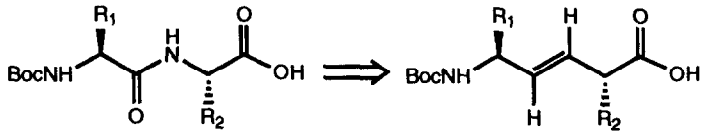
Double Bond Isosteres of the Peptide Bond: Synthesis and Biological Activity of Cholecystokinin (CCK) C-Terminal Hexapeptide Analogs

BioMed. Chem. **1993**, *1*, 161

Youe-Kong Shue, Michael D. Tufano, George M. Carrera, Jr, Hana Kopecka, Sharon L. Kuyper, Mark W. Holladay, Chun Wei Lin, David G. Witte, Thomas R. Miller, Mike Stashko and Alex M. Nadzan
Neuroscience Research, Pharmaceutical Product Division, Abbott Laboratories, Abbott Park, IL 60064



	R_1	R_2
Ia	$CH_2CH(CH_3)_2$	H
Ib	H	3-Indolylmethyl
Ic	3-Indolylmethyl	$(CH_2)_3CH_3$
Id	$CH_2CH(CH_3)_2$	CH_2CO_2-tBu
Ie	CH_2CO_2-tBu	CH_2Ph

(2,3)-α-Methylenepenams: Synthesis and *In Vitro* Activity

BioMed. Chem. **1993**, *1*, 173

C.-C. Wei, K.-C. Luk, K. F. West, J. L. Roberts, D. Pruess, D. W. Moore, R. Yang, T. Steppe, P. Rossman, M. Weigele and D. D. Keith
Roche Research Center, Nutley, NJ 07110

A series of α-methylene penicillins was synthesized and SAR were studied. The α-isomers were found to be chemically reactive and biologically active in contrast to the β-isomers. In addition, the α-isomers have broader spectrum of *in vitro* activity than the corresponding penicillins. Generally, the α-isomers are more active against gram-negative bacteria than the corresponding penicillins, but slightly weaker in potency towards gram-positive organisms.

Soft Drugs–XIV. Synthesis and Anticholinergic Activity of Soft Phenylsuccinic Analogs of Methatropine

BioMed. Chem. **1993**, *1*, 183

R. H. Hammer,[1,2] E. Gunes,[1] G. N. Kumar,[1] W. M. Wu,[1] V. Srinivasan[2] and N. S. Bodor[1]
[1] *Center for Drug Discovery, Box 100497, JHMHC, College of Pharmacy, University of Florida, Gainesville, FL 32610*
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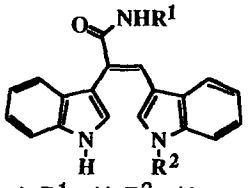
Three soft drug analogs and a metabolite of methatropine based on phenylsuccinic structural moiety were synthesized and tested for activity. In an *in vivo* assay, the soft drugs were found to be two orders of magnitude less potent than methatropine while the carboxylate metabolite was found to be one order of magnitude less potent than the soft drugs.

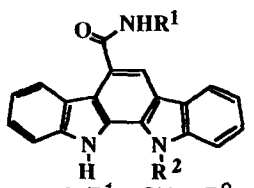
STUDIES ON PROTEIN KINASE C INHIBITORS; STRUCTURE-ACTIVITY RELATIONSHIPS IN INDOLOCARBAZOLE AND BIS-INDOLE SERIES.

BioMed. Chem. **1993**, *1*, 189

Serge FABRE, Michelle PRUDHOMME* Université Blaise Pascal, Laboratoire de Chimie Organique Biologique, URA 485, 63177 Aubière Cedex France; Maryse RAPP Unité INSERM U71, Rue Montalembert, 63005 Clermont-Ferrand, France.



1 $R^1 = H$; $R^2 = H$
2 $R^1 = CH_3$; $R^2 = H$
3 $R^1 = CH_3$; $R^2 = CH_3$



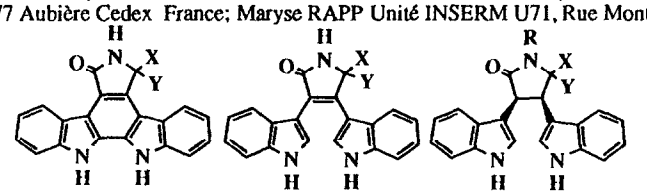
4 $R^1 = CH_3$; $R^2 = H$
5 $R^1 = CH_3$; $R^2 = CH_3$

Amides **1-5** were synthesized. The absence of inhibitory effect on protein kinase C showed that a rigid cyclic structure of the amide moiety is a requirement for biologiocal activity.

PROTEIN KINASE C INHIBITORS; STRUCTURE-ACTIVITY RELATIONSHIPS IN K252c RELATED COMPOUNDS.

BioMed. Chem. **1993**, *1*, 193

Serge FABRE, Michelle PRUDHOMME* Université Blaise Pascal, Laboratoire de Chimie Organique Biologique, URA 485, 63177 Aubière Cedex France; Maryse RAPP Unité INSERM U71, Rue Montalembert, 63005 Clermont-Ferrand, France.



A_1: X = Y = O B_1: X = Y = O C_1 : X = Y = O; R = H
A_2: X = H; Y = OH B_2: X = H; Y = OH C_2: X = H; Y = OH; R =H
A_3: X = Y = H B_3 X = Y = H C_3: X =Y= H; R = H
C_4: X = Y = O; R = CH_2OH

The syntheses of protein kinase C inhibitors, structurally related to the microbial metabolite K252c (A_3), are described. The rigidity of the framework is varied and the functional groups in the amide heterocycle are modified. The inhibitory potencies against protein kinase C and protein kinase A are described.

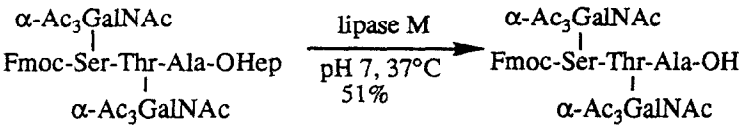
BioMed. Chem. **1993**, *1*, 197

CHEMOENZYMATIC SYNTHESIS OF O-GLYCOPEPTIDES CARRYING THE TUMOR ASSOCIATED T_N-ANTIGEN STRUCTURE

Peter Braun[a], Herbert Waldmann[b]* , Horst Kunz[a]*

[a]Universität Mainz, Institut f. Organ. Chemie, Becherweg 18-20, D-6500 Mainz

[b]Universität Karlsruhe, Institut f. Organ. Chemie, Richard-Willstätter-Weg 2, D-7500 Karlsruhe



BioMed. Chem. **1993**, *1*, 209

CONFORMATIONALLY RESTRICTED ANALOGUES OF THE POTENT CCK-B ANTAGONIST CI-988

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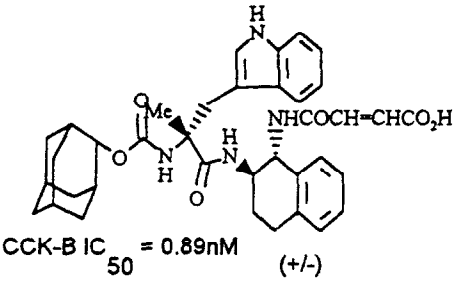
The synthesis and structure-activity relationships (SAR) for a series of conformationally restricted analogues of the selective cholecystokinin (CCK) antagonist CI-988 are described.



BioMed. Chem. **1993**, *1*, 219

Inhibition of Rat Liver Microsomal Lipid Peroxidation Elicited by 2,2-Dimethylchromenes and Chromans Containing Fluorinated Moieties Resistant to Cytochrome P-450 Metabolism

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Department of Biological Organic Chemistry, C.I.D. (C.S.I.C.), J. Girona, 18, 08034 Barcelona, Spain

2,2-Dimethylchromenes and chromans containing cytochrome P-450 resistant 2,2,2-trifluoroethoxy aryl substituents were synthesized and their activity as lipid peroxidation inhibitors evaluated and compared with that exhibited by the corresponding non-fluorinated derivatives.

BioMed. Chem. **1993**, *1*, 227

Synthesis and Biological Evaluation of Tetrademethyl Isocolchicine Derivatives as Inhibitors of DNA Topoisomerase Action *In Vitro*

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Four tetrademethyl isocolchicine analogs were prepared and evaluated as inhibitors of mammalian DNA topoisomerases *in vitro*. All compounds inhibited topoisomerase II-dependent DNA unknotting by a mechanism which did not involve "cleavable-complex" formation. *N*-Deacetylation as well as *N*-substitution with the (3',4',5'-trihydroxybenzoyl)-group afforded compounds which were less selective, based on their added ability to inhibit topoisomerase I-mediated DNA relaxation.