

## Tetrahedron Prize for Creativity in Organic Chemistry 2005 B. Giese

*Edited by:* Herbert Waldmann

*Department of Chemical Biology, Max-Planck Institute for Molecular Biology, 44227 Dortmund, Germany  
and*

*Department of Chemical Biology, Universität Dortmund, 44227 Dortmund, Germany*

### Contents

#### Preface

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Biographical sketch: Professor Bernd Giese

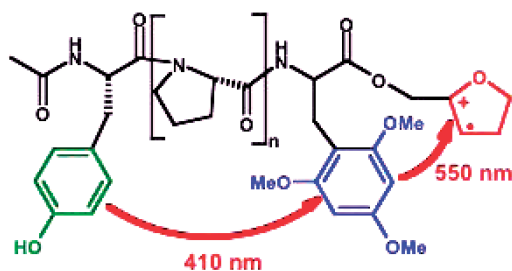
p 6137

#### AWARDEE'S ARTICLE

##### Electron transfer through DNA and peptides

pp 6139–6143

Bernd Giese\*



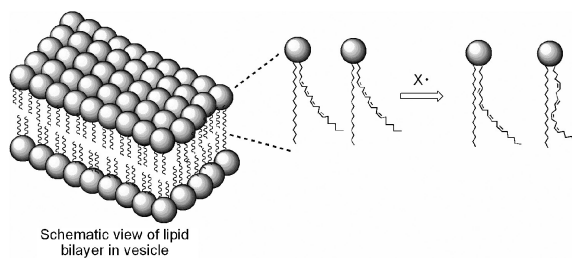
Electron transfer through DNA and peptides occurs in a multistep hopping mechanism.

#### PERSPECTIVE

##### *trans*-Fatty acids and radical stress: What are the real culprits?

pp 6144–6148

Chrysostomos Chatgililoglu,\* Carla Ferreri, Ioannis N. Lykakis and Peter Wardman

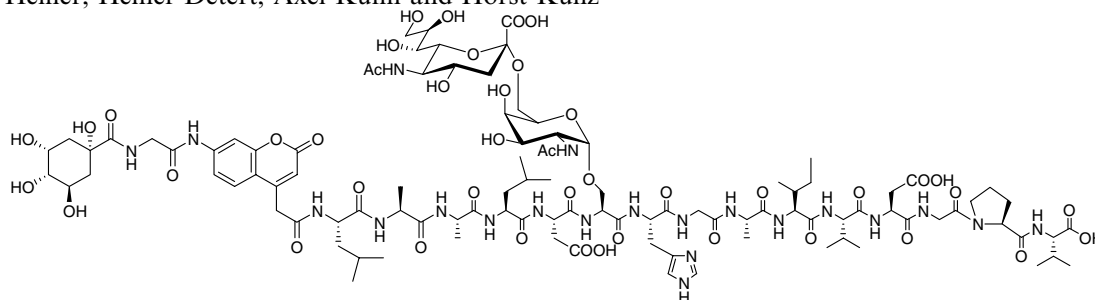


## SPECIAL ISSUE ARTICLES

**Hydrophilic photolabelling of glycopeptides from the murine liver–intestine (LI) cadherin recognition domain**

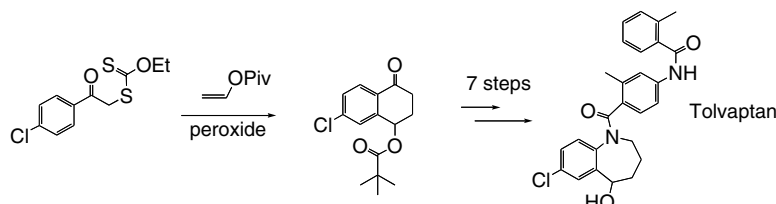
pp 6149–6164

Sebastian Heiner, Heiner Detert, Axel Kuhn and Horst Kunz\*

**A flexible approach for the preparation of substituted benzazepines: Application to the synthesis of tolavaptan**

pp 6165–6173

Alejandro Cordero-Vargas, Béatrice Quiclet-Sire and Samir Z. Zard\*

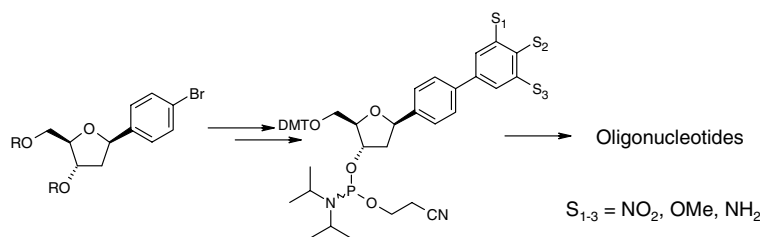


A flexible preparation of benzazepine derivatives using a series of radical and ionic reactions is reported. This approach was applied to the synthesis of tolavaptan, a very promising vasopressin V<sub>2</sub> receptor antagonist currently in clinical trials.

**Synthesis of functionalized biphenyl-C-nucleosides and their incorporation into oligodeoxynucleotides**

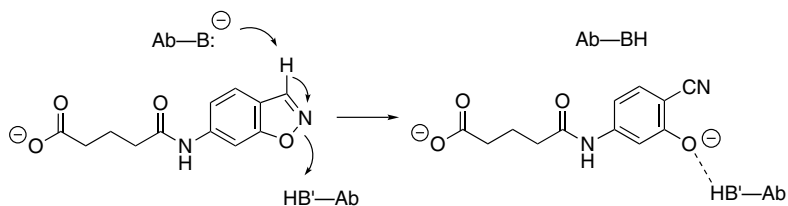
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Alain Zahn and Christian J. Leumann\*

**Toward bifunctional antibody catalysis**

pp 6189–6196

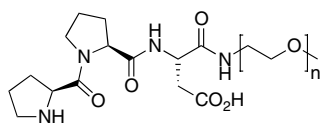
Kazuya Kikuchi, Renate B. Hannak, Mao-Jun Guo, Anthony J. Kirby\* and Donald Hilvert\*



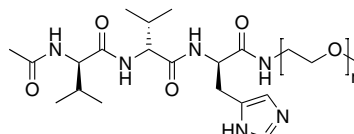
**Peptide–polyethylene glycol conjugates: Synthesis and properties of peptides bearing a C-terminal polyethylene glycol chain**

pp 6197–6201

Jessica Grun, Jefferson D. Revell, Matteo Conza and Helma Wennemers\*



asymmetric catalyst for aldol reaction

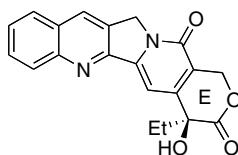


selectively bound by a diketopiperazine receptor

**Synthesis and biological assays of E-ring analogs of camptothecin and homocamptothecin**

pp 6202–6212

Raghuram S. Tangirala, Smitha Antony, Keli Agama, Yves Pommier, Bradley D. Anderson, Robert Bevins and Dennis P. Curran\*

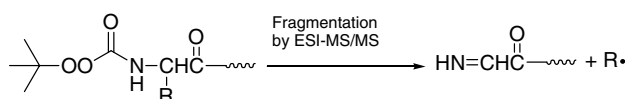


Analogues of the anti-tumor agent camptothecin with both closed E-rings (lactone and ether) and open E-rings (reduced acid, hydrazide, and protected Weinreb amide) have been prepared and tested in topoisomerase and cellular assays. The results provide insights into the structural features of the camptothecin E-ring that affect biological activity.

**N-Terminal amino acid side-chain cleavage of chemically modified peptides in the gas phase: A mass spectrometry technique for N-terminus identification**

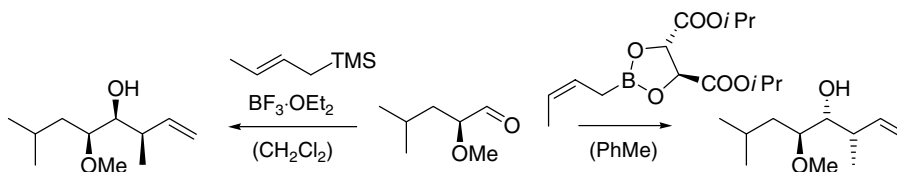
pp 6213–6222

Almary Chacon, Douglas S. Masterson, Huiyong Yin, Daniel C. Liebler and Ned A. Porter\*

i<sup>+</sup>**Stereoselective allyl transfer to chiral α-methoxycarbaldehydes: A model study related to the C-9/C-15 fragment of geldanamycin**

pp 6223–6234

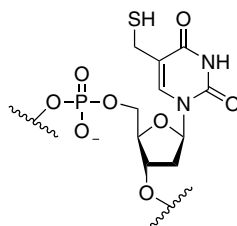
Tony Horneff, Eberhardt Herdtweck, Sören Randoll and Thorsten Bach\*



# Synthesis of DNA oligonucleotides containing 5-(mercaptomethyl)-2'-deoxyuridine moieties

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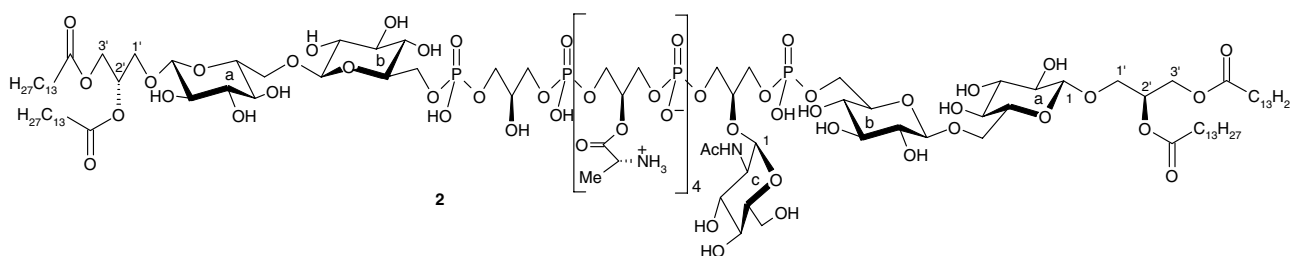
Benjamin Bornemann and Andreas Marx\*



# A *Staphylococcus aureus* lipoteichoic acid (LTA) derived structural variant with two diacylglycerol residues

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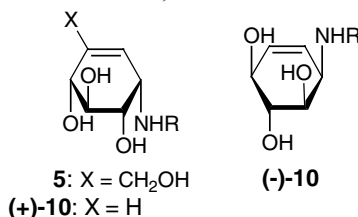
A. Stadelmaier, I. Figueroa-Perez, S. Deininger, S. von Aulock, T. Hartung and R.R. Schmidt\*



# Search for $\alpha$ -glucosidase inhibitors: New N-substituted valienamine and conduramine F-1 derivatives

pp 6255–6282

Robert Lysek, Catherine Schütz, Sylvain Favre, Anthony C. O'Sullivan, Christian Pillonel, Thomas Krülle, Pierre M. J. Jung, Imma Clotet-Codina, José A. Esté and Pierre Vogel\*

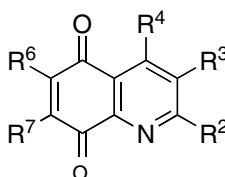


A solid-phase synthesis of new N-substituted valienamines has been developed and new synthesis of (–)-conduramine F-1, (+)-*ent*-conduramine F-1, and their N-derivatives is presented. The inhibitory activities of these new compounds toward  $\alpha$ -glucosidases are compared.

# Biological evaluation of newly synthesized quinoline-5,8-quinones as Cdc25B inhibitors

pp 6283–6287

Janine Cossy,\* Damien Belotti, Marni Brisson, John J. Skoko, Peter Wipf\* and John S. Lazo

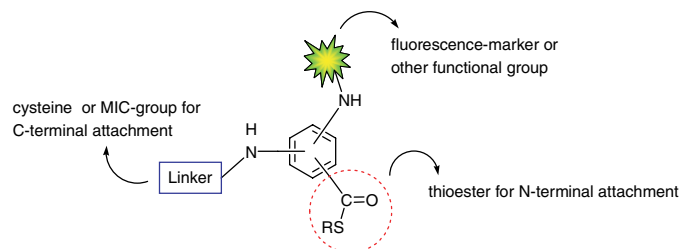


The structure–activity relationship of a focused series of C2-, C3-, or C4-modified quinoline-5,8-quinones on Cdc25B inhibition was interrogated in vitro. Two compounds also inhibited HeLa cell growth.

**A generic building block for C- and N-terminal protein-labeling and protein-immobilization**

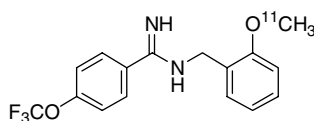
pp 6288–6306

Anja Watzke, Marta Gutierrez-Rodriguez, Maja Köhn, Ron Wacker,  
Hendrik Schroeder, Rolf Breinbauer, Jürgen Kuhlmann, Kirill Alexandrov,  
Christof M. Niemeyer, Roger S. Goody\* and Herbert Waldmann\*

**REGULAR ARTICLES****Towards NR2B receptor selective imaging agents for PET—synthesis and evaluation of N-[<sup>11</sup>C]-(2-methoxy)benzyl (E)-styrene-, 2-naphthyl- and 4-trifluoromethoxyphenylamidine**

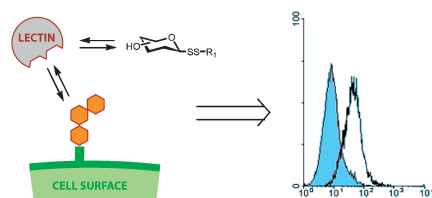
pp 6307–6313

Erik Årstad,\* Stefan Platzer, Achim Berthele, Lyn S. Pilowsky,  
Sajinder K. Luthra, Hans-Jürgen Wester and Gjermund Henriksen

**Glycosyldisulfides from dynamic combinatorial libraries as O-glycoside mimetics for plant and endogenous lectins: Their reactivities in solid-phase and cell assays and conformational analysis by molecular dynamics simulations**

pp 6314–6326

Sabine André, Zhichao Pei, Hans-Christian Siebert, Olof Ramström\* and Hans-Joachim Gabius



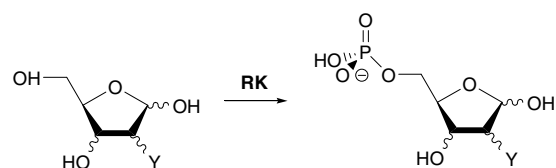
Binding of lectins to cell surface ligands triggers many medically relevant effects. Glycosyldisulfides from dynamic combinatorial libraries can interfere with these processes, as monitored by fluorescent cell assays.

**Ribokinase from *E. coli*: Expression, purification, and substrate specificity**

pp 6327–6332

Dmitry V. Chuvikovskiy, Roman S. Esipov,\* Yuri S. Skoblov, Larisa A. Chupova,  
Tatyana I. Muravyova, Anatoly I. Miroshnikov, Seppo Lapinjoki and Igor A. Mikhailopulo\*

Ribokinase (RK) was expressed in the *Escherichia coli* ER2566 cells, purified from sonicated cells by double chromatography to afford a preparation with specific activity of 75 μmol/minmg protein. Besides D-ribose and 2-deoxy-D-ribose, RK was found to catalyze the 5-O-phosphorylation of D-arabinose, D-xylose and D-fructose in the presence of ATP and potassium and magnesium ions; L-ribose and L-arabinose are not substrates for the recombinant enzyme. A new radiochemical method for monitoring the formation of D-ribofuranose-5-[<sup>32</sup>P]phosphate in the presence of [γ-<sup>32</sup>P]ATP and RK is reported.

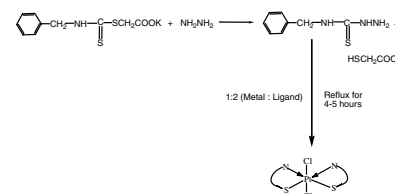


**Synthesis, characterization, antibacterial and cytotoxic study of platinum (IV) complexes**

pp 6333–6340

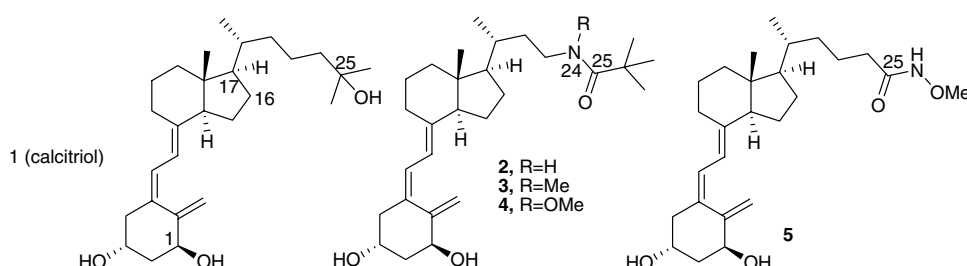
A. K. Mishra,\* S. B. Mishra, N. Manav, D. Saluja, R. Chandra and N. K. Kaushik\*

Platinum (IV) complexes  $[\text{Pt}(\text{L})_2\text{Cl}_2]$  [where, L=benzyl-*N*-thiohydrazide ( $\text{L}^1$ ), (benzyl-*N*-thio)-1,3-propanediamine ( $\text{L}^2$ ), benzaldehyde-benzyl-*N*-thiohydrazone ( $\text{L}^3$ ) and salicylaldehyde-benzyl-*N*-thiohydrazone ( $\text{L}^4$ )] have been synthesized. The thiohydrazides, thiodiamine and thiohydrazones can exist as thione-thiol tautomer and coordinate as a bidentate N–S ligand. Platinum (IV) complexes of the thiohydrazide, thiodiamine and thiohydrazones were characterized by elemental analysis, IR, mass, electronic and  $^1\text{H}$  NMR spectroscopic studies. The complexes were also screened for antibacterial and cytotoxic activity. Thermodynamic parameters such as activation energy ( $E_a$ ), apparent activation entropy ( $S^\ddagger$ ) and enthalpy change ( $\Delta H$ ) for the dehydration and decomposition reactions of the complexes have also been evaluated.

**Highly antiproliferative, low-calcemic, side-chain amide and hydroxamate analogs of the hormone  $1\alpha,25$ -dihydroxyvitamin  $\text{D}_3$** 

pp 6341–6348

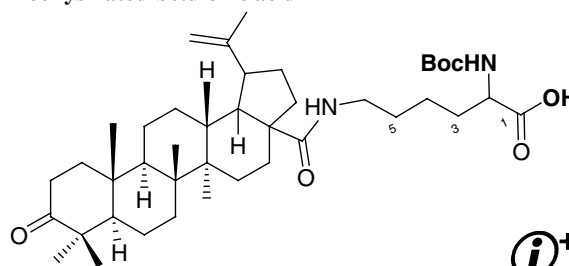
Sandra Sinishtaj, Heung Bae Jeon, Patrick Dolan, Thomas W. Kensler and Gary H. Posner\*

**Boc-lysinated-betulonic acid: A potent, anti-prostate cancer agent**

pp 6349–6358

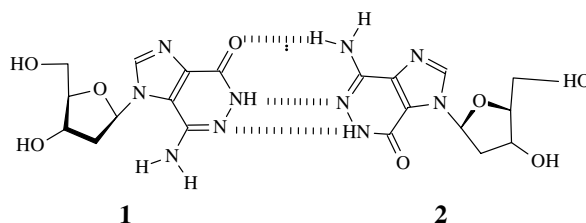
Brij B. Saxena,\* Lei Zhu, Meirong Hao, Eileen Kisilis, Meena Katdare, Ozgur Oktem, Arkadiy Bomshteyn and Premila Rathnam

Boc-lysinated-betulonic acid has been synthesized as a hydrophilic, novel compound which has shown potent anti-cancer activity in vitro. In in vivo tests in athymic mice, Boc-lysinated-betulonic acid inhibited the growth of xenografts up to 92%. Studies indicate that this compound causes cell death by apoptosis.

**Boc-lysinated-betulonic acid****Nucleosides with self-complementary hydrogen-bonding motifs: Synthesis and base-pairing studies of two nucleosides containing the imidazo[4,5-*d*]pyridazine ring system**

pp 6359–6367

Ravi K. Ujjinamatada, Robin L. Paulman, Roger G. Ptak and Ramachandra S. Hosmane\*

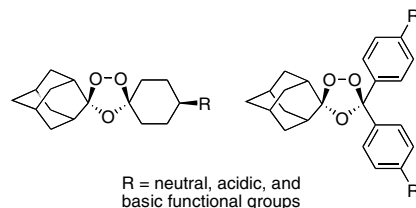


$^1\text{H}$  NMR-based base-pair studies as well as the results of in vitro anti-HIV screening of two isomeric nucleosides containing the title heterocyclic ring system are reported.



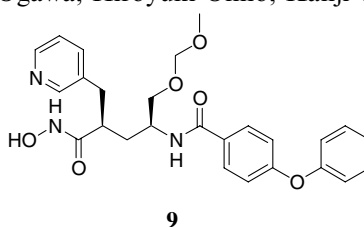
**Effect of functional group polarity on the antimalarial activity of spiro and dispiro-1,2,4-trioxolanes** pp 6368–6382

Yuxiang Dong, Yuanqing Tang, Jacques Chollet, Hugues Matile, Sergio Wittlin, Susan A. Charman, William N. Charman, Josefina Santo Tomas, Christian Scheurer, Christopher Snyder, Bernard Scorneaux, Saroj Bajpai, Scott A. Alexander, Xiaofang Wang, Maniyan Padmanilayam, Srinivasa R. Cheruku, Reto Brun and Jonathan L. Vennerstrom\*

**Design and synthesis of an orally active matrix metalloproteinase inhibitor**

pp 6383–6403

Shingo Yamamoto, Shingo Nakatani,\* Masahiro Ikura, Tsuneyuki Sugiura, Yoshitaka Nishita, Satoshi Itadani, Koji Ogawa, Hiroyuki Ohno, Kanji Takahashi, Hisao Nakai and Masaaki Toda

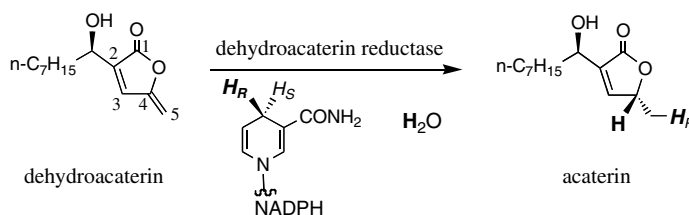


A series of 4-(4-phenoxy)benzoylamino-4-methoxymethoxymethyl butyric acid hydroxamates were found to exhibit strong inhibitory activity against MMP-2, MMP-9, and MMP-3. Among the compounds tested, **9** showed in vivo activity against MMP-3 after oral administration.

**Biosynthesis of acaterin: Mechanism of the reaction catalyzed by dehydroacaterin reductase**

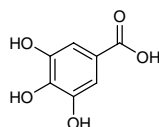
pp 6404–6408

Sayaka Nakano, Wataru Sakane, Hiroshi Oinaka and Yoshinori Fujimoto\*

**Relationship between the lipophilicity of gallic acid *n*-alkyl esters' derivatives and both myeloperoxidase activity and HOCl scavenging**

pp 6409–6413

Rober Rosso, Tiago O. Vieira, Paulo C. Leal, Ricardo J. Nunes, Rosendo A. Yunes and Tânia B. Creczynski-Pasa\*

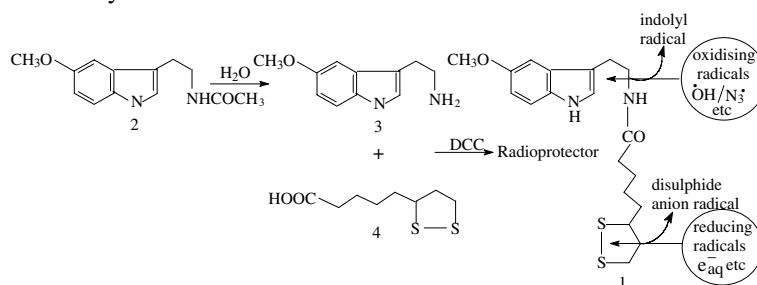


Fourteen derivatives from the gallic acid with respective lipophilicity were studied evidencing the structure–activity relationship in the inhibition of myeloperoxidase and the hypochlorous acid scavenger activities.

### Synthesis, pulse radiolysis, and in vitro radioprotection studies of melatoninolipoamide, a novel conjugate of melatonin and $\alpha$ -lipoic acid

pp 6414–6419

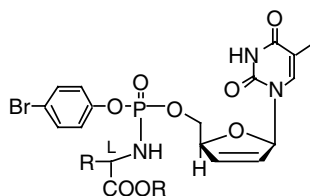
S. R. Venkatachalam,\* A. Salaskar, A. Chattopadhyay,\* A. Barik, B. Mishra, R. Gangabhagirathi and K. I. Priyadarsini\*



### Effect of alkyl groups on the cellular hydrolysis of stavudine phosphoramidates

pp 6420–6433

T. K. Venkatachalam, M. Sarquis, S. Qazi and F. M. Uckun\*

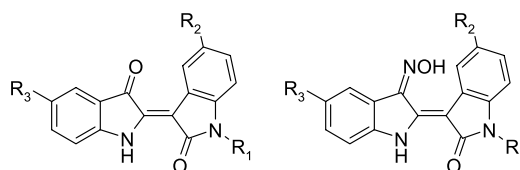


We examined the effect of cellular metabolism of three alkyl substituted amino acid ester phosphoramidate derivatives of stavudine in different cell lines. Marked cell-to-cell differences were found in both the rate of hydrolysis and chiral selectivity. This selectivity implies that different enzymes may be involved in the metabolism of these compounds depending on the cell type involved.

### Synthesis of novel 5-substituted indirubins as protein kinases inhibitors

pp 6434–6443

Anne Beauchard, Yoan Ferandin, Stéphane Frère, Olivier Lozach, Méline Blairvacq, Laurent Meijer, Valérie Thiéry\* and Thierry Besson

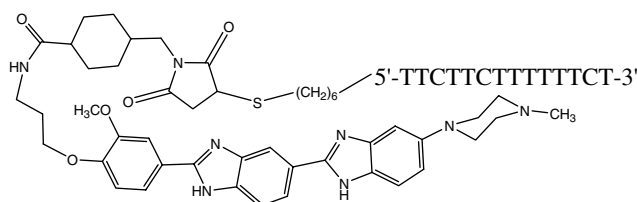


The effects of 34 new indirubin derivatives on CDK1/cyclin B, CDK5/p25, and GSK-3, as well as on SH-SY5Y human neuroblastoma cell survival, were investigated.

### Triple helix stabilization by covalently linked DNA–bisbenzimidazole conjugate synthesized by maleimide–thiol coupling chemistry

pp 6444–6452

Akash K. Jain, Satish Kumar Awasthi and Vibha Tandon\*



Conjugation of a bisbenzimidazole with DNA was done using SMCC, a heterobifunctional crosslinking reagent, by a simple methodology. Conjugate was characterized by ESMS. Triple helix formation studies were done with the conjugate.





**OTHER CONTENTS**

**Bioorganic & Medicinal Chemistry Reviews and perspectives**  
**Instructions to contributors**

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**p I**

\*Corresponding author

Ⓜ<sup>+</sup> Supplementary data available via ScienceDirect

**COVER**

Ribonucleotide Reductases (RNR) are radical-containing enzymes that catalyze the conversion of ribonucleotides to 2'-deoxyribonucleotides. The occurring intramolecular electron transfer is investigated by model peptides. The graphic was designed by Michael Graber from the Bernd Giese's research group using in part the following PDB entries: 1RLR (Uhlin, U., Eklund, H. *Nature* **1994**, 370, 533–539) and 1XSM (Kauppi, B., Nielsen, B. B., Ramaswamy, S., Larsen, I. K., Thelander, M., Thelander, L., Eklund, H. *J. Mol. Biol.* **1996**, 262, 706–720).

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