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# Bioorganic & Medicinal Chemistry

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## Bioorganic & Medicinal Chemistry Volume 18, Issue 8, 2010

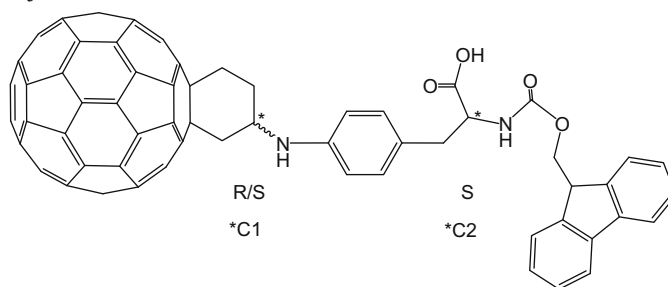
### Contents

#### ARTICLES

##### Nanoscale enzyme inhibitors: Fullerenes inhibit carbonic anhydrase by occluding the active site entrance

pp 2822–2828

Alessio Innocenti, Serdar Durdagi, Nadjmeh Doostdar, T. Amanda Strom, Andrew R. Barron, Claudiu T. Supuran\*

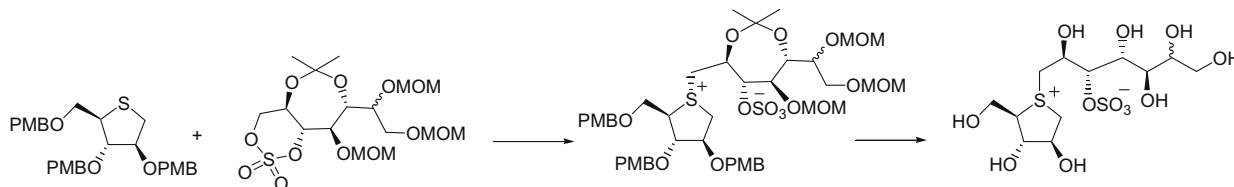


$K_i = 8.21 \mu\text{M}$  (CA II);  $9.19 \mu\text{M}$  (CA IX);  $0.79 \mu\text{M}$  (CA XII).

##### Synthesis of a biologically active isomer of kotalanol, a naturally occurring glucosidase inhibitor

pp 2829–2835

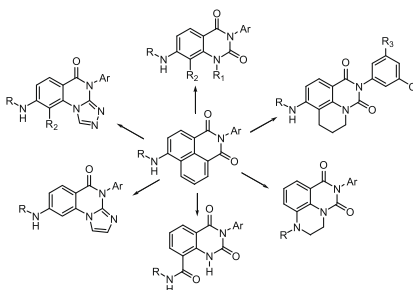
Razieh Eskandari, Kumarasamy Jayakanthan, Douglas A. Kuntz, David R. Rose, B. Mario Pinto\*



##### Allosteric inhibitors of hepatitis C virus NS5B polymerase thumb domain site II: Structure-based design and synthesis of new templates

pp 2836–2848

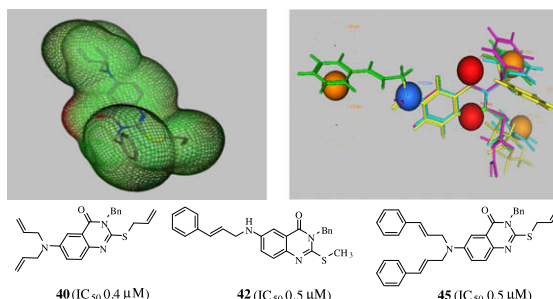
Savina Malancona\*, Monica Donghi, Marco Ferrara, Josè I. Martin Hernando, Marco Pompei, Silvia Pesci, Jesus M. Ontoria, Uwe Koch, Michael Rowley, Vincenzo Summa



### Non-classical antifolates. Part 2: Synthesis, biological evaluation, and molecular modeling study of some new 2,6-substituted-quinazolin-4-ones

pp 2849–2863

Fatmah A. M. Al-Omary, Laila A. Abou-zeid, Mahmoud N. Nagi, El-Sayed E. Habib, Alaa A.-M. Abdel-Aziz, Adel S. El-Azab, Sami G. Abdel-Hamide, Mohamed A. Al-Omar, Abdulrahman M. Al-Obaid, Hussein I. El-Subbagh\*



### Synthesis of a novel series of diphenolic chromone derivatives as inhibitors of NO production in LPS-activated RAW264.7 macrophages

pp 2864–2871

Guo-Biao Liu, Jian-Liang Xu, Mei Geng, Rui Xu, Rong-Rong Hui, Jian-Wei Zhao, Qiang Xu, Hong-Xi Xu, Jian-Xin Li\*

A series of diphenolic chromone derivatives were synthesized and their inhibitory activity on nitric oxide production was evaluated. Three of them exhibited quite potent inhibitory activity without obvious cytotoxicity.

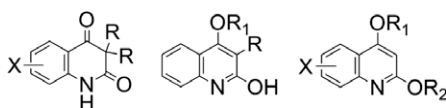
| Compd     | R | $IC_{50}$ |            |
|-----------|---|-----------|------------|
|           |   | $\mu$ M   | $\mu$ g/mL |
| <b>6f</b> |   | 0.35      | 0.11       |
| <b>6g</b> |   | 0.80      | 0.27       |
| <b>6h</b> |   | 0.61      | 0.20       |



### Synthesis and anti-HIV activity of alkylated quinoline 2,4-diols

pp 2872–2879

Nafees Ahmed, Keyur G. Brahmabhatt, Sudeep Sabde, Debashis Mitra\*, Inder Pal Singh, Kamlesh K. Bhutani\*



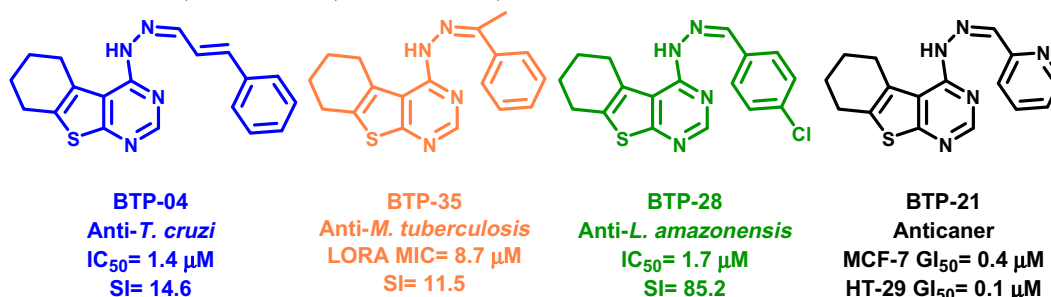
We synthesized 47 alkylated derivatives of quinoline 2,4-diol and tested for anti-HIV activity in human CD4<sup>+</sup> T cell line CEM-GFP, infected with HIV-1<sub>NL4.3</sub>. Compounds **6**, **9** and **23** showed  $IC_{50}$  of 2.35, 3.23 and 3.89  $\mu$ M, respectively.



### Trypanoside, anti-tuberculosis, leishmanicidal, and cytotoxic activities of tetrahydrobenzothienopyrimidines

pp 2880–2886

José C. Aponte, Abraham J. Vaisberg, Denis Castillo, German Gonzalez, Yannick Estevez, Jorge Arevalo, Miguel Quiliano, Mirko Zimic, Manuela Verástegui, Edith Málaga, Robert H. Gilman, Juan M. Bustamante, Rick L. Tarleton, Yuehong Wang, Scott G. Franzblau, Guido F. Pauli, Michel Sauvain, Gerald B. Hammond\*

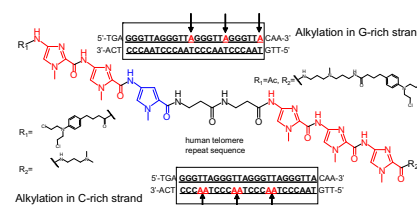


### Alkylation of a human telomere sequence by heterotrimeric chlorambucil PI polyamide conjugates

pp 2887–2893

Gengo Kashiwazaki, Toshikazu Bando\*, Ken-ichi Shinohara, Masafumi Minoshima, Hana Kumamoto, Shigeki Nishijima, Hiroshi Sugiyama\*

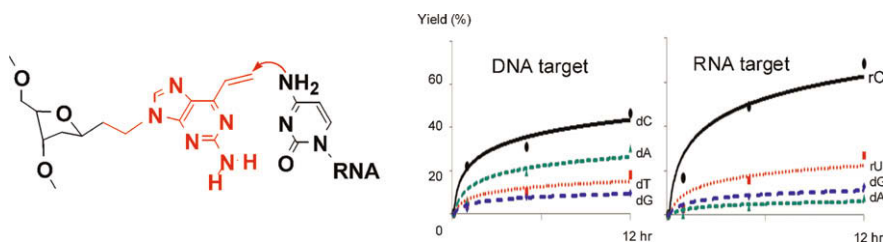
We designed and synthesized human telomere alkylating *N*-methylpyrrole-*N*-methylimidazole (PI) polyamide conjugates (**1–6**). The C-type conjugates **1–3** possessed a chlorambucil moiety at the C terminus, whereas the N-type conjugates **4–6** had one of these moieties at the N terminus. The DNA alkylating activity of these conjugates was evaluated by high-resolution denaturing polyacrylamide gel electrophoresis using a 220 bp DNA fragment containing the human telomere repeat sequence 5'-(GGGTAA)<sub>4</sub>-3'/5'-(TAACCC)<sub>4</sub>-3'. C-type conjugates are designed to alkylate the G-rich-strand-containing 5'-GGGTAA-3' and N-type conjugates were designed to alkylate the complementary C-rich strand-containing 5'-TAACCC-3' sequence. The difference between conjugates **1–3** and **4–6** lies in the linker region between the polyamide moiety and chlorambucil. Conjugates **1** and **4** efficiently alkylated the 5'-GGTTAGGGTTA-3' and 5'-CCCTAACCTAA-3' sequences, respectively, by recognizing 11 bp in the presence of distamycin A (Dist), in a heterotrimeric manner: one long alkylating polyamide conjugate (**1–6**) and two short partners (Dist).



### The alkyl-connected 2-amino-6-vinylpurine (AVP) crosslinking agent for improved selectivity to the cytosine base in RNA

pp 2894–2901

Yosuke Taniguchi, Yusuke Kurose, Takamasa Nishioka, Fumi Nagatsugi, Shigeki Sasaki\*

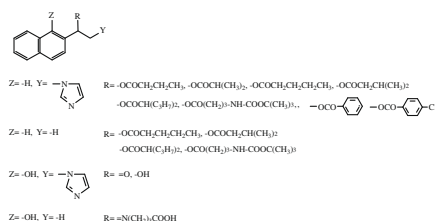


The ethylene-connected 2-amino-6-vinylpurine (AVP) crosslinking agent exhibited improved reactivity and selectivity to the cytosine base in RNA.

### Synthesis, anticonvulsant and antimicrobial activities of some new 2-acetylnaphthalene derivatives

pp 2902–2911

Arzu Karakurt\*, Meral Özalp, Şamil Işık, James P. Stables, Sevim Dalkara

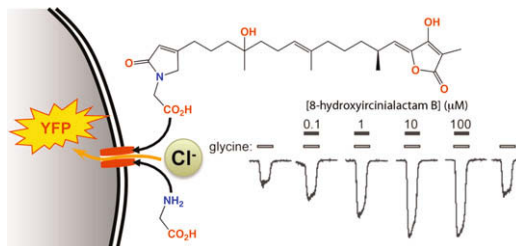


As a part of our interest on (arylalkyl)imidazole anticonvulsant compounds we describe herein the design and synthesis of a series of acetylnaphthalene derivatives and evaluation of their anticonvulsant/antimicrobial activities. These compounds were variously substituted at the alkyl chain between naphthalene and imidazole rings. The most potent compounds were the ester derivatives with imidazole ring.

### Ircinialactams: Subunit-selective glycine receptor modulators from Australian sponges of the family Irciniidae

pp 2912–2919

Walter Balansa, Robiul Islam, Frank Fontaine, Andrew M. Piggott, Hua Zhang, Timothy I. Webb, Daniel F. Gilbert, Joseph W. Lynch, Robert J. Capon\*



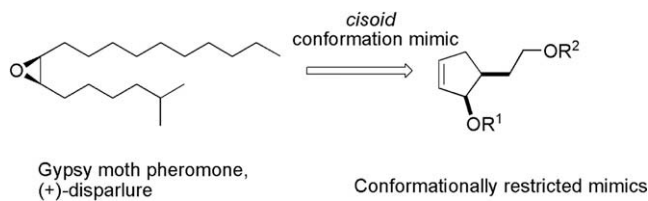
Screening an extract library of marine invertebrates yielded new glycyl lactam sesterterpenes with potent and subunit selective modulatory properties against  $\alpha 1$  and  $\alpha 3$  glycine receptor (GlyR) chloride channels isoforms.



**Synthesis and biological activity of conformationally restricted gypsy moth pheromone mimics**

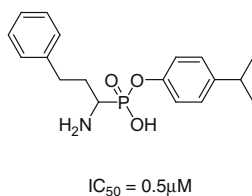
pp 2920–2929

Hao Chen, Yongmei Gong, Regine M. Gries, Erika Plettner\*

**New aromatic monoesters of  $\alpha$ -aminoalkylphosphonic acids as inhibitors of aminopeptidase N/CD13**

pp 2930–2936

Renata Grzywa, Anna M. Sokol, Marcin Sieńczyk, Magdalena Radziszewicz, Beata Kościółek, Michael P. Carty, Józef Oleksyszyn\*

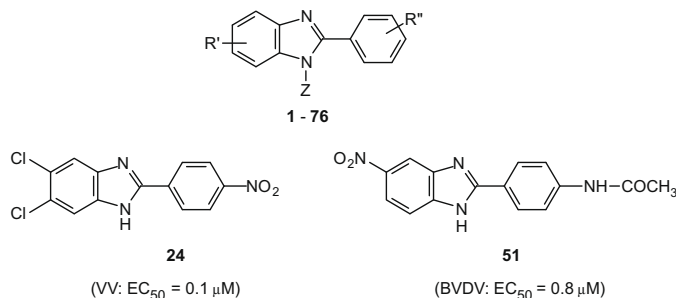


Structure–activity relationship (SAR) studies of phosphonate APN inhibitors.

**Antiviral activity of benzimidazole derivatives. II. Antiviral activity of 2-phenylbenzimidazole derivatives**

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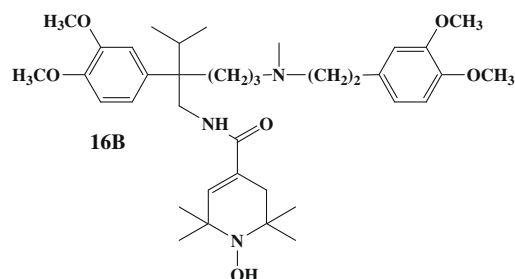
Michele Tonelli\*, Matteo Simone, Bruno Tasso, Federica Novelli, Vito Boido, Fabio Sparatore, Giuseppe Paglietti, Sabrina Pricl, Gabriele Giliberti, Sylvain Blois, Cristina Ibba, Giuseppina Sanna, Roberta Loddo, Paolo La Colla\*

**Synthesis and study of new paramagnetic and diamagnetic verapamil derivatives**

pp 2954–2963

Balázs Bognár, Shabnam Ahmed, M. Lakshmi Kuppusamy, Karupaiyah Selvendiran, Mahmood Khan, József Jekő, Olga H. Hankovszky, Tamás Kálai, Periannan Kuppusamy, Kálmán Hideg\*

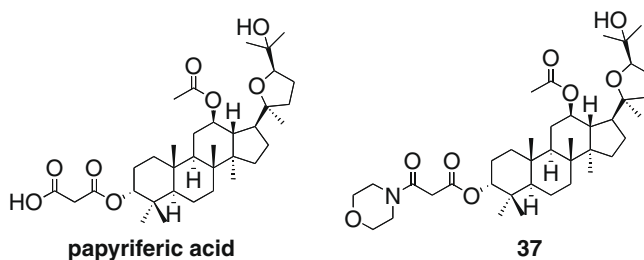
New derivatives of verapamil modified with nitroxides and their precursors were synthesized and screened for reactive oxygen species (ROS)-scavenging activities. Among the new verapamil derivatives compound **16B** proved to be the best ROS scavenger in vitro.



**Papyriferic acid derivatives as reversal agents of multidrug resistance in cancer cells**

pp 2964–2975

Juan Xiong, Masatoshi Taniguchi, Yoshiki Kashiwada\*, Michiko Sekiya, Takashi Yamagishi, Yoshihisa Takaishi

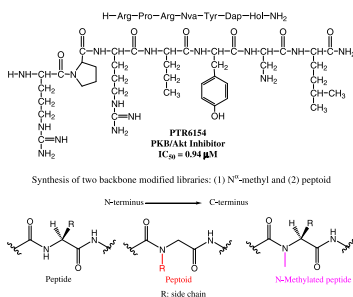


Forty-one derivatives of papyriferic acid were prepared and evaluated for their effect on reversing MDR against KB-C2 cells. Compound **37** significantly reversed the  $IC_{50}$  value of colchicine against KB-C2 cells to 0.059  $\mu$ M (185-fold reversion) at 5  $\mu$ g/mL.

**Synthesis and structure–activity relationship studies of peptidomimetic PKB/Akt inhibitors: The significance of backbone interactions**

pp 2976–2985

Yftah Tal-Gan, Noam S. Freeman, Shoshana Klein, Alexander Levitzki, Chaim Gilon\*



\*Corresponding author

i+ Supplementary data available via ScienceDirect

**COVER**

An insight into biologically relevant chemical space showing the scaffolds of potential natural-product based inhibitors orbiting their target, the protein structure of protein 11-beta steroid dehydrogenase (PDB code 1xu7). Graphic produced using Pymol (<http://www.pymol.org>). [M. A. Koch, A. Schuffenhauer, M. Scheck, S. Wetzel, M. Casaulta, A. Odermatt, P. Ertl, H. Waldmann, Charting biologically relevant chemical space: A structural classification of natural products (SCONP), *PNAS* **2005**, 102, 17272–17277 and S. Wetzel, H. Waldmann, Cheminformatic analysis of natural products and their chemical space, *Chimia* **2007**, 61(6), 355–360].

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ISSN 0968-0896