



Universiteit
Leiden
The Netherlands

Synthesis of mycobacterial phenolic glycolipids

Dijk, J.H.M. van

Citation

Dijk, J. H. M. van. (2022, October 13). *Synthesis of mycobacterial phenolic glycolipids*. Retrieved from <https://hdl.handle.net/1887/3480227>

Version: 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/1887/3480227>

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

Synthesis of Mycobacterial Phenolic Glycolipids

Proefschrift

ter verkrijging van
de graad van doctor aan de Universiteit Leiden,
op gezag van rector magnificus prof.dr.ir. H. Bijl,
volgens besluit van het college voor promoties
te verdedigen op donderdag 13 oktober 2022
klokke 16:15 uur

door

Jan Hessel Michiel van Dijk

geboren te 's-Gravenhage
in 1992

Promotores:

Prof. dr. J.D.C. Codée

Prof. dr. G.A. van der Marel

Promotiecommissie

Prof. dr. H.S. Overkleeft

Dr. D.V. Filippov

Prof. dr. A. Geluk

Prof. dr. A.J. Minnaard

Dr. T.L. Lowary

Leids Universitair Medisch Centrum

Rijksuniversiteit Groningen

Academia Sinica

"The chase is better than the catch"

Scooter

Table of Contents

	Abbreviations	7
Chapter 1	Developments in the Synthesis of Mycobacterial Phenolic Glycolipids	13
Chapter 2	Synthetic Phenolic Glycolipids for the Diagnosis of Leprosy	45
Chapter 3	Synthesis of Phthiocerol alkyne	85
Chapter 4	Synthesis of PGLs originating from The Mycobacterium tuberculosis complex	105
Chapter 5	Synthesis of PGLs originating from M. leprae and M. haemophilum	151
Chapter 6	Synthesis of PGLs originating from M. kansasii and M. gastri	197
Chapter 7	Aglycone analogues of Phenolic Glycolipids	261
Chapter 8	Summary and Future Prospects	304
	Nederlandse Samenvatting	319
	List of Publications	329
	Curriculum Vitae	331
	Dankwoord	333

List of Abbreviations

Ac	Acetyl
All	Allyl
APT	Attached Proton Test
aq	Aqueous
arom	Aromatic
atm	Atmosphere
Bn	Benzyl
BSA	Bovine Serum Albumin
Bu	Butyl
Bz	Benzoyl
cat	Catalytic
Cbz	Carboxybenzyl
COSY	Correlation Spectroscopy
C_q	Quarternary carbon
CSA	Camphorsulfonic acid
d	Doublet
DABCO	Triethylenediamine
DBU	1,8-Diazabicyclo[5.4.0]undec-7-ene
DCE	1,2-Dichloroethane
DCM	Dichloromethane
DDQ	2,3-dichloro-5,6-dicyano- <i>para</i> -benzoquinone
DIBAL-H	Di- <i>iso</i> -butylaluminium hydride
DIC	<i>N,N</i> -di- <i>iso</i> -propylcarbodiimide
DIPEA	<i>N,N</i> -di- <i>iso</i> -propylethylamine
DMAP	<i>N,N</i> -dimethylaminopyridine
DMF	<i>N,N</i> -dimethylformamide
DMP	2,2-Dimethoxypropane or Dess-Martin Periodinane
DMSO	Dimethylsulfoxide
dppf	1,1'-Bis(diphenylphosphino)ferrocene

EDAA	Ethyl diazoacetate
EDC	1-Ethyl-3-(3-dimethylaminopropyl)carbodiimide
ELISA	Enzyme-Linked ImmunoSorbent Assay
eq	Molar equivalents
Et	Ethyl
GPL	Glycopeptidolipid
HAS	Human Serum Albumin
HFIP	1,1,1,3,3,3-hexafluoroisopropanol
HMBC	Hetereonuclear Multiple Bond Correlation
HMPA	<i>N,N,N,N,N</i> -hexamethylphosphoramidate
HOSA	Hydroxylamine- <i>O</i> -sulfonic acid
HRMS	High Resolution Mass Spectrometry
HSQC	Hetereonuclear Single Quantum Coherence
IDCP	Iodonium di- <i>sym</i> -collidine perchlorate
Ig	Immunoglobuline
IL	Interleukin
IR	Infrared
<i>J</i>	<i>J</i> -coupling
LDA	Lithium di- <i>iso</i> -propylamide
M	Molar
m	Multiplet
mCPBA	<i>meta</i> -Chloroperbenzoic acid
Me	Methyl
Nap	2-methylnaphtyl
NBS	<i>N</i> -bromosuccinimide
NIS	<i>N</i> -iodosuccinimide
NMR	Nuclear Magnetic Resonance
NTEC	<i>N</i> -thiophenyl- ϵ -caprolactam
<i>p</i>	Para
PGL	Phenolic Glycolipid

Ph	Phenyl
PIP	<i>para</i> -iodophenyl
Piv	Pivaloyl
PMB	<i>para</i> -methoxybenzyl
PMP	<i>para</i> -Methoxyphenyl
PNP	<i>para</i> -Nitrophenyl
q	Quartet
quant	Quantitative
rt	Room temperature
s	Singlet
sat	Saturated
<i>t</i>	Tertiary
t	Triplet
TBA	Tetrabutylammonium
T-BINAP	2,2-Bis(di- <i>para</i> -tolylphosphino)-1,1-binaphthyl
TBS	<i>tert</i> -Butyldimethylsilyl
TES	Triethylsilyl or Triethylsilane
Tf	Trifluoromethylsulfonyl
TFA	Trifluoroacetic acid
TFAA	Trifluoroacetic acid anhydride
THF	Tetrahydrofuran
TIPS	Tri- <i>iso</i> -propylsilyl
TLC	Thin Layer Chromatography
TMS	Trimethylsilyl or Tetramethylsilane
TMU	<i>N,N,N</i> -tetramethylurea
TNF-α	Tumor necrosis factor α
Tol	Toluene
TRIF	Toll-interleukin-receptor-domain-containing adapter-inducing interferon β
Trt	Triphenylmethyl / Trityl

Abbreviations

Ts	<i>para</i> -Toluenesulfonyl
TTBP	2,4,6-Tri- <i>tert</i> -butylpyrimidine
UV	Ultraviolet
δ	Chemical shift
ν	Wavenumber

