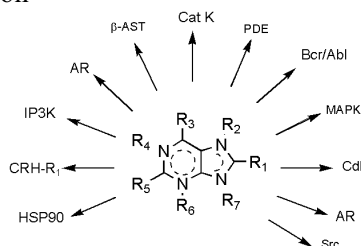


## Contents

### REVIEW

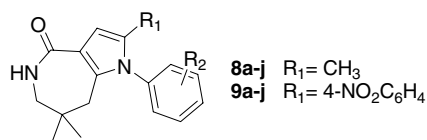
- The purines: Potent and versatile small molecule inhibitors and modulators of key biological targets** pp 3987–4006  
Michel Legraverend\* and David S. Grierson



Different combinations of substituents  $R_1$ – $R_7$  on the purine ring lead to compounds displaying potent and selective activity against a wide range of protein targets.

### ARTICLES

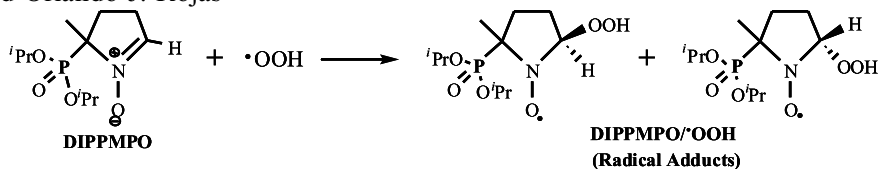
- Tetrahydropyrrolo[3,2-*c*]azepin-4-ones as a new class of cytotoxic compounds** pp 4007–4016  
Roberto Martínez,\* J. Gustavo Ávila, Ma. Teresa Ramírez, Araceli Pérez and Ángeles Martínez



The synthesis of the title compounds was achieved using dimedone as starting material. The observed cytotoxic activity depends of substituent joined to C-2 ( $R_1$ ) of the pyrrole moiety.

- Quantitative  $^{31}\text{P}$  NMR detection of oxygen-centered and carbon-centered radical species** pp 4017–4028

Dimitris S. Argyropoulos,\* Hongyang Li, Armino R. Gaspar, Kamilah Smith,  
Lucian A. Lucia and Orlando J. Rojas

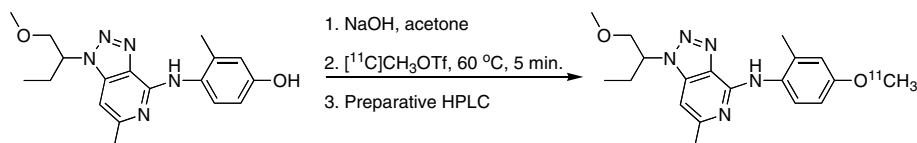


In this study, quantitative  $^{31}\text{P}$  NMR spin trapping techniques were used as effective tools for the detection and quantification of many free radical species. The radicals react with 5-diisopropoxy-phosphoryl-5-methyl-1-pyrroline-*N*-oxide (DIPPMPPO) producing stable spin adducts, which can be detected and accurately quantified using  $^{31}\text{P}$  NMR spectroscopy. This effort forms the foundations for the understanding of the nature, identity, and mechanisms of radical activity in a variety of biological and biochemical reactions involving radical processes.

**Synthesis and in vivo evaluation of [ $^{11}\text{C}$ ]SN003 as a PET ligand for CRF $_1$  receptors**

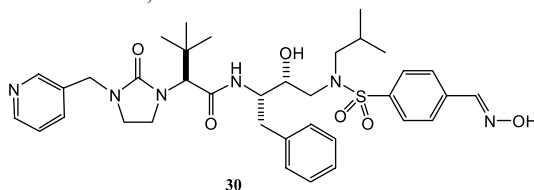
pp 4029–4034

J. S. Dileep Kumar,\* Vattoly J. Majo, Gregory M. Sullivan, Jaya Prabhakaran, Norman R. Simpson, Ronald L. Van Heertum, J. John Mann and Ramin V. Parsey

**Synthesis, antiviral activity, and pharmacokinetic evaluation of P3 pyridylmethyl analogs of oximinoarylsulfonyl HIV-1 protease inhibitors**

pp 4035–4046

John T. Randolph,\* Peggy P. Huang, William J. Flosi, David DeGoey, Larry L. Klein, Clinton M. Yeung, Charles Flentge, Mingua Sun, Chen Zhao, Tatyana Dekhtyar, Hongmei Mo, Lynn Colletti, Warren Kati, Kennan C. Marsh, Akhteruzzaman Molla and Dale J. Kempf

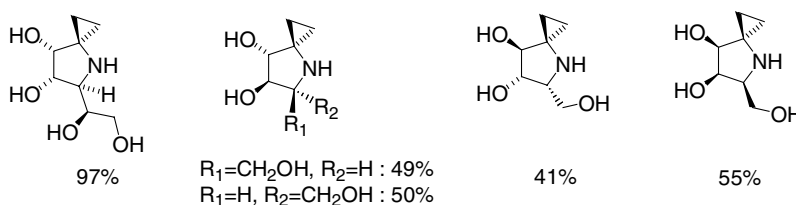


A series of potent inhibitors of HIV-1 protease designed to be equally effective at inhibiting both wild-type virus and a mutant strain of virus (A17) highly resistant to lopinavir is described.

**Spirocyclopropyl pyrrolidines as a new series of  $\alpha$ -L-fucosidase inhibitors**

pp 4047–4054

Christophe Laroche, Jean-Bernard Behr,\* Jan Szymoniak, Philippe Bertus, Catherine Schütz, Pierre Vogel and Richard Plantier-Royon\*

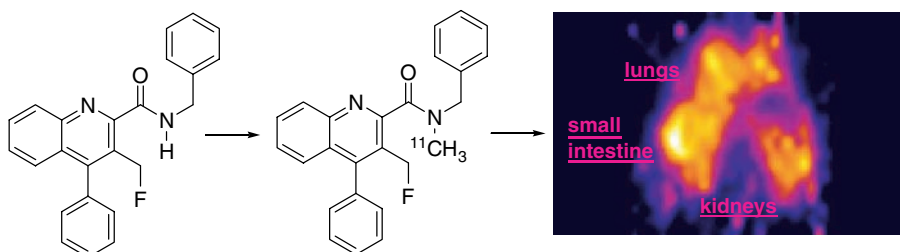


% inhibition of  $\alpha$ -L-fucosidase from bovine kidney at 1 mM concentration.

**Synthesis, labeling, and biological evaluation of halogenated 2-quinolinecarboxamides as potential radioligands for the visualization of peripheral benzodiazepine receptors**

pp 4055–4066

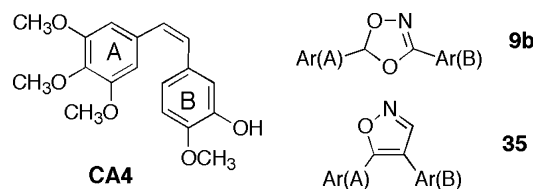
Andrea Cappelli,\* Mario Matarrese, Rosa Maria Moresco, Salvatore Valenti, Maurizio Anzini, Salvatore Vomero, Elia Anna Turolla, Sara Belloli, Pasquale Simonelli, Maria Azzurra Filannino, Michela Lecchi and Ferruccio Fazio



**Isoxazole-type derivatives related to combretastatin A-4, synthesis and biological evaluation**

pp 4067–4077

Julia Kaffy, Renée Pontikis,\* Danièle Carrez, Alain Croisy, Claude Monneret and Jean-Claude Florent

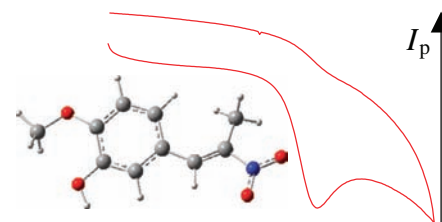
Derivative such as **9b** and **35** have been prepared and investigated. **$\beta$ -Nitrostyrene derivatives as potential antibacterial agents:**

pp 4078–4088

**A structure–property–activity relationship study**

Nuno Milhazes, Rita Calheiros, M. Paula M. Marques, Jorge Garrido, M. Natália D. S. Cordeiro, Cátia Rodrigues, Sandra Quinteira, Carla Novais, Luísa Peixe and Fernanda Borges\*

An interactive study was developed combining the synthesis of a series of  $\beta$ -nitrostyrene and  $\beta$ -methyl- $\beta$ -nitrostyrene derivatives and the evaluation of their antibacterial profile, along with the simultaneous determination of some physicochemical parameters, namely their conformational behaviour, redox potential and lipophilicity.

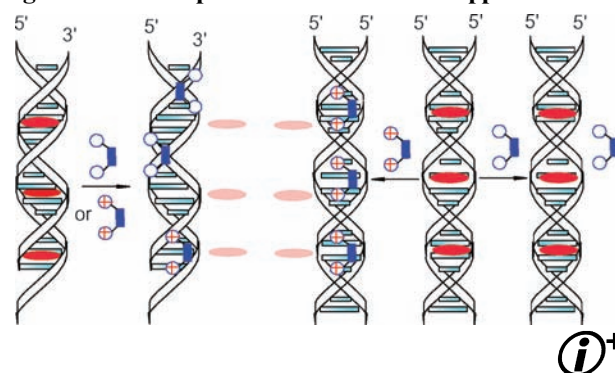
**Binding of actinomycin C<sub>1</sub> (D) and actinomycin to base-modified oligonucleotide duplexes with parallel chain orientation**

pp 4089–4100

Hong Li, Xiaohua Peng, Peter Leonard and Frank Seela\*

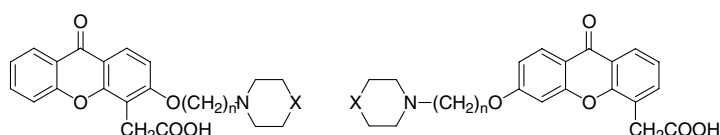
Actinomycin displaces the pre-bound ethidium bromide in anti-parallel DNA but not in parallel DNA, while actinomycin leads to displacement in both DNA structures. Highly fluorescent ethidium bromide, Low fluorescent ethidium bromide,

Actinomycin D, Actinomycin.

**New derivatives of xanthene-4-acetic acid: Synthesis, pharmacological profile and effect on TNF- $\alpha$  and NO production by human immune cells**

pp 4101–4109

Silvia Gobbi,\* Federica Belluti, Alessandra Bisi, Lorna Piazzini, Angela Rampa, Antonella Zampiron, Mariagnese Barbera, Anna Caputo and Maria Carrara



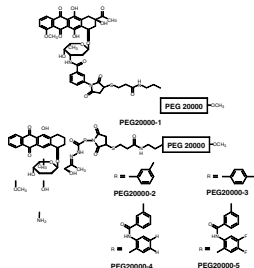
New derivatives of xanthene-4-acetic acid were synthesised and tested for their antitumour effects.



### Correlation of the acid-sensitivity of polyethylene glycol daunorubicin conjugates with their in vitro antiproliferative activity

pp 4110–4117

Paula C. A. Rodrigues, Thomas Roth, Heinz H. Fiebig, Clemens Unger, Rolf Mülhaupt and Felix Kratz\*

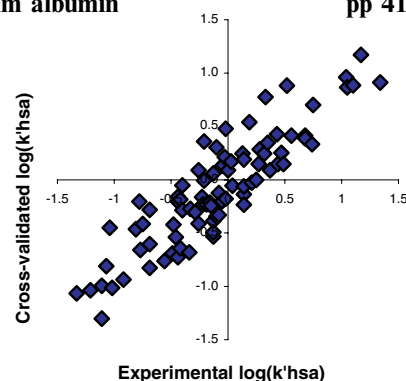


### In silico ADME modelling 2: Computational models to predict human serum albumin binding affinity using ant colony systems

pp 4118–4129

Sitarama B. Gunturi, Ramamurthi Narayanan\* and Akash Khandelwal

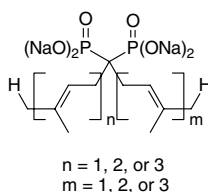
Computational models for the prediction of human serum albumin binding affinity are derived using 94 diverse compounds, 327 molecular descriptors, ant colony systems—a stochastic method and multiple linear regressions. Validation tests demonstrate that the models possess excellent predictive power and can be applied to whole medicinal chemical space for virtual screening studies. Interpretation of the physical meaning of the selected descriptors suggests that human serum albumin binding affinity is dependent principally on hydrophobic interactions, solubility, size and shape.



### Synthesis and biological activity of isoprenoid bisphosphonates

pp 4130–4136

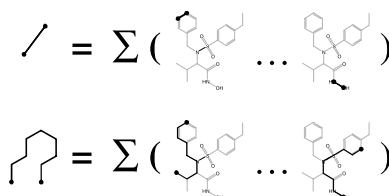
Larry W. Shull, Andrew J. Wiemer, Raymond J. Hohl and David F. Wiemer\*



### Linear and nonlinear QSAR study of *N*-hydroxy-2-[(phenylsulfonyl)amino]acetamide derivatives as matrix metalloproteinase inhibitors

pp 4137–4150

Michael Fernández, Julio Caballero\* and Alain Tundidor-Camba

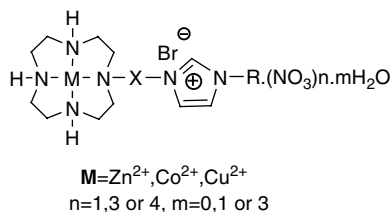


Schematic representation of the 2D autocorrelation vectors used in the QSAR study of *N*-hydroxy-2-[(phenylsulfonyl)amino]-acetamide derivatives as matrix metalloproteinase inhibitors.

**Monometallic complexes of 1,4,7,10-tetraazacyclododecane containing an imidazolium side: Synthesis, characterization, and their interaction with plasmid DNA**

pp 4151–4157

Qiang-Lin Li, Jun Huang, Qin Wang, Ning Jiang, Chuan-Qin Xia, Hong-Hui Lin, Jiang Wu\* and Xiao-Qi Yu\*

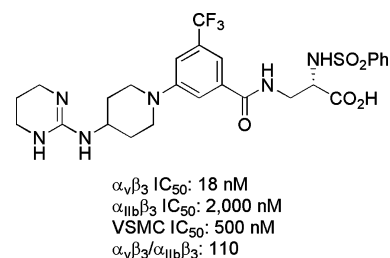
**Tricyclic pharmacophore-based molecules as novel integrin  $\alpha_v\beta_3$  antagonists.**

pp 4158–4181

**Part IV: Preliminary control of  $\alpha_v\beta_3$  selectivity by *meta*-oriented substitution**

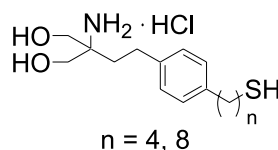
Dai Kubota, Minoru Ishikawa, Midori Ishikawa, Naokazu Yahata, Shoichi Murakami, Kazuyuki Fujishima, Masafumi Kitakaze and Keiichi Ajito\*

We found an  $\alpha_v\beta_3$  selective antagonist to demonstrate the in vivo efficacy of  $\alpha_v\beta_3/\alpha_{IIb}\beta_3$  dual antagonists processing a tricyclic pharmacophore.

**Preparation of antibodies against a novel immunosuppressant, FTY720, and development of an enzyme immunoassay for FTY720**

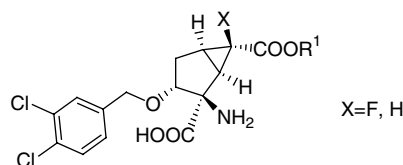
pp 4182–4192

Norimasa Matsumoto,\* Takeyuki Kohno, Shuji Uchida, Takaaki Shimizu, Haruko Kusumoto, Ryoji Hirose, Kazuo Yanada, Wasako Kurio, Shoji Yamaguchi, Kazuhito Watabe and Tetsuro Fujita

**Prodrugs of 3-(3,4-dichlorobenzoyloxy)-2-amino-6-fluorobicyclo[3.1.0]hexane-2,6-dicarboxylic acid (MGS0039): A potent and orally active group II mGluR antagonist with antidepressant-like potential**

pp 4193–4207

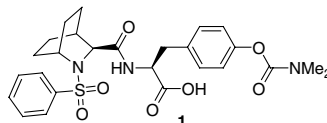
Akito Yasuhara,\* Masato Nakamura, Kazunari Sakagami, Toshiharu Shimazaki, Ryoko Yoshikawa, Shigeyuki Chaki, Hiroshi Ohta and Atsuro Nakazato



**Selection of a 2-azabicyclo[2.2.2]octane-based  $\alpha_4\beta_1$  integrin antagonist as an inhaled anti-asthmatic agent**

pp 4208–4216

Edward C. Lawson,\* Rosemary J. Santulli,\* Alexey B. Dyatkin, Scott A. Ballentine, William M. Abraham, Sandra Rudman, Clive P. Page, Lawrence de Garavilla, Bruce P. Damiano, William A. Kinney and Bruce E. Maryanoff

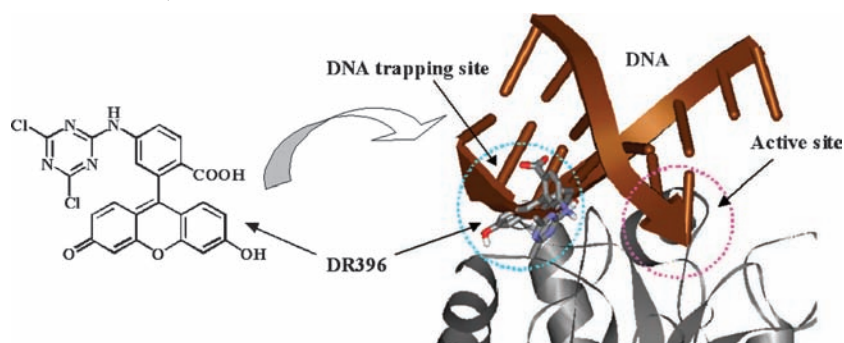


A number of potent  $\alpha_4\beta_1$  antagonists were evaluated for safety and efficacy, and **1** was selected as a lead candidate. The synthesis of compound **1** was optimized and scaled up, so that it could be evaluated in allergen-sensitive sheep and ovalbumin-sensitized guinea pigs. It was found to block changes in airway resistance, hyper-responsiveness, and inflammatory cell number.

**Structure basis for the inhibitory mechanism of a novel DNase  $\gamma$ -specific inhibitor, DR396**

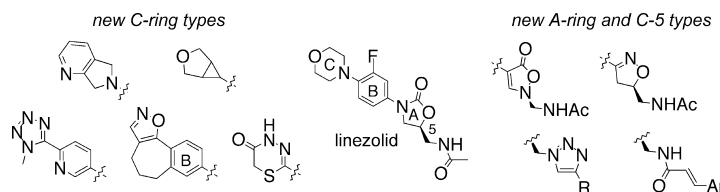
pp 4217–4226

Satoshi Sunaga, Atsushi Yoshimori, Daisuke Shiokawa and Sei-ichi Tanuma\*


**Recent developments in the identification of novel oxazolidinone antibacterial agents**

pp 4227–4240

Adam R. Renslo,\* Gary W. Luehr and Mikhail F. Gordeev

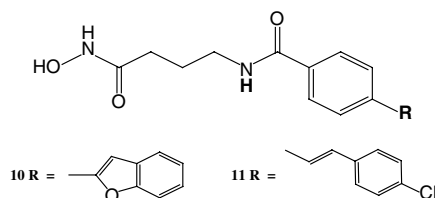


This review describes recent efforts directed at the discovery of new antibacterial oxazolidinones. New structures and structure–activity relationships (SARs) are discussed in the context of earlier work in the field.

**Discovery of a new chemical lead for a matrix metalloproteinase inhibitor**

pp 4241–4252

Masahiro Ikura,\* Shingo Nakatani, Shingo Yamamoto, Hiromu Habashita, Tsuneyuki Sugiura, Kanji Takahashi, Koji Ogawa, Hiroyuki Ohno, Hisao Nakai and Masaaki Toda

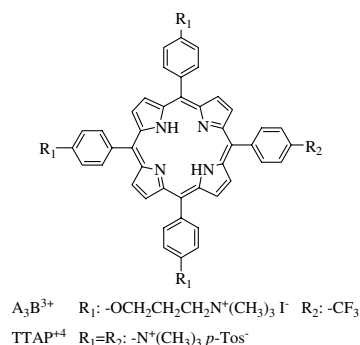


A series of *N*-benzoyl  $\gamma$ -aminobutyric hydroxamic acids were synthesized and evaluated as matrix metalloproteinase inhibitors. Optimization of the *N*-benzoyl residue and  $\gamma$ -amino butyric hydroxamic acid moiety resulted in the discovery of two novel MMP inhibitors (compounds **10** and **11**).

**Photodynamic inactivation of *Escherichia coli* immobilized on agar surfaces by a tricationic porphyrin** pp 4253–4259

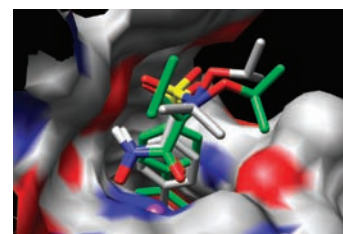
Daniel A. Caminos and Edgardo N. Durantini\*

The photodynamic activity of 5,10,15-tris[4-(3-*N,N,N*-trimethylammoniumpropoxy)-phenyl]-20-(4-trifluoromethylphenyl)porphyrin iodide ( $A_3B^{3+}$ ) has been studied in vitro on a typical Gram-negative bacterium *Escherichia coli* immobilized on agar surfaces. The studies show that the tricationic  $A_3B^{3+}$  porphyrin is an interesting sensitizer with potential applications in photodynamic inactivation of bacteria growing as localized foci of infection.

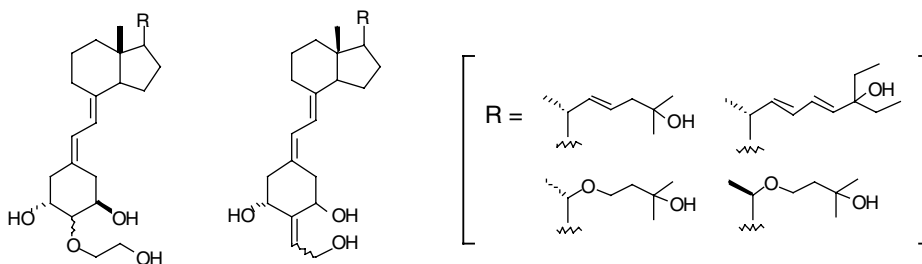
**Amber force field implementation, molecular modelling study, synthesis and MMP-1/MMP-2 inhibition profile of (*R*)- and (*S*)-*N*-hydroxy-2-(*N*-isopropoxybiphenyl-4-ylsulfonamido)-3-methylbutanamides** pp 4260–4276

Tiziano Tuccinardi, Adriano Martinelli,\* Elisa Nuti, Paolo Carelli, Federica Balzano, Gloria Uccello-Barretta, Gillian Murphy and Armando Rossello\*

Superimposition of (*R*)- (grey) and (*S*)-*N*-hydroxy-2-(*N*-isopropoxybiphenyl-4-ylsulfonamido)-3-methylbutanamide (green) docked into MMP-2.

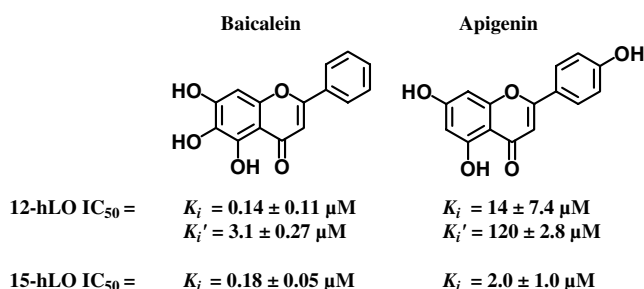
**Synthesis and biological activities of new 1 $\alpha$ ,25-dihydroxy-19-norvitamin D<sub>3</sub> analogs with modifications in both the A-ring and the side chain** pp 4277–4294

Masato Shimizu,\* Yukiko Miyamoto, Emi Kobayashi, Mika Shimazaki, Keiko Yamamoto, Wolfgang Reischl and Sachiko Yamada

**Baicalein is a potent in vitro inhibitor against both reticulocyte 15-human and platelet 12-human lipoxygenases**

pp 4295–4301

Joshua D. Deschamps, Victor A. Kenyon and Theodore R. Holman\*

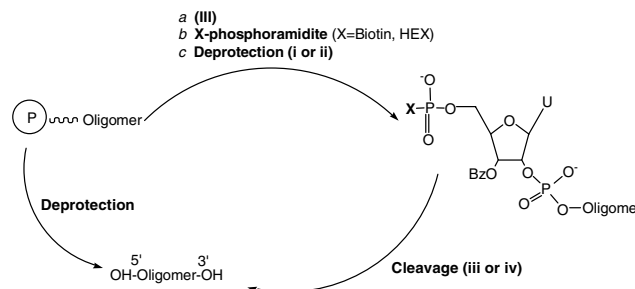


**A new synthetic protocol for labeled oligonucleotides, using a chemically cleavable universal linker**

pp 4302–4309

Shweta Mahajan, S. Patnaik, P. Kumar,\* R. P. Gandhi and K. C. Gupta\*

A two-step general technique for labeling of synthetic oligonucleotides is projected. To incorporate cleavable property in oligonucleotides, a new universal linker based on uridine nucleoside has been synthesized. The linkage between the label and the oligonucleotide is essentially stable under post-synthesis cleavage.

**OTHER CONTENTS****Bioorganic & Medicinal Chemistry Reviews and Perspectives**

pp 4310–4312

**Summary of instructions to authors**

p I

\*Corresponding author

i\* Supplementary data available via ScienceDirect

**COVER**

Docking of (*R*)-*N*-hydroxy-2-(*N*-isopropoxybiphenyl-4-ylsulfonamido)-3-methylbutanamide into MMP-2 [Tuccinardi, T.; Martinelli, A.; Nuti, E.; Carelli, P.; Balzano, F.; Uccello-Barretta, G.; Murphy, G.; Rossello, A. *Bioorg. Med. Chem.* **2006**, *14*, 3987].



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