Solid-Supported Combinatorial and Parallel Synthesis of Small-Molecular Weight Compound Libraries

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PERGAMON
An Imprint of Elsevier Science

ELSEVIER SCIENCE Ltd
The Boulevard, Langford Lane
Kidlington, Oxford OX5 1GB, UK

Library of Congress Cataloging-in-Publication Data
A catalog record from the Library of Congress has been applied for.

British Library Cataloguing in Publication Data
A catalogue record from the British Library has been applied for.

First Edition 1998

ISBN 0 08 043258 1 Hardcover
ISBN 0 08 043257 3 Flexicover

The paper used in this publication meets the requirements of ANSI/NISO Z39.48-1992 (Permanence of Paper).

Printed in the Netherlands.

TETRAHEDRON ORGANIC CHEMISTRY SERIES
Series Editors: J E Baldwin, FRS & R M Williams

VOLUME 17

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* In Preparation

This book is dedicated to

Sir Jack E. Baldwin
(Waynflete Professor of Chemistry, Oxford UK)

and

Prof. Dr. Heinz Heimgartner
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FOREWORD

The words "Combinatorial Chemistry" have different meanings to different people, ranging from split and mix strategies to parallel synthesis using robots, and embracing the whole range of preparative chemistry from organic molecules, to catalyst ligands, and even inorganic solids. All of these activities have in common an attempt to expand the diversity of structure available to the chemist as well as the access to this diversity, permitting the discovery of new and valuable biological acid material properties. In this outstanding survey of combinatorial organic chemistry the authors Obrecht, who has established a new combinatorial chemistry company called *Polyphor*, and Villalgardo have brought together the literature, including that from 1998, and have concisely analysed the applications and achievements of this new field. This work will be of value to all chemists engaged in preparative work, both in industry and academe.

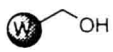
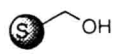
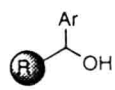
J E Baldwin, FRS

List of Abbreviations

Ac	acetyl
acac	acetylactone
ACD	available chemicals directory
ACE	angiotensin converting enzyme
ADP	adenosine diphosphate
AIBN	azoisobutyronitrile
Ala	L-alanine
Arg	L-arginine
Asn	L-asparagine
Asp	L-aspartate
ATP	adenosine triphosphate
9-BBN	9-borabicyclo[3.3.1]nonane
BHA	benzhydrylamine
Bn	benzyl
Boc	*tert*-butoxycarbonyl
Bpoc	2-(4-biphenylyl)isopropyloxycarbonyl
Bu	butyl
Bz	benzoyl
CAE	carbonyl alkyne exchange reaction
CAN	ceric ammonium nitrate
Cbz	benzyloxycarbonyl
CNS	central nervous system
COD	1,5-cyclooctadiene
COS	combinatorial organic synthesis
Cys	L-cysteine
DAMGO	[D-Ala, MePh^4, Gly-01^5]enkephalin
DBU	1,8-diazabicyclo[5.4.0]-undec-7-ene
DCC	*N,N'*-dicyclohexylcarbodiimide
DDQ	2,3-dichloro-5,6-dicyanobenzoquinone
DEAD	diethyl azodicarboxylate
DIAD	diisopropyl azodicarboxylate
DIBAH	diisobutylaluminium hydride
DIC	*N,N'*-diisopropylcarbodiimide
DIEA	*N,N*-diisopropyl-*N*-ethylamine
DMA	*N,N*-dimethylacetamide
DMAD	dimethyl acetylenedicarboxylate

DMAP	*N*,*N*-dimethylaminopyridine
DME	ethylene glycol dimethyl ether
DMF	*N*,*N*-dimethylformamide
DMS	dimethylsulfide
DMSO	dimethylsulfoxide
DMT	dimethoxytrityl
DNA	desoxyribonucleic acid
DTBP	2,6-di-(*tert*-butyl)pyridine
DVB	divinylbenzene
EDCI	1-ethyl-3-[3-(dimethylamino)propyl]carbodiimide
ELISA	enzyme linked immunosorbant assay
Et	ethyl
FAB	fast atom bombardment
Fmoc	9-fluorenylmethoxycarbonyl
FT	Fourier transform
GABA	γ-aminobutyric acid
GC	gas chromatography
Gln	L-glutamine
Glu	L-glutamate
Gly	L-glycine
HATU	azabenzotriazolyl-*N*,*N*,*N*',*N*'-tetramethyluronium hexafluorophosphate
HBTU	2-(1H-benzotriazole-1-yl)-1,1,3,3-tetramethyluronium hexafluorophosphate
His	L-histidine
HIV	human immunodeficiency virus
HMB	*p*-(hydroxymethyl)benzoyloxy-methyl
HMDS	hexamethyldisilazane
HMP	(hydroxymethyl)phenoxy)acetic acid
HOBt	1-hydroxybenzotriazole
HPLC	high performance liquid chromatography
HTS	high throughput screening
Ile	L-isoleucine
IR	infrared spectroscopy
LAH	lithium aluminium hydride
LDA	lithium *N*,*N*-diisopropylamide
Leu	L-leucine
LPCS	liquid-phase combinatorial synthesis
LPE	liquid-phase extraction
Lys	L-lysine

m-CPBA	*m*-chloroperbenzoic acid
MALDI-TOF	matrix-assisted, laser desorption ionisation time-of-flight MS
MAS-NMR	magic-angle spinning NMR
MBHA	*p*-methylbenzhydrylamine
Me	methyl
Met	L-methionine
MMP	matrix metalloproteinase
Mpc	2-(4-methylphenyl)isopropyloxycarbonyl
MS	mass spectroscopy
Mtr	methoxytrityl
NBS	*N*-bromosuccinimide
NGF	nerve growth factor
NMM	*N*-methylmorpholine
NMO	*N*-methylmorpholine *N*-oxide
NMP	*N*-methylpyrrolidinone
NMR	nuclear magnetic resonance
NVOC	*N*-nitroveratryloxycarbonyl
PAL	5-(4-Fmoc-aminomethyl-3,5-dimethoxyphenoxy)valeric acid
PAM	phenylacetamidomethyl
PCD	pyridinium dichromate
PCR	polymerase chain reaction
PEG	polyethylene glycol
Pfp	pentafluorophenyl
Ph	phenyl
Phe	L-phenylalanine
PNA	peptide-nucleic acid
PPOA	4-(2-bromopropionyl)-phenoxyacetic acid
PPTS	pyridinium *p*-toluene sulfonic acid
Pro	L-proline
PS	polystyrene
PSP	polymer-supported perruthenate
PSQ	polymer-supported quenching procedure
PTBD	polymer-supported 1,5,7-triazabicyclo[4.4.0]dec-5-ene
PVPCC	poly(4-vinylpyridinium chlorochromate)
py	pyridine
PyBOP	(benzotriazole-1-yl)-oxy-tris-pyrrolidino-phosphonium hexafluorophosphate
PyBrOP	bromo-tris-pyrrolidino-phosphonium hexafluorophosphate
RAM	*Rink* amide resin

RNA	ribonucleic acid
SCAL	safety catch amide linkage
Ser	L-serine
SPE	solid-phase extraction
SPOS	solid phase organic synthesis
Su	succinimidyl
TADDOL	α, α, α', α'-tetraaryl-1,3-dioxolane-4,5-dimethanol
TBAF	tetrabutylammonium fluoride
TBTU	*O*-(benzotriazole-1-yl)tetramethyluronium tetrafluoroborate
TCEP	tris-(2-carboxyethyl)phosphine
TES	triethylsilyl
Tf	trifluoromethanesulfonyl (triflyl)
TFA	trifluoroacetic acid
TFE	2,2,2-trifluoroethanol
THF	tetrahydrofuran
Thr	L-threonine
TIPS	triisopropylsilyl
TLC	thin layer chromatography
TMEDA	tetramethylethylenediamine
TMG	tetramethylguanidine
TMS	trimethylsilyl
Trp	L-tryptophane
Ts	*p*-toluolsulfonyl
Tyr	L-tyrosine
UV	Ultraviolet spectroscopy
Val	L-valine
XAL	[[9-[(9-fluorenylmethyloxycarbonyl)amino]xanthen-2(or 3)-yl]oxy]alkanoic acid
	Polystyrene resin (cf. *Chapter 1.7, Table 1.7.1*)
	*Wang* resin (cf. *Chapter 1.7, Table 1.7.1*)
	*Sasrin* resin (cf. *Chapter 1.7, Table 1.7.1*)
	*Rink* resin (cf. *Chapter 1.7, Table 1.7.1*)

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