American Chemical Society

National Awards Nomination Packet

Ernest Guenther Award in the Chemistry of Natural Products:2018
for: Robert Boeckman

Received: 10/27/2015 *Cycle Year: 2*

"For the development of enantio- and diastereo-controlled synthetic methodology and the creative application of that methodology to the total synthesis of stereochemically complex natural products."

NOMINATOR:

Clayton Heathcock

5235 Alhambra Valley Rd
Martinez, CA 94553-9765
UNITED STATES

Tel: (925)229-2944
Fax: (925)229-2944
Email: heathcock@berkeley.eduXXX

- Have you discussed this award nomination with the nominee? *Yes*

NOMINEE:

Robert Boeckman

Univ of Rochester Chemistry
PO Box 270216
Rochester, NY 14627-0216
UNITED STATES

Tel: (716)624-2023
Email: rkb@rkbmac.chem.rochester.eduXXX

ACS Current Member: Yes
Years of Service: 50
Date of birth: 01/01/1944
Present Position: Marshall D. Gates,Jr. Professor of Chemistry
Industry: Academia

SAFETY PROTOCOLS:

- Does the nominee employ and require good safety protocols and practices in his/her laboratory? *Yes*

SUPPORTER 1

Rick Danheiser

Massachusetts Inst of Tech
77 Massachusetts Ave Rm 18-298
Cambridge, MA 02139-4301
UNITED STATES

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SUPPORTER 2

Steven Weinreb

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Recommendation:

I am writing to nominate Professor Robert K. Boeckman, Jr. for the Ernest Guenther Award in the Chemistry of Natural Products. Bob has been a long-time leader in the development of new synthetic strategies and methodologies and the application of these methods to the stereo-controlled synthesis of complex molecules of natural origin. His efforts have encompassed a structurally diverse group of natural products including terpenes, alkaloids, polyether ionophores, macrolides, anthracyclines, complex tetramic and tetronic acids. He always attempted to incorporate tests of physical principles and theory to provide deeper insights into the design and implementation of stereo-controlled synthetic reactions.In the area of terpenoid synthesis, Bob focused on the novel structures of the sesterterpenoids which contain an array of medium ring substructures. He pioneered use of conformational theory as a tool to define direct methods for stereo-controlled functionalization of these substructures. Early on, these efforts have resulted in the total synthesis of -Gorgonene, and employed a novel stereo-controlled tandem conjugate addition-annulation to the only total synthesis of ()-Gascardic Acid.Boeckman was among the first to systematically develop the intramolecular Diels-Alder strategy and devise methodology for the stereo-controlled assembly of functionalized polycyclic rings systems, and to recognize and exploit influence of remote heteroatoms and substituents on the regiochemistry and stereochemistry of cycloadditions. These studies led to very concise, convergent synthetic routes to daunomycinone, adriamycinone and aklavinone. He was among the first to employ allylic substituents and Z-diene elements as facial stereocontrol elements in IMDA reactions and to employ acetal tethers bearing a controlling chiral center, which led to the enantioselective synthesis of ()-X-14547A, (-)-Ikarugamycin, ()-Marasmic Acid, ()-Lycorine and the major subunits of Tetronolide. He devised a conceptually clever fragmentation strategy used for the first total synthesis of the eight-membered ring sesterterpene Ceroplastol. The only total synthesis of the germacranolide ()-Eremantholide A was completed by the Boeckman group utilizing a novel application of the Ramberg-Bcklund rearrangement as a ring contraction to create the highly functionalized 10-membered ring.Bobs efforts extend to synthesis of nitrogen containing natural products including alkaloids. He extended cyclopropyl imine rearrangement devising the milder, more versatile cyclopropyl iminium ion analog, that along with a novel intramolecular Diels-Alder cycloaddition, led to the first total synthesis of the amaryllidacea alkaloid Lycorine.Bob was the first to generalize and exploit the metalation of cyclic vinyl ethers demonstrating that these versatile intermediates have great value in synthesis. These efforts led to a novel, enantiospecific total synthesis of the spiroketal ionophore Calcimycin. He has developed novel masked carbonyl synthons delivered via their derived diorganocuprate complexes and was the first to prepare and utilize copper hydride "ate" complexes for conjugate reduction of carbonyl compounds. More recently, Boeckman has developed a novel approach to 1,2-diazadienes and pyrazolones via a novel palladium catalyzed [4 1] carbonylation sequence. Bobs long term interest in applications of pericyclic reactions to synthesis has led to novel applications of the anionic oxy-Cope rearrangement to the concise, first, non-relay total synthesis of ()-Pleuromutilin, Exploration of the retroClaisen rearrangement for the enantioselective synthesis of functionalized medium ring oxygen and nitrogen heterocycles led a unique total synthesis of ( )-Laurenyne.Boeckman pioneered a new acylketene mediated macrocyclization strategy that was applied to the first total synthesis of ( )-Ikarugamycin, the macrolide (-)-Kromycin, and ( )-Tetronolide. He also pioneered new methodology for the construction complex -acyl tetramic acids, and employed it in total syntheses of (-)-Methyl Ydiginate and ()-Tirandamycin.More recently, Boeckman pioneered a family of novel camphor lactam derived auxiliaries and ligands for creation of stereocenters, including quaternary, with high enantioselectivity using Diels-Alder, alkylation, and aldol, reactions and a novel preparation of chiral mixed acetals. He used this chemistry for synthesis of ( )-Cassioside, and a general synthesis of the antitumor polyol Bengamides. A new protocol for controlling the stereochemistry of Claisen rearrangements using bidentate Lewis acids was employed as a key transformation for total synthesis of ( )-Saudin.Boeckmans contributions to asymmetric catalysis include a novel application of oxazaborolidine catalysts to enantioselective vinylogous aldol reactions as part of concise total synthesis of (-)-Rasfonin. He and his group also solved the difficult problem of enantioselective hydroxymethylation of aldehydes using TMS diphenyl prolinol catalysis and employed it in a second generation total synthesis of (-)-Rasfonin, a novel apoptosis inducer. Boeckman also very recently described the first preparation and use of chiral isoamidium salts for enantioselective Diels-Alder reactions.Accordingly I give him my strongest endorsement as an exceptionally strong candidate for the Ernest Guenther Award in the Chemistry of Natural Products.

BIOGRAPHICAL SKETCH

Provide the following information for the Senior/key personnel and other significant contributors.
Follow this format for each person. **DO NOT EXCEED FIVE PAGES.**

NAME: Boeckman, Robert K., Jr. (cell# 585-734-0014)

eRA COMMONS USER NAME (credential, e.g., agency login): rboeckman

POSITION TITLE: Marshall D. Gates Jr. Professor of Chemistry

EDUCATION/TRAINING *(Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable. Add/delete rows as necessary.)*

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	Completion Date MM/YYYY	FIELD OF STUDY
Carnegie Institute of Technology, Pittsburgh, PA	B.S.	06/1966	Chemistry
Brandeis University, Waltham, MA	Ph.D.	06/1970	Organic Chemistry
Columbia University, New York, NY	NIH Postdoctoral Fellow	09/1970-08/1972	Organic Chemistry

A. Personal Statement

The goal of this program is to provide interdisciplinary training for graduate students at the chemistry-biology interface. I have been involved in graduate education since 1972 and through the years I have collaborated with scientists from the medical school, the biology department and the pharmaceutical industry. During the last 40 years, my research group and I have published in excess of 130 research publications, reviews, and book chapters principally in areas of synthetic organic chemistry: both new synthetic methodology as well as synthesis of complex biologically relevant targets. I have a strong background in training scientists in the fields of synthetic organic and medicinal chemistry. With industrial collaborators, my group and I have also published several articles in the area of medicinal chemistry/drug development. My extensive experience as a synthetic organic chemist has also been invaluable for my position as an Associate Editor for the ACS Journal of Organic Chemistry for almost 20 years.

During my recently completed ten year tenure as Chair of the Chemistry Department, I encouraged the implementation of PLTL (Peer-Led Team Learning) in general and organic chemistry courses that was championed by the late Professor Jack Kampmeier and supported the innovative extension of the methodology into laboratory courses. The PLTL model has led to an increased sense of collaboration and involvement in the department by the faculty, and both undergraduate and graduate students.

Over the past 41 years, I have mentored more than 80 predoctoral students (including 18 women), 75 postdoctoral fellows, and several undergraduate students for their senior research theses. Many of my previous trainees are highly distinguished professors at universities all over the world, and some hold very prominent positions in industry and government. In addition to the awards that I have received for my work in synthetic chemistry over the years, including the ACS Arthur C. Cope Scholar Award, I was especially honored to receive the University of Rochester's highest award for graduate education - the William H. Riker University Award for Graduate Teaching in 2009.

I currently advise 8 graduate students, including two women and one first year student whom I co-advise with a professor in the UR Medical Center. I continue to enjoy my interactions with students at all levels, and am well

prepared and committed to successfully carry out the training and mentoring in synthetic organic and medicinal chemistry as outlined in the proposed training grant.

B. Positions and Honors

Positions and Employment:

1972-75 Assistant Professor of Chemistry, Wayne State University, Detroit, MI
1976-78 Associate Professor of Chemistry, Wayne State University, Detroit, MI
1979-80 Professor of Chemistry, Wayne State University, Detroit, MI
1980-2002 Professor of Chemistry, University of Rochester, Rochester, NY
2002-present Marshall D. Gates Jr. Professor of Chemistry
2003-2013 Chair, Department of Chemistry, University of Rochester

Professional Service and Experience

1981-present Consultant, Novartis Pharmaceuticals Inc., Cambridge MA / Emeryville CA / Basel CH / Horsham UK / Shanghai CN / Changshu CN
1982-2001 Consultant, Ricerca Corp., Painesville OH
1980-84 Member & Chairman, NIH Medicinal Chemistry Study Section
1983-88 Member, Editorial Advisory Board, *Journal of Organic Chemistry*
1986-2009 Consultant, Eastman Kodak Co., Rochester NY
1987 Vice-Chairman, Gordon Research Conference on Natural Products
1988 Chairman, Gordon Research Conference on Natural Products
1988-1996 Member, Editorial Board, *Organic Syntheses*
1996-present Member, Editorial Advisory Board, *Organic Syntheses*
1988-present Consultant, Procter & Gamble Pharmaceuticals Co, Cincinnati OH & Norwich NY
1991-2004 Consultant, Aventis Pharmaceuticals Co., Vitry Sur Seine & Romainville, France
1994-1998 Consultant, Johnson & Johnson Biological Diagnostics, Rochester NY
1997-present Associate Editor, *Journal of Organic Chemistry*, American Chemical Society
1999-2001 Consultant, Emisphere Technologies Inc. Tarrytown, NY
2000-2002 Chair-Elect, Chairman & Past Chair, Organic Div. of the Am. Chem. Soc.
2001-2003 Member, Editorial Advisory Board of the Canadian Journal of Chemistry
2001-present Member, Board of Directors, *Organic Syntheses, Inc.*
2002-2012 Vice President, *Organic Syntheses, Inc.*
2004-2008 Consultant, Sanofi-Aventis SA Vitry-sur-Seine France
2008-2010 Consultant, Onco-Tools LLC. Philomath OR
2008-present Member Ed. Adv. Board, *Targets in Heterocyclic Systems Chemistry & Properties*
2012 Consultant, Oncolyze Inc. New York, NY
2012-present President, *Organic Syntheses, Inc*

Honors

1973 Wayne State University Faculty Research Award
1976-80 Alfred P. Sloan Fellowship
1976-81 NIH Career Development Award
1979 Probus Club Academic Achievement Award of Wayne State University
1980 Timmy Lecturer, Emory University, Atlanta Ga.
1990 Japanese Society for the Promotion of Science, Fellowship
1991 The Bergmann Lecturer, Yale University, New Haven CT.
1992-93 Alexander Von Humbolt Stiftung, Senior Faculty Research Prize
1992 Upper Rhine Lecturer of the German Chemical Society
1996-2001 Marshall Gates Scholar, University of Rochester
1997 Archer Lecturer, Rensselaer Polytechnic Institute, Troy NY
2001 Lutz Lecturer, University of Virginia, Charlottesville VA
2006 American Chemical Society Arthur C. Cope Scholar Award
2008 C. L. Stevens Endowed Lectureship in Chemistry, Wayne State University Detroit MI

2009 William H. Riker University Award for Graduate Teaching
2009 Elected as Fellow to the American Chemical Society
2010 Elected Fellow of the American Association for the Advancement of Science
2010 Ireland Lecturer, University of Virginia, Charlottesville, VA

C. Contributions to Science

1. My group and I have worked in the area of complex molecule synthesis for more than 43 years. The targets have been chosen for the most part based on three major factors: 1) the novelty of the structure, 2) demonstrated significant and potentially important biological activity, and 3) amenability to the application of novel methodology which had either been developed in our laboratory or which would be developed in order to address the synthetic challenges of the target structure. We have been particularly interested in compounds with antitumor activity.

a. Boeckman, R.K., Ferreira, M.R.D., Mitchell, L.H., Shao, P.C., Neeb, M.J. & Fang, Y. (2011). Studies culminating in the total synthesis and determination of the absolute configuration of (-)-saudin. Tetrahedron, 67(51), 9787-9808. Doi 10.1016/j.tet.2011.09.067

b. Boeckman, R.K., Shao, P.C., Wrobleski, S.T., Boehmler, D.J., Heintzelman, G.R. & Barbosa, A.J. (2006). Toward the development of a general chiral auxiliary. A total synthesis of (+)-tetronolide via a tandem ketene-trapping [4+2] cycloaddition strategy. J Am Chem Soc, 128(32), 10572-10588. Doi 10.1021/Ja0581346

c. Boeckman, R.K., Clark, T.J. & Shook, B.C. (2002). The development of a convergent and efficient enantioselective synthesis of the bengamides via a common polyol intermediate. Helvetica Chimica Acta, 85(12), 4532-4560.

d. Boeckman, R.K., Weidner, C.H., Perni, R.B. & Napier, J.J. (1989). An Enantioselective and Highly Convergent Synthesis of (+)-Ikarugamycin. J Am Chem Soc, 111(20), 8036-8037. Doi 10.1021/Ja00202a066

2. A number of the important biologically-active target molecules possess medium ring substructures. We have been especially interested in synthetic approaches to such molecules/ Over the years we have completed novel synthetic routes to a number of such substances including the Cereplastol, Pleuromutilin, Laurenyne and Eremantholide.

a. Boeckman, R.K., Zhang, J. & Reeder, M.R. (2002). Synthetic and mechanistic studies of the retro-Claisen rearrangement 4. An application to the total synthesis of (+)-Laurenyne. Org Lett, 4(22), 3891-3894. Doi 10.1021/Ol0267174

b. Boeckman, R.K., Yoon, S.K. & Heckendorn, D.K. (1991). Synthetic Studies Directed toward the Eremantholides .2. A Novel Application of the Ramberg-Backlund Rearrangement to a Highly Stereoselective Synthesis of (+)-Eremantholide-A. J Am Chem Soc, 113(25), 9682-9684. Doi 10.1021/Ja00025a049

c. Boeckman, R.K., Springer, D.M. & Alessi, T.R. (1989). Synthetic Studies Directed toward Naturally-Occurring Cyclooctanoids .2. A Stereocontrolled Assembly of (+/-)-Pleuromutilin Via a Remarkable Sterically Demanding Oxy-Cope Rearrangement. J Am Chem Soc, 111(21), 8284-8286. Doi 10.1021/Ja00203a043

d. Boeckman, R.K., Arvanitis, A. & Voss, M.E. (1989). Synthetic Studies Directed toward Naturally-Occurring Cyclooctanoids .1. Total Synthesis of (+/-)-Ceroplastol-I. J Am Chem Soc, 111(7), 2737-2739. Doi 10.1021/Ja00189a070

3. We have developed and introduced over 25 new synthetic methodologies useful for the preparation of complex molecules. Among these are: 1) the metallation of cyclic vinyl ethers and their reaction with electrophiles, 2) the first demonstration of conjugate reduction by CuH as an –ate complex, 3) copper catalyzed tandem conjugate addition and annulation/alkylation, 4) introduction of the cyclopropyliminium ion rearrangement, 5) methods for introduction and use of dioxenones as acylketene precursors for cyclizations to macrocyclic lactams and lactones, 6) Contruction of strained medium mings using the Ramberg-Backlund rearrangement, 7) development and use of the camphor lactam class of chiral auxiliaries including use to prepare enantiometically pure mixed acetals chrial at the acetal center, 8) discovery and development of the templated intramolecular S_N2' cyclization for preparation of enantiomerically pure cyclobutanes, 9) development of the RetroClaisen rerangement as a route to enantiomerically pure oxepines, azepines, oxacenes and azocenes, 10) development of the first practical organocatalytic asymmetric hydroxymethylation, 11) development of the use of chiral isoamidium salts as dienophiles for asymmetric cycloaddtion reactions, 12) development of shelf stable recyclable catalysts for Cr(II) mediated chemistry.

a. Boeckman, R.K., Biegasiewicz, K.F., Tusch, D. & Miller, J.R. (2015). Organocatalytic Enantioselective α-Hydroxymethylation of Aldehydes: Mechanistic Aspects and Optimization. J Org Chem, 80, 4030-4045. Doi 10.1021/acs.joc.5b00380

b. Boeckman, R.K., Miller, Y. & Ryder, T.R. (2010). Diels-Alder Reactions of Cyclic Isoimidium Salts. Org Lett, 12(20), 4524-4527. Doi 10.1021/Ol101831b

c. Boeckman, R.K., Genung, N.E., Chen, K. & Ryder, T.R. (2010). Synthetic and Mechanistic Studies of the Aza-Retro-Claisen Rearrangement. A Facile Route to Medium Ring Nitrogen Heterocycles. Org Lett, 12(7), 1628-1631. Doi 10.1021/Ol100397q

d. Boeckman, R.K. & Hudack, R.A. (1998). A variant of the Takai-Utimoto reaction of acrolein acetals with aldehydes catalytic in chromium: A highly stereoselective route to anti diol derivatives. Journal of Organic Chemistry, 63(11), 3524-3525.

4. We have worked in the area of bisphosphonate chemistry preparing a licensed drug candidate for treatment of osteoporosis and a tool useful to undertand the mode of binding of bis phosponate drugs in the active site of farnesyl pyrophosphate synthase thus inhibiting osteoclast function responsible for bone resporption. More recently as part of a collaboration prepared a potent new antifungal drug candidate active against *Candidia sp.* and *Cryptococcus sp.* with a novel mode of action. We have also been participating in collaborations aimed at the development of bis-phosphonate drug conjugates as prodrugs for bone-targeted delivery of a variety of drugs including inhibitors of rheumatoid arthritis therapy mediated bone resorption, antitumor drugs, and epigenetic inhibitors. The first example of these conjugates have been prepared and have shown activity *in vitro*.

a. Boeckman, R.K., Miller, Y., Savage, D. & Summerton, J.E. (2011). Total synthesis of a possible specific and effective acid-targeted cancer diagnostic, a camphor derived bis-N-oxide dimer. Tetrahedron Letters, 52(17), 2243-2245. Doi 10.1016/j.tetler.2011.01.028

b. Ebetino, F.H., Dunford, J.E., Song, X., Boeckman, R.K., Roze, C., McKenna, C.E., Russel, R.G. & Barnetts, B.L. (2007). Stereochemical evidence of the mode of binding of nitrogen containing bisphosphonates in farnesyl diphosphate synthase. Bone, 40(6), S307-S308.

Complete List of Published Work:
http://scholar.google.com/citations?hl=en&user=dcKSpJEAAAAJ&cstart=40&sortby=pubdate&view_op=list_works

D. Research Support

Ongoing Research Support

UR Marshall D. Gates Professorship Research Fund — Boeckman(PI) — 2001-present
Goal: Unrestricted support

ACS Arthur C. Cope Scholar Award — Boeckman(PI) — 2006-present
Goal: Unrestricted support

RO1 AI097142-03 — Krysan (PI) — 07/01/2012-06/30/2017
Phosphoinositide-dependent kinase-1 as an antifungal drug target
Goal: Development of novel fungal specific Kinase inhibitors for the treatment of resistant fungal infections
Role: co-PI

1R01-1AR063650-02S1 — Xing(PI) — 05/01/2015-04/30/2016
NIH/NIAMS
Study of osteoblast regulation in TNF-mediated bone loss-generating bone targeted proteasome inhibitor
Role: co-PI

1RO1-AG046320-01 — Seluanov(PI) — 09/01/2013-08/31/2018
Regulation of Genome Stability by SIRT6
Role: Senior Key Person

Recently Completed Research Support

UR Drug Development Delivery Pilot Award Program — Boyce(PI) — 07/01/2013-06/30/2015
Targeting Chloroquine to Bone using Novel Bisphosphonate Prodrug Technology
Role : co-PI

UR Drug Development Delivery Pilot Award Program — Xing(PI) — 07/01/2014-06/30/2015
Targeting Velcade to Bone using Novel Bisphosphonate Prodrug Technology
Role: co-PI

CHE 0946653 — Boeckman(PI) — 02/01/2011- 1/31/2014
NSF
Acquisition of a Liquid Chromatograph / Mass Spectrometer
Role: co-PI (Dinnocenzo)

CHE 0840410 — Boeckman (PI) — 08/01/2009-12/31/2010
NSF
Acquisition of a Matrix-Assisted Laser Desorption/Ionization Time of Flight (MALDI-TOF)
Role: co-PI (Nilsson)

PUBLICATIONS – Robert K. Boeckman, Jr

1. The Total Synthesis of (±)- β-Gorgonene, R. K. Boeckman, Jr. and S. M. Silver, *J. Org. Chem.*, **40**, 1755 (1975).
2. A Total Synthesis of Gascardic Acid, R. K. Boeckman, Jr., D. M. Blum, and S. D. Arthur, *J. Am. Chem. Soc.*, **101**, 5060 (1979).
3. Stereocontrol in the Intramolecular Diels-Alder Reaction 1. An Application to the Total Synthesis of (±) Marasmic Acid, R. K. Boeckman, Jr. and S. S. Ko, *J. Am. Chem. Soc.*,**102**, 7146 (1980).
4. Cyclic Vinyl Ether Carbanions II: Preparation and Application to the Synthesis of Carbonyl Compounds, R. K. Boeckman, Jr. and K. J. Bruza, *Tetrahedron*, **37**, 3997 (1981).
5. A Flexible New Synthetic Route to Daunomycinone, Adriamycinone and Their 6-Deoxy Analogs, R. K. Boeckman, Jr. and S. H. Cheon, *J. Amer. Chem. Soc.*, **105**, 4112 (1983).
6. Synthetic Studies Directed Toward Naturally Occurring Cyclooctanoids. 1. Total Synthesis of (±)-Ceroplastol I, R. K. Boeckman Jr., A. Arvanitis, and M. E. Voss *J. Am. Chem. Soc.*, **111**, 2737 (1989).
7. An Enantioselective and Highly Convergent Synthesis of (+)-Ikarugamycin, R.K. Boeckman, Jr., C.H. Weidner, R.B. Perni, and J.J. Napier, *J. Am. Chem. Soc.*, **111**, 8036 (1989).
8. Synthetic Studies Directed Toward Naturally Occurring Cyclooctanoids 2. A Stereocontrolled Assembly of (±)-Pleuromutilin *Via* A Remarkable Sterically Demanding Oxy-Cope Rearrangement, R. K. Boeckman, Jr., D. N. Springer, and T. R. Alessi *J. Am. Chem. Soc.*, **111**, 8284 (1989).
9. A New, Highly Efficient, Selective Methodology for Formation of Medium-Ring and Macrocyclic Lactones via Intramolecular Ketene Trapping: An Application to a Convergent Synthesis of (-)-Kromycin, Robert K. Boeckman Jr. and James R. Pruitt, *J. Am. Chem. Soc.*, **111**, 8286 (1989).
10. Synthetic Studies Directed Toward the Eremantholides 2. A Novel Application of the Ramberg-Bäcklund Rearrangement to a Highly Stereoselective Synthesis of (+)-Eremantholide A, R.K. Boeckman, Jr., S.K. Yoon, and D.K. Heckendorn, *J. Am. Chem. Soc*. **1991**, *113*, 9682-9863.
11. Toward the Development of a General Chiral Auxiliary 4. A Remarkable, Highly Diastereoselective, Auxiliary-Mediated Substitution: Application to an Enantioselective Synthesis of the Cyclohexene Subunit of (+)-Tetronolide, R. K. Boeckman, Jr. and S. T. Wrobleski, *J. Org. Chem.*, **1996**, *61*, 7238-39.
12. A Variant of the Takai-Utimoto Reaction of Acrolein Acetals with Aldehydes Catalytic in Chromium: A Highly Stereoselective Route to Anti Diol Derivatives, Robert K. Boeckman, Jr. and Raymond A. Hudak *J. Org. Chem.*, **1998**, *63*, 3524-3525.
13. Synthetic and Mechanistic Studies Of The Retro-Claisen Rearragement 4. Application to an Enantioselective Total Synthesis of (+)-Laurenyne, R. K. Boeckman, Jr., J. Zhang, and M. R. Reeder *Org. Lett.*, **2002**, *4*, 3891-3894.
14. The Development of a Convergent Efficient Enantioselective Synthesis of the Bengamides *via* a Common Polyol Intermediate R. K. Boeckman, Jr. and T. J. Clark, and B. J. Shook *Helv. Chim. Acta*, **2002**, *85*, 4532-4560.
15. Toward the Development of a General Chiral Auxiliary 7. A Novel Total Synthesis of (+)-Tetronolide using a Tandem Ketene-Trapping [4+2] Cycloaddition Strategy, R.K.

Boeckman, Jr., P. Shao, S. T. Wrobleski, G. R. Heintzelman, D. J. Boehmler, and A. J. Barbosa *J. Am. Chem. Soc.* **2006** *128*, 10572-10588.

16. Toward the Development of a General Chiral Auxiliary 11. Enantioselective Alkylation and a New Catalytic Asymmetric Addition of Silyloxyfurans: Application to a Total Synthesis of (-)-Rasfonin, R. K. Boeckman, Jr., J. E. Pero, and D. J. Boehmler *J. Am. Chem. Soc.* **2006** *128*, 11032-11033.
17. Direct Enantioselective Organocatalytic Hydroxymethylation of Aldehydes Catalyzed by α,α-Diphenylprolinol Trimethylsilyl Ether, Robert K. Boeckman, Jr., and John R. Miller *Org. Lett.* **2009**, *11*, 4544-4547.
18. Isoamidinium Salts: A New Class of Chiral and Achiral Dienophiles for Diels-Alder Reactions, R. K. Boeckman Jr., Yan Miller, and Todd R. Ryder *Org. Lett.* **2010**, *12*, 4524-4527.
19. Studies Culminating in the Total Synthesis and Determination of the Absolute Configuration of (-)-Saudin, R. K. Boeckman , Jr., M. R. d-R. Ferreira, L. H. Mitchell, P. Shao, M. J. Neeb, and Y. Fang *Tetrahedron* **2011**, *67*, 9787-9808.
20. Organocatalytic Enantioselective alpha-Hydroxymethylation of Aldehydes: Mechanistic Aspects and Optimization. R. K. Boeckman; K. F. Biegasiewicz; D. J. Tusch; J. R. Miller, *J Org Chem*, **2015**, *80*, 4030.

MASSACHUSETTS INSTITUTE OF TECHNOLOGY
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Rick L. Danheiser
Arthur C. Cope Professor of Chemistry

MIT Room 18-298
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October 26, 2015

Guenther Award Selection Committee
American Chemical Society

Dear Members of the Award Committee,

I am pleased to write in support of the nomination of **Robert K. Boeckman** for the Ernest Guenther Award in the Chemistry of Natural Products. Professor Boeckman's research has significantly advanced our ability to accomplish the total synthesis of structurally complex natural products. His research has encompassed studies on several diverse classes of natural products (terpenoids, alkaloids, macrolides, anthracyclinones), and he and his group have also made a number of significant contributions through the development of new synthetic strategies and tactics.

Notable contributions in the area of new synthetic methodology by Professor Boeckman in the 1970s included the development of a number of useful organocuprate reagents and synthetic builiding blocks based on metallated vinyl ethers. In both areas, Boeckman was at the forefront of very active fields of research. In the early 80s, Boeckman turned his attention to the development of the intramolecular Diels-Alder (IMDA) reaction for complex molecule synthesis, and here again he was a key contributor in what was at the time a highly competitive and active area of research. The development of the "cyclopropyliminium ion rearrangement" represents another significant contribution from the Boeckman lab in the 1980s in the area of synthetic methodology development.

In my judgment, however, Professor Boeckman's most significant contributions to our science involve his work on the total synthesis of complex natural products. In this research, Boeckman has defined the scope and limitations of the field, and demonstrated new strategic approaches to several important classes of naturally occurring molecules.

On a number of occasions his lab was the first to complete the total synthesis of a formidable target attracting the interest of a number of research groups around the world.

Thus, in 1979 Boeckman reported the first total synthesis of gascardic acid, a tricyclic sesterterpene whose structure features a highly condensed array of five-, six-, and seven-membered rings. This was one of the very first successful total syntheses of a C-25 terpenoid. In 1989, Boeckman described an elegant total synthesis of ceroplastol I, a sesterterpene with a five-eight-five tricarbocyclic core. This work was published back-to-back with Kishi's first total synthesis of ophiobolin, a related sesterterpene. The same year, Boeckman also reported the first total synthesis of ikarugamycin (back to back with a synthesis by Paquette); a highlight of the Boeckman approach was the application of a stereocontrolled IMDA reaction to construct the formidable as-indacene core of this natural product. Last, but not least, in 2002 the Boeckman lab reported the first enantioselective total synthesis of (-)-saudin, an extremely challenging molecule whose synthesis was achieved using a remarkable Lewis acid-mediated Claisen rearrangement strategy.

Over the years, the Boeckman group has accomplished groundbreaking total syntheses of numerous other prominent natural products, including beta-gorgonene (1975), cerulenin (1977), marasmic acid (1980), aklavinone (1982), tirandamycin (1986), calcimycin (1987), cassioside (1996), and laurenyne (2002). On the basis of these numerous and significant contributions I believe Professor Boeckman is a very strong and worthy candidate for the ACS Ernest Guenther Award.

Sincerely yours,

Rick L. Danheiser
A. C. Cope Professor

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To whom it may concern:

I am very pleased to enthusiastically support the nomination of Professor Robert K. Boeckman for the 2016 ACS Ernest Guenther Award in the Chemistry of Natural Products. I have known Bob professionally for many years and am quite familiar with his research since in general we work in similar areas. Bob is a highly visible member of the synthetic organic chemistry community, and virtually everyone is well aware of his work. He has been involved in a number of aspects of synthetic organic methodology and in the total synthesis of natural products. His productivity has been very high, the quality of the work has been exceptional, and he is a leader in natural products chemistry.

Bob's research over the years is striking in that he has targeted a very diverse array of complex, important natural products, and has provided creative solutions in the syntheses which he has developed. Rather than reiterate what is outlined in detail in Professor Heathcock's nomination letter, let me note that Bob has completed an impressive number of natural product total syntheses. Especially notable is his work on pleuromutilin, saudin, and tetronolide. These and other molecular structures that he has attacked are complicated, difficult targets. During the course of this work, he has made major creative contributions to the field of natural products research.

In summary, I believe Bob is a truly outstanding nominee for the Ernest Guenther Award and he richly deserves such recognition. He has sustained a highly productive research program that has contributed to the practice of organic chemistry through important new synthetic protocols directed towards the total syntheses of a number of important natural products. Many of his accomplishments in the general area of total synthesis have become benchmarks by which progress in the field is measured. This work exemplifies his adept touch in practicing the art of organic synthesis. His research is highly innovative and creative as well as being quite diverse. I can strongly support his nomination for this award.

Sincerely yours,

Steven M. Weinreb