THE MIDLAND CHEMIST
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The Midland Section is looking forward to a great year...mark your calendars!

Another successful Project SEED program: Laura Schmidt, one of three Project SEED students in 2003, spent the summer on a research project at Saginaw Valley State University, pg. 3

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In This Issue...

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Please submit all articles and photographs to the editor, Ann Birch. Instructions for article submission are on the Midland Section web site, as is contact information for other staff members. Authors can also contact Ann directly with any questions.

Cover photo by Peggy Hill.

Chair Column

A New Year Begins

Joe Ceraso, Chair
ACS Midland Section

The year 2004 is another year of exciting opportunities for members of the American Chemical Society and those of you who enthusiastically volunteer your time throughout the year to implement local Midland Section ACS programs. As chair for the Midland Section in 2004, I would first like to extend my congratulations to last year's chair, Mike Owen, and the board of directors for the outstanding leadership and programs offered by the Midland Section. I learned a lot from Mike, who is certainly a motivating and inspirational leader. It is rewarding to be part of an organization that thrives on bringing science and chemistry to its members and the community with its various communications, member programs, public education, and student programs.

We have several new faces on the board and heading up committees this year. Jennifer Dingman is a director, Deb McNett is secretary, and Maneesh Bahadur is chair of the Nominations and Elections Committee (NEC). Many board members, committee chairs, and volunteers are continuing in their former roles or taking on new roles, for which I am very grateful. Petar Dvornic, Don Miller, and Dave Stickles are directors; Pat Smith is Chair-elect; Doug Beyer is treasurer. Gary Kozerski provided excellent leadership on last year's NEC. This year, he will be the committee chair for Careers and Professional Relations. Buford Lemon and Dale LeCaptain have volunteered to co-chair the Fall Scientific Meeting in 2004. In addition, the committee chair for the 2006 Central Regional Meeting is Kurt Brandstadt. Over the course of the next two years, members will be receiving communications on the progress of the 2006 Central Regional Meeting plans. Finally, a special recognition and thanks to Ann Birch, editor of *The Midland Chemist*, for her outstanding contributions and persistent excellence in our Section communications.

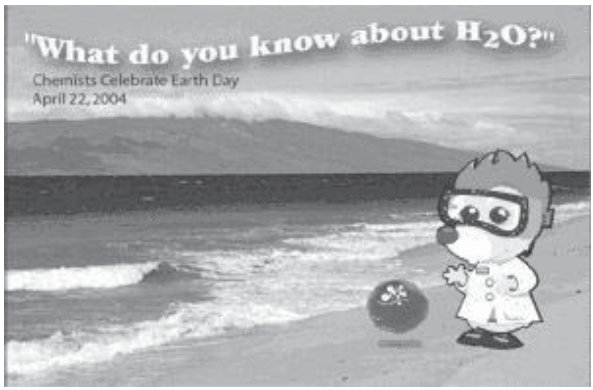
At our first board meeting this year, we approved the budget for 2004. Our spending in the last two years has exceeded our funding. We try to maintain a reserve ratio of 2 to 1. That is, the value of our long-term investments should be at least two times the annual budget. At this time we are at a ratio of 1.5+ and climbing. With the improvement in the economy, our long-term investments are improving considerably. Although The Dow Chemical Company Foundation reduced 2003 funding to 60% of 2002 funding, we are very grateful for the 2004 support with an

increase of 20% over 2003. With the current 2004 budget, the Section will be able to offer the full range of programs that have been offered in the last two years. Economic conditions in the last 2 years have taken a toll with a drop in membership nationally and locally. One of the section goals which we have this year is to increase membership 5%.

Joe Ceraso

Chemists Celebrate Earth Day, April 22, 2004

From National ACS



Members of the American Chemical Society's Committee on Community Activities invite you to participate in Chemists Celebrate Earth Day on April 22, 2004. The program is a joint effort between the ACS Committee on Community Activities, the Committee on Environmental Improvement, and the Green Chemistry Institute. Chemists Celebrate Earth Day provides volunteers with an opportunity to showcase chemistry's contributions to sustaining a healthy planet and environment as part of the annual Earth Day celebration.

The 2004 theme for Chemists Celebrate Earth Day is "What do you know about H_2O?" As part of the celebration, the American Chemical Society is sponsoring a music-video competition for students in grades K–12. The contest encourages students to produce a music video best illustrating the theme "What Do You Know About H_20?" As the unifying event, local sections are asked to participate in "Testing Rain Water," an activity designed to measure the acidity of rainwater in area communities and to compare results online to national findings. For more information, contact the ACS Office of Community Activities at 1-800-227-5558, ext. 6078. For information on Midland Section Earth Day activities, contact Gretchen Kohl, 989-496-8200, gretchen.kohl@dowcorning.com.

Students Experience Project SEED 2003

Article and photos by Peggy Hill

In her second year in the SEED program, Meghan Burleigh did her research at CMU.

Another summer of Project SEED has come and gone with three more students leaving their indelible traces of impact on the labs that hosted them. Meghan Burleigh, back for a second year of Project SEED, worked with Dale LeCaptain at Central Michigan University, while two new students, Laura Schmidt and Kristin Beach, ran investigations with Dave Karpovich at Saginaw Valley State University and Frances Fournier at Dow Corning, respectively. All three young women enjoyed research successes that in each case contributed significantly to their mentor's research goals and boosted their own self-perceptions in the process.

One of the greatest things about this program is the change in self-perception that these students undergo as the result of their SEED experience. Time and time again, as I interview students for the program, most of them ask the same question with the same sheepish hesitancy: "But I don't think I know enough—can *I* do research? Can *I* contribute?"

That glaze of doubt doesn't melt away when I reassure them that, yes, of course they will not only be capable of the work, but by the time the summer draws to a close, they'll be explaining their findings to everyone else. And, they do—the majority of our SEED students do very well, proving to themselves and everyone else that their contributions are valuable ones. It just takes some day-to-day work on their part to reach the level of self-assurance that I can't supply for them in my speeches. Our 2003 students are good examples.

Meghan Burleigh worked out a practical method for recycling salts that arise as by-products of industrial fermentation processes. She was able to lay the groundwork for an electrodialysis method under the guidance of

her mentor, Dale LeCaptain at CMU. Dale requested another student just like her for next summer—the highest praise possible for a SEED student. Frances Fournier said the same about Meghan last year after she and Meghan worked together in a SEED I experience. And now we've let her slip out of state to attend college in Arizona at Embry-Riddle College where she is halfway through her freshman year.

Laura Schmidt did research on agricultural products with Dave Karpovich at SVSU.

Laura Schmidt left her mark on the research lab of Dave Karpovich at SVSU where she explored chemical methods for turning agricultural waste into useful new materials. Her SEED I project expanded on previous work in which carboxy- methylation of corncob powder (a polysaccharide-based material) was used to create a hard, but breakable solid. Laura worked on toughening this potentially useful material by adding natural fibers to create composites and using differential scanning calorimetry to characterize them. She also looked at acylating natural starches from corn, rice, and tapioca with succinic anhydride and then processing these with soy protein to create tough, new composites. An athlete at Shepherd High School, Laura has endured a history of sports-related knee problems and the procedures necessary to deal with them, making her kind of "tough" herself.

Kristin Beach worked with Frances Fournier at Dow Corning on antifoams.

Kristin Beach loves the beach, but opted to spend her 2003 summer

immersed in antifoam instead of seafoam. Working with Frances Fournier at Dow Corning, Kristin completed an ambitious project to characterize antifoams used with acrylic coating systems. Her day-to-day vocabulary changed quite a bit as a result, leaving Kristin's mother to wonder exactly *what* her daughter was doing when words like "viscosity," "draw-down," "defoaming," and "persistence" spilled over into conversations at home. Kristin was building a valuable database of performance information that will help Dow Corning assess where and how certain products might best be used. Now she's working on completing her senior year at Midland Christian School and planning for college.

The contributions of the 2003 mentors made this program successful. Much time and effort was spent by these people to develop suitable projects and then mentor students through 8 to 10 weeks of full-time work. Of special note are the contributions of Dave Karpovich, who has mentored SEED students each year for the past four years and is now co-chairing the Project SEED committee.

SEED I Students	**Preceptor**
Laura Schmidt	David Karpovich
Shepherd H.S.	Dept of Chemistry, SVSU

Project: Preparation of Biodegradable Composite Materials from Agricultural Waste and Food Products

Kristin Beach	Frances Fournier
Midland Christian School	Dow Corning

Project: Antifoam Characterization of Acrylic Coatings

SEED II Student	**Preceptor**
Meghan Burleigh	Dale LeCaptain
Mt. Pleasant H.S.	Dept of Chemistry, CMU

Project: Electrodialysis of Sodium Sulfate into an Acid and Base

Call for Nominations

2004 Science Teaching and Education Volunteer Awards

By Petar Dvornic

Each year the Midland Section of the American Chemical Society presents awards to recognize outstanding achievement in teaching of the chemical sciences. Nominations for the 2004 awards are invited. Awards are presented for outstanding achievement in the following areas:

- Elementary Level Science Education
- Middle Level Science Education
- High School Chemistry Teaching
- College Chemistry Teaching

Candidates for these awards must be educators at schools in the five-county geographical area of the Midland Section: Bay, Gratiot, Isabella, Midland, and Saginaw Counties.

The Science Education Volunteer of the Year award is presented to an individual who makes a substantial contribution to science learning in the Midland Section through voluntary efforts.

Recipients of all awards will be selected by the Awards Committee. Nominators should write a letter indicating the award and describing the attributes of the candidate. Supporting letters from students, colleagues, supervisors, and community leaders are strongly encouraged. The deadline for nominations is **March 12, 2004.** Electronic or fax submissions are acceptable. All submissions must be accompanied by the name, position, address, and phone number of the nominator. Award recipients as well as high school and college student award recipients and Chemistry Olympiad winners will be honored at the 2004 Science Education Recognition Dinner on April 22, 2004, at the Dow 47 Building Cafeteria in Midland.

The Awards Committee greatly appreciates the efforts involved in nominating someone and thanks you for helping to recognize deserving educators in our section. *Parents: Does your child have a great science teacher? If so, consider nominating him/her and pass this flier along to that teacher's principal or section head.* Please submit nominations to:

Petar Dvornic
Chair, ACS Awards Committee
Michigan Molecular Institute
1910 W. Saint Andrews Rd.
Midland, MI 48640-2696
Fax: 989-832-5560
E-mail: dvornic@mmi.org

A list of previous recipients of the awards is provided on the next page.

	Elementary Level Science Education	***Middle Level Science Education***
1992	Karen Ziemelis	Derrell Steffen
1993	Lela Wade	Laurie Hepinstall
1994	Constance A. Dullock	JoAnn Kraut
1995	Joan Klopcic	not awarded
1996	Mark Hackbarth	Barbara J. Bibbee
1997	Denise Koppleberger, Cheryl Ruthig	Gary J. Johnson
1998	Barbara McGivern	not awarded
1999	John Clark	not awarded
2000	Sue Burtch, Robin Harshman-Rogers, Vicki Richard, Clare Jorgensen	not awarded
2001	Cathy Egerer, Amy Hindbaugh-Marr	not awarded
2002	Maureen Becker	Joel Mikusko
2003	Leon Katzinger	not awarded

	High School Chemistry Teaching	***College Chemistry Teaching***
1989	Robert Wallace	Joan Sabourin
1990	Gary Ronk	Bob Howell
1991	not awarded	Robert Kohrman
1992	John Clark, Edna Konwinski	Scott Hill
1993	Mary Irons	Ajit Sharma
1994	Jo Ann Pelkki	Laura Vosejpka
1995	not awarded	George Eastland
1996	Sandra Schafer	Martin Spartz
1997	Mary Fredell	Philip Squattrito
1998	Dale Ressler	Thomas Delia
1999	Robert Enszer	Steven Keinath
2000	Steven Kelly	James Hutchison
2001	William Stokes	Sandra Smith
2002	Robert Hansen	Margaret Hill
2003	not awarded	Dale Meier

Science Education Volunteer

1992	Gregg Young	1998	Carlton Beyer
1993	Peter Bonk	1999	William Albe
1994	Peter Moehs	2000	Karol Childs
1995	Gretchen Kohl	2001	Donald Petersen
1996	John Blizzard, Richard Van Effen	2002	Joan McMahon
1997	Marvin Tegen	2003	John Blizzard

New Chemistries

Making Sense of Antisense Technology

by Kristine Danowski

Antisense oligonucleotides are short, single-stranded (ss) synthetic nucleic acids designed to block the formation of the target protein by complementary (Watson-Crick) binding to the corresponding target mRNA or pre-mRNA. The target is translated into protein, hence it is the "sense" strand. The ss oligonucleotide blocks translation, hence it is the "antisense" strand. As long as the sequence of the gene and mRNA are known, an antisense oligonucleotide can be synthesized to bind to it. Researchers in the field theorize that RNase H, an enzyme that selectively cleaves RNA-DNA hybrids, mediates the antisense effect of ss oligonucleotides inside biological cells. The idea of antisense oligonucleotides as therapeutic agents was first developed in the 1960s and 1970s.

Antisense technology is used increasingly in various *in vitro* and *in vivo* model drugs, and is being developed as a therapeutic agent against viral infections, cardiovascular disease, inflammatory disorders, hematological disease, and cancer. More importantly, in the last few years the effectiveness of a number of therapeutic oligonucleotides has been tested in clinical trials. In 1998, FDA approved the first antisense drug, Vitravene™, for the treatment of cytomegalovirus retinitis in people with AIDS.

In order to be effective, antisense oligonucleotides need stability against nucleases, the ability for cellular uptake, a strong affinity for their target, and the ability to initiate RNAse H activity. However, some properties of antisense oligonucleotides can decrease their effectiveness. For example, their sequence, the nature of their internucleotide linkages, their polyanionic structure, and their ability to stimulate the immune system can interfere with their intended action and cause side effects. The overall effect of these ss oligonucleotides is the sum of antisense and non-antisense action.

Figure 1 shows these molecular properties schematically. An effective antisense oligonucleotide (ON) should be stable to nucleases and taken up by cells. In addition, ONs should have strong affinity for the target mRNA, and should activate RNase H for RNA cleavage. Based on the nucleotide sequence and the nature of the internucleotide linkages, however, ONs display additional properties that may interfere with the specificity and mechanism of action of the ON. Two major properties are the polyanionic nature and immune stimulation. As shown in the figure in a generalized way, the polyanionic nature and immune stimulation may produce biological activities and side effects that compromise the specificity and action of a given oligonucleotide.

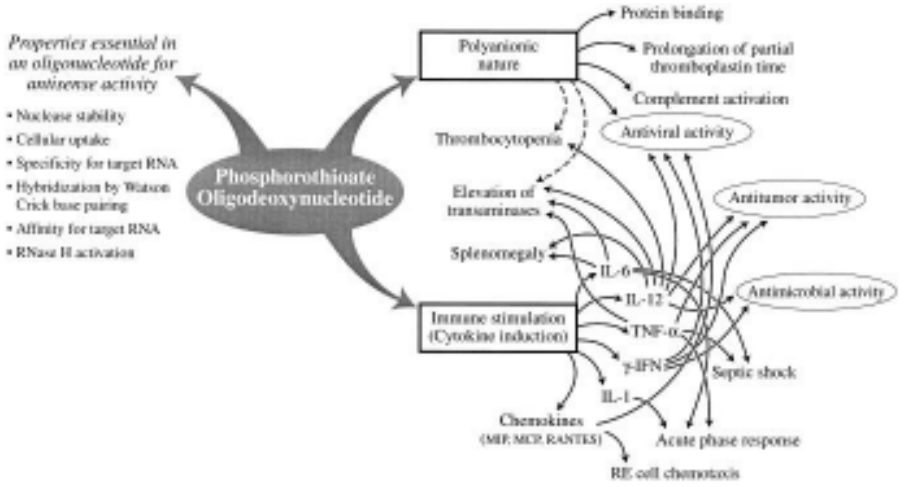


Figure 1. Factors affecting the mechanism of action of antisense oligonucleotides. IFN, interferon; IL, interleukin; MCP, monocyte chemoattractant protein; MIP, macrophage inflammatory protein; RANTES, regulated-upon-activation and normal T-cell expressed and secreted; RE, reticulo-epithelial. Reproduced from Agrawal (1999), with permission of the copyright holder, Elsevier Science, Amsterdam.

The first antisense oligonucleotides were synthesized in the 1960s as unmodified phosphodiesters. These phosphodiesters often contained alkylating or other types of reactive groups to generate irreversible binding to the target sequence in order to prevent the polymerase or ribosome from reading through the target DNA or RNA. However, oligonucleotides with naturally occurring phosphodiester bonds were found to degrade rapidly *in vitro* and *in vivo* and to be poorly taken up by living cells. To solve these problems, backbone modifications, which involve changes to the internucleotide phosphate residue, were among the first developed. These modifications include the replacement of one of the nonbridged oxygen atoms by either a CH_3 group (methylphosphonates), an NR_2 group (phosphoramidates), an OR group (phosphotriesters), or a sulfur molecule (phosphorothioates.) Currently, phosphorothioate is the most frequently used oligonucleotide modification. Figure 2 illustrates these common modifications of antisense oligonucleotides.

Uptake of phosphorothioate oligonucleotides by living cells is as poor as that of unmodified phosphodiester oligonucleotides. In addition, the complexes between phosphorothioate oligonucleotides and mRNA are less stable than those between the corresponding phosphodiester oligonucleotide and RNA. However, phosphorothioates are more resistant to nuclease cleavage than phosphodiesters. Also, when complexed to mRNA, phosphorothioates stimulate cleavage by RNase H as efficiently as

unmodified phosphodiesters. These latter two characteristics give phosphorothioates the edge. Currently the vast majority of antisense oligonucleotides in clinical trials are phosphorothioates.

To be clinically effective, antisense oligonucleotides must have appropriate design and chemistry. These affect not only target hybridization, but also extra- and intracellular biological stability, their ability to avoid undesirable cellular compartmentalization, and their efficient uptake and accumulation. The main barrier is achieving systemic delivery of the oligonucleotide to the correct target in the desired time frame to achieve target gene modulation. For systemic delivery to be successful, antisense oligonucleotides must avoid degradation and protein binding long enough in the blood to ensure that they reach target cells intact and in sufficient quantities to attain the desired level of gene modulation when they reach their intracellular target mRNA.

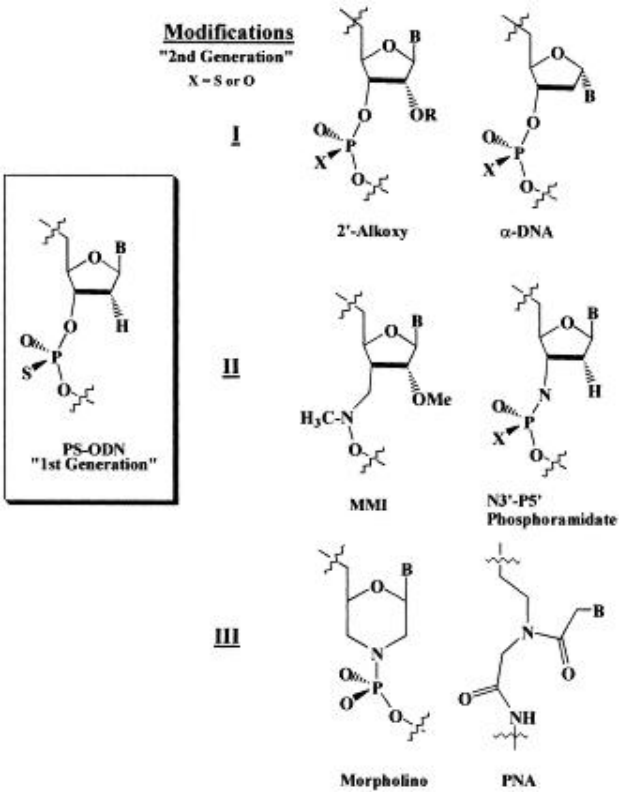


Figure 2. Structure of some antisense oligonucleotide modifications. PS-ODN, phosphorothioate oligodeoxynucleotide; MMI, methylene(methylimino); PNA, peptide nucleic acid. Reproduced from Baker and Monia (1999), with permission of the copyright holder, Elsevier Science, Amsterdam.

The major obstacles to widespread application of antisense oligonucleotides as therapeutic agents are targeting to the specific cell of interest and intracellular delivery. Free oligonucleotides have a half-life of 0.5–1 h when administered directly. Therefore, various delivery methods, such as attaching ligands or linkers, liposomes, dendrimers, carrier peptides, direct central nervous system, or oral administration are under develop-

ment. Currently, cationic liposomes are the most widely used delivery method. They are composed of positively charged lipid bilayers that are complexed to anionic oligonucleotides. Features of cationic liposomes that make them versatile and attractive for DNA delivery include simplicity of preparation, the ability to complex large amounts of DNA to transfect many different cell types, and low toxicity. In addition, cationic liposomes have a high affinity for most negatively charged cell membranes. Currently they represent the most successful delivery method for antisense oligonucleotides. The next few years should see more antisense drugs approved as researchers solve stability and delivery problems.

Further Reading

1. Agrawal, S. Importance of nucleotide sequence and chemical modifications of antisense oligonucleotides. *Biochim Biophys Acta. Gene Structure and Expression* 1999, *1489*, 53.
2. Baker, BF and Monia, BP. Novel mechanisms for antisense-mediated regulation of gene expression. *Biochim Biophys Acta. Gene Structure and Expression* 1999, *1489*, 3.
3. Gillis, J. After years of failure, a code for cures?; DNA advances lift promise of antisense technology. *The Washington Post*, June 24, 2003, page E01.
4. Pirollo, KF *et. al*. Antisense therapeutics: from theory to clinical practice. *Pharmacology & Therapeutics* 2003, *99*(1), 55.
5. Stein, CA, ed. *Perspectives in Antisense Science*. Boston: Kluwer Academic Publishers, 1999.

Bringing Science to Life in 2003

By Mike Ferrito

The National Chemistry Week activities reported in the December 2003 issue of *The Midland Chemist* are just a small part of the program's agenda. Since 1995, 2,500 teachers have attended workshops such as those offered in 2003:

"Bringing Science to Life in the Classroom" includes 16 hands-on demonstrations using "accessible" chemicals. This workshop is aligned with Michigan science education objectives and the level of science can be adjusted to grade level (K-12). Workshops and participation in 2003 included U. of M. Flint (19), Shepherd (51), West Branch (24), and Mt. Pleasant (32).

"Clowning Around with Polymers" includes 12 hands-on demonstrations using "accessible" chemicals and plastics. This workshop is also aligned with Michigan science education objectives and the level of science can be adjusted to grade level (K–12). Supplemental supplies are provided by the American Plastics Council. Workshops and participation in 2003 included Ravenhill (15), Bay Arenac (8), West Branch (34).

In summary, Project Science Literacy 2003 highlights include:

- Nine teacher training session with 161 participants
- National ACS Earth Day award received for West Branch activities
- Phoenix Award Honorable Mention for NCW activities in West Branch
- NCW activities were mentioned in a recent *C&E News* article
- Provided PlastiVan to six area schools in coordination with NCW and teacher training session
- Accumulation and distribution of chemistry equipment

If you have questions about the program or are interested in joining our enthusiastic group of volunteers, please contact Mike Ferrito, m.ferritto@dowcorning.com, 989-496-3244.

Sponsors of Project Science Literacy include ACS Midland Section, Delta College, Alden B. Dow Museum of Science and Art, Mid-Michigan Section-Society of Plastics Engineers, Mid-Michigan Section-American Institute of Chemical Engineers, The Dow Chemical Company, and Dow Corning Corporation. Volunteers include:

John Blizzard	Mike Ferritto	Todd Hogan
Gretchen Kohl	Janet Smith	Gina Malczewski
Marvin Tegen	Paul Popa	Claudia Douglas
Joan Sabourin	Dick Skochdopole	Joe Kchodl
Charles Roth	Barbara Roth	

In Past Issues of *The Midland Chemist*

By Wendell L. Dilling, Midland Section Historian

- **30 Years Ago This Month**—Theodore W. Selby, president of Savant, Inc., has been appointed chairman of Research and Development Div. VII of ASTM Committee D-2. This division will develop tests on lubricants, fuels, and hydraulic fluids used in transportation and industry.
- **20 Years Ago This Month**—Bob Howell, in his Chairman's Corner column, stated that recently much has been written about the deplorable state of science education in our K–12 schools. The consensus would seem to be that 1) this situation poses a long-range threat to our national security and well-being, 2) rectification of the situation will be a long process, and 3) recovery efforts should be initiated and pursued as vigorously as possible.
- **10 Years Ago This Month**—The 75th anniversary of the formation of the Midland Section occurred in 1994. The following was written in a feature article, "Formation of the Section—The Initial Years": The year 1919 saw the beginnings of the Midland Section of the ACS in the form of an updated petition to the national ACS Council for a section charter. On December 8, 1919, the president of the ACS granted, in writing, a charter to the Midland Section. Herbert H. Dow was elected as the first chairman of the Section and served until June 1921.

Important Dates on the ACS Midland Section Calendar

Feb. 9	Midland Section board meeting, Delta College Midland Center, Rm. 12, 7:00 p.m.
Feb. 9	Deadline for March issue of *The Midland Chemist.*
Feb. 16	Prof. Ali Zand, Kettering University, title to be announced, CMU Seminar Series, Central Michigan University, Dow 175, 4:00 p.m., reception preceding in Dow 264 at 3:30 p.m. (Anton Jensen, 989-774-3125).
Mar. 1	Deadline for April issue of *The Midland Chemist.*
Mar. 8	Midland Section board meeting, Delta College Midland Center, Rm. 12, 7:00 p.m.
Mar. 12	Deadline for submitting nominees for teaching and volunteer awards (Petar Dvornic, dvornic@mmi.org)
Mar. 22	Dr. Josh Coon, University of Virginia, "Novel Methods for Proteomic Analysis of Post-Translational Modifications" (Alumni Lecture), CMU Seminar Series, Central Michigan University, Dow 175, 4:00 p.m., reception preceding in Dow 264 at 3:30 p.m. (Anton Jensen, 989-774-3125).

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