JULIUS REBEK, JR.

Director, The Skaggs Institute for Chemical Biology
and
Professor of Chemistry, Department of Chemistry
The Scripps Research Institute

Biographical Sketch

Julius Rebek, Jr. was born in Hungary in 1944 and lived in Austria from 1945-49. He and his family then settled in the U.S.A. in Kansas. He received his undergraduate education at the University of Kansas in 1966, and obtained the Ph.D. degree from the Massachusetts Institute of Technology (1970) for studies in peptide chemistry with Professor D.S. Kemp. As an Assistant Professor at the University of California at Los Angeles (1970-1976) he developed the three-phase test for reactive intermediates. In 1976 he moved to the University of Pittsburgh where he rose to the rank of Professor of Chemistry and developed cleft-like structures for studies in molecular recognition. In 1989 he returned to the Massachusetts Institute of Technology, where he was the Camille Dreyfus Professor of Chemistry and devised synthetic, self-replicating molecules. In July of 1996, he moved his research group to The Scripps Research Institute to become the Director of The Skaggs Institute for Chemical Biology, where he continues to work in molecular recognition and self-assembling systems.

Biographical Data

Birth date: April 11, 1944; Beregszasz, Hungary

Education: B.A. University of Kansas, 1966
Ph.D. Massachusetts Institute of Technology, 1970

Positions: University of California, Los Angeles
Assistant Professor, 1970-1976

University of Pittsburgh
Associate Professor, 1976-1979
Professor, 1980-1989

Massachusetts Institute of Technology, Cambridge, MA
Professor, 1989-1991
Camille Dreyfus Professor of Chemistry, 1991-1996

The Scripps Research Institute, La Jolla, CA
Director, The Skaggs Institute for Chemical Biology
and Professor of Chemistry, 1996

Honors and Awards

NSF Predoctoral Fellow, 1967-1970
Eli Lilly Award, 1972-1974
A. P. Sloan Fellow, 1976-1978
A. von Humboldt Fellow, 1981
J. S. Guggenheim Fellow, 1986
A.C. Cope Scholar Award, 1991
American Academy of Arts and Sciences, 1993
National Academy of Science, 1994
Highland Park High School Hall of Fame, 1995
NIH Merit Award, 1996
James Flack Norris Award in Physical Organic Chemistry, ACS, 1997
American Association for Advancement of Science Fellow, 2000
Hungarian Academy of Science, 2001
American Institute of Chemists, Chemical Pioneer Award, 2002
Ronald Breslow Award for Achievement in Biomimetic Chemistry, ACS 2004
Medal of the Academy of Sciences; Prague, Czech Republic, 2005
Medal of the National Academy of Sciences, Letters and Arts; Modena, Italy 2005
European Academy of Science (Academia Europaea) Member, 2005
Distinguished Scientist Award, ACS, San Diego, California, 2006
Evans Award, Ohio State University, 2006
University of Oregon Creativity Award in Chemistry, Dance and Music, 2007

Recent Plenary Lectures and Symposia

17th Symposium on Chirality, Parma, Italy 2005
American Chemical Society, Anaheim, California, 2004
American Chemical Society, San Francisco, California, 2006
Alfred Nobel Symposium, Sånga Säby, Sweden, 2004
G.D. Ch. Lecturer, Mainz, Germany, 2006
2nd Center for Bioactive Molecular Hybrid Lectures, Seoul, Korea, 2006
1st European Chemical Congress, Budapest, 2006
American Chemical Society, Chicago, Illinois, 2007
10th Ibn Sina Conference of Heterocyclic Chemistry, Luxor, Egypt, 2007
ACS, Chicago, IL, Breslow Award Symposium, 2007

Named Lectureships

Organic Synthesis, Inc. Lecturer, Notre Dame, 1986
J. Clarence Karcher Lecturer, University of Oklahoma, 1988
Frontiers of Science Lectures, Texas A & M University, 1989
Dow Lectures, Michigan State University, 1989
Merck Lecturer, University of Sherbrooke, 1990
Distinguished Lecture Series, University of Florida, 1990
Bender Lectures, Northwestern University, 1990
Abbot Lecturer , Yale University, 1991

H. M. Friedman Lecturer, Rutgers University, 1991
Phillips Lectures, Haverford College, 1991
Special Lecture Series, Scripps Research Institute, 1991
Organic Synthesis, Inc. Lecturer, Colorado State Univ. 1991
MIKI Keynote Lecturer, University of Kansas, 1991
Merck Lecturer, Lehigh University, 1992
Merck Lecturer, University of Montreal, 1992
Franklin Lecturer, University of Kansas, 1992
Bio Mega Lecturer, Montreal, 1993
Miles Lecturer, University of New Hampshire, 1993
Syntex Lecturer, University of Colorado, 1993
Wm. Rauscher Lecturer, Rensselaer Polytechnic, 1993
Seman Lecturer, Kent State University, 1994
Robert Robinson Memorial Lecturer, Oxford, 1994
Welch Foundation Lecturer, Texas Universities, 1994
Linus Pauling Lecturer, Stanford University, 1995
E. K. C. Lee Lecturer, UC Irvine, 1995
Kilpatrick Lecturer, Illinois Institute of Technology, 1996
Lord Lectureship, Allegheny College, 1996
Watkins Lectureship, Wichita State University, 1997
Hirschman Lecturer, Oberlin College, 1998
Oersted Lecturer, Technical University of Denmark at Lyngby, 1998
S.C. Lind Lectureship, University of Tennessee, Knoxville, 1998
Lyle Dawson Lecturer, University of Kentucky, 1998
Reynold Fuson Lectureship, University of Nevada, Reno, 1999
Brantford Chemicals Distinguished Lecturer, Queen's University, Canada, 1999
David Ginsburg Memorial Lecture, Israel Institute of Technology, Israel, 2000
Schlemper Distinguished Lecture in Chemistry, University of Missouri, 2000
Priestley Lecturer, Pennsylvania State University, 2000
Martino Steer Memorial Lecturer, Modena University, Italy, 2000
Johnson Lecturer, Yale University, 2001
Lipscomb Lecturer, University of South Carolina, 2001
Gomberg Lecturer, University of Michigan, 2001
Guthikonda Lecture, Columbia University, 2001
Henry J. Shine Endowment Lecturship, Texas Tech University, 2001
Jack Fox Lecture, Memorial Sloan-Kettering Cancer Center, 2002
Consensus Lecturer, Tufts University, 2002
Woodward Scholar, Harvard University, 2002
Molecular Science Forum, Chinese Academy of Sciences, 2003
Robert Levine Lecture, University of Pittsburgh, 2003
ICI Lecture, Third Bristol Synthesis Meeting, Bristol, UK, 2003
Inaugural Winstein Lecture, University of California Los Angeles, 2004
Evans Award Lecturer, Ohio State University, 2006
Chemistry Day Lecturer, University of Montreal, 2006
Chemistry Week Lecturer, Georgetown University, 2006
Wyeth Lecturer, Princeton University, 2006
Barker Lecturer, University of Maryland, 2007
Haberman Lecturer, Marquette University, 2007

Recent Lectures at Universities and Companies

2004 University of Kyoto; University of Tokyo; University of Shizuoka; Sankyo, Tokyo; Nanotechnology Institute, UCLA; 3rd Symposium on Creation of Novel Nanomaterials, Osaka,; Frontiers in Chemistry, La Jolla, CA;

2005: University of Paris V, France; University of Parma, Italy; University of Padua, Italy; University of Venice, Italy; Novartis, Basel, Switzerland; Imperial College, London, UK; Academy of Science, Prague;

2006: Ecole Normal Superior, Paris, France; University of Rennes, France; Stockholm University, Sweden; Goteborg/Chalmers University, Sweden; Lund University, Sweden; Rohm & Haas, Philadelphia, PA; Wyeth, Princeton University, New Jersey; New York University, New York, NY; Schering-Plough, Cambridge, MA; California Institute of Technology, Pasadena, CA; University of Wuertzburg, Germany; Tokyo Institute of Technology, Japan

Research Interests

Molecular Diversity, Molecular Recognition, Self-Replicating and Self-Assembling Systems.

Editorial Advisory Boards:

Journal of Molecular Recognition, 1987-1995
Chemtracts, 1987-1996
Bioorganic and Medicinal Chemistry Letters, 1991-
Bioorganic and Medicinal Chemistry, 1991-
Journal of the Chemical Society, Perkin Transactions, 1992-
Chemistry and Biology, 1994-
Accounts of Chemical Research, 1996-1998
Journal of Organic Chemistry, 1996-
Current Opinion in Chemistry Biology, 1997-
Tetrahedron Publications, 1991-
Progress in Physical Organic Chemistry, 1998-
Journal of Supramolecular Chemistry, 2001-

Scientific Advisory Boards:

Commercial
Amira (RepliGen), Cambridge, Massachusetts 1990 -1994
Procept, Cambridge, Massachusetts 1991-1997
Darwin Molecular, Seattle, Washington 1992-1995
Cubist Pharmaceuticals, Cambridge, Massachusetts 1992-2001

Discovery Partners International, La Jolla, California, 1996-2001
EPIgen, La Jolla, California, 1996-2001
Synteni (Incyte), Fremont, California, 1997-2001
LaunchCyte, Pittsburgh, PA, 2000-2002
Neogenesis, Cambridge, Massachusetts, 1997-2003
Personal Chemistry, Uppsala, Sweden, 1999-2003
Activx, La Jolla, CA, 2001-2004
Kémia, La Jolla, CA, 2002-

Institutional
University of Chicago, Physical Sciences Division, Chicago, Illinois, 2000-
National Cancer Institute, National Institutes of Health, Bethesda, MD, 2001-
The Institute of Chemical Research of Catalonia, Spain, 2001-
University of Oxford, Elector, Chair in Chemical Biology, 2001-

PUBLICATIONS

1. D. S. Kemp and Julius Rebek, Jr. Peptide Racemization Mechanism. A Kinetic Isotope Effect as a Means of Distinguishing Enolization from Oxazolone Formation, *J. Am. Chem. Soc*. **1970**, *92*, 5792.

2. D. S. Kemp, Zmira Bernstein and Julius Rebek, Jr. Racemization during Peptide Couplings Using the Mixed Anhydride, N-Hydroxysuccinimide Ester, 8-Hydroxyquinoline Ester, and Acyl Azide Methods, *J. Am. Chem. Soc*. **1970**, *92*, 4756.

3. Julius Rebek and David Feitler, An Improved Method for the Study of Reaction Intermediates. The Mechanism of Peptide Synthesis Mediated by Carbo-diimides, *J. Am. Chem. Soc*. **1973**, *95*, 4052.

4. Julius Rebek and David Feitler, Mechanism of the Carbodiimide Reaction II. Peptide Synthesis on the Solid Phase, *J. Am. Chem. Soc.* **1974**, *96*, 1606.

5. William R. Roush, David Feitler and Julius Rebek, Jr. Polymer-Bound Tosyl Azide, *Tetrahedron Lett.* **1974**, 1391.

6. Julius Rebek, Jr. Stephen F. Wolf and Allen B. Mossman, Substituted Peroxycarbamic Acids as Epoxidizing Agents, *J. Chem. Soc. Chem*. *Comm*. **1974**, 711.

7. J. Rebek and F. Gavina, The Three-Phase Test for Reactive Intermediates. Cyclobutadiene, *J. Am. Chem. Soc.* **1974**, *96*, 7112.

8. D. S. Kemp, S.-W. Wang, J. Rebek, Jr. R. C. Mollan, C. Banquer and G. Subramanyam, Peptide Synthesis with Benzisoxazolium Salts--II. Activation Chemistry of 2-ethyl-7-hydroxybenzisoxazolium Fluoroborate; Coupling Chemistry of 3-acyloxy-2-hydroxy-N-ethylbenzamides, *Tetrahedron*, **1974**, *30*, 3955.

9. D. S. Kemp, S. J. Wrobel,Jr. S.-W. Wang, Z. Bernstein and J. Rebek, Jr. Peptide Synthesis with Benzisoxazoline Salts--III. Utility of 7-hydroxy-2-ethyl-benzisoxazolium Fluoroborate in the Synthesis of Peptides, *Tetrahedron*, **1974**, *30*, 3969.

10. Julius Rebek, David Brown and Stephen Zimmerman, The Three-Phase Test for Reaction Intermediates. Nucleophilic Catalysis and Elimination Reactions, *J. Am. Chem. Soc.* **1975**, *97*, 454.

11. J. Rebek and F. Gavina, The Three-Phase Test for Reaction Intermediates. Metaphosphates, *J. Am. Chem. Soc.* **1975**, *97*, 1591.

12. J. Rebek and D. Feitler, Peptide Synthesis with Carbodiimide. III. Racemization, *Int. Peptide Protein Res.* **1975**, *7*, 167.

13. J. Rebek, Mechanisms of Peptide Synthesis with Carbodiimides, in *Peptides 1974*, Proceedings of the Thirteenth European Peptide Symposium, Kiryat Anavim Israel, April 28- May 3, 1974. Edited by Yecheskel Wolman, John Wiley & Sons, New York (**1975**), p. 27.

14. J. Rebek and F. Gavina, The Three-Phase Test for Reaction Intermediates. Evidence for Monomeric Metaphosphates, *J. Am. Chem. Soc.* **1975**, *97*, 3221.

15. Julius Rebek, Jr. and F. Gavina, The Three-Phase Test. Detection of Free Cyclobutadiene, *J. Am. Chem. Soc.* **1975**, *97*, 3453.

16. J. Rebek, S. Zimmerman and D. Brown, New Probes for the Study of Acylation Reactions, *J. Am. Chem. Soc.* **1975**, *97*, 4407.

17. J. W. Goers, V. N. Schumaker, M. M. Glovsky, J. Rebek and H. J. Muller-Eberhard, Complement Activation by a Univalent Hapten-Antibody Complex, *J. Biol. Chem.* **1975**, *250*, 4918.

18. J. Rebek, D. Brown and S. Zimmerman, The Mechanism of the Carbodiimide Reaction, IV, *Peptides: Chemistry, Structure and Biology*, R. Walter and J. Meienhofer, Eds. Ann Arbor Michigan, **1975**, p. 371.

19. J. Rebek and D. Brown, Nucleophilic Catalysis of Acyl Transfers, *Peptides 1976*, A Loffet, Ed. Brussels Univ. Press, Brussels, Belgium, **1976**, p. 61.

20. J. Rebek, F. Gavina, D. Brown and S. Zimmerman, The Three-Phase Test for Reactive Intermediates, *Polym. A.C.S. Div. Polym. Chem.* **1976**, *17*, 230.

21. L. T. Scott, J. Rebek, L. Ovsyanko and C. Sims, Organic Chemistry on the Solid Phase: Site-Site Interactions on Functionalized Polystyrene, *J. Am. Chem. Soc.* **1977**, *99*, 625.

22. J. Rebek and J.-C. Gehret, Progress on the Synthesis of Mitosenes, *Heterocycles*, **1977**, *6* ,1531.

23. J. Rebek, F. Gavina and C. Navarro, The Three-Phase Test: The Conant-Swan Reaction, *Tetrahedron Lett.* **1977**, 3021.

24. J. Rebek and J.-C. Gehret, A Synthetic Approach to the Mitosenes, *Tetrahedron Lett.* **1977**, 3027.

25. J. Rebek, S. Wolf and A. Mossman, Singlet Oxygen and Epoxidation from the Dehydration of Hydrogen Peroxide, *J. Org. Chem.* **1978**, *43*, 180.

26. J. Rebek and J. E. Trend, On Binding to Transition States and Ground States: Remote Catalysis, *J. Am. Chem. Soc.* **1978**, *100*, 4315.

27. S. Wolf, C. S. Foote and J. Rebek, Chemistry of Singlet Oxygen. XXIX. A Specific Three-Phase Kautsky Test for Singlet Oxygen, *J. Am. Chem. Soc.* **1978**, *100*, 7770.

28. J. Rebek, F. Gavina and C. Navarro, The Three-Phase Test: Intermediates in Phosphate Transfer Reactions, *J. Am. Chem. Soc.* **1978**, *100*, 8113.

29. J. Rebek, D. Brown and J. Horton, The Three-Phase Test: Intramolecular Nucleophilic Catalysis, *Israel. J. Chem.* **1978**, *17*, 316.

30. J. Rebek and J. E. Trend, On the Rate of Site-Site Interactions in Functionalized Polystyrenes, *J. Am. Chem. Soc.* **1979**, *101*, 737.

31. J. Rebek and R. McCready, A New Class of Epoxidation Reagents, *Tetrahedron Lett.* **1979**, 1001.

32. J. Rebek, R. McCready, S. Wolf and A. Mossman, New Oxidizing Agents from the Dehydration of Hydrogen Peroxide, *J. Org. Chem.* **1979**, *44*, 1485.

33. J. Rebek, Mechanistic Studies Using Solid Supports: The Three-Phase Test, Tetrahedron Reports, #60, *Tetrahedron*, **1979**, *35*, 723.

34. J. Rebek, R. V. Wattley, S. Chakravorti and J. E. Trend, Allosteric Effects in Organic Chemistry: Site-Specific Binding, *J. Am. Chem. Soc.* **1979**, *101*, 4333.

35. J. Rebek and R. McCready, New Epoxidation Reagents Derived from Alumina and Silicon, *Tetrahedron Lett.* **1979**, 4337.

36. Joseph A. Horton, Charles Kerber, John M. Herron, Julius Rebek, Reduction of Edge Position Uncertainty on Computed Tomographic (CT) Scans, *Proc. Soc. Phot. Instr. Eng.* **1979**, Vol. 207, p. 222-223.

37. J. Rebek and R. V. Wattley, New Macrocyclic Polyethers with Remote Binding Sites, *J. Het. Chem.* **1980**, *17*, 749-751.

38. J. Rebek and R. V. Wattley, Allosteric Effects: Remote Control of Ion Transport Selectivity, *J. Am. Chem. Soc.* **1980**, *102*, 4853-54.

39. J. Rebek and R. McCready, Olefin Epoxidation with å-Substituted Hydroperoxides, *J. Am. Chem. Soc.* **1980**, *102*, 5602-5605.

40. J. Rebek, Jr. and Y. K. Shue, Total Synthesis of Rugulovasines, *J. Am. Chem. Soc.* **1980**, *102*, 5426-27.

41. J. Rebek, Jr. T. Costello and R. V. Wattley, Large Rate Enhancements Through Preferential Binding to Transition States, *Tetrahedron Lett.* **1980**, 2379-80.

42. J. Rebek, Russell McCready, Raymond Wolak, Olefin Epoxidation with å-Hydroperoxides of Esters, Amides, Ketones and Nitriles, *Chem. Commun.* **1980**, 705.

43. J. Rebek, Jr. and R. McCready, Intermolecular Epoxidation with the H2O/Ortho Ester System, *Tetrahedron Lett.* **1980**, *21*, 2491.

44. J. Rebek, Jr. R. V. Wattley, T. Costello, R. Gadwood and L. Marshall, On Binding in Subunit Systems, *J. Am. Chem. Soc.* **1980**, *102*, 7398-7400.

45. J. Rebek, Jr. and Steven Shaber, Recent Progress Toward the Synthesis of Mitosenes, *Heterocycles*, **1981**, *15*, 161-163.

46. J. Rebek, Progress in the Development of New Epoxidation Reagents, *Heterocycles*, **1981**, *15*, 517-545.

47. J. Rebek, Jr. and S. Shaber, Total Synthesis of a Mitosene *Heterocycles*, **1981**, *15*, 1173-1177.

48. J. Rebek, Jr. R. V. Wattley, T. Costello, R. Gadwood and L.Marshall, Allosteric Effects: Binding Cooperativity in a Subunit Model, *Angew. Chem. Int.* **1981**, *93*, 584-585.

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50. J. Rebek, Jr. and D. F. Tai, A New Synthesis of Lysergic Acid, *Tetrahedron Lett*. **1983**, *24*, 859-860.

51. J. Rebek, Jr. and Dar-Fu Tai, Synthesis of Setoclavine *Heterocycles*, **1983**, *20*, 583-584.

52. J. Rebek, Jr. and Luann Marshall, Allosteric Effects: An On-Off Switch, *J. Am. Chem. Soc.* **1983**, *105*, 6668-6670.

53. K. Onan, J. Rebek, Jr. T. Costello and L. Marshall, Allosteric Effects: Structural & Thermodynamic Origins of Binding in Cooperativity in a Subunit Model, *J. Am. Chem. Soc.* **1983**, *105*, 6759-6760.

54. J. Rebek, Jr. D.-F. Tai and Y. K. Shue, Synthesis of Ergot Alkaloids from Tryptophan, *J. Am. Chem. Soc.* **1984**, *106*, 1813-1819.

55. J. Rebek, Jr. Binding Forces, Equilibria and Rates: New Models for Enzymic Catalysis, *Acc. Chem. Res.* **1984**, *17*, 258-264.

56. J. Rebek, Jr. L. Marshall, R. Wolak and J. McManis, Epoxidations With Selective Peracids, *J. Am. Chem. Soc.* **1984**, *106*, 1170-1171.

57. J. Rebek, Y. K. Shue and D.-F. Tai, Rugulovasines: Synthesis, Structure and Interconversions, *J. Org. Chem.* **1984**, *49*, 3540-3545.

58. J. Rebek, Jr. and T. Costello, Binding Forces and Catalysis: Rate Enhancements Through Chelation at a Remote Site, *Heterocycles*, **1984**, *22*, 2191-2194.

59. J. Rebek, Jr. S. H. Shaber, Y. K. Shue, J. C. Gehret and S. Zimmerman, The Total Synthesis of a Mitosene, *J. Org. Chem.* **1984**, *49*, 5164-5174.

60. J. Rebek, Jr. B. Askew, N. Islam, M. Killoran, D. Nemeth and R. Wolak, Synthetic Receptors: Size and Shape Recognition Within a Molecular Cleft, *J. Am. Chem. Soc.* **1985**, *107*, 6736-6738.

61. J. Rebek, Jr. and David Nemeth, Molecular Recognition: Three-Point Binding Leads to a Selective Receptor for Aromatic Amino Acids, *J. Am. Chem. Soc.* **1985**, *107*, 6738-6739.

62. J. Rebek, Jr. L. Marshall, R. Wolak, K. Parris, M. Killoran, B. Askew, D.Nemeth and N. Islam, Convergent Functional Groups: Synthetic and Structural Studies, *J. Am. Chem. Soc.* **1985**, *107*, 7476-7481.

63. J. Rebek, Jr. T. Costello, L. Marshall, R. Wattley, R. Gadwood, and K. Onan, Allosteric Effects in Organic Chemistry: Binding Cooperativity in a Model for Subunit Interactions, *J. Am. Chem. Soc.* **1985**, *107*, 7481-7487.

64. J. Rebek, Jr. T. Costello, R. Wattley, Binding Forces and Catalysis - The Use of Bipyridyl-Metal Chelation to Enhance Reaction Rates, *J. Am. Chem. Soc.* **1985**, *107*, 7487-7493.

65. J. Rebek, Jr. L. Marshall, J. McManis and R. Wolak, Convergent Functional Groups II: Structure and Selectivity in Olefin Epoxidation with Peracids, *J. ORerg. Chem.* **1986**, *51*, 1649-1653.

66. J. Rebek, Jr. S. Luis and L. R. Marshall, Slow Complexation Rates of Crown Ethers: What's Taking So Long?, *J. Am. Chem. Soc.* **1986**, *108*, 5011-5012.

67. J. Rebek, Jr. and D. Nemeth, Molecular Recognition: Ionic and Aromatic Stacking Interactions Bind Complementary Functional Groups in a Molecular Cleft, *J. Am. Chem. Soc.* **1986**, *108*, 5637-5638.

68. J. Rebek, Jr. R. J. Duff, W. E. Gordon and K. Parris, Convergent Functional Groups Provide a Measure of Stereoelectronic Effects at Carboxyl Oxygen, *J. Am. Chem. Soc.* **1986**, *108*, 6068-6069.

69. J. Rebek, Jr. B. Askew, M. Killoran, D. Nemeth and F.-T. Lin, Convergent Functional Groups III: A Molecular Cleft Recognizes Substrates of Complementary Size, Shape and Functionality, *J. Am. Chem. Soc.* **1987**, *109*, 2426-2431.

70. J. Rebek, Jr. B. Askew, D. Nemeth and K. Parris, Convergent Functional Groups IV: Recognition and Transport of Amino Acids Across a Liquid Membrane, *J. Am. Chem. Soc.* **1987**, *109*, 2432-2434.

71. J. Rebek, Jr. Model Studies in Molecular Recognition, *Science*, **1987**, *235*, 1478-1484.

72. J. Rebek, Jr. D. Nemeth, P. Ballester and F.-T. Lin, Molecular Recognition: Size & Shape Specificity In The Binding Of Dicarboxylic Acids, *J. Am. Chem. Soc.* **1987**, *109*, 3474-3475.

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74. J. Rebek, Jr. B. Askew, P. Ballester, C. Buhr, S. Jones, D. Nemeth and K. Williams, Molecular Recognition: Hydrogen Bonding and Stacking Interactions Stabilize a Model for Nucleic Acid Structure, *J. Am. Chem. Soc.* **1987**, *109*, 5033-5035.

75. J. Rebek, Jr. B. Askew, P. Ballester, C. Buhr, A. Costero, S. Jones and K. Williams, Molecular Recognition: Watson-Crick, Hoogsteen and Bifurcated Hydrogen Bonding in a Model for Adenine Recognition, *J. Am. Chem. Soc.* **1987**, *109*, 6866-6867.

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77. J. A. Moore, D. R. Robello, J. Rebek, Jr. R. Gadwood, Synthesis of Dibenzoheptalene Bislactones Via a Double Intramolecular Cannizzaro Reaction, *Org. Prep. Proc. Intl.* **1988**, *20*, 87-92.

78. J. Rebek, Jr. B. Askew, P. Ballester, A. Costero, Convergent Functional Groups V: Ternary Complexes in the Molecular Recognition of β-Aryl Ethylamines, *J. Am. Chem. Soc.* **1988**, *110*, 923-927.

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81. K. S. Jeong and Julius Rebek, Jr. Molecular Recognition: Hydrogen Bonding and Aromatic Stacking Converge to Bind Cytosine Derivatives, *J. Am. Chem. Soc.* **1988**, *110*, 3327-3328.

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93. J. Rebek, Jr. New Molecular Shapes for Recognition and Catalysis, *J. Inc. Phen.* **1989**, *7*, 7-17.

94. J. Rebek, Jr. On the Structure of Histidine and its Role in Enzyme Active Sites, *Structural. Chem.* **1989**, *1*, 129.

95. J. Rebek, Jr. Stereoelectronic Effects in Molecular Recognition, in *Molecular Recognition: Chemical and Biochemical Problems*, Royal Soc. of Chemistry Special Publication #78, **1989**, 211-218.

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97. J. Rebek, Jr. Recognition and Catalysis Using Molecular Clefts, *Chemtracts*, **1989**, *2*, 337-352.

98. J. Rebek, Jr. Model Studies in Molecular Recognition, *J. Heterocyclic Chem.* **1990**, *27*, 111-117.

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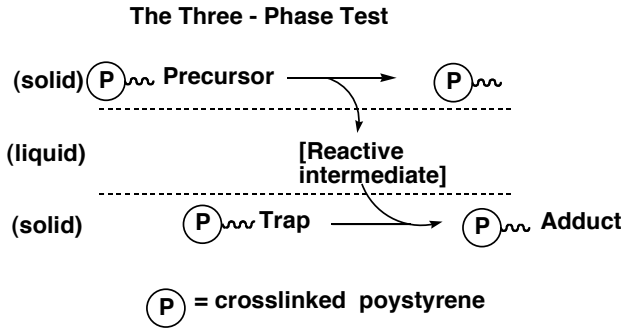
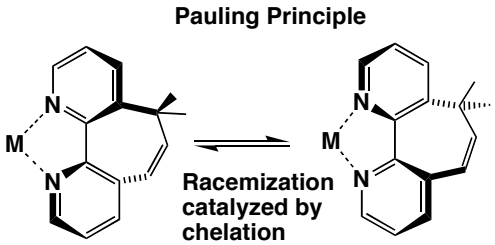
Julius Rebek, Jr.

Career Summary

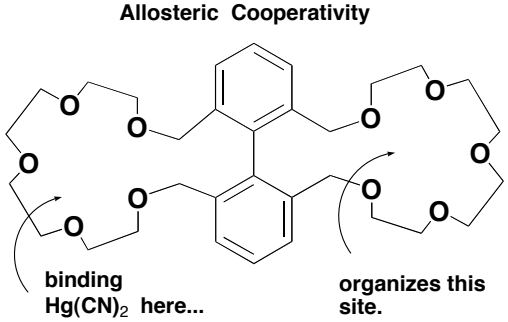
My independent research began in 1970, with a method to detect reactive intermediates. This was invented through application of polymer-bound reagents. A precursor for the reactive intermediate was covalently attached to one solid phase while a trap was attached to a second such support. When transfer takes place between the solid phases, it requires the existence of a reactive intermediate, free in solution as shown below. Among the reactive species detected by this "Three Phase Test" were cyclobutadiene, singlet oxygen, monomeric metaphosphate, and acyl imidazoles.[i]

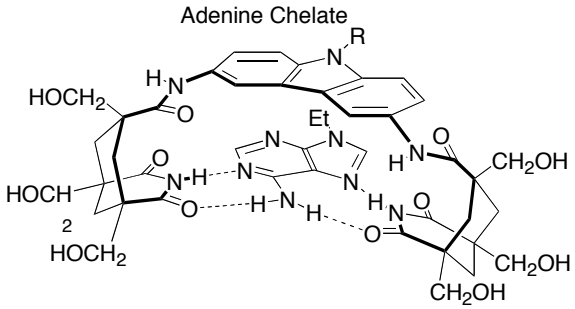
A of model the Pauling principle - catalysis by maximum binding to the transition state – was devised in 1978. A physical processes, the racemization of the bipyridyl shown below was chosen. The transition structure features coplanar aryl rings and a binding force — the chelation of a metal by bipyridyl —shows maximum metal/ligand attraction at the coplanar geometry.[ii] The biaryl bond acts like a fulcrum and binding induces a mechanical stress elsewhere in a molecule. This was one of the first molecular machines, a rotor.





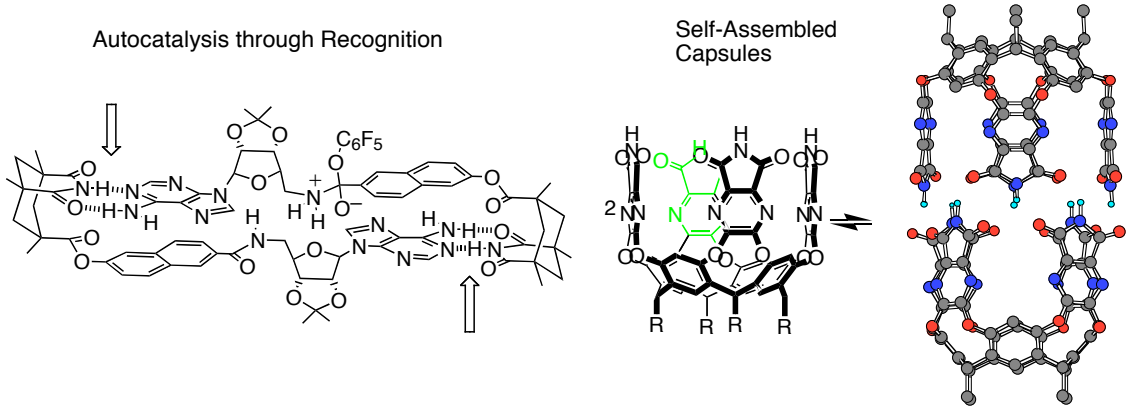
Other bipyridyls and biphenyls were designed in the 1980's as synthetic models of allosteric effects shown below. One involved two identical and mechanically coupled binding sites and it showed positive cooperativity in binding of covalent mercury compounds.[iii,iv] Rotors are still the most abundant chemical models for allosteric effects, and are present in many of the molecular machines pursued in other laboratories today.





Efforts in molecular recognition in the 1980's, led to cleft-like shapes[v] for recognition of ions and biorelevant nonionic targets. Using derivatives of Kemp's triacid it was possible to arrange functional groups that "converged" to create the recognition site. Shown above is a bisimide that chelates adenine in water.[vi] Versions with carboxyl groups[vii] became widely used elsewhere as models for metalloenzymes (the XDK structures)[viii] and in our laboratory to probe stereoelectronic effects.

In 1990, these studies culminated in a synthetic, self-complementary that acted as a template for its own formation. It showed autocatalysis based on molecular recognition and was the first synthetic system to show a primitive sign of life: self-replication.[ix] The template grasps the reactants by hydrogen bonding at both ends as indicated below, left. This self-complementary "recipe" has been incorporated in numerous self-replicating systems synthesized in other research groups.



Through a collaboration with Javier de Mendoza in 1993, we managed to create a self-assembling capsule that completely surrounded small target molecules. These reversibly formed capsules,[x] have become a tool of modern physical organic chemistry: capsules have defined the proper filling of space in the solution phase,[xi,xii] created a fluid model of alkane recognition[xiii] and introduced a new departure in molecular machinery - the spring-loaded device.[xiv] They are also vehicles for new classes of stereochemistry,[xv,xvi] chambers for chemical reactions,[xvii] places where reaction intermediates are stabilized and amplified,[xviii] and small spaces that are chiral. [xix] Capsules have also allowed observation single solvent/solute interactions in liquids.[xx] A cylindrical capsule of nanometric dimensions[xxi] is shown above, it selects congruent guests singly or pairwise[xxii] that fill the space appropriately.

In recent years we have pursued synthetic protein surface mimetics.[xxiii] Through a collaboration with Tamas Bartfai these show biological activities in animal models of disease[xxiv,xxv]

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