# RICHARD G. LAWTON
## vita abstract

Richard G. Lawton is an Arthur F. Thurnau Professor & Professor of Chemistry Emeritus at The University of Michigan, Ann Arbor. He identified his passion and excitement for chemistry at the age of 8 and was mentored in those early years by graduate students of Professors Bill Dauben & Henry Rappoport. A native of Berkeley, Rich received his B.S. from The College of Chemistry, University of California, Berkeley in 1956. He worked in the research group of Dr. Karl Folkers at Merck (Rahway) for almost 2 years, waiting to be drafted into the U.S. Army and after being drafted he served as an organic chemist at Walter Reed Army Institute of Research. After military service he entered graduate school obtaining his Ph.D. in 1962 from the University of Wisconsin, Major Professor: Dr. E. E. van Tamelen. Rich accepted an academic position at the University of Michigan in 1962. He was a Lilly Grantee in Organic Chemistry 1967-1969; John S. Guggenheim Foundation Fellow, Aachen, Germany, 1978-1979 International Academic Partnerships Fellow, Aachen, Germany, 1983-84. Visiting Professor at the Laboratorium fur Organische Chemie, Eidgenossische Technische Hochschule,. Zurich, Switzerland 1986-87. The Rutgers University Organic Synthesis, Inc. Lecturer, 1988. University of Michigan Amoco Teaching Award, 1989; LS&A Excellence in Teaching Award, 1991, 1992 & 1997; University of Michigan Arthur F. Thurnau Professor, 1993. Over the years Rich has been a consultant to Colgate Palmolive Research Laboratories, the du Pont Company, (New England Nuclear Laboratories) and Abbott Diagnostics. His research accomplishments include the first $\pi$-participation ring closure to the norbornyl system; the design and first synthesis of corannulene; the biogenetic-type synthesis of cedrene; the $\alpha$, $\alpha$'-annelation synthesis of bicyclic and spiro systems; the design and construction of molecular yardsticks; the diazopyruvoyl (DAP) photo-activated cross-linking probe and the design, synthesis and chemistry of Equilibrium Transfer Alkylating Cross-linkers as "walking" reagents for cross-linking and tethering of bio-molecules.

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b. August 29, 1934 - Berkeley, California

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***Education:***

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|---|---|
| B.S.(1956) | University of California, College of Chemistry, Berkeley, California. Senior Thesis: Migratory Aptitude of the Trifluoromethyl Group [with Dr. Elliot Bergman]. Junior Project: Study of the Hammick Reaction [with Dr. Henry Rapoport]. |
| Ph.D.(1962) | University of Wisconsin, Department of Chemistry, Madison, Wisconsin. Major Professor: Dr. E. E. van Tamelen. Thesis: Biogenetically Patterned Laboratory Syntheses in the Strychnine-Curare Alkaloid Series. |

***Academic Experience, Awards & Honors:***

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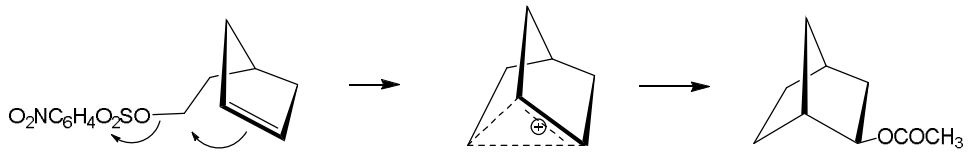
| 1962-2000 | University of Michigan Instructor (1962-1964); Assistant Professor (1964-1967); Associate Professor (1967-1970); Professor (1970-2000) Professor Emeritus (2000-). |
| 1961-1962 | **Owen D. Young Fellow**, University of Wisconsin Graduate Award in Chemistry, General Electric Company. |
| 1967-1969 | **Lilly Grantee in Organic Chemistry** at the University of Michigan. |
| 1970-1971 | **University of Wisconsin**, Madison. Visiting Professor of Chemistry (1970-1971) |
| 1971 (summer) | **University of Illinois**, Champaign-Urbana, Illinois. Visiting Professor of Chemistry. |
| 1978-1979 | **John Simon Guggenheim Foundation Fellowship (1978-1979)**. Guest of the Deutsches Wollforschungsinstitut, Aachen Germany. Hosts were Dr. Helmut Zahn and Dr. Dietrich Brandenberg. |
| 1983-1984 | **International Grant for Academic Partnerships**. Aachen, Germany. |
| 1986-1987 | **Eidgenossische Technische Hochschule, Laboratorium fur Organische Chemie. Zurich, Switzerland**. Visiting Professor, Host Prof. Dieter Seebach. |
| 1988 | **Rutgers University Organic Synthesis, Inc. Lecture**. |
| 1989 | **University of Michigan Amoco Teaching Award**. |
| 1991 | **LS&A Excellence in Teaching Award** |
| 1992 | **LS&A Excellence in Teaching Award** |
| 1993 | **Arthur F. Thurnau Professor, University of Michigan** |
| 1997 | **LS&A Excellence in Teaching Award** |

***Important Scientific Contributions:***

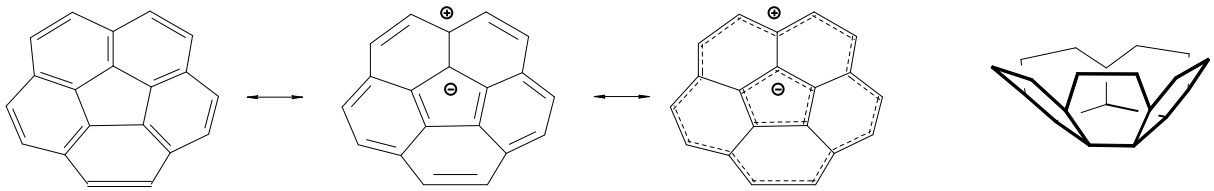
- First example and demonstration of π-double bond participation to produce the norbornyl ring system through the non-classical carbocation




R. G. Lawton, "1,5-Participation in the Solvolysis of 2-(3-Cyclopentenyl)ethyl p-Nitrobenzenesulfonate", ***J. Am. Chem. Soc.*** **1961**, *83*, 2399.

An introspective viewpoint and some history of this story can be found in Brian Coppola's "Deeper Beneath the Surface of the Chemical Article: Richard G. Lawton and the Norbornyl Cation Problem". *The Chemical Intelligencer*; April, **1998**, p 40.

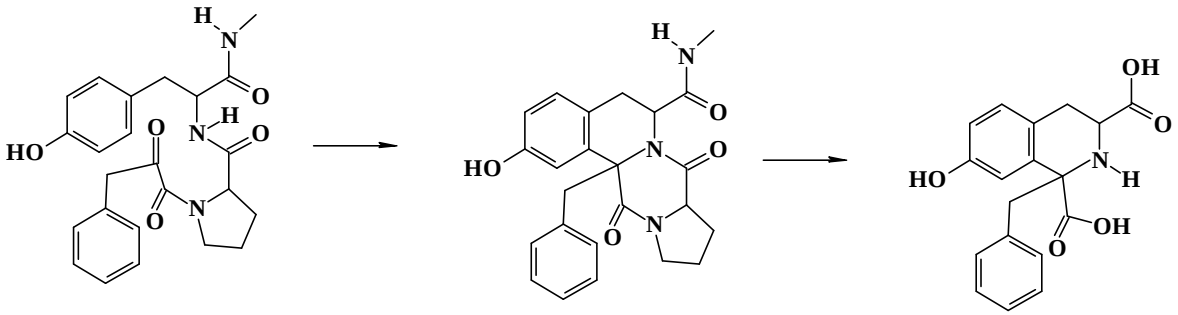
- First design and synthesis of *Corannulene*, a bowl shaped aromatic hydrocarbon consisting of a cyclic array of 5 fused benzene rings designed to test the confrontation of bond angle strain and aromaticity.



Barth, W. E.; Lawton, R. G.; "Dibenzo(*ghi*,*mno*)fluoranthene", *J. Am. Chem. Soc*. **1966**, *88*, 380.

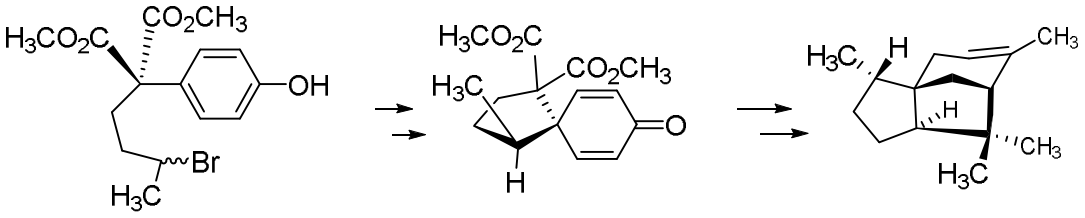
W. E. Barth & R. G. Lawton, "The Synthesis of Corannulene", *J. Am. Chem. Soc*. **1971**, *93*, 1730.

- First use of the *multiple interactions of reactive carbonyl groups with amide backbone chains of peptides* for the biogenetically-patterned construction of alkaloids and peptide alkaloids.



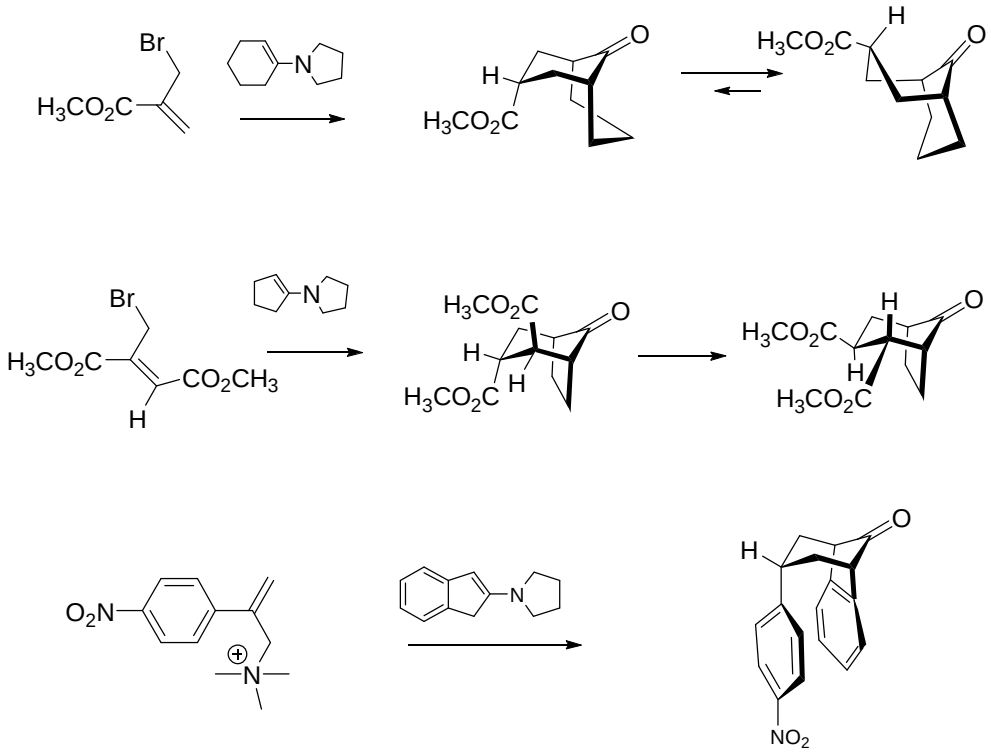
B. W. Dominy, G. Krejcarek & R. G. Lawton, "The Interaction of Reactive Functional Groups Along Peptide Chains. A Model for Alkaloid Biogenesis", ***Chem. Commun.*** **1968**, *22*, 1450.

- *Biogenetically-patterned Total Synthesis of Cedrene* demonstrating the first example of the intramolecular base abstraction of a proton with stereospecific formation of a double bond.



T. G. Crandall & R. G. Lawton, "A Biogenetic-type Synthesis of Cedrene", ***J. Am. Chem. Soc***. **1969**, *91*, 2127.

- Design, reagent synthesis, demonstration and application of the α,α'-Annelation Reaction and its use in the construction of bicyclic and spiro ring systems.



R. P. Nelson & R. G. Lawton, "On the a,a'-Annelation of Cyclic Ketones", ***J. Am. Chem. Soc***. **1966**, *88*, 3884.

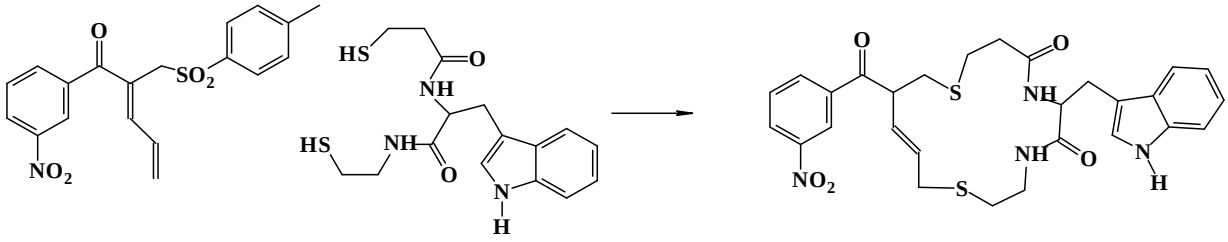
Nelson, R. P.; McEuen, J. M.; Lawton, R. G.; "The α,α'-Annelation of Cyclic Ketones. Synthesis of Bicyclo[3.2.1]octane Derivatives", *J. Org. Chem*. **1969**, *34*, 1225.

McEwen, J. M.; Nelson, R. P.; Lawton, R. G.; "The α,α'-Annelation of Cyclic Ketones. Synthesis and Conformational Properties of Bicyclo[3.3.1.]nonane Derivatives", *J. Org. Chem*. **1970**, *35*, 690.

Dunham, D. J.; Lawton, R. G.; "The Synthesis of Spiro Systems by the α,α'-Annelation Process", *J. Am. Chem. Soc*. **1971**, *93*, 2075.

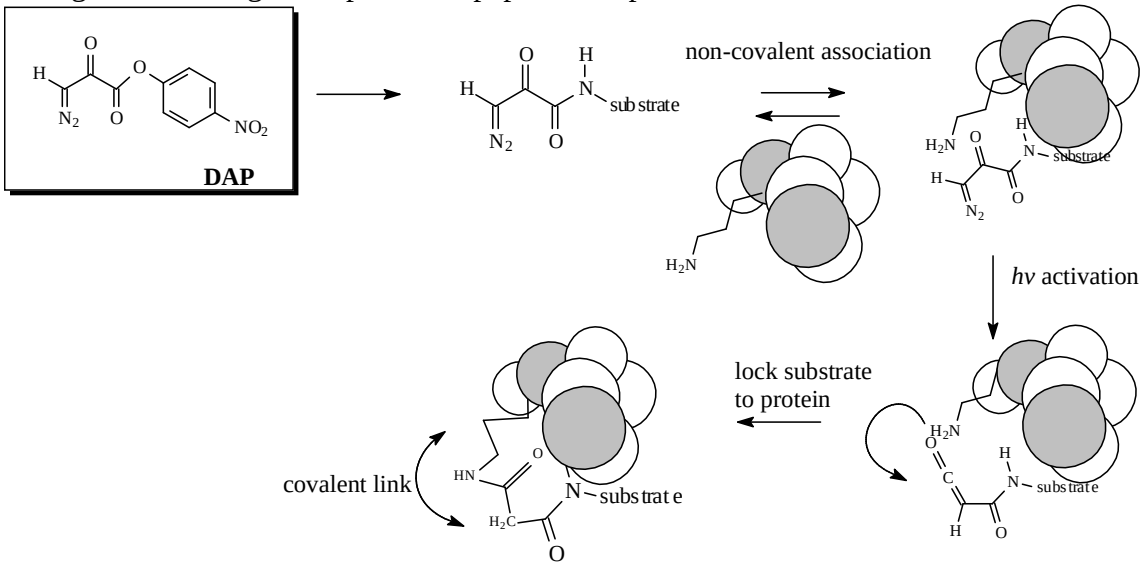
Chen, Y.-S.; Kampf, J. W.; Lawton, R. G.; "Intramolecular Photoinduced Electron Transfer: A Dimethylaniline Constrained to the Face of a Naphthalene through a Bicyclic Scaffold". *Tetrahedron Lett*. **1997**, *38*, 7815-7818

❖ Design, reagent synthesis and use of ***molecular yardsticks*** or extended ETAC reagents for the synthesis of macrocyclic frameworks and protein cross-linking through consecutive, differential Michael reactions.



Steve J. Brocchini, Martin Eberle & Richard Lawton "Molecular Yardsticks. Synthesis of Extended Equilibrium Transfer Alkylation Cross-link Reagents & their use in the Formation of Macrocycles." ***J. Am. Chem. Soc.*** **1988**, *110*, 5211-5212.

❖ Reagent design, construction and use of the diazopyruvoyl function for the photocross-linking and tethering of bioprobes to peptide and proteins.




Goodfellow, V. S.; Setteneri, M.; R. G. Lawton. "*p*-Nitrophenyl 3-diazopyruvate and Diazopyruvamides. A New Family of Photoactivatable Cross-linking Bioprobes" *Biochemistry* **1989**, *28* 6346-6360.

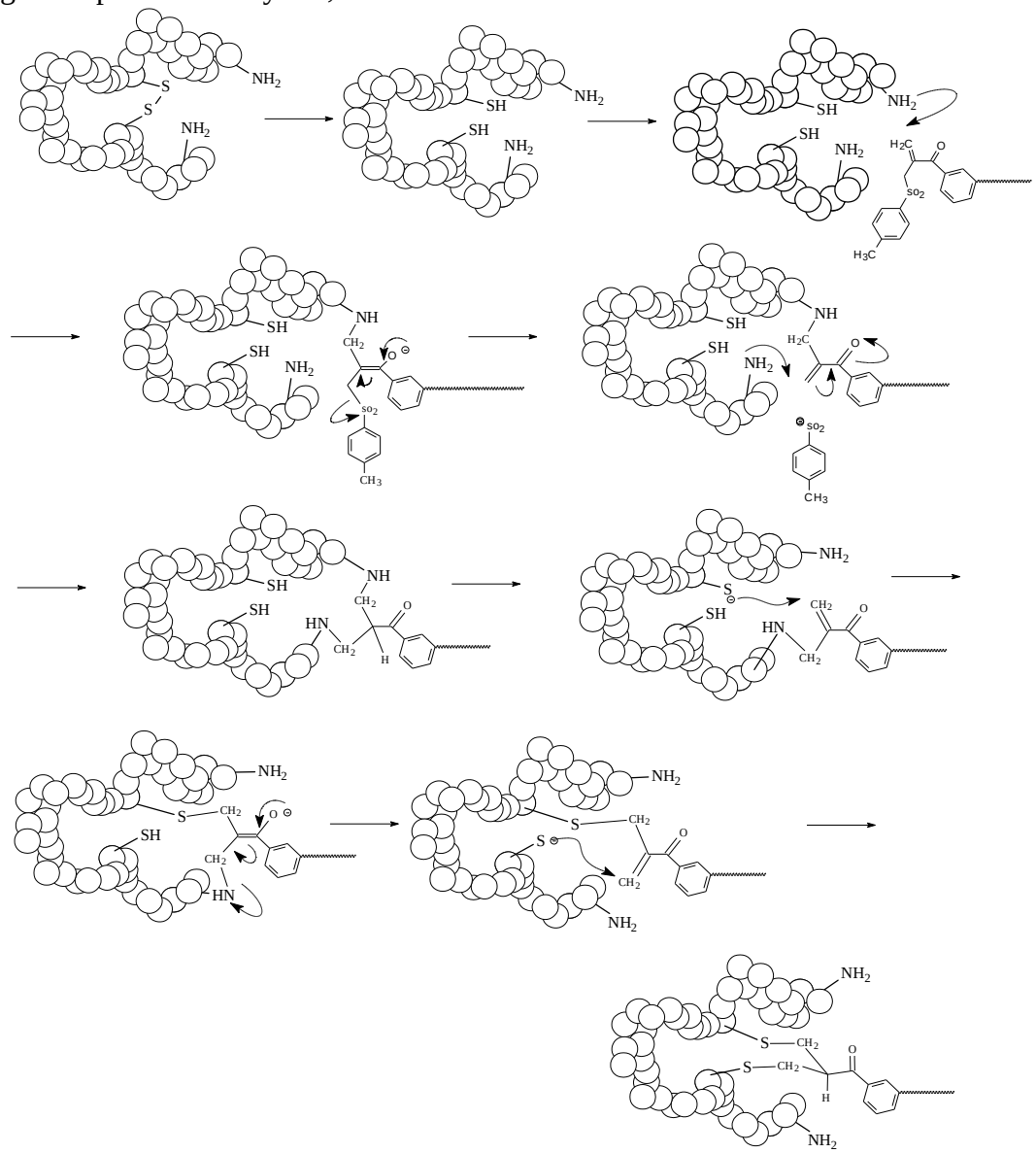
Harrison, J.K.; Gnegy, M.E.; Lawton, R.G. "Development of a Novel Photoaffinity Calmodulin Probe: Cross-linking of Purified Adenylate Cyclase from Bovine Brain." *Biochemistry*. **1989**, *28*, 6023-6027.

Taylor, J. M., Jacob, G. G., Lawton, R. G., Neubig, R. R., "Cross-linking of α2-Adrenergic receptor to G-proteins", *J. Cellular Biochemistry* **1993**, *17c* 221.

Taylor, J. M., Jacob-Mosier, G. G., Lawton, R. G., Neubig, R. R., "A new thiol specific photoactivatable crosslinking regent. Conjugation of an α2-adrenergic receptor peptide to G-protein." *Peptides*, **1994**, *15*, 829-834.

Taylor, J. M., Jacob-Mosier, G. G., Lawton, R. G., Remmers, A. E., Neubig, R. R.,. "Binding of an α2-adrenergic receptor third intercellular loop peptide to Gβ and the amino terminus of Gα". *J. Biol. Chem.***1994**, *45*, 27618-27624.

- Design, reagent synthesis and demonstration of *Equilibrium Transfer Alkylating Cross-link (ETAC; "Eee-tac")* reagents which interact with residues on enzyme, protein and antibody chains to cross-link by means of consecutive Michael reactions forming equilibrium established bridges. The links can transfer from one residue to another in a stepwise "walking" or "pivoting" fashion to give a unique and efficient chemical modification and tethering of bioprobes to enzymes, antibodies and other biomacromolecules.



S. Mitra & R. G. Lawton, "Reagents for the Cross-Linking of Proteins by Equilibrium Transfer Alkylation", ***J. Am. Chem. Soc***. **1979**, *101*. 3097.

Frederick A. Liberatore, Robert D. Comeau, James M. McKearin Daniel A. Pearson, Benjamin Q. Belonga, Stephen J. Brocchini, John Kath, Terri Phillips, Kira Oswell & Richard G. Lawton, "Site Directed Modification and Cross-linking of a Monoclonal Antibody with Equilibrium Transfer Alkylating Cross-link Reagents" ***Bioconjugate Chemistry*** **1990**, *1*, (Jan-Feb) 36-50.

***Total Cumulative list of Publications:***

1. Bergman, E.; Lawton, R. G.; Tai, S. "Preparation and Cationic Rearrangement of Some Trifluoroalkyl Derivatives", Abstracts, p. 11M, 134th Meeting of the American Chemical Society, September, 1955.
2. van Tamelen, E. E.; Dolby, L. J.; Lawton, R. G., "A Biogenetically Patterned Laboratory Synthesis in the Strychnine-Curare Alkaloid Series", *Tetrahedron Lett.* **1960,** *19*, 30.
3. Lawton, R. G.; "1,5-Participation in the Solvolysis of 2-(3-Cyclopentenyl)ethyl p-Nitrobenzenesulfonate", *J. Am. Chem. Soc.* **1961,** *83*, 2399.
4. Barth, W. E.; Lawton, R. G.; "Dibenzo(*ghi,mno*)fluoranthene", *J. Am. Chem. Soc.* **1966,** *88*, 380.
5. Nelson, R. P.; Lawton, R. G., "On the α,α'-Annelation of Cyclic Ketones", *J. Am. Chem. Soc.* **1966,** *88*, 3884.
6. Janata, J.; Gendell, J.; Barth, C. Ling. W.; Backes, L.; Mark, H. B.; Lawton, R. G.; "Concerning the Anion and Cation Radicals of Corannulene", *J. Am. Chem. Soc.* **1967**, *89*, 3056.
7. Dominy, B. W.; Lawton, R. G." 5-Benzylidinedioxalane-2,4-dione. The Cyclic Enol Carbonic Anhydride of Phenylpyruvic Acid", *Chem. Commun.* **1968**, *22*, 1448. Presentation, 1968 ACS Meeting, San Francisco, California.
8. Dominy, B. W.; Krejcarek, G.; Lawton, R. G. "The Interaction of Reactive Functional Groups Along Peptide Chains. A Model for Alkaloid Biogenesis", *Chem. Commun.* **1968**, *22*, 1450.
9. Janata, J. R.; Gendell, J.; Lawton, R. G.; Mark Jr., H. B. "The Reduction of Aromatic Hydrocarbons. I. Polarographic and Electron Spin Resonance Studies of 4,5-Methylenephenanthrene", *J. Am. Chem. Soc.* **1968**, *90*, 5226.
10. Crandall, T. G.; Lawton, R. G.; "A Biogenetic-type Synthesis of Cedrene", *J. Am. Chem. Soc.* **1969**, *91*, 2127.
11. Nelson, R. P.; McEuen, J. M.; Lawton, R. G.; "The α,α'-Annelation of Cyclic Ketones. Synthesis of Bicyclo[3.2.1]octane Derivatives", *J. Org. Chem.* **1969**, *34*, 1225.
12. Dominy, B. W.; Lawton, R. G.; "3-Benzylidene-2,5-diketopiperazine", *J. Org. Chem.* **1969**, *34*, 2013.
13. McEwen, J. M.; Nelson, R. P.; Lawton, R. G.; "The α,α'-Annelation of Cyclic Ketones. Synthesis and Conformational Properties of Bicyclo[3.3.1.]nonane Derivatives", *J. Org. Chem.* **1970**, *35*, 690.
14. Barth, W. E.; Lawton, R. G.; "The Synthesis of Corannulene", *J. Am. Chem. Soc.* **1971**, *93*, 1730.
15. Dunham, D. J.; Lawton, R. G.; "The Synthesis of Spiro Systems by the α,α'-Annelation Process", *J. Am. Chem. Soc.* **1971**, *93*, 2075.
16. Dunham, D. J.; Lawton, R. G.; "Spiro Intermediates in Sesquiterpene Rearrangements and Synthesis", *J. Am. Chem. Soc.* **1971**, *93*, 2075.
17. Haslanger, M.; Lawton, R. G.; "A Facile Preparation of the Ethylene Glycol Monoketal of Cyclohexane 1,4-Dione", *Synthetic Comm.* **1964**, *4(3)*, 155.
18. Ice, R. D.; Wieland, D. M.; Beierwaltes, W. H.; Lawton, R. G.; Redmon, M. J.; "Concentration of Dopamine Analogs in the Adrenal Medulla", *J. Nucl. Med.* **1975**, *16*, 1147.
19. Weiss, D. S.; Haslanger, M.; Lawton, R. G.; "Photochemistry of Methyl 1-Methylbicyclo[3.3.1]nonan-9-one-3-carboxylates", *J. Am. Chem. Soc.* **1976**, *98*, 1050.

20. Haslanger, M.; Zawacky, S.; Lawton, R. G.; "Solvolysis of Benzobicyclo[3.2.1]octenylmethyl Tosylates", *J. Org. Chem.* **1976**, *41*, 1807.
21. Holmes, T. J.; Lawton, R. G.; "Cysteine Modification and Cleavage of Proteins with 2-Methyl-N1-benzenesulfonyl-N4-bromoacetylquinonediimide", *J. Am. Chem. Soc.* **1977**, *99*, 1984.
22. Anderson, N. G.; Lawton, R. G.; "Intramolecular Photochemical Closure to 4-Tryptophane Substituted Tiglate Derivatives", *Tetrahedron Lett.* **1977**, 1843.
23. Mitra, S.; Lawton, R. G.; "Reagents for the Cross-Linking of Proteins by Equilibrium Transfer Alkylation", *J. Am. Chem. Soc.* **1979**, *101*, 3097.
24. Lawton, R. G.; "Reaction of Insulin Derivatives with ETAC Reagents", in *Proceedings of the 2nd International Insulin Symposium*, Aachen **1979**, Walter deGruyter Publishers.
25. Mueller, L. G.; Lawton, R. G.; "A Ring Expansion Synthesis of Fused trans-α-Methylene-γ-lactones", *J. Org. Chem.* **1979**, *44*, 4741.
26. Claiborne, A.; Hemmerich, P.; Massy, V.; Lawton, R. G.; "Reaction of 2-Thio-FAD-reconstituted p-Hydroxybenzoate Hydroxylase with Hydrogen Peroxide. Formation of a Covalent Flavin-Protein Linkage", *J. Biol. Chem.* **1983**, *258*, 5433-5439.
27. Holmes, T. J.; Jr., Lawton, R. G.; "Preparation of Non-Symmetrical *p*-Benzoquinonediimides for Evaluation as Protein Cleavage Reagents", *J. Org. Chem.***1983**, *48*, 3146-3150.
28. Holmes, T. J.; Jr.,; Lawton, R. G.; "A Comparison of CYSSOR Analogues in the Cysteine-specific Chemical Cleavage of Ovalbumin", *Internat. J. Pep. Protein Res.* **1984**, *23*, 282.
29. Chemistry of Protein Cross-linking and Chemical Modification Reagents for publication in J. Meienhoffers PEPTIDES series.
30. Brocchini, S. J.; Eberle, M.; Lawton, R.; "Molecular Yardsticks. Synthesis of Extended Equilibrium Transfer Alkylation Cross-link Reagents & their use in the Formation of Macrocycles." *J. Am. Chem. Soc* **1988**, *110*, 5211-5212.
31. Eberle, M.; Lawton, R. G.; "Thioalkylation of Meldrum's acid: Protected Alkylidene Derivatives of Isopropylidene Malonate." *Helvitica Chimica Acta*. **1988**, *71*, 1974-1982.
32. Liberatore, F. A.; Comeau, R. D.; Lawton, R. G.; "Heterobifunctional Cross-linking of a Monoclonal Antibody with CYSSOR 2-Methyl-N-benzenesulfonyl-N4-bromoacetyl-quinonediimide." *Biochem. Biophys. Research Comm.* **1989**, *158*, 640-645.
33. Goodfellow, V. S.; Setteneri, M.; R. G. Lawton. "*p*-Nitrophenyl 3-diazopyruvate and Diazopyruvamides. A New Family of Photoactivatable Cross-linking Bioprobes" *Biochemistry* **1989**, *28* 6346-6360.
34. Harrison, J.K.; Gnegy, M.E.; Lawton, R.G. "Development of a Novel Photoaffinity Calmodulin Probe: Cross-linking of Purified Adenylate Cyclase from Bovine Brain." *Biochemistry*. **1989**, *28*, 6023-6027.
35. Liberatore, F. A.; Comeau, R. D.; McKearin, J. M.; Pearson, D. A.; Belonga, B. Q.; Brocchini, S. J.; Kath, J.; Phillips, T.; Oswell, K.; Lawton, R. G.; "Site Directed Modification and Cross-linking of a Monoclonal Antibody with Equilibrium Transfer Alkylating Cross-link Reagents" *Bioconjugate Chemistry* **1990**, *1* (Jan-Feb), 36-50.
36. del Rosario, R. B.; Brocchini, S. J.; Lawton, R. G.; Wahl, R. L.; Smith, R.; "Sulfhydral Site-Specific Cross-linking of a Monoclonal Antibody by a Fluorescent Equilibrium Transfer Alkylating Cross-link Reagent." *Bioconjugate Chemistry* **1990**, *1*, 50-58.
37. del Rosario R., Brocchini, S.J., Baron, L.A., Lawton, R.G., Smith, R.H. Jackson G.A., Scott, P.A. Clavo, A.C., Fischer, S. J., Wahl, R.L., "Sulfhydral Site-specific Radiolabeling of Monoclonal Antibodies Using Equilibrium Transfer Alkylation Cross-

link Reagents: Application To The Biotin/streptavidin Methodology." *J. Nucl. Med.* **1989**, *30*, 832.

38. del Rosario R., Brocchini, S.J., Baron, L..A., Lawton, R.G., Smith, R.H. Jackson G.A., Scott, P.A. Clavo, A.C., Fischer, S. J., Wahl, R.L. 1989,"New Strategies For Sulfhydral Site-specific Labeling Of Monoclonal Antibodies Using Biotin/streptavidin and Equilibrium Transfer Alkylation Cross-link (ETAC) Reagents." *4th International Conference on Monoclonal Antibody Immunoconjugates for Cancer*, March **1989**, San Diego, CA.
39. Brocchini, S.J.; Retherford, C.; Schmiedeskamp, M.; del Rosario, R.; Wahl, R.L. & Lawton, R.G. "Macrocycles From Extended Equilibrium Transfer Alkylation Cross-link Reagents. Double-armed and Water Soluble Molecular Yardsticks." *American Chemical Society 31st National Organic Symposium,* June **1989**, Ithaca,NY.
40. del Rosario R., Brocchini, S.J., Baron, L.A., Lawton, R.G., Smith, R.H. Jackson G.A., Scott, P.A. Clavo, A.C., Fischer, S. J. & Wahl, R.L. 1990) "ETAC Reagents: A New Class Of Sulfhydral Site-specific Radiolabeling Probes For Antibodies." *International Symposium of Radiopharmaceutical Chemistry,* June 1990. Princeton, NJ.
41. del Rosario R., Brocchini, S.J., Baron, L.A., Lawton, R.G., Smith, R.H. Jackson G.A., Scott, P.A. Clavo, A.C., Fischer, S. J., Wahl, R.L., Preparation of Streptavidin-Biotinylated Antibodies Using Protein A: Relevance of Complex Size to Tissue Uptake. *J. Nucl. Med.* **1990**, *31*, 904.
42. del Rosario R., Lawton, R.G. & Wahl, R.L., Synthesis and Radiolabeling of Tyrosyl ETAC: A New Sulfhydral Site Specific Antibody Cross-linking and Radioiodination Reagent. *J. Nucl. Med.* **1991**, *32*, 915.
43. del Rosario R., Brocchini, S.J., Baron, L.A., Lawton, R.G., Smith, R.H. Jackson G.A., Scott, P.A. Clavo, A.C., Fischer, S. J. & Wahl, R.L.; ETAC Reagents: A New Class of Sulfhydral Site-Specific Radiolabeling Probes for Antibodies. *J. Labeled Compounds and Radiopharmaceuticals* **1991**, *30*, 193-195.
44. del Rosario R., Baron, L.A., Lawton, R.G., Wahl, R.L. Streptavidin-Biotinylated IgG Conjugates; A Simple Procedure for Reducing Polymer Formation *Nucl. Med Biol.* 1992, *19*, 417-421.
45. Taylor, J. M., Jacob, G. G., Lawton, R. G., Neubig, R. R., Cross-linking of $\alpha_2$-Adrenergic receptor to G-proteins *J. Cellular Biochemistry* **1993**, *17c* 221.
46. Jacob, G. G.,Taylor, J. M., Neubig, R. R., Lawton, R. G., The Development of a New Family of Thiol Specific Photoactivatable Cross-linking Agents. American Chemical Society, Division of Organic Chemistry, 206$^{th}$ ACS National Meeting, Chicago, IL, Abstract 38.
47. Taylor, J. M., Jacob-Mosier, G. G., Lawton, R. G., Neubig, R. R., A new thiol specific photoactivatable crosslinking regent. Conjugation of an α2-adrenergic receptor peptide to G-protein. *Peptides,* **1994,** *15*, 829-834.
48. Taylor, J. M., Jacob-Mosier, G. G., Lawton, R. G., Remmers, A. E., Neubig, R. R.,. Binding of an α2-adrenergic receptor third intercellular loop peptide to Gβ and the amino terminus of Gα. *J. Biol. Chem.***1994**, *45*, 27618-27624.
49. Jacob Mosier, G. G.; Lawton, R. G., The Development of a New Family of Thiol Specific Photoactivatable Cross-linking Agents, *J. Org Chem.* **1995**, *60*, 6953-6958.
50. Coppola, B. P.; R. G. Lawton. "Who Has the Same Substance that I Have". A Blueprint for Collaborative Learning Activities. *J. Chem. Educ.* **1995**, *72*, 1120.

51. M. Taylor, Mosier G. G. Jacob, R. G. Lawton, M. VanDort and R. R. Neubig. Receptor and membrane interaction sites on G{beta}. A receptor-derived peptide binds to the carboxyl terminus.. *J. Biol. Chem.* **1996**, Feb 16; *271* (07): 3336.
52. Ege, S. N., Coppola, B. P.; Lawton, R. G.; The University of Michigan Undergraduate Chemistry Curriculum. 1. Philosophy, Curriculum and the Nature of Change, *J. Chem. Educ*. **1997**, *74*, 74-83
53. Ege, S. N., Coppola, B. P.; Lawton, R. G.; The University of Michigan Undergraduate Chemistry Curriculum. 2. Instructional Strategies and Assessment, *J. Chem. Educ*. **1997**, *74*, 84-94.
54. Chen, Y.-S.; Lawton, R. G. "An Efficient Synthetic Route to 2-(1, 2-Dithiolan-3-yl)acetic acid. Trisnorlipoic Acid and Amide Derivatives." *Tetrahedron Lett*. **1997**, 38, 5785-5788
55. Yaun-Shek Chen, Jeff W. Kampf and Richard G. Lawton. Aromatic Stacking in Folded Architectures through Hydrogen Bonding. *Tetrahedron Lett*. **1997,** 38, 5781-5184.
56. Brocchini, S. J.; Lawton, R. G.; Titanium Chelation in Regioselective Michael Additions to Conjugated Dienones and Trienones. *Tetrahedron Lett*. **1997,** *38***,** 6319-6323.
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**Narrative Resume - Dr. Richard G. Lawton**
**University of Michigan, Ann Arbor Michigan**
b. August 29, 1934; Berkeley, California

***Dr. Richard G. Lawton*,** a native of Berkeley, California, received his B.S. degree from the College of Chemistry at the University of California, Berkeley, in 1956 and his Ph.D. in organic chemistry from the University of Wisconsin, Madison, in 1962. His advisor in his undergraduate years was Dr. William G. Dauben. Bill Dauben and many of his graduated students [particularly Al Markhart and his wife Misty] and post-doctorals had served to nurture Rich's interest in organic chemistry in his junior high school days, a fascination that was initiated at the age of 8 through seeing a chemistry-set in a store window. This fascination with organic chemistry and molecular architecture continues today. While an undergraduate at Berkeley, Rich worked with Dr. Elliot Bergman on a senior project: "Migratory Aptitude of the Trifluoromethyl Group" and with Dr. Henry Rapoport on the chemistry of the "Hammick Reaction".

At the University of Wisconsin, Dr. Eugene van Tamelen served as research director. The theme of Lawton's doctoral research was "The Biogenetic-type Synthesis of Strychnine Alkaloids". During this graduate period, Lawton independently conceived, accomplished and published as a Communication in the *Journal of the American Chemical Society*, the first example of a ring closure demonstrating π-participation to give the non-classical ion leading to the bicyclic norbornyl system.

In the intervening years between his graduate and undergraduate careers, Rich worked as a chemist at the Merck, Sharp and Dohme Research Laboratories in Rahway, New Jersey in the Isolation Structure Determination Group then headed by Dr. Karl Folkers while waiting to be drafted. He was drafted into the U.S. Army in 1957 and after basic training completed his service at Walter Reed Army Institute of Research, Walter Reed Hospital, Washington, D.C. During these years (1957-59), he participated in the design and synthesis of amino mercaptans for use as anti-radiation drugs.

After obtaining his Ph.D. degree in 1962 at Wisconsin, he accepted an appointment at the University of Michigan, Ann Arbor. He served at Instructor at Michigan until 1964, as Assistant Professor until 1967, as Associate Professor (with tenure) until 1970. He is now Professor of Chemistry (Emeritus} and an Arthur F. Thurnau University Professor (1993). In the 1970-1971 academic years he was invited to serve as Visiting Professor at the University of Wisconsin, Madison, and at the University of Illinois, Champaign-Urbana.

In the 1978-79 academic years, Professor Lawton was awarded a Guggenheim Foundation Fellowship for studies involving the chemical interactions of functional groups on protein chains. This fellowship year was devoted to study, writing and research at the Deutsches Wöllforschunginstitut in Aachen, West Germany, in collaboration with the research group of Professor Helmut Zahn. The chemical and biochemical research involved the application of a new family of protein modification reagents designed by the Lawton group to the study of insulin cross-linking. Biochemical techniques of the Zahn Laboratories for insulin chemistry were acquired and new techniques were developed to study the unique type of cross-linking agents being synthesized in Ann Arbor. The relationship with the Aachen group has continued since that time and he returned to Aachen during the summer of 1983 to continue his research efforts on cross-linking reagents. Dr. Lawton has also been associated with the Swiss Federal

Technical University, the Eidgenossische Technische Höchschule, Laboratorium fur Organische Chemie, Zurich, where he was a Visiting Professor with Professor Dieter Seebach in 1987-88.

Dr. Lawton's research interests are highly varied. Early in his career at Michigan, he developed strategies for the synthesis of strained aromatic compounds which reflected a confrontation of the factors of strain and aromaticity. The unique bowl-shaped compound, corannulene, was envisioned and pathways for its synthesis designed and elaborated. The molecule was eventually synthesized by graduate student Wayne Barth in about 27 steps. This corannulene synthesis remained unique for over 25 years. The structure has now been synthesized again several times by different routes and on large scale. There is a tremendous amount of interest in this corannulene structure because it has the same carbon skeleton as a portion of the framework of buckministerfullerene or Buckyball, the C 60 compound attracting so much attention in the popular and scientific literature.

Lawton's research group, including Rodger Nelson, John McEuen, Dave Dunham and Marty Haslanger, was responsible for the design and development of a new technique for the construction of bridged bicyclic and spiro compounds, the α,α'-annelation reaction, a reaction based upon successive Michael reactions and now known as the "Lawton facilitated $S_N2'$ chemistry". With Terry Crandall, Rich designed and accomplished a biogeneticly patterned and stereoselective synthesis of the terpene cedrene following the general mechanistic route discovered earlier in the π-participation cyclization study.

A continuing interest of his research is the design, synthesis and chemistry of reagents and structures which serve as tools for the identification of interactions between reactive functional groups on peptide and protein chains. The idea is an extension of the concepts of neighboring group participation chemistry to the chemical modification of biomaterials. The theme has universal applications for organic, bio and molecular bio-chemistry. These ideas were first formulated and the first entries in the area of synthesis were accomplished with Beryl Dominy, Gary Krejcarek, Doug Raber and Tom Holmes. Both chemical reagents created as well as the modified protein structures derived from combining of reagents and native proteins have potential for unique medicinal and biochemical studies. Further, the concept of the interaction of reactive functional groups on protein chains coupled with the strategies of the α,α'-annelation reaction has provided new types of chemical modification and cross-linking reagents for proteins. These are described as **e**quilibrium **t**ransfer **a**lkylation **c**ross-links, or ETAC reagents, and this specific work was initiated with Sumita Mitra. These reagents allow the covalent linking of proteins in either an intra- or intermolecular fashion, yet the reagents still retain a mobile character so that they can, under certain conditions, transfer from one protein residue to another or to another protein. ETAC reagents are engineered so that nucleophilic residues on a protein chain, such as lysine amino, histidine imidazole, etc., will undergo a Michael addition reaction with the subsequent loss of a group which will generate a new, previously latent, conjugated double bond on the reagent now attached to the protein. A second Michael reaction is then possible, yielding a linked protein either in an intra- or intermolecular mode. When the second nucleophile attacks the conjugated double bond, again an anion intermediate is formed now connecting both the first and second residues. Dual cysteine sulphydryls or the case of one of the SH groups of a reduced cystine pair, are special examples, since no other nucleophiles on the protein will be able to compete for the Michael addition site. Depending on the nucleophiles now attached, the intermediate carbon anion can be protonated to give cross-linked sites or it can fragment in either of two directions:

**1)** reverse Michael to return to the condition having the reagent attached only to the first residue with the simultaneous reformation of the conjugated double bond

or,

**2)** reverse Michael in the alternate direction to release the bond attached to the first residue allowing the transfer of the reagent moiety completely to the second residue again with the simultaneous reformation of the conjugated double bond.

Now free from the attachment to the first site, the reagent can pivot so that Michael addition from a third neighboring site can occur. The process can continue, allowing the reagent moiety to shift from one residue to another by a cascade of consecutive equilibrium Michael reactions to eventually form the most thermodynamically stable bridge. This will be a site between reduced cystines if they are available. It is this transfer path that makes the reagents unique and special as protein modification reagents.

ETAC links between cysteine thiols, especially those that are derived from a cystine by reduction of the S-S bond, are particularly stable since the SH groups must be close in space and these SH groups are significantly more nucleophilic than any other neighboring groups in a protein. The SH groups were originally joined so they must be in proximity to one another and they are about 10,000 times more nucleophilic than a $NH_2$ group in the Michael addition process. The transfer process is automatically arrested because the equilibrium amount of the reverse Michael moiety and of the thiolate anion is small and another thiol (in solution) cannot compete for the Michael acceptor site against the neighboring cysteine thiol at that point. Thus, these reagents have the possibility of "walking", "pivoting", "skipping" or "jumping" along the protein chain from one nucleophilic amino acid side chain to another (lysine) until a stable link (reduced cystines) within the protein framework or protein aggregate structure is attained. The new bridge is "anchored" into place at these two select, abutting and strongly nucleophilic sites of the original cystine unit and serves as a linking point to spectral and radioactive bioprobe indicators. Attachment of the linkers and their tethered bioprobes to antibodies gives a series of special and unique diagnostic reagents.

With Steve Brocchini and post-Doctoral Martin Erberle, these ETAC reagents have been extended by adding to the length of the conjugated Michael acceptor system to create "molecular yardsticks" that bridge the nucleophilic residues of proteins and also cyclize simple frameworks to give unique macrocycles. Research is directed to the design, synthesis and development of reagent structures that can be used in protein biochemistry as molecular tools and probes for the identification of bioorganic mechanisms and interactions. Reagents for the selective cleavage of proteins at cysteine residues has been designed developed and studied [CYSSOR reagents]. Reagents for the chemical synthesis of proteins through selective fragment condensation are also now being created and developed. An active area is the development of photoactivatable reagent probes that was initiated with Val Goodfellow for photo activated covalent modification and cross-linking of proteins [DAP group]. This work was continued with Gay Jacob-Mosier on the development of *bis*-DAP reagents and DAP reagents for connection to thiols. Dr. Lawton continues to both participate in and enjoy laboratory bench chemistry. Rich served as research advisor for 22 Ph. D. students over the 40 years of his academic career.

In addition to active participation in Chemistry Department affairs and programs, for the past several years Dr. Lawton has served as research advisor for graduate students in Medicinal Chemistry in the College of Pharmacy. He has been active in the Executive Committee of this

Interdepartmental program. Dr. Lawton has served as the Organic Division Coordinator for two years starting 1985. He has served as an internal university consultant to Dr. William Beierwaltes(now retired) of the Department of Nuclear Medicine concerning the construction of organ selective organic molecules containing radioactive atoms for diagnostic and radiotherapy and has an active collaboration with Dr. Richard Wahl in Nuclear Medicine of the attachment of bioprobes to antibodies. Further, he has served on numerous doctoral committees in the Biochemistry Department and on the Executive Committee of the Biophysics Group at the Institute of Science and Technology and as the LSA representative to the Bio Medical Research Counsel of the Medical School.

A major commitment of time and effort was the intimate involvement in the construction of the new W. H. Dow Chemistry Building finished in 1989. Rich was a major contributor to the design and appointment of the research laboratories of this building and played an active role in the construction of the building which has received the praise of all chemists and educators who have seen and visited the Department. He served continuously on the planing and building committee for over 15 years.

The Lawton group has continued collaborations with the research groups of Dr. Helmut Zahn (now retired) and Dr. Deitrich Brandenburg of the Deutsches Wöllforschungsinstitut, Aachen, Germany regarding insulin cross-linking; with the research group of Dr. Charles Williams of the Veterans Administration Hospital, Department of Biochemistry and the University of Michigan involving the design of probes for glutathione reductase and amino acid oxidase enzyme systems; with Dr. Michael Welsh, Department of Anatomy and Cell Molecular Biology regarding calmodulin cross-linking reagent probes and with the research group of Dr. Vince Massey of the Department of Biological Chemistry regarding design of probes of flavin enzyme systems; with Dr. Richard Wahl of the Department of Nuclear Medicine on the attachment of radioactive and fluorescent probes to antibodies for diagnostic and cancer chemotherapy.

Rich Lawton has served as a consultant for the Research Laboratories of the Colgate-Palmolive Company, New Jersey, for the last twenty years. Dr. Lawton has also served as a consultant for the former New England Nuclear now a division of the DuPont Company, their Immunopharmaceuticals Organic chemistry and Analysis group.

Teaching assignments at the University of Michigan have been in every organic lecture and laboratory offered. He has taught Sophomore Organic Chemistry (classes of 250-400) and Laboratory, a two-semester sequence, both lecture and laboratory, Qualitative Organic Analysis, Organic Spectroscopy, Honors Organic Chemistry (undergraduate), Special Topics Courses in bioorganic mechanisms and biosynthesis (joint Biochemistry-Chemistry), graduate courses in natural products and synthesis as well as in physical-organic chemistry and mechanisms.

Dr. Lawton was a major participant in the development of a chemistry program for the Inteflex medical students. These are students enrolled simultaneously in the College of Literature, Science and Arts and also in Medical School (a six-year program). A freshman chemistry (one semester), organic chemistry (one semester) and bioorganic chemistry sequences prepares these students for both biochemistry and physiology. The course contains lecture, laboratory and recitation components. The Chemistry Department of the University has been involved continuously in the evolution of a new curriculum for undergraduate chemistry students. This involves a restructuring of the sequence of both lecture and laboratory courses for

chemistry students and Rich Lawton, along with Dr. Brian Coppola and Dr. Seyhan Ege, has been a major participant in this process.

In 1988 Professor Lawton was awarded the University of Michigan Good Teaching Award for excellence in Undergraduate teaching. The citation composed from letters and comments from his students to the Awards committee reads:

> "You have often stated that "I don't teach." All who have been associated with you know that this means you provide the way for self-discovery: learning. Your high standards are presented to students as attainable goals, along with the strong encouragement, accessibility, humor, sensitivity and patience that it takes to support and promote the effort. Both your colleagues and your students describe you in the same consistent terms, and the message is therefore very clear.
>
> Large classrooms of intense pre-professional students, ready to do battle for grades in organic chemistry, are inspired and converted by your own involvement in and enthusiasm for the subject. Students are presented with a model of how one should think rather than what one should think. The opportunity to experience the trial and error which builds proficiency is constantly reinforced in the classroom, in personal interactions, on examinations and in the laboratory.
>
> You serve as a role model and resource for younger colleagues who benefit from your expertise in the classroom. In your research laboratory, you have provided expert training for future researchers in bio-organic chemistry at both the undergraduate and graduate levels. Your strong commitment to solving difficult research problems has contributed to your success in building bridges between chemistry and biology.
>
> In recognition of your outstanding contributions to your students and colleagues, the University is proud to present you with the Amoco Good Teaching Award."

Recognition of Rich's contributions to undergraduate and graduate teaching has continued. In each of the years 1991, 1992 and 1997, Rich was awarded the LS & A College Excellence in Teaching Award and in 1993 the University named Professor Lawton as an Arthur F. Thrunau University Professor for outstanding contributions to undergraduate teaching. Rich moved to Professor Emeritus status in the year 2000.

Rich was married to the former Anne Bender of Vienna, Virginia (Washington, D.C.), a biological research assistant for many years at the University of Michigan in the Department of Neurobiology. Anne died of cancer Jan. 9 2013. The family consists of five children; the oldest is now 56, the youngest 48, including four boys and a girl. Deborah graduated from the University of Wisconsin, Madison, 1992, in German & Geography with a year spent in Freiburg, Germany; David graduated in 1991 from the University of Wisconsin, Milwaukee in Graphic Arts. Eric received his BS in Engineering Mechanics & Mathematics, University of Wisconsin, Madison (1986) and his MS in Applied Mechanics at the University of Michigan Engineering graduate school (1988). John received his BS in Electrical Engineering, Michigan Technological University, Houghton (1988) and Steve, a degree in Industrial Technology from Eastern Michigan University/Washtenaw College (1986). Rich's hobbies include home remodeling, wind-surfing and travel-color photography—[see www.richlawton.zenfolio.com]. Rich still maintains his “hobby”, love and passion for molecular architecture and organic chemistry research. He continues to “tinker” in the laboratory with his own hands.