RICHARD A. WALTON
Lecture in Inorganic Chemistry

A Radical Solution for C(sp^3)–C(sp^3) Bond Formation during the Biosynthesis of Macrocyclic Membrane Lipids

Professor Squire J. Booker
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Archaea synthesize isoprenoid-based ether-linked membrane lipids, which enable them to withstand extreme environmental conditions, such as high temperatures, high salinity, and low or high pH values. In some archaea, such as *Methanocaldococcus jannaschii*, these lipids are further modified by forming carbon–carbon bonds between the termini of two lipid tails within one glycerophospholipid to generate the macrocyclic archaeol or forming two carbon–carbon bonds between the termini of two lipid tails from two glycerophospholipids to generate the macrocycle glycerol dibiphytanyl glycerol tetraether (GDGT). GDGT contains two 40-carbon lipid chains (biphytanyl chains) that span both leaflets of the membrane, providing enhanced stability to extreme conditions. How these specialized lipids are formed has puzzled scientists for decades. The reaction necessitates coupling two completely inert sp^3-hybridized carbon centers, which has not been observed in nature. Here we use X-ray crystallography, high-resolution mass spectrometry, chemical synthesis, and biochemical analyses to show that the gene product of *mj0619* from *M. jannaschii*, which encodes a radical S-adenosylmethionine enzyme, is responsible for biphytanyl chain formation during synthesis of both the macrocyclic archaeol and GDGT membrane lipids.

Squire J. Booker is an Evan Pugh Professor of Chemistry and of Biochemistry and Molecular Biology, and the Eberly Family Distinguished Chair in the College of Science at the Pennsylvania State University. He is also an investigator of the Howard Hughes Medical Institute. He received a B.A. degree with a concentration in chemistry from Austin College (Sherman, TX) in 1987 and a Ph.D. in biochemistry from the Massachusetts Institute of Technology in 1994, where he was supervised by Prof. JoAnne Stubbe. He received an NSF–NATO postdoctoral fellowship to study at the Université René Descartes in Paris, France under the supervision of Dr. Daniel Mansuy, and then an NIH postdoctoral fellowship to study at the Institute for Enzyme Research at the University of Wisconsin under the supervision of Prof. Perry Frey. He joined the faculty at Penn State in 1999, and was promoted to Associate Professor in 2005, Professor in 2013, Eberly Family Distinguished Chair in Science in 2017, and Evan Pugh Professor in 2018. Booker's research focuses on natural product biosynthesis and metalloenzymology, with a particular interest in the methylation or sulfidation of unactivated carbon centers, and the use of S-adenosylmethionine and iron-sulfur clusters in enzyme catalysis. In addition to his scientific endeavors, he is heavily involved in mentoring young scientists, particularly those from groups historically underrepresented in the sciences. Among other awards, Booker received a CAREER award from the National Science Foundation, a Presidential Early Career Award in Science and Engineering (PECASE), an ACS Cope Scholar award in 2011, the Hans Neurath Award from the Protein Society in 2022, and the Merck Award and Ruth Kirschstein Diversity in Science Award in 2023 from the American Society of Biochemistry and Molecular Biology. He was elected a fellow of the American Association for the Advancement of Science in 2013, a member of the American Academy of Arts and Sciences in 2017, and a member of the National Academy of Sciences in 2019. Currently, he is an Associate Editor for the ACS journal Biochemistry and Deputy Editor for ACS Bio & Med Chem Gold.

Thursday, November 7, 2024 | **4:30 pm** | **WTHR 104**

Reception beginning at 3:45pm in the Leighty Commons

PURDUE UNIVERSITY | James Tarpo Jr. and Margaret Tarpo Department of Chemistry