

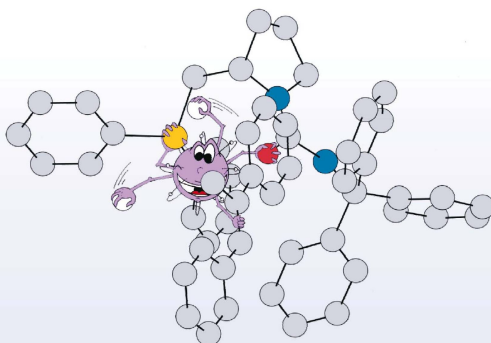


Denise Rageot (Autor)
**Chiral Proline-Based Ligands for Iridium-Catalyzed
Asymmetric Hydrogenation**



**CHIRAL PROLINE-BASED LIGANDS
FOR IRIIDIUM-CATALYZED
ASYMMETRIC HYDROGENATION**

Denise Rageot



Cuvillier Verlag Göttingen
Internationaler wissenschaftlicher Fachverlag

<https://cuvillier.de/de/shop/publications/6100>

Copyright:
Cuvillier Verlag, Inhaberin Annette Jentsch-Cuvillier, Nonnenstieg 8, 37075 Göttingen,
Germany
Telefon: +49 (0)551 54724-0, E-Mail: info@cuvillier.de, Website: <https://cuvillier.de>



List of Abbreviations	1
CHAPTER 1	
IRIDIUM-CATALYZED ASYMMETRIC HYDROGENATION AS A TOOL FOR ORGANIC SYNTHESIS	5
1.1 Introduction	7
1.2 Transition Metal-Catalyzed Asymmetric Hydrogenation: a Historical Perspective	8
1.3 Metal-Catalyzed Asymmetric Hydrogenation in Industrial Processes	13
1.3.1 Rhodium and Ruthenium Catalysts for Asymmetric Hydrogenation in Industrial Processes	13
1.3.2 Iridium Catalysts for Asymmetric Hydrogenation in Industrial Processes	15
1.4 Iridium-Catalyzed Asymmetric Hydrogenation in Natural Product Synthesis	17
1.4.1 Privileged Chiral Bidentate Ligands for Iridium	17
1.4.1.1 Bidentate Ligands for Asymmetric Hydrogenation of C–C Double Bonds	18
1.4.1.2 Bidentate Ligands for the Asymmetric Hydrogenation of C–N Double Bonds	23
1.4.1.3 Bidentate Ligands for the Asymmetric Hydrogenation of C–O Double Bonds	24
1.4.2 Natural Product Syntheses Involving an Iridium-Catalyzed Asymmetric Hydrogenation	25
1.5 Challenges for Metal-Catalyzed Asymmetric Hydrogenations	28
1.6 Objectives of this Work	29
CHAPTER 2	
PROLINE-BASED P,O LIGANDS FOR IRIDIUM-CATALYZED ASYMMETRIC HYDROGENATION	33
2.1 Metal-Catalyzed Asymmetric Reactions Involving Bidentate P,O Ligands	35
2.2 An Amidophosphine Representing Proline-Based P,O Ligands for Iridium-Catalyzed Asymmetric Hydrogenation	37
2.2.1 Initial Results	38
2.2.2 Analysis of the Coordination Mode to Iridium	40
2.3 Proline-Based Carbamatophosphines Ligands	44
2.3.1 Synthesis of Proline-Based Carbamatophosphines	44
2.3.2 Iridium-Catalyzed Asymmetric Hydrogenations with Carbamatophosphine Ligands	48
2.4 Proline-Based Amidophosphines Ligands	51
2.4.1 Synthesis of Proline-Based Amidophosphines	52
2.4.2 Iridium-Catalyzed Asymmetric Hydrogenations with Amidophosphine Ligands	54



2.5	Proline-Based Ureaphosphines Ligands	64
2.5.1	Trisubstituted Ureaphosphines Ligands	65
2.5.1.1	Synthesis of Trisubstituted Ureaphosphines	65
2.5.5.2	Iridium-Catalyzed Asymmetric Hydrogenations with Trisubstituted Ureaphosphine Ligands	70
2.5.2	Tetrasubstituted Ureaphosphines Ligands	82
2.5.2.1	Synthesis of Tetrasubstituted Ureaphosphines	82
2.5.2.2	Iridium-Catalyzed Asymmetric Hydrogenations with Tetrasubstituted Ureaphosphine Ligands	85
2.6	Iridium-Catalyzed Asymmetric Hydrogenation of Other Substrates, Using Proline-Based P,O Ligands	95
2.7	Model Rationalizing the Enantioselectivity	98
2.8	Conclusion	99

CHAPTER 3

PROLINE-BASED P,N LIGANDS FOR IRIDIUM-CATALYZED ASYMMETRIC HYDROGENATION **101**

3.1	P,N Ligands for Iridium-Catalyzed Asymmetric Hydrogenation	103
3.1.1	P,N Ligands Forming a Six-Membered Metallacycle with Iridium	103
3.1.2	P,N Ligands Forming a Non-Six-Membered Metallacycle with Iridium	106
3.2	Proline-Based P,N Ligands	108
3.2.1	Synthesis of Proline-Based P,N Ligands	110
3.2.2	Iridium-Catalyzed Asymmetric Hydrogenations with Proline-Based P,N Ligands	116
3.2.2.1	Initial Results	116
3.2.2.2	Screening of Various Hydrogenation Substrates	118
3.3	Conclusions and Outlook	123

CHAPTER 4

PHOSPHINOHYDRAZONE LIGANDS FOR IRIDIUM-CATALYZED ASYMMETRIC HYDROGENATION **127**

4.1	SAMP/RAMP Hydrazones in Asymmetric Synthesis	129
4.1.1	The SAMP/RAMP Hydrazone Methodology	129
4.1.2	SAMP Hydrazones as Ligands in Organometallic Chemistry	131
4.2	Phosphinohydrazones Ligands	133
4.2.1	Synthesis of Phosphinohydrazones Ligands and Iridium Complexes	133
4.2.1.1	Ketohydrazone Ligands	134
4.2.1.2	Aldhydrazone Ligands	143



4.2.2	Iridium-Catalyzed Asymmetric Hydrogenations with Proline-Based Phosphinohydrazones Ligands	147
4.3	Conclusion	148

CHAPTER 5

PROLINE-BASED LIGANDS FOR PALLADIUM-CATALYZED ALLYLIC

	ALKYLATION REACTION	151
5.1	Privileged Chiral Ligands for Asymmetric Catalysis	153
5.2	Chiral Ligands for the Palladium-Catalyzed Allylic Alkylation Reaction	157
5.3	Palladium-Catalyzed Allylic Alkylation Reaction with Proline-Based Ligands	157
5.3.1	Initial Results	159
5.3.2	Palladium-Catalyzed Allylic Alkylation with Amido- and Ureaphosphine Ligands	159
5.3.3	Analysis of the Coordination Mode to Palladium	161
5.4	Conclusions and Outlook	164

CHAPTER 6

EXPERIMENTAL PART

		167
6.1	General Information	169
6.1.1	Working Techniques and Reagents	169
6.1.2	Analytical Methods	170
6.2	General Synthetic Procedures	172
6.3	Proline-Based P,O Ligands: Preparation and Analytical Data	176
6.3.1	Carbamatophosphines (S)-L _C and Precursors	176
6.3.2	Amidophosphines (S)-L _A and Precursors	185
6.3.3	Trisubstituted Ureaphosphines (S)-L _{U3} and Precursors	204
6.3.4	Tetrasubstituted Ureaphosphines (S)-L _{U4} and Precursors	232
6.4	Proline-Based P,O Ligand/Iridium Complexes: Preparation and Analytical Data	251
6.5	Proline-Based P,N Ligands: Preparation and Analytical Data	259
6.5.1	Benzoxazole phosphines (S)-L _{Ox} and Precursors	259
6.5.2	Benzothiazole phosphines (S)-L _{Th} and Precursors	266
6.5.3	Benzimidazole phosphines (S)-L _{Im}	274
6.6	Proline-Based P,N Ligand/Iridium Complexes: Preparation and Analytical Data	275
6.7	Phosphinohydrazones and Precursors: Preparation and Analytical Data	286
6.8	Hydrogenation Reactions: Procedures and Analytical Data	296



6.8.1	General Information, Working Techniques, and Standard Procedures	296
6.8.2	Hydrogenation Substrates and Products	298
6.9	Allylic Alkylation Reactions: Procedures and Analytical Data	306
6.9.1	Standard Procedure	306
6.9.2	Allylic Alkylation Substrates and Products	306
6.10	Crystallographic Data	308
 SUMMARY		 311