

**A new photoprobe for studying biological activities of secreted phospholipases A<sub>2</sub>**

pp 295–305

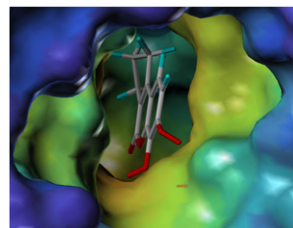
Lidija Kovačič, Jernej Šribar, Igor Križaj\*

Ammodytin (Atx) is a snake venom phospholipase A<sub>2</sub> (sPLA<sub>2</sub>s) with presynaptic toxicity, anticoagulant activity and the ability to influence cell cycle progression. These multiple physiological activities make this molecule a promising tool for studying processes influenced by the highly homologous mammalian sPLA<sub>2</sub>s—for example cell proliferation and apoptosis. Secreted PLA<sub>2</sub>s can act on cells as enzymes or as ligands for cellular receptors. To further characterize the sPLA<sub>2</sub>-binding molecules in cells we have developed a new method based on AtxC and a biotin-containing cross-linking reagent sulfo-SBED which possesses both an amine-reactive and a photo-reactive site, together with a biotin moiety that enables specific detection and affinity-based concentration. The biological activity of the AtxC derivatized by sulfo-SBED was demonstrated by biotin-tagging of calmodulin and R25, both known AtxC targets, but not of other proteins. In addition, using the new protocol we specifically labelled 14-3-3 proteins, protein disulfide isomerase and two unknown proteins of 45 and 46 kDa in the mitochondrial-synaptosomal fraction of porcine cerebral cortex, none of which could be tagged by the previously used methods. The new methodology, which can be used for any sPLA<sub>2</sub>, constitutes a novel approach to discovering and purifying sPLA<sub>2</sub>-binding proteins, to studying the topology of their respective complexes and to following sPLA<sub>2</sub>s in different biological systems.

**A high-throughput screening approach to anthrax lethal factor inhibition**

pp 306–312

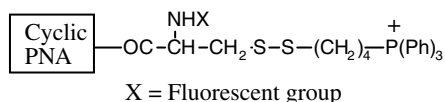
Sherida L. Johnson, Li-Hsing Chen, Maurizio Pellecchia\*



**A “Ready-To-Use” fluorescent-labelled-cysteine-TBTP (4-thiobutyltriphenylphosphonium) synthon to investigate the delivery of non-permeable PNA (peptide nucleic acids)-based compounds to cells**

pp 313–326

Mohamed Mehiri, Sergio Caldarelli, Audrey Di Giorgio, Thibault Barouillet, Alain Doglio, Roger Condom, Nadia Patino\*



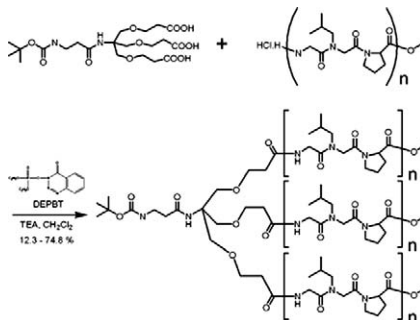
Conjugation of a fluorescent-labelled-cysteine-TBTP (4-thiobutyltriphenylphosphonium) synthon to a non-permeable compound (cyclic PNA-based compound) enables its efficient homogenous delivery into the cytoplasm of cells (visualized by fluorescence microscopy).

## Facile and efficient assembly of collagen-like triple helices on a TRIS scaffold

pp 327–337

Weibo Cai\*, Dustin Wong, Garth A. Kinberger, Sen Wai Kwok, Joseph P. Taulane, Murray Goodman

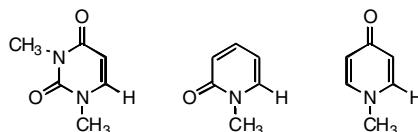
The TRIS scaffold, Boc- $\beta$ -Ala-TRIS-(OH)<sub>3</sub>, was utilized to assemble triple helices composed of the Gly-Nleu-Pro sequence (Nleu denotes *N*-isobutylglycine). The scaffold assembly can be achieved efficiently through direct coupling between long peptide chains and the TRIS scaffold using DEPBT, a recently developed peptide coupling reagent. CD spectroscopy and thermal denaturation studies demonstrated that Boc- $\beta$ -Ala-TRIS-[(Gly-Nleu-Pro)<sub>*n*</sub>-OMe]<sub>3</sub> exhibits triple helicity in H<sub>2</sub>O when *n* equals 5, 6, and 8, while the shorter analogs (where *n* = 1 and 4) do not. TRIS-assembled structures possess several advantages over the KTA- and TREN-assembled structures previously reported from our laboratory (where KTA and TREN denotes *cis*-1,3,5-trimethyl cyclohexane-1,3,5-tricarboxylic acid and *tris*-(2-aminoethyl)amine, respectively). The protecting groups on the scaffold and at the C-terminus of the TRIS-assembled peptides can be readily removed to synthesize collagen mimetic dendrimers and metal-complexing collagen-like peptides respectively, both of which can lead to further enhanced thermal stability.



## Carbanions from decarboxylation of orotate analogs: Stability and mechanistic implications

pp 338–343

Fong Ying Yeoh, Roxanne R. Cuasito, Christina C. Capule, Freeman M. Wong, Weiming Wu\*

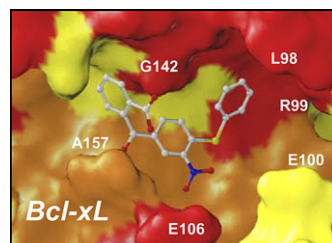


The p*K*<sub>a</sub>'s of the 6-CH groups of 1,3-dimethyluracil, *N*-methyl-2-pyridone, and *N*-methyl-4-pyridone were determined through their reactions with bases derived from carbon acids with known p*K*<sub>a</sub> and the reactions of their corresponding carbanions with the carbon acids. No correlation between the stability of the carbanions and the rate of decarboxylation of corresponding carboxylic acids was found.

## Structure-based discovery of a new class of Bcl-x<sub>L</sub> antagonists

pp 344–353

Michele F. Rega, Marilisa Leone, Dawoon Jung, Naomi J.H. Cotton, John L. Stebbins, Maurizio Pellecchia\*



## CORRIGENDUM

Corrigendum to “Hydrogen transfer pathways of the asymmetric reduction of  $\alpha,\beta$ -unsaturated ketone mediated by baker’s yeast” [*Bioorg. Chem.* 34 (2006) 158–166]

p 354

Yuan Chu, Ben-Li Zhang\*, Virginie Silvestre, Jin-Pei Cheng\*

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