

Contents

1	Nominine	1
	Kevin M. Peese and David Y. Gin	
1.1	Introduction and Classification	1
1.2	Pharmacology	2
1.3	Biosynthesis	3
1.4	Previous Synthetic Work	3
1.4.1	Total Synthesis of Nominine [19a]	4
1.4.2	Synthetic Studies Toward the Hetisine Alkaloids	6
1.5	Strategy and Retrosynthesis	7
1.6	Synthesis	9
1.7	Complete Synthesis	20
	References	21
2	Nakiterpiosin	25
	Shuanhu Gao and Chuo Chen	
2.1	Background	25
2.2	Synthesis of the 6,6,5,6 Steroidal Skeleton	26
2.2.1	The Biomimetic Approaches	27
2.2.2	The Ring-by-Ring Approaches	28
2.2.3	Miscellaneous	28
2.3	Synthesis of Nakiterpiosin	31
2.4	Biology of Nakiterpiosin	34
	References	34
3	The Kinamycins	39
	Seth B. Herzon	
3.1	Introduction	39
3.2	Structure Elucidation	41
3.3	Biological Activity and Mechanism of Action Studies	43
3.4	Biosyntheses of the Kinamycins	45

3.5	Syntheses of the Kinamycins	46
3.5.1	Synthesis of (–)-Kinamycin C [24]	46
3.5.2	Synthesis of (±)- <i>O</i> -Methyl-Kinamycin C [32]	51
3.5.3	Syntheses of (–)-Kinamycins C, F, and J [39]	54
3.5.4	Synthesis of (–)-Kinamycin F [45]	59
	References	64
4	A Short Synthesis of Strychnine from Pyridine	67
	David B. C. Martin and Christopher D. Vanderwal	
4.1	Introduction	67
4.2	Synthesis of Strychnine: A Historical Perspective	68
4.3	Structural Challenges	71
4.4	Background: Zincke Aldehydes	73
4.5	Background: Intramolecular Cycloadditions of Indoles	75
4.6	Development of the Intramolecular Diels–Alder Cycloaddition of Tryptamine-Derived Zincke Aldehydes	78
4.7	Synthesis of Norfluorourarine	80
4.8	Protecting Groups Are Not Always Evil	84
4.9	Strategies for D-Ring Formation for Strychnine	87
4.10	Some Unusual Approaches to C15–C20 Bond Formation	92
4.11	A Successful Route to Strychnine	93
4.12	Conclusions	98
	References	99
5	Bryostatin 7	103
	Yu Lu and Michael J. Krische	
5.1	Introduction	103
5.2	Pharmacology	104
5.3	Biosynthesis	106
5.4	Previous Synthetic Work	108
5.4.1	Total Synthesis of Bryostatin 7 (Masamune 1990)	108
5.4.2	Total Synthesis of Bryostatin 2 (Evans 1998)	110
5.4.3	Total Synthesis of Bryostatin 3 (Nishiyama and Yamamura 2000)	112
5.4.4	Total Synthesis of Bryostatin 16 (Trost 2008)	113
5.4.5	Synthesis of Bryostatin 1 (Keck 2011)	115
5.4.6	Synthesis of Bryostatin 9 (Wender 2011)	117
5.5	Strategy and Retrosynthesis	118
5.6	Synthesis	120
5.6.1	Synthesis of A-Ring Fragment 68	120
5.6.2	Synthesis of C-Ring Fragment 69	121
5.6.3	Fragment Union and Total Synthesis of Bryostatin 7	123
5.7	Conclusion	127
	References	127

6	Serratezomine A	131
	Julie A. Pigza and Jeffrey N. Johnston	
6.1	Introduction and Classification	131
6.2	Pharmacology	132
6.3	Biosynthesis	133
6.4	Previous Synthetic Work	136
6.4.1	Total Synthesis of Serratinine	136
6.4.2	Synthetic Approaches Towards the Framework of Serratinine	138
6.5	Strategy and Retrosynthesis	139
6.6	Synthesis	141
6.7	Complete Synthesis	152
	References	152
7	Hypocrellin/Cercosporin	157
	Carol A. Mulrooney, Erin M. O'Brien, and Marisa C. Kozlowski	
7.1	Introduction	157
7.2	Biological Activity	159
7.3	Previous Synthetic Work	161
7.3.1	Synthesis of (–)-Phleichrome and (–)-Calphostin A,D [30]	161
7.3.2	Synthesis of (–)-Calphostin D [31]	162
7.3.3	Synthesis of (–)-Phleichrome and (–)-Calphostin A [32a]	163
7.3.4	Synthesis of (–)-Calphostin A–D [33a]	164
7.4	Conformational Properties	166
7.5	Strategy and Retrosynthesis	167
7.6	Synthesis	170
7.6.1	Synthesis of (–)-Hypocrellin A	170
7.6.2	Synthesis of (+)-Phleichrome and (+)-Calphostin D	172
7.6.3	Synthesis of (+)-Cercosporin	174
7.7	Synthesis of Perylenequinone Analogs	175
	References	179
8	Phomactin A	183
	Yu Tang, Kevin P. Cole, and Richard P. Hsung	
8.1	Introduction	183
8.1.1	Isolation	183
8.1.2	Biosynthesis	185
8.1.3	Medicinal Chemistry	185
8.1.4	Synthetic Challenges	185
8.2	The Architecturally Distinctive ABD-Tricycle	186
8.2.1	Retrosynthetic Analysis	186
8.2.2	Approaches to the Oxa-Annulation Precursor	188
8.2.3	An Improved Synthesis of Oxa-Annulation Precursor . . .	190

8.2.4	Key Oxa-Annulation and the D-Ring Atropisomerism . . .	191
8.2.5	A Formal Synthesis of (–)-Phomactin A	194
8.3	Lessons Learned from the Challenging Structural Topology . . .	195
8.3.1	Oxidations of C3 and C3a in B-Ring	195
8.3.2	Reduction of C8a and C8b at the AB-Ring Junction . . .	196
8.3.3	Homologation at C5a in the A-Ring	197
8.4	Completion of the Total Synthesis	202
8.4.1	The Diene Route	202
8.4.2	The Allyl Alcohol Route	203
8.4.3	The Vinyl Epoxide Route	203
8.5	Conclusion	207
	References	207
9	(+)-11,11'-Dideoxyverticillin A	211
	Justin Kim and Mohammad Movassaghi	
9.1	Introduction and Classification	211
9.2	Pharmacology	213
9.3	Biosynthesis	214
9.4	Previous Synthetic Work	216
9.4.1	Previous Approaches to the C3–C3' Dimeric Linkages . . .	217
9.4.2	Previous Approaches to the Epidithiodiketopiperazine Motif	218
9.4.3	Total Synthesis of Epidithiodiketopiperazine Alkaloids . .	220
9.5	Strategy and Retrosynthesis for (+)-11,11'-Dideoxyverticillin A .	222
9.5.1	Synthesis of (+)-11,11'-Dideoxyverticillin A	223
9.5.2	Generalization to the Epipolythiodiketopiperazine Alkaloids	230
9.6	Conclusion	231
	References	231
10	Retigeranic acid	235
	David R. Adams and Tomáš Hudlický	
10.1	Introduction	235
10.2	Isolation and Structure	236
10.3	Biosynthesis	238
10.4	Approaches to Total Synthesis	239
10.4.1	Hudlický	239
10.4.2	Fallis	241
10.4.3	Fraser-Reid	243
10.4.4	Trauner	244
10.5	Total Syntheses	247
10.5.1	Corey	247
10.5.2	Paquette	249
10.5.3	Wender	252
10.5.4	Hudlický	255
10.6	Conclusions and Future Perspectives	256
	References	256

11 Total Synthesis of the Lycopodium Alkaloid Complanadine A	259
Richmond Sarpong and Daniel F. Fischer	
11.1 Introduction	259
11.2 Biosynthesis	259
11.3 Biological Activity	262
11.4 The Siegel Synthesis of Complanadine A	263
11.5 Strategy and Retrosynthesis	264
11.6 Borylative C–H Functionalization	267
11.6.1 Benzene Ring Functionalization: Hartwig Synthesis of Taiwaniaquinol B	267
11.6.2 Pyrrole Ring Functionalization: Gaunt Synthesis of Rhazinicine	268
11.6.3 Indole Ring Functionalization: Movassaghi Synthesis of the Asperazine Core	269
11.7 Completion of the Complanadine A Synthesis	269
11.8 Application of the Strategy to Lycopladines F and G	270
11.9 Conclusion	271
References	271
Index	273

Total Synthesis of Natural Products
At the Frontiers of Organic Chemistry

Li, J.J.; Corey, E.J. (Eds.)

2012, XVI, 279 p., Hardcover

ISBN: 978-3-642-34064-2