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Bioorganic &
Medicinal
Chemistry

Bioorganic & Medicinal Chemistry Vol. 14, No. 4, 2006

Contents

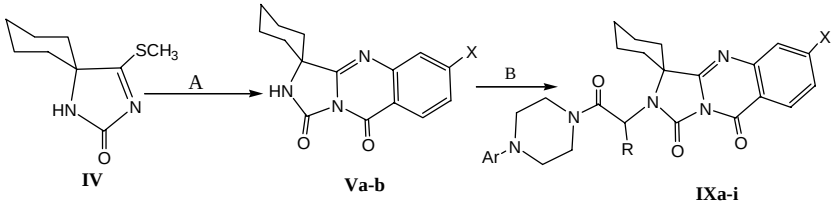
PERSPECTIVE

The benefits of the multi-target approach in drug design and discovery **pp 896–897**
L. Michel Espinoza-Fonseca*

Promiscuous binding has been considered to be a problem in the design and development of new drugs against a given disease. However, promiscuity in molecular recognition is not all bad news, and scientists are currently taking advantage of the emerging 'promiscuous binding' or 'multi-target approach' in medicinal chemistry.

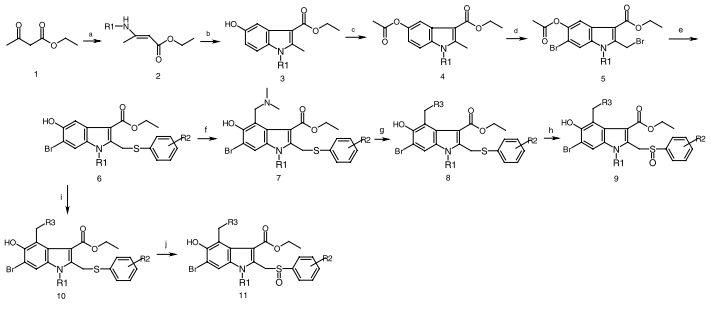
ARTICLES

Ligand design and synthesis of new imidazo[5,1-*b*]quinazoline derivatives as α_1-adrenoceptor agonists and antagonists **pp 898–910**
Mohamed A. H. Ismail,* Mohamed N. Y. Aboul-Enein, Khaled A.M. Abouzid and Rabah A. T. Serya

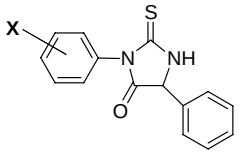


A) Anthranilic Acids B) 1-Aryl-4-Chloroacylpiperazines

Synthesis and in vitro anti-hepatitis B virus activities of some ethyl 6-bromo-5-hydroxy-1*H*-indole-3-carboxylates **pp 911–917**
Huifang Chai, Yanfang Zhao, Chunshen Zhao and Ping Gong*

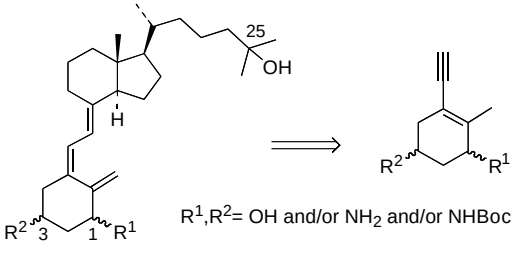


Synthesis, molecular modelling and enzymatic evaluation of (±)3,5-diphenyl-2-thioxoimidazolidin-4-ones as new potential cyclooxygenase inhibitors pp 918–927
Marie P. Gauthier, Catherine Michaux, Stéphanie Rolin, Caroline Vastersaegher, Xavier de Leval, Fabien Julémont, Lionel Pochet and Bernard Masereel*

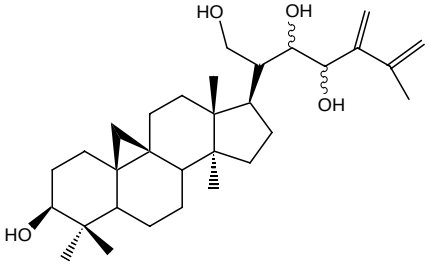


Substituted (±)2-thioxoimidazolin-4-ones were synthesized in order to design new type-2 cyclooxygenase (COX-2) inhibitors. Some of them completely inhibit human recombinant COX-2 at 50 μM. In human blood, the inhibitory potency of these drugs was disappointing and attributed to a poor aqueous stability of these imidazolidinones.

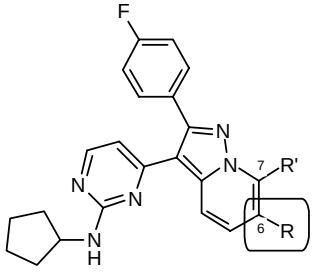
Versatile synthesis and biological evaluation of 1,3-diamino-substituted 1α,25-dihydroxyvitamin D_3 analogues pp 928–937
Daniel Oves, Susana Fernández, Miguel Ferrero, Roger Bouillon, Annemieke Verstuyf and Vicente Gotor*



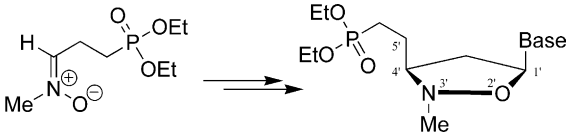
Tyrosinase inhibitory cycloartane type triterpenoids from the methanol extract of the whole plant of *Amberboa ramosa* Jafri and their structure–activity relationship pp 938–943
Mahmud Tareq Hassan Khan,* Sher Bahadar Khan and Arjumand Ather



Synthesis of C-6 substituted pyrazolo[1,5-*a*]pyridines with potent activity against herpesviruses pp 944–954
Scott H. Allen,* Brian A. Johns, Kristjan S. Gudmundsson, George A. Freeman, F. Leslie Boyd, Jr., Connie H. Sexton, Dean W. Selleseth, Katrina L. Creech and Kelly R. Moniri

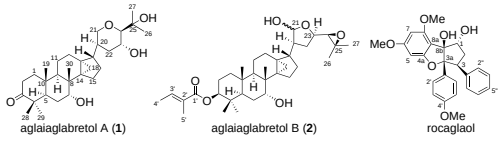


Synthesis and biological evaluation of phosphonated carbocyclic 2′-oxa-3′-aza-nucleosides **pp 955–959**
Ugo Chiacchio, Daniela Iannazzo,* Anna Piperno,* Roberto Romeo, Giovanni Romeo, Antonio Rescifina and Monica Saglimbeni



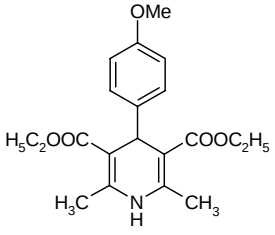
Activity-guided isolation of cytotoxic constituents from the bark of *Aglaia crassinervia* collected in Indonesia **pp 960–972**
Bao-Ning Su, Heebyung Chai, Qiuwen Mi, Soedarsono Riswan, Leonardus B. S. Kardono, Johar J. Afriastini, Bernard D. Santarsiero, Andrew D. Mesecar, Norman R. Farnsworth, Geoffrey A. Cordell, Steven M. Swanson and A. Douglas Kinghorn*

Three new glabretal-type triperpenoids, aglaiaglabretols A–C, and nine known compounds, were isolated from the bark of *Aglaia crassinervia*. The cytotoxic activity of all isolates and several chemical transformation products was evaluated. The known cyclopenta[*b*]benzofuran, rocaglaol, was found to be significantly cytotoxic and comparable in potency to the positive controls, paclitaxel and camptothecin. Aglaiaglabretol B (**2**) was further tested in an in vivo hollow fiber model.



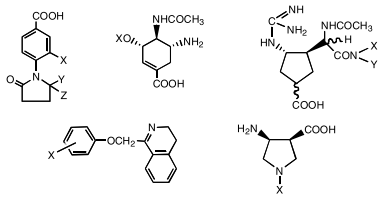
Microwave-assisted synthesis of antimicrobial dihydropyridines and tetrahydropyrimidin-2-ones: Novel compounds against aspergillosis **pp 973–981**
Anil K. Chhillar, Pragya Arya, Chandrani Mukherjee, Pankaj Kumar, Yogesh Yadav, Ajendra K. Sharma, Vibha Yadav, Jyotsana Gupta, Rajesh Dabur, Hirday N. Jha, Arthur C. Watterson, Virinder S. Parmar,* Ashok K. Prasad* and Gainda L. Sharma*

Synthesis and antifungal activity studies on 4-aryl-1,4-dihydropyridine and 4-aryl-1,2,3,4-tetrahydropyrimidin-2-one derivatives against pathogenic strains of *Aspergillus fumigatus* and *Candida albicans* reveal that diethyl 4-(4-methoxyphenyl)-2,6-dimethyl-1,4-dihydropyridin-3,5-dicarboxylate is the most active compound.



A QSAR study on influenza neuraminidase inhibitors **pp 982–996**
Rajeshwar P. Verma and Corwin Hansch*

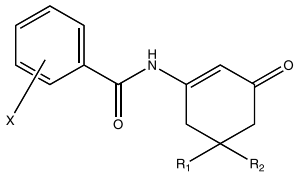
Quantitative structure–activity relationships have been performed for different sets of compounds with respect to their activities toward influenza neuraminidase.



Enaminones 9. Further studies on the anticonvulsant activity and potential type IV phosphodiesterase inhibitory activity of substituted vinylic benzamides pp 997–1006

Alan J. Anderson, Jesse M. Nicholson, Oladapo Bakare, Ray J. Butcher, Tiffany L. Wilson and K. R. Scott*

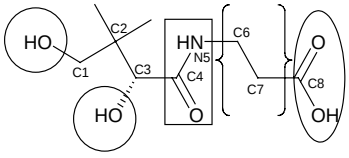
An improved method for the synthesis of benzamides via parallel solution-phase chemistry is presented. These compounds were evaluated for anticonvulsant activity as well as evaluation as potential inhibitors of phosphodiesterase type IV for use as antiasthmatics.



X = H; 3-Cl; 3,4-di OCH_3; 3-$O(CH_2)_3CH_3$,4-OCH_3; 3-*O*-cyclopentyl, 4-OCH_3
R_1 = H or CH_3
R_2 = H or CH_3

Structure–activity relationships and enzyme inhibition of pantothenamide-type pantothenate kinase inhibitors pp 1007–1020

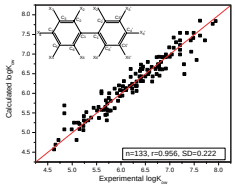
Kristopher G. Virga, Yong-Mei Zhang, Roberta Leonardi, Robert A. Ivey, Kirk Hevener, Hee-Won Park, Suzanne Jackowski, Charles O. Rock and Richard E. Lee*



Structure–activity relationships were determined for three series of pantothenamide-type pantothenate kinase inhibitors through their evaluation in vivo against a panel of four PanK enzymes and for antimicrobial activity.

QSPR models for polychlorinated biphenyls: *n*-Octanol/water partition coefficient pp 1021–1028

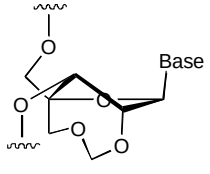
J. Padmanabhan, R. Parthasarathi, V. Subramanian* and P. K. Chattaraj*



The success of any QSPR model depends on the selection of proper descriptors. Exploring the usefulness of descriptors, especially, conceptual DFT based global electrophilicity index (ω) along with the energy of lowest unoccupied molecular orbital (E_{LUMO}) and the number of chlorine substituents (N_{Cl}) in analyzing the lipophilic behaviour ($\log K_{ow}$) for 133 PCBs congeners is assessed. Existence of high correlation indicates the significance of the developed model in property prediction.

Synthesis and properties of 2′-*O*,4′-*C*-methyleneoxymethylene bridged nucleic acid pp 1029–1038

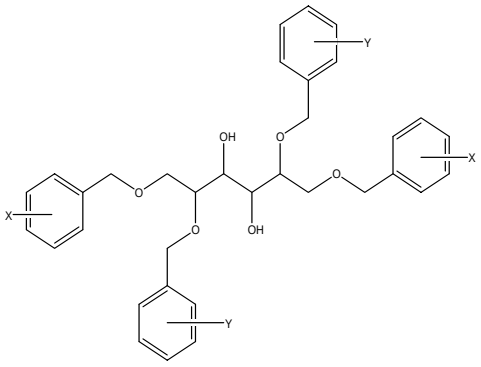
Yoshiyuki Hari, Satoshi Obika, Ryo Ohnishi, Ken Eguchi, Tomohisa Osaki, Hirofumi Ohishi and Takeshi Imanishi*



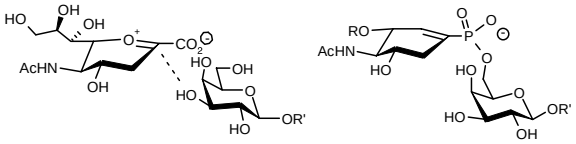
2',4'-BNA^{COC}

QSAR by LFER model of HIV protease inhibitor mannitol derivatives using FA-MLR, PCRA, and PLS techniques pp 1039–1046
J. Thomas Leonard and Kunal Roy*

HIV protease inhibitory data of mannitol derivatives have been subjected to quantitative structure–activity relationship study by linear free energy related model of Hansch using FA-MLR, PCRA, and PLS techniques.



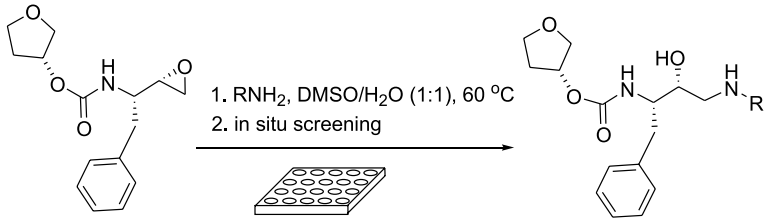
Building a successful structural motif into sialylmimetics—cyclohexenephosphonate monoesters as pseudo-sialosides with promising inhibitory properties pp 1047–1057
Hansjörg Streicher* and Heike Busse



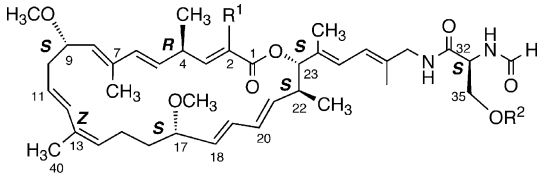
Sialyl-Transfer Pseudo-Sialoside

A systematic synthetic approach to sialylmimetics containing a cyclohexenephosphonate scaffold has been developed which allows their incorporation into pseudo-disaccharidic systems. Thus, mimicking of the full structural space displayed by natural sialosides as substrates, products or as intermediates in enzymatic reactions is possible and inhibitory activity toward selected sialidases is obtained.

Epoxide opening in water and screening in situ for rapid discovery of enzyme inhibitors in microtiter plates pp 1058–1062
Fu-Sen Liang, Ashraf Brik, Ying-Chuan Lin, John H. Elder and Chi-Huey Wong*



Absolute stereochemistry and antitumor activity of iejimalides pp 1063–1067
Kohei Nozawa, Masashi Tsuda, Haruaki Ishiyama, Takuma Sasaki, Takashi Tsuruo and Jun'ichi Kobayashi*

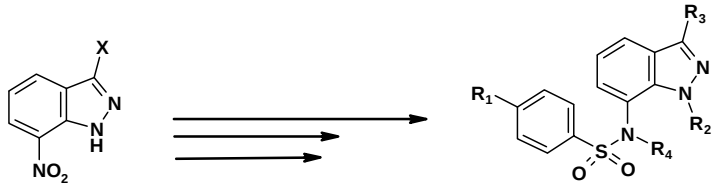


lejimalide A (**1**) R^1=H, R^2=H
lejimalide C (**3**) R^1=H, R^2=SO_3Na
lejimalide D (**4**) R^1=CH_3, R^2=SO_3Na

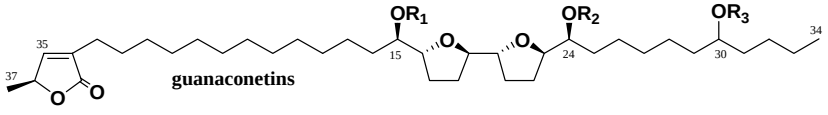
Combination of porphyrins and DNA-alkylation agents: Synthesis and tumor cell apoptosis induction **pp 1068–1077**
Hanping He, Yan Zhou, Feng Liang, Dongqing Li, Juanjuan Wu, Li Yang, Xiang Zhou,* Xiaolian Zhang* and Xiaoping Cao

A series of porphyrin–DNA cross-linking conjugates were synthesized. Their cytotoxicities to tumor cells were tested using MTT assays first. Then, HeLa cell apoptosis induced by these cationic porphyrins under the light was examined by laser confocal microscopy, flow cytometric analysis, and further confirmed by observing the morphological changes and DNA fragmentation mainly.

Synthesis and biological evaluation of *N*-(7-indazolyl)benzenesulfonamide derivatives as potent cell cycle inhibitors **pp 1078–1088**
L. Bouissane, S. El Kazzouli, S. Léonce, B. Pfeiffer, E. M. Rakib, M. Khouili and G. Guillaumet*

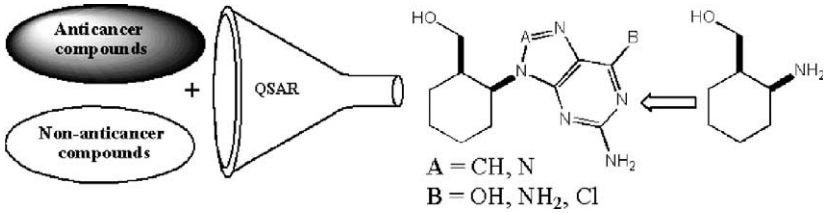


Guanaconetins, new antitumoral acetogenins, mitochondrial complex I and tumor cell growth inhibitors **pp 1089–1094**
Nadia Chahboune, Isabel Barrachina, Inmaculada Royo, Vanessa Romero, Jairo Sáez, José R. Tormo, Nuria De Pedro, Ernesto Estornell, M. Carmen Zafra-Polo, Fernando Peláez and Diego Cortes*



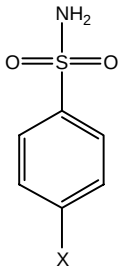
Four new natural and two semisynthetic 15,24,30-trioxygenated acetogenins were tested as mitochondrial complex I enzymatic inhibitors as well as growth of several tumor cell lines. Placement of acetyl groups along the alkyl chain modulated the potency of the bis-tetrahydrofuranic acetogenins.

Stochastic entropy QSAR for the in silico discovery of anticancer compounds: Prediction, synthesis, and in vitro assay of new purine carbanucleosides **pp 1095–1107**
Humberto González-Díaz,* Dolores Viña, Lourdes Santana, Erik de Clercq and Eugenio Uriarte*

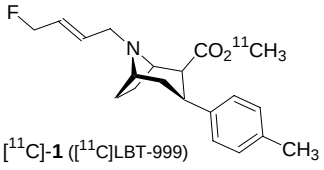


QSAR study on *para*-substituted aromatic sulfonamides as carbonic anhydrase II inhibitors using topological information indices **pp 1108–1114**
Georgia Melagraki, Antreas Afantitis, Haralambos Sarimveis,* Olga Igglessi-Markopoulou and Claudiu T. Supuran

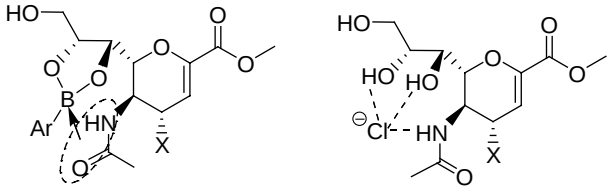
A QSAR study on *para*-substituted sulfonamide carbonic anhydrase inhibitors is performed using topological information indices. Different statistically significant multiparametric models have shown that the physiologically relevant isoform CA II can be successfully modeled using this topological information approach.



Synthesis, radiosynthesis and in vivo preliminary evaluation of [^{11}C]LBT-999, a selective radioligand for the visualisation of the dopamine transporter with PET **pp 1115–1125**
Frédéric Dollé,* Patrick Emond, Sylvie Mavel, Stéphane Demphel, Françoise Hinnen, Zoïa Mincheva, Wadad Saba, Heric Valette, Sylvie Chalon, Christer Halldin, Julie Helfenbein, Joël Legaillard, Jean-Claude Madelmont, Jean-Bernard Deloye, Michel Bottlaender and Denis Guilloteau

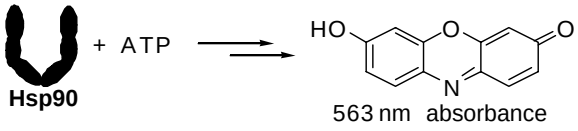


Improving the membrane permeability of sialic acid derivatives **pp 1126–1133**
Timothy M. Altamore, Peter J. Duggan* and Guy Y. Krippner

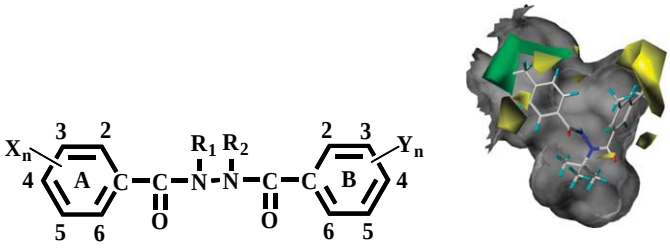


The transport of sialic acid derivatives through a lipophilic membrane, promoted by a boronic acid and an ammonium chloride, was investigated.

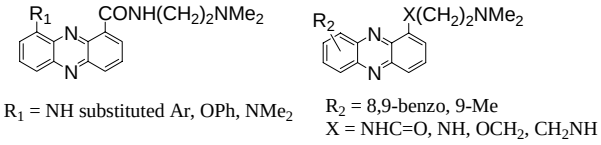
Development and optimization of a useful assay for determining Hsp90's inherent ATPase activity **pp 1134–1142**
Christopher Avila, Boris A. Kornilayev and Brian S. J. Blagg*



High-throughput screening of ecdysone agonists using a reporter gene assay followed by 3-D QSAR analysis of the molting hormonal activity **pp 1143–1159**
Craig E. Wheelock, Yoshiaki Nakagawa,* Toshiyuki Harada, Nobuhiro Oikawa, Miki Akamatsu, Guy Smagghe, Dimitra Stefanou, Kostas Iatrou and Luc Swevers



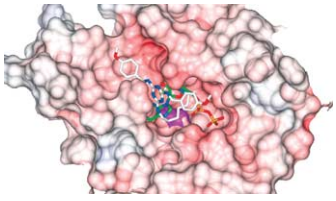
Phenazine-1-carboxamides: Structure–cytotoxicity relationships for 9-substituents and changes in the H-bonding pattern of the cationic side chain **pp 1160–1168**
Swarna A. Gamage,* Gordon W. Rewcastle, Bruce C. Baguley, Peter A. Charlton and William A. Denny



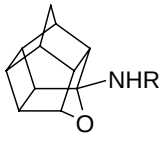
R_1 = NH substituted Ar, OPh, NMe_2

R_2 = 8,9-benzo, 9-Me
X = NHC=O, NH, OCH_2, CH_2NH

Identification of 12Cysβ on tubulin as the binding site of tubulyzine **pp 1169–1175**
Yeoun Jin Kim, Dan L. Sackett, Matthieu Schapira, Daniel P. Walsh, Jaeki Min, Lewis K. Pannell and Young-Tae Chang *

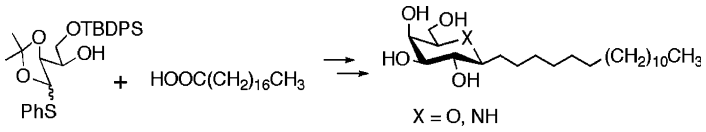


Effect of polycyclic cage amines on the transmembrane potential of neuronal cells **pp 1176–1181**
Erika Grobler, Anne Grobler, Cornelis J. Van der Schyf and Sarel F. Malan*



Pentacycloundecylamine derivatives influence the profile of KCl-induced membrane depolarization and cause an overall reduction in cell membrane depolarization.

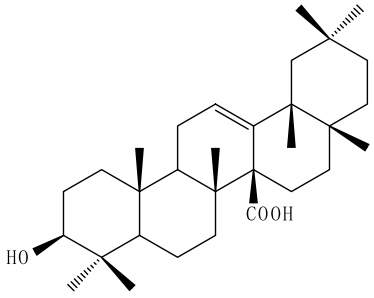
C-Glycoside analogues of β-galactosylceramide with a simple ceramide substitute: Synthesis and binding to HIV-1 gp120 pp 1182–1188
Line A. Augustin, Jacques Fantini* and David R. Mootoo*



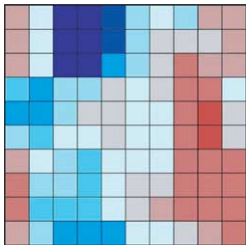
The synthesis and HIV-1 gp120 binding of a *C*- and an aza-*C*-glycoside analogues of β-galactosylceramide that contain a simple C-17 hydrocarbon chain as a ceramide substitute are described. Both compounds were prepared from stearic acid, and a carbohydrate-derived thioacetal alcohol, and showed potent and specific affinity for gp120.

Induction of apoptosis in HeLa cells by 3β-hydroxy-12-oleanen-27-oic acid from the rhizomes of *Astilbe chinensis* pp 1189–1198
Hong-Xiang Sun,* Quan-Fang Zheng and Jue Tu

3β-Hydroxy-12-oleanen-27-oic acid (ATA) was an antitumor active oleanane-type triterpenoid from the rhizomes of *Astilbe chinensis*. ATA was structurally very similar to oleanolic acid, with the only difference being interchange of the carboxyl and methyl groups at the C-14 and C-17 positions. In this study, we investigated the induction of apoptosis in HeLa cells by ATA and the putative pathways of its actions.

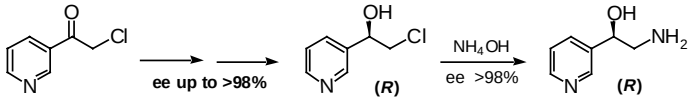


QSAR analysis of phenolic antioxidants using MOLMAP descriptors of local properties pp 1199–1206
Sunil Gupta, Susan Matthew, Pedro M. Abreu and João Aires-de-Sousa*

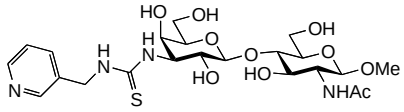


Counterpropagation neural networks (CPG NNs) were trained with MOLMAP descriptors to predict antioxidant activity. The red neurons in the output layer of the CPG NN predicted high antioxidant activity and those in blue predicted inactivity.

A chemoenzymatic scalable route to optically active (*R*)-1-(pyridin-3-yl)-2-aminoethanol, valuable moiety of β_3-adrenergic receptor agonists pp 1207–1214
Maria Grazia Perrone, Ernesto Santandrea, Erika Giorgio, Laura Bleve, Antonio Scilimati* and Paolo Tortorella

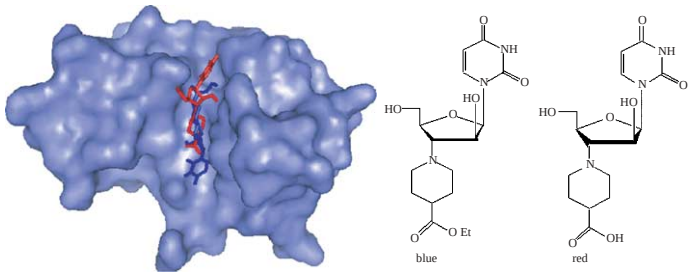


Thioureido *N*-acetyllactosamine derivatives as potent galectin-7 and 9N inhibitors **pp 1215–1220**
B. A. Salameh, A. Sundin, H. Leffler and U. J. Nilsson*

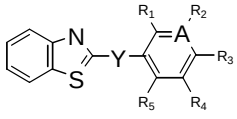


K_d 23 μM against galectin-7 and K_d 47 μM against galectin-9N

3′-*N*-Alkylamino-3′-deoxy-*ara*-uridines: A new class of potential inhibitors of ribonuclease A and angiogenin **pp 1221–1228**
Tushar K. Maiti, Soumya De, Swagata Dasgupta* and Tanmaya Pathak*

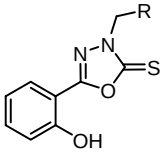


Solid phase combinatorial synthesis of benzothiazoles and evaluation of topoisomerase II inhibitory activity **pp 1229–1235**
Suk-June Choi, Hyen Joo Park, Sang Kook Lee, Sang Woong Kim, Gyoonhee Han and Hea-Young Park Choo*



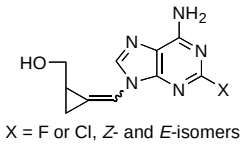
Solid phase synthesis of 2-(substituted-phenyl)benzothiazoles and evaluation of their cytotoxicity and topoisomerase II inhibition activity are described.

Novel 5-(2-hydroxyphenyl)-3-substituted-2,3-dihydro-1,3,4-oxadiazole-2-thione derivatives: Promising anticancer agents **pp 1236–1246**
Ahmed S. Aboraia, Hamdy M. Abdel-Rahman,* Nadia M. Mahfouz and Mahmoud A. EL-Gendy

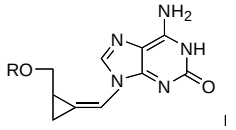


A series of 5-(2-hydroxyphenyl)-3-substituted-2,3-dihydro-1,3,4-oxadiazole-2-thione derivatives was synthesized and tested for anticancer activity.

Synthesis, antiviral, and antitumor activity of 2-substituted purine methylenecyclopropane analogues of nucleosides **pp 1247–1254**
Xinrong Qin, Xinchao Chen, Kun Wang, Lisa Polin, Earl R. Kern, John C. Drach, Elizabeth Gullen, Yung-Chi Cheng and Jiri Zemlicka*

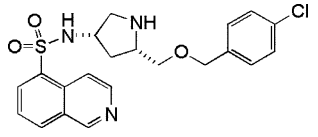


X = F or Cl, *Z*- and *E*-isomers



R = H or $MeO_2CCH(CH_3)NHP(O)(OC_6H_5)$, *R*- and *S*-enantiomers

Structure-based design of isoquinoline-5-sulfonamide inhibitors of protein kinase B **pp 1255–1273**
Ian Collins,* John Caldwell, Tatiana Fonseca, Alastair Donald, Vassilios Bavetsias, Lisa-Jane K. Hunter, Michelle D. Garrett, Martin G. Rowlands, G. Wynne Aherne, Thomas G. Davies, Valerio Berdini, Steven J. Woodhead, Deborah Davis, Lisa C. A. Seavers, Paul G. Wyatt, Paul Workman and Edward McDonald*



Novel pyrrolidine-derived isoquinoline-5-sulfonamide inhibitors of PKB were designed, and investigated crystallographically and in cellular assays.

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*Corresponding author
ⓘ+ Supplementary data available via ScienceDirect

COVER

Calculated low-energy complex between galectin-7 and a C3′-thiourea-derivatized *N*-acetyllactosamine showing an interaction between a protonated pyridine and a galectin-7 glutamate side chain. B. A. Salameh, A. Sundin, H. Leffler and U. J. Nilsson.

Indexed/Abstracted in: Beilstein, Biochemistry & Biophysics Citation Index, CANCERLIT, Chemical Abstracts, Chemistry Citation Index, Current Awareness in Biological Sciences/BIOBASE, Current Contents: Life Sciences, EMBASE/Excerpta Medica, MEDLINE, PASCAL, Research Alert, Science Citation Index, SciSearch, TOXFILE

ISSN 0968-0896