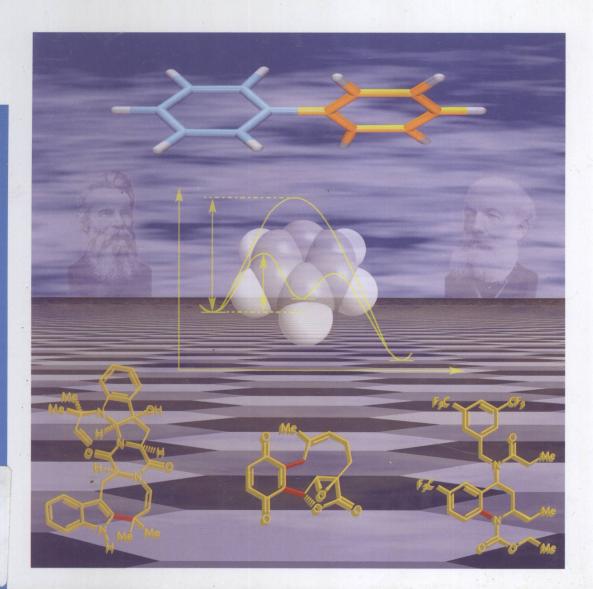
Modern Arylation Methods



0621.25 M689.3

Modern Arylation Methods

Edited by Lutz Ackermann







WILEY-VCH Verlag GmbH & Co. KGaA

The Editors

Prof. Dr. Lutz Ackermann

Georg-August-Universität Göttingen Institut für Organische Chemie und Biomolekulare Chemie Tammannstr. 2 37077 Göttingen Germany All books published by Wiley-VCH are carefully produced. Nevertheless, authors, editors, and publisher do not warrant the information contained in these books, including this book, to be free of errors. Readers are advised to keep in mind that statements, data, illustrations, procedural details or other items may inadvertently be inaccurate.

Library of Congress Card No.: applied for

British Library Cataloguing-in-Publication Data A catalogue record for this book is available from the British Library.

Bibliographic information published by the Deutsche Nationalbibliothek

The Deutsche Nationalbibliothek lists this publication in the Deutsche Nationalbibliografie; detailed bibliographic data are available on the Internet at http://dnb.d-nb.de>.

© 2009 WILEY-VCH Verlag GmbH & Co. KGaA, Weinheim

All rights reserved (including those of translation into other languages). No part of this book may be reproduced in any form – by photoprinting, microfilm, or any other means – nor transmitted or translated into a machine language without written permission from the publishers. Registered names, trademarks, etc. used in this book, even when not specifically marked as such, are not to be considered unprotected by law.

Composition SNP Best-set Typesetter Ltd., Hong Kong Printing betz-druck GmbH, Darmstadt Bookbinding Litges & Dopf GmbH, Heppenheim

Printed in the Federal Republic of Germany Printed on acid-free paper

ISBN: 978-3-527-31937-4

Modern Arylation Methods

Edited by Lutz Ackermann

Further Reading

de Vries, J. G., Elsevier, C. J. (Eds.)

The Handbook of Homogeneous Hydrogenation

3 Volumes 2007

ISBN: 978-3-527-31161-3

Yamamoto, H., Ishihara, K. (Eds.)

Acid Catalysis in Modern Organic Synthesis

2 Volumes 2008

ISBN: 978-3-527-31724-0

Oro, L. A., Claver, C. (Eds.)

Iridium Complexes in Organic Synthesis

2009

ISBN: 978-3-527-31996-1

Hiersemann, M., Nubbemeyer, U. (Eds.)

The Claisen Rearrangement Methods and Applications

2007

ISBN: 978-3-527-30825-5

Bolm, C., Hahn, F. E. (Eds.)

Activating Unreactive Substrates

The Role of Secondary Interactions

2009

ISBN: 978-3-527-31823-0

Sheldon, R. A., Arends, I., Hanefeld, U.

Green Chemistry and Catalysis

2007

ISBN: 978-3-527-30715-9

Preface

Arenes and heteroarenes are essential substructures of numerous compounds with activities that are relevant to a variety of important areas of research, ranging inter alia from medicinal chemistry and biology to materials sciences. As a result, the selective preparation of these omnipresent moieties is of the utmost relevance to synthetic chemists, both in industry and academia. The introduction of already existing aryl- or heteroaryl-groups-which we recognize today as 'arylation chemistry' – arguably constitutes the most generally applicable approach to accomplish this task. Thus, the recent growing impact of—and also interest in—arylation chemistry is reflected by the increasing numbers of references that contain the term 'arylation' {SciFinder Scholar (October 2008): 41 (1968), 124 (1978), 178 (1988), 188 (1998), 755 (2007)}. Hence, Modern Arylation Methods summarizes the diverse aspects of arylation reactions, with a particular focus on recent developments in this area. Within the book, following a brief introduction, industrial practitioners review important transition metal-catalyzed cross-coupling reactions, as well as carbon-heteroatom bond-forming processes. The influence of catalytic strategies-and particularly of those that employ transition metal complexes-on arylation reactions with haloalkanes, alkenes, alkynes and carbonyl compounds as substrates is subsequently described. The next three chapters detail not only the experimental observations but also the mechanistic considerations of ecologically benign C-H bond functionalization reactions. Finally, the book concludes with two chapters on arylations, which involve arynes or radicals as key intermediates, and a summary of photochemically initiated transformations. I hope that this topical selection will be useful to the reader, and that it will serve as a stimulus for further exciting developments in this rapidly evolving research area.

The chapters of this book were written by internationally renowned authorities, to whom I am very thankful for such outstanding contributions. I also wish to express my gratitude to Elke Maase, Rainer Münz, Hans-Jochen Schmitt and the staff of the editorial team of Wiley-VCH for their continuous help during this project. Further, I gratefully acknowledge the assistance of my coworkers during

Modern Arylation Methods. Edited by Lutz Ackermann Copyright © 2009 WILEY-VCH Verlag GmbH & Co. KGaA, Weinheim ISBN: 978-3-527-31937-4 XIV | Preface

the editorial process, particularly of Sergei I. Kozhushkov, Stefan Beußhausen and Gabriele Keil-Knepel. Most importantly, I am deeply thankful to Daniela Rais for her invaluable advice, encouragement and support.

Göttingen, December 2008

Lutz Ackermann

List of Contributors

Lutz Ackermann

Institut für Organische und Biomolekulare Chemie Georg-August-Universität Göttingen Tammannstrasse 2 37077 Göttingen Germany

Angelo Albini

University of Pavia Department of Organic Chemistry Viale Taramelli 10 27100 Pavia Italy

Erick M. Carreira

ETH Zürich Laboratorium für Organische Chemie HCI H 335 Wolfgang-Pauli-Strasse 10 8093 Zürich Switzerland

Yu Chen

Department of Chemistry Iowa State University Ames, Iowa 50011 USA

Christian Defieber

ETH Zürich Laboratorium für Organische Chemie HCI H 335 Wolfgang-Pauli-Strasse 10 8093 Zürich Switzerland

Paula de Mendoza

Institute of Chemical Research of Catalonia (ICIQ) Av. Països Catalans 16 43007 Tarragona Spain

Valentina Dichiarante

University of Pavia Department of Organic Chemistry Viale Taramelli 10 27100 Pavia Italy

Antonio M. Echavarren

Institute of Chemical Research of Catalonia (ICIQ) Av. Països Catalans 16 43007 Tarragona Spain

Maurizio Fagnoni

University of Pavia Department of Organic Chemistry Viale Taramelli 10 27100 Pavia Italy

Shingo Ito

International Research Center for Elements Science Institute for Chemical Research Kyoto University, Uji Kyoto 611-0011 Japan

Richard C. Larock

Department of Chemistry Iowa State University Ames, Iowa 50011 USA

Steven V. Lev

Department of Chemistry University of Cambridge Cambridge CB2 1EW United Kingdom

Adam Littke

Biogen Idec Department of Process Chemistry 14 Cambridge Center Cambridge, MA 02142 USA

Masahiro Miura

Osaka University Department of Applied Chemistry Faculty of Engineering Suita Osaka 565-0871 Iapan

Masaharu Nakamura

International Research Center for **Elements Science** Institute for Chemical Research Kyoto University, Uji Kyoto 611-0011 Japan

Steven P. Nolan

Institute of Chemical Research of Catalonia (ICIQ) Av. Països Catalans 16 43007 Tarragona Spain

Martin Oestreich

Organisch-Chemisches Institut Westfälische Wilhelms-Universität Münster Corrensstrasse 40 48149 Münster Germany

Tetsuya Satoh

Osaka University Department of Applied Chemistry Faculty of Engineering Suita Osaka 565-0871 Japan

Björn Schlummer

Saltigo GmbH 51369 Leverkusen Germany

Ulrich Scholz

Boehringer Ingelheim Pharma GmbH & Co. KG 55216 Ingelheim am Rhein Germany

Birte Schulte

Organisch-Chemisches Institut Westfälische Wilhelms-Universität Münster Corrensstrasse 40 48149 Münster Germany

Armido Studer

Organisch-Chemisches Institut Westfälische Wilhelms-Universität Münster Corrensstrasse 40 48149 Münster Germany

Andrew W. Thomas

Discovery Chemistry F. Hoffmann-La Roche, Ltd 4070 Basel Switzerland

Verena T. Trepohl

Organisch-Chemisches Institut Westfälische Wilhelms-Universität Münster Corrensstrasse 40 48149 Münster Germany

Santiago E. Vaillard

Organisch-Chemisches Institut Westfälische Wilhelms-Universität Münster Corrensstrasse 40 48149 Münster Germany

Rubén Vicente

Institut für Organische und Biomolekulare Chemie Georg-August-Universität Göttingen Tammannstrasse 2 37077 Göttingen Germany

Mihai S. Viciu

ETH Zürich Department of Chemistry and Applied Biosciences Swiss Federal Institute of Technology HCI H 232 8093 Zürich Switzerland

Contents

	Preface XIII	
	List of Contributors XV	
1	Arylation Reactions: A Historical Perspective 1	
	Lutz Ackermann	
1.1	Structure and Bonding of Benzene 1	
1.2	Syntheses of Substituted (Hetero)Arenes, and the Contents	
	this Book 3	
	Abbreviations 18	
	References 18	
2	Metal-Catalyzed Coupling Reactions with Aryl Chlorides,	
	Tosylates and Fluorides 25	
	Adam Littke	
2.1	Introduction 25	
2.2	Coupling Reactions of Aryl Chlorides 26	
2.2.1	Nickel-Catalyzed Cross-Couplings of Aryl Chlorides 27	
2.2.2	Palladium-Catalyzed Cross-Coupling Reactions 29	
2.2.2.1	Suzuki Reaction 29	
2.2.2.2	Stille Reaction 42	
2.2.2.3	Hiyama Coupling 45	
2.2.2.4	Negishi Coupling 49	
2.2.2.5	Kumada Coupling 51	
2.3	Coupling Reactions of Aryl Fluorides 53	
2.4	Coupling Reactions of Aryl Tosylates 56	
2.5	Conclusions 59	
	Abbreviations 60	
	References 61	
	Neterences 01	

Modern Arylation Methods. Edited by Lutz Ackermann Copyright © 2009 WILEY-VCH Verlag GmbH & Co. KGaA, Weinheim ISBN: 978-3-527-31937-4

3	Palladium-Catalyzed Arylations of Amines and α-C-H Acidic
	Compounds 69
	Björn Schlummer and Ulrich Scholz
3.1	Introduction 69
3.2	Palladium-Catalyzed Arylations of Amines 70
3.2.1	Historical Development 70
3.2.2	Catalytic Systems 72
3.2.2.1	Palladium Sources 73
3.2.2.2	Ligands 73
3.2.2.3	Bases 83
3.2.2.4	Solvents 84
3.2.3	Aryl Halides 85
3.2.4	Arylsulfonic Acid Esters 86
3.2.5	Heteroaromatic Electrophiles 87
3.2.6	Amines as Nucleophiles 89
3.2.7	Amine Derivatives as Nucleophiles 90
3.2.8	Applications 92
3.2.9	Mechanistic Aspects 94
3.2.10	Chirality 95
3.3	Palladium-Catalyzed Arylations of α-C–H Acidic Compounds 96
3.3.1	Historical Development 96
3.3.2	Catalytic Systems 98
3.3.3	α-Arylations of Esters 98
3.3.4	α-Arylations of Malonates and α-Cyano Esters 102
3.3.5	α-Arylations of Ketones 103
3.3.6	α-Arylations of Amides 104
3.3.7	α-Arylations of Nitriles 106
3.4	Summary and Conclusions 109
	Abbreviations 111
	References 112
4	Copper-Catalyzed Arylations of Amines and Alcohols with
	Boron-Based Arylating Reagents 121
	Andrew W. Thomas and Steven V. Ley
4.1	Introduction 121
4.2	Discovery and Development of a New O-H Bond
	Arylation Reaction: From Stoichiometric to Catalytic
	in Copper 123
4.3	Mechanistic Considerations 125
4.4	Miscellaneous Applications 127
4.4.1	Additional Applications with ArB(OH) ₂ 127
4.4.2	Alternatives to ArB(OH) ₂ 128
4.4.3	Alternatives to Phenols 131
4.5	Development of a New N–H Bond Arylation Reaction 132
4.5.1	Stoichiometric in Copper 132

4.5.2 4.6 4.6.1 4.6.2	Alternatives to Boronic Acids 138 Development of a New N–H Bond Arylation Reaction: Catalytic in Copper 138 Proposed Mechanism 140 Additional Important Non-N–H Arylation Examples 147
4.7	Summary and Conclusions 149 Abbreviations 151 References 152
5	Metal-Catalyzed Arylations of Nonactivated Alkyl (Pseudo)Halides via Cross-Coupling Reactions 155 Masaharu Nakamura and Shingo Ito
5.1	Introduction 155
5.2	Palladium-Catalyzed Arylations of Alkyl (Pseudo) Halides 156
5.3	Nickel-Catalyzed Arylations of Alkyl (Pseudo)Halides 163
5.4	Iron-Catalyzed Arylations of Alkyl (Pseudo) Halides 168
5.5	Copper- and Cobalt-Catalyzed Arylations of Alkyl
	(Pseudo)Halides 174
	Abbreviations 179
	References 179
6	Arylation Reactions of Alkynes: The Sonogashira Reaction 183 Mihai S. Viciu and Steven P. Nolan
6.1	Introduction 183
6.2	Palladium-Catalyzed Reactions: Ligands and Reaction Protocols 185
6.2.1	Phosphine-Based Ligands 185
6.2.1.1	Copper-Free Catalytic Systems 186
6.2.1.2	Hemilabile Ligands 188
5.2.1.3	Ionic Liquids as Reaction Media 190
5.2.1.4	Reactions in Aqueous Media 190
5.2.1.5	Recyclable Phosphine-Based Catalytic Systems 191
5.2.2	N-Heterocyclic Carbene Ligands for Sonogashira Coupling 192
5.2.3	Palladacycles as Catalysts in Sonogashira Reactions 197
5.2.4	Nitrogen-Coordinating Ligands 199
5.3	Alternative Metal Catalysts 205
5.3.1	Nickel-Catalyzed Sonogashira Reaction 205
5.3.2	Ruthenium-Based Catalytic Systems 206
5.3.3	Indium-Based Catalytic Systems 207
5.3.4	Copper-Based Catalytic Systems 207
5.4	Mechanism of the Sonogashira Reaction 208
5.4.1	Palladium- and Copper-Based Catalytic Systems 209
5.4.2	Copper-Free Catalytic Systems 210
5.5	Concluding Remarks 214
	Abbreviations 215
	References 216

7	Palladium-Catalyzed Arylation Reactions of Alkenes (Mizoroki-Heck Reaction and Related Processes) 221 Verena T. Trepohl and Martin Oestreich
7.1	Introduction 221
7.2	Mizoroki–Heck Arylations 222
7.2.1	Mechanistic Considerations 222
7.2.2	Intermolecular Mizoroki–Heck Arylations 225
7.2.2.1	Intermolecular Arylations 225
7.2.2.2	Asymmetric Intermolecular Arylations 232
7.2.2.3	Directed Intermolecular Arylations 235
7.2.3	Intramolecular Mizoroki–Heck Arylations 239
7.2.3.1	Intramolecular Arylations 239
7.2.3.2	Asymmetric Intramolecular Arylations 239
7.2.3.3	Desymmetrizing Intramolecular Arylations 245
7.3	Reductive Mizoroki–Heck-Type Arylations 248
7.3.1	Mechanistic Considerations 249
7.3.2	Intermolecular Arylations: The Bicyclo[2.2.1]heptane Case 250
7.3.3	Reductive Mizoroki–Heck-Type Arylation in Action 252
7.4	Oxidative Mizoroki–Heck-Type Arylations 254
7.4.1	Mechanistic Considerations 254
7.4.2	Intermolecular C–C Bond Formation 255
7.4.2.1	Arenes as Nucleophiles 255
7.4.2.2	Hetarenes as Nucleophiles 256
7.4.3	Intramolecular C–C Bond Formation 259
7.4.3.1	Arenes as Nucleophiles 259
7.4.3.2	Hetarenes as Nucleophiles 261
	Abbreviations 264
	References 264
8	Modern Arylations of Carbonyl Compounds 271 Christian Defieber and Erick M. Carreira
8.1	Introduction 271
8.2	Enantioselective Arylation of Aldehydes 271
8.2.1	Zinc-Mediated Asymmetric Arylation of Aldehydes 271
8.2.2	Rhodium-Catalyzed Asymmetric Arylation of Aldehydes 274
8.3	Enantioselective Arylation of Ketones 276
8.3.1	Enantioselective Arylation of Aryl-Alkyl-Substituted Ketones 276
8.3.2	Enantioselective Arylation of Isatins 277
8.3.3	Enantioselective Arylation of Trifluoromethyl-
	Substituted Ketones 277
8.4	Enantioselective Arylation of Imines 278
8.4.1	Zinc-Mediated Enantioselective Phenylation of Imines 278
8.4.2	Rhodium-Catalyzed Enantioselective Arylation of Imines 279
8.4.3	Rhodium-Catalyzed Diastereoselective Arylation
	of Imines 280

8.5	Conjugate Asymmetric Arylation 281
8.5.1	Aryl Sources for the Conjugate Asymmetric Arylation 281
8.5.2	Ligand Systems 282
8.5.3	Conjugate Arylation with Diphosphine–Palladium(II) Complexes 284
8.5.4	Enantioselective Conjugate Arylation of α,β -Unsaturated
	Aldehydes 285
8.5.5	Enantioselective Conjugate Arylation of Maleimides 286
8.5.6	Additional Acceptors for Rhodium/Diene-Catalyzed Conjugate Arylation 288
8.5.7	Enantioselective Conjugate Arylation of 2,3-Dihydro-4-Pyridones 289
8.5.8	Enantioselective Conjugate Arylation of Coumarins 290
8.5.9	Conjugate Arylation of Chiral, Racemic α,β-Unsaturated Carbonyl
0.0.7	Compounds 290
8.5.10	Conjugate Asymmetric Arylation of 3-Substituted α,β-unsaturated
	Carbonyl Compounds 291
8.5.11	1,6-Addition of Arylboronic Acids to α,β,γ,δ-Unsaturated
	Carbonyl Compounds 291
8.6	Tandem Processes 293
8.6.1	Rhodium-Catalyzed Enantioselective Conjugate
	Arylation–Protonation 293
8.6.2	Rhodium-Catalyzed Conjugate Arylation–Aldol-Addition 295
8.6.3	Rhodium-Catalyzed Conjugate Arylation–Allylation 296
8.6.4	Rhodium-Catalyzed Sequential Carbometallation-Addition 296
8.7	Enantioselective Friedel–Crafts Arylation 298
8.7.1	Metal-Catalyzed Enantioselective Friedel–Crafts Arylations 298
8.7.2	Organocatalysis in Friedel–Crafts Arylation 300
8.8	Conclusions 303
	Abbreviations 304
	References 304
9	Metal-Catalyzed Direct Arylations (excluding Palladium) 311
	Lutz Ackermann and Rubén Vicente
9.1	Introduction 311
9.2	Rhodium-Catalyzed Direct Arylations 312
9.2.1	Rhodium-Catalyzed Direct Arylations of Arenes 312
9.2.2	Rhodium-Catalyzed Direct Arylations of Heteroarenes 317
9.3	Ruthenium-Catalyzed Direct Arylations 320
9.3.1	Ruthenium-Catalyzed Direct Arylations with Organometallic
	Reagents 320
9.3.2	Ruthenium-Catalyzed Direct Arylations with Aryl (Pseudo)
0.4	Halides 322
9.4	Iridium-, Copper- and Iron-Catalyzed Direct Arylations 327
9.5	Conclusions 330
	Abbreviations 330
	References 331

10	Palladium-Catalyzed Direct Arylation Reactions 335 Masahiro Miura and Tetsuya Satoh
10.1	Introduction 335
10.2	Intermolecular Arylation of Functionalized Arenes 337
10.2.1	Reaction of Phenols and Benzyl Alcohols 337
10.2.2	Reaction of Aromatic Carbonyl and Pyridyl Compounds 341
10.2.3	Reaction of Miscellaneous Aromatic Substrates 345
10.3	Intramolecular Reaction of Haloaryl-Linked Arenes 346
10.4	Intermolecular Arylation Reactions of Heteroaromatic Compounds 348
10.4.1	Reaction of Pyrroles, Furans and Thiophenes 348
10.4.2	Described CT 11 1 0 1 1 1 1 1
10.4.3	Describer of C' Mr. 1 127
10.5	Concluding Remarks 357
10.5	Abbreviations 358
	References 358
	References 330
11	Mechanistic Aspects of Transition Metal-Catalyzed Direct Arylation Reactions 363
	Paula de Mendoza and Antonio M. Echavarren
11.1	Introduction 363
11.2	Palladium-Catalyzed Intramolecular Direct Arylation 363
11.3	Intermolecular Metal-Catalyzed Direct Arylation of Arenes 372
11.4	Metal-Catalyzed Heteroaryl–Aryl and Heteroaryl–Heteroaryl Bond Formation 374
11.5	Direct Arylation via Metallacycles 380
11.6	Cross-Dehydrogenative Couplings 388
11.7	Summary 391
	Abbreviations 391
	References 392
12	Arylation Reactions Involving the Formation of Arynes 401
12.1	Yu Chen and Richard C. Larock
12.1	Introduction 401
12.2	Generation of Arynes 402
12.3	Electrophilic Coupling of Arynes 404
12.3.1	Formation of Monosubstituted Arenes by Proton Abstraction 405
12.3.2	Aryne Insertion into a Nucleophilic–Electrophilic σ-Bond 410
12.3.3	Three-Component Coupling Reactions via Aryl Carbanion Trapping by an External Electrophile 417
12.3.4	Miscellaneous 422
12.4	Pericyclic Reactions of Arynes 427
12.4.1	Diels–Alder Reactions 427
12.4.2	[2+2] Cycloadditions 441
12.4.3	[3+2] Cycloadditions 443

12.4.4	Ene Reaction 446
12.4.5	Miscellaneous 447
12.5	Transition Metal-Catalyzed Reactions of Arynes 449
12.5.1	Transition Metal-Catalyzed Cyclizations 449
12.5.1.1	Palladium/Nickel-Catalyzed [2+2+2] Cycloadditions 449
12.5.1.2	Palladium-Catalyzed Cyclization Involving Carbopalladation
	of Arynes 457
12.5.1.3	Transition Metal-Catalyzed Carbonylations 461
12.5.1.4	Miscellaneous 462
12.5.2	Transition Metal-Catalyzed Coupling Reactions 462
12.5.2.1	Insertion of Arynes into σ -Bonds 462
12.5.2.2	Three-Component Coupling of Arynes Involving
	Carbopalladation 465
12.6	Summary 468
	Abbreviations 468
	References 469
13	Radical-Based Arylation Methods 475
	Santiago E. Vaillard, Birte Schulte and Armido Studer
13.1	Introduction 475
13.2	S _{RN} 1-Type Radical Arylations 475
13.2.1	Intermolecular S _{RN} 1 Reactions 476
13.2.2	Intramolecular S _{RN} 1 Reactions 479
13.3	Homolytic Aromatic Substitutions 480
13.3.1	Intramolecular Homolytic Aromatic Substitutions 480
	Arylations Using Nucleophilic C-Centered Radicals 480
	Arylations Using Electrophilic C-Centered Radicals 485
13.3.1.3	Radical Aryl Migration Reactions 486
13.3.2	Intermolecular Homolytic Aromatic Substitutions 489
13.3.2.1	Arylation with Nucleophilic C-Centered Radicals 489
13.3.2.2	Arylation with Electrophilic C-Centered Radicals 493
13.3.2.3	r
13.4	Arylations Using Aryl Radicals 496
13.4.1	Additions onto Olefins: Meerwein Arylation 496
13.4.2	Cyclizations Using Aryl Radicals 498
13.4.3	Phosphonylation of Aryl Radicals 502
13.5	Conclusions 502
	Abbreviations 503
	References 503
14	Photochemical Arylation Reactions 513
111	Valentina Dichiarante, Maurizio Fagnoni and Angelo Albini
14.1	Introduction 513
14.2	Photochemical Formation of Aryl–C Bonds 517
14.2.1	Intermolecular Formation of Arvl–Alkvl Bonds 517