

Table of Contents

Volume 12: Five-Membered Heteroarenes with Two Nitrogen or Phosphorus Atoms

12.1	Product Class 1: Pyrazoles	
12.1.5	Pyrazoles A. C. Götzinger and T. J. J. Müller	2017
12.1.5	Pyrazoles	1
12.1.5.1	Synthesis by Ring-Closure Reactions	2
12.1.5.1.1	By Formation of One N—C and Two C—C Bonds	2
12.1.5.1.1.1	Fragments N—N—C, C, and C	2
12.1.5.1.1.1.1	Method 1: One-Pot Synthesis of Phosphonyl- and Sulfonylpyrazoles from Aldehydes and a Bestmann–Ohira Reagent	2
12.1.5.1.1.1.2	Method 2: Synthesis from Aldehydes, 1,3-Dicarbonyls or Analogues, and Diazo Compounds	3
12.1.5.1.2	By Formation of Two N—C Bonds	5
12.1.5.1.2.1	Fragments C—C—C and N—N	5
12.1.5.1.2.1.1	From 1,3-Dicarbonyl Compounds (and Synthetic Equivalents) and Hydrazines	5
12.1.5.1.2.1.1.1	Method 1: Synthesis from Alk-2-en-1-ones with a Leaving Group in Position 3 and Hydrazines	5
12.1.5.1.2.1.1.1.1	Variation 1: From Haloalkenones or Sulfonylalkenones and Hydrazines ...	5
12.1.5.1.2.1.1.1.2	Variation 2: From Enaminones and Hydrazines	7
12.1.5.1.2.1.1.1.3	Variation 3: From α,β -Unsaturated- β -alkoxy Ketones and Hydrazines ...	9
12.1.5.1.2.1.1.1.4	Variation 4: From α,β -Unsaturated- β -(alkylsulfanyl) Ketones and Hydrazines	10
12.1.5.1.2.1.1.2	Method 2: Synthesis from Alk-2-en-1-ones and Hydrazines Followed by Dehydrogenation	12
12.1.5.1.2.1.1.3	Method 3: Synthesis from Alk-2-en-1-ones and Tosylhydrazine Followed by Elimination	14
12.1.5.1.2.1.1.4	Method 4: Synthesis from β,γ -Unsaturated α -Oxo Esters and Hydrazones	14
12.1.5.1.2.1.1.5	Method 5: Synthesis from Propargylic Aldehydes and Hydrazines	15
12.1.5.1.2.1.1.5.1	Variation 1: From 3-Ferrocenylpropynal	15
12.1.5.1.2.1.1.5.2	Variation 2: From (Het)aryl Iodides, Propynal Diethyl Acetal, and Hydrazine	16
12.1.5.1.2.1.1.6	Method 6: Synthesis from Alk-2-yn-1-ones and Hydrazines	18
12.1.5.1.2.1.1.7	Method 7: Synthesis from Dialkyl Acetylenedicarboxylates, Phenylhydrazine, and Aryl Chlorides	20

12.1.5.1.2.1.1.8	Method 8:	Synthesis from Alk-3-yn-1-ones and Hydrazines	20
12.1.5.1.2.1.1.9	Method 9:	Synthesis from 1,3-Diketones and Hydrazines	21
12.1.5.1.2.1.1.9.1	Variation 1:	From Dioxo Oximes and Hydrazine Hydrate	23
12.1.5.1.2.1.1.9.2	Variation 2:	From 1,3-Diketones, Allyltrimethylsilanes, and Hydrazines ...	24
12.1.5.1.2.1.1.9.3	Variation 3:	From 1,3-Diketones and Sulfonylhydrazines	25
12.1.5.1.2.1.1.9.4	Variation 4:	From Acetylacetone, Adamantyl Diazirine, and Arylmetal Species	26
12.1.5.1.2.1.1.10	Method 10:	Synthesis from 1,3-Diketones and Arylhydrazones	28
12.1.5.1.2.1.1.11	Method 11:	Synthesis from β -Oxo Esters and Hydrazine Hydrochloride ..	29
12.1.5.1.2.1.1.12	Method 12:	Synthesis from 1,3-Dicarbonyls, Aryl Halides or Arylboronic Acids, and Di- <i>tert</i> -butyl Azodicarboxylate	30
12.1.5.1.2.1.1.13	Method 13:	Synthesis from β -Oxo Amides and Hydrazines in the Presence of Lawesson's Reagent	31
12.1.5.1.2.1.1.14	Method 14:	Synthesis from β -Oxo Acylsilanes and Hydrazines	32
12.1.5.1.2.1.1.15	Method 15:	Synthesis from 1,3-Diaryl-3-thioxopropan-1-ones or 1,3-Diaryl-3-(methylsulfanyl)prop-2-en-1-ones and Arylhydrazines	33
12.1.5.1.2.1.1.16	Method 16:	Synthesis from β -Oxo Dithioesters or β -Oxo Thioesters and Hydrazines	35
12.1.5.1.2.1.1.17	Method 17:	Synthesis from Sodium Acetylacetonate Hydrate, Aryl Isothiocyanates, and Hydrazine Hydrate	36
12.1.5.1.2.1.1.18	Method 18:	Synthesis from Allenic Ketones and Hydrazines	38
12.1.5.1.2.1.1.19	Method 19:	Synthesis from 3-Chloroenals and Hydrazines	40
12.1.5.1.2.1.1.19.1	Variation 1:	One-Pot Synthesis from Aryl Halides, α -Bromocinnamaldehyde, and Tosylhydrazine	40
12.1.5.1.2.1.1.20	Method 20:	Synthesis from Propargylic Alcohols and Tosylhydrazine or <i>N</i> -Acetyl- <i>N</i> -tosylhydrazine	42
12.1.5.1.2.1.1.21	Method 21:	Synthesis from Enynes or Diynes and Hydrazine	44
12.1.5.1.2.1.1.22	Method 22:	Synthesis from α -Cyano Ketones and Hydrazines	46
12.1.5.1.2.1.1.23	Method 23:	Synthesis from Vinamidinium Salts and Arylhydrazines	46
12.1.5.1.2.1.1.24	Method 24:	Synthesis from Morita–Baylis–Hillman Adducts and Hydrazines	48
12.1.5.1.2.1.1.25	Method 25:	Synthesis from α -Cyanoalkenes Bearing a Leaving Group and Hydrazines	49
12.1.5.1.2.1.1.26	Method 26:	Synthesis from α,β -Bis(tosyloxy) Ketones and Phenylhydrazine	51
12.1.5.1.2.1.1.27	Method 27:	Synthesis from 2-(1,3-Dithian-2-yl) 1,3-Diketones and Hydrazine	52
12.1.5.1.2.1.1.28	Method 28:	Synthesis from α -Epoxy Ketones and Semicarbazide or Hydrazines	52
12.1.5.1.2.1.1.29	Method 29:	Synthesis from Ethyl 3-[(Dimethylamino)methylene]pyruvate or Diethyl 3-[(Dimethylamino)methylene]-2-oxosuccinate and Hydrazines	53
12.1.5.1.2.1.1.30	Method 30:	Synthesis from Alk-3-en-1-ones and Phenylhydrazine	55

12.1.5.1.2.1.2	From Other Compounds and Hydrazine	56
12.1.5.1.2.1.2.1	Method 1: Synthesis from But-3-yn-1-ol and Arylhydrazines	57
12.1.5.1.2.1.2.2	Method 2: Synthesis from Nitroallylic Acetates and Tosylhydrazine	57
12.1.5.1.2.1.2.3	Method 3: Synthesis from 1-Aryl-2-tosyldiazenes and Allylic Carbonates ..	58
12.1.5.1.2.1.2.4	Method 4: Synthesis from 1,3-Diols and Hydrazines	59
12.1.5.1.2.1.2.5	Method 5: Synthesis from Enaminones and Arenediazonium Salts	60
12.1.5.1.2.1.2.6	Method 6: Synthesis from Allyl Aryl Ketones, Arenediazonium Salts, and Sodium Trifluoromethanesulfonate	61
12.1.5.1.3	By Formation of One N—C and One C—C Bond	62
12.1.5.1.3.1	Fragments N—N—C and C—C	62
12.1.5.1.3.1.1	Method 1: Synthesis from Diazo Compounds and Alkynes, Allenes, or Alkenes	62
12.1.5.1.3.1.1.1	Variation 1: From Tosylhydrazones and Alkynes	63
12.1.5.1.3.1.1.2	Method 2: Synthesis from Diazoacetates and Carbonyl Compounds	64
12.1.5.1.3.1.1.3	Method 3: Synthesis from Hydrazones and Alkenes	65
12.1.5.1.3.1.1.4	Method 4: Synthesis from Hydrazones and Alkynes	67
12.1.5.1.3.1.1.5	Method 5: Synthesis from Trichloroacetylhydrazones and β -Oxo Esters ..	68
12.1.5.1.3.1.1.6	Method 6: Synthesis from Hydrazones and Vicinal Diols	69
12.1.5.1.3.1.1.7	Method 7: Synthesis from Hydrazonoyl Halides and Alkynes or Alkenes with a Leaving Group	70
12.1.5.1.3.1.1.8	Method 8: Synthesis from Hydrazonoyl Halides and Carbonyl Compounds	72
12.1.5.1.3.1.1.9	Method 9: Synthesis from Enol Diazoacetates and Donor–Acceptor Substituted Hydrazones	73
12.1.5.1.3.1.1.10	Method 10: Synthesis from a Bestmann–Ohira Reagent and Alkenes or Alkynes	74
12.1.5.1.3.1.1.10.1	Variation 1: From Bestmann–Ohira Reagent and α,β -Unsaturated Aldehydes	75
12.1.5.1.3.1.1.11	Method 11: Synthesis from Ugi Adducts	76
12.1.5.1.3.1.1.12	Method 12: Synthesis from Dialkyl Azodicarboxylates and Allenic Esters ..	77
12.1.5.1.3.1.1.13	Method 13: Synthesis from <i>N</i> -Propargylhydrazones by Rearrangement ...	77
12.1.5.1.3.2	Fragments N—N—C—C and C	78
12.1.5.1.3.2.1	Method 1: Synthesis from Hydrazones under Vilsmeier Conditions	78
12.1.5.1.3.2.2	Method 2: Synthesis from Hydrazones, Dimethylformamide, and Cyanuric Chloride	79
12.1.5.1.3.2.3	Method 3: Synthesis from Hydrazones by Acylation	80
12.1.5.1.3.2.4	Method 4: Synthesis from α -Halo Ketone Hydrazones and Isocyanides ..	82
12.1.5.1.3.2.5	Method 5: Synthesis from Acetophenone Hydrazones and Aldehydes ...	82
12.1.5.1.3.2.6	Method 6: Synthesis from α -Halo Hydrazones and Enals	83
12.1.5.1.4	By Formation of One N—N Bond	84
12.1.5.1.4.1	Fragment N—C—C—C—N	84
12.1.5.1.4.1.1	Method 1: Pyrazole 2-Oxides from β -Nitro Hydrazones	84

12.1.5.1.4.1.2	Method 2:	Synthesis from Cyclopropyl Oximes	85
12.1.5.1.5	By Formation of One N—C Bond		86
12.1.5.1.5.1	Fragment N—N—C—C—C		86
12.1.5.1.5.1.1	Method 1:	Synthesis from Acetylene- or Allene-Bearing Hydrazones	87
12.1.5.1.5.1.2	Method 2:	Synthesis from α,β -Unsaturated Hydrazones	88
12.1.5.1.5.1.3	Method 3:	Synthesis from β -Oxo or β -Carboxy Hydrazones	90
12.1.5.1.5.1.4	Method 4:	Synthesis from Semicarbazones formed by Reaction of 3-Siloxy-1,3-dienes with 1,2-Diazabuta-1,3-dienes	90
12.1.5.1.5.1.5	Method 5:	Synthesis from Acetylenic Nitrosoamines	91
12.1.5.1.5.1.6	Method 6:	Synthesis from Propargylic Hydrazides	92
12.1.5.1.5.1.7	Method 7:	Synthesis from Vinyl Diazo Compounds and Arenediazonium Salts	93
12.1.5.1.5.1.8	Method 8:	Synthesis from 1-Chloro-3-hydrazonopropan-2-ones	94
12.1.5.1.5.1.9	Method 9:	Synthesis from (Difluoroalkenyl)tosylhydrazines	95
12.1.5.1.5.1.10	Method 10:	Synthesis from β -Azo Hydrazones	96
12.1.5.1.6	By Formation of One N—C and One N—N Bond		97
12.1.5.1.6.1	Fragments N—C—C—C and N		97
12.1.5.1.6.1.1	Method 1:	Synthesis from 3-Azidopropenals and Arylamines	97
12.1.5.1.6.1.2	Method 2:	Synthesis from α -(1,3-Dithian-2-yl) Enamine Ketones and Primary Amines	98
12.1.5.1.6.1.3	Method 3:	Synthesis from β -Formyl Enamides and Hydroxylamine	99
12.1.5.1.7	By Formation of One N—N and Two N—C Bonds		100
12.1.5.1.7.1	Fragments C—C—C, N, and N		100
12.1.5.1.7.1.1	Method 1:	Synthesis from an Oxaziridine, Primary Amines, and Heptane- 3,5-dione	100
12.1.5.1.8	By Formation of One C—C and Two N—C Bonds		101
12.1.5.1.8.1	Fragments C—C, C, and N—N		101
12.1.5.1.8.1.1	Method 1:	Synthesis from Acyl Chlorides, Terminal Alkynes, and Hydrazines	101
12.1.5.1.8.1.1.1	Variation 1:	Tetrasubstituted Pyrazoles from Acyl Chlorides, Terminal Alkynes, and Hydrazines with Subsequent Halogenation/ Suzuki Coupling	102
12.1.5.1.8.1.1.2	Variation 2:	Biaryl-Substituted Pyrazoles from Acyl Chlorides, Terminal Alkynes, and Hydrazines with Subsequent Suzuki Coupling ..	104
12.1.5.1.8.1.1.3	Variation 3:	From Glyoxylic Acids, Alkynes, and Hydrazines by In Situ Activation	105
12.1.5.1.8.1.2	Method 2:	Synthesis from Arylglyoxal Monohydrates, Tosylhydrazine, and Alkenes	107
12.1.5.1.8.1.3	Method 3:	Synthesis from Terminal Alkynes, Carbon Monoxide, Aryl Iodides, and Hydrazines	107
12.1.5.1.8.1.4	Method 4:	Synthesis from Phthalimides, Lithium Arylacetylides, and Hydrazines	109

12.1.5.1.8.1.5	Method 5:	Synthesis from Aryl Bromides, Carbon Monoxide, Vinyl Ethers, and Hydrazines	110
12.1.5.1.8.1.6	Method 6:	Synthesis from <i>N</i> -Hydroxyimidoyl Chlorides, Terminal Alkynes, and Hydrazines	111
12.1.5.1.8.1.7	Method 7:	Synthesis from Aldehydes, Terminal Alkynes or Allenes, and Hydrazines	113
12.1.5.1.8.1.8	Method 8:	Synthesis from Aldehydes, 1,3-Dicarbonyl Compounds, and Hydrazines	114
12.1.5.1.8.1.8.1	Variation 1:	From Dimethylformamide Dimethyl Acetal, 1,3-Dicarbonyls, and Hydrazines	117
12.1.5.1.8.1.9	Method 9:	Synthesis from Aldehydes, Malono Derivatives, and Arylhydrazines	119
12.1.5.1.8.1.10	Method 10:	Synthesis from Aldehydes, 1,1-Bis(methylsulfanyl)-2-nitroethene, and Hydrazine	120
12.1.5.1.8.1.11	Method 11:	Synthesis from Aldehydes, Dimethyl Acetylenedicarboxylate, and Arylhydrazines	121
12.1.5.1.8.1.12	Method 12:	Synthesis from Aldehydes, Hydrazines, and Nitroalkenes or Enols	122
12.1.5.1.8.1.13	Method 13:	Synthesis from Alkynes, Isocyanides, Amines, and Hydrazines	123
12.1.5.1.8.1.13.1	Variation 1:	From Alkynes, Isocyanides, and Hydrazines	124
12.1.5.1.8.1.14	Method 14:	Synthesis from Dialkyl Acetylenedicarboxylates, Isocyanides, and Hydrazine Carboxamides	126
12.1.5.1.8.1.15	Method 15:	Synthesis from Aldehydes, Vinyl Azides, and Tosylhydrazine	126
12.1.5.1.8.1.16	Method 16:	Synthesis from Ketone Enolates, Acid Chlorides, and Hydrazines	127
12.1.5.1.8.1.17	Method 17:	Synthesis from Ketones, Diethyl Oxalate, and Hydrazines	129
12.1.5.1.8.1.18	Method 18:	Synthesis from Terminal Alkynes, Carbon Dioxide and Hydrazines	130
12.1.5.1.8.1.19	Method 19:	Synthesis from β -Oxo Esters, 1,1,2,2-Tetrafluoroethyl- <i>N,N</i> -dimethylamine, and Hydrazines	131
12.1.5.1.9	By Formation of One C—C, One N—N, and One N—C Bond		132
12.1.5.1.9.1	Fragments C—C, C—N, and N		132
12.1.5.1.9.1.1	Method 1:	Synthesis from Allenates, Amines, and Nitriles	132
12.1.5.1.9.2	Fragments C—C—N, C, and N		133
12.1.5.1.9.2.1	Method 1:	Synthesis from Oxime Acetates, Anilines, and Paraformaldehyde	133
12.1.5.1.10	By Formation of One C—C and One N—N Bond		134
12.1.5.1.10.1	Fragments N—C—C and C—N		134
12.1.5.1.10.1.1	Method 1:	Synthesis from Enamines and Nitriles	134
12.1.5.1.11	By Formation of One C—C Bond		135
12.1.5.1.11.1	Fragment C—N—N—C—C		135
12.1.5.1.11.1.1	Method 1:	Synthesis from <i>N,N</i> -Disubstituted Hydrazones	135
12.1.5.1.12	By Formation of Two N—C and Two C—C Bonds		136

12.1.5.1.12.1	Fragments C, C, C, and N—N	136
12.1.5.1.12.1.1	Method 1: Synthesis from Aldehydes, Arylglyoxal Monohydrates, and Tosylhydrazine	136
12.1.5.2	Synthesis by Ring Transformation	137
12.1.5.2.1	Ring Enlargement	137
12.1.5.2.1.1	From Three-Membered Carbocycles	137
12.1.5.2.1.1.1	Method 1: Synthesis from <i>trans</i> -1-Acyl-2-arylcylopropanes	137
12.1.5.2.1.2	From Four-Membered Carbocycles	138
12.1.5.2.1.2.1	Method 1: Synthesis from 3-Ethoxycyclobutanones and Hydrazines	138
12.1.5.2.2	Retention of Ring Size	139
12.1.5.2.2.1	Method 1: Synthesis from 1,2,3-Oxadiazolium-5-olates (Sydnones)	139
12.1.5.2.2.1.1	Variation 1: From Sydnones and Alkynes	139
12.1.5.2.2.1.2	Variation 2: From Sydnones and Chalcones	141
12.1.5.2.2.1.3	Variation 3: From Sydnones and Dihaloalkenes	141
12.1.5.2.2.2	Method 2: Synthesis from Isoxazoles	142
12.1.5.2.2.3	Method 3: Synthesis from Isothiazoles	143
12.1.5.2.3	Ring Contraction	144
12.1.5.2.3.1	From Six-Membered Rings	144
12.1.5.2.3.1.1	Method 1: Synthesis from Triazines and α -Chloro Carbanions	144
12.1.5.2.3.1.2	Method 2: Synthesis from 4-Chloroquinolines and Hydrazine	145
12.1.5.2.3.1.3	Method 3: From Cyclic Alkenones and Hydrazine	146
12.1.5.2.4	From One Four- and One Six-Membered Ring	149
12.1.5.2.4.1	Method 1: Synthesis from Thietanones and 1,2,4,5-Tetrazines	149
12.1.5.3	Aromatization	150
12.1.5.3.1	By Dehydrogenation	150
12.1.5.3.1.1	Method 1: Oxidation of Dihydropyrazoles	150
12.1.5.3.1.2	Method 2: Synthesis of 3-Benzoyl-4-styryl-4,5-dihydropyrazoles and Oxidation to the Corresponding Pyrazoles	151
12.1.5.3.1.3	Method 3: Synthesis of 5-(Pyrazol-4-yl)-4,5-dihydropyrazoles and Oxidation to the Corresponding Bipyrazoles	153
12.1.5.3.2	By Elimination	154
12.1.5.3.2.1	Method 1: 1-Acyl-4-iodo-1 <i>H</i> -pyrazoles by Iodine Monochloride Induced Dehydration/Iodination	154
12.1.5.3.2.2	Method 2: Synthesis from 4-(Benzotriazol-1-yl)-4,5-dihydropyrazoles ...	155
12.1.5.3.3	By Addition	158
12.1.5.3.3.1	Method 1: Conjugate Addition of Diarylphosphine Oxides to 4-Alkylidene-2,4-dihydro-3 <i>H</i> -pyrazol-3-ones	158
12.1.5.4	Synthesis by Substituent Modification	159
12.1.5.4.1	Substitution of Existing Substituents	159
12.1.5.4.1.1	Of Hydrogen	159

12.1.5.4.1.1.1	Method 1:	C-Acylation, C-Alkylation, and C-Allylation	159
12.1.5.4.1.1.1.1	Variation 1:	C-Acylation with Carboxylic Acid Anhydrides	159
12.1.5.4.1.1.1.2	Variation 2:	C-Alkylation	161
12.1.5.4.1.1.1.3	Variation 3:	<i>ortho</i> -Allylation of (Phenylsulfinyl)pyrazoles	162
12.1.5.4.1.1.2	Method 2:	Halogenation	163
12.1.5.4.1.1.3	Method 3:	Nitration	166
12.1.5.4.1.1.4	Method 4:	Full Substitution via Regioselective Metalation	168
12.1.5.4.1.2		Of Carbon Functionalities	170
12.1.5.4.1.2.1	Method 1:	Deformylation or Decarboxylation	170
12.1.5.4.1.3		Of Heteroatoms	171
12.1.5.4.1.3.1		Substitution of Halogen	171
12.1.5.4.1.3.1.1	Method 1:	Nitrodeiodination	171
12.1.5.4.1.3.1.2	Method 2:	Nucleophilic Substitution of Chloropyrazoles	172
12.1.5.4.1.3.1.3	Method 3:	Preparation of 3-Substituted Pyrazoles via Bromine–Lithium Exchange	173
12.1.5.4.1.3.1.4	Method 4:	Palladium-Catalyzed Dehalogenation of Halopyrazoles	174
12.1.5.4.1.3.1.5	Method 5:	Pyrazole-4-boronic Acids from 4-Bromopyrazoles	175
12.1.5.4.1.3.2		Substitution of Nitrogen Functional Groups	176
12.1.5.4.1.3.2.1	Method 1:	Nucleophilic Substitution of 3,4,5-Trinitro-1 <i>H</i> -pyrazoles	176
12.1.5.4.2		Addition Reactions	178
12.1.5.4.2.1		Addition of Organic Groups	178
12.1.5.4.2.1.1	Method 1:	N-Alkylation	178
12.1.5.4.2.1.2	Method 2:	N-Arylation	180
12.1.5.4.3		Modification of Substituents	181
12.1.5.4.3.1	Method 1:	C–H Activation of the <i>ortho</i> -Position in <i>N</i> -Arylpyrazoles	181
12.1.5.4.3.2	Method 2:	Pyrazole-Substituted Chalcones from Pyrazole- 4-carbaldehydes	184
12.1.5.4.3.3	Method 3:	Synthesis of 4-(Arylmethyl)pyrazoles from (Pyrazol- 4-yl)methanol Derivatives	185
12.1.5.4.3.4	Method 4:	Conversion of (Trifluoromethyl)pyrazoles into Pyrazolecarboxylic Acids or Pyrazolecarbonitriles	186
12.1.5.4.3.5	Method 5:	Hydrovinylation of Alkynes with 1-Vinylpyrazoles	187
12.1.5.4.4		Cross-Coupling Reactions	188
12.1.5.4.4.1		Cross-Coupling Reactions at Position 1	188
12.1.5.4.4.2		Cross-Coupling Reactions at Position 3	190
12.1.5.4.4.2.1	Method 1:	Of Pyrazol-3-yl Trifluoromethanesulfonates, Nonfluorobutanesulfonates, or Iodides	190
12.1.5.4.4.2.2	Method 2:	1-(Arylmethyl)-3-hetarylpyrazoles by Suzuki Coupling	192
12.1.5.4.4.3		Cross-Coupling Reactions at Position 4	193
12.1.5.4.4.3.1	Method 1:	C–H Activation	193
12.1.5.4.4.3.2	Method 2:	Cross Coupling of 4-Metalated Pyrazole Derivatives	195

12.1.5.4.4.3.3	Method 3:	Cross Coupling of 4-Halopyrazoles with Arylmetal Species ...	197
12.1.5.4.4.4		Cross-Coupling Reactions at Position 5	198
12.1.5.4.4.4.1	Method 1:	C—H Activation	198
12.1.5.4.4.4.2	Method 2:	Suzuki Coupling of Pyrazol-5-yl Trifluoromethanesulfonates .	199
12.1.5.4.4.4.3	Method 3:	Cross Coupling of 5-Metalated Pyrazole Derivatives	201
12.1.5.4.4.5		Multiple Substitution	203
12.1.5.4.4.5.1	Method 1:	C—H Activation	203
12.1.5.4.4.5.2	Method 2:	Regioselective Metalation of Pyrazole <i>N</i> -Oxides	206
12.1.5.4.4.5.3	Method 3:	Regioselective Metalation Using a Switchable Metal-Directing Group	209
12.1.5.4.4.5.4	Method 4:	Tetraaryl-Substituted Pyrazoles by S _N Ar Reaction/Suzuki Coupling/C—H Arylation	211
12.1.5.4.4.5.5	Method 5:	Direct Diarylation with Aryl Bromides	214
12.1.5.4.4.5.6	Method 6:	Synthesis of C3-, C4-, and C5-Phosphonylated Pyrazoles	215

Volume 32:

X—Ene—X (X = F, Cl, Br, I, O, S, Se, Te, N, P), Ene—Hal, and Ene—O Compounds

32.5	Product Class 5: (Organooxy)alkenes		
32.5.3.2	Enol Ethers		2017
	F. Bartels, R. Zimmer, and M. Christmann		
32.5.3.2	Enol Ethers		229
32.5.3.2.1	Functionalization of the Enol Ether Oxygen Atom		229
32.5.3.2.1.1	Method 1:	Reactions of 1,3-Dicarbonyl Compounds with Alcohols	229
32.5.3.2.1.1.1	Variation 1:	Heterogeneous/Immobilized Catalysts	229
32.5.3.2.1.1.2	Variation 2:	Homogeneous Condensation of 1,3-Dicarbonyl Compounds and Alcohols	231
32.5.3.2.1.2	Method 2:	Reaction of 2-Hydroxy-1 <i>H</i> -indole-3-carbaldehydes with Alcohols	231
32.5.3.2.1.3	Method 3:	Enolate Methylation	232
32.5.3.2.1.4	Method 4:	O-Methylation of α -Trifluoromethylsulfonyl Ketones	232
32.5.3.2.1.5	Method 5:	O-Allylation of 1,3 Diketones	233
32.5.3.2.1.6	Method 6:	Anaerobic Oxidative Free-Radical Cyclization	233
32.5.3.2.1.7	Method 7:	Reaction of 1,3-Dicarbonyl Compounds with Difluorocarbene	234
32.5.3.2.1.8	Method 8:	Reaction of 1,3-Dicarbonyl Compounds with Diaryliodonium Salts	235
32.5.3.2.2	Formation of the α -C—O Bond		236
32.5.3.2.2.1	Method 1:	Reactions of Alkenyl Halides or Alkenyl Boronates with Alcohols or Phenols	236

32.5.3.2.2.1.1	Variation 1:	Conjugate Addition/Elimination	236
32.5.3.2.2.1.2	Variation 2:	Copper-Mediated C—O Bond Forming Reactions	238
32.5.3.2.2.2	Method 2:	Alkoxylation Reactions	243
32.5.3.2.2.3	Method 3:	Additions to Alkynes	243
32.5.3.2.2.3.1	Variation 1:	Additions of Alcohols to Alkynes under Basic Conditions	243
32.5.3.2.2.3.2	Variation 2:	Metal-Catalyzed Additions of Alcohols or Phenols to Alkynes ·	246
32.5.3.2.2.3.3	Variation 3:	Intramolecular Additions of Hydroxyalkyl-Substituted Alkynes	248
32.5.3.2.3		Substitution at the α -Carbon Atom	252
32.5.3.2.3.1	Method 1:	Palladium-Catalyzed Synthesis of Enol Ethers	252
32.5.3.2.3.1.1	Variation 1:	Continuous-Flow Heck Reaction	252
32.5.3.2.3.1.2	Variation 2:	Oxidative Heck Reaction	252
32.5.3.2.3.1.3	Variation 3:	Suzuki–Miyaura Cross Coupling	254
32.5.3.2.3.1.4	Variation 4:	Stille Cross Coupling	255
32.5.3.2.3.2	Method 2:	Nickel-Catalyzed Suzuki–Miyaura Cross-Coupling Reaction ..	256
32.5.3.2.3.3	Method 3:	Lithiation of Enol Ethers and Reaction with Electrophiles	257
32.5.3.2.3.3.1	Variation 1:	α -Formylation of Enol Ethers	257
32.5.3.2.3.3.2	Variation 2:	α -Alkylamino Functionalization of Enol Ethers	257
32.5.3.2.4		Substitution at the β -Carbon Atom	259
32.5.3.2.4.1	Method 1:	Heck Reaction	259
32.5.3.2.4.2	Method 2:	Acylation of Enol Ethers	260
32.5.3.2.5		Formation of the Enol Ether C=C Bond by Condensation Reactions	260
32.5.3.2.5.1	Method 1:	Julia Alkenation	260
32.5.3.2.5.1.1	Variation 1:	Reaction of Lactones with Sulfones	260
32.5.3.2.5.1.2	Variation 2:	Reaction of Lactones with Fluoroalkyl-Substituted Sulfones ·	264
32.5.3.2.5.1.3	Variation 3:	Reaction of Alkoxyalkyl-Substituted Sulfones with Aldehydes ·	266
32.5.3.2.5.2	Method 2:	Wittig Reaction	267
32.5.3.2.5.2.1	Variation 1:	Reaction of Ketones with (Methoxymethylene)triphenylphosphorane	267
32.5.3.2.5.2.2	Variation 2:	Reaction of Aldehydes with Phosphonium Salts	267
32.5.3.2.5.2.3	Variation 3:	Wittig–Horner Reaction	268
32.5.3.2.5.3	Method 3:	Direct Conversion of Lactones into Enol Ethers Using Organotitanium Reagents	269
32.5.3.2.5.3.1	Variation 1:	Using the Tebbe Reagent	269
32.5.3.2.5.3.2	Variation 2:	Using the Petasis Reagent	270
32.5.3.2.5.4	Method 4:	Other Condensation Reactions	270
32.5.3.2.6		Enol Ether Formation by Metathesis Reaction	271
32.5.3.2.6.1	Method 1:	Formation of Acyclic Enol Ethers	271
32.5.3.2.6.1.1	Variation 1:	Molybdenum- and Ruthenium-Catalyzed Cross Metathesis ..	271
32.5.3.2.6.1.2	Variation 2:	Catalytic Enantioselective Ring-Opening Cross Metathesis Using Molybdenum Catalysts	274
32.5.3.2.6.1.3	Variation 3:	Ruthenium-Catalyzed Ring-Opening Cross Metathesis	276

32.5.3.2.6.1.4	Variation 4:	Enantioselective Ruthenium-Catalyzed Ring-Opening Cross Metathesis	277
32.5.3.2.6.2	Method 2:	Synthesis of Cyclic Enol Ethers Using a Suzuki–Miyaura Cross Coupling/Ring-Closing Metathesis Sequence	278
32.5.3.2.7		Thermolysis and Pyrolysis	281
32.5.3.2.7.1	Method 1:	Thermolysis of Bis(allenes)	281
32.5.3.2.7.2	Method 2:	Pyrolysis of Azetidinones and Their Thio Analogues	282
32.5.3.2.8		Formation of the C=C Bond by Reduction	282
32.5.3.2.8.1	Method 1:	Hydrogenation of Alkynyl Ethers	282
32.5.3.2.8.2	Method 2:	Hydride Reduction of Alkynyl Ethers	285
32.5.3.2.8.3	Method 3:	Cross-Dehydrogenative C—C Bond Forming Reaction of Alkynyl Ethers	287
32.5.3.2.8.4	Method 4:	Palladium-Catalyzed Cross Addition of Alkynes to Alkynyl Ethers	288
32.5.3.2.9		Formation of Enol Ethers through Cycloaddition and Cyclization Reactions ...	289
32.5.3.2.9.1	Method 1:	Cycloaddition Reactions	290
32.5.3.2.9.1.1	Variation 1:	[4 + 2] Cycloaddition	290
32.5.3.2.9.1.2	Variation 2:	Hetero Diels–Alder Reaction	290
32.5.3.2.9.2	Method 2:	Cyclization Reactions	292
32.5.3.2.9.2.1	Variation 1:	Gold-Catalyzed Cyclization	292
32.5.3.2.9.2.2	Variation 2:	Oxidation-Induced Cyclization	297
32.5.3.2.10		Transformation of sp -Hybridized β -Carbon into sp^2 -Hybridized β -Carbon ...	298
32.5.3.2.10.1	Method 1:	Cycloadditions with Alkoxyallenes	299
32.5.3.2.10.1.1	Variation 1:	Gold-Catalyzed [4 + 2] Cycloaddition	299
32.5.3.2.10.1.2	Variation 2:	Gold-Catalyzed [2 + 2] Cycloaddition	300
32.5.3.2.10.2	Method 2:	Additions to Alkoxyallenes	302
32.5.3.2.10.2.1	Variation 1:	Samarium(II) Iodide Mediated Additions to Methoxyallene ..	302
32.5.3.2.10.2.2	Variation 2:	Additions of Perfluoroalkanesulfinyl Chlorides to Alkoxyallenes	303
32.5.3.2.10.3	Method 3:	Ring Closure/Ring Opening Sequence of Alkoxyallene Derivatives	303
32.5.3.2.10.3.1	Variation 1:	Via Dihydrofurans	303
32.5.3.2.10.3.2	Variation 2:	Via 1,2-Oxazines	305
32.5.3.2.10.4	Method 4:	Intramolecular Pauson–Khand Reaction of Alkynyl-Substituted Alkoxyallenes	308

Volume 40:
Amines, Ammonium Salts, Amine N-Oxides,
Haloamines, Hydroxylamines and Sulfur Analogues,
and Hydrazines

40.1	Product Class 1: Amino Compounds		
40.1.1.5.2.4	The Mannich Reaction		2017
	C. Schneider and M. Sickert		
40.1.1.5.2.4	The Mannich Reaction		315
40.1.1.5.2.4.1	Metal-Catalyzed Mannich Reactions		315
40.1.1.5.2.4.1.1	Method 1: Direct Metal-Catalyzed Mannich Reactions		315
40.1.1.5.2.4.1.1.1	Variation 1: Reaction with Aldimines		316
40.1.1.5.2.4.1.1.2	Variation 2: Reaction with Ketimines		325
40.1.1.5.2.4.1.2	Method 2: Direct Vinylogous Metal-Catalyzed Mannich Reactions		330
40.1.1.5.2.4.1.2.1	Variation 1: Reaction with Aldimines		330
40.1.1.5.2.4.1.2.2	Variation 2: Reaction with Ketimines		333
40.1.1.5.2.4.1.3	Method 3: Indirect Metal-Catalyzed Mannich Reactions		335
40.1.1.5.2.4.1.3.1	Variation 1: Reaction with Aldimines		335
40.1.1.5.2.4.1.3.2	Variation 2: Reaction with Ketimines		339
40.1.1.5.2.4.1.4	Method 4: Metal-Catalyzed Vinylogous Mukaiyama–Mannich Reactions		341
40.1.1.5.2.4.1.4.1	Variation 1: Reaction with Aldimines		341
40.1.1.5.2.4.1.4.2	Variation 2: Reaction with Ketimines		346
40.1.1.5.2.4.2	Direct Organocatalyzed Stereoselective Mannich Reactions		348
40.1.1.5.2.4.2.1	Method 1: Reactions with Aldimines		349
40.1.1.5.2.4.2.1.1	Variation 1: <i>syn</i> -Selective Mannich Reactions of Ketones Catalyzed by Chiral Amines via Enamine Catalysis		349
40.1.1.5.2.4.2.1.2	Variation 2: <i>syn</i> -Selective Mannich Reaction of Aldehydes Catalyzed by Chiral Amines via Enamine Catalysis		350
40.1.1.5.2.4.2.1.3	Variation 3: <i>anti</i> -Selective Mannich Reaction of Ketones Catalyzed by Chiral Amines via Enamine Catalysis		355
40.1.1.5.2.4.2.1.4	Variation 4: <i>anti</i> -Selective Mannich Reaction of Aldehydes Catalyzed by Chiral Amines via Enamine Catalysis		359
40.1.1.5.2.4.2.1.5	Variation 5: Mannich Reaction of Acetaldehydes Catalyzed by Chiral Amines via Enamine Catalysis		366
40.1.1.5.2.4.2.1.6	Variation 6: Mannich Reaction Catalyzed by Chiral Guanidine Derivatives		367
40.1.1.5.2.4.2.1.7	Variation 7: Mannich Reactions Catalyzed by Chiral Phosphoric, Sulfonic, and Carboxylic Acids and Derivatives		371
40.1.1.5.2.4.2.1.8	Variation 8: Mannich Reaction Catalyzed by Bifunctional Chiral Catalysts Based on Urea and Thiourea Motifs		376
40.1.1.5.2.4.2.1.9	Variation 9: Mannich Reaction Catalyzed by Cinchona Alkaloid Derivatives		383

40.1.1.5.2.4.2.1.10 Variation 10:	Mannich Reaction Catalyzed by Phase-Transfer and Ion-Pair Catalysts	386
40.1.1.5.2.4.2.1.11 Variation 11:	Mannich Reaction Catalyzed by N-Heterocyclic Carbenes	389
40.1.1.5.2.4.2.2 Method 2:	Reaction with Ketimines	392
40.1.1.5.2.4.2.2.1 Variation 1:	Mannich Reaction of Ketimines with Ketones Catalyzed by Chiral Amines via Enamine Catalysis	392
40.1.1.5.2.4.2.2.2 Variation 2:	Mannich Reaction of Ketimines with Aldehydes Catalyzed by Chiral Amines via Enamine Catalysis	396
40.1.1.5.2.4.2.3 Method 3:	Three-Component Reactions	398
40.1.1.5.2.4.2.3.1 Variation 1:	Three-Component Reaction of Ketones, Amines, and Aldehydes via Enamine Catalysis	398
40.1.1.5.2.4.2.3.2 Variation 2:	Three-Component Mannich Reactions Catalyzed by Chiral Phosphoric Acids and Derivatives	401
40.1.1.5.2.4.2.3.3 Variation 3:	Mannich Reaction Catalyzed by Bifunctional Chiral Catalysts Based on (Thio)Urea Motifs	403
40.1.1.5.2.4.2.3.4 Variation 4:	Mannich Reaction Catalyzed by Enzymes	404
40.1.1.5.2.4.2.4 Method 4:	Reaction with Imine Surrogates	405
40.1.1.5.2.4.2.4.1 Variation 1:	Mannich Reaction of Imine Surrogates Catalyzed by Chiral Amines via Enamine Catalysis	405
40.1.1.5.2.4.2.4.2 Variation 2:	Mannich Reaction of Imine Surrogates Catalyzed by Bifunctional Thioureas	408
40.1.1.5.2.4.2.4.3 Variation 3:	Mannich Reaction of Imine Surrogates Catalyzed by Phase-Transfer Catalysts	410
40.1.1.5.2.4.2.5 Method 5:	Reaction with Hydrazones	412
40.1.1.5.2.4.2.5.1 Variation 1:	Mannich Reaction of Hydrazones Catalyzed by Bifunctional Amine Thioureas	412
40.1.1.5.2.4.3	Indirect Organocatalyzed Stereoselective Mannich Reactions	413
40.1.1.5.2.4.3.1 Method 1:	Reaction with Aldimines	414
40.1.1.5.2.4.3.1.1 Variation 1:	Indirect Mannich Reaction Catalyzed by Bifunctional Amine Thioureas	414
40.1.1.5.2.4.3.1.2 Variation 2:	Indirect Mannich Reaction Catalyzed by Chiral Phosphoric Acids	416
40.1.1.5.2.4.3.2 Method 2:	Indirect Mannich Reaction of Imine Surrogates	420
40.1.1.5.2.4.3.2.1 Variation 1:	Indirect Mannich Reaction Catalyzed by Chiral Phosphoric Acids and Analogues	420
40.1.1.5.2.4.4	Direct Organocatalyzed Stereoselective Vinylogous Mannich Reactions	424
40.1.1.5.2.4.4.1 Method 1:	Reaction with Aldimines	424
40.1.1.5.2.4.4.1.1 Variation 1:	Vinylogous Mannich Reactions Catalyzed by Bifunctional Thioureas	424
40.1.1.5.2.4.4.1.2 Variation 2:	Vinylogous Mannich Reactions Catalyzed by Cinchona Alkaloids	426
40.1.1.5.2.4.4.2 Method 2:	Reaction with Ketimines	429
40.1.1.5.2.4.4.2.1 Variation 1:	Vinylogous Mannich Reactions Catalyzed by Cinchona-Based Alkaloids	429

40.1.1.5.2.4.4.3	Method 3:	Reactions with Imine Surrogates	431
40.1.1.5.2.4.4.3.1	Variation 1:	Vinylogous Mannich Reactions Mediated by Phase-Transfer Catalysts	431
40.1.1.5.2.4.5	Indirect Organocatalyzed Stereoselective Vinylogous Mannich Reactions		431
40.1.1.5.2.4.5.1	Method 1:	Reaction with Aldimines	432
40.1.1.5.2.4.5.1.1	Variation 1:	Indirect Vinylogous Mannich Reactions Catalyzed by Chiral Phosphoric Acids	432
40.1.1.5.2.4.5.1.2	Variation 2:	Indirect Vinylogous Mannich Reactions Catalyzed by Disulfonimides	436
40.1.1.5.2.4.5.2	Method 2:	Three-Component Reactions	438
40.1.1.5.2.4.5.2.1	Variation 1:	Indirect Vinylogous Mannich Reactions Catalyzed by Chiral Phosphoric Acids	438
Author Index			447
Abbreviations			467