

**BIOGRAPHICAL SKETCH**

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NAME Harold Kohn	POSITION TITLE Kenan Professor of Medicinal Chemistry and Natural Products		
eRA COMMONS USER NAME hal_kohn			
EDUCATION/TRAINING (Begin with baccalaureate or other initial professional education, such as nursing, and include postdoctoral training.)			
INSTITUTION AND LOCATION	DEGREE (if applicable)	YEAR(s)	FIELD OF STUDY
University of Michigan, Ann Arbor	B.S.	1966	Chemistry
Penn State University, University Park	Ph.D.	1971	Chemistry
Columbia University, New York	Post Doc.	1971-1973	Chemistry

**A. Positions and Honors. Professional Experience** 1966-1969: Research Assistant with Dr. R.E. Counsell, Professor of Pharmacy and Internal Medicine, The University of Michigan, Ann Arbor, Michigan; 1967-1971: Research Fellow with Dr. R. A. Olofson, Professor of Chemistry, The Pennsylvania State University, University Park, PA; 1971-1973: Research Associate with Dr. R. C. D. Breslow, Mitchill Professor of Chemistry and University Professor, Columbia University, New York, NY; 1973-1978: Assistant Professor; 1978-1983: Associate Professor, Dept. of Chemistry, University of Houston, Houston, TX; 1981: Visiting Research Scientist with Dr. S. J. Benkovic, Eberly and Pugh Professor of Chemistry, The Pennsylvania State University, University Park, PA; 1983-1995: Professor, Dept. of Chemistry, University of Houston, Houston, TX; 1995-1999: M.D. Anderson Professor of Chemistry, Dept. of Chemistry, University of Houston, Houston, TX; 1993-1999: Professor of Biochemical and Biophysical Sciences, Department of Biochemical and Biophysical Sciences, University of Houston, Houston, TX; 1999-2005: Kenan Professor and Chair, Division of Medicinal Chemistry and Natural Products, School of Pharmacy, University of North Carolina, Chapel Hill, NC; 1999-present: Kenan Professor, Division of Medicinal Chemistry and Natural Products, School of Pharmacy, University of North Carolina, Chapel Hill, NC; Member, Lineberger Cancer Center – University of North Carolina. **Honors and Awards** 1966-1969: NSF Traineeship; 1969-1970: NIH Predoctoral Fellowship; 1971-1973: NIH Postdoctoral Fellowship; 1977-1981: Alfred P. Sloan Research Fellowship; 1977-1982: Dreyfus Teacher-Scholar Award; 1993: University of Houston Research Excellence Award.

**B. Peer-reviewed Publications** (selected references from >150 peer-reviewed publications)

- Abuzar, S. & Kohn, H. (1988). Observations on the Activation of Bicyclomycin. *J. Am. Chem. Soc.* 110, 4089-4090.
- Zwiefka, A., Kohn, H. & Widger, W.R. (1993). Transcription Termination Factor Rho: The Site of Bicyclomycin Inhibition in *Escherichia coli*. *Biochemistry* 32, 3564-3570.
- Zhang, Z. & Kohn, H. (1994). Chemical, Biochemical, and Biological Studies of Select C(1) Triol Modified Bicyclomycins. *J. Am. Chem. Soc.* 116, 9815-9826.
- Li, V.-S., Choi, D., Tang, M.-s. & Kohn, H. (1996). Concerning *In Vitro* Mitomycin–DNA Alkylation. *J. Am. Chem. Soc.* 118, 3765-3766.
- Choi, D., Stables, J.P. & Kohn, H. (1996). Synthesis and Anticonvulsant Activities of N -Benzyl 2-Acetamido-propionamide Derivatives. *J. Med. Chem.* 39, 1907-1916.
- Magyar, A., Zhang, X., Kohn, H. & Widger, W.R. (1996). The Antibiotic Bicyclomycin Affects the Secondary RNA Binding Site of *Escherichia coli* Transcription Termination Factor Rho. *J. Biol. Chem.* 271, 25369-25374.
- Park, H.-g., Zhang, X., Widger, W.R. & Kohn, H. (1996). The Role of the C(1) Triol Group in Bicyclomycin: Synthesis and Biochemical and Biological Properties. *J. Org. Chem.* 61, 7750-7755.
- Santillán, Jr., A., Park, H.-g., Zhang, X., Lee, O.-S., Widger, W.R. & Kohn, H. (1996). The Role of the [4.2.2] Bicyclic Unit in Bicyclomycin: Synthesis, Structure, Chemical, Biochemical, and Biological Properties. *J. Org. Chem.* 61, 7756-7763.
- Park, H.-g., Zhang, Z., Zhang, X., Widger, W.R. & Kohn, H. (1996). The Role of the C(5)-C(5a) Exomethylene Group in Bicyclomycin: Synthesis, Structure, and Biochemical and Biological Properties. *J.*

- Org. Chem. 61, 7764-7776.
- Cho, H., Park, H.-g., Zhang, X., Riba, I., Gaskell, S.J., Widger, W.R. & Kohn, H. (1997). Design, Syntheses, and Evaluations of Bicyclomycin-Based Rho Inactivators. J. Org. Chem. 62, 5432-5440.
  - Santillán, Jr., A., Zhang, X., Widger, W.R. & Kohn, H. (1998). 5a-Methyl-Substituted Bicyclomycins: Synthesis and Chemical, Biochemical, and Biological Properties. J. Org. Chem. 63, 1290-1298.
  - Santillán, Jr., A., Zhang, X., Hardesty, J., Widger, W.R. & Kohn, H. (1998). Role of the C(6)-Hydroxy Group in Bicyclomycin: Synthesis, Structure, and Chemical, Biochemical, and Biological Properties. J. Med. Chem. 41, 1185-1194.
  - Riba, I., Gaskell, S.J., Cho, H., Widger, W.R. & Kohn, H. (1998). Evidence for the Location of Bicyclomycin Binding to the *Escherichia coli* Transcription Termination Factor Rho. J. Biol. Chem. 273, 34033-34041.
  - Magyar, A., Zhang, X., Abdi, F., Kohn, H. & Widger, W.R. (1999). Identifying the Bicyclomycin Binding Domain through Biochemical Analysis of Antibiotic-Resistant Rho Proteins. J. Biol. Chem. 274, 7316-7324.
  - Wang, S. & Kohn, H. (1999). Studies on the Mode of Action of BMS-181174 and KW-2149: The Reactivity of 7-N-(Mercaptoethyl)mitomycin C. J. Med. Chem. 42, 788-790.
  - Vincent, F., Widger, W.R., Openshaw, M., Gaskell, S.J. & Kohn, H. (2000). 5a-Formylbicyclomycin: Studies on the Bicyclomycin-Rho Interaction. Biochemistry 31, 9067-9076.
  - Vincent, F., Openshaw, M., Trautwein, M., Gaskell, S.J., Kohn, H., & Widger, W.R. (2000). Rho Transcription Factor: Symmetry and Binding of Bicyclomycin. Biochemistry 31, 9077-9083.
  - Vincent, F., Srinivasan, J., Santillán, Jr., A., Widger, W.R. & Kohn, H. (2001). C(5)-C(5a)-Modified Bicyclomycins: Synthesis, Structure, and Biochemical and Biological Properties. J. Org. Chem. 66, 2251-2264.
  - Andurkar, S. V., Béguin, C., Stables, J.P. & Kohn, H. (2001). Synthesis and Structural Studies of Aza-analogues of Functionalized Amino Acids: New Anticonvulsant Agents. J. Med. Chem. 44, 1475-1478.
  - Na, Y., Li, V.-S., Nakanishi, Y., Bastow, K.F. & Kohn, H. (2001). Synthesis, DNA Cross-linking Activity, and Cytotoxicity of Dimeric Mitomycins. J. Med. Chem. 44, 3453-3462.
  - LeTiran, A., Stables, J.P. & Kohn, H. (2001). Functionalized Amino Acid Anticonvulsants: Synthesis and Pharmacological Evaluation of Conformationally Restricted Analogues. Bioorg. & Med. Chem. 9, 2693-2708.
  - Lee, S.H. & Kohn, H. (2002). Efficient Synthesis of Medium-Sized Cyclic Ether Diamines. J. Org. Chem. 67, 1692-1695.
  - Na, Y., Wang, S. & Kohn, H. (2002). 7-N-(Mercaptoalkyl)mitomycins: Implications of Cyclization for Drug Function. J. Am. Chem. Soc. 124, 4666-4677.
  - Shen, M., LeTiran, A., Xiao, Y., Golbraikh, A., Kohn, H. & Tropsha, A. (2002). QSAR Analysis of Functionalized Amino Acid Anticonvulsant Agents Using k-Nearest Neighbor and Simulated Annealing-PLS Methods. J. Med. Chem. 45, 2811-2823.
  - LeTiran, A., Stables, J.P., & Kohn, H. (2002). Design and Evaluation of Affinity Labels of Functionalized Amino Acid Anticonvulsants. J. Med. Chem. 45, 4762-4773.
  - Xu, Y., Kohn, H. & Widger, W.R. (2002). Mutations in Rho Transcription Termination Factor That Affect RNA Tracking. J. Biol. Chem. 277, 30023-30030.
  - Weber, T.P., Widger, W.R. & Kohn, H. (2002). The Mg<sup>2+</sup> Requirements for Rho Transcription Termination Factor: Catalysis and Bicyclomycin Inhibition. Biochemistry 41, 12377-12383.
  - Weber, T.P., Widger, W.R. & Kohn, H. (2003). Metal Dependency for Transcription Factor Rho Activation. Biochemistry 42, 1652-1659.
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  - Lee, S.H. & Kohn, H. (2003). Phosphine-Assisted Rearrangement of 4,5-Dihydroxy-1,2-Dithianes to 4-Hydroxy-3 Mercaptotetrahydrothiophenes. Heterocycles 60, 47-56.
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  - Kim, M.G., Bodor, E.T., Wang, C., Harden, T.K. & Kohn H. (2003). C(8) Substituted Azabicyclo[3.3.1]non-3-enes and C(8) Substituted 1-Azabicyclo[3.3.1]nonan-4-ones: Novel Muscarinic Receptor Antagonists. J. Med. Chem. 46, 2216-2226.
  - Brogan, A.P., Widger, W.R. & Kohn, H. (2003). Bicyclomycin Fluorescent Probes: Synthesis, Biochemical,

Principal Investigator/Program Director (Last, First, Middle): Kohn, Harold

- Biophysical, and Biological Properties, *J. Org. Chem.* 68, 5575-5587.
- Weber, T.P., Widger, W.R. & Kohn, H. (2003). Metal-1,4-Dithio-2,3-dihydroxybutane Chelates: Novel Inhibitors of the Rho Transcription Termination Factor, *Biochemistry* 42, 9121-9126.
  - Béguin, C., Andurkar, S.V., Jin, A.Y., Stables, J.P., Weaver, D.F. & Kohn, H. (2003). Functionalized Amido Ketones: New Anticonvulsant Agents, *Bioorg. Med. Chem.* 11, 4275-4285.
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  - Vedejs, E., Naidu, B.N., Klapars, A., Warner, D.L., Li, V.-S., Na, Y. & Kohn, H. (2003). Synthetic Enantiopure Aziridinomitosenes; Preparation, Reactivity, and DNA Alkylation Studies, *J. Am. Chem. Soc.*, 125, 15796-15806.
  - Lee, S.H. & Kohn, H. (2004). Cyclic Disulfide C(8) Iminoporfirromycin: Nucleophilic Activation of a Porfirromycin, *J. Am. Chem. Soc.*, 126, 4281-4292.
  - Béguin, C., LeTiran, Arnaud, Stables, J.P. & Kohn, H. (2004). N-Substituted Amino Acid N'-Benzylamides: Synthesis, Anticonvulsant and Metabolic Activities, *Bioorg. Med. Chem.*, 12, 3079-3096.
  - Kim, M.G., Bodor, E.T., Harden, T.K. & Kohn, H. (2004). C(8) Substituted 1-Azabicyclo[3.3.1]non-3-enes: A Novel Scaffold for Muscarinic Receptor Ligands, *Bioorg. Med. Chem.*, 12, 2357-2367.
  - Shen, M., Béguin, C., Golbraikh, A., Stables, J.P., Kohn, H. & Tropsha, A. (2004). Application of Predictive QSAR Models to Database Mining: Rational Discovery of Novel Anticonvulsant Lead Compounds, *J. Med. Chem.*, 47, 2356-2364.
  - LeMagueres, P.; Im, H.; Ebalunode, J.; Strych, U.; Benedik, M.J.; Briggs, J.M.; Kohn, H. & Krause, K.L. (2005). The 1.9 Å Crystal Structure of Alanine Racemase from *Myobacterium tuberculosis* Contains a Conserved Entryway into the Active Site, *Biochemistry*, 44, 1471-1481.
  - Skordalakes, E., Brogan, A.P., Park, B.S., Kohn, H. & Berger, J.M. (2005). Structural Mechanism of Inhibition of the Rho Transcription Termination Factor by the Antibiotic Bicyclomycin, *Structure*, 13, 99-109.
  - Brogan, A.P., Verghese, J., Widger, W.R., & Kohn, H. (2005). Bismuth-dithiol Inhibition of the *Escherichia coli* rho transcription termination factor, *J. Inorg. Biochem.*, 99, 841-845.
  - Brogan, A.P., Widger, W.R., Bensadek, D., Riba-Garcia, I., Gaskell, S.J., & Kohn, H. (2005). Development of a Technique to Determine Bicyclomycin-Rho Binding and Stoichiometry by Isothermal Titration Calorimetry and Mass Spectrometry, *J. Am. Chem. Soc.*, 127, 2741-2751.
  - Lee, S.H. & Kohn, H. (2005). 7-N,7'-N'-(1'',2''-Dithianyl-3'',6''-dimethylenyl)-bismitomycin C: Synthesis and Nucleophilic Activation of a Dimeric Mitomycin, *Organic & Biomol. Chem.*, 3, 471-482.
  - Lee, S.H., Brodnick, R.L., Glish, G.L. & Kohn, H. (2005). 3,8,11,16-Tetrakis(aminomethyl)-1,2,9,10-tetrathia-cyclohexadecane Tetra-trifluoroacetic Acid: Synthetic Precursor to a Novel Thio-Substituted Diamine, *Tetrahedron*, 61, 1749-1754.
  - Jin, A.Y., Kohn, H., Béguin, C., Andurkar, S.V., Stables, J.P., & Weaver, D.F. (2005). A Quantitative Structure-Activity Relationship Study for  $\alpha$ -Substituted Acetamido-N-Benzylacetamide Derivatives: A Novel Anticonvulsant Drug Class, *Can. J. Chem.*, 83, 37-45.
  - Duncan, G.E. & Kohn, H. (2005). The Novel Antiepileptic Drug Lacosamide Blocks Behavioral and Brain Metabolic Manifestations of Seizure Activity in the 6 Hz Psychomotor Seizure Model. *Epilepsy Res.*, 67, 81-87.
  - Kohn, H., & Widger, W. (2005). The Molecular Basis for the Mode of Action of Bicyclomycin, *Curr. Drug. Targets: Infect. Disord.*, 5, 273-295.
  - Park, B.S.; Widger, W.R. & Kohn, H. (2006). Fluorine-substituted Dihydrobicyclomycins: Synthesis, Biochemical and Biological Properties, *Bioorg. Med. Chem.*, 14, 41-61.

## C. Research Support

1 R01 NS054112-01 Kohn (PI)

Project Dates: 07/01/06-06/30/10

Agency: NIH/NINDS

Title: Novel Methods to Identify Targets of the Neurological Agent (R)-Lacosamide

The major goals of this study is to identify the (R)-lacosamide binding targets in the brain proteome using mRNA-display technologies.

Principal Investigator/Program Director (Last, First, Middle): Kohn, Harold

Completed

Schwarz Pharma, Kohn (PI)

Project Dates: 12/15/01 – 12/14/05

Agency: Schwarz Pharma

Title: (R)-N-Benzyl-2-acetamido-3-methoxypropionamide: Sites and Mechanism of Drug Function

The major goals of this project are to learn the neuroanatomical distribution of lacosamide, a new antiepileptic agent discovered in our laboratories currently in phase III clinical trials – for epilepsy and neuropathic pain.

5 R01 GM 37934-16 Kohn (PI)

Project Dates: 07/01/99 – 12/31/04

Agency: NIH/GM

Title: Studies on the Mode of Action of Bicyclomycin

The major goals of this project were to elucidate the mechanism of drug function and the site of bicyclomycin binding with the *Escherichia coli* rho transcription termination factor.

1 R01 CA/GM 29756-17, Kohn (PI)

Project Dates: 07/01/96 – 05/31/01

Agency: NIH

Title: Mitomycins Unravalled

The major goals of this project were to delineate the pathways for mitomycin activation and DNA adduction.

North Carolina Biotechnology Center, Kohn (PI)

Project Dates: 07/01/02 – 06/30/04

Agency: North Carolina Biotechnology Center

Collaborative Funding Assistance Program

Title: (R)-N-Benzyl-2-acetamidopropionamide: Sites and Mechanism of Drug Function

The major goals of this project were to characterize the pathway(s) of lacosamide function using electrophysiology.

NIH AI-46340, Krause, K. (PI)

Project Dates: 09/01/00 – 12/31/04

Agency: NIH/AI

Title: Drug Design for Treating Opportunistic Infection in AIDS

The major goals of this project were to design and evaluate new agents that specifically target alanine racemase.