



Heteroannulations mediated by titanium imido complexes : methods development and applications to the total syntheses of ($\frac{1}{2}$)-monomorine I and (+)-preussin
by Paul Leo McGrane

A thesis submitted in partial fulfillment of the requirements for the degree of Doctor of Philosophy in Chemistry
Montana State University
© Copyright by Paul Leo McGrane (1993)

Abstract:

Highly reactive titanium imido complexes have been generated by the reaction of primary amines with monocyclopentadienyl titanium (IV) complexes. These transient imido complexes have been trapped via intramolecular [2 + 2] cycloadditions with tethered alkynyl moieties. This transformation has been used to prepare a variety of representative heterocycles via catalytic (CpTiCl₃ mediated) and stoichiometric [CpTi(CH₃)₂Cl mediated] annulations of alkynylamines.

Additionally, the azatitanetines generated in stoichiometric [2+2] imido-alkyne cycloadditions have been shown to engage nucleophiles in subsequent bond-forming reactions.

The utility of these new methods in natural products synthesis was shown by their use in concise total syntheses of (\pm)-monomorine I and (+)-preussin.

HETEROANNULATIONS MEDIATED BY TITANIUM IMIDO COMPLEXES:
METHODS DEVELOPMENT AND APPLICATIONS TO THE TOTAL
SYNTHESES OF (±)-MONOMORINE I AND (+)-PREUSSIN

by

Paul Leo McGrane

A thesis submitted in partial fulfillment
of the requirements for the degree

of

Doctor of Philosophy

in

Chemistry

MONTANA STATE UNIVERSITY
Bozeman, Montana

January, 1993

D378

m178

ii

APPROVAL

of a thesis submitted by

Paul Leo McGrane

This thesis has been read by each member of the thesis committee and has been found to be satisfactory regarding content, English usage, format, citations, bibliographic style, and consistency, and is ready for submission to the College of Graduate Studies.

12/20/92
Date

Tom Zylus
Chairperson, Graduate Committee

Approved for the Major Department

1/7/93
Date

John R. Cemer
Head, Major Department

Approved for the College of Graduate Studies

1/11/93
Date

R. L. Brown
Graduate Dean

STATEMENT OF PERMISSION TO USE

In presenting this thesis in partial fulfillment of the requirements for a doctoral degree at Montana State University, I agree that the Library shall make it available to borrowers under rules of the Library. I further agree that copying of this thesis is allowable only for scholarly purposes, consistent with "fair use" as prescribed in the U.S. Copyright Law. Requests for extensive copying or reproduction of this thesis should be referred to University Microfilms International, 300 North Zeeb Road, Ann Arbor, Michigan 48106, to whom I have granted "the exclusive right to reproduce and distribute copies of the dissertation in and from microfilm and the right to reproduce and distribute by abstract in any format."

Signature

P. Ler McNamee

Date

1-10-93

Dedicated to the memory of my father and namesake, Leo Charles McGrane. May your Irish eyes always smile upon us.

ACKNOWLEDGEMENTS

As the successful compilation of a thesis is rarely an individual effort, there are a number of people who need to be acknowledged for their contributions.

Professor Tom Livinghouse has served most effectively as my research advisor and as a guide through the labyrinth of methods development and natural product synthesis. Professors A.C. Craig, P.W. Jennings and B.P. Mundy provided willing and capable guidance. The office staff, Mr. Lee David and Dr. Joe Sears furnished valuable services.

Dr. Mike Jensen was a valued coworker on the methods development portion of this work, and provided suggestions on the synthesis of monomarine I. Former group members Dr. Scott Haring and Klark Hanson, and current members Lydia McKinstry, Greg Luedtke and Derek Sheehan were available for discussion and lent their particular expertise as needed.

Mrs. Barb Hamblet deserves thanks for her word processing services. Her skill and patience are much appreciated.

Without the support and encouragement of my family and friends this work would not have been completed. My wife Michelle has been invaluable in this endeavor. Not only has she provided a loving home, she is also the chief architect behind the structures and spectra in this thesis.

Thank you all and God bless.

TABLE OF CONTENTS

	Page
INTRODUCTION	1
BACKGROUND	4
RESULTS AND DISCUSSION	20
Methods Development	20
The Total Synthesis of (\pm)-Monomorphine I (1)	33
The Enantioselective Total Synthesis of (+)-Preussin (2)	43
CONCLUSION	60
EXPERIMENTAL	61
2,4-Cyclopentadien-1-yltrimethylsilane	63
Cyclopentadienyltitanium trichloride	64
Mixture of 1-chloro-5-phenylpent-4-yne and 1-bromo-5-phenylpent-4-yne(15)	64
1-Iodo-5-phenylpent-4-yne(16)	65
Mixture of 1-Chloronon-4-yne and 1-bromonon-4-yne(21)	66
1-Iodonon-4-yne	66
7-Iodo-1-phenylhept-1-yne(35)	66
2-(2-Bromoethyl)-2-methyl-1,3-dioxolane(43)	67
2,2-Ethylenedioxydec-5-yne(24)	67
Dec-5-yn-2-one(25)	68
Dec-5-yn-2-ylamine(26)	69
6-Phenylhex-5-yn-2-ylamine(7)	70

TABLE OF CONTENTS--Continued

	Page
5-Phenylpent-4-yn-1-ylamine(3)	70
Non-4-yn-1-ylamine(5)	71
6-Phenylhex-5-yn-1-ylamine(9)	72
Dec-5-yn-1-ylamine(11)	73
Pent-4-yn-1-ylamine(28)	73
3,4-Dihydro-5-(phenylmethyl)-2H-pyrrole(4)	74
2-(Phenylmethyl)-3,4,5,6-tetrahydro- pyridine(10)	75
3,4-Dihydro-5-pentyl-2H-pyrrole(6)	76
3,4-Dihydro-2-methyl-5-(phenylmethyl)- 2H-pyrrole(8)	77
3,4-Dihydro-2-methyl-5-pentyl-2H-pyrrole(27)	77
2-Pentyl-3,4,5,6-tetrahydropyridine(12)	78
3,4-Dihydro-5-methyl-2H-pyrrole(29)	78
Reaction of 13 with Isobutyronitrile	78
(E,E)-2,2-Dimethyl-4,6-octadiene-1- ylamine(32)	79
(Z)-5-Phenyl-4-penten-1-ylamine(30)	80
6-Methyl-5-hepten-2-ylamine(31)	80
5,5-Ethylenedioxyhex-2-yne(44)	81
2,2-Ethylenedioxyhept-5-yn-7-ol(45)	82
2,2-Ethylenedioxy-7-iodohept-5-yne(47)	83
O-2,3,5,6-Tetrahydropyran-2-ylhydroxyl- amine(40)	84
(E) and (Z)-O-(2,3,5,6-Tetrahydropyran-	

TABLE OF CONTENTS--Continued

	Page
2-yl)-hexan-2-one oxime(41)	84
O-(2,3,5,6-Tetrahydropyran-2-yl)- 2,2-ethylene-dioxytridec-5-yn- 7-one oxime(48)	85
(±) 7-amino-2,2-ethylenedioxytridec-5-yne(39)	86
(±) 2-Butyl-3,4-dihydro-5-(4,4-ethylene- dioxypentyl)-2H-pyrrole(38)	87
(±) 2-Butyl-5-(4,4-ethylenedioxy- pentyl)-2 β ,3,4,5 β -tetrahydro-1H-pyrrole(37)	87
(±)-Monomorine(1)	88
Undec-2-yn-1-ol(52)	89
1-Bromoundec-2-yne(53)	90
L-Phenylalanine methyl ester hydrochloride	90
Methyl N-(diphenylmethylene)-L-phenylalani- nate(55)	91
(2S, 3S) and (2S, 3R)-2-[N-(diphenyl- methylene)amino]-1-phenylhex-5-yn- 3-ol(59) and (60)	91
(2S, 3S)-2-[N-(diphenylmethylene)amino]- 1-phenylhex-5-yn-3-ol(59)	92
(2S, 3R)-2-[N-(diphenylmethylene)amino]- 1-phenylhex-5-yn-3-ol(60)	93
(4S, 5S)-5-(Phenylmethyl)-4-(prop-2'-yn-1'-yl)- 2-oxazolidinone(61)	94
(2S, 3S)-3-benzyloxy-2-[N-(diphenylmethylene) amino]-1-phenylhex-5-yne(63)	94
(2S, 3S)-3-benzyloxy-2-[N-(diphenylmethylene) amino]-1-phenyl-6-(thiomethyl)hex-5-yne(64)	95
(2S, 3S)-3-benzyloxy-2-[N-(diphenylmethylene)	

TABLE OF CONTENTS--Continued

	Page
amino]-1-phenyltetradec-5-yne(65)	96
(2S,3S)-3-benzyloxy-1-phenyltetradec-5-yn- 2-ylamine(51)	97
(2S,3S)-3-benzyloxy-1-phenylhex-5-yn- 2-ylamine(71)	98
5-Nonyl-2-(phenylmethyl)pyrrole(68)	99
N-Carbomethoxy-5-nonyl-2-(phenylmethyl) pyrrole(70)	100
Octanoyl Nitrile(74)	101
(4S,5S)-4-benzyloxy-2-[2'-cyano- 1'-nonen-1'-yl]-5-(phenylmethyl)-2H- pyrrole(76)	101
(2S,3S,5R)-4-benzyloxy-2-[2'-cyano-1'-nonen- 1'-yl]-1-methyl-5-(phenylmethyl)-pyrrolidine(77) .	102
Diastereomeric Nitriles(78)	104
(2S,3S,5R)-1-methyl-5-nonyl-2-(phenylmethyl)-3- pyrrolidinol(2)	104
REFERENCES	106
APPENDIX	114

LIST OF TABLES

Table		Page
1	Results of CpZr(CH ₃) ₂ Cl Annulation Study	19
2	Results of CpTiCl ₃ and CpTi(CH ₃) ₂ Cl Annulation Studies	29
3	Solvent and Reagent Purification	63

LIST OF FIGURES

Figure		Page
1	Linear and Bent Molybdenum Bisimido Complex	4
2	(+)-Monomorphine I (1) and (+)-Preussin (2)	13
3	Dichlorotitanium Imido Complex	14
4	Silyl Substituted Titanium Imido Complexes	15
5	(+)-Monomorphine I (1)	33
6	(+)-Preussin (2)	44
7	Proposed Transition States for Cycloaddition	52
8	^1H NMR Spectrum of 1-Iodo-5-phenylpent-4-yne(16)	115
9	^{13}C NMR Spectrum of 1-Iodo-5-phenylpent-4-yne(16)	116
10	^1H NMR Spectrum of 1-Iodonon-4-yne	117
11	^{13}C NMR Spectrum of 1-Iodonon-4-yne	118
12	^1H NMR Spectrum of 7-Iodo-1-phenylhept-1-yne(35)	119
13	^{13}C NMR Spectrum of 7-Iodo-1-phenylhept-1-yne(35)	120
14	^1H NMR Spectrum of 2,2-Ethylenedioxydec-5-yne(24)	121
15	^{13}C NMR Spectrum of 2,2-Ethylenedioxydec-5-yne(24)	122
16	^1H NMR Spectrum of Dec-5-yn-2-one(25)	123
17	^{13}C NMR Spectrum of Dec-5-yn-2-one(25)	124
18	^1H NMR Spectrum of Dec-5-yn-2-ylamine(26)	125

LIST OF FIGURES--Continued

Figure		Page
19	¹³ C NMR Spectrum of Dec-5-yn-2-ylamine(26)	126
20	¹ H NMR Spectrum of 2,2-ethylenedioxy-5-phenylhex-5-yne(23)	127
21	¹ H NMR Spectrum of 6-Phenylhex-5-yn-2-ylamine(7)	128
22	¹³ C NMR Spectrum of 6-Phenylhex-5-yn-2-ylamine(7)	129
23	¹ H NMR Spectrum of 5-Phenylpent-4-yn-1-ylamine(3)	130
24	¹³ C NMR Spectrum of 5-Phenylpent-4-yn-1-ylamine(3)	131
25	¹ H NMR Spectrum of Non-4-yn-1-ylamine(5)	132
26	¹³ C NMR Spectrum of Non-4-yn-1-ylamine(5)	133
27	¹ H NMR Spectrum of 6-Phenylhexanenitrile	134
28	¹ H NMR Spectrum of 6-Phenylhex-5-yn-1-ylamine(9)	135
29	¹³ C NMR Spectrum of 6-Phenylhex-5-yn-1-ylamine(9)	136
30	¹ H NMR Spectrum of Dec-5-yn-1-ylamine(11)	137
31	¹³ C NMR Spectrum of Dec-5-yn-1-ylamine(11)	138
32	¹ H NMR Spectrum of Pent-4-yn-1-ylamine(28)	139
33	¹³ C NMR Spectrum of Pent-4-yn-1-ylamine(28)	140
34	¹ H NMR Spectrum of 3,4-Dihydro-5-(phenylmethyl)-2H-pyrrole(4)	141
35	¹³ C NMR Spectrum of 3,4-Dihydro-5-(phenylmethyl)-2H-pyrrole(4)	142

LIST OF FIGURES--Continued

Figure		Page
36	¹ H NMR Spectrum of 2-(Phenylmethyl)- 3,4,5,6-tetrahydro-pyridine(10)	143
37	¹³ C NMR Spectrum of 2-(Phenylmethyl)- 3,4,5,6-tetrahydro-pyridine(10)	144
38	¹ H NMR Spectrum of 3,4-Dihydro- 5-pentyl-2H-pyrrole(6)	145
39	¹³ C NMR Spectrum of 3,4-Dihydro- 5-pentyl-2H-pyrrole(6)	146
40	¹ H NMR Spectrum of 3,4-Dihydro- 2-methyl-5-(phenylmethyl)-2H- pyrrole(8)	147
41	¹³ C NMR Spectrum of 3,4-Dihydro-2-methyl-5- (phenylmethyl)-2H-pyrrole(8)	148
42	¹ H NMR Spectrum of 3,4-Dihydro-2-methyl-5- pentyl-2H-pyrrole(27)	149
43	¹³ C NMR Spectrum of 3,4-Dihydro-2-methyl-5- pentyl-2H-pyrrole(27)	150
44	¹ H NMR Spectrum of 2-Pentyl-3,4,5,6- tetrahydropyridine(12)	151
45	¹³ C NMR Spectrum of 2-Pentyl-3,4,5,6- tetrahydropyridine(12)	152
46	¹ H NMR Spectrum of 3,4-Dihydro-5-methyl- 2H-pyrrole(29)	153
47	¹³ C NMR Spectrum of 3,4-Dihydro-5-methyl- 2H-pyrrole(29)	154
48	¹ H NMR Spectrum of (E,E)-2,2-Dimethyl- 4,6-octadiene-1-ylamine(32)	155
49	¹³ C NMR Spectrum of (E,E)-2,2-Dimethyl- 4,6-octadiene-1-ylamine(32)	156

LIST OF FIGURES--Continued

Figure		Page
50	¹ H NMR Spectrum of (Z)-5-Phenyl-4-penten-1-ylamine(30)	157
51	¹³ C NMR Spectrum of (Z)-5-Phenyl-4-penten-1-ylamine(30)	158
52	¹ H NMR Spectrum of 6-Methyl-5-hepten-2-ylamine(31)	159
53	¹³ C NMR Spectrum of 6-Methyl-5-hepten-2-ylamine(31)	160
54	¹ H NMR Spectrum of 5,5-Ethylenedioxyhex-2-yne(44)	161
55	¹³ C NMR Spectrum of 5,5-Ethylenedioxyhex-2-yne(44)	162
56	¹ H NMR Spectrum of 2,2-Ethylenedioxyhept-5-yn-7-ol(45)	163
57	¹³ C NMR Spectrum of 2,2-Ethylenedioxyhept-5-yn-7-ol(45)	164
58	¹ H NMR Spectrum of 2,2-Ethylenedioxyhept-5-yn-7-ol methane sulfonate ester(46)	165
59	¹³ C NMR Spectrum of 2,2-Ethylenedioxyhept-5-yn-7-ol methane sulfonate ester(46)	166
60	¹ H NMR Spectrum of 2,2-Ethylenedioxy-7-iodohept-5-yne(47)	167
61	¹³ C NMR Spectrum of 2,2-Ethylenedioxy-7-iodohept-5-yne(47)	168
62	¹ H NMR Spectrum of O-2,3,5,6-Tetrahydropyran-2-ylhydroxyl-amine(40)	169
63	¹³ C NMR Spectrum of O-2,3,5,6-Tetrahydropyran-2-ylhydroxyl-amine(40)	170
64	¹ H NMR Spectrum of (E) and (Z)-O-(2,3,5,6-Tetrahydropyran-2-yl)-hexan-2-one oxime(41)	171

LIST OF FIGURES---Continued

Figure		Page
65	^{13}C NMR Spectrum of (E) and (Z)-O-(2,3,5,6-Tetrahydropyran-2-yl)-hexan-2-one oxime(41)	172
66	^1H NMR Spectrum of O-(2,3,5,6-Tetrahydropyran-2-yl)-2,2-ethylene-dioxytridec-5-yn-7-one oxime(48)	173
67	^{13}C NMR Spectrum of O-(2,3,5,6-Tetrahydropyran-2-yl)-2,2-ethylene-dioxytridec-5-yn-7-one oxime(48)	174
68	^1H NMR Spectrum of (\pm) 7-amino-2,2-ethylene-dioxytridec-5-yne(39)	175
69	^{13}C NMR Spectrum of (\pm) 7-amino-2,2-ethylene-dioxytridec-5-yne(39)	176
70	^1H NMR Spectrum of (\pm) 2-Butyl-3,4-dihydro-5-(4,4-ethylene-dioxypentyl)-2H-pyrrole(38)	177
71	^{13}C NMR Spectrum of (\pm) 2-Butyl-3,4-dihydro-5-(4,4-ethylene-dioxypentyl)-2H-pyrrole(38)	178
72	^1H NMR Spectrum of (\pm) 2-Butyl-5-(4,4-ethylenedioxy-pentyl)-2 β ,3,4,5 β -tetrahydro-1H-pyrrole(37)	179
73	^{13}C NMR Spectrum of (\pm) 2-Butyl-5-(4,4-thylenedioxy-pentyl)-2 β ,3,4,5 β -tetrahydro-1H-pyrrole(37)	180
74	^1H NMR Spectrum of (\pm)-Monomorphine(1)	181
75	^{13}C NMR Spectrum of (\pm)-Monomorphine(1)	182
76	^1H NMR Spectrum of Undec-2-yn-1-ol(52)	183
77	^{13}C NMR Spectrum of Undec-2-yn-1-ol(52)	184
78	^1H NMR Spectrum of 1-Bromoundec-2-yne(53)	185
79	^{13}C NMR Spectrum of 1-Bromoundec-2-yne(53)	186
80	^1H NMR Spectrum of Methyl L-Phenylalaninate	187

LIST OF FIGURES--Continued

Figure		Page
81	^{13}C NMR Spectrum of Methyl L-Phenylalaninate	188
82	^1H NMR Spectrum of Methyl N-(diphenylmethy- ene)-L-phenylalaninate(55)	189
83	^{13}C NMR Spectrum of Methyl N-(diphenylmethy- lene)-L-phenylalaninate(55)	190
84	^1H NMR Spectrum of (2S,3S)-2-[N-(diphenyl- methylene)amino]-1-phenylhex-5-yn-3-ol(59) .	191
85	^{13}C NMR Spectrum of (2S,3S)-2-[N-(diphenyl- methylene)amino]-1-phenylhex-5-yn-3-ol(59) .	192
86	^1H NMR Spectrum of (2S,3R)-2-[N-(diphenyl- methylene)amino]-1-phenylhex-5-yn-3-ol(60) .	193
87	^{13}C NMR Spectrum of (2S,3R)-2-[N-(diphenyl- methylene)amino]-1-phenylhex-5-yn-3-ol(60) .	194
88	^1H NMR Spectrum of (4S,5S)-5-(Phenylmethyl)- 4-(prop-2'-yn-1'-yl)-2-oxazolidinone(61) . .	195
89	^{13}C NMR Spectrum of (4S,5S)-5-(Phenylmethyl)- 4-(prop-2'-yn-1'-yl)-2-oxazolidinone(61) . .	196
90	^1H NMR Spectrum of (2S,3S)-3-benzyloxy- 2-[N-(diphenylmethylene)amino]-1-phenylhex- 5-yne(63)	197
91	^{13}C NMR Spectrum of (2S,3S)-3-benzyloxy- 2-[N-(diphenylmethylene)amino]-1-phenylhex- 5-yne(63)	198
92	^1H NMR Spectrum of (2S,3S)-3-benzyloxy- 2-[N-(diphenylmethylene)amino]-1-phenyl- 6-(thiomethyl)hex-5-yne(64)	199
93	^{13}C NMR Spectrum of (2S,3S)-3-benzyloxy- 2-[N-(diphenylmethylene)amino]-1-phenyl- 6-(thiomethyl)hex-5-yne(64)	200

LIST OF FIGURES--Continued

Figure		Page
94	¹ H NMR Spectrum of (2S,3S)-3-benzyloxy-2-[N-(diphenylmethylene)amino]-1-phenyltetradec-5-yne(65)	201
95	¹³ C NMR Spectrum of (2S,3S)-3-benzyloxy-2-[N-(diphenylmethylene)amino]-1-phenyltetradec-5-yne(65)	202
96	¹ H NMR Spectrum of (2S,3S)-3-benzyloxy-1-phenyltetradec-5-yn-2-ylamine(51)	203
97	¹³ C NMR Spectrum of (2S,3S)-3-benzyloxy-1-phenyltetradec-5-yn-2-ylamine(51)	204
98	¹ H NMR Spectrum of (2S,3R)-3-benzyloxy-1-phenyltetradec-5-yn-2-ylamine(66)	205
99	¹³ C NMR Spectrum of (2S,3R)-3-benzyloxy-1-phenyltetradec-5-yn-2-ylamine(66)	206
100	¹ H NMR Spectrum of (2S,3S)-3-benzyloxy-1-phenylhex-5-yn-2-ylamine(71)	207
101	¹³ C NMR Spectrum of (2S,3S)-3-benzyloxy-1-phenylhex-5-yn-2-ylamine(71)	208
102	¹ H NMR Spectrum of 5-Nonyl-2-(phenylmethyl)pyrrole(68)	209
103	¹³ C NMR Spectrum of 5-Nonyl-2-(phenylmethyl)pyrrole(68)	210
104	¹ H NMR Spectrum of N-Carbomethoxy-5-nonyl-2-(phenylmethyl)pyrrole(70)	211
105	¹³ C NMR Spectrum of N-Carbomethoxy-5-nonyl-2-(phenylmethyl)pyrrole(70)	212
106	¹ H NMR Spectrum of Octanoyl Nitrile(74)	213
107	¹³ C NMR Spectrum of Octanoyl Nitrile(74)	214

LIST OF FIGURES--Continued

Figure		Page
108	¹ H NMR Spectrum of (4S,5S)-4-benzyloxy-2-[2'-cyano-1'-nonen-1'-yl]-5-(phenylmethyl)-2H-pyrrole(76)	215
109	¹³ C NMR Spectrum of (4S,5S)-4-benzyloxy-2-[2'-cyano-1'-nonen-1'-yl]-5-(phenylmethyl)-2H-pyrrole(76)	216
110	¹ H NMR Spectrum of (2S,3S,5R)-4-benzyloxy-2-[2'-cyano-1'-nonen-1'-yl]-1-methyl-5-(phenylmethyl)-pyrrolidine(77)	217
111	¹³ C NMR Spectrum of (2S,3S,5R)-4-benzyloxy-2-[2'-cyano-1'-nonen-1'-yl]-1-methyl-5-(phenylmethyl)-pyrrolidine(77)	218
112	¹ H NMR Spectrum of Diastereomeric Nitriles(78)	219
113	¹³ C NMR Spectrum of (2S,3S,5R)-1-methyl-5-nonyl-2-(phenylmethyl)-3-pyrrolidinol(2)	220

ABSTRACT

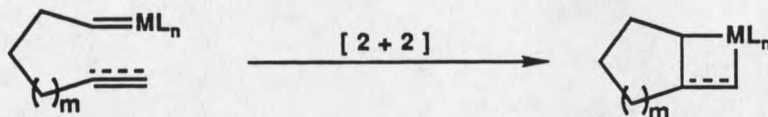
Highly reactive titanium imido complexes have been generated by the reaction of primary amines with monocyclopentadienyl titanium (IV) complexes. These transient imido complexes have been trapped *via* intramolecular [2 + 2] cycloadditions with tethered alkynyl moieties. This transformation has been used to prepare a variety of representative heterocycles *via* catalytic [CpTiCl_2 mediated] and stoichiometric [$\text{CpTi}(\text{CH}_3)_2\text{Cl}$ mediated] annulations of alkynylamines.

Additionally, the azatitanetines generated in stoichiometric [2 + 2] imido-alkyne cycloadditions have been shown to engage nucleophiles in subsequent bond-forming reactions.

The utility of these new methods in natural products synthesis was shown by their use in concise total syntheses of (\pm)-monomorine I and (+)-preussin.

INTRODUCTION

The development of transition metal mediated carboannulation methods has greatly enhanced the chemist's ability to elaborate the cyclic skeletons of many biologically active carbogens. Two powerful examples of these methods are intramolecular carbene cycloaddition^{1,2} and ligand cyclization reactions³ (Eq. 1 and Eq. 2).



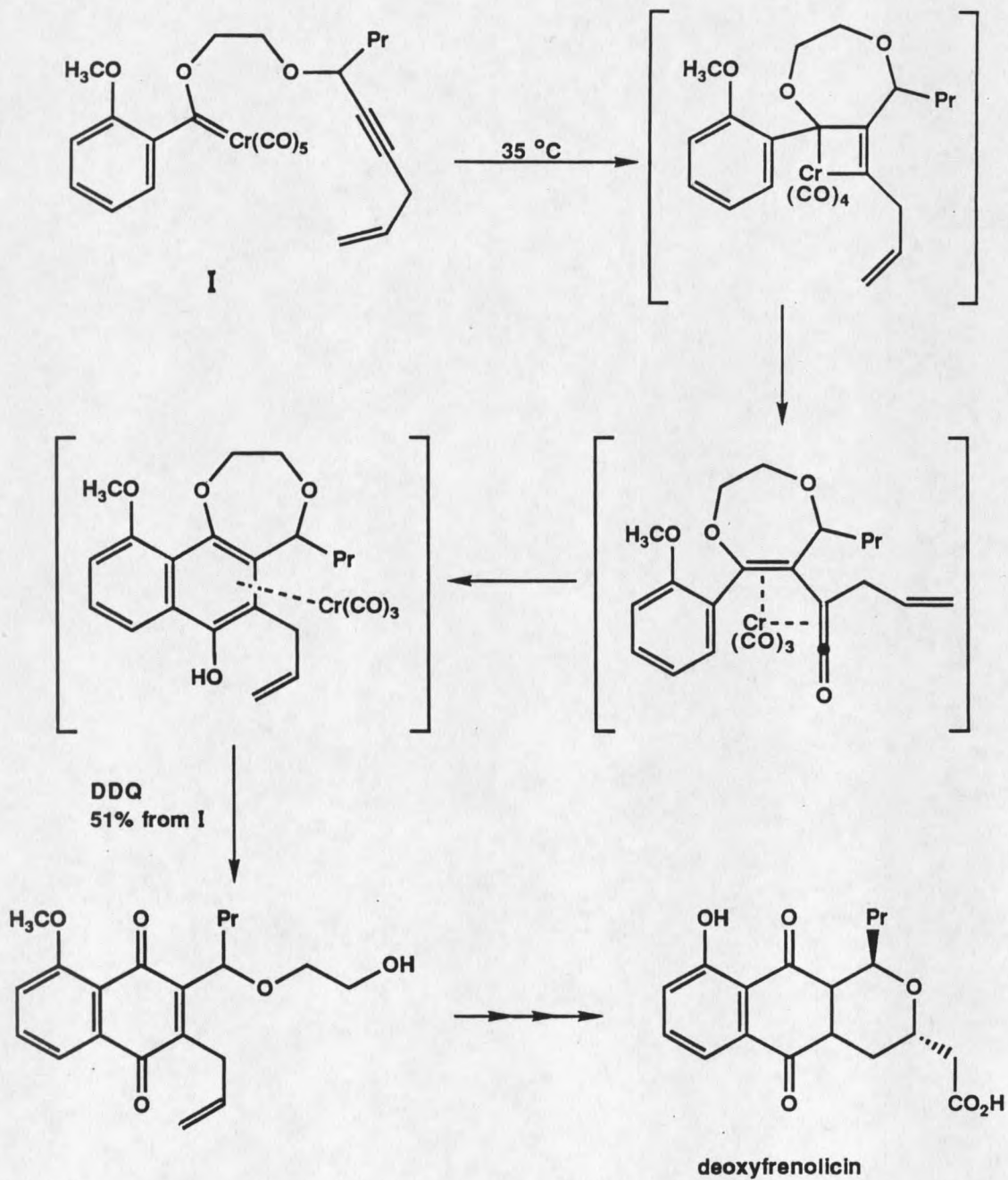
Eq. 1



Eq. 2

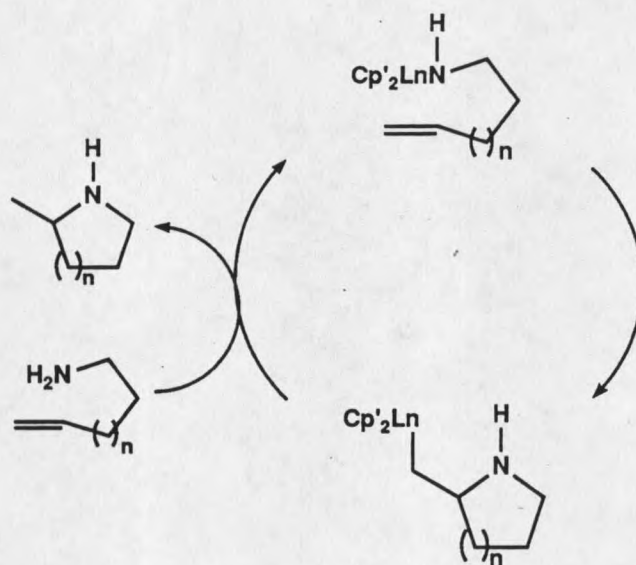
While the reactions in Eq. 1 and Eq. 2 both effect ring annulation, the [2 + 2] cycloaddition of Eq. 1 has the added advantage of generating a metallocyclobutane or metallocyclobutene which may serve as an intermediate for further elaboration. The utility of intramolecular carbene-alkyne cycloadditions in natural product synthesis was

exemplified by Semmelhack's synthesis of deoxyfrenolicin⁴
(Scheme 1).



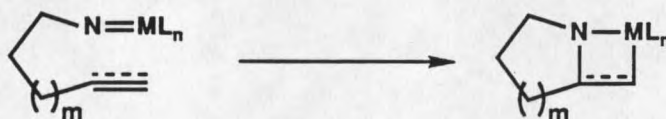
Scheme 1

The analogous transformations of amido and imido complexes that would lead to heterocyclic products have received little or no attention. Recently, Marks described the catalytic hydroamination of terminal alkenes proceeding via amidolanthanide complexes^{5,6} (Scheme 2).



Scheme 2

Prior to the work reported in this thesis, there were no examples of the imido analog of the intramolecular carbene cycloaddition reaction. As with the carbene-olefin cycloaddition, imido complex-olefin cycloadditions could potentially provide exploitable metallocyclic intermediates (Eq. 3).



Eq. 3

