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Symposium-in-Print

Tetrahedron Young Investigator Award 2006 Jonathan Ellman

Edited by: Chi-Huey Wong

Academia Sinica, Taipei, Taiwan
and

Department of Chemistry, The Scripps Research Institute, La Jolla, CA 92037, United States

Contents

Preface

Biographical sketch: Professor Jonathan Ellman

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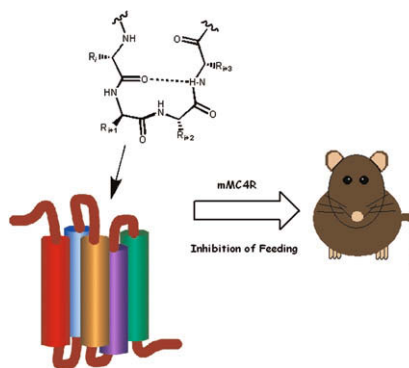
p 951

SPECIAL ISSUE ARTICLES

β -Turn secondary structure and melanocortin ligands

Erica M. Haslach, Jay W. Schaub, Carrie Haskell-Luevano*

pp 952–958

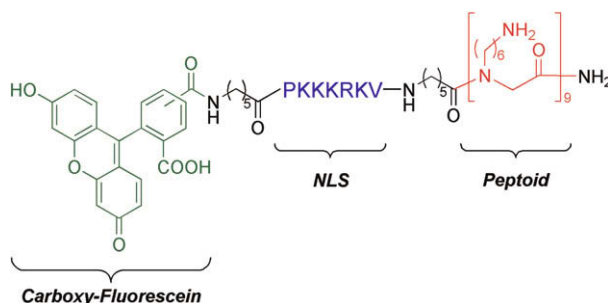


Synthesis, penetrability and intracellular targeting of fluorescein-tagged peptoids and peptide-peptoid hybrids

Asier Unciti-Broceta, Franziska Diezmann, Chiung Ying Ou-Yang,
Mario Antonio Fara, Mark Bradley*

pp 959–966

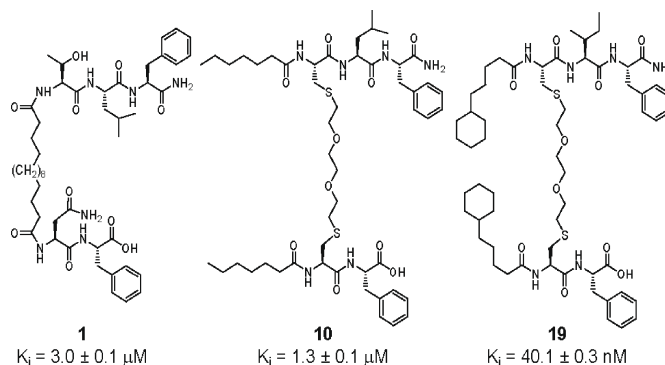
A cell-penetrating peptoid nonamer conjugated to the SV40 nuclear localization signal (NLS) permitted rapid and specific intracellular trafficking and targeting to the cell nucleus, facilitating nuclei staining of live cells with a non-DNA-intercalating fluorescent probe.



Sidechain-linked inhibitors of HIV-1 protease dimerization

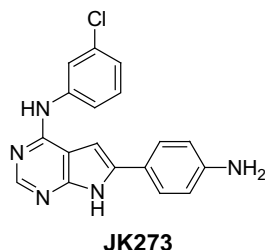
Michael J. Bowman, Jean Chmielewski*

Differential modification of acyl groups and sidechain functionality within uniquely crosslinked dimerization inhibitors of HIV-1 protease provided diverse structures with the most potent inhibitory constants in the low nM range.



A small molecule inhibitor of $\alpha 4$ integrin-dependent cell migration

Jongkook Lee, Jiyong Hong, Tae-Gyu Nam, Eric C. Peters, Anthony P. Orth, Bernhard H. Geierstanger, Lawrence E. Goldfinger, Mark H. Ginsberg, Charles Y. Cho*, Peter G. Schultz*

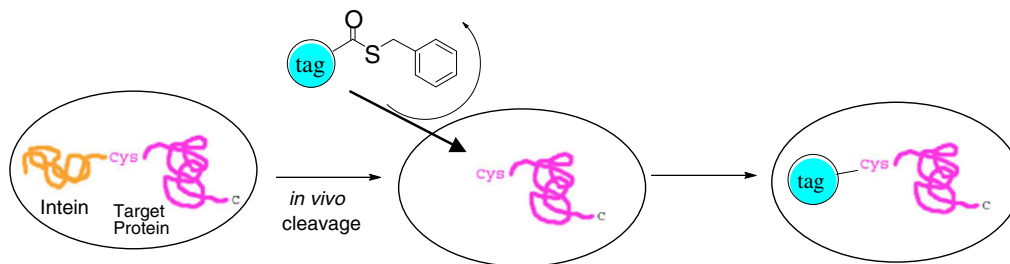


A small molecule inhibitor of $\alpha 4$ integrin-dependent cell migration was identified through a cell-based screen of small molecule libraries.



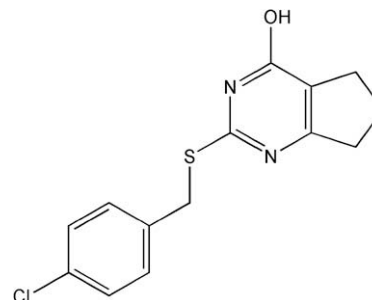
Site-specific covalent labeling of proteins inside live cells using small molecule probes

Souvik Chattopadhyaya, Rajavel Srinivasan, Dawn S. Y. Yeo, Grace Y. J. Chen, Shao Q. Yao*



High throughput screening of potentially selective MMP-13 exosite inhibitors utilizing a triple-helical FRET substrate

Janelle L. Lauer-Fields, Dmitriy Minond, Peter S. Chase, Pierre E. Baillargeon, S. Adrian Saldanha, Roma Stawikowska, Peter Hodder, Gregg B. Fields*

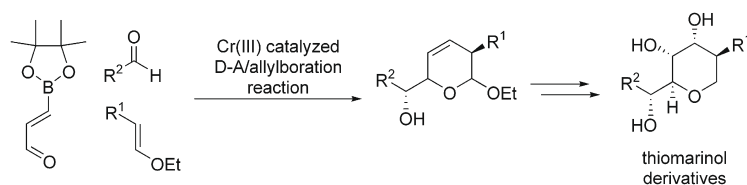


pp 990–1005

Synthesis and preliminary antibacterial evaluation of simplified thiomarinol analogs

pp 1006–1017

Olivier Marion, Xuri Gao, Sandra Marcus, Dennis G. Hall*

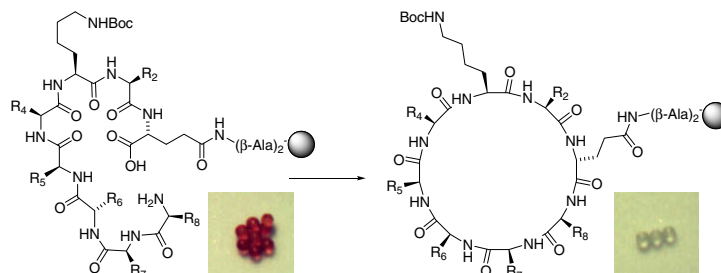


Simplified derivatives of the thiomarinol class of antibiotics were prepared via a catalytic enantioselective inverse electron demand hetero [4 + 2] cycloaddition/allylboration tandem reaction. These analogs were tested for antimicrobial activity using a standard disk diffusion assay.

**On-bead cyclization in a combinatorial library of 15,625 octapeptides**

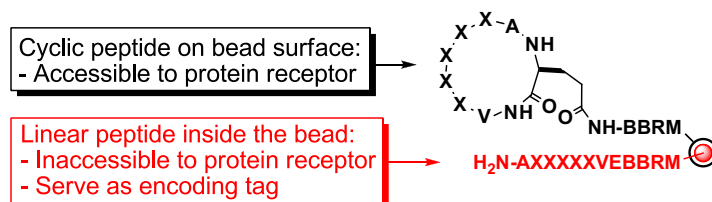
pp 1018–1025

Viviana S. Fluxa, Jean-Louis Reymond*

**Synthesis and screening of a cyclic peptide library: Discovery of small-molecule ligands against human prolactin receptor**

pp 1026–1033

Tao Liu, Sang Hoon Joo, Jeffrey L. Voorhees, Charles L. Brooks, Dehua Pei*

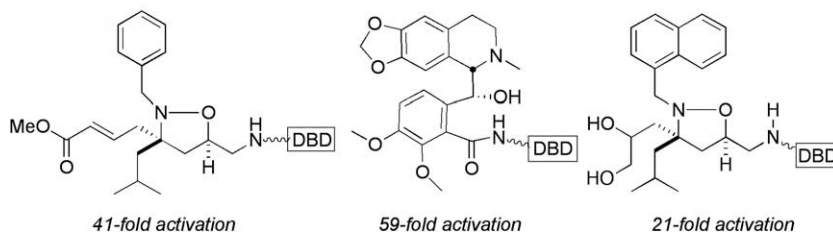


A cyclic peptide library was screened against the extracellular domain of human prolactin receptor and ligands with low-micromolar dissociation constants were discovered.

Expanding the repertoire of small molecule transcriptional activation domains

pp 1034–1043

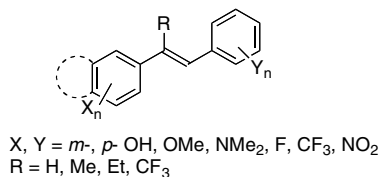
Ryan J. Casey, Jean-Paul Desaulniers, Jonas W. Hojfeldt, Anna K. Mapp*

Small molecule transcriptional activation domains

Synthesis and biological evaluation of a library of resveratrol analogues as inhibitors of COX-1, COX-2 and NF- κ B

pp 1044–1054

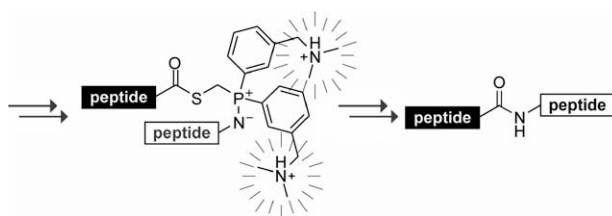
Soo Sung Kang, Muriel Cuendet, Denise C. Endringer, Vicki L. Croy, John M. Pezzuto, Mark A. Lipton*



Coulombic effects on the traceless Staudinger ligation in water

pp 1055–1063

Annie Tam, Ronald T. Raines*



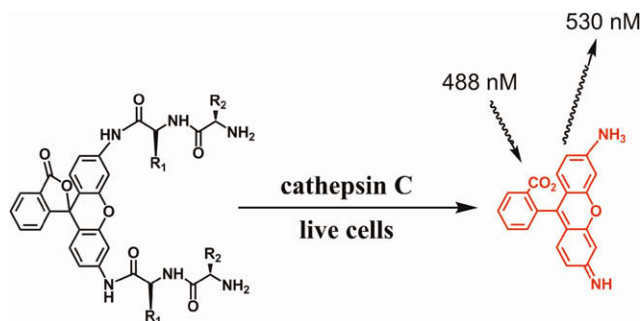
Consideration of Coulombic interactions enables phosphinothiols to mediate a traceless Staudinger ligation efficiently in water.



Substrate optimization for monitoring cathepsin C activity in live cells

pp 1064–1070

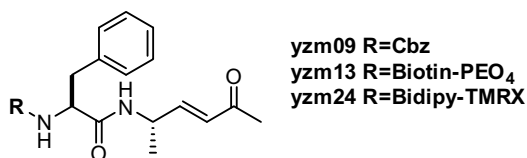
Jun Li, H. Michael Petrassi, Christine Tumanut, Brian T. Masick, Christopher Trussell, Jennifer L. Harris*



Evaluation of α,β -unsaturated ketone-based probes for papain-family cysteine proteases

pp 1071–1078

Zhimou Yang, Marko Fonović, Steven H. L. Verhelst, Galia Blum, Matthew Bogoy*

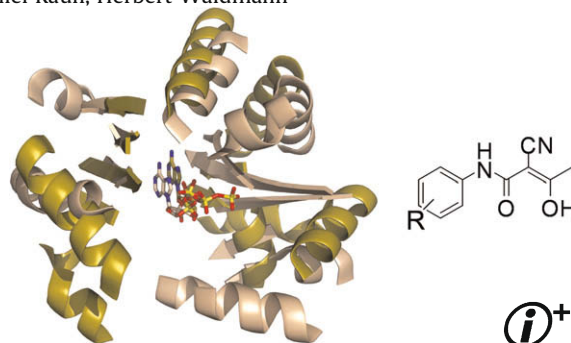
Activity-based probes based on α,β -unsaturated ketone label papain-family cysteine proteases (Cat B and Cat L) in mouse tissue lysates, cell lysate, and intact cells.

ATP competitive inhibitors of D-alanine–D-alanine ligase based on protein kinase inhibitor scaffolds

pp 1079–1087

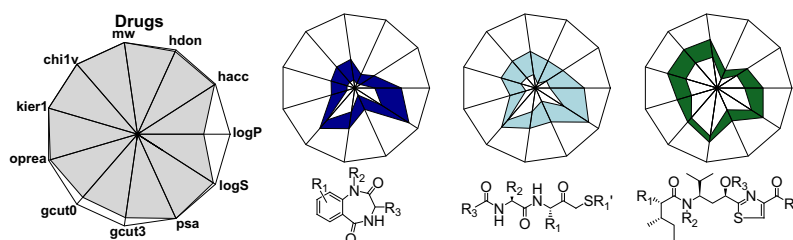
Gemma Triola, Stefan Wetzel, Bernhard Ellinger, Marcus A. Koch, Katja Hübeler, Daniel Rauh, Herbert Waldmann*

New inhibitors for D-alanine–D-alanine ligase can be found based on the similarity of the ATP binding site of kinases and D-alanine–D-alanine ligase.

**A road less traveled by: Exploring a decade of Ellman chemistry**

pp 1088–1093

Anang A. Shelat, R. Kiplin Guy*

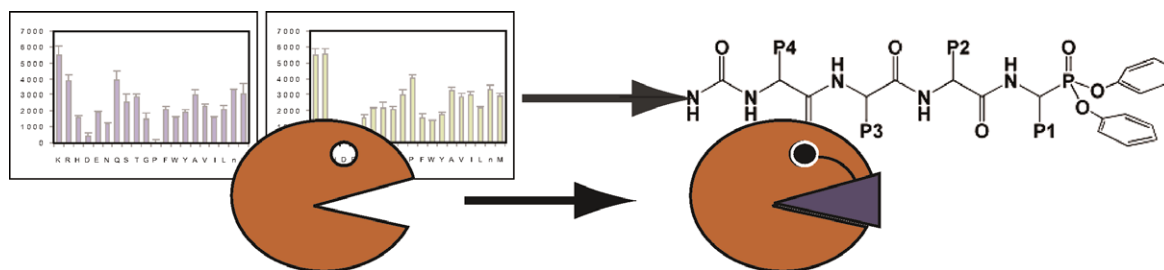


Analysis of the physicochemical properties of eight libraries produced by the Ellman group indicates that they cover a wide span of biologically relevant chemical space.

Using specificity to strategically target proteases

pp 1094–1100

Mark D. Lim, Charles S. Craik*

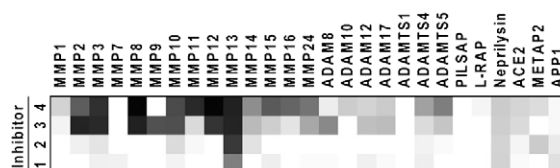


Library-based approaches for screening the substrate specificity of a protease (shown as 'Pacman') as a strategy to develop specific and potent peptidic and small molecule inhibitors.

Ranking the selectivity of PubChem screening hits by activity-based protein profiling: MMP13 as a case study

pp 1101–1108

Ryuichiro Nakai, Cleo M. Salisbury, Hugh Rosen, Benjamin F. Cravatt*



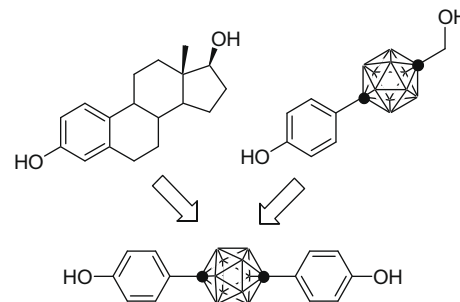
REGULAR ARTICLES

Synthesis and biological evaluation of *p*-carborane bisphenols and their derivatives: Structure–activity relationship for estrogenic activity

pp 1109–1117

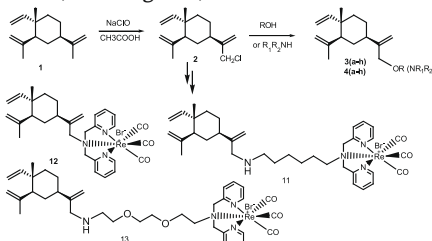
Takumi Ogawa, Kiminori Ohta, Toru Iijima, Tomoharu Suzuki, Shigeru Ohta, Yasuyuki Endo*

Carborane as a spherical hydrophobic pharmacophore: A series of *p*-carborane bisphenol derivatives were designed and synthesized as candidate estrogen receptor α (ER α) ligands. Bis(4-hydroxyphenyl)-*p*-carborane showed high binding affinity for human ER α and potent estrogenic activity in transactivation and cell proliferation assays with MCF-7 cells.

**Synthesis and in vitro anti-proliferative activity of β -elemene monosubstituted derivatives in HeLa cells mediated through arrest of cell cycle at the G1 phase**

pp 1118–1124

Yanhong Sun, Guifeng Liu, Yuangqing Zhang, Hua Zhu, Yunfeng Ren, Yu-Mei Shen*

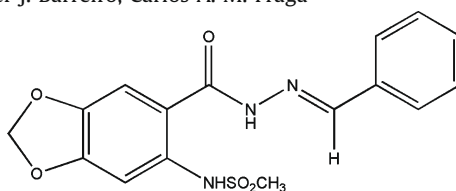


β -Elemene monosubstituted derivatives were synthesized. The in vitro anti-proliferative activity of β -elemene monosubstituted amine and $\text{Re}(\text{CO})_3$ - β -elemene derivatives in human cervix epitheloid carcinoma HeLa cells were improved significantly compared with both of ether derivatives and parent β -elemene. These derivatives could reduce Rb phosphorylation and cyclin D1 protein expression to arrest the cell cycle at G1 phase.

Novel 6-methanesulfonamide-3,4-methylenedioxyphenyl-*N*-acylhydrazones: Orally effective anti-inflammatory drug candidates

pp 1125–1131

Jorge L. M. Tributino, Carolina D. Duarte, Rodrigo S. Corrêa, Antonio C. Doriguetto, Javier Ellena, Nelilma C. Romeiro, Newton G. Castro, Ana Luisa P. Miranda, Eliezer J. Barreiro, Carlos A. M. Fraga*



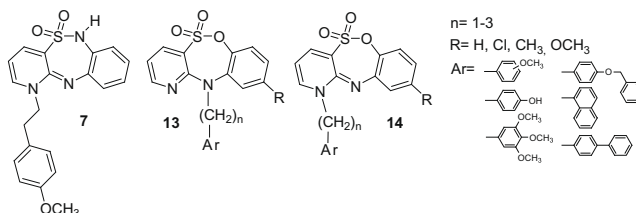
LASSBio-930 (1c)

We describe herein the discovery of NAH-derivative LASSBio-930 (**1c**) as a novel in vivo anti-inflammatory and anti-hyperalgesic prototype, that acts as non-selective COX inhibitor.

**Benzopyrindooxathiazepine derivatives as novel potent antimitotic agents**

pp 1132–1138

Sebastien Gallet, Nathalie Flouquet, Pascal Carato, Bruno Pfeiffer, Pierre Renard, Stéphane Léonce, Alain Pierré, Pascal Berthelot, Nicolas Lebegue*

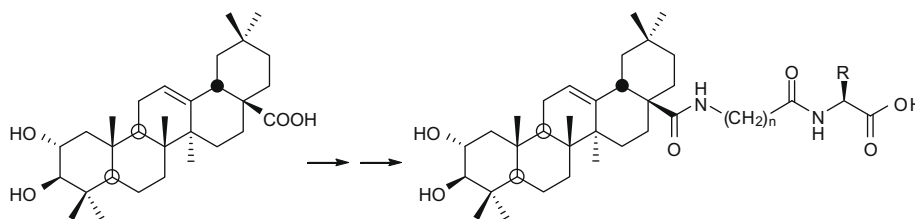


Herein, we describe the structure–activity relationship study of a new 1-(arylalkyl)-11*H*-benzo[*f*]-1,2-dihydropyrido[3,2-*c*][1,2,5]oxathiazepine 5,5-dioxide series of antimitotic agents. The pharmacological results obtained from previous works allowed us to identify compound **1** as a new cytotoxic agent inhibiting tubulin polymerization. We have undertaken the synthesis of its non-methylated analogue **7** and have extended our investigations to a novel, structurally related benzopyrindooxathiazepine dioxide series **9** and **10**.

Solution- and solid-phase synthesis and anti-HIV activity of maslinic acid derivatives containing amino acids and peptides

pp 1139–1145

Andres Parra*, Francisco Rivas*, Pilar E. Lopez, Andres Garcia-Granados, Antonio Martinez, Fernando Albericio, Nieves Marquez, Eduardo Muñoz



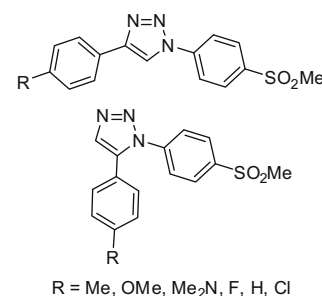
A solid-phase method for the preparation of maslinic acid derivatives has been described, to achieve derivatives that are not cytotoxic and show potent anti-HIV activity.

**Synthesis and cyclooxygenase inhibition of various (aryl-1,2,3-triazole-1-yl)-methanesulfonylphenyl derivatives**

pp 1146–1151

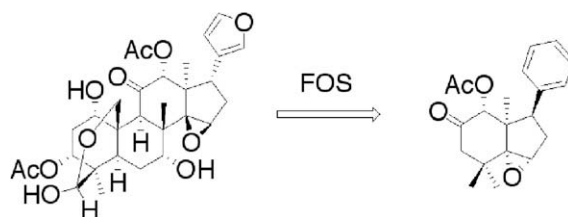
Frank Wuest*, Xinli Tang, Torsten Kniess, Jens Pietzsch, Mavanur Suresh

1,4- and 1,5-diaryl substituted 1,2,3-triazoles were synthesized by either Cu(I)-catalyzed or Ru(II)-catalyzed 1,3-dipolar cycloaddition reactions between 1-azido-4-methane-sulfonylbenzene and a panel of various *para*-substituted phenyl acetylenes (4-H, 4-Me, 4-OMe, 4-NMe₂, 4-Cl, 4-F). All compounds were used in in vitro cyclooxygenase (COX) assays to determine the combined electronic and steric effects upon COX-1 and COX-2 inhibitory potency and selectivity.

**Function-oriented synthesis applied to the anti-botulinum natural product toosendanin**

pp 1152–1157

Yuya Nakai, William H. Tepp, Tobin J. Dickerson, Eric A. Johnson, Kim D. Janda*

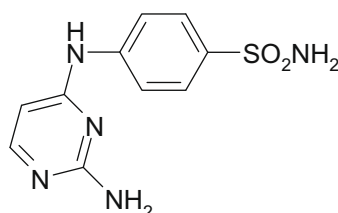


Botulinum neurotoxins (BoNTs) are the most lethal poisons known, while the natural product toosendanin has demonstrated efficacy against the BoNTs. To unravel toosendanin's efficacy, Function-Oriented Synthesis (FOS) was examined.

Carbonic anhydrase inhibitors: Inhibition of the β -class enzyme from the yeast *Saccharomyces cerevisiae* with sulfonamides and sulfamates

pp 1158–1163

Semra Isik, Feray Kockar, Meltem Aydin, Oktay Arslan, Ozen Ozensoy Guler, Alessio Innocenti, Andrea Scozzafava, Claudiu T. Supuran*



Ki (scCA) = 15.1 nM; Ki (hCA I) = 109 nM; Ki (hCA II) = 33 nM

In vitro solubility, stability and permeability of novel quercetin–amino acid conjugates

pp 1164–1171

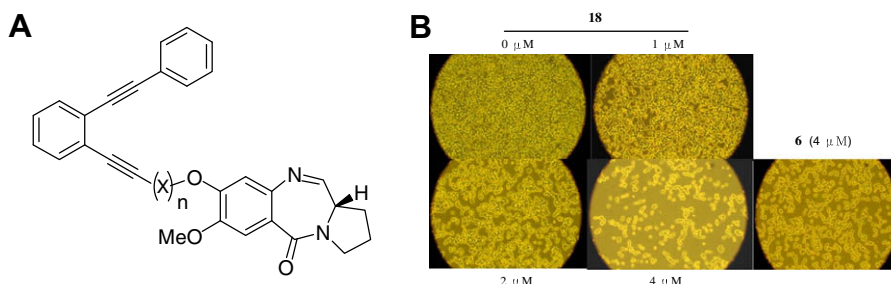
Mi Kyoung Kim, Kwang-su Park, Woon-seok Yeo, Hyunah Choo, Youhoon Chong*

	Quercetin (Qu)	Qu-E
Structure	$R_1 = R_2 = H$	$R_1 = (S)\text{-CONHCH}(\text{CH}_2\text{CH}_2\text{CO}_2\text{H})\text{CO}_2\text{H}$, $R_2 = H$ $R_1 = H$, $R_2 = (S)\text{-CONHCH}(\text{CH}_2\text{CH}_2\text{CO}_2\text{H})\text{CO}_2\text{H}$
Solubility in water (μM)	50	2649
Stability ($t_{1/2}$)		
PBS buffer	–	> 17 h
Cell lysate	–	180 min
Relative cell permeability	1.0	5.2

Synthesis and antitumor activity of novel enediyne-linked pyrrolo[2,1-c][1,4]benzodiazepine hybrids

pp 1172–1180

Wan-Ping Hu, Jium-Jia Liang, Chai-Lin Kao, You-Chiang Chen, Chung-Yu Chen, Feng-Yuan Tsai, Ming-Jung Wu, Long-Sen Chang, Yeh-Long Chen, Jeh-Jeng Wang*

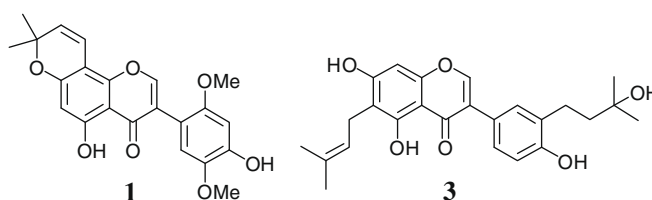


(A) Structure of the enediyne-PBD conjugate agents. (B) The apoptotic morphology after treatment with compound (6, 18) on 293T.

**Death receptor 5 targeting activity-guided isolation of isoflavones from *Milletia brandisiana* and *Ardisia colorata* and evaluation of ability to induce TRAIL-mediated apoptosis**

pp 1181–1186

Hiroyuki Kikuchi, Takashi Ohtsuki, Takashi Koyano, Thaworn Kowithayakorn, Toshiyuki Sakai, Masami Ishibashi*

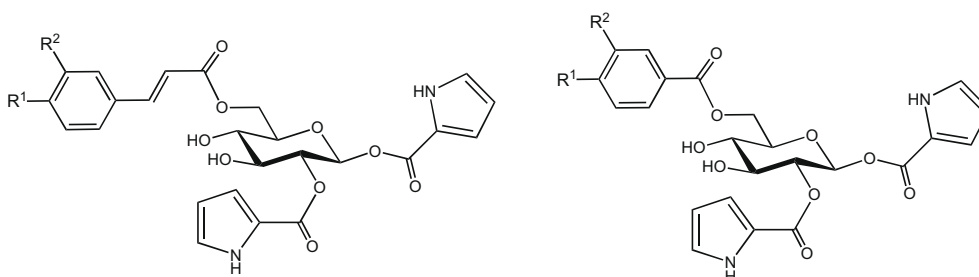


On screening for compounds that enhance DR5 expression, a new isoflavone, coloratanin A (**3**) was isolated from *Ardisia colorata*. In addition, we described that 4'-demethyltoxicarol isoflavone (**1**) sensitized TRAIL-resistant AGS cells to TRAIL-induced apoptosis by up-regulations of DR5 expression.

Synthesis of buprestins D, E, F, G and H; structural confirmation and biological testing of acyl glucoses from jewel beetles (Coleoptera: Buprestidae)

pp 1187–1192

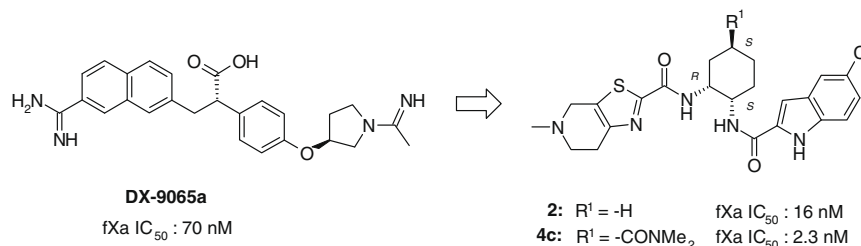
Sebastian Ryczek, Konrad Dettner, Carlo Unverzagt*



Discovery of *N*-[(1*R*,2*S*,5*S*)-2-[[[(5-chloroindol-2-yl)carbonyl]amino]-5-(dimethylcarbamoyl)cyclohexyl]-5-methyl-4,5,6,7-tetrahydrothiazolo[5,4-*c*]pyridine-2-carboxamide hydrochloride: A novel, potent and orally active direct inhibitor of factor Xa

pp 1193–1206

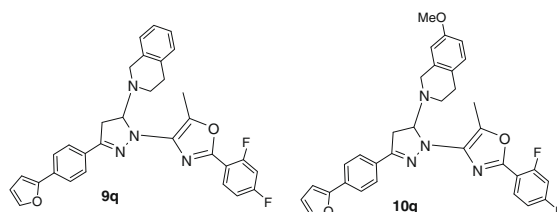
Tsutomu Nagata *, Toshiharu Yoshino, Noriyasu Haginoya, Kenji Yoshikawa, Masatoshi Nagamochi, Syozo Kobayashi, Satoshi Komoriya, Aki Yokomizo, Ryo Muto, Mitsuhiro Yamaguchi, Ken Osanai, Makoto Suzuki, Hideyuki Kanno



Synthesis, structure and antibacterial activity of new 2-(1-(2-(substituted-phenyl)-5-methyloxazol-4-yl)-3-(2-substituted-phenyl)-4,5-dihydro-1*H*-pyrazol-5-yl)-7-substituted-1,2,3,4-tetrahydroisoquinoline derivatives

pp 1207–1213

Xin-Hua Liu *, Jing Zhu, An-na Zhou, Bao-An Song *, Hai-Liang Zhu, Lin-Shan bai, Pinaki S. Bhadury, Chun-Xiu Pan



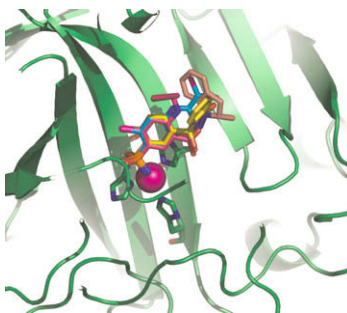
A series of new 2-(1-(2-(substituted-phenyl)-5-methyloxazol-4-yl)-3-(2-substituted-phenyl)-4,5-dihydro-1*H*-pyrazol-5-yl)-7-substituted-1,2,3,4-tetrahydroisoquinoline derivatives were synthesized. The results showed that compounds **9q** and **10q** can strongly inhibit *Staphylococcus aureus* DNA gyrase and *Bacillus subtilis* DNA gyrase.



Carbonic anhydrase inhibitors. Comparison of chlorthalidone, indapamide, trichloromethiazide, and furosemide X-ray crystal structures in adducts with isozyme II, when several water molecules make the difference

pp 1214–1221

Claudia Temperini, Alessandro Cecchi, Andrea Scozzafava, Claudiu T. Supuran *

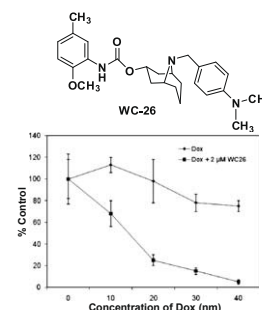


New *N*-substituted 9-azabicyclo[3.3.1]nonan-3α-yl phenylcarbamate analogs as σ₂ receptor ligands: Synthesis, in vitro characterization, and evaluation as PET imaging and chemosensitization agents

pp 1222–1231

Wenhua Chu, Jinbin Xu, Dong Zhou, Fanjie Zhang, Lynne A. Jones, Kenneth T. Wheeler, Robert H. Mach *

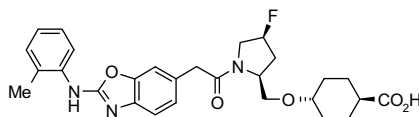
Two highly selective and potent σ₂ receptor ligands, **WC-26** and **WC-59** were synthesized. **WC-26** significantly increases the ability of doxorubicin to kill breast tumor cells at low concentrations where there is no cell kill from either drug alone.



A novel and potent VLA-4 antagonist based on *trans*-4-substituted cyclohexanecarboxylic acid

pp 1232–1243

Fumihito Muro*, Shin Iimura, Yoshiyuki Yoneda, Jun Chiba, Toshiyuki Watanabe, Masaki Setoguchi, Gensuke Takayama, Mika Yokoyama, Tohru Takashi, Atsushi Nakayama, Nobuo Machinaga



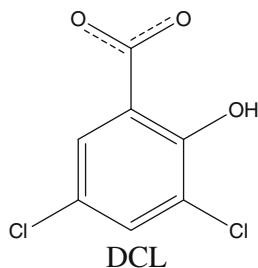
11b: VLA-4/VCAM-1 binding assay, $IC_{50} = 2.8$ nM

The discovery of *trans*-4-substituted cyclohexanecarboxylic acid derivative **11b** as a novel and potent VLA-4 antagonist is reported.

Correlation of binding constants and molecular modelling of inhibitors in the active sites of aldose reductase and aldehyde reductase

pp 1244–1250

Vincenzo Carbone, Hai-Tao Zhao, Roland Chung, Satoshi Endo, Akira Hara, Ossama El-Kabbani*

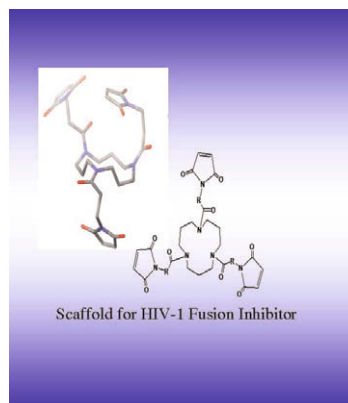


Molecular modelling and inhibitor binding constants are reported for aldose and aldehyde reductases.

Conformational analysis of trimeric maleimide substituted 1,5,9-triazacyclododecane HIV fusion scaffolds

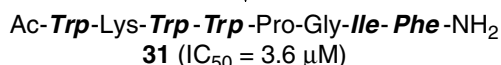
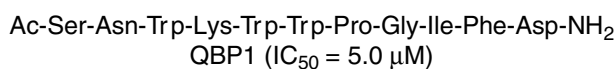
pp 1251–1258

Sarah Remmert, Heather Hollis, Carol A. Parish*

**Structure–activity relationship study on polyglutamine binding peptide QBP1**

pp 1259–1263

Kenji Tomita, H. Akiko Popiel, Yoshitaka Nagai*, Tatsushi Toda, Yuji Yoshimitsu, Hiroaki Ohno, Shinya Oishi*, Nobutaka Fujii



Xaa = Indispensable Amino Acid Residues

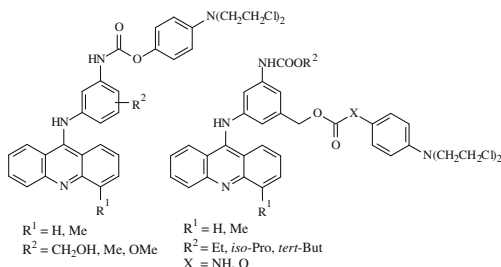
Structure–activity relationship study on polyglutamine binding peptide 1 (QBP1) identified a minimum octapeptide sequence **31** exerting inhibitory activity against polyglutamine aggregation.



Novel DNA-directed alkylating agents: Design, synthesis and potent antitumor effect of phenyl N-mustard-9-anilinoacridine conjugates via a carbamate or carbonate linker

pp 1264–1275

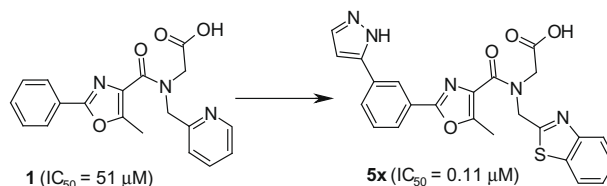
Naval Kapuriya, Kalpana Kapuriya, Huajin Dong, Xiuguo Zhang, Ting-Chao Chou, Yu-Ting Chen, Te-Chang Lee, Wen-Chuan Lee, Tung-Hu Tsai, Yogesh Naliapara, Tsann-Long Su *



Towards Gram-negative antivirulence drugs: New inhibitors of HldE kinase

pp 1276–1289

Nicolas Desroy*, François Moreau, Sophia Briet, Géraldine Le Frallie, Stephanie Floquet, Lionel Durant, Vanida Vongsouthi, Vincent Gerusz, Alexis Denis, Sonia Escaich

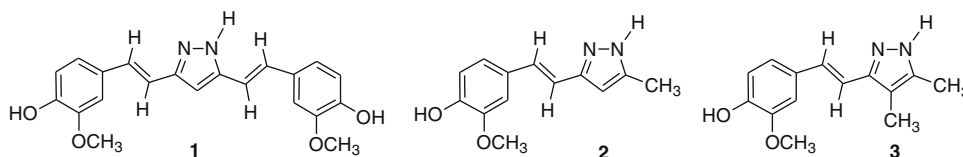


Discovery of new inhibitors of HldE kinase by high throughput screening and structure–activity relationship optimization provided a promising lead series for the development of new Gram-negative antimicrobial agents.

Synthesis and biological evaluation of curcuminoid pyrazoles as new therapeutic agents in inflammatory bowel disease: Effect on matrix metalloproteinases

pp 1290–1296

R. M. Claramunt*, L. Bouissane, M. P. Cabildo, M. P. Cornago, J. Elguero, A. Radziwon, C. Medina *

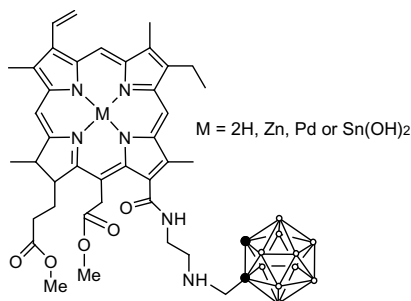


Curcuminoid pyrazoles (**1–3**), have demonstrated activity in the biological assays used as models (MMPs inhibition) for inflammatory bowel disease.

Novel boronated chlorin e_6 -based photosensitizers: Synthesis, binding to albumin and antitumour efficacy

pp 1297–1306

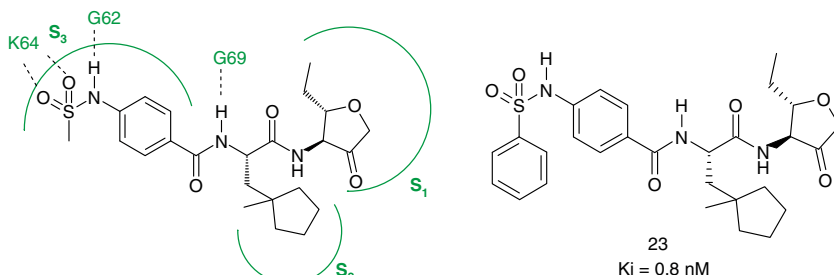
Valentina A. Ol'shevskaya*, Roza G. Nikitina, Arina N. Savchenko, Marina V. Malshakova, Alexander M. Vinogradov, Galina V. Golovina, Dmitry V. Belykh, Alexander V. Kutchin, Mikhail A. Kaplan, Valery N. Kalinin, Vladimir A. Kuzmin, Alexander A. Shtil



New boronated derivatives of chlorin e_6 for anticancer photodynamic therapy.

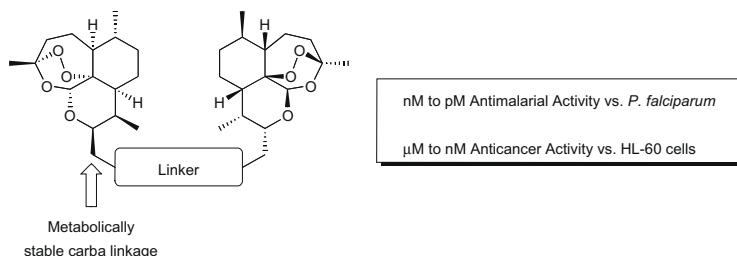
Solid-phase parallel synthesis and SAR of 4-amidofuran-3-one inhibitors of cathepsin S: Effect of sulfonamides P3 substituents on potency and selectivity pp 1307–1324

Susana Ayasa, Charlotta Lindquist, Tatiana Agback, Kurt Benkestock, Björn Classon *, Ian Henderson, Ellen Hewitt, Katarina Jansson, Anders Kallin, Dave Sheppard, Bertil Samuelsson



Synthesis and biological evaluation of extraordinarily potent C-10 carba artemisinin dimers against *P. falciparum* malaria parasites and HL-60 cancer cells pp 1325–1338

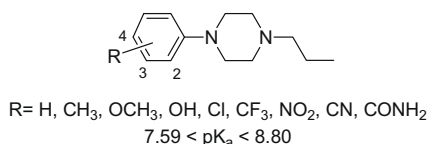
James Chadwick, Amy E. Mercer, B. Kevin Park, Richard Cosstick, Paul M. O'Neill *



A series of artemisinin dimers incorporating a metabolically stable C-10 carba-linkage have been prepared, several of which show remarkable in vitro antimalarial activity (as low as 30 pM) versus *Plasmodium falciparum* and in vitro anticancer activity in the micromolar to nanomolar range versus HL-60 cell lines.

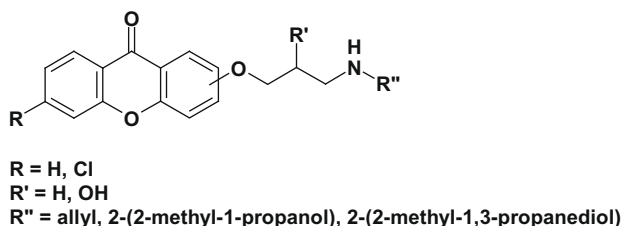
Determination of 1-aryl-4-propylpiperazine pK_a values: The substituent on aryl modulates basicity pp 1339–1344

Enza Lacivita *, Marcello Leopoldo, Paola De Giorgio, Francesco Berardi, Roberto Perrone



Preliminary evaluation of pharmacological properties of some xanthone derivatives pp 1345–1352

Henryk Marona *, Natalia Szkaradek, Anna Rapacz, Barbara Filipek, Małgorzata Dybała, Agata Siwek, Marek Cegła, Edward Szneler

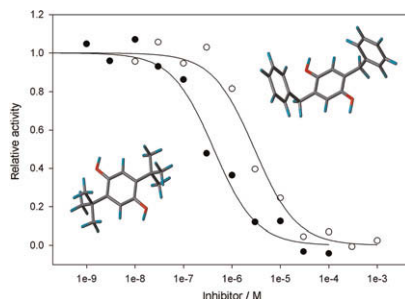


Selected xanthone derivatives, expected to reveal cardiovascular properties, were synthesized and tested for their antiarrhythmic, antihypertensive and anticonvulsive activity, as well as for the α_1 - and β_1 -adrenoceptor binding affinities.

Structure-based virtual screening for novel inhibitors of the sarco/endoplasmic reticulum calcium ATPase and their experimental evaluation

pp 1353–1360

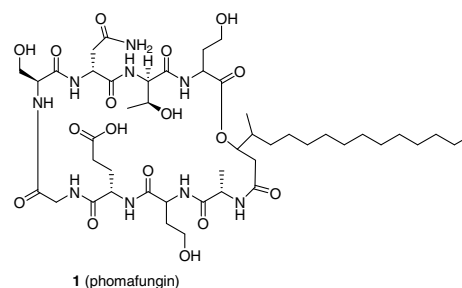
Joel Deye, Christopher Elam, Michael Lape, Robert Ratliff, Kayla Evans, Stefan Paula *



Isolation, structure and biological activity of phomafungin, a cyclic lipodepsipeptide from a widespread tropical *Phoma* sp.

pp 1361–1369

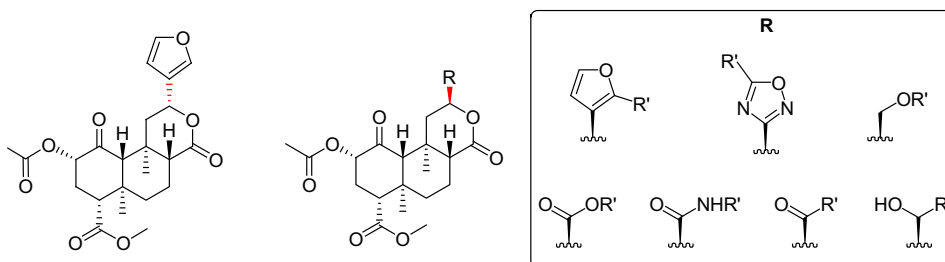
Kithsiri Herath, Guy Harris, Hiranthi Jayasuriya, Deborah Zink, Scott Smith, Francisca Vicente, Gerald Bills, Javier Collado, Antonio González, Bo Jiang, Jennifer Nielsen Kahn, Stefan Galuska, Robert Giacobbe, George Abruzzo, Emily Hickey, Paul Liberator, Deming Xu *, Terry Roemer, Sheo B. Singh *



Modification of the furan ring of salvinorin A: Identification of a selective partial agonist at the kappa opioid receptor

pp 1370–1380

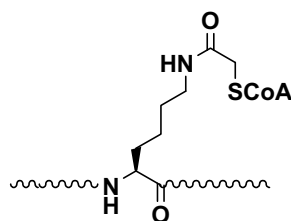
Cécile Béguin *, Katharine K. Duncan, Thomas A. Munro, Douglas M. Ho, Wei Xu, Lee-Yuan Liu-Chen, William A. Carlezon Jr., Bruce M. Cohen



Bisubstrate Inhibitors of the MYST HATs Esa1 and Tip60

pp 1381–1386

Jiang Wu, Nan Xie, Zhikun Wu, Ying Zhang, Yujun George Zheng *

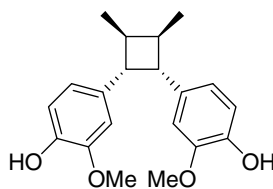


Isolation, structure elucidation and cytotoxic evaluation of endiandrin B from the Australian rainforest plant *Endiandra anthropophagorum*

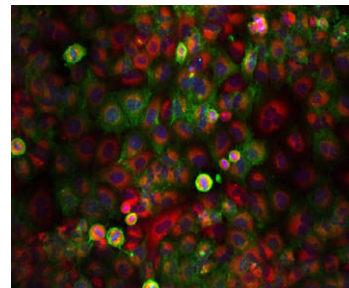
pp 1387–1392

Rohan A. Davis*, Emma C. Barnes, James Longden, Vicky M. Avery, Peter C. Healy

Chemical investigations of *Endiandra anthropophagorum* resulted in the isolation of a new cyclobutane lignan endiandrin B, together with the known natural products, endiandrin A, and (–)-dihydroguaiaretic acid. All compounds were evaluated for their cytotoxicity towards human lung carcinoma cells (A549) using high-content screening.



Endiandrin B

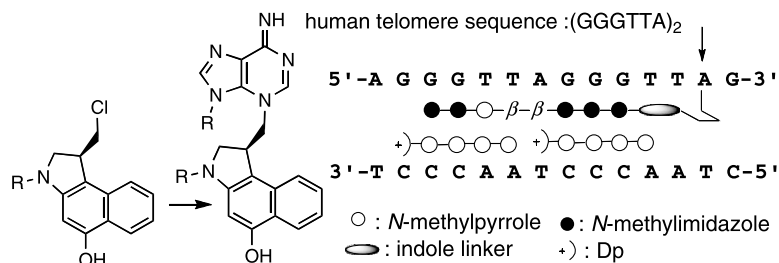


Cooperative alkylation of double-strand human telomere repeat sequences by PI polyamides with 11-base-pair recognition based on a heterotrimeric design

pp 1393–1397

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

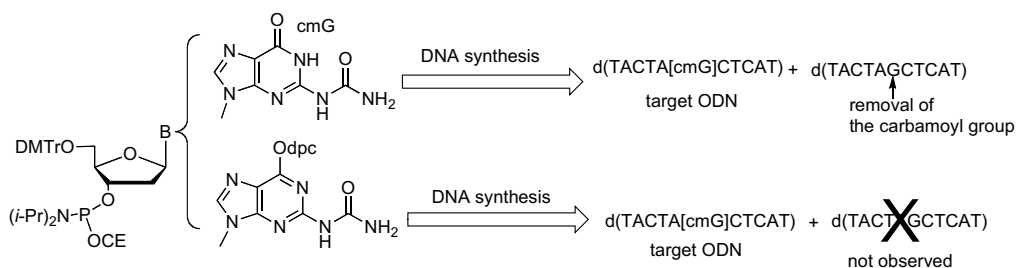
We designed and synthesis of alkylating conjugates **5–7** and their partner *N*-methylpyrrole-*N*-methylimidazole (PI) polyamides **8, 9**. The DNA alkylating activities of conjugates **5–7** were evaluated by high-resolution denaturing polyacrylamide gel electrophoresis with a 219 base pair (bp) DNA fragment containing the human telomere repeat sequence. Conjugate **5** efficiently alkylated the sequence, 5'-GGTTAGGGTTA-3', in the presence of partner PI polyamide **8** or distamycin A (Dist). In contrast, the heterodimer system of **5** with **9** showed very weak alkylating activity. Accordingly, this heterotrimeric system of **5** with two short partners is an expedient way to attain improved precision and extension of the recognition of DNA sequences.



Synthesis of oligodeoxynucleotides incorporating 2-*N*-carbamoylguanine and evaluation of the hybridization properties

pp 1398–1403

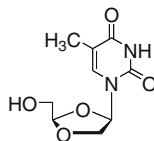
Takeshi Sasami, Yoko Odawara, Akihiro Ohkubo, Mitsuo Sekine*, Kohji Seio*



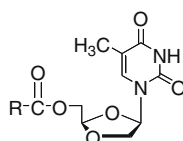
5'-*O*-Aliphatic and amino acid ester prodrugs of (–)-β-D-(2*R*,4*R*)-dioxolane-thymine (DOT): Synthesis, anti-HIV activity, cytotoxicity and stability studies

pp 1404–1409

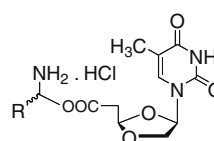
Yuzeng Liang, Ashoke Sharon, Jason P. Grier, Kimberly L. Rapp, Raymond F. Schinazi, Chung K. Chu*



DOT




DOT Prodrugs



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*Corresponding author

+ Supplementary data available via ScienceDirect**COVER**

A 1.5 Å crystal structure of a small molecule inhibitor identified by the Substrate Activity Screening method in complex with cathepsin S (2H7J). The figure was produced using Pymol (www.pymol.org).

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