Dear Colleagues:

On behalf of the Division of Organic Chemistry of the American Chemical Society and the Department of Chemistry of the University of Utah, we welcome you to Salt Lake City, the site of the 39th National Organic Chemistry Symposium (NOS 2005).

The National Organic Chemistry Symposium is the premier event sponsored by the Division of Organic Chemistry of the American Chemical Society. The symposium is held biennially in June of odd numbered years to highlight the recent advances in organic chemistry research. The first National Symposium on Organic Chemistry was held in Rochester, NY, in December 1925, under the auspices of the Rochester Section and the Division of Organic Chemistry of the American Chemical Society. The early meetings were held in December but that changed later to June. There was an interruption during WWII but the symposium was resumed with a meeting in Boston in 1947 and continued to be held biennially since then. In 1959, the Roger Adams Award was established and the Award Address became a significant focus of the symposium. The relaxed program that is spread over four days in beautiful surroundings gives the attendees a chance to talk Chemistry and become better acquainted. The University of Utah, the host of this year's meeting, will continue this tradition. With views of the mountains, the city, and the Great Salt Lake, it will provide this year's meeting with perfect surroundings to relax and talk about Chemistry.

As in the long tradition of the past National Organic Chemistry Symposia, the 39th Symposium features a very distinguished and impressive list of speakers. The main program consists of 13 of the most eminent speakers, and is augmented by the address of the 2005 Roger Adams Awardee, Jerrold Meinwald. The lectures are presented during morning and evening sessions at the elegant Kingsbury Hall auditorium.

The poster presentations, which have become a major part of the NOS program, will be held in the evenings (Sunday to Wednesday) from 9:00 – 12:00 at the Scholarship Reception Room located at the 4th floor of the Rice-Eccles Stadium and Reception Tower with a breathtaking view of the city and surrounding mountains. This year we have over 420 posters presentations spread over the four nights. Wednesday evening will feature a conference dinner to all attendees at the Rice-Eccles Stadium Olympic Plaza.

Salt Lake City and the State of Utah offer a wealth of natural and unnatural attractions. The University of Utah Conference Services has arranged several excursions to visit and enjoy several of the many local attractions.

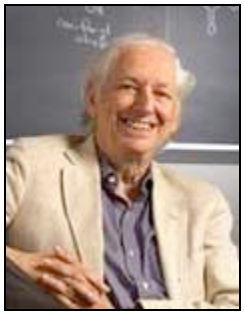
We thank the outstanding faculty of the Chemistry Department for their support and providing about 50 volunteers to help throughout the conference and the many activities. We thank the Conference Services for doing everything to provide the convenience and the relaxed atmosphere that is a trademark of this symposium. Most of all, we thank you for attending and being part of this great symposium.

Welcome to Salt Lake City.

Ahmed F. Abdel-Magid
Johnson & Johnson
Pharmaceutical Research & Development

Jon D. Rainier
Chemistry Department
The University of Utah

39th National Organic Chemistry Symposium
Plenary Speakers

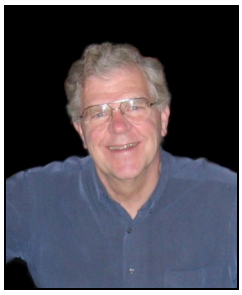


Roger Adams Awardee
Professor Jerrold Meinwald
Cornell University
Department of Chemistry and
Chemical Biology
Ithaca, NY 14853-1301
Presenting: Tues., June 14, 7:30 pm

Professor Stephen Buchwald
MIT
Department of Chemistry
Room 18-490
77 Massachusetts Avenue
Cambridge, MA 02139
Presenting: Mon., June 13, 7:00 pm

Professor Justin Du Bois
Stanford University
Department of Chemistry
S G MUDD, Rm. #191
Stanford, California, 94305-5080
Presenting: Thurs., June 16, 9:00 am

Professor M. Reza Ghadiri
Scripps Research Institute
Department of Chemistry
Beckman Center for Chemical Sciences
(BCC 104)
La Jolla, CA 92037
Presenting: Tues., June 14, 10:30 am



Professor John T. Groves
Princeton University
Department of Chemistry
203 Hoyt Laboratory
Princeton, NJ 08544
Presenting: Wed., June 15, 11:45 am

Professor Steven Ley
Cambridge University
Department of Chemistry
Lensfield Road, Cambridge, CB2 1EW, UK
Presenting: Mon., June 13, 9:00 am

Dr. Bruce Maryanoff
Johnson & Johnson Pharmaceutical
Research and Development
Welsh & McKean Roads
P.O. Box 776
Spring House, PA 19477
Presenting: Tues., June 14, 11:45 am

Professor Jeffrey Moore
University of Illinois
Department of Chemistry
470 Roger Adams Laboratory
600 S. Mathews Avenue
Urbana, IL 61801
Presenting: Tues., June 14, 8:30 am

Professor K.C. Nicolaou
Scripps Research Institute
Department of Chemistry
10550 North Torrey Pines Road, La Jolla, California 92037
Presenting: Wed., June 15, 7:30 pm

Professor Alanna Schepartz
Yale University
Department of Chemistry
P.O. Box 208107
New Haven, CT 06520-8107
Presenting: Mon., June 13, 8:15 pm

Professor Matthew Sigman
University of Utah
Department of Chemistry
315 So. 1400 E. Room 2020
Salt Lake City, UT 84112
Presenting Thurs., June 16, 10:45 am

Professor Amos B. Smith, III
University of Pennsylvania
Department of Chemistry
Philadelphia, PA 19104-6323
Presenting Mon., June 13, 10:45 am

Dr. Richard Tillyer
Merck Research Laboratories
Merck & Co. Inc.,
P.O. Box 2000
Rahway, NJ 07065
Presenting: Wed., June 15, 10:30 am

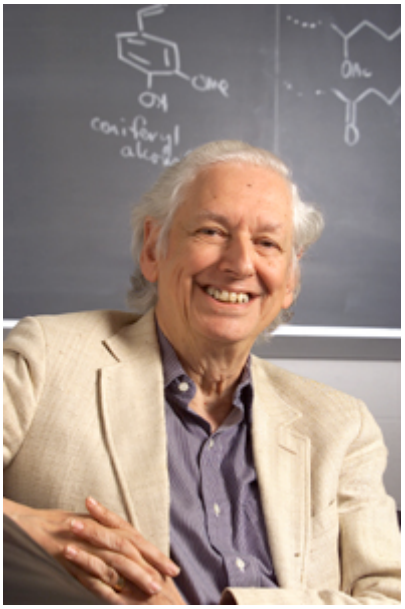
Professor Dan Yang
University of Hong Kong
Room 602
Chong Yuet Ming Chemistry Building
Pokfulam Road
Hong Kong
Presenting: Wed., June 15, 8:30 am

39th National Organic Chemistry Symposium
The Roger Adams Award in Organic Chemistry

The Roger Adams Award in Organic Chemistry is sponsored jointly by the American Chemical Society, Organic Reactions, Inc., and Organic Synthesis, Inc. The award recognizes the distinguished career of Roger Adams, who played a vital role in each of these three organizations. He was Chairman of the Board of Directors as well as President of the American Chemical Society, and he co-founded *Organic Syntheses* and *Organic Reactions*.

The award is made biennially to an individual, without regard to nationality, for outstanding contributions to research in organic chemistry. The award consists of a gold medal, a sterling silver replica of the medal, and an honorarium of twenty-five thousand dollars. It is presented as the biennial National Organic Chemistry Symposium of the Division of Organic Chemistry of the American Chemical Society. The awardee is a featured lecturer in the program of the symposium.

The recipient of this year's Roger Adams Award is Professor Jerrold Meinwald of Cornell University "for his broad contributions to organic chemistry, including extensive chemical studies of insect and plant defense and communication mechanisms, which have helped shape contemporary chemical ecology." Professor Meinwald's Award Address entitled "*Recent Advances in the Chemistry of Natural Products: Death and Transfiguration of a Classical Discipline*" will be delivered on Tuesday evening June 14, 2005.



39th National Organic Chemistry Symposium

Organizers

Ahmed F. Abdel-Magid
Johnson & Johnson Pharmaceutical Research and Development
Symposium Executive Officer

Jon D. Rainier
University of Utah
Local Symposium Chair

Organizing Committee

University of Utah

Peter Beal
Janis Louie
Mathew Sigman
Ilya Zharov
Saundra Reiber

University of Utah Conference Services

Perry Hacker
Amber Chisholm
Meghan Webb

39th National Organic Chemistry Symposium
ACS Division of Organic Chemistry Officers

Executive Committee Members

	2004	*2005*
Chair	William Greenlee	Huw M. L. Davies
Past Chair	Edwin Vedejs	William Greenlee
Chair Elect	Huw M. L. Davies	Kathlyn Parker
Secretary Treasurer	James H. Rigby	James H. Rigby
Secretary/Treasurer-Elect		Gary Molander
National Program Chair	Robert D. Larsen	Robert D. Larsen
39th NOS Executive Officer	Ahmed F. Abdel-Magid	Ahmed F. Abdel-Magid
Members-at-large	P. Andrew Evans	P. Andrew Evans
	Sarah E. Kelly	Donna M. Huryn
	Marie E. Krafft	Marie E. Krafft
	John R. Stille	Peter G. M. Wuts
	Lisa McElwee-White	Lisa McElwee-White
	Steven C. Zimmerman	Steven C. Zimmerman
Councilors	Michael P. Doyle	Michael P. Doyle
	Franklin A. Davis	Franklin A. Davis
	Kathlyn Parker	Kathlyn Parker
	Barry B. Snider	Barry B. Snider
Alternate Councilors	Victor Snieckus	Victor Snieckus
	Cynthia A. Maryanoff	Cynthia A. Maryanoff
	Robert Volkmann	Robert Volkmann
	Stephen W. Kaldor	Paul L. Feldman

39th National Organic Chemistry Symposium

Events Sponsorship

We appreciate the sponsorship of the following events;

Sunday evening poster session and mixer: Beilstein-Institut
Tuesday evening poster session and mixer: Sponsored by ACS Publications

We acknowledge the following for advertising sponsorship:

ACS Publications
Elsevier

39th National Organic Chemistry Symposium Exhibitors

We wish to acknowledge the following companies who have chosen to share their products and information with the Symposium participants.

Exhibitor booths will be located in Rice-Eccles Stadium

Exhibitor hours correspond with poster sessions and social mixers.

ACS Publications

Beilstein-Institut

Chemical Communications

Drug Discovery Alliances

Elsevier

Sigma-Aldrich

39th National Organic Chemistry Symposium Sponsors

We acknowledge and appreciate the unrestricted generous financial support and sponsorship by the following organizations.

Abbott Laboratories
Boehringer Ingelheim
Bristol-Myers Squibb Company
Chembridge Research Laboratories
Chiron
Cordis Corporation
Drug Discovery Alliances, Inc.
DuPont
Eastman Chemical Company
Eli Lilly and Company
Frontier Scientific
Gilead Sciences, Inc.
GlaxoSmithKline
Idaho Technology Inc.
J-Star Research Inc.
Johnson and Johnson, Pharmaceutical Research & Development, L.L.C
Merck Research Laboratories
NPS Pharmaceuticals
Pfizer
Regis Technologies, Inc
Roche Bioscience
Rohm and Haas Company
Sigma- Aldrich
Syrrx
Schering-Plough
Wyeth

General Information

Alcohol

The University is an alcohol free campus. Use, possession or distribution of alcoholic beverages of any type on University premises except as permitted by law and University regulations is prohibited. Empty Alcohol containers are not permitted in the residence halls.

Altitude

The University of Utah is located at 4,657 feet (1420 meters) above sea level and rises to above 10,000 feet (3,220 meters) in the mountains. Some guests may experience altitude sickness. The symptoms of altitude sickness are headaches, nausea, fatigue and/or shortness of breath. Altitude sickness generally disappears within 48 hours. Altitude sickness is almost entirely preventable and can be significantly minimized when the following guidelines are followed: exercise in moderation the first few days; drink more water than usual; reduce alcohol intake - which has a greater effect at this altitude; eat food high in carbohydrates and avoid salty foods.

ATM Machine

There are two ATM Machines located on the first floor of the Olpin Union and one in the Heritage Center.

Campus Parking

Free parking will be available in the University Guest House and Residence Halls lots identified for National Organic Chemistry Symposium participants. A no-charge parking lot is available at Rice-Eccles stadium.

Computer Services & Photocopying

Computers are available in the Multi-Media Lab in the J. Willard Marriott Library (enter from the west side of the building). Limited access computer kiosks are available at the Union free of charge. At the University Guest House an internet ID and password can be purchased to be used with a laptop for $5.00. Photocopying is available in the Olpin Union on the first floor.

Conference Services

General information for the 39th National Organic Chemistry Symposium is available during registration hours: Sunday June 12, 1:00 pm – 9:00 pm and Monday June 13, 7:30 am – 3:00 pm at the Registration Desk located in meeting rooms A & B of the University Guest House as well as the University Guest House front desk open 24 hours.

Dining

Meal plan:

For those of you who have purchased the meal plan:

Breakfast and Dinner will be served at the Peterson Heritage Center. Breakfast is Monday thru Saturday 6:30 am to 9:00 am, Sunday 10:00 am to 2:00 pm. Dinner Monday thru Sunday 4:30 pm to 7:30 pm.

Lunch will be served at the Olpin Union. The menus are as follows:

Hot Lunch Option

Monday, June 13

Caesar Salad, Garlic Parmesan Breadsticks, Ratatouille, Fettuccini with Marinara, Chicken Parmesan, Cheese Cake with Strawberry Topping.

Tuesday, June 14

Penne Pasta Salad with Crumbled Feta and Roasted Vegetables, Butterflake Rolls with Butter, Seared Eye of Round Beef with Roasted Shallot Sauce, Garlic Smashed Potatoes, Dill Buttered Carrots, Chocolate Chip Cookies.

Wednesday, June 15
Fiesta Salad Tossed In Cilantro Lime Dressing, Make-Your-Own Fajitas: Flour Tortillas, Marinated Chicken with Sour Cream, Cheddar Cheese, Salsa, Sliced Jalapeños, and Diced Tomatoes, Spanish Rice, Pinto Beans, Cinnamon Sugar Churros.

Thursday, June 16
Tossed Garden Salad with Raspberry Vinaigrette and Ranch, Assorted Dinner Rolls with Butter, Turkey Breast Roasted with Caramelized Onions and Cranberries, Rosemary Roasted Potatoes, Baby Green Beans, and Apple Pie with Crème Fraiche.

Box Lunch Option
Monday, June 13
Marinated Chicken Breast Sandwich on Chibata Bread/Roasted Veggie (Vegetarian Option), Bag of Chips, Rice Krispie, Canned Beverage/ 12 oz. Bottled Water, Disposable Ware.

Tuesday, June 14
Assorted Meat Sandwiches on Wheat or White Bread, Bag of Chips, Cookie, Canned Beverage/ 12 oz. Bottled Water, Disposable Ware.

Wednesday, June 15
Chicken Caesar Wrap: Grilled Chicken, Romaine Lettuce, Parmesan Cheese, and Caesar Dressing, Bag of Chips, 7-Layer Bar, Canned Beverage/ 12 oz. Bottled Water, Disposable Ware.

Thursday, June 16
All American Subs: Ham, Turkey, Roast Beef, Cheddar Cheese, Bag of Chips, 7-Layer Bar, Canned Beverage/ 12 oz. Bottled Water, Disposable Ware.

Olpin Union Food Options:
Located on the first floor of the Olpin Union, you will find a wide variety of food and beverage options including: pizza, sandwiches, to hot entrees served all day long, and a small convenience store. Food Court in the Olpin Union will be open Monday –Friday from 7:30 a.m. – 2:30 p.m., Closed Saturday & Sunday.

The following are located within walking distance of the University

Chop Suey Luey's	200 S 1328 E	581-1155	Chinese food, reasonably priced; delivery available
The Pie	200 S 1320 E	528-0193	Pizza, beverages, and music; delivery available
Sono Express	200 S 1318 E	582-2800	Japanese food
Gandolfo's	201 S 1300 E		Subs/sandwiches
Subway	221 S 1300 E	582-5001	Subs
B&D Burgers	222 S 1300 E	582-7200	Burgers and shakes
Gepetto's Italian	230 S 1300 E	583-1010	Pizza and pasta
Einstein Brothers	240 S 1300 E	583-1757	Bagels, sandwiches, and coffee
Market Street Broiler	360 S 1300 E	583-8808	Seafood and steak
7-Eleven	209 S 1300 E	581-0998	Open 24 hours
Red Hanger Cleaners	209 S 1300 E	582-7677	Dry cleaning
Kinkos	200 S University	583-3480	Copies and printing
University Pharmacy	200 S 1320 E	582-7624	Pharmacy and deli

Emergency/Medical

On campus, report emergencies to the Campus Police at 5-COPS (5-2677). There are blue light phones located throughout the campus. At your hotel, please contact the front desk or dial 9-911 for assistance in dealing with an emergency.

Game Room

Located on the first floor of the Olpin Union you will find a Bowling Alley, Billiards, Video Games, and the very popular Dance Machine for your enjoyment.

Local Recreation Venues

A complete list of activities from Salt Lake City can be found in you Visitors Guide located with your registration material.

J. Willard Marriott Library

The library is a shared asset of the academic community, dedicated to teaching users how to find, evaluate, and incorporate knowledge in scholarly and research endeavors. With a welcoming environment, the library ties the academic community to varied cultural and scholarly traditions. The library has more than 2.5 million volumes, 14,530 current print serials, and access to a growing body of full-text electronic resources including 10,000 full-text journals.

Utah Museum of Fine Arts

The Utah Museum of Fine Arts is the primary cultural resource for the visual arts in Utah. It is the state's only public institution that acquires and exhibits a general collection of art objects selected for quality and representation of the principal artistic styles and periods of civilization. Museum hours are Tuesday through Friday 10:00 am to 5:00 pm, Wednesday 10:00 am to 8:00 pm Saturday and Sunday 11:00 am to 5:00 pm and Closed Mondays and Holidays. Admission is $4 for adults and $2 for seniors.

Red Butte Garden

Red Butte Garden is a center of botanical and ecological display. Plant collections include native and non-native species that are adaptable to the climate of the Intermountain West. Red Butte Garden features 25 acres of display gardens and collections of dwarf conifers, flowering perennials, ornamental grasses, and aquatic plants. Surrounding natural areas offer four miles of hiking trails for environmental education. Hours are Tues. - Saturday 9:00 am - 9:00 pm, Sunday 9:00 am - 5:00 pm. There is an admission fee of $5 for adults, $3 for seniors, and $3 for children.

Utah Museum of Natural History

The Utah Museum of Natural History holds the Intermountain West's major archaeological, biological, and paleontological collections, which are highlighted in the museum's five exhibit halls: geology, biology, ecology, anthropology, and minerals. About 225 exhibits illustrate Utah's unique resources in natural history. Museum hours are Monday 9:30 am – 8:00 pm, Tues. – Saturday 9:30 am – 5:30 pm, Closed Sundays. There is an admission fee of $6 for adults, $3.50 for seniors, and $3.50 for children.

Lost and Found/Message Board

If you have lost something or need to get a message to someone, do not hesitate to use the message board located in Kingsbury Hall.

Maps

See back cover

Post Office

The Post Office is located inside the University Bookstore, at the north end of the building.

Poster Setup and Teardown

Poster Setup: Sunday through Wednesday 10:00 am - 6:00 pm day of presentation.
Poster Teardown: Monday through Thursday by 1:00 pm (day after poster session).
Exception: Wednesday posters must be taken down immediately following the poster session.

Security
Badges must be worn during all Symposium meals events.

Shuttle Schedule
See inside of back cover

Telephone Information
Telephones are available throughout Olpin Union, Heritage Center and Rice Stadium.

Transportation
Buses will be running from the University Guest House, Residence Halls, University Park Marriott and Chase Suites to the University of Utah campus throughout the conference. There will be an increased amount of buses during the rush hour periods, mornings and evenings. Light rail is also available running from downtown Salt Lake City to the University of Utah campus throughout the day and evening for a nominal fee. A campus shuttle schedule is located on the inside back cover

University Bookstore
University Bookstore, located just west of the Olpin Union offers a wide variety of textbooks, office supplies, computer software, gifts, clothing, and more. The University Bookstore gladly offers a 20% discount to all NOS participants. A coupon is included in your registration materials. The hours of operation during the conference are:

Monday, Wednesday, Thursday and Friday	8:00 am to 5:30 pm
Tuesdays	8:00 am to 5:30 pm
Saturdays	Closed

University of Utah

From its beautiful campus at the foothills of the Wasatch Mountains in Salt Lake City, the University reaches out to its diverse student body (who come from all 29 Utah counties, all 50 states, and 111 foreign countries) and to the larger community with top-rated academic departments, extensive service-learning opportunities, competitive athletics, wide-ranging cultural offerings, and innovative medical programs.

The U opened as the University of Deseret in 1850. The name was changed to the University of Utah in 1892, and classes began in the current campus location (Fort Douglas) in 1900.

U of U Stats:

Total enrollment:	28,933
Residents:	24,719
Nonresidents:	4,214
Undergraduate:	22,775
Graduate:	6,158
Off-campus enrollment:	1,719

Volunteers
There will be volunteers located throughout campus during the conference. The volunteers will be wearing Yellow ACS Shirts and should be easy to locate. If you have problems locating a volunteer, do not hesitate to ask University of Utah students any questions you may have.

Walk-In Medical Facilities

University Hospital, located on the east side of campus is a full service hospital that can handle all medical emergencies and health problems.

Excursions

HISTORIC CITY TOUR

TOUR DESCRIPTION: Celebrate Salt Lake City on a tour that includes some of the city's most famous sites and buildings. Begin at the Capitol, the city's crowning jewel. The view from the front steps is magnificent. Murals lining the Georgian marble rotunda walls tell the story of the settling of the Old West. See the Beehive House, Brigham Young's beautifully restored home. While living in the home, Young was Territorial Governor and President of the Mormon Church. The tour includes a drive past the elegant mansions on South Temple. Many of these homes were built with wealth derived from the Park City mining boom of the late 1800's. One of these homes is the Governor's Mansion, which is the largest in the United States. See the University of Utah's Rice/Eccles Stadium, site of the opening and closing ceremonies for the 2002 Winter Olympic and Paralympic Games, and Old Fort Douglas, site of the 2002 Olympic Athlete's Village. Visit Pioneer Trail State Park and This-Is-The-Place Monument at the mouth of Emigration Canyon. This monument stands as a tribute to the men, women and children who were instrumental in settling this area. En route back to downtown, guests will view Trolley Square, a unique shopping center built in trolley barns from the early 1900's.

INCLUDES: Round trip transportation, uniformed guide and narration, all in-house coordination by Meetings America.
DURATION: 3 Hours
COST: $18 per person (30 person minimum)

PARK CITY & OLYMPIC SPORTS PARK

TOUR DESCRIPTION:" Victorian Silver to Olympic Gold", Utah Olympic Sports Park. Visit Park City, and the Utah Olympic Sports Park, site of the bobsleigh, luge, ski jumping, and Nordic combined events of the 2002 Winter Olympics. The 387-acre facility was opened in 1993. The 1,335-meter bobsleigh/luge track with five start areas is one of only 12 competition-certified refrigerated tracks in the world. Our park guide will take us to the top of the ski jumps, where we can peer over the top - or stand by the bobsleigh track as the athletes race by. Ski jumps for 90- and 120-meter Nordic events are used for training and competition year-round. We'll also visit the Alf Engen Olympic interactive museum on site. The next stop is Park City, which had its beginnings in the mining boom of the late 19th century. Learn about its colorful History as it changed from a mining town to a world famous ski resort. Spend time browsing the unique shops and galleries on historic Main Street or enjoy lunch on your own at one of the many eclectic restaurants.

INCLUDES: Round trip transportation, uniformed guide and narration, all in-house coordination by Meetings America, Admission to the Olympic Sports Park and tour with a park guide.
DURATION: 3 Hours
COST: $30 per person (30 person minimum)

KNOW YOUR ROOTS

EVENT DESCRIPTION: Get help from trained genealogists. Get on board one of the most exciting hobbies sweeping the nation, in the nation's best place to learn it: Genealogy. The Family History Library of The Church of Jesus Christ of Latter-day Saints has the world's largest collection of genealogical records in the world. Today the library has information on more than 2 billion names, 711,000 microfiche, and 278,000 books. With the help of more than 3,400 satellite libraries in 65 countries, the Family History Library is constantly expanding the collection. One of its branches is probably in the city where you live! So if you've been wondering about your family history, come on in! Who knows? You might be related to royalty. There are two levels for this program - according to your interest, experience and level of involvement:

1. One on One Consultation

- Excellent for those who have begun some research
- One hour spent with a professional genealogist
- Pedigree Chart mailed out to registrants and returned three weeks before your trip to SLC
- Questions on difficult lines discussed
- Professional recommendations

2. Shaking the Family Tree Min: 8 Max: 24

- Excellent for the beginning Genealogist
- Learn the Soundex System, which is necessary to read the 1930 census
- Provide name of family member who was head of household in 1930 and his/her location in the U. S.
- Orientation of Family History Library Access international genealogical index & computer indexes compiled by LDS Church
- Learn to use the Internet to continue your research.

INCLUDES: All in-house coordination by Meetings America
DURATION: Length varies depending on the program
COST: (no transportation included) 1.One on One $50; 2.Shaking the Family Tree $12

GREAT SALT LAKE & KENNECOTT COPPER MINE

TOUR DESCRIPTION: Kennecott Copper Mine, Visit the classics… the most famous sites associated with Salt Lake City. The Great Salt Lake is the largest salt-water body of its kind in the world. At 20% saline, compared to the ocean's 2 - 3%, swimmers can bob and float like corks. Guests will learn about the lake's turbulent Ice Age history, its romantic past as the "Coney Island of the West," and its present-day significance regarding weather, industry, recreation, and as a migratory bird habitat. After stopping at the lake's marina for an up-close view, it's on to the Copper Mine. This mine is so enormous that shuttle Astronauts can identify it from space! If the Sears Tower were set in the bottom of the open-pit, it would reach only halfway to the top. Nine million people could be seated for a game if the open-pit were a football stadium. Since mining operations began in 1906, five billion tons of ore have been extracted. Besides copper, trace amounts of gold and silver are found in this mineral rich area.

INCLUDES: Round trip transportation, uniformed guide and narration, all in-house coordination by Meetings America, Admission to the copper mine (weather permitting), Stop at the Great Salt Lake Marina.
DURATION: 3 Hours
COST: $20 (30 person minimum)

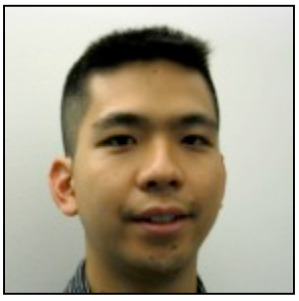
39th National Organic Chemistry Symposium
ACS Organic Division
Graduate Fellows and Sponsors

Listed below are the 29 advanced graduate students who are awarded Division of Organic Chemistry Graduate Fellowships in the past two years. All of these students are here at the Symposium with poster presentations. Next to their name is listed the session and poster number where they will be presenting and the companies that sponsored their awards. Also listed are the names of their institutions, faculty research advisors, and the companies that sponsored these awards. The Division is pleased to honor these extraordinary students and to gratefully acknowledge the substantial financial support provided by their generous sponsors.

2004-2005 Fellowship Winners

Erik J. Alexanian

Sponsor: GlaxoSmithKline
University: Princeton University
Advisor: Erik J. Sorensen



Irwin Chen

Sponsor: Wyeth Research
University: Massachusetts Institute of Technology
Advisor: Alice Ting

Andrew D. Cohen

Sponsor: Aventis Pharmaceuticals
University: Johns Hopkins University
Advisor: John P. Toscano

Jennifer M. Heemstra

Sponsor: Nelson J. Leonard ACS DOC Fellowship, sponsored by Organic Syntheses, Inc.
University: University of Illinois at Urbana-Champaign
Advisor: Jeffrey S. Moore

Audris Huang

Sponsor: Pfizer, Inc.
University: University of California at Irvine
Advisor: Larry E. Overman

Peter D. Jarowski

Sponsor: Organic Reactions, Inc.
University: University of California at Los Angeles
Advisors: Ken N. Houk and Miguel A. Garcia-Garibay

Jennifer E. Klare

Sponsor: Organic Syntheses, Inc.
University: Columbia University
Advisors: Colin Nuckolls

Tamara E. Munsch

Sponsor: Schering-Plough Research Institute
University: Purdue University
Advisor: Paul G. Wenthold

David A. Nicewicz

Sponsor: Novartis Pharmaceuticals
University: University of North Carolina at Chapel Hill
Advisor: Jeffrey S. Johnson

Jason T. Roland

Sponsor: Albany Molecular Research, Inc.
University: University of California at Irvine
Advisor: Zhibin Guan

Jennifer M. Schomaker

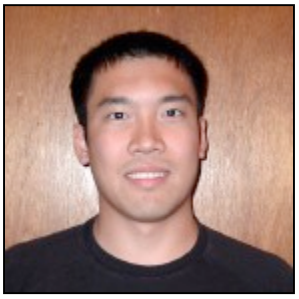
Sponsor: Eli Lilly and Company
University: Michigan State University
Advisor: Babak Borhan

W. Michael Seganish

Sponsor: The Procter & Gamble Company
University: University of Maryland at College Park
Advisor: Philip DeShong

Raissa M. Trend

Sponsor: Bristol Myers Squibb Foundation
University: California Institute of Technology
Advisor: Brian Stoltz



Jimmy Wu

Sponsor: Merck Research Laboratories
University: Harvard University
Advisor: David A. Evans

2003-2004 Fellowship Winners

Christopher T. Calderone

Sponsor: Bristol Myers Squibb Foundation
University: Harvard University
Advisor: David R. Liu

Kacey A. Claborn

Sponsor: Organic Reactions, Inc.
University: University of Washington
Advisor: Bart Kahr

Kevin P. Cole

Sponsor: Schering-Plough Research Institute
University: University of Minnesota
Advisor: Richard P. Hsung

Benjamin L. Frankamp

Sponsor: The Procter & Gamble Company
University: University of Massachusetts, Amherst
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39th National Organic Chemistry Symposium
Schedule of Events

SATURDAY, JUNE 11, 2005

7:00 am – 2:00 pm	Fly Fishing Tour	Depart from University Guest House

SUNDAY, JUNE 12, 2005

1:00 pm – 9:00 pm	Registration	University Guest House
9:00 pm – 12:00 am	Opening Mixer/Poster Session A Exhibitor Booths	Rice-Eccles

MONDAY, JUNE 13, 2004

Presiding: Ahmed F. Abdel-Magid (Johnson & Johnson PRD)

7:30 am – Noon	Registration	University Guest House
8:30 am – 9:00 am	Welcome & Opening Remarks	Kingsbury
9:00 am – 10:00 am	**Steven V. Ley** Cambridge University *Development of New Methods for Organic Synthesis*	Kingsbury
10:00 am – 10:15 am	Questions	
10:15 am – 10:45 am	Break	
10:45 am – 11:45 pm	**Amos B. Smith, III** University of Pennsylvania *Total Synthesis of Architecturally Complex Natural and Unnatural Products: Challenges, Excitement and Frustrations*	
11:45 am – Noon	Questions	
1:00 pm – 5:00 pm	Historic City Tour Know Your Roots Park City/Olympic Tour	Depart from Student Union

EVENING SESSION

Presiding: Jon D. Rainer (University of Utah)

7:00 pm – 8:00 pm	**Stephen L. Buchwald** Massachusetts Institute of Technology *Metal-Catalyzed Cross-Coupling Reactions: Progress, Applications and Mechanistic Studies*	Kingsbury
8:00 pm – 8:15 pm	Questions	
8:15 pm – 9:15 pm	**Alanna Schepartz** Yale University *Designing Molecules for Protein and Cell Surfaces*	Kingsbury
9:15 pm – 9:30 pm	Questions	
9:30 pm – Midnight	Mixer and Poster Session B Exhibitor Booths	Rice-Eccles

TUESDAY, JUNE 14, 2005
Presiding: Peter Beal (University of Utah)

8:20 am – 8:30 am	Introductory Remarks	Kingsbury
8:30 am – 9:30 am	**Jeffrey S. Moore** University of Illinois *Foldamer Heterosequences: Modular and Customizable Molecular Containers*	
9:30 am – 9:45 am	Questions	
9:45 am – 10:30 am	Break	
10:30 am – 11:30 am	**M. Reza Ghadiri** Scripps Research Institute *Self-Assembling Peptide Nanotubes: Design and Biological Applications*	Kingsbury
11:30 am – 11:45 pm	Questions	
11:45 am – 12:45 pm	**Bruce Maryanoff** Johnson & Johnson PRD *Structure-Based Drug Design Applied to Serine Protease Inhibitors*	Kingsbury
12:45 pm – 1:00 pm	Questions	
1:00 pm – 5:00 pm	Know Your Roots Park City/Olympic Tour	Depart from Student Union

EVENING SESSION
Presiding: Huw M.L. Davies (SUNY Buffalo)

7:30 pm – 8:45 pm	**Roger Adams Awardee Address:** **Jerrold Meinwald** Cornell University *Recent Advances in the Chemistry of Natural Products: Death and Transfiguration of a Classical Discipline*	Kingsbury
9:00 pm – Midnight	Mixer and Poster Session C Exhibitor Booths	Rice-Eccles

WEDNESDAY, JUNE 15, 2005

Presiding: Ilya Zharov (University of Utah)

8:20 am – 8:30 am	Introductory Remarks	
8:30 am – 9:30 am	**Dan Yang** University of Hong Kong *Catalytic Asymmetric Cyclization Reactions for Natural Product Synthesis*	Kingsbury
9:30 am – 9:45 am	Questions	
9:45 am – 10:30 am	Break	
10:30 am – 11:30 am	**Richard Tillyer** Merck & Co. *Asymmetric Hydrogenation: A Standard Platform for Practical Drug Synthesis*	Kingsbury
11:30 am – 11:45 am	**John T. Groves** Princeton University *The Chemical Biology of Iron - Trafficking, Signaling and Intervention*	Kingsbury
12:45 pm – 1:00 pm	Questions	
1:00 pm – 5:00 pm	Historic City Tour Know Your Roots	Depart from Student Union

EVENING SESSION

Presiding: Janice Louie (University of Utah)

5:00 pm – 7:00 pm	Conference Banquet	Rice-Eccles Stadium Olympic Plaza
7:30 pm – 8:30 pm	**K.C. Nicolaou** Scripps Research Institute *Perspectives in Total Synthesis*	Kingsbury
8:30 pm – 8:45 pm	Questions	
9:00 pm – Midnight	Mixer and Poster Session D Exhibitor Booths	Rice-Eccles

THURSDAY, JUNE 16, 2005
Presiding: P. Andrew Evans (Indiana University)

8:50 am – 9:00 am	Introductory Remarks	
9:00 am – 10:00 am	**Justin Du Bois** Stanford University *C-H Oxidation Reactions as Enabling Methodologies for Organic Synthesis*	Kingsbury
10:00 am – 10:15 am	Questions	
10:15 am – 10:45 am	Break	
10:45 am – 11:45 am	**Matthew S. Sigman** University of Utah *Metal-Catalyzed Oxidations for Organic Synthesis*	Kingsbury
11:45 am – Noon	Questions	
Noon	Closing Remarks	Kingsbury
1:00 pm – 5:00 pm	Know Your Roots Fly Fishing Tour	Depart from Student Union

Lecture Abstracts

RECENT ADVANCES IN THE CHEMISTRY OF NATURAL PRODUCTS: DEATH AND TRANSFIGURATION OF A CLASSICAL DISCIPLINE

Jerrold Meinwald

Department of Chemistry and Chemical Biology
Cornell University
Ithaca, NY 14853-1301, USA

Natural products chemistry no longer commands quite the excitement it did a half century ago, when it occupied center stage in the field of organic chemistry. Roger Adams himself, with his studies of the *Senecio* alkaloids, gossypol, and tetrahydrocannabinol, had been a pioneer in the field. D. H. R. Barton's conformational analysis rationalized much of steroid and triterpene chemistry. "Woodward's Rules" had greatly increased the utility of ultraviolet spectroscopy in structure determination. Newly available double-beam infrared spectrometers brought the even greater power of infrared spectroscopy to bear on structural problems. The ability of single crystal X-ray diffraction to reveal the full, three-dimensional structures of important natural products, such as cholesterol and penicillin, had been dramatically demonstrated. Early "biogenetic" theories had begun to guide structural hypotheses, and actual biosynthetic pathways were becoming accessible to direct experimental study, especially as a consequence of the availability of ^{14}C, ^{13}C, ^{18}O, ^{3}H, and ^{2}H for isotopic tracer experiments. The determination of the structures of naturally occurring compounds isolated from plant, animal, and microbiological sources on the basis of chemical and physical evidence was an exciting intellectual endeavor requiring a very broad range of analytical skills. The necessity of combining totally different types of evidence which were generally called upon to fully characterize a new natural product gave this sort of research the character of a highly sophisticated intellectual game, and the "proof" of a structure was as satisfying as the solution of a Sherlock Holmes mystery.

Synthesis played a central role in advancing the study of natural products as well. With rapid advances in physical organic chemistry, unprecedented structural selectivity and the control of stereochemistry based on an understanding of reaction mechanisms became possible. Gilbert Stork's brilliant synthesis of cantharidin called the organic chemical community's attention to the value of incorporating stereochemical reasoning into synthetic strategy. It was becoming much easier to confirm postulated structures by rational synthesis in the second half of the 20th century than it had been in the first.

"Recent Advances in the Chemistry of Natural Products" was a much used Woodwardian lecture title (especially convenient when the great master was not quite sure which of his ongoing investigations would be ripe for presentation at the time a lecture needed to be presented). This ubiquitous title always succeeded in generating a wonderful atmosphere of excitement and anticipation within a lecture audience. Woodward's lectures, models of clarity, elegant language, and brilliant analysis, beautifully illuminated by

structural formulas precisely drawn with colored chalk, artfully combined elements of structure elucidation, mechanistic reasoning, and synthesis; they went a long way towards defining the entire discipline.

The study of the chemistry of living organisms has long been motivated by two rather different desires. The more fundamental has been chemists' desire to answer the most basic questions, such as that posed in the English nursery rhyme, *What Are Little Girls Made Of?* What exactly are the chemicals of life? Of comparable importance, however, has been the desire for *useful knowledge:* how can our study of the molecules of nature be used for the development of drugs, dyes, pesticides, fibers, flavors, fragrances, etc. Natural products chemistry can properly be regarded as the mother of organic chemistry, since its pursuit gave birth to the realization that the chemistry of carbon compounds needed to be elucidated for its own sake in order for any substantial understanding of the chemistry of life to be achieved. By the mid-20th century, natural products chemistry had entered a "Golden Age". It has continued to advance rapidly not only as a result of the remarkable creativity of synthetic organic chemists, but also as a consequence of the spectacular development of NMR spectroscopy, mass spectrometry, and X-ray crystallography, as well as unimaginable advances in chromatographic techniques.

In fact, so successful have we been in natural product isolation, structure determination, and synthesis in the last half-century that we have come dangerously close to putting ourselves out of business. Have not most interesting natural products already been discovered? Cannot we count on the possibility of devising a rational synthesis of any new natural product that we might want in quantity? Why should anyone look for novel drugs or pesticides by studying secondary metabolites, when combinatorial chemistry can provide libraries of millions of new and readily patentable compounds which can be examined by high throughput screening techniques in a very short time? Are not genomics and proteomics the chemistries of the future? These questions deserve thoughtful consideration. But there is no doubt that the answers that they have already received in the last decade or so have resulted in a dramatic shift of both interest and resources away from natural products chemistry in both industry and academia. The challenge of "small molecule" isolation, structure determination, and synthesis is no longer what it was. Although not literally dead, the classical discipline of natural products chemistry appears to be at least temporarily indisposed.

In this paper, I will describe some old and some new research endeavors, emphasizing my attempts to avoid the most well-trodden paths. At the suggestion of my good friend, Michael Cava, I used the opportunity of my 1952 appointment at Cornell to build on the earlier work of McElvain to establish the structure of nepetalactone, the active ingredient of catnip. It turned out that the application of the isoprene rule led directly to the correct structure. Beginning in the late 1950's, the opportunity to collaborate with a young biological colleague, Thomas Eisner, provided the possibility for the collaborative pursuit of some problems at the chemistry/biology interface which were almost totally devoid of competitors. The questions we asked were not simply what new compounds could we find in nature, and not only what are the structures of important signaling and defensive molecules in the world of insects and their relatives, but also how these compounds are acquired or biosynthesized, and what behavioral responses do they elicit. By seeking to elucidate the

roles of natural products in the lives of the organisms that produce them, we have been able to ask and answer questions that had been largely ignored by the chemical community. In this research newly developed, non-destructive, microscale, analytical techniques capable of characterizing biologically interesting compounds with unanticipated structures, often present in complex mixtures, are essential.

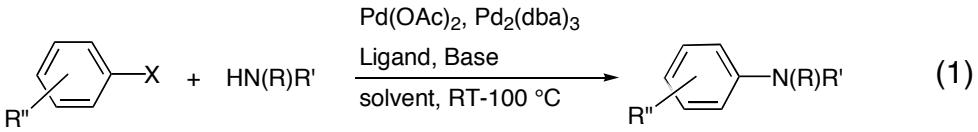
What can we hope to learn from chemical studies of biotic interactions? Since intra-specific and inter-specific chemical interactions have important functions in the lives of all organisms, from microbes to mammals, exploration of this body of chemistry greatly deepens our understanding of biology at the molecular level. There are bound to be applications of such knowledge. From an increased understanding of subjects such as host/parasite, vector/target species, or predator/prey interactions, or the chemistry of pheromonal communication, microbiological and higher plant interactions in the soil, and extremophile chemical ecology, there is every reason to anticipate significant benefits to medicine and agriculture. In spite of two centuries of chemical research, most of nature's chemistry remains unexplored. Right now, we are losing species at a very high rate. The need to reduce this rate is urgent, as is the need to learn as much as we can from the earth's biodiversity. Considering both this challenge and the opportunity to meet it, the stage is set for a Second Golden Age of the Chemistry of Natural Products. There is every reason to expect it to occur in the 21st century!

Metal-catalyzed Carbon-Carbon and Carbon-Heteroatom Bond-Forming Processes: Progress, Applications and Mechanistic Studies

Stephen L. Buchwald
Department of Chemistry
Massachusetts Institute of Technology

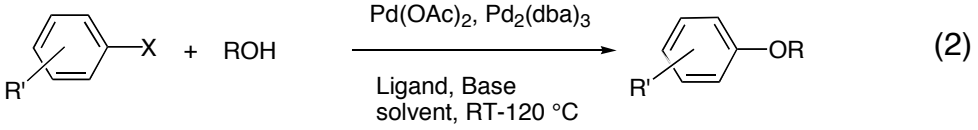
Cross-coupling methodology has had an undeniable impact on the way that synthetic chemists operate. Their use has permeated areas of chemistry ranging from the total synthesis of natural products, the preparation of combinatorial libraries, the construction of new ligands and the assembly of macromolecular structures. As the power of this technology becomes increasingly apparent, the need for ever more general and active catalysts remains. In this lecture I will describe some of our efforts over the past few years to access increasingly effective catalyst systems to affect cross-coupling processes.

Amongst the differing flavors of cross-coupling chemistry, we have been particularly focused on the development of new and improved versions of method for Pd-catalyzed carbon-nitrogen (eq 1) and carbon-oxygen (eq 2) bond formation.



(1)

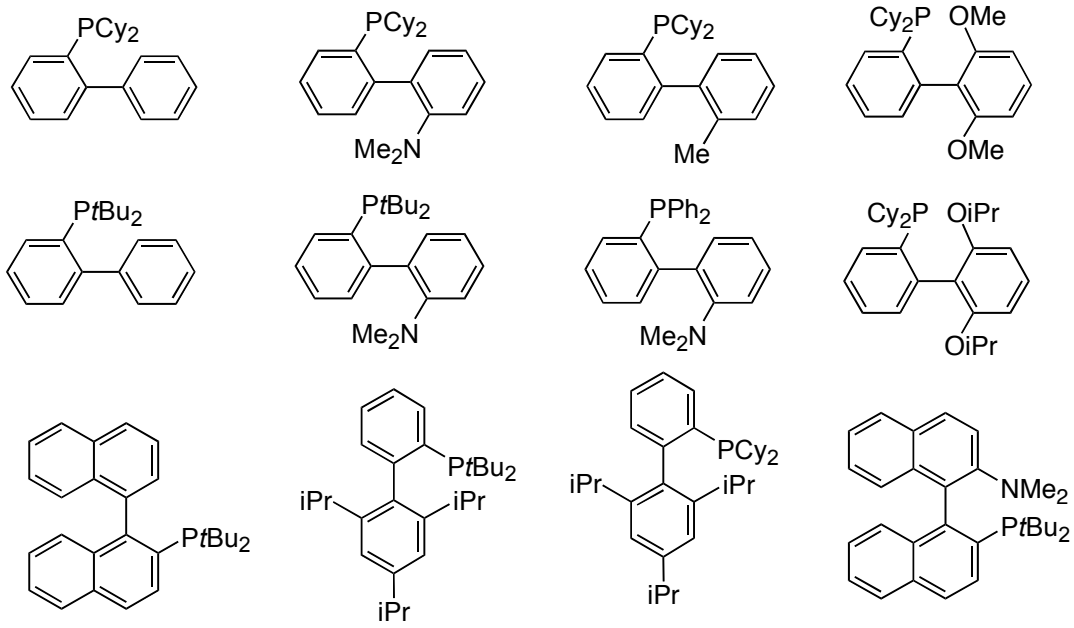
In our initial forays into defining catalysts for carbon-nitrogen bond formation, our work focused on the use of BINAP, initially enantiomerically pure and subsequently in



(2)

Racemic form. In recent years, however, our work has utilized the bulky, electron-rich dialkyl phosphinobiaryl ligands shown in Figure 1. These ligands can be readily prepared in a single step using a procedure based on classical benzyne chemistry. We

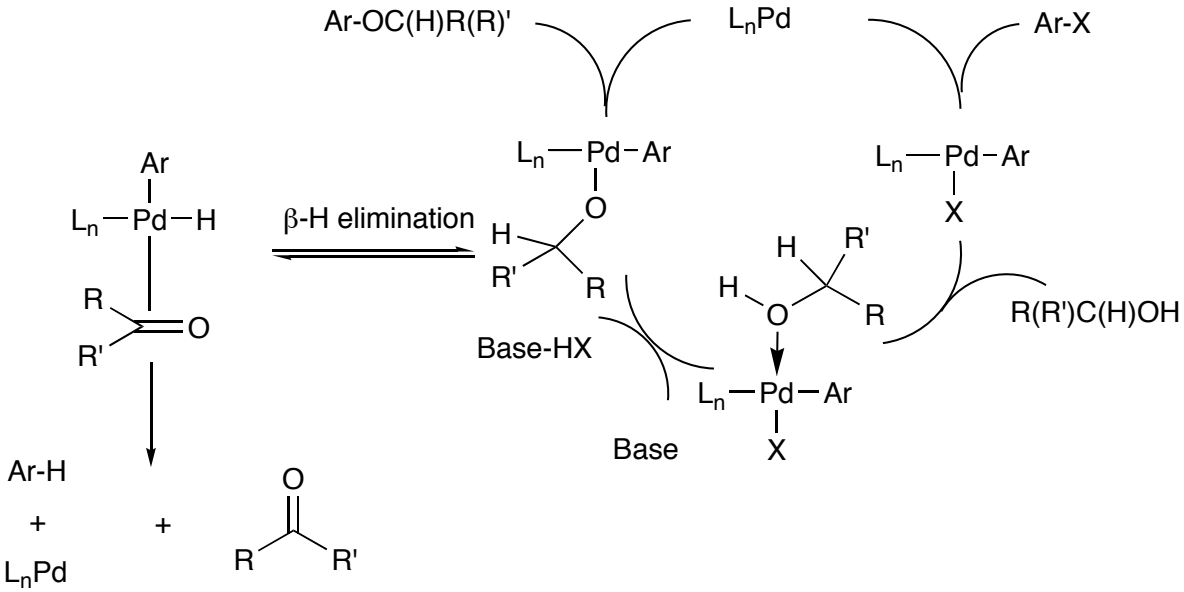
Figure 1



have prepared well over 100 of these phosphines by this route. These have also been used on a moderately large scale and over 100 Kg of these ligands have been produced in a collaborative venture between Rhodia Pharma Solutions and Lanxess. In this lecture I will detail our use of these ligands to provide active and general catalysts for the formation of aromatic carbon-nitrogen bonds between a variety of amines and aryl/heteroaryl chlorides, bromides and tosylates.

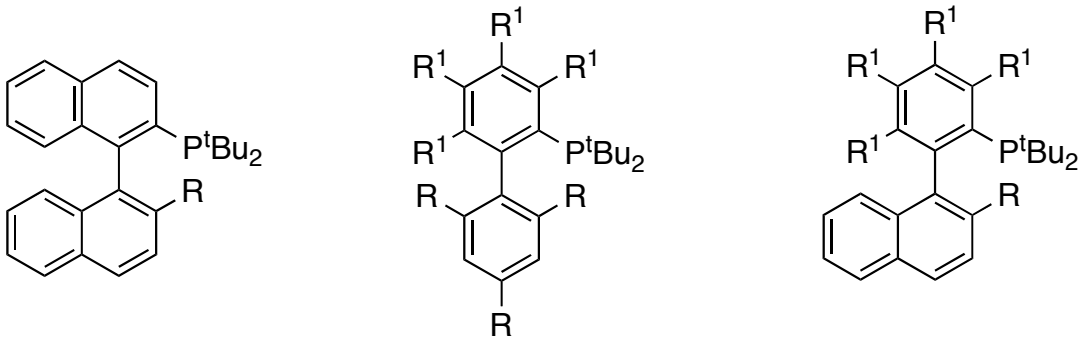
Much less well-developed has been the analogous transformation to form aromatic carbon-oxygen bonds (eq 2). A generic mechanistic outline for this process is shown in Scheme 1. This is entirely analogous to what is seen for the C-N bond-forming reaction; the major difference is in the carbon-heteroatom bond-forming step. Specifically, while reductive elimination from a palladium (aryl) amido intermediate is relatively fast, that from the corresponding palladium (aryl) alkoxide is not. Instead, in the reactions of primary or secondary alcohols, β-hydride elimination either dominates or is competitive. Thus, a significant amount of dehydrohalogenated arene is often seen. In order to overcome this problem we have developed a series of new, extremely

Scheme 1



bulky ligands as shown in Figure 2. With these ligands, we have been able to couple both primary and secondary alcohols with a variety of aryl bromides and chlorides. Moreover, we have developed the first method for the coupling of allylic alcohols with aryl halides. This success is remarkable given the facility of Tsuji-Trost processes involving phenyl allyl ethers.

Figure 2



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2. Jiang, L.; Buchwald, S.L. "Palladium-Catalyzed Aromatic Carbon-Nitrogen Bond Formation." In *Metal-Catalyzed Cross-Coupling Reactions*, 2nd edition; de Meijere, A.; Diederich, F.; Eds.: Wiley-VCH: Weinheim, Germany, 2004, Vol. 2, Ch. 13, pp 699-760 and references therein.

3. Schlummer, B., and Scholz U. "Palladium-Catalyzed C-N and C-O Coupling - A Practical Guide from an Industrial Vantage Point" *Adv. Synth. Catal.* **2004***, 346*, 1599-1626 and references therein.

4. Vorogushin, A.V.; Huang, X. and Buchwald, S.L. " Use of Tunable Ligands Allows for Intermolecular Pd-Catalyzed C-O Bond Formation." Accepted for publication to *J. Am. Chem. Soc.* and references therein.

C-H Oxidation Reactions as Enabling Methodologies for Organic Synthesis

Justin Du Bois
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Stanford, CA 94305-5080

OVERVIEW. A central objective of our research program is aimed at the invention of highly selective oxidation reactions having general utility for the synthesis of amines and amine derivatives. These efforts have manifest in the development of a unique, catalytic C–H amination process that makes possible the facile and efficient oxidative cyclization of carbamate and sulfamate esters. The heterocyclic products obtained are themselves precursors to 1, 2– and 1, 3–amino alcohols as well as other functionalized amine structures. A general discussion of this C–H amination methodology and highlights of its application for the assembly of nitrogen-rich marine natural products will be presented.

REACTION DEVELOPMENT. We have described new strategies for the selective conversion of saturated C–H bonds to carbinolamine stereocenters. Our methods have general utility and make available large numbers of amine derivatives from inexpensive and easily prepared 1° carbamate and sulfamate ester starting materials. Reactions are conducted with catalytic amounts of a Rh^{2+}-carboxylate dimer, $PhI(OAc)_2$ as the terminal oxidant, and MgO as an essential additive. Intramolecular C–H insertion occurs at allylic, benzylic, 3°, and 2° C–H sites to afford versatile heterocyclic structures that can be transformed readily into 1,2- and 1,3-substituted amine derivatives (Figure 1). C–H Insertion processes of this type using nitrogen-based oxidants appear only sparingly throughout the literature, and such reactions are seldom applied to the synthesis of polyfunctionalized materials. Our method, however, offers suitable control of the intermediate oxidizing species so as to make possible highly chemo-, regio-, and diastereoselective transformations. One application of this reaction is found in the preparation of building-block type structures such as 1,3–diamines and β-amino acids. A second opportunity to employ C–H amination chemistry is presented within the context of multi-step synthesis for the intermediate or late-stage introduction of C–N stereocenters. This latter concept forms the basis of our strategy to assemble tetrodotoxin and aconitine (see below). In all, we feel that these inventions have altered the way in which one approaches the synthesis of nitrogen-containing compounds.

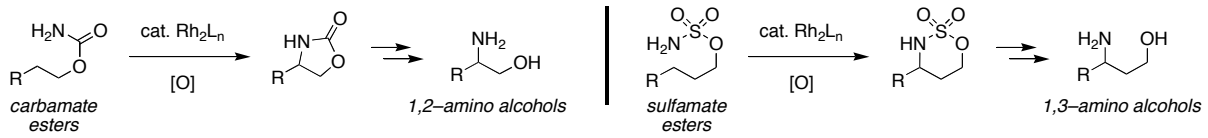

Figure 1. Selective C–H amination reactions for the synthesis of amines and amine derivatives.

Products from C–H insertion of sulfamate esters serve as useful precursors to β-amino alcohols and acids, as well as other 1,3–difunctionalized amine derivatives. Such structural types are found commonly in naturally occurring compounds and therapeutic agents. We have been investigating the reactivity properties of oxathiazinane heterocycles and have noted these compounds to be extremely useful electrophiles, subject to a host of ring-opening reactions with disparate reagents (Figure 2). Cyclic amines and polyfunctionalized acyclic amino alcohols are representative classes of targets that are now made available through straightforward, high yielding protocols elucidated by our lab. More recently, we have identified conditions for conducting Ni-catalyzed cross-coupling reactions between *N*–alkyloxathiazinane derivatives and Grignard reagents. We are currently attempting to extend this reaction methodology to include coupling processes with organozinc and

boronic acid reagents. The development of general C–C bond forming protocols with cyclic sulfamate starting materials should extend greatly the number of possible applications for these unique heterocycles.

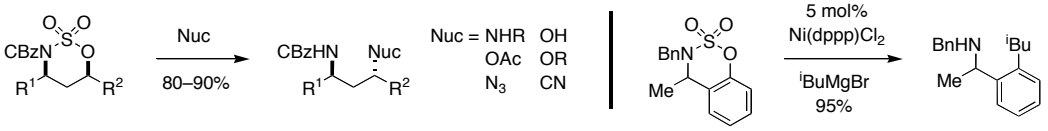

Figure 2. Ring-opening reactions of oxathiazinane heterocycles.

We wish to define systematically the factors that influence regio- and stereoselectivity in Rh-catalyzed C–H amination reactions. Through our investigations using differentially substituted sulfamate esters, we have shown that the rate of C–H bond insertion can be influenced by steric and electronic effects, and that such differences are sufficient to offer reasonable levels of product regiocontrol. In addition, we have observed that the α-C–H positions of ethereal groups are particularly active substrates for this oxidation process. These finding has been exploited in order to generate a series of *N*,*O*–acetal oxathiazinanes for use as iminium ion equivalents (Figure 3). The coupling of allylsilane, silyl enol ether, silyl ketene acetal, and alkynylzinc nucleophiles to such compounds occurs smoothly with Lewis acid promoters and furnishes products rich in structural complexity. Observed levels of diastereoselectivity in these iminium ion additions generally exceed 10:1, the sense of induction for which is rationalized through a hybrid Stevens-Felkin-Ahn stereochemical model. Applications of this chemistry have been envisioned for the synthesis of both saxitoxin and aconitine; both targets are currently being pursued (see below).

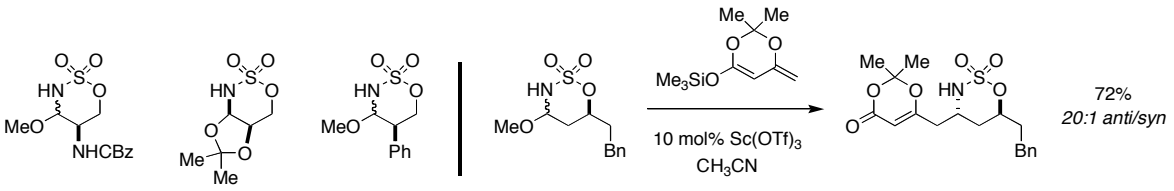

Figure 3. Synthesis and reactivity of *N*,*O*–acetal oxathiazinanes, novel iminium ion surrogates.

Protocols for C–H amination have been extended to intra- and *inter*molecular olefin aziridination (Figure 4). Formation of bicyclic aziridines through oxidation of unsaturated sulfamates has proven particularly powerful, as these unusual heterocycles may be easily manipulated into polyfunctionalized acyclic structures. Such compounds are being exploited as key intermediates in syntheses of both welwitindolinone D and agelastatin A. In addition, a method for intermolecular alkene functionalization has evolved from our studies, which enables reactions to be performed conveniently and with limiting amounts of the starting olefin. The alkoxylsulfonylated products are versatile electrophiles from which myriad amine derivatives may be prepared. We believe that our process provides an optimal solution to this longstanding problem in reaction design. Future efforts will continue to improve and to expand the scope of this chemistry and will concentrate on the development of asymmetric catalysts for olefin aziridination. These latter studies converge nicely with concurrent research to identify new, chiral transition metal complexes that promote enantioselective C–H bond amination reactions.

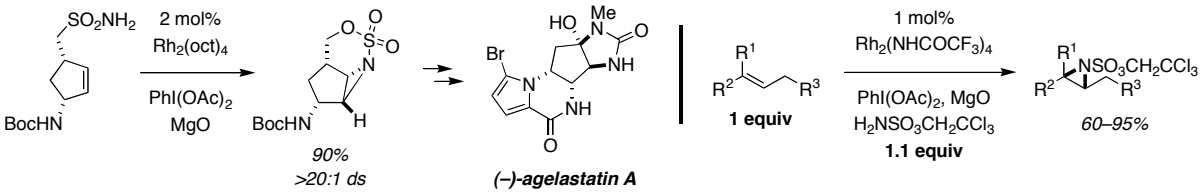

Figure 4. New protocols for catalytic intra- and intermolecular olefin aziridination.

MECHANISTIC ANALYSIS AND CATALYST DESIGN. As part of our ongoing investigations, we wish to identify other transition metal catalyst structures that operate with efficiencies comparable to or exceeding those of the dinuclear Rh complexes. Our ability to modify the ligand framework around the catalytic metal center should enable us to influence regio- and stereoselectivity in the C–H bond amination event. To achieve such promise, a deeper understanding of the reaction mechanism for Rh-catalyzed C–H insertion is needed. By employing a combination of substrate probes and kinetics analysis, we have been able to obtain compelling support for the generation of a Rh-nitrene as the active oxidant. In addition, our data gives evidence for the rapid modification of the catalyst structure upon reaction initiation. These insights have led us to prepare tethered dicarboxylate Rh dimers (i.e., $Rh_2(esp)_2$) with the expectation that such complexes should display enhanced kinetic stability towards carboxylate dissociation (Figure 5). Remarkable catalyst turnover numbers are indeed observed for intramolecular C–H amination using these new systems. In addition, such catalysts have enabled us to formulate high yielding methods for C–H insertion with urea and sulfamide substrates, a long-standing problem in our lab. Perhaps even more exciting, high yielding *inter*molecular C–H bond amination has now been successfully achieved with the advent of $Rh_2(esp)_2$. As shown in Figure 5, substrates containing benzylic C–H centers are smoothly converted to amine derivatives under conditions that employ limiting amounts of the starting material. The oxidation of 2° C–H groups can also be achieved, though product yields are lower on average. Nonetheless, the efficiency of these process establishes a high-water mark for intermolecular C–H amination. Second and third generation designs of tethered dicarboxylate Rh dimers are currently being investigated. Additionally, chiral complexes fashioned in this way are being examined for asymmetric C–H bond oxidation.

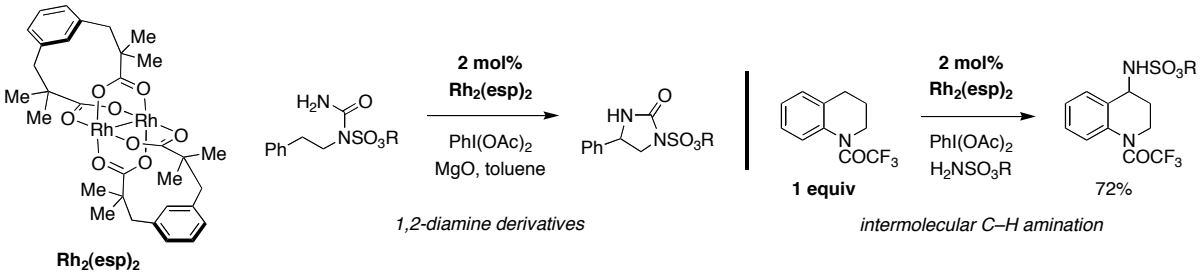

Figure 5. New Rh catalysts display remarkable activity for novel intra- and intermolecular amination reactions.

Self-Assembling Peptide Nanotubes: Design and Biological Applications

M. Reza Ghadiri, ***Departments of Chemistry and Molecular Biology, and The Skaggs Institute for Chemical Biology, The Scripps Research Institute, 10550 North Torrey Pines Road, La Jolla, CA 92037.***

Self-assembling peptide nanotubes are a versatile class of supramolecular structures with expanding utility in materials and biological settings. Cyclic peptides made up of an even number of alternating D- and L-α-amino acid residues, and increasingly other types of macrocyclic ring structures based on β^3-amino acids, α,γ-amino acids, δ-amino acids, oligoureas, and heterocyclic backbone α,ε-amino acids structures, have been used to form hydrogen-bonded hollow tubular supramolecular ensembles. By appropriate choice of the sequence and amino acid residues employed, cyclic D, L-α-peptides and cyclic β^3-peptides can be designed to spontaneously partition into lipid membranes and self-assemble into functional ion channels and pore structures. Rationally designed membrane channels and pore structures show remarkable ion transport efficiencies (>10^7 ions·sec^{-1}), size selective

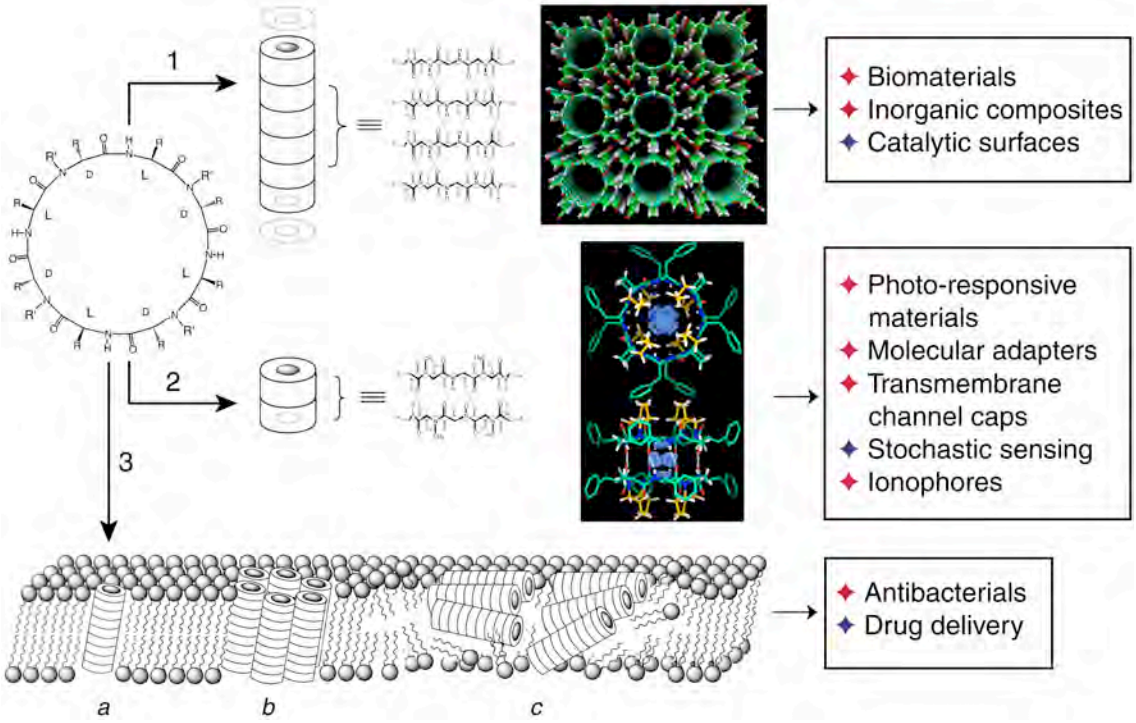

Figure. 1) Cyclic peptides with secondary amide backbone (R'=H) give extended β-sheet like hollow tubular structures with organized surface functional group presentations that can be employed in biomaterials design, formation of transition metal oxide nanocomposites, and heterogeneous catalysis. 2) Backbone substituted cyclic D,L-α-peptides form hydrogen-bonded cylindrical dimers that are useful in a number of applications (box). 3) Appropriately designed cyclic peptides self-assemble in lipid membranes to form channels and pore structures. They display sequence-dependant modes of membrane permeabilization consistent with a) intrapore; b) barrel-stave; and c) carpet-like mechanisms of action. Membrane active self-assembling cyclic peptides display potent and selective antimicrobial activities and may have potential utility as novel drug delivery agents.

molecular transport activities, and potent antimicrobial effects. In this lecture I will highlight various design principles employed in our laboratory for the preparation of synthetic peptide nanotubes. In particular I will discuss the mechanism-based rationale used in the design and discovery of membrane active self-assembling cyclic D,L-α-peptides and their emerging utility as a novel class of antimicrobial agents.

Antibacterial Cyclic Peptide Nanotubes. The emergence of multidrug resistant infections is on the rise worldwide at an alarming pace highlighting the need for novel therapeutic agents. We have shown that six- and eight-residue cyclic D, L-α-peptides act preferentially on gram-positive and/or gram-negative bacterial membranes compared to mammalian cells, increase membrane permeability, collapse transmembrane ion potentials, and cause rapid cell death. The effectiveness of this class of materials as selective antibacterial agents is highlighted by the high efficacy observed against lethal methicillin-resistant *Staphylococcus aureus* infections in mice. Cyclic D, L-α-peptides are proteolytically stable, easy to synthesize, and can be derived from a potentially vast membrane active sequence-space. The unique abiotic structure of the cyclic peptides and their quick bactericidal action may also contribute to limit temporal acquirement of drug resistant bacteria. The low molecular weight D, L-α-peptides thus offer an attractive complement to the current arsenal of naturally derived antibiotics and hold considerable promise in combating a variety of existing and emerging infectious diseases. In this lecture, I will highlight our recent advances in the design, synthesis, biophysical, and biological evaluation of cyclic D, L-α-glycopeptides.

Antiviral Cyclic Peptide Nanotubes. Diverse virus families have evolved to exploit the acidification of endosomal compartments to gain entry into cells. I will describe that a supramolecular approach based on cyclic D, L-α-peptides can be used to selectively target and inhibit viral infections through this central biochemical pathway. Using adenovirus as a model non-enveloped virus, we have determined that an eight-residue cyclic D,L-α-peptide, selected from a directed combinatorial library, can specifically prevent the development of low pH in endocytic vesicles, arrest the escape of virions from the endosome, and abrogate adenovirus infection without an apparent adverse effect on cell viability. The likely generality of this approach against other pH-dependent viral infections is supported by the inhibition of type-A influenza virus escape from endosomes in the presence of the same peptide. Our studies thus suggest that the design of membrane-active supramolecular species capable of selectively targeting endosomes involved in virus entry could offer a new and fertile ground in the design and discovery of broad-spectrum antiviral therapeutics.

The Chemical Biology of Iron

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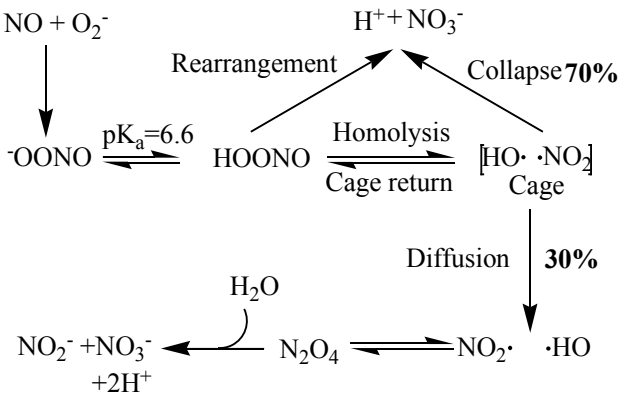
Abstract. The chemistry of iron is central to life processes. Organisms must recruit iron from their environment, control iron storage and trafficking within cells, assemble the complex, iron-containing redox cofactors of metalloproteins and manage a myriad of biochemical transformations by those enzymes.[1] The coordination chemistry and the variable oxidation states of iron provide the essential mechanistic machinery of this metabolism. Our current understanding of several aspects of the chemistry of iron in biology will be discussed with an emphasis on (i) reactive nitrogen species such as peroxynitrite that result *in vivo* from aberrations in nitric oxide signalling pathways, (ii) the development of novel, catalytic iron complexes that ameliorate peroxynitrite damage and (iii) recent studies of the interactions amphiphilic iron siderophores with lipid membranes.

The Chemistry and Biology of Peroxynitrite

The formation of peroxynitrite from the reaction of cellular NO with superoxide was first proposed by Beckman.[2] The reaction between NO and $O_2^{\bullet-}$ that produces peroxynitrite has since been determined to proceed with a rate constant of 10^{10} $M^{-1}s^{-1}$.[3, 4] It has been suggested that this species decomposes to form the hydroxyl radical and NO_2, which cause of oxidative injury in tissues. Peroxynitrite is stable only in its deprotonated state. Peroxynitrous acid is a weak acid with a pK_a of 6.6-6.8. Accordingly, peroxynitrite is stable only in strongly alkaline solutions. Upon protonation, peroxynitrite rapidly decomposes to nitrate with a first-order rate constant of 1.2 s^{-1} at 25°C.[5] The mechanism of this process has been the subject of considerable controversy.[6-10] The current consensus mechanism involves the formation of a caged radical pair of ·OH and $\cdot NO_2$ as the intermediate species during the decomposition of peroxynitrous acid, as shown in Scheme 1. Existence of a tightly-associated, hydrogen bonded intermediate comprised of NO_2 and OH radicals has been supported by density functional theory calculations.[11] The free energy was estimated at 15 kcal/mol relative to cis-peroxynitrous acid, which is comparable to the 17 kcal/mol determined for conversion of peroxynitrous acid to nitric acid [12]. This intermediate is believed to have the high oxidation ability that is associated with ·OH in solution.

Scheme 1. Peroxynitrite reaction pathways *in vitro*.



Because of its complex decomposition chemistry, peroxynitrite is a versatile yet very strong oxidant. In many cases it can oxidize substrates by either one or two electrons. The one-electron redox potential of peroxynitrite has been determined to be $E°'(ONOOH, H^+/NO_2, H_2O) = 1.6 \pm 0.1$ V, which puts it in reach of many substrates, including thiols, phenols, metalloproteins, and Fe-S clusters [5]. The two-electron redox potential of peroxynitrite has also been determined to be $E°'(ONOOH, H^+/NO_2^-, H_2O) = 1.3 \pm 0.1$ V [5]. Such a high redox potential renders the oxidation of sulfides and other biologically relevant oxidizable groups feasible.

Peroxynitrite reacts with a wide range of biological molecules such as phenols, lipids, DNA, Fe-S clusters, hemes, and thiols, as will be discussed in greater detail in this chapter. A particularly important reaction that deserves special mention is the capture of peroxynitrite by dissolved CO_2. $CO_2(aq)$ reacts with deprotonated

peroxynitrite to form an unstable nitrosoperoxycarbonate, $ONOOCO_2^-$, which rapidly homolyzes to form $\cdot NO_2$ and $CO_3^{-}\cdot$ radicals [13]. The radical yield from this reactions is much higher then from the self-decay of peroxynitrous acid, and as a result, the oxidative reactivity of peroxynitrite is significantly increased in the presence of CO_2.[14]

Another unique feature of peroxynitrite chemistry is its ability to diffuse across lipid membranes, presumably ass the conjugate acid. The calculated permeability coefficient for $ONOO^-$ is 8.0×10^{-4} $cm \cdot s^{-1}$, which compares favorably with that of water and is approximately 400 times greater than that of superoxide. This permeability makes $ONOO^-$ an extremely effective oxidant that is able to penetrate cells and compartments far from its origin.[15, 16]

Lipid peroxidation is another common modification generated by peroxynitrite [17]. The oxidation of lipids leads to many cytotoxic effects such as the loss of membrane integrity and formation of lipid-derived reactive species that form adducts with other cellular targets and ultimately results in cellular apoptosis. [18-20]

Important modifications of proteins by peroxynitrite include oxidations [21-23] and nitrosations [24] of cysteines, and hydroxylations [25] and nitrations of tyrosine residues [26-28] that result in enzyme inactivation. Nitration of tyrosine, which has been detected in a large number of proteins upon exposure to peroxynitrite, has been recognized as one of the most important cytotoxic and regulatory effects of peroxynitrite in cells. [29] Recent proteomic exploration of protein nitration during inflammatory challenge has sholwn that a wide variety of proteins show significant levels of nitration. [30]

Metalloproteins are particularly sensitive to damage by peroxynitrite, and iron and manganese proteins are often readily oxidized by peroxynitrite. For example, Fe-S clusters found in many redox active enzymes [31-35] are rapidly oxidized by peroxynitrite, effectively shutting down electron transport in these enzymes. Manganese superoxide dismutase is a key mitochondrial detoxification enzyme that is also hypersensitive to peroxynitrite inactivation. [36, 37]

Tyrosine nitration has been demonstrated in a variety of pathophysiological conditions, including diabetes. In the pancreatic islets of spontaneous autoimmune diabetic mice, a significant increase in tyrosine nitration was found and the degree of beta-cell destruction showed a good correlation with the frequency of nitrotyrosine-positive beta-cells. It was therefore proposed that the intra-islet formation of peroxynitrite plays an active role in the pathogenesis of diabetes. The observation that nitrotyrosine formation is present in the cardiovascular system of diabetic animals and humans, coupled with the fact that exposure of blood vessels of heart preparations to peroxynitrite leads to vascular and cardiac dysfunction led to the suggestion that peroxynitrite may play an active role in the pathogenesis of diabetic cardiovascular failure. A direct demonstration of the pathogenetic role of peroxynitrite requires pharmacological tools which have the ability to powerfully neutralize peroxynitrite *in vivo*. We have described the synthesis and characterization of an iron porphyrin, FP15, that is a potent peroxynitrite decomposition catalyst in a variety of animal models.[38] Using FP15, direct evidence has been obtained for the pathogenetic role of peroxynitrite in diabetic islet cell destruction, as well as in diabetic cardiovascular dysfunction. FP15 has also been shown to protect against the cardiotoxicity of doxorubicin.[39]

Iron Acquisition by Pathogens

The principal strategy for bacterial response to iron restriction is to secrete siderophores, a family of small organic compounds with a highly selective iron-chelating ability.[40] The ability of pathogens to mobilize iron from abundant host iron-containing proteins is essential for bacterial survival upon infection.[41] However, accomplishing this goal is not trivial since hosts have developed a variety of strategies to restrict bacterial access to iron. Among those strategies are iron withdrawal from serum transferrin, increased synthesis of ferritins, and the secretion of lipocalins to scavenge microbial sideorphores. Consequently, invading pathogens have either to resort to less down-regulated iron sources, such as heme iron for *Staphylococcus aureus*, or to actively compete with hosts for this restricted iron pool. Pathogenic siderophores have proved to be remarkably adaptable in the latter process.

Amphiphilic siderophores, a subset of siderophores with both hydrophilic iron chelating moieties and lipophilic hydrocarbon chains, have recently attracted attention, because of their dual abilities for iron acquisition and membrane interaction.[42-45] Particularly, a significant number of these amphiphiles are those isolated from

pathogens, such as mycobactins from *Mycobacterium* strains.[46] Although the iron-acquisition properties of *hydrophilic* siderophores have been extensively characterized, little is known about the properties of these *amphiphiles*. In particular, specific mechanisms pathogenic amphiphile-mediated iron acquisition from biologically important iron sources have begun to be illuminated only recently. Given the bulky hydrophobic chains adjacent to the iron-chelating moieties in these amphiphiles,[42] a key question is to what extent do these siderophores benefit from the membrane-binding properties and what molecular properties are keys to successful function..

Our interest in this aspect of iron trafficking has stimulated us to examine acinetoferrin,[47] a citrate-based amphiphilic siderophore from the antibiotic-resistant strain *Acinetobacter*.[48, 49] This amphiphile also shows the ability to cross-deliver iron to notorious mycobacterial pathogens.[50]

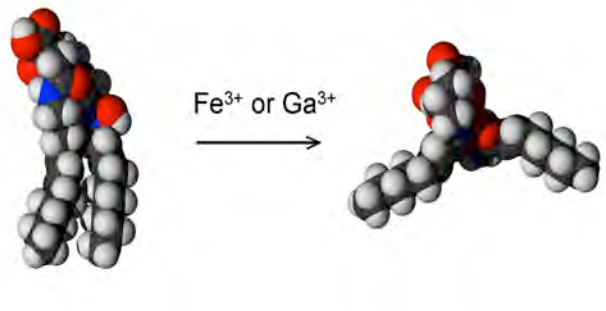


Figure 1. Dramatic change of acinetoferrin (**Af**) conformation upon metal coordination.

We recently reported the 3-D structure and the membrane properties of Af, and showed that the two hydroxamate-conjugated *trans*-2-octenoyl chains in Af play important roles in its membrane partitioning and trans-membrane permeability (Figure 1).[45] The diffusion properties of Af and its iron complex suggest that this amphiphile might be able to access host intracellular iron pool upon diffusion.[51] This part of the lecture will focus on Af-mediated, structure-related iron acquisition from iron citrate (often rich for iron-overloaded patients) and the iron transport protein, and, in particular, on the role of the two seemingly awkward hydrocarbon chains in Af. The findings here not only will have an impact on understanding siderophore-related virulent functions,[41, 52, 53] but also can be applicable to designing amphiphile-derived iron scavengers[54-56] for treating reperfusion injury,[57] breast cancer[58] and malaria.[59, 60]

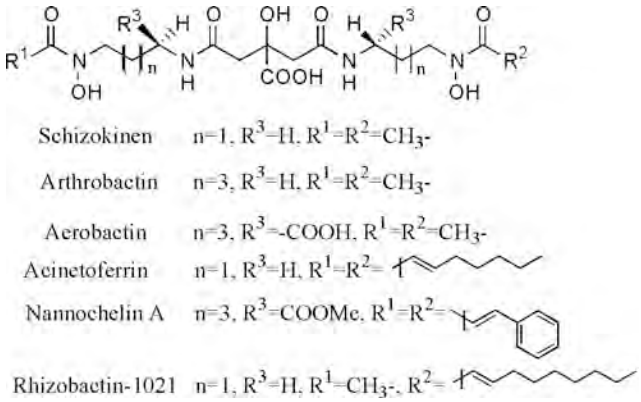


Figure 2. Structures of citrate-based suderophores.

Our results show[61] that both aqueous-phase **Af** and lipid-phase **Af** can successfully acquire iron from transferrin with only a 2-fold slower rate for the latter. The overall rates here are comparable to those of the artificially optimized iron chelators and the catechol-based siderophores. These observations are remarkable, given the two sterically-hindered, terminal *trans*-2-octenoyl chains in **Af**. This increased iron-chelating ability for **Af** must be attributed to its hydroxamate-conjugated double bonds, since schizokinen (**Sz**) and aerobactin, the less-bulky **Af** analogues without such electron-donating moieties, show the much weaker ability to mobilize transferrin iron. Aqueous-phase **Af** and lipid-phase **Af** also rapidly remove iron from polymeric iron citrate. All these results suggest that **Af** achieves the superior abilities for the iron acquisition and membrane interaction simply by assembling the hydroxamate-conjugated *trans*-2-alkenoyl chain. This strategy probably has been adopted by other such-moiety-containing siderophores, such as mycobactins and carboxymycobactins.

The amphiphilic marine aquachelins have recently been shown by Butler, *et al*. to be photoreactive.[62] The iron-hydroxamate chromophore absorbs visible light and the resulting ligand-to-metal charge-transfer chemistry causes an internal reduction of the iron(III) to iron(II) and oxidation of the organic portion of the siderophore. Significantly, this photochemical redox transformation causes a cleavage of the molecule such that the hydrophobic side chain and two of the iron-binding ligands are lost. This could have important implications for how iron is recycled in a marine environment that is critically short of iron near the surface.

Acknowledgments

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PERSPECTIVES IN TOTAL SYNTHESIS

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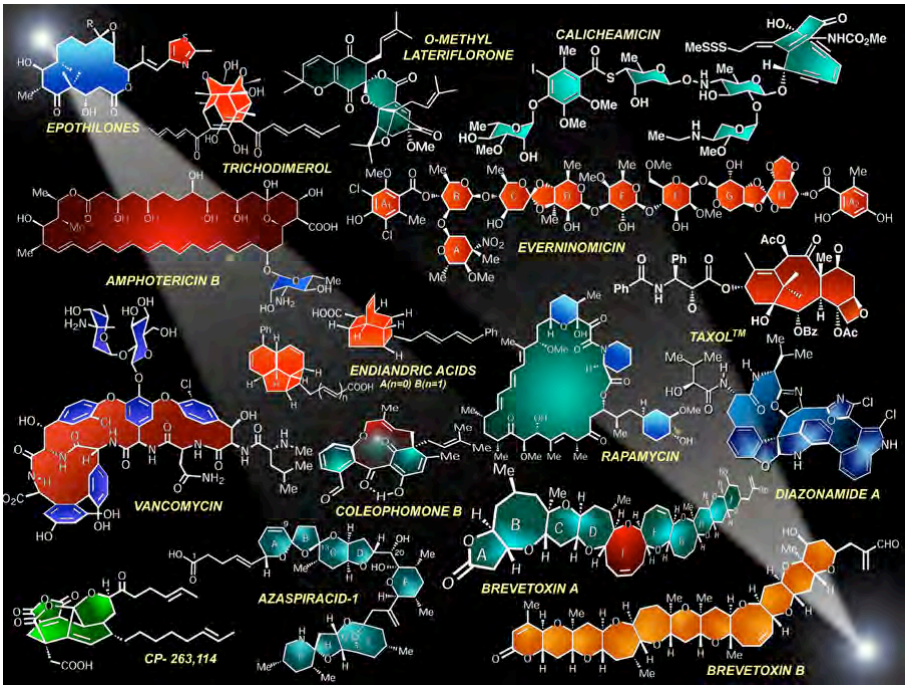
Problems in total synthesis are defined by natural products possessing novel molecular architectures which provide unique opportunities for discovery and invention in chemistry, biology, and medicine. The artistry of total synthesis lies both in the originality and elegance by which the individual steps are orchestrated within the overall synthetic strategy and in the architecture of the designs of synthesized analogs with potential biological activity. Accomplishments in total synthesis of such complex molecules symbolize the state of the art of chemical synthesis and have a major impact by finding applications in everyday endeavors of researchers in drug discovery and development, chemical biology and material science, among other disciplines. A number of examples of total syntheses from our laboratories of bioactive natural products (see structures below) and associated discoveries and inventions in new synthetic technologies and chemical biology will be discussed.[1–5]



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"Development of New Methods for Organic Synthesis"

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http://www.ch.cam.ac.uk/CUCL/staff/svl.html
http://leygroup.ch.cam.ac.uk

The search for new ways to assemble molecules continues to be an important driver for organic synthesis. The biological activity and the exquisite structural diversity associated with many natural products stimulate invention by challenging the current state of the art synthetic methodology. The preparation of biologically active and many other functional material from small, commercially available building blocks inevitably involves more that one synthetic step. For most modern drugs and other complex molecules, it is not uncommon to require at least 10 steps and sometimes many more.
Our research involves the discovery and development of new synthetic methods and their application to biologically active systems. Our group has published extensively on the synthesis of natural products and to date more than 100 target compounds have been synthesised. (see http://leygroup.ch.cam.ac.uk)
In order to make molecules more efficiently and economically, we believe a much better practical solution for the preparation of large chemical libraries rather than use solid phase organic synthesis would be to use solid-supported reagents in a designed sequential and multi-step fashion. In combination with advances in the use of scavenging agents and catch and release techniques or flow methods even greater opportunities for organic synthesis become apparent.

This lecture will give some recent results from the group.

Structure-Based Drug Design Applied to Serine Protease Inhibitors

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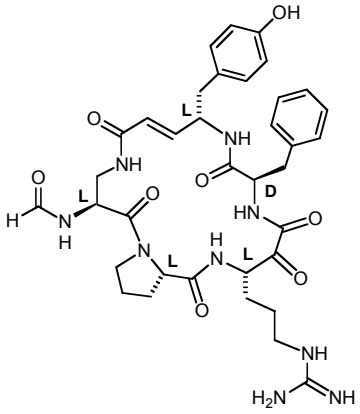
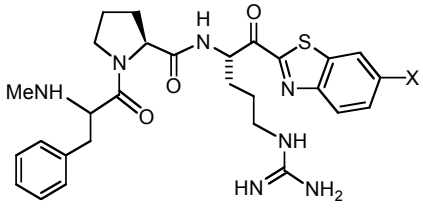
This presentation will be an odyssey in structure-based drug discovery, dealing with serine protease inhibitors. Serine proteases cleave amide bonds in peptides and proteins by the agency of a key, active-site serine residue, which is part of the His–Asp–Ser catalytic triad. The discovery of inhibitors for thrombin, tryptase, cathepsin G, and chymase will be discussed.

In 1991, we initiated a research effort to identify potent inhibitors of thrombin, a serine protease that is central to thrombosis and hemostasis. A thrombin inhibitor, especially an orally active agent, would be therapeutically useful as an anticoagulant/antithrombotic drug, such as for the treatment of deep-vein thrombosis and acute coronary syndrome. We adopted a then-cutting-edge approach involving protein structure-based drug discovery. Initially, we became intrigued with a macrocyclic peptide marine natural product, cyclotheonamide A (CtA), that inhibits thrombin and trypsin (Fig. 1). We obtained the crystal structure of CtA•thrombin (Fig. 2), completed a total synthesis of CtA, and explored CtA structure–function relationships. The structural features of the CtA co-crystal led to the idea of suitably occupying the S1' subsite of thrombin, which is not utilized by the standard D-Phe-Pro-Arg thrombin recognition motif (Fig. 2). We synthesized and evaluated a series of α-ketoheterocycle derivatives, which led to potent α-ketobenzothiazole-based inhibitors RWJ-50353 (K_i = 0.2 nM) and RWJ-51438 (K_i = 2 nM) (Fig. 1). This study constituted some of the earliest results with respect to transition-state-mimetic protease inhibitors bearing heterocycle-activated ketones.

Figure 1. Structures of thrombin inhibitors.



CtA

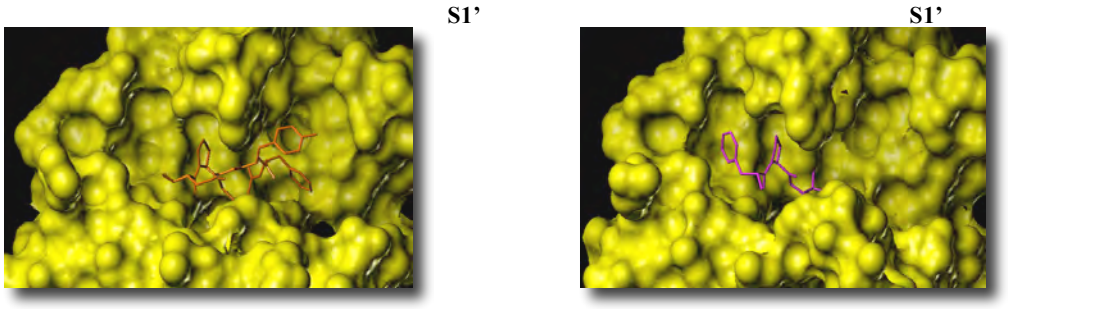


RWJ-50353 X = H
RWJ-51438 X = CO_2H

In probing the minimal structural features for potent thrombin inhibition, we identified trypsin inhibitor RWJ-51084 (Fig. 3), which also turned out to inhibit tryptase. Tryptase is one of the few serine proteases capable of cleaving and activating protease-activated receptor 2 (PAR-2), a target under study by our team of scientists. This enzyme, a principal component of mast cell secretory granules, is released following cell

activation and stimulates inflammatory processes. For example, mast cell tryptase is important in the pathogenesis of allergic disorders such as asthma. The crystal structure of human mast cell tryptase (Bode and coworkers, 1998), which shows a homotetramer with an active site analogous to that of trypsin, was used to guide ligand design. We arrived at RWJ-58643 (Fig. 3A; two diastereromers, mixture at *), a benzothiazole-based dipeptide tryptase inhibitor (K_i = 5 nM) with good selectivity relative to other serine proteases (except trypsin). RWJ-58643 was very efficacious in a sheep model of asthma on aerosol administration (Fig. 3B). RWJ-56423 (Fig. 3A), a single diastereomer of RWJ-58643, was advanced into human clinical studies.

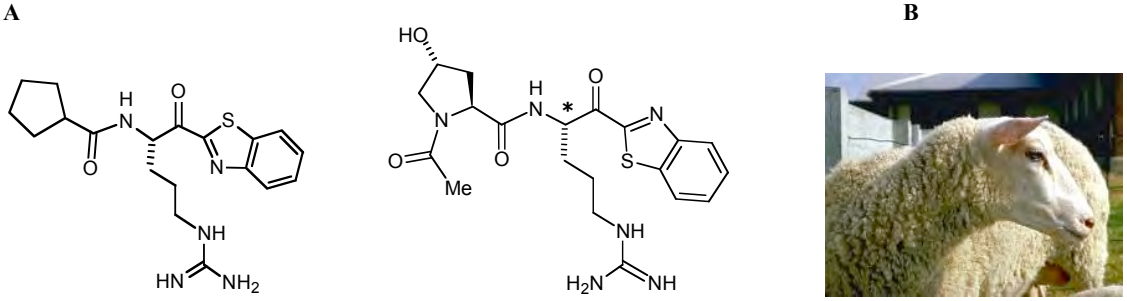
Figure 2. Active site of thrombin occupied by inhibitors (x-ray crystallography).



CtA•thrombin D-Phe-Pro-Arg-CH_2Cl•thrombin

Figure 3. Panel A: Structures of trypsin and tryptase inhibitors. Panel B: A friendly sheep.

A **B**

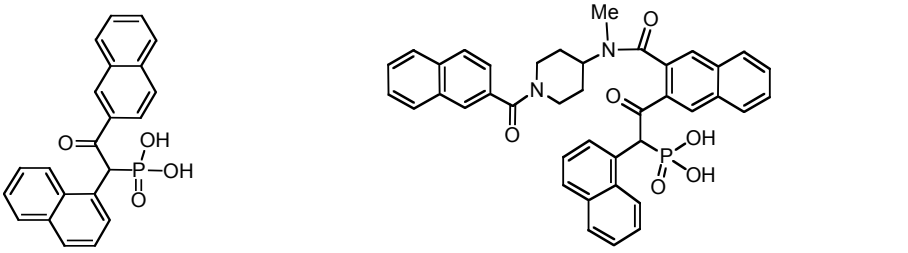


RWJ-51084 RWJ-56423

Our research on tryptase inhibitors established asthma, a chronic disease of the airways and lungs, as a therapeutic direction. Although the mechanism of asthma is unknown, a plausible hypothesis centers on airway inflammation, an important facet of which is the recruitment of neutrophils, eosinophils, and mast cells to the site of injury. Neutrophils are also important in chronic obstructive pulmonary disease (COPD), for which there is a large unmet medical need. Proteases released from neutrophils have local and systemic effects because they can degrade constituents of extracellular matrix and trigger the release of pro-inflammatory mediators. Cathepsin G (Cat G), a serine protease contained within the azurophilic granules of neutrophils, is released on activation and degranulation. Relative to chronic lung inflammation, Cat G can degrade matrix proteins, damage airway epithelial cells, and stimulate vascular permeability. Since inhibitors of Cat G had not been effectively investigated in inflammatory conditions, we sought to discover a small-molecule, nonpeptide inhibitor of Cat G for evaluation in preclinical animal models. From high-throughput

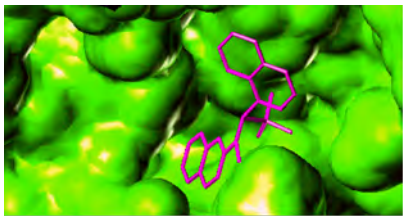
screening (HTS) of the Johnson & Johnson Compound Library, we identified JNJ-785096 (RWJ-48345) as a modest inhibitor of Cat G (IC_{50} = 4 μM) (Fig. 4). This HTS hit was particularly exciting because of its novel chemical structure: a bis-naphthyl-β-ketophosphonic acid. We were fortunate to obtain the crystal structure of JNJ-785096•Cat G, which revealed the key interactions in the active site (Fig. 5). Thus, to optimize potency we installed a suitable appendage to occupy the hydrophobic S3/S4 domain of Cat G. JNJ-10311795 (RWJ-355871) is a potent Cat G inhibitor (K_i = 38 nM) with good selectivity relative to many other serine proteases. Surprisingly, we found that JNJ-10311795 is a very potent inhibitor of chymase (K_i = 2 nM), a mast cell serine protease that also plays an important role in the pathogenesis of asthma. This *dual* inhibitor of Cat G and chymase markedly reduced neutrophil counts in the peritoneal fluid in a rat peritonitis model on intravenous administration and was efficacious in the sheep model of asthma on aerosol administration. We determined the crystal structures of JNJ-10311795•Cat G and JNJ-10311795•chymase, which reveal two different modes of interaction within the active site of each enzyme. JNJ-10311795 was selected for clinical development for the treatment of chronic airway inflammation, including asthma and COPD. We have been pursuing follow-up work on this first-in-class agent to obtain an orally active dual inhibitor.

Figure 4. Structures of cathepsin G and chymase inhibitors.



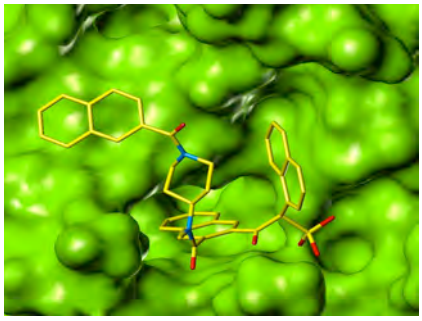
JNJ-785096 JNJ-10311795

Figure 5. Active site of Cat G occupied by inhibitors (x-ray crystallography).



S3 / S4

JNJ-785096

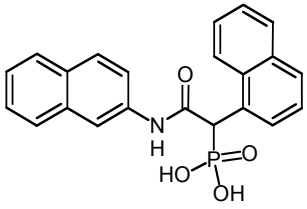


S3 / S4

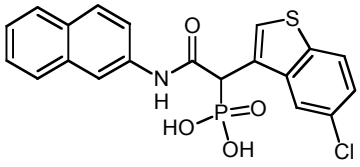
JNJ-10311795

Selective inhibitors for Cat G and chymase would help advance our understanding of the mechanisms of action of our dual inhibitor. In this vein, we have been seeking an orally active, selective Cat G inhibitor and an orally active, selective chymase inhibitor. We identified JNJ-10307635, a β-amidophosphonic acid, as a selective chymase inhibitor (IC_{50} = 200 nM) (Fig. 6). Lead optimization around this structural platform furnished JNJ-10326017 (Fig. 6), a potent, selective chymase inhibitor (IC_{50} = 32 nM). JNJ-10326017 was efficacious in the sheep model of asthma on aerosol administration. We solved the crystal structure of JNJ-10326017•chymase and used the resulting information in a structure-based optimization protocol, which led to a series of potent, selective, orally active chymase inhibitors. A lead compound (K_i = 29 nM) with oral efficacy in the sheep model of asthma, and oral bioavailability in rats and dogs, was selected for clinical development.

Figure 6. Structures of selective chymase inhibitors.



JNJ-10307635



JNJ-10326017

Over nearly 15 years of research, our odyssey in structure-based drug discovery has taken several twist and turns. Although we were successful in identifying potent thrombin inhibitors, the project ultimately did not advance to the clinical stage due to a lack of oral bioavailability. Even today, there are no *oral* thrombin inhibitor drugs on the market, or filed with regulatory authorities, excluding one with a prodrug format. Our foray into the pulmonary inflammation arena proved much more propitious. Thus, three new chemical entities were selected for clinical development: a tryptase inhibitor, a dual Cat G/chymase inhibitor, and a selective chymase inhibitor. Hopefully, a useful drug to benefit patients will emerge from our perseverance in this field of study.

Shape-Persistent Nanoscale Objects - Folded Oligomers and Other Well-Defined Molecular Architectures

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This lecture will cover three areas of ongoing research in my group, related to the general problem of preparing and studying large, but well-defined organic molecules. Unlike proteins and nucleic acids, synthetic macromolecules often possess considerable chemical heterogeneity and their backbones typically explore the ensemble of random conformations. Learning to design synthetic polymers that fold into well-defined, compact shapes will enable chemists to capitalize on features intrinsic to chain molecules including modularity, information rich surfaces, and cooperativity and dynamics of the "folding reaction".[1, 2] Among other things, such nanoscale objects are of interest as scaffolds for displaying biomolecules, as building blocks for self-assembling materials, and as hosts for molecular recognition and supramolecular chemistry. This abstract provides background references and general introductions to the three lecture topics, while the lecture itself will focus on recent results.

m-Phenylene Ethynylene Foldamers and Heterosequenced Oligomers

m-Phenylene ethynylene (*m*PE) oligomers (Fig. 1) undergo a folding reaction in which the ensemble of random conformations is cooperatively transformed into an ordered helical arrangement.[3-5] To observe this reaction at room temperature in common organic solvents, a critical chain length (ca. 8 monomer units) must be exceeded. The side chains dictate the backbone's solubility[6, 7] and the side-chain-linking-group influences the strength of the interaction between adjacent, pi-stacked rings.[8, 9] Chlorohydrocarbon solvents are especially effective at solubilizing the backbone and thus function as "denaturants" of the helical structure.[7]

Despite numerous analytical advances, characterization of oligomers in solution remains a major challenge. To overcome these limitations, we have made extensive use of the chain length dependence test (CLDT). The chain length dependence test is the measurement of an observable quantity over a homologous series of discrete oligomers that

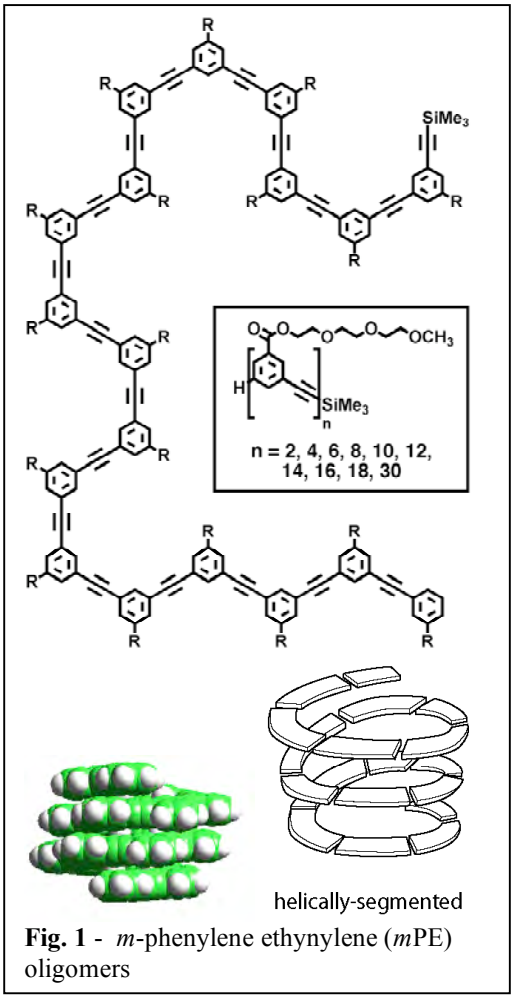

Fig. 1 - *m*-phenylene ethynylene (*m*PE) oligomers

vary systematically in their number of monomer units. While simple in concept, the trends obtained from CLDT studies often provide valuable insight into the behavior of macromolecules that would be difficult to obtain from any single measurement. For instance, the CLDT is useful for studying the structure and properties of chain molecules, such as their conformation in solution,[4, 10] packing in the solid state,[11] and specific intrachain interactions.[12] Applications of the CLDT will be presented throughout the lecture.

The natural segmentation of chain molecules into monomeric units together with the ordered conformation mentioned above provides a unique opportunity to control the spatial disposition of functional groups over nanoscale dimensions, both in the interior of the helical cavity and along the outer surface (Fig. 1). Such control requires the preparation of heterosequenced oligomers in which monomers can be arranged in a prescribed order. Making use of an insoluble solid support is also desirable in order to accomplish the simultaneous synthesis of many sequences in parallel fashion. Ongoing efforts aimed at developing automated procedures for the rapid (1-2 days), parallel synthesis of 20-mer *m*PEs will be described.

Nanoscale Compartments and Reactive Sieving

The compact helical conformation shown in Fig. 1 generates a three-dimensional internal cavity with a diameter larger than 8Å. Lining the inner walls with specific functional groups whose spatial position is determined by chain sequence offers a potentially powerful and general platform for creating information-rich surfaces to bind guests with high affinity and high specificity. We have already demonstrated that the cavity can bind small hydrophobic molecules such as monoterpenes.[13] For rod-shaped guest molecules such as piperazine **1** (Fig. 2), guest-host affinity also depends on length-complementarity[14, 15] and surface functionality.[16] A major challenge is to design sequences in which the binding pocket has a shape that is complementary to the guest. Borrowing sequence design tools from protein chemistry may offer a rational approach to identify heterosequences that are complementary to a given target. In collaboration with Prof. Jeffery G. Saven (UPenn), we are using a statistical computer aided design algorithm[17] originally developed for protein sequences to optimize *m*PEs for specific guests.

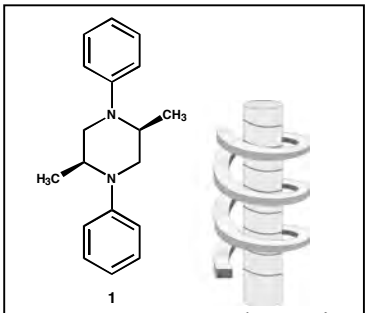

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Fig. 2 - Schematic diagram of a rod-shaped guest (e.g. **1**) bound to a

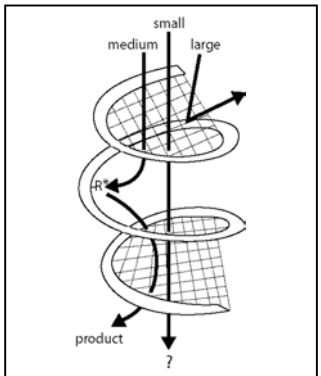

Fig. 3 - Reactive sieving by a helical

Beyond simple guest-host binding, the concept of reactive sieving is being pursued. A long-range goal is to create a catalyst that selectively activates substrates of a certain size (Fig. 3). Ideally, only those substrates having a size complementary to the interior cavity will participate in the reaction. Recent progress toward this objective will be presented.[18, 19]

Dynamic Oligomerization and Polymerization

Reversible polymerization reactions are of interest for the rational design of stimuli-responsive polymeric materials. Here we exploit the cooperative nature of the folding reaction to promote a reversible oligomerization[20-22] or polymerization[23] of chain segments (Fig. 4). Dynamic covalent bonds and reversible metal-ligand coordination bonds[24] have been used to achieve folding-driven reactions. In the case of dynamic covalent bonds, metathesis reactions have three characteristics that make them ideal for this purpose: they are: (1) reversible, (2) fast in the presence of a catalyst but immeasurably slow in the absence of a catalyst, and (3) energetically balanced meaning that bond energy changes are similar on both sides of a metathesis equilibrium. A consequence of (3) is that supramolecular chemistry can tip the balance of reaction equilibria – i.e., noncovalent interactions can drive covalent chemical changes. The products are thus determined by intrachain interactions and entropic considerations.

Fig. 4 - An example of folding-driven oligomerization involving imine metathesis. The metathesis equilibrium constant, K^{MET}, is on the order of unity. Under conditions where K^{FOLD} is greater than unity, the formation of longer oligomers is favored.

For *m*PE oligomers, alkyne metathesis is an obvious choice. Molybdenum alkylidyne **2** is a conveniently prepared[25] catalyst precursor for room-temperature alkyne metathesis (Fig. 5). The active catalyst, generated by ligand exchange with electron-deficient phenols, exhibits good functional group and solvent compatibility.[26] Surprisingly, when dialkynylarenes are subjected to metathesis conditions, macrocycles rather than linear polymers are obtained as the thermodynamic product.[27] To avoid deep thermodynamic traps and control the outcome of these reactions, we introduced the idea of "starter sequences".[28] Starter sequences are short oligomers whose ends can undergo metathesis but whose internal segments are joined by linkages that do not participate in metathesis. Starter sequences appear to polymerize by an interesting "nucleation-elongation" mechanism,[29, 30] where the nucleation step involves oligomer growth up to the critical chain length of helix formation.

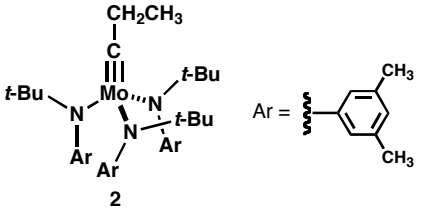

Fig. 5 - A conveniently prepared catalyst precursor for room-temperature alkyne metathesis.

Acknowledgments

With deep gratitude, I thank the excellent coworkers whose names appear in the following references. Contributions not yet published from Christian Ray, Erin Elliot, Ron Smaldone, Jay Wackerly, Dr. Haim Weissman and Prof. Jeffery Saven (University of Pennsylvania) will be presented during the lecture. Financial support from the National Science Foundation and the Department of Energy made this research possible.

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Miniature Proteins and Non-Proteins

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Department of Molecular, Cellular, and Developmental Biology
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A major focus of our research is the design of new classes of molecules that bind protein surfaces with high affinity and specificity, and the use of these molecules to probe the functional roles of discrete protein-protein interactions in normal and pathological cellular processes. We engineer these useful molecules in three ways: by incorporating novel function within a natural miniature protein scaffold, by designing protein folds not previously observed in Nature, and by reconstructing functional epitopes within an altogether non-natural foldamer context (Figure 1).

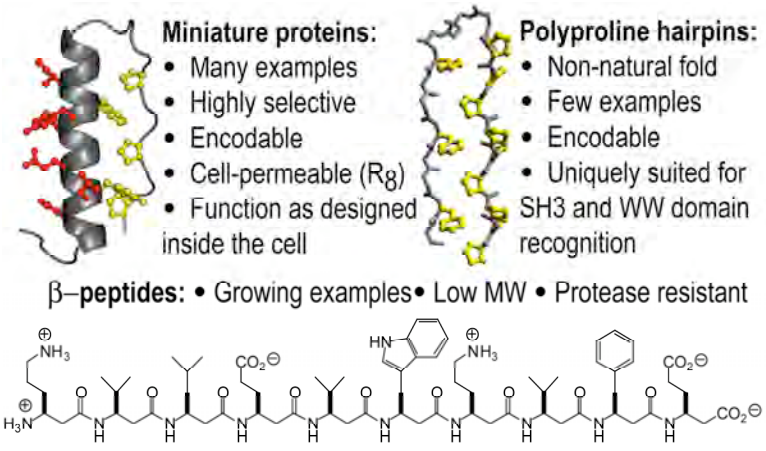
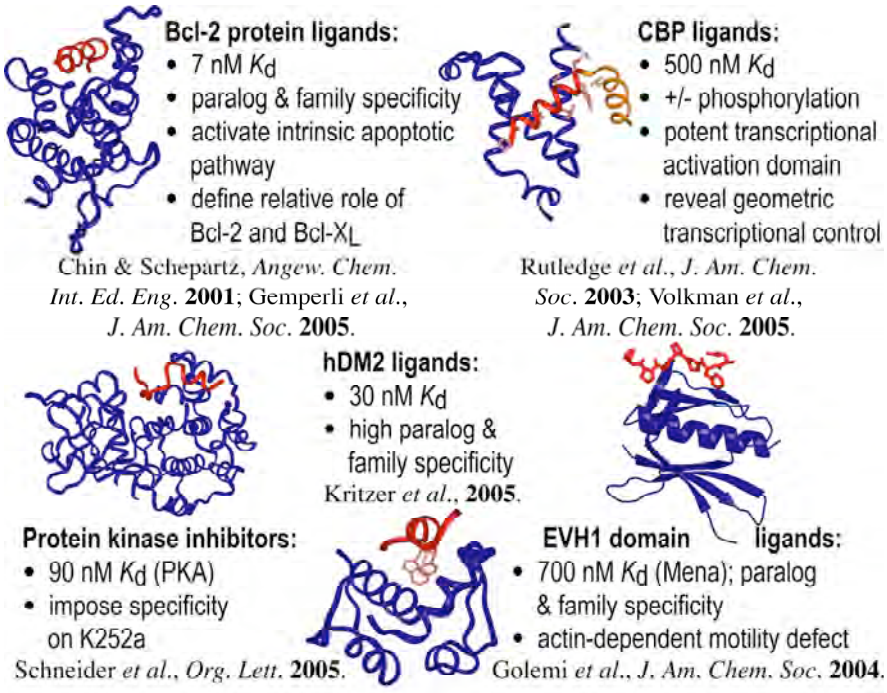


Figure 1. Three classes of molecules to probe, inhibit, or reconfigure protein-protein interactions *in vitro* and *in vivo*.

Functional miniature proteins based on a natural scaffold. The miniature proteins studied most extensively in our lab are highly engineered variants of a natural miniature protein known as avian pancreatic polypeptide (aPP). aPP-based miniature proteins are designed using a process called protein grafting [1-7] in which those residues that comprise a natural α– or type II polyproline (PPII)–helical recognition epitope are introduced onto the solvent-exposed α– or PPII–helical face of aPP [8,9]. Our laboratory has used this procedure, often in combination with directed evolution, to create miniature proteins with high affinities for a diverse array of targets including duplex DNA [1,2,4,10], the anti-apoptotic proteins Bcl-X_L [11] and Bcl-2 [7], the oncoprotein hDM2 (manuscript in preparation), the transcriptional coactivator CBP [5,12], and the EVH1 domain of Mena [6]. Most recently we have used protein grafting to generate a miniature protein-K252a conjugate that selectively inhibits protein kinase A [13] (Figure 2).

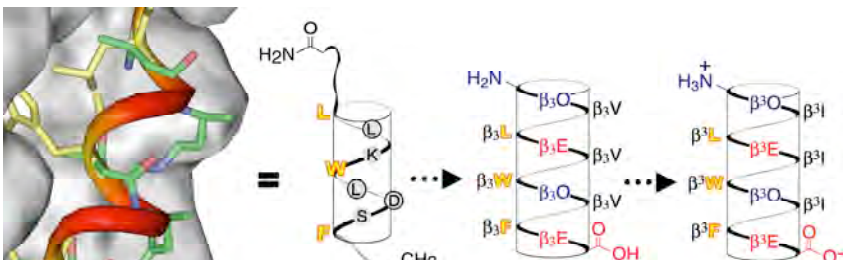
aPP-based miniature proteins possess several useful and interesting properties that will be highlighted in the first phase of this lecture. In addition to exhibiting high affinities for their targets, many aPP-based miniature proteins display high levels of specificity, distinguishing effectively between closely related DNA sequences [2,4,10] or protein family members [6,7]. In addition, since they are comprised of natural α–amino acids, miniature protein structure and/or function can be optimized easily by directed evolution. When tagged with a short transducing sequence such as R_8, miniature proteins cross the plasma membrane, tolerate cellular proteases, and function as designed inside the cell. Alternatively, when substituted for

a promiscuous recognition domain within a larger protein, a miniature protein can, in theory, impose predictable specificity on an otherwise abstruse molecular interaction inside the cell.



The polyproline hairpin: a rationally designed miniature protein not previously observed in Nature. Protein domains that recognize type II polypoline helices – molecules that include SH3, WW, and EVH1 domains, among others – are components of most, if not all, cellular signaling pathways. While there now exist many examples of aPP-based miniature proteins that recognize the deep protein clefts used to bind α–helices [5,7,11-14], and one example of an aPP-based miniature protein that binds with high affinity to an EVH1 domain [6], few molecules, natural or otherwise, discriminate effectively, in the nanomolar concentration range, among the shallow PPII-recognition grooves found within SH3 and WW domains. It is well known that interactions between PPII helices and aromatic side chains stabilize both *intermolecular* interactions with SH3 or WW domains and *intramolecular* interactions within the cores of several miniature proteins, including aPP itself [15]. We recently asked whether these stabilizing interactions could be transplanted into a new miniature protein context: a peptide hairpin containing two, anti-parallel PPII helices (Figure 1). In the second phase of this lecture I will describe the result of this investigation, and illustrate use of a simple FRET assay to optimize helix-helix interactions and the sequence of the intervening β–turn to generate molecules that possess cooperative thermal melting transitions and a high level of PPII content as monitored by CD; preliminary NMR data show clear evidence for aromatic-proline packing. I will also describe how these molecules might be applied as inhibitors or mediators of discrete SH3 and WW domain interactions inside the cell.

β-peptide foldamers: Miniature non-proteins? Our group has also pursued a



complementary approach towards molecules that can inhibit or re-configure protein-protein interactions inside the cell [16]; these results will constitute the final section of the lecture. In this case, our approach exploits the unique properties of β–peptides [17-19]: high protease stability [20,21], favorable pharmacodynamics [22], and, when folded, the ability to recapitulate an extended and highly variable recognition surface in a very small non-protein package. To fully realize these advantages for applications in biology, we designed a short β-peptide that possessed the combined attributes of high water solubility, high 14-helix stability, and six variable positions, by judicious positioning of charged residues and termini [23,24]. Using the same protein grafting strategy that proved successful in the context of aPP-based miniature proteins, we then designed a highly 14-helical β-peptide that bound the hDM2 oncoprotein with high/mid nanomolar affinity [25], and developed a one-bead-one compound library and high throughput screening protocol to identify derivatives with mid/low nanomolar affinities for hDM2 (Figure 3). High-resolution structural analysis of these β-peptides [26] has provided unexpected insight and a general model for utilizing β-peptide 14-helices as α-helix mimetics. Indeed, another β-peptide α-helix mimetic that binds a HIV gp41 construct and inhibits gp41-mediated membrane fusion in cell-cell syncytia assays has also been prepared in our group. This bioactive β-peptide has fueled our optimism that β-peptides can act as effective inhibitors of therapeutically important protein-protein interactions *in vivo*.

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Design and Mechanistic Studies of Palladium-Catalyzed Oxidations for Organic Synthesis

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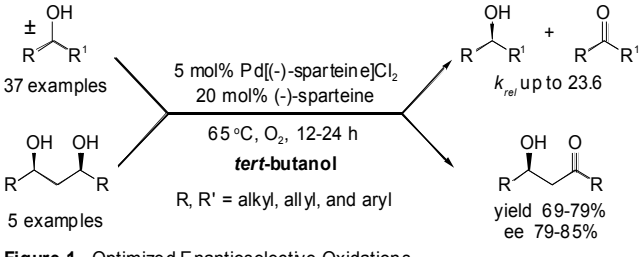
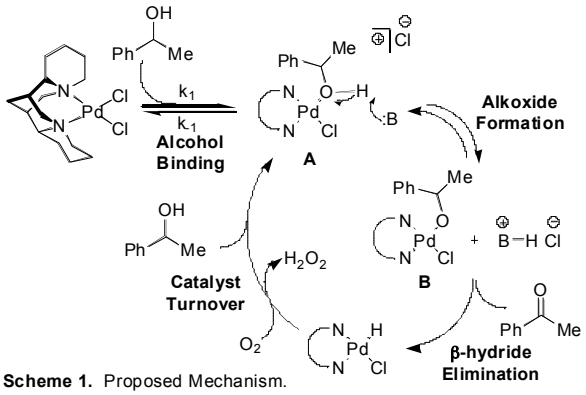
The development of catalytic oxidations using practical terminal oxidants such as molecular oxygen or simple peroxides, represents a central challenge in catalysis. Critical to the development of such potentially practical catalysts is a fundamental understanding of the mechanistic features which lead to a robust and selective catalytic system. Within this regard, our group has focused on the development of new Pd(II)-catalysts for various oxidation reactions wherein mechanistic analysis has played a vital role in catalyst design.



Alcohol Oxidation: Based on the original report by Uemura and coworkers of ligand accelerated catalysis within a Pd(II) catalyzed aerobic alcohol oxidation,[i] we selected to explore the development of catalysts for the oxidative kinetic resolution of secondary alcohols. Using a mainly empirical approach, it was discovered that the addition of (-)-sparteine to Pd(II) sources results in a good catalyst for the aerobic oxidative kinetic resolution of secondary alcohols (Figure 1).[ii]

A significant limitation of this system is the requirement of (-)-sparteine. (-)-Sparteine is only readily available as a single antipode and is a difficult template to optimize through systematic structural variations. With this in mind, it became clear that establishing the precise role(s) of (-)-sparteine in the oxidation and determining its influence on the enantiodiscrimination would provide the basis for future catalyst development. Therefore, a detailed mechanistic investigation was undertaken. The kinetic studies revealed an intriguing mechanistic situation in which the rate limiting step changes from alkoxide formation to β-hydride elimination when the concentration of (-)-sparteine is increased (Scheme 1).[iii]



Scheme 1. Proposed Mechanism.

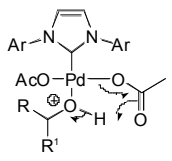


Figure 2. New Catalyst Design.

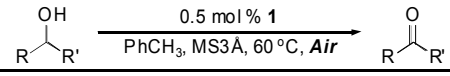
New Catalysts for General Alcohol Oxidation: In addition to developing new enantioselective oxidation systems, we have used this mechanistic insight to improve the practicality of general Pd(II)-catalyzed aerobic oxidations. While developing a Pd-catalyst that is effective for aerobic alcohol oxidation at room temperature,[iv] we found

that excess amine ligand inhibits the oxidation through a pre-equilibrium between different catalytic species. The active catalytic species in this system contains only one amine ligated to the palladium. Based on this information, we envisioned using a single monodentate ligand which could support the Pd catalyst throughout the catalytic cycle. Within this proposal, it was reasoned that a base masked as an anionic ligand could in principle facilitate an intramolecular deprotonation (Figure 3).

Figure 3. Aerobic Oxidation Catalyst **1**.

Not only should this enhance the rate of deprotonation, but also the accessibility of a coordination site for β-hydride elimination. Using isolated Pd(IiPr)$(OAc)_2$-H_2O, **1** (Figure 3), at 0.5 mol%, a variety of benzylic, aliphatic, and allylic alcohols were cleanly oxidized to the corresponding aldehyde or ketone, and high yields of the isolated products could be obtained. Up to 1000 turnovers can be achieved using activated substrates. Increasing the amount of added acetic acid allows removal of the oxygen balloon, and the reaction can be carried out under an ambient atmosphere (Table 1).[v] This is notable as it is a rare example of a homogeneous Pd-catalyst for aerobic alcohol oxidation, which does not require special conditions to increase the oxygen concentration in the reaction. In elucidating the mechanistic details of this catalytic system, we have made two fascinating observations:[vi] (1) an unusually large primary KIE of 5.5 ± 0.1 was measured for *sec*-phenethyl alcohol and (2) [AcOH] simultaneously modulates the rate of oxidation of the alcohol, the reoxidation of the Pd catalyst, and the decomposition of the Pd catalyst.

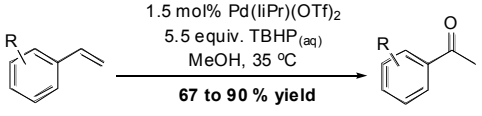
Table 1. Oxidation of Alcohols Using Air.



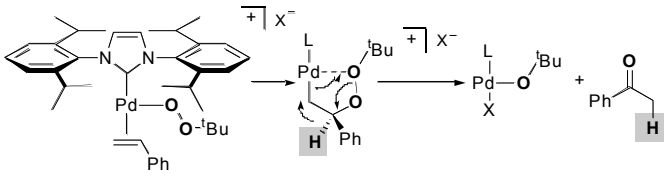
Entry	Substrate	R	R'	Time	%Yield[a,b]
1[c,d]	**2a**	Ph	CH_3	14 h	>99 (97)
2[e]	**2l**	4-$OMeC_6H_4$	CH_3	14 h	>99 (93)
3[e]	**2c**	3-$CF_3C_6H_4$	CH_3	20 h	>99
4[e]	**2m**	4-$CH_3C_6H_4$	H	14 h	>99
5[f]	**2f**	$CH_3(CH_2)_7$	CH_3	14 h	99 (91)
6[e]	**2n**	1-indanol		14 h	>99
7[e]	**2h**	*cis*-4-methylcyclohexanol		14 h	96

[a] GC conversion [b] Isolated yield in parenthesis [c] 5 mol % HOAc [d] 1.0 g

Extension to Olefin Oxidation: The Wacker oxidation is a very useful and well-studied reaction for the oxidation of olefins to ketones. Additionally, it is the simplest Pd(II)-catalyzed functionalization of olefins and is serving as a template for developing more diverse reactions in our laboratory. However, the generality of many of the reported Wacker oxidations is poor especially for substrates that are susceptible to polymerization. This is presumably due to the requirement of greater than stoichiometric amounts of Cu(II)-salts. Our initial goal was to develop a catalyst that requires only O_2 as the terminal oxidant.



(1)



Scheme 2. Proposed hydride shift mechanism.

However, through our studies, we found that simple peroxides are much more effective in the oxidation of styrenyl derivatives (eq. 1).[vii] Through isotopic labeling studies of this system, an alternative mechanism in which the nucleopalladated intermediate undergoes a hydride shift rather than β-hydride elimination has been proposed (Scheme 2). This mechanistic motif allows for unique approaches to Pd(II) catalysis which shall be discussed.

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Evolution of a Gram-Scale Total Synthesis of the Antitumor Agent (+)-Spongistatin 1: Challenges, Excitement, and Frustrations

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In 1993, the research groups of Pettit,[viii] Fusetani[ix] and Kitagawa,[x] independently disclosed the isolation of minute amounts of several congeners of the spongistatin family of bis-spiroketal macrolides that displayed extraordinary cytotoxicity (i.e., subnanomolar) against a wide variety of human cancer cell lines, including melanoma, lung, colon and brain. Named interchangeably the spongistatins, cinachyrolides, and the altohyrtins, these architecturally daunting natural products have attracted wide interest both in the synthetic and biomedical communities. The initial structural assignments of the Kitagawa group,[xi] including absolute stereochemical designations, were subsequently confirmed by the total syntheses of (+)-altohyrtin C [spongistatin 2 (**2**)] by Evans *et al*.[xii] and (+)-altohyrtin A [spongistatin 1 (**1**)] by Kishi and coworkers[xiii] (Figure 1).[xiv] The elegant syntheses at Harvard University demonstrated unequivocally that the altohyrtins and the spongistatins were indeed identical.

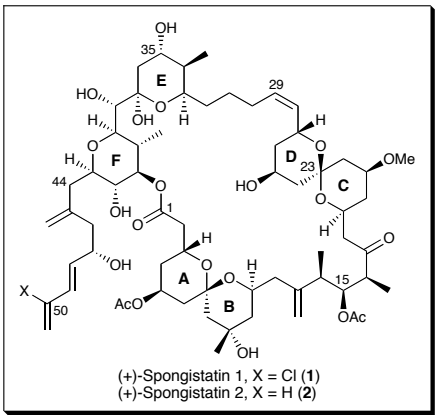


Figure 1

Intrigued both by the impressive pharmacological properties and complex architecture of the spongistatin bis-spiroketal macrolides, we initiated a synthetic program at Penn to develop a scalable route to (+)-**1**. Our enthusiasm for this program derived from our recent experience with the one-gram scale synthesis of the antitumor agent (+)-discodermolide, which was subsequently licensed by Novartis Pharmaceuticals, Inc., and with the aid of the Paterson end-game, led to clinical evaluation.[xv]

This lecture, as outlined below, will describe the status of our current efforts to develop a scalable (ca. one-gram) synthesis of (+)-spongistatin 1 (**1**). Towards this end, we have achieved three total syntheses of the spongistatin antitumor agents to date (Figure 2), the first in 2001 of (+)-spongistatin 2 (**2**),[xvi] a second in 2003 of (+)-spongistatin 1 (**1**),[xvii] and a third in 2004, again of (+)-spongistatin 1 (**1**).[xviii] It is the latter synthesis which we believe

holds the promise of providing material sufficient for preclinical evaluation. Importantly, lessons learned from our earlier ventures, as well as those derived from the Evans and Kishi syntheses, have proven critical to the success of this program.

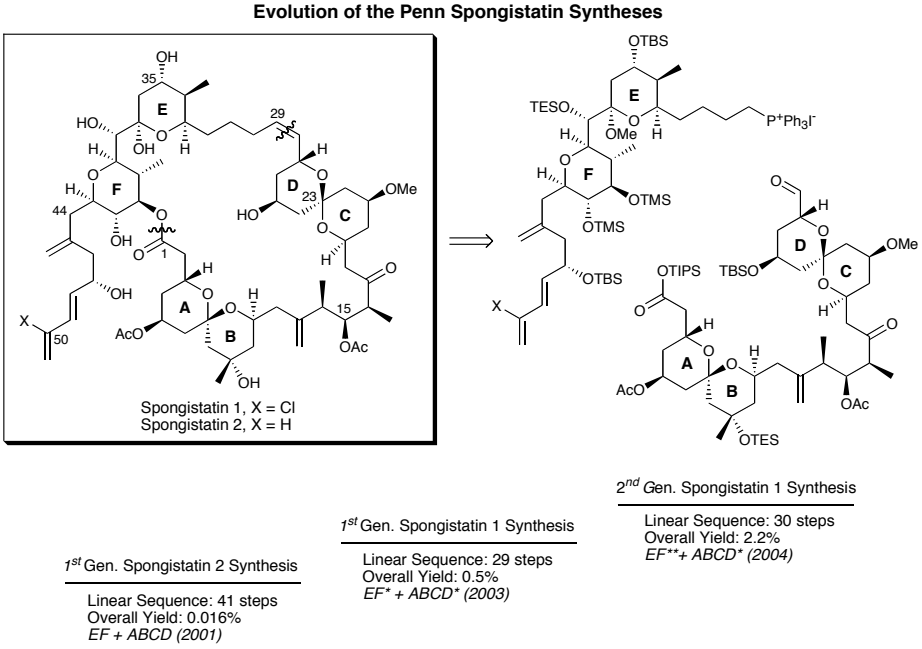
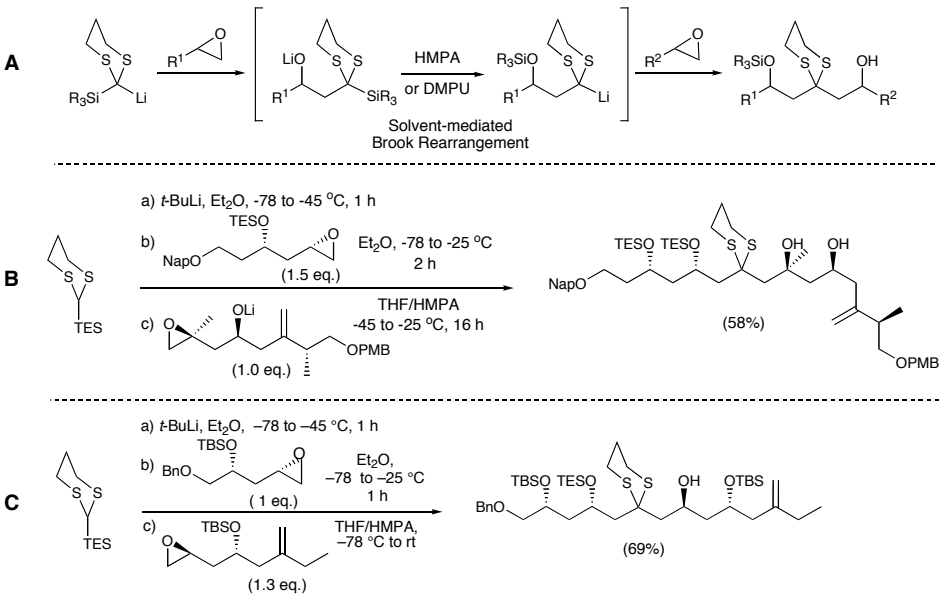


Figure 2

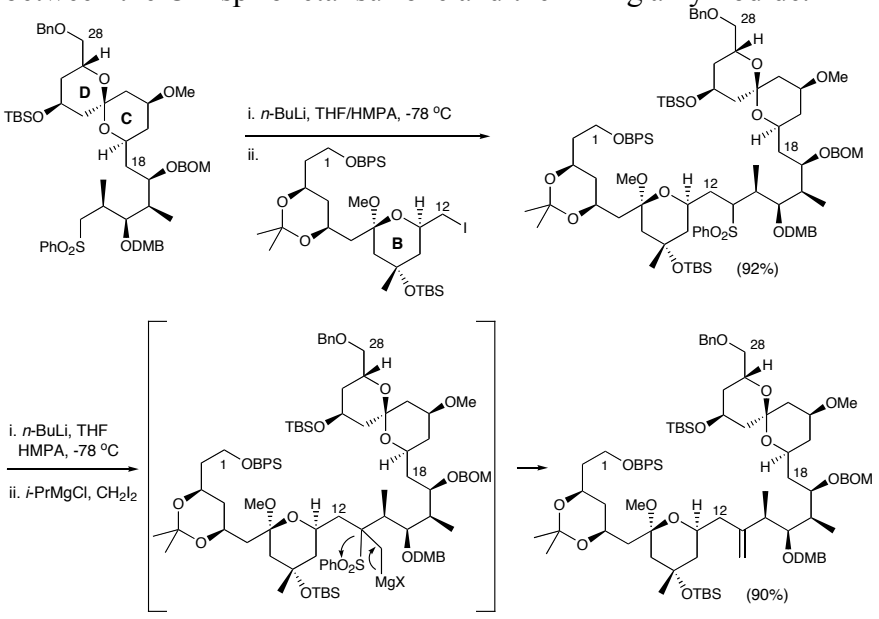
A central, critical feature of most successful total syntheses of architecturally complex natural products entails the efficient union of highly functionalized advanced intermediates. In this regard, we have devised and/or exploited several strategic fragment union tactics as our spongistatin program has evolved. We include here the development of the multicomponent dithiane linchpin coupling exploiting a variety of electrophiles including epoxides,[xix] aziridines,[xx] and carbonyl compounds,[xxi] the Julia olefination, which allows fragment union with simultaneous introduction of an exo-methylene group,[xxii] and the Petasis-Ferrier union/rearrangement tactic,[xxiii] which enables the facile construction of 2,6-cis disubstituted tetrahydropyran ring systems.

The utility of dithiane nucleophiles as acyl anion equivalents has led to numerous applications in Smith group total syntheses.[xxiv] More specifically, the multicomponent dithiane/epoxide linchpin coupling tactic (Scheme 1A) enables the rapid, stereoselective construction of orthogonally functionalized 1,5-diols, which are a common feature in advanced intermediates *en route* to spongistatin 1 (Scheme 1B, 1C).[xxv]



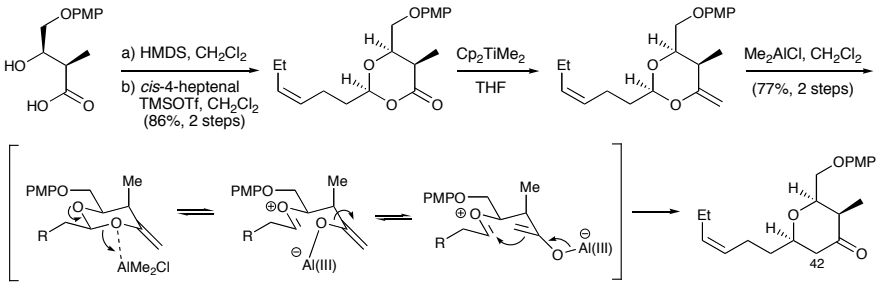
Scheme 1

Likewise, the Julia olefination/methylenation sequence[xxii] has enabled a strategic fragment union in the context of our efforts toward the spongistatins (Scheme 2). Of note is the overall efficiency of the two-step protocol (83%), during which a key C-C bond is formed between the CD-spiroketal sulfone and the B-ring alkyl iodide.



Scheme 2

A third transformation that is exploited with great success is the Petasis-Ferrier union/rearrangement, which enables the facile elaboration of 2,6-cis-disubstituted tetrahydropyran ring systems. Here, condensation of a β-hydroxy acid and an aldehyde, followed by methylenation of the resultant dioxanone, affords an enol acetal (Scheme 3). Treatment with Me_2AlCl then prompts a rearrangement to afford the desired tetrahydropyran intermediate.



Scheme 3

In summary, the application of each of the above mentioned strategic transformations in the context of the large-scale total synthesis of spongistatin 1 (**1**) will be described.

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Asymmetric Hydrogenation: A Standard Platform for Practical Drug Synthesis

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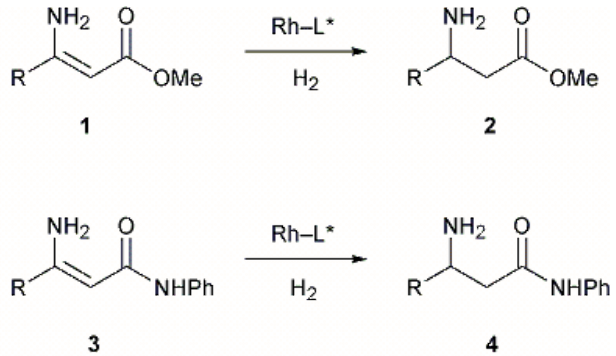
Asymmetric hydrogenation is widely recognized as one of the most powerful methods for synthesis of optically active molecules. While extremely attractive from an industrial perspective (high chemical/optical yields possible, no waste, standard equipment) asymmetric hydrogenation does not feature prominently in manufacturing processes for pharmaceuticals. At Merck, asymmetric hydrogenation has been established as a standard platform technology through the strong collaboration of synthetic, mechanistic, and analytical chemistry, and through investment in substantial ligand libraries and powerful screening/analytical tools.

A goal of our platform approach is to apply asymmetric hydrogenation technology, early in the drug development cycle, to the synthesis of all chiral targets conceivably accessible via hydrogenation, regardless of literature precedent. This has led to the discovery of new and highly practical applications of this methodology, some of which have subsequently been applied at the manufacturing scale. This presentation will highlight some of our recent successes in this area.

Asymmetric hydrogenation of substituted enamines such as **1** (Fig. 1) was recently reported by our laboratory and is possibly the most straightforward and effective synthesis of beta-amino acid derivatives available currently. This conversion is achieved via rhodium-catalyzed, direct asymmetric hydrogenation of ***unprotected*** β-enamino esters and amides, is broad in scope, and has been applied successfully at the manufacturing scale. Mechanistic studies implicate the corresponding imine as the substrate for hydrogenation.



a: R = Ph; **b**: R = 4-MeO-Ph; **c**: R = 4-F-Ph;
d: R = $PhCH_2$–; **e**: R =3-Py

Fig. 1. Highly efficient synthesis of β-amino acid derivatives via asymmetric hydrogenation of unprotected enamines.

A remarkable, pressure-dependent, catalytic, asymmetric hydrogenation of an α, β-unsaturated carboxylic acid was also recently developed, which provides the corresponding chiral saturated acid with excellent selectivity. Mechanistic studies revealed that the hydrogenation proceeds via a complex isomerization / hydrogenation reaction network.

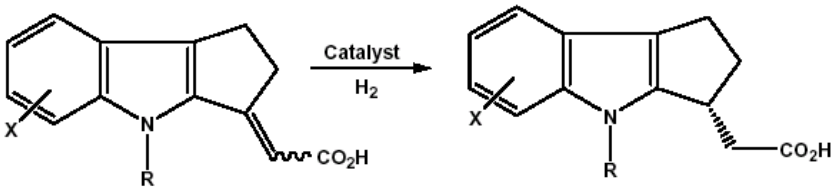


Fig. 2. Asymmetric hydrogenation of an α, β-unsaturated carboxylic acid.

Along with these detailed examples, a brief summary of other novel and practical applications of asymmetric hydrogenation technology will be provided, highlighting the clear potential to expand the scope and utility of this approach far beyond that reported in the literature and currently accepted as state of the art.

Catalytic Asymmetric Cyclization Reactions for Natural Product Synthesis

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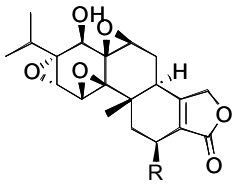
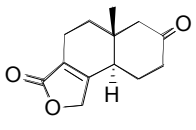
Chinese medicinal plant *Tripterygium wilfordii* Hook F, also called Lei Gong Teng (Thunder God Vine), is a rich source of bioactive natural products. For example, triptolide, tripdiolide, wilforonide, and subglutinol exhibit potent anti-cancer, anti-tumor, anti-inflammatory and immunosuppressive activities (Figure 1). Their structural complexity has presented significant synthetic challenges and inspired us to develop new methods for organic synthesis. In our program on chemistry and biology of those natural products, we have developed a series of oxidation methods (ketone-catalyzed epoxidation, C–H bond oxidation, and peroxynitrite decomposition) and cyclization methods. Here we describe our recent results on catalytic asymmetric cyclization reactions, which range from atom and group transfer radical cyclization to transition metal-catalyzed cyclization, and their applications in the construction of various carbocycles and heterocycles found in many bioactive natural products.

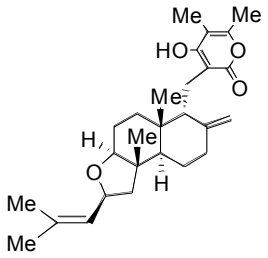
Figure 1



(–)-triptolide (R = H)
(–)-tripdiolide (R = OH)



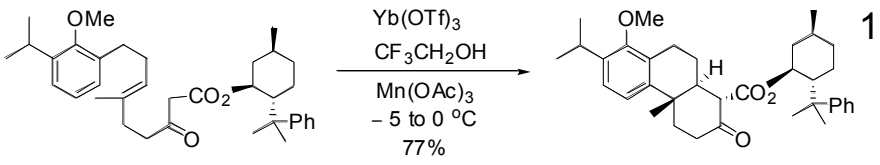
wilforonide



subglutinol A

We first employed $Mn(OAc)_3$-mediated oxidative free-radical cyclization reactions as a key step to construct the tricyclic core of triptolide. We have discovered that lanthanide triflates can catalyze $Mn(OAc)_3$-mediated oxidative radical cyclization reactions, resulting in significant increase in stereoselectivity and yield (Scheme 1). Using Lewis acid catalysis and chiral auxiliaries, we have accomplished the first enantioselective total synthesis of triptolide and wilforonide.

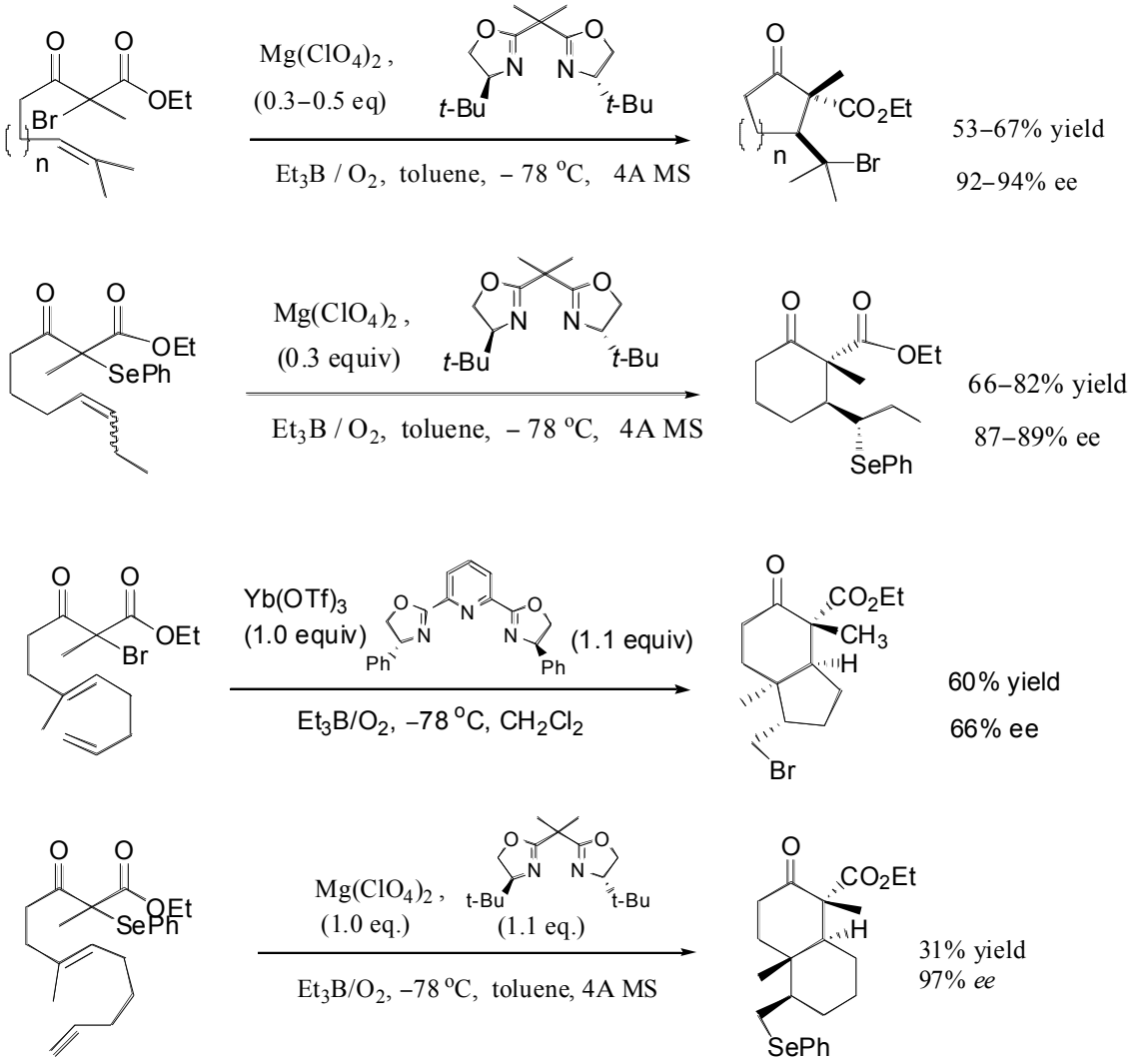
Scheme 1



38:1 *dr*

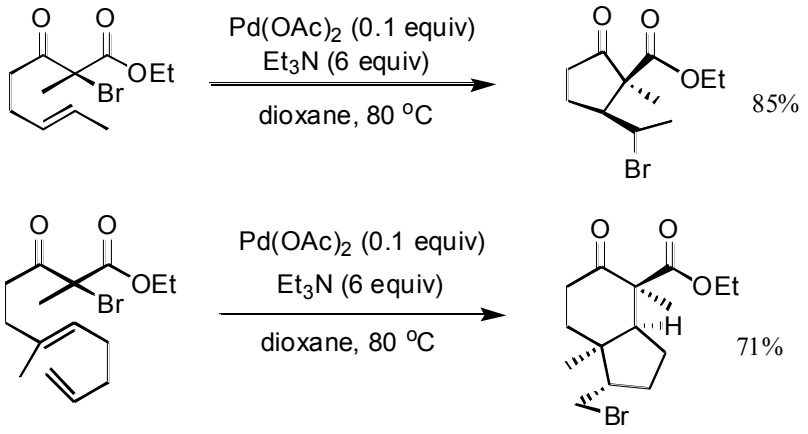
We then turned our attention to developing catalytic enantioselective radical cyclization methods. As an important class of radical reactions, atom or group transfer radical cyclization represents a powerful and atom-economic approach to the ring construction. We have found that catalytic amounts of Lewis acid $Mg(ClO_4)_2$, combined with a chiral bis(oxazoline) ligand, could promote atom or group transfer radical cyclization reactions of unsaturated -keto esters, resulting in 2,3-disubstituted ketones in excellent enantioselectivity (up to 94% ee) (Scheme 2). We have also found that Lewis acids effectively catalyzed atom or group transfer tandem radical cyclization of a series of unsaturated β-keto esters to provide various polycyclic ring skeletons with moderate to good yields and excellent stereoselectivities. The first enantioselective tandem radical cyclization promoted by chiral Lewis acids has been achieved in both atom transfer and group transfer reactions with up to 97% ee (Scheme 2).

Scheme 2



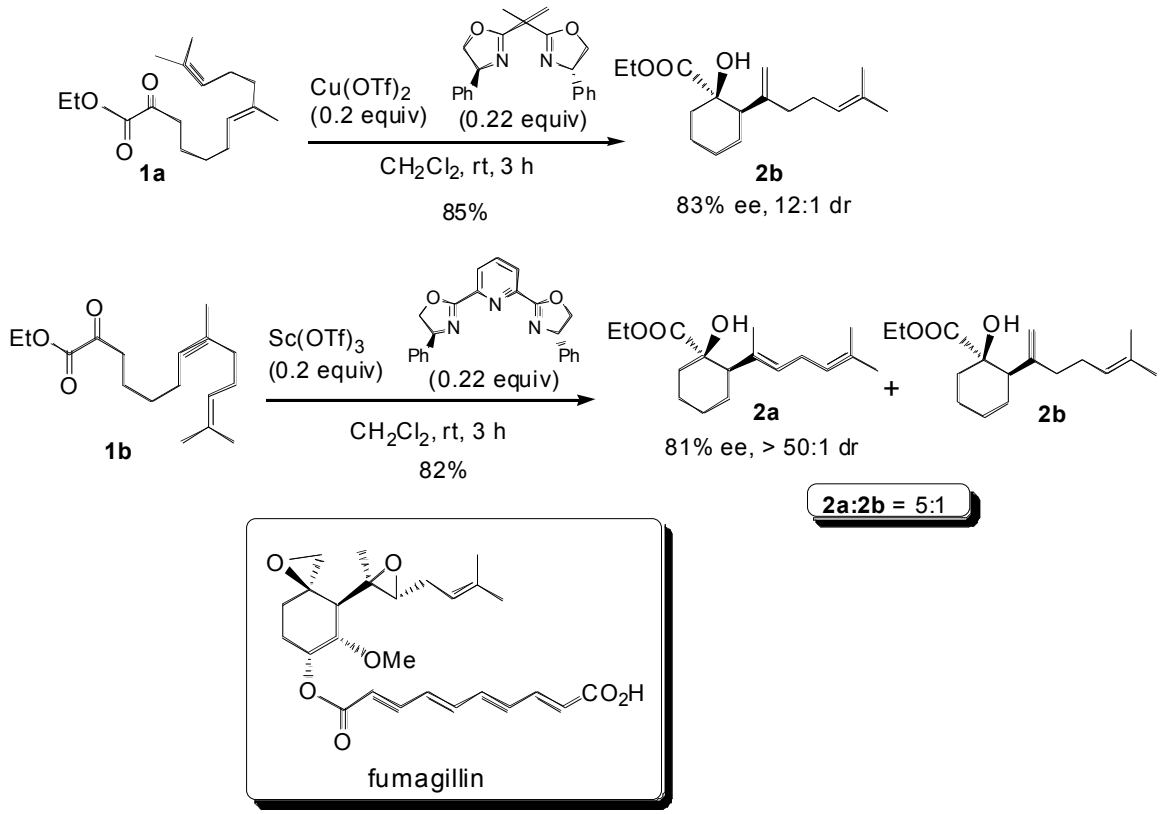
In addition, we have found $Pd(OAc)_2$ can catalyze bromo atom transfer cyclization reaction in the presence of Et_3N, and this reaction is also applicable to the tandem cyclization case (Scheme 3). Preliminary mechanistic studies indicate that these Pd-catalyzed atom transfer reactions may not proceed via a radical pathway.

Scheme 3



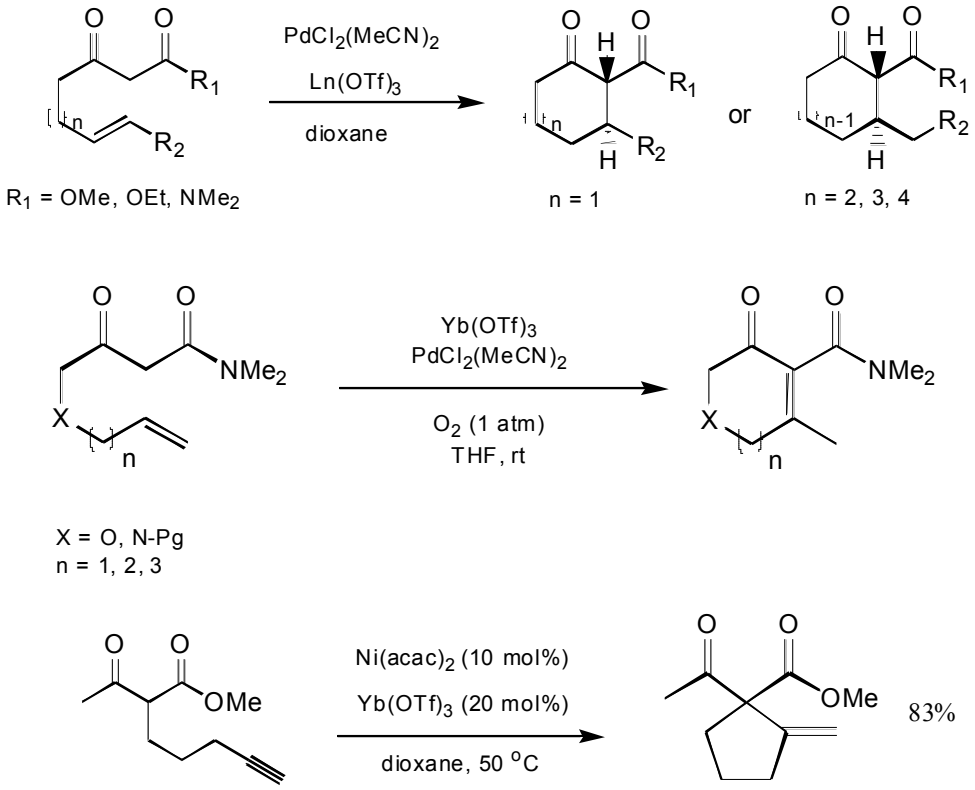
Besides radical cyclization reactions, we have uncovered a Lewis acid-catalyzed enantioselective carbonyl cyclization reaction of unsaturated α-keto esters (Scheme 4). This method has been employed in the enantioselective total synthesis of fumagillin family of angiogenesis inhibitors.

Scheme 4



More recently, we have investigated several transition metal-catalyzed cyclization reactions, including lanthanide triflates-promoted Pd-catalyzed intramolecular hydroalkylation reaction and oxidative cyclization reaction under aerobic conditions, as well as lanthanide triflates-promoted Ni-catalyzed Conia-ene reaction of β-dicarbonyl compounds with alkynes (Scheme 5).

Scheme 5



Schedule of Presenters – Poster Session A Sunday, June 12, 2005

A1 CROSS METATHESIS OF SUGARS AND FATTY ACIDS WITH LYSINE AND CYSTEINE
***Andrew D. Abell* and Andrea J. Vernall**
University of Canterbury
Department of Chemistry, Christchurch, New Zealand

A2 THE SYNTHESIS OF CYCLIC β-AMINO ACIDS FROM METHIONINE, ALLYLGLYCINE AND SERINE
Andrew D. Abell, Kelly H. Anderson, and James Gardiner
University of Canterbury
Peptidomimetic Group, Christchurch, New Zealand

A3 α-ARYLATION OF KETONES: PALLADIUM CATALYZED COUPLING OF ENAMINES AND ARYLHALIDES
James C. Adrian, Jr., Tian Tian
Union College
Department of Chemistry, Schenectady, NY 12308

A4 PHOSPHONATES DERIVED FROM 4-HYDROXYBENZAMIDES AS FUNCTIONAL CHAR-FORMING FLAME RETARDANTS
***Richard C. Ahn* and Bob A. Howell**
Central Michigan University
Center for Applications in Polymer Science, Mt. Pleasant, MI 48859-0001

A5 METHOLOGY AND MECHANISTIC STUDIES OF RING-OPENING/CROSS-METATHESIS (ROCM) REACTIONS OF NORBORNENE DERIVATIVES
Clement Osei Akoto* and Jon D. Rainier
University of Utah
Department of Chemistry, Salt Lake City, Utah – 84112

A6 PALLADIUM-CATALYZED RING-FORMING AMINOACETOXYLATION OF ALKENES
Erik J. Alexanian, Chulbom Lee, Erik J. Sorensen
Princeton University
Department of Chemistry, Princeton, NJ 08544

A7 SOME TRANSFORMATIONS OF 1, 2-EPOXY-3-CHLOROPROPANE
M.A. Allahverdiyev, A. M. Magerramov, A. N. Khalilov, F. N. Nagiyev
Baku State University
23 Z.Khalilov, Baku-Azerbaijan

A8 NMR INVESTIGATIONS INTO THE CONFORMATION AND RELATIVE STEREOCHEMISTRY OF ACYCLIC POLYPROPIONATE MOTIFS
Carolyn E. Anderson,[1] David K. Britt,[1] Christopher D. Anderson,[2] Scott D. Rychnovsky,[2] Daniel J. O'Leary[1]
1. Department of Chemistry, Pomona College, 645 North College Avenue, Claremont, California 91711
2. Department of Chemistry, University of California, Irvine, 516 Rowland Hall, Irvine, California 92697

A9 REGIO- AND STEREOSELECTIVE [4 + 3] CYCLOADDITION USING CHIRAL ALLENAMIDES
Jennifer E. Antoline, Jian Huang, and Richard P. Hsung*
University of Minnesota
Department of Chemistry, 207 Pleasant St. S.E., Minneapolis, MN 55455

A10 DESIGN, SYNTHESIS, AND CHARACTERIZATION OF PH SENSITIVE DENDRIMERS
***Amy M. Balija* and Steven C. Zimmerman**
University of Illinois at Urbana-Champaign

A11 SIMPLE SYNTHESIS OF FLUORENES IN A ONE-POT METHOD
Bimal K. Banik,* Indrani Banik and Curtis Logan
University of Texas-Pan American
Department of Chemistry, 1201 West University Drive, Edinburg, Texas 78541

A12 SM/NBS-INDUCED REDUCTIVE DIMERIZATION OF CARBONYL COMPOUNDS
Bimal K. Banik*,* Indrani Banik and Nacer Aounallah
University of Texas-Pan American
Department of Chemistry, 1201 West University Drive, Edinburg, Texas 78541

A13 IMIDAZOLE-4,5-DICARBOXYLIC ACID AS A SCAFFOLD FOR THE DISCOVERY OF CYTOTOXIC COMPOUNDS AGAINST HL-60 CELLS
Paul W. Baures‡, Elisabeth M. Perchellet†, and Jean-Pierre Perchellet†
‡Department of Chemistry, Bowdoin College, 6600 College Station, Brunswick, ME 04011 and †Anti-Cancer Drug Laboratory, Kansas State University, Division of Biology, Ackert Hall, Manhattan, KS 66506-4901

A14 SOLUTION AND SOLID-STATE INVESTIGATION OF INTERMOLECULAR HYDROGEN BONDING IN IMIDAZOLE-4,5-DICARBOXYLIC ACID DERIVATIVES
Paul W. Baures†, Adam W. Caldwell†, Chris R. Cashman†, Marie T. Masse†, Ethan B. Van Arnam†, and Rebecca R. Conry‡
†Bowdoin College
Department of Chemistry, 6600 College Station, Brunswick, ME 04011
‡Colby College
Department of Chemistry, 5764 Mayflower Hill, Waterville, ME 04901

A15 NOVEL ACYL ANION DONORS UTILIZED FOR CYANIDE-CATALYZED BENZOIN TYPE REACTIONS.
Cory C. Bausch, Jeffrey S. Johnson
University of North Carolina-Chapel Hill
Department of Chemistry, Chapel Hill, North Carolina 27599

A16 BIOMIMETIC TOTAL SYNTHESIS OF SNF4435C AND SNF4435D
Christopher M. Beaudry and Dirk Trauner
University of California, Berkeley

A17 DESIGN, SYNTHESIS AND BIOLOGICAL EVALUATION OF MONOPYRROLINONE-BASED HIV-1 PROTEASE INHIBITORS POSSESSING AUGMENTED P2 SIDE-CHAINS
1. Jason J. Beiger, Adam K. Charnley, Hironori Harada, Louis-David Cantin, Craig S. Kenesky, Ralph Hirschmann, and Amos B. Smith, III
2. Sanjeev Munshi, David B. Olsen, Mark W. Stahlhut, William A. Schleif, and Lawrence C. Kuo
1. University of Pennsylvania, Department of Chemistry, Philadelphia, Pennsylvania 19104
2. Merck Research Laboratories, West Point, Pennsylvania 19486

A18 NICKEL CATALYZED CROSS-COUPLING OF CYCLIC ANHYDRIDES: MECHANISM, SCOPE, AND APPLICATION TO THE SYNTHESIS OF LIGNAN NATURAL PRODUCTS
Eric A. Bercot and Tomislav Rovis*
Colorado State University
Department of Chemistry, Fort Collins, CO 80523

A19 STEREOSELECTIVE SYNTHESIS OF *N*-PROTECTED PYRROLIDINES FROM γ-(*N*-BOC-AMINO)- OR γ-(*N*-ACYLAMINO)ALKENES
Myra Beaudoin Bertrand and John P. Wolfe*
University of Michigan
Department of Chemistry, 930 N. University Ave., Ann Arbor, MI, 48109-1055

A20 A NOVEL DIASTEREOSELECTIVE SYNTHESIS OF (*Z*)-1-CHLORO-1-TRIMETHYLGERMYL-1-ALKENES
Narayan G. Bhat* and Magaly Salinas
University of Texas-Pan American
Department of Chemistry, 1201 West University Drive, Edinburg, Texas

A21 A HIGHLY REGISELECTIVE SYNTHESIS OF *GEM*-DIMETALLOALKANES CONTAINING BORON AND GERMANIUM
Narayan G.Bhat*,Matthew B. Carroll and Wendy C. Lai
University of Texas-Pan American

Department of Chemistry, 1201 West University Drive, Edinburg, Texas

A22 L-ALLYSINE ETHYLENE ACETAL AS A VERSATILE CHIRAL BUILDING BLOCK FOR NATURAL PRODUCT SYNTHESIS

***Richard H. Blaauw*[1] *Marloes A. Wijdeven,*[1,2] *Peter N.M. Botman,*[1] *Quirinus B. Broxterman,*[3] *Hans E. Schoemaker*[3] *and Floris P.J.T. Rutjes*[2]**

1. Chiralix B.V., P.O. Box 31070, 6503 CB Nijmegen, The Netherlands.
2. Radboud University Nijmegen, Institute for Molecules and Materials, Toernooiveld 1, 6525 ED Nijmegen, The Netherlands.
3. DSM Research, Life Sciences – Advanced Synthesis, Catalysis and Development, P.O. Box 18, 6160 MD Geleen, The Netherlands

A23 THE SYNTHESIS OF PHTHALAZINONES, PYRIDAZINONES AND TRIAZINONES AS INSECTICIDE LEADS

Janice Black, Mike Turnbull
Jealotte Hill Research Centre
Syngenta, Jealotts Hill, Berkshire, UK

A24 PROBING THE STRUCTURAL BASIS FOR ANTI-TUBERCULOSIS AND ANTI-CANCER ACTIVITY IN AMAMISTATIN AND MYCOBACTIN ANALOGS

Brian S. Bodnar, Marvin J. Miller, Kelley A. Fennell, Garrett Moraski, Abraham Sheinkman, and Helen Zhu
University of Notre Dame
Department of Chemistry and Biochemistry, 251 Nieuwland Science Hall, Notre Dame, IN 46556

A25 SYNTHESIS OF POLYMERIC EXPANDED CARBOHELICENES

Margel C. Bonifacio and Benjamin T. King*
University of Nevada, Reno
Department of Chemistry/216, Reno, NV 89557

A26 "PROGRESS TOWARDS THE TOTAL SYNTHESIS OF OKILACTOMYCIN AND CHROLACTOMYCIN"

Todd Bosanac and Amos B. Smith, III
University of Pennsylvania
Department of Chemistry, Monell Chemical Senses Center, and Laboratory for Research on the Structure of Matter, Philadelphia, PA 19104-6323

A27 APPROACHES TOWARD THE TOTAL SYNTHESIS OF CITRINADIN A

Vyacheslav Boyarskikh and Jon D. Rainier*
Department of Chemistry, University of Utah
315 South 1400 East, Salt Lake City, Utah 84112

A28 SYNTHESIS OF TETRAHYDROBENZOCYCLOHEPTENONES POSSESSING AN OXAZOLIDINONE MOIETY. USEFUL TEMPLATES FOR THE SYNTHESIS OF OXAZOLIDINONE ANTIBACTERIAL AGENTS

[1]Frederick Boyer, [2]Louis Chupak, [1]Susan Hagen, [2]Wenhua Jiao [2]Takushi Kaneko, [2]Karina Romero [1]Jim Kramer, [1]J. V. N. Vara Prasad
1. Pfizer Global Research and Development, Michigan Laboratories, Ann Arbor, MI 48105;
2. Pfizer Global Research and Development, Groton Laboratories, Groton, Connecticut 06340

A29 OXYGEN NANOSENSOR WITH DENDRITIC PROTECTION AND TWO-PHOTON ABSORBING ANTENNA

Raymond P. Briñas, Thomas Troxler, Robin M. Hochstrasser and Sergei A. Vinogradov
University of Pennsylvania
Departments of Biochemistry and Biophysics and of Chemistry, Philadelphia, PA 19104

A30 RAPID SYNTHESIS OF COMPLEX ARYLETHYNYLENE-BUTADIYNE OLIGOMERS UTILIZING AN IN SITU ETHYNYLSILANE DEPROTECTION REACTION

Allen F. Brooks, Batoul S. Dagher, Jeffrey P. Guina, Anne E. Labut, and Matthew J. Mio*
University of Detroit Mercy
Department of Chemistry and Biochemistry, 4001 West McNichols Road, Detroit, MI 48221-3038

A31 ORGANIC CHEMISTRY BETWEEN INORGANIC LAYERS: SUPRAMOLECULAR CHIRALITY IN LAYERED MATERIALS

Ernesto Brunet, Olga Juanes, Hussein M. H. Alhendawi , Carlos Cerro,Mayte Aranda and Juan Carlos Rodríguez Ubis
Universidad Autónoma de Madrid
Department of Organic Chemistry, Faculty of Sciences C-I, Cantoblanco, 28049-Madrid, Spain

A32 TARGETING D609 TO PHOSPHATASE EXPRESSING CANCER CELL LINES

Adam Bryson, Patrick Meier
Washington State University
Department of Chemistry, Pullman, WA 99163

A33 IMINIUM SALT CATALYSTS FOR ASYMMETRIC EPOXIDATION: THE FIRST HIGH ENANTIOSELECTIVITIES, INCLUDING THE HIGHLY ENANTIOSELECTIVE SYNTHESIS OF LEVCROMAKALIM

Benjamin R. Buckley and Philip C. Bulman Page*
Loughborough University
Department of Chemistry, Loughborough, Leicestershire, LE11 3TU, England

A34 DIASTEREOSELECTIVE SYNTHESIS OF HEXAHYDROPYRROLO [1, 2-*A*]-QUINOLINES BY A TANDEM REDUCTION-DOUBLE REDUCTIVE AMINATION REACTION

Richard A. Bunce and James E. Schammerhorn
Oklahoma State University
Department of Chemistry, Stillwater, Oklahoma 74078-3071

A35 REGIOSPECIFIC GENERATION AND ALLYLATION OF NONSTABILIZED KETONE ENOLATES VIA A TRANSITION METAL-CATALYZED DECARBOXYLATIVE CLAISEN REARRANGEMENT

Erin C. Burger and Jon A. Tunge
University of Kansas
Department of Chemistry, 1251 Wescoe Hall Dr., Lawrence, KS 66045

A36 ACYLATED PHLOROGLUCINOL SYNTHETIC STUDIES

Joseph A. Burlison, David G. J. Young,* and Dongxiang Zeng
University of Tennessee
Department of Chemistry, 552 Buehler Hall, Knoxville, TN 37996-1600

A37 PARALLEL SYNTHESIS OF 2-AMINO-4-HETEROARYL PYRIMIDINES

Matthew G. Bursavich, Sabrina Lombardi, and Adam M. Gilbert
Wyeth Research
Exploratory Medicinal Chemistry, 401 North Middletown Road, Pearl River, NY

A38 RADICAL REACTIONS MEDIATED BY CYCLOBUTADIENEIRON TRICARBONYL

Jeffrey H. Byers*, Yong Zhang, Benjamin Zegarelli, Tina Dimitrova, Sumaya Huque, and Stephen F. Sontum
Middlebury College
Department of Chemistry and Biochemistry, Middlebury, VT 05753

A39 RACEMIC AND OPTICALLY ACTIVE 2-METHOXY-4-OXATETRADECANOIC ACIDS: NOVEL SYNTHETIC FATTY ACIDS WITH SELECTIVE ANTIFUNGAL PROPERTIES

***Néstor M. Carballeira*[1], Rosann O'Neill[1], Keykavous* Parang[2]**
1. University of Puerto Rico, Department of Chemistry, P.O. Box 23346, San Juan, Puerto Rico 00931-3346
2. University of Rhode Island, Department of Biomedical and Pharmaceutical Sciences, College of Pharmacy, Kingston

A40 DESIGN AND SYNTHESIS OF SYNTHETIC COFACTORS FOR IN VITRO SELECTION OF RNA-CLEAVING DNAZYME.

Dorn L. Carranza and Robert R. Kane
Baylor University
Department of Chemistry and Biochemistry

A41 HINDERANCE AS A TOOL IN THE ENANTIOSELECTIVE TOTAL SYNTHESIS OF *HOMO*-SPHINGOSINE FROM L-ASPARTIC ACID

Joel A. Castillo-Melendez*, *A. M. P. Koskinen*
Helsinki University of Technology
Laboratory of Organic Chemistry, FIN-02015 TKK, Finland

A42 APPROACH TO THE TOTAL SYNTHESIS OF MASSILEUNICELLIN-I

Yonghai Chai, Zonghong Mou, and Matthias McIntosh.
University of Arkansas
Department of Chemistry and Biochemistry, 205 Science Bldg, Fayetteville, AR 72701

A43 *C*-NITROSO COMPOUNDS AND THEIR CYCLOADDUCTS AS NO DONORS

***Harinath Chakrapani* and Eric J. Toone**
Duke University
Department of Chemistry, B120 Levine Science Research Center, Durham, NC 27708

A44 HOMOENOLATE/ACYLVINYL REAGENTS CATALYZED BY N-HETEROCYCLIC CARBENES

Audrey Chan, Brooks E. Maki, Karl A. Scheidt
Northwestern University
Department of Chemistry, 2145 Sheridan Road, Evanston, Illinois 60208

A45 STUDIES TOWARDS THE TOTAL SYNTHESIS OF HETEROSCYPHIC ACID A *VIA* OXIDATIVE RADICAL CYCLIZATION AND ORGANOIRON METHODOLOGY

***Subhabrata Chaudhury*, William A. Donaldson**
Marquette University
Department of Chemistry, P.O. Box 1881, Milwaukee, WI 53201-1881

A46 SYNTHESIS AND MOLECULAR RECOGNITION OF HYODEOXYCHOLIC ACID-UREA CONJUGATE

Nam-Ju Cho*, Ki-Soo Kim, Hong-Seok Kim
Kyungpook National University,
Department of Applied Chemistry, Daegu 702-701, Korea

A47 SYNTHESIS OF BROMINATED ARYL PHOSPHATES AS DUAL ACTION FLAME ETARDANTS FOR POLYMERIC MATERIALS

Young-Jun Cho and Bob A. Howell
Central Michigan University
Department of Chemistry, Center for Applications in Polymer Science, Mt. Pleasant, MI 48859-0001

A48 STILLE COUPLINGS OF STEREOCHEMICALLY DEFINED □-HETEROATOM-SUBSTITUTED BENZYLSTANNANES

***J. Michael Chong* and Kevin W. Kells**
University of Waterloo
Department of Chemistry, Waterloo, Ontario, Canada

A49 STERICALLY DIRECTED FUNCTIONALIZATION OF AROMATIC C-H BONDS: SELECTIVE BORYLATION *ORTHO* TO CYANO GROUPS IN ARENES AND HETEROCYCLES.

***Ghayoor A. Chotana*, Michal A. Rak, Milton R. Smith, III**
Michigan State University
Department of Chemistry, East Lansing, MI 48824

A50 SHORT OLIGOPEPTIDES LINKED TO NUCLEOPHILIC CATALYSTS AFFORD STEREOSELECTIVE ACYLATION OF SECONDARY ALCOHOLS

Tammy Chu*, Cristina Clause, Clark Santee, Nance Yuan and Ahamindra Jain
University of California, Berkeley
325 Latimer Hall, Berkeley, CA 94720-1460

A51 FLUORESCENCE SENSING OF ANIONS THROUGH H-BONDING STABILIZATION OF ANION-RECEPTOR ADDUCTS

Yun Mi Chung, Kyo Han Ahn*
Pohang University of Science and Technology
Department of Chemistry and Center for Integrated Molecular Systems, Division of Molecular and Life Science, San 31, Hyoja-dong, Pohang 790-784, Republic of Korea

A52 ENANTIOMORPHOUS TWIN DOMAINS REVEALED BY CIRCULAR DICHROISM IMAGING MICROSCOPY

Kacey Claborn, Eileen Puklin-Faucher, Miki Kurimoto, Werner Kaminsky, and Bart Kahr
University of Washington
Department of Chemistry, Box 351700, Seattle, WA 98195

A53 TANDEM INTRAMOLECULAR NICHOLAS AND PAUSON-KHAND REACTIONS FOR THE SYNTHESIS OF TRICYCLIC HETEROCYCLES

Kristina D. Closser, Miriam M. Quintal, Kevin M. Shea
Smith College
Clark Science Center, Northampton, MA 01063

A54 SYNTHESIS OF HELIANNUOL ANALOGUES

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A55 FIRST TOTAL SYNTHESIS OF AERVINE: A GENERAL APPROACH TO METHOXY SUBSTITUTED CANTHIN-6-ONES

Patrick M. Cobb, Steven Mennen, Brian Zick, and Kevin M. Czerwinski
University of Wisconsin-Stevens Point
Department of Chemistry, Stevens Point WI 54481

A56 THE MECHANISM OF THE PHOTOINDUCED ACYLATION OF AMINES BY *N*-ACYL-5, 7-DINITROINDOLINE AS DETERMINED BY TIME-RESOLVED INFRARED SPECTROSCOPY

Andrew D. Cohen[†], Celina Helgen[‡], Christian G. Bochet[‡], John P. Toscano[†]
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[‡]Department of Chemistry, University of Fribourg, CH-1700 Fribourg, Switzerland

A57 PROGRESS TOWARDS PHOMACTIN A

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University of Minnesota
207 Pleasant St. SE, Minneapolis MN, 55455

A58 Process Development and Synthesis of the β-1, 3-Glucan Synthase Inhibitor Cancidas®

David A. Conlon, Kevin Belyk, William R. Leonard, Jr., Ji Liu, Dean Bender and David L. Hughes
Merck Research Laboratories
Department of Process Research, P. O. Box 2000 Rahway, New Jersey 07065

A59 MECHANISTIC INSIGHT INTO WACKER-TYPE OXIDATIONS UTILIZING PD (IIPR) (OTS) 2 AND *TERT*-BUTYLHYDROPEROXIDE

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A60 TOWARD A FUNCTIONALIZED HELICENE

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University of Nevada, Reno
Department of Chemistry/216, Reno, NV 89557

A61 DYNAMIC KINETIC RESOLUTION OF ZIRCONAAZIRIDINES
Sarah A. Cummings, Jon A. Tunge, and Jack R. Norton*
Columbia University
Department of Chemistry, 3000 Broadway, New York, NY 10027

A62 SYNTHESIS OF *CIS*-1, 3-DIAMINOCYCLOPENTANE AND CYCLOPENTENE 5-HT$_7$ RECEPTOR LIGANDS
N. R. Curtis, S. Hartmann, P. A. Hunt, C. G. Thomson, E. J. Armstrong, M. S. Beer, A. Heald, R. Newman, J. A. Stanton, G. McAllister and J. J. Kulagowski
The Neuroscience Research Centre
Merck Sharp & Dohme Research Laboratories, Terlings Park, Harlow, Essex, CM20 2QR, U.K.

A63 SYNTHESIS OF FUSED TRIAZOLO IMIDAZOLE DERIVATIVES BY SEQUENTIAL VAN LEUSEN/ALKYNE-AZIDE CYCLOADDITION REACTIONS.
Daria Darczak, Alan F Gasiecki, Vijaya Gracias and Stevan W. Djuric
Abbott Laboratories
Scaffold-Oriented Synthesis, Medicinal Chemistry Technologies, Dept R4CP, AP10-1, 100 Abbott Park Road, Abbott Park, IL 60064-6099

A64 INDOLE-DITERPENOID SYNTHETIC STUDIES. PROGRESS TOWARDS THE TOTAL SYNTHESIS OF (–)-NODULISPORIC ACID D AND (+)-NODULISPORIC ACID F.
Akin H. Davulcu, Laszlo Kurti, Amos B. Smith, III*
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Department of Chemistry, Monell Chemical Senses Center and Laboratory for Research on the Structure of Matter, Philadelphia, PA, 19104

A65 AN ITERATIVE PATHWAY TO SUBSTITUTED OLIGOACENES VIA NICKEL-ARYNES AND 1, 3-DIYNES
Kimberly R. Deaton and Mary S. Gin
University of Illinois
Champaign-Urbana 600 S. Matthews Ave., Roger Adams Lab, Box 72-5, Urbana, IL 61801

A66 PD-CATALYZED DIRECTED OXIDATION OF C-H BONDS
Lopa V. Desai, Kami L. Hull, Melanie S. Sanford
University of Michigan
930 N. University, Ann Arbor, MI 48103

A67 MECHANISTIC INVESTIGATIONS INTO PD-CATALYZED C-H ACTIVATION/OXIDATION REACTIONS
Allison R. Dick, Melanie S. Sanford
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A68 PROCESS RESEARCH AND DEVELOPMENT TOWARDS A SELECTIVE AND PARTIAL GABA RECEPTOR INVERSE AGONIST
Nga M. Do, Stephané Caron, Ruth E. McDermott
Pfizer Inc.
PGRD Groton Laboratories, Groton, CT 06340

A69 THE FIRST DESYMMETRISATION OF A CENTROSYMMETRIC MOLECULE BY AN ENANTIOSELECTIVE C-C BOND FORMATION.
Karen Dodd, Dr Adam Nelson, (Dr Robert Narquizian, Roche)
University of Leeds

A70 APPLICATIONS OF RING-CLOSING METATHESIS TO THE SYNTHESIS OF SUBSTITUTED QUINOLIN-2(1H)-ONES
Claude Dufresne, Joannie Minville and Claudio Sturino
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A71 NICKEL-CATALYZED CYCLOADDITION OF ALKYNES AND ISOCYANATES

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A72 SYNTHESIS OF HETEROCYCLIC QUINONES THROUGH BASE CATALYZED REARRANGEMENT OF 2-ACYLAMINO-3-AZIDO-1, 4-NAPHTHAQUINONES

Abdel Moneim El-Ghanam
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Faculty of Science, Chemistry Department, Ibrahimia, P.O. Box 426, Alexanderia, Egypt

A73 HIGHLY PRODUCTIVE ROUTE TO A (Z)-2, 3-BIARYL-4-HYDROXYBUT-ENOIC ESTER VIA A NOVEL GRIGNARD CARBOMETALATION FOLLOWED BY SEQUENTIAL IN SITU TRAP WITH CO_2 AND ACETIC ANHYDRIDE

F. Conrad Engelhardt, Yao-Jun Shi, Cameron J. Cowden, David A. Conlon, Brenda Pipik, George Zhou, James M. McNamara, and Ulf-H. Dolling
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A74 NUCLEIC ACID MOLECULAR BEACONS BASED ON G-SUBSTITUTED PNA

Ethan Englund, Daniel Appella
National Institutes of Health
Laboratory of Bioorganic Chemistry, NIDDK, DHHS, 9000 Rockville Pike, Bldg. 8 Rm. 1A 23, Bethesda, MD 20892

A75 THE PURSUIT OF OPTICALLY ACTIVE CI-1041 (PD 0205881)

Margaret C. Evans, Jeffrey Kallemeyn, Duane VandenBrink, Justin Weaver, Marvin Hoekstra, Denis Sobieray
Pfizer PGRG,
Holland Chemical Research and Development

A76 TOWARDS THE SYNTHESIS OF THE MARINE NATURAL PRODUCT, IISOCYANOADOCIANE

Kelly Ann Fairweather and Lewis N. Mander
Australian National University
Research School of Chemistry, Canberra, ACT 0200

A77 BESTATIN DERIVATIVES AS POTENTIAL SMALL-MOLECULE INHIBITORS OF BACTERIAL METHIONINE AMINOPEPTIDASE

Neil T. Fairweather, Jane F. Djung, Shari J. Soper, Jack S. Amburgey, William L. Seibel, Alan W. Curnow, Jeremy M. Howard, Artem Evdokimov, and Matthew Pokross
Procter and Gamble Pharmaceuticals
8700 Mason Montgomery Road, Mason, Ohio 45040

A78 SYNTHESIS OF A WELL-DEFINED PAMAM DENDRIMER-PLATINUM DRUG CONJUGATE

Daming Fan and Bob Howell
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Center for Applications in Polymer Science, Mt. Pleasant, MI 48859-0001

A79 TOWARDS A POLYETHYLENE KNOT

Edward E. Fenlon and Shin Lin Goh
Franklin & Marshall College
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A80 SYNTHESIS AND STUDY OF AMAMISTATIN B AND ANALOGS AS POTENTIAL ANTI-CANCER AND ANTI-TUBERCULOSIS AGENTS

Kelley A. Fennell and Marvin J. Miller
University of Notre Dame
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A81 BENZOTHIAZOLE-BASED HISTAMINE H_3 RECEPTOR ANTAGONISTS: SYNTHETIC STUDIES AND DISCOVERY OF POTENT BINDING PROPERTIES

***D. Fernando**[1], **S. Chang**[1], **Y. Ku**[1], **A. Bhatia**[1], **M. Cowart**[2], **T. Esbenshade**[2], **A. Hancock**[2]
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2. Dept. of Neuroscience Research

A82 SYNTHESIS OF SYMMETRICALLY π-EXTENDED PORPHYRINS *VIA* OXIDATIVE AROMATIZATION

***Olga S. Finikova,**[1] **Andrei V. Cheprakov**[2] **and Sergei A. Vinogradov**[1]
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2. Department of Chemistry, Moscow State University, 119899 Moscow, Russia

A83 UNIQUE FRAGMENTATION OF PENTAFLUORBENZYLIC ALCOHOLS: A DEMONSTRATION OF $C_6F_5^-$ AS A GOOD LEAVING GROUP

Henry C. Fisher** **and Charles M. Garner
Baylor University
Department of Chemistry & Biochemistry, One Bear Place Box #97348, Waco, TX 76798-7348

A84 PREPARATION OF 1-(2-[2-ISOXAOL-3-YLBENZOFURAN-5-YLOXY]ETHYLAMINO)-3-PHENOXY-2(S)-OL

Darrell E. Fox**, **Keith DeVries, William M. Snyder, Sara Reynolds and Harry Watson
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Pfizer Inc, Groton, CT 06340, MS 8118D-4015, Pfizer, Inc, Eastern Point Road, Groton, CT 06340

A85 THE EFFECTS OF CHIRAL AND ACHIRAL PROMOTERS ON DIASTEREOSELECTIVITIES IN INTRAMOLECULAR PAUSON-KHAND REACTIONS

Amanda K. Freeman**, **Kristina D. Closser, Miriam M. Quintal, Kevin M. Shea
Smith College
Clark Science Center, Northampton, MA 01063

A86 SYNTHESIS OF NOVEL (LYSO)PHOSPHATIDIC ACID ANALOGS AS LPP INHIBITORS.

***Joanna Gajewiak**,[1] **Glenn D. Prestwich**[1], **Andrew J. Morris**[2]
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A87 A NEW SYNTHESIS OF N1 SUBSTITUTED CYTOSINE ANALOGUES

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A88 RECYCLING OF HOMOGENOUS CATALYSTS USING MAGNETIC NANOPARTICLES AS SOLUBLE SUPPORTS

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Southern Illinois University
Department of Chemistry and Biochemistry, Carbondale, IL 62901-4409

A89 SYNTHESIS OF GPR40 AGONISTS

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GlaxoSmithKline
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A90 ENANTIOSELECTIVE INTRAMOLECULAR FORMAL *AZA*-[3 + 3] CYCLOADDITION REACTION

Aleksey I. Gerasyuto**, **Richard Hsung, and Nadiya Sydorenko
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A91 SYNTHESIS AND SAR OF NEW BENZOFURAN HISTAMINE-3 RECEPTOR ANTAGONISTS
Gregory A. Gfesser, Ramin Faghih, Youssef L. Bennani, Michael P. Curtis, Timothy A. Esbenshade, Arthur A. Hancock, Marlon D. Cowart
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Neuroscience Research, Global Pharmaceutical Research and Development, 100 Abbott Park Road, Abbott Park, IL 60064

A92 DIRECT ARYLATION OF π-DEFICIENT AZINES VIA C-H BOND ACTIVATION CATALYZED BY RUTHENIUM COMPLEXES
Kamil Godula and Dalibor Sames
Columbia University in the City of New York
Department of Chemistry, 3000 Broadway MC 3133, New York, NY 10027

A93 ACTIVATION OF NKT CELLS BY ENDOGENOUS AND EXOGENOUS GLYCOSPHINGOLIPIDS DURING INFECTION
Randal D. Goff, Jochen Mattner, Carlos Cantu III, Dapeng Zhou, Ying Gao, Luc Teyton, Albert Bendelac, Paul B. Savage
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Dept. of Chemistry and Biochemistry, Provo, UT 84602

A94 DISCOVERY OF A HELIX-THREADING PEPTIDE INHIBITOR OF THE PROKARYOTIC S15—16S RRNA COMPLEX
Barry D. Gooch and Peter A. Beal
University of Utah
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A95 THE DEVELOPMENT OF CASPASE INHIBITORS: TOOLS TO STUDY NEURODEGENERATIVE DISEASE
David R. Goode, Anil K. Sharma, Paul J. Hergenrother
University of Illinois-Urbana/Champaign
CLSL Box 35-6, 600 S. Matthews, Urbana, IL 61802

A96 A RADICAL CASCADE APPROACH TO THE TOTAL SYNTHESIS OF LYCONADIN A
Seth W. Grant, Koudi Zhu, Steven L. Castle
Brigham Young University
Department of Chemistry and Biochemistry, C100 BNSN, Provo, Utah 84602

A97 A HIGHLY EFFICIENT CATALYTIC OPPENAUER REACTION SYSTEM FOR ALCOHOL OXIDATION
Christopher R. Graves, Bi-Shun Zeng, and SonBinh T. Nguyen
Northwestern University
Department of Chemistry and Institute for Environmental Catalysis, 2145 Sheridan Road, Evanston, IL 60208-3113

A98 SOLUTION PHASE PARALLEL SYNTHESIS OF 2-ALKYL/ARYL-4-AMINOBENZIMIDAZOLES
Daniel M. Green, John Rogers and Jeffrey C. Pelletier
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Chemical and Screening Sciences, 500 Arcola Road, Collegeville, PA 19426

A99 SYNTHESIS OF HETEROAROMATIC AMIDE ISOSTERES AS NK-1 ANTAGONISTS.
Steven J. Green; Albert Amegadzie; Jessie L. Bishop; Jeffrey D. Cohen; Jeffrey W. Cramer; Kevin Gardinier; Donald R. Gehlert; Erik J. Hembre; Jian Eric Hong; Smriti Iyengar; Louis N. Jungheim; Dominic L. Li; Michael A. Robertson; Kenneth A. Savin; Daniel G. Smith
Eli Lilly and Company
Lilly Research Laboratories, Lilly Corporate Center, Indianapolis, IN 46285

A100 EFFICIENT CYCLIZATION OF 1-BROMO-2, 7- AND 1-BROMO-2, 8-ENYNES MEDIATED BY INDIUM
Phil Ho Lee, Sundae Kim, and Jun Hwan Shim
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Department of Chemistry, Chunchon 200-701, Republic of Korea

A101 EFFICIENT SYNTHESIS OF BICYCLO [6.4.0] DODECANES VIA INTERMOLECULAR TANDEM CROSS-COUPLING/ [4+4] AND [4+2] CYCLOADDITIONS MEDIATED BY PD-IN

Phil Ho Lee, *Kooyeon Lee, and Jun Hwan Shim*
Kangwon National University
Department of Chemistry, Chunchon 200-701, Republic of Korea

A102 SYNTHESIS OF ARYLAMIDE DENDRIMERS WITH FLEXIBLE LINKERS *VIA* FISCHER'S HALOACYL HALIDE METHOD

Sergei A. Vinogradov and Michael E. Yurchenko
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Department of Biochemistry and Biophysics, Philadelphia, PA 19104

A103 AN ENANTIOSELECTIVE PREPARATION OF RING FUSED 1-FLUOROCYCLOPROPANE-1-CARBOXYLATE DERIVATIVES: *EN ROUTE* TO AN MGLUR 2 RECEPTOR AGONIST MGS0028

Fei Zhang*, Zhiguo J. Song, Dave Tschaen and R. P. Volante
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A104 CHEMICALLY MODIFIED OPALS AS THIN PERMSELECTIVE NANOPOROUS MEMBRANES

Andrew K. Bohaty, Michael Newton, Henry S. White, Ilya Zharov
University of Utah
Department of Chemistry, Salt Lake City, UT, 84112

A105 SHAPE-PERSISTENT PYRAZINE-CONTAINING MOLECULES FOR NANOSCALE ASSEMBLY

Julie Cichelli, Olga Schepelina, and Ilya Zharov
University of Utah
Department of Chemistry, 315 S. 1400 E., Salt Lake City, UT 84112

A106 *POLYANIONIC DENDRON AGENTS FOR CANCER IMAGING AND THERAPY*

Kristin Galie, Alexis Mollard, and Ilya Zharov
University of Utah
Department of Chemistry, 315 S. 1400 E., Salt Lake City, UT 84112

Schedule of Presenters – Poster Session B Monday, June 13, 2005

B1 COBALARUBICIN: A NEW CYTOTOXIC VITAMIN B12 DRUG THAT IS EFFECTIVE AGAINST BREAST CANCER IN MICE

Charles B. Grissom,[1] Alanna L. Eilers,[3] Weiping Li,[3] Xiaohui Liu,[3] Ned M. Weinshenker,[3] and Frederick G. West[2]
1. University of Utah, Department of Chemistry, 315 S. 1400 E., Salt Lake City, UT 84112-0850
2. University of Alberta, Department of Chemistry, W5-67 Chemistry Centre, Edmonton, Alberta T6G 2G2, Canada
3. MantiCore Pharmaceuticals Inc., 2401 S. Foothill Blvd., Salt Lake City, UT 84109

B2 INTRACELLULAR SINGLE MOLECULE ANALYSIS OF RECEPTOR-MEDIATED ENDOCYTOSIS OF FLUORESCENT COBALAMIN

Charles B. Grissom, Robert A. Horton, Karla S. McCain, and Joel M. Harris
University of Utah
Department of Chemistry, 315 S. 1400 E., Salt Lake City, UT 84112-0850

B3 PREPARATION OF A FLUORESCENT CYCLOSPORINE CONJUGATE

Jonathan Grote, Jeffrey Fishpaugh, and Sushil Rege
Abbott Laboratories
Core R & D Life Science Chemistry Department, Abbott Diagnostic Division, 100 Abbott Park Rd. Abbott Park, IL 60064-6016

B4 STUDIES TOWARDS THE ASYMMETRIC TOTAL SYNTHESIS OF THE MITOMYCINS

Daniel A. Gubler and Robert M. Williams
Colorado State University
Department of Chemistry, Fort Collins, CO 80523

B5 ADVANCED UNIVERSAL SOLID SUPPORTS FOR OLIGONUCLEOTIDE SYNTHESIS

A. P. Guzaev
AM Chemicals LLC
4065 Oceanside Blvd. Suite M, Oceanside, CA 92056

B6 PROGRESS TOWARD THE SYNTHESIS OF (-)-TETRANORLABDANE OXIDE FROM ABIETIC ACID

Christian Hamann, Ryan Lutz, Robert Rapp, and Gary Willman
Albright College
Department of Chemistry & Biochemistry, 13th & Bern Streets Reading, PA 19612

B7 CONTINUOUS ORGANIC SYNTHESIS IN A SPINNING TUBE-IN-A TUBE™ (STT™) REACTOR: TEMPO-CATALYZED OXIDATION OF ALCOHOLS BY HYPOCHLORITE

Philip D. Hampton,* Lisa M. Heath,‡ Rick Boydson‡
* Department of Chemistry, California State University Channel Islands, Camarillo CA.
‡ Kreido Laboratories, Camarillo, One University Drive, California State University Channel Islands, Camarillo, CA 93012

B8 SYNTHESIS AND EPR STUDY OF ETHYL CARBONATE/SPIN LABEL FUNCTIONALIZED PAMAM DENDRIMERS

Hye Jung Han and Mary J. Cloninger*
Montana State University
Department of Chemistry and Biochemistry and Center for Bioinspired Nanomaterials, 108 Gaines Hall, Bozeman, MT 59717

B9 RUTHENIUM-CATALYZED ALDER ENE REACTION OF BORYLATED ALKYNES: TOTAL SYNTHESIS OF DACTYLOLIDE AND ZAMPANOLIDE

Eric C. Hansen, Daesung Lee
University of Wisconsin-Madison
1101 University Ave. Madison, WI 53706

B10 SYNTHESIS OF THE DPP-IV INHIBITOR MK-0431

Karl Hansen, Jaume Balsells, Spencer Dreher, Yi Hsiao, Norihiro Ikemoto, Michele Kubryk, Jinchu Liu, Eugenia Njolito, Michael Palucki, Nelo Rivera, Dietrich Steinhuebel, Joseph D. Armstrong III, David Askin and Edward J. J. Grabowski
Merck Research Laboratories
Department Process Research, Rahway, New Jersey 07065

B11 STUDIES DIRECTED TOWARDS THE ASSEMBLY OF THE BINARY VINCA ALKALOIDS: A STRATEGY FOR THE SYNTHESIS OF (+)-VINBLASTINE

Michael J. Harvey and Martin G. Banwell
Australian National University
Research School of Chemistry, Institute of Advanced Studies, A.C.T. 0200, Australia

B12 SYNTHETIC HIGH-AFFINITY CARBOHYDRATE LIGANDS FOR SHIGA TOXIN

Duane M. Hatch and Suri S. Iyer
University of Cincinnati
Department of Chemistry, Cincinnati, OH -45221

B13 A STEREOSELECTIVE RADICAL STRATEGY LEADING TO β- SUBSTITUTED α- AMINO ACIDS.

Liwen He; Steven L. Castle
Brigham Young University
Department of Chemistry and Biochemistry, Provo, UT 84602

B14 FOLDING-PROMOTED REACTIVITY AND TUNABLE STRUCTURE OF PYRIDINE-CONTAINING *M*-PHENYLENE ETHYNYLENE HELICAL CAVITANDS

Jennifer M. Heemstra and Jeffrey S. Moore
University of Illinois at Urbana-Champaign
Departments of Chemistry and Materials Science & Engineering, 600 South Mathews Avenue, Urbana, IL 61801

B15 CAN β-HYDROXYOLEFIN CLEAVAGE BE CATALYZED BY LEWIS ACIDS?
Amanda L. Henry,‡ James R. Vyvyan,*,‡ and Steven H. Dillman†
Western Washington University
Department of Chemistry‡ and Department of Engineering Technology†, 516 High Street, Bellingham, WA 98255

B16 PROGRESS TOWARD FLUOROUS SOLUBLE CROWN ETHERS FROM A NATURAL PRODUCT
Jessica R. Herron and Martin J. Campbell
Henderson State University
Department of Chemistry, Box 7633, Arkadelphia, AR 71999

B17 THEORETICAL AND SYNTHETIC INVESTIGATION OF 2-PYRROLINES VIA 1,5-DIPOLAR ELECTROCYCLIZATIONS
Amber M. Hibberd, Jess L. Burleson, Derrek N. Woodbury and Don L. Warner
Boise State University
Department of Chemistry, 1910 University Dr., Boise, ID 83725-1520

B18 TAILORING ANALGESIA
Anne-Cécile Hiebel (1), Gabriella De Martino (1), Richard B. Rothman (2), Christina M. Dersch (2), Jeffrey Deschamps (3), Arthur E. Jacobson (1), Kenner C. Rice (1)
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2. Clinical Psychopharmacology Section, NIDA, Addiction Research Center, Baltimore, MD 21224
3. Laboratory for the Structure of Matter, Naval Research Laboratory, Washington, D.C. 20375

B19 SYNTHESIS OF C_1/C_3-SUBSTITUTED CYCLOALKYL [*b*] INDOLES
M. C. Hillier; J. –F. Marcoux; D. Zhao; E. J. J. Grabowski; R. D. Tillyer
Merck & Co.
Department of Process Research, Merck & Co., PO Box 2000, Rahway, NJ 07065

B20 A NEW SERIES OF ORGANOZIRCONIUM COMPOUNDS
Cameron L. Hilton and Benjamin T. King*
University of Nevada, Reno
Department of Chemistry, 216, Reno, NV 89557

B21 $BIBR_3$ INITIATED CYCLIZATION-ADDITION REACTIONS: TOTAL SYNTHESIS OF (+)-(*S, S*)-(*CIS*-6-METHYLTETRAHYDROPYRAN-YL) ACETIC ACID, ITS *TRANS*-DIASTEREOMER AND EFFECT OF NUCLEOPHILE ON OXOCARBENIUM ION ADDITIONS
Robert J. Hinkle, Yajing Lian, Nichole D. Litvinas, Alex T. Jenkins, Daniel C. Burnette
The College of William and Mary
Department of Chemistry, P. O. Box 8795, Williamsburg, VA 23187-8795

B22 A NEW SYNTHESIS OF COUMARINS, 4-HYDROXY-2-NAPHTHOIC ACIDS AND BENZYLIDENESUCCINIMIDES USING BAYLIS-HILLMAN REACTION
Wan Pyo Hong, Young Seok Song and Kee-Jung Lee*
Hanyang University
Department of Chemical Engineering, Seoul 133-791, Korea

B23 REGIOCONTROLLED, PALLADIUM-CATALYZED BISFUNCTIONALIZATION OF ALLENYL ESTERS. MULTI-COMPONENT COUPLING APPROACHES TO HIGHLY SUBSTITUTED α,β-UNSATURATED δ-LACTONES
Chad D. Hopkins, Lisa Guan and Helena C. Malinakova
University of Kansas

B24 POLY(STYRENE) CONTAINING NO HEAD-TO-HEAD UNITS
Bob A. Howell and Khaekhai Chaiwong
Central Michigan University
Center for Applications in Polymer Science, Mt. Pleasant, MI 48859-0001

B25 SYNTHESIS OF NOVEL ANALOGUES OF ANTIMYCIN A_3
Zilun Hu, Xiang-Jun Jiang and We Han*
Bristol-Myers Squibb Pharmaceutical Research Institute
Department of Discovery Chemistry, P.O. Box 5400, Princeton, NJ 08543

B26 A NEW ASYMMETRIC SYNTHESIS OF PYRROLIDINOINDOLINES. APPLICATION FOR THE PRACTICAL TOTAL SYNTHESIS OF (–)-PHENSERINE

Audris Huang, Jeremy J. Kodanko, and Larry E. Overman
University of California at Irvine
Department of Chemistry, 516 Rowland Hall, Irvine, CA 92697–2025

B27 IDENTIFICATION, SYNTHESIS, AND MECHANISTIC STUDY OF FORMATION OF DEGRADANTS OF GARENOXACIN, A QUINOLONE ANTIBIOTIC

Yande Huang[1], Venkatapuram Palaniswamy[1], Stephan Taylor[1], Joel Young[1], Xin Bu[1], Frank Rinaldi[1], Richard Gedamke[1], Nona Khaselev[1], Hiroyuki Yamamoto[2]
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2. Toyama Chemical Co. Ltd., Research Laboratories, 4-1, Shimo-okui 2-chome, Toyama 930-8508, Japan

B28 PYRIDINE DIRECTING GROUPS FOR SELECTIVE SP^3 C-H ACTIVATION AND OXIDATION

Kami L. Hull, Lopa V. Desai, Melanie S. Sanford
The University of Michigan
930 N. University, Ann Arbor, MI 48109

B29 A UNIDIRECTIONAL CROSSLINKING STRATEGY FOR HIV-1 PROTEASE DIMERIZATION INHIBITORS

You Seok Hwang and Jean Chmielewski
Purdue University
Department of Chemistry, 560 Oval Dr. West Lafayette, IN 47907

B30 SYNTHETIC STUDIES TOWARD PLEUROTIN

Shinya Iimura, Sonia Rodríguez, and Peter Wipf
University of Pittsburgh
219 Parkman Ave., Chevron Science Center, Pittsburgh, PA 15260

B31 EFFORTS TOWARDS THE TOTAL SYNTHESIS OF PSYMBERIN

Karthik Iyer and Jon D. Rainier*
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Department of Chemistry, Salt Lake City, Utah – 84112

B32 AUXILIARY MEDIATED SYNTHESIS OF SMALL CYCLIC PEPTIDES

T. P. Jansen, H. Bieräugel, J. van Maarseveen, H. Schoemaker, H. Hiemstra
Van't Hoff Institute for Molecular Science
UvA, Nieuwe Achtergracht 129, 1018 WS Amsterdam, the Netherlands

B33 COMBINED TETHERED/TEMPLATED CYCLIZATIONS TOWARDS SMALL CYCLIC PEPTIDES

T. Paul Jansen,[1] Jasper Springer,[1] Hans Bieräugel,[1] Hans E. Schoemaker,[2] Henk Hiemstra[1] and Jan H. van Maarseveen[1]
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B34 RADICAL AROMATIC SUBSTITUTION REACTIONS ON ARENE-CHROMIUM TRICARBONYLS

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B35 POLYYNES: POLYHEDRANES, POLYMERIZATION, AND PI-CONJUGATION

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B36 ASYMMETRIC ALKENYL ZIRCONOCENE/ZINC ADDITIONS TO ALDEHYDES

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B37 FULLERENE-COATED DENDRIMERS
***Anton W. Jensen*,* Brijesh S. Maru, Kalpesh Gala, and Xi Zhang**
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B38 BRASSININ OXIDASE, A PHYTOALEXIN DETOXIFYING ENZYME PRODUCED BY THE PHYTOPATHOGENIC FUNGUS *LEPTOSPHAERIA MACULANS*: INDUCTION, PARTIAL PURIFICATION, AND SUBSTRATE SPECIFICITY
Mukund Jha*, Okeola O. G., and M. Soledade C. Pedras
University of Saskatchewan
Department of Chemistry, 110 Science Place, Saskatoon SK S7N 5C9, Canada

B39 DETOXIFICATION PATHWAYS OF THE CRUCIFEROUS PHYTOALEXIN BRASSININ: SYNTHESES, METABOLISM AND BIOLOGICAL EVALUATION OF METABOLIC PROBES
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B40 ENANTIOSELECTIVE DIRECT INTERMOLECULAR ALDOL REACTIONS WITH ENANTIOTOPIC GROUP SELECTIVITY AND DYNAMIC KINETIC RESOLUTION. APPLICATION TO THE SYNTHESIS OF (-)-SERRICORNIN
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B41 CONCISE SYNTHESIS OF ALKYL ANALOGUES OF LYSOBISPHOSPHATIDIC ACIDS
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B42 CL-PIQ: A SECOND-GENERATION ASYMMETRIC ACYLATION CATALYST
Hui Jiang* and Vladimir B. Birman
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B43 THE FIRST KINETIC RESOLUTION OF RACEMIC OXAZOLIDINONES VIA CATALYTIC, ENANTIOSELECTIVE N-ACYLATION
Hui Jiang*, Eric W. Uffman and Vladimir B. Birman
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B44 SYNTHETIC STUDIES OF CARBOCYCLIC SINEFUNGIN
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B45 RING-CLOSING METATHESIS APPROACH TO *S*-HETEROCYCLES
***María Jiménez* and Paul R. Hanson**
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B46 STUDIES TOWARD AN ASYMMETRIC TOTAL SYNTHESIS OF QUININE
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B47 A HIGHLY STEREOSELECTIVE SYNTHESIS OF C5 DERIVATIVES OF 3-ALKYL-7-CHLORO-5-TRIFLUOROMETHYLBENZO-1, 4-DIAZAPIN-2-ONES ACHIEVED THROUGH CHIRAL INDUCTION BY ENLISTING A CHIRAL C3 SUBSTITUENT
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B48 EFFORTS TOWARDS THE SYNTHESIS OF BREVENAL: SYNTHESIS OF THE C-E RINGS
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B49 THE TOTAL SYNTHESIS OF GAMBIEROL
Henry W. B. Johnson, Utpal Majumder, Jason M. Cox, Jon D. Rainier*
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B50 DETERMINATION OF THE ACTIVE CATALYTIC SPECIES DURING ALDEHYDE HYDROGENATION VIA *IN SITU* IR SPECTROSCOPY AND REACTION MODELING
Jeffrey B. Johnson, Charles P. Casey
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B51 NEW CHEMISTRY FOR OXYGEN-INDEPENDENT PHOTODYNAMIC THERAPY STRATEGIES
Paul B. Jones, Robert G. Brinson and Sarah L. Leonard
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B52 PHOTOINDUCED ENERGY TRANSFER IN SACOGLOSSAN POLYPROPIONATES
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B53 PROGRESS TOWARDS THE TOTAL SYNTHESES OF THE NATURAL PRODUCTS ACUTUMINE AND HASUBANONINE
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B54 C-H ACTIVATION/OXIDATION OF AROMATIC C-H BONDS
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B55 PHOTOCHEMICAL GENERATION OF REACTIVE ENEDIYNES. SYNTHESIS AND PHOTOCHEMISTRY OF CYCLIC ENEDIYNES INCORPORATING 2-DIAZO-1, 3-DICARBONYL MOIETY.
Grigori V. Karpov, Vladimir V. Popik
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B56 DOUBLE CUVET-ISES: *IN SITU* ESTIMATION OF ENANTIOSELECTIVITY AND RELATIVE RATE FOR CATALYST SCREENING
Kannan R. Karukurichi, Sangeeta Dey, Weijun Shen and David B. Berkowitz
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B57 SYNTHESIS OF NOVEL VINBLASTINE LIKE LIBRARIES
Mira Kaselj, Yuko Isome, Zhimin Wang, Demosthenes Fokas, Ji-Feng Liu, Daniel Yohannes and Carmen M. Baldino
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B58 DIASTEREOSELECTIVE REDUCTIONS OF A-CHIRAL A-ALKOXY TOSYL HYDRAZONES
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B59 STUDIES TOWARD THE SYNTHESIS OF THE NATURAL PRODUCT RADERMACHOL

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B60 MULTICOMPONENT LINCHPIN COUPLING OF SILYL DITHIANES EMPLOYING AN *N*-TS AZIRIDINE AS THE SECOND ELECTROPHILE: APPLICATION TO THE SYNTHESIS OF ALKALOIDS

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B61 TRIFLUOROACETOPHENONE-BASED COLORIMETRIC SENSORS FOR SELECTIVE VISUALIZATION OF CYANIDE ION

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B62 INTRAMOLECULAR HYDROAMINATIONS OF AMINOALKENES AND AMINOALKYNES CATALYZED BY BIS (THIOPHOSPHINIC AMIDATE) ZR (IV) COMPLEX

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[‡]Department of Chemistry, Montana State University, Bozeman, MT 59717

B63 CATALYTIC ASYMMETRIC METHALLYLATION OF KETONES WITH AN (H_8-BINOLATE)TI-BASED CATALYST

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B64 *IN SITU* ORGANOZINC REAGENTS GENERATION FROM ALKYL BROMIDES & ITS CATALYTIC ASYMMETRIC ADDITIONS TO ALDEHYDES

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B65 SYNTHETIC STUDY OF (-)-CASSINE VIA ASYMMERTIC AMINOHYDROXYLATION AND REDUCTIVE AMINATION

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B66 PREPARATION OF ENANTIOPURE 2-ACYL MORPHOLIN-5,6-DIONE FROM THE REACTION OF 2-ACYLAZIRIDINE AND METHYL OXALYL CHLORIDE

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B67 ORGANIZING AND BINDING MOLECULES TO METAL SURFACES

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B68 DEVELOPMENT OF HIGHLY STEREOSELECTIVE ASYMMETRIC 6□-AZAELECTROCYCLIZATION TOWARD NEW STRATEGY FOR CHIRAL PIPERIDINE SYNTHESIS

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B69 APPLICATION OF DIASTEREOSELECTIVE UGI REACTION TO NATURAL PRODUCTS SYNTHESIS

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B70 SYNTHESIS OF SOME TETRAHYDRONAPTHALENE CARBOXYLIC ACID SULFONAMIDES AS METHIONINE AMINOPEPTIDASE-2 (METAP2) INHIBITORS

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B71 TOWARDS SADDLENE

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B72 SILETANYLMETHYLLITHIUM: AN AMBIPHILIC ORGANOSILANE

Mariya V. Kozytska and Gregory B. Dudley
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B73 PEPTIDE QUINOLINE CONJUGATES: A NEW CLASS OF RNA-BINDING MOLECULES

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B74 PROCESS RESEARCH FOR THE SYNTHESIS OF ABT-239, A POTENT AND SELECTIVE H_3 ANTAGONIST

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B75 DESIGN AND SYNTHESIS OF PHOTOCLEAVABLE PHOSPHOLIPID ANALOGS.

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B76 HIGH-PRESSURE-PROMOTED UNCATALYZED TRANSFORMATION OF TRICHLOROETHYL CARBAMATES TO UREAS

Koji Kumamoto, Saleha Azad, Kaoru Uegaki, and Hiyoshizo Kotsuki
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B77 HIGH-PRESSURE-PROMOTED UNCATALYZED KETALIZATION OF KETONES AND OXY-MICHAEL/KETALIZATION OF CONJUGATED ENONES

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B78 TOTAL SYNTHESIS OF (+)-HONGOQUERCIN A. A FORMAL [3 + 3] CYCLOADDITION REACTION CATALYZED BY LEWIS ACIDS.

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B79 Progress Toward the Total Synthesis of (+)-Nodulisporic ACID A AND B: APPROACHES FOR THE CONSTRUCTION OF THE HIGHLY STRAINED CDE TRICYCLE

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B80 EFFICIENT CONSTRUCTION OF STEROIDS USING A DOMINO INTRAMOLECULAR DIELS-ALDER REACTION

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B81 A HIGHLY SELECTIVE AG (I) IONOPHORE BASED ON 1, 3, 5-TRIS (2-ARYLTHIOMETHYL)-2, 4, 6-TRIMETHYLBENZENE

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B82 SYNTHESIS AND SELF-ASSEMBLY OF FUNCTIONALIZED 1-AZA-ADAMANTANETRIONES

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B83 SYNTHESIS AND BIOLOGICAL EVALUATION OF NOVEL HETEROCYCLIC QUINONES AS INHIBITORS OF THE DUAL SPECIFICITY PROTEIN PHOSPHATASE CDC25C

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B84 EVALUATION OF A2E AND OTHER AMINO-RETINOID COMPOUNDS IN LIPOFUSCIN AND MELANOLIPOFUSCIN

Mary Lawyer-Alvarez, D. Joshua Cameron, McKenzie R. Pew, Glenn L. Walker, Jeffrey L. Swallow, Sarah Warburton, Craig D. Thulin, Heidi R. Vollmer-Snarr
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B85 AN EFFICIENT SYNTHESIS OF CHIRAL 1,2-DIAMINES USING AN ENANTIOMERICALLY PURE AZIRIDINE-2-METHANOL

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B86 ENYNE METATHESIS AND METALLOTROPIC [1,3]-SHIFT OF RUTHENIUM CARBENES

Daesung Lee and Mansuk Kim
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B87 ONE-POT PD-CATALYZED HYDROSTANNATION/STILLE REACTION WITH ACID CHLORIDES AS THE ELECTROPHILE.

Kyoungsoo Lee, Wenzheng Chung, Elli A. Toskey, William P. Gallagher and Robert E. Maleczka, Jr.
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B88 IN AND PD-MEDIATED INTER- AND INTRAMOLECULAR COUPLING REACTIONS OF ARYL AND VINYL HALIDES

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B89 INDIUM-CATALYZED REGIOSELECTIVE ADDITION OF ORGANOGALLIUM REAGENTS TO CARBONYL COMPOUNDS

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B90 MULTIPLE MUTATIONS WITHIN HIV-1 PROTEASE DIMERIZATION INHIBITORS VIA AN IN SITU SYNTHESIS AND SCREENING METHOD

Song-Gil Lee, Jean Chmielewski
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B91 ORGANOMETALLIC REAGENTS FOR C-F BOND ACTIVATION

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B92 LEWIS BASE-CATALYZED ADDITIONS OF TRIALKOXYSILYLALKYNES

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B93 SYNTHETIC APPLICATION OF ACYLNITROSO DIELS-ALDER DERIVED AMINOCYCLOPENTENOLS: STEREOSELECTIVE TOTAL SYNTHESIS OF (+)-STREPTAZOLIN AND ITS ANALOGUES BY USING TEMPORARY SILICON-TETHERED RCM STRATEGY

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B94 UTILIZING X-RAY CRYSTAL ANALYSIS TO IMPROVE PK PROPERTY OF TGF-β INHIBITOR

Hong-yu Li,[1] William T. McMillen,[1] Charles R. Heap,[5] Chi-Hsin R. King,[5] Yan Wang,[1] David K Clawson,[1] Parsons Stephen,[1] Faming Zhang,[1] Denis J McCann,[2] Elizabeth A. Dierks[2] J. Ott[2] Lei Yan,[3] Robert M. Campbell,[4] Bryan D. Anderson,[4] Jill R. Wagner,[4] Jonathan M. Yingling[3], J. Scott Sawyer[5]
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B95 PD (II)/PD (0) CATALYZED SEQUENTIAL SYNTHESIS OF COUMARINS

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B96 EFFICIENT SYNTHESIS OF 2'-*C*-β-METHYLGUANOSINE

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B97 LARGE SCALE SYNTHESIS OF (*S*)-2-HYDROXYAMINO-2-PHENYLETHANOL

Wenke Li, Timothy Towne, Gregory Wayne, Steve Wittenberger and Steve Richter
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B98 RELATIVE AND ABSOLUTE STEREOCHEMISTRY OF SAGITTAMIDES A AND B
***Sarah C. Lievens* and Tadeusz F. Molinski**
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B99 FORAYS IN TOTAL SYNTHESIS: THE RETRO-CLAISEN REARRANGEMENT OF MARINE NATURAL PRODUCTS
***Troy Lister* and Michael V. Perkins**
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Adelaide, Australia

B100 MOLECULES DESIGNED TO AFFORD COOLING SENSATIONS ALSO BIND TO RECEPTORS FOUND IN PROSTATE CANCER CELLS
Amanda Liu, Zaihleen Keller, Audrey Tedesco, Lok-Him Yu, Dolly Pham and Ahamindra Jain*
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B101 ASYMMETRIC CYCLIZATION OF QUINONE DERIVATIVES
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B102 TOTAL SYNTHESIS OF APOPTOLIDINONE
Qingsong Liu, Bin Wu, Gary A. Sulikowski
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B103 RECENT DEVELOPMENTS IN NAZAROV CYCLIZATION CHEMISTRY
Alison J. Frontier, Wei He, Mesfin Janka, Richard Eisenberg, Tulay Aygan Atesin
University of Rochester
Rochester NY 14627

B104 BRØNSTED ACID-CATALYZED ASYMMETRIC IMINE AMIDATION
Gerald B. Rowland, Haile Zhang, Emily B. Rowland, Yong Wang, Spandan Chennamadauvani, Jian Shu Zhao and Jon C. Antilla*
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B105 A CONCISE SYNTHESIS OF A-GALACTOSYLCERAMIDE KRN 7000
***Kuangiang Gao* and Robert M. Moriarty**
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B106 A NOVEL NON-COVALENT LINKING CONCEPT
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B107 NOVEL DERIVATIVES OF 2-ARYL-3-HYDROXYQUINOLIN-4(1*H*)-ONES AND THEIR ANTICANCER ACTIVITY
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Schedule of Presenters – Poster Session C Tuesday, June 14, 2005

C1 EFFICIENT REGIOSELECTIVE PD-CATALYZED COUPLING REACTIONS OF IODOPYRIMIDINES AND FUSED-RING IMIDAZOLES
Yanbin Liu, Mark A. Ashwell, Jifeng Liu, Robert Selliah, Russ Graceffa, Mary O'Donnell, Woj Wrona
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C2 STUDIES TOWARDS TOTAL SYNTHESIS OF ROSTRATIN B-D

Zhuqing Liu and Jon Rainier*
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C3 TOWARDS THE SYNTHESIS OF (-)-EUONYMINOL

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C4 SILICON AS A LEWIS ACID IN ASYMMETRIC SYNTHESIS

Pamela J. Lombardi, James L. Leighton
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C5 EFFICIENT SYNTHESIS OF PYRAZOLES AS NOVEL PROGESTERONE RECEPTOR ANTAGONISTS

Qing Lu, Lara S. Kallander, Dennis A. Holt, David W. Gray, Roy M. Katso, Rosie Tarafdar, HY Cheng, Xiaoliu X. Geng, Scott K. Thompson
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C6 DESIGN AND SYNTHESIS OF DICYANOMETHYLENEDIHYDROFURAN (DCDHF) SINGLE-MOLECULE FLUOROPHORES WITH EXTENDED CONJUGATION LINKAGES

Zhikuan Lu[1], Na Liu[1], Hui Wang[1], Robert J. Twieg[1], Sam Lord[2], Kallie Willets[2], W. E. Moerner[2]
1 Department of Chemistry, Kent State University, Kent, OH 44242
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C7 EXPLOITING THE METASTABILITY OF AMINO CARBINOLS AND AMINO ALKOXIDES; DEVELOPMENT OF A NEW AUXILIARY FOR THE PICTET-SPENGLER REACTION AND A NOVEL FORMYLATING REAGENT

Amanda C. Lucas, Darren J. Dixon*, Jeremy C. Prodger
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University Chemical Laboratory, Lensfield Rd., Cambridge CB2 1EW, UK

C8 SYNTHESIS OF HETEROCYCLES ON THE BASE OF THIOCARBAMIDE

A. M. Magerramov, A. R. Guseynova, I. A. Bunyad-zadeh, M. A. Allahverdiyev
Baku State University
23 Z.Khalilov, Baku-Azerbaijan

C9 PROGRESS TOWARD THE TOTAL SYNTHESIS OF GUANACASTEPENE A

Sarah V. Maifeld and Daesung Lee*
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Department of Chemistry, Madison, WI 53706

C10 A C-GLYCOSIDE CENTERED STRATEGY TOWARDS THE TOTAL SYNTHESIS OF GAMBIERIC ACID A

Utpal Majumder, Scott W. Roberts, and Jon D. Rainier*
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Department of Chemistry, 315 South 1400 East Salt Lake City, UT 84112-0850

C11 BIOMIMETIC SYNTHESIS OF ANTIMALARIAL NAPHTHOQUINONES

Jeremiah P. Malerich and Dirk Trauner
University of California – Berkeley

C12 SYNTHESIS AND CHARACTERIZATION OF NOVEL FURANOCOUMARINS

Ivica Malnar,[a] Ivaylo Jivkov Elenkov,[a] Lidija Lerman,[a] Andreja Čempuh Klonkay,[a] Anita Filipović Sučić,[a] Dinko Žiher,[a] Nada Košutić Hulita,[b] Boška Hrvačić,[a] Stribor Marković,[a] Mladen Merćep,[a] and Milan Mesić[a]
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C13 CYANOVIRIN-N BINDING TO MANα1—MAN FUNCTIONALIZED DENDRIMERS

Shane L. Mangold[‡], Joel R. Morgan[‡], Angela M. Gronenborn[†] and Mary J. Cloninger[‡]

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C14 SYNTHESIS OF FUNCTIONALIZED THIOPHENE DERIVATIVES

Jesse J. Manikowski and Christopher J. Bungard

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Medicinal Chemistry Department, 770 Sumneytown Pike, P.O. Box 4, West Point, PA 19486-0004

C15 DIRECT SYNTHESIS OF METHYL 2-DIAZO-4-ARYL-3-BUTENOATES AND THEIR REACTIVITY VIA AN ENANTIOSELECTIVE C-H ACTIVATION/COPE REARRANGEMENT-ELIMINATION PATHWAY

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C16 BLEACHABLE VISIBLE SENSITIZERS FOR ELECTRON-TRANSFER PHOTOCHEMICAL ACID GENERATION

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C17 DEVELOPMENT OF REACTIONS INVOLVING DIAZO COMPOUNDS: THE TANDEM BAMFORD-STEVENS-CLAISEN AND MOLECULAR MOUSTRAPS.

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C18 SYNTHESIS OF NUCLEOSIDE ANALOGS FOR THE STUDY OF RNA-BINDING PROTEINS

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C19 NICKEL-CATALYZED ADDITIONS OF ALKYNES AND NITRILES

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C20 SYNTHETIC UTILITY OF FUNCTIONALLY-ACTIVE PHOSPHATE TETHERS

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C21 REDUCTIVE AMINATION OF KETONES AND ALDEHYDES UTILIZING AMMONIA SALTS AND SODIUM TRIACETOXYBOROHYDRIDE

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C22 SYNTHESIS OF NON-RACEMIC 1, 2-DISUBSTITUTED CYCLOPROPANES

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C23 TRANSITION METAL-CATALYZED ALLYLIC AMINATION VIA DECARBOXYLATIVE COUPLING OF ALLYLIC CARBAMATES

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C24 EFFICIENT SYNTHESES OF POTENT SELECTIVE SEROTONIN REUPTAKE INHIBITORS (SSRIS)
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C25 A MANGANESE (0) MEDIATED DIASTEREOSELECTIVE SYNTHESIS OF SUBSTITUTED DIAMINES
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C26 STUDIES TOWARD THE ENANTIOSELECTIVE TOTAL SYNTHESIS OF CANANODINE
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C27 DIMERISATION OF TERMINAL AZIRIDINES TO GIVE PROTECTED (*E*)-2-ENE-1, 4-DIAMINES
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C28 ASYMMETRIC CYCLOPROPANATION OF OLEFINS WITH OPTICALLY ACTIVE (SALEN) RUTHENIUM (II) COMPLEXES
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C29 DISCOVERY AND OPTIMIZATION OF OXAZOLINE BASED LIGANDS FOR USE IN ENANTIOSELECTIVE ADDITION OF ALLYLIC HALIDES TO ALDEHYDES AND KETONES
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C30 SYNTHESIS AND REACTIONS OF SUBSTITUTED DENDRALENES
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C31 SYNTHESIS OF NOVEL BI-FUNCTIONAL SELECTIVE SEROTONIN REUPTAKE INHIBITORS
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C32 DEVELOPMENT OF NEW CATALYSTS FOR ORGANIC SYNTHESIS
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C33 DEVELOPMENT OF A PRACTICAL PROCESS TO A PHARMACEUTICALLY USEFUL CYCLOBUTANONE
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C34 DEVELOPMENT OF THE TWO-STEP INTERMOLECULAR STETTER
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C35 ENANTIODIVERGENT SYNTHESES OF INOSITOL PHOSPHATES AND ANALOGS THEREOF

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C36 SYNTHESIS OF VANADIUM SUBSTITUTED POLYOXOTUNGSTATE METALLODENDRIMERS

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C37 SULFUR MEDIATED HETEROCYCLE AND MACROCYCLE SYNTHESIS

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C38 IN SITU RECYCLING OF ORGANOTIN HYDRIDES: THE DEVELOPMENT OF A ONE-POT STILLE/HYDROSTANNATION REACTION

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C39 PROGRESS TOWARD THE TOTAL SYNTHESIS OF CERCOSPORIN VIA A COPPER-CATALYZED ASYMMETRIC BIARYL COUPLING REACTION

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C40 THERMOCHEMISTRY OF N-DEHYDROPHENYLNITRENES (N = 2, 3, OR 4): EXPERIMENTAL CONFIRMATION OF A DOUBLET GROUND STATE FOR AN ORGANIC TRIRADICAL

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C41 A BIOMIMETIC STRATEGY FOR CATALYTIC CONJUGATE ADDITIONS OF CARBONYL ANIONS IN WATER

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C42 STEREOELECTRONIC CONTROL OF PROTEIN STRUCTURE

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C43 MONOOXIDATION OF HETEROAROMATICS

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C44 METALLOPHOSPHITE-INDUCED NUCLEOPHILIC ACYLATION OFα,β-UNSATURATED AMIDES: FACILITATED CATALYSIS BY A DIASTEREOSELECTIVE RETRO [1, 4] BROOK REARRANGEMENT

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C45 REMOTE CHIRALITY TRANSFER FROM EPOXIDES

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C46 STEREOSELECTIVE SYNTHESIS OF 2(1-INDENYL) TETRAHYDROFURANS AND PYRROLIDINES VIA INTRAMOLECULAR CARBOAMINATION AND CARBOETHERIFICATION
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C47 MECHANISTIC STUDIES OF THE REACTION OF TRIS (2, 2, 2-TRIFLUOROETHYL) PHOSPHITE WITH DIARYLIODONIUM SALTS
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C48 [1, 3] RING CONTRACTION OF 7-MEMBERED HETEROCYCLES
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C49 SYNTHESIS OF A NOVEL ANSA-SECOSTEROID CORE FOR A COMPOUND LIBRARY
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C50 CATALYTIC ALDOL-TRANSFER REACTIONS
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C51 NOVEL CHIRAL PSEUDOALKALOIDS FROM CAMPHOR
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C52 TOTAL SYNTHESIS OF RAMESWARALIDE A
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C53 THREE-COMPONENT COUPLING REACTIONS OF SILYLGLYOXYLATES, ALKYNES, AND ALDEHYDES: A CHEMOSELECTIVE ONE-STEP GLYCOLATE ALDOL CONSTRUCTION
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C54 A COMPLETE PROGRAM TOWARD PELORUSIDE A AND ANALOGUES: METHODOLOGY, CONFORMATIONAL ANALYSIS, AND TOTAL SYNTHESIS
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C55 ASYMMETRIC C–H INSERTION OF RH (II) STABILIZED CARBENOIDS INTO ACETALS: A CLAISEN CONDENSATION EQUIVALENT
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C56 SYNTHESIS OF C-GLUCOSYL-α-SERINE AND ALANINE BY A CROSS METATHESIS/ CYCLIZATION STRATEGY
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C57 THE DESIGN AND SYNTHESIS OF STRUCTURALLY NOVEL ANTIBACTERIAL COMPOUNDS RELATED TO β-LACTAM ANTIBIOTICS

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C58 SYNTHETIC APPROACHES TO PLAKORTHETHERS AND THE CORE OF PSEUDOMONIC ACID

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C59 THE DIASTEREOSELECTIVE SYNTHESIS OF QUATERNARY SUBSTITUTED THIOINDOLINES FROM SULFUR YLIDE INTERMEDIATES

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C60 IP_3 SENSING IN PHYSIOLOGICAL CONDITIONS USING TANSITION-METAL-BASED CHEMOSENSING ENSEMBLES

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C61 [1, 4]-WITTIG REARRANGEMENTS OF □-ALKOXYSILANES

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C62 ARMCHAIR GRAPHITIC STRIPS

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C63 REACTIONS DUE TO THE ACIDIC NATURE OF α–METHYL H OF 1, 4-NAPHTHOQUINONES.

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C64 SYNTHESIS AND METAL BINDING ABILITY OF THIOGLYCOSIDE DENDRIMERS

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C65 SYNTHESIS OF ASMARINE ANALOGUES

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C66 NEW SYSTEMS FOR CATALYTIC ASYMMETRIC EPOXIDATION USING IMINIUM SALT CATALYSTS

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C67 NEW PHASE-TRANSFER CATALYSTS FOR THE SYNTHESIS OF β-HYDROXY α-AMINO ACIDS VIA ALDOL REACTIONS

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C68 STUDIES TOWARDS THE SYNTHESIS OF DIFFERENTIALLY SUBSTITUTED BICYCLIC MALONAMIDES FOR MATERIALS APPLICATIONS

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C69 A CONCISE SYNTHESIS OF A NOVEL ANTIANGIOGENIC TYROSINE KINASE INHIBITOR

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C70 AZA-HELICENES AS MOLECULAR MACHINES

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C71 SUPEROXIDE DISMUTASE MIMETICS: SYNTHESIS AND STRUCTURE-ACTIVITY RELATIONSHIP STUDY OF GLYOXYLATE- AND GLYOXAMIDE-DERIVED METALLOPORPHYRINS

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C72 NEW DIOXOPIPERAZINES FROM THE PLANT PATHOGEN *LEPTOSPHAERIA MACULANS/PHOMA LINGAM* AND THEIR IMPLICATIONS ON THE BIOSYNTHESIS OF SIRODESMINS

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C73 STUDIES ON THE BIOSYNTHESIS OF PHYTOALEXINS FROM THE WILD CRUCIFER ERUCASTRUM GALLICUM

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C74 STEREOSELECTIVE DIALKYLATION REACTIONS TO FORM CONTIGUOUS STEREOGENIC QUATERNARY CARBON CENTERS IN NATURAL PRODUCT SYNTHESIS

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C75 SYNTHESIS OF 3-DEAZA-3,3-DIFLUOROURIDINE AND RELATED NUCLEOSIDES: POTENTIAL MODULATORS OF THE CYTOSINE NUCLEOSIDE BIOSYNTHETIC MANIFOLD

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C76 SOLUTION AND SOLID-PHASE SYNTHESIS OF HCV POLYMERASE INHIBITORS

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C77 PREPARATION OF ALL STEREOISOMERS OF 3-FLUORO-4-AMINOMETHYLPYRROLIDINE

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C78 NOVEL REACTIONS OF DIHALOCYCLOPROPANES FOR THE ASSEMBLY OF FUNCTIONALISED GIBBANES

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C79 SYNTHESIS AND CHARACTERIZATION OF 2, 5'-DI-TERT-BUTYL-6, 13-DIKETO-5, 14-DIHYDRO-5, 14[1', 2']-BENZENOPENTACENE

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C80 (*S, S*)-*TRANS* CYCLOPENTANE PNA: AN OPTIMIZED PROBE FOR NUCLEIC ACID DETECTION

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C81 SYNTHESIS OF POLYPROPIONATE MOTIFS: APPLICATION OF A TANDEM MUKAIYAMA/ FREE RADICAL-BASED REDUCTION SEQUENCE

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C82 STUDIES TOWARDS THE TOTAL SYNTHESIS OF PAMEROLIDE A

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C83 BIOISOTERIC REPLACEMENT OF PHENOL IN THE OPIOID ANTAGONIST LY255582, 3-[1-(3-CYCLOHEXYL-3-HYDROXY-PROPYL)-3, 4-DIMETHYL-PIPERIDIN-4-YL]-PHENOL

Steven J. Quimby, Mike Statnick, Jamie McKinzie, Todd Suter, Ryan Favors, Mike Mangold, Nita Patel, Joe Woodland, Elizabeth Thomas, Miles Siegel, and Charles H. Mitch

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C84 PALLADIUM CATALYZED REDUCTION OF AROMATIC AND ALIPHATIC NITRO COMPOUNDS TO AMINES. A ONE-POT REDUCTIVE CONVERSION TO AMIDES, CARBAMATES, AND SULFONAMIDES

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C85 LIGAND BASED OPTIMIZATION OF ENANTIOSELECTION IN HYDROGEN BOND PROMOTED HETERO DIELS-ALDER REACTION

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C86 SYNTHETIC EFFORTS TOWARDS THE SYNTHESIS OF 3, 3' DISUBSTITUTED MEO-BIPHEP DERIVATIVES INCORPORATING THE "3, 5 DIALKYL META-EFFECT"

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C87 SEMI-SYNTHESIS AND SAR STUDY ON C-10 HALO AND C-12 HYDROXY PROSTAGLANDIN A_2

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C88 A CONVERGENT SECOND GENERATION SYNTHESIS OF (+)-PHORBOXAZOLE A AND IDENTIFICATION OF HIGHLY CYTOTOXIC ANALOGS THROUGH SAR STUDIES

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C89 A HIGHLY ENANTIO- AND DIASTEREOSELECTIVE CATALYTIC INTRAMOLECULAR STETTER REACTION

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C90 BIOORGANIC FIRST: A NEW MODEL FOR THE COLLEGE CHEMISTRY CURRICULUM

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C91 NOVEL AROMATIC COMPOUNDS BY TANDEM MICHAEL-CLAISEN REACTIONS

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C92 TOWARDS THE TOTAL SYNTHESIS OF (+)-ACUTIPHYCIN: UTILIZATION OF HOMOALDOL METHODOLOGY IN THE PREPARATION OF ENANTIOSELECTIVE ACETATE ALDOL

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C93 EXPANDING THE ROLE OF α-HALOALDEHYDES IN ASYMMETRIC SYNTHESIS

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C94 THEORETICAL CONFIRMATION OF THE EXPERIMENTAL RAMAN SPECTRA OF THE LOWER-ORDER DIAMONDOID MOLECULE: CYCLOHEXAMANTANE ($C_{26}H_{30}$)

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C95 TWO-STEP THREE CARBON ALDEHYDE HOMOLOGATION

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C96 DFT STUDY OF THE DIASTEREOSELECTIVE EPOXIDATION OF CYCLIC ENOL ETHERS BY DIMETHYLDIOXIRANE

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C97 OLEFIN METATHESIS IN CARBON DISULFIDE

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C98 MODULAR DOMAIN STRUCTURE: A NEW BIOMIMETIC APPROACH FOR ADVANCED POLYMER PROPERTIES

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C99 SMALL-MOLECULE DIVERSITY ACCESSED THROUGH ITERATED BRANCHING REACTION PATHWAYS AND DNA-TEMPLATED SYNTHESIS

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C100 SITE-SPECIFIC LABELING OF CELL SURFACE PROTEINS USING BIOTIN LIGASE

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C101 REGIOSELECTIVE ADDITION OF ALLYLGALLIUM REAGENTS TO TERMINAL ALKYNES

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C102 INDIUM-MEDIATED SELECTIVE ALLENYLATION AND PROPARGYLATION AT C-4 POSITION OF 2-AZETIDINONES AND ITS CYCLIZATION CATALYZED BY $AUCL_3$

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C103 REACTIONS OF SEMIBULLVALENE AND ITS DERIVATIVES

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C104 SPERMINE PARTICIPATES IN OXIDATIVE GUANINE DEGRADATION IN DNA LEADING TO DEOXYRIBOSYLUREA

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C105 AN EFFICIENT SYNTHESIS OF A $GABA_A$ $\alpha_{2,3}$-SELECTIVE ALLOSTERIC MODULATOR VIA A SEQUENTIAL PD-CATALYZED CROSS-COUPLING APPROACH

Mark S. Jensen, R. Scott Hoerrner, Wenjie Li, Dorian P. Nelson, Gary J. Javadi, Peter G. Dormer, Dongwei Cai, Robert D. Larsen
Department of Process Research, Merck Research Labs, Rahway NJ 07765

Schedule of Presenters – Poster Session D Wednesday, June 15, 2005

D1 ENZYME-ASSISTED SYNTHESIS OF PHOSPHOLIPID ANALOGUES: FLUOROGENIC REPORTERS OF PHOSPHOLIPASE A HEAD GROUP SELECTIVITY
Tyler M. Rose and Glenn D. Prestwich
University of Utah
Medicinal Chemistry Department, 419 Wakara Way, Suite 205, Salt Lake City, UT 84108

D2 INTERMOLECULAR FREE RADICAL ADDITION REACTIONS OF α-NITRO ESTERS AND KETONES AND β-KETO ESTERS
Ian J. Rosenstein and Louis J. Vaickus
Hamilton College
Department of Chemistry, 198 College Hill Road, Clinton, NY 13323

D3 SOME SCALE-UP ISSUES AND SOLUTIONS
Bruno Roy, John Scheigetz and Robert Zamboni.
Merck Frosst Centre for Therapeutic Research,
P.O. Box 1005, Pointe Claire-Dorval, Quebec H9R 4P8

D4 STRUCTURE-ACTIVITY RELATIONSHIP STUDY OF MYRIAPORONES
Myriam Roy, Hua Cheng, and Richard E. Taylor*
University of Notre Dame
Department of Chemistry and Biochemistry, Notre Dame, IN 46556

D5 INVESTIGATING THE ROLE OF INTERFACIAL POLAR SIDECHAIN IDENTITY IN THE STABILITY AD SPECIFICITY OF COILED-COIL ASSEMBLY
Shannon J. Ryan, Yongda Zhang, Alan J. Kennan
Colorado State University
Department of Chemistry, Fort Collins, CO, 80523

D6 SYNTHESIS AND CATALYTIC REACTIONS OF NEW CHIRAL PINCER-TYPE TRANSITION METAL COMPLEXES
DoWook Ryu, Myeong Sik Yoon, and Kyo Han Ahn*
Pohang University of Science and Technology
Department of Chemistry and Center for Integrated Molecular Systems Division of Molecular and life Sciences, San 31 Hyojadong, Pohang, Kyeongbuk 790-784, Korea

D7 STUDIES TOWARDS THE TOTAL SYNTHESIS OF (±)-PEROPHORAMIDINE AND (±)-DIHYDROFLUSTRAMINE C
Amir Sabahi and Jon D. Rainier*
University of Utah
Department of Chemistry, 315 South 1400 East, Salt Lake City, UT 84112

D8 ISOTOPIC NITROGEN EXCHANGE IN TETRAZINES; IS THE POTENTIAL ENERGY SURFACE A MONKEY SADDLE?
Dhandapani V. Sadasivam and David M. Birney
Texas Tech University
Lubbock, TX 79409-1061

D9 TOTAL SYNTHESIS OF (+)-DACTYLOLIDE
Carina C. Sanchez, Gary E. Keck
University of Utah
Department of Chemistry, Salt Lake City, UT 84112

D10 THE PREPARATION OF POLYETHER SUBSTITUTED POLY (PHENYLENEVINYLENES) FOR USE IN LIGHT EMITTING DEVICES
Elizabeth M. Sanford, David L. Weatherly, Kyle A. Cox, Alexis M. Johnson and Gregory M. Borst
Hope College
Department of Chemistry, P. O. Box 9000, Holland, MI 49422

D11 ENANTIOSELECTIVE [2, 3]-WITTIG REARRANGEMENT FEATURING CHIRALITY TRANSFER FROM EPOXIDE

Michiko Sasaki, Kei Takeda*
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Department of Synthetic Organic Chemistry, Graduate School of Biomedical Sciences, 1-2-3, Kasumi, Minami-Ku, Hiroshima 734-8551, Japan

D12 ENANTIOSELECTIVE SYNTHESIS OF AMINES AND AMIDES THROUGH CATALYTIC ASYMMETRIC RING-CLOSING METATHESIS

Elizabeth S. Sattely,‡ G. Alexander Cortez,‡ David C. Moebius,‡ Amir H. Hoveyda,‡ and Richard R. Schrock#
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#Massachusetts Institute of Technology, Department of Chemistry, Cambridge, MA 02139

D13 BINDING OF MANNOSE-FUNCTIONALIZED DENDRIMERS WITH PEA (PISUM SATIVUM) LECTIN

Kristian H. Schlick, Rachel A. Udelhoven, Gregory C. Strohmeyer, Mary J. Cloninger*
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D14 SYNTHESIS OF DIASTEREOMERICALLY AND ENANTIOMERICALLY PURE SUBSTITUTED TETRAHYDROFURANS, PYRROLIDINES AND OTHER USEFUL COMPOUNDS VIA SULFUR YLIDES

Jennifer M. Schomaker, Babak Borhan, Somnath Bhattacharjee, Keith A. Korthals, Veera Pulgam Reddy, William D. Wulff
Michigan State University
East Lansing, MI 48824

D15 New NMR-Based Strategies for Natural Products Discovery

Frank C. Schroeder, Andrew E. Taggi, Matthew Gronquist and Jerrold Meinwald
Cornell University
Department of Chemistry and Chemical Biology, Baker Laboratory, Ithaca, New York 14853

D16 UNDERSTANDING AND DEVELOPING PD-CATALYZED AEROBIC ALCOHOL OXIDATIONS

Mitchell J. Schultz, Ryan S. Adler, Steven S. Hamilton, David R. Jensen, Wiktor Zierkiewicz, Timofei Privalov, Matthew S. Sigman
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D17 PROGRESS TOWARDS A TOTAL SYNTHESIS OF AN IEJIMALIDE

Dirk Schweitzer, John Kane, Jamie Zigterman, Paul Helquist
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D18 PYRROLE CARBINOLS: POWERFUL PLATFORMS FOR STEREOSELECTIVE NATURAL PRODUCT SYNTHESIS

Mark S. Scott, Darren J. Dixon, Chris A. Luckhurst
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D19 CHARACTERIZATION OF EDIBLE FILMS BASED ON EXTRACTED GLUTEN FROM TWO TYPE IRANIAN WHEAT

Soheila Sedaghat ; Farzam Ghamisi ; Morteza Khosravi
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Department of Chemistry, North Tehran Branch, Tehran –Iran

D20 NEW GUAIANOLIDES FROM TANACETUM *FRUTICULOSUM* LEDEB

Soheila Sedaghat ; Abdolhossein Rustaiyan
Islamic Azad University
Department of Chemistry, North Tehran Branch, Tehran –Iran

D21 FACILITATED ANION TRANSPORT ACROSS PHOSPHATIDYLCHOLINE BILAYERS
Jennifer L. Seganish, Jeffery T. Davis
University of Maryland
Department of Chemistry and Biochemistry, College Park, MD

D22 APPLICATION OF ARYL SILOXANE COUPLING METHODOLOGY TO THE SYNTHESIS OF ALLOCOLCHICINE
W. Michael Seganish and Philip DeShong
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D23 A UNIQUE, SELF-ASSEMBLED, ZONAL POLYMER SYSTEM BASED ON ZINC (II), COPPER (II), AND AN ORGANIC BACKBONE
S. Russell Seidel, Joseph S. Campanelli, and Russell Ainbinder
Dowling College
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D24 DESIGN, SYNTHESIS AND BIOLOGICAL ACTIVITY OF NOVEL HYDROXAMIC ACID ANTIMYCOTIC ANTIBIOTIC (HAAA) NEOENACTIN A ANALOGS, DERIVATIVES AND SIDEROPHORE CONJUGATES
A. K. Sheinkman,[1] M. J. Miller,[1] P. A. Miller,[1] C. Schous,[1] V. Girijavallabhan,[1] N. Niyaz ,[1] Robert F. Murphy,[1] U. Möllmann[2]
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2. Hans-Knöll Institute for Natural Products Research, Jena, Germany

D25 A RAPID PREPARATION OF 5-SUBSTITUTED-3-HYDROXY-1-AMIDOBENZENES FROM 3-SUBSTITUTED HALOBENZENES VIA A C-H BORYLATION/AMIDATION/OXIDATION PROCESS
Feng Shi, Milton R. Smith, III and Robert E. Maleczka, Jr.*
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D26 ROUTES TO UNIQUE 2*H*-INDAZOLES: SYNTHETIC AND MECHANISTIC INVESTIGATION INTO COARCTATE CYCLIZATIONS
Laura D. Shirtcliff, Jazmin Rivers, Michael M. Haley
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D27 TOWARDS THE SYNTHESIS OF EVONINIC ACIDS.
Lena Shukla[1], Dr. Alan C. Spivey[1] and Dr. Judy F. Hayler[2]
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D28 A TEMPORARY *P*-TETHER/RCM APPROACH TO AMINE CONTAINING BUILDING BLOCKS
Stephen R. Sieck, and Paul R. Hanson
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D29 β-GALACTOSIDASE ENZYME FRAGMENT COMPLEMENTATION BASED PROTEASE HTS ASSAYS
R. Singh, T. Naqvi, N. Charter and R.M. Eglen
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42501 Albrae Street, Fremont, CA-94538

D30 Novel Inhibitors of Fatty Acid Amide Hydrolase
S.Y. Sit,[1] Kai Xie,[1] Hongfeng Deng,[1] Kevin Burris,[2] Robert Bertekap,[2] Kim W. McIntyre,[3] David J. Shuster,[3] Clotilde Bourin,[2] Fred Machet,[2] Ping Chen,[2] Joe Polino,[2] and Charles M. Conway[2]
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D31 SYNTHESIS OF IRREVERSIBLE ANTAGONISTS OF CGRP RECEPTORS.

D. David Smith, Christopher K Taylor, Peter W. Abel, Martin Hulce
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D32 SYNTHESIS OF SUBSTITUTED 3, 4-DIBENZOYLFUROXANS

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D33 SOLID-PHASE REAGENTS FOR THE TRACELESS STAUDINGER LIGATION

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D34 SYNTHETIC STUDIES TOWARDS THE CONSTRUCTION OF THE LEFT-HAND RING OF CELOGENTIN C

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D35 DESIGN AND SYNTHESIS OF BENZOSUBERENE ANALOGS OF COMBRETASTATIN AS TUBULIN BINDING COMPOUNDS

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D36 FIRST IPSO-FUNCTIONALIZATION OF META-TERPHENYL COMPOUNDS WITH BROMO- AND HYDROXYMETHYL GROUPS

C. Stanciu, A.R.Fox, A.F. Richards, M.M.Olmstead and P.P.Power
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D37 STUDIES DIRECTED TOWARDS THE TOTAL SYNTHESIS OF THE ERYTHRINAN AND HOMOERYTHRINAN ALKALOIDS

Pauline C. Stanislawski and Martin G. Banwell
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Research School of Chemistry, Australian National University, Canberra, ACT 0200

D38 IDENTIFICATION OF 4-(INDAZOL-3-YL)-PHENOLS AS A PATHWAY SELECTIVE ESTROGEN RECEPTOR LIGANDS

Robert J. Steffan [1], Edward Matelan [1], Mark A. Ashwell [7], William J. Moore[1], Matora Fiorey[8], William R. Solvibile [1], Eugene Trybulski [1], Christopher C. Chadwick [6], Susan Chippari [2], Thomas Kenney [2], Richard C. Winneker[2], Amy Eckert[3], Lisa Borges-Marcucci[3], Steven J. Adelman[3], James C. Keith[4], Yelena Leatherby[4], Leo Albert [4], Zhang Xu[5], Lydia Mosyak[5] and Douglas C. Harnish[3]
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D39 TOWARDS THE ENANTIOSELECTIVE DESYMMETRISATION OF A NOVEL CENTROSYMMETRIC DILACTONE

Will Stephen and Paul Wyatt,
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D40 MECHANISTIC STUDIES ON THE COPPER-CATALYZED *N*-ARYLATION OF AMIDES

***Eric R. Strieter*[†] *Donna G. Blackmond*[‡] *and Stephen L. Buchwald*[†]**
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D41 A NEW APPROACH TO THE SYNTHESIS OF J-113397, THE FIRST NON-PEPTIDE ORL1 RECEPTOR ANTAGONIST

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D42 S_NAR REACTION ON BIPHENOLS: MONO VS. BIS SELECTIVITY AS A FUNCTION OF BASE EQUIVALENTS

Kevin Sullivan, Chaoyu Xie, Michael Laurila, John Pu, and David Mitchell
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Chemical Product Research and Development Division, Indianapolis, IN 46285

D43 OXIDATION OF ORGANOCUPRATES WITH "SUB-STOICHIOMETRIC" OXIDANT AND THE SYNTHESIS OF STRAINED MEDIUM RINGS

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D44 A STEREOSELECTIVE FORMAL AZA-[3 + 3] CYCLOADDITION APPROACH TOWARD A TOTAL SYNTHESIS OF (-)-CYLINDRICINE C.

Jacob J. Swidorski; Jiashi Wang; Richard P. Hsung*
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D45 CHIRAL ENALS AND TETRONAMIDES IN FORMAL AZA-[3 + 3] CYCLOADDITION REACTIONS. SYNTHESIS OF PIPERIDINYL HETEROCYCLES.

Nadiya Sydorenko, Richard Hsung, and Eymi Vera
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D46 NONREDUCTIVE DEIODINATION OF IODOPHENOLS IN THE PRESENCE OF AMINES

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D47 WATER-SOLUBLE REAGENTS FOR TRACELESS STAUDINGER LIGATION

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D48 3, 4-DIHYDROXYPROLINES: SYNTHESIS, CONFORMATION AND ROLE IN NATURE

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D49 SYNTHESIS OF A TRANSITION-STATE ANALOG FOR THE HYDROLYSIS OF THE ZEARALENONE LACTONE

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D50 NICKEL-CATALYZED CYCLOADDITIONS OF UNACTIVATED CARBONYLS WITH UNSATURATED HYDROCARBONS

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D51 SYNTHESIS OF A NOVEL PEPTIDIC PHOTOAFFINITY PROBE FOR THE PTP-1B ENZYME

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D52 ASYMMETRIC CYCLOPROPANE SYNTHESIS

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D53 SYNTHESES OF FIDUXOSIN METABOLITES THROUGH SELECTIVE AROMATIC HYDROXYLATION

Zhenping Tian*, Jianzhang Mei, Lynda Dai, Shyamal Parekh, and Albert Thomas
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D54 KINETIC STUDY OF ORGANOTRIFLUOROBORONATES IN SUZUKI-MIYAURA COUPLINGS

Robert Todd, Michael Singer, Peng Gao and Kanth Josyula.
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D55 TOWARDS THE TOTAL SYNTHESIS OF HEMIBREVETOXIN B

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D56 MECHANISTIC EXPLORATIONS OF PALLADIUM (II) OXIDATION CHEMISTRY

Raissa M. Trend*, Brian M. Stoltz
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D57 PRACTICAL AND EFFICIENT ROUTE TO (S)-γ-FLUOROLEUCINE

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D58 SYNTHESIS, TAUTOMERIC STATES AND CRYSTAL STRUCTURE OF ETHYL 2-H-AND 2-METHYLQUINAZOLINE-4-YLIDEN CYANACETATE

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D59 TOWARDS A TOTAL SYNTHESIS OF THE CORNEXISTINS: TAKING ADVANTAGE OF AN OBSERVED RETRO-ALDOL

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D60 CONFORMATIONAL CONTROL FOR HETEROTROPIC COOPERATIVITY

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D61 PROGRESS TOWARDS THE TOTAL SYNTHESIS OF (+) - SORANGICIN A

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D62 ONE-POT CONVERSION OF BROMOTHIOAMIDES TO AMINOBENZOTHIAZOLES VIA A TANDEM PALLADIUM-CATALYZED INTRAMOLECULAR ARYLATION/BUCHWALD-HARTWIG AMINATION REACTION

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D63 SYNTHESES OF DIENES CONTAINING COBALT-COMPLEXED ALKYNES AND THEIR REACTIVITY IN DIELS-ALDER REACTIONS

Florina A. Voica, Elizabeth A. Crawford, Kevin M. Shea
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D64 AN RCM/X-MET SEQUENCE TO COMPLEX POLYOL SUBUNITS

Josh D. Waetzig, Alan Whitehead and Paul R. Hanson
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D65 MULTI-KILOGRAM SCALE ENANTIOSELECTIVE SYNTHESIS OF A VITRONECTIN RECEPTOR ANTAGONIST

Michael D. Wallace, Michael A. McGuire, Lynn Goldfinger, Marvin S. Yu, Susan Shilcrat, Li Liu, and Wenning Dai
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D66 HELICAL POLYELECTROLYTE MOLECULAR ACTUATORS

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D67 RUTHENIUM CATALYZED DECARBOXYLATIVE INSERTION OF ELECTRONPHILES

Chao Wang and Jon A. Tunge
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D68 STEREOSELECTIVE SYNTHESIS OF (E)-VINYLBORONIC ESTERS *VIA* A ZR MEDIATED HYDROBORATION OF ALKYNES

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D69 INVESTIGATION OF DNA CROSS-LINKING BY AZIRIDINOMITOSENES

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D70 STUDIES TOWARDS THE TOTAL SYNTHESIS OF BRYOSTATIN 1: PREPARATION OF THE PYRAN ANNULATION AB-RING PRECUSOR

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D71 METHYLTRANSFERASE-MEDIATED DNA ALKYLATION AND POST-ENZYMATIC CONJUGATION VIA SYNTHETIC COFACTOR MIMICS

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D72 SYNTHESIS AND SAR STUDY OF 3-ACYL-2, 6-DIAMINOPYRIDINE ANALOGS AS CYCLIN-DEPENDENT KINASE INHIBITORS

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D73 THE BIOCHEMICAL PROPERTIES OF *N*6-(2-DEOXY-D-PENTOFURANOSYL)-6-DIAMINO-5-FORMAMIDO-4-HYDROXYPYRIMIDINE (FAPY•DG)

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D74 A PRACTICAL ROUTE FOR THE KILOGRAM-SCALE PRODUCTION OF *CIS*-3-METHYLAMINO-4-METHYLPIPERIDINES

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D75 MULTIVALENT ACTIVATION IN PHOSPHATE TRIESTERS: HARNESSING LATENT LEAVING GROUP ABILITY IN BICYCLIC PHOSPHATES.

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D76 TRANS-CYCLOPENTANE PEPTIDE NUCLEIC ACIDS (TCYPPNA) MONOMERS: SYNTHESIS AND APPLICATIONS IN PNA: DNA COMPLEXES

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D77 MANNOSE/GLUCOSE FUNCTIONALIZED DENDRIMERS AS TOOLS FOR PROBING TUNABLE MULTIVALENCY

***Mark L. Wolfenden** and Mary J. Cloninger*
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D78 BORABENZENE AS A DIENE IN DIELS-ALDER REACTIONS: SYNTHESIS AND CHARACTERIZATION OF BORABARRELENE ANALOGUES

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D79 MACROCYCLIC ARTIFICIAL β-SHEETS

R. Jeremy Woods, Omid Khakshoor, and James S. Nowick
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D80 ASYMMETRIC SYN-SELECTIVE SCANDIUM-CATALYZED ENE REACTIONS

***Jimmy Wu**, David A. Evans*
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D81 ASYMMETRIC SYNTHESES OF PROPARGYLAMINES VIA 3, 3'-DISUBSTITUTED BINAPHTHOL MODIFIED ALKYNYL BORONATES

T. Robert Wu, J. Michael Chong
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D82 *SELECTIVE INTRAMOLECULAR ACYL MIGRATION: A PRACTICAL APPROACH TO PREPARE C-3, 5-ACYL FURANOSES*

Feng Xu, Bryon Simmons, Kimberly Savary, Chunhua Yang, Robert A. Reamer
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D83 BIOMIMETIC CASCADE REACTIONS IN ORGANIC SYNTHESIS: TOTAL SYNTHESES OF 1-*O*-METHYLLATERIFLORONE AND GAMBOGIN

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D84 DESIGN AND SYNTHESIS OF PHOSPHATASE-RESISTANT ANALOGS OF PHOSPHATIDYLINOSITOL 3-PHOSPHATE

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D85 BIOMIMETIC AND TOTAL CHEMICAL SYNTHESIS OF AMINO-RETINOID COMPOUNDS: POTENTIAL APPLICATIONS IN CANCER AND AGE-RELATED MACULAR DEGENERATION

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D86 FORMATION OF GUANIDINOHYDANTOIN FROM THE OXIDATION OF GUANOSINE VIA SINGLET OXYGEN

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D87 A SIMPLE SYNTHESIS OF 4-CHLORO-5-HYDROXY-1*H*-BENZO [*G*] INDOLES AND 4, 9-DIOXO-1*H*-BENZO [*F*] INDOLES

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D88 OXYGENG PROMOTED PD(II) CATALYSIS FOR CROSS-COUPLING OF BORON COMPOUNDS AND ALKENES

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D89 THE EFFECT OF APPLYING MIXED ORGANOMETALLIC REAGENTS TOWARDS THE DESYMMETRIZATION OF CYCLIC ANHYDRIDES

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D90 HIGHLY STEREOSELECTIVE REDUCTIVE AMINATION OF AMINO ESTERS WITH NEW SOLUBLE STERICLLY HINDERED SODIUM TRIACYLOXYBOROHYDRIDE REAGENTS

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D91 SYNTHESIS OF BENZOAZEPINONES AND ISOQUINOLINONES VIA PALLADIUM-CATALYZED ADDITION OF TETHERED AMIDES TO PHENYL ACETYLENES
Ying Yu and David Mitchell
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D92 TOWARD THE TOTAL SYNTHESIS OF XESTOCYCLAMINE A
Heedong Yun and Samuel J. Danishefsky
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D93 COPPER (II) PROMOTED DIAMINATION OF UNACTIVATED OLEFINS
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D94 TANDEM SIGMATROPIC REARRANGEMENTS IN THE SYNTHESIS OF PINNATOXINS
Armen Zakarian and Matthew J. Pelc
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D95 CATALYTIC ASYMMETRIC ALKYLATIVE DESYMMETRIZATION OF CYCLIC ANHYDRIDES AND ITS APPLICATION TO THE SYNTHESES OF NATURAL PRODUCTS
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D96 SYNTHESIS OF *N*-PHENETHYL *PARA*-E- AND *PARA*-F-OXIDE-BRIDGED HENYLMORPHANS
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D97 CHEMICAL SYNTHESIS OF ENANTIOMERIC GERANYLGERANYLGLYCERYL PHOSPHATES TO CHARACTERIZE THE DGGGP SYNTHASE
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D98 REGIOSELECTIVE RING OPENING OF EPOXIDES WITH HYDRAZIDES-APPLICATION TO THE SYNTHESIS OF D_3-LABELLED REYATAZ™
Huiping Zhang, Samuel J. Bonacorsi, Jr., Bang-Chi Chen, Leslie W. Leith, J. Kent Rinehart, Balu Balasubramanian and Joel C. Barrish
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D99 DEVELOPMENT OF HIGH-LOAD REAGENTS VIA ROM POLYMERIZATION
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D100 DESIGN, SYNTHESIS AND BIOLOGICAL EVALUATION OF NOVEL "UNIVERSAL" B-LACTAMS
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D101 AN EFFICIENT AND PRACTICAL SYNTHESIS OF RWJ-339489, A MIXED V_{1A}/V_2 RECEPTOR ANTAGONIST

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D102 2-THIOINDOLE CYCLIZATIONS TO FORM SPIROINDOLINES: ENTRY INTO MULTICYCLIC NATURAL PRODUCTS

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D103 NICKEL CATALYZED REARRANGEMENTS OF VINYLCYCLOPROPANES AND CYCLOPROPYLEN-YNES

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D104 ALLYL CROSS-COUPLING REACTIONS USING ALLYL ACETATES MEDIATED BY PD-IN-$INCL_3$

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D105 SYNTHESIS OF POLYAZA PYRIMIDINES FROM KETENE N, S-ACETALS

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