SHORT CURRICULUM VITAE AND MOST SIGNIFICANT PUBLICATIONS

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Curriculum Vitae

Since 2006, Plato A. Magriotis, Ph.D., is an Associate Professor of Medicinal Chemistry at the Department of Pharmacy, School of Health Sciences at the University of Patras in Greece and a Research Affiliate with the Department of Chemistry at New York University. Magriotis received his Ph.D. in Chemical Biology working with Professor Francis Johnson at the Department of Chemistry of Stony Brook University in 1983 and did Postdoctoral work at Harvard University (1983-1986) with Nobel Laureate Professor E. J. Corey. He began his academic career at West Virginia University and when presented with a very attractive offer to join Merck & Co. as a senior scientist, he joined the Medicinal Chemistry Department of Merck Pharmaceutical Company in New Jersey. Before assuming his present position, he moved back to Academia as an Adjunct Professor of Chemistry at New York University in 2002. Magriotis' research program focuses on the development of new methodology for the synthesis of relevant pharmacophores applied in drug discovery such as β-Lactams and Piperazines.

Courses

Organic Chemistry
Medicinal Chemistry III

Research Activities

Importance of Catalytic Enantioselective Synthesis of Saturated N-Heterocucles in Medicinal Chemistry and Chemical Biology

The important requirement for approval of a new drug, in case it happens to be chiral, that both enantiomers of the drug be studied in detail,[1] have focused the attention of synthetic organic and medicinal chemists on the development of new methods for catalytic asymmetric synthesis especially of relevant saturated N-heterocycles. Despite the success of chirally modified transition-metal catalysts in asymmetric synthesis, in the form of the Nobel Prize in Chemistry in 2001, the field of asymmetric organic synthesis has, since then, been dominated by organocatalysts due to their ability to catalyze a variety of fundamentally important transformations in medicinal chemistry and therefore chemical biology. One example is the Staudinger synthesis of β-lactams representing one class of saturated N-

[1] Stinson, S. E. *Chem. Eng. News* **2000**, *78*, 55-78.

heterocycles and continuing to provide unique opportunities for the discovery of new derivatives with novel pharmacological profiles.[2] Specifically, β-lactams have recently been found to have potential as the basis for treatments for neurological disorders including amyotrophic lateral sclerosis (ALS), also known as Lou Gehrig's disease.[3] Although significant progress has been made in asymmetric organocatalytic Staudinger synthesis of β-lactams since the inaugural and pioneering investigations by Lectka and coworkers around the turn of the century,[4] the same did not hold true regarding the development of a novel Gilman-Speeter process for the catalytic enantioselective synthesis of β-lactams.[5] Efforts directed at this latter goal are ongoing in this Laboratory.

On the other hand, the piperazine ring, besides defining a major class of saturated N-heterocycles, has been classified as a priviledged structure in Medicinal Chemistry since it is more than frequently found in biologically active compounds including several marketed blockbuster drugs such as Glivec (Imatinib) and Viagra (Sildenafil).[6] Actually, an analysis of all U.S. FDA approved small molecule drugs found that 21% contained saturated 6-membered N-heterocycles with an additional heteroatom (N, piperazines; O, morpholines; S, thiomorpholines).[7] Indeed, 13 of the 200 best-selling small molecule drugs in 2012 contain a piperazine ring.[8] In the vast majority of these molecules, however, the piperazine ring is not substituted on any of its carbon atoms. Specifically, analysis of the piperazine substitution pattern reveals a luck of structural diversity, with almost every single drug in this category (83%) containing a substituent at both the N1- and N4-positions compared to only a few drugs having a substituent at any other position (C2, C3, C5, and C6).[4] Significant chemical space that is closely related to that known to be biologically relevant, therefore, remains unexplored. In order to explore this chemical space, an efficient and enantioselective synthesis of C-substituted piperazines must be designed and developed.[9] Efforts toward the implementation of this particular target are also ongoing in this Laboratory. Since piperazine derivatives have been reported to elicit a broad spectrum of pharmacological activities including antidepressant, anticancer, antihelmentic, antibacterial, antifungal, antimycobacterial, antimalarial, antituberculant, anticonvulsant,[6] and anti-AIDS;[10] one can easily comprehend that the sky will be the limit, as far as novel drug development is concerned, once this catalytic enantioselective process will be fully developed.

Publications

"A New Cr(VI) Reagent for the Catalytic Oxidation of Secondary Alcohols to Ketones." Corey, E. J.; Barrette, E.-P.; Magriotis, P. A. *Tetrahedron Lett.* **1985**, *26*, 5855-5858.

"Total Synthesis and Absolute Configuration of 7,20-Diisocyanoadociane." Corey, E. J.; Magriotis, P. A. *J. Am. Chem. Soc.* **1987**, *109*, 287-289.

"Stereoselective Construction and Synthetic Applications of Phenylthio Substituted Iodoolefins." Magriotis, P. A.; Doyle, T. J.; Kim, K. D. *Tetrahedron Lett.* **1990**, *31*, 2541-2544.

"A New Stereoselective Synthesis of (Z)-Vinylsilane Allylic Alcohols." Kim, K. D.; Magriotis, P. A. *Tetrahedron Lett.* **1990**, *31*, 6137-6140.

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[2] Galletti, P.; Giacomini, D. *Current Medicinal Chem.* **2011**, *18*, 4265-4283.
[3] Rothstein, J. D. et al. *Nature* **2005**, *433*, 73-77.
[4] (a) Lectka, T. et al. *J. Am. Chem. Soc.* **2000**, *122*, 7831-7832. (b) Magriotis, P. A. *Eur. J. Org. Chem.* **2014**, 2647-2657.
[5] Magriotis, P. A. *Angew. Chem. Int. Ed.* **2001**, *40*, 4377-4379.
[6] (a) Alam, M. et al. *Eur. J. Med. Chem.* **2015**, *102*, 487-529. (b) Ye, Z.; Gettys, K. E.; Dai, M. *Beilstein J. Org. Chem.* **2016**, *12*, 702-715.
[7] Vitaku, E.; Smith, D. T.; Njardarson, *J. Med. Chem.* **2014**, *57*, 10257-
[8] Nelson, A. et al. *Org. Biomol. Chem.* **2014**, *12*, 2584-2591.
[9] (a) Gettys, K. E.; Ye, Z.; Dai, M. *Synthesis* **2017**, *49*, 2589-2604. (b) Vo, C.-V. T; Luescher, M. U.; Bode, J. W. *Nat. Chem.* **2014**, *6*, 310-314.
[10] Nathans, R.; Cao, H.; Sharova, N.; Ali, A.; Sharkey, M.; Stranska, R.; Stevenson, M.; Rana, T. M. *Nature. Biotechnology* **2008**, *26*, 1187-1192.

"A Highly Selective Synthesis of Versatile (E)-1-Phenylthio Vinylstannanes." Magriotis, P. A.; Brown, J. T.; Scott, M. E. *Tetrahedron Lett.* **1991**, *32,* 5047-5050.

"A Novel Approach to the Synthesis of Enediynes." Magriotis, P. A.; Scott, M. E.; Kim, K. D. *Tetrahedron Lett.* **1991**, *32,* 6085-6088.

"Synthesis of Phenylthioacetylene." Magriotis, P. A.; Brown, J. T. *Org. Synth*. **1993**, *72,* 252-264.

"Novel Generation of Alkynyl Ketenes: Efficient Synthesis of β,γ-Alkynyl Lactones." Magriotis, P. A.; Scott, M. E.; Vourloumis, D.; Tarli, A. *Tetrahedron Lett.* **1993**, *34,* 2071-2074.

"Ireland-Claisen Rearrangement of Enediyne Lactones: Tandem Claisen-Bergman Strategy for Tetrahydronaphthalene Synthesis." *Magriotis, P. A.; Kim, K. D. J. Am. Chem. Soc.* **1993**, *115,* 2972-2973.

"t-Butoxyacetylene." Magriotis, P. A. In *Encyclopedia of Reagents for Organic Synthesis;* Paquette, L. A. Ed.; John Wiley & Sons: Chichester, **1995***; Vol 2,* 826-827.

"Methylthioacetylene." Magriotis, P. A. In *Encyclopedia of Reagents for Organic Synthesis;* Paquette, L. A. Ed.; John Wiley & Sons: Chichester, **1995***; Vol 5,* 3586-3587.

"Phenylthioacetylene." Magriotis, P. A. In *Encyclopedia of Reagents for Organic Synthesis;* Paquette, L. A. Ed.; John Wiley & Sons: Chichester, **1995***; Vol 6,* 4067-4068.

"Direct Catalytic Enantioselective Reduction of Achiral α,β-Ynones. Strong Remote Steric Effects Across the C-C Triple Bond." Helal, C. J.; Magriotis, P. A.; Corey, E. J. *J. Am. Chem. Soc.* **1996**, *118,* 10938-10939.

SIGNIFICANT RESEARCH ACHIEVEMENTS AFTER THE TURN OF CENTURY

Publications

"Recent Progress in the Enantioselective Synthesis of β-Lactams: Development of the first Catalytic Approaches" Magriotis, P. A. *Angew. Chem., Int. Ed. Engl.* **2001**, *40,* 4377-4379.

"Neues uber die enantioselektive Synthese von β-Lactamen: Entwicklung der ersten Katalytischen Ansatze" Magriotis, P. A. *Angew. Chem.* **2001**, *113,* 4507-4509.

"The Discovery of Sulfonylated Dipeptides as Potent VLA-4 Antagonists" Hagmann, W. K.; Durette, P. L.; Lanza, T.; Kevin, N. J.; de Laszlo, S. E.; Kopka, I. E.; Young, D.; **Magriotis, P. A.**; Li, B.; Lin, L. S.; Yang, G.; Kamenecka, T.; Chang, L. L.; Wilson, J.; MacCoss, M.; Mills, S. G.; Van Riper, G.; McCauley, E.; Egger, L. A.; Kidambi, U.; Lyons, K.; Vincent, S.; Stearns, R.; Colletti, A.; Teffera, J.; Tong, S.; Fenyk-Melody, J.; Owens, K.; Levorse, D.; Kim, P.; Schmidt, J. A.; Mumford, R. A. *Bioorg. Med. Chem. Lett.* **2001**, *11,* 2709-2713.

"N-Tetrahydrofuroyl-(L)-Phenylalanine Derivatives As Potent VLA-4 Antagonists" Yang, G. X.; Chang, L. L.; Truong, Q.; Doherty, G. A.; **Magriotis, P. A**.; de Laszlo, S. E.; Li, B.; MacCoss, M.;Kidambi, U.; Egger, L. A.; McCauley, E.; Van Riper, G.; Mumford, R. A.; Schmidt, J. A.; Hagmann, W. K. *Bioorg. Med. Chem. Lett.* **2002**, *12,* 1497-1500.

"Substituted N-(3,5-Dichlorobezenesulfonyl)-L-Prolyl-Phenylalanine Analogues as Potent VLA-4 Antagonists" Kopka, I. E.; Young, D.; Lin, L.; Mumford, R. A.; **Magriotis, P. A.**; MacCoss, M.; Mills, S. G.; Van Riper, G.; McCauley, E.; Egger, L.; Kidambi, U.; Schmidt, J. A.; Lyons, K.; Stearns, R.; Vincent, S.; Colletti, A.; Wang, Z.; Tong, S.; Wang, J.; Zheng, S.; Owens, K.; Levorse, D.; Hagmann, W.

K. *Bioorg. Med. Chem. Lett.* **2002**, *12*, 637-640.

"Substituted 3-Amino Biaryl Propionic Acids as Potent VLA-4 Antagonists" Kopka, I. E.; Lin, L. S.;Mumford, R. A.; Lanza, T.; **Magriotis, P. A.**; Young, D.; deLaszlo, S. E.; MacCoss, M.; Mills, S. G.; Van Riper, G.; McCauley, E.;Lyons, K.; Vincent, S.; Egger, L. A.; Stearns, R.; Colletti, A.; Tong, S.; Owens, K.; Levorse, D.; Schmidt, J. A.; Hagmann, W. K. *Bioorg. Med. Chem. Lett.* **2002**, *12*, 2415-2418.

"The Discovery of Acylated β-Amino Acids as Potent and Orally Bioavailable VLA-4 Antagonists" Lin, L. S.; Kopka, I. E.; Mumford, R. A.; **Magriotis, P. A.**; Lanza, T.; Durette, P. L.; Kamenecka, T.; Young, D. N.; deLaszlo, S. E.; McCauley, E.; Van Riper, G.; Kidambi, U.; Egger, L. A.; Tong, X.; Lyons, K.; Vincent, S.; Stearns, R.; Colletti, A.; Teffera, J.; Fenyk-Melody, J.; Schmidt, J. A.; MacCoss, M.; Hagmann, W. K. *Bioorg. Med. Chem. Lett.* **2002**, *12*, 611-614.

"Novel Applications of the Schöllkopf Chiral Auxiliary: A New and Efficient Enantioselective Synthesis of β-Lactams Possessing a C-4 Quaternary Stereocenter" Vassiliou, S.; Dimitropoulos, C.; Magriotis, P. A. *Synlett* **2003**, 2398-2400.

"A New Method for the Functionalization of [60] Fullerene: An Unusual 1,3-Dipolar Cycloaddition Leadind to a C_{60} Housane Derivative" Zhou, Z.; Magriotis, P. A. *Org. Lett.* **2005**, *7*, 5849-5851.

"Improved Schöllkopf Construction of Quaternary α-Amino Acids: Efficient Enantioselective Synthesis of Integrin LFA-1 Antagonist BIRT-377" Vassiliou, S.; Magriotis, P. A. *Tetrahedron: Asymmetry* **2006**, *17*, 1754-1757.

"Efficient Enantioselective Synthesis of Orthogonally Protected (R)-α-Alkylserines Compatible with the Solid Phase Peptide Synthesis" *Tetrahedron Letters* **2006**, *47*, 7339-7341.

"Synthesis of the Metabotropic Receptor Ligand (2S)-α-(Hydroxyymethyl)- glutamic acid and its Fmoc Protected Derivatives" Yiotakis A.; **Magriotis, P. A.**; Vassiliou, S. *Tetrahedron: Asymmetry* **2007**, *18*, 873-877.

"Importance of Mechanistic Drug Metabolism Studies in Support of Drug Discovery: A Case Study with a N-Sulfonylated dipeptide VLA-4 Antagonist in Rats" Tang, W.; Stearns, R. A.; Chen, Q.; Bleasby, K.; Teffera, Y.; Colletti, A.; Hafey, M.; Evers, R.; Dean, D. C.; **Magriotis**, **P. A**.; Lanza, T.J.; Lin, L.S.; Hagmann, W.K.; Baillie, T.A. *Xenobiotica* **2008**, *38*, 223-237.

"Progress in Asymmetric Organocatalytic Synthesis of β-Lactams" Magriotis P. A. *Eur. J. Org. Chem.* **2014**, 2647-2657.

"Synthetic Approaches to the Stereochemically Complex Antitumor Drug Ecteinascidin-743: A Marine Natural Product by the Name Yondelis® or Trabectidin" Magriotis, P. A.; in Stereochemistry and Global Connectivity: The Legacy of Ernest L. Eliel.; Cheng et al. Ed.; *Volume 2*; Chapter 5, pp. 61-78. ACS Symposium Series, American Chemical Society: Washington, DC, **2017**.

Invited Talks

"Studies toward the Synthetic Application of the Bergman and Myers Reactions" Department of Chemistry, New York University (Colloquium, Invited lecture); February 2002.

"Novel Applications of the Schöllkopf Chiral Auxiliary: A New and Efficient Enantioselective Synthesis of β-Lactams Possessing a C-4 Quaternary Stereocenter" Dimitropoulos, C.; Vassiliou, S.; Magriotis, P. A. American Chemical Society, 226th National Meeting (Oral Presentation), New York, NY, September 2003.

"Asymmetric Synthesis of α-Amino Acids and β-Lactams: From Auxiliary-Driven to Catalytic

Enantioselective Methodology" Department of Chemistry, State University of New York at Stony Brook (Invited Lecture), July 2005.

"Synthesis of Small Molecules as Integrin Antagonists. Asymmetric Synthesis of α-Amino Acids and β-Lactams: From Auxiliary-Driven to Catalytic Enantioselective Methodology."Center for Neurologic Diseases, Harvard Medical School and Brigham and Women's Hospital; (Ivited Seminar), Boston, MA, August 2005.

"Synthesis of Small Molecules as Integrin Antagonists. Asymmetric Synthesis of α-Amino Acids and β-Lactams." Institute of Physical Chemistry (Chemical Biology), NCSR <<DEMOCRITOS>> (Invited Seminar), Athens, Greece, September 2006.

"S-Oxide Activated Mannich Reactions in Medicinal Chemistry: Enantioselective Synthesis of Substituted
β-Lactams." Psarra, V.; Magriotis, P. A. 3rd Hellenic Symposium on Organic Synthesis. From Chemistry to Biology, Medicine and Materials Science (Invited Short Lecture), University of Athens, Athens, Greece, October 2009.

"Studies toward the Total Synthesis of Ecteinascidin-743: New SyntheticTechnology in Medicinal Chemistry." Magriotis, P. A.; Invited Lecture, Department of Pharmacy, University of Bari, Italy, December 2009.

"Studies Toward the Total Synthesis of Ecteinascidin-743: New Synthetic Technologies in Medicinal Chemistry." Psarra, V.; Magriotis, P. A. 11th Conference on Medicinal Chemistry: Drug Discovery and Design (Invited Short Lecture), University of Patras; Rio, Patras, Greece, April 2010.

"Studies Toward a Novel Total Synthesis of Ecteinascidin-743: New Synthetic Technologies in Medicinal Chemistry." Magriotis, P. A. Francis Johnson Symposium (Invited Lecture) Department of Pharmacological Sciences, SUNY at Stony Brook; Stony Brook, New York, USA, October 2010.

"Studies toward the Total Synthesis of the Anticancer Drug and Marine Natural Product Yondelis" Magriotis, P. A. (Invited Lecture) , 2nd Conference of Pharmaceutical Sciences, University of Patras, Rio, Greece, October 2014.

"Drug Development from Marine Natural Products: The Case of the Anticancer Drug Yondelis" Magriotis, P. A. (Invited Lecture) 1st Conference of Applied Pharmacy, Met Hotel, Thessaloniki, Greece, April 2015.

"Design and Development of Novel methodology for the Synthesis of Substituted Piperazines Inspired by the Mechanism of Action of the Antitumor Drug and Marine Natural Product Yondelis" Magriotis, P. A. (invited Lectuire) , 3rd Conference of Pharmaceutical Sciences, Aristotle University of Thessaloniki, Thessaloniki, Greece, February, 2017.

Organisation (member) of international conferences:
International Conference on Stereochemistry *(Sao Paulo, Brazil, August 18-19, 2016).*
European Chemistry Conference *(Rome, Italy, June 11-13, 2018).* *http://chemistry-conference.com/scientific-committee.html*

Patents
Co-inventor on the following U.S. patent application: "Preparation of Substituted β-Alanine Derivatives as Cell Adhesion Inhibitors." Durette, P. L.;Hagmann, W. K.; Kopka, I. E.; MacCoss, M.; Mills, S. G.;Mumford, R. A.; **Magriotis, P. A.** (PCT Application WO 99 26,921) *Chem. Abstr.* **1999**, *131*, 5529n.

ACADEMIC AND PROFESSIONAL HONORS-AWARDS (RESEARCH GRANTS)

Peer Reviewer Status in several Scientific Journals (Tetrahedron Letters, Journal of Organic Chemistry, Journal of the American Chemical Society, Organic Letters, Synthesis Letters, Angewandte Chemie International Edition, Tetrahedron: Asymmetry, European Journal of Organic Chemistry, Medicinal Chemistry Letters)
Member of the Editorial Board of the Journal Chemical Biology and Pharmaceutical Chemistry. http://www.imedpub.com/journal-chemical-biology-pharmaceutical-chemistry/.

Member of the Editorial Board of the Journal of Medicinal Chemistry and Drug Design
https://sciforschenonline.org/journals/medicinal-chemistry-drug-design/editorial-board.php

Member of the Editorial Board of Drug Designing & Intellectual Properties International Journal
http://lupinepublishers.us/ddipij/editorial-committee.php

Award for Excellence in Teaching, 1982, SUNY at Stony Brook, Department of Chemistry.

Merck Fellowship, 8/9/95-9/9/96, Visiting Professorship, Harvard University, Department of Chemistry and Chemical Biology (Mentor: Professor Elias J. Corey)

ACS-PRF #20811-G1, "Asymmetric Synthesis via Binaphthyl Derived Organometallic Reagents." 9/1/88-8/31/90, $18,000.

NSF #CHE-8913626, "Purchase of a Gas Chromatography/Mass Spectrometer System." 9/1/89-8/31/90, $40,819.

American Cancer Society #IN-181, "Studies on the Synthesis of the Power-ful Cell Growth Inhibitor Cephalostatin I." 8/1/89-7/31/91, $7,500.

NSF #CHE-901242, "Group Travel for U.S. Participants in 8th International IUPAC Conference on Organic Synthesis; Helsinki, Finland, July 23-27, 1990."; $1,500.

American Cancer Society #CH-496, "A Unified Strategy for the Synthesis of Enediyne Antitumor Antibiotics." 7/1/90-6/30/92, $160,000.

NSF #CHE-9120098, "Purchase of an Automated Single-Crystal X-Ray Diffractometer." 12/1/91-5/31/93, $108,000.

SmithKline Beecham Pharmaceuticals, "The Enediyne Route to the Synthesis of Taxol and Related Compounds." 6/1/92, $2,000.

Stavros Niarchos Foundation. "Purchase of Chiral HPLC Instrumentation" October 2017. € 40.000.