



Universiteit
Leiden
The Netherlands

Small changes for long term impact : optimization of structure kinetic properties : a case of CCR2 antagonists

Vilums, M.

Citation

Vilums, M. (2014, November 20). *Small changes for long term impact : optimization of structure kinetic properties : a case of CCR2 antagonists*. Retrieved from <https://hdl.handle.net/1887/29811>

Version: Corrected Publisher's Version

License: [Licence agreement concerning inclusion of doctoral thesis in the Institutional Repository of the University of Leiden](#)

Downloaded from: <https://hdl.handle.net/1887/29811>

Note: To cite this publication please use the final published version (if applicable).

Cover Page



Universiteit Leiden



The handle <http://hdl.handle.net/1887/29811> holds various files of this Leiden University dissertation.

Author: Vilums, Maris

Title: Small changes for long term impact : optimization of structure kinetic properties : a case of CCR2 antagonists

Issue Date: 2014-11-20

LIST OF PUBLICATIONS

M. Vilums, A.J.M. Zweemer, S. Dekkers, Y. Askar, H. de Vries, J. Saunders, D. Stamos, J. Brussee, L.H. Heitman, A.P. IJzerman. Design and Synthesis of Novel Small Molecule CCR2 Antagonists: Evaluation of 4-Aminopiperidine Derivatives. In preparation.

M. Vilums, A.J.M. Zweemer, A. Dilanchian, J.P.D. van Veldhoven, H. de Vries, J. Brussee, D. Stamos, J. Saunders, L.H. Heitman, A.P. IJzerman. Evaluation of (4-Arylpiperidin-1-yl)cyclopentanecarboxamides as High Affinity and Long Residence Time Antagonists for the CCR2 Receptor. In preparation.

M. Vilums, A.J.M. Zweemer, F. Barmare, A.M.F. van der Gracht, D.C.T. Bleeker, Z. Yu, H. de Vries, R. Gross, J. Clemens, P. Krenitsky, J. Brussee, D. Stamos, J. Saunders, L.H. Heitman, A. P. IJzerman. When Structure-Affinity Relationships Meet Structure-Kinetics Relationships: 3-((Inden-1-yl)amino)-1-isopropyl-cyclopentane-1-carboxamides as CCR2 Antagonists. In preparation.

M. Vilums, J. Heuberger, L.H. Heitman, A.P. IJzerman. Indanes – Properties, Preparation, and Presence in Ligands for G Protein-Coupled Receptors. *Med Res Rev.* Submitted.

A.J. Zweemer, J. Bunnik, M. Veenhuizen, F. Miraglia, E.B. Lenselink, **M. Vilums**, H. de Vries, A. Gibert, S. Thiele, M.M. Rosenkilde, A.P. IJzerman, L.H. Heitman. Discovery and Mapping of an Intracellular Antagonist Binding Site at the Chemokine Receptor CCR2. *Mol Pharmacol.* 2014 Oct;86(4):358-68

M. Vilums, A. J. M. Zweemer, Z. Yu, H. de Vries, J. M. Hillger, H. Wapenaar, I. A. E. Bollen, F. Barmare, R. Gross, J. Clemens, P. Krenitsky, J. Brussee, D. Stamos, J. Saunders, L. H. Heitman, A. P. IJzerman. Structure–Kinetic Relationships –An Overlooked Parameter in Hit-to-Lead Optimization: A Case of Cyclopentylamines as Chemokine Receptor 2 Antagonists. *J. Med. Chem.* 2013, 56, 7706–7714

M. Vilums, J. Overman, E. Klaasse, O. Scheel, J. Brussee, A. P. IJzerman. Understanding of Molecular Substructures that Contribute to hERG K⁺ Channel Blockade: Synthesis and Biological Evaluation of E-4031 Analogues. *ChemMedChem* 2012, 7, 107 – 113

M.van der Steen, **M. Vilums**, C. V. Stevens. Synthesis of novel urethanes from a castor oil derived C22-acyloin. *Arkivoc* 2011, (ix), 261-271.

A. Krauze, E. Liepins, **M. Vilums**, G. Duburs. A new regioselective synthesis of 2-methoxymethyl-3-oxo-2,3-di-hydro-7H-thiazolo[3,2-a]pyridine-8-carboxylic acid methylamide. *Chem. of Heterocyc. Comp.*, 2009, Nr 2, 250-252.

H. Kazoka, A. Krauze, **M. Vilums**, L. Chernova, L. Sile and G. Duburs. Synthesis of 6'-carbamoylmethylthio-5'-cyano-1',4'-dihydro-3,4'-bipyridine-3'-carboxylic and 6'-carbamoylmethylthio-5'-cyano-1',4'-dihydro-4,4'-bipyridine-3'-carboxylic esters and investigation of their stability. 2. Esters of 6'-carbamoylmethyl-thio-5'-cyano-1',4'-dihydro-4,4'-bipyridine-3-carboxylic acids. *Chem. of Heterocyc. Comp.*, 2007, Nr 6, 708-714.

A. Krauze, **M. Vilums**, L. Sile, G. Duburs. Alternative products in one-pot reaction of benzyldenemalononitrile, N-methyl-2-thiocarbamoylacetamide, and ω-bromoacetophenone. *Chem. of Heterocyc. Comp.*, 2007, Nr 5, 653-657.

H. Kazoka, A. Krauze, **M. Vilums**, L. Chernova, L. Sile and G. Duburs. Synthesis and investigation of the stability of esters of 6'-carbamoylmethylthio-5'-cyano-1',4'-dihydro-3,4'-and-4,4'-bipyridine-3'-carboxylic acids 1. Esters of 6'-carbamoylmethylthio-5'-cyano-1',4'-dihydro-3,4'-bipyridine-3'-carboxylic acids. *Chem. of Heterocyc. Comp.*, 2007, 43, 1, 50-57.

A. Krauze, R. Danne, **M. Vilums**, Z. Kalme, L. Chernova, L. Sile, G. Duburs. Synthesis of new partially hydrogenated 6-alkylthio-2,4-diaryl-3-ethoxycarbonylpyridine-5-carbonitriles. (in Latvian) *Latv. Kim.Z.*, 2007, 2, 3.

A. Krauze, L. Chernova, **M. Vilums**, L. Sile, G. Duburs. Green one-pot multicomponent synthesis of 4-aryl-6-carbamoylmethylthio-5-cyano-2-methyl-1,4-dihydropyridine-3- carboxylic acid methyl esters. *Heterocycl. Commun.*, 2006, 12, 3/4, 281-286.

A. Krauze, L. Baumanė, L. Sile, L. Chernova, **M. Vilums**, R. Vitolina, G. Duburs, J. Stradins. Synthesis, cardiovascular activity, and electrochemical oxidation of nitriles of 5-ethoxycarbonyl-2-methyl-thio-1,4-dihydropyridine-3-carboxylic acid. *Chem. of Heterocyc. Comp.*, 2004, Vol. 40, No. 7, pp.876-887

AFTERWORD

Always keep your mind open and continue learning...

From my supervisors – Hans, John, Dean, Laura and Ad

“Efficiency is doing things right. Effectiveness is doing the right things”

From my colleagues:

Leiden University – Annelien, Arnault, Bart, Clara, Dennis, Dong, Elaine, Ellen, Elisabeth, Gerard, Henk, Indira, Jaco, Joao, Joey, Julien, Lence, Miriam, Maarten, Patricia, Rob, Rongfang and Thea

Vertex Pharmaceuticals Inc. – Farhana, Paul, Raymond, Jeremy, Mike and Silvia

“Growth is never by mere chance; it is the result of forces working together”

James Cash Penney

From my students – Jeroen, Julia, Hannah, Guido, Joleen, Arthur, Jules, Sebastian, Arien, Youssry, and all the minors

“Supervision is an opportunity to bring someone back to their own mind, to show them how good they can be”

Nancy Kline, ‘Time to Think’

From my very first real chemistry teacher – Erika

“Just come and have a try...”