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Design and synthesis of paramagnetic probes for structural biology

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**Design and synthesis of paramagnetic
probes for structural biology**

Wei-Min Liu

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Wei-Min Liu

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Cover Image: Model of CLaNP-7 attached to Cyt *c* N56C/L58C.

Cover designed by Ching-Ya, Huang

The investigations described in this thesis were performed at the Protein Chemistry department of the Leiden Institute of Chemistry, Leiden University, Leiden, the Netherlands.

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'Lanthanoids: These elements perplex us in our researches, baffle us in our speculations, and haunt us in our very dreams. They stretch like an unknown sea before us; mocking, mystifying and murmuring strange revelations and possibilities.'- *Sir William Crookes, Royal Society of Chemistry, 1887*

To My Family

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List of abbreviations

<i>aq</i>	aqueous
AzF	<i>p</i> -azido phenylalanine
Boc	<i>tert</i> -butyloxycarbonyl
calcd.	Calculated
CLaNP	caged lanthanoid NMR probe
CuAAC	copper-catalyzed 1,3-dipolar azide-alkyne cycloaddition
Cyt <i>c</i>	cytochrome <i>c</i>
Cys	cysteine
δ	chemical shift
d	doublet
Da	Dalton
dd	double doublet
DCM	dichloromethane
DHP	3,4-dihydropyran
DIPEA	diisopropylethyl amine
DMF	<i>N,N</i> -dimethylformamide
DMSO	dimethylsulfoxide
DOTA	1,4,7,10-tetraazacyclododecane-1,4,7,10-tetraacetate
DTPA	diethylene triamine pentaacetic acid
DTT	dithiothreitol
EDC	1-ethyl-3-(3-dimethyl-aminopropyl)-carbodiimide
equiv.	molar equivalent
h	hour(s)
HATU	1-[Bis(dimethylamino)methylene]-1H-1,2,3-triazolo[4,5- <i>b</i>]pyridinium 3-oxid hexafluorophosphate
His	histidine
HOBt	<i>N</i> -hydroxybenzotriazole
HPLC	high performance liquid chromatography
HRMS	high resolution mass spectrometry
Hz	Hertz
IR	infrared
<i>J</i>	coupling constant
K	Kelvin
LC/MS	liquid chromatography/mass spectrometry
M	molar
m	multiplet
<i>m</i> CPBA	meta-chloroperoxybenzoic acid
MeCN	acetonitrile
min	minute(s)
MsCl	methanesulfonylchloride
<i>m/z</i>	mass-to-charge ratio

NHS	<i>N</i> -hydroxysuccinimide
NMR	nuclear magnetic resonance
<i>p</i>	para
Paz	pseudoazurin
PCS	pseudocontact shift
ppm	parts per million
PPTs	pyridinium <i>p</i> -toluenesulfonate
PRE	paramagnetic relaxation enhancement
q	quartet
RT	room temperature
s	singlet
sat.	saturated
SDS-PA gel	sodium dodecyl sulphate-poly acrylamide gel electroforesis
Su	succinimidyl
t	triplet
TBTA	<i>tris</i> -(Benzyltriazolylmethyl)amine
THP	tetrahydropyranyl
HTFA	trifluoroacetic acid
TLC	thin layer chromatography