Dana K. Winter

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EDUCATION

2011-Present	Fonds de recherche du Québec-Nature et technologies (FRQNT)[1] Postdoctoral Fellow Advisor: Professor John A. Porco, Jr., Boston University, Boston, MA.
2005-2011	Ph.D. in Organic Chemistry Advisors: Professors Claude Spino and Jean Lessard Université de Sherbrooke, Sherbrooke, QC.
2001-2005	Bachelor of Sciences, *magna cum laude* with honors, Biopharmaceutical Sciences Medicinal Chemistry Co-op, University of Ottawa, Ottawa, ON

HONORS AND AWARDS

2011-2013	FRQNT Fellowship for Postdoctoral Research
2009-2010	FRQNT Award for Doctoral in Research
2009-2010	Valorization of student work, U. de Sherbrooke
2007-2009	National Sciences and Engineering Research Council of Canada (NSERC)[2] Doctoral Scholarship
2005-2007	NSERC Master's Scholarship
2006-2007	Valorization of student work, U. de Sherbrooke
2006-2007	Gene H. Kruger Scholarship
2004-2005	Dean's Merit Scholarship for Excellence, U. of Ottawa
2001-2002	Admission scholarship, U. of Ottawa

RESEARCH EXPERIENCE

02/2011-Present — FRQNT Postdoctoral Fellow, Boston University

Advisor: Professor John A. Porco, Jr.

Total Synthesis of Tetrahydroxanthone Natural Products: kibdelone and isokibdelone family.

- Completed the first total synthesis of kibdelone A (manuscript in preparation).
- Optimized a novel metal-mediated biaryl formation/iodine oxidative photocyclization sequence towards the common core of both kibdelones and isokibdelones.
- Elaborated an improved second generation route towards the tetrahydroxanthone ring system of the kibdelones.

2005-2011 — NSERC/FRQNT Ph.D. Fellow, Organic Chemistry, Université de Sherbrooke

Advisors: Professors Claude Spino & Jean Lessard

- Determined the scope and mechanism of the novel photochemical rearrangement of *N*-heterosubstituted lactams through the synthesis and contraction of various lactams.
- Elaborated a viable synthetic route to an advanced intermediate towards (+)-gephyrotoxin.

[1] FRQNT is a granting agency of the Quebec government which provides awards based on competitions held to determine the highest level of achievement.

[2] NSERC is a granting agency of the Canadian government which provides awards based on competitions held to determine the highest level of achievement.

– Mentored five undergraduate students (one summer student and five honors students).

01/2005-05/2005 Honors thesis in Chemistry, University of Ottawa
Advisor: Dr. Robert Ben
-Elucidated the importance of amide linkage in Protein-ice interaction through the synthesis of Modified C-linked Antifreeze Glycoproteins (AFGPs) Analogues.

04/2004-12/2004 Chemistry Co-op Intern
Pfizer Global Research & Development, Ann Arbor, Michigan, USA
Supervisor: Dr. Joseph S. Warmus
– Optimized and elaborated synthetic routes towards desired medicinal chemistry targets.
– Studied the importance of chirality in a novel intramolecular cyclization.

01/2003-08/2003 Research Assistant (Medicinal Chemistry Department)
Isis Pharmaceutical, Carlsbad, California, USA
Supervisor: Dr. Elizabeth Jefferson
– Synthesized antibacterial and antiviral heterocycles using solution and solid phase chemistry (drug discovery program).
– Prepared and optimized the synthesis of medicinal chemistry drug leads targeting specific areas of RNA.

SCIENTIFIC COMMUNICATIONS

Publications

1) Drouin, A.; Winter, D.K.; Pichette, S.; Aubert-Nicol, S.; Lessard, J.; Spino, C. Photochemical Rearrangement of *N*-mesyloxylactams: stereospecific formation of *N*-heterocycles. *J. Org. Chem.* **2011**, *76*, 164-169.
2) Winter, D.K.; Drouin, A.; Lessard, J.; Spino, C. Photochemical Rearrangement of *N*-Chlorolactams: A new route to *N*-Heterocycles through Concerted Ring Contraction. *J. Org. Chem.* **2010**, *75*, 2610-2618.
3) Jefferson, E.A.; Seth, P.P.; Robinson, D.R.; Winter, D.K., Miyaji, A.; Risen, L.M.; Bertrand, M.; Osgood, S.A.; Swayze, E.E. Optimizing the antibacterial activity of a lead structure discovered by "SAR by MS" technology. *Bioorganic & Medicinal Chemistry Letters*, **2004**, *14*, 5257-5261.
4) Jefferson, E.A.; Seth, P.P.; Robinson, D.R.; Winter, D.K., Miyaji, A.; Risen, L.M.; Osgood, S.A.; Swayze, E.E. Biaryl Guanidine inhibitors of in vitro HCV-IRES activity. *Bioorganic & Medicinal Chemistry Letters*, **2004**, *14*, 5139-5143.

Oral Presentations

1) Boston Symposium on Organic and Bioorganic Chemistry, Merck Research labs, Boston, MA (September 2012): Winter, D.K.*; Porco, J.A. Total Synthesis of kibdelones A-C and progress towards their congeners isokibdelones A-C.
2) Boston Women in Chemistry Symposium, Boston, MA (September 2011): Winter, D.K.*; Sloman D.; Porco, J.A. Progress towards the Total Synthesis of kibdelone A and isokibdelone A.
3) 93rd Canadian Chemistry Conference and Exhibition, Toronto, Ont. (June 2010): Winter, D.K.*; Drouin, A., Lessard. J.; Spino, C. Photochemical Rearrangement of *N*-substituted lactams: A new route to *N*-heterocycles to concerted ring-contraction.
4) ACS national Fall meeting -Philadelphia, Pensylvania, USA (August 2008):

Winter, D.K.*; Drouin, A., Lessard. J.; Spino, C. Ring-contraction of *N*-chlorolactams and *N*-mesylates: a new route to a wide variety of *N*-heterocycles.

5) Quebec/Ontario Minisymposium of Synthethic and Bioorganic Chemistry- London, Ontario, Canada (November 2006): Winter, D.K.*; Drouin, A., Lessard. J.; Spino, C. Scope and mechanism of the ring-contraction of *N*-Chlorolactams: towards the better understanding and application of the rearrangement.

Posters

1) CMLD Symposium, Chemical Synthesis: Advances and Applications (June 2012): Winter, D.K.*, Porco, J. A. Progress towards the total synthesis of kibdelone A and isokibdelone A.
2) Novartis Networking Event (April 2012):Winter, D.K.*, Porco, J. A. Progress towards the total synthesis of kibdelone A and isokibdelone A.
3) Keith Fagnou Organic chemistry Symposium-Ottawa, Ont. (May 2010): Winter, D.K.*; Drouin, A., Pichette, S.; Aubert-Nicol, S.; Lessard. J.; Spino, C. Photochemical Rearrangement of *N*-substituted lactams: A new route to *N*-heterocycles to concerted ring-contraction.
4) AstraZeneca R&D Chemistry Symposium- Laval, Quebec, Canada (October 2008): Winter, D.K.*; Drouin, A., Lessard. J.; Spino, C. Ring-contraction of *N*-chlorolactams and *N*-mesyloxylactams: a new route to a wide variety of *N*-heterocycles.
5) Pfizer Global Research & Development Michigan Symposium (Autumn 2004) and Pfizer Global Research & Development Intern Symposium (Summer 2004)

TEACHING AND OUTREACH EXPERIENCE

Teaching

09/2009-12/2009 Course Lecturer
Université de Sherbrooke, Sherbrooke, QC
CHM 101: Structure and reactivity (2 classes of 40 students)
- Subjects covered: nomenclature, conformation, chirality, reaction mechanism, functional group proprieties, polymer and organic synthesis.

08/ 2008-12/ 2008 Course Lecturer
Université de Sherbrooke, Sherbrooke, QC
CHM 302: Organic and Inorganic Laboratory Techniques (2 classes of 50 students)
- Subjects covered: 1H NMR, IR, acid-base principals (pKa), purification techniques
- Responsible for weekly pop quiz creation and correcting, review of misunderstood class material, laboratory experiments and final exam preparation.

2005-2007 Technical Advisor CHM 302 and CHM 400
Université de Sherbrooke, Sherbrooke, QC
- Guided undergraduate students through basic and elaborate organic chemistry techniques, corrected lab books and helped explain subjects covered in class.

Outreach

2011-2012 Boston Women in Chemistry Seminar Coordinator.

Summer 2009 ''Le Salésien'': Seminar given to high school students about the opportunities that a career in chemistry can offer.

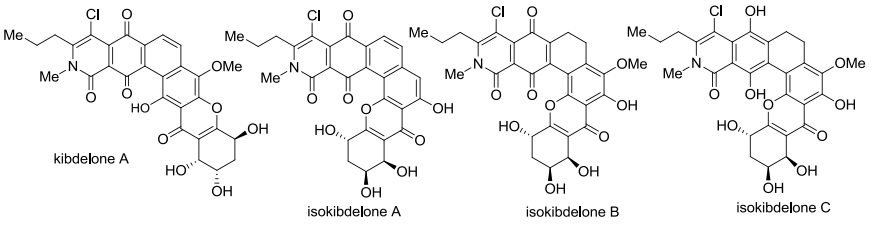
2006-2009 ''Petits Debrouillards'': Chemistry laboratory demonstrations for summer camp groups to get children involved in science and chemistry.

REFERENCES AVAILABLE UPON REQUEST

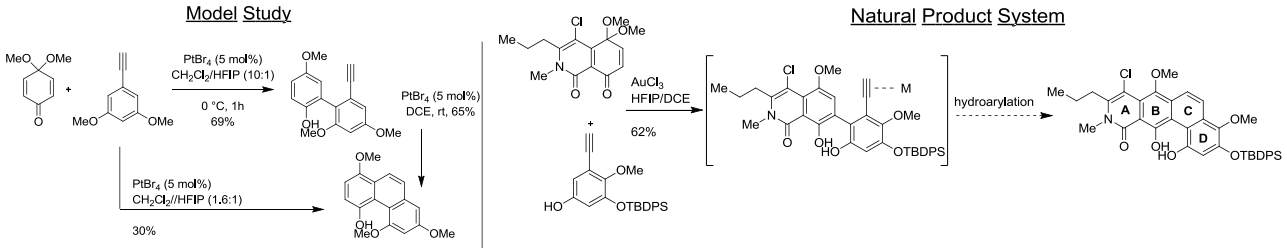
Dr. Dana K. Winter, Research Summary

Porco Research Group, Boston University:

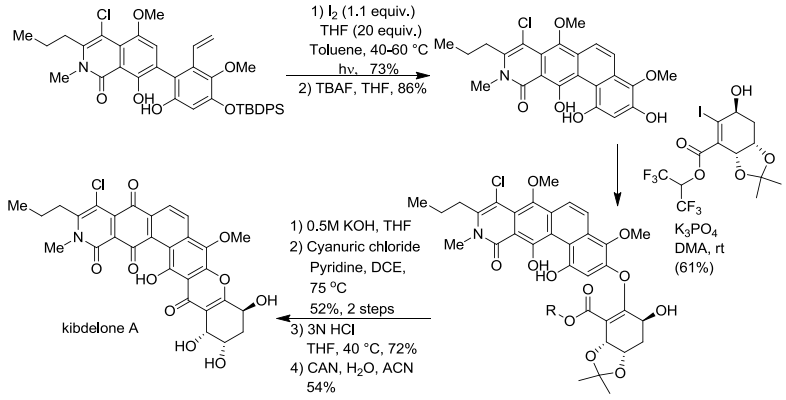
Total Synthesis of kibdelone A and progress towards the isokibdelones A-C.



Kibdelones A-C and the isokibdelones A-C belong to a small family of cytotoxic agents which possess broad and interesting biologically activities. Both series of natural products possess common ABCD ring systems but diverge in their connectivity of the E/F ring system. We believed that the ABCD core of these natural products could be synthesized by a tandem Friedel-Craft /hydroarylation cascade between an appropriate alkyne and quinone monoketal.

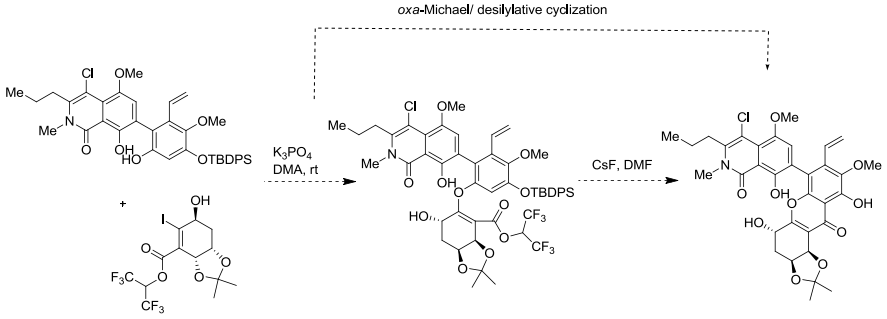


Model studies using a simple system showed great promise towards this synthetic sequence but failed in the real natural product system. Only the initial Friedel-Crafts addition was found to be successful and this even after extensive screening of conditions for further hydroarylation to construct the C ring. Accordingly an alternative novel sequence using an iodine-mediated oxidative photochemical electrocyclization was therefore successfully developed.

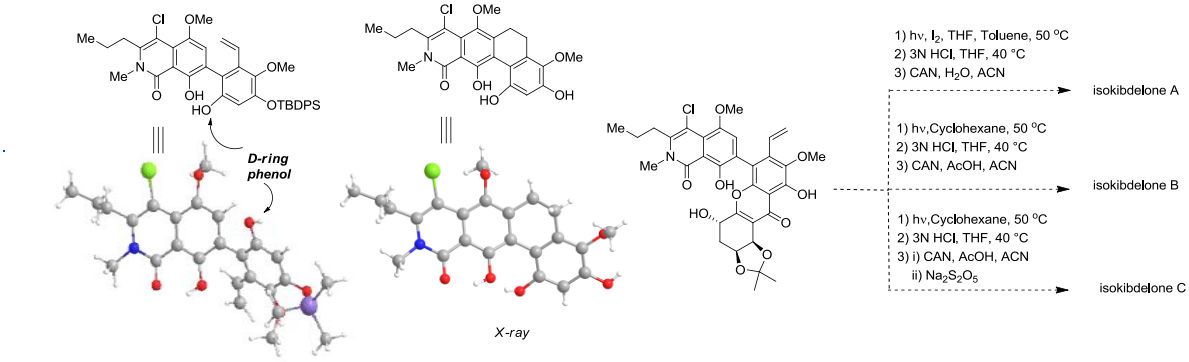


The construction of the tetrahydroxanthone ring system for the kibdelones and related natural products was recently accomplished and improved by changing the electronics of the ester of the initial iodo-cyclohexene F-ring for both the kibdelone cores and simpler phenols. We have found that an HFIP ester on the iodo-cyclohexene ring displayed improved reactivity in the *oxa*-Michael fragment coupling with both the ABCD ring core and with simpler phenols. A one pot process for tetrahydroxanthone formation was possible with simple phenols but was not with the natural product moiety. An alternative sequence employing a saponification/cyanuric chloride cyclization followed by deprotection of the acetonide moiety of the F-ring and oxidation of the B ring using CAN in water/CH_3CN was developed and afforded kibdelone A. A careful study of the pH of the final CAN oxidation revealed that acidic conditions were unfavorable due to increased oxidation of the D ring.

Our current focus is aimed on the total synthesis of the isokibdelone family. We plan to utilize the bisected nature of the biaryl moiety to promote a novel *oxa*-Michael /desilylative Friedel Craft cyclization to construct the tetrahydroxanthone core of this series of natural products. Examination of a molecular model of the biaryl shows that the D ring phenol is not hydrogen bonded such as in its ABCD ring conformation (X-Ray). This should therefore increase its reactivity in comparison to the phenol in the closed ring system which is part of a hydrogen bond network.



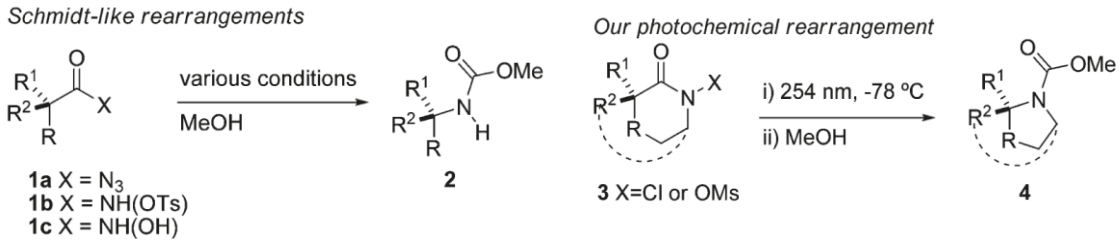
The desilylative Friedel Craft cyclization on simple models has shown to be viable and is currently under investigation for the natural product system. Once the tetrahydroxanthone obtained, isokibdelones (A-C) may be obtained depending on the nature of the electrocyclic ring closure and specific conditions used to oxidize the B ring which were previously developed during the kibdelone series.



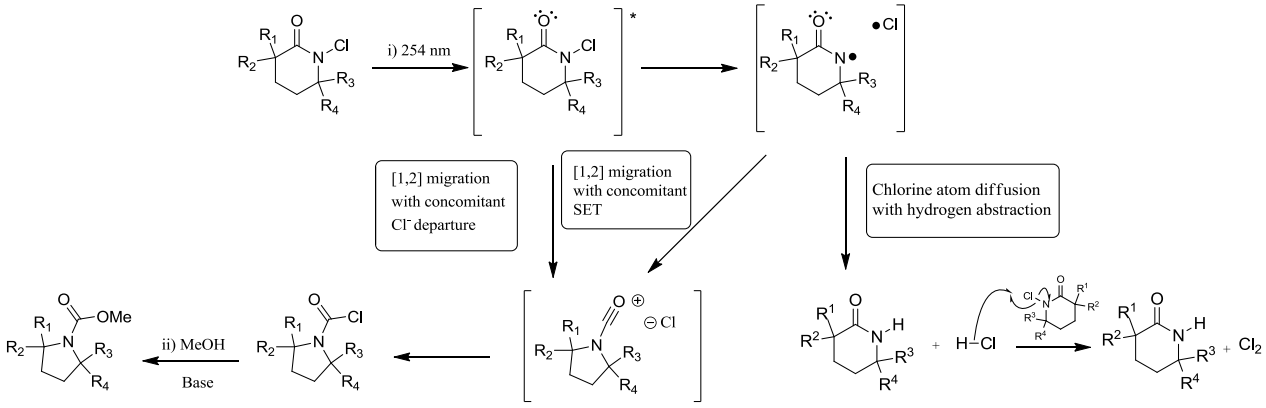
Spino/Lessard Research Groups, Université de Sherbrooke:

Development of a new methodology for *N*-heterocycle synthesis *via* photochemical rearrangement of *N*-heterosubstituted lactams and its application towards the synthesis of (+)-gephyrotoxin.

Alkaloids are known to possess a variety of interesting pharmacological properties. It is therefore important to develop short and efficient routes to synthesize them. The Spino/Lessard group serendipitously discovered a novel ring contraction allowing the direct conversion of *N*-chlorolactams to their corresponding ring-contracted *N*-heterocycles upon photolysis. This methodology is complementary to other know rearrangements but utilizing cyclic amides which are not potential substrates for such methods.

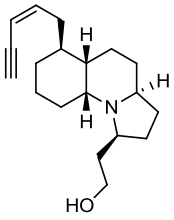


An exhaustive scope and mechanistic study was completed through the synthesis and contraction of several *N*-chlorolactams.[3] Results show that the rearrangement occurs with a variety of substrates and that the greater the substitution at the migrating carbon, the greater the yield of product. Importantly, stereochemistry at the migrating carbon is conserved in the product. Rearranged products were isolated as their methyl carbamates in yields varying from 17% to 58%, with the major side product being the recyclable parent lactam (**3,** X = H). This side product stemmed from a secondary competing radical pathway originating from lactamyl radicals generated from homolytic cleavage of the N-Cl bond. The nature of the [1,2] migration of this novel reaction involves ionic species which can be generated either from the decay of the electronic or vibrational excited state, via a yet unknown mechanism.

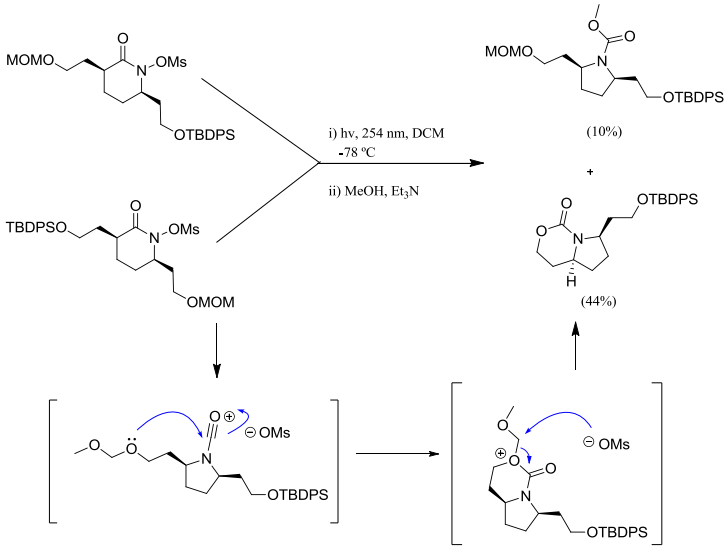


Optimization through radical chain inhibition was attempted through solvent, temperature and additives screens; and by changing the nature of the leaving group on the lactam (**3**, X= Cl, OMs, OTs). To our delight, yields increased to a range of 65-86%, inhibiting all parent lactam formation, and showed the same general scope by changing to *N*-mesyloxylactams (**3**, X = OMs).[4]

This new ring-contraction therefore opens a new and viable route for the synthesis of a variety of *N*-heterocycles and potentially to alkaloids using very mild reaction conditions. At the end of my Ph.D., two short and expeditive synthetics routes utilizing this novel methodoly were developped to an advanced synthetic intermediate towards the synthesis (+)-gephyrotoxin. The isolated product obtained during the photochemical rearrangement displayed a great futur potential for this novel reaction: the intramolecular trapping of reaction intermediates.



(+)-gephyrotoxine



[3] **Winter, D.K.**; Drouin, A.; Lessard, J.; Spino, C. *J. Org. Chem.* **2010**, 75, 2610-2618.
[4] Drouin, A.; **Winter, D.K.**; Pichette, S.; Aubert-Nicol, S.; Lessard, J.; Spino, C. *J. Org. Chem.* **2011**, *76*, 164-169.