prodes; appl. 19.3.1984; E-prior. 21.3.1983).
US 4 548 952 (Prodes; 22.10.1985; appl. 15.3.1984; E-prior. 21.3.1983).

alternative synthesis:
ES 2 020 146 (Prodesfarma; appl. 29.5.1990).

Formulation(s): cream 1.5 %; vial 150 mg; tabl. 100 mg

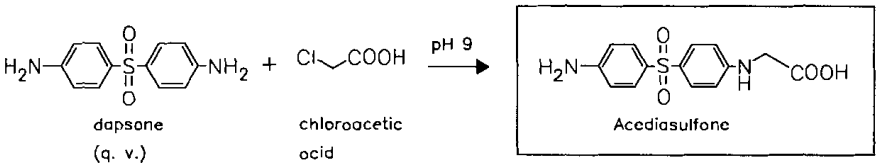
Trade Name(s):
GB: Preservex (Bristol-Myers Squibb; 1992)

Acediasulfone

ATC: S02
Use: antibacterial, cytotoxic agent

RN: 80-03-5 MF: $C_{14}H_{14}N_2O_4S$ MW: 306.34 EINECS: 201-243-7
CN: *N*-[4-[(4-aminophenyl)sulfonyl]phenyl]glycine

monosodium salt
RN: 127-60-6 MF: $C_{14}H_{13}N_2NaO_4S$ MW: 328.32 EINECS: 204-852-6



dapsone
(q. v.)

chloroacetic
acid

Acediasulfone

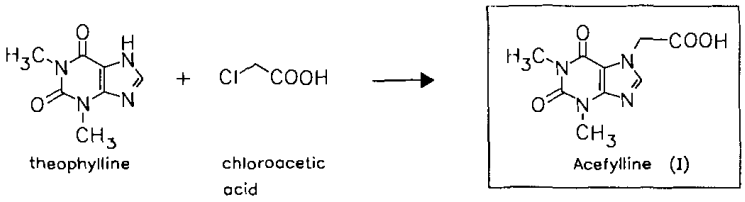
Reference(s):
CH 254 803 (Cilag; appl. 1946).
CH 278 482 (Cilag; appl. 1949).
US 2 589 211 (Parke Davis; 1952; appl. 1948).
US 2 454 835 (Parke Davis; 1948; prior. 1943).
US 2 751 382 (Cilag; 1956; D-prior. 6.7.1953).

Trade Name(s):
D: Ciloprin (Cilag-Chemie)-comb.; wfm

Acefylline

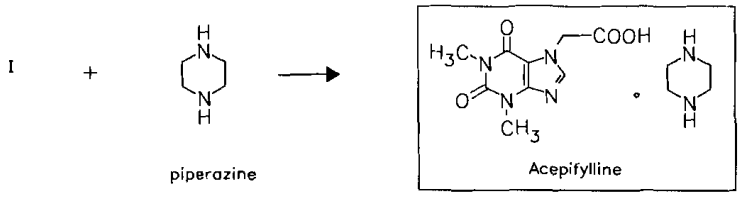
ATC: R03B
Use: cardiotonic, diuretic, antispasmodic, bronchodilator

RN: 652-37-9 MF: $C_9H_{10}N_4O_4$ MW: 238.20 EINECS: 211-490-2
LD_{50}: 1180 mg/kg (M, i.p.); 2733 mg/kg (M, p.o.)
CN: 1,2,3,6-tetrahydro-1,3-dimethyl-2,6-dioxo-7*H*-purine-7-acetic acid



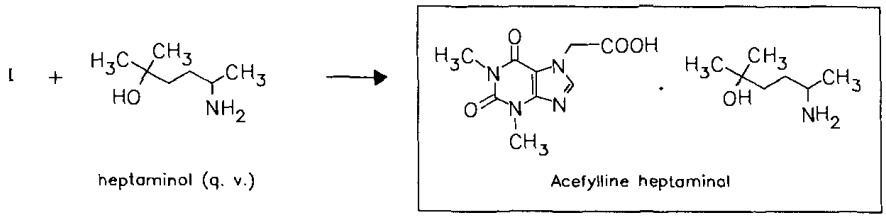
Acepifylline

RN: 18833-13-1 MF: $C_9H_{10}N_4O_4 \cdot xC_4H_{10}N_2$ MW: unspecified EINECS: 242-614-3
CN: 1,2,3,6-tetrahydro-1,3-dimethyl-2,6-dioxo-7*H*-purine-7-acetic acid compd. with piperazine



Acefylline heptaminol

RN: 59989-20-7 MF: $C_9H_{10}N_4O_3 \cdot C_8H_{19}NO$ MW: 367.45 EINECS: 262-012-4
CN: 1,2,3,6-tetrahydro-1,3-dimethyl-2,6-dioxo-7*H*-purine-7-acetic acid compd. with 6-amino-2-methyl-2-heptaminol (1:1)



Reference(s):
Blaisse, J.: Bull. Soc. Chim. Fr. (BSCFAS) **1949**, 769.

Formulation(s): amp. 500 mg/200 ml; drg. 250 mg; suppos. 500 mg; tabl. 250 mg (acepifylline); drg. 250 mg; inj. 0.5 g; suppos. 0.5-1 g

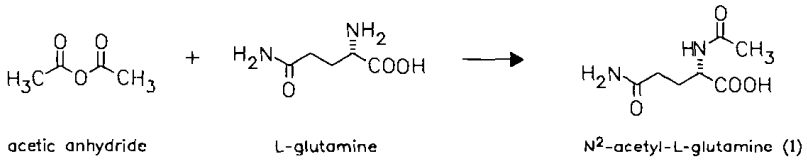
Trade Name(s):

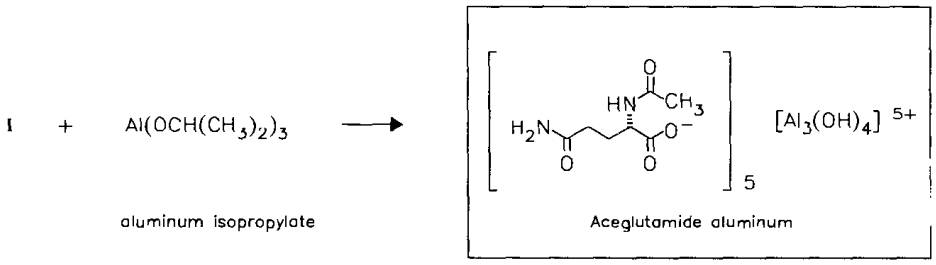
D:	Etaphydel (Delalande; as acepifylline); wfm	F:	Sureptil (Synthélabo; as acefylline-heptaminol)-comb.	GB:	Etophylate (Delalande; as acepifylline); wfm
				I:	Sureptil (Delalande Isnardi)-comb.

Aceglutamide aluminum

ATC: A02AB; N06B
Use: peptic ulcer therapeutic

RN: 12607-92-0 MF: $C_{35}H_{59}Al_3N_{10}O_{24}$ MW: 1084.85
LD_{50}: 460 mg/kg (M, i.v.); 13.1 g/kg (M, p.o.);
400 mg/kg (R, i.v.); >14.5 g/kg (R, p.o.)
CN: pentakis(N^2-acetyl-L-glutaminato)tetrahydroxytrialuminum





Reference(s):
DOS 2 127 176 (Kyowa Hakko; appl. 1.6.1971; J-prior. 5.6.1970).
US 3 787 466 (Kyowa Hakko; 22.1.1974; J-prior. 5.6.1970).

preparation of N^2-acetyl-L-glutamine:
Reddy, A.V; Ravindranath, B.: Synth. Commun. (SYNCAV) **22** (2), 257 (1992).
Synge: Biochem. J. (BIJOAK) **33**, 673 (1939).

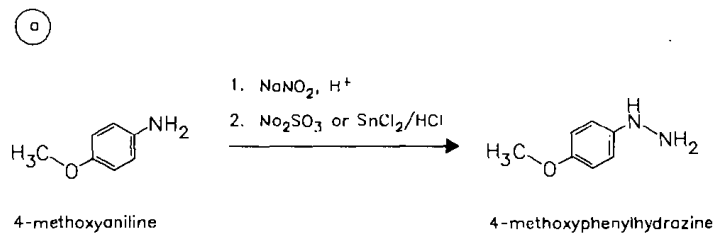
Formulation(s): gran. 700 mg

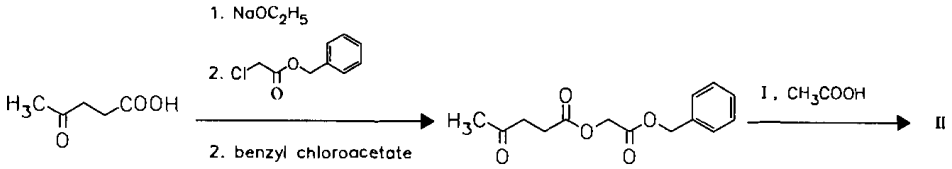
Trade Name(s):
J: Glumal (Kyowa Hakko)

Acemetacin

ATC: M01AB11
Use: non-steroidal anti-inflammatory

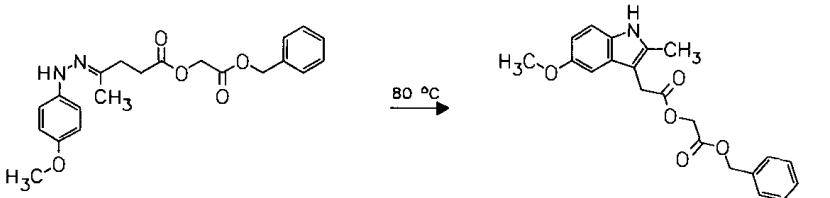
RN: 53164-05-9 MF: $C_{21}H_{18}ClNO_6$ MW: 415.83 EINECS: 258-403-4
LD_{50}: 55 mg/kg (Mm, p.o.); 18.42mg/kg (Mf, p.o.);
24.2 mg/kg (Rm, p.o.); 30.1 mg/kg (Rf, p.o.)
CN: 1-(4-chlorobenzoyl)-5-methoxy-2-methyl-1*H*-indole-3-acetic acid carboxymethyl ester





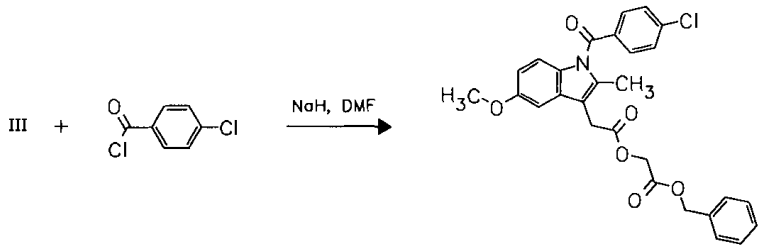
levulinic acid

benzyl levulinoyloxyacetate



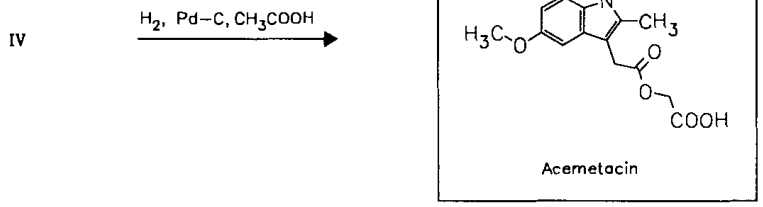
benzyl [2-(4-methoxyphenylhydrazono)-valeryloxy]acetate (II)

benzyl (5-methoxy-2-methyl-3-indolyl-acetoxy)acetate (III)



4-chloro-benzoyl chloride

benzyl [1-(4-chlorobenzoyl)-5-methoxy-2-methyl-3-indolylacetoxy]acetate (IV)



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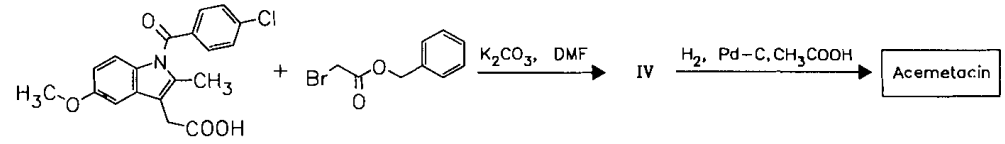


indometacin (q. v.)

benzyl bromo-acetate

Reference(s):

DOS 2 234 651 (Tropon; appl. 14.7.1972).
FR 2 192 828 (Tropon; appl. 13.7.1973; D-prior. 14.7.1972).
US 3 910 952 (Troponwerke Dinklage; 7.10.1975; appl. 28.6.1973; D-prior. 14.7.1972).

preparation of 4-methoxyphenylhydrazine *from* 4-methoxyaniline (*p*-anisidine):
Lee, A.-R. et al.: J. Heterocycl. Chem. (JHTCAD) **32** (1), 1-12 (1995).
Clade, D.W. et al.: J. Chem. Soc., Perkin Trans. 2 (JCPKBH) , 909-916 (1982).
DE 70 459 (Riedel; 12.11.1891).
Altschul: Ber. Dtsch. Chem. Ges. (BDCGAS) **25**, 1849 (1892).

preparation of benzyl levulinoyloxyacetate:
Boltze, K.-H.; Brendler, O.; Jacobi, H.; Opitz, W.; Raddatz, S. et al.: Arzneim.-Forsch. (ARZNAD) **30** (8a), 1314-1325 (1980).

Formulation(s): cps. 30 mg, 60 mg; s. r. cps. 90 mg

Trade Name(s):

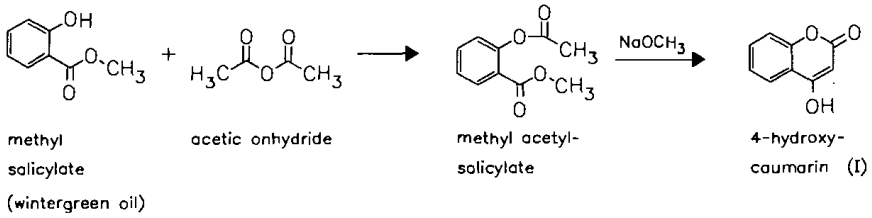
D:	Rantudil (Bayer; 1980)	I:	Acemix (Bioprogress)	J:	Rantudil (Kowa; 1984)
GB:	Emflex (Merck)		Solar (Bioindustria)		

Acenocoumarol

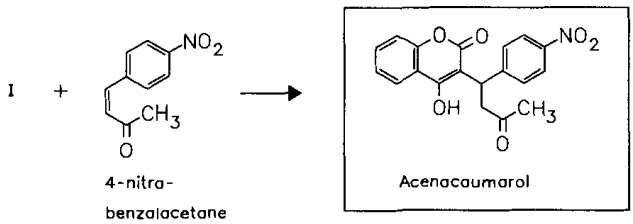
(Acenocumarin; Nicoumalone)

ATC: B01AA07
Use: anticoagulant

RN: 152-72-7 MF: $C_{19}H_{15}NO_6$ MW: 353.33 EINECS: 205-807-3
LD_{50}: 115 mg/kg (M, i.p.); 1470 mg/kg (M, p.o.);
513 mg/kg (R, p.o.)
CN: 4-hydroxy-3-[1-(4-nitrophenyl)-3-oxobutyl]-2*H*-1-benzopyran-2-one



methyl salicylate (wintergreen oil) | acetic anhydride | methyl acetylsalicylate | 4-hydroxycoumarin (I)



Reference(s):
US 2 648 862 (Geigy; 1953; CH-prior. 1950).

Formulation(s): tabl. 1 mg, 4 mg

Trade Name(s):

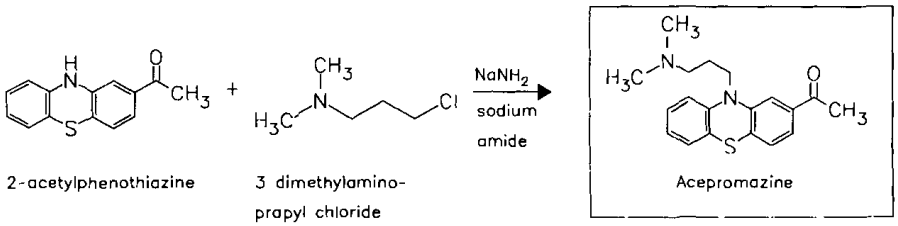
D:	Sintrom (Geigy); wfm	GB:	Sinthrome (Geigy)	J:	Sintrom (Ciba-Geigy)
F:	Sintrom (Novartis)	I:	Sintrom (Novartis)	USA:	Sintrom (Geigy); wfm

Acepromazine

ATC: N05AA04
Use: neuroleptic, anti-emetic, tranquilizer

RN: 61-00-7 MF: $C_{19}H_{22}N_2OS$ MW: 326.46 EINECS: 200-496-0
LD_{50}: 59 mg/kg (M, i.v.)
CN: 1-[10-[3-(dimethylamino)propyl]-10*H*-phenothiazin-2-yl]ethanone

maleate (1:1)
RN: 3598-37-6 MF: $C_{19}H_{22}N_2OS \cdot C_4H_4O_4$ MW: 442.54 EINECS: 222-748-9
LD_{50}: 65 mg/kg (M, i.v.);
95 mg/kg (R, i.v.); 400 mg/kg (R, p.o.)



2-acetylphenothiazine + 3 dimethylamino-propyl chloride → Acepromazine

Reference(s):
DE 1 049 865 (Bayer; appl. 7.9.1955).
Schmitt, J. et al.: Bull. Soc. Chim. Fr. (BSCFAS) **1957**, 938, 1474.

Formulation(s): drops 1 mg/10 drops; syrup 2.5 mg; tabl. 10 mg (as maleate)

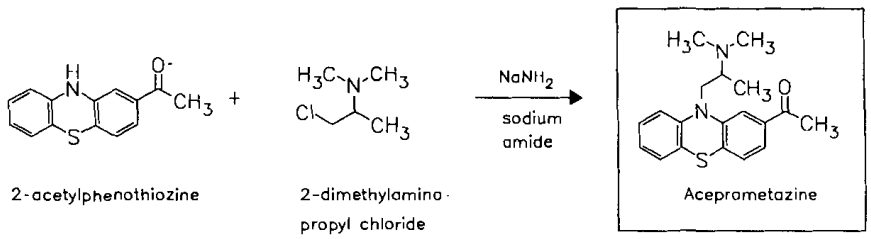
Trade Name(s):
F: Noctran (Menarini)-comb. J: Plebal (Fujinaga-Sankyo)-comb.

Acepromethazine

ATC: N05AA
Use: neuroleptic, antitussive

RN: 13461-01-3 MF: $C_{19}H_{22}N_2OS$ MW: 326.46 EINECS: 236-661-9
LD_{50}: 517 mg/kg (M, p.o.)
CN: 1-[10-[2-(dimethylamino)propyl]-10*H*-phenothiazin-2-yl]ethanone

maleate
RN: 7455-18-7 MF: $C_{19}H_{22}N_2OS \cdot C_4H_4O_4$ MW: 442.54



2-acetylphenothiozine + 2-dimethylamino-propyl chloride → Acepromethazine

Reference(s):
DE 1 049 865 (Bayer; appl. 7.9.1955).

Formulation(s): tabl. 13.55 mg (as maleate in combination with 400 mg meprobramate)

Trade Name(s):

D:	Clindorm (Midy)-comb.		Noctran (Menarini)-comb.
F:	Mépronizine (Sanofi)-comb.	J:	Noctran (Clin-Midy-Sanofi); wfm

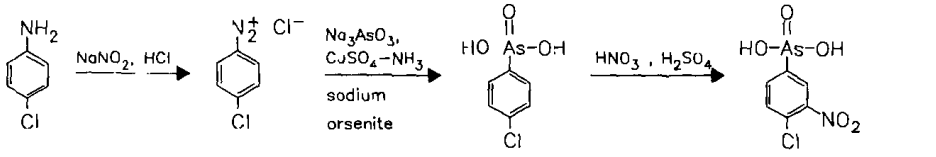
Acetarsol

(Acetarsone)

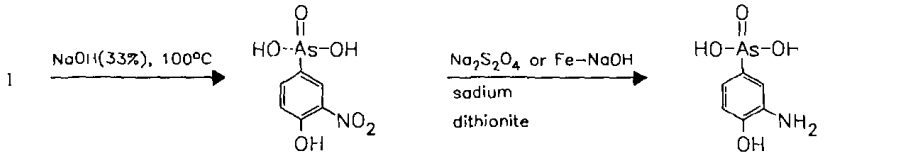
ATC: A07AX02; G01AB01; P01CD02
Use: antiprotozoal (trichomonas)

RN: 97-44-9 MF: $C_8H_{10}AsNO_5$ MW: 275.09 EINECS: 202-582-3
LD_{50}: 180 mg/kg (M, i.v.); 4 mg/kg (M, p.o.)
CN: [3-(acetylamino)-4-hydroxyphenyl]arsonic acid

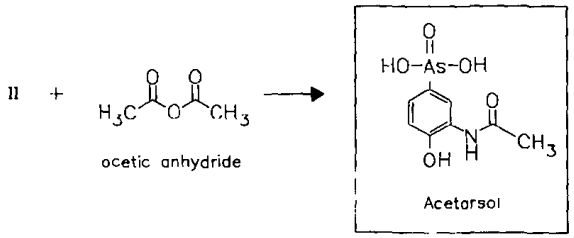
monosodium salt
RN: 5892-48-8 MF: $C_8H_9AsNNaO_5$ MW: 297.07 EINECS: 227-573-1



4-chloroaniline — 4-chlorobenzenediazonium chloride — 4-chlorophenylarsonic acid — 4-chloro-3-nitrophenylarsonic acid (I)



4-hydroxy-3-nitrophenylarsonic acid — 3-amino-4-hydroxyphenylarsonic acid (II)



Reference(s):
Raiziss, G.W.; Gavron, J.L.: J. Am. Chem. Soc. (JACSAT) **43**, 583 (1921).
Raiziss, G.W.; Fisher, B.C.: J. Am. Chem. Soc. (JACSAT) **48**, 1323 (1926).
DRP 250 264 (H. Bart; appl. 1910).
DRP 245 536 (Hoechst; appl. 1911).
DRP 224 953 (Hoechst; appl. 1909).

Formulation(s): collutorium (mouth wash) 0.5 mg/100 g

Trade Name(s):

F:	Arpha collutoire (Fournier)-comb.; wfm	Gynoplix (Doms-Adrian); wfm	Humex collutoire (Fournier)-comb.; wfm
	Collargent acétarsol (Sarbach)-comb.; wfm	Gynoplix (Théraplix)-comb.; wfm	Humex Fournier collutoire (Fournier)-comb.; wfm

	Polygynax (Innothéra)-comb.; wfm		Sanogyl (Pharmascience)-comb.; wfm	I:	Gynoplix (Vaillant)
	Polygynax Virgo (Innothéra)-comb.; wfm	GB:	Sanogyl (Vilette); wfm	J:	Neo Osvarsan (Banyu)
	Pyorex (Bailly-Speab)-comb.; wfm		Pyorex (Bengue)-comb.; wfm		Osvarsan (Banyu)
			S. V. C. (May & Baker)		

Acetazolamide

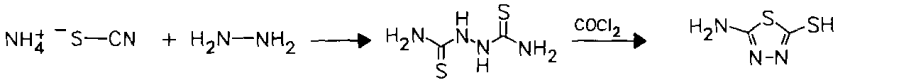
(Acetazoleamide)

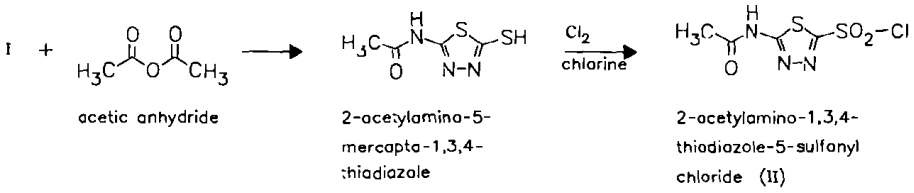
ATC: S01EC01
Use: diuretic

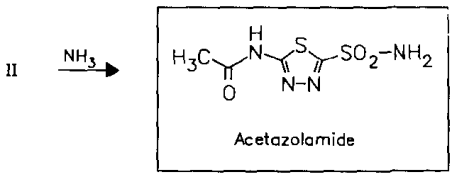
RN: 59-66-5 MF: $C_4H_6N_4O_3S_2$ MW: 222.25 EINECS: 200-440-5

LD_{50}: 1175 mg/kg (M, i.p.); >3000 mg/kg (M, i.v.); 4300 mg/kg (M, p.o.); >3000 mg/kg (M, s.c.); 2750 mg/kg (R, i.p.);
>1500mg/kg (g. p., s.c.)
>2000 mg/kg (dog, i.v.);

CN: *N*-[5-(aminosulfonyl)-1,3,4-thiadiazol-2-yl]acetamide







Reference(s):
US 2 554 816 (American Cyanamid; 1951; prior. 1950).
Roblin, R.O.; Clapp, J.W.: J. Am. Chem. Soc. (JACSAT) **72**, 4890 (1950).

similar process:
US 2 980 679 (Omikron-Gagliardi; 18.4.1961; I-prior. 4.4.1957).

Formulation(s): amp. 500 mg; cream 10 %; lyo. 500 mg; powder 500 mg; s. r. cps. 500 mg; tabl. 125 mg, 250 mg

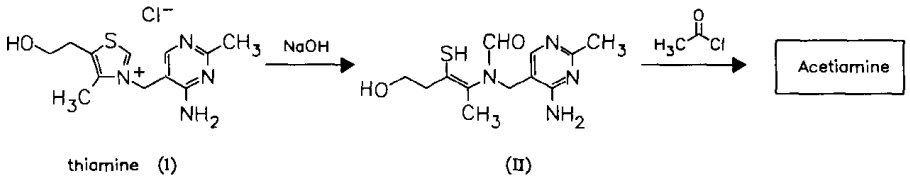
Trade Name(s):

D:	Diamox (Lederle)		Diamox Sustets (Lederle); wfm		Diamox S. R. (Lederle-Takeda)
	Diuramid (medpharm)				
	Glaupax (CIBA Vision)	I:	Diamox (Cyanamid)		Didoc (Sawai)
F:	Défiltran (Labs. Jumer)	J:	Acetamox (Santen)		Donmox (Hotta)
	Diamox (Théraplix)		Atenezol (Tsuruhara)		Zohnox (Konto)
GB:	Diamox (Storz)		Diamox (Lederle-Takeda)	USA:	Diamox (Lederle)

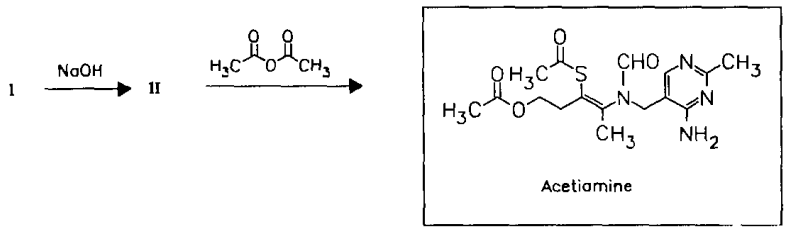
Acetiamine

ATC: A11
Use: vitamin B_1-derivative, neurotropic analgesic

RN: 299-89-8 MF: $C_{16}H_{22}N_4O_4S$ MW: 366.44
CN: ethanethioic acid *S*-[1-[2-(acetyloxy)ethyl]-2-[[(4-amino-2-methyl-5-pyrimidinyl)methyl]formylamino]-1-propenyl] ester



thiamine (I) (q. v.) (II)



Reference(s):
US 2 752 348 (Takeda; 1956; J-prior. 1952).
Matsukawa, T.; Kawasaki, H.: Yakugaku Zasshi (YKKZAJ) **23**, 705 (1953).
Gauthier, B. et al.: Ann. Pharm. Fr. (APFRAD) **21**, 655 (1963).

Formulation(s): drg. 50 mg

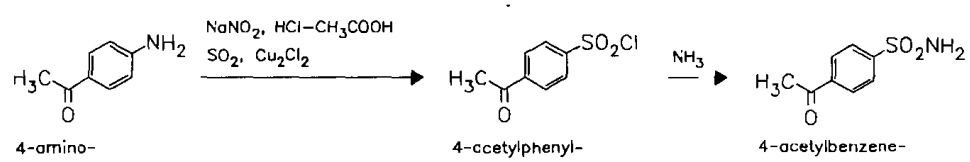
Trade Name(s):

D:	Thiancurone (Rhône-Poulenc); wfm	F:	Algo-Névriton (Pharmuka); wfm

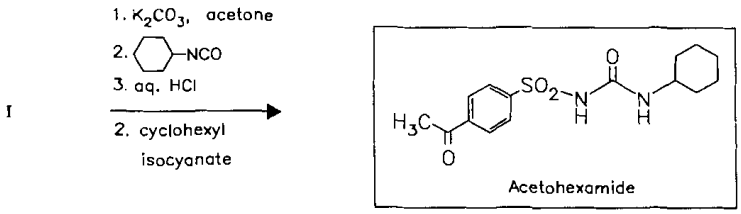
Acetohexamide
(Cyclamide)

ATC: A10BB31
Use: antidiabetic

RN: 968-81-0 MF: $C_{15}H_{20}N_2O_4S$ MW: 324.40 EINECS: 213-530-4
LD_{50}: >2500 mg/kg (M, p.o.); 5g/kg (R, p.o.)
CN: 4-acetyl-*N*-[(cyclohexylamino)carbonyl]benzenesulfonamide



4-amino-acetophenone — 4-acetylphenyl-sulfonyl chloride — 4-acetylbenzene-sulfonamide (I)



Reference(s):
US 3 320 312 (Lilly; 16.5.1967; prior. 28.4.1960).
DE 1 177 631 (Lilly; appl. 21.4.1961; USA-prior. 28.4.1960).
DE 1 135 891 (Hoechst; appl. 30.6.1960).

Formulation(s): tabl. 250 mg, 500 mg

Trade Name(s):

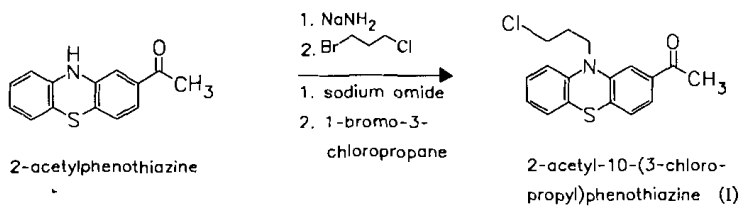
GB:	Dimelor (Lilly); wfm	J:	Dimelin (Shionogi)
I:	Dimelor (Lilly); wfm	USA:	Dymelor (Lilly)

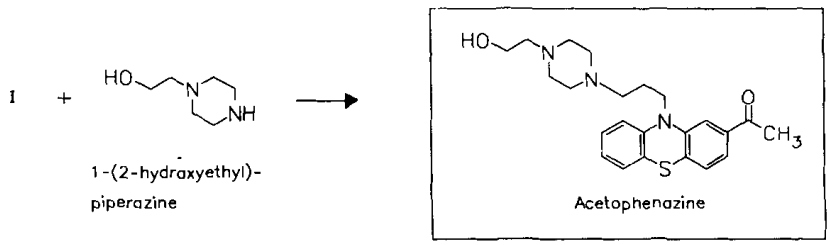
Acetophenazine

ATC: N05AB07
Use: neuroleptic, antipsychotic

RN: 2751-68-0 MF: $C_{23}H_{29}N_3O_2S$ MW: 411.57
CN: 1-[10-[3-[4-(2-hydroxyethyl)-1-piperazinyl]propyl]-10*H*-phenothiazin-2-yl]ethanone

maleate (1:2)
RN: 5714-00-1 MF: $C_{23}H_{29}N_3O_2S \cdot 2C_4H_4O_4$ MW: 643.71 EINECS: 227-202-3
LD_{50}: 71 mg/kg (M, i.v.);
60 mg/kg (R, i.p.); 39 mg/kg (R, i.v.); 415 mg/kg (R, p.o.)





Reference(s):
US 2 985 654 (Schering Corp.; 23.5.1961; prior. 21.9.1956).

Formulation(s): tabl. 20 mg (as dimaleate)

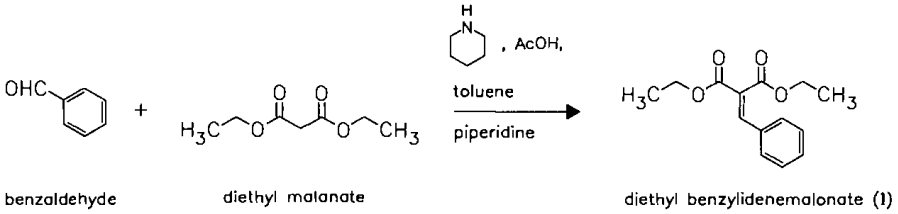
Trade Name(s):
USA: Tindal (Schering); wfm

Acetorphan

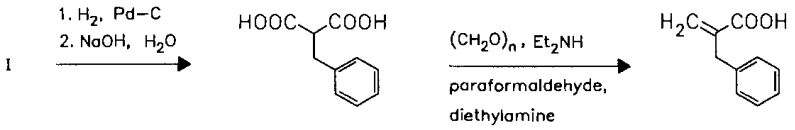
(Racecadotril)

ATC: A07XA04
Use: antisecretory, enkephalinaseinhibitor

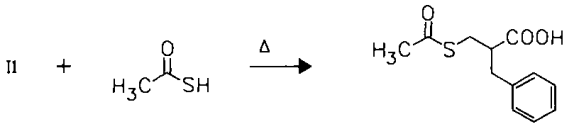
RN: 81110-73-8 MF: $C_{21}H_{23}NO_4S$ MW: 385.48
CN: (±)-*N*-[2-[(Acetylthio)methyl]-1-oxo-3-phenylpropyl]glycine phenylmethyl ester



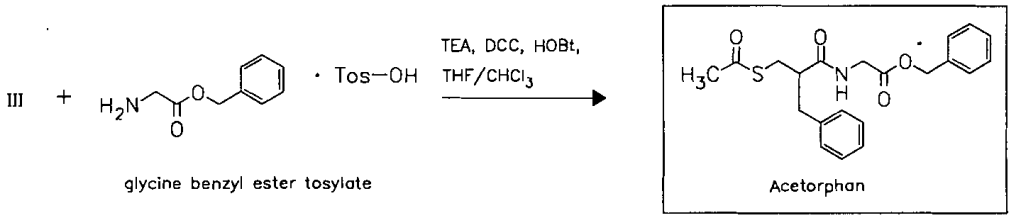
benzaldehyde diethyl malonate diethyl benzylidenemalonate (I)



benzylmolonic acid 2-benzylacrylic acid (II)

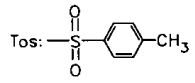


thioacetic acid (±)-2-acetylthiomethyl-3-phenylpropianic acid (III)



glycine benzyl ester tosylate

Acetorphan



Reference(s):
EP 38 758 (Roques, B. et al.; appl. 17.4.1981; F-prior. 17.4.1980).
EP 729 936 (Soc. Civile Bioprojet; appl. 1.3.1996; F-prior. 3.3.1995).

synthesis of III:
Mannich, C.; Ritsert, K.: Ber. Dtsch. Chem. Ges. (BDCGAS) **57**, 1116 (1924).

Formulation(s): cps. 100 mg

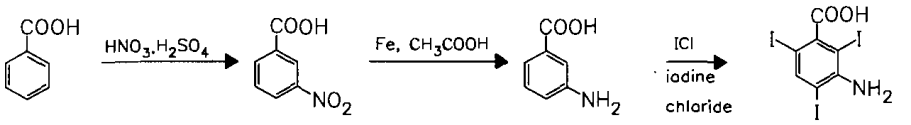
Trade Name(s):
F: Tiorfan (Bioprojet; 1993)

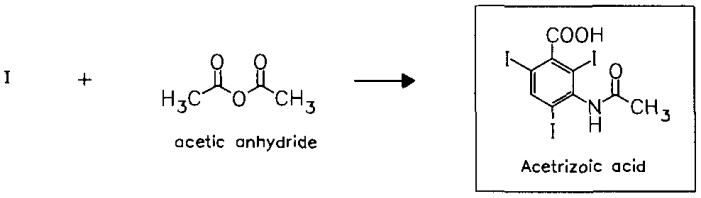
Acetrizoic acid

ATC: V08AA07
Use: X-ray contrast medium

RN: 85-36-9 MF: $C_9H_6I_3NO_3$ MW: 556.86 EINECS: 201-600-7
LD_{50}: 8000 mg/kg (M, i.v.); 20 g/kg (M, p.o.)
CN: 3-(acetylamino)-2,4,6-triiodobenzoic acid

meglumine salt (1:1)
RN: 22154-43-4 MF: $C_9H_6I_3NO_3 \cdot C_7H_{17}NO_5$ MW: 752.08
LD_{50}: 10.1 g/kg (M, i.v.)
sodium salt
RN: 129-63-5 MF: $C_9H_5I_3NNaO_3$ MW: 578.85 EINECS: 204-956-1
LD_{50}: 12156 mg/kg (M, i.m.); 7800 mg/kg (M, i.v.);
6400 mg/kg (R, i.v.);
5200 mg/kg (rabbit, i.v.);
5600 mg/kg (cat, i.v.);
6300 mg/kg (dog, i.v)





Reference(s):
US 2 611 786 (Mallinckrodt; 1952; appl. 1950; prior. 21.7.1948).
Wallingford et al.: J. Am. Chem. Soc. (JACSAT) **74**, 4365 (1952).

3-amino-2,4,6-triiodobenzoic acid:
Kretzer: Ber. Dtsch. Chem. Ges. (BDCGAS) **30**, 1944 (1897).

Formulation(s): vial. 250 mg/ml, 500 mg/ml

Trade Name(s):

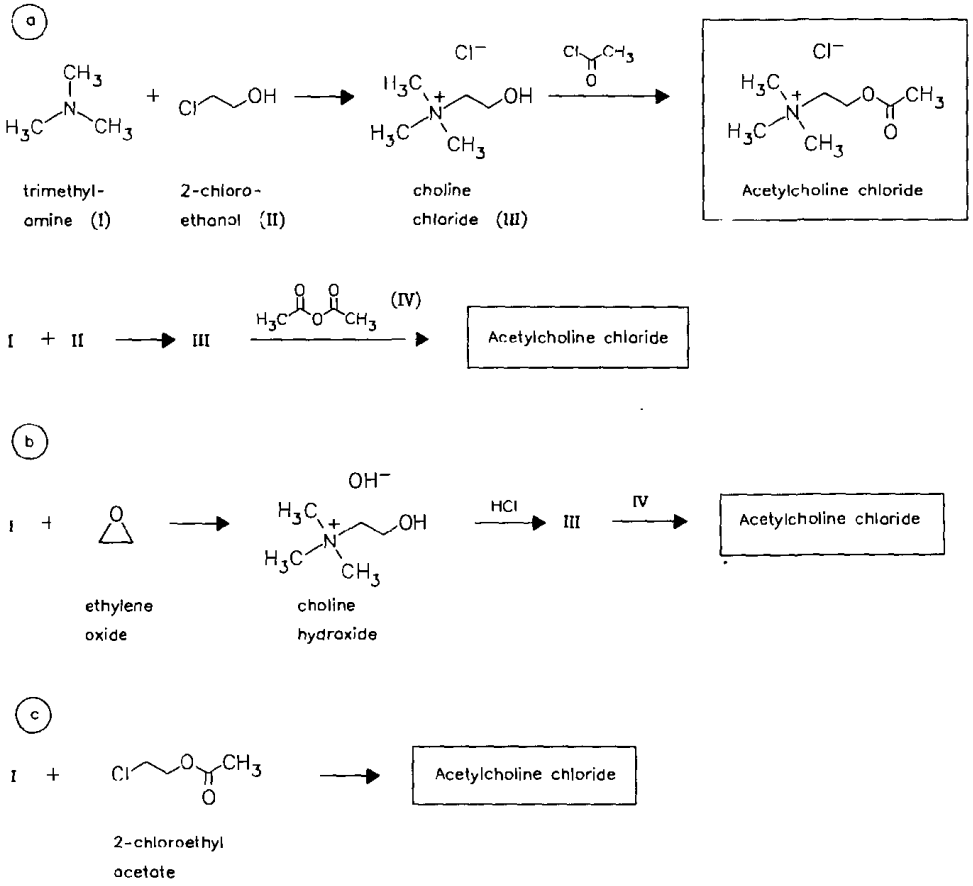
F:	Vasurix (Guerbet); wfm	J:	Diaginol (Banyu); wfm	Pyelokon-R
GB:	Diaginol (May & Baker); wfm	USA:	Cystocon (Mallinckrodt); wfm	(Mallinckrodt); wfm Salpix (Ortho); wfm

Acetylcholine chloride

ATC: S01EB09
Use: parasympathomimetic, miotic, vasodilator (peripheral)

RN: 60-31-1 MF: $C_7H_{16}ClNO_2$ MW: 181.66 EINECS: 200-468-8
LD_{50}: 10 mg/kg (M, i.v.); 3 g/kg (M, p.o.);
22 mg/kg (R, i.v.); 2500 mg/kg (R, p.o.)
CN: 2-(acetyloxy)-*N*,*N*,*N*-trimethylethanaminium chloride

hydroxide
RN: 56-13-3 MF: $C_7H_{17}NO_3$ MW: 163.22
bromide
RN: 66-23-9 MF: $C_7H_{16}BrNO_2$ MW: 226.11 EINECS: 200-622-4
LD_{50}: 170 mg/kg (M, s.c.)



Reference(s):
Baeyer, A. v.: Justus Liebigs Ann. Chem. (JLACBF) **142**, 235 (1867).
Nothnagel: Arch. Pharm. (Weinheim, Ger.) (ARPMAS) **232**, 265 (1894).
Fourneau, E.; Page, H.J.: Bull. Soc. Chim. Fr. (BSCFAS) [4] **15**, 544 (1914).
DE 801 210 (BASF; appl. 1948).
US 1 957 443 (Merck & Co.; 1934; appl. 1931).
US 2 012 268 (Merck & Co.; 1935; appl. 1931).
US 2 013 536 (Merck & Co.; 1935; appl. 1931).

Formulation(s): amp. 20 mg; eye drops 1 %

Trade Name(s):

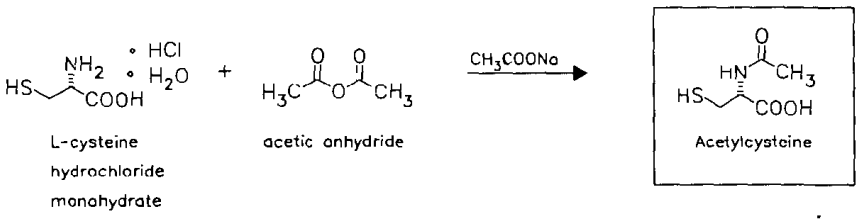
D:	Miochol-E (CIBA Vision)	J:	Acetylcholine (Roche)
I:	Farmigea acetilcolina (Farmigea); wfm		Neucholin-A (Zeria); wfm Ovisot (Daiichi); wfm

Acetylcysteine

ATC: R05CB01; S01XA08; V03AB23
Use: mucolytic agent

RN: 616-91-1 MF: $C_5H_9NO_3S$ MW: 163.20 EINECS: 210-498-3
LD_{50}: 400 mg/kg (M, i.p.); 3800 mg/kg (M, i.v.); 7888 mg/kg (M, p.o.);
1140 mg/kg (R, i.v.); 5050 mg/kg (R, p.o.);
700 mg/kg (dog, i.p.); 700 mg/kg (dog, i.v.); >1 g/kg (dog, p.o.)
CN: *N*-acetyl-L-cysteine

monosodium salt
RN: 19542-74-6 MF: $C_5H_8NNaO_3S$ MW: 185.18 EINECS: 243-143-6
LD_{50}: 3800 mg/kg (M, i.v.);
2559 mg/kg (R,i.v.)
monoammonium salt
RN: 50807-78-8 MF: $C_5H_9NO_3S \cdot H_3N$ MW: 180.23



Reference(s):
US 3 091 569 (Mead Johnson;. 28.5.1963; appl. 26.8.1960).
US 3 184 505 (Mead Johnson; 18.5.1965; appl. 18.6.1962).
Smith, H.A.; Gorin, G.: J. Org. Chem. (JOCEAH) **26**, 820 (1961).

ammonium salt (mucolysis of bronchial mucus by nebulization):
DOS 2 305 271 (Bristol-Myers; appl. 2.2.1973; USA-prior. 3.2.1972).

Formulation(s): amp. 300 mg (as monosodium salt); cps. 200 mg; eff. tabl. 100 mg, 200 mg, 600 mg; f. c. tabl. 100 mg, 200 mg, 600 mg; gran. 10 mg, 100 mg, 200 mg, 600 mg; lyo. for syrup 100 mg; syrup 200 mg/10 ml; tabl. 100 mg, 200 mg, 600 mg

Trade Name(s):

D: ACC (Hexal)
Acemuc (betapharm)
Fluimucil-100/-200 (Zambon)
Rinofluimucil (Inpharzam)-comb.
numerous combination and generic preparations

F: Broncoclar (Oberlin)
Codotussyl (Whitchall)
Euronac (Europhta)
Exomuc (Bouchara)
Fluimucil (Zambon)
Fluimucil Antibiotic 750 (Zambon)
Genac (Génévrier)
Mucolator (Abbott)
Mucomyst (Bristol-Myers Squibb)
Mucothiol (SCAT)
Rhinofluimucil (Débat)-comb.
Solmucol (Génévrier)
Tixair (Byk)

GB: Ilube (Alcon)-comb.
Parvolex (Evans)

I: Brunac (Bruschettini)
Fluimucil (Zambon)
Mucisol (Deca)
Rinofluimucil (Zambon)-comb.

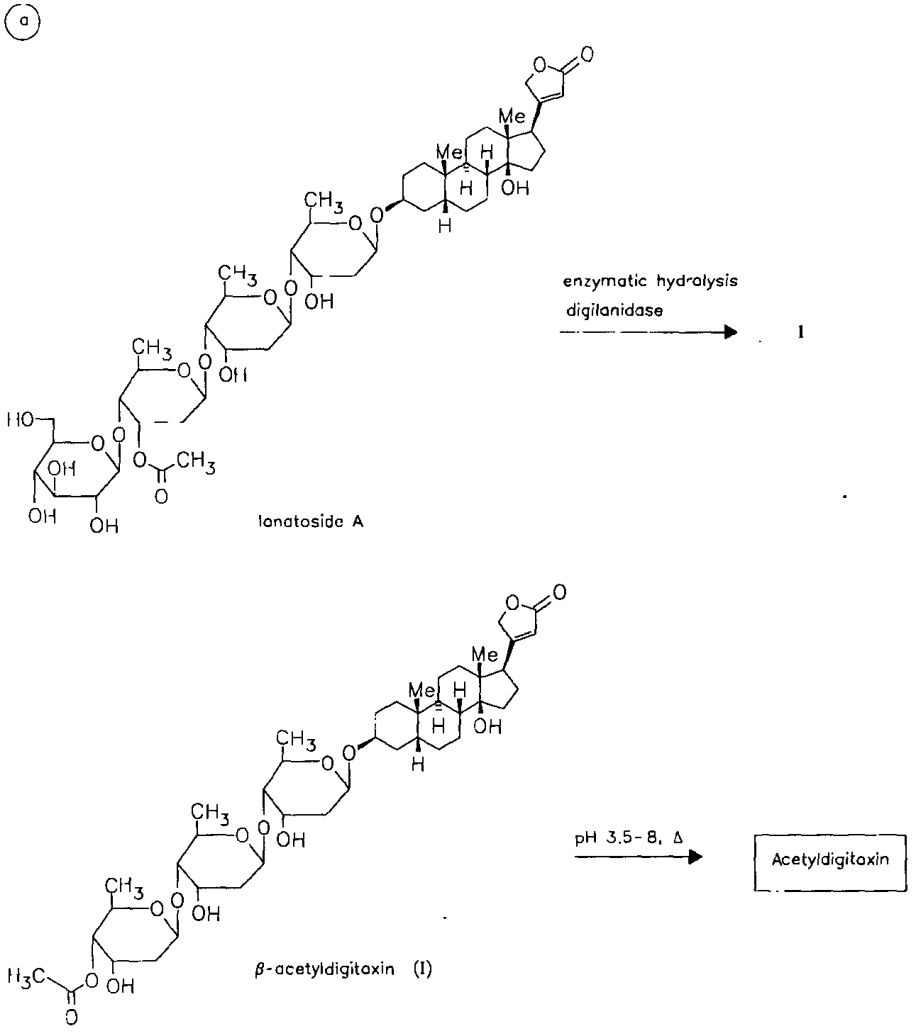
J: Acetein (Senju)
Mucofilin Sol. (Eisai)

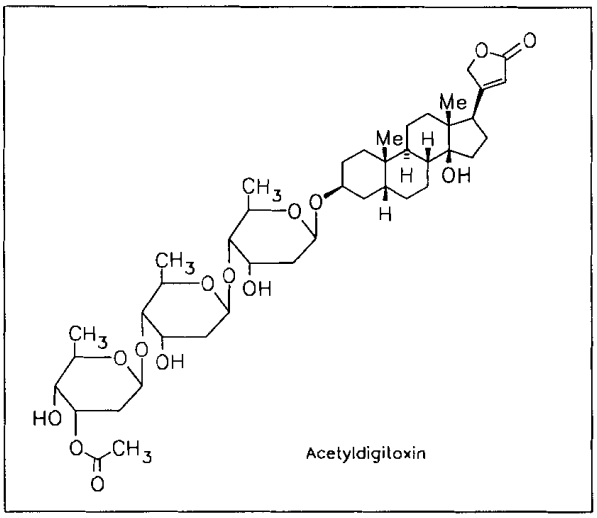
USA: Mucosit (Dey)

Acetyldigitoxin

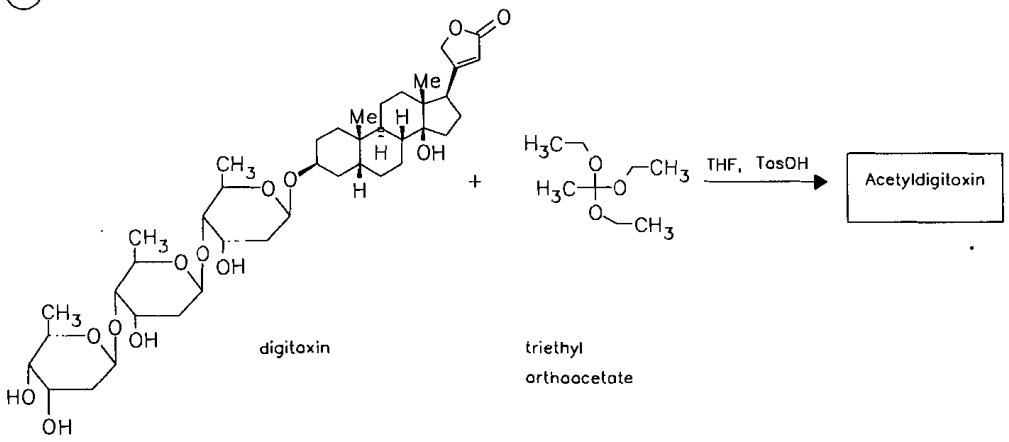
ATC: C01AA01
Use: cardiotonic, cardiac glycoside

RN: 1111-39-3 MF: $C_{43}H_{66}O_{14}$ MW: 806.99 EINECS: 214-178-4
LD_{50}: >30 mg/kg (g. p., p.o.);
514 µg/kg (cat, i.v.); 250 µg/kg (cat, p.o.)
CN: (3β,5β)-3-[(*O*-3-*O*-acetyl-2,6-dideoxy-β-D-*ribo*-hexopyranosyl-(1→4)-*O*-2,6-dideoxy-β-D-*ribo*-hexopyranosyl-(1→4)-2,6-dideoxy-β-D-*ribo*-hexopyranosyl)oxy]-14-hydroxycard-20(22)-enolide





b



Reference(s):

a Stoll, A. et al.: Helv. Chim. Acta (HCACAV) **34**, 397 (1951).
Gisvold, O.: J. Pharm. Sci. (JPMSAE) **61**, 1320 (1972).
HU 155 716 (Richter Gedeon; appl. 20.1.1968).
DE 925 047 (Sandoz; appl. 1954; CH-prior. 1952).

b DE 2 010 422 (Boehringer Ing.; appl. 5.3.1970).

alternative synthesis:

DE 2 206 737 (Boehringer Mannh.; appl. 12.2.1972) (α-Acetyldigoxin, q. v.).

Formulation(s): tabl. 0.2 mg

Trade Name(s):

D: Acylanid (Sandoz); wfm F: Acylanid (Sandoz); wfm USA: Acylanid (Sandoz); wfm

α-Acetyldigoxin

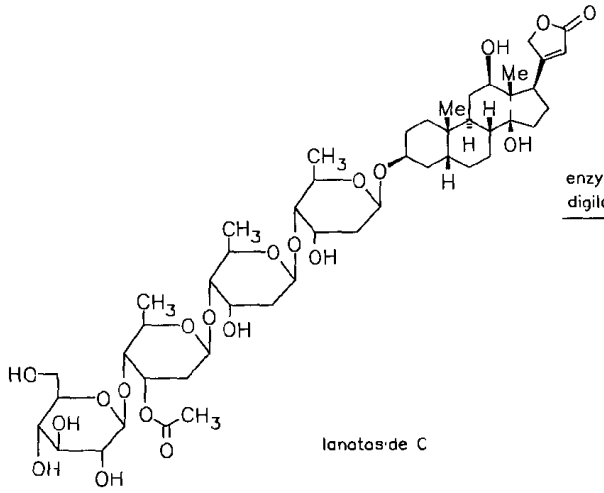
ATC: C01AA02
Use: cardiotonic, cardiac glycoside

RN: 5511-98-8 MF: $C_{43}H_{66}O_{15}$ MW: 822.99 EINECS: 226-855-1

LD_{50}: 3300 µg/kg (g. p., p.o.);
200 µg/kg (cat, p.o.)

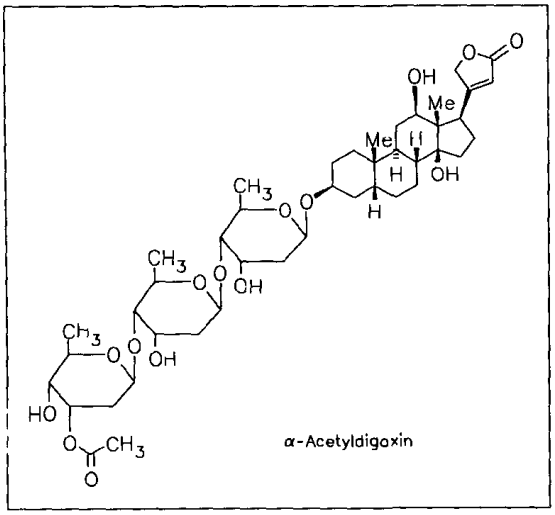
CN: (3β,5β,12β)-3-[(*O*-3-*O*-acetyl-2,6-dideoxy-β-D-*ribo*-hexopyranosyl-(1→4)-*O*-2,6-dideoxy-β-D-*ribo*-hexopyranosyl-(1→4)-2,6-dideoxy-β-D-*ribo*-hexopyranosyl)oxy]-12,14-dihydroxycard-20(22)-enolide

(a)



enzymatic hydrolysis
digilanidase

α-Acetyldigoxin



(b)

digilanide

(lanatoside A, B, C)

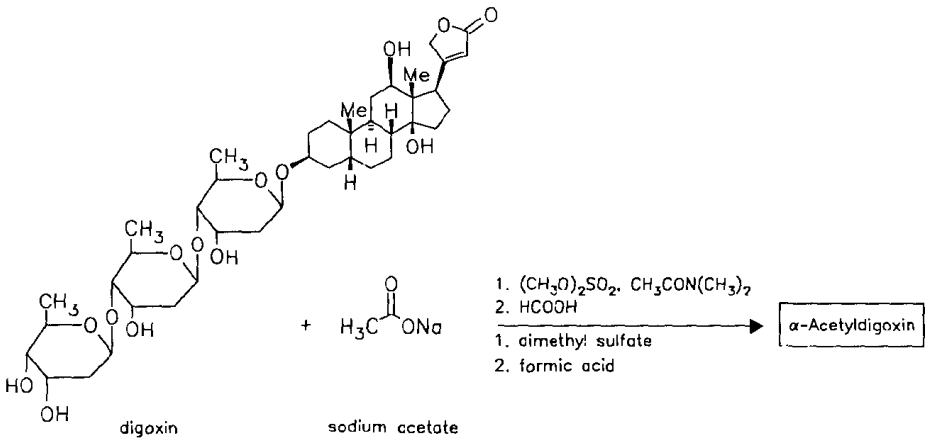
enzymatic hydrolysis

acetyldigitoxin
+
acetyldigoxin
+
acetylgitoxin

partition of the methanol solution between H_2O and $CHCl_3$

α-Acetyldigoxin

(c)



Reference(s):

a Fieser, L.F.; Fieser, M.: Steroide, p. 801, Verlag Chemie, Weinheim 1961.
b GB 1 162 614 (Heilmittelwerke Wien; appl. 1.2.1968; A-prior. 7.2.1967).
Gisvold, O.: J. Pharm. Sci. (JPMSAE) **61**, 1320 (1972).

alternative syntheses:

DE 2 010 422 (Boehringer Ing.; appl. 5.3.1970). (Acetyldigitoxin, q. v.).
Rietbrock, N.; Kuhlmann, J.: Naunyn-Schmiedeberg's Arch. Pharmacol. (NSAPCC) **279**, 413 (1973).

Formulation(s): sol. 0.5 mg/ml; tabl. 0.25 mg, 0.2 mg

Trade Name(s):

D:	Card-Hydergin (Sandoz)-comb.; wfm	Lanadigin (Promonta); wfm	Nitro-Sandolanid (Sandoz)-comb.; wfm
	Digi-Complamin (Beecham-Wülfing)-comb.; wfm	Lanadigin EL (Promonta); wfm	Sandolanid (Sandoz)
		Lanadigin + Theophyllin (Promonta)-comb.; wfm	F: Acygoxine (Sandoz); wfm
			I: Cedigossina (Sandoz)

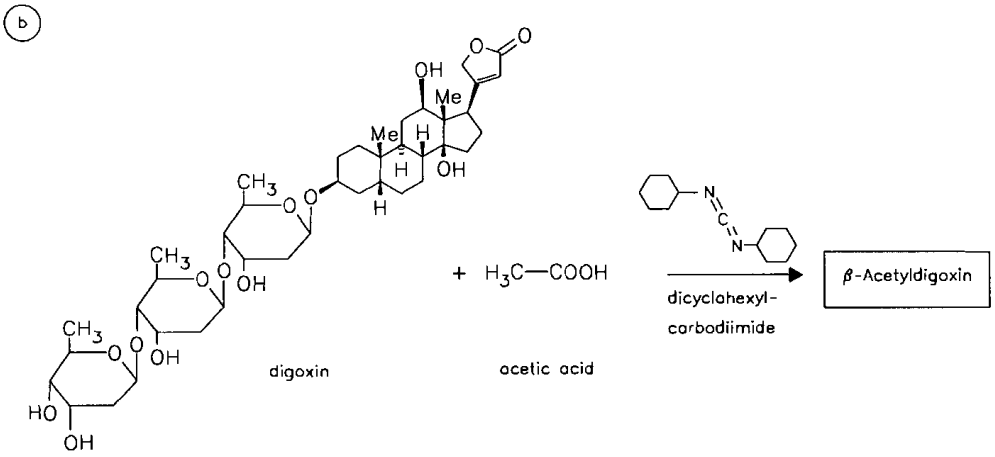
β-Acetyldigoxin

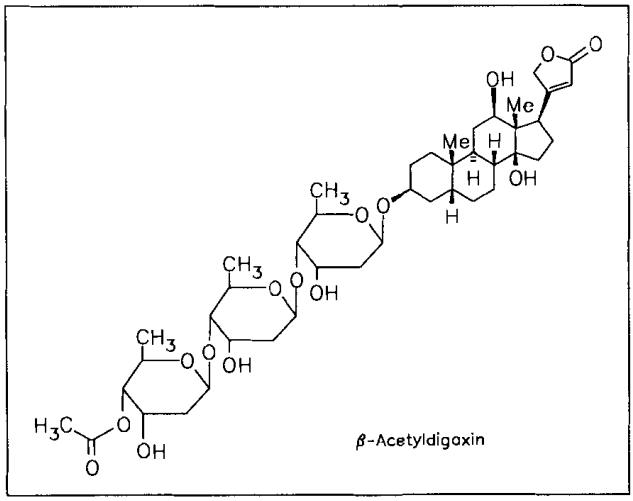
ATC: C01AA02
Use: cardiotonic, cardiac glycoside

RN: 5355-48-6 MF: $C_{43}H_{66}O_{15}$ MW: 822.99 EINECS: 226-337-5
LD_{50}: 2400 µg/kg (g. p., p.o.);
422 µg/kg (dog, p.o.)
CN: (3β,5β,12β)-3-[(*O*-4-*O*-acetyl-2,6-dideoxy-β-D-*ribo*-hexopyranosyl-(1→4)-*O*-2,6-dideoxy-β-D-*ribo*-hexopyranosyl-(1→4)-2,6-dideoxy-β-D-*ribo*-hexopyranosyl)oxy]-12,14-dihydroxycard-20(22)-enolide

(a) isolation and extraction from the leaves of Digitalis lanata

(b)





Reference(s):

a Hopponen, R.E.; Gisvold, O.: J. Am. Pharm. Assoc. (JPHAA3) **41**, 146 (1952).
Rangaswami, S. et al.: Indian J. Pharm. (IJPAAO) **17**, 253 (1955).

b HU 7 147 (Richter Gedeon; appl. 5.6.1972).

alternative syntheses:

Haberland, G.: Arzneim.-Forsch. (ARZNAD) **15**, 481 (1965).
Graf, E.; Pfaff, J.: Arch. Pharm. (Weinheim, Ger.) (ARPMAS) **307**, 943 (1974).
DOS 2 826 532 (LEK tovarna farm.; appl. 16.6.1978; YU-prior. 22.6.1977).

medical use:

DOS 1 921 307 (Boehringer Ing.; appl. 25.4.1969) addition to DOS 1 767 553.

Formulation(s): tabl. 0.1 mg, 0.2 mg

Trade Name(s):

D: Beta-Acetyldigoxin (ratiopharm)
Beta-Acetyldigoxin R.A.N. = glycotop (R.A.N.)
Beta-Acetyldigoxin-ratiopharm 0,1 mg/0,2 mg (ratiopharm)
Digostada 0.2/-mite (Stadapharm)
Digostade (Stada)
Digotab (ASTA Medica AWD)
Digox (ct-Arzneimittel)
Digoxin-Didier (Hormosan)
Gladixol (Corax)

Kardiamed (Medice) Novodigal (Beiersdorf) Stillacor (Wolff)	I:	numerous combination preparations Beta-Acigoxia (Inverni della Beffa); wfm	Cardioreg (Nattermann); wfm

Acetylsalicylic acid

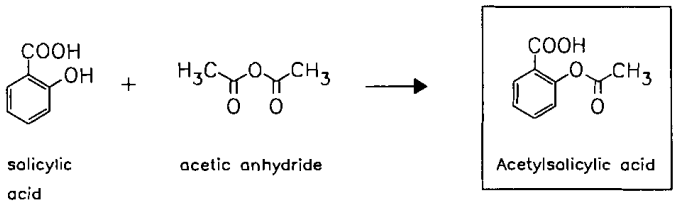
(Acidum acetylsalicylicum; Aspirin)

ATC: A01AD05; B01AC06; M01BA03; N02BA01; N02BA51

Use: analgesic, antipyretic, antirheumatic, platelet aggregation inhibitor

RN: 50-78-2 MF: $C_9H_8O_4$ MW: 180.16 EINECS: 200-064-1
LD_{50}: 280 mg/kg (M, i.p.); 250 mg/kg (M, p.o.); 1520 mg/kg (M, s.c.); 340 mg/kg (R, i.p.); 200 mg/kg (R, p.o.); 1600 mg/kg (R, s.c.); 1075 mg/kg (g. p., p.o.); 1010 mg/kg (rabbit, p.o.); 681 mg/kg (dog, i.v.); 700 mg/kg (dog, p.o.)
CN: 2-(acetyloxy)benzoic acid

aluminum salt
RN: 147-31-9 MF: $C_{27}H_{21}AlO_{12}$ MW: 564.44
calcium salt
RN: 69-46-5 MF: $C_{18}H_{14}CaO_8$ MW: 398.38 EINECS: 200-707-6
lithium salt
RN: 552-98-7 MF: $C_9H_7LiO_4$ MW: 186.09 EINECS: 209-029-5
sodium salt
RN: 493-53-8 MF: $C_9H_7NaO_4$ MW: 202.14 EINECS: 207-777-7
LD_{50}: 730 mg/kg (M, i.p.); 1450 mg/kg (R, i.p.)
magnesium salt
RN: 132-49-0 MF: $C_{18}H_{14}MgO_8$ MW: 382.61 EINECS: 205-062-4
LD_{50}: 620 mg/kg (M, s.c.)
lysine salt (1:1)
RN: 62952-06-1 MF: $C_9H_8O_4 \cdot C_6H_{14}N_2O_2$ MW: 326.35
LD_{50}: 950 mg/kg (M, i.v.); 3270 mg/kg (M, p.o.); 1525 mg/kg (R, i.v.); 4350 mg/kg (R, p.o.)



Reference(s):
Ullmanns Encykl. Tech. Chem., 3. Aufl., Vol. **13**, 90.
US 3 235 583 (Norwich Pharmacal; 15.2.1966; appl. 22.7.1964).

acetylation in presence of pyridine *for avoidance of formation of* acetylsalicylic anhydride *and* acetylsalicylsalicylic acid*:*
DOS 2 635 540 (A. L. de Week, H. Bundgaard; appl. 6.8.1976).

acetylation in presence of H_2SO_4*:*
US 2 731 492 (J. Kamlet; 1956; appl. 1954).

crystallization:
US 2 890 240 (Monsanto; 1959; appl. 1957).

aluminum salts:
DRP 585 986 (Chinoin; appl. 1931; H.-prior. 1931).
US 2 698 332 (Reheis Comp.; 1954; appl. 1951).
US 2 918 485 (Keystone Chemurgic Corp.; 1959; appl. 1955).
GB 888 666 (Hardman & Holden; appl. 1959).

aluminum acetylsalicylate glutaminate:
DOS 2 909 829 (Kyowa Hakko; appl. 13.3.1979; J-prior. 13.3.1978).

Formulation(s): cps. 325 mg, 500 mg, suppos. 125 mg, 150 mg, 300 mg; tabl. 50 mg, 75 mg, 100 mg, 300 mg, 500 mg

Trade Name(s):

D:
Alka-Seltzer (Bayer)
Aspirin (Bayer; 1899)
Aspisol (Bayer; as DL-lysine salt)
Aspro (Roche Nicholas)
ASS Dura (durachemie)
ASS-ratiopharm (ratiopharm)
Godamed (Pfleger)
Micristin (OPW)
Miniasal (OPW)
Romigal (Romogal-Werk)
Santasal (Merckle)
Togal (Togal)
numerous combination preparations

F:
Actron (Bayer)-comb.
Afebry (Galephar)-comb.
Alka-Seltzer (Bayer)-comb.
Antigrippine (SmithKline Beecham)-comb.
Aspégic 500 (Synthélabo; as lysine salt)
Aspirine Bayér (Bayer)
Aspirine duRhône (Bayer)
Aspirine pH 8 (3M Santé)
Aspirine Upsa (UPSA)
Aspirine Upsa Vitamine C (UPSA)-comb.
Aspirine Vitamine C (Oberlin)-comb.
Aspirisucre (Arkomedika)
Aspro (Nicholas)
Catalgine (Schwarz)
Claragine (Nicholas)
Kardégic (Synthélabo)
Rhonal (Théraplix)
Sargépirine (ASTA Médica)
Solupsan (UPSA)
numerous combination preparations

GB:
Angettes (Bristol-Myers)
Aspan (Hoechst)-comb.
Aspirin (Bayer)
Caprin (Sinclair)
Disprin CO (Reckitt & Colman)
Nu-Seals Aspirin (Lilly)
Post MI (Ashbourne)
numerous combination preparations

I:
Ac Acsal (Formulario Naz.; Tariff. Nazionale; Scfm; Icma; Farmacologico Milanese)
Acesal (Geymonat)
Alupir (Farmacologico Milanese; as aluminum salt)
Aspergum (Farmades)
Aspirina (Bayer)
Aspirinetta (Bayer)
Aspro (Roche)
Bufferin (Bristol-Myers Squibb)
Cemirit (Bayer)
Endydol (Guidotti)
Kilios (Carlo Erba)
numerous combination preparations

J:
generic preparations

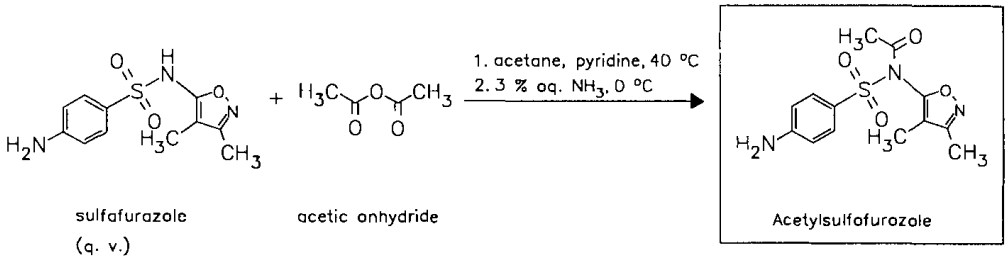
USA:
Acuprin (Richwood)
Ecotrin (SmithKline Beecham Consumer)
Equagesic (Wyeth-Ayerst)
Fiorinal (Novartis)
Halfprin (Kramer)
Norgeric (3M)
Percotan (Endo)
Roboxisal (Robins)

Acetylsulfafurazole

(Acetylsulfisoxazole; Sulfisoxazole Acetyl)

ATC: S01AB
Use: antibacterial

RN: 80-74-0 MF: $C_{13}H_{15}N_3O_4S$ MW: 309.35 EINECS: 201-305-3
CN: *N*-[(4-aminophenyl)sulfonyl]-*N*-(3,4-dimethyl-5-isoxazolyl)acetamide



Reference(s):
US 2 721 200 (Roche; 1955; appl. 1953).

Formulation(s): susp. 500 mg/5 ml

Trade Name(s):
USA: Eryzole (Alra) Pediazole (Ross)

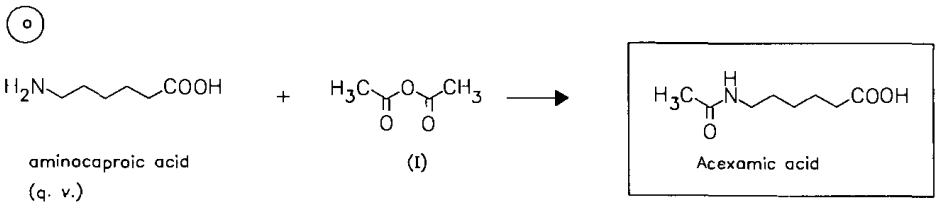
Acexamic acid

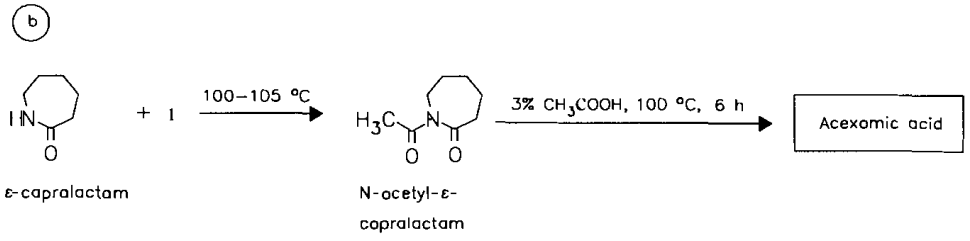
(Acide acexamique)

ATC: D03A
Use: antifibrinolytic

RN: 57-08-9 MF: $C_8H_{15}NO_3$ MW: 173.21 EINECS: 200-310-8
CN: 6-(acetylamino)hexanoic acid

sodium salt
RN: 7234-48-2 MF: $C_8H_{14}NNaO_3$ MW: 195.19 EINECS: 230-635-0





Reference(s):
Offe, H.A.: Z. Naturforsch., B: Anorg. Chem., Org. Chem., Biochem., Biophys., Biol. (ZENBAX) **2**, 182 (1947).
FR-M 2 332 (Rowa; appl. 1963).

Formulation(s): amp. 5 g (as sodium salt); cps. 300 mg (as zinc salt); ointment 5 % (as sodium salt); susp. 300 mg (as zinc salt)

Trade Name(s):
F: Plasténan (Isopharm) Plasténan Néomycine (Isopharm)-comb.
I: Plastenan (Italfarmaco); wfm

Aciclovir

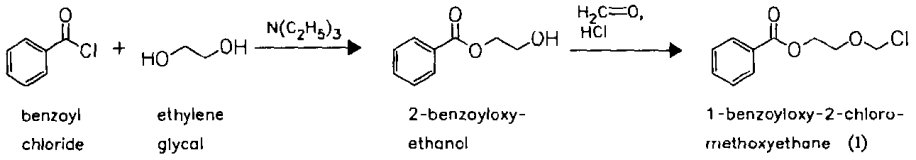
(Acyclovir; Acycloguanosine)

ATC: D06BB03; J05AB01; S01AD03
Use: antiviral

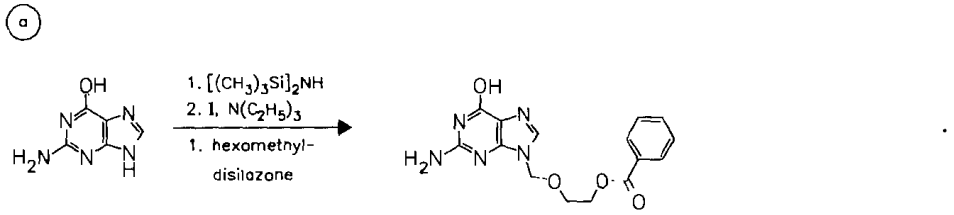
RN: 59277-89-3 MF: $C_8H_{11}N_5O_3$ MW: 225.21 EINECS: 261-685-1
LD_{50}: 1000 mg/kg (M, i.p.); 1118 mg/kg (M. i.v.); >10000 mg/kg (M, p.o.); 1118 mg/kg (M, s.c.); 860 mg/kg (R, i.p.); 910 mg/kg (R, i.v.); >20000 mg/kg (R, p.o.); 620 mg/kg (R, s.c.)
CN: 2-amino-1,9-dihydro-9-[(2-hydroxyethoxy)methyl]-6*H*-purin-6-one

monosodium salt

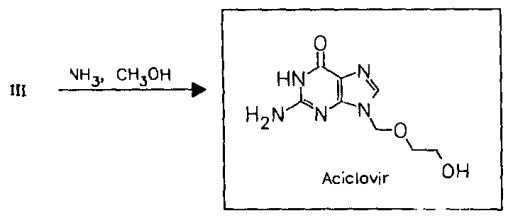
RN: 69657-51-8 MF: $C_8H_{10}N_5NaO_3$ MW: 247.19
LD_{50}: 999 mg/kg (M, i.p.); >10000 mg/kg (M, p.o.); 1210 mg/kg (R, i.p.); >600 mg/kg (R, i.v.); >20000 mg/kg (R, p.o.); 650 mg/kg (R, s.c.)

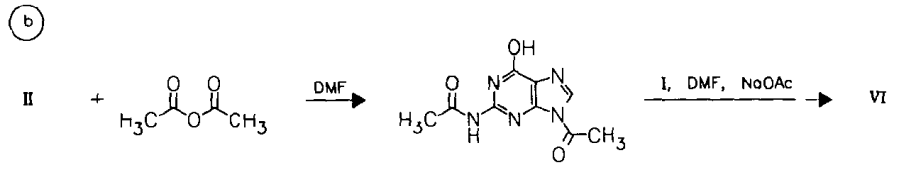


benzoyl chloride | ethylene glycol | 2-benzoyloxy-ethanol | 1-benzoyloxy-2-chloro-methoxyethane (I)

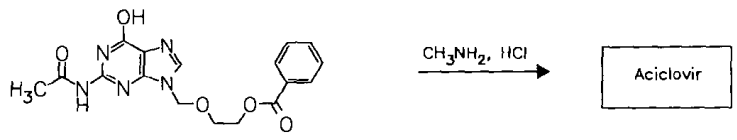


guanine (II) | 9-(2-benzoyloxyethoxy-methyl)guanine (III)



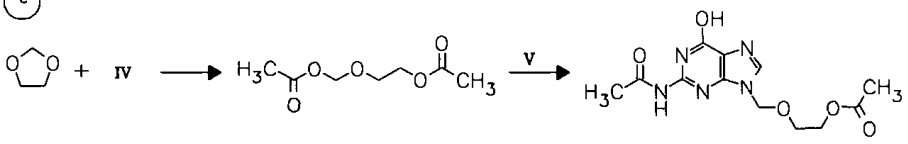


(IV) | N^2,9-diacetylguanine (V)



N^2-acetyl-9-(2-benzoyloxy-ethoxymethyl)guanine (VI)

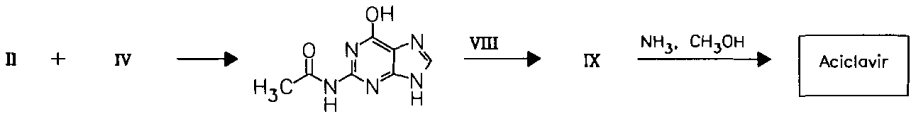
(c)



1,3-dioxolone (VII) — 2-acetoxyethyl ocetaxymethyl ether (VIII) — "diacetylaciclavir" (IX)

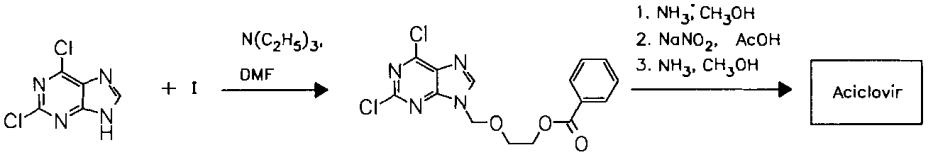
IX $\xrightarrow{NH_3,\ CH_3OH}$ Aciclovir

(d)



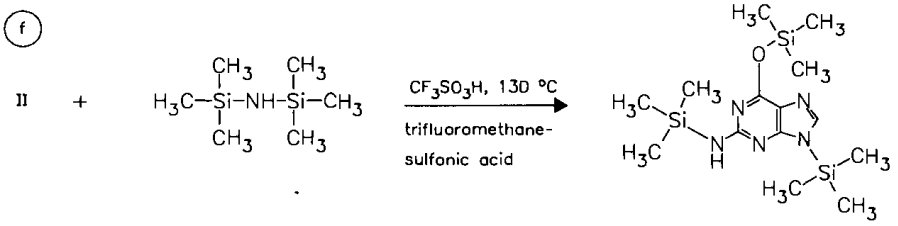
N^2-acetylguanine

(e)

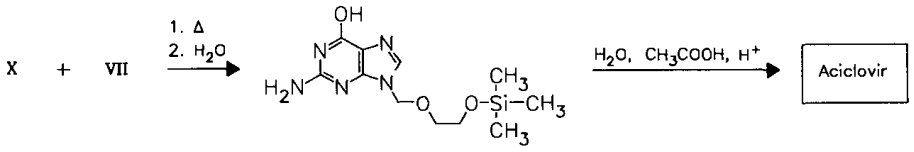


2,6-dichloropurine

(f)

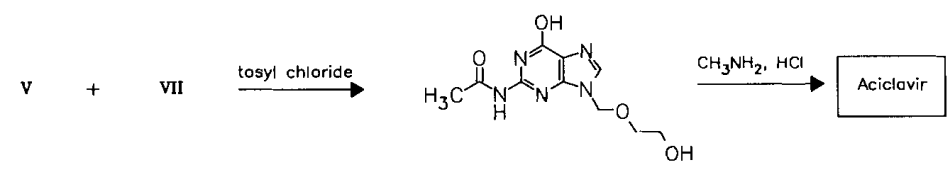


hexamethyldisilazane — (X)



9-(2-trimethylsilyloxyethoxymethyl)guanine

(g)



"monoocetylociclovir"

Reference(s):
Schaeffer, H.J. et al.: Nature (London) (NATUAS) **272**, 583 (1978).
DE 2 539 963 (Wellcome; appl. 2.9.1975; GB-prior. 2.9.1974).
US 4 199 574 (Wellcome; 22.4.1980; GB-prior. 2.9.1974).
GB 1 523 865 (Burroughs Wellcome; GB-prior. 2.9.1974).
c GB 1 567 671 (Wellcome; appl. 26.8.1977; USA-prior. 27.8.1976).
Matsumoto, H. et al.: Chem. Pharm. Bull. (CPBTAL) **36**, 1153 (1988).
f EP 709 385 (Roche; appl. 13.7.1995; USA-prior. 26.7.1994, 27.4.1995).

alternative synthesis from 4-aminoimidazole-5-carboxamide:
WO 9 011 283 (GEA Farm.; 4.10.1990; DK-prior. 20.3.1989).

alternative synthesis via formylguanine:
WO 9 507 281 (Recordati; appl. 3.2.1994; I-prior. 10.9.1993).

synthesis using 1,3-dioxolane:
US 5 567 816 (Syntex; appl. 27.4.1995; USA-prior. 27.7.1994).

improved procedures:
DE 19 536 164 (Boehringer Ingelheim; D-prior. 28.9.1995).
WO 9 724 357 (Mallinckrodt; appl. 17.12.1996; USA-prior. 28.12.1995).
DE 19 604 101 (B. Lehmann; 6.2.1996).
EP 806 425 (Lupin Lab.; EP-prior. 9.4.1996).
US 5 792 868 (Ajinomoto; appl. 18.3.1994; J-prior. 18.9.1991).

Formulation(s): cps. 200 mg; cream 50 mg/g; eye ointment 30 mg/g; susp. 8 %; tabl. 200 mg, 400 mg, 800 mg; vial 250 mg, 500 mg

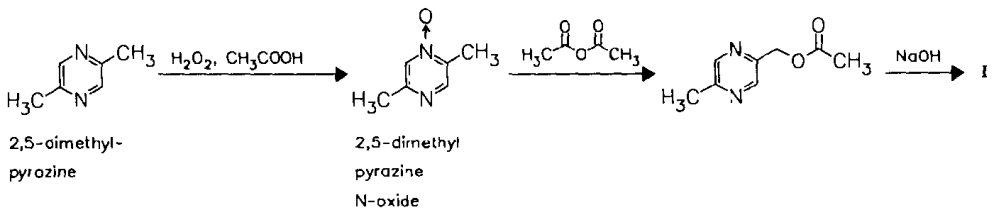
Trade Name(s):

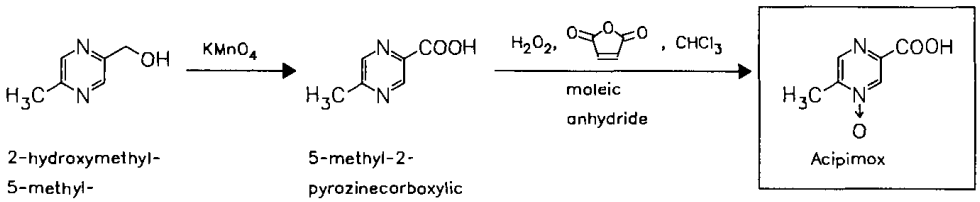
D:	Zovirax (Glaxo Wellcome; 1983)	Alovir (Foletto)			Sifiviral (SIFI)
		Avirase (Lampugnani)			Zovirax (Wellcome; 1984)
F:	Activir (Warner-Lambert)	Avyclor (Bioprogress)	J:		Zovirax (Seimitomo-Wellcome; 1985)
	Zovirax (Wellcome; 1983)	Cycloviran (Sigma-Tau)			
GB:	Herpetad (Boehringer Ing.)	Dravyr (Drug Research)	USA:		Zovirax (Glaxo Wellcome; 1985)
	Zovirax (Glaxo Wellcome; 1981)	Efrivir (Aesculapius-Bs)			
I:	Aciviran (Ripari-Gero)	Esavir (Boniscontro & Gazzone)			
	Acyvir (Delalande Isnardi)	Neviran (Coli)			

Acipimox

ATC: C10AD06
Use: antihyperlipoproteinemic

RN: 51037-30-0 MF: $C_6H_6N_2O_3$ MW: 154.13 EINECS: 256-928-3
LD_{50}: 3500 mg/kg (M, p.o.)
CN: 5-methylpyrazinecarboxylic acid 4-oxide





2-hydroxymethyl-5-methyl-pyrazine (I)

5-methyl-2-pyrazinecarboxylic acid

Reference(s):
US 4 002 750 (Carlo Erba; 11.1.1977; I-prior. 28.4.1972).
US 4 051 245 (Carlo Erba; 27.9.1977; I-prior. 28.4.1972).
DOS 2 319 834 (Carlo Erba; appl. 18.4.1973; I-prior. 28.4.1972).
GB 1 361 967 (Carlo Erba; appl. 12.4.1973; I-prior. 28.4.1972).
Brubrogi, V. et al.: Eur. J. Med. Chem. (EJMCA5) **15**, 157 (1980).

5-methyl-2-pyrazinecarboxylic acid:
Pitré, D. et al.: Chem. Ber. (CHBEAM) **99**, 364 (1966).

2-hydroxymethyl-5-methylpyrazine:
Klein, B. et al.: J. Org. Chem. (JOCEAH) **26**, 129 (1961).

Formulation(s): cps. 25 mg, 250 mg

Trade Name(s):
I: Olbetam (Pharmacia & Upjohn; 1985)

Aclarubicin

(Aclacinomycin A)

ATC: L01DB04
Use: antineoplastic

RN: 57576-44-0 MF: $C_{42}H_{53}NO_{15}$ MW: 811.88 EINECS: 260-824-3
LD_{50}: 22.6 mg/kg (M, i.p.); 33.7 mg/kg (M, i.v.)
CN: [1*R*-(1α,2β,4β)]-2-ethyl-1,2,3,4,6,11-hexahydro-2,5,7-trihydroxy-6,11-dioxo-4-[[2,3,6-trideoxy-4-*O*-[2,6-dideoxy-4-*O*-[(2*R*-*trans*)-tetrahydro-6-methyl-5-oxo-2*H*-pyran-2-yl]-α-L-*lyxo*-hexopyranosyl]-3-(dimethylamino)-α-L-*lyxo*-hexopyranosyl]oxy]-1-naphthacenecarboxylic acid methyl ester

hydrochloride
RN: 75443-99-1 MF: $C_{42}H_{53}NO_{15} \cdot HCl$ MW: 848.34