

- Abuse tests, 19
Acarbose, 119, 120. *See also* Precose
Accupril[®], 148–150
ACE, 130–131, 144–146, 160. *See also*
 Angiotensin-converting enzyme
Acetone, as unreactive byproduct, 22
Acetonide, 100
Acetonitrile, 18
N-Acetylaziridine, 108
N-Acetyl gemifloxacin, 61
N-Acetyl-neuraminic acid, 111
Acetylde, 87, 90
Acetylthiophene, 207
Acne, 41
Acquired immunodeficiency syndrome.
 See AIDS
Active transport, 227
Actos, 117, 122, 124
Acute exacerbations of chronic bronchitis
 and pneumonia, 47, 57, 60
Acute maxillary sinusitis, 47
Acute pyelonephritis, 47
Acylation, 86
Adalat[®], 159, 162–163. *See also* Nifedipine
Adderall[®], 241, 244, 246–247
Addition sequence, 19–20
Addition–elimination reaction, 46–47, 52
ADHD, 241–257
Adipogenesis, 121
ADME (absorption, distribution, metabolism,
 elimination), 2
Adrenal insufficiency, 33
Adrenaline, 242–243
Adrenergic, 202
Adsorbents, 23
Age-dependent PK, 162
Agitation, effectiveness of, 13, 20
AIDS, 84, 86, 90, 92
Albumin plasma protein binding, 131
Albumin, 122, 123
AlCl₃, 177
Aldehyde oxidase, 219
Aldoketoreductases, 34
Aldol condensation, 78
Aldol, 253
Aldosterone receptor blocker, 160
Aldosterone, 37
Allosteric, 84, 85, 217
Allyl isomerization, 103
Alpha-glucosidase inhibitors, 120–121
Alpha-keto phosphonate, 5
 α 2 δ , 225, 227
Altace[®], 151–154
Amantadine, 96
Ambien[®], 215
American Cyanamid, 221
Amidine, 138–139
Amido-Grignard, 207
Amination, 209, 210
 γ -Aminobutyric acid, 225. *See also* GABA
Aminoglutethimide, 34, 37
Aminoguanidine, 222
Aminoiminomethanesulfonic acid, 112
Aminolysis, 205, 245, 254–255
(R)-(–)-2-Amino-1-propanol, 54
(S)-(+)-2-Amino-1-propanol, 52, 54, 57
Aminopyrazole, 222
Amlodipine besylate, 159, 164–165. *See also*
 Norvasc[®]
Ammonolysis, 107
Amphetamine, 241, 243–247. *See also*
 Adderall[®]
Amphotericin B, 72
Anaerobes, 41, 57, 64
Analytical methods, 16
Anastrozole, 31, 34, 36. *See also* Arimidex[®]
Andrenosteroidogenesis, 35
Androgens, 33
Angiotensin AT1 antagonists, 129–131
Angiotensin AT2, 130–131

- Angiotensin converting enzyme, 130–131, 160. *See also* ACE
- Angiotensin I, 130–131, 144–145
- Angiotensin II antagonists, 160
- Angiotensin II, 130–131, 144–145
- Anion exchange chromatography, 228, 231, 232
- Anion, 204, 207
- Antacid, 45, 48, 61
- Anthrax, 47
- Antiangina, 162
- Antidepressant, 200–202
- Antiglucocorticoids, 200
- Anti-hyperglycemic, 124
- Antisolvent, 22
- Anxiolytic, 217
- Apolipoprotein A-V, 124
- Apolipoprotein B, 187
- Apparent clearance. *See* CL/F
- Aqueous methylamine, 205
- Aqueous sodium hydroxide, 204
- Aranidipine, 160, 161. *See also* Bec[®]
- Arbuzov reaction, 156
- Area under the curve. *See* AUC
- Arimidex, 31, 34, 36
- Aromasin, 31, 35
- Aromatase inhibitors, 31–38
 - Type I aromatase inhibitors, 34
 - Type II aromatase inhibitors, 34, 36–38
- Arylacetonitrile, 204
 - Condensation with ketones, 204
- Arylation, 193
- ASN-1377642, 6
- Aspartic acid, 85
- Aspergillosis, 73
- Aspergillus fumigatus*, 74, 77
- Astra-Zeneca, 31, 148, 159, 163, 169, 174
- Asymmetric Diels–Alder, 107
- Asymmetric epoxidation, 254–255
- Asymmetric hydrogenation, 237
- Asymmetric synthesis, 220
- Asymmetrically Induced Crystallization, 208
- Atamestane, 34
- Atomoxetine, 241, 243–244, 253–257.
 - See also* Straterra[®]
- Atorvastatin, 125, 171. *See also* Lipitor[®]
- Attention Deficit Hyperactivity Disorder.
 - See also* ADHD
- AUC (area under the curve), 45, 48, 58, 61, 98, 124, 125, 162, 220
- Autoimmune disease, 118
- Avandia[®], 1117, 121–122
- Avelox[®]. *See also* moxifloxacin
- Azabicyclo[3.3.0] octane-3-carboxylic acid, 152, 153
- Azelnidipine, 159, 165–166.
 - See also* Calblock[®]
- 2-Azetidinone, 185
- Azide, 99, 100, 102, 106, 110, 111, 205
- Azidoacetamide, 100
- Azidoamine, 100
- Aziridine, 99, 100, 103, 104, 106, 109
- AZT, 86, 90
- B. anthracis*. *See also* *Bacillus anthracis*
- Bacillus anthracis*, 47. *See also*
 - B. anthracis*
- Baclofen, 226
- Bacterial meningitis, 40
- Bacterial resistance, 44
- Bactericidal, 44
- Bacteriostatic, 44
- Baker's yeast, 54, 255
- BALF, 98
- Barbiturates, 216
- Barfknecht, C., 246
- Barnidipine hydrochloride, 160, 161.
 - See also* Hypoca[®]
- Batch processing. *See* semi-batch processing, 20
 - limitations vs. continuous operations, 21–22
- Batches, strategy
 - Phase 1 and toxicology
 - Purity goals, 15
 - Bridging, 16
 - Phase 2 and beyond, 15–26
- Bayer, 39, 43, 159
- Baylis–Hillman conditions, 237
- Baypress[®], 160, 161. *See also* Nitrendipine
- BBr₃, 178
- Bcr-Abl kinase, 4
- Bec[®], 160, 161. *See also* Aranidipine
- Beckmann rearrangement, 150
- Benazepril, 150–151. *See also* Lotensin[®]
- Benazeprilat, 150
- Benidipine hydrochloride, 160, 161.
 - See also* Coniel[®]
- Benzodiazepines, 216
- Benzoxazines, 40, 49, 51–56

- Benzoxazinone, 88
Benzoyl peroxide. *See* BPO
Benzyl-(*R*)-(-)-mandelate, 177
Benzylation, 87
Benzyloxycarbonyl-*L*-phenylalanine, 152
Bicyclic aminal, 204
Biguanides, 119–120
Bile excretion, 133
Bioavailability (%F), 23, 24, 38, 45, 48, 57, 61, 98, 146, 203
BioCryst Pharmaceuticals, 98
Biodegradable polymer, 246, 250
Biota, 95, 110, 111
Biphenylbenzyl bromide, 135–136, 139
Biphenyltetrazolyl bromide, 136–137
BIRB, 796, 5
bis(heteroaryl)piperazine, 90
bis-acetoxyboronates, 59–60
Bischler indole synthesis, 173
Blaise reaction, 178
 β -Blockers, 160
Blood pressure, 160
Blood-brain-barrier, 226, 227
BMS-354825, 5
Boc group, deprotection, 17–18
Boehringer Ingelheim, 83, 85, 139
Boldenone, 42
Borane-dimethylsulfide complex, 211
Borane-*t*-butylamine, 171
Boronate chelate, 174
Boronate ester, 189
Boronic acid, 133–134
Bothrops jararaca, 145
BPO, 36
Bradykinin, 144–145
Breast cancer, 31–38
 Estrogen-dependent, 33
Breast carcinoma, 32
Bristol-Myers Squibb, 43, 117, 125, 146, 149, 154
Bromoacetamidation, 108
N-Bromoacetamide. *See* NBA, 108
Bromohydrin, 178
Bronchoalveolar lining fluid. *See* BALF
Brown, H. C., 254
Bupropion, 201, 202
t-Butyl acetoacetate, 173
t-Butyl bromoacetate, 178
n-Butyl lithium, 87, 171
Butylmagnesium diisopropylamide, 207
C. pneumoniae. *See also Chlamydia pneumoniae*
C2C12 N myoblasts, 121
C3H10T/2 cell line, 121
Calblock[®], 159, 165–166. *See also* Azelnidipine
Calcium channel blocker, 159–167
Calcium channel, 159–162, 227
Calslot[®], 160, 161. *See also* Franidipine hydrochloride
Candesartan cilexetil, 129, 131–132, 136–137
Candesartan, 136. *See* CV11974
Candida albicans, 72, 74, 77
Candida Antarctica Lipase B (CALB), 210
Candida Antarctica, 220
Candidosis, 73, 76
Captopril, 145, 146
Carbonyldiimidazole, 92, 218
N-Carboxyanhydride. *See* NCA, 21, 147, 148, 149
Carboxylesterases, 221
Carboxylic acid metabolite, 133
Carcinogen, 18
Cardene SR[®], 160, 161. *See also* Nicardipine hydrochloride
Cardiovascular disease, 130
Caspase, 5
Cathepsin G, 5
CCR5, 6
CD₄, 85, 86
Celgene, 241, 249
Central nervous system. *See also* CNS
C–H activation, 251
C–H insertion reaction, 233
Chemical space, 7
Chinese star anise, 101
Chiral hydride, 208
Chiral inducer, 177
Chiral resolution, 181
Chiral, 207, 208, 212, 220
Chirazyme L-2, 105, 220
Chirotech, 237
Chlamydia pneumoniae, 60. *See also* *C. pneumoniae*
Chloral hydrate, 216
Chloride ion channels, 217
Chlorination, 13, 78
Chloroacetyl chloride, 172
Chlorodimethylsilane, 180

- Chloroform, 18
 Chloromethyloxirane, 205
 Cholesterol Absorption Inhibitor (CAI), 184
 Cholesterol biosynthesis, 170
 Cholesterol, 33, 183
 Chromatography
 Plug, 23
 Preparative, 16, 22
 Chu-Li synthesis, 46
 Chu-Mitscher synthesis, 46, 52–54
 Cialis[®]. *See* tadalafil, 24
 CIAT. *See* crystallization-induced asymmetric transformation, 24–25, 151
 Ciba-Geigy, 40, 41, 150
 CIDR. *See* crystallization-induced dynamic resolution, 24–25
 Cimetidine, 219
 Cinaldipine, 160, 161. *See also* Siscrad[®]
 Cinoxacin, 41
 Cipro[®]. *See also* ciprofloxacin
 Ciprofloxacin, 41, 43, 47, 48, 57, 60, 64.
 See also Cipro[®]
cis-trans mixture, 205
 CL/F, 123
 Clearance, 48, 58, 61
 Clinafloxacin, 41, 42, 43, 44, 45
 cLogP, 2–3
 Clotrimazole, 72–73
 C_{max}, 38, 48, 58, 61, 98, 121, 125, 162, 220
 CMO. *See* contract manufacturing organization, 13
 CNS (central nervous system), 200, 226, 227, 239, 242, 245,
 Co-activators, 121
 Cocktail, 84, 86, 90, 92
 Co-distillation, 20
 COG. *See* cost of goods, 15, 23–26
 Combinatorial chemistry, 7
 Community acquired pneumonia (CAP), 47, 60
 Community acquired respiratory traction infection (CART), 57
 Compactin, 170
 Concerta[®], 241, 244, 250
 Condensation, 204
 Configuration, 205, 208
 Coniel[®], 160, 161. *See also* Benidipine hydrochloride
 Conjugate addition, 62
 Continuous operations, 16, 21–22
 Contract manufacturing organization.
 See CMO, 13
 Contract research organization. *See* CRO, 13
 Convergent routes, 17
 Corey epoxidation, 77
 Corey, E. J., 106–108
 Corey–Bakshi–Shibata (CBS) reduction, 189
 Corey–Kim oxidation, 96
 Coronary heart disease, 130, 170
 Corticotrophin-releasing factor
 antagonist, 200
 Cost of goods. *See* COG, 15, 23–26
 CP-96, 345, 6
 C-reactive Protein, 187
 Crestor[®], 169, 174–176. *See also* Rosuvastatin
 CRO. *See* contract research organization, 13
 Cryptococcosis, 73
Cryptococcus neoformans, 74, 77
 Crystal engineering, 23
 Crystallization vs. precipitation, 17
 Crystallization, 49, 52, 53, 58, 59
 Crystallization-induced asymmetric transformation. *See* CIAT, 24–25, 151
 Crystallization-induced dynamic resolution.
 See CIDR, 24–25
 Curtius rearrangement, 106, 228
 CV11974, 136
 Cycle times, 19
 [3 + 2]-Cycloaddition, 106
 Cyclophosphamide, 38. *See also* Cytosan[®]
 Cyclopropane, 205, 207
 Cyclopropylmethyl ketone, 177
 9-Cyclopropylpyrimidinones, 46
 Cylert[®], 243
 Cymbalta[®], 199, 253. *See also* Duloxetine
 CYP1A1, 34, 123
 CYP1A2, 218
 CYP2A6, 35
 CYP2B6, 90, 220
 CYP2C19, 35, 125
 CYP2C8, 34, 121, 123, 220
 CYP2C9, 34, 121, 125, 133, 135, 218
 CYP2D6, 34, 92, 203
 CYP3A4, 34, 35, 73, 86, 92, 123, 125, 133, 162, 217, 218, 219, 220, 221
 CYP51, 72. *See also*
 lanosterol-14 α -demethylase
 Cytochrome P450 inhibition, 2, 72–73
 Cytochrome P450 isoforms, 2, 217.
 See also CYP

- Cytotoxicity, 85, 87
Cytosan[®], 38
- DA, 200, 201, 202. *See also* dopamine
Daiichi, 39, 48
Dalcipran[®], 199. *See also* Milnacipran
DANA, 97
DAT (dopamine transporter), 202, 242, 253
Davies, H., 251
Daytrana[®], 241, 244, 250
DCC, 149–150
DDQ, 175
DEA scheduling, 243. *See also* U.S. Drug
Enforcement Agency
DEAD, 99
DEAE-Toyopearl 650 M, 51
Deallylation, 103, 104
Dean-Stark apparatus, 35, 246–247
Decarboxylation, 61, 78
Decomposition of activated intermediates, 13
Dehydrogenation, 175
Delavirdine, 83, 84, 90, 91
N-Demethylation, 207
Depression, 199–202
Deprotonation, 189, 205
20,22-Desmolase, 34
Dess-Martin periodinane, 109
Desymmetrization, 106
DiaBeta[®], 119
Diabetes, 117–125
 Type 1 diabetes, 118
 Type 2 diabetes, 118–124
Diabetic coma, 118
Diabetic ketoacidosis, 118
Diastereocontrol, 107
Diastereomeric salt formation, 220
Diastereoselectivity, 189
Diastolic blood pressure, 160
DIBAL, 176
L-Dibenzoyl-tartaric acid, 152
Dichloromethane. *See* methylene chloride,
 18–19
1,2-Dichloroethane, 18
2,3-Dichloropropene, 11
Diels–Alder, 105
Diethanolamine boronic ester, 65, 66
Diethyl azodicarboxylate. *See* DEAD
Diethyl ether, 18
Diethyl oxalate, 21
Diethyl-3-hydroxygluturate, 176
Diethylamine, 205
(*R,R*)-Diethyl tartrate, 178
Differential scanning calorimetry and
 exothermic processes, 13
Diflucan, 71, 76
Difluoroborates, 52, 60
Dihydropyridine, 159–167
Diisopropyl ether, 18
Diltiazem, 160, 162
1,2-Dimethoxyethane. *See* DME and
 glyme, 18
2,2-Dimethoxypropane, 181
Dimethylamine, 207
Dimethylbenz[*a*]-anthracene. *See* DMBA
Dimethylsulfide, 20
Dimethylsulfoxide. *See* DMSO, 20
Dioxane, 18
Diphenylphosphoryl azide, 106
Direct isolation, 22, 23
Disiamyl borane, 181
Diskhaler, 97
Displacement, 86
Diuretics, 160
DMBA, 37
DME. *See* 1,2-dimethoxyethane and
 glyme, 18
DMSO. *See* dimethylsulfoxide, 20
DNA gyrase, 43, 44, 45, 46. *See also*
 Topoisomerase II
DNA, 43, 44
Domino sequence, 103
Dopamine reuptake transporter. *See* DAT
Dopamine, 200, 242–243, 246. *See also* DA,
 Monoamine
Dose/Day, 203
Drug resistance, 85
Drug-drug interaction, 35
Drying, 23
DSM IV, 242
Duloxetine, 199, 202–203, 207–212, 253.
 See also Cymbalta[®]
Dynamic equilibrium, 24
Dyslipidemia, 124
- E. coli*, 44, 47, 48, 101. *See also*
 Escherichia coli
E. R. Squibb & Sons, 153
Econazole, 72–73
Efavirenz, 83, 84, 87, 90
Effexor[®], 199. *See also* Venlafaxine

- Efflux pumps, 44
- Efonidipine hydrochloride ethanol, 160, 161.
See also Landel[®]
- Electrostatic discharge, 18
- Elegance in simplicity, 26
- Eli Lilly, 199, 241, 243, 253–257
- Elimination half-life, 203
- Elimination route, 203
- Enalapril maleate, 21, 146–147.
See also Vasotec[®]
- Enalaprilat, 146
- Enamide, 222
- Enamine, 219, 223
- Enantiomer, Enantiomeric, 199, 207–212
- Enantioselective, 189, 208, 211, 212
- Enantioselectivity, 220
- Enoxacin, 41
- Enterococcus* spp., 48
- Enterohepatic recirculation, 187
- Enzymatic hydrolytic desymmetrization, 106
- Enzymatic reduction, 255
- Enzymatic resolution, 51, 220, 238
- Epoxide, 99, 100, 102, 104, 178
- Eprosartan mesylate, 130–131, 138–139
- ER, 33
- Ergosterol, 72
- Escherichia coli*, 44, 47, 48, 101.
See also *E. coli*
- Ester enolate-imine condensation, 187
- Ester hydrolysis, 136, 138–139
- Ester prodrug, 136
- Estorra[®], 216
- Estrogen receptor, 124. *See also* ER
- Estrogen, 32, 33
- Eszopiclone, 216, 220. *See also* Estorra[®] and Lunesta[®]
- Ethanolamine, 103, 104, 106
- Etherification, 207, 209, 211, 212
- 1-Ethyl-3-(3-(dimethylamino) propylcarbodiimide), 92
- Ethyl formate, 207
- Ethyl isobutrylacetate, 226
- Ethylene glycol, 18, 19
- Ethylmethylphosphinic acid, 154
- Evans' chiral oxazolidinone, 234
- Evans-Aldol condensation, 189
- Evista[®], 33
- Exemestane, 31, 35. *See also* Aromasin[®]
- Exotherms and liability on scale, 17
- 5-Exo-trig halogen atom transfer radical cyclization, 232
- EXP 3174, 132–133
- EXP 3179, 132–133
- Extended operations, 13–14, 24, 25
 Additions, 13
 Carboxylation through Grignard, 13–14
- Extracellular pathogens, 60
- Ezetimibe, 183. *See also* Zetia[®]
- Ezetrol, 183. *See also* Zetia[®]
- Fab H, 4. *See also*, β -Ketoacyl carrier protein synthase III
- Factive[®]. *See also* gemifloxacin
- Famotidine, 124
- Farmitalia Carlos Erba S.r.l, 31, 35
- FDA, 42, 43, 47, 57, 64, 243, 249. *See also* U.S. Federal Drug Administration
- Feline leukemia virus, 85
- Felodipine, 159, 163–164. *See also* Plendil[®]
- Femara[®], 31, 34, 37–38
- Fenofibrate, 125
- Filtration, problems with crystalline needles, 23
- First-pass elimination, 162, 163
- Fischer indole synthesis, 171
- Fleroxacin, 41, 42
- Floxin[®]. *See also* ofloxacin
- Fluconazole 71, 76–77. *See also* Diflucan[®]
- Flumazenil, 217
- Flumequine, 41
- Fluorobenzene, 177
- 1-Fluoronaphthalene, 207
- Fluorouracil, 38. *See also* 5-FU
- Fluoxetine, 201, 253. *See also*, Prozac[®]
- Fluroquinolones, 40, 41, 44, 45, 47–64
- Fluvastatin, 169, 171–174. *See also* Lescol[®]
- fMRI, 242
- Foams, difficulties in formulating, 23
- Focalin[®], 241, 244, 249–250
- Folic acid analog, 32
- Foreman, R., 245
- Formestane, 34
- Formulating the API, 23
- Formulations (novel) 243–244, 246–247, 249–250
- Fosfluconazole 71, 80. *See also* Prodig[®]
- Fosinopril sodium, 154–156. *See also* Monopril[®]
- Fosinoprilat, 154

- Fourier transform infrared. *See* FTIR, 14
Fractional crystallization, 147, 156
Franiidine hydrochloride, 160, 161.
 See also Calslot[®]
Fraser–Reid coupling, 81
Friedel–Crafts acylation, 77, 171, 177, 223
Friedel–Crafts alkylation, 155
FTIR, in Grignard-carboxylation, 14
5-FU, 32
- G protein-coupled receptors, 6
GABA receptor binding, 44–45
GABA, 216, 225, 226. *See also* γ -amino butyric acid
GABA_A agonists, 215
GABA_A subunits, 217
GABA_A, 215
Gabapentin, 225–232, 239. *See also* Neurontin[®]
[³H]-Gabapentin, 226, 227
Gag-pol, 84
Garenoxacin (T-3811), 39, 41, 42, 44, 45, 47, 64–66
Gas evolution and liability on scale, 17
Gastrointestinal infections, 40
Gatifloxacin, 41, 42, 43, 44, 57, 60, 64.
 See also Tequin[®]
Gemfibrozil, 124
Gemifloxacin, 39, 41, 42, 43, 47, 48, 60–64.
 See also Factive[®]
Gene transcription, 120
Genotoxicity, 44
Gerster–Hayakawa synthesis, 46, 48
GG167. *See* zanamivir or Relenza[®]
Gilead, 95, 96, 98, 99
Ginkgo leaves, 101
Glargine, 118. *See also* Lantus[®]
GlaxoSmithKline, 95, 96, 110, 111, 117
Gleevec[®], 4. *See also* imitinib
Glimepiride, 119. *See also* Amaryl[®]
Glipizide[®], 119. *See also* Glucotrol[®]
Glitazones, 120–125
Glomerular filtration, 98
Glucokinase, 120
Glucophage[®], 119
Glucose transporter GLUT-4, 121
Glucose, 1117–118
Glucotrol[®], 119
Glucuronic acid, 121
Glucuronidation, 124
O-Glucuronidation, 187
Glucuronide, 38, 58, 61
GLUT4 glucose transporter, 121
Glyburide, 119. *See also* DiaBeta[®] or Glynase PresTab[®] or Micronase[®]
(*S*)-Glycerol acetone, 55
Glyme. *See* 1,2-dimethoxyethane and DME, 18
Glynase PresTab[®], 119
Glyset[®], 124–125
Gould–Jacobs reaction, 46, 48, 49
Gram-negative, 40, 41, 44, 48, 57, 60, 64
Gram-positive, 40, 41, 43, 44, 48, 57, 60, 64
Grapefruit juice, 162
Green procedure, 204
Grepafloxacin, 41, 42
Grignard reaction, 14
Grignard, 171
Grohe–Heitzer cycloacylation, 46–47, 52–53, 58, 61
GS-4071, 97, 98
Guanidine, 111, 112
Guareschi salt, 228
Gynecological infections, 40
- H. influenzae*. *See* *Haemophilus influenzae*
H5N1 strain of avian flu, 96
Haemagglutinin (HA), 96
Haemophilus influenzae, 47, 48, 57, 60, 64.
 See also *H. influenzae*
Half-life ($T_{1/2}$), 34, 36, 38, 45, 58, 61, 86, 90, 92, 121, 122, 125, 130, 132, 135, 137–139, 160, 162
Hantzsch, 160, 162
Hass, H., 245
HBTU, 17
HDL cholesterol, 124
Heat transfer rate, slower on scale, 13
Heat transfer, benefits of continuous processing, 21
Hemisuccinate, 46
Hemolytic-uremic syndrome, 42
Hemoprotein, 40
Henry Reaction, 245
Hepatic cytochrome P450 enzymes, 98
Hepatic esterases, 98
Hepatic metabolism, 162
Hepatotoxicity, 42
Heptane, 18
HERG, 2–3

- Hippocampal, Hippocampus, 200
 Histamine receptors, 202
 Hite, G., 248
 HIV, 83, 84, 85, 87, 90, 91, 92
 HMG-CoA-reductase inhibitor, 169–182
 HMG-CoA-reductase, 170
 HMPA, 175
 HOBt, 149
 Hoechst, 151
 Hofmann rearrangement, 231
 Homogeneous reactions *vs.* suspensions, 25
 Homology modeling, 6
 5-HT, 200, 201, 202. *See also* Serotonin,
 Monoamine
 Adrenergic/5-HT Dual Antagonist, 202
 5-HT Antagonist/Reuptake
 Inhibitor, 202
 5-HT Transporter. *See also* SERT, 202
 Humalog[®], 118
 Human immunodeficiency virus. *See* HIV
 Hydrazine, 205
 Hydroboration, 180, 250–251
 Hydrobromic Acid, 205
 Hydrogen Chloride, 209
 Hydrogenation, 56, 58, 62, 64, 204, 205,
 211, 212
 Catalytic, 211
 Palladium on Carbon, 205
 Rhodium on Alumina Catalysis, 204
 Ruthenium-catalyzed, 212
 Hydrogenolysis, 177, 246
 Hydrosilylation, 180
 Hydroxylation, 86, 90, 92
 β -Hydroxyketone, 174
 17 α -Hydroxyprogesterone, 37
 Hypercholesterolemia, 170, 184
 Hyperglycemia, 54, 122, 123
 Hyperinsulinemia, 122
 Hypertension, 130, 144–145, 160
 Hypertriglyceridemia, 122
 Hypnotic, 217, 220
 Hypoca[®], 160, 161. *See also* Barnidipine
 hydrochloride
 Hypoglycemia, 53–54, 121

 Imidate salt, 135–136, 138–139
 Imidazole antifungal drugs, 72–73
 Imidazolecarbaldehyde, 133, 138–139
 Imidazopyridine, 218
 Iminium salt, 173

 Imipramine, 201
 Impurity profile, 15–16
 In silico modeling, 2
 Inactivators, 40
 Indiplon, 216, 221
 Influenza, 95–98
 1918 Spanish influenza, 95
 1957 Asian influenza, 95
 1968 Hong Kong influenza, 96
 Influenza A and B, 96
 Inhibitory neurotransmitter, 225
 In-process controls. *See* IPC, 16
 Insomnia, 216
 Insulin analogs, 118
 Insulin Aspart., 118. *See also* NovoLog[®]
 Insulin pump, 118
 Insulin resistance, 118
 Insulin, 117–120
 Intracellular pathogens, 60
 Iodination, 210, 211
 Iodobenzene, 207
 Iodolactamization, 143
 IPC. *See* In-process controls, 16
 Irbesartan, 129, 135–136
 3-Isobutyl GABA, 226, 234
 γ -Isobutylglutaric acid, 236
 Isocarboxazid, 201
 Isocyanate, 106
 Isoforms, 217
 Isoindolines, 44, 64, 65, 66
 Isotopic small labeling, 244–245
 Isotopomers, 210
 Itraconazole 71, 74–76. *See also* Sporanox[®]
 Ixel[®], 199. *See also* Milnacipran

 Johnson & Johnson, 98, 241, 250
 Jones oxidation, 35

K. pneumoniae, *See* *Klebsella pneumoniae*
 K103 N, 85, 87, 91
 Karpf and Trussardi, 102
 K_d, 121
 Ketalisation, 74
 Ketene, 188
 Ketene-imine cycloaddition, 187
 β -Ketoacyl carrier protein synthase III,
 4. *See also* Fab H
 Keto amine, 207, 208, 211, 212
 Keto ester, 212
 Ketoconazole, 72–74, 124

- Kidney excretion, 133–138
Kim, Choung U., 96
Kinetic resolution, 210, 211
King Pharmaceuticals, 151
Klebsella pneumoniae, 47, 57. *See also* *K. pneumoniae*
Knapp protocol, 107
Knoevenagel condensation, 138–139, 164, 229
Knoevenagel reaction, 25
Kowa, 169, 177
- L. pneumophila*. *See also* *Legionella pneumophila*
Lacidipine, 160, 161. *See also* Lasirex[®]
D-Lactic acid dehydrogenase, 151
Lactic acidosis, 120
Lactone, 205
Lactonization, 100, 173
L-amino acid transporter, 226, 227
Lamisil[®], 72
Landel[®], 160, 161. *See also* Efonidipine hydrochloride ethanol
Lanosterol-14 α -demethylase, 72. *See also* CYP51
Lantus[®], 118
Large-scale synthesis, 204
Lasirex[®], 160, 161. *See also* Lacidipine
LCMS, 7
LDL-C, 184
Legionella pneumophila, 60. *See also* *L. pneumophila*
Lercanidipine, 160, 161. *See also* Zanedip[®]
Lescol[®], 169, 171–174. *See also* Fluvastatin
Letrozole, 31, 34, 37–38. *See also* Femara[®]
Levaquin[®]. *See also* levofloxacin
Levofloxacin, 39, 41, 42, 43, 45, 46, 47–57, 58, 60, 64. *See also* Levaquin[®]
Lewis acids, 102
LG Life Sciences, 39, 43
Liability from accidents, 12
LiAlD₄, 245
LiAlH₄, 178, 208, 211
Ligand-bound PPAR heterodimerises, 121
Lindlar's catalyst, 112
LiNH₂, 178
Lipase B, 220
Lipitor[®], 171. *See also* Atorvastatin
LIPOLASE[®], 100L, 239
Lipoprotein lipase, 51, 124
Lisinopril, 147–148. *See also* Zestril[®]
Lispro, 118. *See also* Humalog[®]
Lithium Aluminum Hydride, 178, 208, 211. *See also* LiAlH₄
Lithium Diethylamide, 205
Livalo[®], 169, 177–181. *See also* Pitavastatin
L-leucine, 234
Lomefloxacin, 41, 43. *See also* Maxaquin[®]
Losartan potassium, 129, 132–134
Lossen rearrangement, 228
Lotensin[®], 150–151
LPL Amano 3, 51
L-type calcium channel, 162, 163, 164
Lumpectomy, 38
Lunesta[®], 216, 220
Lung cancer, 32
Lyrica[®], 225, 227. *See also* pregabalin
- M. catarrhalis*. *See also* *Moraxella catarrhalis*
M₂ ion channel inhibitors, 96
Madin–Darby canine kidney. *See* MDCK
Major Depressive Disorder, 200. *See also* MDD
(*S*)-(+)-Mandelic Acid, 207
Mannich reaction, 207
Mannich-type reaction, 218
MAOI (monoamine oxidase inhibitor), 201
Markovnikov addition, 245
Mastectomy, 32
Maxaquin[®]. *See also* lomefloxacin
Maximal electroshock model, 226
mCPBA, 175
MDCK, 97
MDD, 200–202. *See also* Major Depressive Disorder
Mechanism of action, 122
Medicinal chemistry, 1
Meglitinides, 119
Meldrum's acid, 232
Merck, 43, 87, 133–134, 146–148
Metabolism, 86, 90, 92, 186, 217
Metabolite, 132–133, 186, 203, 219
Metaboloids, 186
Metal-halogen exchange, 65
Metallation, 76, 78, 207
Metallopeptidase, 144–145
Metformin, 119, 125. *See also* Glucophage[®]
Methanesulfonic acid, to remove Boc group, 17
Methanesulfonyl chloride, 19–20

- Methicillin resistant, 57, 64
 Methicillin susceptible, 47
 Methotrexate, 32
 Methylacetoacetate, 171
 (*R*)-Methylbenzylamine, 236
 Methylene chloride. *See* dichloromethane, 18–19
 (*S*)-Methylisothiourea, 111, 175
 Methylphenidate, 241, 244, 247–253.
See also Ritalin[®], Concerta[®], Focalin[®], Daytrana[®]
N-Methylpiperazine, 49, 50, 53
 Michael addition, 57, 229, 236
 Miconazole, 72–73
 Micromixing, 20
 Micronase, 119
 Microreactors, 21
 Miglitol, 120. *See also* Glyset[®]
 Milnacipran, 199, 202–203, 205–207.
See also Ixel, Dalcipran
 Minimum agitation volume, 13
 Minimum inhibitory concentration (MIC), 48, 57, 60, 64
 Mirtazapine, 201, 202
 Mitsunobu inversion, 209
 Mitsunobu reaction, 55–56, 110, 155, 254–256
 Mixed-anhydride couplings, 17
 Molecular sieves, 25
 Monoamine, 200, 201, 202
 Monoamine Neurotransmitters, 200
 Monoamine Oxidase A, B, 202
 Monoamine Oxidase Inhibitors, 201.
 See also MAOI
 Monoamine Transporters, 200
 Monoamine re-uptake inhibitor, 253
 Monopril[®], 154–156
Moraxella catarrhalis, 48, 57, 60, 64.
 See also *M. catarrhalis*
 Morphology, 84
 Mouse muscle satellite cells, 121
 Moxifloxacin, 39, 41, 42, 43, 44, 47, 48, 57–60, 64. *See also* Avelox[®]
 MT-2 cells, 90
 Mukaiyama aldol condensation, 195
 Muraglitazar, 117, 124–125. *See also* Pargluva[®]
 Muscarinic Receptors, 202
 Muscle relaxant, 217
 Mutagenicity, 18
 Mutants, 85, 87, 91
 Double, 87
 Single, 87
Mycoplasma pneumoniae, 60. *See also* *M. pneumoniae*
 Nabenhauer, F., 245
 NADPH, 40
 Nalidixic acid, 41, 45, 48
 [1-¹⁴C]-Naphthalene, 210
 Naphthyridines, 40, 60–62
 National Sleep Foundation, 216
 NBA, 108. *See also* *N*-Bromoacetamide
 NCA, 21, 147, 148, 149. *See also* *N*-carbonic anhydride
 NDA, 16. *See* New Drug Application
 NE, 200, 201, 202. *See also* Norepinephrine
 NE Transporter, 202. *See also* NET
 NE/DA Dual Reuptake Inhibitor, 202
 Selective NE Reuptake Inhibitor, 202.
 See also NRI
 Needles, crystalline, problems in scale-up, 23
 Nefazodone, 201, 202
 Negishi cross-coupling, 188
 Neiman-Pick C1 Like Protein, 187
Neisseria spp., 48
 Nelfinavir mesylate. *See* Viracept[®], 19–20
 NET (norepinephrine transporter), 202, 253.
 See also NE
 Neu5Ac2en. *See* DANA
 Neuraminidase inhibitors, 95–114
 Neurocrine Biosciences, 216, 221
 Neurontin[®], 225, 226
 Neuropathic pain, 226
 Neurotransmission, Neurotransmitter, 200
 Neurotransmitter, 217, 243
 Nevirapine, 83, 84, 85, 86
 New Drug Application (NDA), 16, 39, 42, 47, 64. *See also* NDA
 Nicardipine hydrochloride, 160, 161. *See also* Cardene SR[®]
 Nicotinamide adenine dinucleotide phosphate.
 See NADPH
 Nifedipine, 160, 161. *See also* Adalat[®]
 Nilvadipine, 160, 161. *See also* Nivadil[®]
 Nimodipine, 160, 161. *See also* Nimotop[®]
 Nimotop[®], 160, 161. *See also* Nimodipine
 Nisoldipine, 160, 161. *See also* Syscor[®]
 Nisoxetine, 253
 Nissan Chemical, 169, 177

- Nitration, 139
Nitrendipine, 160, 161. *See also* Baypress[®]
Nivadil[®], 160, 161. *See also* Nilvadipine
NK-1, 6
NMR, 5, 7
NNRTI, 84, 90
Nolvadex, 33
Non-nucleoside reverse transcriptase inhibitor.
 See NNRTI
Non-stimulant, 253
Noradrenaline, 243
Norepinephrine reuptake transporter.
 See NET
Norepinephrine, 199, 200, 202, 243.
 See also NE, Monoamine
 Dual Selective Serotonin Norepinephrine
 Reuptake Inhibitors, 199. *See also*
 SSNRI
Norfloxacin, 41, 43, 48. *See also* Noroxin[®]
Noroxin[®]. *See* norfloxacin
Norvasc[®], 159, 164, 165. *See also* Amlodipine
 besylate
Norvir[®]. *See* ritonavir, 23–24
Nosocomial (hospital-acquired) infections,
 47, 60
Novartis, 31, 150, 169, 171, 241, 248,
 250–252
Novartis/Ciba-Geigy, 134–135
NovoLog[®], 118
NRTI, 84, 85, 86, 90, 92
NSAID, 45
Nuclear hormone receptor, 124
Nucleophilic Aromatic Substitution.
 See S_NAr
Nucleophilic Attack, 205
Nucleoside reverse transcriptase inhibitor.
 See NRTI
Numbering up, 21

Ofloxacin, 41, 43, 47, 48, 49. *See also* Floxin[®]
Olefin metathesis, 7
Oligonucleotide-directed mutagenesis, 91
Olmesartan medoxomil, 129, 131–132,
 137–138. *See also* RNH-6270
Once-a-day therapy, 203
Onset, 200, 201, 203
Optical resolution, 49, 50, 58, 207–208
Optically active, 207, 208, 211, 220
Oral bioavailability, 3, 131–132, 136–139,
 227. *See also* bioavailability

OROS technology, 250
Ortho metallation, 87
Ortho-lithiation, 133
Ortho-McNeil (Johnson & Johnson), 39, 43
Oscient, 39, 43
Oseltamivir, 95–110. *See also* Tamiflu[®]
Osteomyelitis, 40
Outsourcing, 3
Oxacillin resistant, 64
Oxalyl chloride, 14
Oxazaborolidines, 209
Oxazolidinone, 106
Oxazoline, 111, 112
Oxidation
 Corey–Kim oxidation, 96
 Dess–Martin periodinane, 109
 Jones oxidation, 35
 Swern oxidation, 13, 134–135
 TPAP, 176
 With DMSO, 20
4-Oxo-1,4-dihydro-[1,8]-naphthyridine, 40
4-Oxo-1,4-dihydrocinoline, 40
4-Oxo-1,4-dihydroquinolone, 40
5-Oxo-5,8-dihydropyrido-[2,3-d]-pyrimidine,
 40
7-Oxo-2,3-dihydro-7H-pyrido-[1,2,3,-d,e]-
 1,4-benzoxazine, 40
4H-4-Oxoquinolizine, 40

P. aeruginosa. *See Pseudomonas aeruginosa*
P38 kinase, 4–5
P450_{arom}, 33–34
Palladium bis-triphenylphosphine dichloride
 [Pd(PPh₃)₂Cl₂], 65, 66
Palladium on carbon, 92, 205
Palladium, 100, 103–106, 111, 147,
 150, 152, 153, 155
Palladium-mediated coupling, 177, 178
Pancreas, 118–120
Pancreatic islet β cell function, 124
Pancreatic islet, 124
Pannizon, L., 248
parC, 44
parE, 44
Pargluva[®], 117, 124–125
Parikh–Doering oxidation, 62, 63
Parke–Davis, 227
Partial seizures, 227
PAT. *See* process analytical technology
 initiative, 21

- PdCl₂, 181
 Pemoline, 243
 Penicillin resistant, 47, 57
 Pentane, 18
 Peramivir, 98
 Perel, J., 250
 Peripheral blood mononuclear cells, 87, 90
 Peripheral vasodilator, 164
 Periphery, 120
 Peroxides, 18
 Peroxisome proliferator response elements. *See* PPREs
 Peroxisome proliferator-activated receptor. *See* PPAR
 PET, 112, 242
 Pfizer, 31, 43, 148, 159, 164, 234, 236, 237, 238
 Pharmacia, 43
 Pharmacodynamics, 217
 Pharmacokinetics, 37, 48, 57, 61, 121, 122, 160, 217, 219, 220, 243, 246–247, 250
 Phase-transfer catalyst, 36, 204
 Phenyl tetrazole, 133
 PhI(OAc)₂, 178
 Phosgene, 147, 150
 Phosphonium ylide, 176
 Phosphorus oxychloride, 13
 Phototoxicity, 42, 43, 44, 45
 Physical states, 23–24
 Pictet-Spengler condensation, 24
 Pierre Fabre Laboratories, 199
 Pig liver esterase. *See* PLE
 Pinner reaction, 230
 Pioglitazone hydrochloride, 117, 122, 124. *See also* Actos[®]
 Pipemidic acid, 41
 Pipercolic acid, 250–251
 Pitavastatin, 169, 177–181. *See also* Livalo[®]
 Pivaloyl chloride, 17
 Plane of symmetry, 177
 Plasma concentration, 48, 58, 61
 Platinum, 155
 PLE, 106
 Plendil[®], 159, 163, 164. *See also* Felodipine
 Polymerase, 84, 85, 87, 91
 DNA-dependent DNA polymerase, 84
 Escherichia coli polymerase, 87
 Human DNA polymerase, 85, 87
 RNA-dependent DNA polymerase, 84
 Thymus DNA polymerase, 85
 Polymorphs, 23–24
 Polyphosphoric ester, 49, 55, 56. *See also* PPE
 Positron emission topography. *See* PET
 Post-herpetic neuralgia, 226, 227
 Potassium phthalimide, 205
 Potassium *t*-butoxide, 14
 PPAR agonists, 120–125
 PPAR dual agonist (γ/α), 124
 PPAR, 120–125
 PPAR- α agonists, 124
 PPAR- γ agonist, 120–125
 PPAR- γ receptor, 121
 PPE. *See* Polyphosphoric ester
 PPE. *See* protective personnel equipment, 12, 17
 PPREs, 121
 Prandin[®], 119
 Pravacol[®], 170. *See also* Pravastatin
 Pravastatin, 170. *See also* Pravacol[®]
 Precose[®], 120
 Pregabalin, 225–227, 234, 236, 238, 239. *See also* Lyrica[®]
 Prinivil, 147–148. *See also* Zestril[®]
 Process analytical technology initiative. *See* PAT, 21
 Process optimization, 13, 14, 16–17, 19–23, 24–26
 Prochiral, 177
 Prodif[®], 71, 80–81
 Prodrug, 80, 97, 146, 244
 Productivity, 16, 17, 20
 Progesterone receptor, 124
 Progesterone, 33
 1,2-Propane diol, 18
 Propargylic alcohol, 178
 Prostatitis, 40
 Protease inhibitors, 84, 86, 90, 92
 Protective personnel equipment. *See* PPE, 12, 17
 Protein binding, 45, 48, 58, 61, 203
 Protein-bound, 120, 162–166
 Prozac[®], 253
Pseudomonas aeruginosa, 47, 48, 51. *See also* *P. aeruginosa*
Pseudomonas Cepacia (PS-D), 211
 Pseudopolymorphs. *See* solvates, 23
 Pyridine hydrogenation, 248
 (1*R*, 2*S*)-*N*-Pyrrolidinylnorephedrine, 87

- QSAR, 3D, 8
QT prolongation, 42
Quinapril, 148–150. *See also* Accupril®
Quinaprilat, 149
(–)-Quinic acid, 100
Quinolone generations, 40–42
Quinolones, 39–69
- R86183, 84, 85
Raloxifene, 33. *See also* Evista®
Ramipril, 151–154. *See also* Altace®
Ramiprilat, 151
Raney-Cobalt catalyst, 106
Raney-Nickel, 49, 51, 62, 63, 101, 123, 124,
147, 148, 232, 239, 246–247
RAS, 144–145
Reactor chips, 7
Reagents, air-sensitive, 17
Rearrangement, Dimroth, 19
Reboxetine, 201, 202
Recombinant human PPAR- α and PPAR- γ
receptors, 124
Recrystallization, 177, 181, 220
Reductive Alkylation, 204
Reductive amination, 92, 134–135, 244, 246
Relenza®, 95–97, 110–112
Renal elimination, 120
Renal tubular secretion, 98
Renin angiotensin system, 130. *See also* RAS
Renin, 130
Renin-angiotensin, 160
Repaglinide, 119. *See also* Prandin®
Repke, D., 247
Rescriptor®, 83. *See also* Delavirdine
Residue product, 13
Resolution, 80, 200, 207–208, 210–211,
220
Retinoid X receptor. *See* RXR
Reuptake®, 199, 201, 202. *See also* Serotonin,
Norepinephrine
5-HT Antagonist/Reuptake Inhibitor, 202
NE/DA Dual Reuptake Inhibitor, 202
Selective NE Reuptake Inhibitor, 202. *See
also* SNRI
Dual Selective Serotonin Norepinephrine
Reuptake Inhibitors, 199. *See also*
SSNRI
Selective Serotonin Reuptake Inhibitors,
201. *See also* SSRI
Reverse transcriptase. *See* RT
- Rhodium on aluminum oxide, 204, 231
Rhodium, 204, 212
Rhone-Poulenc Rorer, 220
Rifampicin, 219
Rimantadine, 96
Ritalin®, 241, 244
Ritalinic acid, 249
Ritonavir. *See* Norvir, 23–24
RNH-6270, 131–132, 137–138
Roche, 95, 96, 104
Rosiglitazone maleate, 117, 121, 122.
See also Avandia®
[¹⁴C]-Rosiglitazone maleate, 122
Rosuvastatin, 169, 174–176. *See also* Crestor®
Route design, 24–26
Route of Administration, 203
RT, 84, 85, 87, 91
Rugged operations, 16, 19, 20, 24
Rule-of-Five, 3–4
Ruthenium, 212
Diphosphine/diamine ruthenium complex,
212
Diphosphine ruthenium complex, 212
RXR, 121, 124
- S. aureus*. *See also* *Staphylococcus aureus*
S. pneumoniae. *See also* *Streptococcus
pneumoniae*
S. pyogenes. *See also* *Streptococcus pyogenes*
Safe operations, 12
Safety hazard assessments, 12
SAM, 38
Sandoz, 169, 171
Sankyo, 137, 159, 177
Sanofi, 135–136
Sanofi-Aventis, 151, 215, 220
Saponification, 46
SAR, 98, 187. *See also* Structure Activity
Relationship
Sartans, 130
SBDD, 97
Scalable processes, 16
Scale down to scale up, 15
SCH-48461, 185
SCH-58235, 186
Schedule IV drug classification, 217
Schering-Plough, 39, 47, 64, 185
Secondary alcohol metabolite. *See* SAM
Sedatives, 217
Seizures, 226

- Selective Estrogen Receptor Modulator.
See SERM
- Selective NE Reuptake Inhibitor, 202.
See also SNRI
- Selective Serotonin Reuptake Inhibitors,
 201. *See also* SSRI
- Semi-batch processing. *See* batch
 processing, 20
- As alternative to batch processing for
 ketoester formation, 21–22
- Sepracor, 216, 220
- SERM, 33
- Serotonergic, 202, 203
- Adverse Events, 203
- Receptors, 202
- Serotonin re-uptake transporter. *See* SERT
- Serotonin, 199–202. *See also* 5-HT,
 Monoamine
- Dual Selective Serotonin Norepinephrine
 Reuptake Inhibitors, 202. *See also*
 SSNRI
- Selective Serotonin Reuptake Inhibitors,
 201. *See also* SSRI
- Serratia marcescens*, 59
- SERT (serotonin transporter), 202, 253. *See
 also* Serotonin, Transporter
- Sexually transmitted diseases, 40
- Shafi'ee, A., 248
- Sharpless, K. B., 254–255
- Shibasaki, 109, 110
- Shigella spp.*, 48
- (–)-Shikimic acid, 99–102, 105
- Shiongi, 169, 174
- Shire, 241, 250
- Sialic acid, 97, 111
- Sialidase, 97
- Side-effects, 90, 92
- [3,3]-Sigmatropic rearrangement, 171
- Simian immunodeficiency
 virus, 85
- Simvastatin, 125, 170. *See also* Zocor[®]
- Sinusitis, 47, 57
- Siscrad[®], 160, 161. *See also* Cinaldipine
- Sitafloxacin, 41, 42
- Skin structure infections, 47, 57
- Sleep, 216
- Slow-release formulation, 246, 250
- SmithKline Beecham, 138–139
- S_N2 displacement, 36, 37, 38
- S_NAr reaction, 38, 53, 256
- SNRI (serotonin norepinephrine reuptake
 inhibitor), 202–203. *See also* Serotonin
- SODAS technology. *See* OROS technology
- Sodium borohydride, 218
- Sodium sulfate, 16, 19
- Sodium triacyloxyborohydrides, 54
- Solid phase synthesis, 7
- Solubility, 2
- Solution phase synthesis, 7
- Solvates. *See* polymorphs, 23
- Solvent displacement, 17
- Solvent selection, 18–19
- Sonata[®], 215
- Sonolyses, 20
- Sparfloxacin, 41, 42, 44, 45, 57
- Specifications, 16
- Sporanox[®], 71, 74
- Squalene epoxidase, 92
- Src SH2, 6
- SSNRI (selective serotonin norepinephrine
 reuptake inhibitor), 199, 202–203.
See also Serotonin, Norepinephrine,
 Reuptake
- SSRI (selective serotonin reuptake inhibitor),
 201–203. *See also* Serotonin, Reuptake
- Stability, of process streams and isolated
 compounds, 23
- Staphylococcus aureus*, 44, 47, 48, 57, 64.
See also *S. aureus*
- Staphylococcus epidermis*, 151
- Static mixer, 20–21
- Statins, 169–182
- Steady-state plasma level, 41
- Stereoselective, 204, 208
- Stille reaction, 65, 66, 209
- Stimulant, 242–243, 253
- Stocrin[®], 83. *See also* Efavirenz and Sustiva[®]
- STR. *See also* Structure Toxicity
 Relationship
- Straterra[®], 241, 243, 253
- Streptococcus pneumoniae*, 47, 48, 57,
 60, 64. *See also* *S. pneumoniae*
- Streptococcus pyogenes*, 57, 64. *See also*
S. pyogenes
- Structure-Activity Relationship, 44, 45.
See also SAR
- Structure-based drug design, 2, 4.
See also SBDD
- Structure-Toxicity Relationship, 44, 45.
See also STR

- Sub-Saharan Africa, 84
Substance P antagonist, 200
Suicide inhibitors, 40
Sulfathiazole, 23
Sulfonylurea drugs, 119
SUMIPAX OA-4200 column, 49
Sustiva[®], 83. *See also* Efavirenz
Suzuki cross-coupling, 65–66, 133–134
Swern oxidation, 13, 134–135
Synapse, 200
Synergistic effect, 90
Syn-reduction, 174
Synthetic chemistry, 1
Synthetic methodology, 7
Sycor[®], 160, 161. *See also* Nisoldipine
- $T_{1/2}$, 98, 146, 160, 162
Tadalafil. *See* Cialis[®], 24
Takeda, 117, 136–137
Tamiflu[®], 95–110
Tamoxifen, 33. *See also* Nolvadex
D-(+)-Tartrate, 58–59
L-(+)-Tartrate, 58–59
TCA (tricyclic antidepressants), 201–202
T_{max} (time to maximum concentration), 203
Technology transfer, 20
Telescoping, 25–26
Telmisartan, 130–132, 139
Temafloracin, 41, 42, 44
Temperatures
 Cryogenic, 16, 17
 High, 16
 In multi-purpose equipment, 16
Teprotide, 145
Tequin[®]. *See also* gatifloxacin
Teratogen, 18
Terbinafine, 72. *See also* Lamisil[®]
Testosterone 5 α -reductase, 34
Tetrabutylammonium sulfate, 204
Tetrahydroisoquinoline, 149
Teva, 53
TFA. *See* trifluoroacetic acid, 17, 24
Thermal convergence, 205
Thermolyses, 20
Thiazolidine-2,4-dione, 122
Thiazolidinediones. *See* TZDs
Thionyl chloride, 205, 218, 220
Thiophene, 207, 209, 210, 212
Thrombin, 5
Tiagabine, 227
Tioconazole 72–73
Tissue factor VIIa complex, 5
 T_{max} , 98, 121, 146
TNF- α , 120
Tolerance, 217
Toluenesulfonic acid. *See* *p*-TsOH, 17–18
Tomoxetine, 253. *See also* Straterra[®]
Topoisomerase II, 43. *See also* DNA gyrase
Topoisomerase IV, 43, 44
Tosufloxacin, 41, 42, 43, 44
Toxicity, 85
Toyama, 39
TPAP, 176
Transdermal formulation, 250
Transesterification, 106, 177
Transferability, 13
Transition-metal catalyzed cross-coupling reactions, 7
Transketalization, 100, 101
Transmembrane, 162
Transporter, 146, 148, 200, 202.
 See also Serotonin, Norepinephrine, Monoamine
 5-HT Transporter, 202. *See also* SERT
 NE Transporter, 202. *See also* NET
Tributyltin azide, 134–136
2,2,2-Trichloroethyl chloroformate, 207
1,2,3-Trichloropropane, 11
Tricyclic Antidepressants, 201.
 See also TCA
Tricyclic dipyridodiazepinone, 85
Trifluoroacetamide, 148
Trifluoroacetic acid. *See* TFA, 17, 24
Triglycerides, 124
Triisopropylborate, 65
Trimethylsilylanyl-propynal, 181
Tri-*n*-butylstannylvinyl ethoxide, 171, 172
Triphenylmethyl group deprotection, 133–134, 136
Triphenylphosphite methyl iodide, 50
N-Tritylaziridine, 99
Tritylphenyl tetrazole, 133
Trovafloracin, 41, 42, 44
p-TsOH. *See* toluenesulfonic acid, 17–18
Tumor necrosis factor- α . *See* TNF- α , 120
Type 2 diabetes, 117–124
Tyramine reuptake, 201
Tyrosine kinase inhibitor, 19
TZDs, 120–125

- U.S. Federal Drug Administration.
See FDA
- U.S. Drug Enforcement Agency.
See DEA
- Uncomplicated skin infections, 47, 57
- Unit operations, 19–22, 23
- Upjohn, 90
- Upper and lower respiratory
infections, 40
- Ureas, unsymmetrical *and* symmetrical, 22
- Urinary tract infections, 40, 47
- Use-tests, 12
-
- Valsartan, 129, 131–132, 134–135
- Vascular tissue, 164
- Vasotec[®], 21, 146–147. *See also* enalapril
- Venlafaxine, 199, 202–204. *See also* Effexor[®]
- Verapamil, 160, 162
- Vfend[®], 71, 77
- Vigabatrin, 227
- Vilsmeier–Haack reaction, 133, 173
- Vilsmeier–Haack reagent, 35
- Vinyl silane, 178
- Viracept[®]. *See* nelfinavir mesylate, 19–20
- Viral RNA, 85
- Viramune[®], 83. *See also* nevirapine
- Viscous oils, difficulties in
formulating, 23
- Volume of distribution (V_d), 38, 48, 58,
61, 203
- von Itzstein, 110
- Voriconazole, 71, 77–80. *See also* Vfend[®]
- Vyvanse[®], 244
-
- (*R*)-Warfarin, 125
- (*S*)-Warfarin, 125
- Warner-Lambert, 148
- Weinreb amide, 250–251
- Winkler, J., 249
- Wittig olefination, 176
- Wittig reaction, 250
- Wohl–Ziegler reaction, 36
- Woodward, Robert Burns, 95
- Workup, 22–23
- Wyeth, 215
- Wyeth-Ayerst Laboratories, 199
-
- X-ray crystal structures, 84
- X-ray crystallography, 4
- X-ray diffraction, 108
-
- Y(O^{*i*}Pr)₃, 109
- Y181C, 85, 87
- Yb(OTf)₃, 102
- Ytterbium trifluoromethanesulfonate.
See Yb(OTf)₃
-
- Zaleplon, 215, 219. *See also* Sonata[®]
- Zanamivir, 95–97, 110–112.
See also Relenza[®]
- Zanedip[®], 160, 161. *See also* Lercanidipine
- Zestril[®], 147–148
- Zetia[®], 183
- Zinc powder, 207
- Zocor[®], 170. *See also* Simvastatin
- Zolpidem, 215, 217. *See also* Ambien[®]
- Zopiclone, 220