

## Peoffesor Kjell Undheim

### A Tribute



Kjell Undheim obtained his B.Sc.Tech.(Honours) in Industrial Biochemistry at UMIST, Manchester, England in 1956, and was awarded a Parke Davis Fellowship for Ph. D. studies in organic chemistry under the supervision of Professor H. N. Rydon at UMIST. When Professor Rydon moved to University of Exeter in 1957, Undheim went with him to complete his Ph.D. studies in Exeter in early 1959. Subsequently, in 1973 he received the D.Sc. degree from the University of Exeter. He also holds the dr.philos degree from the University of Oslo, Norway.

He joined the group of Professor Carl Djerassi at Stanford University, California, for his postdoctoral training in 1959. After one year he was employed as a research chemist at Geigy Pharmaceuticals, New York; in the Astra Laboratories in Södertälje, Sweden, and at Nycomed in Oslo, Norway, before joining the Chemistry Department, University of Oslo in late 1965 as an Associate Professor. In 1970 he was appointed Professor in pharmaceutical organic chemistry at

the Institute of Pharmacy, University of Oslo, but two years later he was appointed Professor in organic chemistry at the Department of Chemistry and returned to the organic chemistry section where he has been working since.

Sabbatical leaves have been spent with Professor Barry Trost, then at the University of Wisconsin, Madison, USA; with Professor Teruaki Mukayama, then at University of Tokyo, Tokyo, Japan; and with Professor Desmond Brown, Australian National University, Australia.

Undheim is a member of The Norwegian Academy of Technical Sciences.

During all his university career Undheim has worked in close contact with pharmaceutical industry and fine chemical companies, frequently on collaborative projects. Besides publications, the collaborative work has resulted in a number of patent applications. On leave from his University, he was for a few years Director of Medicinal Chemistry at Bioreg, a Nycomed company with emphasis on immunology modulators.

More than 300 publications have come out of the Undheim research group. The group has hosted a great number of postdoctorals and many students have received the M.Sc. and Ph.D. degrees under his supervisions. Several of his former students have become professors in Norway. In exchange programs with Universities in Cairo, Egyptian postdoctoral students have since become professors in Egypt. Another collaborative site has been the University in Iasi, Romania, where several of the staff members in organic chemistry have received research training in his group in Oslo.

Undheim is an author of chapters in handbooks and encyclopedia. He authored the Chapter on «*Five-membered Rings (One Oxygen or Sulfur and At least One Nitrogen Atom) Fused with Six-membered Rings (At least one nitrogen Atom).*» in the first edition of *Comprehensive Heterocyclic Chemistry* (A. R: Katritzky, C. W. Rees). In the second edition, his chapter was on «*Pyrimidines and Their Benzo derivatives*». Aspects of organotitanium and -zirconium chemistry were reviewed together with coworkers in the reference work «*Encyclopedia of Reagents for Organic Synthesis*» (L. A: Paquette). The chapter on «*Heteroaromatics via Palladium-Catalyzed Cross Coupling*» in Handbook of «*Organopalladium Chemistry for Organic Synthesis*» (E.-i. Negishi) is about to be published. Reviews also include *Tetrahedron. Symposium-in-Print* articles on the applications of organometallics in synthesis and an early review together with coworker on «*Organometallics in Coupling Reactions in  $\pi$ -Deficient Azaheterocycles*» in *Advances in Heterocyclic Chemistry*.

Undheim has worked in several areas of synthetic organic chemistry starting with his initial training in heterocyclic chemistry during his Ph.D. studies on the synthesis of antifolates. Industrial work was associated with CNS active cyclic amino acid analogues, semisynthetic  $\beta$ -lactams and X-ray contrast agents. Industrial collaborative efforts have been on nucleoside and nucleotide prodrugs as antiHIV agents, metaphase arrestors for synchronization of cell division as adjuvants in treatment with cytotoxic drugs, and on aminoid structures as immune modulators.

Major efforts have been devoted to studies of gas phase structures of ionic and mesoionic molecules in the mass spectrometer, and on syntheses of betaines and mesoionic hetarenes. Early, major efforts were on development of transition metal-catalyzed cross-coupling reactions

in  $\pi$ -deficient heteroarenes. The main emphases in recent years have been on stereoselectivity in the construction of constrained or rigidified amino acid analogues and peptides, and on the stereocontrolled construction of rigidified metallocenes for stereoselective catalytic applications.

### Selected Publications of Kjell Undheim (1989 - date)

1. Efskind, J.; Rømming, C.; Undheim, K. "Stereocontrolled construction of rigid tricyclic bis( $\alpha$ -amino acid) derivatives by Ru(II)-catalyzed cascade and Diels-Alder reactions" *J. Chem. Soc., Perkin Trans. 1* **2001**, 2697.
2. Aburel, P. S.; Rømming, C.; Ma, K.; Undheim, K. "Synthesis of  $\alpha$ -hydroxy and  $\alpha$ -oxospiranes through ruthenium(II)-catalyzed ring-closing metathesis" *J. Chem. Soc., Perkin Trans. 1* **2001**, 1458.
3. Aburel, P. S.; Rømming, C.; Undheim, K. "Rhodium(II)-carbenoid C-H insertion reactions in the synthesis of  $\alpha,\beta$ -dioxospiro systems" *J. Chem. Soc., Perkin Trans. 1* **2001**, 1024.
4. Ahmad, I.; Falck-Pedersen, M. L.; Undheim, K. "Synthesis of silacycloalkenes and silaspiroenes by Ru(II)-catalyzed ring-closing metathesis reactions" *J. Organomet. Chem.* **2001**, 625, 160
5. Wang, J.; Falck-Pedersen, M. L.; Rømming, C.; Undheim, K. "The Pauson-Khand Reaction in the Synthesis of Bicyclic Rigid  $\alpha$ -amino Acids". *Synth. Commun.* **2001**, 31, 1141.
6. Undheim, K.; Efskind, J. "Ru(II)-Catalyzed Ring Closing Metathesis in Stereoselective Spiroannulations and Cascade Reactions of Cyclic Dipeptide Substrates." *SYMPOSIA-IN-PRINT, "Carbene Complexes in Organic Chemistry" Tetrahedron* **2000**, 56, 4847.
7. Hammer, K.; Wang, J.; Falck-Pedersen, M. L.; Rømming, C.; Undheim, K. "Stereoselectivity in the synthesis of conformationally constrained vicinally dihydroxylated cyclic  $\alpha$ -amino acids" *J. Chem. Soc., Perkin Trans. 1* **2000**, 1691.
8. Falck-Pedersen, M. L.; Rømming, C.; Undheim, K. "Palladium Mediated Carbosubstitutions in Spiranes" *Tetrahedron* **1999**, 55, 8525.
9. Efskind, J.; Rømming, C.; Undheim, K. "Ru(II)-Catalysis in the preparation of sterically congested and stereochemically homogeneous heterospiroenes" *J. Chem. Soc., Perkin Trans. 1* **1999**, 1677.
10. Sirbu, D.; Falck-Pedersen, M. L.; Rømming, C.; Undheim, K. "Palladium Mediated Substitutions and Rearrangements in Spiro[4,4]nonanes" *Tetrahedron* **1999**, 55, 5703-6712.
11. Sandnes, R. W.; Gacek, M. and Undheim, K. "A Simple Synthesis of the Macrocyclic 1,4,7,10-Tetraazacyclododecane" *Acta Chem. Scand.* **1998**, 52, 1402-1404.
12. Hammer, K.; Undheim, K. "Ru(II)-Catalyzed Ring Closing Metathesis in Stereoselective Syntheses of Constrained Homoserine Analogues" *Tetrahedron* **1998**, 54, 10837-10850.
13. Hatlelid, J.; Benneche, T.; Undheim, K. "Synthesis of Prodrugs as Bridged Nucleosides" *Acta Chem. Scand.* **1998**, 52, 1270-1274.
14. Møller, B.; Undheim, K. "Cyclic  $\alpha$ -amino Acids by Pd-Mediated Cycloisomerization and Coupling Reactions" *Tetrahedron* **1998**, 54, 5789-5804.

15. Kremminger, P.; Undheim, K. "Synthesis of orthogonally protected hydroxylated azalkene- $\alpha,\alpha'$ -bridged bis( $\alpha$ -glycine) and dihydroxylysine derivatives" *Tetrahedron Asymmetry* **1998**, *9*, 1183-1189.
16. Efskind, J.; Benneche, T.; Undheim, K. "Stereoselective Synthesis of Alkenyl  $\alpha,\alpha'$ -Bridged Bis(glycines) using Palladium Promoted Substitution in the Bridge" *Acta Chem. Scand.* **1997**, *51*, 942-952.
17. Rødbotten, S.; Benneche, T.; Undheim, K. "Stereoselective Synthesis of Alkynylglycines and  $\alpha,\alpha'$ -Alkynyl-Bridged Bis(glycines)" *Acta Chem. Scand.* **1997**, *51*, 873-880.
18. Hatlelid, J.; Benneche, T.; Undheim, K. "Tin-Pummerer Rearrangement in the Synthesis of O,S-Acetal Derivatives" *Acta Chem. Scand.* **1997**, *51*, 1092-1095.
19. Neset, S.; Hope, H.; Undheim, K. "Stereoselective Synthesis of Cyclopropane-1,2-bis(Glycine) Derivatives" *Tetrahedron* **1997**, *53*, 10459-10470.
20. Hammer, K.; Undheim, K. "Ruthenium-Catalyzed Enyne Metathesis in Stereoselective Preparation of Cyclic 1-Amino-1-Carboxylic Acids" *Tetrahedron* **1997**, *53*, 1060-10614.
21. Kremminger, P.; Undheim, K. "Asymmetric Synthesis of Unsaturated and Bis-Hydroxylated (*S,S*)-2,7-Diaminosuberic Acid Derivatives" *Tetrahedron* **1997**, *53*, 6925-6936.
22. Hammer, K.; Undheim, K. "Synthesis of Conformationally Restricted Serine Derivatives Through Ruthenium(II)-Catalyzed Ring Closing Metathesis" *Tetrahedron* **1997**, *53*, 5925-5936.
23. Hammer, K.; Benneche, T.; Hope, H.; Undheim, K. "Stereoselective Synthesis of Thiophenedimethyl- and Benzenedimethyl  $\alpha,\alpha'$ -Bridged Bis(glycines)" *Acta Chem. Scand.* **1997**, *51*, 392-402.
24. Lu, Q.; Mangalagiu, I.; Benneche, T.; Undheim, K. "Trialkylalanes in Palladium-Catalyzed C-Alkylations of Azines" *Acta Chem. Scand.* **1997**, *51*, 302-306.
25. Møller, B. S.; Benneche, T.; Undheim, K. "Palladium Catalysis in Bridge-Forming Reactions Between Stereoselectively Substituted Glycine Auxiliaries" *Tetrahedron* **1996**, *52*, 8807-8812
26. Falck-Pedersen, M. L. and Undheim, K. "Asymmetric Synthesis of Phenylbis(glycines)" *Tetrahedron* **1996**, *52*, 7761-7770
27. Hammer, K.; Hatlelid, J.; Grøtli, M.; Arukwe, J.; Klaveness, J.; Rise, F.; Undheim, K. "Ether, Carbonates and Urethane Deoxynucleoside Derivatives as Prodrugs" *Acta Chem. Scand.* **1996**, *50*, 609-622.
28. Mangalagiu, I.; Benneche, T.; Undheim, K. "Trialkylalanes in Palladium-Catalyzed Chemo- and Regioselective Alkylations" *Tetrahedron Lett.* **1996**, *37*, 1309-1312
29. Undheim, K.; Benneche, T. "Organometallics in Coupling Reactions in  $\pi$ -Deficient Azaheterocycles" A Review. *Advances in Heterocyclic Chemistry.* **1995**, *62*, 305-418.
30. Grøtli, M.; Undheim, K. "Synthesis of 2'-Deoxy-2'-Allylnucleosides by Radical Reactions" *Acta Chem. Scand.* **1995**, *49*, 217-224.
31. Williams, L.; Booth, S.; Undheim, K. "An Approach to  $\alpha$ -substituted Amines" *Tetrahedron* **1994**, *50*, 13697-13708

32. Undheim, K.; Williams, L. "The  $\alpha$ -Alkylation of Amines via a 1,5-Hydrogen Shift" *J. C.S. Chem. Commun.* **1994**, 883-884.
33. Fischer, P.; Solbakken, M.; Undheim, K. "Solution Synthesis of a Dimeric Pentapeptide: Diketopiperazine Cyclisation of Glu-Asp Dipeptide Esters and Asp-Racemisation During Segment Condensation" *Tetrahedron* **1994**, *50*, 2277-2288.
34. Sandosham, J.; Undheim, K. "Stannylation in the Electrophilic 2- and 4/6-Pyrimidine Position and The Use of Stannylpyrimidines in Coupling and Tin-Lithium Exchange Reactions" *Tetrahedron* **1994**, *50*, 275-284.
35. Sandosham, J.; Undheim, K. "Synthesis of Pyrimidine Triflates and Palladium-Catalyzed Coupling with Organotin and Organozinc Reagents" *Heterocycles* **1994**, *37*, 501-514.
36. Benneche, T.; Strande, P.; Oftebro, R.; Undheim, K. "Pyrimidinone as Reversible Metaphase Arresting Agents" *Eur. J. Med. Chem.* **1993**, *28*, 463-472.
37. Sandosham, J.; Undheim, K.; Rise, F. "Regioselective Substitution in Triflyloxy-pyrimidines and Chloropyrimidines using Tin and Zinc Reagents" *Heterocycles* **1993**, *35*, 235-244.
38. Undheim, K.; Benneche, T. "Metallation and Metal-Assisted Bond Formation in  $\pi$ -electron Deficient Heterocycles" *Acta Chem. Scand.* **1993**, *47*, 102-121.
39. Falck-Pedersen, M. L.; Benneche, T.; Undheim, K. "Palladium-Catalyzed Rearrangements of 2-Cyclopentenylloxypyrimidines in the Preparation of Carbonucleosides" *Acta Chem. Scand.* **1993**, *47*, 72-79.
40. Falck-Pedersen, M. L.; Benneche, T.; Undheim, K. "Palladium Catalysis in Allylic Rearrangements of Propenyl 2-Pyrimidinyl Carbonates to 1-Propenyl-2(1H)-pyrimidinones" *Acta Chem. Scand.* **1993**, *47*, 63-67.
41. Gaare, K.; Repstad, T.; Benneche, T.; Undheim, K. "Preparation of 5-(Pyrrolylcarbonyl)- and 5-(Imidazolylcarbonyl)pyrimidines" *Acta Chem. Scand.* **1993**, *47*, 57 - 62.
42. Møller, B. S.; Falck-Pedersen, M. L.; Benneche, T.; Undheim, K. "Regioselectivity in the Alkylation of Ambient 2-Pyrimidinone Anions" *Acta Chem. Scand.* **1992**, *46*, 1219-1222.
43. Gundersen, L.-L.; Rise, F.; Undheim, K. "Aryl- and Alkynyltri-isopropoxytitanium Reagents in Regioselective Carbon-Carbon Bond Formation in Azines" *Tetrahedron* **1992**, *48*, 5647-5656.
44. Keilen, G.; Benneche, T.; Gaare, K.; Undheim, K. "Peroxy-molybdenum Complexes in Sulfide to Sulfone Oxidations" *Acta Chem. Scand.* **1992**, *46*, 867-871.
45. Gundersen, L.-L.; Benneche, T.; Rise, F.; Gogoll, A.; Undheim, K. "Regiochemistry and Stereochemistry in Pd(0)-Catalyzed Allylic Alkylation of Nucleoside Bases" *Acta Chem. Scand.* **1992**, *46*, 761-771.
46. Benneche, T.; Keilen, G.; Solberg, J.; Oftebro, R.; Undheim, K. "Synthesis and Studies of Alkynyl Pyrimidinones as Metaphase Inhibitors" *Acta Chem. Scand.* **1991**, *45*, 731-735.
47. Benneche, T.; Keilen, G.; Hagelin, G.; Oftebro, R.; Undheim, K. "Synthesis and Studies of Metaphase-Arresting Pyrimidinones" *Acta Chem. Scand.* **1991**, *45*, 177-185.
48. Arukwe, J.; Benneche, T.; Undheim, K. "Synthesis of 5-Stannylpyrimidines and their Use in Pd-Catalyzed Ketone Formation" *J. Chem. Soc. Perkin Trans. I* **1989**, 255-259.

49. Majeed, A. J.; Antonsen, Ø.; Benneche, T.; Undheim, K. "Stannylation Reactions and Cross-Couplings in Pyrimidines" *Tetrahedron* **1989**, *45*, 993-1006.
50. Zheng, J.; Undheim, K. "Organocerium(III) Reagent from Pyrimidine in Carbon Bond-Forming Reactions" *Acta Chem. Scand.* **1989**, *43*, 816-818.
51. Gundersen, L.-L.; Benneche, T.; Undheim, K. "Chloromethoxysilanes as Protecting Reagents for Sterically Hindered Alcohols" *Acta Chem. Scand.* **1989**, *43*, 706-709.
52. Rise, F.; Undheim, K. "Sodium 2-Mercaptoethanesulfonate in Reversible Adduct Formation and Water Solubilization" *Acta Chem. Scand.* **1989**, *43*, 489-492.
53. Solberg, J.; Undheim, K. "Regiochemistry in Pd-catalyzed Organotin Reactions with Halopyrimidines" *Acta Chem. Scand.* **1989**, *43*, 62-68.
54. Antonsen, Ø.; Benneche, T.; Undheim, K. "Synthesis of Unsaturated Chloromethyl Ethers" *Acta Chem. Scand.* **1989**, *43*, 56-61.