The versatility of asymmetric aminoethyl-tetrazines in bioorthogonal chemistry

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List of Publications

Fluorogenic Bifunctional trans-Cyclooctenes as Efficient Tools for Investigating Click-to-Release Kinetics
A. J. C. Sarris, M. A. R. de Geus, E. Maurits, T. Hansen, M. S. Kloet, K. Kamphorst, W. ten Hoeve, M. S. Robillard, A. Pannwitz, S. A. Bonnet, J. D. C. Codée, D. V. Filippov, H. S. Overkleeft, S. I. van Kasteren
Chem. Eur. J. **2020**, 26, 44, 9900-9904 DOI: 10.1002/chem.201905446

Fast and pH-Independent Elimination of *trans*-Cyclooctene by Using Aminoethyl-Functionalized Tetrazines
A. J. C. Sarris, T. Hansen, M. A. R. de Geus, E. Maurits, W. Doelman, H. S. Overkleeft, J. D. C. Codée, D. V. Filippov, S. I. van Kasteren
Chem. Eur. J. **2018**, 24, 18075-18081 DOI: 10.1002/chem.201803839

Methyltetrazine as a small live-cell compatible bioorthogonal handle for imaging enzyme activities in situ
D. Torres-García, M. A. T. van de Plassche, E. van Boven, T. van Leeuwen, M. G. J. Groenewold, A. J. C. Sarris, Luuk Klein, H. S. Overkleeft, S. I. van Kasteren
RSC Chem. Biol. **2022**, 3, 1325-1330 DOI: 10.1039/D2CB00120A

Live-Cell Imaging of Sterculic Acid – a Naturally Occurring 1,2-Cyclopropene Fatty Acid – by Bioorthogonal Reaction with Turn-On Tetrazine-Fluorophore Conjugates
K. Bertheussen, M. van de Plassche, T. Bakkum, B. Gagestein, I. Ttofi, A. J. C. Sarris, H. S. Overkleeft, M. van der Stelt, S. I. van Kasteren
Angew. Chem.Int. Ed. **2022**, 61, e202207640 DOI: 10.1002/anie.202207640

The development of a broad-spectrum retaining β-exo-galactosidase activity-based probe
C.L. Kuo, Q. Su, A. M. C. H. van den Nieuwendijk, T. J. M. Beenakker, W. A. Offen, L. I. Willems, R. G. Boot, A. J. C. Sarris, A. R. A. Marques, J. D. C. Codée, G. A. van der Marel, B. I. Florea, G. J. Davies, H. S. Overkleeft, J. M. F. G. Aerts
Org. Biomol. Chem. **2023**, 21, 7813-7820 DOI: 10.1039/D3OB01261A

Mechanism-based heparanase inhibitors reduce cancer metastasis in vivo
C. de Boer, Z. Armstrong, V. A. J. Lit, U. Barash, G. Ruijgrok, I. Boyango, M. M. Weitzenberg, S. P. Schröder, A. J. C. Sarris, N. J. Meeuwenoord, P. Bule, Y. Kayal, Neta Ilan, J. D. C. Codée, I. Vlodavsky, H. S. Overkleeft, G. J. Davies, L. Wu
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Chemical Control over T-Cell Activation in Vivo Using Deprotection of trans-Cyclooctene-Modified Epitopes
A. M. F. van der Gracht, M. A. R. de Geus, M. G. M. Camps, T. J. Ruckwardt, A. J. C. Sarris, J. Bremmers, E. Maurits, J. B. Pawlak, M. M. Posthoorn, K. M. Bonger, D. V. Filippov, H. S. Overkleeft, M. S. Robillard, F. Ossendorp, S. I. van Kasteren
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Quantification of Bioorthogonal Stability in Immune Phagocytes Using Flow Cytometry Reveals Rapid Degradation of Strained Alkynes
T. Bakkum, T. van Leeuwen, A. J. C. Sarris, D. M. van Elsland, D. Poulcharidis, H. S. Overkleeft, S. I. van Kasteren
ACS Chem. Biol. **2018**, 13, 5, 1173-1179 DOI: 10.1021/acschembio.8b00355

A pH-Sensitive, Colorful, Lanthanide-Chelating Paramagnetic NMR Probe
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J. Am. Chem. Soc. **2012**, 134, 41, 17306–17313 DOI: 10.1021/ja307824e

Curriculum Vitae

Alexi Johannes Christaki Sarris was born on the 29th of July 1986 in Eindhoven. During his pre-university education (VWO) developed an strong interest in chemistry and biology. After following an introductory course on organic chemistry at the University of Leiden, he found his passion and went on to study the bachelor chemistry program "Molecular Science and Technology", a cooperation of fundamental (in)organic chemistry (University of Leiden) and Chemical Technology (University of Delft). After the first year a focus on the University of Leiden program was made, including a minor of in-depth chemistry courses. In the final year, a chemistry research internship was conducted at the Bio-organic Synthesis Department (Biosyn), part of the Leiden Institute of Chemistry (LIC). While working on "*Synthesis, analysis and reaction of caged lanthanide NMR probes*", his supervisor Wei-Min Lui provided great guidance and was an inspiration for him to continue in the research focused organic chemistry field. In 2012 he obtained his Bachelor's degree.

He went on to study the chemistry master program with a specialization in research at the University of Leiden. This included a major focus on all aspects of organic chemistry, supplemented with virology, biology, catalysis and electrochemistry courses. After an extensive master research internship at Biosyn on "*Solid Phase Synthesis of Coxsackievirus B3W VPg-Nucleopeptides*" under the guidance of Geoffroy P.P. Gential, in 2015, he obtained his Master's degree with *cum laude* distinction (GPA 8.6).

He was then offered a PhD position at Biosyn (Prof. Dr. Hermen S. Overkleeft) within the group of Prof. Dr. Sander I. van Kasteren, where "click"-type bioorthogonal chemistry was employed to explore the interface between chemistry and immunology. He was also participating in the multidisciplinary educational programme of the institute of chemical immunology (ICI), and followed a wide variety of courses within the ICI-programme on relevant scientific subjects. During his PhD, he worked on various projects focused on tetrazine-alkene mediated IEDDA chemistry and its application in biology and supervised multiple students. Most of these projects are included in this thesis, and parts of the work were presented (as poster) on various conferences including CHAINS.

He was employed at the University of Leiden until 2020, and continued his career outside of academia within the field of chemistry and biology, including biotech research and regulatory work.

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The final part of the thesis comes with the acknowledgements to everyone contributing to the work described in this thesis. I would like to thank Sander for all his support and advice during my PhD, allowing me to find my path in the wonderful world of tetrazines and “click”-chemistry, and always being supportive to the projects I was working on. Without his knowledge and guidance this thesis would not contain the work I am so proud of. I would also like to thank Hermen providing insights and experience whenever I needed a clear direction in my projects. I would like to thank all the people working at Biosyn, the professors, assistant-professors, technicians and other employees were always happy to provide their time and expertise when it was required and keeping the entire department running. A special mention goes to Dima, besides being the person I would go to whenever I had any theoretical or practical question about the chemistry I was performing during my PhD, he has been a great chemistry teacher throughout my education and a positive influence in my path to becoming a professional chemist.

Over the years I’ve had the pleasure to work alongside many PhD students, post-docs, and intern students. Special mentions go to Michel, Jerre, Thomas and Shimrit, Ward, Daniël and Anouk as the people that I’ve got to know really well and consider my friends, everyone at the DM-Labs who were my daily colleagues and comrades during my PhD, everyone within the Sander-group, and also everyone within the Biosyn-group. Last but not least I am very thankful to the students I worked with Luuk, Nancy and Dyone, who showed amazing skill and perseverance in their projects and were, besides contributing to this thesis, a true enjoyment to supervise and spend my time with. Looking back to this, I am truly happy to have met each and all of you, and I am certain that in between all the fun, conversations and cups of coffee, these interactions have provided me the knowledge and strength to succeed and overcome all the difficulties in the path towards my goals.

Finally, I would like to thank my friends and family. My father and my brothers have always been very supportive throughout my PhD and after. And, most importantly, my wife Ruth and my children Elias and Hannah. Deciding to become a parent, twice, during my PhD was a very challenging and the most rewarding decision in my life. Ruth, you were a tremendous help to me for all my struggles. During periods of long and energy draining days at the lab, but also the time after leaving the University lab. With my most precious experiments successful and the book mapped out in my head, the only thing left was to write the thesis. Unfortunately things usually don’t go as we plan them. I went For two years I was stuck working in terrible and toxic work environments, leaving me struggling with emotions I couldn’t imagine. During this time, you and our children have been my joy, my beacons of hope and have kept me going even when everything felt too much. With the thesis now finally written, this chapter in my life comes to an end and hopefully, surely, will lead to a bright and exciting new one.