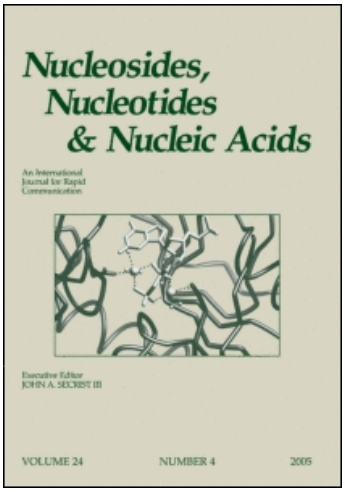

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Introduction

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NUCLEOSIDES, NUCLEOTIDES & NUCLEIC ACIDS
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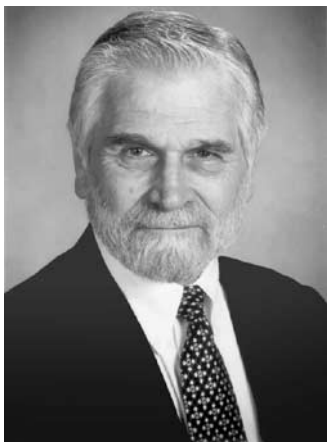
Introduction



Leroy B. Townsend

A 70TH BIRTHDAY TRIBUTE TO LEROY B. TOWNSEND

I first met Leroy at a New York Academy of Sciences conference entitled ''Chemistry, Biology, and Clinical Uses of Nucleoside Analogs'' on September 4, 1974. I was sitting at a counter in a small New York City restaurant having breakfast on the first day of the meeting when a very friendly extrovert with long dark hair and beard sat down next to me and asked if I were attending the conference. After introducing ourselves and chatting for a few minutes, I realized this Townsend guy was one of the invited speakers and that he must be somewhat well known even though I had never heard of him! At that time I wasn't particularly interested in getting to know a chemist from Utah but since he seemed to know a lot of people at the meeting, I asked him if he could point out Lee Bennett to me. Lee was someone I did want to meet because he had several drug-resistant cell lines in which I was interested. He did so but it wasn't until later in the meeting and after talking with Lee that I realized this friendly chemist was already quite well known and respected for his considerable work in heterocyclic and nucleoside chemistry.

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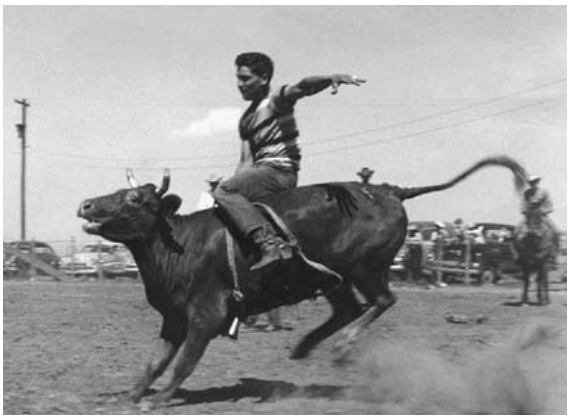
Over the next few years I noted with interest that many of the nucleosides that Townsend's group synthesized were structurally related to vidarabine (arabinosyladenine) and other nucleosides that I studied as a biochemist working with antivirals. Consequently it was with considerable excitement that I supported the effort to recruit Leroy to the University of Michigan in 1979. Since then, it has been my privilege to work closely with him on collaborative research projects and to be his colleague in the Interdepartmental Graduate Program in Medicinal Chemistry which he chaired for 20 years. In light of his many accomplishments it is altogether fitting and proper that we dedicate this issue of *Nucleosides, Nucleotides & Nucleic Acids* to Leroy because his entire career has been dedicated to the application of organic chemistry for the discovery and development of novel heterocycles and nucleosides as potential drugs.

Leroy was born in west Texas on December 20, 1933. I have no direct knowledge of this time, but if ranch life was anything like I've heard, Leroy had a very active and demanding upbringing. And if Leroy was anything as a child like he is now, his parents also had a very active and demanding time raising him! The following picture provides some insight into his teen-age years.



L.B. Townsend, high school rodeo, circa 1948.

After graduating from high school at age 16, Leroy went to New Mexico State University in Las Cruces to major in engineering and play football. After one year, he left the university to work in the oilfields. He eventually became the derrick man who works over 100 feet in the air on a small platform, the most dangerous and demanding job in the oilfield. From west Texas a football scholarship took him to New Mexico Highlands University which was a very different life from that on top of an oil derrick. Another major change occurred when a young assistant professor by the name of Roland K. Robins told Leroy that if he didn't get the highest score in the class on the next exam in organic chemistry, he'd fail the course. This would have meant that he could kiss his football scholarship and military deferment goodbye. Never one to shy away from a challenge, that's exactly what he did. Leroy not only passed the course, he also found a mentor and friend for life in R.K. Robins. He also discovered his passion for organic chemistry. During this time he made the best decision of his life when he married Sammy Beames with whom he celebrated their 50th anniversary this past September.

Leroy completed his B.S. degree at New Mexico Highlands University in 1955 with a double major in chemistry and mathematics. He then decided to pursue a graduate degree

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in chemistry under R.K.'s mentorship, completing his M.S. in chemistry in 1957. After graduation he volunteered for duty in the U.S. Navy's Officer Training School and reported to Newport, RI. Following commissioning as an officer, he volunteered for the very challenging one-year training program to become a deep sea and SCUBA diver and underwater ordnance disposal expert. He was assigned to the U.S.S. Mulberry which was an ordnance recovery and diving ship with the only floating double lock decompression chamber on the West Coast. The following photograph shows Leroy and some of the explosive ordnance disposal (E.O.D.) divers he commanded while on the Mulberry.

L.B. Townsend (center, kneeling) and his dive team, deck of U.S.S. Mulberry, *circa* 1958 (left picture) and relaxing shore side some time later (right picture).

His initial duties were restricted to being the E.O.D. and diving officer. However—following a pattern to be repeated several times in his professional career—even though Leroy came aboard as the lowest ranking officer (ensign), he served in essentially every department on board the ship and left the Navy in 1960 as the ship's commanding officer.

L.B. Townsend, Commanding Officer, U.S.S. Mulberry.

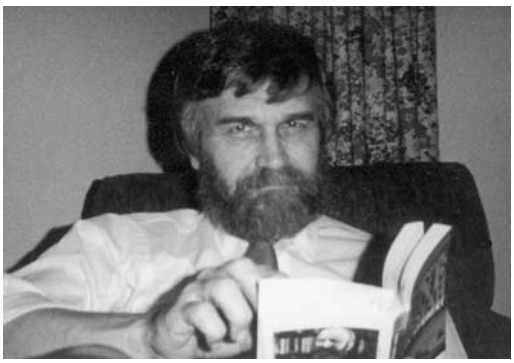
Following his four-year Navy career, Leroy rejoined R.K. Robin's research group then at Arizona State University. He obtained his Ph.D. from Arizona State in 1965 and went with R.K. to the University of Utah in 1965 as an assistant research professor and the assistant director of the Cancer Chemotherapy National Service Center at Utah.

Leroy B. Townsend and Roland K. Robins, University of Utah, 1967.

In 1967 he was appointed as an Assistant Professor of Medicinal Chemistry and an Assistant Research Professor of Chemistry. In 1971 he was promoted to the associate level and in 1975 to the levels of full professor in medicinal chemistry and chemistry. In 1979 he made the second best decision of his life and moved to the University of Michigan as Professor and Chair of Medicinal Chemistry in the College of Pharmacy and Professor of Chemistry in the College of Literature, Sciences and the Arts.

Whether at Arizona State, Utah, or Michigan, Leroy's scholarship has earned him worldwide recognition and a reputation for excellence in the design and synthesis of heterocyclic compounds as potential agents to treat cancer and infectious diseases. Cancer research is the area in which Leroy first was recognized for major contributions. He and his collaborators were the first to chemically synthesize the naturally-occurring nucleoside antibiotics tubercidin, toyocamycin and sangivamycin. The latter compound was advanced to clinical testing. He and his group also were the first to characterize and synthesize more than ten other nucleoside antibiotics including showdomycin the first in a new class of compounds, the C-nucleoside antibiotics. This work included not only synthetic chemistry but also the development of new physical–chemical

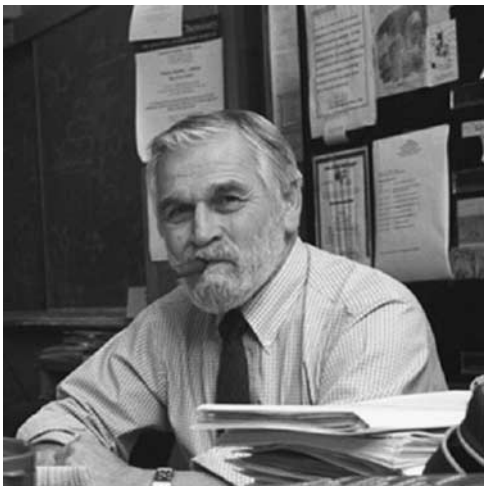
techniques for structure elucidation and proof. Other work in the nucleoside area led to the synthesis of triciribine, a compound which was advanced to phase II clinical investigations for ovarian cancer.



Relaxing (?) at home during days in Utah. (*View this art in color at www.dekker.com.*)

Leroy also has been successful in research aimed at developing drugs to treat parasitic diseases. His studies sponsored by the World Health Organization (W.H.O.) led to the design and synthesis of a series of benzimidazole heterocycles which are active against filariasis—a disabling parasitic disease prevalent in tropical climates. The compounds which Leroy has discovered are very active in low dosage and are the only compounds known which are active against both the juvenile and adult forms of the worm.

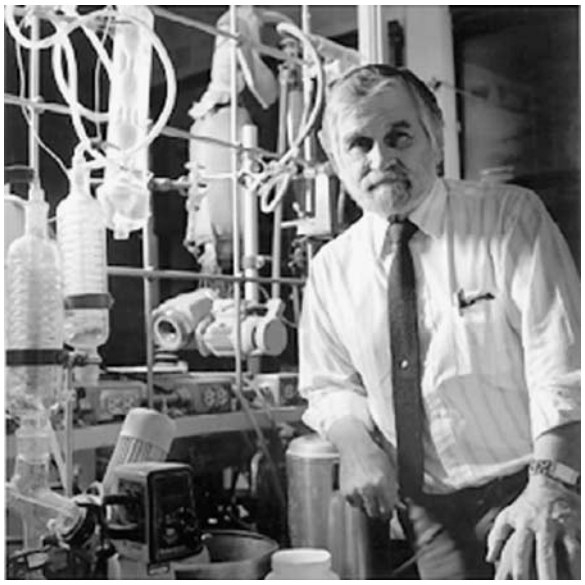
Recent significant progress also has been made in Leroy's work with antiviral drugs. In collaboration with me, two series of compounds have been discovered which are highly active against human cytomegalovirus (HCMV)—the virus which causes



Leroy B. Townsend, Michigan days.

retinitis in AIDS patients, pneumonitis in bone marrow transplant patients, and is one of the leading causes of birth defects in the U.S. These new compounds are active against HCMV at non-toxic concentrations and are active against drug-resistant strains of the virus because they act by a new mechanism. In collaboration with colleagues at Glaxo Wellcome Co., an analog of these compounds has been made which has undergone successful preclinical evaluation and now is resuming phase II clinical trials. In addition to these compounds, another compound (triciribine, mentioned above) has been found to be active against HIV and to act by a new mechanism.

For a single individual to discover drugs which may be used to treat a diversity of diseases such as cancer, filariasis, herpes, and AIDS is significant and unusual. These discoveries are a result of hard work and a broad diversity of talents; namely, Leroy's ability to lead and inspire students and collaborators plus his considerable knowledge in both chemistry and relevant biology.



Townsend ''prep'' lab, University of Michigan.

During this time of great productivity in research and scholarship, Leroy also has been very active in service to local, national, and international scientific groups and organizations. He was co-founder of the International Roundtable on the Chemistry and Biological Activity of Nucleosides & Nucleotides, and co-founder of the International Society of Heterocyclic Chemistry. He has served on the board of directors of the International Society for Antiviral Research and as Chair of the Pharmaceutical Sciences section of the American Association for the Advancement of Science. He also was president of the International Society of Heterocyclic Chemistry, and has held virtually every elected position—including president—of the Division of Medicinal

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Chemistry of the American Chemical Society. He also has served on grant review bodies and study sections for the National Science Foundation, the American Cancer Society, the National Institutes of Health (in both bioorganic chemistry and in medicinal chemistry), the Canadian Heritage Foundation, NATO, the World Health Organization, the World Health Organization steering committee on the chemotherapy of malaria, and the advisory committee on AIDS to the director of the National Institute of Allergy and Infectious Diseases.

Leroy is a member of the editorial board of several journals in heterocyclic and nucleoside chemistry, as well as the editor and author of the series of books on organic synthesis entitled, ''Improved and New Synthetic Procedures, Methods, and Techniques'' and he has been the organizer of local and national meetings as well as international symposia. His most recent effort was organizing and chairing the 25th National Medicinal Chemistry Symposium which was held at the University of Michigan in 1996. Chairing this meeting was unique because he became the only Division member to chair two National Medicinal Chemistry Symposia, the 15th at the University of Utah and the 25th at Michigan.

Leroy speaking at his 60th birthday celebration. (*View this art in color at www.dekker.com.*)

Professor Townsend is no less energetic in his dedication to his students and to teaching. He has taught pharmacy students, undergraduate and graduate medicinal chemistry students, and undergraduate and graduate chemistry students with distinction. He has mentored research projects for undergraduate students, minority undergraduate students, M.S. students, Ph.D. students, and postdoctoral fellows. His demanding but friendly mentoring of students has resulted in exceptional training of, and exceptional performance by his students. His Saturday morning research group meetings have become a virtual institution with his students and postdoctoral fellows. These regular meetings serve as an arena for training in research methodology, discussion of research

results, review of publications and grants, and critiques of scientific literature as well as the Michigan football, basketball and hockey teams.

Townsend 50th Anniversary Celebration, Santa Fe, New Mexico, 2003. Left to right seated on wall: Rick Kopenhefer, Lisa Kopenhefer, Billy K., LBT & Sammy, Linda Townsend, Joshua T., Byron Townsend. Seated on ground: Kelly Townsend McKenna, Dana K., Cameron Issel. (*View this art in color at www.dekker.com.*)

In the last several years Leroy's accomplishments have been recognized by a number of institutions and organizations. In 1993 he received the Distinguished Faculty Award for the University of Michigan from the Michigan Association of Governing Boards of State Universities. In 1994 he received the Division of Medicinal Chemistry's Edward E. Smissman—Bristol Myers Squibb Award. In 1994 he also received the T.O. Soine Memorial Lecturer Award from the University of Minnesota and the Distinguished Alumnus Award from New Mexico Highlands University. In 1995 he became a Fellow of the American Association for the Advancement of Science. In 1997 he received an honorary Doctor of Science degree from the University of Nebraska. In 1998 he was honored for co-founding the International Roundtable on the Chemistry and Biological Activity of Nucleosides & Nucleotides and in 1999 he was the recipient of an honorary doctorate (honaris causa) of the University from the Universite Montpellier II, France. The year 2001 brought two more honors, the Gertrude B. Elion Award for Scientific Excellence from the International Society for Antiviral Research and the Volwiler Research Achievement Award from the American Association of Colleges of Pharmacy.

All these awards notwithstanding, I know what Leroy values above all is his family. Sammy, their children Lisa and Byron, and their spouses, and the grandchildren are of utmost importance to him and sources of great pride and satisfaction.

Leroy and Sammy Townsend, International Conference on Antiviral Research Banquet, Prague, Czech Republic, March 2001. (*View this art in color at www.dekker.com.*)

In closing, happy birthday my friend! I know there won't be 70 more, but I do hope and pray there will be many more to share with your family, friends, colleagues, and students—and that there are some very active antiviral compounds yet to be synthesized.

John C. Drach
Ann Arbor, Michigan
January 2004

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