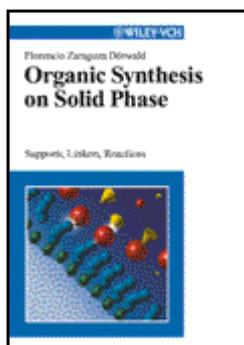


*Book Received**

Organic Synthesis on Solid Phase. (Supports, Linkers, Reactions). By Zaragoza Dörwald, Florencio. Wiley-VCH, Weinheim, 2000. Pages: 474, Hardcover. Price: 271.86 DM / 139.- EUR / 241.- SFR. ISBN 3-527-29950-5

Received: 1 December 2001



Organic synthesis on solid supports is a rapidly developing methodology, which offers several advantages if compared to traditional synthesis in solution. In recent years the number of substance classes that can be synthesised on solid phase has quickly increased, and solid-phase synthesis is becoming a valuable alternative to traditional synthesis - in particular when large numbers of different compounds in small quantities are needed for screening.

This exhaustive and systematically organised reference work gives an in-depth view on organic syntheses on insoluble polymers from the basic principles to the newest developments. The work quickly guides the reader to any particular type of reaction and to the best method for preparing a given class of compounds on solid support.

Many tables with clear presentation collect valuable information about the feasibility of a given reaction on solid support, and a wealth of information is opened up to the reader through a thoroughly worked out and comprehensive reference list. This makes the book the first stop when it comes to synthesising your compounds on solid support.

General Techniques and Analytical Tools for Solid-Phase Organic Synthesis

Supports for Solid-Phase Organic Synthesis

Linkers for Solid-Phase Organic Synthesis

Preparation of Organometallic Compounds

Preparation of Hydrocarbons

Preparation of Alkyl and Aryl Halides
Preparation of Alcohols and Ethers
Preparation of Sulfur Compounds
Preparation of Organoselenium Compounds
Preparation of Nitrogen Compounds
Preparation of Phosphorus Compounds
Preparation of Aldehydes and Ketones
Preparation of Carboxylic Acid Derivatives
Preparation of Carbonic Acid Derivatives
Preparation of Heterocycles
Preparation of Oligomeric Compounds
Index

Table of Contents:

Glossary and Abbreviations	XIV
Experimental Procedures	XX
1 General Techniques and Analytical Tools for Solid-Phase Organic Synthesis	1
1.1 General Techniques for Performing Syntheses on Insoluble Supports	1
1.2 Strategies for Parallel Synthesis	3
1.3 Analytical Methods for Support-bound Intermediates	5
1.3.1 Combustion Analysis	5
1.3.2 Colorimetric Assays	5
1.3.3 Infrared Spectroscopy	7
1.3.4 Mass Spectrometry	7
1.3.5 Nuclear Magnetic Resonance Spectroscopy	7
1.4 Strategies for the Selection of Reactions and Reagents for Parallel Solid-Phase Synthesis	8
2 Supports for Solid-Phase Organic Synthesis	13
2.1 Polystyrene	14
2.1.1 Microporous Styrene--Divinylbenzene Copolymers	14
2.1.1.1 Swelling Behavior	15
2.1.1.2 Chemical Stability	17
2.1.1.3 Functionalization	17
2.1.2 Macroporous Styrene--Divinylbenzene Copolymers	19
2.1.3 Miscellaneous Polystyrenes	20
2.2 Poly(ethylene glycol)--Polystyrene Graft Polymers	21
2.3 Poly(ethylene glycol)	22
2.4 Polyacrylamides	22
2.5 Polyacrylamide--PEG Copolymers	24
2.6 Silica	25
2.7 Polysaccharides	26
2.8 Miscellaneous Supports	27
3 Linkers for Solid-Phase Organic Synthesis	33
3.1 Linkers for Carboxylic Acids	35
3.1.1 Linkers for Acids Cleavable by Acids or Other Electrophiles	35
3.1.1.1 Benzyl Alcohol Linkers	35
3.1.1.2 Diarylmethanol (Benzhydrol) Linkers	37

- 3.1.1.3 Trityl Alcohol Linkers 37
- 3.1.1.4 Non-Benzylic Alcohol Linkers 38
- 3.1.2 Linkers for Acids Cleavable by Bases or Nucleophiles 39
 - 3.1.2.1 Benzyl Alcohol Linkers 40
 - 3.1.2.2 Non-Benzylic Alcohol Linkers 40
 - 3.1.2.3 Miscellaneous Linkers Cleavable by Bases or Nucleophiles 43
- 3.1.3 Photocleavable Linkers for Carboxylic Acids 45
- 3.1.4 Linkers for Acids Cleavable by Transition Metal Catalysis 47
- 3.1.5 Linkers for Acids Cleavable by Enzymes 49
- 3.2 Linkers for Thiocarboxylic Acids 50
- 3.3 Linkers for Amides, Sulfonamides, Carbamates, and Ureas 50
 - 3.3.1 Benzylamine Linkers 51
 - 3.3.2 (Diarylmethyl)amine and Tritylamine Linkers 55
 - 3.3.3 Linkers for Amides Cleavable by Nucleophiles 59
 - 3.3.3.1 Nucleophilic Cleavage of Alkyl Esters 59
 - 3.3.3.2 Nucleophilic Cleavage of Aryl Esters 61
 - 3.3.3.3 Nucleophilic Cleavage of Oxime and Related Esters 63
 - 3.3.3.4 Nucleophilic Cleavage of Amides and Carbamates 63
- 3.4 Linkers for Hydroxamic Acids and Hydrazides 63
- 3.5 Linkers for Carboxylic Esters 67
 - 3.5.1 Linkers for Esters Cleavable by Nucleophiles 67
 - 3.5.2 Linkers for Lactones Cleavable by Electrophiles or Oxidants 70
- 3.6 Linkers for Primary and Secondary Aliphatic Amines 71
 - 3.6.1 Benzylamine, (Diarylmethyl)amine, and Tritylamine Linkers 72
 - 3.6.2 Carbamate Attachment 74
 - 3.6.3 Miscellaneous Linkers for Aliphatic Amines 76
- 3.7 Linkers for Tertiary Amines 77
- 3.8 Linkers for Aryl- and Heteroaryl amines 79
- 3.9 Linkers for Guanidines and Amidines 81
- 3.10 Linkers for Pyrroles, Imidazoles, Triazoles, and Tetrazoles 84
- 3.11 Linkers for Alcohols and Phenols 85
 - 3.11.1 Attachment as Ethers 85
 - 3.11.2 Attachment as Silyl Ethers 89
 - 3.11.3 Attachment as Acetals 91
 - 3.11.4 Attachment as Esters 91
 - 3.11.5 Miscellaneous Linkers for Alcohols and Phenols 94
- 3.12 Linkers for Thiols 96
- 3.13 Linkers for Alkyl and Aryl Halides 99
- 3.14 Linkers for Aldehydes and Ketones 99
 - 3.14.1 Attachment as Enol Ethers, Enamines, and Imines 100
 - 3.14.2 Attachment of Carbonyl Compounds as Acetals 100
 - 3.14.3 Miscellaneous Linkers for Aldehydes and Ketones 103
- 3.15 Linkers for Olefins 103
 - 3.15.1 Linkers for Olefins Cleavable by β -Elimination 104
 - 3.15.2 Linkers for Olefins Cleavable by Olefin Metathesis 108
- 3.16 Linkers for Alkanes and Arenes 110

- 3.16.1 Cleavage followed by Decarboxylation 110
- 3.16.2 Cleavage of Silanes and related Compounds 111
- 3.16.3 Reductive Cleavage of Carbon--Oxygen and Carbon--Nitrogen Bonds 114
- 3.16.4 Reductive Cleavage of Carbon--Phosphorus, Carbon--Sulfur, and Carbon--Selenium Bonds 116
- 3.17 Non-Covalent Linkers 118
 - 3.17.1 Ion-Exchange Resins 118
 - 3.17.2 Transition Metal Complexes 118
 - 3.17.3 Miscellaneous Non-Covalent Linkers 119
- 4 Preparation of Organometallic Compounds 133
 - 4.1 Group I and II Organometallic Compounds 133
 - 4.2 Group III Organometallic Compounds 136
 - 4.3 Group IV Organometallic Compounds 137
 - 4.4 Transition Metal Complexes 138
- 5 Preparation of Hydrocarbons 143
 - 5.1 Preparation of Alkanes 143
 - 5.1.1 Preparation of Alkanes by Hydrolysis of Organometallic Compounds 143
 - 5.1.2 Preparation of Alkanes by Hydrogenation and Reduction 143
 - 5.1.3 Preparation of Alkanes by Carbon--Carbon Bond Formation 145
 - 5.1.3.1 Coupling Reactions with Group I Organometallic Compounds 145
 - 5.1.3.2 Coupling Reactions with Group II Organometallic Compounds 146
 - 5.1.3.3 Coupling Reactions with Boranes 147
 - 5.1.3.4 Coupling Reactions with Arylpalladium Compounds 148
 - 5.1.3.5 Alkylations with Alkyl Radicals 149
 - 5.1.3.6 Preparation of Cycloalkanes 150
 - 5.2 Preparation of Alkenes 151
 - 5.2.1 Preparation of Alkenes by β -Elimination and Reduction 151
 - 5.2.2 Preparation of Alkenes by Carbonyl Olefination 152
 - 5.2.2.1 By Wittig Reaction 152
 - 5.2.2.2 By Aldol and Related Condensations 155
 - 5.2.2.3 By Other Carbonyl Olefinations 156
 - 5.2.3 Preparation of Alkenes by Olefin Metathesis 156
 - 5.2.4 Preparation of Alkenes by C-Vinylation 159
 - 5.2.5 Preparation of Cycloalkenes by Cycloaddition 163
 - 5.3 Preparation of Alkynes 165
 - 5.4 Preparation of Biaryls 168
- 6 Preparation of Alkyl and Aryl Halides 177
 - 6.1 Preparation of Alkyl Halides 177
 - 6.2 Preparation of Aryl and Heteroaryl Halides 181
- 7 Preparation of Alcohols and Ethers 185
 - 7.1 Preparation of Alcohols 186
 - 7.1.1 Reduction of Carbonyl Compounds 186
 - 7.1.2 Addition of Carbon Nucleophiles to C--O Double Bonds 187
 - 7.1.3 Miscellaneous Preparations of Alcohols 191
 - 7.1.4 Protective Groups for Alcohols 193
 - 7.1.4.1 Protective Groups Cleavable by Acids 193

- 7.1.4.2 Protective Groups Cleavable by Nucleophiles 195
- 7.2 Preparation of Ethers 197
 - 7.2.1 Preparation of Dialkyl Ethers 197
 - 7.2.2 Preparation of Alkyl Aryl Ethers 200
 - 7.2.3 Preparation of Diaryl Ethers 204
- 8 Preparation of Sulfur Compounds 209
 - 8.1 Preparation of Thiols 209
 - 8.2 Preparation of Thioethers 211
 - 8.3 Preparation of Sulfoxides and Sulfones 215
 - 8.4 Preparation of Sulfonamides 216
 - 8.5 Preparation of Sulfonic Esters 221
- 9 Preparation of Organoselenium Compounds 227
- 10 Preparation of Nitrogen Compounds 229
 - 10.1 Preparation of Amines 229
 - 10.1.1 Preparation of Amines by Aliphatic Nucleophilic Substitution 229
 - 10.1.1.1 With Support-Bound Alkylating Agents 229
 - 10.1.1.2 By Alkylation of Support-Bound Amines 233
 - 10.1.2 Preparation of Amines by Aromatic Nucleophilic Substitution 233
 - 10.1.2.1 With Support-Bound Arylating Agents 233
 - 10.1.2.2 By Arylation of Support-Bound Amines 237
 - 10.1.3 Preparation of Amines by Addition of Amines to C=C Double Bonds 239
 - 10.1.4 Preparation of Amines by Reduction of Imines 239
 - 10.1.5 Preparation of Amines by Reaction of Carbon Nucleophiles with Imines or Aminals 242
 - 10.1.6 Preparation of Amines by Reduction of Amides and Carbamates 245
 - 10.1.7 Preparation of Amines by Reduction of Nitro Compounds 246
 - 10.1.8 Preparation of Amines by Reduction of Azides 247
 - 10.1.9 Miscellaneous Preparations of Amines 248
 - 10.1.10 Protective Groups for Amines 249
 - 10.1.10.1 Carbamates 250
 - 10.1.10.2 Amides 256
 - 10.1.10.3 Cyclic Imides 257
 - 10.1.10.4 Enamines 258
 - 10.1.10.5 Imines 259
 - 10.1.10.6 N-Alkyl and N-Aryl Derivatives 259
 - 10.1.10.7 N-Sulphenyl and N-Sulfonyl Derivatives 260
 - 10.2 Preparation of Quaternary Ammonium Salts 261
 - 10.3 Preparation of Hydrazines and Hydroxylamines 262
 - 10.4 Preparation of Azides 263
 - 10.5 Preparation of Diazo Compounds 264
 - 10.6 Preparation of Nitro Compounds 265
- 11 Preparation of Phosphorus Compounds 274
 - 11.1 Phosphonic Acid Derivatives 274
- 12 Preparation of Aldehydes and Ketones 275
 - 12.1 Preparation of Aldehydes and Ketones by C-Acylation 275
 - 12.2 Preparation of Aldehydes and Ketones by Oxidation 277
 - 12.3 Miscellaneous Preparations of Aldehydes and Ketones 278

- 13 Preparation of Carboxylic Acid Derivatives 285
 - 13.1 Preparation of Amides 285
 - 13.1.1 Preparation of Amides by Acylation of Amines with Isolated Acylating Agents 285
 - 13.1.2 Acylation of Amines with Acylating Reagents Formed In Situ 288
 - 13.1.2.1 Activation of Acids with Carbodiimides 290
 - 13.1.2.2 Activation of Acids with Phosphonium Salts 294
 - 13.1.2.3 Activation of Acids with Uronium Salts 296
 - 13.1.3 Miscellaneous Preparations of Amides 298
 - 13.1.4 Preparation of Amides by C-Alkylation of Other Amides 300
 - 13.1.5 Preparation of Amides by N-Alkylation of Other Amides 301
 - 13.2 Preparation of Hydroxamic Acids and Hydrazides 302
 - 13.3 Preparation of Carboxylic Acids 303
 - 13.4 Preparation of Carboxylic Esters 304
 - 13.4.1 Preparation of Esters from Support-Bound Alcohols 304
 - 13.4.1.1 Esterification of Support-bound Alcohols with N-Protected α -Amino Acids 309
 - 13.4.2 Preparation of Esters from Support-Bound Alkylating Agents 311
 - 13.4.3 Preparation of Esters from Support-Bound Carboxylic Acids 313
 - 13.4.4 Preparation of Esters by Chemical Modification of Other Esters 315
 - 13.5 Preparation of Thiol Esters 315
 - 13.6 Preparation of Amidines and Imino Ethers 315
 - 13.7 Preparation of Nitriles and Isonitriles 318
 - 13.8 Preparation of Imides 319
 - 13.9 Preparation of Thioamides 321
- 14 Preparation of Carbonic Acid Derivatives 327
 - 14.1 Preparation of Carbodiimides 327
 - 14.2 Preparation of Isocyanates and Isothiocyanates 328
 - 14.3 Preparation of Guanidines 329
 - 14.4 Preparation of Ureas 331
 - 14.5 Preparation of Thioureas and Isothioureas 334
 - 14.6 Preparation of Carbamates 335
 - 14.7 Preparation of Carbonates and Miscellaneous Carbonic Acid Derivatives 338
- 15 Preparation of Heterocycles 343
 - 15.1 Preparation of Epoxides and Aziridines 343
 - 15.2 Preparation of Azetidines and Thiazetidines 344
 - 15.3 Preparation of Pyrroles and Pyrrolidines 345
 - 15.4 Preparation of Indoles and Indolines 350
 - 15.5 Preparation of Furans and Tetrahydrofurans 354
 - 15.6 Preparation of Benzofurans and Dihydrobenzofurans 356
 - 15.7 Preparation of Thiophenes 358
 - 15.8 Preparation of Imidazoles 361
 - 15.9 Preparation of Hydantoin (2,4-Imidazolidinediones) and Thiohydantoin 363
 - 15.10 Preparation of Benzimidazoles 367
 - 15.11 Preparation of Isoxazoles 369
 - 15.12 Preparation of Oxazoles and Oxazolidines 373
 - 15.13 Preparation of Thiazoles and Thiazolidines 373
 - 15.14 Preparation of Pyrazoles 374

- 15.15 Preparation of Triazoles, Tetrazoles, Oxadiazoles, and Thiadiazoles 376
- 15.16 Preparation of Pyridines and Dihydropyridines 378
- 15.17 Preparation of Tetrahydropyridines and Piperidines 380
- 15.18 Preparation of Fused Pyridines 382
- 15.19 Preparation of Pyridazines (1,2-Diazines) 387
- 15.20 Preparation of Pyrimidines (1,3-Diazines) 389
- 15.21 Preparation of Quinazolines 391
- 15.22 Preparation of Pyrazines and Piperazines (1,4-Diazines), and Fused Derivatives thereof 394
 - 15.22.1 Preparation of Diketopiperazines 394
 - 15.22.2 Preparation of Miscellaneous 1,4-Diazines and Quinoxalines 397
- 15.23 Preparation of Triazines 398
- 15.24 Preparation of Pyrans and Benzopyrans 399
- 15.25 Preparation of Oxazines and Thiazines 400
- 15.26 Preparation of Azepines and Larger Heterocycles with one Nitrogen Atom 402
- 15.27 Preparation of Diazepines, Thiazepines, and larger Heterocycles with more than one Heteroatom 404
- 16 Preparation of Oligomeric Compounds 413
 - 16.1 Peptides 414
 - 16.1.1 Merrifield's Peptide Synthesis 414
 - 16.1.2 The Boc Strategy 415
 - 16.1.3 The Fmoc Strategy 417
 - 16.1.4 Side-Chain Protection 419
 - 16.1.5 Backbone Protection 420
 - 16.1.6 Cyclic Peptides 421
 - 16.2 Oligonucleotides 422
 - 16.2.1 Historical Overview 422
 - 16.2.2 The Phosphotriester Method 424
 - 16.2.3 The Phosphoramidite and H-Phosphonate Methods 425
 - 16.2.4 Oligonucleotide Analogs 428
 - 16.3 Oligosaccharides 428
 - 16.3.1 Glycosylation with Glycosyl Bromides 429
 - 16.3.2 Glycosylation with Glycosyl Sulfoxides 430
 - 16.3.3 Glycosylation with Glycosyl Thioethers 431
 - 16.3.4 Glycosylation with Miscellaneous Glycosyl Donors 431
 - 16.4 Miscellaneous Oligomeric Compounds 433
 - 16.4.1 Oligoamides 433
 - 16.4.1.1 Oligoglycines 434
 - 16.4.1.2 Peptide Nucleic Acids (PNA) 434
 - 16.4.2 Oligoesters 436
 - 16.4.3 Oligoureas and Oligothiureas 436
 - 16.4.4 Oligocarbamates 437
 - 16.4.5 Oligosulfonamides 438
 - 16.4.6 Oligomeric Phosphoric Acid Derivatives 438
 - 16.4.7 Peptide-Derived Oligomeric Compounds 439
 - 16.4.8 Oligomers Prepared by C-C Bond Formation 439
 - 16.4.9 Dendrimers 441

17 Index 449

**Editor's Note:* The brief summary and the contents of the books are reported as provided by the author or the publishers. Authors and publishers are encouraged to send review copies of their recent books of potential interest to readers of *Molecules* to the Editor-in-Chief (Dr. Shu-Kun Lin, MDPI, Saengergasse 25, CH-4054 Basel, Switzerland. Tel. +41 79 322 3379, Fax +41 61 302 8918, E-mail: molinfo@mdpi.org). Some books will be offered to the scholarly community for the purpose of preparing full-length reviews.

© 2001 by MDPI (<http://www.mdpi.org>).