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(1S,2S)-2-อะมิโนไซโคลเพนเทนคาร์บอกซิลิกแอซิดเป็นตัวเชื่อม



นางช่อถัฏดา ศรีสุวรรณเกศ

ศูนย์วิทยทรัพยากร  
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SYNTHESIS AND DNA-BINDING PROPERTIES OF PYRROLIDINYL  
PEPTIDE NUCLEIC ACIDS BEARING (1*S*,2*S*)-2-AMINOCYCLOPENTANE  
CARBOXYLIC ACIDS SPACER



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ช่อศักดิ์ดา ศรีสุวรรณเกษ : การสังเคราะห์และสมบัติการจับยึดดีเอ็นเอของพิวโรลิดินิล  
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งานวิจัยนี้เป็นการพัฒนาวิธีการสังเคราะห์เพปไทด์นิวคลีอิกแอซิด (พีเอ็นเอ) ชนิดใหม่ที่มีเบสผสม  
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 และพีเอ็นเอชนิดนี้แสดงการจับยึดกับดีเอ็นเอได้ดีกว่าอาร์เอ็นเอและตัวพีเอ็นเอเอง

ศูนย์วิทยทรัพยากร  
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KEY WORD : PEPTIDE NUCLEIC ACID / PNA / ACPC PNA.

CHOLADDA SRISUWANNAKET: SYNTHESIS AND DNA-BINDING PROPERTIES OF PYRROLIDINYL PEPTIDE NUCLEIC ACIDS BEARING (1*S*,2*S*)-2-AMINOCYCLOPENTANECARBOXYLIC ACIDS SPACER. THESIS ADVISOR: ASSOC. PROF. TIRAYUT VILAIVAN, D.Phil. 180 pp. ISBN 974-14-1291-7

A solid phase protocol for the synthesis of a new peptide nucleic acid (PNA) carrying all four nucleobases has been developed. The PNA monomers in this research consist of a nucleobase-modified pyrrolidine derivatives with *cis*-D stereochemistry and (1*S*,2*S*)-2-aminocyclopentanecarboxylic acid (ACPC). The optimized solid phase synthesis conditions include the use of Pfp-activated monomer with HOAt and DIEA for 30 minutes in the coupling step. For capping step, lauroyl chloride and DIEA were used in order to facilitate the purification of PNA. The average coupling yield in each step was generally over 95 %. A number of mixed bases PNA with 5-15 mer in length were successfully synthesized by this protocol.  $T_m$  studies with complementary DNA showed that the PNA can form a stable hybrid with high affinity and sequence specificity for Watson-Crick type base pairing (A-T, C-G) exclusively in an antiparallel fashion. These PNA also exhibited a strong preference for binding to DNA over RNA and over self pairing.

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## LIST OF ABBREVIATIONS

$\delta$	chemical shift
$\mu\text{L}$	microliter
$\mu\text{mol}$	micromole
$[\alpha]_{\text{D}}$	specific rotation
A	adenine
$\text{A}^{\text{Bz}}$	$N^4$ -benzoyladenine
Ac	acetyl
$\text{Ac}_2\text{O}$	acetic anhydride
AcOH	acetic acid
aq	aqueous
Boc	<i>tert</i> -butoxycarbonyl
br	broad
Bz	benzoyl
c	concentration
C	cytosine
calcd	calculated
$\text{C}^{\text{Bz}}$	$N^4$ -benzoylcytosine
CCA	$\alpha$ -cyano-4-hydroxy cinnamic acid
$\text{CDCl}_3$	deuterated chloroform
d	doublet
$\text{D}_2\text{O}$	deuterium oxide
DCM	dichloromethane
DIAD	diisopropylazodicarboxylate
DIC	diisopropyl carbodiimide
DIEA	$N,N'$ -dimethylaminopyridine
DMAP	4-dimethylaminopyridine
DMF	$N,N'$ -dimethylformamide
$\text{DMSO-}d_6$	deuterated dimethylsulfoxide
DNA	deoxyribonucleic acid
Dpm	diphenylmethyl
EDC.HCl	$N$ -(3-dimethylaminopropyl)- $N'$ -ethyl-carbodiimide hydrochloride



equiv	equivalent (s)
FAB <sup>+</sup>	positive ion fast atom bombardment (mass spectrometry)
Fmoc	9-fluorenylmethoxycarbonyl
FmocCl	9-fluorenylmethyl chloroformate
FmocOSu	9-fluorenylsuccinimidyl carbonate
g	gram
G	guanine
G <sup>Ibu</sup>	<i>N</i> <sup>2</sup> -isobutyrylgaunine
h	hour
HATU	<i>O</i> -(7-azabenzotriazol-1-yl)- <i>N,N,N',N'</i> -tetramethyluronium hexafluorophosphate
HOAt	1-hydroxy-7-azabenzotriazole
HPLC	high performance liquid chromatography
Ibu	isobutyryl
<i>J</i>	coupling constant
Lys	lysine
m	multiplet
MALDI-TOF	matrix-assisted laser desorption/ionization-time of flight
MeCN	acetonitrile
MeOH	methanol
MeOTs	methyl tosylate
mg	milligram
MHz	megahertz
min	minute
mL	milliliter
mM	millimolar
mmol	millimole
mp.	melting point
mRNA	messenger ribonucleic acid
MS	mass spectrometry
nm	nanometer
NMR	nuclear magnetic resonance
Npe	2-(4-nitrophenyl)ethyl
°C	degree celcius

OD <sub>xxx</sub>	optical density at xxx nm (= A <sub>xxx</sub> )
Pfp	pentafluorophenyl
PfpOH	pentafluorophenol
PfpOTfa	pentafluorophenyl trifluoroacetic acid
PG	an unspecified protecting group
Ph	phenyl
PNA	peptide nucleic acid or polyamide nucleic acid
ppm	part per million
R <sub>f</sub>	retention factor
RNA	ribonucleic acid
s	singlet
t	triplet
T	thymine
T <sup>Bz</sup>	<i>N</i> <sup>3</sup> -benzoylthymine
TFA	trifluoroacetic acid
THF	tetrahydrofuran
TLC	thin layer chromatography
T <sub>m</sub>	melting temperature
t <sub>R</sub>	retention time
Ts	<i>p</i> -toluenesulfonyl (=tosyl)
UV	ultraviolet
X	an unspecified leaving group

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