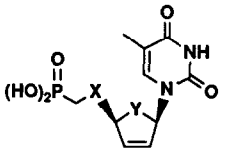
GRAPHICAL ABSTRACTS

BioMed. Chem. Lett. **1992**, 2, 367

SYNTHESIS AND HIV ACTIVITY OF PHOSPHONATE ISOSTERES OF D4T MONOPHOSPHATE

Choung Un Kim*, Joanne J. Bronson*, Louis M. Ferrara, and John C. Martin
Bristol-Myers Squibb Company, Pharmaceutical Research Institute, Wallingford, CT 06492

The synthesis and antiviral activity of phosphonate isosteres of 2',3'-didehydro-2',3'-dideoxythymidine monophosphate (d4T-MP) are described.



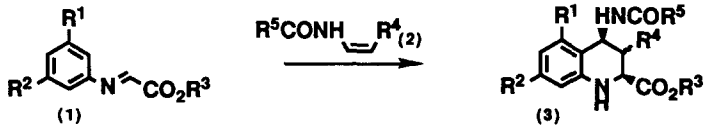
X = Y = O
X = CH_2, Y = O
X = O, Y = CH_2

BioMed. Chem. Lett. **1992**, 2, 371

Synthesis of *cis* and *trans* 4-Amido-2-Carboxyterahydrquinolines, High Affinity Ligands at the Glycine site of the NMDA Receptor.

Graeme I. Stevenson*, Paul D. Leeson, Micael Rowley, Ian Sanderson and Ian Stansfield, Merck Sharp and Dohme Research Laboratories, Neuroscience Research Centre, Terlings Park, Harlow, Essex, CM20 2QR, UK.

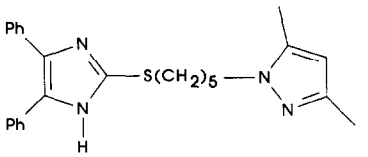
N-Aryliminoesters (1) react with enamides (2) under Lewis acid catalysis to afford *cis* 4-amido-2-carboxytetrahydroquinolines (3). The products of this reaction are easily converted to the biologically active *trans* conformers.



BioMed. Chem. Lett. **1992**, 2, 375

RP 70676: A POTENT SYSTEMICALLY AVAILABLE INHIBITOR OF ACYL-CoA:CHOLESTEROL O-ACYL TRANSFERASE (ACAT)

M.J. Ashton*, A.W. Bridge, R.C. Bush, D.I. Dron, N.V. Harris*, G.D. Jones, D.J. Lythgoe, D. Riddell, and C. Smith
Rhone-Poulenc Rorer, Central Research, Dagenham Research Centre, Dagenham, Essex, RM10 7XS (UK)



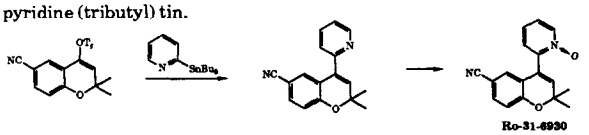
RP 70676 is a potent inhibitor of ACAT that is readily bioavailable in rabbits with significant levels of parent compound present in plasma for up to 6 hours after an oral dose.

BioMed. Chem. Lett. **1992**, 2, 381

A NEW EFFICIENT SYNTHESIS OF Ro-31-6930, A POTENT POTASSIUM CHANNEL ACTIVATOR, AND ITS ANALOGS

Sung-eun Yoo,* Jee Hee Suh, Sang Jo Lee and Nakcheol Jeong*
Korea Research Institute of Chemical Technology, Daedeogdanji P.O. Box 9, Daejeon, Korea

A potent potassium channel activator, Ro-31-6930 and its analogs were prepared efficiently by employing Pd(O) mediated coupling of the enol triflates and pyridine (tributyl) tin.

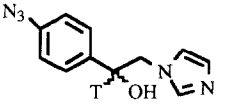


Ro-31-6930

BioMed. Chem. Lett. **1992**, *2*, 383

Synthesis and Evaluation of Photoaffinity Probes Directed at Lanosterol 14α-Demethylase ($P\text{-}450_{14DM}$) Gerard D. Wright and John F. Honek; Guelph-Waterloo Center for Graduate Work in Chemistry, Department of Chemistry, University of Waterloo, Waterloo, Ontario, Canada N2L 3G1

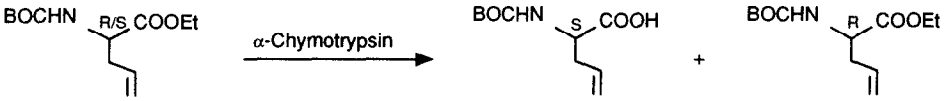
A series a aromatic azides which could act as potential photoaffinity probes for the yeast lanosterol 14α-demethylase ($P\text{-}450_{14DM}$) were prepared. One of these, 1-[^{3}H]-p-azidophenyl-2-(1-imidazolyl)ethanol, has been demonstrated to label purified $P\text{-}450_{14DM}$ from Saccharomyces cerevisiae. These results provide the framework for future labeling experiments.



BioMed. Chem. Lett. **1992**, *2*, 387

α-Chymotrypsin Catalyzed Enantioselective Hydrolysis of Alkenyl-α-Amino Acid Esters

Bettina Schricker, Klaus Thirring, Heinz Berner
Sandoz Forschungsinstitut, Brunnerstraße 59, A-1235 Wien, Austria



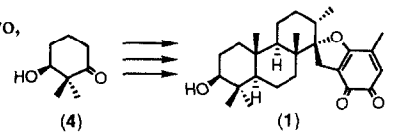
The title reaction was carried out with differently substituted amino acid esters, giving high chemical yields (up to 99%) and stereoselectivity (ee 86-96%).

BioMed. Chem. Lett. **1992**, *2*, 391

SYNTHESIS AND ABSOLUTE CONFIGURATION OF (–)-STYPOLDIONE

Kenji Mori* and Yasuo Koga
Department of Agricultural Chemistry, The University of Tokyo, Yayoi 1-1-1, Bunkyo-ku, Tokyo 113, Japan

Conversion of (*S*)-3-hydroxy-2,2-dimethylcyclohexanone (**4**) to (–)-stypoldione (**1**), a marine toxin, established its absolute configuration as depicted in (**1**).



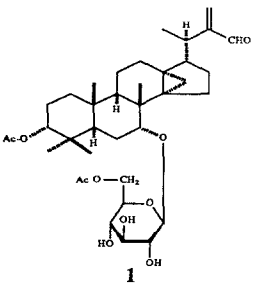
BioMed. Chem. Lett. **1992**, *2*, 395

CUMINDYSOSIDE A, A NOVEL CYTOTOXIC TRISNORTRITERPENE GLUCOSIDE WITH A 14, 18-CYCLOAPOEUPHANE-TYPE SKELETON FROM *DYSOXYLUM CUMINGIANUM*

Yoshiki Kashiwada,[a] Toshihiro Fujioka,[a] Jer-Jang Chang,[b] Ih-Sheng Chen,[c] Kunihide Mihashi,[d] and Kuo-Hsiung Lee [a]*

[a]*Natural Products Laboratory, Division of Medicinal Chemistry and Natural Products, School of Pharmacy, University of North Carolina, Chapel Hill, North Carolina 27599, USA,* [b]*Department of Pathology, School of Medicine, University of North Carolina, Chapel Hill, North Carolina 27599, USA,* [c]*Natural Products Research Center, Kaohsiung Medical College, Kaohsiung, Taiwan,* [d]*Faculty of Pharmaceutical Sciences, Fukuoka University, Fukuoka 814-01, Japan*

Cumindysoside A, a novel trisnortriterpene glucoside with a 14, 18-cycloapoeuphane-type skeleton, has been isolated from *Dysoxylum cumingianum* as a cytotoxic principle. Its structure was established from spectroscopic evidence.



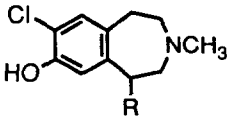
1

BioMed. Chem. Lett. **1992**, *2*, 399

DOPAMINE RECEPTOR BINDING PROPERTIES OF SOME 2,3,4,5-TETRAHYDRO-1*H*-3-BENZAZEPINE-7-OLS WITH NON-AROMATIC SUBSTITUENTS IN THE 5-POSITION

Wei K. Chang, Marjorie Peters, Vicki P. Fevig, Joseph A. Kozlowski, Gouwei Zhou, Derek B. Lowe, Henry Guzik, Robert D. McQuade, Ruth Duffy, Vicki L. Coffin, and Joel G. Berger*, Schering-Plough Research Institute, 60 Orange St., Bloomfield, New Jersey 07003

A series of benzazepine-7-ols related to the dopamine D-1 antagonist SCH-23390 (R=Ph) in which the R substituent is non-aromatic were synthesized. Several possess considerable D-1 receptor affinity and selectivity.



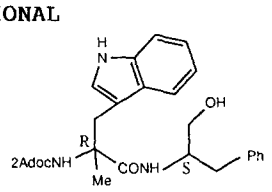
BioMed. Chem. Lett. **1992**, *2*, 403

THE USE OF A PROLINE RING AS A CONFORMATIONAL RESTRAINT IN CCK-B RECEPTOR "DIPEPTOIDS".

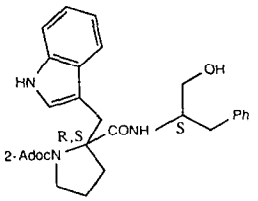
Christopher I. Fincham, David C. Horwell, Giles S. Ratcliffe and David C. Rees.*

Parke-Davis Neuroscience Research Centre Addenbrookes Hospital Site, Hills Road, Cambridge CB2 2QB, UK.

Examination of molecular dynamics of **2b** and an X-ray crystal structure led to synthesis of **7**.



2b

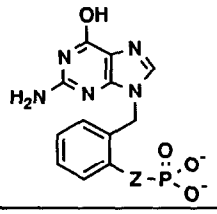


7

BioMed. Chem. Lett. **1992**, *2*, 407

Phosphonate derivatives of N-9 benzylguanine: a new class of potent purine nucleoside phosphorylase inhibitors

S. Halazy, A.Eggenspiller, A. Ehrhard and C.Danzin, Marion Merrell Dow, Strasbourg,France



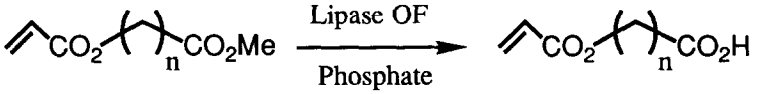
Depicted compounds with Z = $CHFCF_2$, CH=CF or CH=CH were prepared and found to be the most potent inhibitors of purine nucleoside phosphorylase reported so far.

BioMed. Chem. Lett. **1992**, *2*, 411

PREPARATION OF CARBOXYALKYL ACRYLATE BY LIPASE-CATALYZED REGIOSELECTIVE HYDROLYSIS OF CORRESPONDING METHYL ESTER

EIICHIRO FUKUSAKI, SHUJI SENDA, YUTAKA NAKAZONO, HIROYUKI YUASA and TETSUO OMATA

Medical and Membrane Research Laboratory, Nitto Denko Co.1-1-2, Shimohozumi, Ibaraki, Osaka 567, Japan



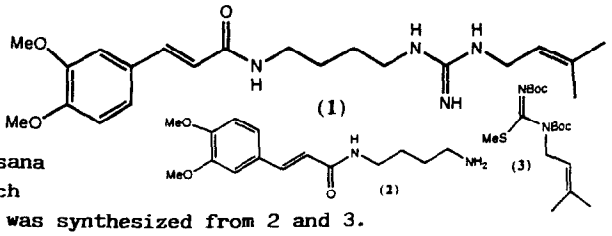
2 (n=1,3,5) **1** (n=1,3,5)

BioMed. Chem. Lett. **1992**, *2*, 415

CARACASANAMIDE, A NOVEL HYPOTENSIVE AGENT FROM VERBESINA CARACASANA

G. Delle Monache,B. Botta,F. Delle Monache, R. Espinal, S. C. de Bonnevaux, C. De Luca, M. Botta, F. Corelli, and M. Carmignani
Centro Chimica Recettori, U.C.S.C., Largo F. Vito 1, 00168 Roma, Italy

The hypotensive agent from Verbesina caracasana is shown to be a novel guanidino-amide, which occurs in (Z)-and (E)-forms. The latter (1) was synthesized from 2 and 3.



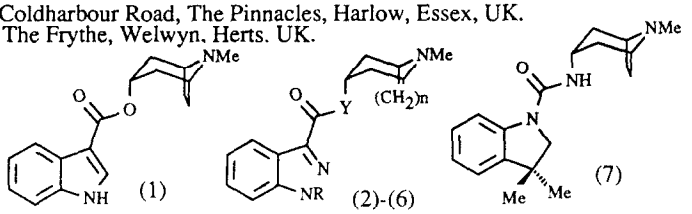
BioMed. Chem. Lett. **1992**, *2*, 419

INDAZOLE AS AN INDOLE BIOISOSTERE: 5-HT$_4$ RECEPTOR ANTAGONISM

A.J. Kaumann[a], F.D. King* and R.C. Young[a]

*SmithKline Beecham Pharmaceuticals,Coldharbour Road, The Pinnacles, Harlow, Essex, UK.
[a]SmithKline Beecham Pharmaceuticals, The Frythe, Welwyn, Herts. UK.

A comparison of the potencies of the indole ICS 205-930 (1), The indazoles (2)-(6) and the indoline (7) as 5-HT$_3$ and 5-HT$_4$ receptor antagonists is described.

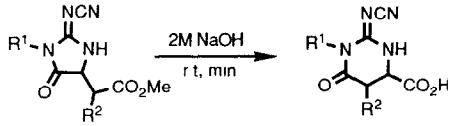


BioMed. Chem. Lett. **1992**, *2*, 421

Facile Rearrangement of 5-Carbomethoxymethyl-2-cyanoiminoimidazolones. Synthesis of 6-Carboxyhexahydropyrimidines, Potential Dihydrorotate Dehydrogenase Inhibitors.

Vern M. Delisser, Peter J. Garratt, Simon N. Thorn and Roger Wrigglesworth
Department of Chemistry, University College London, Gordon Street, London WC1H 0AJ, U.K. and Sandoz Institute for Medical Research, Gower Place, London WC1E 6BN, U.K.

5-Carbomethoxy-2-cyanoiminoimidazolones rearrange to 6-carboxyhexahydropyrimidines with dilute base at room temperature

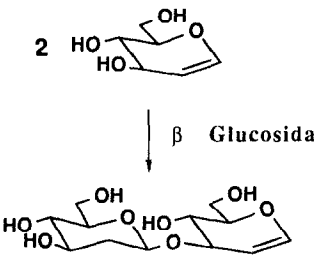


BioMed. Chem. Lett. **1992**, *2*, 423

GLYCOSIDASES CATALYZED SYNTHESIS OF 2-DEOXY-β-GLYCOSIDES

Sylvie Bay, Danièle Cantacuzène
Unité de Chimie Organique, UA CNRS 487, Département de Biochimie et Génétique Moléculaire, Institut Pasteur, 28 rue du Dr Roux 75724 Paris (France)

β-glycosidases are used for the stereoselective glycosylation of glycals. The one pot preparation of 2-deoxy-β-glycosides containing potentially sensitive glycal units is very advantageous since no protection-deprotection steps are required

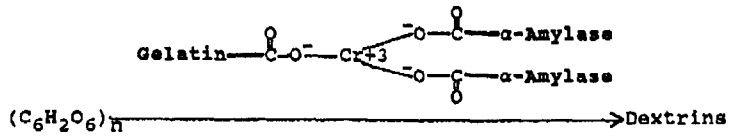


BioMed. Chem. Lett. **1992**, *2*, 427

IMMOBILIZATION OF ALPHA-AMYLASE INTO GELATIN FILMS WITH VARIOUS CROSS-LINKERS

Bayramoglu, Z., Akbulut*, U., Sungur, S., Department of Chemistry,
Middle East Technical University, 06531-Ankara, Turkiye

Abstract - α-amylase was immobilized into photographic gelatin by cross-linking with chromium(III)acetate, chromium(III)sulfate, potassium chromium(III)sulfate and formaldehyde. Polyester film strips were coated with immobilized α-amylase.



BioMed. Chem. Lett. **1992**, *2*, 433

UREASE IMMOBILIZATION INTO POLY(ACRYLAMIDE)-GELATIN GELS

Elçin, M., Sungur, S., Akbulut*, U., Department of Chemistry,
Middle East Technical University, 06531-Ankara, Turkiye

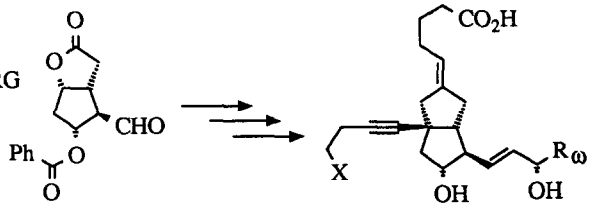
Abstract - Poly(acrylamide)-gelatin gels were used as carrier system for urease immobilization.

BioMed. Chem. Lett. **1992**, *2*, 439

SYNTHESIS OF CHEMICALLY STABLE 9-SUBSTITUTED CARBACYCLIN DERIVATIVES AND THEIR BIOLOGICAL USE

P. Deicke, U. Klar*, H. Vorbrüggen
Research Laboratories of Schering AG,
Müllerstr. 170-178, W-1000 Berlin 65, FRG

Several 9-substituted carbacyclin derivatives were synthesized and their biological properties evaluated.

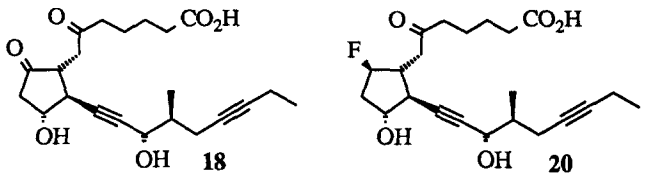


BioMed. Chem. Lett. **1992**, *2*, 445

SYNTHESIS OF POTENT 6-OXO AND 9-FLUORO-PGE$_1$-DERIVATIVES AND THEIR BIOLOGICAL PROPERTIES

U. Klar*, A. Pletsch,
W. Skuballa, H. Vorbrüggen
Research Laboratories of
Schering AG, Müllerstr. 170-178
W-1000 Berlin 65, FRG

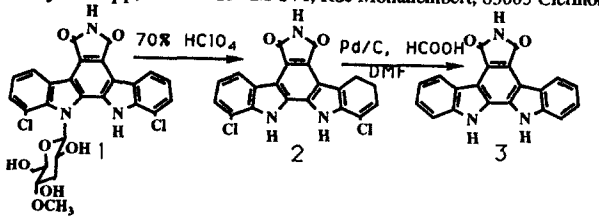
The synthesis of derivatives **18** and **20** as well as their biological data are presented.



BioMed. Chem. Lett. **1992**, *2*, 449

PREPARATION OF SYNTHONS FOR THE SYNTHESIS OF PROTEIN KINASE C INHIBITORS FROM REBECCAMYCIN.

Serge Fabre , Michelle Prudhomme*
Université Blaise Pascal, Laboratoire de Chimie Organique Biologique, URA 485, 63177 Aubière Cedex - France.
and Maryse Rapp, Unité INSERM U71, Rue Montalembert, 63005 Clermont-Ferrand, France.

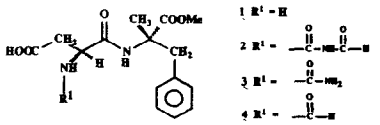


An efficient method to obtain PKC inhibitors precursors from the antitumor antibiotic Rebeccamycin is presented.

BioMed. Chem. Lett. **1992**, *2*, 453

NEW ASPARTAME-LIKE SWEETENERS CONTAINING L-(αMe)Phe

S. Polinelli, Q.B. Broxterman, H.E. Schoemaker, W.H.J. Boesten, M. Crisma[a], G. Valle[a], C. Toniolo[a] and J. Kamphuis*
DSM Research, Bio-organic chemistry section, P.O. Box 18, 6160 MD Geleen, The Netherlands
[a]University of Padova, Department of Organic Chemistry and Biopolymer Research Centre, CNR, Via Marzolo 1, 35131 Padova, Italy

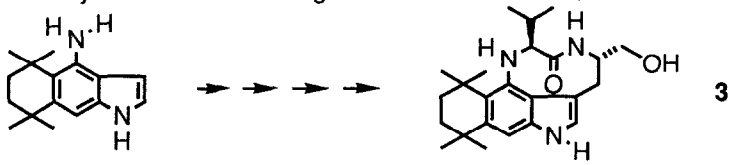


BioMed. Chem. Lett. **1992**, *2*, 457

SYNTHESIS AND BIOLOGICAL ACTIVITY OF A 5,6-SUBSTITUTED TELEOCIDIN

Robert R. Webb II,* and Michael C. Venuti, Bioorganic Chemistry Department, Genentech, Inc., 460 Pt. San Bruno Blvd., South San Francisco, California 94080

The synthesis and biological evaluation of 5,6-substituted teleocidin **3** is reported.



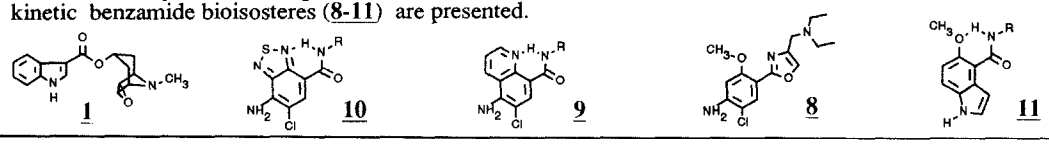
3

BioMed. Chem. Lett. **1992**, *2*, 461

DESIGN AND SYNTHESIS OF NOVEL LIGANDS FOR THE 5-HT$_3$ AND THE 5-HT$_4$ RECEPTOR

E.Blum, K.H.Buchheit, H.H.Buescher, R.Gamse, E.Kloeppner, H.Meigel,
C.Papageorgiou, R.Waelchli and L.Revesz*)
Preclinical Research, Sandoz Pharma AG, CH-4002 Basle

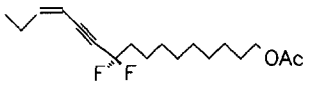
Abstract: A novel highly potent 5-HT$_3$ antagonist and Tropisetron analogue (1) is described with an increased efficacy to inhibit cisplatin induced emesis in ferrets. Four novel structural classes of gastroprokinetic benzamide bioisosteres (8-11) are presented.



BioMed. Chem. Lett. **1992**, *2*, 467

SYNTHESIS OF (Z)-10,10-DIFLUORO-13-HEXADECEN-11-YNYL ACETATE, NEW DIFLUORO ANALOGUE OF THE SEX PHEROMONE OF THE PROCESSIONARY MOTH

J. Feixas, F. Camps and A. Guerrero*
Department of Biological Organic Chemistry, C.I.D. (CSIC)
Jordi Girona Salgado 18-26. 08034-Barcelona, Spain

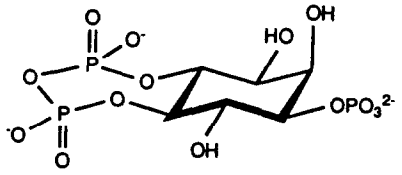


The synthesis, biological activity and some physicochemical features of the compound are reported.

BioMed. Chem. Lett. **1992**, *2*, 471

TOTAL SYNTHESIS OF *MYO*-INOSITOL-1-PHOSPHATE-4,5-PYROPHOSPHATE, A NOVEL SECOND MESSENGER ANALOGUE, VIA *MYO*-INOSITOL-1-PHOSPHATE-4,5-BISPHOSPHOROTHIOATE

N J Noble, D Dubreuil and B V L Potter*
School of Pharmacy and Pharmacology,
University of Bath, Claverton Down,
Bath BA2 7AY, UK.

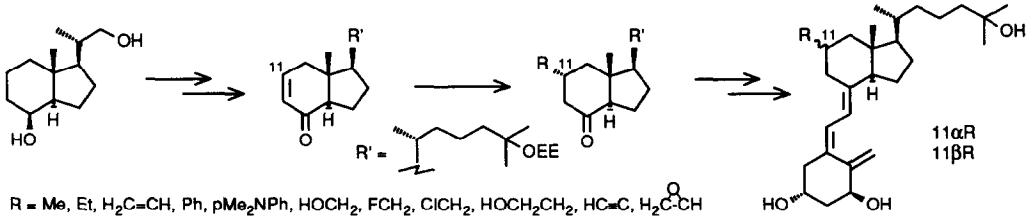


Myo-inositol 1-phosphate 4,5-bisphosphorothioate is converted into *myo*-inositol 1-phosphate 4,5-pyrophosphate using N-bromosuccinimide.

BioMed. Chem. Lett. **1992**, *2*, 477

SYNTHESIS OF (C-11)-SUBSTITUTED ANALOGUES OF 1α,25-$(OH)_2$-VITAMIN D_3

C. D'Halleweyn, D. Van Haver, J. Van der Eycken, P. De Clercq and M. Vandewalle*
Lab. Org. Synth., Univ. of Gent, Krijgslaan 281 (S4), B-9000 GENT (Belgium)



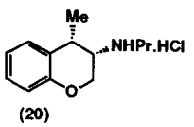
R = Me, Et, H_2C=CH, Ph, pMe_2NPh, $HOCH_2$, FCH_2, $ClCH_2$, $HOCH_2CH_2$, HC≡C, H_2C-CH (O)

BioMed. Chem. Lett. **1992**, *2*, 481

THE PREPARATION OF NOVEL DOPAMINE ANALOGUES VIA PALLADIUM CATALYSED CYCLISATION REACTIONS

Antony J. Davies, Richard J.K. Taylor,* David I. Scopes and Alan H. Wadsworth
School of Chemical Sciences, University of East Anglia, Norwich, NR4 7TJ, U.K.
and Glaxo Group Research, Park Road, Ware, SG12 0PJ, U.K.

A range of tetrahydronaphthalene and benzopyran derivatives (e.g. 20, in homochiral form) have been prepared using the intramolecular Heck reaction and related palladium-catalysed cyclisation-anion capture procedures.

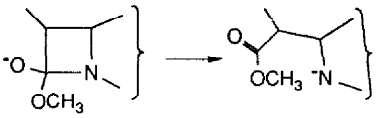


(20)

BioMed. Chem. Lett. **1992**, *2*, 485

AM1 STUDY ON TETRAHEDRAL INTERMEDIATES OF THE AMIDES OF β-LACTAM ANTIBIOTICS AND METHANOL

Keepyung Nahm
Specialty Chemicals, R&D Center, LUCKY LTD., P.O. Box 10, Science Town, Dae-Jeon 305-343, South Korea



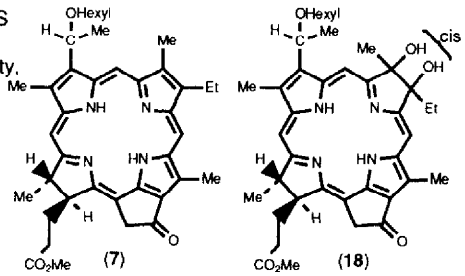
Tetrahedral intermediates on methanolysis of several model β-lactam antibiotics were studied pictorially and energetically with semiempirical AM1 method.

BioMed. Chem. Lett. **1992**, *2*, 491

STRUCTURE/ACTIVITY RELATIONSHIPS AMONG PHOTOSENSITIZERS RELATED TO PHEOPHORBIDES AND BACTERIOPHEOPHORBIDES

Ravindra K. Pandey, Fuu-Yau Shiau, Adam B. Sumlin, Thomas J. Dougherty, and Kevin M Smith*. Department of Chemistry, University of California, Davis, CA 95616, and Department of Radiation Medicine, Roswell Park Memorial Institute, 666 Elm St , Buffalo, NY 14263, USA

Structure/activity relationships for a number of photosensitizers which are of potential value in photodynamic therapy of tumors are presented. These sensitizers are members of the pheophorbide (e.g. **7**) and bacteriopheophorbide (e.g. **18**) series

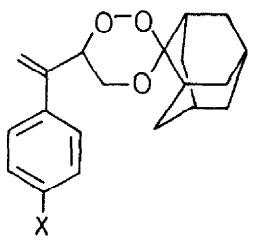


BioMed. Chem. Lett. **1992**, *2*, 497

SYNTHESIS OF IN VIVO POTENT ANTIMALARIAL 1,2,4-TRIOXANES

Chandan Singh[a*], Dharmendra Misra[a], Gunjan Saxena[a] and Subhash Chandra[b], Divisions of Medicinal Chemistry and Parasitology, Central Drug Research Institute, Lucknow 226 001, India

Abstract : The synthesis of a new class of in vivo potent antimalarial 1,2,4-trioxanes is reported.



BioMed. Chem. Lett. **1992**, *2*, 501

6-CARBOXYMETHYL-2-AZABICYCLO[2.2.1]HEPTANE ENANTIOMERS: MUSCARINIC ACTIVITIES OF RIGID ANALOGUES OF ARECOLINE

E. Pombo-Villar*, P. Supavilai, H.P.Weber, and H.W.G.M.Boddeke,
Sandoz Pharma Ltd., CH-4002 Basel, Switzerland

(1*R*,4*R*,6*R*)-(-)-6-Carbomethoxy-2-azabicyclo[2.2.1]heptane **8a**, its N-methyl analogue **2a** and their enantiomers **8b** and **2b** have been prepared as rigid analogues of arecoline **1**, and their cholinergic activities evaluated.