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Cyclophellitol and its derivatives: synthesis and application as beta-glycosidase inhibitors

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Cyclophellitol and Its Derivatives

Synthesis and Application
as Retaining β -Glycosidase Inhibitors

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Kah-Jee Li

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List of Abbreviations

4-mu	4-methylumbelliferyl	DBU	1,8-diazabicyclo[5.4.0]undec-7-ene
ABP	activity-based probe	DCE	dichloroethane
ABPP	activity-based protein profiling	DCM	dichloromethane
Ac	acetyl	dd	double doublet
ACN	acetonitrile	ddd	double double doublet
Ada	adamantane	ddt	double double triplet
AMP	5-(adamantan-1-yl-methoxy)- pentyl	DMAP	4-(<i>N,N</i> -dimethylamino)pyridine
AMP-	<i>N</i> -[5-(adamantan-1-yl-methoxy)- pentyl]-1-deoxynojirimycin	DMDO	dimethyldioxirane
DNM		DMF	<i>N,N</i> -dimethylformamide
APT	attached proton test	DMSO	dimethylsulfoxide
aq.	aqueous	DMTF	<i>N, N</i> -dimethylthioformamide
Ar	aromatic	DNP	2,4-dinitrophenyl
Asp	aspartic acid	DNPC	2,4-dinitrophenyl- β -cellobioside
Bn	benzyl	dt	double triplet
Boc	<i>tert</i> -butoxycarbonyl	EEDQ	2-ethoxy-1-ethoxycarbonyl-1,2- dihydroquinoline
Boc ₂ O	di- <i>tert</i> -butyldicarbonate	EG	endoglucanase
BODIPY	boron-dipyrromethane	eq	molar equivalents
br	broad	ERT	enzyme replacement therapy
BSA	bovine serum albumin	Et	ethyl
Bz	benzoyl	<i>et al.</i>	<i>et alii</i> (and others)
Bu	butyl	Et ₃ N	triethylamine
cald.	calculated	Et ₂ O	diethyl ether
CBE	conduritol β -epoxide	EtOAc	ethyl acetate
CBH	cellobiohydrolase	EtOH	ethanol
COSY	correlation spectroscopy	g	gram(s)
CMT	chaperone-mediated therapy	Gal	D-galactose
C _q	quarternary carbon atom	GalF	D-galactosyl fluoride
d	doublet	GBA	glucocerebrosidase
δ	chemical shift	GBA2	β -glucosidase 2
Da	Dalton	GBA3	cytosolic β -glucosidase

GCS	glucosylceramide synthase
Glc	D-glucose
GlcF	D-glucosyl fluoride
Glu	glutamic acid
h	hour (s)
HPLC	high-performance liquid chromatography
HRMS	high resolution mass spectrometry
HSQC	heteronuclear single quantum coherence
Hz	Hertz
IC ₅₀	half maximal inhibitory concentration
<i>J</i>	coupling constant
LC/MS	liquid chromatography/mass spectrometry
LPH	lactase-phlorizin hydrolase
m	multiplet
M	molar (s)
m/z	mass to charge ratio
<i>m</i> CBPA	<i>meta</i> -chloroperoxybenzoic acid
Me	methyl
MeOH	methanol
mg	milligram(s)
MHz	mega Hertz
min	minute(s)
mL	millilitre(s)
mmol	millimol(s)
Ms	methanesulfonyl (mesyl)
MS	mass spectrometry
NaH	sodium hydride
NBS	<i>N</i> -bromosuccinimide
NIS	<i>N</i> -iodosuccinimide
NMR	nuclear magnetic resonance
PAGE	polyacrylamide gel electrophoresis
Pd/C	palladium on charcoal

Ph	phenyl
ppm	parts per million
<i>p</i> TsOH	<i>para</i> -toluenesulfonic acid
q	quartet
rt	room temperature
s	singlet
SRT	substrate reduction therapy
t	triplet
TBAF	tetrabutylammonium fluoride
TBAI	tetrabutylammonium iodide
TBS	<i>tert</i> -butyldimethylsilyl
TBTA	<i>N,N,N</i> -tris((1-benzyl-1 <i>H</i> -1,2,3-triazol-4-yl-methyl)amine
<i>t</i> Bu	<i>tert</i> -butyl
td	triple doublet
TFA	trifluoroacetic acid
THF	tetrahydrofuran
TLC	thin layer chromatography
Tr	trityl
Ts	<i>para</i> -toluenesulfonyl
UV	ultraviolet
WT	wild-type

Note: the one and three letter codes for the amino acids follow the recommendations of IUPAC. *J. Biol. Chem.* **1968**, 243, 3557-3559 and *J. Biol. Chem.* **1972**, 247, 977-983

