

## I. BIOGRAPHICAL DATA

A. James M. Cook

Date of Birth: August 6, 1945

### B. Education

BS in Chemistry with Honors, West Virginia University, 1963-1967.

PhD, Organic Chemistry, University of Michigan, 1968-1971 with Professor Philip LeQuesne; Thesis Title: I. Alkaloidal N-Oxides in Hallucinogenic Drugs. II. Studies on the Alkaloids of *Alstonia muelleriana* Domin."

Postdoctoral Appointment: "Synthesis of the Antitumor, *Vinca* Alkaloids," University of British Columbia," 1972-1973 with Professor James P. Kutney.

### C. Positions Held

Laboratory Technician, Fikes Chemicals, Nitro, W. Va., 1964-1965.

Supervisor of Research Laboratory and Pilot Plant, Fikes Chemicals, Summer 1965-1966.

Plant Foreman, Thiourea Production, Fikes Chemicals, Nitro, WV, Summer, 1967, Mr. Elmer Fike, President.

Graduate Student, University of Michigan, Ann Arbor, 1968-1971.

NIH Postdoctoral Fellow, University of British Columbia, 1972-1973.

Assistant Professor of Chemistry, UW-Milwaukee, September 1973-1979.

Associate Professor of Chemistry, UW-Milwaukee, September 1979-1986.

Professor of Chemistry, University of Wisconsin-Milwaukee, 1986-present.

Chair, Department of Chemistry, 1996-1999.

University Distinguished Professor, 2002-present

### D. Special Honors and Award

Member of Phi Lambda Upsilon Chemistry Honorary.

General Mills Summer Fellowship (1969); NASA Traineeship (1969).

Univ. of Michigan "Travel Award" for Excellence in Teaching and Research (1971).

National Institutes of Health Predoctoral Fellowship (1970-1972).

National Institutes of Health Postdoctoral Fellowship (1972-1973).

UW-Milwaukee Foundation Award for Research (1981).

National Institute for Alcohol and Drug Abuse Study Section for Contracts (1985).

Member of 3-Man Review Committee to Evaluate CNS Program for G.D. Searle and Co., Skokie, IL (1986).

NSF Study Panel - Review of SBIR Grants (1987-1989), NIH (BNP-adhoc, 1994).

Milwaukee Section ACS Award in Chemistry (1989). NIMH Study Panel-Program on Psychotherapeutic Drug Development (1997); Medications Development (Contracts) 2003.

WiSys (Wisconsin System) 2006 Innovation Scholar Award.

UW – Milwaukee 2007 Innovator Award.

Hector DeLuca Scientific Achievement Award from BIOFORWARD (October 12, 2022).

Japanese Society for the Promotion of Science Fellowship (2001).

Faculty of the Year 2016-17, Chemistry and Biochemistry, UW-Milwaukee and 2018-2019.

Member, Editorial Advisory Board, *Journal of Medicinal Chemistry* (1996-2001).

Editorial Advisory Board, *Medicinal Chemistry Research* (1996-2015).

Member, Editorial Board, Expert Opinion on Therapeutic Patents (1999-2016).

Member, Editorial Advisory Board, Current Topics in Medicinal Chemistry (2001- 2016).

Member, Editorial Advisory Board, Current Organic Synthesis (2002-2016).

Member, Editorial Board, Clinical Pharmacology: Advances and Applications (2016-2018).

Member, Editorial Board, Drug Design, Development and Therapy (2007-2016).

Member, Editorial Board, Journal of Clinical Pharmacology (2009-2016).

Member, Editorial Advisory Board, International Journal of Drug Design and Discovery (2009 - 2016).

## II. GRANTS, CONTRACTS AND RESEARCH AWARDS

### A. External Funds

Research Corporation, "Synthesis of Antihypertensive Agents," \$6,625, 1974-1976.

National Institutes of Health, "The Synthesis of Alpha and Beta Adrenergic Antagonists," \$117,000, 1976-1980.

Department of the Army, "Synthesis of Antimalarial Agents from 1,6-Diazaphenylene Derivatives," \$135,000, 1977-1980.

National Science Foundation, U. Weiss and J.M. Cook (P.I.), "General Method for the Synthesis of Cyclopentanoid Compounds," \$97,500, 1979-1982.

Petroleum Research Foundation, "Synthetic Approach Toward Planar Tetracoordinate Carbon," \$30,000, 1980-1982.

Aldrich Chemical-Alfred Bader, "Medicinal Chemistry and Polyquinanes." (unrestricted funds) \$10,000, 1979-1982.

Money donated to program from other contributors, \$10,000.

National Science Foundation, U. Weiss and J.M. Cook (P.I.), "General Approach for the Synthesis of Polyquinanes," \$175,990, 1982-1985.

Shell Development Company, "Biological Screening of Compounds," \$7,612, 1984-1985.

National Institutes of Health, "β-Carbolines: Search for Valium Agonists and Antagonists," \$220,000, 1985-1987.

Shaw Foundation, "Synthesis of Anxiolytic Agents With No Sedative-Hypnotic Effects and Search for Selective Hypnotic Agents," \$3,500, 1986-1987.

University of Wisconsin-Sea Grant, "The Persistence of Organic Pollutants in a Great Lakes Estuary," \$77,877, 1986-1988. Cook (Associate, 15% of Award).

Petroleum Research Fund, "Synthetic Approach Toward Planar Four Coordinate Carbon," \$52,500, 1986-89. Project SEED, \$1,000, 1987.

Petroleum Research Fund, Summer Research Supplement, \$4,500, 1988.

National Institute of Drug Abuse, "Characterization of Bz Receptors and Punished Responding," \$66,000, 1988-1989.

National Institutes of Health, "General Approach for the Synthesis of Macroline Alkaloids," \$165,000, 1986-1989.

National Institutes of Environmental Health Sciences, "Purchase of Analytical HPLC," \$9,704, 1988-1989.

National Science Foundation, "General Approach Toward the Synthesis of Polyquinenes," \$180,500, 1986-1990.

Searle Research Laboratories, "The Synthesis of β-Carbolines as Cognitive Enhancers," \$10,000, 1987-1992.

Monsanto Agricultural Division, \$6,600, 1989-1992.

Private Donation, \$25,000, 1989-1994.

National Institutes of Mental Health, "β-Carbolines: Search for Valium Agonists and Antagonists," \$470,000, 1988-1993.

National Science Foundation, "Fenestrane Approach to Planar Tetracoordinate Carbon," \$215,800, 1991-1994.

NIH Small Instrumentation Grant. "Purchase of an IR," \$13,000, 1995.

National Institute of Mental Health, "Rigid Probes: Modeling Selective Anxiolytics for BzR," \$580,000, 1991-1996.

Merck-Sharp and Dohme, England, "Synthesis of Ligands Selective for α5 or α6 Benzodiazepine Receptor Sites. II.

Characterization of the GABA/Cl<sup>-</sup> Channel," \$38,000, 1993-1996.

NSF, "Upgrade of NMR Spectroscopy Laboratory", One of 5 Principle Contributors (D. Petering, P.I.) \$245,000, (University match \$245,000, 1995).

ASTRA and Dupont Companies, "Broad Screening of Organic Compounds," \$27,600, 1997-2000.

ASTRA/ARCUS, "Broad Screening of Organic Compounds, \$67,000, 1997-99.

CALBIOCHEM, Tryprostatin B, \$4000, 1998-1999.

National Institute of Mental Health "Selective Anxiolytics *via* BzR Subtype Specific Ligands," \$655,043, 1996-2000.

Eli Lilly, "Broad Screening of Organic Compounds," \$13,800, 2000-2002.

Wyeth-Ayerst, Fellowship for Student Salaries, Screening," \$20,000, 2000-2002.

Aldrich Chemical Company, \$20,000, 2000-2002.

National Institutes of Health, "Ligands that Modulate Memory," \$146,000, 2000-2002(with Dr. Helmstetter, Psychology); 40% to Chemistry.

National Institute of Health (NIMH), "Selective Anxiolytics *via* BzR Subtype Specific Ligands," (minority postdoctoral supplement), \$118,000, 12/1/03-11/30/05.

NIH SBIR (subcontract) "Attenuation of Memory Impairment Using BDZR Ligands," \$48,756 (DC+IC) 2003-2005.

National Institute of Mental Health, "Selective Anxiolytics *via* BzR Subtype Specific Ligands," \$1,687,717, 2000-2006.

National Institute of Health, NIMH, "Selective Anxiolytics *via* BzR Subtype Specific Ligands," \$221,000, 12/1/03-11/30/06.

Searle Laboratories, "Process Development Chemistry," Donation of Equipment, \$80,000, 2000-2005. \$130,000 more, 2004-2008.

National Institutes of Health (NIAAA), (IUPUI/U of Maryland, subcontract with Harry June) "GABA<sub>A</sub> Receptor Subunits in Alcohol Reinforcement," \$330,000, 2002-2008.

Bristol Myers Squibb, Unrestricted Funds for Medicinal Chemistry, \$95,000, 2004 – 2008.

Bristol Myers Squibb (WISIS License Agreement) \$280,000, 2006 – 2008.

Aldrich Chemical, Purchase of Chemical Compounds, \$35,000, 2005-2009.

Biotechnology Alliance Collaborative Grant Program with Marquette University and Medical College of Wisconsin. "Cysteine Prodrugs in the Treatment of Schizophrenia," \$56,000. 2006-2008.

Wisconsin Applied Research Program (WITAG) with UW-LaCrosse, "Synthesis of Substituted Phenoxytyrenes as Novel Antimicrobial Agents," \$23,500. 2006 – 2008.

UW-Milwaukee, Research Growth Initiative, "Novel GABA(A) Ligands for Treating Alzheimers-related Cognitive Deficits," \$215,257. 2006 – 2008.

National Institutes of Health (Johns Hopkins University subcontract, Dr. Elise Weerts), "Preclinical Assessment of Medications for Alcohol Abuse," \$66,000. 2007 – 2009.

Catalyst Grant, Lynde and Harry Bradley Foundation, "Synthesis of Beta Carbolines to Treat Alcohol Abuse," \$60,908 (7/1/08 – 6/30/09 –extended to December 31, 2009).

NIH, SBIR with David Baker at Marquette University and Promentis, "Cysteine Prodrugs to Treat Schizophrenia," Total UW-Milwaukee amount, \$285,895, 2008-2011.

National Institutes of Health (University of Maryland subcontract, Dr. Harry June), NIAAA "Alcoholism and Anxiety: Novel Benzodiazepine Treatments," \$60,000 (2009-2010).

Research Growth Initiative, " New GABAergic Drugs to Treat Epilepsy Devoid of Sedative Ataxic and Amnesic Side Effects which Do Not Develop Tolerance," \$130, 944.

Catalyst Grant, Lynde and Harry Bradley Foundation, "Synthesis of Nonsedating Anticonvulsants," \$60,000 (7/1/2010-6/30/2011).

National Institutes of Health (Johns Hopkins University subcontract, Dr. Nancy Ator), "GABA(A)-Alpha 5 Cognitive Enhancers: Pharmacology and Neuropsychology in Macaques," \$300,000. 2007 – 2012.

National Institutes of Drug Abuse (P.I. David Baker, Marquette), "Targeting System Xc- for the Treatment of Drug Addiction," \$201,000 (2009-2012).

National Institutes of Health (Harvard Medical School subcontract, Dr. James Rowlett, P. I.), "Novel GABA – A Modulators as Cognitive Enhancers," \$600,000 (UWM-share), July, 2010 – June 30, 2016.

NIAAA (Harvard Medical School subcontract, Dr. Donna Platt) "GABA(A) Receptor Subtype Mechanisms in Non Human Primate Models of Alcohol Abuse," \$183,750. 2006 – 2017. (36,000/year)

Dupont Pharmaceuticals, Ag Division. Purchase of Chemical Compounds, \$34,800, 2005 – 2017.

MiTAG (UW-Milwaukee), Synthesis of Subtype Selective GABAergic Agents to Treat Schizophrenia, \$95,000, 2007-2017.

NIH "Synthesis of Alpha2/Alpha3 GABA Agonists to Treat Neuropathic Pain" J. M. Cook (P.I.), \$1,323,000, (2012-2017).

NIH "New Therapeutic Agents to treat Schizophrenia," J. M. Cook (P.I.) \$1,880,000 (2013-2018).

UWM-Grant "Purchase of a Mass Spectrometer," J. M. Cook (P.I.) \$76,058 (2013).

UWM Foundation Catalyst Grant "Pharmacological Proof of Concept for a First-in-Class Asthma Therapy," J. M. Cook (P.I.) \$50,000 (2014-2015).

NIH "Development of a GABA (A) Agonist to Control Airway Hyperresponsiveness and Inflammation in Asthma", J. M. Cook (P.I.), \$1,400,000 (2014-2019).

NIH "Development of New Drugs for Asthma by Targeting GABA (A) Receptors in the Lung (C. Emala, PI), UWM-subcontract, J.M. Cook (P.I.) \$200,808 (2015-2019).

## **PRESENT**

NIDA "Tolerance and Physical Dependence after Chronic Benzodiazepine Treatment", J. M. Cook (UWM P.I.) \$582,517 (2016 – 2021), James Rowlett (P.I. Miss State Med School).

NIH-NIDA "Development of Non-sedative Parasitic Selective Benzodiazepines to Treat the Neglected Tropical Disease Schistosomiasis", J. M. Cook (UWM P.I.) \$117,000 (10/1/2020 – 9/30/2022).

NIH "GABA(A) Receptor Subtype Mechanisms in Nonhuman Primate Models of Alcohol Abuse", J. M. Cook (UWM P.I.) \$220,000 (11/01/2020 – 10/31/2025).

NIDA "Benzodiazepines and Polydrug Use", S. Huskinson (UMMC P.I.), J. M. Cook (UWM P.I.) \$383,642 (07/01/2021 – 06/30/2026).

## **PENDING**

DOD "A Novel Subunit-selective Potentiator of GABA(A) Receptors for Treatment of Post Traumatic Epilepsy", J. M. Cook (UWM P.I.) \$53,895 (04/01/2021 – 03/31/2024).

NIH "KRM-II-81 as a Novel Treatment for Post-Traumatic Epilepsy", J. M. Cook (UWM P.I.) \$21,280 (04/01/2021 – 03/31/23).

DOD "KRM-II-81 as a Novel Treatment for Pain" J. M. Cook (UWM P.I.) under construction (07/01/2021 – 06/30/2024).

## **B. Internal Funds: James M. Cook, P.I.**

Graduate School Research Award, "The Synthesis of Antihypertensive Agents," \$7,894, 1974-1975.

Graduate School Research Award, "The Synthesis of Antihypertensive Agents," \$3,400, 1975-1976.

Graduate School Research Award, "The Synthesis of Cardiosensitive and Chronoselective Antihypertensive Agents," \$4,200, 1976-1977.

Graduate School Research Award, "The Synthesis of Antileishmanial Agents," \$4,200, 1982-1983.

Graduate School Seed Money, c. \$2,500, 1981-1982.

Graduate School Matching Funds *vis a vis* Grant Proposals, c. \$30,000, 1974-1984.

Graduate School Matching Funds *vis a vis* Grant Proposals, \$40,000, 1985-1987.

Shaw Foundation, \$1,000 (133-H654).

Graduate School Matching Funds *vis a vis* Grant Proposals, \$30,000, 1988.

Graduate School Matching Funds *vis a vis* Grant Proposals, \$45,000, 1989-1990.

Graduate School Matching Funds *vis a vis* Grant Proposals, \$33,000, 1991-1992.

Graduate School Matching Funds *vis a vis* Grant Proposals, \$56,000, 1993-1995.

Graduate School Matching Funds *vis a vis* Grant Proposals, \$50,000, 1996-1997.

Graduate School Matching Funds *vis a vis* Grant Proposals, \$40,000, 1997-1998.

Graduate School Matching Funds *vis a vis* Grant Proposals, \$30,000, 1998-1999.

Graduate School Matching Funds *vis a vis* Grant Proposals, \$40,000, 1999-2000.

Graduate School Bridging Funds for Anxiolytics, \$50,000, 2005

MiTag grant (\$85,000), 2007-2008.

Research Growth Initiative (\$215, 000), 2006-2008

Catalyst Grant (\$60,000), 2008-2009

Catalyst Grant (\$50,000), 2013-2014

Catalyst Grant (\$56,000), 2014-2015

### III. RESEARCH

#### A. Scholarly Publications

1. "Alstonerine, a New Indole Alkaloid from *Alstonia muelleriana*," J.M. Cook and P.W. LeQuesne, *Chem. Commun.*, 1306-1307 (1969).
2. "The Structure of Alstonisidine: A Novel Dimeric Indole Alkaloid," J.M. Cook and P.W. LeQuesne, *J. Org. Chem.*, **36**, 582-586 (1970).
3. "Some Aspects of Drug Usage, Trade and Plant Domestication Among the Yanomamo Indians of Venezuela and Brazil," N. Chagnon, P.W. LeQuesne, and J.M. Cook, *Acta Cient. Venezolana*, **21**, 186-193 (1970).
4. "Yanomamo Hallucinogens: Anthropological, Botanical and Chemical Findings," N. Chagnon, P.W. LeQuesne, and J.M. Cook, *Current Anthropology*, **12**, 72-74 (1971).
5. "Macralstonine from *Alstonia muelleriana*," J.M. Cook and P.W. LeQuesne, *Phytochem.*, **10**, 737-738 (1971).
6. "A Model Iron-Catalyzed Biomimetic Cyclization of a Cyclic Tryptamine N-Oxide," G. Scherer, C. Dorschel, J.M. Cook, and P.W. LeQuesne, *J. Org. Chem.*, **37**, 1083-1085 (1971).
7. "Biomimetic Synthesis and Structure of the Bisindole Alkaloid Alstonisidine," D.E. Burke, J.M. Cook, and P.W. LeQuesne, *Chem. Commun.*, 697 (1972).
8. "Biomimetic Synthesis of the Bisindole Alkaloid Macralstonine," D.E. Burke, J.M. Cook, C. DeMarkey, and P.W. LeQuesne, *Chem. Commun.*, 1346-1347 (1972).
9. "Further Alkaloids of *Alstonia muelleriana*," D.E. Burke, G.A. Cook, J.M. Cook, H. Lazar, K. Heller, and P.W. LeQuesne, *Phytochem.*, **12**, 1467-1474 (1973).
10. "Biomimetic Synthesis of Villalstonine and Alstonisidine," D.E. Burke, J.M. Cook, and P.W. LeQuesne, *J. Amer. Chem. Soc.*, **95**, 546-553 (1973).
11. "Studies on *Vinca* Alkaloids. The Structure of Vincarodine," J.P. Kutney, G. Cook, J. Cook, I. Itoh, J. Clardy, J. Fayos, P. Brown, and G. Svoboda, *Heterocycles*, **2**, 73-78 (1974).
12. "11-Methoxyakuammicine from *Alstonia muelleriana*," J.M. Cook and P.W. LeQuesne, *J. Org. Chem.*, 1367 (1975).
13. "Studies on the Synthesis of Bisindole Alkaloids. Structure and Absolute Configuration of 18'-Epi-4'-Epi-Vinblastine, 18'-Decarbometh-oxy-18'-Epi-4'-Epi- Vinblastine and 18'-Epi-3',4'-Dehydrovinblastine," J.P. Kutney, J. Cook, K. Fuji, A.

Treasurywala, J. Clardy, J. Fayos, and H. Wright, *Heterocycles*, **3**, 205-212 (1975).

14. "Total Synthesis of Indole and Dihydroindole Alkaloids. VIII. Studies on the Synthesis of Bisindole Alkaloids in the Vinblastine-Vincristine Series. The Chloro-indolenine Approach," J.P. Kutney, J. Beck, F. Bylsma, J.M. Cook, W. Cretney, K. Fuji, R. Imhof, and A. Treasurywala, *Helv. Chim. Acta*, **58**, 1690-1719 (1975).
15. "Reaction of 1,2 and 1,3 Dicarboxyl Compounds with Dimethyl  $\beta$ -Ketoglutarate. I. Synthesis of Methyl 5,6,7,8-Tetrahydro-5-oxocoumarin- $\beta$ -(4<sup>1</sup>H)-Acetate," D. Yang, J. Oehldrich, D. Foerst, and J.M. Cook, *J. Org. Chem.*, **41**(4), 743 (1976).
16. "Reactions of Dicarboxyl Compounds with Dimethyl  $\beta$ -Ketoglutarate. II. Simple Synthesis of Compounds of the [10.3.3] and [6.3.3] Propellane Series," J.M. Cook and D. Yang, *J. Org. Chem.*, **41**, 1903-1907 (1976).
17. "Pictet-Spengler Condensations in Refluxing Benzene," J. Sandrin, D. Soerens, L. Hutchins, E. Richfield, F. Ungemach, and J.M. Cook, *Heterocycles*, **4**, 1101-1105 (1976).
18. "<sup>13</sup>C-NMR of 1,3-Disubstituted 1,2,3,4-Tetrahydro- $\beta$ -Carbolines," J. Sandrin, D. Soerens, and J.M. Cook, *Heterocycles*, **4**, 1249-1255 (1976).
19. "Reactions of Dicarboxyl Compounds with Dimethyl  $\beta$ -Ketoglutarate. IV. Isolation of 1:1 Adducts," J. Oehldrich, M. Mueller, D. Wichman, D. Yang, J.M. Cook, and U. Weiss, *J. Org. Chem.*, **41**, 4053-4058 (1976).
20. "Reactions of Dicarboxyl Compounds with Dimethyl  $\beta$ -Ketoglutarate. V. Simple Synthesis of Tricyclo [6.3.0.0<sup>1-5</sup>]undecane-3,7,9-Trione: A Novel Cyclopentanoid Compound," J. Oehldrich, J.M. Cook, and U. Weiss, *Tetrahedron Lett.*, 4549- 4552 (1976).
21. "Reactions of Dicarboxyl Compounds with  $\beta$ -Ketoglutaric Acid III: Synthesis of 4-Hydroxy-3,4-diphenylcyclopent-2-enone-2-carboxylic Acid," J. Oehldrich and J.M. Cook, *Can. J. Chem.*, **55**, 82-84 (1977).
22. "Reactions of Dicarboxyl Compounds with Dimethyl  $\beta$ -Ketoglutarate. VI. Revision of the Structure of the Reaction Product of Cyclohexane-1,3-dione and Dimethyl  $\beta$ -Ketoglutarate and Conversion into 4-Substituted-5,6,7,9 -Tetrahydro-5-oxo-2- quinolones," J. Oehldrich and J.M. Cook, *J. Org. Chem.*, **42**, 889-894 (1977).
23. "Synthesis of 1,2,3,4-Tetrahydro- $\beta$ -Carbolines," J. Sandrin, D. Soerens, P. Mokry, and J.M. Cook, *Heterocycles*, **6**, 1133-1139 (1977).
24. "Reaction of Carbonyl Compounds with Dimethyl  $\beta$ -Ketoglutarate. Synthesis of Bicyclic Furan Derivatives," O. Campos and J.M. Cook, *J. Hetero. Chem.*, **14**(5), 711-715 (1977).
25. "General Method for the Synthesis of [n.3.3]Propellanes, n  $\geq$  3," R. Weber and J.M. Cook, *Can. J. Chem.*, **56**, 198-192 (1978).
26. "Synthesis of the Antibiotic ( $\pm$ )-Pyridindolol," G.S. Wu, E. Yamanaka, and J.M. Cook, *Heterocycles*, **9**, 175-183 (1978).
27. "Synthesis of a Tetraketone of the Tetracyclo[5.5.1.0.<sup>4,13</sup>O<sup>10,13</sup>]tridecane ("Staurane") Series," R. Mitschka, U. Weiss, and J.M. Cook, *J. Am. Chem. Soc.*, **100**, 2973-2974 (1978).
28. "The Spiroindolenine Intermediate: A Review," F. Ungemach and J.M. Cook, *Heterocycles*, **9**, 1089-1119 (1978).
29. "Simple Entry into the 1,6-Diazaphenalene Ring System," M.I. El-Sheikh, J.-C. Chang, and J.M. Cook, *Heterocycles*, **9**, 1561-1570 (1978).
30. "Study of the Pictet-Spengler Reaction in Aprotic Media: Synthesis of the  $\beta$ -Galactosidase Inhibitor, Pyridindolol," D. Soerens, J. Sandrin, F. Ungemach, P. Mokry, G.S. Wu, E. Yamanaka, L. Hutchins, M. DiPierro, and J.M. Cook, *J. Org. Chem.*, **44**, 535-545 (1979).
31. "Selenium Dioxide Entry into 3-Acylindoles," O. Campos and J.M. Cook, *Tetrahedron Lett.*, 1025-1028 (1979).
32. "Synthesis of 1,6-Diazaphenalene, a Vinylogous Imidazole," J.-C. Chang, M.I. El- Sheikh, and J.M. Cook, *Heterocycles*, **12**, 903-907 (1979).
33. "Stereospecific Synthesis of *Trans*-1,3-Disubstituted-1,2,3,4-Tetrahydro  $\beta$ -Carbo-lines," F. Ungemach, M. DiPierro, R. Weber, and J.M. Cook, *Tetrahedron Lett.*, 3225-3228 (1979).
34. "A Convenient Preparation of Cyclopentane-1,2-dione," J. Wrobel and J.M. Cook, *Synthetic Commun.*, **10**, 333-337 (1980).
35. "General Method for the Assignment of Stereochemistry of 1,3-Disubstituted-1,2,3,4- Tetrahydro- $\beta$ -Carbolines by Carbon-13 Spectroscopy," F. Ungemach, D. Soerens, R. Weber, M. DiPierro, O. Campos, P. Mokry, J.V. Silverton, and J.M. Cook, *J. Am. Chem. Soc.*, **102**, 6976-6984 (1980).



36. "Selenium Dioxide Oxidations in the  $\beta$ -Carboline Area," O. Campos, M. DiPierro, M. Cain, R. Mantei, A. Gawish, and J.M. Cook, *Heterocycles*, **14**, 975-984 (1980).
37. "New Perspectives on the Semmler-Wolff Aromatization Reaction," M.I. El-Sheikh and J.M. Cook, *J. Org. Chem.*, **45**, 2585-2587 (1980).
38. "Stereospecific Synthesis of 1,3-Disubstituted-1,2,3,4-Tetrahydro  $\beta$ -Carbolines," F. Ungemach, M. DiPierro, R. Weber, and J.M. Cook, *J. Org. Chem.*, **46**, 164-168 (1981).
39. "General Approach for the Synthesis of Polyquinanes: Stereospecific, Regiospecific Entry into the Tetracyclo[6.6.0.0<sup>1,5</sup>.O<sup>8,12</sup>]tetradecane System," A. Gawish and J.M. Cook, *Tetrahedron Lett.*, **22**, 211-214 (1981).
40. "3-Hydroxymethyl  $\beta$ -Carboline Antagonizes Some Pharmacologic Actions of Diazepam," P. Skolnick, S.M. Paul, K.C. Rice, S. Barker, J.M. Cook, R. Weber, and M. Cain, *Eur. J. Pharmacol.*, **69**, 525-527 (1981).
41. "Reaction of Dicarboxyl Compounds with Dimethyl 3-ketoglutarate. Influence of Steric Effects on Success of the Condensation," K. Avasthi, M.N. Deshpande, W.-C. Han, U. Weiss, and J.M. Cook, *Tetrahedron Lett.*, **22**, 3475-3478 (1981).
42. "The Chemistry of 1,6-Diazaphenalene. Electrophilic Substitution and Reaction with Singlet Oxygen," K. Avasthi, S.-J. Lee, J.M. Cook, J.E. Pickett, and H.H. Wasserman, *Heterocycles*, **16**, 1453-1461 (1981).
43. "General Approach for the Synthesis of Polyquinanes, Facile Generation of Molecular Complexity via Reaction of 1,2-Dicarboxyl Compounds with Dimethyl 3-keto-glutarate," R. Mitschka, J. Oehldrich, K. Takahashi, J.M. Cook, U. Weiss, and J.V. Silverton, *Tetrahedron* (Symposium in Print, ed. by L.A. Paquette), **37**, 4521-4542 (1981).
44. "Synthesis of 1,6-Diazaphenalene," M.I. El-Sheikh, J.C. Chang, A. Harmon, K. Avasthi, and J.M. Cook, *J. Org. Chem.*, **46**, 4188-4193 (1981).
45. "Chemistry of 1,6-Diazaphenalene, Halogenation," S.-J. Lee and J.M. Cook, *Heterocycles*, **16**, 2125-2131 (1981).
46. "Regiospecific Cleavage of Strained Tri- and Tetraquinane  $\beta$ -Diketones via a Retro- Claisen Reaction," W.C. Han, K. Takahashi, J.M. Cook, U. Weiss, and J.V. Silverton, *J. Am. Chem. Soc.*, **104**, 318-321 (1982).
47. "Do Benzodiazepine Receptors Play a Role in Sleep Regulation? Studies with the Benzodiazepine Antagonist, 3-Hydroxymethyl- $\beta$ -Carboline," W. Mendelson, M. Cain, J.M. Cook, S.M. Paul, and P. Skolnick, in "Beta-Carbolines and Isoquinolines," ed. by Earl Usdin, A.R. Liss, Inc., New York, 233-252 (1982).
48. " $\beta$ -Carbolines and Benzodiazepine Receptors: Structure-Activity Relationships and Pharmacologic Activity," P. Skolnick, E.F. Williams, J.M. Cook, M. Cain, K.C. Rice, J.M. Crawley, and S.M. Paul, in "Beta-Carbolines and Isoquinolines," ed. by Earl Usdin, A.R. Liss, Inc., New York, 253-262 (1982).
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D. **Non-refereed Publications** (including major in-house reports): Progress reports were written to NIH as part of grants.

E. **Papers Presented at Professional Meetings**

"Synthesis of Propellanes with Large and Medium-sized Rings from Cyclic  $\alpha$ -Diketones and Dimethyl  $\beta$ -Ketoglutarate," J. Cook and D. Yang, presented at the 7th Central Regional Meeting of the American Chemical Society, West Virginia University, Morgantown, WV, May 28-30, 1975, Abstract No. 122.

"Chemistry of 1,2- and 1,3-Dicarbonyl Compounds with Dimethyl  $\beta$ -Ketoglutarate: Synthesis of Methyl-2,3,5,6,7,8 - Hexahydro - 2, 5 - dioxo - 4 H- 1-benzopyran-<sup>4'</sup> -Acetate," J. Cook, D. Yang, J. Oehldrich, and U. Weiss, presented at the 6th Natural Products Symposium of the West Indies, Mona, Jamaica, January 4-10, 1976.

"Synthesis of Beta Carbolines: Pictet-Spengler Condensations in Refluxing Benzene," J. Sandrin, D. Soerens, L. Hutchins, E. Richfield, F. Ungemach, and J. Cook, presented at the 10th Middle Atlantic Regional Meeting of the American Chemical Society, Temple University, Philadelphia, PA, February 24, 1976, Abstract No. K-25.

"Reactions of 1,2 and 1,3-Dicarbonyl Compounds with Dimethyl  $\beta$ -Ketoglutarate: Preparation of 1:1 Adducts," D. Yang, J. Oehldrich, and J.M. Cook, presented at the 10th Middle Atlantic Regional Meeting of the American Chemical Society, Temple University, Philadelphia, PA, February 25, 1976, Abstract No. K-41.

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"Studies in the Indole Alkaloid Area: C-13 NMR of 1,3-Disubstituted-1,2,3,4- Tetrahydro  $\beta$ -Carbolines," J. Sandrin, G.S. Wu, F. Ungemach, and J.M. Cook, presented at the 11th Great Lakes Regional Meeting of the American Chemical Society, Stevens Point, WI, June 6-8, 1977, Abstract No. 180.

"Studies in the Indole Alkaloid Area: Pictet-Spengler Reactions in Refluxing Benzene," D. Soerens, O. Campos, E. Yamanaka and J.M. Cook, presented at the 11th Great Lakes Regional Meeting of the American Chemical Society, Stevens, Point, WI, June 6-9, 1977, Abstract No. 181.

"Reactions of Dicarboxyl Compounds with Dimethyl  $\beta$ -Ketoglutarate: Synthesis of Cyclopentanoid Derivatives," J.M. Cook, J. Oehldrich, and R. Weber, presented at the 11th Great Lakes Regional Meeting of the American Chemical Society, Stevens Point, WI June 6-8, 1977, Abstract No. 182.

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"Studies Directed toward the Synthesis of 3-Acylindole Bases," O. Campos and J.M. Cook, presented at the Joint Central-Great Lakes Regional Meeting of the American Chemical Society, Butler University, Indianapolis, IN, May 24-26, 1978, Abstract No. 30.

"Studies Directed Toward the Synthesis of Indole Alkaloid, *Suaveoline*," D. Soerens and J.M. Cook, presented at the Joint Central-Great Lakes Regional Meeting of the American Chemical Society, Butler University, Indianapolis, IN, May 24-26, 1978, Abstract No. 31.

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"Synthesis of 1,6-Diazaphenalene, a Vinylogous Imidazole," M.I. El-Sheikh, J.-C. Chang, R. Weber and J.M. Cook, American Chemical Society Great Lakes Regional Meeting, Rockford College, Rockford, IL, June 4-5, 1979, Abstract No. 206.

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"General Approach to the Synthesis of Cyclopentanoid Compounds: Studies Directed Toward the Preparation of Staurane and

Modhephene," J.M. Cook, 8th Natural Products Symposium, University of the West Indies, Mona, Jamaica, January 7-11, 1980.

"*In Vitro* Inhibition of [<sup>3</sup>H] Diazepam Binding to Benzodiazepine Receptors by  $\beta$ -Carbolines," K.C. Rice, P. Skolnick, S.M. Paul, S. Barker, J.M. Cook, R. Weber, and M. Cain, presented at the 2nd Chemical Congress of the North American Continent, August 24-29, 1980, Las Vegas, NV, Abstract No. MEDI-069.

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"Selenium Dioxide and DDQ Oxidations in the Indole Area," J.M. Cook, R. Mantei, M. Cain, and M. DiPierro, presented at the 2nd Chemical Congress of the North American Continent, August 24-29, 1980, Las Vegas, NV, Abstract No. ORGN-341.

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"Studies Directed toward the Synthesis of Potential Antimalarial Agents. Synthesis of 9-Methoxy and 9-Amino-1,6-diazaphenalene Derivatives," R. Weber, J. Chang, M.I. El-Sheikh and J.M. Cook, 14th Great Lakes Regional Meeting, June 4-6, 1980, Western Illinois University, Macomb, IL, Abstract No. 140.

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"Anomalous Action of Benzodiazepine Antagonists in Preventing 3-Carbomethoxy- $\beta$ -Carboline (BCCM)-Induced Convulsions," M. Schwei, M. Cain, J. Cook, S. Paul, and P. Skolnick, ASPET Meeting, Louisville, KY, August, 1982.

"Reaction of 1,6-Diazaphenalene with Electrophiles. Theoretical and Experimental Results," R. Weber, S.J. Lee, J.M. Cook, and W. England, 16th Annual Meeting of Great Lakes American Chemical Society Region, Illinois State University, Normal, IL, June 7-9, 1982, Abstract No. 184.

" $\beta$ -Carbolines: Synthesis, Neurochemical and Pharmacological Actions on Brain Benzodiazepine Receptors," M. Cain, F. Guzman, R. Weber, J.M. Cook, K.C. Rice, and P. Skolnick, 16th Annual Meeting of Great Lakes American Chemical Society Region, Illinois State University, Normal, IL, June 7-9, 1982, Abstract No. 185.

"General Approach Toward the Synthesis of Polyquinanes. Entry into the Triquinacene Ring System," G. Lannoye, V. Honkan, U. Weiss, S. Bertz, and J.M. Cook, 16th Annual Meeting Great Lakes American Chemical Society Region, Illinois State University, Normal, IL, June 7-9, 1982, Abstract No. 201.

"Reaction of Dicarbonyl Compounds with Dimethyl 3-Ketoglutarate, Influence of Steric Effects on Success of the Condensation," M.N. Deshpande, G. Kubiak, W.C. Han, U. Weiss and J.M. Cook, 16th Annual Meeting Great Lakes American Chemical Society Region, Illinois State University, Normal, IL, June 7-9, 1982, Abstract No. 206.

"General Approach for the Synthesis of Polyquinanes. Synthesis of Modhephane and Triquinacene *via* the Weiss Reaction," V. Honkan, G. Lannoye, J. Wrobel, S. Bertz, K. Takahashi and J.M. Cook, 184th American Chemical Society National Meeting, Kansas City, MO, September 12-17, 1982, Abstract No. ORG-134.

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"Benzosubstituted Benzodiazepine Probes With Which to Study the Topography of the Agonist Pharmacophore of the BzR," Weijiang Zhang, H. Diaz-Arauzo and J.M. Cook, 1991 Joint Central-Great Lakes Regional Meeting of The American Chemical Society, Indiana University-Purdue University at Indianapolis, Indiana, May 29-31, 1991, Abstract No. 340.

"Stereospecificity of the Pictet-Spengler Reaction. Kinetic versus Thermodynamic Control," K. Czerwinski, L. Deng and J.M. Cook, 1991 Joint Central-Great Lakes Regional Meeting of The American Chemical Society, Indiana University-Purdue University at Indianapolis, Indiana, May 29-31, 1991, Abstract No. 356.

"Studies Directed Toward the Enantiospecific Synthesis of the Suaveoline Alkaloids. Application of the Oxy-Cope Rearrangement to the Construction of the Pyridine E-Ring," F.Yu, X. Fu and J.M. Cook, 1991 Joint Central-Great Lakes Regional Meeting of The American Chemical Society, Indiana University-Purdue University at Indianapolis, Indiana, May 29-31, 1991, Abstract No. 403.

"Carboxyl-Mediated Pictet-Spengler Reaction. Synthesis of Antileukemic Cytotoxic Canthine-6-one Alkaloids," K. Narayanan and J.M. Cook, 1991 Joint Central-Great Lakes Regional Meeting of The American Chemical Society, Indiana University-Purdue University at Indianapolis, Indiana, May 29-31, 1991, Abstract No. 404.

"General Approach to the Synthesis of Macroline/Sarpagine Alkaloids. Recent Progress Directed Toward the Synthesis of Na-Methylsarpagine, Talpinine, Talcarpine, and Other *Alstonia* Alkaloids," L.K. Hamaker, Y. Bi and J.M. Cook, 1991 Joint Central-Great Lakes Regional Meeting of The American Chemical Society, Indiana University-Purdue University at Indianapolis, IN, May 29-31, 1991, Abs. No. 405.

"Studies on the Pictet-Spengler Reaction. New Strategies for the Synthesis of Ring-A Methoxylated Indole Alkaloids," M.S. Allen, K. Narayanan and J.M. Cook, 32nd Meeting of the American Society of Pharmacognosy: International Research Congress on Natural Products, Chicago, IL, July 21-26, 1991, Abstract No. O-42.

"Recent Progress Toward the Synthesis of Macroline/Sarpagine Alkaloids," L.K. Hamaker, Y. Bi, F. Yu, X. Fu and J.M. Cook, 32nd Annual Meeting of the American Society of Pharmacognosy: International Research Congress on Natural Products, Chicago, IL, July 21-26, 1991, Abstract No. O-43.

"Probes to Study the Structure and Function of the Benzodiazepine (Valium) Receptor. The Synthesis of a New Selective Anxiolytic/Anticonvulsant Agent," M. Allen, H. Diaz and J.M. Cook, MONA Symposium 1992, Natural Products & Medicinal Chemistry, University of the West Indies, Mona, Jamaica, January 6-10, 1992.

"Molecular Yardsticks. Probing the Dimensions of the Benzodiazepine Receptor Agonist/Inverse Agonist Binding Site With Rigid Planar Ligands," W. Zhang, H. Diaz-Arauzo, L. Dorn, M. Martin, P. Skolnick and J.M. Cook, 203rd ACS National Meeting, San Francisco, April 5-10, 1992, MED 184.

"General Approach to the Synthesis of Macroline/Sarpagine Alkaloids. Total Synthesis of Raumacline, Suaveoline, and 19,20-Dehydrotalcarpine," X. Fu, Y. Bi, L.K. Hamaker, F. Y. and J.M. Cook, 203rd ACS National Meeting, San Francisco, April 5-10, 1992, ORG-490.

"Receptor Mapping of the Benzodiazepine Binding Site," K.F. Koehler, T.J. Hagen, H. Diaz-Arauzo, M.S. Allen, G. Constantino, P. Skolnick and J.M. Cook, 25th Great Lakes Regional ACS Meeting, Milwaukee, WI, June 1-3, 1992, ORG-153.

"Study of the Topography of the Agonist Pharmacophore at the Benzodiazepine Receptor Binding Site," W. Zhang and J.M. Cook, 25th Great Lakes Regional ACS Meeting, Milwaukee, WI, June 1-3, 1992, ORG-180.

"Predictive Binding of  $\beta$ -Carboline Inverse Agonists and Antagonists *via* the CoMFA Approach," A.J. LaLoggia, M.S. Allen, K. Koehler, (G.D. Searle), P. Skolnick and J.M. Cook, 25th Great Lakes Regional ACS Meeting, Milwaukee, WI, June 1-3,

1992, ORG-181.

"Stereospecificity in the Pictet-Spengler Reaction," K.M. Czerwinski, L. Deng and J.M. Cook, 25th Great Lakes Regional ACS Meeting, Milwaukee, WI, June 1-3, 1992, ORG-184.

"Studies Directed Toward the Enantiospecific Preparation of Macroline, Affinisine and N<sub>a</sub>-Methylsarpagine," Y. Bi and J.M. Cook, 25th Great Lakes Regional ACS Meeting, Milwaukee, WI, June 1-3, 1992, ORG-193.

"General Approach to the Synthesis of Macroline/Sarpagine Alkaloids. Recent Progress Directed Toward the Synthesis of Alstophylline, Talpinine, Talcarpine, and Other *Alstonia* Alkaloids," L.K. Hamaker, M.S. Allen and J.M. Cook, 25th Great Lakes Regional ACS Meeting, Milwaukee, WI, June 1-3, 1992, ORG-195.

"Studies Directed Toward the Enantiospecific Synthesis of the Suaveoline Alkaloids. Application of the Anionic Oxy-Cope Rearrangement to the Construction of the Pyridine E-Ring," F. Yu and J.M. Cook, 25th Great Lakes Regional ACS Meeting, Milwaukee, WI, June 1-3, 1992, ORG-197.

"General Approach to the Synthesis of Macroline/Sarpagine Alkaloids. Total Synthesis of Raumacline, N<sub>b</sub>-Methyl Raumacline, and Suaveoline," X. Fu and J.M. Cook, 25th Great Lakes Regional ACS Meeting, June 1-3, 1992, ORG-198.

"Molecular Yardsticks. Rigid Benzodiazepine Receptor Ligands to Probe the Spatial Dimensions of the Binding Site," M.J. Martin, L.J. Dorn, K.F. Koehler, P. Skolnick and J.M. Cook, 25th Great Lakes Regional ACS Meeting, Milwaukee, WI, June 1-3, 1992, ORG-263.

"Molecular Yardsticks: Studying the Topography of the Agonist Pharmacophore at the Benzodiazepine Receptor Binding Site," W. Zhang, P. Skolnick and J.M. Cook, 204th ACS National Meeting, August 23-28th, 1992, MED-71.

"General Approach to the Enantiospecific Synthesis of the Suaveoline/Ajmaline Alkaloids: Application of the Anionic Oxy-Cope Rearrangement to the Construction of the Pyridine E-Ring," F. Yu, X. Fu and J.M. Cook, 204th ACS National Meeting, August 23-28th, 1992, ORG-27.

"Mechanism-Driven *Trans*-Stereospecificity in the Pictet-Spengler Reaction," K.M. Czerwinski, L. Deng and J.M. Cook, 204th ACS National Meeting, August 23-28th, 1992, ORG-80.

"General Approach to the Synthesis of Macroline/Sarpagine Alkaloids: The Enantiospecific Preparation of Macroline and Related Alkaloids," Y. Bi and J.M. Cook, 204th ACS National Meeting, August 23-28th, 1992, ORG-99.

"Enantiospecific Approach Toward the Synthesis of Alstonerine, Alstophylline, and 10,20-Dehydrotalcarpine," L.K. Hamaker, M.S. Allen and J.M. Cook, 204th ACS National Meeting, August 23-28th, 1992, ORG-100.

"Molecular Yardsticks. Rigid Probes to Study the Topography of the Benzodiazepine Receptor Site," NIMH Workshop, Keystone, Colorado, September, 1992.

"Beta Carbolines: The Design of Pharmacologic Probes for the Study of Anterior Hypothalamic Function," M.J. Martin, K. Koehler and J.M. Cook, Cellular Consequences of Sleep, Maui, Hawaii, March 13-17, 1993.

"The Agonist Pharmacophore of the Benzodiazepine Receptor. Synthesis of a Selective Anticonvulsant/Anxiolytic," E.D. Cox, M.S. Reddy and J.M. Cook, 33rd National Organic Symposium, Bozeman, Montana, June 13-17, 1993, Abs. A-50.

"Complete *Trans* Stereoselectivity in the Aprotic Pictet-Spengler Reaction," K.M. Czerwinski and J.M. Cook, 33rd National Organic Symposium, Bozeman, Montana, June 13-17, 1993, Abs. A-54.

"Enantiospecific Approach Towards the Synthesis of Macroline/Sarpagine/Ajmaline Alkaloids," L.K. Hamaker, Y. Bi, F. Yu and J.M. Cook, 33rd National Organic Symposium, Bozeman, Montana, June 13-17, 1993, Abs. A-93.

"Synthetic and Computer Assisted Analysis of the Structural Requirements for Selective High Affinity Ligand Binding to 'Diazepam-Insensitive' Benzodiazepine Receptors," K. Koehler, P. Skolnick, R. Liu, Q. Huang, Z-Q Gu and J.M. Cook, 33rd National Organic Symposium, Bozeman, Montana, June 13-17, 1993, Abs. B-3.

"Design, Synthesis and Evaluation of Indoleamine-2,3-Dioxygenase Inhibitors to Combat Aberrant Tryptophan Metabolism," A.C. Peterson, M.T. Migawa, J.M. Cook, R.R. Brown and J.A. Will, 33rd National Organic Symposium, Bozeman, Montana, June 13-17, 1993, Abs. B-48.

"A Study of the Topography of the Agonist Pharmacophore at the Benzodiazepine Receptor Binding Site and Its Effect on Activity," W. Zhang, P. Skolnick and J.M. Cook, 33rd National Organic Symposium, Bozeman, Montana, June 13-17, 1993, Abs. B-135.

"Synthesis and Evaluation of Inhibitors to Combat Aberrant Tryptophan Metabolism Catalyzed by Indoleamine 2,3-Dioxygenase," A.C. Peterson, M.T. Migawa, J.M. Cook, R.R. Brown and J.A. Will, 206th ACS National Meeting, Chicago,

Illinois, August 22-27, 1993, MEDI-242.

"Study of the Agonist Pharmacophore of the Benzodiazepine Receptor. The Synthesis of Anxiolytic Anxiolytics," W. Zhang, P. Skolnick and J.M. Cook, 206th ACS National Meeting, Chicago, Illinois, August 22-27, 1993, MEDI-196.

"Studies Directed Toward the Enantiospecific Preparation of the Bisindole Alkaloid Macralstonidine. The Total Synthesis of (+)-Macroline and (+)-Affinisine," Y. Bi, and J.M. Cook, 206th ACS National Meeting, Chicago, Illinois, August 22-27, 1993, ORGN-67.

"Approach to the Enantiospecific Synthesis of Norsuaveoline, Macrophylline, and the Related Desmethylnorphylline," F. Yu and J.M. Cook, 206th ACS National Meeting, Chicago, Illinois, August 22-27, 1993, ORGN-68.

"Enantiospecific Approach Towards the Synthesis of Macroline/Sarpagine Alkaloids," L.K. Hamaker, M.S. Allen and J.M. Cook, 206th ACS National Meeting, Chicago, Illinois, August 22-27, 1993, ORGN-69.

"Stereochemical Control of the Pictet-Spengler Reaction," K. Czerwinski, K. Koehler and J.M. Cook, 206th ACS National Meeting, Chicago, Illinois, August 22-27, 1993, ORGN-70.

"Effect of Novel  $\beta$ -Carboline Compounds on Pentobarbital Induced Sleep," C. LeBeaux, K. Campbell-Prue, J. Cook and G. Yutrzenka, American Indian Research Opportunities Conference, Bozeman, Montana, August 12-13, 1993.

"Effect of Novel  $\beta$ -Carboline Compounds on Pentobarbital Induced Incoordination," K. Campbell-Prue, C. LeBeaux, J. Cook and G. Yutrzenka, American Indian Research Opportunities Conference, Bozeman, Montana, August 12-13, 1993.

"Enantiospecific Approach Towards the Synthesis of Macroline/Sarpagine/Ajmaline Alkaloids," J.M. Cook, Y. Bi, L.K. Hamaker and M.S. Allen, Fifteenth Mona Symposium in Natural Products and Medicinal Chemistry, Mona, Jamaica, January 3-7, 1994.

"Synthesis and SAR Study of Selective High-Affinity Ligands That Bind to Diazepam- Insensitive Benzodiazepine Receptors," presented at the 207th ACS National Meeting, San Diego, CA, March 13-17, 1994, MEDI-187.

"Chemical and Computer-Assisted Study of the Agonist Pharmacophore of the Benzodiazepine Receptor," W. Zhang, P. Skolnick and J.M. Cook, presented at the 207th ACS National Meeting, San Diego, CA, March 13-17, 1994, MEDI-188.

"Stereoselective Pictet-Spengler Reactions: Application to the Synthesis of Optically Active Tetrahydro  $\beta$ -Carbolines," M.S. Reddy and J.M. Cook, presented at the 207th ACS National Meeting, San Diego, CA, March 13-17, 1994, ORGN-312.

"General Approach for the Synthesis of Macroline-Sarpagine Alkaloids: Enantiospecific Synthesis of (+)Macroline and a Partial Synthesis of (+)Villalstonine," Y. Bi, L. Hamaker and J.M. Cook, presented at the 207th ACS National Meeting, San Diego, CA, March 13-17, 1994, ORGN-444.

"Effect of 3-Substituted  $\beta$ -Carbolines on Pentobarbital (PB) Induced Sleep," G.J. Yutrzenka, C. LeBeaux, K. Campbell-Prue and J.M. Cook, XII International Congress of Pharmacology, Montreal, Quebec, July 24-29, 1994.

"Mode of Action of  $\beta$ -Carboline Convulsants on the Insect Nervous System and Their Potential as Insecticides," J.R. Bloomquist, A.J. LaLoggia, M.S. Reddy and J.M. Cook, presented in the summer of 1994.

"Chemical and Computer-Assisted Development of the Inclusive Pharmacophore for the Benzodiazepine Receptor," James Cook, presented at the 28th Middle Atlantic Regional Meeting of the ACS, University of Maryland, Baltimore County, Baltimore, MD, May 25-27, 1994, ABS 112.

"Synthesis and SAR Study of Selective High Affinity Ligands Which Bind to Benzodiazepine Receptor Subtypes," R. Liu, P. Zhang, P. Skolnick and J.M. Cook, presented at the Joint Great Lakes, Central Regional ACS Meeting, University of Michigan, Ann Arbor, MI, June 1-3, 1994, ABS 314.

"Synthesis and SAR Study of Novel Imidazobenzodiazepines Which Bind to Diazepam- Insensitive Benzodiazepine Receptors," P. Zhang, R. Liu, P. Skolnick and J.M. Cook, presented at the Joint Great Lakes, Central Regional ACS Meeting, University of Michigan, Ann Arbor, MI, June 1-3, 1994, ABS 315.

"Synthesis of 3,4,6-Trisubstituted  $\beta$ -Carbolines. Probing the Dimensions of the Lipophilic Pockets in the BzR Site(s)," E. Cox and J.M. Cook, presented at the Joint Great Lakes, Central Regional ACS Meeting, University of Michigan, Ann Arbor, MI, June 1-3, 1994, ABS 316.

"Evaluation of Competitive and Non-competitive Inhibitors of Indoleamine 2,3-Dioxygenase to Combat Aberrant Tryptophan Metabolism in Immunological Disease States," A.C. Peterson, E. Cox, J.M. Cook, R.A. Arend and R.R. Brown, presented at the Joint Great Lakes, Central Regional ACS Meeting, University of Michigan, Ann Arbor, MI, June 1-3, 1994, ABS 319.

"A Chemical and Computer Assisted Study of the Inclusive Pharmacophore of the Benzodiazepine Receptor," W. Zhang and

J.M. Cook, presented at the Joint Great Lakes, Central Regional ACS Meeting, University of Michigan, Ann Arbor, MI, June 1-3, 1994, ABS 320.

"Enantiospecific Synthesis of Macrolin/Sarpagine/Ajmaline-Related Alkaloids *via* the Pictet-Spengler Reaction," Y. Bi, L. Hamaker and J.M. Cook, presented at the Joint Great Lakes, Central Regional ACS Meeting, University of Michigan, Ann Arbor, MI, June 1-3, 1994, ABS 358.

"Enantiospecific Approach Towards the Synthesis of the Macroline-Related Alkaloids Alstophylline and Macralstonine," L. Hamaker, M.S. Allen and J.M. Cook, presented at the Joint Great Lakes, Central Regional ACS Meeting, University of Michigan, Ann Arbor, MI, June 1-3, 1994, ABS 381.

"The Aza-Wittig Approach to the Enantiospecific Synthesis of Norsuaveoline, Macrophylline, and the Related Desmethylnorphylline," F. Yu and J.M. Cook, presented at the Joint Great Lakes, Central Regional ACS Meeting, University of Michigan, Ann Arbor, MI, June 1-3, 1994, ABS 396.

"Studies Directed Toward the Enantiospecific Synthesis of *Alstonia*, *Gardneria*, and *Voacanga* Oxindole Alkaloids," A.C. Peterson and J.M. Cook, presented at the Joint Great Lakes, Central Regional ACS Meeting, University of Michigan, Ann Arbor, MI, June 1-3, 1994, ABS 399.

"Synthetic Approach to Angular Tetraquinanes Related to 14 $\pi$  Cyclo pentapentalenes," M.S. Reddy and J.M. Cook, presented at the Joint Great Lakes, Central Regional ACS Meeting, University of Michigan, Ann Arbor, MI, June 1-3, 1994, ABS 402.

"Stereochemical Control of the Pictet-Spengler Reaction," K. Czerwinski, K. Koehler and J.M. Cook, presented at the Joint Great Lakes, Central Regional ACS Meeting, University of Michigan, Ann Arbor, MI, June 1-3, 1994, ABS 403.

"The Total Synthesis of Roeharmine, (+)Norroecarboline, and (-)-1,2,3,4- Tetra-hydroroeharmine," M. Sreenivasa Reddy and J.M. Cook, presented at the Joint Great Lakes, Central Regional ACS Meeting, University of Michigan, Ann Arbor, MI, June 1-3, 1994, ABS 428.

"Search for  $\alpha 5$  Benzodiazepine Receptor Subtype Specific Ligands Based on the Structure of Sarmazenil (Ro 15-4513)," R.Y. Liu, N.P. Gillard, Z-Q. Gu, K. Rice, R. McKernan and J.M. Cook. Presented at the 56th Annual Scientific Meeting of the College on Problems of Drug Dependence, The Breakers, West Palm Beach, June 18-23, 1994, Oral Communications VI.

"Chemical and Computer-Assisted Study of the Inclusive Pharmacophore/Receptor Model of the Benzodiazepine Receptor Binding Site," W. Zhang, R. Liu, Q. Huang, P. Zhang, K.F. Koehler and J.M. Cook, presented at the 208th National ACS Meeting, Washington, D.C., August 21-25, 1994, MED-191.

"Use of  $\beta$ -Carbolines to Further Differentiate the Agonist/Inverse Agonist Pharmacophore at the BzR," E.D. Cox and J.M. Cook, presented at the 208th National ACS Meeting, Washington, D.C., August 21-25, 1994, MED-192.

"Synthesis and SAR Study of Novel Imidazobenzodiazepines at Diazepam- Insensitive and Diazepam-Sensitive Benzodiazepine Receptors," P. Zhang, W. Zhang, R. Liu and J.M. Cook, presented at the 208th National ACS Meeting, Washington, D.C., August 21-25, 1994, MED-195.

"Total Synthesis of Roemeria Alkaloids. A Study of the Racemization in (-)-1,2,3,4- Tetrahydroroeharmine," M.S. Reddy and J.M. Cook, presented at the 208th National ACS Meeting, Washington, D.C., August 21-25, 1994, ORG 259.

"Enantiospecific Approach Toward the Synthesis of the *Alstonia* Alkaloid Alstophylline and the Bisindole Macralstonine," L.K. Hamaker and J.M. Cook, presented at the 208th National ACS Meeting, Washington, D.C., August 21-25, 1994, ORG 269.

"Studies Toward the Enantiospecific Synthesis of Suaveoline Alkaloids. Aza-Wittig Approach to the Construction of the Pyridine E-Ring Systems," F. Yu and J.M. Cook, presented at the 208th National ACS Meeting, Washington, D.C., August 21-25, 1994, ORG 270.

"Studies Directed Toward the Diastereoselective Synthesis of *Alstonia* Oxindole Alkaloids," A.C. Peterson and J.M. Cook, presented at the 208th National ACS Meeting, Washington, D.C., August 21-25, 1994, ORG 271.

"Recent Advances in GABA<sub>A</sub>/Benzodiazepine Receptor Subtype Selectivity," J.M. Cook, 27th Annual Mardi Gras Symposium on Chemistry in Drugs of Abuse: Recent Advances in Chemistry and Pharmacology, University of New Orleans, February 24, 1995.

"Synthesis of Ligands Selective for the  $\alpha 5$  Benzodiazepine Receptor (BzR) Subtype," R.Y. Liu, P.W. Zhang, N.P. Gillard, R. McKernan and J.M. Cook, presented at the 209th National ACS Meeting, Anaheim, CA, April 2-6, 1995, MED 1.

"Evidence for Cleavage Across the C(1)N(2) Bond in the Epimerization of 1,2,3,4-Tetrahydro- $\beta$ -Carbolines," E.D. Cox, L.K. Hamaker, M.S. Reddy, P. Zhang, K. Czerwinski and J.M. Cook, presented at the 209th National ACS Meeting, Anaheim, CA, April 2-6, 1995. ORG 356.



"Stereospecific Approach to 19,20-Dehydro-10-methoxytalcarpine. The Enantio-specific Synthesis of 5-Methoxy-D-(+)-or L-(-)-tryptophan," P.W. Zhang and J.M. Cook, presented at the 28th Great Lakes Regional Meeting of the ACS, La Crosse, WI, June 5-8, 1995, #142.

"A Chemical and Computer Assisted Study of the Inclusive Pharmacophore of the Benzodiazepine Receptor," Q. Huang, W. Zhang and J.M. Cook, presented at the 28th Great Lakes Regional Meeting of the ACS, La Crosse, WI, June 5-8, 1995, #169.

"Scission of the C(1)-N(2) Bond in the Epimerization of 1,2,3,4-Tetrahydro  $\beta$ -Carbolines," E.D. Cox, M. S. Reddy and J.M. Cook, presented at the 28th Great Lakes Regional Meeting of the ACS, La Crosse, WI, June 5-8, 1995, #183.

"Synthesis and SAR Study of Novel Imidazobenzodiazepines Which Bind to 'Diazepam-Insensitive' GABA<sub>A</sub> Receptors," P. Zhang, R. Liu, B. Harris, P. Skolnick and J.M. Cook, presented at the 28th Great Lakes Regional Meeting of the ACS, La Crosse, WI, June 5-8, 1995, #199.

"Synthesis and Study of Ligands Selective for the  $\alpha 5\beta 2\gamma 2$  BzR Subtype," R.Y. Liu, P.W. Zhang, N.P. Gillard, R. McKernan and J.M. Cook, presented at the 28th Great Lakes Regional Meeting of the ACS, La Crosse, WI, June 5-8, 1995, #200.

"Studies Directed Toward the Rapid Construction of Angular Tetraquinanes Related to  $14\pi$  Cyclopentapentalenes," S. Van Ornum, M.S. Reddy and J.M. Cook, presented at the 28th Great Lakes Regional Meeting of the ACS, La Crosse, WI, June 5-8, 1995, #210.

"Pharmacophore Mapping: Synthesis of Ligands Selective for the  $\alpha 5\beta 2\gamma 2$  BzR Site," R.Y. Liu, P.W. Zhang, Q. Huang, N.P. Gillard, R. McKernan and J.M. Cook, presented at the 57th Annual Scientific Meeting of the College on Problems of Drug Dependence, Scottsdale, Arizona, June 10-15, 1995, P.S. II #35.

"Synthesis of Novel Imidazobenzodiazepines: The Selective Ligands for the GABA<sub>A</sub> Receptor Subtype," P. Zhang, R. Liu, P. Skolnick and J.M. Cook, presented at the 210th ACS National Meeting, Chicago, Illinois, August 20-24, 1995, MEDI-0148.

"Chemical and Computer-Assisted Study of the Inclusive Pharmacophore of the Benzodiazepine Receptor," Q. Huang, W. Zhang and J.M. Cook, presented at the 210th ACS National Meeting, Chicago, Illinois, August 20-24, 1995, MEDI -159.

"Synthesis of Ligands Selective for the  $\alpha$ -5 Benzodiazepine Receptor (BzR) Subtype," R.Y. Liu, P.W. Zhang, N.P. Gillard, R. McKernan and J.M. Cook, presented at the 210th ACS National Meeting, Chicago, Illinois, August 20-24, 1995, MEDI-160.

"Enantiospecific Synthesis of Macroline/Sarpagine/Ajmaline-related Indole Alkaloids *via* the Pictet-Spengler Reaction," J. Li, L. Hamaker, K. Czerwinski, P. Zhang and J.M. Cook, presented at the 210th ACS National Meeting, Chicago, Illinois, August 20-24, 1995, ORGN-212.

"Studies Toward the Synthesis of the Antiamoebic Bisindole Alkaloid (-)-Macrocarpamine: The Partial Synthesis of (-)-Anhydromacrosalpine-methine," T. Gan and J.M. Cook, presented at the 210th ACS National Meeting, Chicago, Illinois, August 20-24, 1995, ORGN-213.

"Stereospecific Approach to 19,20-Dehydro-10-methoxytalcarpamine: The Enantio-specific Synthesis of 5-Methoxy-D-(+)- or L-(-)-Tryptophan," P. Zhang, T. Gan and J.M. Cook, presented at the 210th ACS National Meeting, Chicago, Illinois, August 20-24, 1995, ORGN-214.

"Studies Directed Toward the Diastereoselective Synthesis of *Alstonia* Oxindole Alkaloids," A.C. Peterson, P. Yu and J.M. Cook, presented at the 210th ACS National Meeting, Chicago, Illinois, August 20-24, 1995, ORGN-215.

"Scission of the C(1)-N(2) Bond in the Epimerization of 1,2,3,4-Tetrahydro- $\beta$ -Carbolines," E.D. Cox, L.K. Hamaker, M.S. Reddy, P. Zhang, K.M. Czerwinski and J.M. Cook, presented at the 210th ACS National Meeting, Chicago, Illinois, August 20-24, 1995, ORGN-216.

"Studies Directed Toward the Construction of Angular Tetraquinanes Related to  $14\pi$  Cyclopentapentalenes," S.G. van Ornum, M.S. Reddy and J.M. Cook, presented at the 210th ACS National Meeting, Chicago, Illinois, August 20-24, 1995, ORGN-217.

"Studies Directed Toward Enantiospecific Synthesis of the Antiamoebic Alkaloid Macrocarpamine and 10-Methoxymacrocarpamine," J.M. Cook and T. Gan, presented at the Sixteenth Mona Symposium on Natural Products and Medicinal Chemistry, Mona, Jamaica, January 8-12, 1996.

"Partial Synthesis of the Antiamoebic Alkaloid Macrocarpamine *via* the Asymmetric Pictet-Spengler Reaction," J.M. Cook and T. Gan, presented at the 211th ACS National Meeting, New Orleans, March 23-28, 1996, ORGN-116.

"The Partial Synthesis of the Antiamoebic Alkaloid Macrocarpamine *via* The Asymmetric Pictet-Spengler Reaction," T. Gan and J.M. Cook presented at the 29th Great Lakes Regional ACS Meeting, Illinois State University, Normal, IL, May 19-22, 1996, Abstract No. 130.

"Studies Directed Toward the Construction of Angular Tetraquinanes Related to  $14\pi$  Cyclopentapentalenes," S. van Ornum,

M.S. Reddy and J.M. Cook, presented at the 29th Great Lakes Regional ACS Meeting, Illinois State University, IL, May 19-22, 1996, Abstract No. 251.

"Synthesis of Ligands Selective for the  $\alpha 5$  Benzodiazepine Receptor (BzR) Subtype," R. Liu, P.W. Zhang, N.P. Gillard, R. McKernan and J.M. Cook, presented at the 29th Great Lakes Regional ACS Meeting, Illinois State University, Normal, IL., May 19-22, 1996, Abstract No. 255.

"Enantiospecific Synthesis of Macroline/Sarpagine/Ajmaline-Related Indole Alkaloids *via* The Pictet-Spengler Reaction," J. Li, L. Hamaker, K. Czerwinski, P. Zhang and J.M. Cook, presented at the 29th Great Lakes Regional ACS Meeting, Illinois State University, Normal, IL, May 19-22, 1996, Abstract No. 256.

"Scission of The C(1)-N(2) Bond in the Epimerization of 1,2,3,4-Tetrahydro  $\beta$ -Carbolines," E. Cox, L.K. Hamaker, M.S. Reddy, P. Zhang, K. Czerwinski and J.M. Cook, presented at the 29th Great Lakes Regional ACS Meeting, Illinois State University, Normal, IL, May 19-22, 1996, Abstract No. 257.

"General Approach to The Diastereoselective Synthesis of Alstonia Oxindole Alkaloids," P. Yu, A. Peterson and J.M. Cook, presented at the 29th Great Lakes Regional ACS Meeting, Illinois State University, Normal, IL, May 19-22, 1996, Abstract No. 258.

"Studies of the Pharmacophore-Receptor Models for Benzodiazepine Receptor Subtypes: Binding Affinities of Substituted  $\beta$ -Carbolines for  $\alpha\beta\gamma 2$  (X=1,2,3,5 or 6) Subtypes and a Comparative Molecular Field Analysis," Q. Huang, E.D. Cox, T. Gan, D.W. Bennett and J.M. Cook, presented at the 212th ACS National Meeting, Orlando, Florida, August, 25-29, 1996, MEDI-0157.

"Partial Synthesis of The Antiamoebic Alkaloid Macrocarpamine *via* the Asymmetric Pictet-Spengler Reaction," T. Gan and J.M. Cook, presented at the 212th ACS National Meeting, Orlando, Florida, August 25-29, 1996, ORGN-0042.

"The *cis* the *trans* Epimerization 1,2,3,4-Tetrahydro  $\beta$ -carbolines Employed in the Total Synthesis of Indole Alkaloids: Further Evidence for Cleavage Across the C(1) - N(2) Bond," E. Cox, J. Li, P. Yu, and J.M. Cook, presented at the 212th ACS National Meeting, Orlando, Florida, August, 25-29, 1996, ORGN-0044.

"Studies Directed Toward the Construction of Angular Tetraquinanes Related to  $14\pi$ -Cyclopentapentalenes," S. Van Ornum, M. Reddy and J.M. Cook, presented at the 212th ACS National Meeting, Orlando, Florida, August 25-29, 1996, ORGN-0068.

"Generation of Four Five-membered Rings in a One-pot process: Studies Toward the Synthesis of Dicyclopenta[a,e]pentalene *via* the Tandem Pauson-Khand Reaction," S.G. Van Ornum, M. S. Reddy, and J.M. Cook, presented at the 213th ACS National Meeting, San Francisco, CA, April 13-17, 1997, ORGN-0498.

"Enantiospecific Total Synthesis of Tryprostatin A," T. Gan and J.M. Cook, presented at the 213th ACS National Meeting, San Francisco, CA, April 13-17, 1997, ORGN-0595.

"Enantiospecific Total Synthesis of (+)-Ajmaline and Alkaloid G *via* the Asymmetric Pictet-Spengler Reaction," J. Li, and J.M. Cook, presented at the 213th ACS National Meeting, San Francisco, CA, April 13-17, 1997, ORGN-0455.

"Evidence for the Conservation of Conformational Topography at Five Major GABA<sub>A</sub>/Benzodiazepine Receptor Subsites: Potent Affinities of the S-Enantiomers of Framework-constrained 4,5-Substituted Pyrroloimidazobenzodiazepines," Q. Huang, R. Liu, J.M. Cook and R.M. McKernan, presented at the 213th ACS National Meeting, San Francisco, CA, April 13-17, 1997, MEDI-0175.

"A Study of Pharmacophore/Receptor Models for Benzodiazepine Receptor Subtypes and SAR Study *via* a Ligand-mapping Approach," Q. Huang, E.D. Cox, T. Gan, X. He, C. Ma, and J.M. Cook, presented at the 213th ACS National Meeting, San Francisco, CA, April 13-17, 1997, MEDI-0040.

"Synthesis of Polyquinanes *via* the Tandem Pauson-Khand Reaction. Studies Directed Toward the Preparation of Dicyclopenta[a,d]pentalene and Dicyclopenta-[a,e]pentalene," S.G. Van Ornum, and J.M. Cook, presented at the 30th Great Lakes Regional ACS Meeting, Loyola University, Chicago, IL., May 28-30, 1997, Org 97.

"Enantiospecific Total Synthesis of Tryprostatin A," Tong Gan and James M. Cook, presented at the 30th Great Lakes Regional ACS Meeting, Loyola University, Chicago, IL., May 28-30, 1997, Org 132.

"Conservation of Conformational Topography at Five GABA<sub>A</sub>/Benzodiazepine Receptor Subtypes," Xiaohui He, Qi Huang, Tong Gan, and James M. Cook, presented at the 30th Great Lakes Regional ACS Meeting, Loyola University, Chicago, IL., May 28-30, 1997, Org 203.

"Search for New Antianxiety Agents: Subtype Selectivity at  $\alpha 1\beta 3\gamma 2$  and  $\alpha 5\beta 3\gamma 2$  Receptor Subtypes," Chunrong Ma, E.D. Cox, R. McKernan and J.M. Cook, presented at the 30th Great Lakes Regional ACS Meeting, Loyola University, Chicago, IL., May 28-30, 1997, Org 204.

“General Approach to the Enantiospecific Synthesis of *Alstonia* Oxindole Alkaloids,” Peng Yu, F. Yu, T. Wang, A.C. Peterson and J.M. Cook, presented at the 30th Great Lakes Regional ACS Meeting, Loyola University, Chicago, IL., May 28-30, 1997, Org 216.

“Enantiospecific Total Synthesis of (+)-Ajmaline *via* the Asymmetric Pictet-Spengler Reaction,” Jin Li and J.M. Cook, presented at the 30th Great Lakes Regional ACS Meeting, Loyola University, Chicago, IL., May 28-30, 1997, Org 217.

“Approach to the Enantiospecific Total Synthesis of Quebrachidine and Vincamajine,” Tao Wang, P. Yu, J. Li and J.M. Cook, presented at the 30th Great Lakes Regional ACS Meeting, Loyola University, Chicago, IL., May 28-30, 1997, Org 218.

“Approach to Sarpagine Indole Alkaloids. Stereospecific Synthesis of (6S, 10S)-2-Methoxy-9-Oxo-12-benzyl-6,7,8,9,10,11-hexahydro-6,10-imino-5H-cyclooct [b]indole *via* the Asymmetric Pictet-Spengler Reaction,” S. Zhao, Q. Huang, R. Liu, P. Zhang and J.M. Cook, presented at the 30th Great Lakes Regional ACS Meeting, Loyola University, Chicago, IL., May 28-30, 1997, Org 219.

“Generation of Four Five-Membered Rings in a One Pot Process. Studies Directed Toward the Synthesis of Dicyclopenta[a,e]pentalene *via* the Tandem Pauson-Khand Reaction,” S.G. Van Ornum and J.M. Cook, presented at the 30th Great Lakes Regional ACS Meeting, Loyola University, Chicago, IL., May 28-30, 1997, Org 231.

“Conservation of Conformational Topography at Five GABA<sub>A</sub>/Benzodiazepine Receptor Subtypes,” Q. Huang, X. He, T. Gan and J.M. Cook, presented at the 59th Annual Scientific Meeting of the College on Problems of Drug Dependence, Nashville, TN, June 14-19, 1997, Oral Communications III.

“Pharmacophore - receptor Models for Five Major Benzodiazepine Receptor Subtypes,” J.M. Cook, Q. Huang, E.D. Cox R. Liu, T. Gan, X. He and C. Ma, presented at the 214th ACS National Meeting, Las Vegas, Nevada, September 6-11, 1997, MEDI-124.

“Enantiospecific Total Synthesis of (+)-Ajmaline,” J. Li and J.M. Cook, presented at the 214th ACS National Meeting, Las Vegas, Nevada, September 6-11, 1997, ORGN-190.

“Diastereospecific Synthesis of Ketooxindoles: Potential Intermediates for the Synthesis of Alstonisine as well as Voacanga-related Oxindole Alkaloids,” P. Yu and J.M. Cook, presented at the 214th ACS National Meeting, Las Vegas, Nevada, September 6-11, 1997, ORGN-340.

“Studies Directed Toward the Synthesis of Dicyclopenta[a,e]pentalene and Dicyclopenta [a,d]pentalene *via* the Tandem Pauson-Khand Reaction,” S. Van Ornum and J.M. Cook, presented at the 214th ACS National Meeting, Las Vegas, Nevada, September 6-11, 1997, ORGN-356.

“Enantiospecific Synthesis of Ajmaline, Alkaloid G, Talpinine and Talcarpine *via* the Asymmetric Pictet-Spengler Reaction,” J. Li, P. Yu, and J.M. Cook, presented at the Seventeenth Mona Symposium, 1998 in Mona, Jamaica, January 5-9, 1998.

“GABA<sub>ERGIC</sub> Regulation of the Reinforcing Properties of Alcohol in Wistar rats,” C. R. Cason, H. L. June, M. Fredericks, G. Cheatham, A. Chen, J. Cook, T. Gan and J. M. Murphy, 27th Annual Meeting of Society for Neuroscience, New Orleans, October 25-30, 1997, abstract 381.5.

“Exploration of the L2 Region of Pharmacophore/Receptor Models for Benzodiazepine Receptor Subtypes *via* Preparation of Rigidly Substituted Pyrazoloquinolinones (CGS-Series),” Qi Huang, X. He, C. Ma and J.M. Cook, 215th ACS National Meeting, Dallas Texas, March 29-April 2, 1998, abstract MEDI-136.

“Search for Selective Ligands for Benzodiazepine Receptor Subtypes by Probing the Pharmacophore/Receptor Models of GABA<sub>A</sub>/BzR Subtypes *via* Optically Active BzR Ligands,” S. Yu, X. He, C. Ma, X. Liu and J.M. Cook, 215th ACS National Meeting, Dallas, Texas, March 29-April 2, 1998, abstract MEDI-137.

“First Enantiospecific Total Synthesis of Talcarpine and Talpinine from D-(+)-Tryptophan *via* the Asymmetric Pictet-Spengler Reaction,” P. Yu and J.M. Cook 215th ACS National Meeting, Dallas, Texas, March 29-April 2, 1998, abstract ORGN-175.

“Enantiospecific Total Synthesis of (+)-Ajmaline *via* the Asymmetric Pictet Spengler Reaction,” J. Li and J.M. Cook, 215th ACS National Meeting, Dallas, Texas, March 29-April 2, 1998, abstract ORGN-176.

“Synthetic Approach Toward The Synthesis of Dicyclopenta[a,d]pentalene and Dicyclopenta[a,e]pentalene *via* The Tandem Pauson-Khand Reaction,” S.G. Van Ornum and J.M. Cook, 215th ACS National Meeting, Dallas, Texas, March 29-April 2, 1998, abstract ORGN-275.

“Enantiospecific Total Synthesis of (+)-Ajmaline *via* the Asymmetric Pictet-Spengler Reaction,” Jin Li and J.M. Cook, 31st Great Lakes Regional Meeting of the ACS, University of Wisconsin-Milwaukee, Milwaukee, WI, June 1-3, 1998, abst. 185.

“Exploration of Region L2 of Pharmacophore/Receptor Models for GABA<sub>A</sub>/BzR Subtypes,” J.M. Cook, Q. Huang, C. Ma, X.

He and S. Yu, presented at The College on Problems of Drug Dependence, Sixtieth Annual Scientific Meeting, Scottsdale, AZ, June 13-18, 1998, poster session III, #124.

“Enantiospecific Total Synthesis of Talcarpine 1 and Talpinine 2 *via* the Asymmetric Pictet-Spengler Reaction,” Peng Yu and J.M. Cook, 31st Great Lakes Regional Meeting of the ACS, University of Wisconsin-Milwaukee, Milwaukee, WI, June 1-3, 1998, abst. 186.

“The Enantiospecific Total Synthesis of Norsuaveoline *via* The Pictet-Spengler Reaction,” Tao Wang and J.M. Cook, 31st Great Lakes Regional Meeting of the ACS, University of Wisconsin-Milwaukee, Milwaukee, WI, June 1-3, 1998, abst. 187.

“Utility of The Tandem Pauson-Khand Reaction Directed Toward The Synthesis of Dicyclopenta[a,d]pentalene and Dicyclopenta[a,e]pentalene,” M.M. Bruendl, S.G. Van Ornum and J.M. Cook, 31st Great Lakes Regional Meeting of the ACS, University of Wisconsin-Milwaukee, Milwaukee, WI, June 1-3, 1998, abst. 200.

“Synthesis and Evaluation of Functionalized Tryptophan Derivatives and Substituted  $\beta$ -Carbolines As Inhibitors of Indoleamine 2,3-Dioxygenase,” Xiaoxiang Liu, Chunrong Ma, Andrew C. Peterson and J.M. Cook, 31st Great Lakes Regional Meeting of the ACS, University of Wisconsin-Milwaukee, Milwaukee, WI, June 1-3, 1998, abst. 206.

“Enantiospecific Total Synthesis of Tryprostatin A,” Shuo Zhao, Tong Gan, Peng Yu and J.M. Cook, 31st Great Lakes Regional Meeting of the ACS, University of Wisconsin-Milwaukee, Milwaukee, WI, June 1-3, 1998, abst. 227.

“Synthetic Approach Directed Toward The Synthesis of Dicyclopenta[a,d]pentalene and Dicyclopenta[a,e]pentalene *via* the Tandem Pauson-Khand Reaction,” S.G. Van Ornum and J.M. Cook, 31st Great Lakes Regional Meeting of the ACS, University of Wisconsin-Milwaukee, Milwaukee, WI, June 1-3, 1998, abst 235.

“Search for Selective Ligands for  $\alpha 5$ -Benzodiazepine Receptor Subtypes By Probing The Pharmacophore/Receptor Models of GABA<sub>A</sub>/BzR Subtypes *via* Chiral BzR Ligands,” Xiaoxiang Liu and J.M. Cook, 31st Great Lakes Regional Meeting of the ACS, University of Wisconsin-Milwaukee, Milwaukee, WI, June 1-3, 1998, abst 245.

“The Agonist Pharmacophore of The Benzodiazepine Receptor. Synthesis of A Selective Anticonvulsant/anxiolytic,” Chunrong Ma, E.D. Cox, R. McKernan and J.M. Cook, 31st Great Lakes Regional Meeting of the ACS, University of Wisconsin-Milwaukee, Milwaukee, WI, June 1-3, 1998, abst 246.

“Evidence of Conservation of Conformational Topography at Five GABA<sub>A</sub>/BzR Subtypes,” Xiaohui He, Qi Huang, Tong Gan and J.M. Cook, 31st Great Lakes Regional Meeting of the ACS, University of Wisconsin-Milwaukee, Milwaukee, WI, June 1-3, 1998, abst 248.

“Exploration of the L2 Region of Pharmacophore/Receptor Models For Benzodiazepine Receptor Subtypes *via* Preparation of Rigidly Substituted Pyrazoloquinolinones (CGS Series),” Qi Huang, Xiaohui He, Chunrong Ma and J.M. Cook, 31st Great Lakes Regional Meeting of the ACS, University of Wisconsin-Milwaukee, Milwaukee, WI, June 1-3, 1998, abst 249.

“Study of Pharmacophore/Receptor Models for Benzodiazepine Receptor Subtypes *via* Preparation of Rigidly Substituted Pyrazoloquinolinones,” Q. Huang, X. He, S. Yu, C. Ma and J. M. Cook, 216th National ACS Meeting, Boston, MA, August 23-27, 1998, abst MEDI-96.

“Development of Selective Ligands for Benzodiazepine Receptor Subtypes By Manipulating the Stereochemistry of Optically Active BzR Ligands,” S. Yu, X. He, C. Ma, X. Liu and J. M. Cook, 216th National ACS Meeting, Boston, MA, August 23-27, 1998, abst MEDI-97.

“Synthesis and Study of Bz1 Receptor Subtype Specific Ligands,” C. Ma, X. He, S. Yu, R. McKernan and J. M. Cook, 216th National ACS Meeting, Boston, MA, August 23-27, 1998, abst MEDI-98.

“In Search of Inhibitors for the Indoleamine 2,3-dioxygenase (IDO) Enzyme System, X. Liu, C. Ma, A. C. Peterson and J. M. Cook, 216th National ACS Meeting, Boston, MA, August 23-27, 1998, abst ORG-105.

“Photochemical Tandem Pauson-Khand Reaction: Studies Directed Toward The Synthesis of Dicyclopenta[a,f]pentalene and Dicyclopenta[a,e]pentalene,” M. M. Bruendl, S. G. Van Ornum, J. M. Cook, 216th National ACS Meeting, Boston, MA, August 23-27, 1998, abst ORG-117.

“General Approach to The Diastereospecific Synthesis of Indole Alkaloids: Total Synthesis of Talcarpine, Talpinine, Alstonerine, and Anhydromacrosalpine-Methine *via* the Asymmetric Pictet-Spengler Reaction,” P. Yu, J. Li, T. Wang and J. M. Cook, 216th National ACS Meeting, Boston, MA, August 23-27, 1998, abst. ORG-554.

“General Approach to the Synthesis of Sarpagine/Ajmaline Alkaloids: Enantiospecific Total Synthesis of (+)-Ajmaline *via* the Asymmetric Pictet-Spengler Reaction,” J. Li and J. M. Cook, 216th National ACS Meeting, Boston, MA, August 23-27, 1998, abst. ORG-555.



“Total Synthesis of Norsuaveoline From D-(+)-Tryptophan via an Asymmetric Pictet-Spengler Reaction and Regioselective Oxyanion Cope Rearrangement,” T. Wang, P. Yu, J. Li and J. M. Cook, 216th National ACS Meeting, Boston, MA, August 23-27, 1998, abst. ORG-556.

“Enantiospecific Total Synthesis of the Enantiomers of Tryprostatin A and B,” S. Zhao, T. Gan, P. Yu and J. M. Cook, 216th National ACS Meeting, Boston, MA, August 23-27, 1998, abst. ORG-557.

“Study of Pharmacophore/Receptor Models for GABA<sub>A</sub>/BzR Subtypes via QSAR Analysis of Symmetrically Substituted Pyrazoloquinolinones,” X. He, S. Yu, C. Ma, Q. Huang, R. McKernan, and J.M. Cook, 217th National ACS Meeting, Anaheim, CA, March 21-25, 1999, abst. MEDI-095.

“Studies in Search of Memory-enhancing Agents that Act via GABA<sub>A</sub>/Bz Receptors: Part 1. Evidence for the Conservation of Pharmacophoric Descriptors at all DS Sub-types,” S. Yu, X. He, C. Ma, J.M. Cook, 217th National ACS Meeting, Anaheim, CA, March 21-25, 1999, abst. MEDI-096.

“Manipulation of Stereochemistry of Optically Active BzR Ligands: Development of Selective Ligands for Benzodiazepine Receptor Subtypes,” M.M. Bruendl, X. He, C. Ma, J.M. Cook, 217th National ACS Meeting, Anaheim, CA, March 21-25, 1999, abst. MEDI-097.

“Synthesis of [5.5.5.5]- and [5.6.6.5]Tetracycles via the Tandem Pauson-Khand Reaction,” M.M. Bruendl, H. Cao, J.M. Cook, 217th National ACS Meeting, Anaheim, CA, March 21-25, 1999, abst. ORG-271.

“Studies Toward the Enantiospecific Total Synthesis of Pleiocarpamine via a Novel Pictet-Spengler Reaction,” S. Yu, E.D. Cox, J.M. Cook, 217th National ACS Meeting, Anaheim, CA, March 21-25, 1999, abst. ORG-405.

“Novel Synthesis of Optically Active Tryptophan Derivatives,” C. Ma, X. Liu, S. Yu, S. Zhao, J.M. Cook, 217th National ACS Meeting, Anaheim, CA, March 21-25, 1999, abst. ORG-416.

“Synthesis of Chiral Imidazobenzodiazepines Employed in the Development of Selective Ligands for Benzodiazepine Receptor Subtypes,” M.M. Bruendl, X. He, C. Ma, and J.M. Cook, 36th National Organic Chemistry Symposium, University of Wisconsin-Madison, Madison, WI, June 13-17, 1999, abst. 29.

“Study of Pharmacophore/Receptor Models for GABA<sub>A</sub>/BzR Subtypes By Synthesis of Rigidly Substituted Imidazobenzodiazepines and Pyrazoloquinolinones,” X. He, S. Yu, C. Ma, M. Bruendl, and J.M. Cook, 36th National Organic Symposium, University of Wisconsin-Madison, Madison, WI, June 13-17, 1999, abst. 102.

“Approach to the Total Synthesis of Indole Alkaloid Alstophylline,” X. Liu, C. Ma, L. Hamaker, and J.M. Cook, 36th National Organic Symposium, University of Wisconsin-Madison, Madison, WI, June 13-17, 1999, abst. 160.

“Efficient Synthesis of Optically Active Tryptophan and Isotryptophan Derivatives,” C. Ma, X. Liu, S. Yu, X. He, and J.M. Cook, 36th National Organic Symposium, University of Wisconsin-Madison, Madison, WI, June 13-17, 1999, abst. 169.

“Enantiospecific Total Synthesis of Norsuaveoline via Asymmetric Pictet-Spengler Reaction and Regioselective Oxyanion Cope Rearrangement,” T. Wang and J.M. Cook, 36<sup>th</sup> National Organic Symposium, University of Wisconsin-Madison, Madison, WI, June 13-17, 1999, abst. 279.

“Studies Directed Toward the Enantiospecific Total Synthesis of Indole Alkaloid Pleiocarpamine via a Novel Pictet-Spengler Reaction,” S. Yu, E.D. Cox, and J.M. Cook, 36th National Organic Symposium, University of Wisconsin-Madison, Madison, WI, June 13-17, 1999, abst. 302.

“Sarpagine Indole Alkaloids. Stereospecific Synthesis of (6s, 10s)-2-Methoxy-9-oxo-12-benzyl-6,7,8,9,10,11-hexahydro-6,10-imino-5H-cyclooct[b]indole via Asymmetric Pictet-Spengler Reaction,” S. Zhao and J.M. Cook, 36th National Organic Symposium, University of Wisconsin-Madison, Madison, WI, June 13-17, 1999, abst.310.

“Development of Selective Ligands for Benzodiazepine Receptor Subtypes by Manipulating the Stereochemistry of Optically Active BzR Ligands,” M.M. Bruendl, X. He, C. Ma, and J.M. Cook, 218<sup>th</sup> National ACS Meeting, New Orleans, LA, August 22-26, 1999, abst. MEDI-127.

“Search for Selective Ligands for GABA<sub>A</sub>/BZR Subtypes and Their Role as Inverse Agonists/Antagonists in Alteration of Alcohol Dependence,” X. He, C. Ma, M. Bruendl, S. Yu, H. June, R. McKernan, and J.M. Cook, 218<sup>th</sup> National ACS Meeting, New Orleans, LA, August 22-26, 1999, abst. MEDI-128.

“Search for Bz1 Selective Ligands For GABA<sub>A</sub>/Benzodiazepine Receptor Subtypes,” C. Ma, X. He, M. Bruendl, R. McKernan, and J.M. Cook, 218<sup>th</sup> National ACS Meeting, New Orleans, LA, August 22-26, 1999, abst. MEDI-129.

“Total Synthesis of Tryprostatin A and B, and Enantiomers,” S. Zhao, T. Gan, P. Yu and J.M. Cook, 218<sup>th</sup> National ACS Meeting, New Orleans, LA, August 22-26, 1999, abst. ORGN-155.

“General Approach for the Synthesis of Ajmaline and Sarpagine Indole Alkaloids: Enantiospecific Total Synthesis of Norsuaveoline via Asymmetric Pictet-Spengler Reaction,” T. Wang and J.M. Cook, 218<sup>th</sup> National ACS Meeting, New Orleans, LA, August 22-26, 1999, abst. ORGN-156

“Enantiospecific Synthesis of Tryptophans and Tryprostatins via the Schöllkopf Chiral Auxillary,” S. Zhao, C. Ma, and J.M. Cook, MONA Symposium-2000, Mona, Jamaica, January 2-7, 2000.

“Enantiospecific Synthesis of Tryprostatins *via* the Schöllkopf Chiral Auxiliary,” S. Zhao, C. Ma, X. Liu, and J.M. Cook, 219<sup>th</sup> National ACS Meeting, San Francisco, CA, March 26-30, 2000, abst. ORGN- 749.

“General Approach for the Synthesis of Suaveoline and Sarpagine Indole Alkaloids. Enantiospecific Total Synthesis of Norsuaveoline and Vellosimine,” T. Wang and J.M. Cook, 219<sup>th</sup> National ACS Meeting, San Francisco, CA, March 26-30, 2000, abst. ORGN- 752.

“Search for Selective Ligands for GABA<sub>A</sub>/BzR Subtypes and Their Role in Alteration of Alcohol Dependence,” J.M. Cook, X. He, C. Ma, S. Yu, H. June, and R. McKernan, 219<sup>th</sup> National ACS Meeting, San Francisco, CA, March 26-30, 2000, abst. MEDI-101.

“Development of Selective Ligands for Benzodiazepine Receptor Subtypes,” J.M. Cook, C. Ma, X. He, and M.M. Bruendl, 219<sup>th</sup> National ACS Meeting, San Francisco, CA, March 26-30, 2000, abst. MEDI-105.

“Comparison of the Behavioral Effects of Beta-CCt and Flumazenil in Rhesus Monkeys,” C.P. France, L.R. Gerak, C. Ma, and J.M. Cook, 62<sup>nd</sup> Meeting of the College on Problems of Drug Dependence, Oral Communications XVIII, Puerto Rico, June 17-22, 2000.

“Search for Benzodiazepine/GABA<sub>A</sub> Subtype Selective Ligands and Implications in Alcohol Self-Administration,” X. He, C. Ma, H. June, and J.M. Cook, 62<sup>nd</sup> Meeting of the College on Problems of Drug Dependence, Poster Session IV (85), Puerto Rico, June 17-22, 2000.

“General Approach for the Synthesis of Sarpagine/Ajmaline/Corynanthe Alkaloids *via* the Asymmetric Pictet-Spengler Reaction. Enantiospecific Synthesis of Ajmaline, Vellosimine, Geissoschizine and Corynantheidine,” T. Wang, S. Yu, and J.M. Cook, (Planery Lecture), 32<sup>nd</sup> Great Lakes 2000 Regional Meeting of the ACS, Fargo, North Dakota, June 4-6, 2000, abst.74.

“Approach to the Total Synthesis of the Indole Alkaloid N<sub>a</sub>-Methylsarpagine and the Bisindole Alkaloid Macralstonine,” S. Zhao and J.M. Cook, 32<sup>nd</sup> Great Lakes 2000 Regional Meeting of the ACS, Fargo, North Dakota, June 4-6, 2000, abst.93.

“Progress Towards the Total Synthesis of 10-Methoxyanhydromacrosalpine-methine *via* the Asymmetric Pictet-Spengler Reaction, X. Liao, S. Zhao, and J.M. Cook, 32<sup>nd</sup> Great Lakes 2000 Regional Meeting of the ACS, Fargo, North Dakota, June 4-6, 2000, abst. 145.

“Studies Towards the Total Synthesis of the Bisindole Alkaloid Macralstonine,” X. Liu, C. Ma, and J.M. Cook, 32<sup>nd</sup> Great Lakes 2000 Regional Meeting of the ACS, Fargo, North Dakota, June 4-6, 2000, abst. 146.

“Enantiospecific Synthesis of Vellosimine and Norsuaveoline as well as an Approach Toward Quebrachidine,” T. Wang and J.M. Cook, 32<sup>nd</sup> Great Lakes 2000 Regional Meeting of the ACS, Fargo, North Dakota, June 4-6, 2000, abst.150.

“Enantiospecific Approach Towards the Total Synthesis of the Enantiomer of (+) Ajmaline,” Q. Xu, T. Wang, and J.M. Cook, 32<sup>nd</sup> Great Lakes 2000 Regional Meeting of the ACS, Fargo, North Dakota, June 4-6, 2000, abst. 152.

“Construction of [5.5.5.5] Tetracycles via the Tandem Pauson-Khand Reaction and New Entry into [5.8.5] Ring Systems,” H. Cao, S. Van Ornum, M. Bruendl, and J.M. Cook, 32<sup>nd</sup> Great Lakes 2000 Regional Meeting of the ACS, Fargo, North Dakota, June 4-6, 2000, abst. 158.

“General Approach to the Corynanthe Alkaloids: Enantiospecific Total Synthesis of (-) Corynantheidol and (+)-Geissoschizine,” M. Berner, S. Yu, and J.M. Cook, 32<sup>nd</sup> Great Lakes 2000 Regional Meeting of the ACS, Fargo, North Dakota, June 4-6, 2000, abst.173.

“Total Synthesis of the Enantiomer of the Indole Alkaloid Affinisine and Approach to the Total Synthesis of Alstophylline and Macralstonine,” X. Liu, T. Wang, C. Ma, Q. Xu, and J.M. Cook, 220<sup>th</sup> National ACS Meeting, Washington, D.C., August 20-24, 2000, abst. ORG -122.

“General Approach for the Synthesis of (-)Corynantheidine, (-)Corynantheidol, (+)-Geissoschizine, and (-)-Geissoschizol from a Common Intermediate,” M. Berner, S. Yu, and J.M. Cook, 220<sup>th</sup> National ACS Meeting, Washington, D.C., August 20-24, 2000, abst. ORG - 131.

“Approach to the Total Synthesis of the Bisindole Alkaloid Macralstonidine,” S. Zhao and J.M. Cook, 220<sup>th</sup> National ACS

Meeting, Washington, D.C., August 20-24, 2000, abst. ORG - 137.

“Enantiospecific Total Synthesis of the Sarpagine Indole Alkaloid (+)-Vellosoimine as well as a Study Toward the Total Synthesis of the Bisindole Alstonisine,” T. Wang and J.M. Cook, 220<sup>th</sup> National ACS Meeting, Washington, D.C., August 20-24, 2000, abst. ORG - 140.

“Enantiospecific Synthesis of Sarpagine, Ajmaline, and Corynanthe Indole Alkaloids via the Asymmetric Pictet-Spengler Reaction,” (planary lecture), The Twenty-third Gulf Coast Chemistry Conference, Pensacola, Florida, September 14-16, 2000 (Thursday Lecture 2:40).

“Discriminative Stimulus Effects of the Novel 1,4-Benzodiazpine QHII-66 in Ethanol- and Triazolam-Trained Squirrel Monkeys,” S. Lelas, D.M. Platt, J.K. Rowlett, R.D. Spealman, J. Cook, and C. Ma, 30<sup>th</sup> Annual Meeting of the Society for Neuroscience, New Orleans, LA, November 4-9, 2000, Soci. Neurosci. Abst., 26, Part 1, 280 (abst. 103.2).

“Selective GABA<sub>A</sub>  $\alpha$ 1 Subunit Ligands (BCCt, 3PBC) Attenuate Responding Maintained by Ethanol Following Microinjection into the Ventral Pallidum,” M.R. Carroll, K.L. Foster, S. Harvey, P.F. McKay, J.M. Cook and H. June, Alcoholism: Clin. Exp. 24: 47A (abst. 24).

“Development of Selective Ligands for GABA<sub>A</sub>/BzR Subtypes and Their Role in Alteration of Alcohol Dependence,” X. Li, X. He, C. Ma, S. Harvey, and J.M. Cook, 221<sup>st</sup> National ACS Meeting, San Diego, CA, April 1-5, 2001, abst. MEDI-83.

“High-yield Generation of the [5.5.5.5]Tetracyclic Systems *via* Molybdenum Carbonyl Mediated Tandem Pauson-Khand Reaction,” H. Cao and J.M. Cook, 221<sup>st</sup> National ACS Meeting, San Diego, CA, April 1-5, 2001, abst. ORGN-420.

“Approach to the Total Synthesis of 10-Methoxyanhydromacrosalpine-methine *via* the Asymmetric Pictet-Spengler Reaction,” X. Liao, S. Zhao, and J.M. Cook, 221<sup>st</sup> National ACS Meeting, San Diego, CA, April 1-5, 2001, abst. ORGN-586.

“General Approach to the Total Synthesis of Macroline/Sarpagine Indole Alkaloids as well as Their Enantiomers,” X. Liu and J.M. Cook, 221<sup>st</sup> National ACS Meeting, San Diego, CA, April 1-5, 2001, abst. ORGN-591

“General Approach for the Synthesis of Sarpagine Ajmaline and Corynanthe Alkaloids *via* the Asymmetric Pictet-Spengler Reaction,” (planary lecture) Royal Society of Chemistry, Perkin Division, 15<sup>th</sup> Lakeland Symposium: Grasmere, Grasmere Village, UK, May 10-14, 2001, (Friday morning lecture).

“Alcohols Euphoric Properties are Regulated by the GABA<sub>A</sub> Receptor  $\alpha$ 1 Subtype,” W. Yin, M. Carroll, H. June, and J.M. Cook, College on Problems of Drug Dependence, 63<sup>rd</sup> Annual Scientific Meeting, Scottsdale, AZ, June 16-21, 2001, Oral Communications IX (1:45 p.m.).

“Approach to Cyclopentapentalenes. Regiospecific Synthesis of the Highly Functionalized [5.5.5.5]Tetracycles *via* the Molybdenum Carbonyl-Mediated Tandem Pauson-Khand Reaction,” H. Cao, J.M. Cook, and J. Flippen-Anderson, 37<sup>th</sup> National Organic Chemistry Symposium, Montana State University, Bozeman, MT, June 10-14, 2001, abst. 58.

“Research in Search of Selective Ligands for GABA<sub>A</sub>/BzR Subtypes and Their Role in Alteration of Alcohol Dependence,” X. Li, X. He, C. Ma, S. Harvey, and J.M. Cook, 37<sup>th</sup> National Organic Chemistry Symposium, Montana State University, Bozeman, MT, June 10-14, 2001, abst.-122.

“Studies Directed Toward the Antimalarial Bisindole Alkaloid Macralstonine O-Methyl Ether as well as Macralstonine,” X. Liu and J.M. Cook, 37<sup>th</sup> National Organic Chemistry Symposium, Montana State University, Bozeman, MT, June 10-14, 2001, abst.-126.

“Studies Directed Toward the Total Synthesis of the Bisindole Villalstonine,” J. Ma, S. Yu, O.M. Berner, and J.M. Cook, 37<sup>th</sup> National Organic Chemistry Symposium, Montana State University, Bozeman, MT, June 10-14, 2001, abst.-132.

“Studies Directed Toward the Enantiospecific Total Synthesis of Oxindole Alkaloids: Approach to the Total Synthesis of Alstonisine,” X. Wearing, P. Yu, and J.M. Cook, 37<sup>th</sup> National Organic Chemistry Symposium, Montana State University, Bozeman, MT, June 10-14, 2001, abst.-219.

“Search for Benzodiazpine/GABA<sub>A</sub> Subtype Selective Ligands that Reverse Alcohol Self-Administration,” W. Yin, C. Zhang, M. Carroll, H. June, and J.M. Cook, 37<sup>th</sup> National Organic Chemistry Symposium, Montana State University, Bozeman, MT, June 10-14, 2001, abst.-234.

“Study of Pharmacophore/Receptor Models for GABA<sub>A</sub>/BzR Subtypes,” Chunchun Zhang and J.M. Cook, 37<sup>th</sup> National Organic Chemistry Symposium, Montana State University, Bozeman, MT, June 10-14, 2001, abst.-238.

“The Enantiospecific Total Synthesis of the Alstonia Bisindole Alkaloid, Macralstonidine,” X. Liao, S. Zhao, and J.M. Cook, 37<sup>th</sup> National Organic Chemistry Symposium, Montana State University, Bozeman, MT, June 10-14, 2001, abst.-239.

“Enantiospecific Synthesis of a Very Potent Tryprostatin Diastereomer, Active Against Human Cancer Cell Lines,” S. Zhao, X.

- Liu, C. Zhang, A. Morin, K. Smith, T. McDonald, and J.M. Cook, 37<sup>th</sup> National Organic Chemistry Symposium, Montana State University, Bozeman, MT, June 10-14, 2001, abst. 240.
- “Search for Benzodiazepine/GABA(A) Subtype Selective Ligands that Reverse Alcohol Self-Administration,” J. Cook, W. Yin, C. Zhang, X. Li, and H. June, (plenary lecture), 53<sup>rd</sup> Southeastern Regional Meeting of the ACS, Savannah, GA, September 23-26, 2001, plenary lecture, abst. 379.
- “The Enantiospecific Synthesis of Sarpagine, Ajmaline, and Corynanthe Indole Alkaloids *Via* the Asymmetric Pictet-Spengler Reaction,” T. Wang, S. Zhao, X. Liu, and J.M. Cook, 19<sup>th</sup> Meeting of the Northeast Chapter of the International Isotope Society, Pearl River, N.Y., October 26, 2001 (plenary lecture).
- “The Role of the GABA(A)  $\alpha 1$  Subtype in Mediating the Sedative and Anxiolytic Properties of Benzodiazepines,” M.R. Carroll, J. Woods, R.Y. Seyoum, and H. June, presented at the RCM Meeting, 2001.
- “Involvement of GABA(A) Receptors Containing the  $\alpha 5$  Subunit in Nitrous Oxide Withdrawal,” L. Vaughn, R. Lindau, W. Yin, and J.M. Cook, presented at the Neuroscience Meeting, San Diego, CA, 2001.
- “The Role of BZ/ $\alpha 1$  and BZ/ $\alpha 5$  Receptors in Discriminative Stimulus Effects of Triazolam in Squirrel Monkeys,” S. Lelas, J.K. Rowlett, R.D. Spealman, J.M. Cook, X. Li, and W. Yin, presented at the Neuroscience Meeting, San Diego, CA, 2001.
- “Role of GABA(A)/ $\alpha 1$  Receptor Mechanisms in the Discriminative Stimulus Effects of Ethanol in Squirrel Monkeys,” D.M. Platt, J.K. Rowlett, R.D. Spealman, J.M. Cook, and W. Yin, FASEB Summer Research Conference, Arizona, August 2001.
- “Search for Benzodiazepine/GABA(A) Subtype Selective Ligands that Reverse Alcohol Self-Administration,” W. Yin, C. Zhang, M. Carrol, H. June, and J.M. Cook, 21<sup>st</sup> Symposium on Medicinal Chemistry, 10<sup>th</sup> Annual Meeting of the Division of Medicinal Chemistry, Kyoto, Japan, November 28-30th, 2001, (plenary lecture).
- “Enantiospecific Synthesis of Sarpagine, Ajmaline and Corynanthe Alkaloids *via* the Asymmetric Pictet-Spengler Reaction,” T. Wang, S. Zhao, X. Liu, and J.M. Cook, Mini- Symposium of the Society of Synthetic Organic Chemistry(Japan), Chiba, Japan, November 30, 2001 (plenary lecture).
- “The Enantiospecific, Stereospecific Total Synthesis of the Alstonia Bisindole, Macralstonidine,” S. Zhao, X. Liao, and J.M. Cook, The Mona Symposium 2002, Natural Products and Medicinal Chemistry, University of the West Indies, Mona Jamaica, Jan. 7-10, 2002, p.21.
- “Search for Benzodiazepine/GABA<sub>A</sub> Subtype Selective Ligands to Treat Alcohol Abuse,” W. Yin, C. Zhang, H. June, and J.M. Cook, 28<sup>th</sup> National Medicinal Chemistry Symposium, San Diego, CA, June 8-12, 2002 (plenary lecture).
- “Approach to Cyclopentapentalenes: Regiospecific Synthesis of the Highly Functionalized [5.5.5.5]Tetracycles *via* the Molybdenum Carbonyl-Mediated Tandem Pauson-Khand Reaction,” H. Cao, J.M. Cook, and J. Flippen-Anderson, 223<sup>rd</sup> National Meeting of the ACS, Orlando, FL, April 7-11, 2002, abst. ORGN 301.
- “Progress Towards The Synthesis of Antimalarial Bisindole Alkaloids,” X. Liao and J.M. Cook, 223<sup>rd</sup> National Meeting of the ACS, Orlando, FL, April 7-11, 2002, abst. ORGN 104.
- “General Approach for the Synthesis of Indole Alkaloids *via* the Asymmetric Pictet-Spengler Reaction,” J. Cook, 2002 Gordon Research Conference on Heterocyclic Compounds, Salve Regina University, Newport, RI, 2002 (plenary lecture)
- “Search for Benzodiazepine/GABA<sub>A</sub> Subtype Selective Ligands that Reverse Alcohol Self-Administration,” W. Yin, J. Cook, and H. June, 34<sup>th</sup> Great Lakes Regional Meeting of the ACS, Minneapolis, MN, June 2-4, 2002, abst. 85.
- “Enantiospecific Synthesis of a Very Potent Tryprostatin Diastereomer Active Against Human Cancer Cell Lines,” C. Zhang, S. Zhao, and J.M. Cook, 34<sup>th</sup> Great Lakes Regional Meeting of the ACS, Minneapolis, MN, June 2002, abst. 92.
- “Regiospecific Synthesis of the Highly Functionalized [5.5.5.5]Tetracycles,” Hui Cao and J.M. Cook, 34<sup>th</sup> Great Lakes Regional Meeting of the ACS, Minneapolis, MN, June 2-4, 2002, abst. 110.
- “The First Enantiospecific Total Synthesis of Alstonisine from D-(+)-Tryptophan *via* the Asymmetric Pictet-Spengler Reaction,” X. Wearing, P. Yu, and J.M. Cook, 34<sup>th</sup> Great Lakes Regional Meeting of the ACS, Minneapolis, MN June 2-4, 2002, abst. 203.
- “Study of Selective Ligands for GABA/BzR Subtypes and their Role in Alteration of Alcohol Dependence,” X. Li, W. Yin, S. Harvey, and J.M. Cook, 34<sup>th</sup> Great Lakes Regional Meeting of the ACS, Minneapolis, MN, June 2-4, 2002, abst. 78.
- “Approach Toward the Total Synthesis of the Antimalarial Alkaloid Villalstonine,” J. Ma, S. Yu, O. Mathias, and J.M. Cook, 34<sup>th</sup> Great Lakes Regional Meeting of the ACS, Minneapolis, MN, June 2-4, 2002, abst. 90.
- “The Total Synthesis of Bisindole Dispegatrine,” X. Liao and J.M. Cook, 34<sup>th</sup> Great Lakes Regional Meeting of the ACS,



Minneapolis, MN, June 2-4, 2002, abst. 105.

“Search for Benzodiazepine/GABA(A) Subtype Selective Ligands that Reverse Alcohol Self-Administration,” W. Yin, X. Liao, H. June, and J. Cook, 224<sup>th</sup> ACS National Meeting, Boston, MA, August 18-22, 2002, abst. MEDI-244.

“Studies in Search of Memory Enhancing Agents Which Act *via* GABA(A)/BzR Receptors,” X. Li, C. Cook, F.J. Helmstetter, and J.M. Cook, 224<sup>th</sup> ACS National Meeting, Boston, MA, August 18-22, 2002, abst. MEDI-245.

“Enantiospecific Stereospecific Total Synthesis of Alstonisine,” X. Wearing, J.M. Cook, and J.L. Flippen-Anderson, 224<sup>th</sup> ACS National Meeting, Boston, MA, August 18-22, 2002, abst. O361.

“Approach to Cyclopentapentalenes, Regiospecific Synthesis of the Highly Functionalized [5.5.5.5]tetracycles *via* the Molybdenum Carbonyl-mediated Tandem Pauson-Khand Reaction,” H. Cao, J.M. Cook, and J. Flippen-Anderson, 224<sup>th</sup> ACS National Meeting, Boston, MA, August 18-22, 2002, abst. O835.

“The GABA(A) Receptor  $\alpha 1$  Subtype in the Ventral Pallidum Regulates Alcohol-Seeking Behaviors,” W. Yin, C. Zhang, H. June, and J.M. Cook, The 12<sup>th</sup> Neuropharmacology Conference, GABA(A) Receptors in Cellular and Network Excitability, Sheraton World Resort, Orlando, FL, October 31-November 2, 2002, poster P-D05.

“GABA(A)/ $\alpha 1$ , 5HT<sub>1A</sub>, Alcohol and Aggression in Rats,” S.L. Gourley, J.F. Debold, J.M. Cook and K.A. Miczek, Society for Neuroscience 32<sup>nd</sup> Annual Meeting, Orlando, FL, November 2-7, 2002, abstract 607.9.

“Role of GABA<sub>A</sub>/ $\alpha 5$  Receptor Mechanisms in the Discriminative Stimulus Effects of Ethanol in Squirrel Monkeys,” D.M. Platt, J.K. Rowlett, R.D. Spealman, J.M. Cook, and W. Yin, Alcohol Society Meeting, June, 2003.

“Biological Activity of the Tryprostatins and their Diastereomers on Human Carcinoma Cell Lines,” C.C. Zhang, S. Zhao, and J.M. Cook, 225<sup>th</sup> ACS National Meeting, New Orleans, LA, March 23-27, 2003 (abst MEDI-87).

“Studies of Memory Enhancing Agents which act *via* GABA<sub>A</sub>/BzR Receptors,” X. Li, H. Cao, C. Cook, F. Helmstetter, and J.M. Cook, 225<sup>th</sup> ACS National Meeting, New Orleans, LA, March 23-27, 2003 (abst MEDI-221).

“Enantiospecific, Stereospecific Total Synthesis of Alstonisine and Approach to the Total Synthesis of *N*<sub>b</sub>-Demethylalstophylline Oxindole,” Xiangyu Z. Wearing and J.M. Cook, 225<sup>th</sup> ACS National Meeting, New Orleans, LA, March 23-27, 2003 (abst ORG-412).

“Stereospecific, Enantiospecific Total Synthesis of the Sarpagine Indole Alkaloids (*E*)16-Epiaffinisine, (*E*)16-Epinormacusine B and Dehydro-16-epiaffinisine,” Jianming Yu and James M. Cook, 225<sup>th</sup> ACS National Meeting, New Orleans, LA, March 23-27, 2003, Organic Section (March 25<sup>th</sup>).

“ $\alpha 1$  Subunit Containing GABA<sub>A</sub> Receptor Antagonism and Alcohol Heightened Aggressive Behavior in Male Rats,” D.L. Zitzman, J.F. DeBold, S.L. Gourley, J.M. Cook, and K.A. Miczek, Neuroscience Meeting, New Orleans, LA, November 12-17, 2003, #852.5.

“The Reinforcing Effects of Amphetamine in the Selectivity Bred High Alcohol Drinking (HAD-1) and Low Alcohol Drinking (LAD-1) Rat Lines,” J.E. Woods, J. Cook, And H.L. June, Neuroscience Meeting, New Orleans, LA, November 12-17, 2003, #852.12.

“Rational Design of Indoleamine 2,3-Dioxygenase Inhibitors,” A. Martin, C. Austin, J. Mizdrak, V. MacFarlane, C. Zhang, W. Yin, X. Li, J. Jamie, R. Truscott, J. Cook, and R. Griffith, 19<sup>th</sup> Royal Australian Chemical Institute Conference, Lorne, Victoria, Australia, July 6-11, 2003.

“Elucidating Benzodiazepine Receptor Subtype Mechanisms Using Zolpidem and the Putative GABA<sub>A</sub>/ $\alpha 5$  Selective Agonist QH-ii-066,” A.N. Duke, D. Platt, R. Spealman, J.M. Cook, X. Li, and J. Rowlett, Sixty-fifth Annual Scientific Meeting of the College on Problems of Drug Dependence, Bal harbour, FL, June 14-19, 2003.

“The SAR and Possible Treatment of Alcohol Abuse with  $\alpha 1$  Selective Benzodiazepine/ GABA<sub>A</sub> Receptor Antagonists,” James Cook, Sixty-fifth Annual Scientific Meeting on the College on Problems of Drug Dependence, Bal Harbour, FL, June 14-19, 2003. Invited Lecture-Workshop (30 min).

“Search of Benzodiazepine/GABA(A) Subtype Selective Ligands that Reverse Alcohol Self-Administration,” W. Yin, C. Zhang, X. Li, H. June, and J.M. Cook, Sixty-fifth Annual Scientific Meeting of the College on Problems of Drug Dependence, Bal Harbour, FL, June 14-19, 2003.

“Approach Towards the Total Synthesis of Villalstonine,” J. Ma and J.M. Cook, 38<sup>th</sup> National Organic Symposium, Indiana University, Bloomington, IN, June 8-12, 2003, Abstract Number: B64

“Study of the Conformation of GABA<sub>A</sub>-Benzodiazepine Receptor Bivalent Ligands by Low Temperature NMR,” D. Han, F. Holger, X. Li, J.R. Deschamps, H. Cao, J. Ma, W. Yin, and J.M. Cook, 38<sup>th</sup> National Organic Symposium, Indiana University,

Bloomington, IN, June 8-12, 2003, Abstract Number: A76.

“General Approach for the Synthesis of Natural and Non-natural Products via the Tandem Pauson-Khand Reaction: Synthesis of 14 $\pi$  Annulenes and [5.8.5] Systems,” H. Cao, J. Flippen-Anderson and J. M. Cook, 228<sup>th</sup> ACS National Meeting, Philadelphia, PA, August 22-26, 2004 (abst. ORG-390).

“Stereocontrolled Total Synthesis of (-)-11-Methoxy-17-Epivincamajine and (-)-Vincamajinine,” X. Z. Wearing, Y. Yu, F. Rivas and J. M. Cook, Philadelphia, PA, August 22-26, 2004 (abst. ORG-391)

“GABA<sub>A</sub>/ $\alpha$ 1 Receptor Involvement in the Hyperphagic Effect of Benzodiazepines in Squirrel Monkeys,” A. Duke, D. Platt, J. M. Cook, W. Yin and J. K. Rowlett, 66<sup>th</sup> Annual Meeting of the College on Problems of Drug Dependence, San Juan, Puerto Rico, June 12-17, 2004, Poster Session III, Poster 32.

“GABA-A Receptor Mechanisms Underlying Motor Effects of Benzodiazepines in Monkeys,” S. C. Licata, D. M. Platt, A. N. Duke, J. M. Cook, P. V. V. S. Sarma, and J. K. Rowlett, Neuroscience Meeting, San Diego, CA October 22-28 (2004).

“The GABA(A)/ $\alpha$ 1 Receptor-Preferring Antagonist BCCt Does Not Attenuate Benzodiazepine-Induced Suppression of Locomotor Activity,” A. N. Duke, D. M. Platt, W. Yin, J. M. Cook and J. Rowlett, Neuroscience Meeting, San Diego, October 22-28 (2004).

“Search for Benzodiazepine/GABA(A) Subtype Selective Bivalent Ligands That Reverse Alcohol Self-Administration,” W. Yin, C. Zhang, S. S. V. V. Pullela, H. June and J. M. Cook, 227<sup>th</sup> ACS National Meeting, Anaheim, CA March 28 – April 1, 2004 (abst. MEDI 0286).

“Synthesis, in vitro Affinity and Efficacy of the First Bivalent  $\alpha$ 5 Subtype Selective BzR/GABA(A) Antagonist,” X. Li, W. Sieghart, G. R. Wenger and J. M. Cook. 227<sup>th</sup> ACS National Meeting, Anaheim, CA March 28 – April 1, 2004 (abst. MEDI 0348).

“Preparation of Analogs of the Cytotoxic Tryprostatins A and B. Study of Structure Activity Relationships as well as Irreversible Inhibitors for Mechanistic Work,” C. Zhang, J. Ma and J. M. Cook, 227<sup>th</sup> ACS National Meeting, Anaheim, CA March 28 – April 1, 2004 (abst. MEDI 0115).

“Study of the Structure-Activity Relationships of GABA(A)-Benzodiazepine Receptor Bivalent Ligands by Low Temperature NMR Spectroscopy and X-ray Analysis,” D. Han, F. H. Forsterling, X. Li, J. R. Deschamps, H. Cao, and J. M. Cook, 227<sup>th</sup> ACS National Meeting, Anaheim, CA March 28 – April 1, 2004 (abst. MEDI 0285).

“Development of Selective Ligands for Benzodiazepine Receptor Subtypes by Manipulating the Stereochemistry of Optically Active BzR Ligands,” X. Li, J. R. Atack, and J. M. Cook, 227<sup>th</sup> ACS National Meeting, Anaheim, CA March 28 – April 1, 2004 (abst. MEDI 0287).

“MEDI-0285 Also Chosen for Sci-Mix (represented).”

“MEDI-0287 Also Chosen for Sci-Mix (represented).”

Regiospecific, Enantiospecific Total Synthesis of the 12-Alkoxy-substituted Sarpagine Alkaloids, (+)-12-Methoxy-N<sub>a</sub>-Methylvellosimine, (+)-12-Methoxyaffinisine and (-)-Fuchsiaefoline,” H. Zhou, W. Yin and J. M. Cook, 227<sup>th</sup> ACS National Meeting, Anaheim, CA March 28 – April 1, 2004 (abst. ORGN 0444).

“Use of the Molybdenum Hexacarbonyl-Mediated Tandem Allenic Pauson-Khand Reaction for the Synthesis of a Dicyclo[a,e]pentalene,” H. Cao, J. L. Flippen-Anderson, J. L. Chen and J. M. Cook, 227<sup>th</sup> ACS National Meeting, Anaheim, CA March 28 – April 1, 2004 (abst. ORGN 0083).

“Mechanistic Study on the Asymmetric Pictet-Spengler Reaction. Evidence Supporting the Carbocationic Pathway,” D. Han, X. Liu, and J. M. Cook, 227<sup>th</sup> ACS National Meeting, Anaheim, CA March 28 – April 1, 2004 (abst. ORGN 0485).

“First Enantiospecific Total Synthesis of a Quaternary Voachalotine Alkaloid, (+)-Dehydrovoachalotine,” J. Yu, J. Ma, X. Wearing and J. M. Cook, 227<sup>th</sup> ACS National Meeting, Anaheim, CA March 28 – April 1, 2004 (abst. ORGN 0439).

“Progress Toward the Total Synthesis of the Antimalarial Bisindole Alkaloid Villastonine,” J. Ma, C. Zhang, J. Yu, and J. M. Cook, 227<sup>th</sup> ACS National Meeting, Anaheim, CA March 28 – April 1, 2004 (abst. ORGN 0443).

“Progress Toward the Enantiospecific Stereospecific Total Synthesis of N<sub>b</sub>-Demethylalstophylline Oxindole,” X. Z. Wearing and J. M. Cook, 227<sup>th</sup> ACS National Meeting, Anaheim, CA March 28 – April 1, 2004 (abst. ORGN 0483).

“General Approach to the Synthesis of Sarpagine/Macroline Bisindole Alkaloids,” X. Liao, H. Zhou and J. M. Cook, 227<sup>th</sup> ACS National Meeting, Anaheim, CA Mar. 28 – Apr. 1, 2004 (abst. ORGN 0442).

“Stereoselective Total Synthesis of (-)-Vincamajinine and (-)-11-Methoxy-17-epivincamijine,” X. Z. Wearing, J. Yu and J. M.

Cook, 227<sup>th</sup> ACS National Meeting, Anaheim, CA March 28 – April 1, 2004 (abst. ORGN 0484)

“ORGN-0483 Also chosen for Sci-mix (represented).”

“General Approach for the Synthesis of Natural and Non-natural Products via the Tandem Pauson-Khand Reaction. Synthesis of 14 $\pi$  Annulenes and [5.8.5] Systems,” H. Cao, J. Flippen-Anderson and J. M. Cook, 36<sup>th</sup> Great Lakes Regional ACS Meeting, Peoria, IL, October 17-20 (2004), abstract 294.

“Synthesis, In Vitro Affinity and Efficacy of the First Bivalent Alpha 5 Subtype Selective BzR/GABA(A) Antagonist,” W. Yin, F. Rivas, R. Furtmueller, X. Li, W. Sieghart, G. Wenger and J. M. Cook, Neuroscience 2004, San Diego, CA, October 23-27 (2004), Tue, Posterboard MM31.

“Alcohol Drinking in Baboons: Effects of 3-Propyloxy Beta-Carboline,” E. M. Weerts, B. J. Kaminski, W. Yin, P.V.V.S. Sarma and J. M. Cook, College on Problems of Drug Dependence, June 19-25, Orlando, FL (2005).

“Neurochemical and Behavioral Effects of Novel 8-Acetylenyl Analogs of Triazolam,” S. Licata, D. M. Platt, J. M. Cook, H. Zhou, P.V.V.S. Sarma, R. Fürtmueller, W. Sieghart, S. Huck and J. K. Rowlett, 2005 Neuroscience Meeting, November 12-17, Washington, DC (2005).

“General Approach to the Synthesis of Ring-A Alkoxy Substituted Indole Alkaloids via the Asymmetric Pictet-Spengler Reaction,” H. Zhou, X. Liao, J. Ma, A. Wearing and J. M. Cook, The 21<sup>st</sup> Mona Symposium on Natural Products and Medicinal Chemistry, Mona Jamaica, January 3-6 (2006).

“General Approach to the Synthesis of Ring-A Alkoxy Substituted Indole Alkaloids via the Asymmetric Pictet-Spengler Reaction,” J. M. Cook, H. Zhou, X. Liao, J. Ma, and P.V.V.S. Sarma, Abstracts, 37<sup>th</sup> Great Lakes Regional Meeting of the American Chemical Society, Milwaukee, WI, May 31-June 2, 2006, GLRM-307.

“Electronic Effects On the Cis to Trans Epimerization of Pictet-Spengler Produced 1,2,3,4-Tetrahydro- $\beta$ -Carbolines,” M. L. Van Linn, D. Han, H. J. Kumpaty, F. H. Forsterling, J.R. Deschamps, J. M. Cook, Abstracts of Papers, 232<sup>nd</sup> ACS National Meeting, San Francisco, CA, Sept. 10-14, 2006, ORGN-832.

“Synthesis of Optically Active Subtype Selective BZR Ligands,” S. Huang, T. Clayton, M. Dai, R. Edwankar, C. Sawant, J. M. Cook, Abstracts of Papers, 232<sup>nd</sup> ACS National Meeting, San Francisco, CA, Sept. 10-14, 2006, MEDI-502.

“Search For Benzodiazepine/GABA(A) Subtype Selective Ligands That Reverse Alcohol Self-Administration” M. L. Van Linn, E. Weerts, D. Platt, W. Yin, P.V.V.S. Sarma, J. M. Cook, Abstracts, 37<sup>th</sup> Great Lakes Regional Meeting of the American Chemical Society, Milwaukee, WI, May 31-June 2 2006, GLRM-156.

“The SAR Study of Benzodiazepine Receptor Bivalent Ligands by Low Temperature NMR Spectroscopy and X-Ray Analysis,” S. Huang, T. Clayton, M. Dai, W. Yin, J. Ma, R. Edwankar, C. Sawant, M. Van Linn, Y. Teng, M. Johnson, H. F. Forsterling, and J. M. Cook, Abstracts, 37<sup>th</sup> Great Lakes Regional Meeting of the American Chemical Society, Milwaukee, WI May 31 – June 2, 2006, GLRM-155.

“Enantiospecific Synthesis of (+)-N<sub>a</sub>-Methyl-pericyclivine, (-)-N<sub>a</sub>-Methylakuammidine, (+)-10-Methoxy-N<sub>a</sub>-Methylpericyclivine and 10-Hydroxy-N<sub>a</sub>-Methylpericyclivine,” P.V.V.S. Sarma, R. V. Edwankar, C. R. Edwankar, S. Huang, J. M. Cook, Abstracts, 37<sup>th</sup> Great Lakes Regional Meeting of the American Chemical Society, Milwaukee, WI May 31-June 2, 2006, GLRM-143.

“General Approach to the Synthesis of Oxygenated Bisindole Alkaloids,” M. Dai, S. Huang, J. M. Cook, Abstracts, 37<sup>th</sup> Great Lakes Regional Meeting of the American Chemical Society, Milwaukee, WI, May 31-June 2, 2006, GLRM-142.

“General Approach Towards the Total Synthesis of 9-Methoxy Indole Alkaloids: 9-Methoxygeissoschizol, 9-Methoxy-N<sub>b</sub>-Methyl-geissoschizol and the Opioid Analgesic Active Mitragynine,” J. Ma, J. M. Cook, Abstracts, 37<sup>th</sup> Great Lakes Regional Meeting of the American Chemical Society, Milwaukee, WI, May 31-June 2, 2006, GLRM-141.

“Progress Towards the Total Synthesis of the Opioid Analgesic Indole Alkaloids Mitragynine and 7-Hydroxymitragynine as well as the Antimalarial Bisindole 10-Hydroxysambaresine,” J. Ma, W. Yin, J. M. Cook, Abstracts of Papers, 231<sup>st</sup> ACS National Meeting, Atlanta, GA, March 26-30, 2006, ORGN-174.

“General Approach for the Synthesis of 12-Methoxy Substituted Sarpagine Indole Alkaloids Including 12-Methoxy-N<sub>b</sub>-Methyl-voachalotine and Fuschsiaefoline,” H. Zhou, J. M. Cook, Abstracts of Papers, 231<sup>st</sup> ACS National Meeting, Atlanta, GA, March 26-30, 2006, ORGN-173.

“Total Synthesis of Antileishmanial and Antibacterial Alkaloids (+)-N<sub>a</sub>-Methylpericyclivine and (-)-N<sub>a</sub>-Methylakuammidine as well as the Ring A-Oxygenated Natural Products, (+)-10-Methoxy N<sub>a</sub>-Methylpericyclivine and 10-Hydroxy N<sub>a</sub>-Methylpericyclivine,” P.V.V.S. Sarma, J. M. Cook, Abstracts of Papers, 231<sup>st</sup> ACS National Meeting, Atlanta, GA, March 26-30, 2006, ORGN-172.

- “Modulation of Alcohol-heightened Aggression in Mice by  $\alpha$ -5-Containing GABA(A) Receptors,” S. Faccidomo, J. G. Maggin, S. Melief, T. Clayton, J. M. Cook, K. A. Miczek, Society for Neuroscience, October, 2006, Atlanta, GA.
- “Differential Sedative and Motor Effects of GABA(A) Subtype Selective Compounds in Rhesus Monkeys,” A. Duke, D. Platt, S. Licatta, R. Edwankar, S. Huang, J. M. Cook, R. Furtmueller, W. Sieghart, and J. K. Rowlett, Society for Neuroscience, October, 2006, Atlanta, GA.
- “Attenuation of Motor and Sedative-like Effects of Alparzolam by Flumazenil and BCCt in Rhesus Monkeys,” A. Duke, D. M. Platt, J. M. Cook, W. Yin and J. K. Rowlett, CPDD 68<sup>th</sup> Annual Meeting, June 17-22, 2006, Scottsdale, AZ.
- “Synthesis, Pharmacological Studies, and Molecular Modeling of Novel 1,3-Diazapinium Chlorides,” J. A. Grant, Y. A. Jackson, M. Gossel-Williams, T. Clayton, J. M. Cook, Latest Trends in Organic Synthesis, Brock University, St.Catherines, Ontario, CA, 2006.
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“MK-801-Induced Hyperlocomotion in Rats is Affected by Modulation of  $\alpha 5$ -Containing GABA Receptors”, T. Timic, S. Joksimovic, M.M. Poe, J. Ramerstorfer, P. Biawat, T. Radulovic, B. Roth, W. Sieghart, J.M. Cook, M. Savic, 26<sup>th</sup> ECNP Congress, Barcelona, Spain, Oct. 2013.

“PWZ-029 Alleviates NMDA Receptor Antagonist-Induced Deficits in Water Maze and Object Recognition Test in the Rat: Implications for the Treatment of Cognitive Impairment in Schizophrenia”, S. Joksimovic, A. Obradovic, T. Timic, T.



- Radulovic, P. Biawat, J. Kovacevic, M. Milic, B. Batinic, J. Cook, M. Savic, 26<sup>th</sup> ECNP Congress, Barcelona, Spain,, Oct. 2013.
- “Role of Alpha 3 GABH<sub>A</sub> Receptor Modulation in the Anti-Conflict Effects of Benzodiazepine – Type Drugs in Monkeys,” Sawyer, E.; Fischer, B.; Meng, Z.; Poe, M.; Namjoshi, O.; Cook, J.; Rowlett, J., presented at The CPDD Meeting, San Diego, CA. Hilton Bayfront Hotel, June 17-21 (2013).
- “Little Role for Alpha1 GABA-A, Receptor Subtypes in the Reinforcing Effects of Ethanol in Rhesus Monkeys,” Platt D. M., Moran C., Sawyer E., Sirbu M., Van Linn M., Namjoshi O., Clayton T., and Cook J.M., *Alcohol Clin Exp Res* 37:247A. Research Society on Alcoholism 65<sup>th</sup> Annual Meeting, Orlando, FL, 2013.
- “Synthesis of Natural Products and Related Heterocyclic Compounds. Search For Agents to Treat Neuropathic Pain Epilepsy and Anxiety Disorders as well as Simple Molecules to Treat TB and MRSA Infections,” Plenary Lecture, Cook, J.; Edwankar, C.; Poe, M.; Tiruveedhula, P.; Witzigmann, C., 25<sup>th</sup> Mona Symposium on Natural Products and Medicinal Chemistry, UWI, Mona Kingston Jamaica, Jan. 5-9, 2014.
- “Behavioral Effects of the Novel, Benzodiazepine Positive Modulator SH-053-2’F-S-C H<sub>3</sub> in an Immune-Mediated Neurodevelopmental Disruption Model,” Richetto, J.; Labouesse, M.; Poe, M.M.; Cook, J.; Graie, A.; Riva, M.; Meyer, U, presented at the SIRS Congress (2014).
- “Chiral Subtype Selective Imidazobenzodizepines Important as Potential Agents to Treat Schizophrenia,” Poe, M.; Radditz, N.; Baker, D.; Cook, J., 247<sup>th</sup> ACS National Meeting, Dallas, TX, March 16-20 (Abst.MEDI 282), 2014.
- “Design and Synthesis of Novel Small Molecule Stilbenes with Activity Against Gram-Positive Bacteria and Mycobacterium,” Witzigmann, C.; Tiruveedhula, V.; Monte, A.; Schwan, W.; Cook, J.M. 247<sup>th</sup> ACS National Meeting, Dallas, TX, March 16-20 (Abst.MEDI 266), 2014.
- “Design and Synthesis of Novel Antimicrobials for the Treatment of Drug Resistance Bacterial Infections, Including *M. Tuberculosis*,” Tiruveedhula, V.; Witzigmann, C.; Rott, M.; Schwan, W.; Monte, A.; Cook, J.M. 247<sup>th</sup> ACS National Meeting, Dallas, TX, March 16-20 (Abst.MEDI 263), 2014.
- “Selective Pharmacologic Targeting of the GABA<sub>A</sub>α4 Subunit in Airway Smooth Muscle to Alleviate Bronchospasm,” Gene T. Yocum, Ryo Wakita, Michael R. Stephen, James M. Cook, Charles W. Emala, George Gallos.
- “Selective Pharmacologic Targeting of the GABA-A Receptor α4 Subunit in Airway Smooth Muscle to Alleviate Bronchoconstriction” Yocum, G.; Gallos, G.; Ernst, M.; Cook, J.; Emala, C. Anesthesiology 2015, San Diego, California, October 24-28, 2015.
- “Reinforcing Effects of Ethanol are Attenuated by Alpha 5, GABA-A Receptor Inverse Agonists in Monkeys,” Ruedi-Bettschen, D.; Rallapalli, S.; Clayton, T.; Cook, J.; Platt, D.M. 38<sup>th</sup> Annual Research Society on Alcoholism Scientific Meeting, San Antonio, Texas, June 20-24, 2015.
- “A Novel Trojan Horse for IN-vivo Sensitivity Testing of Medulloblastoma Therapies,” Sengupta, S.; Jones, O.; galligaris, Cook. J.; Peo, M.; Methuku, K.; Archer, T.; Francois, J.; Tranchese, F.; Pomeroy, S.; Agar, N.; Langer, R.; 19<sup>th</sup> Society of Neuro-oncology Meeting, Miami, FIA, Nov. 13-16 (2014).
- “Design and Synthesis of Novel β-Carbolines as a GABA<sub>A</sub> Subtype Selective Agent for the Treatment of Alcohol Abuse,” Tiruveedhula, V.; Menthuka, K.; Warnock, K.; June, H.; Cook, J.M., 248<sup>th</sup> ACS National Meeting, San Francisco, CA, August 10-14 (Abst. MEDI 0128), 2014.
- “Inducing Airway Smooth Muscle Relaxation by Targeting the Restricted α-Subunit Repertoire of GABA<sub>A</sub> Receptors Using MD-45,” Stephen, M.J.; Jahan, R.; Gallos, G.; Emala, C.W.; Cook, J.M., 248<sup>th</sup> ACS National Meeting, San Francisco, CA, August 10-14 (Abst. MEDI 057), 2014.
- “Stereospecific Total Synthesis of the Indole Alkaloid Ervindidine: Establishment of the C-6 Hydroxyl Stereochemistry,” Verma, R.S.; Rallapalli, S.K.; Verma, A.R.; Cook, J.M., 248<sup>th</sup> ACS National Meeting, San Francisco, CA, August 10-14 (Abst. MEDI 433), 2014.
- “Effects of Hz-166, a Novel α2 and α3 Subunit-Containing GABA<sub>A</sub> Receptor Agonist, on Inflammatory Pain and Operant Behavior in Mice,” Fischer, F.; Kroll, C.; Poe, M.; Cook, J.M., Presented at The CPDD 76<sup>th</sup> Annual Scientific Meeting, June 14-19, 2014, Caribe Hiltonm, San Juan, Puerto Rico.
- “Tonic Inhibition in the Central Amygdala Controls Anxiety Behavior,” Botta, P.; Kasugal, Y.; Demmou, L.; Xu, C.; Rudolph, U.; Ferraguti, F.; Luthi, A.; Poe, M.M.; Cook, J., PhD Conference in Europe, 2014.
- “Examining the Effect of an α5 Subunit-Containing GABA<sub>A</sub> Receptor-Positive Allosteric Modulator on UCMS-Induced Emotionality Behavior in the Mouse,” Meyer, U.; Poe, M.M.; Cook, J.M.; *et al.* Presented at Conference in Europe, 2014.

“Design and Characterization of a Novel System XC-Substrate,” Raddatz, A.; Neary, M.; Hjelmhaug, J.; Edwarde, M.; Mueller, C.; Xie, X.; Cook, J.; Fucks-Lokensgard, R.; Mantsch, J.; Lobner, D.; Baker, D., Presented at the Fall Meeting of The Society for Neuroscience, 2014.

“Identifying New Treatments for the Brain,” “Electrophysiological Assay and Generation of a Stable Recombinant Cell Line,” Yuan, N.; Poe, M.; Witzigmann, C.M.; Sieghart, W.; Cook, J.M.; Arnold, A.L.; Gordon Research Conference-Ion Channels, South Hadley, MA, July 8<sup>th</sup>, 2014.

“Development of High Throughput Assays to Identify New Alpha Subtype-Selective GABA(A) Receptor Modulators to Treat Anxiety and Depression Disorders,” Yuan, N.; Cook, J.M.; Arnold, A.L.; Gordon Research Seminar- Ion Channels, South Hadley, MA, July 6<sup>th</sup>, 2014 (oral).

“The First Enantiospecific Total Synthesis of Macrosalpine Chloride and Progress Towards the Total Synthesis of Macropine A, B and C,” Rahman, M.; Jahan, R.; Edwankar, R.; Deschamps, J.; Cook, J.M.; 249<sup>th</sup> ACS National Meeting, Denver, Co, March 22-26, (Abst. ORGN 164), 2015.

“Novel Strategy For the Treatment of Asthma by Targeting GABA<sub>A</sub> Receptors in the Lung,” Jahan, R.; Stephen, M.R.; Gallos, G.; Emala, C.; Cook, J.M.; 249<sup>th</sup> ACS National Meeting, Denver, CO, March 22-26, (Abst. MEDI 101), 2015.

“Development of  $\alpha_6\beta_3\gamma_2$  Subtype Selective Ligands for GABA<sub>A</sub> Receptors,” Verma, R.; Witzigmann, C.; Cook, J.M.; 249<sup>th</sup> ACS National Meeting, Denver CO, March 22-26, (Abst. MEDI 275), 2015.

“Design and Synthesis of Novel  $\beta$ -Carbolines as a Potential Anti-Alcohol Agents,” Tiruveedhula, V.V.N. P. B.; Methuku, R.; Warnock, K.T.; June, H.L.; Cook, J.M.; 7<sup>th</sup> Yao Yuan Biotech-Pharma Symposium, University of Illinois at Chicago, Chicago, IL, April 18<sup>th</sup>, 2015 (2015).

“Targeting the Restricted  $\alpha$ -Subunit Repertoire of Bz/GABA<sub>A</sub> Receptors: A Drug Strategy for Bronchoconstrictive Disorders,” Stephen, M.; Jahan, R.; Gallos, G.; Emala, C.; Ernst, M.; Sieghart, W.; Cook, J.M.; 7<sup>th</sup> Yao Yuan Biotech—Pharma Symposium, University of Illinois at Chicago, Chicago, IL, April 18, 2015 (2015).

“Behavioral Effect of Novel Benzodiazepine Analog Methyl 8-Ethynyl-6-(pyridine-2-yl)-4H-benzo{f}imidazo{1,5-a}{1,4}diazepine-3-carboxylate (MP-III-024),” Fischer, B.D.; Hamade, B.Z.; Poe, M.M.; Cook, J.M.; Annual meeting of the American Society for Pharmacology and Experimental Therapeutics: Boston, MA, 2015.

“Reinforcing Effect of Ethanol are Attenuated by Alpha5 GABA-A Receptor Inverse Agonists in Monkeys,” Ruedi-Bettschen, D.; Rallapalli, S.; Clayton, T.; Cook, J.M.; Platt, D.M.; Presented at the RSA Meeting, 2015.

“Selective Pharmacologic Targeting of the GABA  $\alpha_4$  Subunit in Airway Smooth Muscle to Alleviate Bronchospasm,” Yocum, G.; Wakita, R.; Stephen, M.; Cook, J.; Emala, C.; Gallos, G.; Presented at Am Thoracic Meeting, 2015.

“Evidence of Sedative Effects of Benzodiazepines Involving Unexpected GABA Receptor Subtypes,” Rowlett, J.; Duke, A.; Platt, D.; Nasjoshi, O.; Poe, M.; Tiruveedhula, P.; Cook, J.; 77<sup>th</sup> Annual Meeting of The College on Drug Dependence, June 13th-19<sup>th</sup>, Phoenix, Az; Poster Session IV, paper 5 (2015).

“Reduction of Alcohol Self-Administration by 3-ISO-PBC,” Weerts, E.; Tiruveedhula, V.; Cook, J.M.; CPPD Meeting, June 2016.

“Novel  $\alpha_5$  Selective Benzodiazepine Site Ligands,” Rehman, S.; Puthenkalam, R.; Scholze, P.; Steudle, F.; Poe, M.; Li, G.; Cook, J.; Savic, M.; Stamenic, T.; Emala, C.; Gallos, G.; Ernst, M.; *Austrian Society of Neurosciences Meeting*, Austria (2015).

“Enantiospecific Stereospecific Total Synthesis of a Series of C-19 Methyl Substituted Sapagine/Macroline Alkaloids via an Efficient Method of Copper-Mediated Enolate Driven Cross-Coupling Process,” Cook, J.M.; Rahman, Md.; 26<sup>th</sup> Mona Symposium, Mona, UWI JA Jan 3-Jan 7, 2016.

“Design and Regiospecific Synthesis of 3-Substituted  $\beta$ -carbolines as a GABA<sub>A</sub> Subtype Selective Agents for the Treatment of Alcohol Abuse”, V. V. N. Phani Babu Tiruveedhula, Kaitlin Warnock, Harry June, Xenia Simeone, Margot Ernst, Marjorie C. Gondre-Lewis, James M Cook. 250<sup>th</sup> ACS National Meeting, Boston, Massachusetts, August 16-20, (Abst. MEDI 433), 2015.

“Imidazobenzodiazepines for Improving  $\alpha_5$ -GABA<sub>A</sub>R Subtype Selectivity and their Pharmacological Relevance,” M.M. Poe, G. Gallos, R. Puthenkalam, M.M. Savic, C.W. Emala Sr., M. Ernst, J.M. Cook; 250<sup>th</sup> ACS National Meeting, Boston, MA, August 16-20, (Abst. MEDI 70), 2015.

“Selective Targeting of  $\alpha_4\beta_3\gamma_2$  GABA<sub>A</sub> Receptors on Airway Smooth Muscle as a Novel Strategy to Treat Asthma”, Michael Rajesh Stephen, Rajwana Jahan, George Gallos, Charles W. Emala, Margot Ernst, Werner Sieghart, and James M. Cook 250<sup>th</sup> ACS National Meeting, Boston, Massachusetts, August 16-20, (Abst. MEDI 121), 2015.

“First Total-Synthesis of Macroline Indole Alkaloids Macrocarpine A-G via an Efficient, Enolate-Driven, Copper-Mediated Cross-Coupling Process” M. Toufiquir Rahman; Jeffrey R. Deschamps; James M. Cook. ACS Milwaukee Meeting, Carroll University, WI, March 31, 2016.

“Novel Strategy for The Treatment of Asthma by Targeting the  $\alpha 4$  Subunit of GABA<sub>A</sub> Receptors in Airway Smooth Muscle”. Rajwana Jahan, Michael Stephen, Gene T. Yocum, George Gallos, Yi Zhang, Revathi Kodali, Zdravko Varagic, Roshan Puthenkalam, Margot Ernst, Leggy A. Arnold, Douglas Stafford, Charles Emala, James M. Cook. ACS Milwaukee Meeting, Carroll University, WI, March 31, 2016.

“Novel Strategy for The Treatment of Asthma by Targeting the  $\alpha 4$  Subunit of GABA<sub>A</sub> Receptors in Airway Smooth Muscle”. Rajwana Jahan, Michael Stephen, Gene T. Yocum, George Gallos, Yi Zhang, Revathi Kodali, Zdravko Varagic, Roshan Puthenkalam, Margot Ernst, Leggy A. Arnold, Douglas Stafford, Charles Emala, James M. Cook. The 8<sup>th</sup> Yao Yuan Biotech-Pharma Symposium, Chicago, IL, April 23<sup>rd</sup> (Poster # 7), 2016. [Poster and Talk]

“Synthesis of Novel  $\beta$ -carboline as a GABA<sub>A</sub> Subtype Selective Agents for the Treatment of Alcohol Abuse. Regiospecific Solution to the Problem of 3,6-Disubstituted  $\beta$ - and Aza- $\beta$ -carboline Specificity”, V. V. N. Phani Babu Tiruveedhula, Kaitlin Warnock, Harry June, Xenia Simeone, Margot Ernst, Marjorie C. Gondre-Lewis, James M. Cook. The 8<sup>th</sup> Yao Yuan Biotech-Pharma Symposium, Chicago, IL, April 23<sup>rd</sup> (Poster # 10), 2016.

“Synthesis of Novel  $\beta$ -carboline as a GABA<sub>A</sub> Subtype Selective Agents for the Treatment of Alcohol Abuse. Regiospecific Solution to the Problem of 3,6-Disubstituted  $\beta$ - and Aza- $\beta$ -carboline Specificity”, V. V. N. Phani Babu Tiruveedhula, Kaitlin Warnock, Harry June, Xenia Simeone, Margot Ernst, Marjorie C. Gondre-Lewis, James M. Cook. 251<sup>st</sup> ACS National Meeting & Exposition, San Diego, CA, March 13-17, (Abst. MEDI 111), 2016.

“First Total-Synthesis of Macroline Indole Alkaloids Macrocarpine A-G via an Efficient, Enolate-Driven, Copper-mediated Cross-coupling Process” M. Toufiquir Rahman; Jeffrey R. Deschamps; James M. Cook. 251<sup>st</sup> ACS National Meeting, San Diego, CA, March 13-17, (Abst. ORGN 206), 2016.

“Search for Water Soluble  $\alpha$ -6 Bz/GABA(A) Receptor Subtype Selective Ligands in Order to Determine Their *in vivo* Activity” Ranjit S. Verma, Daniel Knutson, Christopher M. Witzigmann, Matheus A. Meirelles Margot Ernst, Werner Sieghart and James M. Cook. 251<sup>st</sup> ACS National Meeting, San Diego, CA, March 13-17, (Abst. ORGN 320), 2016.

"Potential Novel Targets for Schizophrenia: Stereospecific GABAA Receptor Subtype Selective Imidazobenzodiazepines" Guanguan Li; Michael M. Poe; Nicholas J. Raddatz; David A. Baker; Margot Ernst; James M. Cook. 251<sup>st</sup> ACS National Meeting, San Diego, CA, March 13-17, (Abst. MEDI 325), 2016.

"Stereospecific Total Synthesis of Macroline-Related Oxindoles: Macrogentine and Alstonoxine" G.O. Fonseca; M. Ahmed Khan; J. Deschamps; J.M. Cook. 251<sup>st</sup> ACS National Meeting, San Diego, CA, March 13-17, (Abst. ORGN 226), 2016.

“Novel Strategy for The Treatment of Asthma by Targeting the  $\alpha 4$  Subunit of GABA<sub>A</sub> Receptors in Airway Smooth Muscle”. Rajwana Jahan, Michael Stephen, Gene T. Yocum, George Gallos, Yi Zhang, Revathi Kodali, Zdravko Varagic, Roshan Puthenkalam, Margot Ernst, Leggy A. Arnold, Douglas Stafford, Charles Emala, James M. Cook. 251<sup>st</sup> ACS National Meeting, San Diego, CA, March 13-17, (Abst. MEDI 167), 2016.

“Benzodiazepine- GABA<sub>A</sub>  $\alpha 1$  Antagonist 3-Iso-PBC Selectively Reduce alcohol Self- Administration”, E. M. Weerts; A. F. Holtyn; VVNPB Tiruveedhula and J. M. Cook presented at The ISBRA ESBRA joint meeting in Europe, Sept. 2-5 (2016).

“Different Benzodiazepines Seen to Interact Differently with GABA<sub>A</sub> Receptors”, P. Scholze; A. Elgarf; F. Steudle; G. Li; J.M. Cook; M. Ernst; Society for Neuroscience (2016).

“Effects of Ro5-4864 on Methamphetamine Self- Administration in Male and Female Rats”, G. Guerin; S. Harold; S. Porter; C. Schmoutz; J.M. Cook; G. Li; N. Goeders; Society for Neuroscience (2016).

“Targeting The Immune System with Subtype- Selective GABA<sub>A</sub> Receptor Modulators to Alleviate Symptoms”, A. Neiman; G. Forkuo; M. Guthrie; N. Yuan; O.B. Yu; R. Kodali; R. Jahan; M.R. Stephen; M.M. Poe; B. Hartzler; C. W. Emala; J.M. Cook; D.C. Stafford; L. A. Arnold; AAI Annual Meeting, 2016.

“Pharmacodynamics and Pharmacokinetics of Novel GABA<sub>A</sub>  $\alpha$ 4 Subunit Selective Ligands that Treat Bronchoconstriction”, G. Yocum; Y. Zhang; G. Furkuo; M. Guthrie; A. Youmans; R. Jahan; M. Stephen; D.C Stafford; James Cook; Alexander Arnold and Charles Emala; American Respiratory Society Meeting (2016).

“Attaining *in vivo* Selectivity of Positive Modulation of  $\alpha$ 3 GABA<sub>A</sub> Receptors in Rats: A Hard Task”, Batinic B.; Stankovio, T.; Poe, M.M.; Cook, J. M.; Savic, M.M.; *European Society For Neuroscience* (2016).

“Behavioral Effects of Novel GABAA Receptors Positive Allosteric Modulator in Rats”, Lakeisha, Lewter; J.M. Cook; Jun-Xu Li; BBC Meeting, April 4-6, 2016, San Antonio, Texas.

“Reduction of Alcohol Self-administration by 3-Iso-PBC”, E. Weerts, V.V.N.P.B. Tiruveeddhulaad, J.M. Cook, CPDD 78<sup>th</sup> Annual Meeting La Quinta Resort and Club, Palm Springs, CA, June 11-16, 2016.

“Novel  $\alpha$ 5 Selective Benzodiazepine Site ligands”, S. Rehman, R. Puthenkalam, P. Scholze, F. Steudle, M. Poe, G. Li, J.M. Cook, M. Savic, T. Stamenic, C. Emala, G. Gallos, M. Ernst, Medical Neuroscience Cluster, IG Neuropsychopharmacology (2016).

“A Novel GABA(A) Receptor  $\alpha$ 5 Subunit Selective Allosteric Modulator That Does Not Cross The Blood Brain Barrier Relaxes Airway Smooth Muscle Contracted with Diverse Ligands”, G. Yocum, P. Yim, Y. Zhang, J. Perez-Zoghbi, A. Arnold, J. Cook and C. Emala, American Thoracic Society (2017).

“First Total Synthesis of Macroline Indole Alkaloids Macrocarpine A-G via an Efficient, Enolate-Driven Copper- Mediated Cross-Coupling Process”, M. Toufiquir Rahman, Jeffrey R. Deschamps, James M. Cook; ACS Milwaukee Meeting, Carrol University, WI, March 31, 2016.

“Novel Strategy for The Treatment of Asthma by Targeting the  $\alpha$ 4 Subunit of GABAA Receptors in Airway Smooth Muscle”. Rajwana Jahan, Michael Stephen, Gene T. Yocum, George Gallos, Yi Zhang, Revathi Kodali, Zdravko Varagic, Roshan Puthenkalam, Margot Ernst, Leggy A. Arnold, Douglas Stafford, Charles Emala, James M. Cook; ACS Milwaukee Meeting, Carrol University, WI, March 31, 2016.

“Novel GABAAR Agonists Under the Preclinical Development for the Treatment of Asthma” Rajesh, S. M., Jahan, R., Yocum, G. T., Zhang, Y., Varagic, Z., Puthenkulam, R., Gallos, G., Emala, C. W., Margot Ernst, Arnold, L. A., Stafford, D., and Cook. J. M. 5th Annual International Chemical Biology Society Conference, Madison WI, October 24-26, (Abst. 24), 2016.

“Novel Strategy for The Treatment of Asthma by Targeting the  $\alpha$ 4 Subunit of GABA(A) Receptors in Airway Smooth Muscle” Rajwana Jahan, Michael Stephen, Gene T. Yocum, George Gallos, Yi Zhang, Revathi Kodali, Zdravko Varagic, Roshan Puthenkalam, Margot Ernst, Leggy A. Arnold, Douglas Stafford, Charles Emala, James M. Cook. 5th Annual International Chemical Biology Society Conference, Madison WI, October 24-26, (Abst. 25), 2016.

"Enantiospecific, Stereospecific Total Synthesis of a Series of C-19 Methyl Substituted Sarpagine/Macroline Indole Alkaloids via an Efficient Method of Copper-Mediated Enolate-Driven Cross-Coupling Process" Rahman, M.T, Deschamps, J.R., Cook, J.M. 5th Annual International Chemical Biology Society (ICBS) Conference, Madison, WI, October 24-26, (Abst. 108), 2016.

“The Search for Selective and Water Soluble  $\alpha$ 6 Bz/GABA(A) Receptor Subtype Selective Ligands in Order to Determine their *in vivo* Activity” Ranjit Verma, Daniel Knutson, Christopher Witzigmann, James Cook, L.C. Chiou, Margot Ernst. 5th Annual International Chemical Biology Society (ICBS) Conference, Madison, WI, October 24-26, (Abst. 36), 2016.

"Synthesis of Nonsedating and Selective  $\alpha$ 2- or  $\alpha$ 3-GABAAR Agonists as Potential Novel Anxiolytics against Neuropathic Pain" Guanguan Li, Kashi R. Methuku, Michael M. Poe, Jeffrey M. Witkin, Jeffrey M. Schkeryantz, James M. Cook. 5th Annual International Chemical Biology Society Conference, Madison WI, October 24-26, (Abst. 121), 2016.

“Novel Deuterated GABAAR- $\alpha$ 6 Subtype Selective Ligands with Improved Metabolic Stability. Targeting Trigeminal Orofacial Pain, Neuropsychiatric Disorders, & Depression” Knutson, D. E., Verma, R. S., Stephen, M. R., Kodali, R., Arnold, L. A., Cook, J. M., Mihovilovic, M. D., Wimmer, L., Ernst, M., Sieghart, W. 5th Annual International Chemical Biology Society Conference, Madison WI, October 24-26, (Abst. 36), 2016.

“Alpha5 GABAA Receptors, a Potential Therapeutic Target for the Treatment of Alcohol Related Disorders: Evidence from



Rodent Studies” Chandler, C.; Reeves-Darby, J.; Jones, S.; Rahman, M.; Li, G.; Cook, J.; Platt, D. M, 40th Annual RSA Scientific Meeting, Denver, CO, (Poster No. 068, Abst. No. 397), June 2017.

“General strategy for the total synthesis of C-19 methyl substituted sarpagine/macroline indole alkaloids including macrocarpines A-G, peraksine, and dihydroperaksine” Rahman, M. T.; Deschamps, J.R.; Cook, J.M, Oral Presentation (ORGN 654), 253rd ACS National Meeting, San Francisco, CA, April 2017.

“General Strategy for the Total Synthesis of C-19 Methyl Substituted Sarpagine/Macroline Indole Alkaloids” Rahman, M. T.; Deschamps, J. R.; Cook, J. M., 34th H. C. Brown Lectures in Organic Chemistry, Department of Chemistry, Purdue University, (Poster # 50), April 2017.

“Pro-cognitive and neurotrophic effects of a novel molecule enhancing  $\alpha 5$ -GABA-A receptor function in adult or aged mice”, Sibille, E.; Cook, J.; Li, G.; Knutson, D.E; Mian, Y.; Mondal, P.; David, D.J.; Mendez-David, I.; Guilloux, J-P.; Prevot, T.D., ACNP, Orlando, Dec 2019.

#### F. **Invited Lectures Presented at Universities, Industry, etc.**

Carthage College, "Hallucinogenic Principles Employed by Yanomamo Indians of South America," 1973.

Carroll College, "Hallucinogenic Principles Employed by Yanomamo Indians of South America," Fall, 1973.

Ripon College, "Synthesis of Antihypertensive Agents," 1974.

Lakeland College, "Electrophilic-Nucleophilic Additions to Indole Double Bonds," 1974.

Lewis University, "The Use of N-Oxides in the Biomimetic Synthesis of Indole Alkaloids," 1974.

Calvin College, "Synthesis of Antihypertensive Agents," 1975.

National Institutes of Health, *Alstonia* Alkaloids: Structures, Synthesis and Relation to Antihypertensive Agents," 1975.

St. Norberts College, "Isolation and Use of Psychoactive Drugs by the Yanomamo Indians of South America," 1976.

University of Wisconsin-Eau Claire, "The Synthesis of Cyclopentanoid Compounds," 1976.

University of Wisconsin-Parkside, "Isolation and Use of Psychoactive Drugs by the Yanomamo Indians of South America," 1976.

Western Illinois University, "Synthetic and Stereochemical Studies of Disubstituted- 1,2,3,4- tetrahydro- $\beta$ -Carbolines on the Road to Potential Antihypertensive Agents." National Institutes of Health, Bethesda, Maryland, plenary lecture at the Symposium of Bioorganic and Synthetic Chemistry entitled, "Reactions of Dimethyl  $\beta$ -Ketoglutarate and Diketones," in honor of Ulrich Weiss, April 10, 1978.

Northeastern University, "Synthetic and Stereochemical Studies in the  $\beta$ -Carboline Area," July 21, 1978.

University of Wisconsin-River Falls, "Isolation and Use of Psychoactive Drugs by the Yanomamo Indians of South America," September 27, 1978.

University of Wisconsin-Stevens Point, "Isolation and Use of Psychoactive Drugs by the Yanomamo Indians of South America," September 29, 1978.

Marquette University, "General Method for the Synthesis of Cyclopentanoid Compounds," Spring, 1979.

University of Louisville, "General Method for the Synthesis of Cyclo-pentanoid Compounds," Spring, 1979.

Northern Illinois University, "Progress Toward the Synthesis of Staurane and Modhephene," Fall, 1979.

Winona State University, Minnesota, "General Approach toward the Synthesis of C Cyclopentanoid Compounds: Studies Directed Toward Synthesis of Staurane and Modhephene," Fall, 1979.

University of Michigan, "General Approach for the Synthesis of Polyquinanes," Fall, 1980.

University of Wisconsin-Eau Claire, "General Approach for the Synthesis of Polyquinanes," Fall, 1980.

Hope College, "Synthesis of Polyquinanes," Spring, 1980.

Calvin College, "General Approach for the Synthesis of Polyquinanes," Spring, 1980.

University of Wisconsin-Eau Claire, "Synthesis of  $\beta$ -Carbolines: Search for Valium Agonists and Antagonists," Fall, 1981.

University of Wisconsin-Oshkosh, "Synthesis of  $\beta$ -Carbolines: Search for Valium Agonists and Antagonists," Fall, 1981.

Winona State University, "Synthesis of  $\beta$ -Carbolines: Search for Valium Agonists and Antagonists," Fall, 1981.

Vanderbilt University, "General Approach for the Synthesis of Polyquinanes," Summer, 1981.

Illinois State University, "Synthesis of  $\beta$ -Carbolines: Search for Valium Agonists and Antagonists," Fall, 1981.

Searle Laboratories, "Synthesis of  $\beta$ -Carbolines: Search for Valium Agonists and Antagonists," Spring, 1982.

University of Illinois at the Medical Center, Department of Medicinal Chemistry, "Synthesis of  $\beta$ -Carbolines: Search for Valium Agonists and Antagonists," Spring, 1982.

University of Alberta, Canada, "Synthesis of  $\beta$ -Carbolines: Search for Valium Agonists and Antagonists," Fall, 1982.

University of Wisconsin-River Falls, "Synthesis of  $\beta$ -Carbolines: Search for Valium Agonists and Antagonists," Fall, 1982.

Hope College, "General Approach for the Synthesis of Polyquinanes. Synthesis of Modhephene and Triquinacene," Fall, 1982.

Michael Reese Hospital, Department of Anesthesiology, "Synthesis of  $\beta$ -Carbolines: Search for Valium Agonists and Antagonists," Spring, 1983.

University of Minnesota, "General Approach for the Synthesis of Polyquinanes," Spring, 1983.

Elmhurst College, " $\beta$ -Carbolines: Search for Valium Agonists and Antagonists," Spring, 1984.

University of Chicago, "General Approach for the Synthesis of Polyquinanes," Spring, 1984.

University of Wisconsin-River Falls, " $\beta$ -Carbolines: Search for Valium Agonists and Antagonists," Fall, 1983.

Winona State University, "General Approach for the Synthesis of Polyquinanes," Fall, 1985.

College of St. Catherine's, " $\beta$ -Carbolines: Search for New Valium Agonists and Antagonists," Fall, 1985.

National Science Foundation Workshop on Organic Synthesis, "General Approach Toward the Synthesis of Polyquinanes," Pingree Park, Colorado, Summer, 1985.

Illinois State University, " $\beta$ -Carbolines: Search for New Valium Agonists and Antagonists," Spring, 1986.

Eastern Illinois University, " $\beta$ -Carbolines: Search for New Valium Agonists and Antagonists," Spring, 1986.

University of Wisconsin-Eau Claire, " $\beta$ -Carbolines: Search for New Valium Agonists and Antagonists," Spring, 1986.

Ball State University, " $\beta$ -Carbolines: Search for New Valium Agonists and Antagonists," Spring, 1986.

Incell Chemical Co., " $\beta$ -Carbolines: Search for New Valium Agonists and Antagonists," Spring, 1986.

University of Wisconsin-Madison, "General Approach for the Synthesis of Polyquinanes," Spring, 1986.

Wayne State University, "General Approach for the Synthesis of Polyquinanes," Fall, 1986.

University of Wisconsin-Stevens Point, " $\beta$ -Carbolines: Search for Valium Agonists and Antagonists," Fall, 1986.

Uniformed Services University, Bethesda, MD, " $\beta$ -Carbolines: Search for Valium Agonists and Antagonists," Fall, 1986.

College of St. Catherine's, " $\beta$ -Carbolines: Search for New Valium Agonists and Antagonists," Fall, 1985.

Iowa State University, "General Approach for the Synthesis of Polyquinanes," Spring, 1987.

Searle Laboratories, " $\beta$ -Carbolines: Search for Valium Agonists and Antagonists," 1987.

Muskingam College, "Indole Alkaloids: Synthesis of Macroline-Related Alkaloids and Search for the Pharmacophore for the Benzodiazepine Inverse Agonist Site," Fall, 1987.

Eli Lilly & Co., " $\beta$ -Carbolines: Search for New Valium Agonists and Antagonists," Fall, 1987.

University of Louisville, "Indole Alkaloids: Synthesis of Macroline-Related Alkaloids and Search for the Pharmacophore for the Benzodiazepine Inverse Agonist Site," Spring, 1988.

University of Kentucky, "Indole Alkaloids: Synthesis of Macroline-Related Alkaloids and Search for the Pharmacophore for the Benzodiazepine Inverse Agonist Site," Spring, 1988.

Kansas State University, "Indole Alkaloids: Synthesis of Macroline-Related Alkaloids and Search for the Pharmacophore for

the Benzodiazepine Inverse Agonist Site," Spring, 1988.

Utah State University, "Synthesis of Biologically Active Indole Alkaloids," Spring, 1988.

University of Utah, "General Approach to the Synthesis of Polyquinenes," Spring, 1988.

Warner-Lambert-Parke Davis, "Pictet-Spengler Reactions in Aprotic Media. Stereospecific Approach to Macroline-Related Alkaloids," Fall, 1988.

UW-Stevens Point, "Pictet-Spengler Reactions in Aprotic Media. Stereospecific Approach to Macroline-Related Alkaloids," Fall, 1988.

UW-Eau Claire, "Pictet-Spengler Reactions in Aprotic Media. Stereospecific Approach to Macroline-Related Alkaloids," Fall, 1988.

St. Olafs, "Pictet-Spengler Reactions in Aprotic Media. Stereospecific Approach to Macroline-Related Alkaloids," Fall, 1988.

Ohio State University, "Pictet-Spengler Reactions in Aprotic Media. Stereospecific Approach to Macroline-Related Alkaloids," Spring, 1989.

UW-River Falls, "Pictet-Spengler Reactions in Aprotic Media. Stereospecific Approach to Macroline-Related Alkaloids," Fall, 1988.

Ripon College, "Pictet-Spengler Reactions in Aprotic Media, Synthesis of Biologically Active Alkaloids," Fall, 1989.

Michigan Technological University, "Pictet-Spengler Reactions in Aprotic Media, Synthesis of Biologically Active Alkaloids," Fall, 1989.

St. Norbert College, "Pictet-Spengler Reactions in Aprotic Media, Synthesis of Biologically Active Alkaloids," Fall, 1989.

Marquette University, "Pictet-Spengler Reactions in Aprotic Media, Synthesis of Biologically Active Alkaloids," Fall, 1989.

Calvin College, "Pictet-Spengler Reactions in Aprotic Media, Synthesis of Biologically Active Alkaloids," Fall, 1989.

Hope College, "Pictet-Spengler Reactions in Aprotic Media, Synthesis of Biologically Active Alkaloids," Fall, 1989.

ACS Milwaukee Section Award Address, "New Drugs for the Age of Anxiety. Rigid Probes to Study Benzodiazepine (Valium) Receptors," Fall, 1989.

Benedictine College, "Pictet-Spengler Reactions in Aprotic Media, Synthesis of Biologically Active Alkaloids," Spring, 1990.

North Dakota State University, "Stereospecific Synthesis of Macroline-Related Indole Alkaloids," Spring, 1990.

University of North Dakota, "Stereospecific Synthesis of Macroline-Related Indole Alkaloids," Spring, 1990.

Clemson University, "The Structure, Topology and Function of the Benzodiazepine (Valium) Receptor," Fall, 1990.

Loyola of Chicago, "The Structure, Topology and Function of the Benzodiazepine (Valium) Receptor," Fall, 1990.

Illinois State University, "The Structure, Topology and Function of the Benzodiazepine (Valium) Receptor," Fall, 1990.

UW-Oshkosh, "Rigid Probes to Study the Structure, Function and Topology of the Benzodiazepine Receptor. The Synthesis of an Anxiolytic," Spring, 1991.

Kent State University, "General Approach for the Synthesis of Polyquinenes *via* the Weiss Reaction," Spring, 1991.

Searle Research Laboratories, Skokie, Illinois, "Novel Strategies for the Synthesis of Ring-A Methoxylated Indole Alkaloids," June 6, 1991.

ACS Meeting, Rockriver Section, Rockford, Illinois, "Probes to Study the Structure and Function of the Benzodiazepine (Valium) Receptor. The Synthesis of a New Selective Anxiolytic/Anticonvulsant," September 25, 1991.

Abbott Laboratories, Chicago, Illinois, "Studies on the Pictet-Spengler Reaction. Strategies for the Synthesis of Ring-A Methoxylated Indole Alkaloids," January, 1992.

Abbott Laboratories, Chicago, Illinois, "The Age of Anxiety: Probes to Study the Structure and Function of the Benzodiazepine (Valium) Receptor and Its Influence on Everyday Living," January, 1992.

Medical College of Wisconsin, Department of Pharmacology, Milwaukee, WI, "Molecular Yardsticks: Rigid Probes With Which to Study the Structure and Function of the Benzodiazepine Receptor Site," Spring, 1992.

Boston University, Boston, Massachusetts, "Studies on the Pictet-Spengler Reaction. New Strategies for the Synthesis of

Ring-A Methoxylated Indole Alkaloids," Spring, 1992.

Northeastern University, Boston, Massachusetts, "Studies on the Pictet-Spengler Reaction. New Strategies for the Synthesis of Ring-A Methoxylated Indole Alkaloids," Spring, 1992.

University of Illinois-Chicago, "Studies on the Pictet-Spengler Reaction. New Strategies for the Synthesis of Ring-A Methoxylated Indole Alkaloids," Spring, 1992.

University of South Dakota, "Molecular Yardsticks. Rigid Probes With Which to Study the Structure and Function of the Benzodiazepine Receptor," Spring, 1992.

Anaquest, "Studies on the Pictet-Spengler Reaction. New Strategies for the Synthesis of Ring-A Methoxylated Indole Alkaloids," Fall, 1992.

North Carolina State, "Studies on the Pictet-Spengler Reaction. New Strategies for the Synthesis of Ring-A Methoxylated Indole Alkaloids," Fall, 1992.

University of Missouri at Columbia, "Synthetic Organic Chemistry and Drug Design," Spring, 1993.

R.W. Johnson Pharmaceutical Research, "The Inclusive Pharmacophore of Benzodiazepine Receptor Sites," Fall, 1993.

Indiana University-Purdue University at Indianapolis, "Enantiospecific Synthesis of Macroline/Sarpagine/Ajmaline Alkaloids," Fall, 1993.

Promega Corporation, "Computer and Chemical Assisted Development of the Inclusive Pharmacophore of Benzodiazepine Receptors," Spring, 1994.

R.W. Johnson Pharmaceutical Research, "Recent Advances in GABA<sub>A</sub> Receptor Subtype Modeling," Fall, 1994.

National Institutes of Health, "Enantiospecific Synthesis of Macroline/Sarpagine/Ajmaline Alkaloids," Fall, 1994.

National Institutes of Health, "The Inclusive Pharmacophore of Benzodiazepine Receptors and its Relationship to Subsite Selectivity," Fall, 1994.

Xavier University of Louisiana, "Recent Advances in GABA<sub>A</sub>/Benzodiazepine Receptor Subtype Selectivity," Spring, 1995.

Memorial Sloan-Kettering Cancer Center, "Enantiospecific Synthesis of Macroline/ Sarpagine/Ajmaline Alkaloids," Spring, 1995.

Abbott Laboratories, "Enantiospecific Synthesis of Macroline-Related Sarpagine and Ajmaline Indole Alkaloids," Fall, 1995.

University of Wisconsin-Eau Claire, "Enantiospecific Synthesis of Macroline-Related Antimalarial and Antiamoebic Bisindole Alkaloids," Fall, 1995.

University of Chicago, "Enantiospecific Synthesis of Macroline, Sarpagine and Ajmaline Alkaloids. Biomimetic Approach to Bisindoles," Fall, 1995.

Augsburg College, "Synthesis of  $\beta$ -Carbolines as Valium Agonists and Antagonists," Fall, 1995.

University of Wisconsin-River Falls, Enantiospecific Synthesis of Macroline-Related Antimalarial and Antiamoebic Bisindole Alkaloids, Spring, 1996.

Northwestern University, "Enantiospecific Synthesis of (+) Ajmaline and Tryptostatin A.", Spring 1997.

Northwestern University, "Search for Subtype Specific Ligands for BzR Subtypes", Spring, 1997.

Merck, "Enantiospecific Synthesis of Ajmaline, Alkaloid G, Talpinine and Talcarpine via the Asymmetric Pictet-Spengler Reaction," Fall, 1997.

Schering-Plough, "Enantiospecific Synthesis of Ajmaline, Alkaloid G, Talpinine and Talcarpine via the Asymmetric Pictet-Spengler Reaction," Fall, 1997.

Parke-Davis, "Enantiospecific Synthesis of Ajmaline, Alkaloid G, Talpinine and Talcarpine via the Asymmetric Pictet-Spengler Reaction," Fall, 1997.

International Conference Hall, "Construction of Pharmacophore Receptor Models for GABA<sub>A</sub>/ Benzodiazepine Receptor Subtypes," Annual Meeting of the Pharmaceutical Society of Japan, Kyoto, JAPAN, April 1, 1998.

Taiho Pharmaceutical Co, "Construction of Pharmacophore Receptor Models for GABA<sub>A</sub>/ Benzodiazepine Receptor Subtypes," JAPAN, April 3, 1998.



Eisai Pharmaceutical Co., "Enantiospecific Total Synthesis of Sarpagine/Ajmaline Alkaloids via the Asymmetric Pictet-Spengler Reaction," JAPAN, April 6, 1998.

Hokkaido University, "Enantiospecific Total Synthesis of Sarpagine/Ajmaline Alkaloids via the Asymmetric Pictet-Spengler Reaction," Sapporo, JAPAN, April 7, 1998.

FUJI Film Co, "Construction of Pharmacophore Receptor Models for GABA<sub>A</sub>/Benzodiazepine Receptor Subtypes," JAPAN, April 10, 1998.

University of Louisville, "Synthesis of Agents and Antianxiety Agents in Enantiospecific Fashion," April 28, 1998.

Gordon Conference, Regina Salve University, Rhode Island, "Enantiospecific Synthesis of Sarpagine/Ajmaline Alkaloids *via* the Asymmetric Pictet-Spengler Reaction," July 2, 1998.

Eli Lilly and Company, Indianapolis, Indiana, "Enantiospecific Synthesis of Sarpagine/ Ajmaline/Macroline Alkaloids via the Asymmetric Pictet-Spengler Reaction," March, 1999.

University of Illinois at Chicago, "Enantiospecific Synthesis of Ajmaline, Sarpagine Indole Alkaloids," May, 1999.

The 48<sup>th</sup> Gordon Research Conference on Natural Products, New England College, Rhode Island, "General Approach for the Synthesis of Sarpagine/Ajmaline Alkaloids, July, 1999.

Sepracor, Marlborough, MA, "Synthesis of Indoles, Tryptophans and Tryprostatins," October, 1999.

Harvard Medical School, New England Regional Primate Center, Sudbury, MA, "The Search for Subtype Selective Ligands for Bz/GABA<sub>A</sub> Receptors and Effect on Alcohol Self-Administration," October 1999.

Karolinska Institutet, Stockholm, Sweden, General Approach to the Synthesis of Macroline/ Sarpagine/Ajmaline Indoles Alkaloids," October 1999.

Karolinska Institutet and Royal Institute of Chemistry, Novum Lecture, "Search for Benzodiazepine/GABA(A) Subtype Selective Ligands and Implications in Alcohol Self- Administration," October, 1999.

Research Triangle Institute, Research Triangle Park, NC, "Enantiospecific synthesis of Indoles, Tryptophans and Tryprostatins," November, 1999.

Rhône-Poulenc, Research Triangle Park, NC, "Enantiospecific Synthesis of Indoles, Tryptophans and Tryprostatins," November, 1999.

University of Minnesota, Medicinal Chemistry and Pharmacy, Minneapolis, MN, "Search for Benzodiazepine/GABA Subtype Selective Ligands and Implications in Alcohol Self-Administration," November, 1999.

University of Wisconsin-Milwaukee, Department of Psychology and Society for Neuroscience, "Search for Benzodiazepine/GABA Subtype Selective Ligands and Implications in Alcohol Self-Administration," December, 1999.

Indiana University-Purdue University at Indianapolis,"Search for Benzodiazepine/GABA Subtype Selective Ligands," April, 2000.

Pfizer Pharmaceutical Co., "General Approach to the Synthesis of Indole Alkaloids. Enantiospecific Synthesis of Ajmaline, Velloximine, Norsuaveoline and Geissochizine," April, 2000.

R.W. Johnson Pharmaceuticals, "Enantiospecific Total Synthesis of Sarpagine, Ajmaline and Corynanthe Indole Alkaloids," February, 2001.

Pfizer Global Research and Development, "Enantiospecific Synthesis of Sarpagine, Ajmaline and Corynanthe Indole Alkaloids *via* the Asymmetric Pictet-Spengler Reaction," July, 2001.

Dupont Pharmaceuticals, "Enantiospecific Synthesis of Sarpagine, Ajmaline and Corynanthe Indole Alkaloids *via* the Asymmetric Pictet-Spengler Reaction," July, 2001.

Wyeth-Ayerst Pharmaceuticals, "General Approach for the Synthesis of Sarpagine, Ajmaline and Corynanthe Alkaloids *via* the Asymmetric Pictet-Spengler Reaction," October, 2001.

Waseda University, "Enantioselective Synthesis of Sarpagine, Ajmaline and Corynanthe Alkaloids *via* the Asymmetric Pictet-Spengler Reaction," November, 2001.

The University of Tokyo, "Studies on the Synthesis of Antimalarial Bisindole Alkaloids," November, 2001.

Tokyo Institute of Technology, "The Pictet-Spengler Reaction in Milwaukee," November, 2001.

Science University of Tokyo, "The Synthesis of Polyquinenes *via* the Weiss and Tandem Pauson-Khand Reactions," November, 2001.

Institute for Physical Chemistry Research (RIKEN), "Search for Benzodiazepine/GABA(A) Subtype Selective Ligands that Reverse Alcohol Self-Administration," November, 2001.

Hokkaido University, "Enantioselective Synthesis of Sarpagine, Ajmaline and Corynanthe Alkaloids *via* the Asymmetric Pictet-Spengler Reaction, November, 2001.

Tohoku University, "Enantioselective Synthesis of Sarpagine, Ajmaline and Corynanthe Alkaloids *via* the Asymmetric Pictet-Spengler Reaction," November 2001.

Nagoya University, "Studies on the Synthesis of Antimalarial Bisindole Alkaloids," November, 2001.

Kyushu University, "Enantioselective Synthesis of Sarpagine, Ajmaline and Corynanthe Alkaloids *via* the Asymmetric Pictet-Spengler Reaction," November, 2001.

Okayama University, "Studies on the Synthesis of Antimalarial Bisindole Alkaloids," November, 2001.

Tokushima Bunri University, "Enantioselective Synthesis of Sarpagine, Ajmaline and Corynanthe Alkaloids *via* the Asymmetric Pictet-Spengler Reaction," November, 2001.

Osaka University, "Enantioselective Synthesis of Sarpagine, Ajmaline and Corynanthe Alkaloids *via* the Asymmetric Pictet-Spengler Reaction," November, 2001.

Sankyo Company Limited, "Enantioselective Synthesis of Sarpagine, Ajmaline and Corynanthe Alkaloids *via* the Asymmetric Pictet-Spengler Reaction," December, 2001.

University of Tokyo, "Enantioselective Synthesis of Sarpagine, Ajmaline and Corynanthe Alkaloids *via* the Asymmetric Pictet-Spengler Reaction," December, 2001.

Ligand Pharmaceutical, "General Approach to the Synthesis of Indole Alkaloids *via* the Asymmetric Pictet-Spengler Reaction," April, 2002.

UCB Pharmaceutical Co., Boston, MA, "General Approach to the Synthesis of Indole Alkaloids *via* the Asymmetric Pictet-Spengler Reaction," August 2002.

Roche Biosci Inc., Palo Alto, CA, "General Approach for the Synthesis of Indole Alkaloids *via* the Asymmetric Pictet-Spengler Reaction," January 2003.

Wayne State University, "Synthesis of Antimalarial Bisindole Alkaloids *via* the Asymmetric Pictet Spengler Reaction," April 2003.

Eli Lilly & Co., "General Approach for the Synthesis of Macroline, Sarpagine and Ajmaline Indole Alkaloids," Summer 2003.

Sepracore, "Search for Subtype Selective Ligands that Reverse Alcohol Self-Administration," Fall 2003.

UW Stevens Point, "Serendipity Rediscovered: An oxymoron or Rational Drug Design?" Spring, 2005.

Olivet Nazarene University, "The Synthesis of Antimalarial Alkaloids *via* the Asymmetric Pictet-Spengler Reaction," Spring, 2005.

Virginia Commonwealth University, "Serendipity Rediscovered: An Oxymoron or Rational Drug Design?" Spring 2005.

Abbott Laboratories, "General Approach to the Synthesis of Ring-A Alkoxy Substituted Indole Alkaloids *via* the Asymmetric Pictet-Spengler Reaction," Fall, 2005.

Clemson University, "Serendipity Rediscovered: An Oxymoron or Rational Drug Design?" Fall, 2005.

Bristol Meyers Squibb, "Serendipity Rediscovered: An Oxymoron or Rational Drug Design? Development of Orally Active, Nonsedating Anxiolytics," Fall, 2005.

Sepracor, "Serendipity Rediscovered: An Oxymoron or Rational Drug Design? Search for Subtype Selective Ligands," Fall, 2005.

Brandeis University, "General Approach to the Synthesis of Ring-A Alkoxy Substituted Indole Alkaloids *via* the Asymmetric Pictet-Spengler Reaction," Spring, 2006.

WiSys (UW-System), "Serendipity Rediscovered: An Oxymoron or Rational Drug Design," Spring, 2006.

North Carolina State University, "General Approach to the Synthesis of Ring-A Alkoxy Substituted Indole Alkaloids," Spring,

2006.

55<sup>th</sup> Natural Products Gordon Research Conference, “General Approach to the Synthesis of Ring-A Alkoxy Substituted Indole Alkaloids via the Asymmetric Pictet-Spengler Reaction (**Plenary Lecture**),” Tilton, NH, July 23-28, 2006.

Biofine/Sci Update Meeting, “Palladium and Copper-Mediated Strategies for the Asymmetric Synthesis of Antimalarial, Antileishmanial and Antimicrobial Agents, New Directions in Chemical Process Design,” Sanibel Island, Florida, December 2,3 (2008). (**Plenary Lecture**.)

Illinois State University, “Palladium and Copper-Mediated Strategies for the Asymmetric Synthesis of Antimalarial, Antileishmanial and Antimicrobial Agents,” Bloomington-Normal, IL, November (2008).

RTI, “Palladium and Copper-Mediated Strategies for the Asymmetric Synthesis of Antimalarial, Antileishmanial and Antimicrobial Agents,” Raleigh-Durham, NC, October (2008).

Mona Jamaica, Mona Symposium, “General Approach to the Stereospecific Synthesis of the Antileishmanial Alkaloid (+) Dispegatrine and other Alkaloids.” C. Edwankar and James M. Cook, Jan 3-Jan 7, 2012.

Concordia University, “Synthesis of Alpha 2/Alpha3 Agonists to Treat Anxiety Disorders and Neuropathic Pain”. James M. Cook, Fall 2012.

Northern Illinois University, “General Approach to the Stereospecific Synthesis of Bisindole Alkaloids (+)-Dispegatrine, Accedinisine and N'-Demethylaccedinisine”, James M Cook, Nov1, 2012, Dekalb, IL.

Illinois State University, “Synthesis of Alpha 2/Alpha3 Agonists to Treat Anxiety Disorders and Neuropathic Pain”. James M Cook, Nov 1, 2012. Bloomington-Normal, IL.

Medical College of Wisconsin, Synthesis of Nonsedating Anxiolytics Active Against Neuropathic Pain as well as Seizures, Milwaukee, WI, May 30, 2013.

Gunderson Hospital Forum, Lacrosse, WI, “Synthesis of Nonsedating Anxiolytics Active Against Neuropathic Pain as well as Seizures, August 18, 2014.

University of East Anglia, UK, Anorcq Meeting, Synthesis of Bisindole Alkaloids Targeted at Parasitic Diseases as well as Simple Molecules to Treat MRSA Infections, July 2, 2014; Plenary Lecture.

Cook, J. “Synthesis of Bisindole Antimalarial Alkaloids as well as Ligands to Treat Drug Resistant MRSA Infections,” Cambridge Major Laboratories, December 2, 2014.

“Synthesis of Nonsedating Anxiolytics Active Against Neuropathic Pain as well as Seizures,” James M. Cook, Alessandra Di Lio, Zhi-jian Wang, Rahul Edwankar, HannsUlrich Zeilhofer. University of Wisconsin-LaCrosse, Department of Chemistry & Biochemistry, LaCrosse, WI, August, 2015.

“Enantiospecific, Stereospecific Total Synthesis of a Series of C-19 Methyl Substituted Sarpagine-Macroline Indole Alkaloids via an Efficient Method of a Copper-Mediated Enolate Driven Cross-Coupling Process,” James M. Cook, M. Rahman. 26<sup>th</sup> Natural Products and Medicinal Chemistry Symposium, University of the West Indies, Chemistry Department, Mona Campus, Jamaica, January 4-7, 2016.

“Enantiospecific, Stereospecific Total Synthesis of a Series of C-19 Methyl Substituted Sarpagine-Macroline Indole Alkaloids via an Efficient Method of a Copper-Mediated Enolate Driven Cross-Coupling Process,” James M. Cook; M. Toufiquir Rahman. 17<sup>th</sup> Florida Heterocyclic and Synthetic Conference (FloHet 2016), University of Florida, FL, USA, February 28-March 2, 2016.

“Drug Design Stories and Chemical Development” James M. Cook. Industry Leader Seminar Series, Concordia University, WI, April 29<sup>th</sup>, 2016.

“Design of Benzodiazepine/ GABA(A) ergic Subtype Selective Ligands as Potential Nonsedating Treatments for Pain Disorders, Epilepsy and Anxiety Disorders with Little or No Tolerance” James M. Cook, Kashi Reddy Methuku, and Michael M. Poe. The University of Kansas, Lawrence, KS, USA, September 21st, 2016.

“Design of Benzodiazepine/ GABA(A) ergic Subtype Selective Ligands as Potential Nonsedating Treatments for Pain Disorders, Epilepsy and Anxiety Disorders with Little or No Tolerance” James M. Cook, Kashi Reddy Methuku, and Michael M. Poe. Stanford Research Institute, Menlo Park, CA, USA, October 14th, 2016; Also Ohio State U., Feb 21st, 2017.

“General strategy for the total synthesis of C-19 methyl substituted sarpagine/macrolone indole alkaloids including macrocarpines A-G, peraksine, and dihydropersaksine” Rahman, M. T.; Deschamps, J.R.; Cook, J.M. Oral Presentation, 253rd ACS National Meeting, San Francisco, CA, April 4-7, (Abst. ORGN 654), 2017.

“A Novel Asthma Treatment: Targeting the GABA(A) Receptors Present in the Lung”, Rajwana Jahan, Michael Stephen, Gloria S. Forkuo, Revathi Kodali, Margaret L. Guthrie, Amanda N. Nieman, Nicolas M. Zahn, Gene T. Yocum, Margot Ernst, Leggy A. Arnold, Douglas Stafford, Charles Emala, James M. Cook, UWM Department of Chemistry and Biochemistry Awards Day and Symposium, Milwaukee, WI, May 22, 2018.

“Identifying of the Molecular Target for the Potent Antimicrobial Agent TI-I-100 to Treat Drug Resistance Bacteria”, Tiruveedhula, V. V. N. Phani Babu.; Kodali, Revathi.; Han, Lanlan.; Bardy, Sonia L.; Mirza, Shama P.; Silvaggi, Nicholas R.; Stafford, Douglas.; Arnold, Leggy A.; Cook, James M. Nobel Symposium Poster Section, Department of Chemistry and Biochemistry, UW-Milwaukee, September 29, 2017

“Identifying of the Molecular Target for the Potent Antimicrobial Agent TI-I-100 to Treat Drug Resistance Bacteria”, Tiruveedhula, V. V. N. Phani Babu.; Kodali, Revathi.; Han, Lanlan.; Bardy, Sonia L.; Mirza, Shama P.; Silvaggi, Nicholas R.; Stafford, Douglas.; Arnold, Leggy A.; Cook, James M. Research Symposium, Department of Chemistry and Biochemistry, UW-Milwaukee, May 23, 2017

“Identifying of the Molecular Target for the Potent Antimicrobial Agent TI-I-100 to Treat Drug Resistance Bacteria”, Tiruveedhula, V. V. N. Phani Babu.; Kodali, Revathi.; Han, Lanlan.; Bardy, Sonia L.; Mirza, Shama P.; Silvaggi, Nicholas R.; Stafford, Douglas.; Arnold, Leggy A.; Cook, James M. 35th H. C. Brown Lectures in Organic Chemistry, Department of Chemistry, Purdue University, April 13th, (Poster # 22), 2018.

“General Strategy for the Total Synthesis of C-19 Methyl Substituted Sarpagine/Macrolone Indole Alkaloids” Rahman, M. T.; Deschamps, J. R.; Cook, J. M., 34th H. C. Brown Lectures in Organic Chemistry, Department of Chemistry, Purdue University, April 13, (Poster # 50), 2017.

“Total Synthesis of Bioactive Sarpagine/Macrolone/Ajmaline Indole Alkaloids” Cook, J. M.; Rahman, M. T.; Proceedings of the 27th Mona Symposium, University of the West Indies, Mona, Kingston, Jamaica, January 8-11, 2018.

“Total Synthesis of Sarpagine-Related Bioactive Indole Alkaloids” Rahman, M. T., Oral Presentation at Nobel Graduate Seminar, arranged by Milwaukee Institute for Drug Discovery (MIDD) on the occasion of 2016 Chemistry Nobel Laureate Professor Bernard L. Feringa’s visit to The UWM Chemistry Department, September, 2017.

“General Strategy for the Total Synthesis of C-19 Methyl Substituted Sarpagine/Macrolone Indole Alkaloids” Rahman, M. T.; Deschamps, J. R.; Cook, J. M., Department of Chemistry and Biochemistry, University of Wisconsin-Milwaukee Awards Day Symposium, May 23rd, 2017.

“General Strategy for the Total Synthesis of C-19 Methyl Substituted Sarpagine/Macrolone Indole Alkaloids” Rahman, M. T.; Deschamps, J. R.; Cook, J. M., ACS-Milwaukee Meeting, May 3rd, 2017.

“Unprecedented Stereocontrol in the Synthesis of 1,2,3- Trisubstituted Tetrahydro- $\beta$ -carbolines via a New Asymmetric Pictet-Spengler Reaction Towards SarpagineType Indole Alkaloids” Rahman, M. T.; Deschamps, J.R.; Cook, J. M., 35th H. C. Brown Lectures in Organic Chemistry, Department of Chemistry, Purdue University, April 13th, (Poster # 21), 2018.

“Design and synthesis of novel deuterated GABAAR- $\alpha 6$  subtype selective ligands with improved metabolic stability and enhanced bioavailability” Knutson, D. E. K., Revathi; Stephen, Michael R.; Verma, Ranjit S.; Witzigmann, Christopher; Meirelles, Matheus A.; Zahn, Nicolas M.; Huber, Alec T.; Arnold, Leggy; Savic, Miroslav M.; Ernst, Margot; Sieghart, Werner; Cook, James M. In 35th Herbert C. Brown Lectures in Organic Chemistry, Purdue University, 2018.

“Novel Deuterated GABAAR- $\alpha 6$  Subtype Selective Ligands with Improved Metabolic Stability and Enhanced Bioavailability Targeting Trigeminal Orofacial Pain, Neuropsychiatric Disorders, and Depression” Knutson, D. E.; Kodali, R.; Stephen, M. R.;



Zahn, N. M.; Arnold, L. A.; Cook, J. M.; Dobricic, V.; Savic, M. M.; Mihovilovic, M. D.; Treven, M.; Ernst, M.; Sieghart, W. In 254th ACS National Meeting, Washington, DC, 2017.

“Design and synthesis of novel deuterated GABAAR- $\alpha 6$  subtype selective ligands with improved metabolic stability and enhanced bioavailability” Knutson, D. E. K.; Revathi; Stephen, Michael R.; Verma, Ranjit S.; Witzigmann, Christopher; Meirelles, Matheus A.; Zahn, Nicolas M.; Huber, Alec T.; Arnold, Leggy; Savic, Miroslav M.; Ernst, Margot; Sieghart, Werner; Cook, James M. In 255th ACS National Meeting, New Orleans, LA, 2018.

“Synthesis of New Benzodiazepines that Function as  $\alpha 5$ -GABAA Receptor Ligands to Target Group 3 Medulloblastomas” F. Rashid, T. Ahmed, K. R. Methuku, O. Jonas, S. Sengupta, and J. M. Cook, 35th HC Brown Lectures, West Lafayette IN, April 12-13, (poster #38), 2018.

“Synthesis of New Benzodiazepines that Function as  $\alpha 5$ -GABAA Receptor Ligands to Target Group 3 Medulloblastomas” F. Rashid, T. Ahmed, K. R. Methuku, O. Jonas, S. Sengupta, and J. M. Cook, Milwaukee ACS Section, Milwaukee WI, May 3, 2018.

“Design and synthesis of novel deuterated GABAAR- $\alpha 6$  subtype selective ligands with improved metabolic stability and enhanced bioavailability” Knutson, D. E. K.; Revathi; Stephen, Michael R.; Verma, Ranjit S.; Witzigmann, Christopher; Meirelles, Matheus A.; Zahn, Nicolas M.; Huber, Alec T.; Arnold, Leggy; Savic, Miroslav M.; Ernst, Margot; Sieghart, Werner; Cook, James M. UWM Department of Chemistry and Biochemistry Awards Day and Symposium, Milwaukee, WI, May 22, 2018.

“Approach Towards the Total Synthesis of Unnatural Enantiomers of Sarpagine/Macroline Indole Alkaloids” Kamal P Pandey, Md Toufiqur Rahman, James M. Cook. UWM Department of Chemistry and Biochemistry Awards Day and Symposium, Milwaukee, WI, May 22, 2018.

“Design and Synthesis of  $\alpha 5$ -GABAA Receptor Subtype Ligands to Treat Group 3 Medulloblastoma” Md Yeunus Mian, Guanguan Li, Farjana Rashid, Taukir Ahmed, Kashi Reddy Methuku, Oliver Jonas, Soma Sengupta, and James M. Cook. UWM Department of Chemistry and Biochemistry Awards Day and Symposium, Milwaukee, WI, May 22, 2018.

“Unprecedented Stereocontrol in the Synthesis of 1,2,3-trisubstituted Tetrahydro- $\beta$ -carbolines via a New Asymmetric Pictet-Spengler Reaction Towards Sarpagine-type Indole Alkaloids” Rahman, M. T.; Deschamps, J. R.; Cook, J. M., Department of Chemistry and Biochemistry, University of Wisconsin-Milwaukee Awards Day Symposium, May 22, 2018.

"Progress toward the enantiospecific and stereospecific total synthesis of a number of sarpagine-related indole alkaloids including hystrixnine and gelsempervines A and B", Md Zubair Ahmed Khana, Md Toufiqur Rahman, James M. Cook. Department of Chemistry and Biochemistry, University of Wisconsin-Milwaukee Awards Day Symposium, May 22, 2018.

“Synthesis of New Benzodiazepines that Function as  $\alpha 5$ -GABAA Receptor Ligands to Target Group 3 Medulloblastomas” F. Rashid, T. Ahmed, K. R. Methuku, O. Jonas, S. Sengupta, and J. M. Cook. Department of Chemistry and Biochemistry, University of Wisconsin-Milwaukee Awards Day Symposium, May 22, 2018.

“Synthesis of novel imidazobenzodiazepine oxazole bioisosteres as potential  $\alpha 2, 3$  subtype selective GABA(A) receptors agonists with excellent metabolic stability, pharmacokinetics, and anxiolytic efficacy” Li, G.; Methuku, K.R.; Poe, M.M.; Witkin, J.M.; Schkeryantz, J.M.; Ernst, M.; Cook, J.M. 253rd ACS National Meeting, San Fransico, CA, April 2-6, (Abst. MEDI 99), 2017.

“Synthesis of novel imidazobenzodiazepine oxazole bioisosteres as potential  $\alpha 2, 3$  subtype selective GABA(A) receptors agonists with excellent metabolic stability, pharmacokinetics, and anxiolytic efficacy” Li, G.; Methuku, K.R.; Poe, M.M.; Witkin, J.M.; Schkeryantz, J.M.; Ernst, M.; Cook, J.M. UWM annual symposium, Milwaukee, WI, May 23, (Abst. 1), 2017.

“Design and Synthesis of Anxiolytic, Anticonvulsant and Antinociceptive Benzodiazepine/GABA(A)ergic Receptor Subtype Selective Ligands as Potential Nonsedating Treatment for Anxiety Disorders, Epilepsy and Pain Disorders” Li, G.; Witkin, J.M.;

Schkeryantz, J.M.; Cerne, R.; Fisher, J.; Li, J.; Lewter, L.; Freeman, K.B.; Davis, P.; Stafford, D.C.; Arnold, L.A. and Cook, J.M. UWM annual symposium, Milwaukee, WI, May 22, (Abst. 22), 2018.

- 2 years behind on talks

## V. RESEARCH IN PROGRESS

### Current Research:

Major areas of interest at the present time include Medicinal Chemistry, Synthetic Organic Chemistry, and Natural Products Chemistry. More specifically, we are interested in the synthesis of natural products with biological activity or related analogs with enhanced activity. Research of this type has led us into the alkaloid, quinoline, indole,  $\beta$ -carboline, benzodiazepine and coumarin fields. Much of our research effort has been concerned with the synthesis of small molecules active in the CNS, to search for receptor subtype selective activity.

A. The benzodiazepines employed to treat anxiety are a group of compounds with wide therapeutic application as anxiolytics, anticonvulsants, hypnotics and muscle relaxants. However, the sedative-hypnotic, muscle-relaxant, ataxic and amnesic side effects limit their use in the elderly and in many other patients. Recently, a number of  $\beta$ -carbolines were prepared in our laboratory which have intrinsic effects opposite to the benzodiazepines (anxiogenic, convulsant, etc.) and have been employed to study mechanisms in anxiety. Moreover, there is some selectivity [Bz1-selective (Bz1 =  $\alpha 1\beta 3\gamma 2$ ), BCCt and 3-PBC antagonists] in their mode of action in vivo. More importantly, we have recently discovered inverse agonist and antagonist activity in the rigid, planar pyridodiindole Bz receptor ligands which simplifies computer modeling of the receptor subtypes. A collaboration with a network of 19 pharmacologists has been set up to search for selective action, work in progress is detailed below:

1. To prepare new and better anxiolytics. These agents would be selective for antianxiety effects but would not possess sedative-hypnotic, ataxic or muscle-relaxant effects; a BzR selective agonist potentially devoid of abuse potential. We have now prepared anxiolytics devoid of muscle-relaxant, ataxic and sedative-hypnotic effects. These orally active agents are currently being characterized and should be useful in treatment of panic disorders, general anxiety disorders, social anxiety disorders, agrophobias and post traumatic stress disorders. It appears potential abuse potential for these new agents is decreased in comparison to that of Valium, Xanax, etc. We have now developed potent  $\alpha 2/\alpha 3$  agonists active as nonsedating analgesics.
2. Push our  $\alpha 2/\alpha 3$  subtype selective PAMS, which do not develop tolerance nor sedation/ataxia or dependence into the clinic to treat epilepsy neuropathic pain and anxiety.
3. To prepare potent, long-lived, selective (Bz1, Bz2, Bz5, Bz6, etc) benzodiazepine receptor selective agonists and antagonist/inverse agonists. These inverse agonists/ antagonists would be employed to reverse the effects of benzodiazepine-induced anesthesia and to indirectly reverse barbiturate-induced CNS depression. This would help in surgery in the elderly, who oftentimes experience respiratory arrest with the barbiturate/haloalkanes presently in use.
4. Study the effect of anxiogenic agents on the levels of endorphins in the brain (Endocrinology, 1985).
5. Use the SAR of the rigid, planar pyridodiindoles to computer model the topography of each of the benzodiazepine receptor subtypes (Bz1-Bz6). This has been published, but 200 new ligands will be added to this modeling strategy this year.
6. To differentiate between Bz1, Bz5, and Bz6 receptors as well as between Bz1, Bz2 and Bz3 receptor subtypes.
7. To determine if the ability of Ro 15-4513 to reverse the effects of alcohol is mediated by the Bz6 [diazepam-insensitive site (Bz6)] site, the Bz5 site, the Bz1 receptor site or a related site. The  $\alpha 1$  preferring, orally active BzR antagonists, BCCt and 3PBC have recently been shown to reverse alcohol self-administration in rats, and may have clinical potential in the treatment of alcoholism. These agents exhibit very weak anxiolytic activity in alcoholic rat models as well as potentially reversing alcohol self-administration.
8. To employ our Bz5 receptor ligands to design BzR ligands with 200 fold selectivity for Bz5 sites after which the pharmacology of the Bz5 site can be elucidated to use these to enhance cognition and to treat Alzheimer's disease. These compounds are active against alcohol abuse as well.
9. To employ the same approach under 8 with molecular modeling and chemical synthesis to define the pharmacology of Bz1 and Bz6 subtypes.
10. Eventually, with receptor subsite selective ligands, define the exact pharmacology of all major BzR (GABA(A) sites and employ this in drug design for the preparation of anxiolytics, anticonvulsants and sedative hypnotics with decreased abuse potential and a better understanding of tolerance.

11. Study the interrelationship between GABAergic and dopaminergic systems, in regard to the prevention of alcohol/drug abuse. This work is presently underway in collaboration with Dr. Donna Platt and Dr. Weerts.
12. Ultimate goal - to determine the differences at the molecular level between the various BzR sites via modeling, synthesis, site directed mutagenesis, cloning, and X-ray crystallography of irreversibly bound photolabels to the specific GABA(A)/BzR Cl ion channels, beginning with  $\alpha 1\beta 3\gamma 2$  and  $\alpha 5\beta 3\gamma 2$  subtypes.
13. To use Bz5 ( $\alpha 5\beta 3\gamma 2$ ) subtype selective inverse agonists and agonists to push forward our GABA approach for the treatment of Alzheimers disease and age-associated memory impairment in the elderly.
14. A program on Design of  $\alpha 4$  Subtype Selective Ligands for treatment of Asthma.

B. In mammals L-tryptophan and other indoleamines are oxidized to formylkynurenines via the kynurenine pathway by indoleamine 2,3-dioxygenase (IDO) or tryptophan 2,3-dioxygenase (TDO). Although both enzymes catalyze the same transformation, TDO is found only in the liver, while IDO is present in a wide variety of tissues such as brain, lung, and small intestine, as well as macrophages that are found in the CNS. Furthermore, IDO is a 41 kD, monomeric heme containing protein that utilizes superoxide to cleave the 2,3-double bond of indoleamines.

Many inflammatory diseases and neurodegenerative diseases have been hypothetically linked to aberrant L-tryptophan metabolism caused by activation of IDO. Moreover, Heyes and coworkers have recently reported evidence which implicates the activation of IDO in inflammatory diseases, such as AIDS, dementia and wasting, meningitis and sepsis. Interferon  $\gamma$  has been shown to induce the production of IDO. One of the ways in which the body responds to infection by foreign organisms and head injuries is to produce large amounts of interferon-gamma and other immune system activators. High levels of interferon-gamma eventually induce the production of high levels of IDO which results in the catabolism of large amounts of L-tryptophan and the production of high levels of metabolites of the kynurenine pathway. This can lead to extremely high levels of quinolinic acid in the CNS which can effect many neuropathological changes including nerve cell death and dementia.

Recently we have prepared both competitive and noncompetitive (modulatory  $\beta$ -carboline binding site) inhibitors of IDO (Med. Chem. Res., 1993, 1994).  $N^a$ -methyl L(-)-tryptophan is the most active competitive inhibitor reported to date; however, the noncompetitive inhibitors 3-nitro  $\beta$ -carboline and 3-butyl  $\beta$ -carboline look even more promising. We plan, via molecular modeling and chemical synthesis, to search for even more potent inhibitors of IDO in collaboration with Dr. Melvin Heyes and Dr. Markey at NIH as well as Dr. Jamie (Australia). Drs. Mellor and Dunn have recently employed  $N^a$ -methyl-D-tryptophan (prepared first in this laboratory) as an IDO inhibitor with clinical potential. The  $N^a$ -methyl-D-tryptophan, first prepared and reported here in Milwaukee, has been employed by Drs. Mellor and Dunn to shed light on the "pregnancy paradox" and is being studied as a treatment for immune-system related diseases.

C. Multidrug resistance (MDR) in neoplastic cells is usually due to decreased cellular retention of drugs such as vincristine or doxorubicin. An ATP-dependent drug efflux pump has been detected in MDR-1-phenotypic cells and inhibition of the MDR pump is presumably a primary mechanism for reversal of MDR. Although quinine and quinidine are reversal agents and inhibitors of the MDR pump, a mixture of diastereomeric epoxides of quinine 10,11-epoxide was 8 fold more active in inhibiting the MDR pump. It is believed one of the diastereomers of the epoxide is covalently (Mol. Pharmacol., 1994) bonding to the pump. At present, the stereospecific synthesis of both epoxides is under study to determine which is the active agent, and how effective. Moreover, other agents known to inhibit this pump will be converted into epoxides to attempt to increase activity. Goal - find a way to block the pump so that vincristine/etc can kill drug resistant strains of cancer cells. The natural product tryprostatin-A, synthesized first here in Milwaukee, is the most potent inhibitor of breast cancer resistant protein reported to date (Joel Turner). Analogs of this natural product are being synthesized to find even more potent inhibitors of this member of the ABC transporter family. The goals of much of this work are to develop small molecules which can be employed to treat multidrug resistant forms of cancer.

D. The MDR pump is reported to be ubiquitous in nature, consequently, our pure diastereomeric quinine-10,11-epoxides will be employed with quinine and chloroquine in drug resistant strains of *P.falciparum* to determine if this simple approach would be effective in treating drug-resistant strains of malaria.

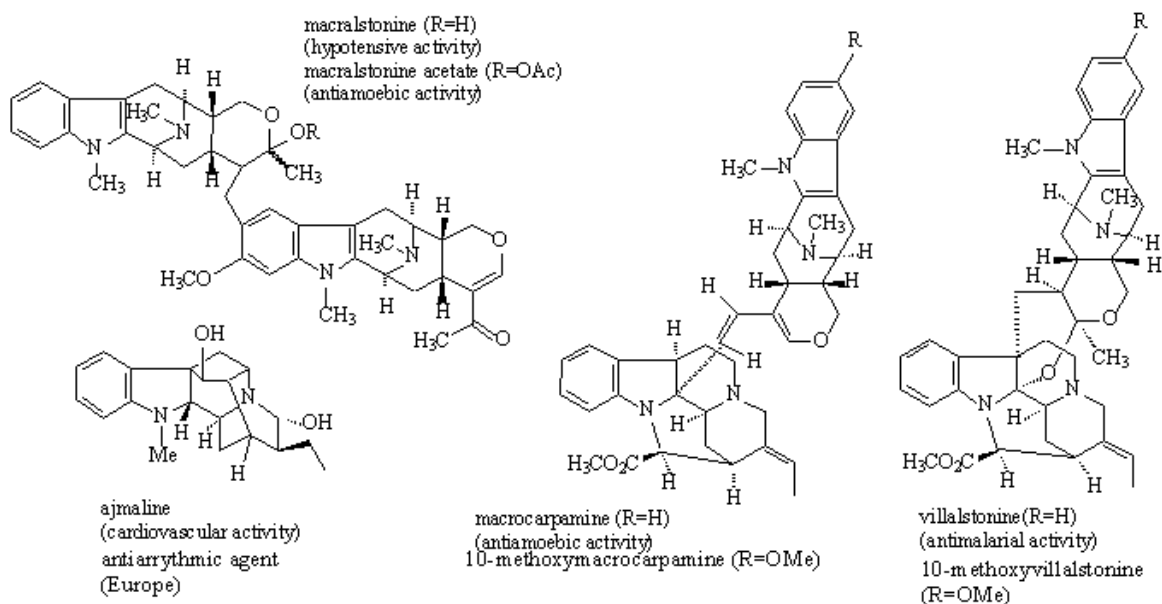
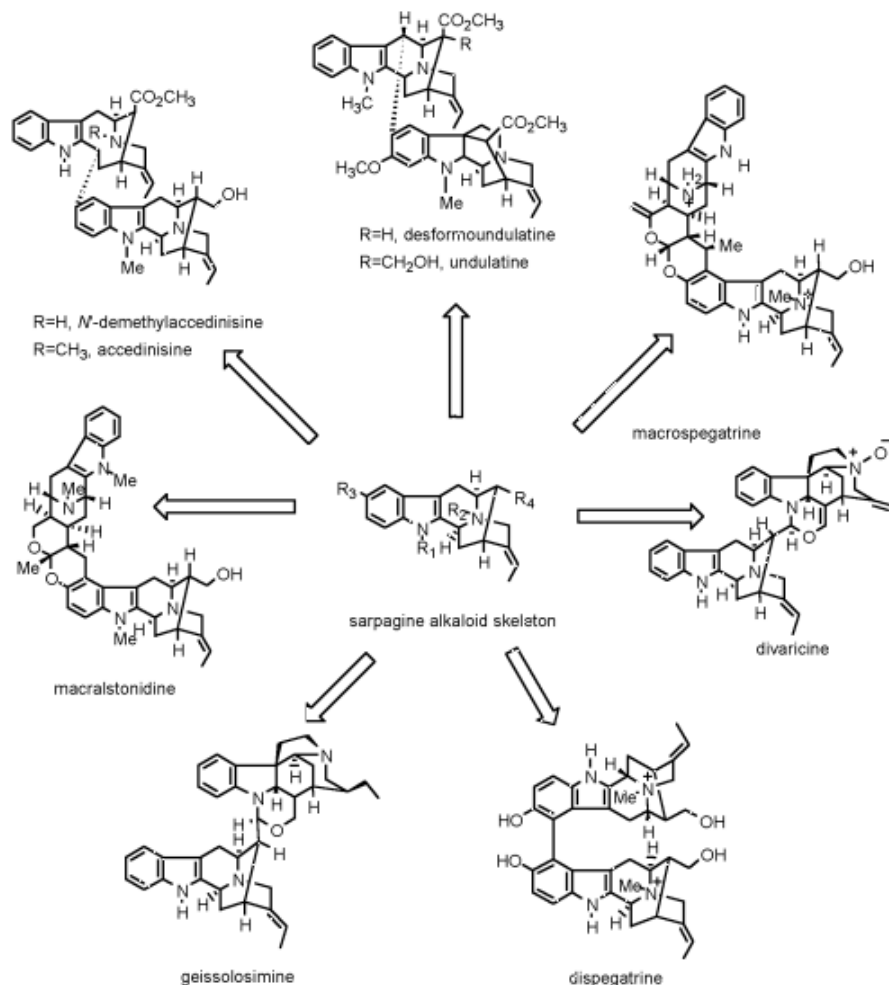


Figure 1

E. During recent years an increasing number of macroline related alkaloids has been isolated from various species of *Alstonia*. At the present time this group contains over 90 indole alkaloids, at least 21 of which are bisindoles. The hypotensive base macralstonine isolated from *Alstonia macrophylla* Wall is a member of this family, as well as the bisindole villalstonine. This latter alkaloid has been found to exhibit potent antimalarial activity against *Plasmodia falciparum*, while the related macrocarpamine is active against *Entamoeba histolytica* and *Plasmodia falciparum*. One of these alkaloids is active against drug resistant strains of *Plasmodia falciparum* while the other is active only at the chloroquine sensitive strain. The activity of these alkaloids confirms the use of *Alstonia angustifolia* in traditional medicine for the treatment of malaria as well as amoebic dysentery.

We have recently completed the total synthesis of dispegatrine (C. Edwankar). The antihypertensive bisindole employed in Chinese medicine. This was completed in 12 steps via our enantiospecific, stereospecific doubly convergent strategy.





**FIGURE 2.** Potential bisindole alkaloid targets from sarpagine alkaloids.

The enantiospecific total synthesis of these bisindole alkaloids (see Figures 1 and 2) as well as the cardiovascularly active alkaloid ajmaline and a number of other macroline related sarpagine alkaloids is being pursued. The synthetic route to these bisindole alkaloids which employs the *trans*, stereospecific Pictet-Spengler reaction developed in this laboratory is both enantiospecific and doubly convergent [J. Am. Chem. Soc. (1994); J. Org. Chem. (2003)]. Recently the total synthesis of the bisindoles macralstonine and macralstonidine [J. Org. Chem. (2003)] as well as the partial synthesis of macrocarpamine and villalstonine has been completed and reported. A number of indole alkaloids (over 30) have been synthesized over the past three years employing the recently developed enolate-driven palladium-catalyzed cross coupling reaction in combination with the asymmetric Pictet-Spengler reaction. A related palladium-mediated method of Larock has been employed to develop the first stereospecific, regiospecific synthesis of 6-methoxy and 7-methoxy (D or L) tryptophan building blocks for total synthesis or as IDO active ligands.

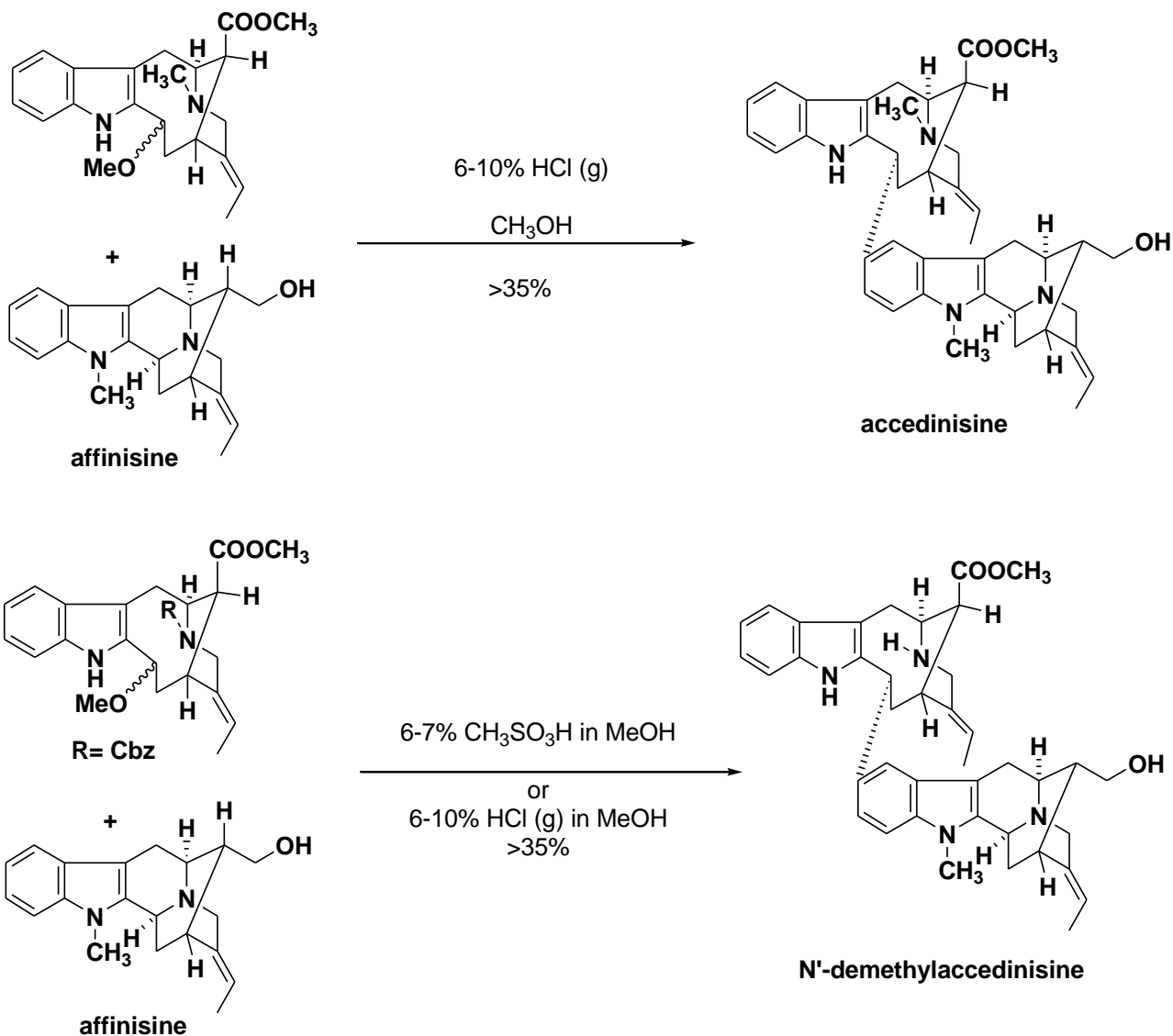
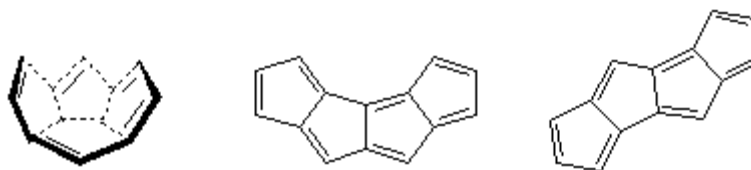
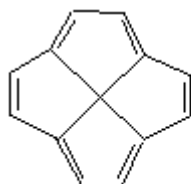


Figure 3: Synthesis of Bisindoles accedinisine and N'-demethylaccedinisine

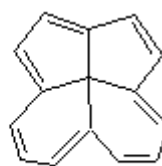
F. Attempts to prepare strained 10pi and 14pi annulenes (see below) termed cyclopentapentalenes in order to study homoconjugation, stability, electron delocalization, aromaticity (bonding character in organic molecules) are underway. The first stable disubstituted linear 14p annulene was recently prepared [J. Am. Chem. Soc. (2003)] in this series with the tandem Pauson-Khand reaction as the key step to generate molecular complexity.



G. We have in progress two projects directed toward the preparation of molecules which may house a planar four coordinate carbon atom. Initial targets are shown below. The Weiss reaction continues to be important in this work.



[5.5.5.5]



[5.5.6.6.]

Licensed Aza Beta Carboline compounds/patents to MPP Group and Addiction Therapeutix Inc. a Milwaukee-based start up company (2008).

Licensed Cysteine prodrugs and patent to Promentis Pharmaceuticals (Baker, Cook; Marquette/UWM), (2008-2009).

WISYS and Neuroamp. WISYS signed an option to license with NeuroAmp on the Alzheimers-Directed Compounds ( $\alpha 5$  Ligands at GABAergic BzR) from the memory deficit patent of Cook, Clayton and Han, assigned to WISYS, NeuroAmp is a new, Milwaukee-based start up company (Physiogenix). Previously, had nonsedating anxiolytic in human phase I clinical trials (had licensed to BMS).

## VI. STATEMENT OF TEACHING RESPONSIBILITIES AT UW-MILWAUKEE

There are a large number of students who enter UW-Milwaukee with career goals directed toward the Health Sciences in various subdisciplines including: premedical, pre dental, preveterinarian, and medical technology. The candidate's expertise in Medicinal Chemistry and Natural Products Chemistry, as well as his experience in Organic Chemistry enables him to teach students, academically, in this area quite readily. He has been responsible for teaching the survey course in Organic Chemistry (341) and the laboratory (342) to students in the medical technology, biology and environmental engineering fields. In addition, he has taught the standard organic sequence (343 and 345) to chemistry, premedical, pre dental, and preveterinarian students, which also included the laboratories 344 and 346. The candidate will continue to teach the above courses at the undergraduate level for it is extremely important to bridge the gap between Organic, Medicinal, and Biological Chemistry. At the graduate level, the candidate is interested in teaching Synthetic Organic and Medicinal Chemistry to students who are enrolled in all disciplines of chemistry. This teaching also includes courses in Medicinal Chemistry, The Biogenesis of Natural Products, A Survey of Natural Products Chemistry and The Total Synthesis of Indole Alkaloids.

### A. Experience as a teacher

#### Courses Taught at the University of Wisconsin-Milwaukee

##### Undergraduate Level

Chemistry 101 General and Organic Chemistry for Nursing Students  
 Chemistry 341 Introductory Survey of Organic Chemistry  
 Chemistry 343 Organic Chemistry, Semester 1  
 Chemistry 345 Organic Chemistry, Semester 2  
 Chemistry 342 Introductory Organic Chemistry Laboratory  
 Chemistry 344 Organic Chemistry Laboratory  
 Chemistry 346 Organic Chemistry Laboratory-Advanced Lab  
 Chemistry 399 Special Chemical Problems-Undergraduate Research  
 Chemistry 599 Special Projects in Chemistry-Undergraduate Research  
 Chemistry 691 Senior Thesis - Undergraduate Research  
 Chemistry 692 Senior Thesis, Capstone Course  
 Chemistry 693 Chemical Literature

##### Graduate Level

Chemistry 740 Modern Methods in Synthetic Chemistry (taught every other year).  
 Chemistry 741 Biogenesis of Natural Products  
 Chemistry 741 Heterocyclic Chemistry  
 Chemistry 741 Medicinal Chemistry  
 Chemistry 741 The Total Synthesis of Indole Alkaloids (taught every other year)  
 Chemistry 781 Modern Industrial Organic Chemistry  
 Chemistry 900 Colloquium  
 Chemistry 912 Graduate Seminar  
 Chemistry 990 Advanced Research - Organic

VII. UNDERGRADUATE AND GRADUATE RESEARCH PROJECTS, THESIS AND DISSERTATIONS DIRECTED.

Undergraduate Research 399, 599, and 691 - Students and their Next Position

*Sandra Neuendorf* - "Study of the Steering Effects in the Nitration of Aromatic Compounds," 1975-1976 (PhD, Biochemistry, UW-Madison, Vice President for Research, Incell Chemical, now UW-Oshkosh Faculty).

*Larry Hutchins* - "Pictet-Spengler Reactions in Refluxing Benzene," 1974-1976 (PhD, University of British Columbia; M.D., UW-Madison, now Marshfield Clinic).

*Steven Tung* - "Synthesis of Indole Alkaloids," (Medical School, believed to be at Columbia University).

*Eric Richfield* - "Studies directed toward the Synthesis of the Indole Alkaloid, Macroline," 1975-1976 (Medical Doctor, Marquette Medical School).

*Nancy Bratanow* - "Studies Directed Toward the Synthesis of Cellulase Inhibitors," 1975-1976 (Medical School, now Associate Professor, Medical College of Wisconsin).

*Cynthia Albanese* - "NMR Spectroscopy of Indole Alkaloids," 1975-1976 (Ph.D. Marquette University)

*Anita Miswald* - "Preparation of Galactose Derivatives," 1976.

*Mechtild Mueller-Johnson* - "Reaction of  $\alpha$ -Diketones with Dimethyl  $\beta$ -Ketoglutarate," 1975-1976 (Graduate School, UW-Milwaukee, Department of Mathematics).

*Robert Schumaker* - "Synthesis of Cyclopentanoid Compounds," 1975.

*Paulann Haas* - "Synthesis of Antimalarial Agents--A Review," 1975.

*Edward Amberger* - "Synthesis of 4-Oxo-4,5,6,7-tetrahydroindole," 1975-1976.

*Neil Palassari* - "Synthesis of Methyl-4-deoxy-4-thio-D-glucopyranoside," 1975-1976 (Graduate School, Biochemistry, University of Minnesota).

*Regina Prenger* - "Studies on Galactose," 1975-1976 (employee in government laboratory).

*David Wichman* - "Chemistry of Aromatic  $\alpha$ -Dicarbonyl Compounds and Dimethyl 3-Keto-glutarate," 1975-1976 (Lecturer, Math, UW-Milwaukee).

*Terri Chipman* - "Preparation of Bioinorganic Laboratory Experiments for Chemistry 342," 1976 (Medical School).

*Janet Koch* - "Amine Oxides," 1976 (MS, Department of Chemistry; Major, Biochemistry).

*Gary Bode* - "Applications of High Pressure Liquid Chromatography--A Review," 1976.

*Robert Weber* - "General Method for the Synthesis of [n.3.3.]propellanes, n3," 1976-1977 (PhD, UW-Milwaukee, CENTOCORE).

*Michael DiPierro* - "Pictet-Spengler Reactions; Synthesis and Stereochemistry," 1977-1979 (PhD, University of Minnesota, Abbott Laboratories; now Pfanstiehl Laboratories).

*Vernon Hasenstein* - "Preparation of 1-Ethyl-1,2,3,4-tetrahydro- $\beta$ -Carboline Derivatives," 1977-1978 (sales representative).

*Frank Ungemach* - "Stereospecific Synthesis of 1,3-Disubstituted-1,2,3,4-Tetrahydro  $\beta$ -Carbolines," (PhD, Vanderbilt University, now Patent Attorney, Amgen).

*John Conrad* - "Synthesis of Bicyclo[3.3.0]octanedione Derivatives," 1977.

*Robert Mantei* - "Studies Directed Toward the Synthesis of the  $\beta$ -Carboline Alkaloid, Crenatine," 1980 (Chemist, Abbott Laboratories).

*Gary Callen* - "Studies Directed Toward the Synthesis of Suaveoline," (Ph.D., University of Michigan, now Abbott Laboratories).

*Paul Larscheid* - "Synthesis of  $\beta$ -Carboline Alkaloids to be Employed as Valium Antagonists," 1980-1985 (Graduate School, UW-Milwaukee, Eli Lilly at one time).

*Mike Alexander* - "Synthesis of Coumarins and Carbostyrils for Mechanistic Studies," 1980 (Graduate School, UW-Madison).



*Jeff Schneider* - "Studies Directed Toward the Synthesis of Antimalarial Agents," 1980 (Graduate School, UW-Milwaukee).

*Jay Wrobel* - "Studies Directed Toward the Synthesis of Modhephene," 1980 (PhD, Cornell; Ayerst Laboratories).

*Mike Schoemaker* - "Studies Directed Toward the Synthesis of 7-Substituted-1,6- Diazaphenalenenes," 1979-1980 (Freeman Chemical Corporation).

*Barry Johnson* - "Entry into 3, 4-Disubstituted  $\beta$ -Carbolines *via* the Claisen Rearrangement," 1983-1984 (PhD, University of California-Berkeley, now Manager, Aldrich Chemical).

*Rick Craig* - "Synthesis of 3, 4-Disubstituted  $\beta$ -Carbolines," 1982-1984, MS degree, Marquette University (now Abbott Laboratories).

*Steve Welsenbach* - "Regiospecific Mono and Dialkylation of *cis*-Bicyclo-[3.3.0]octane-3,7- dione Systems," 1984-1985 (Gross Laboratories).

*Willis Yets* - "General Approach to the Synthesis of Polyquinenes," 1984-1985 (MS in Chemistry, University of California-Riverside, now Ameritech).

*David Remsen* - "Search for Polyaromatic Hydrocarbons from Sediment Taken from Green Bay," 1983-1984 (Graduate school, UW-Madison).

*Deborah Tuskiewicz* - "Synthesis of  $\beta$ -Carbolines," 1984-1985.

*Jeff Names* - "Synthesis of Indole Alkaloids," 1986-1987 (Chemical Industry, Milwaukee).

*Liesl Schindler* - "Synthesis of Inverse Agonists for Bz Receptors." "Synthesis of Polyquinenes." 1987-1989 (PhD, University of Minnesota), Director of Operations in Europe, Shell Oil Co.

*Michael Martin* - "Partition Coefficients of Benzodiazepine Inverse Agonists & Synthesis of Ligands for Valium Receptors." "Synthesis and Alkylation of Pyridodiindoles. Search for New Antianxiety Agents." 1987-1988 (Graduate School, UW-Milwaukee, Chemistry; now Eli Lilly and Company).

*Jeff Schkeryantz* - "Synthesis of Polyquinanes," 1986-1987 (PhD, University of Michigan, Postdoctoral study, Sloan Kettering; now Abbott Laboratories).

*Mark Derkowski* - "Synthesis of  $\beta$ -Carbolines," 1986.

*Adiga Godi* - "Synthesis of 3-Amino  $\beta$ -Carbolines," 1986-1988 (Aldrich Chemical Company).

*Brian Opanski* - "Synthesis of Quinidine Metabolites." "Synthesis of Polyquinenes." 1988 (PhD, University of Colorado, now Senior Design Engineer, Storage Tek).

*Ron Lefever* - "Synthesis of Polyquinenes *via* the Weiss Reaction," 1988 (Incell Chemical, now Aldrich Chemical Co.).

*Anthony J. Laloggia* - " $\beta$ -Carbolines: Synthesis of Inverse Agonists," 1988 (Aldrich Chemical Co.).

*Jerry Menzia* - "Synthesis of Indole Alkaloids," 1988 (Abbott Laboratories).

*Tim Feiter* - Literature Searches on "Indole and Tropane Alkaloids," 1990.

*Mike Magawa* - "Synthesis of Indole-2,3-Dioxygenase Inhibitors," 1991-1993 (PhD, Medicinal Chemistry, University of Michigan).

*Mark Theis* - "Synthesis of Alstonia Alkaloids," 1991-1992.

*Mark Minton*(high school student) -"Synthesis of BzR Ligands," 1992 (Ph.D. student, University of Colorado-Boulder).

*Ann Marie Kuhn* - "Synthesis of IDO Inhibitors," 1994-1995 (Medical School, Washington University).

*Andrew H. Geise* - "Synthesis of IDO Inhibitors," 1994 (PhD student, Medicinal Chemistry, UW-Madison, Fall, 1995).

*Sam Dashi* - "Search for New *Alstonia* Alkaloids," 1994.

*Heidi Pirkov* - "Search for Subtype Specific Ligands for BzR," 1994.

*Chris Plambeck* - "Search for  $\alpha 5\beta 2\gamma 2$  Subtype Specific Ligands for BzR," 1995 (Medical School, MCW).

*Raza Ghadi* - "Organic Chemistry Experiments," (PhD, UW-Madison; Professor, Scripps Research Institute).

*Poitr Kaszyinski* - "Chemistry of Polyquinenes," (PhD, Univ. of Colorado; Assoc. Professor, Vanderbilt Univ.).

*Erik Johnson* - "Synthesis of Polyquinenes," 1997.

Steve Taylor - "Search for New GABA<sub>A</sub>/BzR Antianxiety Agents," 1998-1999.

Dan Mass (high school student) - "Search for New GABA<sub>A</sub>/BzR Antianxiety Agents," 1998.

Yelena Ostrerova - "Synthesis of Potential Antianxiety Agents," 1999. (Aldrich Chemical Company).

Jelena Plavsic - "Synthesis of Antianxiety Agents," 2004. UW-Madison (School of Pharmacy).

Daniel Sem - "Synthesis of Heterocyclic Compounds" now Professor at Concordia University, Department of Chemistry.

Dustin Fisher - "Agents to Treat Neuropathic Pain," 2009.

Ara Tahniyath - "Search for New Antimicrobials," 2009.

Keni-Anne Paulina Francis - "Search for Agents to Treat Schizophrenia," 2009.

Angie Grzybkowska - "Synthesis of Antialcohol Compounds," 2010, now in Medical School.

Jana Beth Plotkin - "Research into Causes of Schizophrenia and Drugs to Treat Alcohol Abuse," 2011-2013.

Matheus Meirelles- "Synthesis of  $\alpha 6\beta 3\gamma 2$  receptor PAM's," 2014-2016.

Rodrigo De Souza- "Synthesis of  $\alpha 6\beta 3\gamma 2$  receptor PAM's," 2015.

C.J. Kleischmidt- "Synthesis of  $\alpha 6\beta 3\gamma 2$  receptor PAM's," 2015.

Demi Woods- "Search for  $\alpha 6$  Subtype Selective Ligands," 2014.

#### Graduate Level - Graduate Students, Thesis Title or Research Project in Progress

Daisy Yang-Lan (MS) - "Synthesis of [10.3.3] Propellane and [6.3.3] Propellane Derivatives," degree conferred August 1976.

James Oehldrich (MS) - "Addition of Activated Methylene Compounds to 1,2-and 1,3-Dicarbonyl Compounds," degree conferred August 1976 (Wisconsin Crime Bureau).

Frank Ungemach (MS) - "Pictet-Spengler Reactions in Refluxing Benzene and Toluene: Synthetic and Stereochemical Consequences of this Condensation," degree conferred in May 1978 (Abbott Laboratories, Group Leader, now Patent Attorney, Amgen).

Dave Soerens (PhD) - "I. Studies of the Pictet-Spengler Reaction in Aprotic Media. II. Studies Directed Toward the Total Synthesis of the Indole Alkaloid, *Suaveoline*," thesis defense completed in August 1978 (3M, now Kimberly Clarke).

Olivia Campos (PhD) - "I. Synthesis of Potential Antihypertensive Agents. II. Studies Directed Toward the Total Synthesis of *Brevicolline*," thesis defense completed in August 1978 (Associate Professor, University of Brasilia, Brazil).

Randall Mitschka (MS) - "Synthesis of Tetracyclo [5.5.1.0<sup>4,13</sup>.0<sup>10,13</sup>] tridecane-2,6,8,12-tetraketone," thesis defense completed in August 1978 (Eli Lilly, now Abbott Laboratories).

Patti Mokry Brettell (MS) - "Pictet-Spengler Reactions in Aprotic Media: Use of Acid-Labile Aldehydes in this Condensation," thesis defense completed in August 1979 (S.C. Johnson and then Kimberly Clarke, now Medical Doctor).

Jen-Chun Chang (MS) - "Synthesis of 1, 6-Diazaphenalene," thesis defense completed in August 1980.

Wen-Ching Han (MS) - "Studies Directed Toward the Synthesis of [5.5.6.6] Fenestrane," thesis defense completed in August 1982 (Squibb).

Mike Cain (PhD) - "I. Synthesis of the  $\beta$ -Carboline Alkaloids Canthine-6-one and Crenatine. II. Synthesis of Benzodiazepine Antagonists," thesis defense completed in December 1982 (Abbott Laboratories).

Shieu-Jeing Lee (MS) - "Chemistry of 1, 6-Diazaphenalene," thesis defense completed in May 1984 (PhD Student, Chemical Engineering, Yale University).

Robert Weber (PhD) - "I. Studies Directed Toward Synthesis of the Alkaloid, *Suaveoline*. II. Construction of Potential Antimalarial Agents," PhD, November 1984 (Mallinkrodt and then CENTOCOR).

Filadelfo Guzman (MS) - "Studies Directed Toward the Synthesis of a Specific Bz<sub>1</sub> Receptor Antagonist," MS in December 1984 (Schering Plough and then Rikker Laboratories).

Mahendra Deshpande (PhD) - "General Approach to the Synthesis of Polyquinenes. Synthesis of Staurane-2,5,8,11-tetraene," thesis defense completed in August 1985 (Abbott Laboratories).

*Mani Venkatachalam* (PhD) - "General Approach to the Synthesis of Polyquinenes *via* the Weiss Reaction," thesis defense completed in August 1986 (Supelco, Inc.).

*Greg Lannoye* (PhD) - "I. Synthesis of Triquinacene *via* the Weiss Reaction. II. Studies Directed Toward the Synthesis of Strained Polyquinenes," thesis defense completed in August 1987 (Abbott Laboratories).

*Greg G. Kubiak* (PhD) - "I. Mechanistic and Synthetic Studies on the Scope of the Weiss Reaction. II. Studies Directed Toward the Preparation of Staurane-1,3,5,7,9,11-Hexaene on the Route Towards Tetracoordinate Planar Carbon," thesis defense completed in May 1989 (Rhône Poulenc).

*Christopher Schultz* (MS) - "Studies Directed Toward the Synthesis of  $\beta$ -Carbolines and Indolocarbazoles as Ligands for the Benzodiazepine Receptor," MS thesis defense completed in August 1987 (PhD Student, Geology).

*Timothy Hagen* (PhD) - "I. The Synthesis of Benzodiazepine Receptor Antagonists and Inverse Agonists. II. The Total Synthesis of the Cytotoxic Indole Alkaloid: 1-Methoxy Canthine-6-one," PhD thesis defense completed in May 1988 (Searle Laboratories).

*Mark L. Trudell* (PhD) - "I. The Synthesis and Study of the Pharmacologic Activity of 7,12-Dihydropyrido[3,2-b:5,4-b']diindoles. A Novel Class of Rigid, Planar Benzodiazepine Receptor Ligands. II. The Total Synthesis of the Indole Alkaloid, ( $\pm$ ) Suaveoline," thesis defense completed in March 1989 (Distinguished Professor, University of New Orleans).

*Sherry Lifer* (MS) - "Studies on the Synthesis, Electrophilic Substitution, and SAR Studies on the Biological Activity of 7,12-Dihydropyrido[3,2-b:5,4-b']diindole," thesis defense completed in August 1987 (Eli Lilly and Co.).

*Hernando Diaz-Arauzo* (MS) - "Synthesis, High Resolution NMR Spectroscopy of the Metabolites of Quinine and Quinidine and Antibody-Mediated Platelet Destruction," MS thesis defense completed in July 1988 (PhD student, UW-Milwaukee).

*Michael Allen* (PhD) - "I. The Synthesis of Benzodiazepine Receptor Antagonists and Long-lived Inverse Agonists *via* the Template Approach. II. The Synthesis of 6-Methoxy-D-(+)-Tryptophans by the Moody Azide-Schollkopf Protocol," PhD Thesis completed January 1992 (Abbott Laboratories).

*Lin-Hua Zhang* (PhD) - "General Strategy for the Synthesis of Macroline/Sarpagine Alkaloids. Enantiospecific Total Synthesis of (-)-Alstonerine," PhD thesis defense completed in March 1990. (Postdoctoral work, University of California-Berkeley, Merck-Dupont Pharmaceutical Co., now Boehringer Ingelheim Pharmaceuticals, Inc.).

*Yun-Chou Tan* (MS) - "Synthesis and Study of the Biological Activity of 7,12-Dihydro-pyrido-[3,2-b:5,4b']diindole Derivatives," thesis defense completed in June 1988 (Ciba Geigy).

*Joseph Sandrin* (PhD writing in progress) - "Stereospecificity of the Pictet-Spengler Reaction," (Vice President, C.M. Hill).

*Xiaoyong Fu* (PhD) - "I. General Approach to the Synthesis of Polyquinenes *via* the Weiss Reaction. The Synthesis of Ellacene and Studies of the Attempted Dimerization to a Substituted Dodecahedrane. II. General Approach to the Synthesis of the Ajmaline Related Alkaloids. Enantiospecific Total Synthesis of (-)-Suaveoline, (-)-Raumacline, and (-)-N<sub>6</sub>-Methyl-raumacline," PhD thesis completed May 1992 (Schering-Plough Pharmaceutical Co.).

*Yingzhi Bi* (PhD) - "General Approach for the Synthesis of Macroline/Sarpagine Indole Alkaloids. Enantiospecific Total Synthesis of (+)-Macroline and a Partial Synthesis of the Bisindole Villalstonine," PhD thesis completed May 1994 (University of California-Berkeley, Postdoctoral Appt., also Affymax Co.; now Bristol Meyers Squibb)

*Li Deng* (MS) - "I. The Synthesis of 7, 12-Dihydropyrido[3,2-b:5,4-b']diindole and Indolo-[3,2-b] isoquinoline Ligands with which to Study the Pharmacophore of the Benzodiazepine Receptor Inverse Agonist Site. II. The Study of *Trans* Diastereoselectivity in the Pictet-Spengler Reaction," thesis defense completed in August 1990 (Harvard University, PhD; now Assistant Professor Brandeis University).

*Paul May* (MS) - "I. Unusual, Non-Proteinogenic Alpha-Amino Acids Derived from Chiral Heterocyclic Templates. II. Asymmetric Epoxidation," thesis defense completed in 1990 (Upjohn).

*Linda Hamaker* (PhD) - "Studies Directed Toward the Synthesis of Ring-A Methoxylated Indole Alkaloids. An Enantiospecific Approach to the Total Synthesis of Alstophylline and the Bisindole Macralstonine," thesis defense completed in August 1995 (Advanced Chem Tech, Louisville, Kentucky, then Texas Biotechnology Corp., now AtheroGenics, Inc.).

*Linda Dorn* (MS) - "Synthesis of Rigid, Planar 8H-Pyrido[1",2":1',2']imidazo[4'5':5,6]-pyrido [3,4,-b]indoles to Study the Topography of the Benzodiazepine Receptor," thesis defense completed in July 1991 (Abbott Labs).

*Michael Martin* (MS) - "Synthesis of Rigid Probes to Define the Dimensions of the Benzodiazepine Receptor Cleft," thesis defense completed in September 1992 (Eli Lilly).

*Kevin Czerwinski* (PhD) - "Studies on the Pictet-Spengler Reaction. I. Stereospecific Synthesis of *Trans*-1,3-Disubstituted-

1,2,3,4-tetrahydro- $\beta$ -carbolines. II. Approach to Cytotoxic Canthin-6-one Alkaloids," thesis defense completed in August 1995 (Professor, University of Wisconsin-Stevens Point).

*Wei Zhang* (PhD) - "I. Chemical and Computer-Assisted Development of an Inclusive Pharmacophore for the Benzodiazepine Receptor. Studies Directed Toward the Synthesis of Anxiolytic Anxiolytics. II. Molecular Yardsticks: Probes to Study the Actual Dimensions of Benzodiazepine Receptors," thesis defense completed in August 1994, (Iowa State University, Postdoctoral research associate; Abbott Laboratories, now Thervance).

*Jacquelyn Behnke* (MS studies) - "NMR Spectroscopy of *Alstonia* Alkaloids." (Aldrich Chemical Co.)

*Hernando Diaz-Araujo* (PhD) - "Synthetic and Computer Assisted Analysis of the Pharmacophore for Agonists at Benzodiazepine Receptors. Synthesis of a Selective Anxiolytic/Anticonvulsant," thesis defense completed in July 1991 (Nalco Oil Company).

*Eric Cox* (PhD) - "I. Synthesis and Evaluation of Analogues of the Partial Agonist 6-propoxy-4-methoxymethyl- -Carboline-3-carboxylic Acid Ethyl Ester and the Full Agonist Zk93423. II. Studies Directed Toward the Enantiospecific Synthesis of the Indole Alkaloid Pleiocarpamine and the Bisindole Alkaloids Villalstonine and Macrocarpamine," thesis defense completed in July 1997 (Pfizer Pharmaceutical Co.).

*Ruiyan Liu* (PhD) - "An Enantiospecific Synthesis of 5-Methoxy-(D)-Tryptophan and Related Indole Amino Acids Which Serve as Building Blocks Required for The Synthesis of Alkaloids and Cyclic Peptides. II. Synthesis and Pharmacological Properties of Novel Imidazobenzo-diazepines: High Affinity, Selective Probes for  $\alpha 5$ -Containing GABA<sub>A</sub> Receptors," thesis defense completed, October 1996 (Pharmacopia).

*Scott Van Ornum* (PhD) - "Studies Directed Toward the Synthesis of Dicyclopenta-[a,e]pentalene and Dicyclopenta[a,f]pentalene via the Tandem Pauson-Khand Reaction," thesis defense completed in April 1998 (Abbott Laboratories, Cedarburg Laboratories, now Professor Concordia University).

*Tong Gan* (PhD) - I. "An Enantiospecific Total Synthesis of (-)-Anhydromacrosalpine-Methine and A Partial Synthesis of The Antiamoebic Bisindole Alkaloid (-)-Macrocarp-amine." II. "Enantiospecific Synthesis of Optically Active 6-Methoxytryptophan Derivatives and Total Synthesis of Tryprostatin A," thesis defense completed in August 1997 (Schering Plough, now MLB).

*Qi Huang* (PhD) - "I. A Chemical and Computer Assisted Approach to Pharmacophore/Receptor Models for GABA<sub>A</sub>/BZ Receptor Subtypes. II Predictive Models for GABA<sub>A</sub>/BzR Subtypes via Comparative Molecular Field Analysis," thesis defense completed in June 1998 (Amgen, now Union Biopharmaceutical co).

*Peng Yu* (PhD) - "Enantiospecific Total Synthesis of the Indole Alkaloids Talpinine, Talcarpine, Alstonerine and Anhydromacrosalpine-methine as well as Studies Directed Toward the Synthesis of the Oxindole Alkaloid Alstonisine," thesis defense completed in February 1999 (Medi Chem Research, now Professor in China).

*Jin Li* (PhD) - "Enantiospecific Total Synthesis of (+)- Ajmaline and Alkaloid G as well as Studies Directed Toward the Total Synthesis of 19-Hydroxy-N<sub>6</sub>-Methylraumacline via the Asymmetric Pictet-Spengler Reaction," thesis defense completed in February 1999 (Pfizer Pharmaceutical Co.; now President of Shenogen Pharmaceutical Co.)

*C. Ma* (PhD) - I. "Efficient Asymmetric Synthesis of Ring-A Substituted Tryptophans. Synthesis of 6-Methoxy-(D)-Tryptophan Required for the Total Synthesis of Ring-A Oxygenated Indole Alkaloids. II. Synthesis of Selective Ligands for GABA<sub>A</sub>/Benzo-diazepine Receptor Subtypes," thesis defense completed in July 2000 (Pfizer, now Takeda Pharmaceutical).

*X. He* (PhD) - "Studies of Molecular Pharmacophore/receptor Models for GABA<sub>A</sub>/BzR Subtypes: Chemical and Computer Assisted Approach in Search of Selective Ligands for GABA<sub>A</sub>/BzR Subtypes," thesis defense completed in August 2000 (COMBI-CHEM, Dupont, now GNF corporation).

*T. Wang* (PhD) - "Enantiospecific Total Synthesis of (+)-Vellosimine, (+)-Normacusine B and (-)-Norsuaveoline as well as an Improved Enantiospecific Total Synthesis of (+)-Ajmaline and (+)-Alkaloid G," thesis defense completed in March 2001 (Schering Plough).

*S. Zhao* (PhD) - "I. The Enantiospecific Total Synthesis of Tryprostatin A and B as well as Their Enantiomers and Mismatched Pairs. II. The Enantiospecific, Stereospecific Total Synthesis of the Ring-A Oxygenated Sarpagine Indole Alkaloids (+)-Majvinine, (+)-10-Methoxyaffinisine, and (+)-N<sub>a</sub>-Methylsarpagine as well as the First Total Synthesis of the Alstonia Bisindole Alkaloid Macralstonidine," thesis defense completed in August 2001 (Ligand Pharmaceutical, now Biogenecide).

*X. Liu* (PhD) - "Enantiospecific Stereospecific Total Synthesis of the Enantiomers of the Indole Alkaloids N<sub>a</sub>-Methylvellosimine, Affinisine and Macroline as well as the Total Synthesis of Indole Alkaloids Trinervine, Alstophylline and the Antimalarial Bisindole Macralstonine." thesis defense completed in February 2002 (postdoctoral position, Yale University, then Wyeth, now Schering-Plough, now Patent Attorney (2012)).



*H. Cao* (PhD) - "Synthesis of  $14\pi$  Dicyclopentapentalenes *via* the Tandem Pauson- Khand Reaction." thesis defense completed in June 2003 (Enanta Pharmaceuticals).

*X. Liao* (PhD) - "The First Total Synthesis of the Indole Alkaloids, Macralstonine, 6-Oxo-alstophylline, 10-Methoxyvellosimine, Lochnerine, Sarpagine, and an Improved Total Synthesis of Macralstonine and Macroline, as well as a Formal Total Synthesis of Dispegatine," thesis defense completed in April , 2007 (postdoctoral position, University of Illinois at Champagne-Urbana, now Professor in Chinese University).

*W. Yin* (PhD) - "I. Synthesis of Optically Active Tryptophan Derivatives with Potential Activity as Indoleamine 2,3-dioxygenase Inhibitors: An Approach *via* Asymmetric Catalytic Hydrogenation. II. Design, Synthesis and Pharmacology of Selective Ligands for  $\alpha_1$ -Containing GABA<sub>A</sub>/benzodiazepine Receptor Subtypes: SAR Studies of  $\beta$ -carbolines at Positions -3 and -6 and Their Corresponding Bivalent Ligands. III. First Enantiospecific Total Synthesis of the Important Biogenetic Intermediates, (+)-Polyneuridine and (+)-Polyneuridine Aldehyde, as well as 16-Epi-Vellosimine and Macusine A," thesis defended Oct.1, 2007; Promentis Pharmaceutical Co (2008-2012).

*X. Li* (PhD) - "Synthesis of Subtype Specific Ligands for BzR/GABA(A) Receptors," thesis defense completed in October 2004 (US Army PHS, was in Aldrich Chemical).

*X. Wearing Zhu* (PhD) - Enantiospecific Stereospecific Total Synthesis of the Oxindole Alkaloid (+)-Alstonisine and Stereocontrolled Total synthesis of (-)-11-Methoxy-17-epivincamajine as well as Studies Directed Toward the Total Synthesis of N<sub>6</sub>-Demethyl-alstophylline," Thesis defense completed in September 2004 (Esai Pharmaceuticals).

*J. Ma* (PhD) - "I. General Approach to the Total Synthesis of 9-Methoxy Substituted Indole Alkaloids: Total Synthesis of the Opioid Agnostic Indole Alkaloid, Mitragynine, as well as 9-Methoxygeissoschizol and 9-Methoxy-Nb-Methylgeissoschizol. II. Studies Toward the Total Synthesis of the Antimalarial Alkaloid Villalstonine," thesis defended September 25, 2006 (Sloan Kettering, NY, now Enanta Pharmaceuticals).

*C. Zhang* (PhD) - "I. The Structure Activity Relationships and Cytotoxic Activity of Analogs of Tryprostatin A and B. Preparation of Irreversible Inhibitors for Studies of Mechanism of Action. II. Pharmacophore/Receptor Models for the GABA<sub>A</sub>/Bz Receptor Subtypes," Thesis defense completed in June 2004 (Pfizer Pharmaceuticals).

*S. Huang* (PhD) - "Synthesis of Optically Active Subtype Selective Benzodiazepine Receptor Ligands," Thesis defended August 9, 2007, job in California startup company.

*Michael Van Linn* (PhD) - " Studies on the Mechanism of the Cis to Trans Epimerization of Cis-1,2,3-Trisubstituted-1,2,3,4 – Tetrahydro  $\beta$ -Carbolines into their Trans Diastereomers *via* Kinetic Analysis," Thesis defended August 26, 2009. Postdoctoral appointment, Drexel University, CML-Labs.

*Yun Teng Johnson* (PhD) - "Synthesis of Subtype Selective Ligands for GABA(A)/Benzodiazepine Receptors Including Homomeric and Heteromeric Bivalent Ligands," Thesis defended August 15, 2009. Pharmacy School (UW-Madison).

*Shamim Ara* (MS) - "Synthesis of Optically Active C-4 Substituted Subtype Selective Imidazobenzodiazepine Receptor Ligands " Thesis defended August, 2010

*Rahul Edwankar* (PhD) - "I. Hz166, A Novel  $\gamma$ -Aminobutyric Acid (A) Receptor Sub-Type Selective Ligand Active Against Neuropathic Pain II. The First Enantiospecific, Stereospecific Total Synthesis Of The C-19 Methyl Substituted Sarpagine Indole Alkaloids 19(S),20(R)-Dihydroperaksine, 19(S),20-(R)-Dihydroperaksine-17-Al And Peraksine. III. Application Of Metal-Carbenoid Chemistry And Brønsted Acid Mediated Cyclization Of Enaminones For The Rapid And Efficient Access To The Tetracyclic (Abce) Skeleton Of The *Strychnos* Alkaloids Contained In Bisindole Alkaloids." Thesis defense completed in November 2010. Post doctoral appointment, University of North Carolina, now at Broad Institute, MIT, MA/GSK.

*Shahjahan Kabir* (PhD) - "I. Development of New Organic Synthetic Methods: Palladium and Copper Catalyzed Carbon-Carbon, Carbon-Sulfur, Carbon-Nitrogen, and Carbon-Oxygen Bond Formation as well as DABCO-Mediated Stereospecific Synthesis of Acrylate Ethers and Amines. Part II. Design, Synthesis and SAR Studies of New Classes of Agents to Treat Drug-Resistant Bacteria, Anthrax and Tuberculosis Infections". August 2011, FDA.

*C. Edwanker* (PhD) – "I. The First Regio- and Atropidiastereoselective Total Synthesis of the Dimeric Indole Alkaloid (+)-Dispegatine, as well as the First Total Synthesis of the Sarpagine Alkaloids (+)-Spegatine, (+)-Lochnerine, and (+)-Lochneram and an Improved Total Synthesis of (+)-10- Methoxyvellosimine, (+)-Lochnerine and (+)-Sarpagine. Part II. Studies Directed Toward the Total Synthesis of the C-19 Methyl Substituted Sarpagine-Macroline Alkaloids (+)-acrosalhine Chloride as well as Macrocarpine A, B and C." Thesis defense completed in December, 2011, Post doctoral appointment, at Broad Institute, MIT, MA



*T. Clayton* (PhD) - "Part I. Unified Pharmacophoric Protein Models Of The Benzodiazepine Receptor Subtypes Part II. Subtype Selective Ligands for 5 Gabaa/Bz Receptors." Thesis defense completed in December, 2011, Vice President R&D, Chromatic Technologies, Inc

*E. Johnson* (PhD) - "Part I. Design and Synthesis of Cysteine / Cystine Prodrugs and Bioisosteres including Symmetrical and Unsymmetrical Disulfides Designed to Increase Cystine Levels in the CNS in Order to Drive the Cystine / Glutamate Antiporter: A Novel Treatment for Schizophrenia and Drug Addiction. Part II. Design and Synthesis of Subtype Selective Ester Bioisosteres of BZR Ligands for GABA<sub>A</sub> / Benzodiazepine Receptors to Enhance Metabolic Stability." December 2012, Head Pharmacist, Milwaukee Hospital.

*S. Rallapalli* (PhD) - "Part I. The First Enantiospecific, Stereospecific Total Synthesis Of The Indole Alkaloid Ervincidine Part II. The Synthesis of Alpha 5 Subtype Selective Ligands for GABA (A) /Benzodiazepine Receptors". December 2012, Postdoctoral appointment, UWM-Milwaukee; Cambridge Major Labs. May, 2014.

*P. Biawat* (MS)-"The Synthesis of Alpha5 Subtype Selective GABA(A)/Benzodiazepine Receptor(s) Ligands," 2014; Sigma-Aldrich Chemical Company.

*G. Fonseca* (PhD) -"Enantiospecific Stereospecific Strategy for The Total Synthesis of Sarpagine and Macroline Related Oxindole Alkaloids: First Total Synthesis of Affinisine Oxindole, Isoalstonisine, Alstoline, Macrogentine, N(1)-Demethylalstonisine, Alstonoxine A And Second Generation Synthesis of Alstonisine". August, 2015. Job in Uruguay, South America.

*M. M. Poe* (PhD) - "Synthesis of Subtype Selective Bz/ GABA(A) Receptors Ligands for the Treatment of Anxiety, Epilepsy and Neuropathic Pain as well as Schizophrenia and Asthma", May, 2016. Postdoctoral appointment, UCONN.

*C. Witzigmann* (PhD) - "Part 1: Design, Synthesis, and Evaluation of Novel Gram-Positive Antibiotics; Part 2: Synthesis of Dihydrobenzofurans via a New Transition Metal Catalyzed Reaction; Part 3: Design, Synthesis, and Evaluation of Bz/GABA<sub>A</sub>  $\alpha$ 6 Positive Allosteric Modulators", December, 2016. Alcam, Germantown, WI.

*V. V. N. Phani Babu Tiruveedhula* (PhD) - "Part-I: Development of a two-step regiospecific synthetic route for multigram-scale synthesis of  $\beta$ -carboline analogs for studies in primates as anti-alcohol agents, Part-II: Design and synthesis of novel antimicrobials for the treatment of drug-resistant bacterial infections, Part-III: A novel synthetic method for the synthesis of the key quinine metabolite (3S)-3-hydroxyquinine", August 2017, University of Wisconsin-Milwaukee. T3 Bioscience; Wonik Materials North America, Germantown, WI.

*Md Toufiqur Rahman* (PhD)- "Part I: Shorter and improved access to the key tetracyclic core of C-19 methyl substituted bioactive sarpagine-macroline-ajmaline indole alkaloids via a new ambidextrous asymmetric pictet-spengler reaction beginning from either D-(+)- or L-(-)-tryptophan, Part II: The total synthesis of a number of bioactive C-19 methyl substituted macroline-sarpagine indole alkaloids including macrocarpines A-G, talcarpine, N(4)-methyl-N(4),21-secotalpinine, deoxyperaksine, dihydroperaksine, talpinine, O-acetylaltalpinine, as well as N(4)-methylaltalpinine" December, 2018. RTI International, NC.

*Guanguan Li* (PhD) – "Synthesis of New Treatments for Bipolar Disorders and Schizophrenia." May 2019.

*Md Zubair Ahmed Khan* (PhD) – "Synthesis of New Treatments for Diseases", 2021. PPD, WI.

*Rajwana Jahan* (PhD) - "Part-I: Design and synthesis of novel drugs to treat asthma by targeting gabaa receptors in the lung, Part II: Design and synthesis of novel  $\alpha$ 2/ $\alpha$ 3 subtype selective gabaar ligands for CNS disorders", May 2019. RTI International, NC.

*Daniel Knutson* (PhD) - "Synthesis of New Drugs to Treat Migraine and Tic disorders", August 2020. A-Chem, WI.

*Farjana Rashid* (PhD) – "Design and synthesis of achiral and chiral benzodiazepines and imidazodiazepines to modulate the activity of GABA<sub>A</sub> receptors for the treatment of cancer, CNS disorders and pain", August 2021. PPD, WI.

*Taukir Ahmed* (PhD) – "The activity of QH-II-66 and its analogs in medulloblastoma, melanoma and non-small cell lung cancer cell lines", May 2022. PPD, WI.

*Md Yeunus Mian* (PhD) – "Design and synthesis of chiral and achiral benzodiazepines and imidazodiazepines as  $\alpha$ -subtype selective gabaar positive modulators to treat schistosomiasis, epilepsy, asthma and some mental disorders", March 2022. Sterling Pharma Solutions, WI.

*Kamal Prasad Pandey* (PhD) – “Part-I: Enantiospecific total synthesis of unnatural enantiomers of C-19 methylated sarpagine/macroline/ajmaline-type biologically active indole alkaloids via pictet-spengler reaction/dieckmann cyclization process, Part-II: Design, synthesis, and characterization of novel gammaaminobutyric acid type a (GABA<sub>A</sub>) receptor ligands for the treatment of neurological disorders including epilepsy, depression, anxiety, pain, and the synthesis of back up compounds for the clinically progressing KRM-II-81 for the treatment of pharmacoresistant epilepsy and dravet syndrome”, Jan 2023, Dupont.

*Dishary Sharmin* (PhD) – “Design, synthesis, and biological evaluation of gabaar subtype selective ( $\alpha_6$ ,  $\alpha_2/3$ , and  $\alpha_5$ ) ligands to treat migraine, neuropathic pain, trigeminal pain, tourette syndrome, epilepsy, anxiety and cognitive disorders as well as asthma”, August 2023. UWM, WI.

*Prithu Mondal* (PhD work in progress) – “Synthesis of New Agents to Treat Depression and Alzheimer’s Disease”.

*Sepideh Rezvanian* (PhD work in progress) – “Synthesis of Agents to Treat Anxiety Disorders, Neuropathic Pain and Epilepsy”.

*Morteza Panahzadeh Khanmiri* (PhD work in progress) – “Strategic Design and Synthesis of Benzodiazepines for Targeted Cancer Therapies and Multi-Disease Treatment Approaches”.

### Postdoctoral Trainees and Visiting Scientists

*Denis Foerst* - "Preliminary Exploration of Synthetic Routes to Antihypertensive and Antimalarial Agents," 1976 (NIOSH, Cincinnati, Ohio).

*Geng Wu* - "Synthesis of Indole Alkaloids and Antihypertensive Agents," 1978 (Ash-Stevens, Detroit, Michigan).

*Etsuji Yamanaka* - "Studies Directed Toward the Total Synthesis of the Indole Alkaloids, Macroline and Pyridindolol," 1977-1978 (Associate Professor, Chiba University, Japan).

*Mustafa El-Sheikh* - "Synthesis of Antimalarial Agents, Chemistry of 1,6-Diazaphenalene," 1977-1979 (Faculty Member, United Arab Emirates).

*Ali Gawish* - "General Approach for the Synthesis of Polyquinanes," 1979-1981 (Research Chemist, ARAMCO then Incell).

*Kazu Takahashi* - "Studies Directed Toward the Synthesis of Modhephene," 1981-1982 (Associate Professor, Industrial Chemistry, Chiba University, now deceased).

*K. Avasthi* - "Studies on the Chemistry of 1,6-Diazaphenalene," "General Approach for the Synthesis of Polyquinanes," 1980-1981 (Chemist, India, now Professor in India).

*Vidya Honkan* - "Synthesis of Modhephene," 1982-1983 (Chemist for the Government, Jamaica, West Indies, deceased in car crash).

*Mikolaj Jawdosiuk* - "Synthesis of Polyquinanes and of Indole Alkaloids," 1983-1985 (Aldrich Chemical Co., now President of CRO).

*N. Fukada* - "Hydrazine-mediated Amination-Oxidation of 4-Oxo-substituted-1,2,3,4-tetra-hydro  $\beta$ -Carbolines," 1984 (Associate Professor, Chiba University).

*Ashok Kumar Gupta* - "Synthetic Approach to Planar Tetracoordinate Carbon *via* the Weiss Reaction," 1987-1990 (Abbott Laboratories).

*Kotha Sambasivarao* - "General Approach to the Synthesis of Polyquinenes *via* the Weiss Reaction. Synthesis of Dicyclopentapentalenes," 1987-1989 (Hoechst Celanese Corporation, now Professor, India).

*Krishnaswamy Narayanan* - "Synthesis of New Ligands for Benzodiazepine Receptors." "Carboxy-mediated Pictet-Spengler Reaction," 1987-1990 (Teaching Position, Mount Mary College).

*Sean Patrick Hollinshead* - "Studies Directed toward the Synthesis of the Macroline-Derived Indole Alkaloid, Alstonisine," 1987-1989 (Pfizer Pharmaceutical Firm, England, now SPHINX, N.C.).

*Robert Badger* - "General Approach to the Synthesis of Polyquinenes. Synthesis of 1,10- Disubstituted Triquinacenes," 1988 (Associate Professor of Chemistry, University of Wisconsin- Stevens Point).

*Mundla S. Reddy* - "I. Enantiospecific Synthesis of Indole Alkaloids *via* the Pictet-Spengler Reaction. II. Fenestrane Approach

Toward a Planar Tetracoordinate Carbon Atom," 1992-1994 (Proctor and Gamble Co., Cincinnati, OH, now President Sreeni Labs, India).

*Andrew Peterson* - "I. Synthesis of Indole 2,3-Dioxygenase Inhibitors. II. Enantiospecific Synthesis of Ajmaline and Alstonisine," 1992-1994 (Clarion Pharmaceuticals, then Columbia Chemical).

*Puwen Zhang* - "I. Enantiospecific Synthesis of Alstonia Alkaloids. II. Synthesis of  $\alpha 5$  Subtype Specific Ligands at BzR," 1993-1995 (Wyeth-Ayerst Pharmaceuticals, now Pharmaron Corp, China).

*Shu Yu* - "I. Synthesis of  $\alpha 1\beta 3\gamma 2$  Selective Ligands for BzR/GABA<sub>A</sub> Receptors. II. Studies on the Total Synthesis of Pleiocarpamine," 1997-1999 (Pfizer).

*M. Bruendel* - "I. Studies on the Tandem Pauson-Khand Reaction. II. Synthesis of New Ligands for BzR/GABA<sub>A</sub> Receptor Subtypes," 1997-1999 (Pfizer).

*Mathias Berner* - "I. Studies in the Enantiospecific Synthesis of Indole Alkaloids. II. Synthesis of Novel Benzodiazepines," 1999-2000 (Postdoctoral position, Professor Enders, now REACHLAW).

*Dongmei Han* - "I. Synthesis of Benzodiazepine Receptor Subtype Specific Ligands. II. The Asymmetric Pictet-Spengler Reaction." (company in California)

*Jianming Yu* - "I. Synthesis of Benzodiazepine Subtype Specific Ligands. II. The Total Synthesis of the Bisindole Alkaloid Alstonisine," 2003-2004 (FMC, then Lundbeck, now Pharma Corp.)

*Hao Zhou* - "I. Synthesis of New Anxiolytic Agents. II. Stereospecific Synthesis of Indole Alkaloids," 2004-2006 (Lundbeck)

*P.V.V.S. Sarma* - "Synthesis of BzR Subtype Selective Anxiolytics," 2004-2006 (Cambridge-Major Labs)

*Felix Rivas* - "Synthesis of BzR Subtype Selective Ligands for Treatment of Epilepsy," 2004-2005, Associate Professor (Chicago State University).

*H. Jain* - "Synthesis of Anticonvulsant and Antimalarial Agents," 2009, Business, India.

*J. Yang* - "Synthesis of Anxiolytic and Antileishmanial Agents," Albany Molecular Research Institute, 2008.

*H. Kumpaty* - "Mechanism of the Pictet – Spengler Reaction." Associate Professor, UW-Whitewater.

*Ross Wang* - "Synthesis of Nonsedating Anticonvulsant and Anxiolytic Agents" 2009-2012, (now Washington University Medical School, Postdoctoral; Now Berkley); Now startup in CA.

*Ojas Namjoshi* - "Synthesis of New  $\alpha 5$  GABA(A)ergic Ligands for Studies on Cognition and Antialcohol Agents." 2008-2012 (RTI, North Carolina).

*Michael Lorenz* - "Synthesis of Cysteine-Cystine Bioisosteres." 2010, BASF, Germany.

*Ranjit Verma* - "Synthesis of Antimicrobial and Anticonvulsant Agents as well as Prodrugs to Treat Schizophrenia." 2009-2011; 2013-2016 (Cytometrix); Now Medical College of Wisconsin, Project Director.

*Sundari K. Rallapalli* - "Synthesis of  $\alpha 5$  GABA(A)ergic Ligands for Studies on Schizophrenia and Neuroblastoma", 2012-2013; (CML, then Analytical Co. in Atlanta).

*Wenyuan Yin* - "Synthesis of Prodrugs to Treat Schizophrenia." 2008-2012 (was Promentis Pharmaceutical Co., now a company on the West Coast).

*Stephen Michael Rajesh* - "Synthesis of  $\alpha 4$ -  $\alpha 6$  GABA(A)ergic Ligands for Treating Asthma, and Agents for Pain." 2013 – 2018; Jubilant Biosynthesis, Bangalore, India.

*Kashi Reddy Methuku* - "Synthesis of  $\alpha 4$ -  $\alpha 6$  GABA(A)ergic Ligands for Treating Asthma, as well as Agents for Pain and Schizophrenia." Alcam, Germantown, WI.

*Ashwini Verma* - "Synthesis of Agents to Treat Schizophrenia and Pain". Medical College of Wisconsin, Program Director.

*Lalit Kumar Golani* – "Synthesis of Agents to Treat Pain and Schizophrenia".

*Dishary Sharmin* – "Synthesis of Agents to Treat Depression, Neuropathic Pain, Epilepsy, and Migraine".

## VIII. CONSULTING SERVICES

Consulted for Aldrich Chemical Company, Milwaukee, on classification of cytochalasin B and the synthesis of dicarbonyl compounds. Fee: \$1,500. Time: Three-five days per year. Paid by Aldrich Chemical. (For details, contact Dr. Alfred Bader, President).

Consulted with the UW-Extension on the thesis of Mr. Paul Thoma. Fee: \$100. Time: One day.

Consulted for Aldrich Chemical on the Synthesis of *cis*-bicyclo[3.3.0]octane-3,7-dione and N<sub>a</sub>-methyltryptophan. \$6,000.00 (10 days) 1979-1985.

Consulted for Incell Chemical. Fee: \$100/day. Time: Four days.

Consulted for Research Biochemical Incorporated on Synthesis of  $\beta$ -Carbolines. Fee: \$4,250. Time: Seven days.

Consulted for Searle Research Laboratories on evaluation of their new CNS program. Fee: \$800/day, for several days. (1986-1987)

Consulted for Eli Lilly. Fee: \$450/day. (1987)

Consulted for Aldrich Chemical. Fee: \$2,500.00, Synthesis of *cis*-bicyclo[3.3.0]octane- 3,7-dione. (1988)

Consulted for Research Biochemical Incorporated on Synthesis of  $\beta$ -Carbolines. Fee: \$1,500.00. (1988)

Consulted for Gillick, Gillick, Murphy, and Wicht (Law Firm) on the case of student Jeff Schkeryantz. Fee: \$500.00. (1988)

Consulted for Parke Davis-Warner Lambert. Fee: \$500.00/day. (1988)

Consulted for Monsanto Chemical Co. (Agr. Division), on Synthesis of Compounds for Biological Screening. Fee: \$6,600. (1989-1990)

Consulted for Aldrich Chemical Co. on the Synthesis of Isoreserpine and other Alkaloids. Fee: \$800. (1989)

Consulted for Searle Laboratories on Compounds for Gastrointestinal Studies. Fee: \$1,000. (1989)

Consulted for Universal Foods on the Isolation of Carminic Acid. Fee: \$1,000. (1989)

Consulted for Aldrich Chemical on the Synthesis of *cis*-Bicyclo[3.3.0]octane-3,7-dione. Fee: \$6,000. (5 days, 1990)

Consulted for Universal Foods on the Structure of New Flavors and Pigments. Fee: \$1,000. (1991)

Consulted for Aldrich Chemical on the Synthesis of New Indoles and  $\beta$ -Carbolines. Fee: \$2,900. (1991)

Consulted for Aldrich Chemical on the Synthesis of Tryptophans. Fee: \$1,700. (1992)

Consulted for Aldrich Chemical on the Synthesis of Tryptophans. Fee: \$2,900. (1993-94)

Consulted for R.W. Johnson Pharmaceutical Co. on Benzodiazepines. Fee: \$1,000. (1994).

Consulted for Aldrich Chemical Co. on the Synthesis of Bicyclo[3.3.0]octane-3,7-dione. Fee: \$7,000. (1994).

Consulted for Aldrich Chemical Co. on the Synthesis of Indoles. Fee: \$1,400. (1994).

Consulted for Abbott Laboratories on Indole Alkaloids. Fee: \$1,500. (1995).

Consulted for Aldrich Chemical Co. on the Synthesis of Indoles. Fee: \$750. (1995).

Consulted for Ciba-Corning on Synthesis of Quinine diols. Fee: \$1,000; \$2,000 donated to the Department of Chemistry. (1995).

Consulted for Aldrich Chemical Co. on the Synthesis of Bicyclooctan-3,7-diones. Fee: \$9,000. (1996).

Consulted for Aldrich Chemical Co. on the Synthesis of Indoles *via* The Moody Azide pyrolysis. Fee \$6,000 (1996).

Consulted for Aldrich Chemical Co. on the Synthesis of Indoles. Fee: \$11,000. (1996).

Consulted for Merck and Co. on Samples for Screening. Fee: \$1,000. (1996).

Consulted for Aldrich Chemical Co. on Synthesis of Heterocycles. Fee \$3,450 (1996-97).

Consulted and Supplied Compounds for Broad Based Screening to ASTRA Pharmaceutical and Dupont. Fee paid to UW-Milwaukee: \$18,350 (1997).

Consulted and Supplied Compounds for Broad Based Screening to ASTRA/ARCUS Pharmaceutical Co. Fee paid to UW-Milwaukee: \$47,000.

Consulted for Aldrich Chemical Co on the Synthesis of Indoles and Polyquinanes. Fee \$20,000 (1997-98).

Consulted and Supplied Compounds for Broad Based Screening to ASTRA/ARCUS Pharmaceutical Co. Fee paid to UW-Milwaukee \$20,000.



Consulted and Supplied Compounds for Broad Screening to Dupont. Fee paid to UW-Milwaukee \$9,000.

Consulted for Cal Biochem on the Synthesis of Trypostatins. Fee \$4,000 (1998).

Consulted for Albany Molecular Research on the Synthesis of Tryptophans. Fee paid to UW-Milwaukee \$4500 (1999).

Consulted for Aldrich Chemical on Synthesis of Indoles. Fee donated to UW-Milwaukee \$1250 (1999).

Consulted for Albany Molecular Research. Fee paid to UW-Milwaukee \$3000 (2000).

Consulted for Dr. Andy Mellor, Georgia Medical School. Fee paid to UW-Milwaukee \$3000 (2000).

Consulted for Aldrich Chemical Company. Fee donated to UW-Milwaukee Foundation (Chemistry) \$20,000 (2000).

Consulted for Pfizer Global Research and Development. \$2500 (2001).

Consulted for Dupont Pharmaceuticals. \$1000 (2001).

Consulted for Aldrich Chemical Company. Fee donated to the UW-Milwaukee Foundation (Chemistry) \$10,000 (2001).

Consulted for Ligand Pharmaceutical. \$500 (2002).

Consulted for UCB Pharmaceutical. \$1000 (2002).

Consulted for Roche Biosci, Inc. \$1500 (2003).

Consulted for Eli Lilly & Co., \$2000 (2003).

Consulted for Sepracore, \$1250 (2003).

Consulted for Aldrich Chemical Company, \$11, 167 (2003).

Consulted for Aldrich Chemical Company, \$5600 (2004).

Consulted for GMP Pharmaceutical Co., \$12,500 (\$8,500 donated to UWM-Foundation) (2005).

Consulted for Abbott Laboratories, \$1500 (2005).

Consulted for Sepracor, \$1000 (2005).

Consulted for Aldrich Chemical Co., \$20,000 (donated to UWM-Foundation) (2005).

Consulted for Aldrich Chemical, \$20,000 (donated to UWM-Foundation) (2006).

Consulted for Xintria Pharmaceutical Corp., 2006

Consulted for Xintria Pharmaceutical Corp., \$8000 (2007).

Consulted for Xintria Pharmaceutical Corp., \$1500 (2008).

Consulted for Cambridge-Major Labs, \$2500 (2008).

Consulted for Physiogenix, \$5000 (2008).

Consulted for MPP Group, \$16,000 (2008).

Consulted for Promentis, \$15,000 (2009).

Consulted for MPP Group, \$12,000 (2009).

Consulted for Aldrich Chemical Co., \$1500-3000 (2009).

Consulted for CML, \$2500 (2009).

Consulted for Promentis, \$15,000 (2010)

Consulted for Addiction Therapeutix, \$12,000 (2010)

Consulted for Promentis, \$18,750 (2011)

Consulted for Addiction Therapeutic, \$7000 (2011)

Consulted for Promentis \$3750 (2012)

Consulted for CML, \$2500 (2010)

Consulted for CML, \$2500 (2011)

Consulted for CML, \$2500 (2012)  
Consulted for HMS, \$5600 (2013)  
Consulted for CML, \$2500 (2013)  
Consulted for CML, \$5500 (2014)  
Consulted for CML, \$5000 (2015)  
Consulted for Cortex Pharmaceutical Co., \$2500 (2015)  
Consulted for Cortex Pharmaceutical Co., \$4000 (2016)  
Consulted for Alcam, \$5000 (2016-Paid in 2015; Dec 31, 2015)  
Consulted for Expansion Therapeutics, \$10,000 (2018 – 2019)  
Consulted for the Medical College of Wisconsin, Dr. Sengupta, on agents to treat bladder pain, \$8000 (2018 – 2019)  
Consulted for the University of Cincinnati on Cancer, \$9000 (2019 – 2020)

## **IX. MEMBERSHIPS**

- The American Chemical Society: Organic & Medicinal Chemistry Divisions
- The Chemical Society
- Society of Neuroscience
- College on Problems of Drug Dependence
- International Congress on Heterocyclic Chemistry
- European Union Academy of Sciences