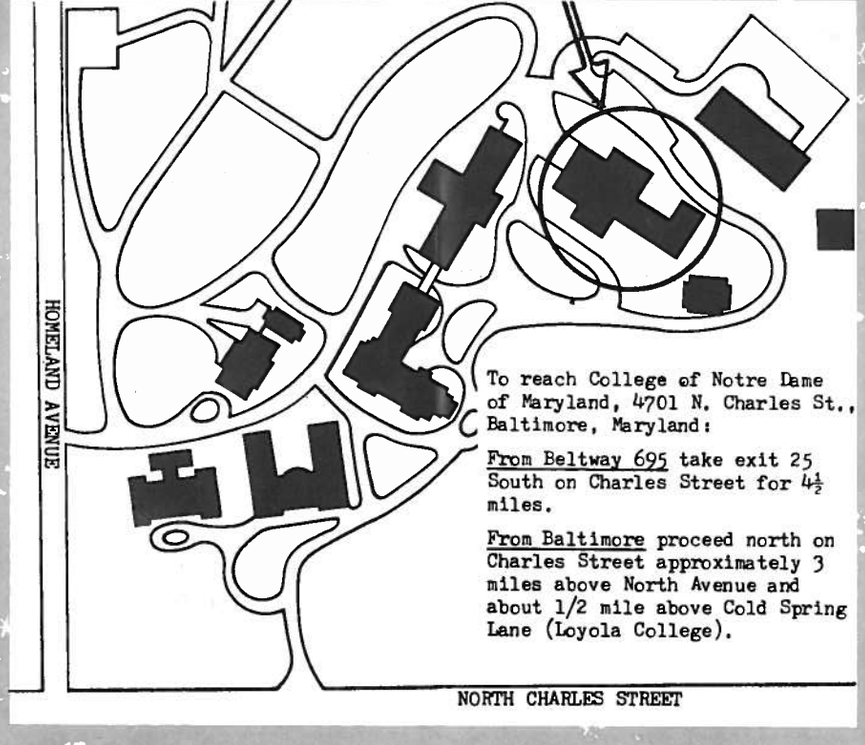
THE CHESAPEAKE CHEMIST

MARYLAND SECTION
AMERICAN CHEMICAL SOCIETY

VOL. XXXI DECEMBER, 1975 NUMBER 9

1975 MARYLAND SECTION AWARD
DR. BENJAMIN WITTEN

PLACE: College of Notre Dame



To reach College of Notre Dame of Maryland, 4701 N. Charles St., Baltimore, Maryland:

From Beltway 695 take exit 25 South on Charles Street for 4½ miles.

From Baltimore proceed north on Charles Street approximately 3 miles above North Avenue and about 1/2 mile above Cold Spring Lane (Loyola College).

DATE: December 17, 1975

MARYLAND SECTION NEWS

HOOD COLLEGE

Dr. Sharron W. Smith is a new member of the Chemistry faculty. Doctor Smith is a biochemist, Ph.D. in biochemistry from the University of Kentucky, who has worked at NIH since obtaining her degree.

Enrollment in general, and in organic, chemistry at Hood is at an all-time high this year. This increase appears to be related to the current emphasis at Hood on career-oriented programs.

Phyllida M. Willis

THE JOHNS HOPKINS UNIVERSITY

At the Opening Ceremony of The Johns Hopkins University Centennial Year it was announced that Dr. Emil H. White has been awarded the D. Mead Johnson Chair in Chemistry and Dr. Alex Nickon has been awarded the Vernon K. Krieble Chair in Chemistry.

Lorraine Torgerson

TOWSON STATE COLLEGE

Our program received accreditation by the American Chemical Society this Summer.

After reviewing hundreds of applications we have hired three new faculty: Robert L. Caret, Ph.D. - Univ. of New Hampshire, Instructor, Organic Chemistry; Lynn B. Rodewald, Ph.D. - Iowa State University, Assistant Professor, Organic Chemistry; Nordulf W. G. Debye, Ph.D. - Cornell Univ., Visiting Instructor, Physical-Inorganic Chemistry.

This Spring we will be moved into our new wing. In addition to our regular day program we are offering the following evening courses: Chemical and Bacteriological Studies on Water Pollution, Physical Chemistry I (Thermodynamics), Research, Special Problems, Essentials of Biochemistry, Organic Chemistry I and II, Essentials of Organic Chemistry, General Chemistry I and II and Chemistry for Non-Scientists. We welcome evening Chemistry majors and other students. Phone (301) 321-3058.

Several of our faculty members were promoted this year: Dr. David Larkin to Assistant Professor, Dr. Linda M. Sweeting to Associate Professor, Dr. Joseph J. Topping to Associate Professor and Dr. Alan S. Wingrove to Associate Professor.

Linda M. Sweeting

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TEACHING POSITIONS AVAILABLE

CHEMISTRY - PART-TIME

Two or three part-time teaching opportunities are expected beginning this spring and probably continuing for some time in the future. Teaching may include both regular courses and a technical training program. M.S. with teaching experience desired, in some combination of organic, inorganic and analytical (instrumental). Must be available for substantial assignments during the day, as well as possible evening teaching. Send resume to;

Chairman, Div. of Science and Math
Essex Community College
Baltimore, Maryland 21237

TEAR-OUT DINNER RESERVATION FORM

Enclosed is $ _____ ($5.50 per person)* for dinner reservations at the College of Notre Dame for the following persons**.

NAME (Please print or type)	AFFILIATION

*Please make checks payable to Maryland Section, ACS, and mail together with reservation form to Mr. John Kolbe, Martin-Marietta Laboratories, 1450 S. Rolling Road, Baltimore, Maryland 21227. Or phone 247-0700, ext. 283 or 261. ASK FOR RESERVATIONS.

**Return by Friday, December 12.

THE CHESAPEAKE CHEMIST

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DECEMBER MEETING

DR. BENJAMIN WITTEN

DATE:

Wednesday, December 17, 1975.

PLACE:

College of Notre Dame of Maryland
4701 N. Charles Street
Baltimore

SPEAKER AND TOPIC:

8:30 p.m. - Le Clerc Hall
Auditorium

THE MARYLAND CHEMIST AWARD
Dr. Benjamin Witten,
Edgewood Arsenal
"The Design of Alkalating Agents with Varying Degrees of Enzymatic or Hydrolytic Stability for use in Chemotherapy"

SOCIAL HOUR:

There will be a social hour after the meeting. Refreshments will be served.

COCKTAILS AND DINNER:

Doyle Building Dining Room
College of Notre Dame of Md.
Cocktails 6:30 - 7:15, courtesy
Beckman Instruments

Hot buffet dinner (7:15) $5.50 per person. Retired chemists, students, and their spouses may attend the dinner at $3.50 each. Reservations are necessary for the dinner.

ACS RESERVATIONS
c/o Martin-Marietta Laboratories

USE THE CONVENIENT FORM THAT
APPEARS ELSEWHERE IN THIS ISSUE

(Or phone: 247-0700, x283 or 261.)

It is not necessary to be a member of the American Chemical Society to attend the dinner or the talks; the talks may be attended without going to the dinner. You are invited to bring your spouse and friends to both the dinner and the meeting.

DR. BENJAMIN WITTEN

Dr. Benjamin Witten was born in Baltimore, Maryland on October 4, 1916. He received his Ph.D. in Organic Chemistry from The Johns Hopkins University in 1940 and then joined the staff of the Technical Command at Edgewood Arsenal, Maryland as a Junior Chemist. He progressed steadily through various positions of responsibility to that of Chief, Chemical Research Division in 1956 and in the reorganization of 1966 became Chief, Organic Chemistry Department (later Branch).

In 1955, he was appointed Assistant in Surgery (Part Time), The Johns Hopkins University School of Medicine, Baltimore, Maryland, a position he holds until the present time. In 1959, he was appointed Research Associate, Division of Surgical Research, Department of Surgery, Sinai Hospital, Balto., Maryland and held this position until June 1972. In July 1972, he was appointed Research Associate, Department of Research Oncology and Cell Biology at Sinai Hospital.

He spent one year (1966-1967) at the Hebrew University under a Secretary of the Army Research and Study Fellowship.

Since his employment at Edgewood Arsenal in 1940, Dr. Witten has been engaged in a program of research in organic chemistry and toxicology leading to the discovery of physiologically active compounds (representing a spectrum of biological effects) and a study of their chemical properties. Areas of investigation include:

1. Research in synthetic organic chemistry with the objective of developing new types of physiologically active compounds.
2. Primary screening in animals of suggested compounds to determine those that should receive detailed biological study for potential testing in man.
3. Development of improved animal screening procedures to insure that animal test methods reflect expected behavior in humans.
4. A study of the chemical properties of physiologically active compounds deemed to be of special interest.

In this program he has been assigned progressively increasing responsibilities. In 1953, he became responsible for the establishment, administration and technical direction of a research program involving a staff of approximately fifty personnel. These consisted of organic chemists, pharmacologists, clerical and sub-professional personnel. In 1959, a multimillion dollar contract program was instituted with industry and universities to supplement the in-house effort. At its peak, more than 200 professional and sub-professional personnel were working under contract on one aspect or another of the program. Dr. Witten organized the technical aspects of these contracts and coordinated the work with the in-house effort to avoid duplication and to obtain the maximum benefit from them.

Specifically, Dr. Witten and his group have made contributions in the following fields:

1. Structure-activity relationship studies of
   a. organophosphorus anticholinesterases,
   b. atropine substitutes (as anticholinergics),
   c. phenothiazine tranquilizers,
   d. morphine substitutes and antagonists,
   e. tetrahydrocannabinols,
   f. chemicals for riot control.
2. Development of synthetic routes for isotopically labeled organophosphorus anticholinesterases for biochemical studies.
3. Development of chemical procedures for the detection and identification of selected air pollutants.
4. Process development studies.
5. Development of toxicity screening procedures in mice and rabbits.

Dr. Witten has also been involved since 1955 in a program of designing mustards and other alkylating agents for use in cancer chemotherapy. In this program, he has collaborated with Dr. Arnold M. Seligman, formerly Surgeon-in-Chief at Sinai Hospital and now Chief, Department of Research Oncology and Cell Biology.

Dr. Witten is a member of the American Chemical Society, the American Association for Cancer Research, the New York Academy of Sciences, and the Army Ordnance Association.

Dr. Witten has served on NIH study panels for the evaluation of proposed grants. In this connection he has made site visits to investigate the adequacy of the laboratory facilities

He has served as evaluator of research proposals submitted to the Army Research Office. These proposals have come from all over the world. In several Army Research Contracts, he has served as the primary scientific liaison.

He has served as an official US representative at International Conferences and has collaborated with his counterparts in these countries.

He has presented scientific papers at national scientific societies, such as the American Chemical Society and American Association for Cancer Research (AACR). In 1963, he served as chairman of one of the chemical sections of AACR.

He has participated in several Army Science Conferences at which papers coauthored by him were presented. His paper in 1964 won a Certificate of Outstanding Achievement.

He served as expert witness and technical adviser in 1971 at a trial of a case in which the Government was charged with infringement of a patent on the meprobamate tranquilizing drug.

Dr. Witten received the following awards and honors: Meritorious Civilian Service Award (1946); Department of the Army Certificate of Achievement (1962); Certificate of Outstanding Achievement at the West Point Army Science Conference (1964); Sustained Superior Performance Award (1966); Secretary of the Army Research and Study Fellowship Award (1966); Sustained High Quality Performance Award (1971); Meritorious Civilian Service Award (1972).

THE DESIGN OF ALKYLATING AGENTS WITH VARYING DEGREES OF ENZYMATIC OR HYDROLYTIC STABILITY FOR USE IN CHEMOTHERAPY

Since World War II mustargen, an alkylating agent, has played an important role in the chemotherapy of certain neoplasms. Its therapeutic dose, however, is close to its lethal dose. A program was undertaken in collaboration with Dr. Arnold Seligman of Sinai Hospital to design more suitable alkylating agents utilizing both enzymatic and chemical approaches.

In the enzymatic approach, the assumption was made, as indicated by histochemical studies of Seligman and coworkers, that some tumor cells are deficient in aliesterases. Recently Dr. Seligman has shown that prostate and prostate carcinoma cells have a high concentration of a unique acid phosphatase. Alkylating agents containing functional groups susceptible to esterase attack were designed with the intent that they be more toxic to the cancer cells than to the host cells. These were syntheisized and evaluated. The more interesting compounds were tested clinically.

In the clinical approach, attention was focussed on the fact that the bone marrow is generally more sensitive to the lethal effects of alkylating agents than are most other parts of the body. A hydrolytically unstable alkylating agent was sought that could be injected intra arterially into the blood servicing the tumor sites. If properly designed, it would remain essentially intact at the tumor site but would degrade rapidly to harmless products before it reached the bone marrow. In this program, alkylating agents were designed and tested that had half lives at pH 7.4 varying from a fraction of a second to hours. Some of the short life compounds have been given clinically.

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