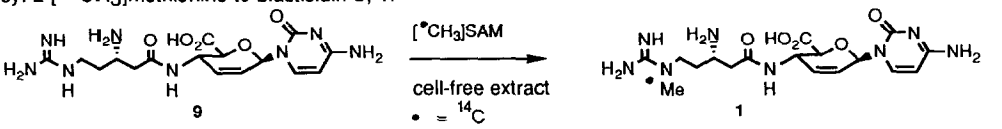
GRAPHICAL ABSTRACTS

BioMed. Chem. Lett. **1991**, *1*, 497

BIOSYNTHESIS OF BLASTICIDIN S. CELL-FREE DEMONSTRATION OF N-METHYLATION AS THE LAST STEP

Jincan Guo and Steven J. Gould*
Department of Chemistry, Oregon State University, Corvallis, Oregon 97331-4003

A cell-free preparation of *Streptomyces griseochromogenes* has been obtained that converted demethylblasticidin S, **9**, and *S*-adenosyl-L-[$^{14}CH_3$]methionine to blasticidin S, **1**.



9 → 1

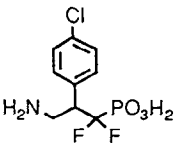
BioMed. Chem. Lett. **1991**, *1*, 501

SYNTHESIS AND BIOLOGICAL EVALUATION OF 3-AMINO-2-(4-CHLOROPHENYL)1,1-DIFLUOROPROPYL PHOSPHONIC ACID

William Howson* and Judy M. Hills
SmithKline Beecham Pharmaceutical Ltd, The Frythe, Welwyn, Herts, AL6 9AR, U.K.

G.Michael Blackburn and Marianne Broekman
Department of Chemistry, Sheffield University, Sheffield, S3 7HF, U.K.

The synthesis of the α-difluoro analogue of the $GABA_B$ antagonist phaclofen is described along with its action on a $GABA_B$ functional assay.



BioMed. Chem. Lett. **1991**, *1*, 503

OBSERVATION OF ENZYME BOUND INTERMEDIATES IN THE BIOSYNTHESIS OF PREUROPORPHYRINOGEN BY PBG DEAMINASE

Robin T. Aplin[a], Jack E. Baldwin[a], Clotilde Pichon[b], Charles. A. Roessner[b], A. Ian Scott[b], Christopher J. Schofield[a], Neal J. Stolowich[b], and Martin J. Warren[c]; *[a]The Dyson Perrins Laboratory and the Oxford Centre for Molecular Sciences, South Parks Road, Oxford, OX1 3QY, U.K.; [b]Center for Biological NMR, Chemistry Department, Texas A and M University, College Station, Texas 77843-3255, U. S. A.; [c]University of London, Queen Mary and Westfield College, Mile End Road, London, E1 4NS.*

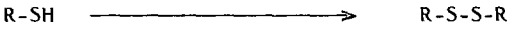
Electrospray mass spectrometry was used to observe covalently bound enzyme-intermediate complexes during the catalytic assembly of the linear tetrapyrrole, preuroporphyrinogen, by the enzyme porphobilinogen deaminase.

BioMed. Chem. Lett. **1991**, *1*, 507

BAKER'S YEAST CATALYSED OXIDATIVE COUPLING OF THIOLS TO DISULFIDES

K Rama Rao* and H M Sampath Kumar
Organic Chemistry-I, Indian Institute of Chemical Technology, Hyderabad 500007, India

Baker's yeast catalyses for the first time the formation of sulfur-sulfur bond.



1 → 2

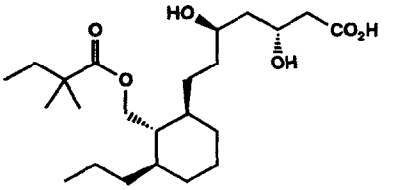
BioMed. Chem. Lett. **1991**, *1*, 509

C-2 Desmethyl Seco-Mevinic Acids. Monocyclic HMG-CoA Reductase Inhibitors

Dinesh V. Patel* and Eric M. Gordon

Bristol-Myers Squibb Pharmaceutical Research Institute
P.O. Box 4000, Princeton, NJ 08543-4000

The C-2 desmethyl seco-mevinic acid **2a** was efficiently prepared from 2-cyclohexen-1-one in 10 steps and 24.7% overall yield, and evaluated as an inhibitor of HMG-CoA reductase.



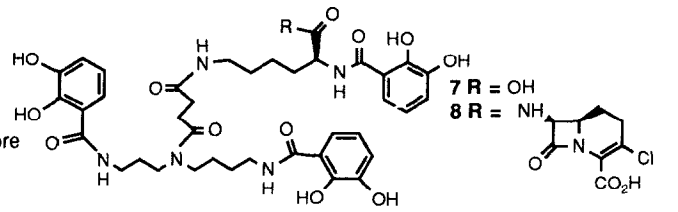
2a

BioMed. Chem. Lett. **1991**, *1*, 513

SYNTHESIS, SIDEROPHORE, AND ANTIMICROBIAL EVALUATION OF A SPERMIDINE-BASED TRICATECHOLATE SIDEROPHORE AND CARBACEPHALOSPORIN CONJUGATE

Julia A. McKee and Marvin J. Miller*
Department of Chemistry and Biochemistry,
University of Notre Dame, Notre Dame, IN, 46556

The synthesis and biological evaluation of a novel spermidine-based tricatecholate siderophore and the corresponding carbacephalosporin conjugate are described.



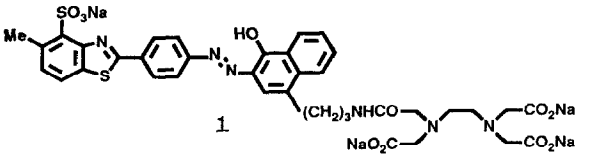
7 R = OH
8 R = NH$_2$

BioMed. Chem. Lett. **1991**, *1*, 519

DESIGN AND SYNTHESIS OF A POTENTIAL AFFINITY/CLEAVING REAGENT FOR BETA-PLEATED SHEET PROTEIN STRUCTURES.

James F Resch*[§], G Scott Lehr[§], and Claude M Wischik[¥]
[§]Medicinal Chemistry Department, ICI Pharmaceuticals Group, Wilmington, DE 19897
[¥]Cambridge Brain Bank Laboratory, MRC Centre, Hills Road, Cambridge, CB2 2QH, England

Bifunctional reagent 1 binds to beta-pleated sheet protein structures, providing a complexation site for ferrous ion



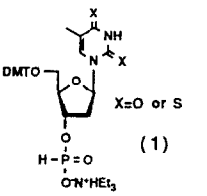
1

BioMed. Chem. Lett. **1991**, *1*, 523

SYNTHESIS AND PROPERTIES OF OLIGOTHYMIDYLATE CONTAINING SULFER-MODIFIED THYMIDINE: EFFECT OF THIATION OF PYRIMIDINE RING ON THE THERMOSTABILITY AND CONFORMATION OF THE DUPLEX

Tomoyasu Ishikawa[†], Fumio Yoneda[†], Kiyoshi Tanaka[§]* and Kaoru Fuji[§]
† Faculty of Pharmaceutical Sciences, Kyoto University, Sakyo-ku, Kyoto 606, Japan
§ Institute for Chemical Research, Kyoto University, Uji, Kyoto 611, Japan

Thiothymidine derivatives(1) was incorporated into oligothymidylates. The alternate strands(2, 3) containing 2-thiothymidine exhibited significant duplex stability with their complementary strands



X=O or S

(1)

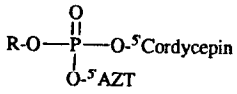
^{2e}Tp(Tp^{2e}Tp)$_3$Tp (2) Tp(^{2e}TpTp)$_6$^{2e}TpT (3)

BioMed. Chem. Lett. **1991**, *1*, 527

O-ALKYL-5',5'-DINUCLEOSIDE-PHOSPHOTRIESTERS AS PRODRUGS OF ANTIVIRAL AND ANTIBIOTIC NUCLEOSIDES

Chris Meier[a)b)] and Tam Huynh-Dinh[a)]; a) Unité de Chimie Organique, URA 487 CNRS, Institut Pasteur, 28, Rue du Docteur Roux, 75724 Paris Cedex 15, France; b) Present address: University of Frankfurt/Main, Niederurseler Hang 29, Postfach, D-6000 Frankfurt/Main, FRG

The syntheses of two new phosphotriester derivatives as prodrugs of AZT and 3'-deoxyadenosine (cordycepin) are described.



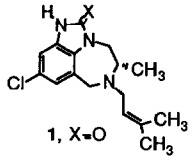
1a: R=C_6H_{13}
1b: R=$C_{16}H_{33}$

BioMed. Chem. Lett. **1991**, *1*, 531

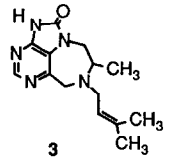
SYNTHESIS OF THE PYRIMIDINE ANALOG OF 4,5,6,7-TETRAHYDROIMIDAZO[4,5,1-*jk*][1,4]-BENZODIAZEPIN-2(1*H*)ONE (TIBO) POTENTIAL FOR HIV-1 INHIBITION

Chih Y. Ho* and Michael J. Kukla
Janssen Research Foundation, Spring House, Pennsylvania 19477

Efficent synthesis of the pyrimidine TIBO analog **3** starting from 9-benzyl-6-chloropurine and testing of its ability to inhibit the replication of the HIV-1 virus in MT-4 cells are described.



1, X=O
2, X=S



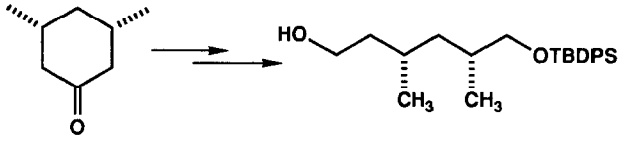
3

BioMed. Chem. Lett. **1991**, *1*, 535

THE ENZYMATIC BAEYER-VILLIGER OXIDATION: SYNTHESIS OF THE C_{11}-C_{16} SUBUNIT OF IONOMYCIN

Michael J. Taschner* and Quin-Zene Chen
Department of Chemistry, The University of Akron,
Akron, Ohio 44325-3601

An efficient synthesis of the C_{11}-C_{16} subunit of ionomycin from *cis*-3,5-dimethyl cyclohexanone using as the enzymatic Baeyer-Villiger oxidation to establish the correct absolute stereochemistry at C_{12} and C_{14} is reported.

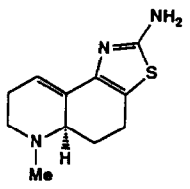


BioMed. Chem. Lett. **1991**, *1*, 539

SYNTHESIS AND DOPAMINERGIC ACTIVITY OF THE ENANTIOMERS OF 6-METHYL-4,5,5a,6,7,8-HEXAHYDROTHIAZOLO[4,5-f]QUINOLIN-2-AMINE (PD 128483).

Juan C. Jaen,[+]* Bradley W. Caprathe,[+] Lawrence D. Wise,[+]
Thomas A. Pugsley,* Leonard T. Meltzer,* and Thomas G. Heffner.*
Depts. of Chemistry[+] and Pharmacology,* Parke-Davis Pharmaceutical Research Division,
Warner-Lambert Company, Ann Arbor, Michigan 48105.

Abstract. The enantiomers of the dopamine (DA) agonist PD 128483 (**1**) have been synthesized and characterized biochemically (D_1, D_2 receptor binding, effects on rat brain DA synthesis), electrophysiologically (inhibition of DA neuron firing) and behaviorally (effects on rat exploratory locomotor activity). While R-(+)-**1** is a potent D_2 agonist that stimulates both pre- and postsynaptic DA receptors, S-(-)-**1** is a weak partial DA agonist able to stimulate only the more sensitive presynaptic DA receptors (DA autoreceptors).



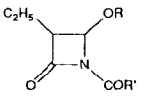
(+)-**1**

BioMed. Chem. Lett. **1991**, *1*, 545

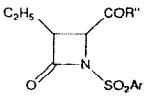
PREVENTION OF HUMAN LEUKOCYTE ELASTASE-MEDIATED LUNG DAMAGE BY 3-ALKYL-4-AZETIDIONES

W. K. Hagmann*, S. K. Shah, C. P. Dorn, L. A. O'Grady, J. J. Hale, P. E. Finke, K. R. Thompson, K. A. Brause, B. M. Ashe, H. Weston, M. E. Dahlgren, A. L. Maycock, P. S. Dellea, K. M. Hand, D. G Osinga, R. J. Bonney, P. Davies, D. S Fletcher, J. B. Doherty
Merck, Sharp, and Dohme Research Laboratories, Rahway, NJ 07065

Simple substituted 4-azetidinones, such as **1** and **2**, are potent inhibitors of human leukocyte elastase-mediated lung damage in hamsters despite being modest inhibitors of the enzyme.



1

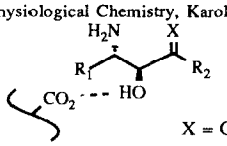


2

BioMed. Chem. Lett. **1991**, *1*, 551

PROBING THE INHIBITION OF LEUKOTRIENE A_4 HYDROLASE BASED ON ITS AMINOPEPTIDASE ACTIVITY

Wei Yuan†, Ziyang Zhong,† Chi-Huey Wong†*, Jesper Z Haeggström¶, Anders Wetterholm¶, and Bengt Samuelsson¶*
†Department of Chemistry, The Scripps Research Institute, 10666 N. Torrey Pines Road, La Jolla, CA 92037,
¶Department of Physiological Chemistry, Karolinska Institute, Box 60 400, S-104 01, Stockholm, Sweden



X = O, S, N

BioMed. Chem. Lett. **1991**, *1*, 557

SUBSTRATE ACTIVATED TIME DEPENDENT INHIBITION OF CARBOXYPEPTIDASE A BY AMINOCYCLOPROPANE CARBOXYLIC ACID DERIVATIVES AND ANALOGUES

by Alison Kemp, M. Catriona Tedford, and Colin J. Suckling*,
Department of Pure and Applied Chemistry, University of Strathclyde, 295 Cathedral Street, Glasgow, G1 1XL.

Abstract· A series of aminocyclopropane carboxylic acid derivatives and analogues that are time dependent inhibitors of carboxypeptidase A has been synthesised Kinetic experiments show surprisingly that the rate of inhibition is increased in the presence of substrate A related secondary alcohol also acts as a time dependent inhibitor of carboxypeptidase A and this result is evaluated in the context of current views on the mechanism of action of carboxypeptidase A.