
Index

A

Acetonide,
 as a protecting group, 150, 157,
 444, 448
 deprotection, 237, 500, 505
 migration, 448
Acetylene,
 alkylation, 458
Acid,
 alkaline hydrolysis of esters, 351
 by Jones oxidation, 170, 402,
 495, 498, 502, 507
 by oxidation of alcohols, 366,
 371, 379, 381
 from aldehyde with hydrogen
 peroxide, 157
 ruthenium-catalyzed oxidation of
 alcohol, 449
Acyl chloride, formation, 199
Acylamidrazone, from amidrazone,
 12
Acylation, 297, 304
 of oxazolidinone, 445
Acyloxazolidinone, 445
 α -Fluoro- α -silyl acetate, synthesis,
 362, 372
Alcohol
 acid reduction with borane, 442
 from aldehyde, 284
 hydride reduction of ester, 151,
 153
 oxidation to acid, 449

Aldehyde
 by alkene oxidation, 284
 by ozonolysis of alkene, 444
 by reduction of Weinreb amide,
 197
 from ester, DIBALH-mediated,
 193, 194
 PCC oxidation of alcohol, 369,
 401
Aldol condensation, 200, 202, 446
Alkene
 allylation of phenylsulfone, 493,
 496, 497, 500
 by selenide oxidation, 474, 476,
 478, 479
Alkene isosteres, 125
Alkylation
 of malonate, 115
 of phenylsulfone, 493, 496, 497,
 500
 with alkyl halides, 284, 285,
 459
 with triflyloxy ester, 115
Alkylhydrazine, coupling with bis-
 PFP carbonate, 91
Allyl, deprotection, 306
Allylation, of phenol, 299
Allylglycine, synthesis, 343
Allytin, in condensation with
 aldehyde, 152
Amalgam, in sulfone removal, 493,
 497, 502, 507

- Amide bond mimetic, oxadiazole, triazole, 1
- Amide
- aminolysis of esters, 370
 - from acid and ammonia, 522
 - from lactam, 401, 402
 - via acyl fluoride, 267
- Amidoxime, from nitriles, 6
- Amidrazone, 11
- Amine
- alkylation of, 244, 246, 248
 - by azide reduction with tin chloride, 301
 - hydrogenation of azide, 184, 244, 248
 - LAH reduction of amide, 370
 - reduction of nitro compounds, 311, 315
- Aminimides, 527
- Amino acids
- coupling
 - with DCC/HOBt, 77
 - with DIC, 60
 - optical resolution, 298
 - racemic synthesis, 297
- Amino lactol, reduction of, 267
- Aminocyclization, 239
- Aminohydroxyethylene, formation, 501
- Anode, 263
- Aryl ether, formation, 293, 303, 308, 310
- Atropisomers, 313
- α -Aza-amino acids, 87
- Azasugars, as peptide mimetics, 227
- Azatides
- biological properties, 98
 - by coupling with bis-PFP carbonate, 91
 - mass spectroscopy, 98
- Azeotrope, in ester formation, 480
- Azeotropic distillation, 141
- Azepane, as peptide mimetic, 227
- Azide
- by bromide replacement with azide, 182
 - by mesylate displacement, 169, 411, 461, 462
 - epoxide opening with, 131
 - Mitsunobu reaction with hydrazoic acid, 243, 248
 - reduction
 - to amine, 170
 - with tin chloride, 301
 - Trisyl-N₃ on enolate, 300
- Aziridine
- by Mitsunobu reaction (Ph₃P), 132
 - by Sharpless epoxidation, 130
 - from β -hydroxy acids, 128
- B**
- Benzodiazepine, 385
- formation, 460
- 1,4-Benzodiazepin-2-one, as peptide mimetic, 227
- Benzoyl
- amino protection, 479
 - deprotection, 483
 - ester
 - formation, 460
 - hydrolysis, 459
- Benzyl
- ether
 - deprotection, 506

- formation, 168, 236, 500, 504
- hydrogenolytic removal, 250, 426
- Benylation, of amine, 314
- β -Hydroxy acid, as aziridine
 - precursors, 130
- Birch reduction, 334, 345, 354, 355
- Bis-aryl, formation, 523
- β -Lactam
 - hydrolysis to α -hydroxy- β -amino acid, 144
 - opening
 - by amino-Wang resin, 147
 - to α -hydroxy- β -amino amide, 145
 - with enolate, 147
 - with methanol/DMAP, 150
 - synthesis, 137
- Boc
 - amine
 - deprotection, 290
 - protection, 132, 240, 246, 391, 462, 477
 - deprotection
 - with iodotrimethylsilane, 16
 - with hydrochloric acid, 214, 247, 249, 304, 308, 314
 - with TFA, 60, 478
 - with TFA/ Et_3SiH , 197, 203
 - protection
 - of amides, DMAP-catalyzed, 143, 290
- Boc-amine synthesis, via Curis
 - rearrangement, 28, 218, 377
- BocON, 377
- BOP, in peptide coupling, 170, 171, 392
- BOP-Cl, in peptide coupling, 61, 392
- Bromide, from alcohol with PBr_3 , 459
- α -Bromination, 181
- Bromoacetyl bromide, in aniline
 - acylation, 388
- β -Strand, 397
- β -Turn, 161
- Butyl nitrate, phenols from anilines, 311, 316
- C
 - Caco-2 monolayers, 48, 66, 82
 - Carbamate, N-alkylation, 504
 - Carbodiimide, in peptide coupling, 393
 - Carbonate, synthesis, 41
 - Carbonyl-diimidazole, in formation of γ -ketoacid, 107
 - CBZ
 - amine protection with, 370
 - removal
 - with $\text{H}_2/\text{Pd.C}$, 78, 220
 - with Hbr, 423, 426, 427
 - C—C bond formation, γ -ketoacid, 107
 - CDI, in formation of γ -ketoacid, 107
 - Cerium ammonium nitrite,
 - oxidation, 143
 - Cesium salts of Boc-amino acids, 42
 - Cis-peptide bond, 417
 - Cleavage
 - from Rink's resin
 - from Wang's resin
 - Conformational constraints, 175, 209, 213, 215
 - cyclo-arginine, 34
 - cyclo-glutamic acid, 34
 - cyclo-glutamine, 34
 - cyclo-methionine, 34

- 2,3-methanoamino acid, 25
Coronamic acid, synthesis, 346
Coumarinic acid, 71
Coupling
 amino acids
 with DIC, 60
 with EDC, 62, 63, 273
 DCC-mediated, 213, 214
 peptide
 BOP-mediated, 170, 171
 with BOP-Cl, 46
 with DCC/HOBt, 77
 with DEPC, 197, 203
 with EDC/HOBt, 44, 46
Curtius rearrangement, in Boc-amine synthesis, 28, 31, 218
Cyanocuprate, in S_N2 opening of aziridine, 126
Cyclic lactone, synthesis, 401, 410
Cyclic peptide, synthesis with BOP-Cl, 60
Cyclic sulfates, 25
Cyclization,
 to δ -lactam, 220
 with BOP-Cl, 60, 80
Cyclohexane, reduction of phenyl, 443
Cyclopropane amino acids,
 synthesis, 346
Cyclopropanes, as conformational restriction, 397, 407
Cyclopropylmorpholinone, 285
Cyclopropylation,
 with cyclic sulfate, 27
 with Johnson sulfoximine, 348
- D**
D-Allose, as peptide mimetic, 227
DCC, in peptide coupling, 303, 428, 429
Deacetylation, removal of trifluoroacetyl, 298
Deamination, with t-butyl nitrate, 311, 316
Dean–Stark trap, 141, 480
Decarboxylation, of malonate, 115
Deoxygenation, of phenol, 316
Deprotection
 of benzyl ether with TFA/Msa, 185
 of Boc, with TFA, 44, 60
 of Fmoc, with piperidine, 60
 of p-MeO-phenyl, 143
 of t-Bu ester, 80
Dess–Martin, 167
D-glucose, as peptide mimetic, 227
Diacylhydrazine, dehydration to 1,3,4-oxadiazoles, 10
Diastereoselectivity, of malonate alkylation with triflate, 120
Diazatides, by coupling with bis-PFP carbonate, 91
Diazoacetate, from pTs-sulfonylhydrazone, 400, 409
Diazomethane
 formation from MNNG, 350
 methyl ester formation, 350, 412, 496
DIBALH
 in reduction to alcohol, 364
 in reduction to aldehyde, 373
Diethyl glutaconate, in cyclopropylation, 30
Dihydroxyethylene isosteres, 137
Diol, by LAH reduction of lactone, 58, 74
Dipeptide isosteres, 137, 281
Dipeptide, hydrolysis, 460
Diphenyl diselenide, in lactone opening, 473, 476, 479

Diphenyl, formation, 523
Diphenylphosphorylazidate, in
 Curtius rearrangement, 28,
 31, 218
Disulfide, reduction with DTT,
 393
 δ -Lactam, 218
Dowex 50 X 8™, 475, 477
DPPA
 cyclic peptide, 433
 in Curtius rearrangement, 218
 in peptide coupling, 307, 433
D-xylose, as peptide mimetic, 227

E

EDC, in coupling, 306, 313
 ϵ -lactam, 218, 221
Electrochemical oxidation, 263
Enolate, formation, 107, 199
Enzymatic stability, 37, 53, 71
Enzyme,
 digestion of isomers, 298
 inhibitors, 137, 189, 339
Epimerization
 of aldehyde, 445,
 DBU-mediated, 168
Epoxide
 as enzyme inhibitor, 189
 by oxidative elimination, 200,
 202
 from diol
 via mesyl ester, 238, 501,
 506
 via Mitsunobu, 154, 237
 opening
 with amines, 155
 with azides, 131
 with carbamate, 501, 506
 with Grignard reagent, 156

Ester
 acid hydrolysis, 475, 477
 by azeotropic distillation, 480
 enzymatic hydrolysis of, 298
 formation
 DMAP/EDC/alcohol, 44, 170
 synthesis, via acetyl chloride/
 methanol, 192
 with base, 29, 32, 96, 303, 351
 with Dowex 50 W™, 14
Esterase-sensitive prodrug, 37, 53,
 71
Ether, allyl, synthesis, 299
Ethylene oxide
 as an electrophile, 473, 476
 as vinyl cation equivalent, 473,
 476
Evans' auxiliary
 attachment, 300
 reductive removal, 301

F

Finkelstein reaction, 42, 286
Fluorochlorocyclopropylation, 379
Fluorolefins, 357
Fluoroolefine, formation, 364, 369,
 372
Fmoc deprotection, with piperidine,
 60
Fmoc protection, 29
Friedel–Crafts
 acylation, 520
 alkylation of 3,5-dimethylphenol,
 58

G

Gauche conformation, 176, 321
Gilman cuprate, in S_N2 opening of
 aziridine, 126

- γ -lactam, 209
Glyoxylic acid hydrate, 220
Grignard reaction, 180, 443
- H**
- Hemiacetal, formation from lactol, 353
Hemiaminal
 by amide reduction with DiBALH/MeOH, 165
 oxidation to ketone, 167
Heterocycles as peptide bond mimics, 1
- HF
 cleavage from resin, 392, 429, 433
 deprotection, 429, 433
HIV-protease inhibitor, 397, 437
Hydrazide
 quaternization to amnides, 531, 532, 533
 use for diacylhydrazines, 10
Hydrazine
 deprotection of phthalimide, 366
 hydrate
 in synthesis of hydrazides, 8
Hydrogenation
 of alkenes, 495
 of azide to amine, 184, 412
Hydrogenolysis
 benzyl group removal, 47, 141, 250
 of amino lactol, 267
 of nitro to amino, 311, 315
Hydrolysis
 enzymatic, of ester, 298
 of dipeptide, 460
 of morpholinone, 288, 289
- Hydroxyacid, from amino acid with NaNO₂, 111
Hydroxyamines
 by Grignard reaction, 156
 from epoxides, 156
Hydroxylactam, by reduction of ketolactam, 168
Hydroxymethylation, with trioxane, 367
- Imidate
 formation with CCl₃CN, 381
 reaction with hydrazide, 11
Imidazolidinone
 acid hydrolysis, 329
 alkylation of, 330
Imine, from aldehyde and *p*-anisidine, 142
Inhibitors, 527
Ion exchange chromatography, 186
 Dowex 50 X 8™, 475, 477
Isobutyl nitrite, in formation of oximine, 399
- J**
- Jones oxidation, 103, 170, 366, 371, 379, 381, 402, 495, 498, 502, 507
- K**
- Ketomethylene peptide isosteres, 103
- L**
- Lactam
 from lactone, 167
 opening with amines, 401, 402
Lactam-bridged dipeptides, 209, 215
Lactol, DIBAH-reduction of lactone, 353

- Lactone
 basic hydrolysis, 462
 formation from ethylene oxide, 473, 476
 reduction to lactol, 353
 ring opening, 474, 476
- Lactonization, 460
- LAH, in reduction to alcohol, 381
- Lead tetraacetate, as oxidative agent, 350
- L-*gluco*-piperidine, scaffold, 230
- L-*gulo*-piperidine, scaffold, 230
- Li/NH₃(l), in oxazinone cleavage, 334, 348, 354
- L-*ido*-azepane, scaffold, 230
- Liquid phase, PEG-supported, 92
- L-*manno*-azepane, scaffold, 230
- Loading, Wang's resin, 60
- M**
- Malonate
 alkylation, 115, 297
 decarboxylation, 115, 297
- Marfey's reagent, 328
- Meldrum acid, in pyrrolidinone synthesis, 217
- Membrane permeability, 37, 53, 71
- Mesyl ester, formation, 237, 242, 246, 250, 285, 411, 461, 501
- 2,3-Methanoamino acids, 25
- 2-Methoxypropene, in acetonide formation, 444
- 4-Methoxyproline, 259
- Methyl ester
 by esterification, 519
 from diazomethane, 350
 from phenol, 520
- Methylation, of amides, 311
- Methylhydrazine, deprotection of phthalimide, 377
- Mitsunobu reaction, 365, 375
- Mixed anhydrides, in peptide coupling, 424
- MMPP, in hydroxylation–lactonization, 460
- MNNP, precursors for diazomethane, 350
- Morpholinone, synthesis, 283
- N**
- Na(0)/NH₃(l), in oxazinone cleavage, 345
- N-alkylation, of carbamate, 504
- NBS, as a brominating agent, 181, 347
- N-methylation
 of amides, 311
 of carbamates, 391
- Norstatine, synthesis, 137
- O**
- Olefination, with α -fluoro- α -trimethylsilylacetate, 364
- Olefine, by Wittig olefination, 13, 198
- Organocuprates, in S_N2' opening of aziridine, 126, 133
- Osmium tetroxide, 284
- 1,2,4-Oxadiazole, synthesis, 1, 5
- 1,3,4-Oxadiazole, synthesis, 1, 8
- Oxalyl chloride, in Swern oxidation, 151
- Oxazinone
 alkylation, 343
 with triflate, 352
 bis-alkylation, 345

- cleavage
 - with lead tetraacetate, 350
 - with $\text{Li(0)/NH}_3(\text{l})$
 - with $\text{Na/NH}_3(\text{l})$
- NBS bromination
- Oxazolidine
 - formation with 2-methoxypropene, 445
 - from serine and dimethoxypropane, 194
- Oxazolidinone
 - acylation of, 179
 - attachment, 300
 - cleavage with H_2O_2 , 183
 - reductive removal of chiral auxiliary, 301, 369, 447
- Oxidation
 - alcohol to acid, 170, 366, 371, 379, 381
 - alcohol to aldehyde, 369
 - aldehyde to acid, with H_2O_2 , 76
 - alkene with NaIO_4 , cat. RuCl_3 , 30
 - Dess–Martin, 167
 - ketone to acid, with hypochloride, 153
 - of alcohol to aldehyde with PCC, 142, 401
 - proline to 4-methoxyproline, 263
 - to aldehyde with pyridine- SO_3 , 443
 - with CAN, 143
 - with lead tetraacetate, 350
 - with osmium tetroxide, 284
- Oxime
 - formation, 521, 522
 - reduction, 521, 522
- Oximine
 - formation, 390
 - reduction with Raney Ni, 390
- Oxirane, synthesis, 189
- Ozone, in selenide conversion to alkene, 474, 476, 478, 479
- Ozonolysis, 157, 267, 275, 411, 444
- P**
- PCC oxidation, 142, 369, 401
- Peptide bond
 - isosteres, 125, 357
 - heterocyclic, 120
 - mimetic, 189, 281
 - ozadiazole, triazole, 1
- Peptide coupling
 - BOP, 392
 - BOP-Cl, 392
 - DCC, 213, 214, 303, 307, 428, 429
 - DIC, 393
 - DPPA, 433
 - mixed anhydrides, 424, 427
 - PFP ester, 310
 - WSCDI, 306, 313, 393, 403, 413
- Periodic acid, in oxidation of alcohols, 449
- Periodinane, in oxidation of alcohols, 167
- Phe-Gly mimetic, oxadiazole, triazole, 1
- Phenylpropionic acid, as a prodrug, 53
- Phthalimide, in Mitsunobu reaction, 365, 375
- Phthaloyl, deprotection, 366, 375
- Pictet–Spengler reaction, 327, 328, 331, 333
- Piperidine, as peptide mimetic, 227
- Plasma stability, 47, 64, 81
- Polyethylene glycol monomethyl ether, 93

- PPTS, 150, 157, 493, 498, 499
Prodrug, 37, 53, 71
Pyridine-SO₃, in oxidation to aldehyde, 443
Pyridinium chlorochromate, oxidation with, 142
Pyridinium *p*-toluenesulfonate (PPTS), 150, 157, 493, 498, 499
Pyrrolidine
 as peptide mimetic, 227
 formation, 493, 497, 506
- R**
- Raney-Ni
 in oxime reduction, 521, 522
 reduction of oximine, 390
REDAL, in reduction of ester to alcohol, 458
Reduction, 364, 373
 azide to amino, 184
 cat. by Pd(BaSO₄)/H₂, 268, 274
 ester to alcohol, 458
 nitro to amino, 311, 315
 of acid with borane/THF, 442
 of aldehyde, 284
 of aldehyde to alcohol, 411
 of azide with tin chloride, 301
 of disulfide to thiol, 393
 of phenyl to cyclohexane, 443
 of Weinreb amide, 197
 TMP ester to alcohol, 364
Reductive animation, 268, 275, 504
Reformatski reaction, 380
Renin inhibitors, 453
Resin
 cleavage with TFA, 97
 loading
 with DIC/amino acids, 60
 with DMAP/DCC, 96
- Rhodium
 catalyst, in cyclopropanation, 401, 410
 on carbon, reduction of aromatics, 443
Ring contraction, via aziridine formation, 242
- S**
- Selenide, conversion to alkene, 474, 476, 478, 479
Selenylaldehyde
 formation of, 195, 198
 in aldol condensation, 200, 202
SEM, deprotection of, 365
SEM-Cl, protection with, 363
Separation, of optical isomers, 298
Sharpless epoxydation, 130
Silyl ether
 deprotection with HF/py, 150, 169
 formation, 237, 241, 301
 removal with TBAF, 145
 TIPS as alcohol protecting group, 141, 142
Silylketenethioacetal, in aldol condensation, 200, 202
S_NAr, 293, 303, 308, 310
Sodium borohydride, in reduction of aldehyde, 411
Solution phase peptide synthesis, 61
Spinacine, 333
Spiromorpholinone, 285, 286, 287
Statine, synthesis, 351, 354
Suicide inhibitors, 189
Sulfone
 alkylation of, 493, 496
 removal with Na-Hg, 493, 497, 502, 507

- Sulfonium salt
 cyclization to lactam, 213, 215
 synthesis, 213, 215
- Swern oxidation, aldehydes to
 alcohols, 131, 151
- Symmetric anhydride, formation, 5
- T**
- TBAF
 removal of TBDMS, 371
 Tmse deprotection, 171
- TBDMS
 alcohol protection, 58, 62, 74,
 237, 241, 301, 368, 462
 deprotection to alcohol, 59, 75,
 238, 242, 314, 378
 removal with TBAF, 371
- TBDPS, deprotection, 169
- t-Bu ester
 deprotection, 389
 formation, 93
- t-Butyl bromoacetate, in aniline
 alkylation, 388
- 1,2,3,4-Tetrahydro-6-OH-
 isoquinoline-3-carboxylate,
 331, 332
- Tetrazole, 417
- Thioester, hydrolysis to acid, 200, 203
- Thiol, formation from disulfide, 393
- THP, removal, 493, 498, 499
- TIC, 321
- Tin chloride, in azide to amine
 reduction, 301
- Tip, 333
- TIPP, 321
- Tmse
 as alcohol-protecting group, 170
 deprotection, 171
- Topographical constraints, 175
- Tosylate, formation, 505
- Trans conformation, 176
- Transition state mimics, 137, 437
- Transport across membranes, 48, 65,
 81
- 1,2,4-Triazole, synthesis, 1, 11
- Trichloroacetonitrile, in imidate
 formation, 381
- Trichloroethanol ester
 deprotection with Zn/AcOH, 46,
 64
 formation with DMAP/EDC/
 alcohol, 44, 61
- Triflate
 as alkylating agent, 352
 formation, 113, 523
- Trifluoroacetyl, deprotection, 298
- Trifluoroacetylation, 297
- Triflyloxy ester, in formation of γ -
 ketoacid, 110
- Trimethyl lock, 53
- Trimethylphosphite, 347
- Trioxane, in hydroxymethylation,
 367
- Trisyl azide, in azide synthesis, 300
- Turn mimetics, 259, 385, 407
- V**
- Vinyl amino acids, 467, 468
- Vinylglycine, alkylation of, 480
- Vinylmagnesium bromide, addition
 to aldehyde, 443
- W**
- Wacker oxidation, alkene to ketone,
 with PdCl₂, O₂, 152
- Wang's resin, loading, 60
- Weinreb amide, 197
- Wittig
 olefination, 131, 347

reagent
via trimethylphosphite, 347

WSCDI, in peptide coupling, 393,
403, 413