Index

The following index can be used to find topical information within the text. A comprehensive index of compounds, reagents, reactions and topics covered in graphical form on even-numbered pages is available at the following website: http://www.worldscibooks.com/chemistry/7815.html

Absolute stereochemistry, of Cecropia juvenile hormone, 453 Absolute stereochemistry, reagent based control of, 185 Acetoacetic ester synthesis, of substituted acetones, 53, 451 Acetylide addition, to ketone, 39 Activated cyclopropanes, opening with thiolate anion, 123 Activating groups (SPh), 509 Acyclic diastereoselection, 3, 5, 13 and the prostaglandins, 123 early application to synthesis, 455 and juvabione, 5 and prostaglandins, 5 and pyrrolizidine alkaloids, 5 and steroids, 5 relationship between prostaglandins and steroids, 125

relationship between prostaglandins and pyrrolizidines, 125 Acyclic stereogenic centers, control of, 29 Acyl anion equivalents, 83, 185 metallated, dithiane as, 77, 517metallated cyanohydrins as, 103 metallated dihydropyran as, 527 metallated furans as, 55 Acylnitroso compounds, in approach to pumiliotoxin-C, 369 Aglycone, 537 Aldol condensation, 269 and Cram's rule, 525 and the Felkin-Ahn rule, 525 intramolecular, vinylogous, 81 intramolecular, 77, 79 minimization of β -elimination during, 77

versus alkylation for carbon-carbon bond formation, 107 Aldol-dehydration, double, intramolecular, 51 Aldol-dehydration, intramolecular, 27, 39 Aldols, synthesis of using crotylation reactions, 527 Alkaloids, total synthesis of, 281 Alkenes, as latent carbonyl groups, 233 Alkylation deconjugative, 35, 37 diastereoselective of ester enolates with arene-chromium tricarbonyls, 179 intramolecular of enamine, 376 intramolecular, of enolate, 253, 261 of enolate, stereoelectronics of, 513 of enolates, 1,2-asymmetric induction model, 157 of imidate anion, 519 versus aldol for carbon-carbon bond formation, 107 Alkyne, semi-hydrogenation to alkene, 105 Allenol ethers, synthesis and hydrolysis to cis-unsaturated aldehyde, 377 Allylation, Pd-mediated, 189 Allylic oxidation, using Corey-Fleet reagent, 427 Allylic rearrangement, promoted by HBr, 39 Allylic strain as a conformational control element, 385 importance in 1,2-asymmetric induction model for enolate alkylation, 157

in planning synthesis of gephyrotoxin, 379 importance of in route to pumiliotoxin-C, 369 role in determining stereochemistry of Diels-Alder, 361 Allylsilanes, model for asymmetric addition to enones, 193 Alternate or ambident functional groups (A-functions), examples of, 209, 211 Aminoketone, β -, construction of via Mannich reaction, 293 Analgesics (painkillers), 405 Androsterone, 29 Annulation reactions (annelation reactions), 23 Anodic oxidation, of amides, 289 Anomeric effect, 505 Anomeric effect, double as stereocontrol element in N,O-acetal formation, 289 in spiroacetals, 523 Anthranilic acid, 371 Arachidonic acid, 73 Arene-chromium tricarbonyl complex, reaction with ester enolates, 179 Aspirin, 75 Asymmetric conjugate addition catalytic, of methyl group to enone, 373 of amide nucleophile to unsaturated ester, 373 Asymmetric Diels-Alder, predictive model for, 93 Asymmetric induction, 1,2-, 159 Asymmetric induction, Cornforth model, 455 Felkin-Ahn model, 455

in conjugate addition reactions, 191 in intramolecular cyclopropanations, 139 relative, 95 Asymmetric reduction, reagent controlled, 61 Asymmetric synthesis, of aldols using crotylation reactions, 527 of prostaglandins, 101 the chiral pool approach, 181 Aziridinium ions, preparation and chemistry of, 435, 437, 439 Azomethine ylids, method of generation for use in cycloadditions, 149

Baeyer-Villiger oxidation, 187, 235, 309, 327, 511, 523, 539, 541 Baeyer-Villiger oxidation, regioselective, 85 Baker's yeast, 187, 195 Bamford-Stevens reaction, 287 Barbier-Wieland degradation, 29 Barton reaction, 105, 339, 381 Batrachotoxin, 337 Beckman rearrangement, 235, 339 Biomimetic synthesis, 41, 291 of morphine, 7, 413 of pumiliotoxin-C, 367, 369 of steroids, 3 **Biosynthesis** of morphine, 411, 413 proposal for Dentrobatid alkaloids, 367 Biosynthetic pathway, 3 Bischler-Napieralski reaction, 299, 305 Blocking groups, 25 Brown allylation, 351

Cahn-Ingold-Prelog (CIP) convention, 167 Calcimycin (A23187), 11, 505-529 Carbene generation, by α -elimination reaction, 433 Carbocation, vinylic, nucleophilic capture of, 57 Carbocycle synthesis, 3 Carbohydrates, as source of chirality, 517 Carbon-hydrogen activation, via Barton reaction, 339 Carbon-hydrogen insertion, of carbene (vinylidene) in approach to morphine, 433 Carbopalladation, approach to prostaglandins, 111 Cecropia juvenile hormone, 11, 445-474 Celebrex, as COX inhibitor, 75 Charge affinity inversion (charge reversal), 211 Chiral auxiliary, for Diels-Alder reaction, 91 phenylglycinol as in synthesis of pumiliotoxin-C, 367, 369 proline as in synthesis of pumiliotoxin-C, 371 Chiral pool approach to asymmetric synthesis, 181, 183, 185, 187 definition, 103 in approach to lasonolide A, 485 in calcimycin synthesis, 517 Chiral reducing agent, design of, 97 Chiral, crotylborane, 527 Chirality transfer, issues of geometry in Ireland-Claisen, 513 Chirality, transfer of, 121

Chloroacrylonitrile, α -, as ketene equivalent in Diels-Alder, 85 Chloronitrile, α -, conversion to ketone, 85 Cholesterol, 3, 17, 19 Cholesterol, biosynthesis of, 41 Cholesterol, synthesis of, 29 Cholic acid, 17 Cladinose, L-, in erythromycin A, 537 Claisen condensation, crossed, 311 Claisen condensations, iterative in biosynthesis of polyacetates, 483 Claisen rearrangement, 197, 343 and transfer of chirality, 121, 513 as enforced S_N2' reaction, 55, 451 enolate, 513 how to see potential for use in synthesis, 451 Johnson-Faulkner, 55 stereochemical course of, 171, 451 Codeine, as cough suppressant, 405 Codeine, conversion to morphine, 411, 413, 421 Colchicine, 561 Collins oxidation, 509 Computer-assisted synthesis design, 282, 283 Configurational stability, of S,Shemiacetal, 543 Conformational analysis in allylic systems within context of ester enolate alkylation, 57 of allylic alcohols, 471 of N-acyltetrahydroisoquinolines, 417 of substituted cyclohexane, 379, 381 Conformational mobility, 543

Conformations, of allylic alcohols and effect on epoxidation stereochemistry, 471 Conjugate addition, to enone for introduction of PG sidechain, 101 Conjugate addition-enolate trapping, 105, 373 Convergence, importance in planning a synthesis, 493 Convergent synthesis, 517, 527, 537 comparison with linear synthesis, 99 importance in synthesis design, 204, 205 of prostaglandins, 105 Cope elimination, 143, 267 Cope rearrangement, 311 in plan for synthesis of reserpine, 309 stereochemistry of, 171 Corey lactone, for prostaglandin synthesis, 89 Corey-Fuchs reaction, 349 Corey-Nicolaou lactonization, 549 Corey-Rucker reagent, in Peterson olefination, 389 Corey-Suggs reduction, 115 Corey-Winter reaction, 263 Cornforth model, for 1,2diastereoselection, 455 Corticosteroids, introduction of C11 oxygen, 31, 35 Corticosteroids, preparation by polyolefin cyclization, 59 Cortisone, 17, 19, 31, 39 Crabtree's catalyst, for directed hydrogenation, 371 Cram selectivity, 509, 525 Crotylation-oxidative cleavage, strategy for polypropionate synthesis, 527

Crotylborane, chiral, 527 Cuprate addition, stereoelectronics of, 517 Curtin-Hammett Principle, 295 Curtius rearrangement, 267, 353 to establish ketene equivalency, 91 Cyanohydrin, metallated as acyl anion equivalent, 103 Cyclic structures, for controlling multiple acyclic stereogenic centers, 515, 521 Cyclization, base-initiated, 523 Cycloaddition, [2+2] of ynamine with enone, 169 Cycloalkene synthesis, general strategy, 103 Cycloalkenes, as latent dicarbonyl compounds, 233 Cyclohexenes, conversion to acylcyclopentanes, 20 Cyclohexenone, from cyclopentene, 51 Cyclooxygenase (COX) in biosynthesis of prostaglandins, 75 inhibitors of, 75 Cyclopentane, from cyclohexene, 77 Cyclopropanation, of alkenes, 123 Cyclopropanation, stereochemistry of intramolecular carbene-alkene reactions, 139 Cyclopropane, geminally activated, 127, 139, 141 Dart-poison frogs, 337 Decahydroquinoline alkaloids, 359 Deconjugation, of enone, 29, 107

Demerol, as analgesic, 405

Desosamine, D-, in erythromycin A 537

Dess-Martin periodinane oxidation, 493 Desulfurization, 253 Desymmetrization in enzyme-mediated reduction, 35 of cyclohexanone, 165 in synthesis of erythronolide A, 539 Deuterium labeling experiments, in design of calcimycin synthesis, 507 Diastereoselection, in carbene-alkene addition reactions, 139 reagent control of, 95 relative within context of prostaglandin synthesis, 95 substrate control of, 95 Diastereoselective hydrogenation, in cyclic system to control stereochemistry, 177 Diastereoselectivity, 1,2-, 513 Diastereoselectivity, 1,4-, 513 Diastereoselectivity, in crotylation reaction, 527 Diastereoselectivity, in prostaglandin synthesis, 119 Dicarbonyl compounds, 1,4-, synthesis of, 55 Diels-Alder reaction, 21, 165, 197 aromaticity as a driving force, 393 in plan for synthesis of reserpine, 309 ketene equivalents, 83 Lewis acid promoted, 83, 91 lowering temperature through use of more reactive dienophile, 91 of nitroalkene and butadiene, 77 of acylnitroso compounds, 145 rate as a function of dienophile, 91

retro, for generation of acylnitroso compound, 147 stereocontrol in, 85 Diels-Alder-retro-aldol, strategy for controlling vicinal stereochemistry, 165 Diels-Alder-retro-Diels-Alder, in plan for synthesis of reserpine, 315 Dienamide synthesis, 361, 363 Difunctional relationships, 5, 7, 205 1,2-, construction of, 219 1,3-, construction of, 217 1,3-, relevance to Mannich reaction, 281 1,4-, and construction of 5membered rings, 227 1,4-, construction of, 221, 223 1,5-, and construction of 6membered rings, 225, 227 1,5-, construction of, 223 and construction of cyclohexanones, 225 and construction of cyclopentanones, 227 classification of, 213 generation by insertion reactions, 235 importance in retrosynthetic analysis, 247 importance in synthetic plan for porantherine, 281 importance in synthetic plan for porantheridine, 287 in analysis of lasonolide A substructures, 483 in approach to pumiliotoxin-C, 371 in Diels-Alder route to pumiliotoxin-C, 365

in retrosynthetic analysis of twistane, 247 in synthesis of triquinacene, 271 reinforcing and interfering, 215 Dipolar cycloaddition, 1,3importance of reversibility in nitrone approach to HTX, 357 azomethine ylid in approach to pyrrolizidine alkaloids, 149 of nitrones in approach to pyrrolizidine alkaloids, 143 Dipole-dipole repulsion, importance in asymmetric Diels-Alder, 93 Directed reactions, 307 addition of free radicals, 116 addition to unactivated alkenes, 111 hydrogenation, heterogenous, 376 hydrogenation, in synthesis of pumiliotoxin-C, 371 Dodecahedrane, relationship to triquinacene, 265 Electrochemistry, anodic oxidation of

Electrochemistry, anodic oxidation of amides, 289 Electrophilic addition, iodolactonization, 87 Electrophilic addition, selectivity between alkenes, 39 Electrophilic functional groups (E-functions), examples of, 209 Elimination, β-, avoidance of, 87 Enantiomer production, of natural products depending upon plant source, 377, 379 Enantiomers, separation by chromatography of chiral support, 429

Enantioselective reduction, using enzymes, 35 Enantioselective synthesis, of twistane using enzymatic reduction, 255 Enantioselectivity, in crotylation reaction, 527 Ene-reactions, intramolecular of Nacylnitroso compounds, 345 Enolate alkylation, stereochemical course of, 513 Enolate protonation, kinetic control of stereochemistry in, 549 Enolate-Claisen, importance of enolate geometry, 513 Enyne synthesis, via Peterson-type olefination, 383 Enzymatic reduction, 35 of ketone to alcohol using Baker's yeast, 187, 195 using horse liver alcohol dehydrogenase (HLAD), 255 Epimerization and thermodynamics, to control stereochemistry in spiroacetals, 529 Epoxidation, stereochemistry in corticosteroid synthesis, 13 Epoxide opening, regioselectivity in, 351 Equilenin, 3, 19 Equivalency concept iodonium ion as proton equivalent, 87 ketene equivalents, 83 1,2-bis-sulfonylethylene as ethylene equivalent, 391 of terminal alkene to aldehyde, 283 Erythromycin, 13, 537-555 Eschenmoser sulfide contraction, 383 Eschweiler-Clark methylation, 267 Estrone, 3, 19

Felkin-Ahn model, for 1,2diastereoselection, 455, 509, 525 (in aldol) Finkelstein reaction, 321, 455 Formyl anion equivalent, lithiated dithiane as. 219 Free radical addition approach to prostaglandins, 115 intermolecular, 115, 117 Free radical allylation, in approach to perhydrohistrionicotoxin, 345 Free radical cyclization conformational analysis of, 485 of N-centered radical in morphine synthesis, 425 stereochemistry of, 321 Free radical intermediate, to avoid β elimination, 87 Functional group relationships, and appearance of synthetic approaches, 395 Functional group transformation (FGT), to establish equivalency, 85, 219 Functional groups, importance of compatability in synthesis design, 205 Functionality, level of, 20 Furans, metalated, as acyl anion equivalents, 55 Furst-Plattner rule in epoxide openings, 295 variation of for nucleophilic opening of bromonium ion, 303 Fusidic acid, 17

Geminally activated cyclopropanes, reactions with amines, 139, 141 Gennari-Still reaction 487, 495

Gephyrotoxin, 9, 374-395, 337 difunctional relationships in, 375 enantioselective synthesis, debate over absolute stereochemistry, 377 structure and determination of absolute configuration, 377 Grieco-Sharpless method, formal dehydration of terminal alcohol, 485, 547 Grob fragmentation, relationship to Julia olefin synthesis, 459 Hastanecine, 141 Heck reaction, intramolecular, as oxidative phenolic coupling alternative, 427 Henry reaction, 77 example of nitro group as an Nfunction, 209 Heroin, as analgesic, 405 Heterogenous catalytic hydrogenation, stereocontrol of, 376, 377 Histrionicotoxin, 7, 335-357, 337 enantioselective synthesis via double-alkylation strategy, 351, 353 of ene-yne substructure via Sonogashira reaction, 351 synthesis of ene-yne substructure via Wittig reaction, 349 synthesis via intramolecular nitrone cycloaddition, 355, 357 Histrionicotoxins, 337 Homosteroid, D-, 20, 33 Horner-Wadsworth-Emmons reaction, 81, 363, 447, 497, 523, 525 Gennari-Still modification of, 487, 495 Hydration of nitriles, catalytic, 371

Hydrazones, as A-functional groups, 211 Hydrogenation, semi, of alkyne, 39 Hydrogenation, stereochemistry of, 25 Imide, size as a cyclohexane substituent, 381 Imides, ketone-like reactivity of, 375 Iminium ion, stereoelectronic model for addition of nucleophile to, 285, 289 Insect sex hormones, 447 Insertion reactions, for generation of difunctional relationships, 235 Intramolecular alkylation, of enamine, 393 conjugate addition, to construct pyrrolidine, 387 delivery of nucleophile in epoxide opening, 301 delivery, of nucleophile via N,Nacetal formation, 295 Ionophores, as a family of natural products, 505 Ionophores, introduction to, 497 Ireland-Claisen, importance of enolate geometry, 513 Isomerization, of cyclopentadienes, 83 Isomerization, Pd-mediated, 37 Isonitriles, as free radical traps, 117 Isotope dilution method, application to morphine synthesis, 413 Iterative reactions, in Cecropia juvenile hormone syntheses, 473 Iterative synthesis, 449 of trisubstituted olefins, 463

Johnson-Faulker Claisen, 451 Johnson-Lemieux oxidation, 283, 437 Jones oxidation, 297 Julia olefin synthesis, 453, 457 relationship to Grob fragmentation, 459 variations of, 457 Julia-Lythgoe-Kocienski olefin synthesis, 485, 489, 491, 493 Juvabione, 5, 29, 159-197 determination of absolute configuration via synthesis, 181 Juvenile hormones, 159, 447

Ketene equivalent chiral, 93 unsaturated ester as, 91 α-chloroacrylonitrile as in Diels-Alder reaction, 293 α-chloroacryloyl chloride as, 91 for Diels-Alder reaction, 83
Ketone reduction, axial delivery of hydride, 29
Kinetic control, of stereochemistry in enolate protonation, 311, 549
Kornblum oxidation, 219, 437

Lanosterol, 41 Lasolocid A (X537A), as an ionophore, 509 Lasonolide A, 11, 479-497, 537 biological activity of enantiomers, 481 Latent C2-axis of symmetry, in design of calcimycin synthesis, 507 Latent carbonyl groups, alkenes as, 233 Laudanosine, 411 LeChatelier's Principle, 21 Limonene, R-, 181, 183 Linear strategy, 517 Linear synthesis, comparison with convergent synthesis, 99

Luciduline intermediate, structural relationship to reserpine intermediate, 309 Lycopodium alkaloids, examples of, 293 Lysine, as chiral pool starting material for porantheridine, 287 Macrolactonization, 497, 537, 543, 549, 551 Macrolides, 11 Mannich reaction and 1,3-difunctional relationships, 281 double intramolecular in sparteine synthesis, 291 in alkaloid synthesis and biosynthesis, 281 Mass spectrometry, in structure determination of dart-poison alkaloids, 337 McGarvey-Fleming model, for asymmetric alkylation of enolates, 157 Mechanisms, importance in synthesis design, 204, 205 Meerwein-Pondorf-Verley reduction, 301 Methadone, as analgesic, 405 Michael addition, deconjugative, 33 Michael reaction, 23 Michael-Michael reaction, of dienolate with acrylate as Diels-Alder equivalent, 327 Midland reduction, 61 Mislow-Evans rearrangement, and transfer of chirality, 121 Mitsunobu reaction, 107, 419, 423 Moffatt-type oxidation, 487

Monensin, as an ionophore 505, 509, 561 Morphine, 7 Morphine, 403-439 and analgesics, 405 biosynthesis of, 411, 413 synthesis via intramolecular electrophilic aromatic substitution, 435 synthesis via perhydrophenanthrene-based approach, 429 N,O-relationships, 1,3-, in alkaloids, 297 N-acyliminium ion cyclizations in Mannich-type reactions with alkenes, 341 in synthesis of gephyrotoxin, 379 N-acylnitroso compounds, intramolecular ene reactions of, 345 Nef reaction, for conversion of N-function to E-function, 209, 221 Neighboring group participation, 301 Neuroscience, importance of dartpoison frogs to, 337 Nitrile chemistry, comparison of pumiliotoxin-C and reserpine syntheses, 367 Nitroalkanes as A-functions, 209 importance of tautomers, 209 Nitrone cycloaddition intramolecular, 297 in pyrrolizidine alkaloid synthesis, 143 to establish 1,3-N,O-relationship, 297

NMR spectroscopy, in structure determination of dart-poison alkaloids, 337 Nonactin, as an ionophore 509 Nucleophilic functional groups (N-functions), examples of, 209 Olefin geometry, importance in establishing vicinal stereochemical relationships, 447 Olefin metathesis, 497 Olefin stereochemistry, as function of boat versus chair transition states in oxy-Cope, 175 Olefin synthesis classification of according to method of construction, 474 trisubstituted, 11 Organopalladium chemistry, 111, 113 Oxetane formation, in competition with Grob fragmentation, 461 Oxidation state adjustment of in PG synthesis, 105 adjustments, in synthesis of reserpine, 317 changes at carbon, 21, 23 importance of in synthesis of reserpine, 311 role in selection of starting materials for synthesis, 185 Oxidation, 511 Oxidation, conversion of amine to ketone, 79 Oxidation, Saegusa, 117 Oxidative cleavage of alkene to ketoaldehyde, 79 Oxidative phenolic coupling a mechanistic interpretation, 413 alternatives to, 419

regiochemical problems in synthesis of morphine, 415, 417 site selective equivalent via arvl diazonium chemistry, 415 Oxime derivatives, as A-functional groups, 211 Oxy-Cope rearrangement in synthesis of luciduline, 293 stereochemistry of, 171 Ozonolysis, 523, 527 Painkillers (analgesics), 405 Perhydrohistionicotoxin retrosynthetic analyses, 339 via N-acyliminium ions and Nacylnitroso compounds, 339 Perhydroindan, 20 Perhydronaphthalene (decalin), 20 Perillaldehyde, 185 Periodate cleavage, of vicinal diol, 525 Peterson olefination, 357 PGA, structure of, 77 PGA₁, synthesis of, 79 PGA₂, the problem of acyclic diastereoselection, 123 PGE_1 , structure of, 77 PGE₁, synthesis of, 79 PGE₂, structure of, 75 PGE_2 , synthesis of, 109 $PGF_{1\alpha}$, synthesis of, 79 $PGF_{2\alpha}$, synthesis of, 117 $PGF_{2\alpha}$, synthesis of, 87 PGF_{2B}, synthesis of, 79 PGG₂, structure of, 75 PGH₂, structure of, 75 Photochemistry, in triquinacene synthesis, 269, 273 Photocycloadditions, directed and intramolecular, 307 Pictet-Spengler reaction, 299, 329

Pictet-Spengler reaction in biosynthesis of morphine, 411 Polyacetates, natural products derived from acetic acid, 483 Polyketides, 13 Polymers, polypropionates as, 537 Polyolefin cyclizations, 43 acetal as initiator, 51 alkynes as terminators, 53 allylic alcohol as initiator, 49 effect of C11 substitutents in approach to corticosteroids, 59 rates as a function of substituents, 63 termination with an allylic silane, 63 termination with ethylene carbonate, 57 termination with nitroethane, 57 Polypropionate natural products, 13, 505.537 calcimycin as, 505 introduction to, 497 repeating unit in, 527 synthesis via crotylation-oxidative cleavage strategy, 527 Porantherilidene, 285 Porantherine, 281 Practical synthesis, of juvabione, 63 Principle of vinylogy, 375 Progesterone synthesis, analysis in terms of difunctional relationships, 229 Progesterone, 17 Propargylic alcohols, use in trisubstituted olefin synthesis, 463 Prostaglandin synthesis, analysis in terms of difunctional relationships, 231

Prostaglandins, 3, 71-127 from arachidonic acid, 73 strategies for synthesis of, 99 Protecting group selection, compatability in complex synthesis, 545 Pumiliotoxin, comparison of Diels-Alder routes to, 359, 365 Pumiliotoxin-C, 7, 358-373 Pummerer rearrangement, 219 Pyrrolizidine alkaloids, 5, 137-151 Quinic acid, as starting material for reserpine, 321 Reaction classification, 207 Reaction conditions, as tool for achieving thermodynamic or kinetic control, 329 Reaction sequencing, importance of in reserpine synthesis, 327, 329 Reactive intermediates, tactics for generation of, 145, 147 Reagent-controlled asymmetric synthesis, in allylation reactions, 491 Recycling, of stereoisomeric alcohols via oxidation-reduction, 87 Reduction of alkynes, control of stereochemistry, 171 of iodide in presence of ester and lactone, 87 selective, of nitroalkane, 79 Reductive homologation, of ketone, 337 Regiochemistry, of N-acyliminium ion cyclizations, 343 Regioselective hydration of alkene, directed, 87 Relative asymmetric induction, 191

Relative stereochemistry, use of cyclic compounds to control, 521 Relay synthesis, 27 of erythromycin A, 551 of morphine, 409 Research, the search part of, 387 Reserpine intermediate, structural relationship to luciduline intermediate, 309 Reserpine, 9, 299-329 as substituted cyclohexane, 299 introduction to, 299 synthetic plan, 299 Reserpine-isoreserpine, stereochemical relationship between, 313, 319, 325 Resolution in enantioselective approach to twistane, 257 of acid as ephedrine salt, 89 of ketone via chiral acetal formation and diastereomer separation, 433 of S,S-hemiacetal in synthesis of erythronolide A, 545 Reticuline, 411 Retroaldol condensation, 165, 167 Retro-Aldol condensation, in plan for synthesis of reserpine, 307 Retro-Claisen condensation, 169 Retro-Diels-Alder, to generate Nacylnitroso reactive intermediate, 345 Retronecine, 143, 145 Retrosynthetic analysis, 20, 205 Ring expansion, cyclopentanone to lactam via Beckmann rearrangement of nitrone, 439 Ring opening reaction, of cyclobutane with relief of strain, 169

Ring synthesis five-membered, 3 six-membered, 3 Robinson annulation, application to perhydrophenanthrene approach to morphine, 429

Saegusa oxidation, 117 Sakurai, reaction, 193 Salutaridine, 413 Schlosser modification of Wittig reaction, 55 Schlosser's base, 527 Seco-acid cyclization of, 545 definition of, 537 Semi-hydrogenation, of alkyne, 141 Sex hormones, 17 Sharpless epoxidation, 351 Sigmatropic rearrangements 2,3- as formal S_N2' reactions, 467-471 and transfer of chirality, 121 Singlet oxygen, use in prostaglandin synthesis, 101 $S_N 2'$ reactions Claisen rearrangements as equivalent of, 343 in approaches to Cecropia juvenile hormone, 467 **Solvolysis** of allylic alcohol, 49 of unsaturated nosylate, 45 Sonogashira reaction, 351 Sparteine, biomimetic synthesis of, 291 Spiroacetals, 505 thermodynamic control over stereochemistry of, 507 and the anomeric effect, 505 Squalene oxide, 43

Squalene, 41 Stacking, π - π , importance in asymmetric Diels-Alder, 93 Starting materials, importance of recognition in synthesis design, 204, 205 Stereochemical control, importance of kinetics and thermodynamic considerations, 325 Stereochemical relationship, control of 1,2 by addition reactions, 123, 139 1,4 by transfer of chirality, 123 by thermodynamics or kinetics, 37 vicinal relationships through Diels-Alder reaction, 167 vicinal relationships, 139 through bowl-shaped nature of reactant, 189 through molecular shape, 301, 321 starting material vs thermodynamics, 521 Stereochemistry importance of controlling relative, 29 in formation of bromohydrin, 39 kinetic vs thermodynamic control of. 435 of addition of acetylide to steroidal ketone, 39 of enolate alkylation, 513 of iminium ion reduction in reserpine synthesis, 305 reagent control of, 97 remote control of in hydrogenation, 383 thermodynamic control in spiroacetal formation, 507 thermodynamic control of epimerization, 527 thermodynamic control over, 505

vicinal, control through kinetic protonation, 169 vicinal, the problem of control in acyclic systems, 161 Stereocontrol acyclic using ring-opening strategy, 537 acyclic and cyclic, 3 importance of order of operations, 45 importance of, 25 of cyclic stereogenic centers by olefin geometry, 53 Stereoelectonics analysis of imine addition reactions, 385 considerations, 329 control in nucleophilic opening of epoxide, 295, 301 control, of stereochemistry in ketone reduction, 541 model for addition of nucleophile to imine, 285 of N-acyliminium ion cyclizations, 341, 343 of cuprate addition, 517 Stereoelectronic effects, on reserpineisoreserpine oxidation-reduction chemistry, 319 Stereorandom synthesis purpose of, 447, 451 value to medicinal chemistry, 81 Stereoselective olefin synthesis, 447 Steric effects, in cis-decalin conformational equilibria, 295 Steroid side chain problem, 157, 159 Steroid synthesis annulation strategy, 35 industrial scale, 35 Steroids, 3

Steroids, ring juncture stereochemistry, 17 Stitching methodology, using boranes, 185 Stork-Danheiser synthesis, 327 Stork-Eschenmoser hypothesis, 43 Strategy, 13, 205 3-component coupling for PG synthesis, 105 allylation-oxidation for use in polyacetate synthesis, 491 for control of vicinal stereochemistry, 119 for molecules containing multiple acyclic stereogenic centers, 515 for synthesis of lasonolide A via intramolecular Stille coupling, 483 for synthesis of lasonolide via macrolactonization reaction, 495 Structure determination, by synthesis, 11, 447, 449, 481 Sulfonium salts, as A-functional groups, 211 Sulfoxides, as A-functional groups, 211 Sulfur-containing heterocycles, use to set stereochemistry in acyclic systems, 473 Swern oxidation, 425, 491 Symmetry as a consideration in retrosynthetic analysis, 375 in approach to porantherine, 281 in synthetic approaches to triquinacene, 265, 269, 273 use of in erythronolide A strategy, 539 **Synthesis** and structure determination, 11

as template for reaction development, 179, 185 as tool for understanding reaction stereochemistry, 193 biomimetic, 3, 41 importance of mechanistic, stereochemical principles during design, 204, 205 selection of key intermediates, 19 to meet demand for supply of compound, 561

Tactics, 13, 205 improvement of for problems in prostaglandin synthesis, 89 Tamao-Fleming oxidation, 327, 485 Tandem reactions, 197 aldol-dehydration-alkylation approach to morphine, 431 radical cyclization-additionelimination approach to morphine, 423 reduction-hydrogenolysis-imine formation-reduction, 363 stereochemistry controlled by thermodynamics versus kinetics, 523 sulfone addition-alkylation approach to morphine, 419, 421 Target-oriented synthesis, necessary considerations, 205 Tautomerization, importance of in determining functional group reactivity, 213 Terpenoids, side chain stereochemistry problem, 5 Testosterone, 29 Thermodynamic control of epimerization stereochemistry, 527

of stereochemistry in ketone alkylation, 541 of stereochemistry, 521 as a stereochemical control element, 305 control of intramolecular aldol regiochemistry, 79 control over stereochemistry, 505 for controlling spiroacetal stereochemistry, 507 Thiele's acid, 269 Three-component coupling, strategy for PG synthesis, 99, 107, 109 Thromboxanes, 93 Tin hydride reductions, catalytic in tin, 93 Todomatuic acid, 163 Torsional strain importance in enolate alkylations, 157 in macrocycle, 543 Total synthesis, as a tool for methodology development, 151 Transannular strain, in macrocycle, 543 Transfer of chirality, 1,2- to 1,4, 513 Transfer of chirality, 121, 513 in Claisen rearrangement, 513 Triquinacene, 7 Triquinacene origin of 5-membered rings in synthesis of, 267, 269 relationship to dodecahedrane, 265 synthesis of, 265-273 Trisubstituted olefin synthesis, Gennari-Still compared with normal HWE reactions, 487 Twistane, 7 Diels-Alder route to, 249, 257 retrosynthetic analysis of, 247 synthesis of, 249-263

Umpolung, 211

VanRheenan oxidation, 541 Vicinal diastereoselection, in addition of metallated vinyl sulfoxide to enone, 195 Vicinal dihydroxylation, with OsO₄, 39 Vicinal stereochemistry control by ring-opening strategy using Baeyer-Villiger, 177, 187 control of by addition to alkenes, 123 control of in oxy-Cope rearrangement, 175 control through alkene addition reactions, 119 control through cycloaddition-ring opening strategy, 169 Vinylogy, the principle of, 215 Vioxx, as COX inhibitor, 75

Water scavenger, use to improve yield in sensitive Diels-Alder reaction, 361 Weinreb amide synthesis, 485 Weiss reaction, in triquinacene synthesis, 271 Williamson ether synthesis, 317, 453, 455 Wittig reaction, 187, 261, 289, 349, 353, 489, 495, 517, for introduction of prostaglandin sidechain, 87 modifications of in stereoselective olefin synthesis, 465 Schlosser modification of, 55, 465 stereochemistry of, 55 Wolf-Kishner reduction, 249, 257, 291, 409

Yamamoto-Peterson olefination (ene-yne synthesis), 383 Ynamine cycloaddition, 169

Z-Olefin synthesis, via Wittig reaction of unstabilized phosphoranes, 55