

Cover Page



Universiteit Leiden



The handle <http://hdl.handle.net/1887/66126> holds various files of this Leiden University dissertation.

**Author:** Vorm, S. van der

**Title:** Reactivity and selectivity in glycosylation reactions

**Issue Date:** 2018-10-11

## List of publications

### **Stereoselective Glycosylations – Additions to Oxocarbenium Ions**

Bas Hagen, Stefan van der Vorm, Thomas Hansen, Gijsbert A. van der Marel and Jeroen D.C. Codée

in: “Selective Glycosylations: Synthetic Methods and Catalysts”, **2017**, editor: Clay S. Bennett, pp 1-28. ISBN: 978-3-527-33987-7

### **The influence of acceptor nucleophilicity on the glycosylation reaction mechanism**

Stefan van der Vorm, Thomas Hansen, Herman S. Overkleeft, Gijsbert A. van der Marel and Jeroen D. C. Codée

*Chemical Science*, **2017**, 8 (3), pp. 1867-1875

### **Stereoselectivity of conformationally restricted glucosazide donors**

Stefan van der Vorm, Herman S. Overkleeft, Gijsbert A. van der Marel and Jeroen D. C. Codée

*The Journal of Organic Chemistry*, **2017**, 82 (9), pp. 4793-4811

### **Mapping the relationship between glycosyl acceptor reactivity and glycosylation stereoselectivity**

Stefan van der Vorm, Jacob M. A. van Hengst, Marloes Bakker, Herman S. Overkleeft, Gijsbert A. van der Marel and Jeroen D. C. Codée

*Angewandte Chemie International Edition*, **2018**, 57 (27), pp. 8240-8244

*Angewandte Chemie*, **2018**, 130 (27), pp. 8372-8376

### **The synthesis of O-1 to O-6 substituted positional isomers of D-glucose-thioether ligands and their ruthenium polypyridyl conjugates**

Lucien N. Lameijer, Julien Le Roy, Stefan van der Vorm, Sylvestre Bonnet

*Manuscript in press, The Journal of Organic Chemistry*

**Conformational Energy Landscapes as a tool to study the glycosylation stereoselectivity of 2-azidofuranoses, 2-fluorofuranoses, and methyl furanosyl uronates**

Stefan van der Vorm, Thomas Hansen, Erwin R. van Rijssel, Rolf Dekkers, Jerre M. Madern, Herman S. Overkleeft, Dmitri V. Filippov, Gijsbert A. van der Marel and Jeroen D. C. Codée

*Manuscript submitted*

**Synthesis, reactivity and stereoselectivity of 4-thio furanosides**

Jerre M. Madern, Thomas Hansen, Erwin R. van Rijssel, Stefan van der Vorm, Herman S. Overkleeft, Gijsbert A. van der Marel, Dmitri V. Filippov and Jeroen D. C. Codée

*Manuscript submitted*

**Defining the S<sub>N</sub>1-side of glycosylation reactions: stereoselectivity of glycopyranosyl cations**

Thomas Hansen, Ludivine Lebedel, Wouter A. Remmerswaal, Stefan van der Vorm, Dennis P.A. Wander, Herman S. Overkleeft, Dmitri V. Filippov, Yves Bleriot, Gijsbert A. van der Marel, Sebastien Thibaudeau, Jeroen D. C. Codée

*Manuscript in preparation*

**Acceptor reactivity in glycosylations**

Stefan van der Vorm, Herman S. Overkleeft, Gijsbert A. van der Marel and Jeroen D. C. Codée

*Manuscript in preparation*

**The impact of 3,4-tethering on the stereoselectivity of a glucosazide donor**

Stefan van der Vorm, Herman S. Overkleeft, Gijsbert A. van der Marel and Jeroen D. C. Codée

*Manuscript in preparation*



OrchID: 0000-0002-4047-9373

## Curriculum vitae - Nederlands

Stefan van der Vorm werd geboren op 28 juli 1988 te Rotterdam. Van 2000 tot 2007 volgde hij middelbaar onderwijs aan het Maerlant College Brielle, waar hij in 2005 het HAVO diploma (met het profiel Natuur & Gezondheid) en vervolgens in 2007 het VWO-atheneum diploma (profielen Natuur & Techniek en Natuur & Gezondheid) behaalde. In 2007 werd begonnen aan de bacheloropleiding Molecular Science & Technology aan de Universiteit Leiden en de Technische Universiteit Delft. Als afstudeerstage werd van januari tot en met augustus 2010 onderzoek verricht onder leiding van prof.dr.ir. J.G.E.M. Fraaije, waarbij eiwitten betrokken bij membraanfusie werden gemodelleerd met behulp van dissipatieve deeltjes dynamica. Na een jaar de opleiding Talen en Culturen van Japan aan de Universiteit Leiden te hebben gevolgd, werd in 2011 op dezelfde locatie begonnen aan de masteropleiding Chemistry, met een onderzoeksspecialisatie in Ontwerp & Synthese. In het kader van deze opleiding werd een onderzoeksstage gevolgd bij de vakgroep Bio-organische Synthese, onder leiding van prof.dr. H.S. Overkleef en prof.dr. G.A. van der Marel. Dit project getiteld “Towards a library of sulfated mannuronic acid oligomers, to study structure-activity relationships” werd begeleid door dr. M.T.C. Walvoort en dr. A.G. Volbeda. In 2013 werd een tweede onderzoeksstage gevolgd aan de Universiteit van Kioto (京都大学), in de groep van prof.dr. J.-I. Yoshida (吉田 潤一), getiteld “Configurational stability of chiral oxyranyllithium intermediates from styrene oxide derivatives” waarbij gebruik werd gemaakt van microreactoren. Na het afronden van de masteropleiding werd het diploma met lof behaald. In december 2013 werd gestart met het in dit proefschrift beschreven promotieonderzoek bij de vakgroep Bio-organische Synthese, onder leiding van prof.dr. G.A. van der Marel, prof.dr. H.S. Overkleef en dr. J.D.C. Codée.

Delen van het onderzoek hier beschreven zijn gepresenteerd op de jaarlijkse NWO-CHAINS conferentie te Veldhoven, middels posterpresentaties (2014, 2015, 2016, 2017) en mondelinge presentaties (2017). Een posterpresentatie is gegeven op het 19<sup>de</sup> European Carbohydrate Symposium 2017 in Barcelona, Spanje, waar het werd bekroond met de prijs voor beste poster.

Sinds april 2018 is hij aangesteld als vakdocent organische chemie aan de Universiteit Leiden.

## Curriculum vitae - English

Stefan van der Vorm was born in Rotterdam, The Netherlands, on July 28th 1988. From 2000 until 2007 he attended the Maerlant College in Brielle, at which secondary education diplomas, with majors in science, were obtained in 2005 (HAVO) and 2007 (VWO-atheneum). In 2007 he commenced with the bachelor education Molecular Science & Technology at Leiden University and Delft University of Technology. As part of the bachelor program, a research internship in the field of molecular modelling was followed, concerning the dissipative particle dynamics study of protein-mediated membrane fusion, under guidance of prof.dr. J.G.E.M. Fraaije. The Bachelor of Science degree was subsequently obtained in 2010, after which he studied Languages and Cultures of Japan at Leiden University for one year. In 2011 the research master program in Chemistry was started with a specialization in Design and Synthesis. During this program a research internship at the Bio-organic Synthesis group, headed by prof.dr. H.S. Overkleef and prof.dr. G.A. van der Marel, of Leiden University was pursued. The title of the project was “Towards a library of sulfated mannuronic acid oligomers, to study structure-activity relationships” and was under daily supervision of dr. M.T.C. Walvoort and dr. A.G. Volbeda. A second research internship was conducted in 2013 at Kyoto University (京都大学), in the group of prof.dr. J.-I. Yoshida (吉田潤一), and was titled “Configurational stability of chiral oxyranyllithium intermediates from styrene oxide derivatives”, making extensive use of microreactors. After conclusion of the master education, the Master of Science degree was received with honors. In December of 2013, the research described in this Ph.D. thesis was started under supervision of prof.dr. H.S. Overkleef, prof.dr. G.A. van der Marel, and dr. J.D.C. Codée, in the Bio-organic Synthesis group of Leiden University.

Parts of the research described herein was presented at the annual Dutch chemistry conference “CHAINS”, Veldhoven, by poster presentations (2014,2015, 2016, 2017) and an oral presentation (2017). A poster was presented at the 19<sup>th</sup> European Carbohydrate Symposium 2017, in Barcelona, Spain, and was rewarded the price for best poster.

Since April 2018 he is appointed as lecturer organic chemistry at Leiden University.

## Appendix: General experimental procedures

All chemicals were of commercial grade and used as received unless stated otherwise. Dichloromethane (DCM) was stored over activated 4 Å molecular sieves for at least 24 h before use. Trifluoromethanesulfonic anhydride (Tf<sub>2</sub>O) was distilled over P<sub>2</sub>O<sub>5</sub> and stored at -20°C under a nitrogen atmosphere. Triethylamine (Et<sub>3</sub>N) was distilled over CaH<sub>2</sub> and stored over KOH pellets. Overnight temperature control was achieved by a FT902 Immersion Cooler (Julabo). Flash column chromatography was performed on silica gel 60 Å (0.04 – 0.063 mm, Screening Devices B.V.). Size-exclusion chromatography was performed on Sephadex (LH-20, GE Healthcare Life Sciences) by isocratic elution with DCM/MeOH (1/1, v/v). Thin-layer chromatography (TLC) analysis was conducted on TLC silica gel 60 plates (Kieselgel 60 F<sub>254</sub>, Merck) with UV detection by (254 nm) and by spraying with 20% sulfuric acid in ethanol or by spraying with a solution of (NH<sub>4</sub>)<sub>6</sub>Mo<sub>7</sub>O<sub>24</sub>·H<sub>2</sub>O (25 g/L) and (NH<sub>4</sub>)<sub>4</sub>Ce(SO<sub>4</sub>)<sub>4</sub>·2H<sub>2</sub>O (10 g/L) in 10% aq. sulfuric acid followed by charring at ±250 °C. TLC-MS analysis was performed on a Camag TLC-MS Interface combined with an API165 (SCIEX) mass spectrometer (eluted with *tert*-butylmethylether/EtOAc/MeOH, 5/4/1, v/v/v + 0.1% formic acid, flow rate 0.12 mL/min). LC-MS analysis was conducted on a Finnigan LCQ Advantage Max mass spectrometer with a Finnigan Surveyor HPLC system eluted with a gradient solvent (8 min, 1 mL/min, 10%-90% CH<sub>3</sub>CN in H<sub>2</sub>O + 1% TFA, total sample run 12 min). High-resolution mass spectrometry (HRMS) was performed on a Thermo Finnigan LTQ Orbitrap mass spectrometer equipped with an electrospray ion source in positive-ion mode (source voltage 3.5 kV, sheath gas flow 10, capillary temperature 275 °C) with resolution  $R = 60.000$  at  $m/z$  400 (mass range of 150-4000) and dioctylphtalate ( $m/z=391.28428$ ) as lock mass, or on a Waters Synapt G2-Si (TOF) equipped with an electrospray ion source in positive mode (source voltage 3.5 kV) and LeuEnk ( $m/z = 556.2771$ ). as internal lock mass. <sup>1</sup>H, <sup>2</sup>H and <sup>13</sup>C NMR spectra were recorded on a Bruker AV-400 NMR, a Bruker DMX-400 NMR instrument (400, 61 and 101 MHz respectively), a Bruker AV-500 NMR instrument (500, 77, 126 MHz respectively), and <sup>19</sup>F spectra were recorded on a Bruker AV-500 NMR (470 MHz). Chemical shifts ( $\delta$ ) are given in ppm relative to tetramethylsilane as internal standard or the residual signal of the deuterated solvent. Coupling constants ( $J$ ) are given in Hz. All given <sup>13</sup>C-APT spectra are proton decoupled. NMR peak assignments were made using COSY and HSQC. If necessary additional NOESY, TOCSY, HMBC, (HMBC-)GATED, and HSQC-HECADE experiments were used to further elucidate the structure. The anomeric product ratios were based on careful analysis of the crude reaction mixture and the purified reaction product by integration of representative <sup>1</sup>H NMR signals. IR spectra were recorded on a Shimadzu FTIR-8300 IR spectrometer and are reported in cm<sup>-1</sup>. Specific rotations were measured on a Propol automatic polarimeter or an Anton-Paar MCP-100 modular circular polarimeter at 589 nm unless otherwise stated.