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## Synthetic Studies Towards Oligonucleotide Derivatives and Conjugates

Delft, P. van

### Citation

Delft, P. van. (2013, September 3). *Synthetic Studies Towards Oligonucleotide Derivatives and Conjugates*. Retrieved from <https://hdl.handle.net/1887/21632>

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**Author:** Delft, Pieter van

**Title:** Synthetic studies towards oligonucleotide derivatives and conjugates

**Issue Date:** 2013-09-03

# Synthetic Studies Towards Oligonucleotide Derivatives and Conjugates

PROEFSCHRIFT

ter verkrijging van  
de graad van Doctor aan de Universiteit van Leiden,  
op gezag van Rector Magnificus prof. mr. C.J.J.M. Stolker,  
volgens besluit van het College voor Promoties  
te verdedigen op dinsdag 3 september 2013  
klokke 16:15 uur

door

**Pieter van Delft**  
geboren te Leiden in 1981

## **Promotiecommissie**

Promotor: Prof. Dr. G. A. van der Marel

Co-promotor: Dr. D. V. Filippov

Overige leden: Prof. Dr. C. A. van Boeckel

Prof. Dr. J. Brouwer

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# List of abbreviations

A	(2'-deoxy-)adenosine	KDa	kilodalton
Ada	adamantoyl	KLH	keyhole limpet hemocyanin
Alk	alkyl	LC/MS	liquid chromatography/ mass spectrometry
BMT	5-benzyl-mercapto-tetrazole	m	multiplet
Bn	benzyl	mcm <sup>5</sup> U	5-methoxycarbonylmethyl-uridine
Boc	<i>tert</i> -butyloxycarbonyl	mcm <sup>5</sup> S <sup>2</sup> U	5-methoxycarbonylmethyl-2-thiouridine
BODIPY	4,4-difluoro-4-bora-3 <i>a</i> ,4 <i>a</i> -diazas-indacene	MMTr	4-methoxytrityl
bs	broad singlet	m/z	mass-to-charge ratio
BSA	bovine serum albumin	NMP	<i>N</i> -methyl-2-pyrrolidone
Bt	benzotriazole	NMR	nuclear magnetic resonance
Bz	benzoyl	NOE	nuclear Overhauser effect
C	(2'-deoxy-)cytidine	Nu	nucleophile
CD	circular dichroism	<i>ON</i>	oligonucleotide
CE	2-cyanoethyl	PAGE	polyacrylamide gel electrophoresis
CPG	controlled pore glass	PBS	phosphate buffer saline
δ	chemical shift	PEG	polyethylene glycol
d	doublet	PES	potential energy surface
d (prefix)	2'-deoxy	PG	protective group
DCA	dichloroacetic acid	PS	polystyrene
dd	doublet of doublets	pTsOH	para-toluenesulfonic acid
ddd	doublet of doublet of doublets	q	quartet
DBU	1,8-diazabicyclo[5.4.0]undec-7-ene	RNA	ribonucleic acid
DCC	<i>N,N'</i> -dicyclohexylcarbodiimide	RP	reversed phase
DCM	dichloromethane	r.t.	room temperature
DCE	1,2-dichloroethane	RITRICO	ribose triazolyl annulated cyclooctyne
DCI	4,5-dicyanoimidazole	s	singlet
DIC	<i>N,N'</i> -diisopropylcarbodiimide	SDS	sodium dodecyl sulfate
DIAD	diisopropyl azo dicarboxylate	SPPS	solid phase peptide synthesis
DIPEA	<i>N,N</i> -diisopropyl-ethylamine	T	2'-deoxy-thymidine
DMAP	4-dimethylamino-pyridine	t	triplet
DMF	dimethylformamide	TAMRA	tetramethylrhodamine
DMTr/DMT	4,4'-dimethoxytrityl	<i>t</i> -Bu	<i>tert</i> -butyl
DNA	2'-deoxyribonucleic acid	TBAF	tetrabutylammonium fluoride
DTT	dithiothreitol	TBAI	tetrabutylammonium iodide
Dup	duplex	TBDMS	<i>tert</i> -butyl dimethylsilyl
ESI	electro spray ionization	TBDPS	<i>tert</i> -butyl-diphenylsilyl
Fmoc	Fluorenylmethyl-oxycarbonyl	TCA	trichloroacetic acid
G	(2'-deoxy-)guanosine	TEAA	triethylammonium acetate
GlcNAc	2-(Acetylamino)-2-deoxy-D-glucose	TES	triethylsilane
HCTU	<i>O</i> -(6-Chlorobenzotriazol-1-yl)- <i>N,N,N',N'</i> -tetramethyluroniumhexafluorophosphate	TIS	triisopropylsilane
HMDS	hexamethyldisilazane	TFA	trifluoroacetic acid
HOBt	<i>N</i> -hydroxy benzotriazole	THF	tetrahydrofuran
HPLC	high performance liquid chromatography	TLC	thin layer chromatography
HRMS	high resolution mass spectrometry	TLR	Toll-like receptor
Im	imidazole	TMS	trimethylsilyl
<i>i</i> -Pr	isopropyl	Ts	<i>para</i> -toluenesulfonyl
IR	infrared spectroscopy	U	uridine
<i>J</i>	coupling constant	UV	ultraviolet

One and three letter aminoacid codes follow the recommendations of the IUPAC as published in *Biochem. J.* **1984**, 219, 345-373.

