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## Understanding Anthracyclines: Synthesis of a Focused Library of Doxorubicin/Aclarubicin - Inspired Structures

Wander, D.P.A.

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**Author:** Wander, D.P.A.

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**Understanding Anthracyclines:  
Synthesis of a Focused Library of  
Doxorubicin/Aclarubicin -  
Inspired Structures**

**PROEFSCHRIFT**

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op gezag van Rector Magnificus prof. mr. C. J. J. M. Stolker  
volgens besluit van het College voor Promoties  
te verdedigen op dinsdag 19 november 2019  
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door

**Dennis Pascal Aron Wander**

Geboren te Spijkenisse in 1991

# Promotiecommissie

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Luck is the residue of design

- *John Milton*

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# List of Abbreviations

Ac	acetyl
AIBN	azobisisobutyronitrile
Alloc	allyloxycarbonyl
app.	apparent
aq.	aqueous
Ag(DPAH) <sub>2</sub>	silver(II) bis-(hydrogen dipicolinate)
b	broad
b.r.s.m.	based on recovered starting material
Bz	benzoyl
cat.	catalytic
CEL	conformational energy landscape
CoA	coenzyme A
cod	1,5-cyclooctadiene
COSY	correlation spectroscopy
d	doublet
dd	doublet of doublets
ddd	doublet of doublets of doublets
ddt	doublet of doublet of triplets
DCE	1,2-dichloroethane
DCM	dichloromethane
DDQ	2,3-dichloro-5,6-dicyano-1,4-benzoquinone
DEAD	diethyl azodicarboxylate
DIPEA	diisopropylethylamine; Hünigs base
DMAP	4-dimethylaminopyridine
DMF	<i>N,N</i> -dimethylformamide
DMP	Dess-Martin periodinane
DMSO	dimethyl sulfoxide
dq	doublet of quartets
DSB	double-stranded break
dt	doublet of triplets
DTBMP	2,6-di- <i>tert</i> -butyl-4-methylpyridine
dtc	doublet of triplet of triplets
EDCI	1-ethyl-3-(3-dimethylaminopropyl)carbodiimide
eq	molar equivalents
FDA	US Food and Drug Administration

HSQC	heteronuclear single-quantum coherence spectroscopy
IDCP	iodonium di- <i>sym</i> -collidine perchlorate
<i>J</i>	coupling constant (Hz)
K <sub>222</sub>	4,7,13,16,21,24-hexaoxa-1,10-diazabicyclo[8.8.8]hexacosane
LC-MS	liquid-chromatography mass spectrometry
<i>m</i>	multiplet
Ms	methylsulfonate
M.S.	molecular sieves
NDMBA	<i>N,N</i> -dimethylbarbituric acid
NIS	<i>N</i> -iodosuccinimide
NMR	nuclear magnetic resonance
o.n.	overnight
OPMP	<i>p</i> -methoxyphenolate
Ph	phenyl
Phen	3,4,7,8-tetramethyl-1,10-phenanthroline
PMB	<i>p</i> -methoxybenzyl
pNBz	<i>p</i> -nitrobenzoyl
ppm	parts per million
pyr.	pyridine
<i>q</i>	quartet
<i>qd</i>	quartet of doublets
quant.	quantitative
ROS	reactive oxygen species
rt	room temperature
<i>s</i>	singlet
SAR	structure-activity relationship
sat.	saturated
Su	succinimide
<i>t</i>	triplet
TBABr	tetra- <i>n</i> -butylammonium bromide
TBAF	tetra- <i>n</i> -butylammonium fluoride
TBS	<i>tert</i> -butyldimethylsilyl
TBSOTf	<i>tert</i> -butyldimethylsilyl trifluoromethanesulfonate
<i>td</i>	triplet of doublets
TES	triethylsilyl
Tf	trifluoromethylsulfonate
TFAc	trifluoroacetyl