Templated Organic Synthesis

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WILEY-VCH

Weinheim · New York · Chichester · Brisbane · Singapore · Toronto

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Library of Congress Card No. applied for.

A catalogue record for this book is available from the British Library.

Deutsche Bibliothek Cataloguing-in-Publication Data:
A catalogue record for this book is available from Der Deutschen Bibliothek

Printed on acid-free and chlorine-free paper.

Composition, Printing and Bookbinding: Konrad Triltsch, D-97070 Würzburg
Printed in the Federal Republic of Germany

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WILEY-VCH

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Preface

Templated synthesis is a timely research area where molecular and supramolecular sciences meet. Moreover, it represents an emerging interface between chemistry, biology, and materials sciences. This multi-author monograph includes authoritative contributions from ten leading research laboratories involved in the development of novel template-assisted organic synthesis at this interface. It demonstrates how non-covalent and covalent templates are successfully applied to control the rate and the regio- and stereoselectivity of molecular and supramolecular organic reactions.

In view of the broad, often indiscriminate use of the words "templates" and "tethers", the scope of the monograph requires careful definition. According to *Webster's Dictionary*, a template is "a gauge, pattern, or mold (as a thin plate or board) used as a guide to the form of a piece being made". The same source defines a tether as "something (as a rope or chain), by which an animal is fastened so that it can range only within a set radius". "Mold" is perhaps the best single word to define a template in the frame of this monograph. Since clear definitions are important, it is appropriate that Chapter 1 provides definitions and describes the roles of templates in organic synthesis.

Either non-covalent or covalent templates need to be absent in the original substrate as well as in the product or, at least, should be removable after having accomplished their task. Tethers should be effective in the transition states of reactions and, by acting as a mold, control the rate and the regio- and stereochemistry. Thus the monograph focuses on reactivity rather than on static structural chemistry. It is intended to promote the use of intermolecular non-covalent interactions, besides steric discrimination, to control reactivity and selectivity. Its content was selected to provide useful template- or tether-based methodology to both expert and novice practitioners in both the molecular and supramolecular sciences.

This book is focused on organic synthesis and reactivity, naturally combining and merging molecular and supramolecular aspects. It includes one contribution (Chapter 5) on templated synthesis of biological polymers and their mimics. A profound discussion of biological templated reactions or inorganic templated synthesis (such as biomineralization) is beyond the scope of this monograph. Likewise, templates (better: scaffolds) in medicinal chemistry are excluded. Thus, carbohydrates or other central scaffolds (or cores), from which functional groups for protein recognition diverge, have sometimes been named as templates. Furthermore, the concept of reversibility, i.e., the removal of a non-covalent or covalent tether after the function of providing a "mold" has been accomplished, is important. This eliminates a variety of supramolecular self-assembly processes as well as "structural templates" such as those used to organize four-helix bundle proteins.

Although all metal-catalyzed reactions such as the Pauson–Khand reaction, Co-catalyzed cyclotrimerization, and metal-catalyzed cross-coupling reactions are templated

reactions in which the metal center acts as template, they are excluded since they have been the subject of the previous monographs, *Modern Acetylene Chemistry* and *Metal-catalyzed Cross-coupling Reactions* from the same editors and publishers as this book.

The requirement for ultimate removal of the covalent template precludes examples in which the reaction has been changed from an intermolecular to an intramolecular one by connecting the reaction partners by some kind of permanent tether which remains in the molecule. Even with this restriction, organic synthesis provides an extremely rich variety of reversible templating and tethering, as illustrated in Chapter 10; here, we would only like to mention the "silicon connection" chemistry introduced by G. Stork. Claimed template effects sometimes deserve critical mechanistic examination, and this is nicely illustrated in Chapter 9.

The increasingly successful use of intermolecular interactions by non-covalent and covalent molecular and polymeric tethers provides an important link between organic synthesis and supramolecular chemistry in this monograph. Synthesis in Nature abundantly takes advantage of non-covalent bonding and templating and, therefore, the chemistry described herein can be rightly qualified as biomimetic. Emphasis is placed upon key developments and important advances, which are illustrated with attractive and useful examples. Areas covered range from molecular imprinting (Chapter 2), molecular recognition and supramolecular self-assembly (Chapters 3 and 4), biomimetic catalysis (Chapter 6), templated synthesis of biopolymers and unnatural oligomers and polymers (Chapters 1, 5, and 8), regio- and stereoselective synthesis of covalent fullerene derivatives (Chapter 7), templated macrocyclizations (Chapters 1 and 9), to the use of temporary connections in organic synthesis (Chapter 10). Carefully chosen references guide the reader through the extensive literature. A useful feature is the inclusion of key synthetic protocols, in experimental format, in six chapters. We are hopeful that the monograph will stimulate the further development of efficient and exciting new templated synthesis methodology in the molecular and supramolecular sciences.

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May 10, 1999

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DNA	deoxyribonucleic acid
DNOE	difference nuclear Orerhauser effect
L-DOPA	3-hydroxy-L-tyrosine
dppe	bis(diphenylphosphino)ethane
DSC	differential scanning calorimetry
DTBP	2,6-di-*tert*-butylpyridine
EDTA	ethylenediaminetetraacetic acid
e.e.	enantiomeric excess
EM	effective molarity
Fmoc	(9*H*-fluoren-9-ylmethoxy)carbonyl
GC	gas chromatography
GDS	guest determining step
HETCOR	{^{1}H-^{13}C}heteronuclear shift correlation
HMDS	hexamethyldisilazane
HMPA	hexamethylphosphoric triamide
HOBT	1-hydroxy-1*H*-benzotriazole
HPLC	high-performance liquid chromatography; high-pressure liquid chromatography (Chapter 8)
h-RNA	homo-RNA
IDCP	iodonium collidine perchlorate
IDCT	iodonium collidine triflate
IMDA	intramolecular Diels–Alder
i-PrOH	isopropanol
KHMDS	potassium hexamethyldisilazide
LDA	lithium diisopropylamide
LNA	locked-nucleic acid
L-selectride	lithium tri-*sec*-butylborohydride
LUMO	lowest unoccupied molecular orbital
MC	Monte Carlo
*m*CPBA	*m*-chloroperoxybenzoic acid
MMA	methyl methacrylate
MMTR	4-methoxytriphenylmethyl
MOM	methoxymethyl
ms	molecular sieves
NBD	norbornadiene
NBS	*N*-bromosuccinimide
NIS	*N*-iodosuccinimide
NFP	*N*-formylpiperidine
NMO	*N*-methylmorpholine *N*-oxide
NMP	*N*-methyl-2-pyrrolidinone
OPNA	oxypeptide-RNA
OTf	trifluoromethane sulfonate
PCC	pyridinium chlorochromate
PDC	pyridinium dichromate

PEG	poly(ethylene glycol)
phen	1,10-phenanthroline
Phth	phthalyl
Piv	pivaloyl
PM3	parametric method 3
PMB	*p*-methoxybenzyl
pMMA	poly(methyl methacrylate)
PNA	peptide-nucleic acid
Pr	propyl
pRNA	pyranosyl-RNA
*p*TSA	*p*-toluenesulfonic acid
py	pyridine
Ra-Ni	Raney nickel
RCM	ring-closing metathesis
RNA	ribonucleic acid
RORCM	ring-opening and ring-closing metathesis
rSNA	dimethylene sulfone RNA
rt	room temperature
RVC	reticulated vitreous carbon
SDDS	sodium dodecylsulfate
T	thymine
TBAF	tetrabutylammonium fluoride
TBDMS	*tert*-butyldimethylsilyl
TBDPS	*tert*-butyldiphenylsilyl
TBS	*tert*-butyldimethylsilyl
Tf	trifluoromethane sulfonyl
TFA	trifluoroacetic acid
THF	tetrahydrofuran
THP	3,4,5,6-tetrahydro-2*H*-pyran-2-yl
TLC	thin layer chromatography
TMP	tetramethylpiperidine
TMS	trimethylsilyl
TMSI	trimethylsilyl iodide
Tr	triphenylmethyl
Ts	*p*-toluenesulfonyl
TsOH	*p*-toluenesulfonic acid
T. S.	transition state
TSA	*p*-toluenesulfonic acid

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