Soft Drugs-XVI. Design, Evaluation and Transdermal Penetration of Novel Soft Anticholinergics Based on Methatropine

BioMed. Chem. **1993**, *1*, 327

G.N. Kumar,[1] R.H. Hammer,[2] and N.S. Bodor[1]
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Nine soft drug analogs of methatropine based on the phenylmalonic structural unit were synthesized and studied. It was found that they are hydrolytically deactivated during a transdermal penetration process. A linear correlation between log partition coefficients (log P) and log permeability coefficients (log K_p) for all compounds tested was found. Topical application of these soft drugs is expected to result in local antisecretory activity with essentially no systemic side effects.

Bioactivity and Molecular Modelling of Diphenylsulfides and Diphenylselenides

BioMed. Chem. **1993**, *1*, 333

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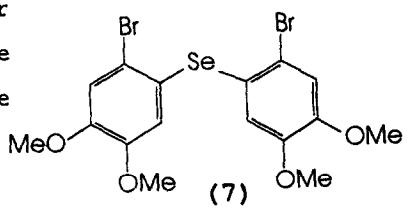
CRC Department of Experimental Chemotherapy, Paterson Institute for Cancer Research, Christie Hospital NHS Trust, Wilmslow Road, Manchester M20 9BX, U.K.

The dibromoselenide (7) has shown some biological effects similar to those of Taxol. Molecular modelling has shown that the bromine atoms play an important role in the biochemistry of this selenide (7).



(7)

BioMed. Chem. **1993**, *1*, 341

PROXYL NITROXIDE OF LITHOCHOLIC ACID : A POTENTIAL SPIN PROBE FOR MODEL MEMBRANES

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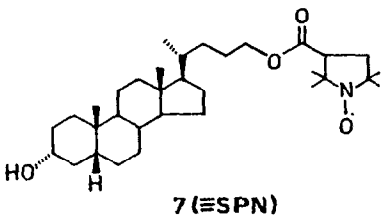
The incorporation and the mode of localization of a new steroidal proxyl nitroxide 7 (SPN) in model membrane system have been ascertained. SPN has been used as a spin probe for studying phase transition and permeability of model membranes.



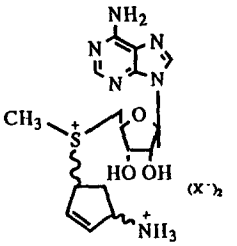
7 (≡SPN)

BioMed. Chem. **1993**, *1*, 349

Preparation of the Pure Diastereomeric Forms of S-(5'-Deoxy-5'-adenosyl)-1-ammonio-4-methylsulfonio-2-cyclopentene and Their Evaluation as Irreversible Inhibitors of S-Adenosylmethionine Decarboxylase from *Escherichia coli*.

Yong Qian Wu and Patrick M. Woster,* Department of Pharmaceutical Sciences, Wayne State University, Detroit, MI 48202

Abstract: The conformationally restricted S-adenosylmethionine analogue AdoMac was prepared in its pure diastereomeric forms, and each diastereomer was evaluated as an irreversible inhibitor of the pyruvoyl enzyme S-adenosylmethionine decarboxylase. The data suggests that these and related analogues may be useful as conformational probes for the catalytic site of the enzyme.



AdoMac

Investigating the s-2 Subsite Selectivity of Alkaline Proteases in Hydrolysis of Diastereo-Peptide Esters and Molecular-Modeling Interpretation

BioMed. Chem. **1993**, *1*, 361

Shui-Tein Chen,[1] Chen-Chen Tu,[1] Shiah-Yun Chen,[1] Hsuan-Cheng Huang[1] and Kung-Tsung Wang[1,2]
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[2]*Department of Chemistry, National Taiwan University, PO Box 23-106, Taipei, Taiwan, 10098, R.O.C.*

Diastereomeric peptide-esters have been used as substrates, and the kinetic constants of the three alkaline proteases, subtilisin Caqrlsberg, alcalase, and Nagarse catalyzed ester-hydrolysis, were measured to investigate the selectivity of the enzyme-catalyzed peptide ester-hydrolysis. All three proteases preferred the substrate which had a small side-chain at the s-2 site.

Intramolecular Carboxylate Catalysis in the Depurination of a 7-Methylguanosine Derivative

BioMed. Chem. **1993**, *1*, 369

Scott A. Van Arman and Anthony W. Czarnik
Department of Chemistry, The Ohio State University, Columbus, OH 43210, U.S.A.

We have compared the pH-independent rates of glycosidic hydrolysis in a carboxylate bearing 7-methylguanosine derivative with those of a reference compound and with that of 7-methylguanosine itself. A *syn*-oriented carboxylate group affords catalysis in the hydrolysis reaction, although the instability of 7-alkylguanosines above pH 7 severely limits the useful pH range that could be studied. The effect of the carboxylate near neutral pH can be viewed in three different ways: it provides a 3-fold acceleration as compared to underivatized 7-methylguanosine, an approximately 30-fold acceleraton when the decelerating effect of the ketal group is considered, and because of slow decomposition of the reference compound under the reaction conditions, we conclude that the carboxylate provides an acceleration of ≥43-fold as compared to the protio reference compound.

Enzymic Acylation of Methyl D- and L-Glycopyranosides: Influence of the 3-Hydroxyl Group

BioMed. Chem. **1993**, *1*, 375

Diego Colombo,[a] Fiamma Ronchetti,[a]* Antonio Scala,[a] Ida Maria Taino[a] and Lucio Toma[b]
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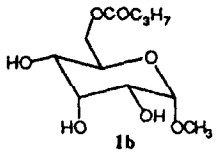
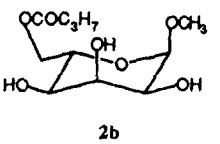
[b]Dipartimento di Chimica Organica, Università di Pavia, Via Taramelli 10, 27100 Pavia (Italy)

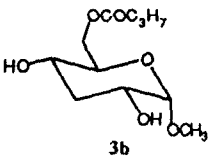
In order to investigate the influence of the 3-hydroxyl group on the regioselectivity of the reaction, compounds **1b-4b** have been submitted to lipase catalyzed butyrylation.



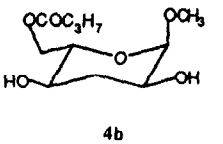
1b



2b



3b



4b

THE SYNTHESIS AND USE OF pp60src-RELATED PEPTIDES AND PHOSPHOPEPTIDES AS SUBSTRATES FOR ENZYMATIC PHOSPHORYLATION STUDIES,

BioMed. Chem. **1993**, *1*, 381

John W. Perich[A*,B], Flavio Meggio[C], Robert M. Valerio[A], R. B. Johns[A], Lorenzo A. Pinna[C] and Eric C. Reynolds[B], [A]*School of Chemistry and* [B]*School of Dental Science, The University of Melbourne, Victoria, Australia, and* [C]*Department of Biological Chemistry, University of Padova, Padova, Italy.*

Abstract: The enzymatic phosphorylation (CK-2) of the auto-phosphorylation site of pp60^{src}, -Asn-Glu-Tyr^{416}-Thr-Ala-, was studied by the use of the following synthetic peptides and phosphopeptides :

Asn-Glu-Tyr(*P*)-Thr-Ala	Asn-Glu-Tyr-Thr-Ala	Asn-Glu-Tyr(Me)-Thr-Ala	Asn-Glu-Ala-Thr-Ala
Asn-Glu-Ser(*P*)-Thr-Ala	Asn-Glu-Phe-Thr-Ala	Asn-Glu-Cha-Thr-Ala	Asn-Ala-Tyr-Thr-Ala

Synthesis and Interaction Studies of ^{13}C Labeled Lactone Derivatives with a Model Protein Using ^{13}C NMR

BioMed. Chem. **1993**, *1*, 389

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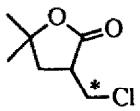
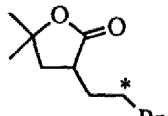
Laboratoire de Dermatochimie associé au CNRS, Université Louis Pasteur Clinique Dermatologique, CHU, F-67091 Strasbourg, France

Two molecules **9** and **14**, representatives of two series of electrophilic lactone derivatives, have been synthesised, labeled with carbon 13 at their reactive sites. The mechanism and the products of the reaction of these two molecules with human serum albumin (HSA) under various reaction conditions have been studied by ^{13}C NMR using DEPT 135 sequences. Results using the protein dissolved in aqueous medium or butylamine (a model nucleophile) dissolved in organic solvent were very similar. These results are entirely consistent with the in vivo allergising activity of these molecules. The validity of the Relative Alkylation Index (RAI) as a predicative model in contact allergy is discussed.



9



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