



**University
of Victoria**

Graduate Studies

PROGRAMME

The Final Oral Examination for the Degree of

DOCTOR OF PHILOSOPHY
(Department of Chemistry)

Thomas Pinter

2009

Simon Fraser University

BSc (Chemistry)

“Tetrazoles are potent anion recognition elements
in a variety of structural contexts”

Tuesday, September, 9th, 2014
12:00 p.m.

David Strong Building, room C114

Supervisory Committee:

Dr. Fraser Hof, Department of Chemistry, UVic (Supervisor)

Dr. Jeremy Wulff, Department of Chemistry, UVic (Member)

Dr. J. Scott McIndoe, Department of Chemistry, UVic (Member)

Dr. Brian Christie, Department of Biochemistry and Microbiology,
UVic (Outside Member)

External Examiner:

Dr. Belinda Heyne, Department of Chemistry, University of Calgary

Chair of Oral Examination:

Dr. Byoung-Chul Choi, Department of Physics and Astronomy,
UVic

Abstract

In efforts to expand the limited amount of functional groups available for anion recognition, a series of highly acidic, strongly hydrogen bond-donating groups were envisaged as suitable candidates. These included the thoroughly studied *N*-aryl sulfonamides along with the less utilized *N*-acyl sulfonamides and tetrazoles. These groups were affixed to a well understood supramolecular platform in calix[4]arene and their binding affinities for various halides and oxyanions probed. It was found that although in its least energetically favourable conformation, that is orthogonal to the aryl group to which it was bound, the tetrazole proved a superior anion binding element.

Noting that tetrazoles prefer co-planarity with aryl neighbours, a series of pyrrolyl-tetrazole anion binding compounds were prepared, first a simple bidentate pyrrolyl-tetrazole which when tested for anion binding affinity demonstrated some of the strongest binding with anions for a bidentate compound ever observed, especially chloride.

It was then conceived to hybridize this new binding motif with the well-known amidopyrrole moiety and two new tetrazolyl-amidopyrroles were constructed. When compared to an ester-functionalized pyrrolyl-tetrazole, binding strength with halides was not much different, leading to the postulation that the amide N-H may just be a spectator in the binding event, and the electron-withdrawing nature of the adjacent carbonyl was what led to the binding potency.

Nonetheless, a new class of diversifiable anion binders with superior strength to analogous amidopyrroles has been constructed and could perhaps be used in a variety of functional applications.

Awards, Scholarships, Fellowships

- 2013 Nora & Mark de Goutiere Memorial Scholarship (UVic Chemistry)
- 2010 Louis C. Clark Memorial Graduate Fellowship (UVic Chemistry)
- 2008 Pacific Northwest Undergraduate Symposium On Organic Chemistry (Awarded best lecture)

2008 Western Canadian Undergraduate Chemistry Conference
(Awarded best lecture-organic chemistry division)

Presentations

1. Pinter, T et al. "Exploring tetrazoles as novel agents for anion binding sensing and transport." Canadian Society of Chemistry National Conference, Calgary, AB, Canada, June 2012. (oral)
2. Pinter, T et al. "Exploring tetrazoles as novel agents for anion binding, sensing and transport." Banff Symposium on Organic Chemistry, Banff AB, Canada, November 2011. (oral)
3. Pinter, T et al. "Exploring tetrazoles and other carboxylic acid bioisosteres as novel agents for anion binding and transport." Canadian Society of Chemistry National Conference, Montreal, QC, Canada, June 2011. (oral)
4. Pinter, T et al. "Exploring tetrazoles and other carboxylic acid bioisosteres as novel agents for anion binding and transport." Franco-Canadian Workshop in Supramolecular Chemistry, Montreal, QC, Canada, June 2011. (poster)
5. Pinter, T et al. "Exploring tetrazoles and other carboxylic acid bioisosteres as novel agents for anion binding and transport." Volcano Conference on Chemical Biology, Pack Forest, WA, USA, March 2011. (oral)
6. Pinter, T; Hof, F. "Synthesis of novel calix[4]arene derived compounds as potential hosts for methylated lysine." Franco-Canadian Workshop in Supramolecular Chemistry, Victoria-Montreal-Paris (teleconference) August 2010. (oral)
7. Pinter, T; Hof, F. "Synthesis of novel calix[4]arene derived compounds as potential hosts for methylated lysine." Volcano Conference on Chemical Biology, Pack Forest, WA, USA, March 2010. (poster)
Pinter, T et al. "Development of a concise and general enantioselective route to 2,5-disubstituted-3-hydroxytetrahydrofurans." Pacific Northwest Undergraduate Symposium on Organic Chemistry, Corvallis, OR, USA, August 2008.(oral)
8. Pinter, T et al. "Development of a concise and general enantioselective route to 2,5-disubstituted-3-

hydroxytetrahydrofurans.” Western Canadian Undergraduate Chemistry Conference, Winnipeg, MB, August 2008. (oral)

Publications

1. Pinter, T; Simhadri, C; Hof, F. “Dissecting the Complex Recognition Interfaces of Potent Tetrazole- and Pyrrole-Based Anion Binders.” *The Journal of Organic Chemistry*, **2013**, 78 (10), 4642-4648.
2. Hof, F; Pinter, T. “Learning from Proteins and Drugs: Receptors That Mimic Biomedically Important Binding Motifs.” *Designing Receptors for the Next Generation of Biosensors*. Springer Series on Chemical Sensors and Biosensors, Vol. 12, pp 33-51. Piletsky, SA; Whitcombe, MJ, eds. Springer –Verlag Berlin Heidelberg, **2013**.
3. Daze, K; Pinter, T; Minaker, SA; Beshara, C; Ibraheem A; Ma, MFC; Courtemanche, RJM; Campbell, RE; Hof, F. “Supramolecular hosts that recognize methyllysines and disrupt the interaction between a modified histone tail and its epigenetic reader protein.” *Chemical Science*, **2012**, 3, 2695-2699. (K. Daze and T. Pinter contributed equally to this work.)
4. Courtemanche, RJM; Pinter, T; Hof F. “Just add tetrazole: 5-(2-Pyrrolo)tetrazoles are simple, highly potent anion recognition elements.” *Chemical Communications*, **2011**, 47, 12688-12690.
5. Pinter, T; Jana, S; Courtemanche, RJM; Hof, F. “Recognition Properties of Carboxylic Acid Bioisosteres: Anion Binding by Tetrazoles, Aryl Sulfonamides, and Acyl Sulfonamides on a Calix[4]arene Scaffold.” *The Journal of Organic Chemistry* **2011**, 76 (10), 3733–3741.
6. Khan, MA; Moktar, J; Mott, PJ; Vu, M; McKie, AH; Pinter, T; Hof, F; Bishop, RE. “Inscribing the Perimeter of the PagP Hydrocarbon Ruler by Site-Specific Chemical Alkylation.” *Biochemistry*, **2010**, 49(42), 9046-9057.
7. Kang, B; Mowat, J; Pinter T; Britton, R. “Development of a Concise and General Enantioselective Approach to 2,5-Disubstituted-3-hydroxytetrahydrofurans.” *Organic Letters*, 2009, 11 (8), 1717-1720.