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## Targeting Platinum Compounds: synthesis and biological activity

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# Targeting Platinum Compounds synthesis and biological evaluation

## PROEFSCHRIFT

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*"It is teachers, not politicians, who control the lifeline of society."*

Yuan-Tseh Lee, Nobel prize Chemistry 1986.

***Aan Daniel***

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## List of abbreviations

A	L-alanine
A2780	human ovarian carcinoma cell line
A2780R	cisplatin-resistant human ovarian carcinoma cell line
ACN	acetonitrile
AcOH	acetic acid
ADEPT	antibody-directed enzyme prodrug therapy
aq	aqueous
Boc	<i>tert</i> -butyloxycarbonyl
BOP	benzotriazol-1-yloxytris(dimethylamino)phosphonium hexafluorophosphate
tBu	<i>tert</i> -butyl
nBuLi	n-butyl lithium
Cat	cathepsin
D	aspartic acid
d	doublet
DCG-0N	active site label for cysteine proteases
DCM	dichloromethane
DIPEA	<i>N,N</i> -diisopropylethylamine
dien	diethylene triamine
DMEM	Dulbecco's modified Eagle's medium
DMF	dimethylformamide
DMSO	dimethyl sulfoxide
DNA	deoxyribonucleic acid
E	L-glutamic acid
ECL	chemiluminescent detection reagent for horseradish peroxidase system
eda	2-aminoethyl glycine
EDTA	ethylene diamine tetraacetic acid
EPR	enhanced permeability and retention
equiv	equivalent
ER	estrogen receptor
ESI	electrospray ionization
Et <sub>2</sub> O	diethyl ether
EtOAc	ethylacetate
FDA	Food and Drug Administration
Fmoc	9-fluorenylmethoxycarbonyl
FPLC	fast protein liquid chromatography
G	L-glycine
GPL	$\alpha_9\beta_1$ -integrin targeting peptide GPLAEIDGIELG
H	L-histidine
h	hour
HMBA	4-hydroxymethylbenzoic acid
HPLC	high performance liquid chromatography
HRP	horseradish peroxidase
I	L-isoleucine
IC <sub>50</sub>	concentration of a compound that induces 50% growth inhibition in cells compared to untreated cells
ICP-OES	Inductively coupled plasma optical emission spectroscopy

J	coupling constant
K	L-lysine
L	L-leucine
L1210	murine leukemia cell-line
L1210R	murine leukemia cell-line resistant to cisplatin
LCMS	liquid chromatography mass spectrometry
LDA	lithium diisopropyl amine
m	multiplet
MBHA	4-methylbenzhydrylamine
MeOH	methanol
min	minute
MS	mass spectroscopy
MTT	3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyl-2H-tetrazolium bromide
<i>m/z</i>	mass to charge ratio
NLS	nuclear localisation signal peptide
NMM	<i>N</i> -methylmorpholine
NMP	<i>N</i> -methyl-2-pyrrolidone
NMR	nuclear magnetic resonance
P	L-proline
PBS	phosphate buffer in saline
Ph	phenyl
PNA	peptide nucleic acid
PVDF	polyvinylidene difluoride membrane
ppb	parts per billion
ppm	parts per million
Q	L-glutamine
q	quartet
RNA	ribonucleic acid
R	L-arginine
rt	room temperature
s	singlet
SAR	structure activity relationships
SDS	sodium dodecyl sulfate
SPOC	solid-phase organic chemistry
SPPS	solid-phase peptide synthesis
sw480 <sup>+/-</sup>	colon carcinoma cell line, displaying (+) or lacking (-) the $\alpha_9\beta_1$ -integrin receptor
t	triplet
TEA	triethyl amine
Tr	trityl
TFA	trifluoroacetic acid
THF	tetrahydrofuran
TMA	tetramethyl ammonium bromide
TMS	trimethylsilane
TSP	3-(trimethylsilyl)-propionic acid-D4, sodium salt
Y	L-tyrosine
Z-FR-AMC	benzyloxycarbonyl-Phe-Arg-aminomethylcumarin