

GEORGE KOKOTOS

Professor

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- 6620 citations (H-index 44)

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EDUCATION

1979 B.Sc. in Chemistry: National and Kapodistrian University of Athens, Greece

1984 D.Phil. in Organic Chemistry: National and Kapodistrian University of Athens, Athens, Greece.

APPOINTMENTS

2011 - 2012 Director of the Institute of Organic and Pharmaceutical Chemistry, National Hellenic Research Foundation, Athens, Greece.

2014 – 2017 Chairman of the Department of Chemistry, National and Kapodistrian University of Athens.

2003 - today Professor, Laboratory of Organic Chemistry, Department of Chemistry, National and Kapodistrian University of Athens.

2003 – today Director of the Master's Program "Organic Chemistry and its Applications in Chemical Industry"

Summer 2014, 2013, 2003 Visiting Professor, Department of Chemistry and Biochemistry and Department of Pharmacology, University of California at San Diego, USA.

1998 - 2002 Associate Professor, Laboratory of Organic Chemistry, Department of Chemistry, National and Kapodistrian University of Athens.

Summer 2000 Guest Researcher, Department of Chemistry and Biochemistry, University of California at San Diego, USA.

1993 - 1997 Assistant Professor, Department of Chemistry, National and Kapodistrian University of Athens.

1988 - 1992 Lecturer, Department of Chemistry, National and Kapodistrian University of Athens.

RESEARCH FIELDS

- Design, synthesis and study of organic compounds presenting pharmacological activity - Novel agents for the treatment of inflammatory diseases, neurological disorders and cancer
- Design, synthesis and study of enzyme inhibitors (phospholipase A₂, autotaxin, HDAC enzymes)

- Development of methodology for the synthesis of bioactive compounds - Organocatalysis – Synthetic Photochemistry Use of enzymes in organic synthesis
- Determination and study of organic compounds using High Resolution Mass Spectrometry – Lipidomics

EDUCATION EXPERIENCE

UNDERGRADUATE COURSES

- Organic Chemistry
- Medicinal Chemistry
- Topics in Bioorganic Chemistry

POSTGRADUATE COURSES

- Chemistry of Biomolecules and Bioactive Compounds
- Synthesis of Biologically Active Organic Compounds
- Natural Products

REVIEWER OF SCIENTIFIC JOURNALS

- Reviewer of more than 60 international journals

MEMBER OF THE EDITORIAL BOARD OF JOURNALS

- Member of the Editorial Board of the journals: *Molecules* (1996-now), *Frontiers in Chemical Biology* (2013-now), *Current Organic Chemistry* (2013-now), *Biomolecules* (2020-now), *European Journal of Lipid Science and Technology* (2007-2008)

AWARDS AND SCHOLARSHIPS

- Graduate Research Fellowship from the National Research Foundation (1979 – 1980)
- Fellowship from the Royal Society of Chemistry (summer 1993)

ADDITIONAL INFORMATION

- More than 190 publications in journals with peer review
- More than 300 conference presentations
- 10 invited book chapters in collective volumes
- Supervision of doctoral thesis:**23**
- Supervision of graduate students:**51**
- Supervision of undergraduate students:**more than 50**
- Reviewer in Research Programs: more than 50

SELECTED RESEARCH GRANTS

- “Preclinical development of autotaxin inhibitors: A new target for the treatment of pulmonary fibrosis and chronic inflammation.” (ΕΡΕΥΝΩ, ΔΗΜΙΟΥΡΓΩ, ΚΑΙΝΟΤΟΜΩ) June 2017 – June 2022.
- “Synthesis of bioactive compounds and study of bioactive compounds using high resolution mass spectrometry.” (Stravros Niarchos Foundation) July 2017 - October 2022.
- “Phospholipases A₂ inhibitors: Developing a drug pipeline for the treatment of inflammatory neurological disorders” (ΣΥΝΕΡΓΑΣΙΑ) 2014-16.
- “Pharmaceutically optimized drug candidate for the treatment of the chronic phase of primary Glomerulonephritis” (Norwegian Research Council) 2014-16.
- “Autotaxin (ATX): A novel therapeutic target in lung cancer” (ΣΥΝΕΡΓΑΣΙΑ) 2012-15.

SELECTED PUBLICATIONS

"Sunlight- or UVA-Light-Mediated Synthesis of Hydroxamic Acids from Carboxylic Acids." O. G. Mountanea, C. Mantzourani, M. G. Kokotou, C. G. Kokotos, G. Kokotos, *Eur. J. Org. Chem.* **2023**, e202300046.

"A Photochemical Protocol for the Synthesis of Weinreb and Morpholine Amides from Carboxylic Acids." A. Bourboula, O. G. Mountanea, G. Krasakis, C. Mantzourani, M. G. Kokotou, C. G. Kokotos, G. Kokotos, *Eur. J. Org. Chem.* **2023**, e202300008.

"The discovery and development of transmembrane serine protease 2 (TMPRSS2) inhibitors as candidate drugs for the treatment of COVID-19." C. Mantzourani, S. Vasilakaki, V.-E. Gerogianni, G. Kokotos, *Expert Opin. Drug Disc.* **2022**, *17*, 231-246.

"N-Acylated and N-Alkylated 2-Aminobenzothiazoles Are Novel Agents That Suppress the Generation of Prostaglandin E₂." M. A. Theodoropoulou, A. Psarra, M. Erhardt, A. Nikolaou, A.-D. D. Gerogiannopoulou, D. Hadjipavlou-Litina, D. Hayashi, E. A. Dennis, A. Huwiler, G. Kokotos, *Biomolecules* **2022**, *12*, 267.

"Free fatty acid profiling of Greek yogurt by liquid chromatography-high resolution mass spectrometry (LC-HRMS) analysis." C. Mantzourani, C. S. Batsika, M. G. Kokotou, G. Kokotos, *Food Res. Inter.* **2022**, *160*, 111751.

"Lipidomics Analysis of Free Fatty Acids in Human Plasma of Healthy and Diabetic Subjects by Liquid Chromatography-High Resolution Mass Spectrometry (LC-HRMS)." Kokotou M.G., Mantzourani C., Batsika C.S., Mountanea O.G., Eleftheriadou .I, Kosta O., Tentolouris N., Kokotos G. *Biomedicines* **2022**, *10*, 1189.

"Identification of a Dual Inhibitor of Secreted Phospholipase A₂ (GIIA sPLA₂) and SARS-CoV-2 Main Protease." Theodoropoulou M.A., Koutoulogenis G.S., Zhang L., Akrani I., Mikros E., Hilgenfeld R., Kokotos G. *Pharmaceuticals* **2022**, *15*, 961.

"Light-promoted oxidation of aldehydes to carboxylic acids under aerobic and photocatalyst-free conditions." C. S. Batsika, C. Koutsilieris, G. S. Koutoulogenis, M. G. Kokotou, C. G. Kokotos, G. Kokotos, *Green Chem.* **2022**, *24*, 6224-6231.

"Nuclear receptor NR5A2 negatively regulates cell proliferation and tumor growth in nervous system malignancies." D. Gkikas, D. Stellas, A. Polissidis, T. Manolakou, M. G. Kokotou, G. Kokotos, P. K. Politis, *PNAS* **2021**, *118*, e2015243118.

"The design and discovery of phospholipase A₂ inhibitors for the treatment of inflammatory diseases". C. S. Batsika, A.-D. D. Gerogiannopoulou, C. Mantzourani, S. Vasilakaki, G. Kokotos, *Expert Opin. Drug Discov.* **2021**, *16*, 1287-1305.

"Saturated Oxo Fatty Acids (SOFAs): A Previously Unrecognized Class of Endogenous Bioactive Lipids Exhibiting a Cell Growth Inhibitory Activity." Batsika C.S., Mantzourani C., Gkikas D., Kokotou M.G., Mountanea O.G., Kokotos C.G., Politis P.K., Kokotos G., *J. Med. Chem.* **2021**, *64*, 5654-5666.

"Changes in the cellular fatty acid profile drive the proteasomal degradation of α -synuclein and enhance neuronal survival." M. Xylaki, I. Boumpourea, M. G. Kokotou, T. Marras, G. Papadimitriou, I. Kloukina, V. Magrioti, G. Kokotos, K. Vekrellis, E. Emmanouilidou, *FASEB J.* **2020**, *34*, 15123-15145.

"Saturated Hydroxy Fatty Acids Exhibit a Cell Growth Inhibitory Activity and Suppress the Cytokine-Induced β -Cell Apoptosis." Kokotou M.G., Kokotos A.C., Gkikas D., Mountanea O.G., Mantzourani C., Almutairi A., Lei X., Ramanadham S., Politis P.K., Kokotos G., *J. Med. Chem.* **2020**, *63*, 12666-12681.

"Lipid mediators and biomarkers associated with type 1 diabetes development." Nelson A.J., Stephenson D.J., Bone R.N., Cardona C.L., Park M.A., Tusing Y.G., Lei X., Kokotos G., Graves C.L., Mathews C.E., Kramer J., Hessner M.J., Chalfant C.E., Ramanadham S. *JCI Insight*, **2020**, *5*, e138034.

" β -Lactones: A Novel Class of Ca²⁺-Independent Phospholipase A₂ (Group VIA iPLA₂) Inhibitors with the Ability To Inhibit β -Cell Apoptosis" C. Dedaki, M. G. Kokotou, V. D. Mouchlis, D. Limnios, X. Lei, C. T. Mu, S. Ramanadham, V. Magrioti, E. A. Dennis, G. Kokotos, *J. Med. Chem.* **2019**, *62*, 2916-2927.

"Small-molecule inhibitors as potential therapeutics and as tools to understand the role of phospholipases A₂" A. Nikolaou, M. G. Kokotou, S. Vasilakaki, G. Kokotos, *BBA - Molecular and Cell Biology of Lipids* **2019**, *1864*, 941-956.

"Hydroxamic acids constitute a novel class of autotaxin inhibitors that exhibit *in vivo* efficacy in a

pulmonary fibrosis model" Nikolaou A., Ninou I., Kokotou M. G., Kaffe E., Afantitis A., Aidinis V., Kokotos G. *J. Med. Chem.* **2018**, *61*, 3697-3711.

"Development of Potent and Selective Inhibitors for Group VIA Calcium-Independent Phospholipase A₂ Guided by Molecular Dynamics and Structure-Activity Relationships" V. D. Mouchlis, D. Limnios, M. G. Kokotou, E. Barbayianni, G. Kokotos, J. A. McCammon, E. A. Dennis, *J. Med. Chem.* **2016**, *59*, 4403-4414.

"Autotaxin, a secreted lysophospholipase D, as a promising therapeutic target in chronic inflammation and cancer" E. Barbayianni, E. Kaffe, V. Aidinis, G. Kokotos *Progr. Lipid Res.* **2015**, *58*, 76-96.

"Synthetic and natural inhibitors of phospholipases A₂: their importance for understanding and treatment of neurological disorders." W.-Y. Ong, T. Farooqui, G. Kokotos, A. A. Farooqui *ACS Chem. Neurosci.* **2015**, *6*, 814-831.

"Inhibition of Ca²⁺-independent phospholipase A₂β (iPLA₂β) ameliorates islet infiltration and incidence of diabetes in NOD mice" Bone R. N., Gai Y., Magrioti V., Kokotou M. G., Ali T., Lei X., Tse H. M., Kokotos G., Ramanadham S. *Diabetes* **2015**, *64*, 541-554.

"Inhibition of group IVA cytosolic phospholipase A₂ by thiazolyl ketones in vitro, ex vivo, and in vivo." Kokotos G., Feuerherm A., J. Barbayianni E., Shah I., Sæther M., Magrioti V., Nguyen T., Constantinou-Kokotou V., Dennis E. A., Johansen B. *J. Med. Chem.* **2014**, *57*, 7523.

"Fluoroketone inhibition of Ca⁽²⁺⁾-independent phospholipase A₂ through binding pocket association defined by hydrogen/deuterium exchange and molecular dynamics." Y. H. Hsu, D. Bucher, J. Cao, S. Li, S. W. Yang, G. Kokotos, V. L. Woods, J. A. McCammon, E. A. Dennis *J. Am. Chem. Soc.* **2013**, *135*, 1330-1337.

"Primary amine-thioureas with improved catalytic properties for "difficult" Michael reactions: Efficient organocatalytic syntheses of (S)-baclofen, (R)-baclofen and (S)-phenibut" M. Tsakos, C. G. Kokotos, G. Kokotos *Adv. Synth. Catal.* **2012**, *354*, 740-746.

"A tripeptide-like prolinamide-thiourea as an aldol reaction catalyst." Fotaras S., Kokotos C.G., Kokotos G. *Org. Biomol. Chem.* **2012**, *10*, 5613-9.

"Phospholipase A₂ enzymes: Physical structure, biological function, disease implication, chemical inhibition, and Therapeutic intervention" E. A. Dennis, J. Cao, Y.-H. Hsu, V. Magrioti, G. Kokotos *Chem. Rev.* **2011**, *111*, 6130-6185.

"Novel pyrrolidine-thiohydantoins/thioxotetrahydropyrimidinones as highly effective catalysts for the asymmetric Michael addition." Kokotos C.G., Limnios D., Triggidou D., Trifonidou M., Kokotos G. *Org. Biomol. Chem.* **2011**, *9*, 3386-3395.

"Potent and selective fluoroketone inhibitors of group VIA calcium-independent phospholipase A₂" G. Kokotos, Y.-H. Hsu, J. E. Burke, C. Baskakis, C. G. Kokotos, V. Magrioti, E. A. Dennis, *J. Med. Chem.* **2010**, *53*, 3602-3610.

"Location of inhibitors bound to group IVA phospholipase A₂ determined by molecular dynamics and deuterium exchange mass spectrometry." J. E. Burke, A. Babakhani, A. A. Gorfe, G. Kokotos, S. Li, V. L. Woods, J. A. McCammon, E. A. Dennis, *J. Am. Chem. Soc.* **2009**, *131*, 8083-8091.

"*Bacillus subtilis* esterase (BS2) and its double mutant have different selectivity in the removal of carboxyl protecting groups" E. Barbayianni, C. G. Kokotos, S. Bartsch, C. Drakou, U. T. Bornscheuer, George Kokotos, *Adv. Synth. Catal.* **2009**, *351*, 2325-2332.

"Differing roles for members of the phospholipase A₂ superfamily in experimental autoimmune encephalomyelitis." Kalyvas A., Baskakis C., Magrioti V., Constantinou-Kokotou V., Stephens D., López-Vales R., Lu J.Q., Yong V.W., Dennis E.A., Kokotos G., David S. *Brain* **2009**, *132*, 1221-1235.

"Primary amine-thioureas based on tert-butyl esters of natural amino acids as organocatalysts for Michael reaction" C. G. Kokotos, G. Kokotos, *Adv. Synth. Catal.* **2009**, *351*, 1355-1362.

"Synthesis of polyfluoro ketones for selective inhibition of human phospholipase A₂ enzymes" C. Baskakis, V. Magrioti, N. Cotton, D. Stephens, V. Constantinou-Kokotou, E. A. Dennis, G. Kokotos *J. Med. Chem.* **2008**, *51*, 8027-8037.

"Synthesis of medicinally interesting polyfluoro ketones via perfluoroalkyl lithium reagents." C. G. Kokotos, C. Baskakis, G. Kokotos, *J. Org. Chem.* **2008**, *73*, 8623-8626.

"Structure-activity relationship of 2-oxoamide inhibition of group IVA cytosolic phospholipase A₂ and group V secreted phospholipase A₂" D. A. Six, E. Barbayianni, V. Loukas, V. Constantinou-Kokotou, D.

Hadjipavlou-Litina, D. Stephens, A. C. Wong, V. Magrioti, P. Moutevelis-Minakakis, S. F. Baker, E. A. Dennis, G. Kokotos, *J. Med. Chem.* **2007**, *50*, 4222-4235.

"Enzymatic removal of carboxyl protecting groups. III. Fast removal of allyl and chloroethyl esters by *Bacillus subtilis* esterase (BS2)." I. Fotakopoulou, E. Barbayianni, V. Constantinou-Kokotou, U. T. Bornscheuer, G. Kokotos, *J. Org. Chem.* **2007**, *72*, 782-786.

"Differential inhibition of group IVA and group VIA phospholipases A₂ by 2-oxoamides." D. Stephens, E. Barbayianni, V. Constantinou-Kokotou, A. Peristeraki, D. A. Six, J. Cooper, R. Harkewicz, R. A. Deems, E. A. Dennis, G. Kokotos, *J. Med. Chem.* **2006**, *49*, 2821-2828.

"Systemic and intrathecal effects of a novel series of phospholipase A₂ inhibitors on hyperalgesia and spinal prostaglandin E₂ release." T. L. Yaksh, G. Kokotos, C. I. Svensson, D. Stephens, C. G. Kokotos, B. Fitzsimmons, D. Hadjipavlou-Litina, X. Y. Hua, E. A. Dennis, *J. Pharmacol. Exp. Ther.* **2006**, *316*, 466-475.

"Enzymatic removal of carboxyl protecting groups. 2. Cleavage of the benzyl and methyl moieties." E. Barbayianni, I. Fotakopoulou, M. Schmidt, V. Constantinou-Kokotou, U. T. Bornscheuer, G. Kokotos, *J. Org. Chem.* **2005**, *70*, 8730-8733.

"Proline-modified poly(propyleneimine) dendrimers as catalysts for asymmetric aldol reactions." E. Bellis, G. Kokotos, *J. Mol. Catal. A: Chem.* **2005**, *241*, 166-174.

"Enzymatic removal of carboxyl protecting groups. 1. Cleavage of the tert-butyl moiety." M. Schmidt, E. Barbayianni, I. Fotakopoulou, M. Hohne, V. Constantinou-Kokotou, U. T. Bornscheuer, G. Kokotos, *J. Org. Chem.* **2005**, *70*, 3737-3740.

"Inhibition of group IVA cytosolic phospholipase A₂ by novel 2-oxoamides in vitro, in cells, and in vivo." G. Kokotos, D. Six, V. Loukas, T. Smith, V. Constantinou-Kokotou, D. Hadjipavlou-Litina, S. Kotsovolou, A. Chiou, C. Beltzner and E. Dennis, *J. Med. Chem.* **2004**, *47*, 3615-3628.

"Novel trifluoromethyl ketones as potent gastric lipase inhibitors." G. Kokotos, S. Kotsovolou, R. Verger, *ChemBioChem* **2003**, *4*, 90-95.

"Synthesis of lipophilic aldehydes and study of their inhibition effect on human digestive lipases." S. Kotsovolou, R. Verger, G. Kokotos, *Org. Lett.* **2002**, *4*, 2625-8.

"Novel 2-oxoamide inhibitors of human group IVA phospholipase A₂." G. Kokotos, S. Kotsovolou, D.A. Six, V. Constantinou-Kokotou, C.C. Beltzner, E.A. Dennis, *J. Med. Chem.* **2002**, *45*, 2891-2893.

"Bis-2-oxoamide triacylglycerol analogues: A novel class of potent human gastric lipase inhibitors" S. Kotsovolou, A. Chiou, R. Verger, G. Kokotos, *J. Org. Chem.* **2001**, *66*, 962-967.

"Synthesis of 2-oxo amide triacylglycerol analogues and study of their inhibition effect on pancreatic and gastric lipases." G. Kokotos, R. Verger, A. Chiou, *Chemistry-A European Journal* **2000**, *6*, 4211-4217.

"Synthesis and study of a lipophilic α -keto amide inhibitor of pancreatic lipase." A. Chiou, T. Markidis, V. Constantinou-Kokotou, R. Verger, G. Kokotos, *Org. Lett.* **2000**, *2*, 347-350.

"A general approach to the asymmetric synthesis of unsaturated lipidic α -amino acids. The first synthesis of α -aminoarachidonic acid." G. Kokotos, J.M. Padron, T. Martin, W.A. Gibbons and V.S. Martin, *J. Org. Chem.* **1998**, *63*, 3741-3744.

"Selective one-pot conversion of carboxylic acids into alcohols." G. Kokotos, C. Noula, *J. Org. Chem.* **1996**, *61*, 6994-6996.

"A general approach to the enantiomeric synthesis of lipidic α -amino acids, peptides and vicinal aminp alcohols." G. Kokotos, J.-M. Padron, C. Noula, W.A. Gibbons, V. Martin, *Tetrahedron: Asymmetry* **1996**, *7*, 857-866.

"A convenient one-pot conversion of *N*-protected amino acids and peptides into alcohols". G. Kokotos, *Synthesis* **1990**, 299-301.