Peter Šilhár, Ph.D.

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Born in Bratislava, Slovak Republic, 1980.
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Summary
Synthetic chemist with an extensive experience in medicinal chemistry and biochemistry. Expertise in advanced organic synthesis, solid-phase synthesis, modern isolation and separation techniques, analytical and spectroscopic methods as well as enzymatic assays, drug design and high-throughput screening. Highly flexible team player with strong written and communication skills seeking to apply his abilities in a goal oriented, progressive and collaborative environment.

Work Experience

API Engineer at Saneca, a.s., Hlohovec, Slovakia (Oct 2016 - Oct 2018)
- Production of validation batches of several APIs (active pharmaceutical intermediates)
- Research and development / optimization in synthesis of active pharmaceutical intermediates

Research scientist at Contipro, a.s., Dolní Dobrouč 56102, Czech Republic (Feb 2016 - Sep 2016)
- Research and development in field of hyaluronic acid and hydrogels
- Preparation of chemically modified hyaluronic acid and its use in hydrogels

Senior Chemist at Moravek Biochemicals, Inc., Brea, California, USA (Dec 2012 – Oct 2015)
- Custom synthesis of radioactively labeled compounds (^{14}C and ^{3}H) as well as custom synthesis with stable isotopes (^{2}H, ^{13}C, ^{15}N)
- Successfully and efficiently performed and finished numerous projects in which the expertise in advanced organic synthesis was certified
- Worked in multi-projects mode with extremely valued ^{14}C and ^{3}H precursors

Research Experience and Education

Postdoctoral Fellow at The Scripps Research Institute, La Jolla, CA, USA (June 2009 – Dec 2012)
Project: Small molecule inhibitors of Botulinum Neurotoxin Proteases
Advisor: Prof. Kim D. Janda
- Designed, synthesized and evaluated numerous small molecule inhibitors of Botulinum Neurotoxin A Protease (BoNT/A)
- Performed SAR of these inhibitors and identified one of the best small molecule antagonist of BoNT/A protease to date
- Conducted enzymatic high-throughput screenings of small libraries against BoNT/A protease

Postdoctoral Fellow at University of Bern, Department of Chemistry and Biochemistry, Bern, Switzerland (April 2007 – May 2009)
Project: Antisense Therapeutics: Nucleic-Acid Analogs with Restricted Conformational Flexibility in the Sugar-Phosphate Backbone.
Advisor: Prof. Christian J. Leumann
- Synthesized novel type of 'bicyclo-nucleosides', incorporated them into oligonucleotides and measured thermal stability data with complementary DNA and RNA
- Introduced and examined an unique modified 'bicyclo-T' nucleoside into oligonucleotides capable of post-synthetic transformation/functionalization
- Supervised and co-developed shorter and more efficient synthesis of 'bicyclo-nucleosides' *via* Rh-catalyzed hydroacylation

Ph.D. in Organic Chemistry at Institute of Chemical Technology in Prague, Czech Republic,
Department of Organic chemistry (2003 – 2007)
Thesis Title: Synthesis and Transformations of Hydroxymethylated Purines, elaborated at Institute of Organic Chemistry and Biochemistry, Academy of Sciences of the Czech Republic.
Thesis Advisor: Prof. Michal Hocek, Ph.D.

- Developed synthetic methodology for introduction of functionalized carbon substituents to purine bases and nucleosides *via* Pd-catalyzed cross-coupling reactions
- Synthesized numerous novel modified nucleosides for testing of biological activity (screened for anticancer, anti-HCV activity)

M.Sc. in Organic Chemistry at Slovak University of Technology in Bratislava, Slovak Republic,
Department of Organic Chemistry (1998 – 2003)
Thesis Title: Synthesis of 2-Aryl-3-methylidenetetrahydrofuranes and their Utilization in 1,3-Dipolar Cycloadditions.
Thesis Advisor: Dr. Eva Jedlovská

- Studied and explored 1,3-dipolar cycloadditions with a novel dipolarophile
- Synthesized several 2-aryl-3-methylidene-tetrahydrofuranes and utilized them in a synthesis of various novel spiro heterocyclic isoxazolines

Experimental techniques
Organic synthesis - multistep organic synthesis, oligonucleotide synthesis and chemistry, organometallic chemistry, cross-coupling reactions, solid support chemistry, combinatorial chemistry, synthesis of radiolabeled molecules (^{3}H and ^{14}C)
Analysis in organic chemistry - NMR, 2D-NMR, MS, HPLC, LC-MS, LC-MS/MS, GC-MS, UV-VIS spectroscopy, optical rotation, flash chromatography, analytical and preparative TLC
Protein biochemistry - enzymatic assays and kinetics (with or without inhibitors)

Languages:
Slovak (native); English (excellent)

Mentoring experience:
2008 – 2009 University of Bern - mentoring and supervising undergraduate student Arben Haziri

Awards
June 2003 – award of Duslo, a.s. for the best diploma thesis at Department of Organic Chemistry, Slovak University of Technology in Bratislava.

List of Publications:

24. Xue, S., Seki, H., Remes, M., Silhar, P., Janda, K., "Examination of alpa-exosite inhibitors against Botulinum neurotoxin A protease through structure-activity relationship studies of chicory acid" *Bioorg. Med. Chem. Lett.* **2017,** 27, 4956.
23. Seki, H., Xue, S., Pellett, S., Šilhár, P., Johnson, E.A., Janda, K.D., "Cellular protection of SNAP-25 against Botulinum Neurotoxin/A: Inhibition of thioredoxin reductase through a suicide substrate mechanism" *J. Am. Chem. Soc.* **2016**, 138, 5568.
22. Seki, H.; Pellett, S.; Šilhár, P.; Stowe, G. N.; Blanco, B.; Lardy, M. A.; Johnson, E. A.; Janda, K. D. "Synthesis/biological evaluation of hydroxamic acids and their prodrugs as inhibitors for Botulinum neurotoxin A light chain" *Bioorg. Med. Chem.* **2014**, 22(3), 1208-1217.
21. Šilhár, P.; Lardy, M. A.; Hixon, M. S.; Shoemaker, C. B.; Barbieri, J. T.; Struss, A. K.; Lively, J. M.; Javor, S.; Janda, K. D. "The C-terminus of Botulinum A Protease Has Profound and Unanticipated Kinetic Consequences Upon the Catalytic Cleft" *ACS Med. Chem. Lett.* **2013**, 4(2), 283–287.
20. Šilhár, P.; Silvaggi, N. R.; Pellett, S.; Čapkova, K.; Johnson, E. A.; Allen, K. N.; Janda, K. D. "Evaluation of adamantane hydroxamates as botulinum neurotoxin inhibitors: synthesis, crystallography, modeling, kinetic and cellular based studies" *Bioorg. Med. Chem.* **2013**, 21(5), 1344-1348.
19. Šilhár, P.; Eubanks, L. M.; Seki, H.; Pellett, S.; Javor, S.; Tepp, W. H.; Johnson, E. A.; Janda, K. D. "Targeting botulinum A cellular toxicity: a prodrug approach" *J. Med. Chem.* **2013**, 56(20), 7870-7879.

18. Šilhár, P.; Alakurtti, S.; Capkova, K.; Feng, X. C.; Shoemaker, C. B.; Yli-Kauhaluoma, J.; Janda, K. D. "Synthesis and evaluation of library of betulin derivatives against the botulinum neurotoxin A protease" *Bioorg. Med. Chem. Lett.* **2011**, *21*, 2229-2231.
17. Šilhár, P.; Leumann, C. J. "Parallel synthesis and nucleic acid binding properties of C(6 ')-alpha-functionalized bicyclo-DNA" *Bioorg. Med. Chem.* **2010**, *18*, 7786-7793.
16. Eubanks, L. M.; Šilhár, P.; Salzameda, N. T.; Zakhari, J. S.; Feng, X. C.; Barbieri, J. T.; Shoemaker, C. B.; Hixon, M. S.; Janda, K. D. "Identification of a Natural Product Antagonist against the Botulinum Neurotoxin Light Chain Protease" *ACS Med. Chem. Lett.* **2010**, *1*, 268–272.
15. Šilhár, P.; Capkova, K.; Salzameda, N. T.; Barbieri, J. T.; Hixon, M. S.; Janda, K. D. "Botulinum Neurotoxin A Protease: Discovery of Natural Product Exosite Inhibitors" *J. Am. Chem. Soc.* **2010**, *132*, 2868–2869.
14. Haziri, A. I.; Šilhár, P.; Renneberg, D.; Leumann, C. J. "Synthesis of the Sugar Building Block of Bicyclo-RNA" *Synthesis* **2010**, *5*, 823-827.
13. Stowe, G. N.; Šilhár, P.; Hixon, M. S.; Silvaggi, N. R.; Allen, K. N.; Moe, S. T.; Jacobson, A. R.; Barbieri, J. T.; Janda, K. D.: ,"Chirality Holds the Key for Potent Inhibition of the Botulinum Neurotoxin Serotype A Protease" *Org. Lett.* **2010**, *12*, 756–759.
12. Luisier, S.; Šilhár, P.; Leumann, C. J.: "Highly β-selective, N-iodosuccinimide-mediated nucleosidation to bicyclo- and tricyclo-nucleosides" *Nucleic Acids Symp. Ser.* **2008**, *52*, 581-582.
11. Šilhár, P.; Hocek, M.; Pohl, R.; Votruba, I.; Shih, I.; Mabery, E.; Mackman, R.: "Synthesis, cytostatic and anti-HCV activity of 6-(*N*-substituted aminomethyl)-, 6-(*O*-substituted hydroxymethyl)- and 6-(*S*-substituted sulfanylmethyl)purine nucleosides" *Bioorg. Med. Chem.* **2008**, *16*, 2329-2366.
10. Hasník, Z.; Šilhár, P.; Hocek, M.: "Hydroxymethylations of Aryl Halides by Pd-Catalyzed Cross-Couplings with (Benzoyloxy)methylzinc Iodide – Scope and Limitations of the Reaction" *Synlett* **2008**, 543–546.
9. Hasník, Z.; Šilhár, P.; Hocek, M.: "Synthesis of (purin-6-yl)acetates and 6-(2-hydroxyethyl)purines via cross-couplings of 6-chloropurines with the Reformatsky reagent" *Tetrahedron Lett.* **2007**, *48*, 5589–5592.
8. Hocek, M.; Šilhár, P.: "Palladium-Catalyzed Cross-Coupling Reactions in C6 Modifications of Purine Nucleosides" *Curr. Protocols Nucleic Acid Chem.* (J. Wiley & Sons., Inc.) **2007**, 1.16.
7. Hocek, M.; Šilhár, P.; Pohl, R.: "Cytostatic and activiral 6-arylpurine ribonucleosides VIII. Synthesis and evaluation of 6-substituted purine 3'-deoxyribonucleotides" *Collect. Czech. Chem. Commun.* **2006**, *71*, 1484-1496.
6. Hocek, M.; Šilhár, P.; Shih, I.; Mabery, E.; Mackman, R.: "Cytostatic and antiviral 6-arylpurine ribonucleosides. Part 7: Synthesis and evaluation of 6-substituted purine L-ribonucleosides" *Bioorg. Med. Chem. Lett.* **2006**, *16*, 5290–5293.
5. Šilhár, P.; Pohl, R.; Votruba, I.; Klepetářová, B.; Hocek, M.: "Synthesis of 6-Amino-, 6-Methyl- and 6-Aryl- 2-(Hydroxymethyl)purine Bases and Nucleosides" *Collect. Czech. Chem. Commun.* **2006**, *71*, 788-803.
4. Šilhár, P.; Pohl, R.; Votruba, I.; Hocek, M.: "Synthesis and Cytostatic Activity of Novel 6-(Difluoromethyl)purine Bases and Nucleosides" *Synthesis* **2006**, 1848-1852.
3. Šilhár, P.; Pohl, R.; Votruba, I.; Hocek, M.: "Synthesis of 2-Substituted 6-(Hydroxymethyl)Purine Bases and Nucleosides" *Collect. Czech. Chem. Commun.* **2005**, *70*, 1669-1695.
2. Šilhár, P.; Pohl, R.; Votruba, I.; Hocek, M.: "The First Synthesis and Cytostatic Activity of Novel 6-(Fluoromethyl)purine Bases and Nucleosides" *Org. Biomol. Chem.* **2005**, *3*, 3001-3007.
1. Šilhár, P.; Pohl, R.; Votruba, I.; Hocek, M.: "Facile and Efficient Synthesis of 6-(Hydroxymethyl)purines" *Org. Lett.* **2004**, *6*, 3225-3228.

Oral Conference Contributions:

2. Šilhár, P.; Hocek, M.; Chemistry of Nucleic Acid Components, 13th Symposium, Špindlerův Mlýn, Czech Republic, September 3-9, 2005.
1. Šilhár, P.; Hocek, M.; 36th Symposium on Catalysis, Prague, Czech Republic, November 8-9, 2004,

Poster Presentations:

7. Šilhár, P.; Hocek, M.; XVII International Roundtable on Nucleosides, Nucleotides and Nucleic Acids, Bern, Switzerland, September 3-7, 2006.
6. Šilhár, P.; Hocek, M.; Summer School "Medicinal Chemistry", Shanghai, China, September 25-28, 2005.
5. Šilhár, P.; Hocek, M.; 2nd Nucleic Acid Chemical Biology PhD Summer School and Symposium, Odense, Denmark, June 19-23, 2005.
4. Šilhár, P.; Hocek, M.; 2nd Summer School "Medicinal Chemistry", University of Regensburg, Regensburg, Germany, October 5-7, 2004.
3. Hocek, M.; Čapek, P.; Šilhár, P.; IUPAC Fifteenth International Conference on Organic Synthesis, Nagoya, Japan, August 1-6, 2004.
2. Jedlovská, E.; P. Šilhár, E.Solčániová; 56th Symposium of Chemical Society, Ostrava, Czech Republic, September 6-9, 2004.
1. Jedlovská, E.; P. Šilhár, E. Solčániová; 10th Blue Danube Symposium on Heterocyclic Chemistry, Vienna, Austria, September 3-6, 2003.