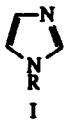
*BioMed. Chem.* **1994,** *2,* 305

**IMIDAZOL-1-YLALKANOIC ACIDS AS EXTRINSIC $^1$H NMR PROBES FOR THE DETERMINATION OF INTRACELLULAR pH, EXTRACELLULAR pH AND CELL VOLUME.** M. S. Gil, P. Zaderenko, F. Cruz,[&] S. Cerdán[&] and P. Ballesteros,* *Departamento de Química Orgánica y Biología, Facultad de Ciencias, UNED, 28040-Madrid, Spain and [&]Instituto de Investigaciones Biomédicas, CSIC, Arturo Duperier 4, 28029-Madrid, Spain*



I

R = $-CH_2CO_2CH_3$; $-CH(CO_2C_2H_5)_2$; $-CH(CH_2CO_2C_2H_5)_2$; $-CH(CO_2C_2H_5)-CH_2CO_2C_2H_5$

Imidazol-1-ylalkanoate esters I have been prepared by reaction of imidazole with α-bromo esters or with α,β-unsaturated esters. The corresponding acids have been obtained by hydrolysis. Esters and acids have been evaluated as extrinsic $^1$H NMR probes for the determination of intracellular pH, extracellular pH and cell volume in rat erythrocytes.

*BioMed. Chem.* **1994,** *2,* 315

**Regulation oF Apoptosis in Leukemic Cells by Analogs of Dynemicin A.**

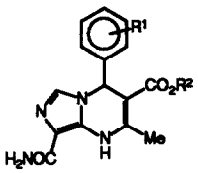
Andrew Hiatt,Robert Merlock, Steven Mauch and Wolfgang Wrasidlo*, Dept. of Cell Biology & Molecular & Exp. Medicine, The Scripps Res. Inst., 10666 N. Torrey Pines Rd., La Jolla, CA..,92037

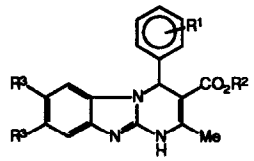
Structural determinants involved in the induction or inhibition of apoptosis of synthetic enediynes are described. Induction of apoptosis did not require the ability of enediynes to bind to DNA. Prevention of apotosis was observed by electronically stabalized analogs against topoisomerase I and II inhibitors, anti-mitotic and DNA anti-metabolite drugs and alkylating agents.

*BioMed. Chem.* **1994,** *2,* 323

**IMIDAZO[1,5-a]PYRIMIDINE AND BENZO[4,5]IMIDAZO[1,2-a]-PYRIMIDINE DERIVATIVES AS CALCIUM ANTAGONISTS**

R.Alajarin,[a] J. J. Vaquero,[a] J. Alvarez-Builla,*[a] M. Fau de Casa-Juana,[b] C. Sunkel,[b] J. G. Priego,[b] P. Gomez-Sal,[c,d] and R. Torres[d] *Deptos de [a]Química Orgánica, [c]Química Inorgánica and [d] Unidad de Rayos X (UCSA), Univ. de Alcalá. 28871-Alcalá de Henares. Madrid. Spain. [b]Laboratorios Alter S. A. Mateo Inurria, nº 30, 28036-Madrid. Spain.*





Several imidazo[1,5-a]pyrimidine and benzo[4,5]imidazo[1,2-a]pyrimidine derivatives were synthesized and evaluated as calcium antagonists. Structural and conformational aspects were studied by X-ray analysis.

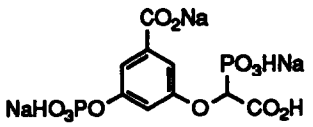
*BioMed. Chem.* **1994,** *2,* 331

**Functionalized 3,5-Dihydroxybenzoates as Potent Novel Inhibitors of EPSP Synthase**

**Michael J. Miller,* Joel E. Ream, Mark C. Walker, and James A. Sikorski**

***Life Sciences Research Center, Monsanto Company***
***700 Chesterfield Parkway North, St. Louis, Missouri 63198***

**Aromatic analogues of the EPSP synthase reaction substrate, product and tetrahedral intermediate were synthesized from 3,5-dihyroxybenzoic acid. These readily accessible analogues are highly effective competitive inhibitors (vs. S3P) of *E. Coli* EPSP synthase indicating that a benzene ring is a very effective substitute for the complex shikimate in EPSP synthase inhibitors.**



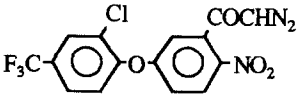
**4, $K_i$ (apparent) = 160 nM**

*BioMed. Chem.* **1994**, *2*, 339

**Synthesis and Properties of a Photoaffinity Labeling Reagent for Protoporphyrinogen Oxidases, the Target Enzymes of Diphenyl Ether Herbicides**

N. O'Connor,[1] R. Mornet,[1] M. Matringe,[2] D. Clair,[2] R. Scalla,2 T.T. Fujimoto and C. Swithenbank[3]
[1]*L.C.O.F.A., Faculté des Sciences, 2 Boulevard Lavoisier, 49045 Angers, France;* [2]*Laboratoire des Herbicides, INRA, BV 21034 Dijon, France;* [3]*Rohm and Haas Company, Research Lab, 727 Norristown Road, Spring House, PA 19447, USA.*

A photoaffinity labeling reagent was designed for probing protoporphyrinogen oxidases. It exhibits similar properties as diphenyl ether herbicides, known as inhibitors of these enzymes.

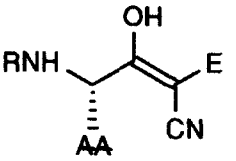



*BioMed. Chem.* **1994**, *2*, 343

**Synthesis of Novel Inhibitors of the HIV-1 Protease: Difunctional Enols of Simple N-Protected amino Acids.**

M. Vaillancourt,[a,b] B. Vanasse,[a] N. Le Berre,[a] E. Cohen[b] and G. Sauvé*,[a]
a) Institut Armand-Frappier, 531 boul. des Prairies, Laval, Qc, Canada H7N 4Z3
b) Dép. de microbiologie et d'immunologie, Université de Montréal, C.P. 6128, Succ.A, Montréal, Qc, Canada, H3C 3J7

A Structure activity relationship study which led to the design of difunctionalized enols of simple amino acids as novel competitive inhibitors of HIV-1 protease is described.

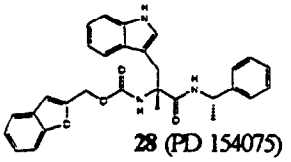



*BioMed. Chem.* **1994**, *2*, 357

**RATIONAL DESIGN OF HIGH AFFINITY TACHYKININ $NK_1$ RECEPTOR ANTAGONISTS**

S Boyle, S Guard, D C Horwell, W Howson, M Higginbottom, K Martin, A T McKnight, M C Pritchard, J O'Toole, J Raphy, D C Rees, E Roberts, K J Watling, G N Woodruff, J Hughes.
*Parke-Davis Neuroscience Research Centre, Addenbrookes Hospital Site, Hills Road, Cambridge CB2 2QB, UK.*

The rational design of a non-peptide tachykinin $NK_1$ receptor antagonist **28**, PD 154075 is described. **28** has a $K_i$ = 0.35 nM for the $NK_1$ receptor binding site in human IM9 cells and is a potent antagonist *in vitro* (guinea-pig ileum bioassay, $K_B$ = 0.3 nM). **28** is active *in vivo* in the guinea-pig bladder plasma extravasation model induced by SPOMe with an $ID_{50}$ of 0.02 mg/Kg iv.



**28** (PD 154075)