

## Contents

### Volume 1

**Foreword** xv

**Preface** xvii

**Acknowledgments** xix

- 1     **Diazo-Mediated Homologation Reactions** 1  
*Nuno R. Candeias and H lio M.T. Albuquerque*
  
- 2     **Lithium Carbenoids in Homologation Chemistry** 79  
*Laura Ielo, Margherita Miele, Veronica Pillari, Laura Castoldi, and Vittorio Pace*
  
- 3     **Streamlining C1 Homologation Reactions Using Continuous Flow Technology: Focus on Diazomethane and Methylithium Chemistry** 143  
*Antimo Gioiello, Giada Ceccarelli, Marco Colella, and Renzo Luisi*
  
- 4     **Magnesium Carbenoids in Homologation Chemistry** 191  
*Tsutomu Kimura and Koto Sekiguchi*
  
- 5     **Homologation Reactions Based on Zinc Carbenoids and Related Reagents** 217  
*Valentina Pirovano and Rub n Vicente*
  
- 6     **Homologations via Carbene-Mediated Rearrangement Reactions** 265  
*Claire Empel, Sripati Jana, and Rene M. Koenigs*
  
- 7     **Oxenoids as Homologation Partners** 287  
*Longyang Dian and Ilan Marek*

- 8 Sulfur Ylides as C1 Homologating Reagents 309**  
*Nikoleta Spiliopoulou, Nikolaos F. Nikitas, and Christoforos G. Kokotos*
- 9 Modern Homologation Reactions of Sulfoxonium Ylides via C–H Activation 353**  
*Jin Zhang, Tao Li, Xiaogang Wang, Yangmin Ma, and Michal Szostak*
- 10 Phosphorus Reagents for Two-, Three-, and Four-Carbon Homologation of Carbonyl Compounds to Functionalized Olefins 401**  
*David Hurem and James McNulty*
- 11 Homologation Tactics with Diborylmethane via  $\alpha$ -Boryl Carbanions 429**  
*Elena Fernández*

## Volume 2

**Foreword xvii**

**Preface xix**

**Acknowledgments xxi**

- 12 Homologation of Boronic Acids and Organoboranes by Transition-Metal-Free Reactions with Diazo Compounds and N-Sulfonylhydrazones 467**  
*Carlos Valdés*
- 12.1 Introduction 467
- 12.2 Seminal Work: Homologation of Alkylboranes with Diazo Compounds and N-Sulfonylhydrazones 468
- 12.2.1 Reactions of Diazo Compounds with Alkylboranes: Hooz Homologation 468
- 12.2.2 Reactions of Alkylboranes and N-Sulfonylhydrazones 469
- 12.3 Reactions of Diazo Compounds and N-Sulfonylhydrazones with Organoboranes and Boronic Acid Derivatives 471
- 12.3.1 Reactions of Boronic Acid Derivatives and Organoboranes with Stable Diazo Compounds 471
- 12.3.2 Reactions of Boronic Acids with N-Tosylhydrazones: Reductive Coupling Reactions 477
- 12.3.2.1 Reductive Couplings with Aryl and Alkyl Boronic Acids 477
- 12.3.2.2 Reactions with Alkenyl and Allenylboronic Acids 482
- 12.3.2.3 Reaction of Alkynyl-N-Sulfonylhydrazones with Boronic Acids 486
- 12.3.3 Homologation of Boronic Acid Derivatives with Diazo Compounds Generated *In Situ* by other Methods 488

12.3.3.1	Reactions with Diazo Compounds Generated by Diazotization of Primary Amines	488
12.3.3.2	Reactions with Diazo Compounds Generated by Oxidation of Hydrazones	491
12.3.3.3	Reactions with Diazo Compounds Generated by Decomposition of Heterocycles	492
12.4	Sequential and Multicomponent Reactions	494
12.4.1	Intermolecular Multicomponent C–C/C–C Bond Forming Reactions	494
12.4.2	Intramolecular Domino Cyclizations	500
12.4.2.1	Intramolecular C–C/C–C Bond Forming Domino Reactions	500
12.4.2.2	Intramolecular C–C/C–N Bond Forming Domino Reactions	505
12.5	Synthesis of Alkyl Boronates by Reaction of Boronic Acids with <i>N</i> -Sulfonyhydrazones	506
12.6	Organocatalytic Asymmetric Homologation of Alkenylboronic Acids with 2,2,2-Trifluorodiazoethane	508
12.7	Conclusions	509
	References	510
<b>13</b>	<b>Stereospecific Reagent-Controlled Homologation Using Carbenoids Generated by Sulfoxide–Metal Exchange</b>	<b>513</b>
	<i>Paul R. Blakemore</i>	
13.1	Introduction: The Promise of Iterative Stereospecific Assembly Using Chiral Carbenoids as Fundamental Building Blocks	513
13.2	Background: The Pioneering Work of Matteson and Hoffmann	515
13.2.1	Stereoinductive Substrate-Controlled Homologation Using Prochiral Dihalomethylolithiums: An Overview of the Matteson Chain Extension Process	515
13.2.2	Sulfoxide–Metal Exchange as a Route to Stereodefined Organometallic Reagents: Hoffmann’s Quest for Enantiomerically Enriched Grignard Reagents	517
13.3	Stereospecific Reagent-Controlled Homologation with $\alpha$ -Chloroalkylmetal Reagents Generated by Sulfoxide–Metal Exchange	518
13.3.1	Enantioselective Synthesis of $\alpha$ -Chloroalkyl Aryl Sulfoxides	519
13.3.2	Sulfoxide–Lithium Exchange from $\alpha$ -Haloalkyl Aryl Sulfoxides	520
13.3.3	Homologation of Boronic Esters with $\alpha$ -Chloroalkylmetal Reagents	523
13.3.3.1	Homologation Studies with $\alpha$ -Chloroalkylmagnesium Chloride Reagents	523
13.3.3.2	Homologation Studies with $\alpha$ -Chloroalkyllithium Reagents	523
13.3.4	Iterative Homologation of Boronic Esters with $\alpha$ -Chloroalkyllithiums	527
13.3.4.1	Programmed Synthesis of Model Stereodiad and Stereotriad Motifs	527
13.3.4.2	Synthesis of Cyclic Targets Related to the Alkaloid Epibatidine	530

13.3.5	Mechanistic Considerations for StReCH with Putative $\alpha$ -Chloroalkyllithiums Generated by the Addition of Organolithiums to $\alpha$ -Chloroalkyl Aryl Sulfoxides	531
13.4	Stereospecific Reagent-Controlled Homologation with Lithiated Oxiranes Generated by Sulfoxide–Metal Exchange	533
13.5	Stereospecific Reagent-Controlled Homologation with Metalated Carbamates and Esters Generated by Sulfoxide–Metal Exchange	536
13.5.1	Enantioselective Synthesis of $\alpha$ -Oxyalkyl Aryl Sulfoxides	537
13.5.2	Homologation with $\alpha$ -Metalated Carbamates and Esters	539
13.6	Concluding Remarks and Outlook	542
	Acknowledgments	544
	References	545
<b>14</b>	<b>Iterative Homologation of Boronic Esters: Assembly Line Synthesis</b>	<b>549</b>
	<i>Kay Yeung and Varinder K. Aggarwal</i>	
14.1	Introduction	549
14.1.1	Substrate-Controlled Homologation of Boronic Esters	549
14.1.2	Reagent-Controlled Homologation of Boronic Esters	550
14.1.2.1	Lithiation–Borylation	551
14.2	Iterative Homologation of Boronic Esters (Assembly Line Synthesis)	554
14.2.1	Application of Assembly Line Synthesis to Molecules with Tailored Shape	555
14.2.2	Application of Assembly Line Synthesis to Polypropionate Fragments	558
14.2.3	Total Syntheses of Natural Products Using Assembly Line Synthesis	561
14.2.3.1	Stemaphylline	561
14.2.3.2	Tatanan A	563
14.2.3.3	Mycolactone Core	564
14.2.3.4	Kalkitoxin	565
14.2.3.5	Hydroxyphthioceranic Acid	566
14.2.3.6	Baulamycins A and B	568
14.3	Conclusion and Outlook	571
	References	572
<b>15</b>	<b>Fluorocarbon Chain Homologation and Elongation Reactions</b>	<b>575</b>
	<i>Qian Wang and Jinbo Hu</i>	
15.1	Introduction	575
15.2	By Use of Carbene-Type C1 Source	575
15.2.1	Homocoupling of Difluorocarbene	575
15.2.2	CF <sub>2</sub> -Insertion into C–Cu Bond	579
15.2.3	CF <sub>2</sub> -Insertion into C–Pd Bond	583
15.3	By Radical or Ionic-Type C1 Source	585

15.4	By Radical Telomerization of Fluoroalkenes	589
15.5	By Radical Polymerization of Fluoroalkenes	590
15.6	Conclusion	592
	References	592
<b>16</b>	<b>Homologation Reactions for the Synthesis of Fluorinated Molecules</b>	<b>595</b>
	<i>Claire Empel, Zhen Yang, and Rene M. Koenigs</i>	
16.1	Introduction	595
16.2	Cyclopropanation Reactions	596
16.2.1	Biocatalytic Cyclopropanation Reactions	603
16.3	Insertion Reactions	605
16.3.1	Insertion Reactions into C–C and C–H Bonds	605
16.3.2	Insertion Reactions into X–H Bonds	605
16.4	gem-Difluoroolefination Reactions	610
16.5	Conclusion and Perspective	614
	References	616
<b>17</b>	<b>Synthesis of Oxiranes and Aziridines from Aldehydes and Imines Using Anionic Homologation Approaches</b>	<b>619</b>
	<i>Michael D. Delost and Jon T. Njardarson</i>	
17.1	Introduction	619
17.2	Brief Summary of Milestones in Darzens Homologations	619
17.2.1	Brief Summary of Milestones in Ylide (Corey–Chaykovsky) Chemistry	621
17.2.2	Brief Summary of Milestones in Carbene Homologations with Diazo Compounds	622
17.3	Selected Darzens Homologation Strategies with $\alpha$ -Halo-Nucleophiles	623
17.3.1	Racemic Darzens Strategies	623
17.3.2	Asymmetric Darzens Strategies	624
17.3.3	Various Asymmetric Cascades Involving Darzens Reactions	626
17.3.4	Darzens Reaction Applications in Total Synthesis	627
17.4	Selected Aza-Darzens Homologation Strategies	632
17.4.1	Non-Asymmetric Aza-Darzens Strategies	632
17.4.2	Asymmetric Aza-Darzens Strategies	633
17.4.2.1	Asymmetric Aza-Darzens Strategies with Chiral Auxiliaries	633
17.4.2.2	Aza-Darzens Strategies through the Utilization of Chiral Ligands	636
17.4.3	Anionic Hopping and Related Cascades	637
17.5	Carbene and Carbenoid Homologation Strategies with $\text{XCH}_2\text{X}$ (and Related Platforms)	638
17.6	Sulfur Ylide Homologation Strategies	642
17.6.1	Chiral Sulfide Architectures and Selected Contributions	642
17.6.2	[2+1] Sulfur Ylide Annulations with Classic Reagents	645
17.6.2.1	Selected Sulfur Ylide Strategies with Chiral Imine Auxiliaries	645

17.6.3	Homologations from <i>In Situ</i> -Derived Sulfur Ylides	646
17.6.4	Selected Non-Sulfur Ylide Homologation Strategies	647
17.7	Selected Carbene Homologation Strategies with Diazo Compounds	648
17.7.1	Aziridinations Through Metal Insertion	648
17.7.2	Lewis Acid-Mediated Aziridinations	649
17.7.3	Aziridinations with Trimethylsilyldiazomethane (TMSD)	651
17.7.4	Bronsted Acid-Mediated Aziridinations	651
17.7.5	Lewis Acid-Mediated Epoxidations	653
17.8	Summary and Outlook	654
	Abbreviations	655
	References	655
<b>18</b>	<b>One-Carbon Homologation and Homologation–Functionalization Reactions of Aldehydes</b>	<b>661</b>
	<i>Timothy S. Snowden</i>	
18.1	Introduction	661
18.2	Overview of One-Carbon Homologation of Aldehydes	662
18.2.1	Wittig-Type Homologations (Levine–Wittig Homologation)	662
18.2.2	Peterson-Type Homologations (Magnus Carbonyl Homologation)	664
18.2.3	Boron-Wittig Homologations (Matteson Carbonyl Homologation)	666
18.2.4	Epoxidation–Meinwald Rearrangement	667
18.2.5	Alkyne Formation–Hydration	668
18.2.6	Henry–Nef Reactions	670
18.2.7	Aldehyde Homologations Using Flow	673
18.3	One-Carbon Homologation–Functionalization of Aldehydes	673
18.3.1	One-Carbon Homologation to Nitroalkanes	673
18.3.2	One-Carbon Homologation to Nitriles	674
18.3.2.1	Reductive Cyanations	675
18.3.2.2	Aldehyde Homologation–Nitrile Synthesis	678
18.3.3	One-Carbon Homologation to Carboxylic Acids	678
18.3.3.1	Phosphonate Reagents	680
18.3.3.2	Peterson-Type Reactions	681
18.3.3.3	Miscellaneous Reactions	682
18.3.4	One-Carbon Homologation to Amides	687
18.3.5	One-Carbon Homologation to Esters	693
18.3.5.1	Ketene Thioacetals	693
18.3.5.2	Miscellaneous Reactions	696
18.3.6	Reductive One-Carbon Homologation to Primary Alcohols	697
18.3.7	One-Carbon Homologation to Sulfones and Sulfonamides	699
18.3.7.1	Homologated Sulfones	699
18.3.7.2	Homologated Sulfonamides	703
18.4	Summary and Outlook	706
	References	706

<b>19</b>	<b>Ring Expansion Homologation: Synthetic Strategies and Reaction Design</b>	<b>713</b>
	<i>James R. Donald and William P. Unsworth</i>	
19.1	Introduction	713
19.2	One-Atom Ring Expansion Homologation	714
19.2.1	Ring Expansion Homologation Promoted by Relief of Ring Strain	714
19.2.2	One-Atom Ring Expansion Homologation Reactions that Work on Multiple Ring Sizes	716
19.2.3	Iterative Methods for One-Atom Ring Expansion Homologation	719
19.3	Ring Expansion Based on Higher Homologation Reactions	721
19.4	Conclusions and Perspective	724
	References	725
<b>20</b>	<b>Dehomologation and Ring Contraction Strategies</b>	<b>727</b>
	<i>Marco Blangetti and Cristina Prandi</i>	
20.1	Introduction	727
20.2	Dehomologation from Carboxylic Acids and Carboxylic Acid Derivatives	727
20.3	Dehomologation from Alcohols	737
20.4	Dehomologation from Carbohydrates	741
20.5	Dehomologation from Aldehydes and Derivatives	747
20.6	Miscellaneous Dehomologations	751
20.7	Conclusions and Outlook	754
	References	755
<b>21</b>	<b>Direct Radical C<sub>1</sub> Homologations</b>	<b>759</b>
	<i>Christoph Hirschhäuser and Hans-Gert Korth</i>	
21.1	Introduction	759
21.2	Radical Additions to C=O and C=N $\pi$ -Bonds	761
21.2.1	Vincinal Radical Addition to C=X Double Bonds	762
21.2.2	Geminal Addition to Carbon Monoxide	766
21.3	Radicals and their Reaction with Tamed Carbenoids	769
21.3.1	Triggering 1,2-Migrations by Hydrogen Atom Transfer (HAT)	772
21.3.2	Triggering 1,2-Migrations by Atom Transfer Radical Addition (ATRA)	776
21.4	Conclusion	781
	References	782
<b>22</b>	<b>Allenation of Terminal Alkynes for Allene Synthesis</b>	<b>785</b>
	<i>Xue Zhang and Shengming Ma</i>	
22.1	Introduction	785
22.2	Original ATA Reaction by Crabbé	785
22.3	Allenation of Terminal Alkynes (ATA): The Racemic Version	786
22.3.1	Synthesis of Monosubstituted Allenes via ATA Reactions with Paraformaldehyde	786

22.3.2	Synthesis of 1,3-Disubstituted Allenes via ATA Reactions with Normal Aldehydes	788
22.3.3	Synthesis of Trisubstituted Allenes via ATA Reactions with Ketones	790
22.4	Enantioselective Allenation of Terminal Alkynes (EATA) with Aldehydes	792
22.4.1	Synthesis of Optically Active 1,3-Disubstituted Allenes via Chiral Ligand Strategy	792
22.4.2	Synthesis of Optically Active 1,3-Disubstituted Allenes via Chiral Amine Strategy	794
22.5	Applications of (E)ATA Reaction	797
22.5.1	Applications of the Racemic ATA Reaction in the Natural Products Synthesis	797
22.5.2	Applications of EATA Reaction in the Natural Products Synthesis	797
22.5.2.1	Synthesis of Natural Products Containing Allene Moieties	797
22.5.2.2	Applications of EATA Reactions in the Syntheses of Natural $\gamma$ -Butyrolactones	801
22.5.2.3	Applications of EATA Reactions in the Synthesis of Jaspine B	804
22.6	Conclusions and Perspectives	805
	References	805
<b>23</b>	<b>Homogeneous Carbon Monoxide Homologation</b>	<b>813</b>
	<i>Ana M. Geer, Deborah L. Kays, and Laurence J. Taylor</i>	
23.1	Introduction	813
23.2	s-Block Metals	813
23.2.1	Early Group 1 and Group 2 Chemistry	814
23.2.2	Reactivity with s-Block Organometallics	814
23.3	p-Block	816
23.3.1	Group 13 (B, Al)	816
23.3.2	Group 14 (Si, Ge)	819
23.3.3	Group 15 (P, Se)	821
23.4	Early d-Block Metals	821
23.4.1	Group 3 (Sc, Y)	821
23.4.2	Group 4 (Ti, Zr, Hf)	822
23.4.3	Group 5 (V, Nb, Ta)	825
23.4.4	Group 6 (Cr, Mo, W)	826
23.4.5	Group 7 (Mn, Tc, Re)	828
23.5	Late d-Block Metals	831
23.5.1	Catalytic Double Carbonylation	831
23.5.2	Group 8 (Fe, Ru, Os)	832
23.5.3	Group 9 (Co, Rh, Ir)	834
23.5.4	Group 10 (Ni, Pd, Pt)	835
23.6	f-Block Metals	835



23.6.1	Rare Earth Chemistry	835
23.6.2	Actinide Chemistry	838
23.7	Conclusion and Outlook	840
	Abbreviations	841
	References	842
<b>24</b>	<b>Homologation Reactions with CO<sub>2</sub></b>	<b>847</b>
	<i>Tamal Roy and Ji-Woong Lee</i>	
24.1	Introduction	847
24.2	Metal Carbenoids as Reagents for CO <sub>2</sub> Homologation	848
24.3	Carbenes in CO <sub>2</sub> Homologation	850
24.4	Umpolung Reactivity of Carbonyl Compounds in CO <sub>2</sub> Homologation	852
24.4.1	Dithioacetals and CO <sub>2</sub> (Corey–Seebach Reaction)	853
24.4.2	Redox Neutral Carboxylation Reactions via Umpolung Strategies	854
24.4.3	Photo Redox Reactions with CO <sub>2</sub>	860
24.5	Carbonylation Reaction Using CO <sub>2</sub> as a CO Surrogate	863
24.5.1	Hydroformylation/Reduction Sequence for Alkenes with CO <sub>2</sub> /H <sub>2</sub>	864
24.6	Methanol Homologation Using CO <sub>2</sub>	867
24.7	CO <sub>2</sub> -Promoted Cyanide Homologation	870
24.8	Conclusion	874
	References	874
	<b>Index</b>	<b>879</b>