



HAL
open science

D-glucosamine as "green" substrate in synthesis of ligands for asymmetric catalysis

Karolina Wojcik

► **To cite this version:**

Karolina Wojcik. D-glucosamine as "green" substrate in synthesis of ligands for asymmetric catalysis. Other. Université Claude Bernard - Lyon I, 2012. English. NNT : 2012LYO10213 . tel-00974873

HAL Id: tel-00974873

<https://theses.hal.science/tel-00974873v1>

Submitted on 7 Apr 2014

HAL is a multi-disciplinary open access archive for the deposit and dissemination of scientific research documents, whether they are published or not. The documents may come from teaching and research institutions in France or abroad, or from public or private research centers.

L'archive ouverte pluridisciplinaire **HAL**, est destinée au dépôt et à la diffusion de documents scientifiques de niveau recherche, publiés ou non, émanant des établissements d'enseignement et de recherche français ou étrangers, des laboratoires publics ou privés.

N° d'ordre : 213-2012

Année 2012

THESE EN COTUTELLE ENTRE L'UNIVERSITE DE LYON 1 ET L'UNIVERSITE
DE MARIA CURIE-SKŁODOWSKA DE LUBLIN

delivrée par
L'UNIVERSITE DE CLAUDE BERNARD LYON 1
pour l'obtention du

DIPLOME DE DOCTORAT
(arrêté du 7 aut 2006)
spécialité chimie

présentée et soutenue publiquement le 22 Octobre 2012 par

KAROLINA WÓJCIK

**D-GLUCOSAMINE AS "GREEN" SUBSTRATE IN SYNTHESIS OF
LIGANDS FOR ASYMMETRIC CATALYSIS.**

(D-GLUKOZAMINA JAKO "ZIELONY" SUBSTRAT W SYNTEZIE LIGANDÓW DLA POTRZEB
KATALIZY ASYMETRYCZNEJ)

Directeurs de thèse :

Dr. E. FRAMERY and Prof. K. M. PIETRUSIEWICZ

JURY: **B. ANDRIOLETTI**
E. FRAMERY
C. GOUX-HENRY
S. JUGE (reviewer)
P. KIELBASIŃSKI (reviewer)
B. MARCINIEC (reviewer)
K. M. PIETRUSIEWICZ

Institut de Chimie et Biologie Moleculaires et Supramoleculaires
Equipe CASYEN
Bat CPE, 43 BD du 11Novembre 1918, 69100 Villeurbanne Cedex France
Department of Organic Chemistry
Maria-Curie Skłodowska University, Gliniana 33, 20-614 Lublin, Poland

L'UNIVERSITE DE
CLAUDE BERNARD
LYON 1



UNIwersytet Marii
Curie-Skłodowskiej
WYDZIAŁ CHEMII



Karolina Wójcik

**D-GLUKOZAMINA JAKO "ZIELONY" SUBSTRAT W
SYNTEZIE LIGANDÓW DLA POTRZEB KATALIZY
ASYMETRYCZNEJ**

***(D-GLUCOSAMINE AS "GREEN" SUBSTRATE IN
SYNTHESIS OF LIGANDS FOR ASYMMETRIC CATALYSIS)***

**Praca doktorska wykonana
w Instytucie Chemii i Biochemii Molekularnej i Supramolekularnej
UCBL1**

**Promotorzy
Prof. dr hab. K. Michał Pietrusiewicz
Dr Eric Framery**

Lublin, 2012

UNIVERSITE CLAUDE BERNARD - LYON 1

Président de l'Université

M. François-Noël GILLY

Vice-président du Conseil d'Administration

M. le Professeur Hamda BEN HADID

Vice-président du Conseil des Etudes et de la Vie
Universitaire

M. le Professeur Philippe LALLE

Vice-président du Conseil Scientifique

M. le Professeur Germain GILLET

Secrétaire Général

M. Alain HELLEU

COMPOSANTES SANTE

Faculté de Médecine Lyon Est – Claude Bernard

Directeur : M. le Professeur J. ETIENNE

Faculté de Médecine et de Maïeutique Lyon Sud –
Charles Mérieux

Administrateur provisoire : M. le Professeur G.
KIRKORIAN

UFR d'Odontologie

Directeur : M. le Professeur D. BOURGEOIS

Institut des Sciences Pharmaceutiques et Biologiques

Directeur : Mme la Professeure C. VINCIGUERRA

Institut des Sciences et Techniques de la
Réadaptation

Directeur : M. le Professeur Y. MATILLON

Département de formation et Centre de Recherche en
Biologie Humaine

Directeur : M. le Professeur P. FARGE

COMPOSANTES ET DEPARTEMENTS DE SCIENCES ET TECHNOLOGIE

Faculté des Sciences et Technologies

Directeur : M. le Professeur F. De MARCHI

Département Biologie

Directeur : M. le Professeur F. FLEURY

Département Chimie Biochimie

Directeur : Mme le Professeur H. PARROT

Département GEP

Directeur : M. N. SIAUVE

Département Informatique

Directeur : M. le Professeur S. AKKOUCHE

Département Mathématiques

Directeur : M. le Professeur A. GOLDMAN

Département Mécanique

Directeur : M. le Professeur H. BEN HADID

Département Physique

Directeur : Mme S. FLECK

Département Sciences de la Terre

Directeur : Mme la Professeure I. DANIEL

UFR Sciences et Techniques des Activités Physiques
et Sportives

Directeur : M. C. COLLIGNON

Observatoire de Lyon

Directeur : M. B. GUIDERDONI

Polytech Lyon

Directeur : M. P. FOURNIER

Ecole Supérieure de Chimie Physique Electronique

Directeur : M. G. PIGNAULT

Institut Universitaire de Technologie de Lyon 1

Directeur : M. C. VITON

Institut Universitaire de Formation des Maîtres

Directeur : M. R. BERNARD

Institut de Science Financière et d'Assurances

Directeur : Mme la Professeure V. MAUME-
DESCHAMPS

Acknowledgments

I want to thank the University of Claude Bernard Lyon 1 for giving me permission to commence this thesis in the first instance, to do the necessary research work and to use departmental facilities.

The first person I would like to thank is my supervisor Dr Eric Framery, for giving me the opportunity of doing my Ph.D. in his group, for his invaluable support and kindness through this time, and for his guidance in the course of scientific research presented here.

I would like to thank to Prof. Kazimierz Michał Pietrusiewicz for allowing me to conduct this research under his supervision, and for all help I received during preparation of this manuscript.

I am also very grateful to Prof. Sylvain Jugé, Prof. Piotr Kiełbasinski and Prof. Bogdan Marciniec for the interest shown in this manuscript by accepting to be referees.

I would like to collectively thank to my research group for making our laboratory a great working environment. Our research group members were always willing to help and advice me so that my research life became smoother. Special thanks go to Prof. Bruno Andrioletti for giving me the opportunity of doing my PhD in his group and Dr Catherine Goux-Henry for their assistance in the laboratory and work that contributed to my project.

For their collaborations I would like to thank to Prof. Florence Popowycz, PhD Marc Baron, Dr Chloe Thieuleux and Doctor Reine Sayah.

This thesis certainly would not have been possible without the love and encouragement of my family and friends. My mom and dad, my grandparents as well as my friends Yassir, Lyonnelle, Shuai and Meriem, have been always support me throughout my time in France. Thank You all.

Abbreviations

$[\alpha]_D$	specific rotation at wavelength of sodium D line
Ac	acetyl
Ar	aryl
atm	atmosphere
bd	broad doublet
BET	Brunauer–Emmett–Teller- Adsorption method for the characterization of porous materials
BINAP	2,2'-Bis(diphenylphosphino)-1,1'-binaphthalene
BINOL	2,2-dihydroxy-1,1-binaphthyl
Bn	benzyl
BOC	<i>t</i> -butoxycarbonyl
bs	broad singlet
Bu	butyl
Bz	benzoyl
Calcd.	calculated
COD	cyclooctadiene
Conv.	conversion
COSY	gradient-selected Correlation Spectroscopy
<i>c</i> -Pr	<i>cyclo</i> -propyl
Cy	cyclohexyl
d	doublet
DAIPEN	1,1-bis(4-methoxyphenyl)-3-methyl-1,2-butanediamine
DCC	dicyclohexylcarbodiimide
DCM	dichloromethane
dd	doublet of doublets
ddd	doublet of doublet of doublets
dddd	doublet of doublet of doublet of doublets
DIPEA	Diisopropylethylamine
DMAP	4-dimethylaminopyridine
DMF	<i>N,N</i> -dimethylformamide
DMSO- <i>d</i> ₆	Dimethyl sulfoxide deuterated
DPEN	Diphenylethylenediamine
DPPBA	diphenylphosphino benzoic acid
dq	doublet of quintets
dqd	doublet of quartets of doublets
dt	doublet of triplets
EDC	1-ethyl-3-(3-dimethylaminopropyl)carbodiimide
<i>ee</i>	enantiomeric excess
equiv	equivalent
<i>er</i>	enantiomeric ratio
ESI	electrospray ionization

<i>et al.</i>	<i>et alia-</i> and others
Et	ethyl
g	gram(s)
GC	gas chromatography
HOBt	1-hydroxybenzotriazol
HPLC	High-Performance Liquid Chromatography
HSQC	heteronuclear single quantum coherence spectroscopy
Hz	hertz
<i>i</i> -Bu	<i>iso</i> -butyl
<i>i</i> -Pr	<i>iso</i> -propyl
IR	infrared
L, Lig	ligand
m	multiplet
<i>m</i> - <i>meta</i>	position of an aryl ring
M	general transition metal
m/z	mass per charge
Me	methyl
Mes	mesityl, -C ₆ H ₂ (CH ₃) ₃
mg	milligram(s)
min	minutes
mL	milliliter(s)
mmol	millimole(s)
MPSO	methyl phenyl sulfoxide
MPSO ₂	methyl phenyl sulfone
MS	mass spectrometry
<i>n</i> -Bu	<i>n</i> -butyl
NMR	nuclear magnetic resonance
Np	naphthyl
Nu	nucleophile
<i>o</i> - <i>ortho</i>	position of an aryl ring
°C	degrees Celsius
OTf	trifluoromethanesulfonate (triflate)
<i>p</i> - <i>para</i>	position of an aryl ring
PEG	poly(ethylene glycol)
Ph	phenyl
Piv	pivaloyl
ppm	parts per million
Pr	propyl
Ps	polystyrene support
q	quartet
R	general alkyl or aryl substituents
<i>rac.</i>	racemate
R _f	Retention Factor
rt	room temperature

s	singlet
SAPC	Supported Aqueous Phase Catalyst
sat.	saturated
SBA-15	Santa Barbara-15
SLPC	Supported Liquid Phase Catalyst
t	triplet
TBDMS	tert-butyldimethylsilyl
TBDPS	<i>t</i> -Butyldimethylsilyl
<i>t</i> -Bu	<i>tert</i> -butyl
Temp.	temperature
TES	triethylsilyl
TFA	trifluoroacetic acid
THF	tetrahydrofuran
TIPS	Triisopropylsilyl
TLC	Thin Layer Chromatography
TMS	trimethylsilyl
Tol	4-methylbenzoyl
TON	Trunover number
Tr	trityl
t_r	retention time
Xyl	3,5-dimethylbenzoyl
δ	chemical shift in NMR spectroscopy
μL	microliter(s)
μmol	micromol(s)
ν	frequency

Table of contents

ACKNOWLEDGMENTS	VII
ABBREVIATIONS	IX
TABLE OF CONTENTS	XIII

General introduction	1
<i>Problem statement</i>	3
<i>Thesis objectives</i>	5
<i>Thesis organization</i>	6
<i>Keywords</i>	6

CHAPTER 1 Bibliography..... 7

INTRODUCTION	9
HOMOGENEOUS CATALYSIS	11
1.1 HOMODONOR D-GLUCOSAMINE BASED LIGANDS.....	11
1.1.1 <i>Monodentate ligands</i>	11
1.1.1.1 Phosphines ligands.....	11
1.1.1.2 Phosphinites ligands.....	12
1.1.1.3 Phosphites and aminophosphine ligands.....	12
1.1.2 <i>Bidentate ligands</i>	13
1.1.2.1 Phosphines ligands.....	13
1.1.2.2 Phosphinites ligands.....	15
1.1.2.3 N/N ligands.....	15
1.2 HETERODONOR D-GLUCOSAMINE BASED LIGANDS.....	18
1.2.1 <i>Bidentate ligands</i>	18
1.2.1.1 P/N ligands.....	18
1.2.1.2 P/O ligands.....	22
1.2.1.3 N/O ligands.....	25
1.2.2 <i>Tridentate ligands</i>	28
1.2.2.1 P/N/S ligands.....	28
1.2.2.2 N/N/N ligands.....	28
1.2.2.3 N/N/O ligands.....	29
1.2.2.4 O/N/O ligands.....	30
1.2.3 <i>Tetradentate ligands</i>	31
1.2.3.1 N/N/O/O ligands.....	31
1.3 GLUCOSAMINE DERIVATIVES AS ORGANOCATALYSTS.....	33
1.4 GLUCOSAMINE DERIVATIVES AS REAGENTS.....	39

HETEROGENEOUS CATALYSIS	40
1.5 COVALENT BONDING WITH POLYSTYRENE RESIN.....	40
1.6 BIPHASIC CATALYSTS.....	41
CONCLUSIONS	43

CHAPTER 2 Ligands for homogeneous catalysis..... 45

INTRODUCTION	47
RESULTS AND DISCUSSION	49
2.1 PREPARATION OF 1,2-DIAMINO-D-GLUCOSAMINE.....	49
2.2 “TROST TYPE” LIGANDS FOR ALLYLIC ALKYLATION.....	53
2.2.1 Amide type ligand.....	53
2.2.2 Imine type ligand.....	55
2.2.3 Allylic alkylation with “Trost type ligand”.....	57
2.3 CATALYST FOR HYDROGENATION.....	60
2.3.1 BINAP-Ru(II) diaminecomplex.....	60
2.3.2 Hydrogenation with BINAP-Ru(II) diaminencomplexes.....	62
2.4 THIOUREA ORGANOCATALYSTS FOR MICHAEL ADDITION.....	64
2.4.1 Synthesis of D-glucosamine based thiourea organocatalysts.....	64
2.4.2 Michael addition with thiourea organocatalysts.....	67
CONCLUSIONS	69
EXPERIMENTAL PART	71
2.5 EXPERIMENTS DEALING WITH SYNTHESIS OF 1,2-B-GLUCODIAMINE.....	71
2.6 EXPERIMENTS DEALING WITH SYNTHESIS OF LIGANDS FOR ALLYLIC ALKYLATION... 76	76
2.7 EXPERIMENTS DEALING WITH SYNTHESIS CATALYST FOR HYDROGENATION.....	82
2.8 EXPERIMENTS DEALING WITH SYNTHESIS OF D-GLUCOSAMINE BASED ORGANOCATALYSTS.....	84

CHAPTER 3 Ligands for heterogeneous catalysis..... 87

INTRODUCTION	89
RESULTS AND DISCUSSION	95
3.1 SUPPORTED AQUEOUS PHASE CATALYST (SAPC) FOR SUZUKI-MIYAJIMA CROSS COUPLING REACTION.....	95
3.1.1 Synthesis of ligand.....	95
3.1.2 Impregnation of catalyst.....	96
3.1.3 Suzuki Miyajima cross coupling.....	97
3.2 PEG-SUPPORTED LIGANDS.....	103
3.2.1 Ligand containing 4-polyethylene arms.....	103
3.2.2 Ligands containing 1- polyethylene arm.....	104
3.2.2.1 Using trityl protecting group.....	105
3.2.2.2 Using silyl protecting group.....	106

3.2.2.3	Using tosyl protecting group	107
3.2.2.4	Introducing azido function	108
3.2.2.5	Introducing alkynyl function	112
3.3	SILICA IMMOBILIZED LIGANDS	113
3.3.1	<i>Silica materials</i>	113
3.3.2	<i>Synthesis of carbohydrate with alkynyl function in β-anomeric position</i>	116
3.3.3	<i>Immobilization of silica with carbohydrate via anomeric position</i>	116
3.3.3.1	Amido type ligand	116
3.3.3.2	Imino type ligand.....	119
3.3.3.3	Complex L-Pd (1 / 1).....	119
3.3.3.4	Complex L-Pd (2 / 1).....	121
CONCLUSIONS		123
EXPERIMENTAL PART		125
3.4	EXPERIMENTS DEALING WITH SAPC SYSTEM.....	125
3.5	EXPERIMENTS DEALING WITH SYNTHESIS OF POLY(ETHYLENE) BASED LIGANDS. ...	129
3.6	EXPERIMENTS DEALING WITH SILICA GRAFTED LIGANDS.....	137

References	143
-------------------------	------------

General conclusions and recommendations for future work....	153
--	------------

ANNEX A <i>Abstract of the PhD Thesis in English</i>	I
<i>Abstract of the PhD Thesis in French</i> <i>(Resume en Français)</i>	I

ANNEX B <i>Abstract of the PhD Thesis in Polish</i> <i>(Streszczenie Dysertacji)</i>	III
--	------------

ANNEX C <i>Supplementary work</i>	XXI
--	------------

General introduction

Problem Statement

“Green chemistry” is a multi-disciplinary concept that has emerged over the past two decades, considering chemical research and engineering that encourages the design of products and processes that minimize the use and generation of hazardous substances.

Anastas and Warner¹ formulated the twelve principles of green chemistry in 1998, which help to explain what the definition means in practice.

THE 12 PRINCIPLES OF “GREEN CHEMISTRY”

- 1. Prevention:** It is better to prevent waste than to treat or clean up waste after it is formed.
- 2. Atom economy:** Synthetic methods should be designed to maximize the incorporation of all materials used in the process into the final product.
- 3. Less hazardous chemical synthesis:** Wherever practicable, synthetic methods should be designed to use and generate substances that possess little or no toxicity to human health and the environment.
- 4. Designing safer chemicals:** Chemical products should be designed to preserve efficacy of function while reducing toxicity.
- 5. Safer solvents and auxiliaries:** The use of auxiliary substances (e.g. solvents or separation agents) should be made unnecessary whenever possible and innocuous when used.
- 6. Design for energy efficiency:** Energy requirements of chemical processes should be recognized for their environmental and economic impacts and should be minimized. If possible, synthetic methods should be conducted at ambient temperature and pressure.
- 7. Use of renewable feedstocks:** A raw material or feedstock should be renewable rather than depleting whenever technically and economically practicable.
- 8. Reduce derivatives:** Unnecessary derivatization (use of blocking groups, protection/ de-protection and temporary modification of physical/ chemical processes) should be minimized or avoided if possible.
- 9. Catalysis:** Catalytic reagents (as selective as possible) are superior to stoichiometric reagents.

¹ P. T. Anastas, J. C. Warner, *Green Chemistry: Theory and Practice*, Oxford University Press, USA, 1998.

10. Design for degradation: Chemical products should be designed so that at the end of their function they do not persist in the environment and break down into innocuous degradation products.

11. Real-time analysis for pollution prevention: Analytical methodologies need to be further developed to allow for real-time, in-process monitoring and control prior to the formation of hazardous substances.

12. Inherently safer chemistry for accident preventions: Substances and the form of a substance used in a chemical process should be chosen to minimize the potential for chemical accidents, including releases, explosions and fires.

These principles identify catalysis as one of the most important tools for realization of assumptions of “green chemistry”². Developing green chemistry methodologies is a challenge that makes need to design chemical products and processes that reduce or eliminate the use and generation of hazardous substances. Industrial catalysis can be divided into heterogeneous and homogeneous catalysis.

Homogeneous catalysis by transition metals is a fundamental methodology used for production of fine chemicals, specially because of its efficiency, reproducibility, high selectivity and mild reaction conditions. Many bonds like C-C, C-H, C-N, C-S or C-O bonds can be accomplished with high yield and enantioselectivity in case of chiral compounds. However using this method we will encounter few obstacles. High catalyst performance requires careful choice of resources (activating metals and chiral ligands, use of harmless solvents and reagents). Other drawback are undesired by-products and difficulties with separation of catalyst from reaction mixture.

Nowadays, mostly chosen methodologies for solving this problem is heterogeneous catalysis. Supporting organometallic complexes in inorganic or organic matrix make recovery and reuse of the catalyst to be easy, but also reduce metallic impurities left in the final products. Heterogeneous catalysts have a longer lifetime for the storage and increased temperatures, they are less susceptible to various forms of pollution and higher resistance to poisons. Finally by choosing appropriate support and its bonding to the support they are able to provide very good activity and selectivity of the catalyst.

² P. T. Anastas, M. M. Kirchhoff, T. C. Williamson, *Appl. Catal. A: General*, 2001, 221, 3-13.

General introduction

Very important is also design and application of new catalysts which are achieving goals of lower energy requirements, catalytic versus stoichiometric amounts of materials, increased selectivity, and decreased use of processing and separation agents.

One of the simplest ways to obtain chiral ligands is to transform or derivatize natural chiral compounds, thus making tedious optical-resolution procedures unnecessary. In the past few years, carbohydrate derivative ligands have been used in wide range of catalytic asymmetric reactions with impressive results. Carbohydrates have many advantages. They are readily available from environmentally friendly feedstocks, they are highly functionalized, and have several stereogenic centers.

Thesis Objectives

- One of the objectives of this thesis was to synthesize conformationally restricted derivative of D-glucosamine: 1,2- β -glucodiamine that could be used as structurally well defined and coming from natural feedstock analogous of *trans*-1,2-cyclohexdiamine.
- Secondly this work assumed to use of such derivative as a starting material in synthesis of chiral ligands, catalysts and organocatalysts.
- In order to use them in different catalytic homogeneous reactions such as allylic alkylation, hydrogenation or organocatalysis.
- Furthermore one of the stipulated aims was preparation of immobilized D-glucosamine based ligands that could be use in heterogeneous catalysis.
- No previous explore was made in area of SAPC (Supported Aqueous Phase Catalyst) system catalysed reaction of Suzuki Miyaura cross coupling, thus, in this study, we were interested in developing methodology which will allows to prepare in simple way immobilized system that could be easy recover and reuse.
- The final objective was to synthesize ligands for heterogeneous catalysis which could be used in biphasic systems or could be grafted in inorganic matrix and easy recovered from reaction mixture.

Thesis Organization

In this manuscript is separated in three parts:

Chapter 1 Bibliography. Brief review of all D-glucosamine based ligands, organocatalysts and reagents- prepared and used in catalytic reactions till April 2012 is discussed.

Chapter 2 Ligands for homogeneous catalysis. In following chapter will be presented preparation of new D-glucosamine based ligands with 1,2-glucodiamino core and their use in reactions of allylic alkylation, hydrogenation, Michael addition.

Chapter 3 Ligands for heterogeneous catalysis. Preparation of D-glucosamine based ligands will be characterized and their immobilization into different heterogeneous systems. Also efficiency of SAPC system in catalytic reaction of Suzuki Myaura cross-coupling will be detailed.

Keywords:

D-glucosamine, „Green chemistry”, allylic alkylation, hydrogenation, organocatalysis, PEG, Silica supported catalysts, SAPC, homogeneous catalysis, heterogeneous catalysis.

CHAPTER 1

Bibliography

Introduction

The chemistry of simple sugars was developed in the end of nineteenth century by Emil Fischer³, and the ring structures were determined in the interwar years by Haworth⁴ and coworkers. Since then carbohydrate received attention of scientists and knowledge about their biological activity was successively enlarged. However their synthetic utility was omitted in favor of aminoacids, vitamins, terpenes or alkaloids. Recently situation change and during last decade use of the carbohydrates as ligands become more popular and developed. Their role has been also expanded to using them as chiral auxiliaries, reagents, and organocatalysts⁵. Finally they start to be used in many asymmetric processes in field of pharmaceutical⁶ and agrochemical industry⁷ but also in production of flavors and fragrances⁸.

In synthetic point of view carbohydrates are excellent starting materials. Most of them are easily available, cheap and they offer a ready source of enantiomerically pure compounds. Another advantage is their stereochemical diversity. Presence of several highly functionalized stereogenic centers gives scientists scope for preparing unique ligands structures which can be used in many asymmetric processes. Only inconvenience in using those molecules could be that only one of enantiomer is easy available when L-sugars are prohibitively expensive. This problem can be easily solved by using pseudoenantiomers. One of the widely used carbohydrates is D-glucosamine (Figure 1.1).

³ "Collection of Emil Fischer Papers" (Bancroft Library, University of California, Berkeley), were summarized by Professor Frieder W. Lichtenhaler in his article (*Angew. Chem. Int. Ed.*, **1992**, 31, 1541-1556).

⁴ (a) H. D. K. Drew, W. N. Haworth, *J. Chem. Soc.*, 1926, 2303-2310 (b) W. N. Haworth, E. L. Hirst, A. Learner, *J. Chem. Soc.*, **1927**, 1040-1047.

⁵ Reviews: a) M. M. K. Boysen, *Chem. Eur. J.*, **2007**, 13, 8648-8659, (b) M. Diéguez, C. Claver, O. Pàmies, *Eur. J. Org. Chem.*, **2007**, 4621-4634, (c) M. Diéguez, O. Pàmies, C. Claver, *Chem. Rev.*, **2004**, 104, 3189-3215; (d) M. Diéguez, O. Pàmies, A. Ruiz, Y. Diaz, S. Castillon, C. Claver, *Coord. Chem. Rev.*, **2004**, 248, 2165-2192.

⁶ For recent reviews see: (a) R. K. Shukla, A. Tiwari, *Critical Reviews in Therapeutic Drug Carrier Systems*, **2011**, 28, 255-292. (b) H. M. I. Osborn, P. G. Evans, N. Gemmell, S. D. Osborne, *Molecular Pathomechanisms and New Trends in Drug Research*, **2003**, 178-190.

⁷ B. Brauckmann, *CLB Chemie in Labor und Biotechnik*, **2003**, 54, 292-295.

⁸ Examples: (a) K-H. Renz, B. Schleifenbaum, J. Uhlemann, F. Saleeb, DE 10219228 **2003**, (b) R. C. McIver, F. Vlad, R. A. Golding Jr, T. D. Leichsenring, D. Benzcedi, WO 2002065858, **2002**, (c) O. Chmiel, R. T.-S. Liu, M. Furrer, D.F. Rushmore, WO 9623423 **1996**.

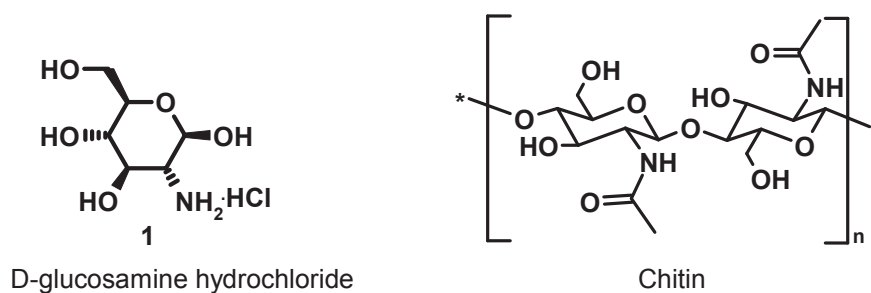


Figure 1.1 Structures of D-glucosamine hydrochloride and chitin.

This amino sugar is obtained by hydrolysis of the polysaccharides like chitosan and chitin, which compose the exoskeletons of crustaceans and other arthropods, cell walls in fungi and many higher organisms. Easy availability of biomass used to obtain Glucosamine make it to be inexpensive material which price is around 1€ for 5 gram (Acros Organics).

Because of the fact that D-glucosamine can be easily functionalized and modified, several types of ligands have been prepared in recent decades.

Large numbers of ‘D-glucosamine cores’ have been developed and used as ligands for different kind of catalytic reactions both in homogeneous and heterogeneous catalysis. This article aims to give an overview of D-glucosamine based ligands, organocatalysts and reagents with pyranose substructure. Furanose, acyclic and heterocyclic structures will not be discussed.

Organization of Chapter 1

This Chapter is separated in two main parts:

- *Homogeneous catalysis*

Firstly compounds used in homogeneous catalysis will be presented and their use as ligands, organocatalysts and reagents. Review is organized according to the type of ligands, and take into account first nature of donor atom (P, N, S, O). In subchapters when large amount of different ligands with the same type of chelation was known in literature, first all ligands are presented followed by their use in catalytic reactions.

- *Heterogeneous catalysis*

Ligands are organized by technique of immobilization of ligand. Firstly ligands grafted in organic matrix of polystyrene will be presented and after ligands used in biphasic media.

Homogeneous catalysis

1.1 Homodonor D-glucosamine based ligands

1.1.1 Monodentate ligands

1.1.1.1 Phosphines ligands

Zapf and co-workers⁹ prepared glucosamine based monophosphines (Figure 1.2).

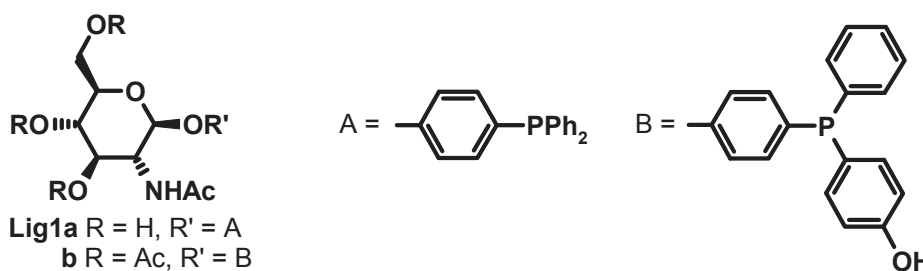
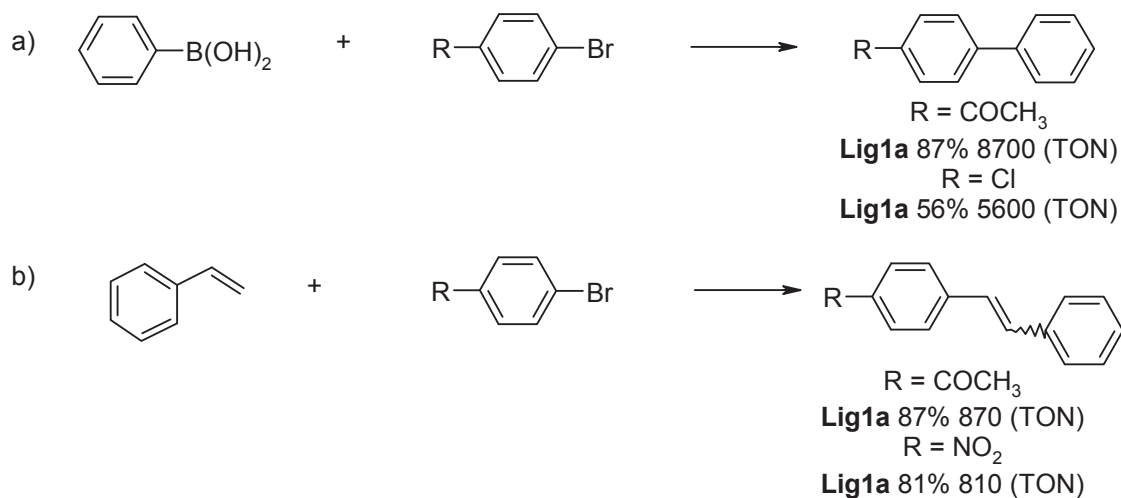


Figure 1.2 Monophosphines based D-glucosamine derived by Zapf.

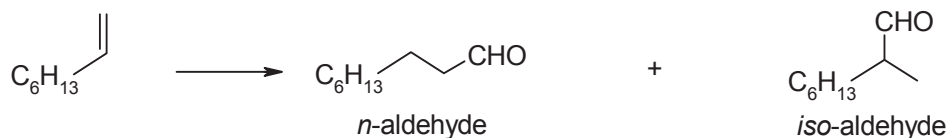
Only **Lig1a** found application in catalytic reactions as biphasic Suzuki-Miyaura cross-coupling and Heck reactions, afforded products with conversions up to 87% and TON up to 8700 (Scheme 1.1).



Scheme 1.1 Reactions: a) Suzuki-Miyaura cross-coupling, b) Heck reaction.

That compound was used also in [Rh]-catalysed hydroformylation in a biphasic and homogeneous medium with low chemoselectivity of the desired branched product (16% of conversion, *n/iso*-selectivity 82 : 18), and enantiomeric excesses were not determined (Scheme 1.2).

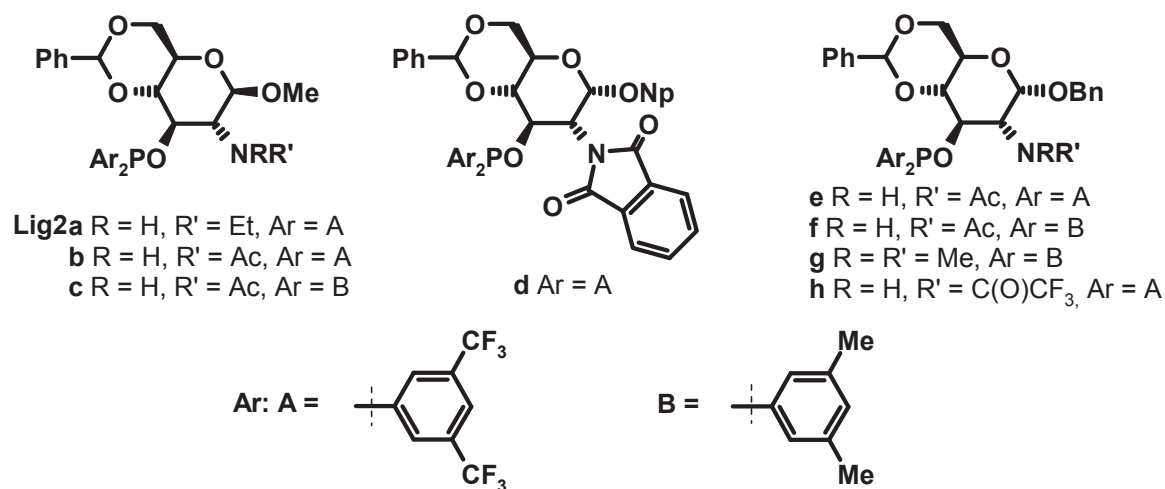
⁹ (a) M. Beller, J. G. E. Krauter, A. Zapf, *Angew. Chem. Int. Ed.*, **1997**, 36, 772-774, (b) M. Beller, J.G.E. Krauter, A. Zapf, S. Bogdanovic, *Catal. Today*, **1999**, 48, 279-290.



Scheme 1.2 Hydroformylation.

1.1.1.2 Phosphinites ligands

In 2002 RajanBabu and Park¹⁰ prepared series of diarylphosphinite ligands **Lig2** which were applied in the [Ni]-catalysed asymmetric hydrovinylation reactions (Figure 1.3).

Figure 1.3 Monodentate phosphinites **Lig2a-h**.

Ligands **Lig2a,g** containing alkyl substituents on nitrogen atom have been found to be totally ineffective. Other ligands formed products of hydrovinylation, with low to moderate enantiomeric excesses up to 64% (Scheme 1.3).

1.1.1.3 Phosphites and aminophosphine ligands

Monophosphites ligands **Lig3** and aminophosphine ligand **Lig4** with glucopyranoside backbone were prepared by RajanBabu and coworkers (Figure 1.4)^{10,11}. and had been employed in [Ni]-hydrovinylation of vinyl arenes (Scheme 1.3).

¹⁰ H. Park, T. V. RajanBabu, *J. Am. Chem. Soc.*, **2002**, 124, 734-735.

¹¹ H. Park, R. Kumareswaran, T. V. RajanBabu, *Tetrahedron*, **2005**, 17, 6352-6367.

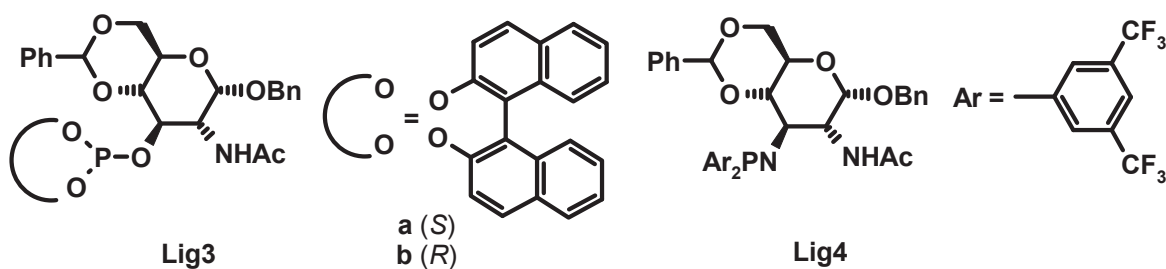
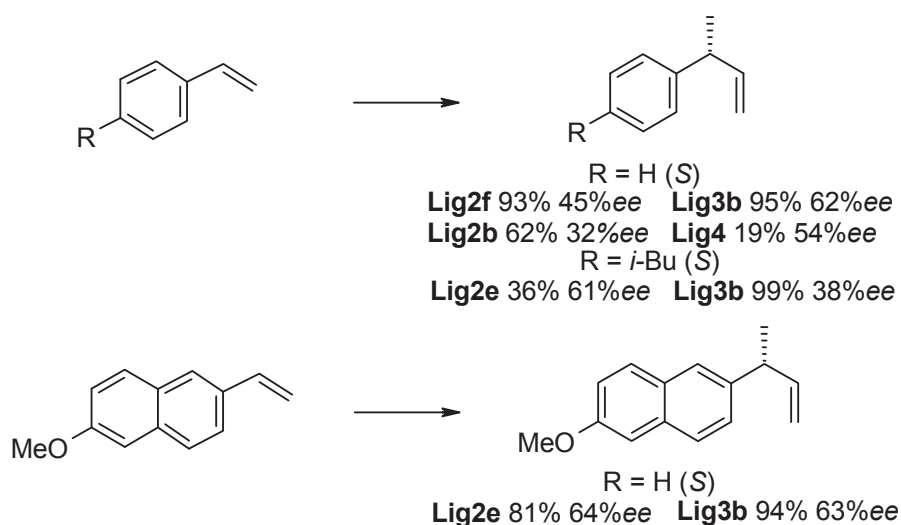


Figure 1.4 Phosphites ligands **Lig3a,b**, and aminophosphine ligand **L4**.

Best results were achieved with ligand **Lig3b** containing in its structure (*R*)-BINAP moiety, 2-methoxy-6-[(*S*)-1-methylallyl]naphthalene was formed with 94% of yield and 63% *ee* (Scheme 1.3).



Scheme 1.3 Asymmetric hydrovinylation reactions.

1.1.2 Bidentate ligands

1.1.2.1 Phosphines ligands

Recently Ruffo *et al.*¹² developed a strategy for preparing ligands **Lig5a-e** with structure similar to already known ligands in which *trans*-cyclohexanediamine¹³ core was replaced by D-glucosamine ring (Figure 1.5).

¹² (a) R. Del Litto, A. De Roma, A. D'Errico, S. Magnolia, F. Ruffo, *Tetrahedron: Asymmetry*, **2006**, 17, 2265-2269, (b) V. Benessere, A. De Roma, F. Ruffo, *ChemSusChem.*, **2008**, 1, 425-430, (c) A. De Roma, F. Ruffo, S. Woodward, *Chem. Commun.*, **2008**, 5384-5386.

¹³ B. M. Trost D. L. Van Vranken, and C. Bingel, *J. Am. Chem. Soc.*, **1992**, 114, 9327-9343.

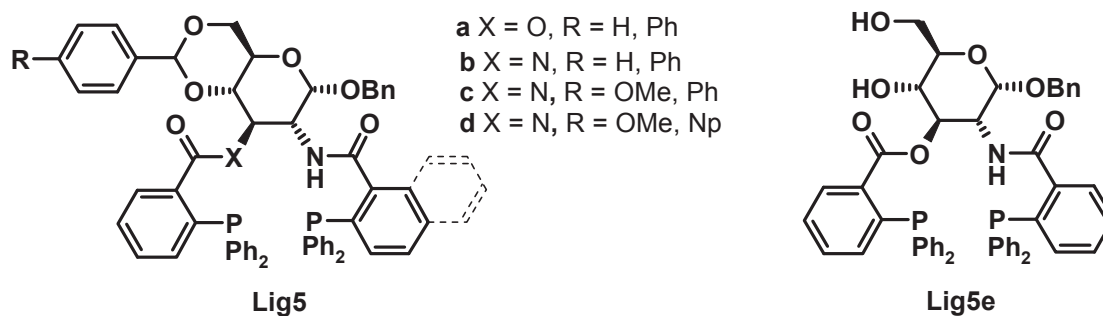
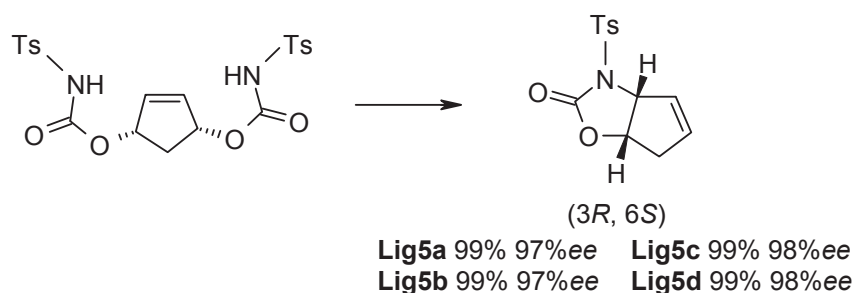


Figure 1.5 Trost type ligands L5.

These ligands have been successfully used in reactions for the carbon–carbon bonds formation such as the asymmetric allylic alkylation of *meso*-2-cyclopenten-1,4-diol biscarbamate promoted by palladium, afforded product with excellent yields 99% and enantioselectivities up to 98% (Scheme 1.4)^{12a,b}.



Scheme 1.4 Asymmetric allylic alkylation.

Ligands **Lig5c,d,e** were also investigated in the copper catalysed Me₂Zn and Et₂Zn conjugate additions to linear enones (Table 1.1)^{12c}.

ligand	R	R'	R''	yield(%)	<i>ee</i> (%)
Lig5c	C ₅ H ₁₁	Me	Me	70	95(<i>R</i>)
	C ₆ H ₁₃	Me	Et	95	93(<i>R</i>)
	<i>i</i> -Pr	Me	Et	79	93(<i>R</i>)
	Me	Et	Et	65	67(<i>S</i>)

Table 1.1 Asymmetric conjugate addition reaction.

Authors found that the most successful ligand **Lig5c** is effective for the addition of both ZnMe₂ and ZnEt₂ to a class of enones possessing only aliphatic substituents with minimal steric profiles. In general, for all substrates this ligand provided better yields (up to 95%) and enantioselectivities (up to 95%).

1.1.2.2 Phosphinites ligands

RajanBabu *et al.*¹⁴ developed new 3,4-diarylphosphinite ligands with a pyranoside backbone (Figure 1.6).

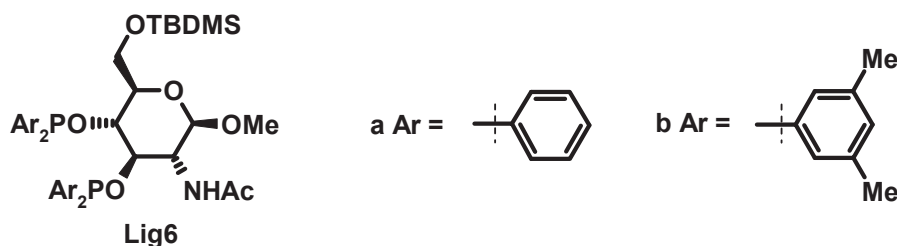


Figure 1.6 3,4-Diarylphosphinite ligands **Lig6**.

These ligands have been successfully applied in the [Rh]-catalysed asymmetric hydrogenation of alkenes which are aromatic and heteroaromatic derivatives of alanine (Table 1.2).

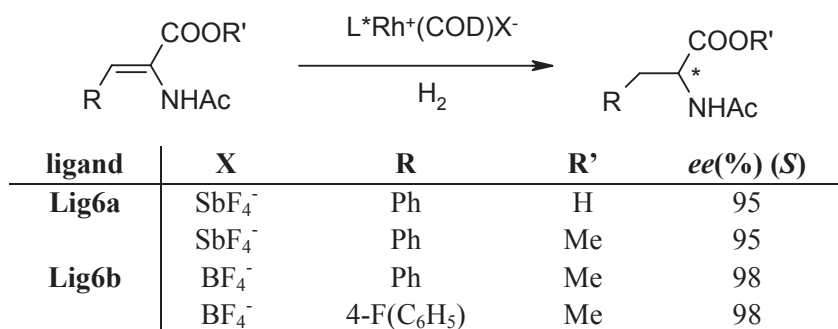


Table 1.2 [Rh]-catalysed asymmetric hydrogenation of alanine derivatives.

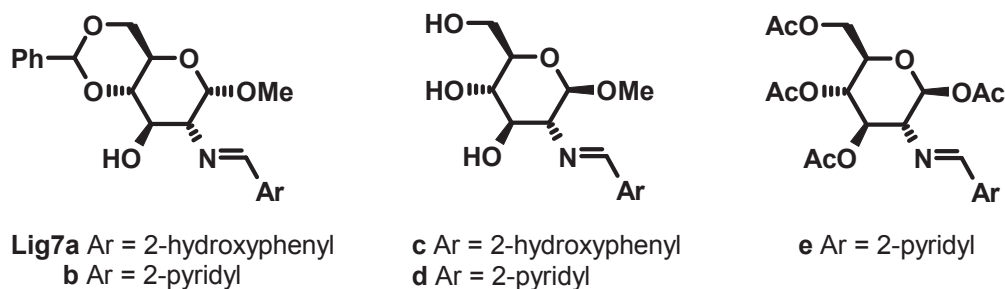
The widely available 2-deoxy-2-acetamido-glucose system **Lig6** was found to be an effective ligand for the production of D-amino acids with excellent enantioselectivities up to 98% *ee*. One of the limitations of those ligands prepared from the chiral pool is that they can catalysed only the formation of one enantiomer.

1.1.2.3 N/N ligands

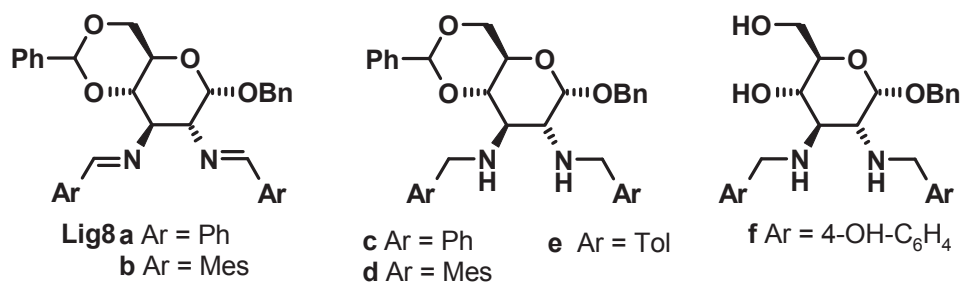
Milner *et al.*¹⁵ presented Schiff- base ligands derived from salicylaldehyde or pyridine-2-carboxaldehyde.

¹⁴ (a) T. V. RajanBabu, T. A. Ayers, A. L. Casalnuovo, *J. Am. Chem. Soc.*, **1994**, 116, 4101-4102. (b) T. V. RajanBabu, T. A. Ayers, G. A. Halliday, K. K. You, J. C. Calabrese, *J. Org. Chem.*, **1997**, 62, 6012-6028.

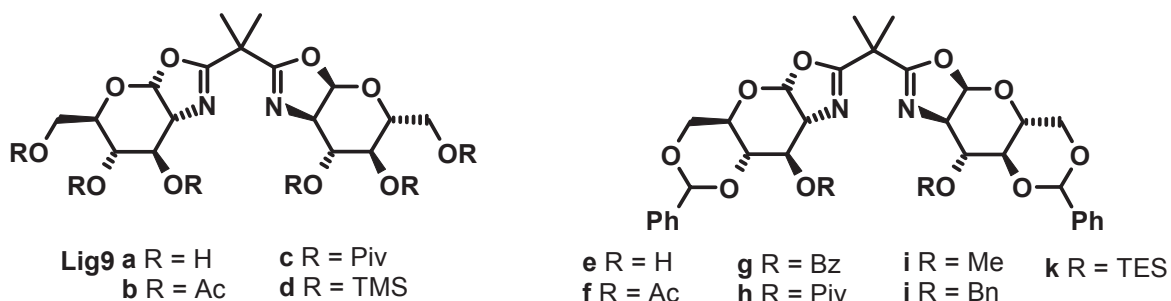
¹⁵ D. A. Holland, D. J. Laidler, D. A. Milner, *J. Mol. Catal.*, **1981**, 119-127.

Figure 1.7 Schiff- base ligands **Lig7**.

Ruffo *et al.*¹⁶ reported the synthesis of chiral diimino and diamino ligands **Lig8** by introducing amino function in 3-rd position in carbohydrate ring (Figure 1.8).

Figure 1.8 Diimino and diamino ligands **Lig8**.

Boysen *et al.*¹⁷ developed new type of carbohydrate-based bis(oxazoline) ligands **Lig9** (Figure 1.9).

Figure 1.9 Carbohydrate-based bis(oxazoline) ligands **Lig9**.

All ligands **Lig7-9** found application in the asymmetric copper(I) catalysed cyclopropanation of haloalkenes (Table 1.3). Ligands **Lig7a-e** as well as ligands **Lig8b-f** gave low to moderate yields and low geometric control. Results obtained with ligands **Lig9** were better however the stereoselectivity of cyclopropanations strongly depend from nature of substituents. For carbohydrate based bis(oxazolines) **Lig9a-d** best results were

¹⁶ (a) C. Borriello, M.E. Cucciolito, A. Panunzi, F. Ruffo, *Tetrahedron: Asymmetry*, **2001**, 12, 2467-2471, (b) C. Borriello, M. E. Cucciolito, A. Panunzi, F. Ruffo, A. Saporito, *Inorg. Chem. Commun.*, **2003**, 6, 1081-1085.

¹⁷ (a) M. Irmak, A. Groschner, M. M. K. Boysen, *Chem. Commun.*, **2007**, 177-179, (b) T. Minuth, M. Irmak, A. Groschner, T. Lehnert, M. M. K. Boysen, *Eur. J. Org. Chem.*, **2009**, 997-1008, (c) T. Minuth, M. M. K. Boysen, *Synlett*, **2008**, 1483-1486.

obtained when hindered as pivaloylated substituent was introduced; the major *cis* diastereomer was generated with 94% *ee* using ligand **Lig9c**. (Table 1.3).

$$\text{alkene} + \text{N}_2=\text{CHCOOR} \xrightarrow{[\text{Cu}]} \text{R1-}\triangle\text{-COOR} + \text{R1-}\triangle\text{-COOR}$$

ligand	alkene	R	Yield	<i>trans/cis</i>	<i>ee</i> _{<i>trans</i>} (%)	<i>ee</i> _{<i>cis</i>} (%)
Lig9b	4-MeOC ₆ H ₄	Et	72	65 : 35	77	80
		<i>t</i> -Bt	63	73 : 27	76	68
	Ph	Et	60	70 : 30	82	82
		<i>t</i> -Bt	44	68 : 32	74	64
Lig9c		Et	86	63 : 37	84	<u>94</u>
Lig9f		Et	90	79 : 21	<u>93</u>	82
Lig9h		Et	90	64 : 36	62	49

Table 1.3 Copper (I) catalysed cyclopropanation of olefins with ethyl or tert-butyl diazoacetates.

With benzyldiene-protected ligands **Lig9e-k**, authors observed steric and electronic effects of the 3-*O* substituent in carbohydrate ring. Small acetyl group gave far better results than those obtained with more bulky acyl residues and ether groups irrespective of their steric demand. The major *trans* diastereomer was formed in 93% *ee* using ligand **Lig9f** with acetyl substituent in 3-*O* position. Authors explain that phenomenon to be caused by conformational effect chair-like conformation which gives best results in combination with the rather small 3-*O* acetyl group. Peracetylated ligands **Lig9b** adopting a twist-like conformation, led to better results with bulky pivalate residues.

Ligand **Lig9b** in combination with copper was investigated also in Henry reaction¹⁸ with a wide range of aromatic, aliphatic and heteroaromatic aldehydes to afford the corresponding nitroalkanols with high enantioselectivity (up to 99%) in excellent yields (up to 95%) (Table 1.4).

$$\text{R-CHO} \xrightarrow{[\text{Cu}]} \text{R-CH(OH)-CH}_2\text{NO}_2$$

Ligand	R	Yield (%)	<i>ee</i> (%)	R	Yield (%)	<i>ee</i> (%)
Lig9b	Ph	85	94	2,5-(MeO) ₂ -C ₆ H ₄	88	92
	4-Cl-C ₆ H ₄	92	92	2,5-(MeO) ₂ -C ₆ H ₄	84	<u>99</u>
	4-Me-C ₆ H ₄	82	91	2-Np	<u>95</u>	90
	2-NO ₂ -C ₆ H ₄	88	91	2-MeO-C ₆ H ₄	82	90

Table 1.4 Enantioselective Henry reaction of aldehydes catalysed by complex of ligand **Lig9b** with copper.

¹⁸ B. V. Subba Reddy, Jimil George, *Tetrahedron: Asymmetry*, **2011**, 22, 1169-1175.

1.2 Heterodonor D-glucosamine based ligands

1.2.1 Bidentate ligands

1.2.1.1 P/N ligands

Carbohydrate oxazoline ligands derived from D-glucosamine can be easily formed, although N-acyl derivatives of this amino carbohydrate first time were described in 1998. Kunz and Gläser¹⁹ developed a phosphine-oxazoline ligand **Lig10a** (Figure 1.10). Uemura and coworkers²⁰ prepared a series of phosphinite-oxazoline ligands **Lig10b-h**.

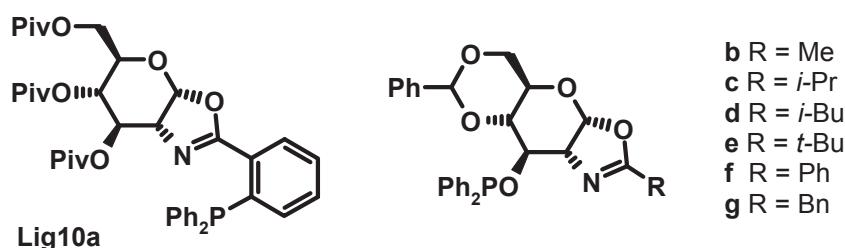


Figure 1.10 Phosphine oxazoline ligands **Lig10**.

Diéguez and Pàmies²¹ had designed a new family of carbohydrate based oxazoline ligands **Lig11-Lig15a-g** in with phosphite group carrying biphenyl residues with bulky substituents or naphthyl residues to position 3 in carbohydrate ring (Figure 1.11).

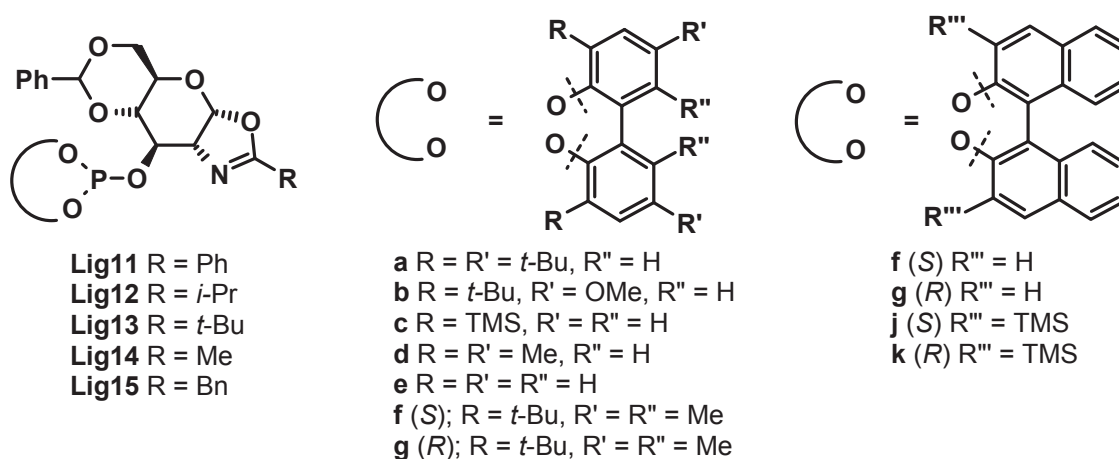


Figure 1.11 Phosphite D-glucosamine oxazoline type ligands **Lig11-15a-g**.

¹⁹ B. Gläser, H. Kunz, *Synlett*, **1998**, 53-54.

²⁰ (a) K. Yonehara, T.; Hashizume, K.; Mori, K.; Ohe, S. Uemura, *Chem. Commun.* **1999**, 415-416, (b) K. Yonehara, T.; Hashizume, K.; Mori, K.; Ohe, S. Uemura, *J. Org. Chem.* **1999**, 64, 9374-9380, (c) K. Yonehara, K. Mori, T. Hashizume, K. G. Chung, K. Ohe, S. Uemura, *J. Organomet. Chem.*, **2000**, 40-49.

²¹ (a) Y. Mata, M. Diéguez, O. Pàmies, C. Claver, *Adv. Synth. Catal.* **2005**, 347, 1943-1947, (b) Y. Mata, M. Diéguez, O. Pàmies, C. Claver, *Org. Lett.* **2005**, 7, 5597-5599, (c) Y. Mata, O. Pàmies, M. Diéguez, *Chem. Eur. J.* **2007**, 13, 3296-3304, (d) M. Diéguez, J. Mazuela, O. Pàmies, J. J. Verendel, P. G. Andersson, *J. Am. Chem. Soc.* **2008**, 130, 7208-7209, (e) J. Mazuela, P. Norrby, P. G. Andersson, O. Pàmies, M. Diéguez, *J. Am. Chem. Soc.*, **2011**, 133, 13634-13645.

Recently Shen *et al.*²² presented glucosamine-based phosphinite ligands **Lig16** and **Lig17**, and Khinar *et al.*²³ elaborated new D-glucosamine based ligands **Lig18** using reaction of ‘click chemistry’ (Figure 1.12).

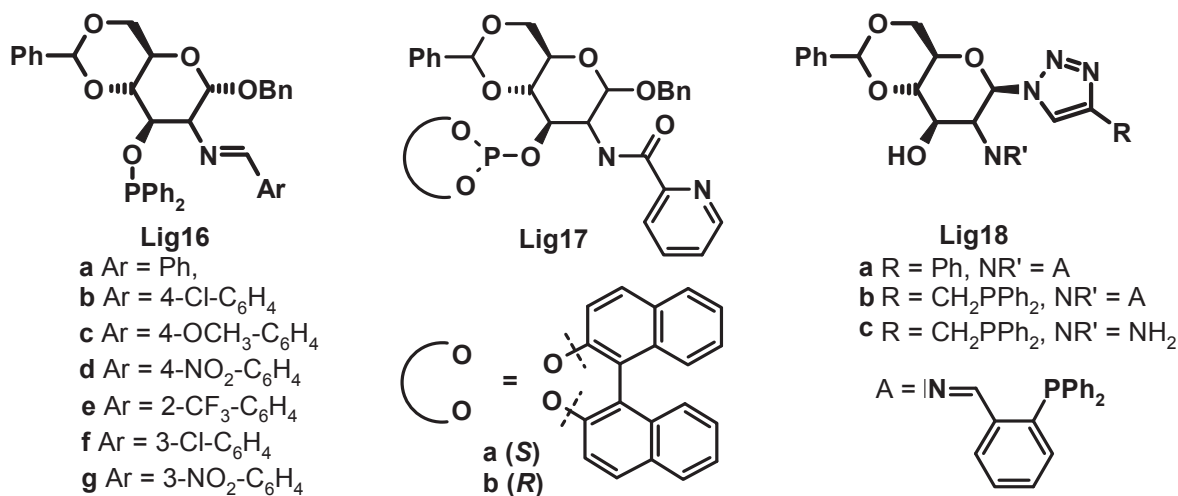
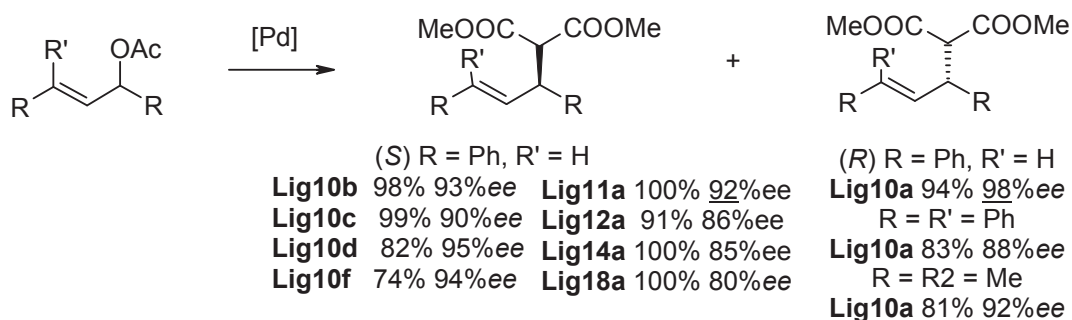


Figure 1.12 Carbohydrate-based phosphate ligands Lig16-17, and phosphine type Lig18.

[Pd] Allylic alkylation.

P/N ligands are well designed for allylic alkylation and most of them find application in this area. Ligands **Lig10-15** had been employed successfully in [Pd]-catalysed enantioselective allylation of dimethylmalonate to symmetrically and nonsymmetrically substituted allyl acetates^{19,20a,b,21a} yielded products in high enantioselectivities up to 98 % *ee* (for phosphine ligand **Lig10a**) (Scheme 1.5).



Scheme 1.5 Asymmetric allylic substitution reactions.

For ligands containing phosphate moiety activities are higher when less sterically demanding substituents are presented (Me>Ph>*i*-Pr>*t*-Bu). Ligand **Lig10b** with the smallest substituent on oxazoline ligand (R = Me) proceed the best enantioselectivity (96% *ee*). The ligands having bulky substituents gave lower *ees*.

²² (a) C. Shen, H. Xia, H. Zheng, P. Zhang, X. Chen, *Tetrahedron: Asymmetry*, **2010**, 21, 1936-1941,

(b) H. Xia, H. Yan, C. Shen, F. Shen, P. Zhang, *Catal. Commun.*, **2011**, 16, 155-158.

²³ N. Khinar, R. Navas, I. Fernández, *Tetrahedron Lett.*, **2012**, 53, 395-398.

Ligands were examined also with other various nucleophiles. Ligands **Lig16** were tested in reaction of allylic alkylation with dimethyl malonate (Scheme 1.5). Best results were obtained for ligand **Lig16d** and that ligand was used in reaction with other nucleophiles (Table 1.5). Good reactivities (up to 94%) and enantioselectivities (up to 93% *ee*) were generated with both bulky and substituted malonates. When benzylamine was used as a nucleophile, the highest enantiomeric excess (95% *ee*) was observed using the chiral ligand **Lig10d** ($R = i\text{-Bu}$). Almost the same level of enantioselectivity (94% *ee*) was achieved using for ligands **Lig10b,11d**.

Ligand	R	R	NuH	Yield(%)	<i>ee</i> (%)
Lig10b	COOEt	Ph	Benzylamine	78	94 (<i>R</i>)
Lig10d				72	<u>95</u> (<i>R</i>)
Lig11a				60	94 (<i>R</i>)
Lig16d	OAc		CH ₂ (COOEt) ₂	<u>94</u>	88 (<i>S</i>)
			CH ₂ (COOBn) ₂	90	88 (<i>S</i>)
		Me	CH ₂ (COOEt) ₂	58	93 (<i>S</i>)

Table 1.5 Allylic substitution with different nucleophiles.

[Pd] Heck reaction

D-glucosamine based phosphinite-oxazolines **Lig10-15** were studied in Heck reactions^{20a,21a,c} with different substrates aryl triflates and led to good yields and enantioselectivities of products, however in many cases was observed also compound obtained by isomerization of desired product (Table 1.6).

X = O				X = CH ₂			
Ligand	R	Yield (%) (conv.)	Ee (%)	Ligand	R	Yield (%) (conv.)	Ee (%)
Lig10d	Ph	100	93	Lig11a	Ph	(100)	94
Lig10g		100	<u>96</u>		1-cyclohexen	(95)	<u>96</u>
Lig11a	1-cyclohexen	(98)	98	Lig11c	Ph	(92)	95
Lig11c	Ph	(97)	99		1-cyclohexen	(93)	96
	1-cyclohexen	(92)	97	Lig14a	Ph	(93)	94
Lig14c	Ph	(98)	<u>99</u>		1-cyclohexen	(92)	94

Table 1.6 Asymmetric intramolecular Heck reaction.

2,3-Dihydrofuran was transformed to 2-aryl-2,5-dihydrofuran using ligand **Lig10g** with 100% of yield, and 96% *ee*). When cyclopentene was used as starting material the most

Bibliography

efficient worked ligand **Lig11a**, coupling product was obtained with 94% *ee* in 100% conversion. Many other substrates and aryl triflates were tested, however yields and enantioselectivities were worse than in presented cases.

[Ir] Hydrogenation

D-glucosamine based oxazoline ligands **Lig11-Lig15a-g** with phosphite moiety were extensively studied in hydrogenation of minimally functionalized olefins^{21d,f}.

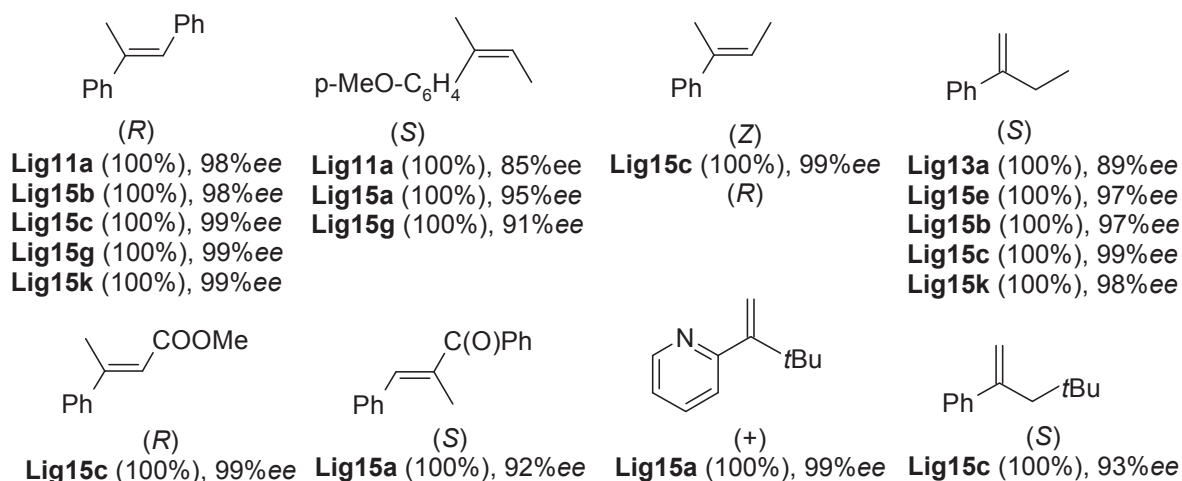


Figure 1.13 Examples of olefins used for hydrogenation and results of catalysis.

Excellent ligands have been identified for a range of substrates, including disubstituted terminal olefins as well as trisubstituted olefins (Figure 1.13).

[Cu] Addition of diethylzinc to acyclic enones.

Ligands **Lig17a,b**, were tested in enantioselective 1,4-conjugate addition of diethylzinc to acyclic enones^{22b}. Authors dedicated more attention for testing ligand containing (S)-BINOL in its structure **Lig17a**. Moderate to high yields (up to 81%) and enantioselectivities (up to 78% *ee*) were obtained (Table 1.7).

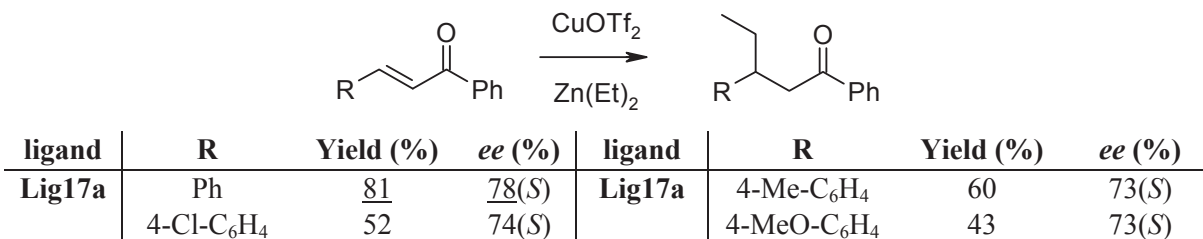


Table 1.7 Addition of diethylzinc to acyclic enones

1.2.1.2 P/O ligands

Our team carried out a synthesis of different phosphino-amido ligands based on D-glucosamine. Among the ligands were compounds with free hydroxyl groups, tetra- or triacetylated containing different substituents in α or β position on anomeric carbon, and each contained phosphine moiety connected with amino function via aromatic ring or aliphatic chain (Figure 1.14)^{24,25}.

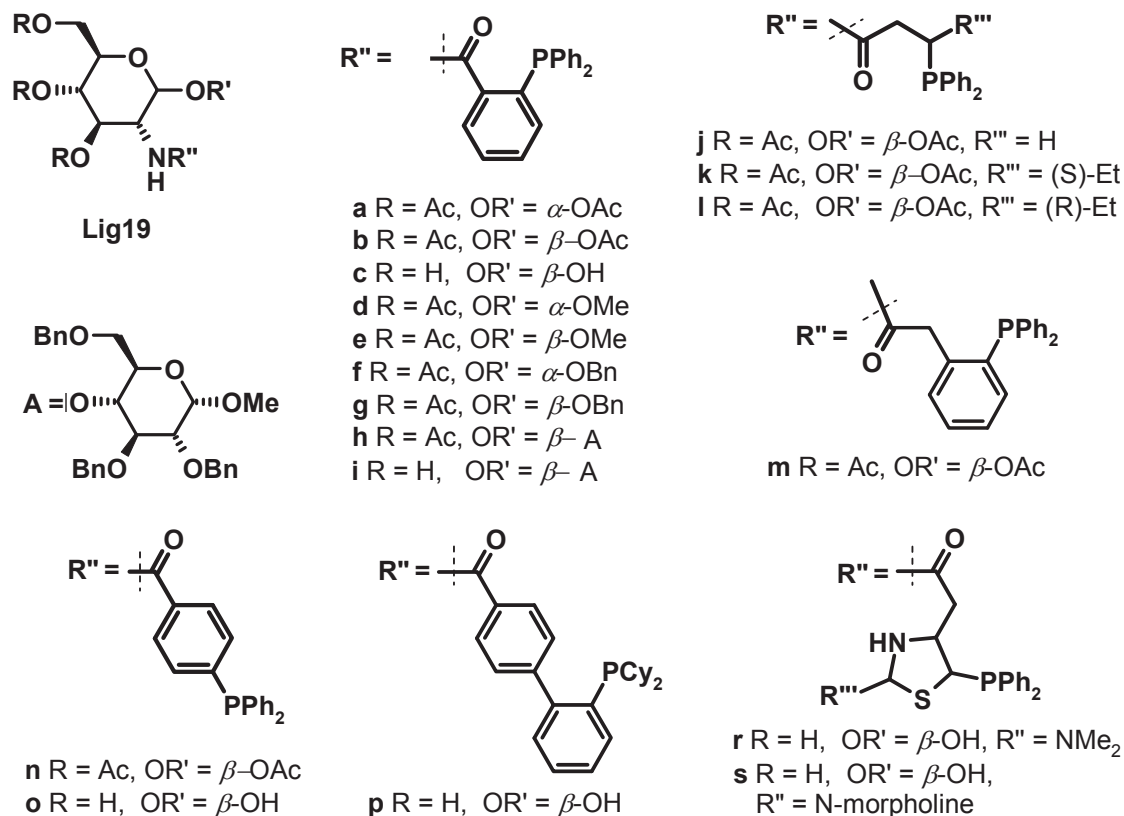


Figure 1.14 Phosphino-amido ligands L28-L30 for allylic alkylation reactions.

Also synthesis of different phosphino-imino **Lig20** and phosphino-amino **Lig21** type ligands was elaborated (Figure 1.15)²⁶.

²⁴ (a) M. Tollabi, E. Framery, C. Goux-Henry, D. Sinou *Tetrahedron: Asymmetry*, **2003**, 14, 3329-3333, (b) A. Konovets, K. Glegoła, A. Penciu, E. Framery, P. Jubault, C. Goux-Henry, K. M. Pietrusiewicz, J. C. Quirion, D. Sinou, *Tetrahedron: Asymmetry*, **2005**, 16, 3183-3187, (c) K. Glegoła, E. Framery, C. Goux-Henry, K. M. Pietrusiewicz, D. Sinou, *Tetrahedron*, **2007**, 63, 7133-7141.

²⁵ (a) S. Parisot, R. Kolodziuk, C. Goux-Henry, A. Iourtchenko, D. Sinou, *Tetrahedron Lett.*, **2002**, 43, 7397-7400, (b) R. Kolodziuk, A. Penciu, M. Tollabi, E. Framery, C. Goux-Henry, A. Iourtchenko, D. Sinou, *J. Organomet. Chem.*, **2003**, 687, 348-391. (c) A. Konovets, A. Penciu, E. Framery, N. Percina, C. Goux-Henry, D. Sinou, *Tetrahedron Lett.*, **2005**, 46, 3205-3208.

²⁶ (a) S. A. Johannesen, K. Glegoła, D. Sinou, E. Framery, T. Skrydstrup, *Tetrahedron Lett.*, **2007**, 48, 3569-3573, (b) K. Glegoła, S. A. Johannesen, L. Thim, C. Goux-Henry, T. Skrydstrup, E. Framery, *Tetrahedron Lett.*, **2008**, 49, 6635-6638.

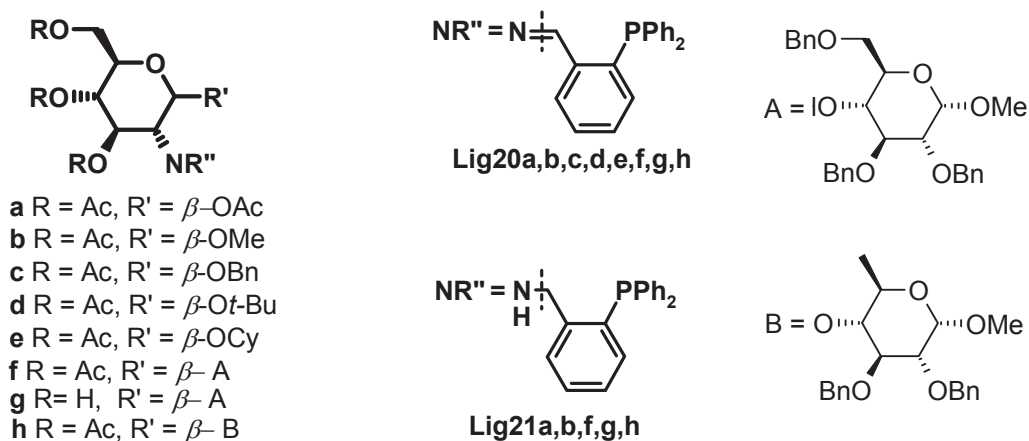


Figure 1.15 Phosphino-imino **Lig20** and phosphino-amino **Lig21** type ligands.

Recently Ruffo and Benessere²⁷, presented ligands **Lig22** in which oxygen in third position in carbohydrate ring was replaced with nitrogen (Figure 1.16).

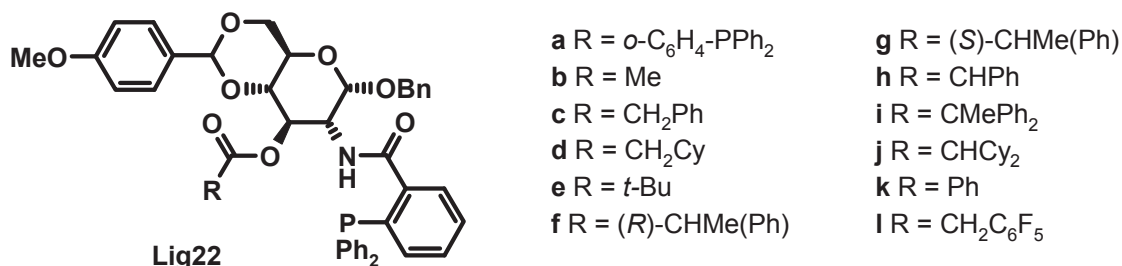


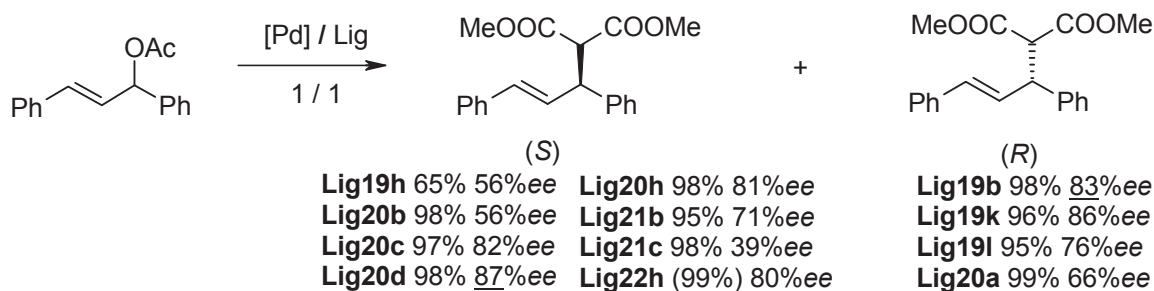
Figure 1.16 Ligands **L22** prepared by Ruffo.

[Pd] Allylic alkylation

Compounds **Lig19-22** were applied in reactions of allylic substitution of 1,3-diphenylprop-2-enyl acetate with dimethyl malonate. Two different ratios of palladium / ligand were investigated. In proportions of palladium / ligand 1 / 1 P,O-chelation type was observed (Scheme 1.6), and with ratio 1 / 2 ligands P,P-chelation took place (Scheme 1.7).

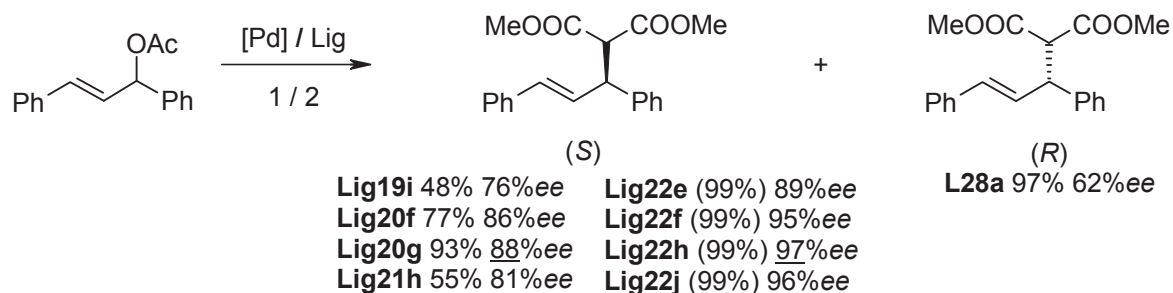
For the first type of chelation (P,O) with phosphino-amido ligands **Lig19** the best results were obtained for **Lig19b** containing acetyl group in β -position on anomeric carbon (98% of yield and 83% *ee* for *R* enantiomer). Among phosphino-imino ligands **Lig20** turned out to be the best **Lig20d** with sterically demanding *tert*-butyl function in anomeric position (98% of yield and 87% *ee* for *S* enantiomer) (Scheme 1.6)

²⁷ (a) V. Benessere, F. Ruffo, *Tetrahedron: Asymmetry*, **2010**, 21, 171-176, (b) V. Benessere, M. Lega, A. Silipo, F. Ruffo, *Tetrahedron*, **2011**, 67, 4826-4831.



Scheme 1.6 Allylic substitution of 1,3-diphenylprop-2-enyl acetate with phosphino-amido, -imino, and -amino ligands **Lig19-22**, using ratio of metal/ligand 1/1.

For ratio palladium / ligand 1 / 2 (P,P-chelation) the biggest efficiency show diphosphine ligands **Lig22**, with catalysed reaction with conversions up to 99% and enantioselectivities up to 97% *ee*. But also good results were obtained with phosphino-imino ligand **Lig20g** containing carbohydrate molecule as bulky substituent in anomeric carbon (93% of yield and 88% *ee*) (Scheme 1.7).



Scheme 1.7 Allylic substitution of 1,3-diphenylprop-2-enyl acetate with phosphino-amido, -imino, and -amino ligands **Lig19-22**, using ratio of metal/ligand 1/2.

Among ligands **Lig19-21** two the best efficient were tested with other nucleophiles. In both cases high yields (up to 96%) and enantioselectivities (up to 97% *ee*) were observed (Table 1.8).

NuH	Lig19b [Pd] / Lig 1 / 1		Lig20g [Pd] / Lig 1 / 2	
	Yield(%)	<i>ee</i> (%)	Yield(%)	<i>ee</i> (%)
MeCH(COOMe) ₂	94	88(S)	/	85(R)
AcNHCH(COOMe) ₂	86	97(S)	96	99(R)
Benzylamine	70	93(S)		
Morpholine	92	81(S)		
(2-Naphtylmethyl)amine	58	93(S)		

Table 1.8 Allylic substitution with different nucleophiles

[Pd] Suzuki Myaura cross-coupling.

Reactivity of ligands **Lig18,20** was studied in reaction of Suzuki-Myaura coupling with different kind of boronic acids and different halides. Results are collected in Table 1.9.

Ar'-B(OH) ₂ + Ar-X		[Pd]	Ar'-Ar
Ligand	Aryl boronic acid Ar'B(OH) ₂	Aryl halide Ar-X	Yield % (conversion)
Lig18c	4-MeC ₆ H ₄ B(OH) ₂	4-Iodonitrobenzene	99
	4-MeOC ₆ H ₄ B(OH) ₂		99
	2,6-diMeC ₆ H ₃ B(OH) ₂		98
	C ₆ H ₅ B(OH) ₂		100
Lig18n		3-Bromonitrobenzene	99
		2-Bromochlorobenzene	(97)
Lig18o	4-CHOC ₆ H ₄ B(OH) ₂	4-Iodonitrobenzene	>99
	C ₆ H ₅ B(OH) ₂		100
Lig18p		4-Bromobenzaldehyde	>99
		4-Bromonitrobenzene	97
	4-MeC ₆ H ₄ B(OH) ₂	4-Chloronitrobenzene	99
	4-CNC ₆ H ₄ B(OH) ₂		99
Lig18s	4-CH ₃ C(O)C ₆ H ₄ B(OH) ₂		98
	C ₆ H ₅ B(OH) ₂	4-Iodonitrobenzene	100
Lig20a		Bromobenzene	(100)

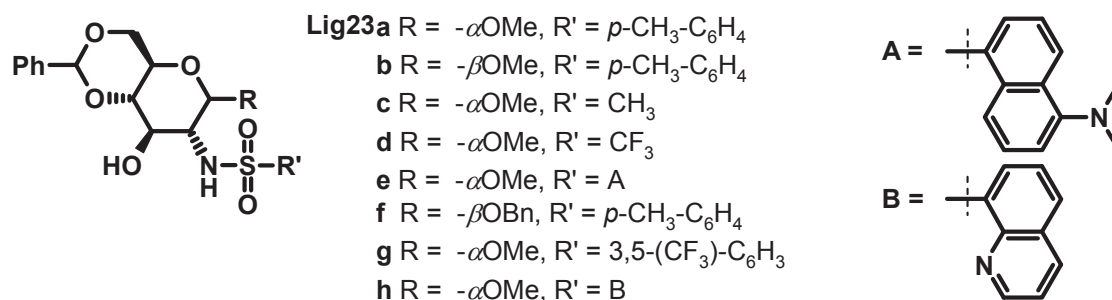
Table 1.9 Suzuki-Miyaura cross-coupling reactions catalysed by ligands **L16e**, **L29-L35**.

Palladium associated with a carbohydrate-based phosphine has been shown to have very high efficiency for the coupling reaction of iodides, chlorides and bromides with electron-rich as well as electron-poor substituents and a wide range of boronic acids. The polyhydroxylated ligands led to more active catalysts than the peracetylated ligands, also in case of ligand **Lig18p** it was possible to recycle the catalyst.

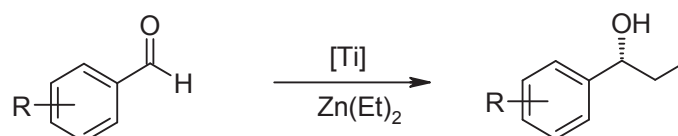
1.2.1.3 N/O ligands

Bauer *et al.*²⁸ presented the synthesis of sulfonamides derived from D-glucosamine (Figure 1.17) and their application as ligands in titanium tetraisopropoxide promoted enantioselective addition of diethylzinc to different aldehydes (Table 1.11).

²⁸ (a) T. Bauer, J. Tarasiuk, K. Pańniczek, *Tetrahedron: Asymmetry*, **2002**, 13, 77-82, (b) T. Bauer, S. Smoliński, *Appl. Catal. A: General*, **2010**, 375, 247-251, (c) T. Bauer, S. Smoliński, P. Gawel, J. Jurczak, *Tetrahedron Lett.*, **2011**, 52, 4882-4884.

Figure 1.17 Sulfonamides ligands **Lig23**.

The catalytic activity of ligands **Lig23a-f** was tested using different aromatic and aliphatic aldehydes.

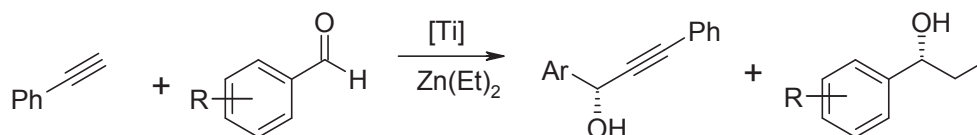


Ligand	R	Yield (%)	ee (%) (R)
Lig23a	H	99	97
	4-OMe	95	89
Lig23d	H	92	94
	3-OMe	74	99
	2-F	84	94
Lig23d	2-Cl	94	98
Lig23e	H	98	94

Table 1.10 Enantioselective addition of phenylacetylene to various aldehydes.

Excellent results generated ligands containing α -configuration on anomeric center, with sterically demanding sulfonamides, yields up to 99% and enantioselectivities up to 99% were obtained (Table 1.10).

Ligands **Lig23** were also tested in phenylacetylene addition to different aldehydes.



Ligand	R	Yield (%)	ee (%) (R)	68:69
Lig23a	H	73	66	95 : 1
Lig23e	H	74	53	98 : 2
Lig23g	H	82	90	99 : 1
	2-OMe	92	94	72 : 28
	2-F	68	92	85 : 15

Table 1.11 Enantioselective addition of phenylacetylene to various aldehydes

Bibliography

In test made with benzaldehyde as model substrate ligand **Lig23g** showed the biggest efficiency. This ligand was chosen for reaction with several aromatic aldehydes and enantiomeric excesses up to 94% were obtained (Table 1.11).

In 2008 Cheng *et al.*²⁹ used D-glucosamine as a natural ligand, in the *N*-arylation of imidazole with aryl and heteroaryl halides using CuI as a catalyst (Table 1.12).

Aryl halide Ar-X	Yield (%)	Aryl halide Ar-X	Yield (%)
Bromobenzene	84	2-Bromothiophene	82
2-Bromonaphtalene	86	3-Bromothiophene	83
1-Bromo-3,5-bis(trifluoromethyl)benzene	<u>91</u>	N-(2-bromo-4-methylphenyl)-2,2,2-trifluoroacetamide	90
4-Bromofluorobenzene	<u>90</u>	2-Chloropyrimidine	<u>95</u>

Table 1.12 *N*-arylation of imidazole catalysed by D-glucosamine.

Different aryl and heteroaryl bromides were used as the substrates and good yields up to 95% were obtained.

Recently³⁰ D-glucosamine was used also in copper catalysed synthesis of primary aryl amines from aryl halides and ammonia (Table 1.13). Various aryl iodides and aryl bromides provided good to excellent yield of the corresponding primary amines.

Aryl halide Ar-X	Yield (%)	Aryl halide Ar-X	Yield (%)
4-Iodobenzoic acid	96	3-Iodobenzophenone	95
4-Iodoanisole	90	2-Bromonitrobenzene	83
4-Bromonitrobenzene	<u>98</u>	1-Iodonaphtalene	95
4-Iodonitrobenzene	<u>98</u>	4-Iodobenzophenone	85

Table 1.13 Synthesis of primary aryl amines catalysed by D-glucosamine.

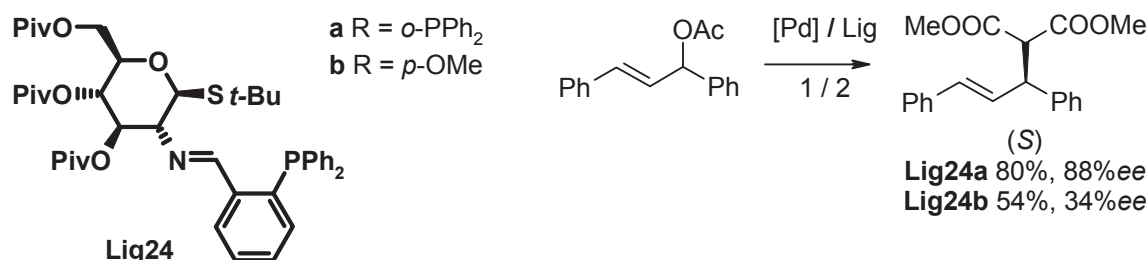
²⁹ D. Cheng, F. Gan, W. Qian, W. Bao, *Green Chem.*, **2008**, 171-173.

³⁰ K. G. Thakur, D. Ganapathy, G. Sekar, *Chem. Commun.*, **2011**, 5076-5078.

1.2.2 Tridentate ligands

1.2.2.1 P/N/S ligands

The tridentate phosphine imine thioglycoside ligand **Lig24a** derived from D-glucosamine (Scheme 1.8)³¹ was found to be a highly efficient catalyst precursor for [Pd]-catalysed asymmetric allylation of 1,3-diphenylpropenylacetate with dimethyl malonate.



Scheme 1.8 D-glucosamine based thioether ligands **Lig24** and their use in allylic allylation reaction

S-enantiomer was obtained with rather good yield 80% and enantiomeric excess 88%. Similar bidentate N/S ligand **Lig24b** without phosphine function was prepared and tested in the same reaction, with bad results (Scheme 1.8).

1.2.2.2 N/N/N ligands

In 2007 Boysen *et al.*³² prepared carbohydrate-derived pyridyl bis(thiazoline) ligands **Lig25** (Figure 1.18).

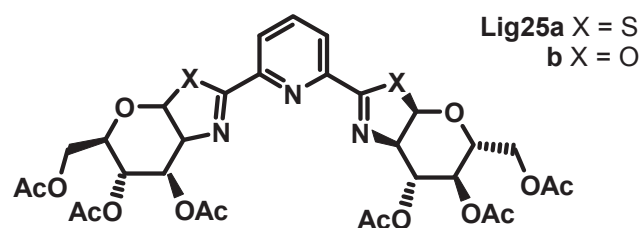


Figure 1.18 Bisoxazoline ligand prepared by Boysen.

Ligand **Lig25a** was used in cyclopropanation reactions. Different substrates were tested, however authors didn't success to obtaining good yields and enantioselectivities of products^{32a}.

Ligand **Lig25b**, was applied in [Cu]-catalysed alkynylations of imines^{32b}. Excellent enantiomeric excess (99% *ee*) was achieved for the alkynylation of imines derived from

³¹ N. Khiar, B. Suárez, I. Fernández, *Inorg. Chim. Acta*, **2006**, 359, 3048-3053.

³² M. Irmak, T. Lehnert, M. M. K. Boysen, *Tetrahedron Lett.*, **2007**, 48, 7890-7893, (b) M. Irmak, M. M. K. Boysen, *Adv. Synth. Catal.*, **2008**, 350, 403-405.

benzaldehyde and aniline with phenylacetylene. Other products were obtained with low to good yields and moderate enantioselectivities (Table 1.14).

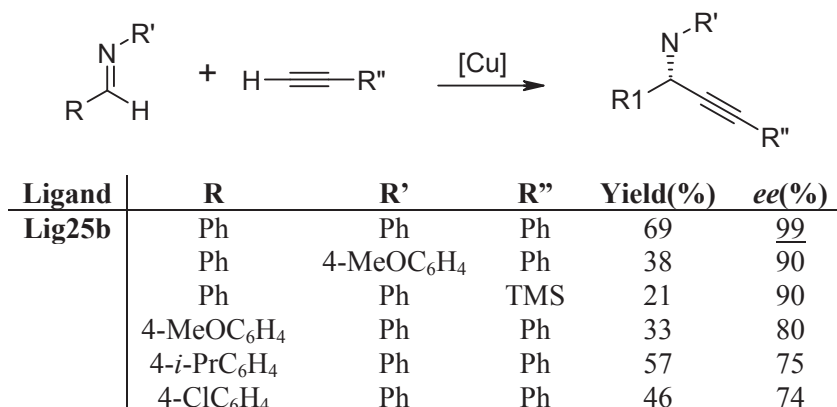


Table 1.14 Enantioselective alkynylation of imines with Lig25b.

1.2.2.3 N/N/O ligands

Ruffo *et al.*³³ prepared tridentate bis(pyridine-2-carboxamides) containing D-glucosamine moiety (Figure 1.19) and applied them in [Mo]-catalysed allylic alkylation by using both methyl (*E*)-3-phenyl-2-propenyl and methyl *rac*-1-phenyl-2-propenyl carbonates and dimethyl malonate as nucleophile under microwave irradiation (Table 1.15).

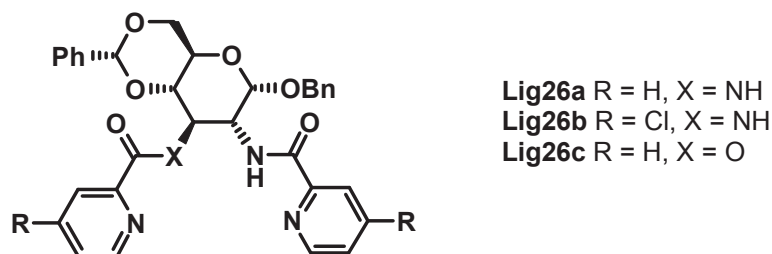
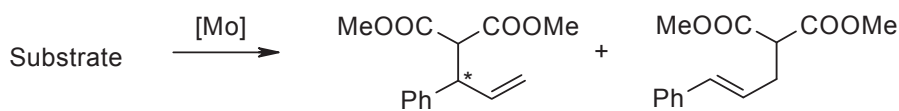


Figure 1.19 Bispyridine ligands Lig26.



Ligand	Substrate	Yield (%) (Conv.)	Regioselectivity (38/39)	ee (%)
Lig26a		90	49 : 1	99 (R)
Lig26b		(42)	12 : 1	87 (R)
Lig26a		90	8 : 1	96

Table 1.15 Asymmetric Allylic Alkylation reaction

³³ V. Benessere, R. Del Litto, F. Ruffo, C. Moberg, *Eur. J. Org. Chem.*, **2009**, 1352-1356.

High enantioselectivity up to 99% *ee* and high regioselectivity were observed for ligands **Lig26** containing amide functions in carbohydrate ring. No product was observed when monoamide **Lig26c** was used as ligand. Authors proofed importance of NH function in 3-rd position of carbohydrate ring.

1.2.2.4 O/N/O ligands

Ruffo et al.³⁴ presented new O/N/O-tridentate ligands, containing Schiff base (Figure 1.20).

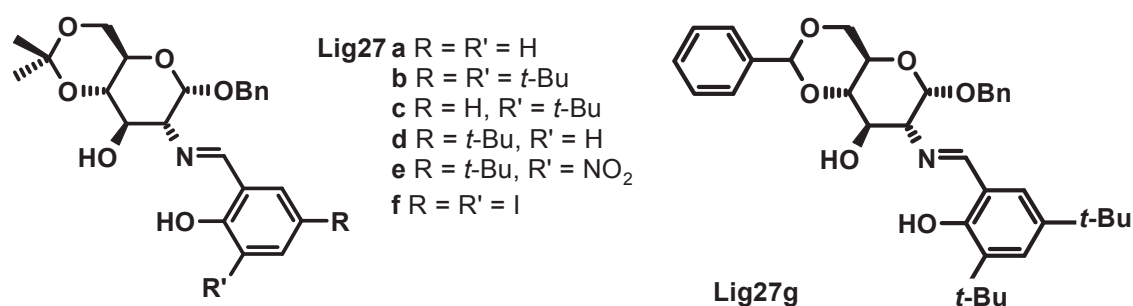
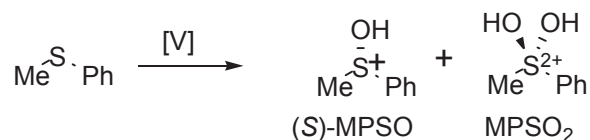


Figure 1.20 Tridentate ligands prepared by Ruffo.

Ligands were used in the [V]-promoted asymmetric oxidation of thioanisole (Table 1.16).



Ligand	Conv. (%)	Selectivity (MPSO/MPSO ₂)	<i>ee</i> (%) (S)	Ligand	Conv. (%)	Selectivity (MPSO/MPSO ₂)	<i>ee</i> (%) (S)
Lig27a	99	95/5	42	Lig27c	99	90/10	26
Lig27b	99	<u>97/3</u>	<u>60</u>	Lig27g	99	85/15	45

Table 1.16 Vanadium-catalysed oxidation of thioanisole.

All tested ligands give excellent conversions. Ligand **Lig27b** was the best choice from all examined. Very good selectivity and enantioselectivity (60% *ee*) was obtained.

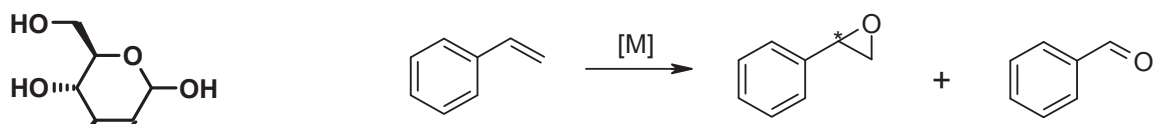
In 2006 other Schiff base carbohydrate ligand **Lig28** was described and used by Muzart *et al.* in [Ru]³⁵- and [Cr]-catalysed³⁶ asymmetric epoxydation of olefins. In all cases results achieved with [Ru] were better comparing to yields obtained with [Cr] complex, and

³⁴ M. E. Cucciolo, R. Del Litto, G. Roviello, F. Ruffo, *J. Mol. Catal. A*, **2005**, 236, 176-181.

³⁵ D. Chatterjee, S. Basak, A. Mitra, A. Sengupta, J. Le Bras, J. Muzart, *Inorg. Chim. Acta.*, **2006**, 359, 1325-1328.

³⁶ D. Chatterjee, S. Basak, J. Muzart, *J. Mol. Catal. A: Chem.*, **2007**, 271, 270-276.

enantioselectivities remain approximately the same. The best results were obtained for 1,2-dihydronaphthalene as substrate. Product of its oxidation was created selectively with 59% of yield and 47% *ee*.



Alkene	[Ru]		[Cr]	
	Oxide Yield (%)	<i>ee</i> (%)	Oxide Yield (%)	<i>ee</i> (%)
Styrene	62	42	34	43
4-Chlorostyrene	65	39	37	45
4-Methylstyrene	60	45	38	41
4-Methoxystyrene	59	37	40	44
1-Methylcyclohexene	32	45	29	39
1,2-Dihydronaphthalene	59	<u>47</u>	38	43

Table 1.17 Epoxydation of styrenes with complexes **Lig28**-[Ru], and **Lig28**-[Cr].

Epoxides were the major products in all cases however many others byproducts were observed: corresponding substituted benzaldehyde usually diols, phenylacetaldehyde for styrenes and 1,2-dihydronaphthalene, and allylic oxidation products for 1-methylcyclohexene).

1.2.3 Tetradentate ligands

1.2.3.1 N/N/O/O ligands

“Salen” type tetradentate ligands **Lig29** (Figure 1.21) were prepared and in combination with Yttrium or Manganese were used as catalysts.

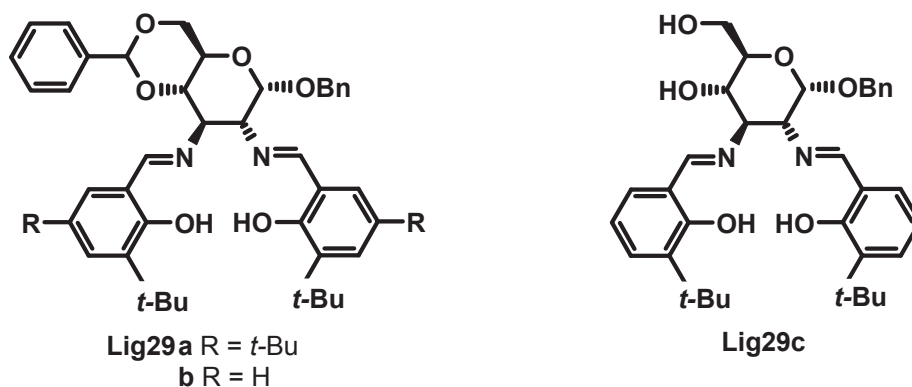
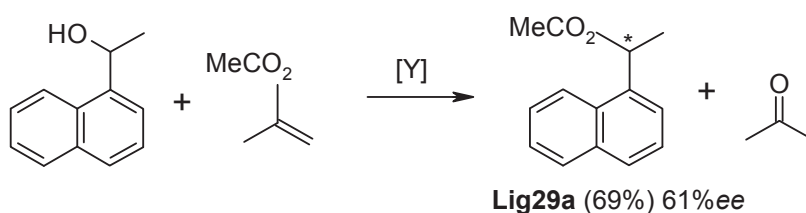


Figure 1.21 Tetradentate ligands prepared by Ruffo.

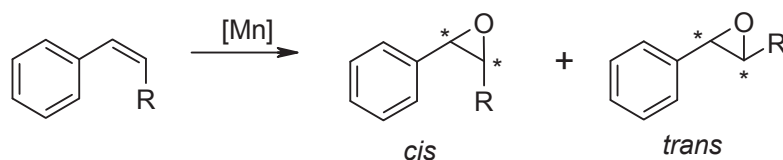
Ligand **Lig29a** was tested with Yttrium in *trans*-acylation between enolesters and chiral secondary alcohols (Scheme 1.9)³⁷.



Scheme 1.9 Transacylation catalysed by ligand **Lig29a**.

Kinetic resolution of 1-(1-naphthyl)ethanol using 2-propenyl acetate as the acyl transfer agent was examined. Product was obtained in enantiomeric excess of 61% with 69% of conversion of starting material.

Activity of ligands **Lig29a,b** was studied in asymmetric epoxydation of styrene and *cis*- β -methylstyrene (Table 1.18)³⁸.



Ligand	Alkene	R	Conv. (%)	Selectivity (<i>cis</i> / <i>trans</i>)	ee (%)
Lig29a	Styrene	H	99	-	50(<i>S</i>)
Lig29b	Styrene	H	99	-	54(<i>S</i>)
Lig29a	<i>cis</i> - β -Methylstyrene	Me	99	95/5	86(1 <i>S</i> ,2 <i>R</i>)
Lig29b	<i>cis</i> - β -Methylstyrene	Me	99	96/4	86(1 <i>S</i> ,2 <i>R</i>)
Lig29d	<i>cis</i> - β -Methylstyrene	Me	99	80/20	80(1 <i>S</i> ,2 <i>R</i>)

Table 1.18 Epoxydation of styrenes with Ligands **Lig29**

In all cases high conversions were obtained (99%), when styrene was used as substrate enantioselectivity was low up to 54% *ee*, using *cis*- β -methylstyrene selectivity of *cis* product was high and desired diastereoisomer (1*S*,2*R*) was obtained with up to 86% *ee*.

³⁷ M. H. Lin, T.V. RajanBabu, *Org. Lett.*, **2002**, 4, 1607-1610.

³⁸ (a) C. Borriello, R. Del Litto, A. Panunzi, F. Ruffo, *Tetrahedron: Asymmetry*, **2004**, 15, 681-686, (b) C. Borriello, R. Del Litto, A. Panunzi, F. Ruffo, *Inorg. Chem. Commun.*, **2005**, 8, 717-721.

1.3 Glucosamine derivatives as organocatalysts

Novel catalytic system which combines carbohydrate and amino acids moiety was subject of interest of three research groups: Machinami *et al.*³⁹ prepared organocatalysts **Lig30a-d**, Agarwal and Peddinti⁴⁰, prepared D-glucosamine based organocatalysts whose include the prolinamides **Lig30e-g** and Pedatella *et al.*⁴¹ prepared catalyst **Lig30h** (Figure 1.22).

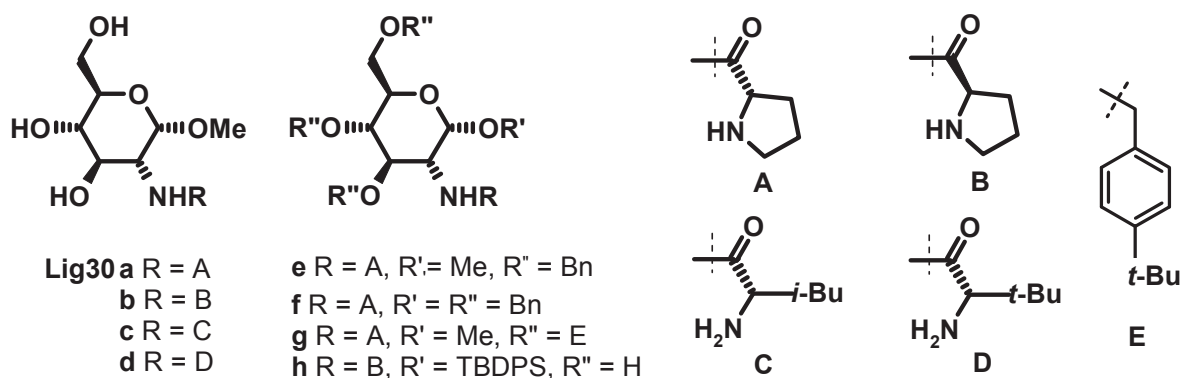
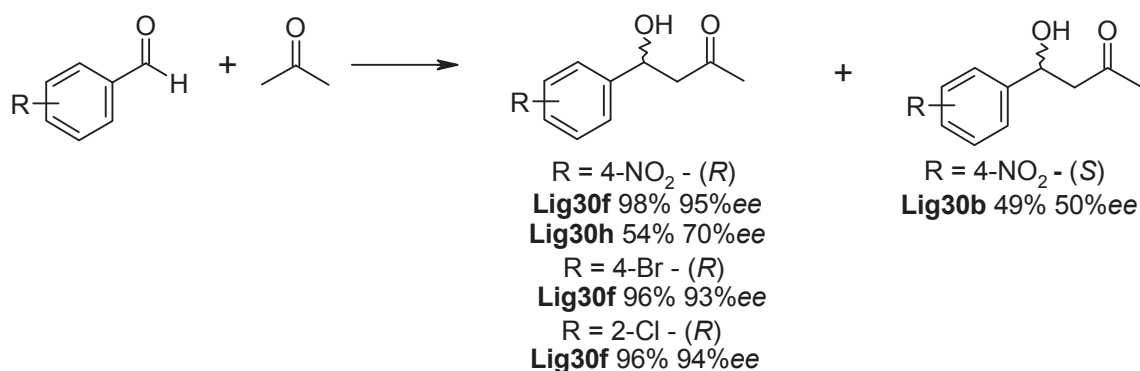


Figure 1.22 D-glucosamine based organocatalysts L44.

Lig30 catalysts were investigated in aldol reaction of acetone and different benzaldehydes in the presence of water. (Scheme 1.10).



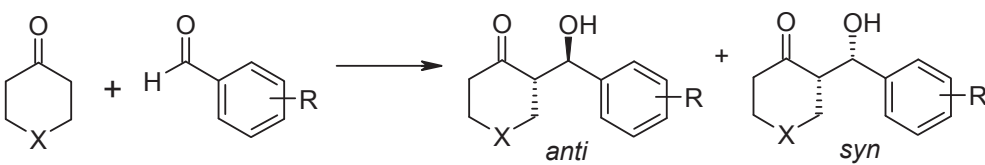
Scheme 1.10 Aldol reaction of aryl aldehydes with acetone 73.

D-glucosamine based prolinamides **Lig30e-h** (Figure 1.22) with different substituents in carbohydrate ring, were used in the aldol reaction between aromatic ketones and aryl aldehydes under solvent free conditions (Table 1.19). In case of **Lig30e-h** the corresponding aldol products with six-membered cyclic ketones as starting materials were obtained in excellent yields with high levels of *anti* diastereoselectivity (up to 99 : 1) and enantioselectivity (up to 99%).

³⁹ A. Tsutsui, H. Takeda, M. Kimura, T. Fujimoto, T. Machinami, *Tetrahedron Lett.*, **2007**, 48, 5213-5217.

⁴⁰ (a) J. Agarwal, R. K. Peddinti, *Tetrahedron: Asymmetry*, **2010**, 21, 1906-1909, (b) J. Agarwal, R. K. Peddinti, *Tetrahedron Lett.*, **2011**, 52, 117-121.

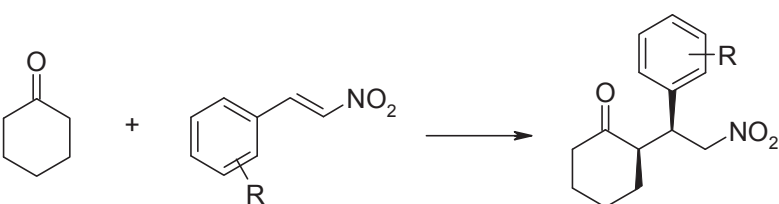
⁴¹ S. Pedatella, M. De Nisco, D. Mastroianni, D. Naviglio, A. Nucci, R. Caputo, *Adv. Synth. Catal.* **2011**, 353, 1443-1446.



Catalyst	X	R	Yield (%)	anti:syn	ee(%) anti
Lig30f	CH ₂	2-Nitro	97	97 : 3	96
	CH ₂	2-Bromo	85	97 : 3	97
	CH ₂	2-Methoxy	86	97 : 3	<u>99</u>
	O	2-Nitro	96	94 : 6	97
	S	2-Nitro	89	98 : 2	97
Lig30h	CH ₂	4-Chloro	99	97 : 3	98
	CH ₂	4-Cyano	99	97 : 3	96
	CH ₂	2-Nitro	96	98 : 2	<u>99</u>
	CH ₂	4-Fluoro	99	96 : 4	98

Table 1.19 Aldol reaction of cyclic ketones with substituted benzaldehydes in the presence of **Lig30**.

Catalysts **Lig30e-g** were tested in Asymmetric Michael addition in solvent free conditions^{40d}.



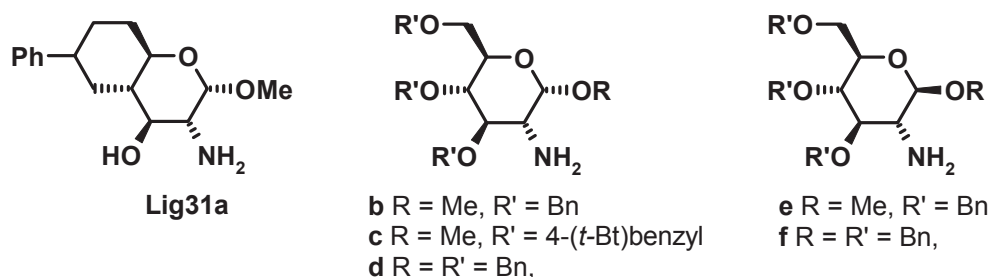
L	R	Yield (%)	dr (syn/anti)	er (syn)
Lig30f	2-NO ₂	96	90 : 10	76 : 24
	3-NO ₂	94	93 : 7	<u>84 : 16</u>
	2-Br	<u>98</u>	86 : 14	77 : 23
	4-Br	92	<u>98 : 2</u>	78 : 22
Lig30g	H	91	95 : 5	-

Table 1.20 The addition of acetylacetone to *b*-nitrostyrenes catalysed by ligands **Lig30**.

The best results were obtained when compound **Lig30f** was used as organocatalyst in the presence of benzoic acid as additive. Michael adducts were generated in high yields (up to 98%) with excellent diastereoselectivities (up to >99 : 1) and moderate enantiomeric ratios (up to 84 : 16) (Table 1.20).

Agarwal and Peddinti⁴² prepared amino organocatalysts **Lig31a-f**. Aldol reaction of cyclic ketones with substituted benzaldehydes however diastereoselectivities as well as enantioselectivities were worse than in case of ligands **Lig30e-h** (Figure 1.23).

⁴² J. Agarwal, R. K. Peddinti, *J. Org. Chem.* **2011**, 76, 3502-3505.

Figure 1.23 Organocatalysts **Lig31a-f**.

Kunz *et al.*⁴³ prepared series of bifunctional urea Schiff base organocatalysts (Figure 1.24).

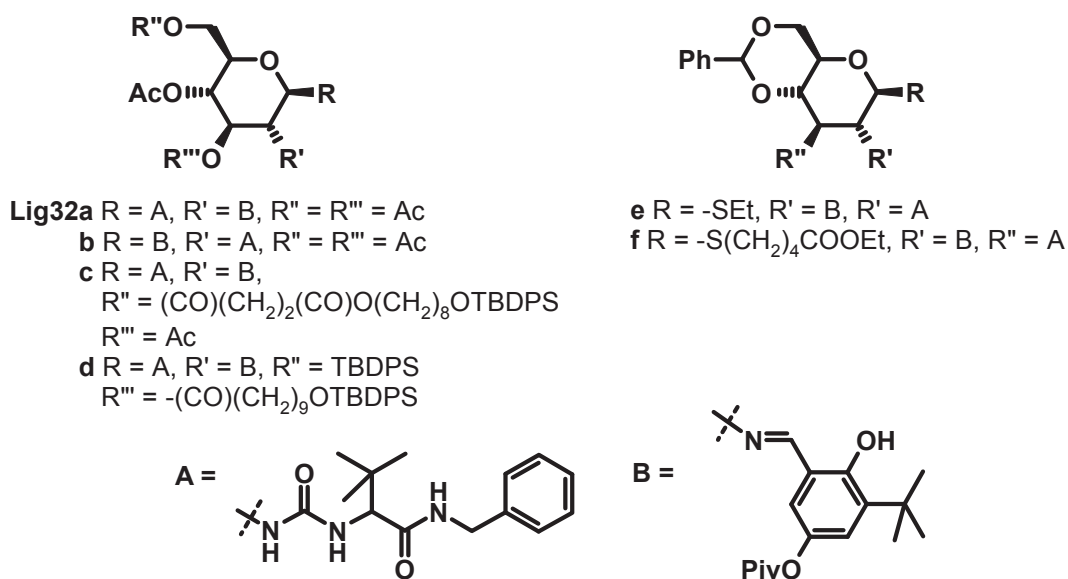
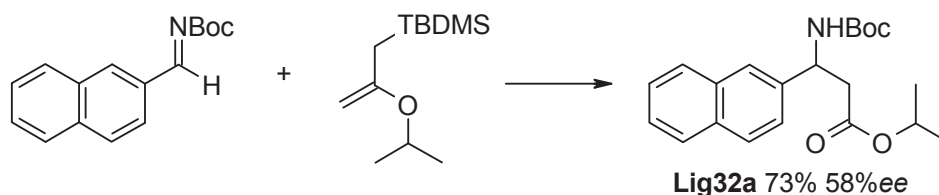


Figure 1.24 Urea organocatalysts.

Urea **Lig32a** was tried in enantioselective Mannich reactions giving rather low selectivity.



Scheme 1.11 Enantioselective Catalysis of the Mannich Reaction.

Other ligands were used in Strecker reaction of different imines with trimethylsilyl cyanide. Best results were obtained for catalyst **Lig32b** containing in anomeric β -position the urea moiety and the Schiff base linked to the 2-amino function, which lead to product with excellent enantioselectivity 95% ee. (Table 1.21). Remaining catalyst proceed to product with poor results.

⁴³ C. Becker, C. Hoben, H. Kunz, *Adv. Synth. Catal.* **2007**, 349, 417-424.

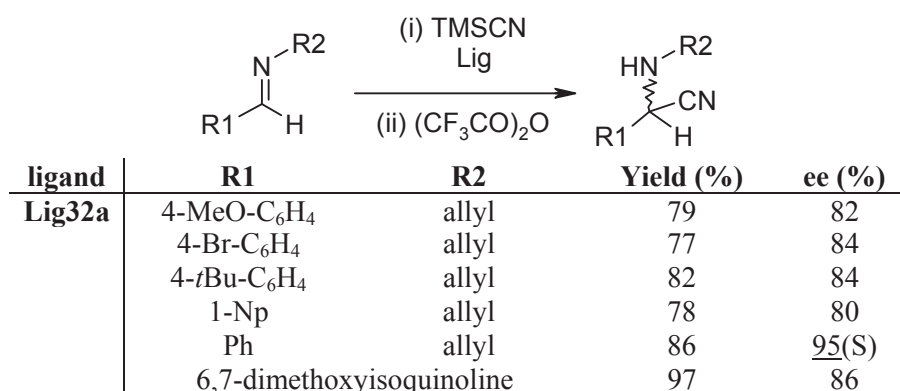


Table 1.21 Hydrocyanation of Imines (Strecker Reaction).

Recently Chen *et al.*⁴⁴ prepared of D-glucosamine-derived amino alcohols **Lig33a-e** (Figure 1.25)

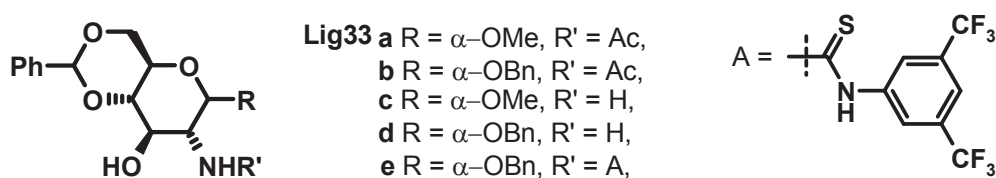


Figure 1.25 Various carbohydrate-derived catalysts screened for aldol reaction.

D-glucosamine hydrochloride and catalysts **Lig33a-e** were tested in the enantioselective aldol reaction of ketones with different isatins derivatives.

In mostly cases reaction occurred with good yields of desired compound, but the *ees* value obtained were poor (Table 1.22).

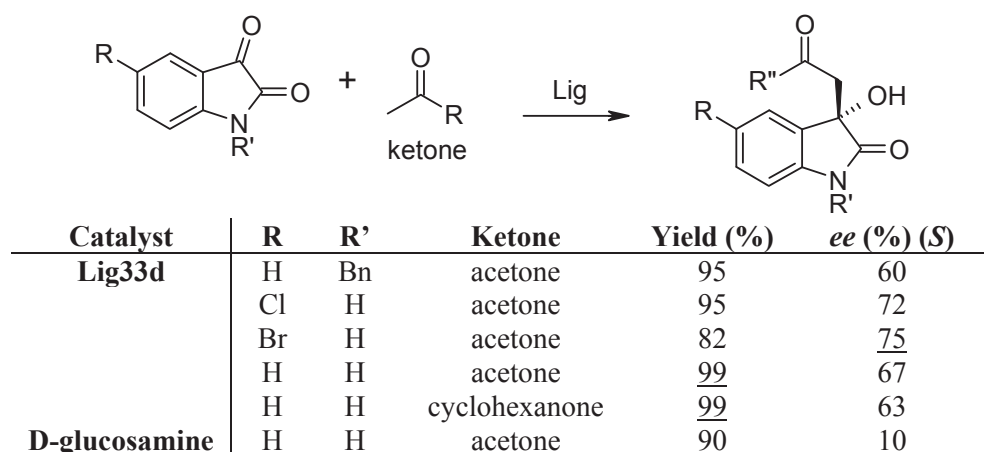


Table 1.22 Organocatalytic enantioselective aldol reaction addition of different ketones to various isatins.

When acetone was used as a substrate reaction occurred with good yields and moderate enantioselectivity up to 75% *ee*. D-glucosamine was also tested in this reaction however enantioselectivity of corresponding product did not reach more than 10% *ee* (Table 1.22).

⁴⁴ C. Shen, F. Shen, H. Xia, P. Zhang, X. Chen, *Tetrahedron: Asymmetry*, **2011**, 22, 708-712.

Other carbohydrate-based bifunctional organocatalysts were prepared by Poletti *et al.*⁴⁵ (Figure 1.26) and used in nucleophilic addition to nitroolefins and imines.

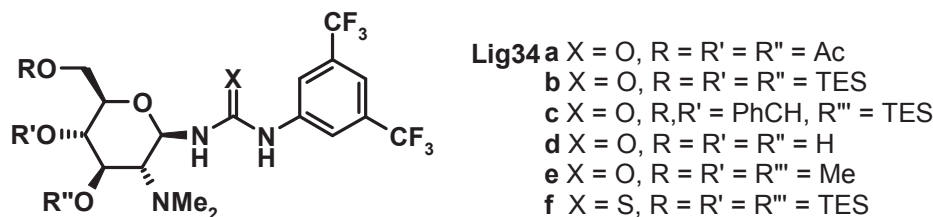


Figure 1.26 Glucosaminylurea-based organocatalysts.

Best results were obtained for catalyst **Lig34b**. in reaction addition of acetylacetone to β -nitrostyrene chemical yields up to 93% and enantioselectivities up to 89% were achieved (Table 1.23)

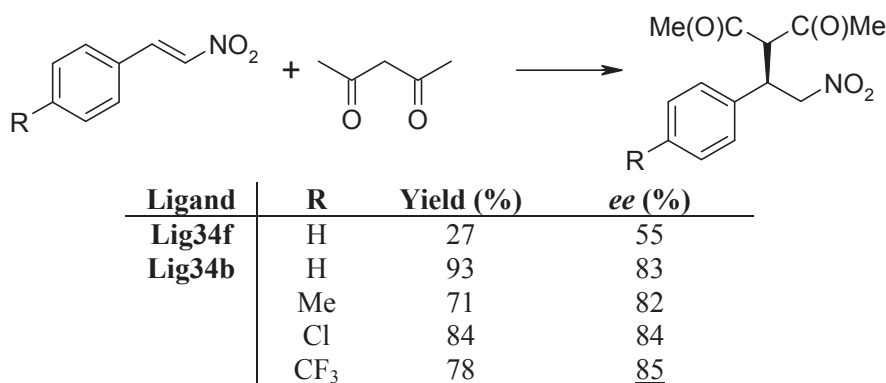
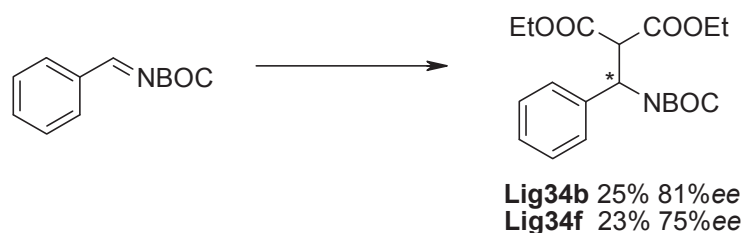


Table 1.23 The addition of acetylacetone to β -nitrostyrenes catalysed by ligands **Lig34**.

These catalysts were also preliminarily investigated as promoters in the addition of diethyl malonate to the *N*-BOC imine of benzaldehyde, affording the product with low yields and moderate enantioselectivities up to 81% *ee*. (Scheme 1.12)



Scheme 1.12 The addition of diethyl malonate to *N*-Boc imines.

In 2009 Boutureira *et al.*⁴⁶ prepared series of ketones, readily available from *N*-acetyl-D-glucosamine **Lig35a-f** (Figure 1.27) and in 2012 Schöberl and Jäger⁴⁷ enlarged library of those compounds for new **Lig35g**, **Lig36,37** organocatalysts.

⁴⁵ A. Puglisi, M. Benaglia, L. Raimondi, L. Lay, L. Poletti, *Org. Biomol. Chem.*, **2011**, 9, 3295-3302.

⁴⁶ O. Boutureira, J. F. McGouran, R. L. Stafford, D. P. G. Emmerson, B. G. Davis, *Org. Biomol. Chem.*, **2009**, 7, 4285-4288.

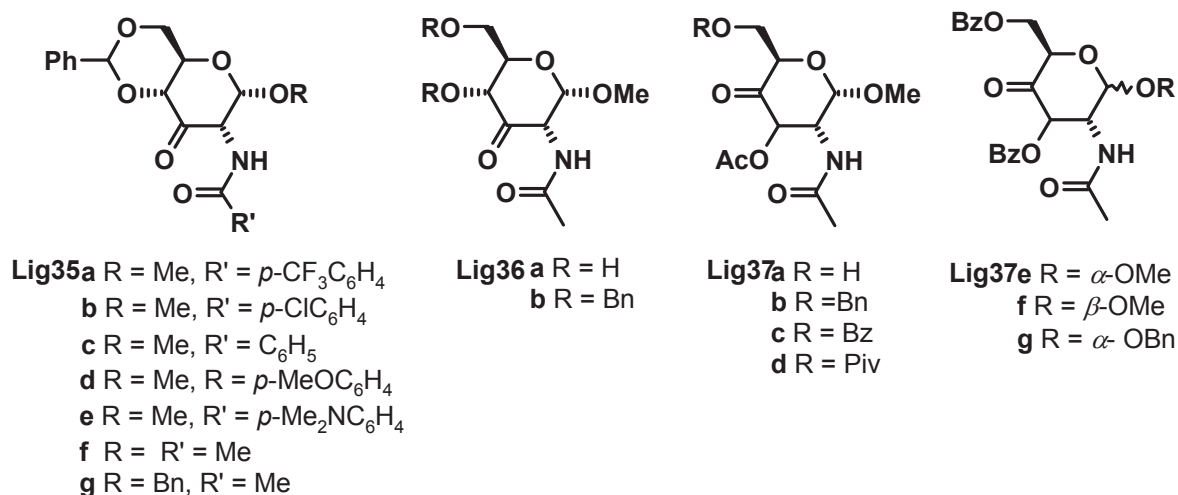


Figure 1.27 Organocatalysts Lig35-37.

Compounds were tested as asymmetric epoxydation catalysts. Different kind of olefins were screened. In case of **Lig35a-f** obtained yields were moderate to good (up to 98%) but yields were not higher than 67% *ee*. For other ligands similarly yields were moderate and enantioselectivities rather low. Best results were obtained for ethyl cinnamate, (enantiomeric ratio for product 90 : 10 *er* (2*R*,3*S*)) (Figure 1.28).

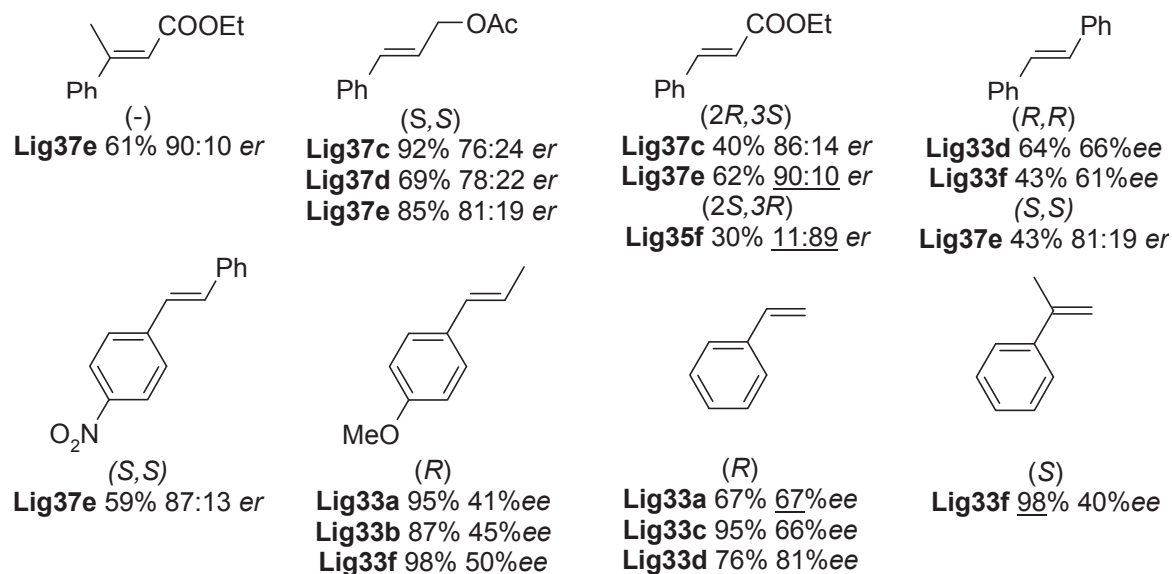


Figure 1.28 Results of asymmetric olefin epoxydation by organocatalysts L35-37.

⁴⁷ C. Schöberl, V. Jäger, *Adv. Synth. Catal.*, **2012**, 354, 790-796.

1.4 Glucosamine derivatives as reagents

Davis *et al.*⁴⁸ presented carbohydrate derived amino alcohols **Lig38-39** (Figure 1.29).

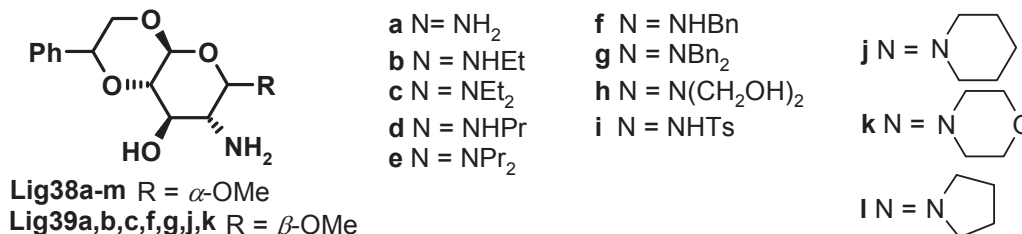
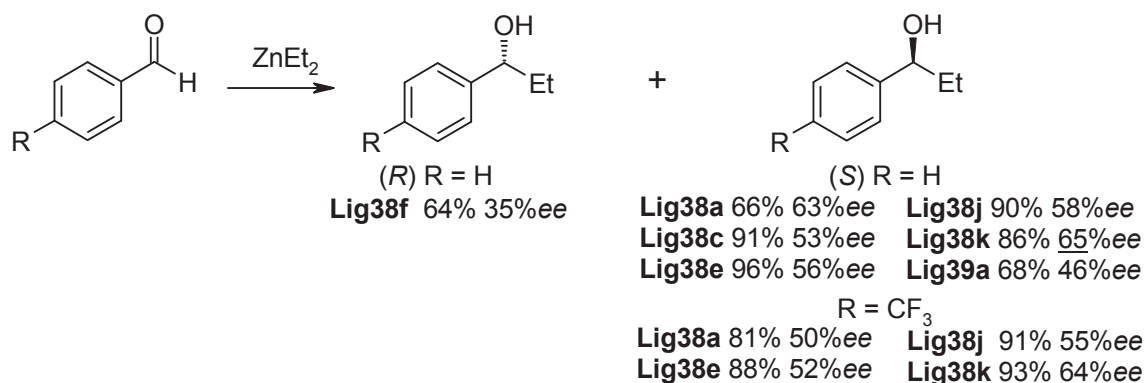


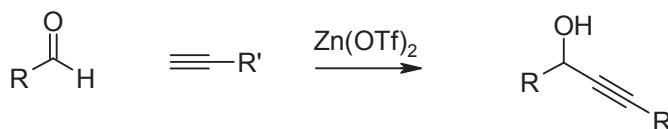
Figure 1.29 Ligands **Lig38-39**.

Those compounds were employed in addition of diethyl zinc to aldehydes. No high results were achieved with any of the substrates used. The highest enantiomeric excess was obtained for benzaldehyde as substrate using ligand **Lig38k** (65% *ee*) (Scheme 1.13).



Scheme 1.13 Addition of diethyl zinc to different aldehydes.

The same ligands were also investigated in the Zn(OTf)₂-mediated addition of alkynes to aldehydes^{48b}. Several alkynes as well as aliphatic and aromatic aldehydes were tested. In mostly cases reaction occurred with excellent enantioselectivities but more disappointing yields (Table 1.24).



Ligand	R	R'	Yield (%)	<i>ee</i> (%)	Ligand	R	R'	Yield (%)	<i>ee</i> (%)
Lig38k	<i>i</i> -Pr	Ph	80	95	Lig39k	Cyclohexyl	HO(CH ₂) ₂	90	98
Lig38l	Cyclohexyl	Ph	94	99		Cyclohexyl	Ph(CH ₂) ₂	89	95
Lig39k	<i>i</i> -Pr	Ph	70	97		<i>t</i> -Bu	Ph(CH ₂) ₂	77	99

Table 1.24 Alkylation of aldehydes.

⁴⁸ (a) D. P. G. Emmerson, R. Villard, C. Mugnaini, A. Batsanov, J. A. K. Howard, W. P. Hems, R. P. Tooze, B. G. Davis, *Org. Biomol. Chem.*, **2003**, 3826-3838, (b) D. P. G. Emmerson, W. P. Hems, B. G. Davis, *Org. Lett.*, **2006**, 8, 207-210.

Heterogeneous catalysis

1.5 Covalent bonding with polystyrene resin

Ruffo *et al.* prepared amido^{12b} and imino^{38b} glucosamine based ligands containing polystyrene resins in their structure. (Figure 1.30).

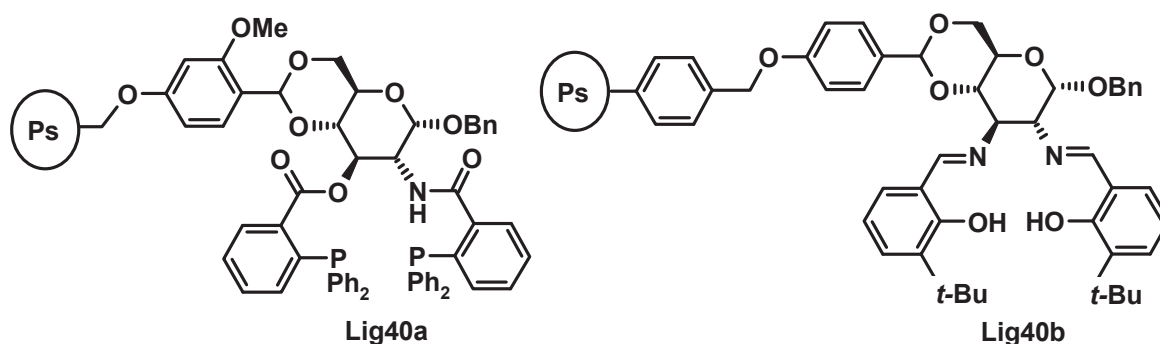
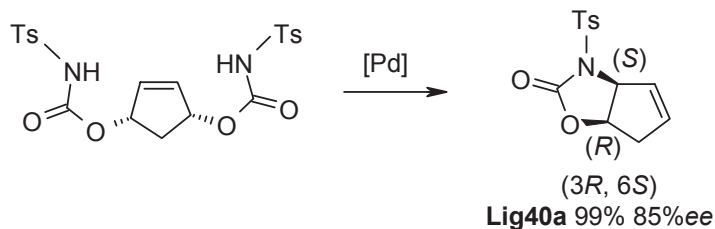


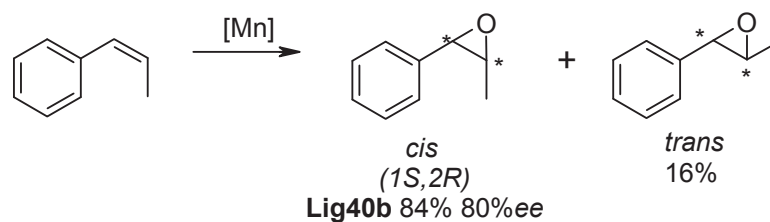
Figure 1.30 Ligands with polystyrene resin prepared by Ruffo.

Ligand **Lig40a** had been successfully used in the asymmetric allylic alkylation of *meso*-2-cyclopenten-1,4-diol biscarbamate promoted by palladium to afford product with excellent yield 99% but rather moderate enantioselectivity 85%. (Scheme 1.14)^{12b}.



Scheme 1.14 Asymmetric allylic alkylation reaction.

“Salen” type tetradentate ligand **Lig40b** (Figure 1.30) was tested in asymmetric epoxydation of *cis*- β -methylstyrene, with rather low selectivity of *cis* product and moderate enantioselectivity 80% *ee*^{38b}.



Scheme 1.15 Epoxydation of *cis*- β -methylstyrene with ligand **Lig40b**

Bibliography

Kunz *et al.*⁴³ prepared series of bifunctional urea Schiff base organocatalysts **Lig41**. Ligands were immobilized on polystyrene either via the carbohydrate **Lig41a,b** or via the amino acid amide **Lig41c** (Figure 1.31).

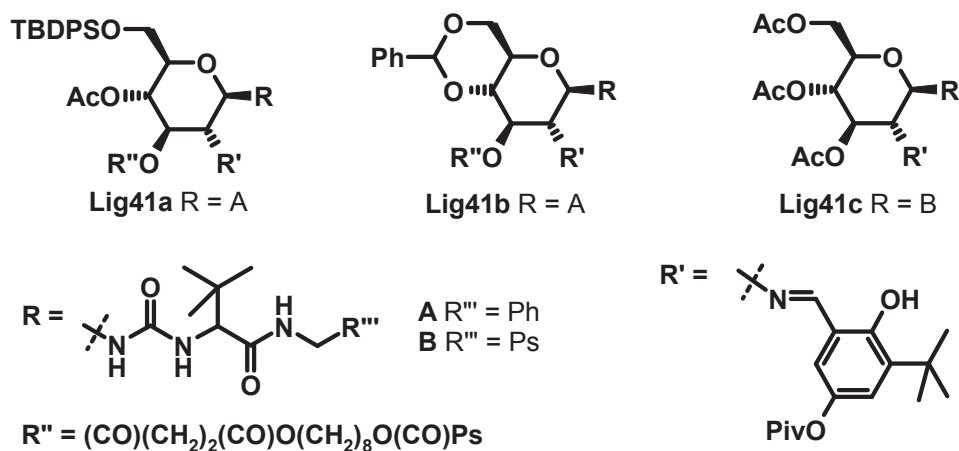
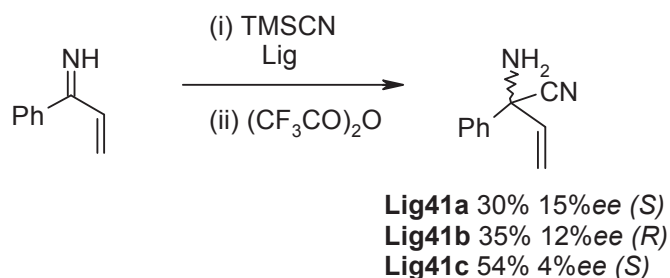


Figure 1.31 Urea organocatalysts.

Ligands were used in Strecker reaction of benzaldimine, with disappointing results. In any case yield did not exceed more than 54% and enantioselectivity was not higher than 15% ee (Scheme 1.16).



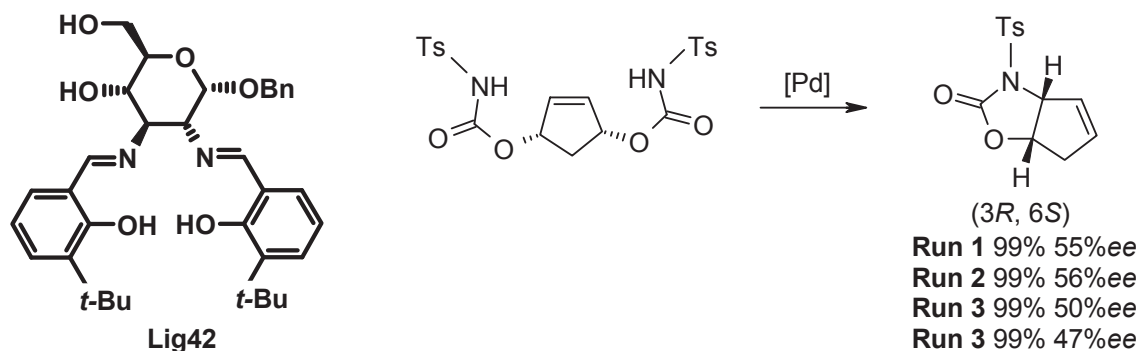
Scheme 1.16 Hydrocyanation of Imines (Strecker Reaction).

1.6 Biphasic catalysts

Ionic liquids are among the most promising green solvents⁴⁹. Their use does not require specific tagging of the catalyst, however ligands should be polar to increase affinity for the ionic liquids and avoid leaching of the catalyst into the organic product phase.

Group of Ruffo prepared ligand **Lig42** and used it in the reaction of allylic alkylation of *meso*-2-cyclopenten-1,4-diol biscarbamate using 1-butyl-3-methylimidazolium tetrafluoroborate (BMIM[BF₄]) as solvent.

⁴⁹ Ionic Liquids in Synthesis (Eds.: P. Wasserscheid, T. Welton), Wiley-VCH, Weinheim, 2003.



Scheme 1.17 Ligand use in ionic liquids.

Product was obtained with full conversion and 55% of *ee*. Catalyst phase was recycled for further runs, four first cycles were reproducible, in further cycles both yield and enantioselectivity progressively decreased (Scheme 1.17).

Uemura and Ohe⁵⁰ prepared water soluble ligand **L19**, bearing a diethylaminomethyl group on the phenyl ring of the phosphinite moiety (Table 1.25). His complex with palladium and [BF₄⁻] worked effectively as a catalyst and provided good enantiomeric excess in allylic alkylation and amination in water or an aqueous/organic biphasic medium. The product could be easily separated from the water-soluble catalyst by phase separation.

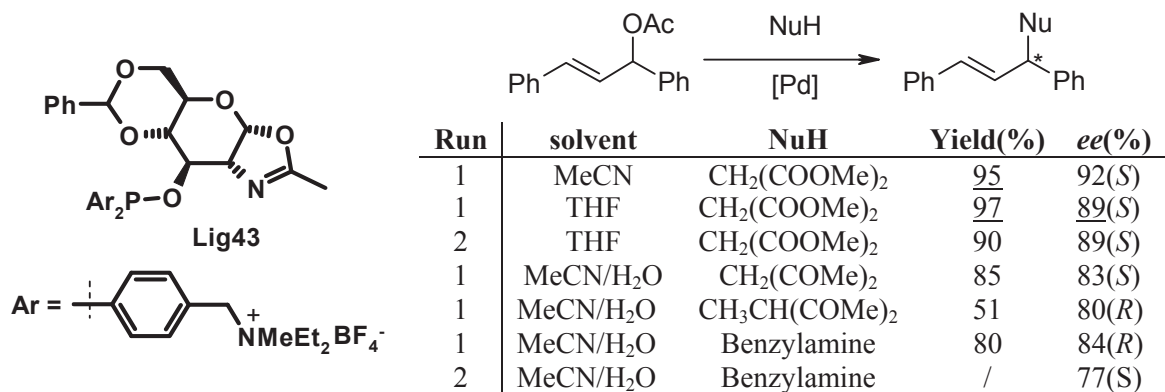


Table 1.25 Water soluble ligand D-glucosamine-oxazoline type and its use in Allylic substitution with different nucleophiles.

Reaction with dimethyl malonate in acetonitrile proceeded smoothly with 95% of yield and 92% *ee*. Excellent results were obtained also in THF, and it was possible to recycle catalyst to obtain 90% of yield and 89% of *ee* in second cycle. When benzylamine was used as a nucleophile in mixture acetonitrile and water, 84% of enantiomeric excess was obtained in first cycle and 77% *ee* in second cycle (Table 1.25).

⁵⁰ T. Hashizume, K. Yonehara, K. Ohe, S. Uemura, *J. Org. Chem.*, **2000**, 65, 5197-5201.

Conclusions

Daunting task hindered preparation of novel carbohydrates cores can seem polarity of unprotected starting material and wide reagent ranges or specialist conditions often required for synthesis. However this review show that easy availability of D-glucosamine together with its low cost, and presence five natural stereogenic centers makes it excellent choice in synthesis of new chiral ligands.

Over few past years D-glucosamine backbone was modified and functionalized in many ways by variation of stereogenic centers and steric properties to gave a large diversity of ligands, organocatalyst and reagents. They had been employed in many catalytic reactions like allylic alkylation, hydrogenation, hydrocyanation, Heck reactions or Suzuki-Miyaura cross-coupling to gave excellent yields. In case of asymmetric catalysis also high control of enantioselectivity was observed and selectivities achieved with glucosamine derivatives are comparable to those obtained with the more traditional derivatives from the chiral pool, what make them interesting alternatives. Despite the fact that many traditional structures of ligands have his equivalent based in carbohydrate, there is steel many ligands that can be replaced with ligands derived from natural chiral pool.

In literature many examples of use of glucosamine based ligands in homogeneous catalysis is described, nevertheless the productivity of catalysts needs to be further improved to achieve high turnover numbers and frequencies. This task can be accomplished by heterogenisation of catalyst.

CHAPTER 2

Ligands for homogeneous catalysis

Introduction

One of the aims of this thesis is to develop a strategy which will let incorporating in a sugar ring essential function of already known ligands derived from *trans*-cyclohexanediamine.

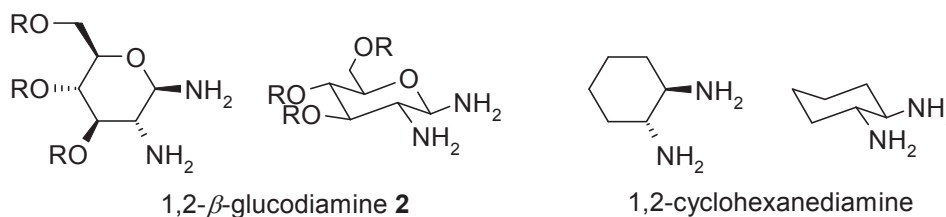


Figure 2.1 Structures of 1,2- β -glucodiamine and 1,2-cyclohexanediamine

This is based on the assumption that that (*1R,2R*)-cyclohexanediamine has a structural analogy with the 1,2- β -glucodiamine frame, because in both cases neighboring amino functions are in *trans*-diequatorial position of a six-member ring (Figure 2.1).

Ligands containing *trans*-diamine function incorporated into frame of D-glucosamine are already known. Ruffo *et al.*^{12,16,33,38} as well as RajanBabu *et al.*³⁷ prepared series of ligands containing two neighboring amino functions in *trans* configuration in second and third positions of carbohydrate ring. Compounds were tested in numbers of asymmetric reactions, in several cases the chiral products were generated with high *ees*. In study on ligands authors proved importance of substituent in second position of carbohydrate ring in coordination of metal, while third position was suitable for introducing steric hindrance or additional coordinating functions next to the metal center.

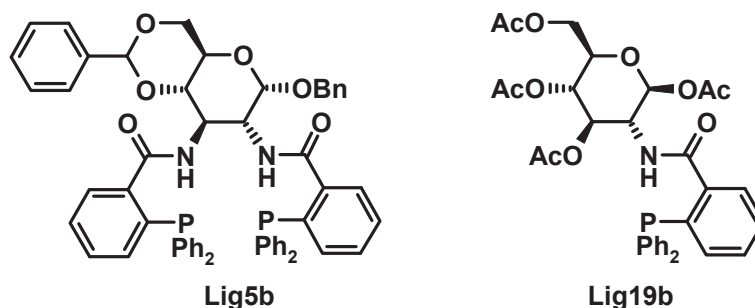


Figure 2.2 Examples of ligands prepared by Ruffo and by our team.

In research made by our team^{24,25} on ligands for allylic alkylation it was proved that anomeric β -position plays an essential function in obtaining high enantiomeric excess.

Combining those knowledge we decide to prepare series of D-glucosamine based ligands, containing two amino functions in first and second position of carbohydrate ring, in order to test them in catalytic reactions of allylic alkylation, hydrogenation and Michael addition.

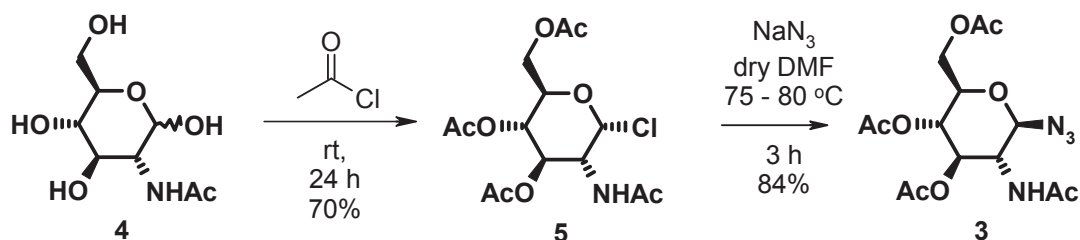
Organization of Chapter 2

The synthesis of carbohydrate chiral pool: *trans*-1,2- β -glucodiamine will be presented at first. The next subsection will concern preparation of amino- and imino- type ligands for allylic alkylation. Furthermore catalyst designed for hydrogenation will be shown. Finally synthesis of thiourea organocatalysts will be described and their use in reaction of Michael addition. And in the end of this chapter, all conditions of reactions and detailed descriptions of compounds will be included in experimental part.

Results and discussion

2.1 Preparation of 1,2-diamino-D-glucosamine.

2-Acetamido-3,4,6-tri-*O*-acetyl-1-azido-2-deoxy- β -D-glucopyranose **3** was easily obtained from *N*-acetyl-D-glucosamine **4** in two steps (Scheme 2.1).



Scheme 2.1 Synthesis of 2-acetamido-3,4,6-tri-*O*-acetyl-1-azido-2-deoxy- β -D-glucopyranose.

The first step was the preparation of 2-acetamido-3,4,6-tri-*O*-acetyl-2-deoxy- α -D-glucopyranosyl chloride **5** from **4** following the method described by Horton⁵¹ with yield 70%. Reaction occurred with formation exclusively of α -anomer, confirmed by ^1H NMR study- signal of anomeric proton with α characteristic low coupling constant $J = 3.7$ Hz (Table 2.1, entry 3).

Entry	Compound	Shift (ppm)	Coupling constant (Hz)
1	4α *	$\delta = 4.62$	$J=4.3\text{Hz}$
2	4β *	$\delta = 4.52$	$J=5.6\text{Hz}$
3	5α	$\delta = 6.18$	$J=3.7\text{Hz}$
4	3β	$\delta = 4.74$	$J=9.3\text{Hz}$
5	6β	$\delta = 4.13$	$J=9.2\text{Hz}$
6	7β	$\delta = 4.86$	$J=9.3\text{Hz}$
7	8β	$\delta = 4.52$	$J=9.0\text{Hz}$
8	2β	$\delta = 3.98$	$J=8.8\text{Hz}$

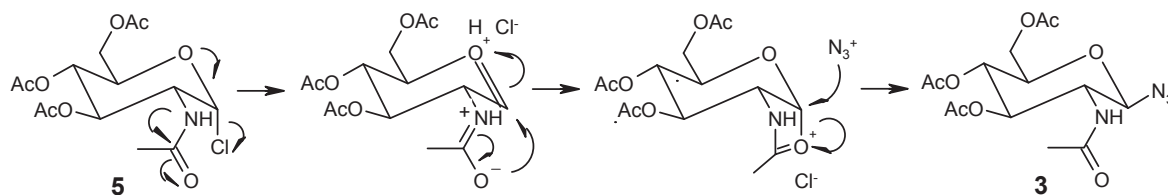
Table 2.1 Chemical shift and coupling constant of H-1 for each carbohydrate in synthesis of 1,2- β -glucodiamine **2** (*starting material **4** is mixture of anomers in ratio **4 α** : **4 β** 87:13).

The second step was treatment of **5** with sodium azide in dry DMF at reflux for 3 hours. This synthesis was described by Cunha⁵² Nucleophilic substitution occurs with inversion of configuration. This fact can be explained by formation of oxazoline ring preceding the

⁵¹ D. Horton, *Org. Synth.*, **1973**, 5, 1-4.

⁵² A. C. Cunha, L. O. R. Pereira, R. O. P. de Souza, M. C. B. V. de Souza, V. F. Ferreira, *Nucleosides, Nucleocides & Nucleic Acids*, **2001**, 20, 1555-1569.

attack of azide anion on anomeric position with form exclusively of β -anomer (Scheme 2.2). ^1H NMR spectra show high coupling constant ($J = 9.3$ Hz) for doublet formation of hydrogen of anomeric center characteristic for β -position (Table 2.1, entry 4).



Scheme 2.2 Mechanism of nucleophilic substitution leading to the formation of **3**.

Next step was reduction of azide **3** to amino group in presence of hydrogen and palladium on carbon. After 14 hours in room temperature and filtration on celite 2-acetamido-3,4,6-tri-*O*-acetyl-1-amino-2-deoxy- β -D-glucopyranose **6** was obtained with 96% of yield (Scheme 2.3).

It has been known that direct cleavage of the acetamide bonds protected amines required harsh conditions such as refluxing in solutions of HCl ⁵³ or $\text{Ba}(\text{OH})_2$ ⁵⁴, which are not compatible with sensitive functionality of carbohydrates. Trying to perform synthesis of compound **2**, starting from **6** method described by Burk and Allen⁵⁵ was tested. According to authors some amides can be activated to hydrolysis by prior conversion to the *N*-BOC amide derivatives and following that selective hydrolysis of the amide with hydrazine leaves the *N*-*tert*-butoxycarbamate in place. However in case of carbohydrate **6** it was impossible for us to deprotect amino function, which probably resulted from the presence of free amino function in neighboring anomeric carbon (Scheme 2.3).

The same reaction starting from azido derivative **3** lead to product of deprotection **7** with rather low yield 38%. Another drawback of this reaction was activity of hydrazine, which next to acetyl form amido function removed acetyls of third and fourth hydroxyl groups and reacetylation was required.

To avoid such problems and problematic purification we prepare 3,4,6-tri-*O*-acetyl-1-azido-2-(*tert*-butyl-carbamate)-2-deoxy- β -D-glucopyranose **8** with 73% of yield by changing acetamido group for *tert*-butoxycarbonyl (BOC) group according to methodology described by Lafont⁵⁶. In next step BOC group was deprotected using trifluoroacetic acid

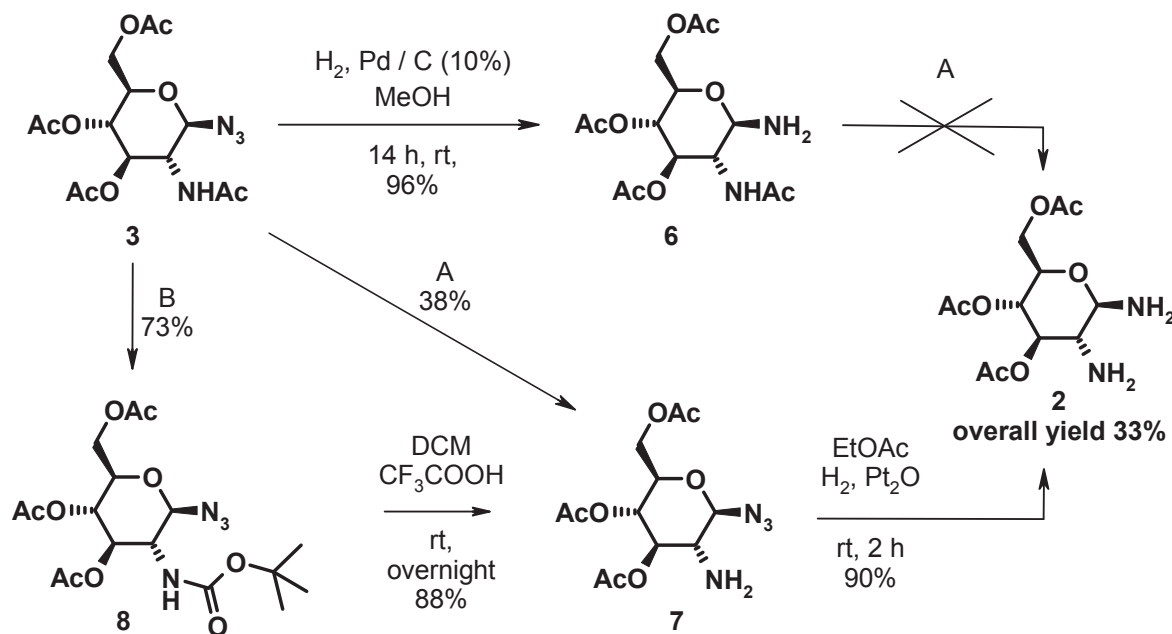
⁵³ G. A. Dilbeck, L. Field, A. Gallo, R. J. Gargiulo, *J. Org. Chem.* **1978**, *43*, 4593-4596.

⁵⁴ X. Hu, W. Zhang, I. Carmichael, A. S. Serianni, *J. Am. Chem. Soc.*, **2010**, *132*, 4641-4652.

⁵⁵ M. J. Burk, J. G. Allen *J. Org. Chem.*, **1997**, *62*, 7054-7057.

⁵⁶ D. Lafont, P. Boullanger, *Tetrahedron: Asymmetry*, **2006**, *17*, 3368-3379.

in dichloromethane in room temperature overnight giving expected product **7** with 88% yield, and 64% after two steps (Scheme 2.3).



A = (i) BOC₂O, DMAP, THF, reflux (ii) NH₂NH₂·H₂O, MeOH, r.t. (iii) TFA, rt.
 B = (i) BOC₂O, DMAP, THF, reflux (ii) MeONa, MeOH, rt (iii) Ac₂O, pyridine

Scheme 2.3 Synthesis of 3,4,6-tri-*O*-acetyl-1,2-β-glucodiamine **2**.

In last step: hydrogenation using Platinum oxide⁵⁷ for 2 hours in room temperature, diamino compound **2** was obtained with very good yield 90%, and overall yield 33% starting from carbohydrate **4** (Scheme 2.3).

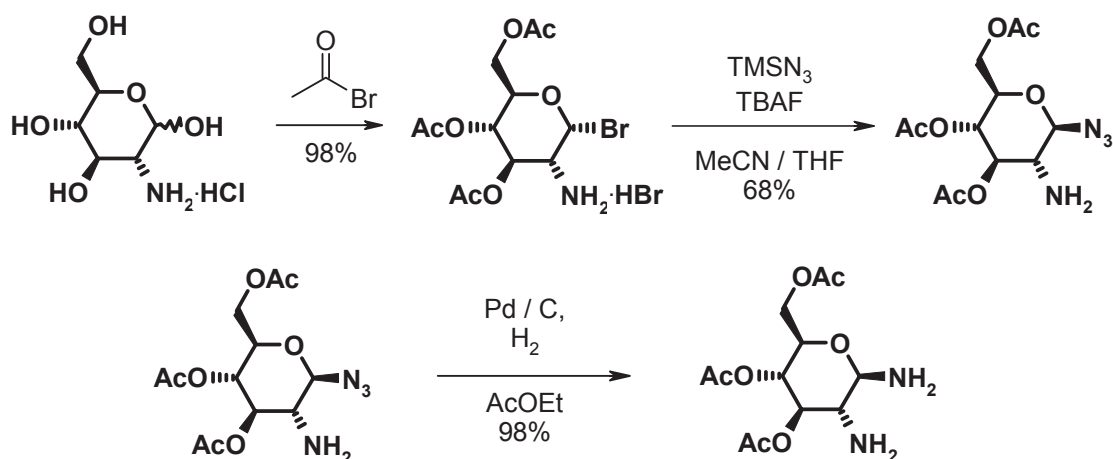
Diamino compound **2** was used as starting material to obtain various ligands for allylic alkylation, hydrogenation, organocatalysis and oxidation.

During work on the preparation the 1,2-diaminoglucosamine group of Ruffo⁵⁸ released article containing other way for preparation mentioned carbohydrate:

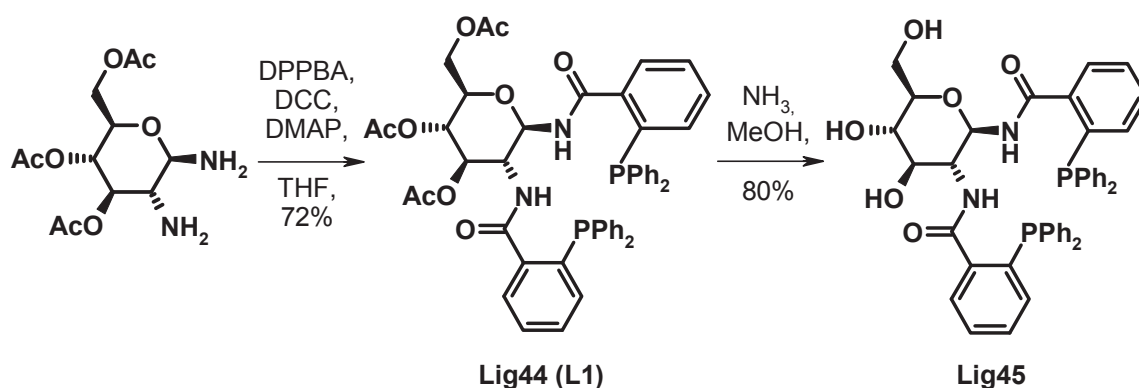
Starting from D-glucosamine **1** 3,4,6-tri-*O*-acetyl-2-deoxy-α-D-glucopyranosyl bromide hydrobromide was prepared using acetyl bromide with 98% of yield. Next mixture TMSN₃/TBAF in THF and acetonitrile was used as a source of azide anion with increased nucleophilicity, thus reaction under these conditions gave diastereomerically pure azido derivative with 68% of yield. Last step hydrogenation using palladium on carbon in ethyl acetate as solvent gave product 3,4,6-tri-*O*-acetyl-1,2-β-glucodiamine **2** with 98% of yield (Scheme 2.4).

⁵⁷ A. Bertho, A. Révész, *Justus Liebigs Annalen der Chemie*, **1953**, 581, 161-167.

⁵⁸ V. Benessere, A. De Roma, R. Del Litto, M. Lega, F. Ruffo, *Eur. J. Org. Chem.*, **2011**, 5779-5782.

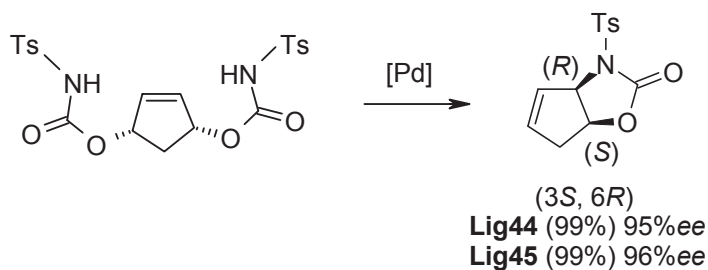
Scheme 2.4 Synthesis of 1,2-diaminoglucosamine **9**.

Authors obtain 1,2-diaminoglucosamine in 65% of overall yield in three steps. Compound that was used in preparation of two ligands. First one **Lig44** was obtained by condensation of **2** with two equivalents of 2-(diphenylphosphino)benzoic acid (DPPBA) while second **Lig45** was prepared by treatment of the acetylated product with methanolic ammonia to completely deprotect the acetyl groups (Scheme 2.5).



Scheme 2.5 Ligands based on 1,2-β-glucodiamine prepared by Ruffo.

Ligands were applied in Pd-catalyzed desymmetrization of *meso*-cyclopent-2-ene-1,4-diol with excellent conversions up to 99% and enantioselectivities up to 96% (Scheme 2.6).

Scheme 2.6 The desymmetrization of *meso*-cyclopent-2-ene-1,4-diol.

2.2 “Troost type” ligands for allylic alkylation.

In 1992 Trost, Van Vranken, and Bingel⁵⁹, introduced C₂-symmetric “Troost modular ligand” (Figure 2.3a). Since then this structure was developed and expanded by using different types of chiral pools and linkers (Figure 2.3b) to create one of the most successfully and broadly applied ligand classes used for asymmetric transition metal-catalyzed C-C or C-heteroatom bond-forming reactions⁶⁰.

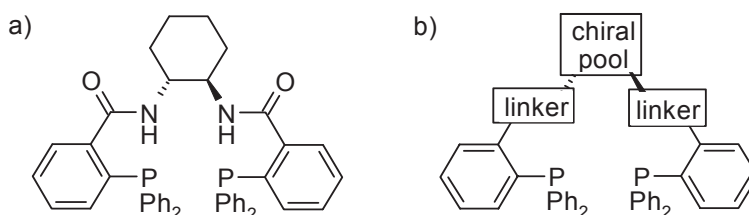


Figure 2.3 a) “Troost modular ligand”, b) general “Troost ligand” system

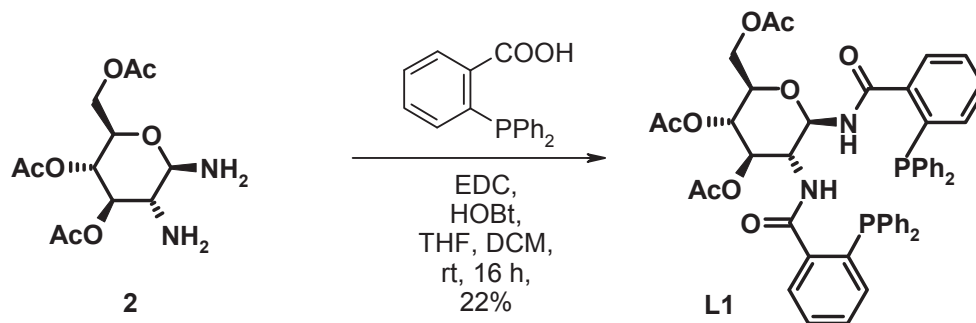
In our team we decided to prepare ligands belong to family of “Troost ligand system” containing 1,2-diamino-D-glucosamine as chiral pool and two types of linkers: amido- or imino-linkers, and to test them in reaction of allylic alkylation with palladium.

2.2.1 Amide type ligand.

By coupling of compound **2** with 2-(diphenylphosphino)benzoic acid in mixture dichloromethane and tetrahydrofuran 1 : 1 using HOBT and EDC as coupling reagents ligand **L1** was prepared and isolated using flash chromatography in only 22% of yield (Scheme 2.7).

⁵⁹ (a) B. M. Trost, D. L. Van Vranken, and C. Bingel, *J. Am. Chem. Soc.*, **1992**, 114, 9327-9343, (b) B. M. Trost, D. L. Van Vranken, C. Bingel, *Angew. Chem., Int. Ed. Engl.*, **1992**, 31, 228-230.

⁶⁰ Examples of using Trost ligand in asymmetric catalysis: (a) B. M. Trost, R. C. Bunt, *J. Am. Chem. Soc.*, **1994**, 116, 4089-4090, (b) B. M. Trost, C. B. Lee, J. M. Weiss, *J. Am. Chem. Soc.*, **1995**, 117, 7247-7248, (c) B. M. Trost, M. G. Organ, G. A. O'Doherty, *J. Am. Chem. Soc.*, **1995**, 117, 9662-9670, (d) B. M. Trost, S. R. Pulley, *J. Am. Chem. Soc.*, **1995**, 117, 10143-10144, (e) B. M. Trost, R. C. Lemoine, *Tetrahedron Lett.*, **1996**, 37, 9161-9164, (f) B. M. Trost, G. R. Cook, *Tetrahedron Lett.*, **1996**, 37, 7485-7488.



Scheme 2.7 Synthesis of “Trost type” carbohydrate based ligand.

Different conditions were tested. It was impossible to increase temperature because degradation of carbohydrate was ongoing, also changing time of reaction led to creation of many phosphorus byproducts present on ^{31}P NMR. Other coupling reagents were also tested. Using DCC / DMAP in catalytic amount in dichloromethane no product was observed, however the same reagents used by Ruffo in big excess and THF as solvent led to creation of desired product with 73% of yield (Scheme 2.5).

Ligand **L1** was characterized by many techniques: ^1H NMR, ^{13}C NMR, ^{31}P NMR, IR, ESI-MS (See experimental part). Spectra analysis allows to confirm the ligands structure and to check his purity. The sugar identity was confirmed by the typical pattern of glucosamine (Figure 2.4, protons H-1 to H-6’).

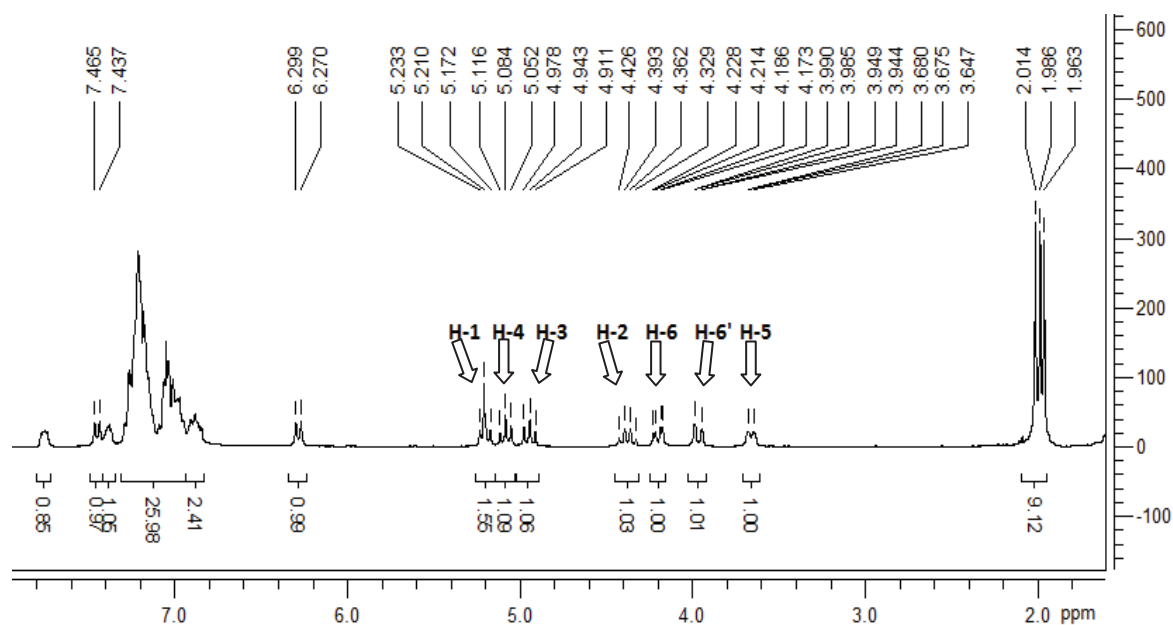


Figure 2.4 ^1H NMR from 1.6 to 8.0 ppm of ligand **L1**.

The formation of the amidic bond was demonstrated by presence of two typical signals at $\delta = 6.28$ ppm and at $\delta = 7.45$ ppm, that appear as doublets due to coupling with the sugar protons (Figure 2.5, protons H-N1 and H-N2).

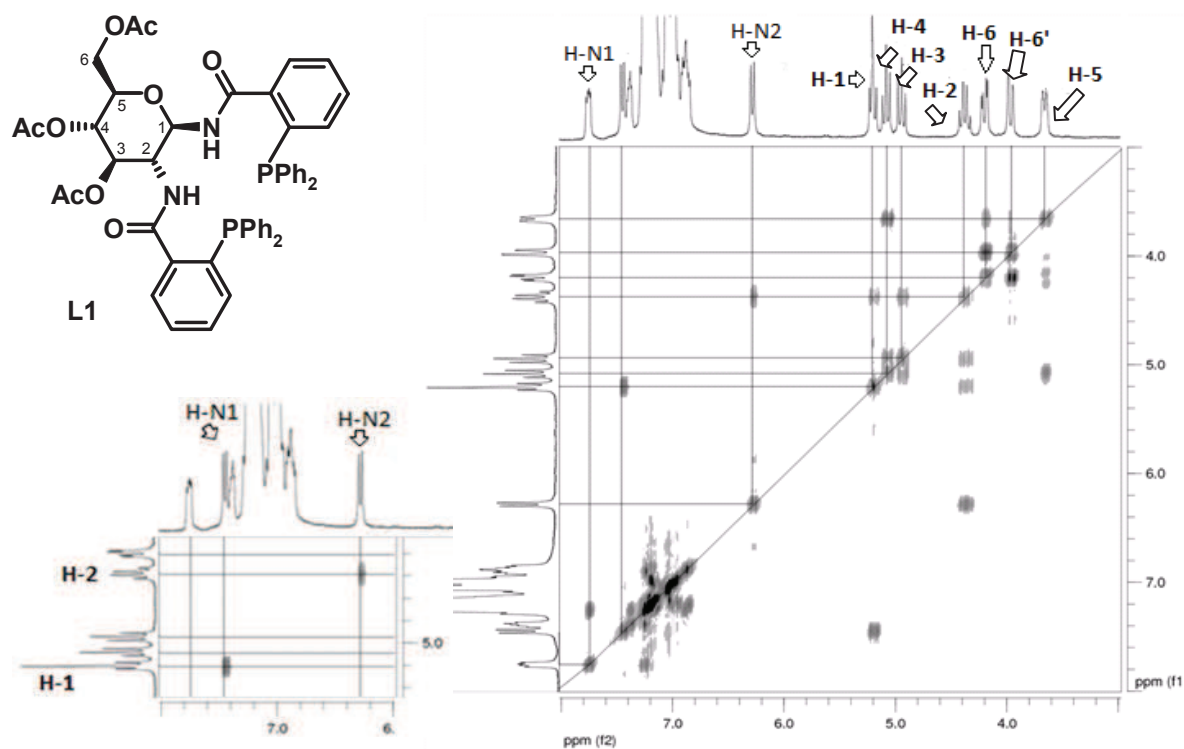
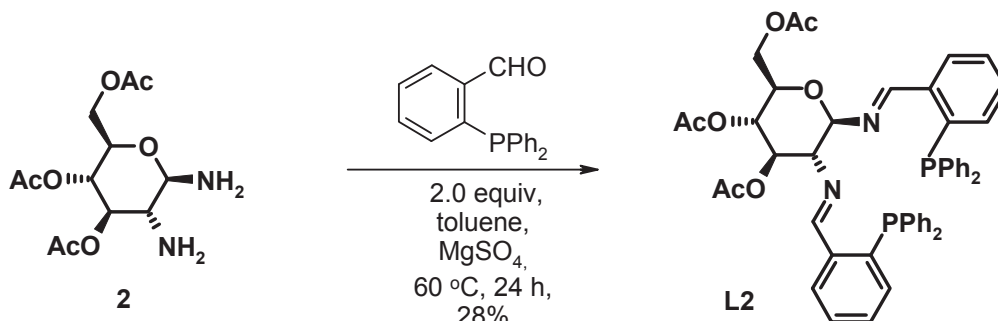


Figure 2.5 COSY ^1H - ^1H from 3.0 to 8.0 ppm for diamido ligand **L1**, and zoom in area of amido bonds 6.0 ppm to 8.0 ppm.

2.2.2 Imine type ligand.

Ligand with similar structure containing imino function was prepared using condensation of anime **2** with 2-(diphenylphosphino)benzoic aldehyde. Toluene was used as solvent, and magnesium sulfate as drying agent (Scheme 2.8). After 24 hours in reaction mixture there is still starting material, and two products of monocondensation, however increasing of time of reaction causes with decreasing amount of starting material and appearing in phosphorus spectra five new signals while amount of diimine ligand **L2** remains the same.



Scheme 2.8 Preparation of imine type ligand **L2**.

Compound was isolated with 28% of yield, and its structure confirmed with ^1H NMR, ^{13}C NMR, ^{31}P NMR, IR, ESI-MS experiments (See experimental part).

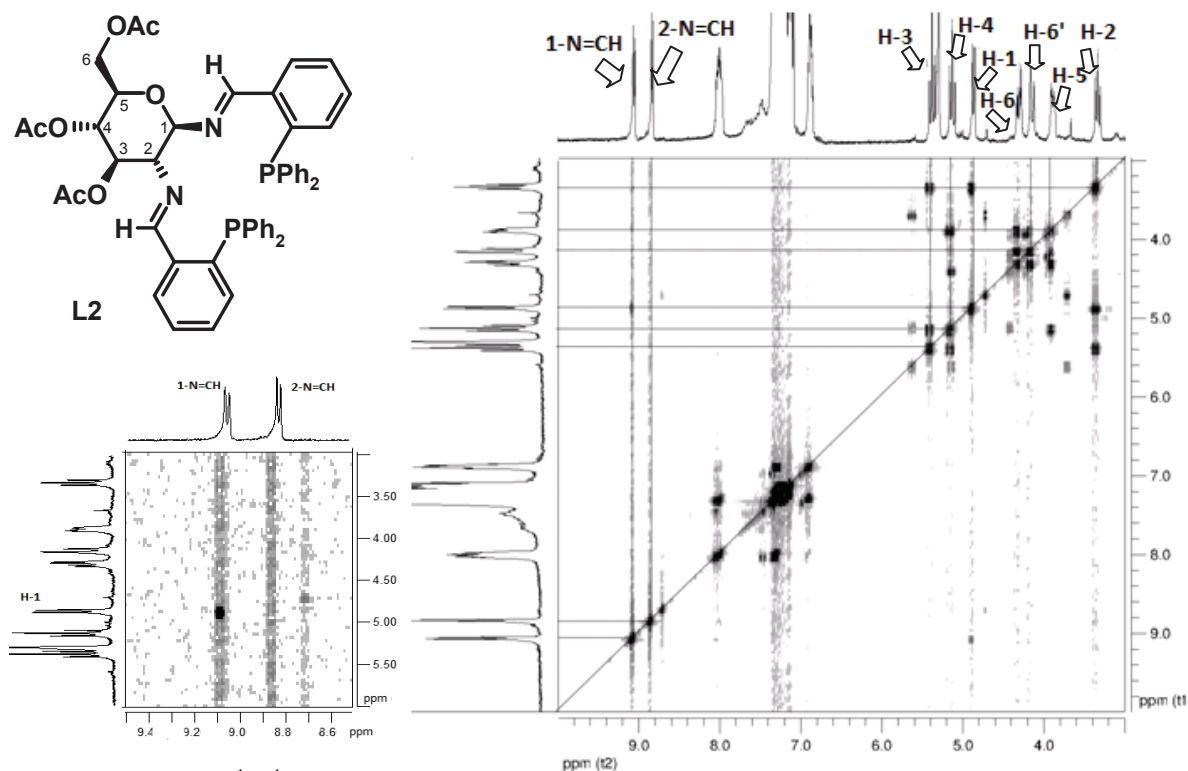


Figure 2.6 COSY ^1H - ^1H from 3.0 to 10.0 ppm for diimino ligand **L2**, and zoom in area of imine bonds 8.3 ppm to 9.5 ppm.

The formation of the two imino bonds of ligand **L2** is pointed out by the presence of the two typical signals at $\delta = 8.76$ ppm (2-N=CH) and $\delta = 8.99$ ppm (1-N=CH), that appears as a doublet due to the coupling with H-2 and H-1 respectively. However in COSY spectra we can observe only coupling between proton in anomeric carbon and proton of imine bond 1N=CH (Figure 2.6).

Unfortunately it was impossible for us to use ligand **L2** in catalytic reactions of allylic alkylation because of his stability. After short time partial degradation to monosubstituted product **10** was observed (Figure 2.7).

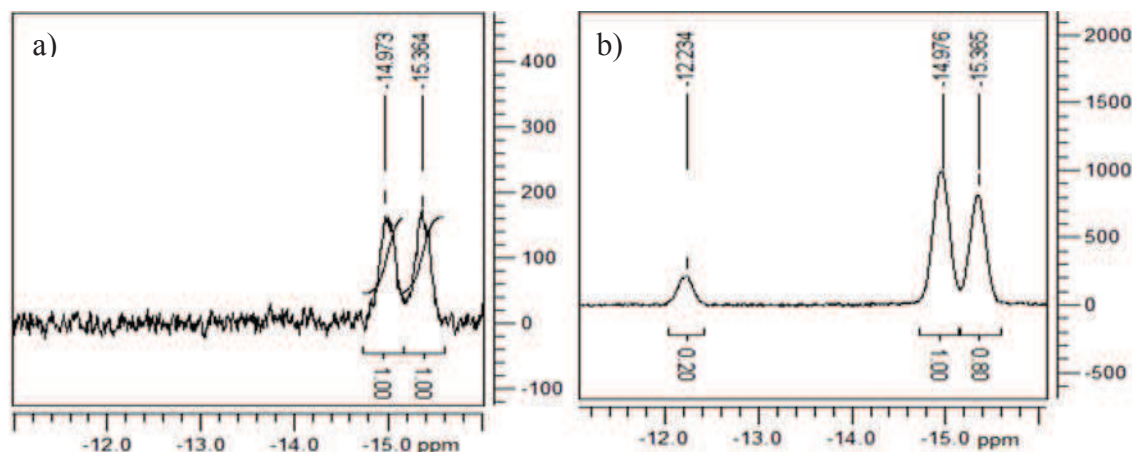


Figure 2.7 ^{31}P NMR from -11.0 to -16.0 ppm for ligand **L2**. a) after purification of reaction mixture b) after 18 hours.

Appearance of new compound was observed also in ^1H NMR spectra (Figure 2.8).

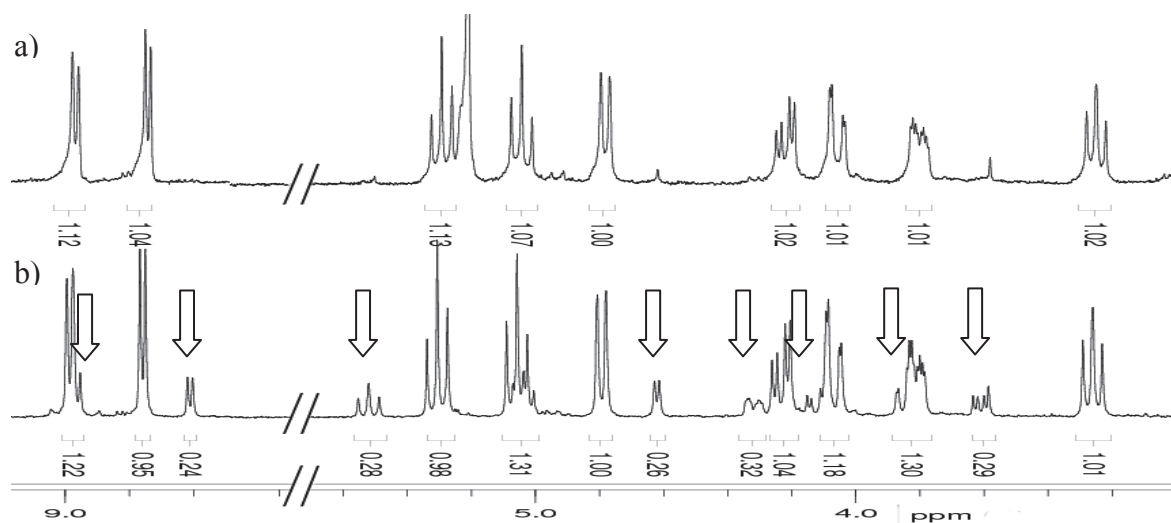
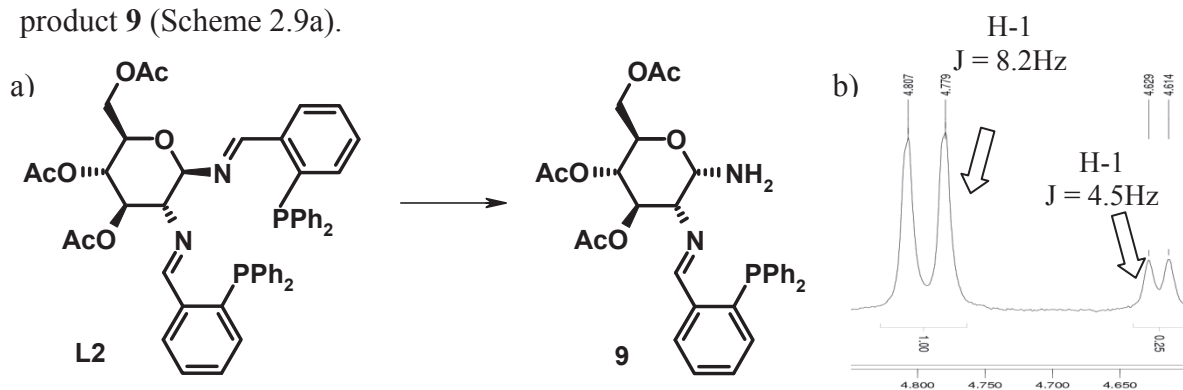


Figure 2.8 ^1H NMR from 3.0 to 5.6 ppm and 8.4 to 9.2 for ligand **L2**. a) after purification of reaction mixture
b) after 18 hours.

Degradation probably occurred by ring opening and led to creation of monocondensated product **9** (Scheme 2.9a).



Scheme 2.9 a) Degradation of ligand **L2** to compound **9**, b) ^1H NMR from 4.60 to 4.85 ppm

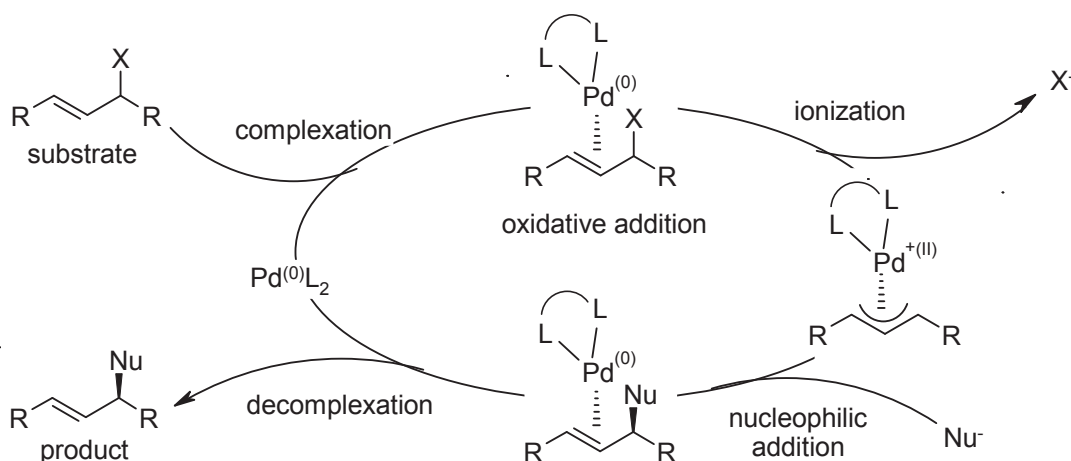
During degradation ongoing inversion of configuration in anomeric position. Signal of H-1 for compound **9** has containing low constant ($J = 4.5\text{Hz}$) (Scheme 2.9b) characteristic for anomeric protons in α position. Monosubstituted product was not isolated.

2.2.3 Allylic alkylation with “Troost type ligand”

It has been applied to a large number of asymmetric allylic alkylations with substrates difficult to control with other systems^{61,62} A wide variety of transition metals are known to catalyze this reaction, however the mostly studied were reactions with palladium.

⁶¹ For review, see: B. M. Trost, M. L. Crawley, *Chem. Rev.*, **2003**, 103, 2921-2943.

⁶² B. M. Trost, A. C. Krueger, R. C. Bunt, J. Zambrano, *J. Am. Chem. Soc.*, **1996**, 118, 6520-6521.



Scheme 2.10 Mechanism of allylic alkylation.

The generally accepted mechanism for [Pd]-catalyzed allylic alkylation contains two key steps: oxidative addition of Pd species, “Pd⁽⁰⁾L₂”, to the allylic electrophile and followed by nucleophilic attack on the resulting Pd(II) allyl cation, to liberate the product and regenerate the Pd(0) complex (Scheme 2.10).

Efficiency of ligand **L1** was tested in the reactions of allylic alkylation. Two typical racemic allylic substrates, 2-acetoxy-1,3-diphenyl-2-propene and 2-acetoxy-1,3-dimethyl-2-propene, and a standard nucleophile, dimethyl malonate, were chosen. (Table 2.2).

Entry	Ligand	R	Solvent	Base	Yield (%)	ee (%)
1	Trost ligand ⁶²	Ph	THF	NaH	24	12
2	L1	Ph	THF	NaH	39	42
3	Trost ligand ⁶²	Me	DCM	Cs ₂ CO ₃	98	92
4	L1	Me	DCM	Cs ₂ CO ₃	0	0
5	L1	Me	THF	NaH	0	0

Trost ligand

Table 2.2 Shortlists and compare of results of allylic alkylation with “Trost ligand”(entry 1, 3) and ligand **L1** (entry 2, 4, 5).

In case of 1,3-Diphenyl-3-acetoxyprop-1-ene, results of allylic alkylation are better comparing to results obtained by Trost (Table 2.2, entry 1,2). Increasing of yield from 24 to 39% was observed as well as increasing of enantioselectivity from 12 to 42% *ee*. When 4-acetoxy-2-pentene was used as starting material reaction occurred with excellent yield and enantioselectivity with “Trost ligand” (Table 2.2, entry 3), when carbohydrate ligand

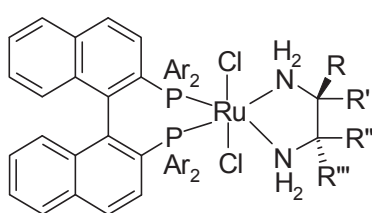
Ligands for homogeneous catalysis

L1 was used as ligand no conversion was observed with neither of used conditions (Table 2.2, entry 4,5).

Despite of better results in case of 1,3-Diphenyl-3-acetoxyprop-1-ene in comparing with results of Trost ligand we decided to stop project and do not study reactivity of ligand **L1** with other substrates. Obtained by us results were not satisfactory. Many other carbohydrate based ligands catalysed reaction of allylic alkylation with better yields and enantioselectivities (see Chapter 1 Scheme 1.5, Scheme 1.6, Scheme 1.7).

2.3 Catalyst for hydrogenation.

BINAP-Ru(II) diaminecomplexes were used first time in 1995 by Noyori^{63a}. Since then they are shown to be efficient, catalyst in many organic transformations. They were used successfully in enantiomeric hydrogenation of simple aromatic^{63b-e}, heteroaromatic^{63f,g}, cyclopropyl^{63h}, dialkyl^{63h}, amino^{63i,j}, olefinic^{63h,k}, and α -alkoxy ketones^{63a,l}. They show great efficiency in chemoselective hydrogenation C=O bonds in presence of C=C bond, also variety of functionalities such as F, Cl, Br, I, CF₃, OCH₃, OCH₂C₆H₅, COOCH(CH₃)₂, NO₂, NH₂, and NRCOR.



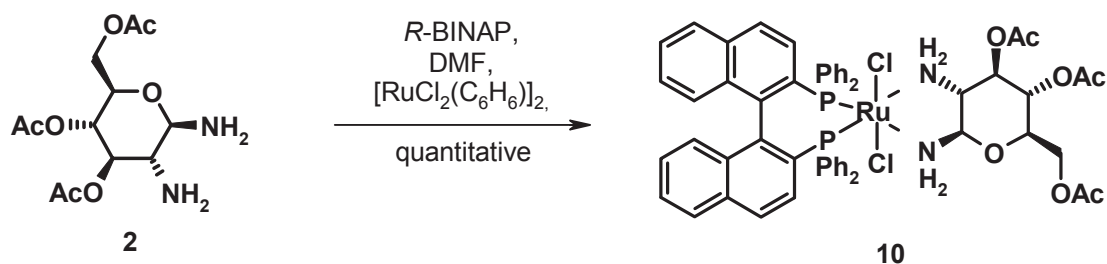
BINAP: Ar = C₆H₅
 TolBINAP: Ar = 4-CH₃C₆H₄
 XylBINAP: Ar = 3,5-(CH₃)₂C₆H₃
 DPEN: R = R''' = C₆H₅,
 R' = R'' = H
 DAIPEN: R = R' = 4-CH₃OC₆H₄
 R'' = H, R''' = (CH₃)₂CH

Figure 2.9 BINAP/diamine-Ru^{II} catalyst developed by Noyori.

2.3.1 BINAP-Ru(II) diaminecomplex

Using procedure establish by Noyori *et al.*^{63a} BINAP-Ru(II) 1,2-diaminecarbohydrare complex **10** was prepared. Treatment of commercially available (*R*)-BINAP with dimmer [RuCl₂(C₆H₆)]₂ and 1,2- β -glucodiamine as diamine source in DMF at 25 °C for three hours gave quantitatively complex **10** (Scheme 2.11).

⁶³ (a) R. Noyori, T. Ohkuma, *Angew. Chem. Int. Ed.*, **2001**, 40, 40-73, (b) T. Ohkuma, H. Ooka, S. Hashiguchi, T. Ikariya, R. Noyori, *J. Am. Chem. Soc.*, **1995**, 117, 2675-2676, (c) H. Doucet, T. Ohkuma, K. Murata, T. Yokozawa, M. Kozawa, E. Katayama, A. F. England, T. Ikariya, R. Noyori, *Angew. Chem. Int. Ed.*, **1998**, 37, 1703-1707, (d) R. Noyori, T. Ohkuma, *Pure Appl. Chem.*, **1999**, 71, 1493-1501, (e) R. Noyori, M. Koizumi, D. Ishii, T. Ohkuma, *Pure Appl. Chem.*, **2001**, 73, 227-232, (f) T. Ohkuma, M. Koizumi, M. Yoshida, R. Noyori, *Org. Lett.*, **2000**, 2, 1749-1751, (g) P. Cao, X. Zhang, *J. Org. Chem.*, **1999**, 64, 2127-2129, (h) T. Ohkuma, M. Koizumi, H. Doucet, T. Pham, M. Kozawa, K. Murata, E. Katayama, T. Yokozawa, T. Ikariya, R. Noyori, *J. Am. Chem. Soc.*, **1998**, 120, 13529-13530, (i) M. Kitamura, T. Ohkuma, S. Inoue, N. Sayo, H. Kumobayashi, S. Akutagawa, T. Ohta, H. Takaya, R. Noyori, *J. Am. Chem. Soc.*, **1988**, 110, 629-631, (j) T. Ohkuma, D. Ishii, H. Takeno, R. Noyori, *J. Am. Chem. Soc.*, **2000**, 122, 6510-6511, (k) T. Ohkuma, H. Ooka, T. Ikariya, R. Noyori, *J. Am. Chem. Soc.*, **1995**, 117, 10417-10418, (l) T. Ohkuma, H. Ikehira, T. Ikariya, R. Noyori, *Synlett*, **1997**, 467-468.



Scheme 2.11 Preparation of ligand for hydrogenation.

Formation of nitrogen-Ru bond was confirmed by shift of protons of starting material on ^1H NMR spectra (Figure 2.10).

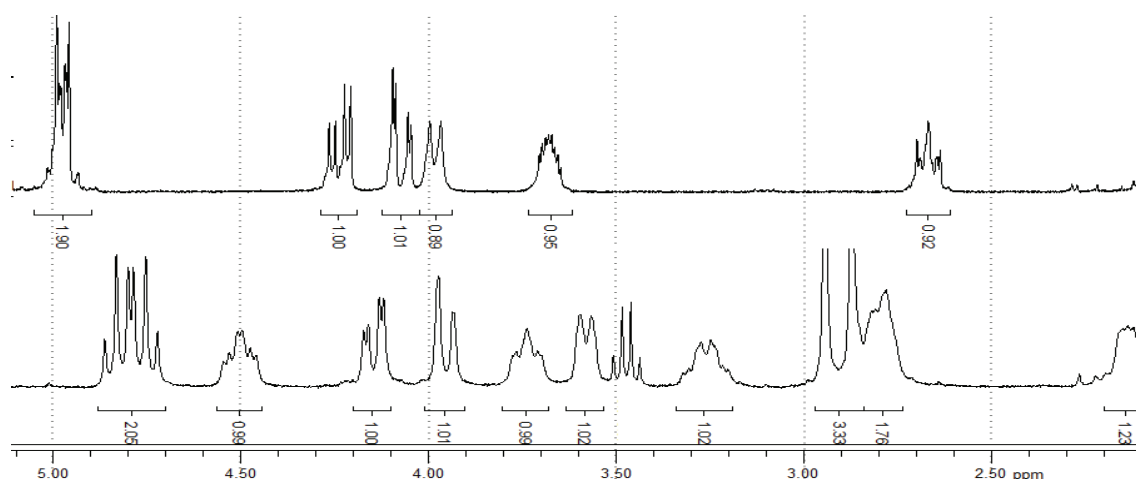


Figure 2.10 ^1H NMR spectra from 2.0 to 5.20 ppm for: a) compound **2**, b) complex **10**.

Also presence of signals in mass spectra corresponding to complex **10**, which were agree with simulation (Figure 2.11).

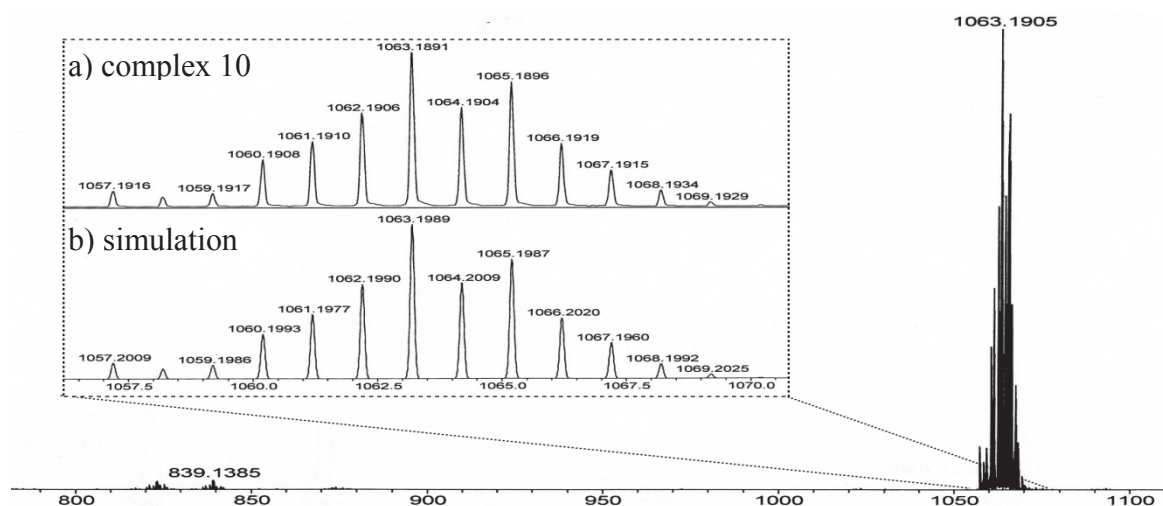
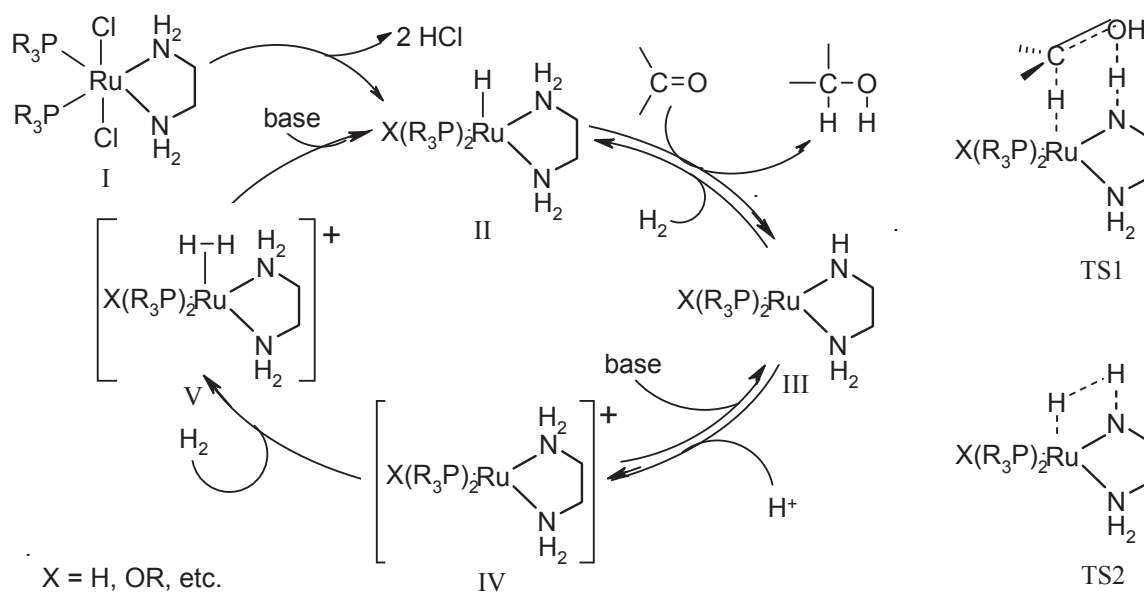


Figure 2.11 ESI-MS spectra for complex **10**.

2.3.2 Hydrogenation with BINAP-Ru(II) diaminencomplexes

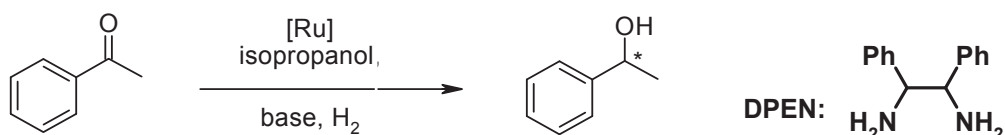
Hydrogenation catalyzed by a BINAP/diamine-Ru^{II} catalyst and an alkaline base is general solution for problem of asymmetric transformation of simple ketones with lack any Lewis basic functionality capable to interact with metal center. Various complexes (Figure 2.9) provided to be effective in hydrogenation of variety of ketones⁶³.

Hydrogenation occurred by nonclassical metal-ligand bifunctional mechanism (Scheme 2.12)^{63a,e}. First complex I is converted into Ruthenium hydride II in presence of base and hydride source (H₂ and isopropanol). Catalytic cycle who carried out between II and III contain two transition states TS1 and TS2. Ru hydride in II reacts with a ketonic substrate via six membered transition state TS1, where hydridic Ru-H and protic N-H plays role in hydrogen delivery to ketones, forming alcoholic product directly, without formation of a metal alkoxide. *Via* transition state TS2 Ru-N dipolar bond splits III to restore hydride II, alternatively II may be regenerated by way of IV and V by action of protonic medium and base (Scheme 2.12).



Scheme 2.12 Catalytic cycle of hydrogenation of ketones with BINAP/diamine-Ru^{II}/strong base combined system.

This [Ru]-complex obtained from *R*-BINAP and compound **2** was used in reaction of hydrogenation of acetophenone (Table 2.3). As a first choice potassium hydroxide was used as a base. In case of Noyori^{63b} complex with DPEN as diamine authors obtained full conversion and 87% *ee* (Table 2.3, entry 1). In the same conditions with complex containing 1,2- β -glucodiamine, no conversion was observed, even when time of reaction was elongated from 3 to 72 hours (Table 2.3, entry 2).



Entry	Amine	Base	Pressure (atm)	Cat. (%)	Time (h)	Conv. (%)	Yield (%)	ee (%)
1	DPEN ^{63b}	KOH	4	0.2	3	100	>99	87
2	2	KOH	4	0.2	72	0	0	-
3	DPEN ^{63d}	<i>t</i> -BuOK	45	0.4 x 10 ⁻⁴	48	100	100	80
4	DPEN	<i>t</i> -BuOK	20	0.2	72	60	40	75
5	2	<i>t</i> -BuOK	10	0.2	48	0	0	-
6	2	<i>t</i> -BuOK	20	0.2	72	0	0	-

Table 2.3 Shortlist and compare of results of hydrogenation of acetophenone with “Noyori ligand” (entry 1, 3, 4) and ligand **L4** (entry 2, 5, 6).

Another base (potassium *tert*-butoxide) was used by group of Noyori^{63d} in a big scale reactions and TON up to 2400000 was achieved. Authors obtain product of hydrogenation with full conversion and 80% of enantiomeric excess (Table 2.3, entry 3). Because it was imposibe for us to repeat exacly the same conditions, reaction with the DPEN was carried out in our laboratory with preasure decreased from 45 to 20 atmosphers and amount of catalyst increased from 0.4 x 10⁻⁴ to 0.2% molar. (Table 2.3, entry 4), to give product of reaction with 60% of conversion and comparable enantiomeric excess 75%. The same condition were applied for complex containing 1,2- β -glucodiamine, unfortunately in this case reaction did not leded to any conversion of starting material (Table 2.3, entries 5, 6).

2.4 Thiourea organocatalysts for Michael addition

Organo-catalyzed asymmetric reactions are becoming an increasingly important field of organic synthesis⁶⁴. First time thiourea organocatalyst based on cyclohexanediamine ring (Figure 2.12) was prepared by Jacobsen⁶⁵ and used in Strecker reaction. In 2003 Takemoto⁶⁶ use similar ligand in nucleophilic addition of nitroolefins, and one year later bifunctional dithiourea organocatalyst was prepared by Nagasawa⁶⁷ and used in Baylis-Hilman reaction. Since then library of those compounds has been enriched, and used successfully in many different kind of reactions⁶⁸.

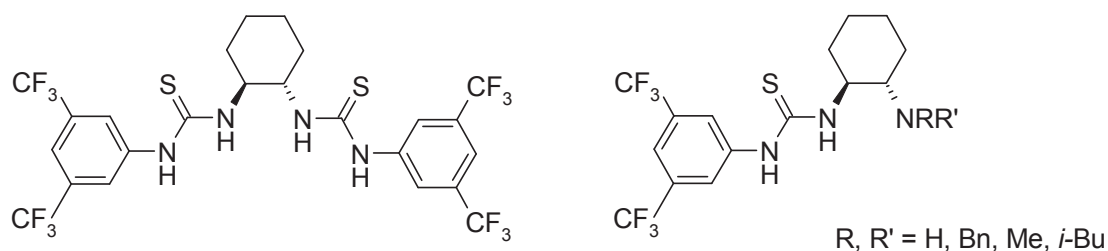


Figure 2.12 Bifunctional thiourea organocatalysts based on cyclohexanediamine.

We decided to prepare three different D-glucosamine based thiourea organocatalysts. Project was made in collaboration with professor Florence Popowycz and PhD student Marc Baron from team CASYEN from University Lyon 1 who carried out tests of reaction of Michael addition between chalcone and nitromethane.

2.4.1 Synthesis of D-glucosamine based thiourea organocatalysts

Three catalyst containing thiourea moiety were prepared. Starting from described above compound **8**, where amino function was protected with BOC group, in two steps we prepared catalyst **L3**, by hydrogenation with platinum oxide, and condensation with thiocyanate compound with 96% of yield. Compound that was used as starting material for

⁶⁴ For recent reviews on asymmetric organocatalysis, see: (a) F. Giacalone, M. Gruttadauria, P. Agrigento, R. Noto, *Chem. Soc. Rev.*, **2012**, 41, 2406-2447, (b) B. R. Buckley, M. M. Farah. *Annu. Rep. Prog. Chem., Sect. B: Org. Chem.*, **2011**, 107, 102-117, (c) The special issue devoted to 'Asymmetric Organocatalysis': *Chem. Rev.*, **2007**, 107, 5413-5883.

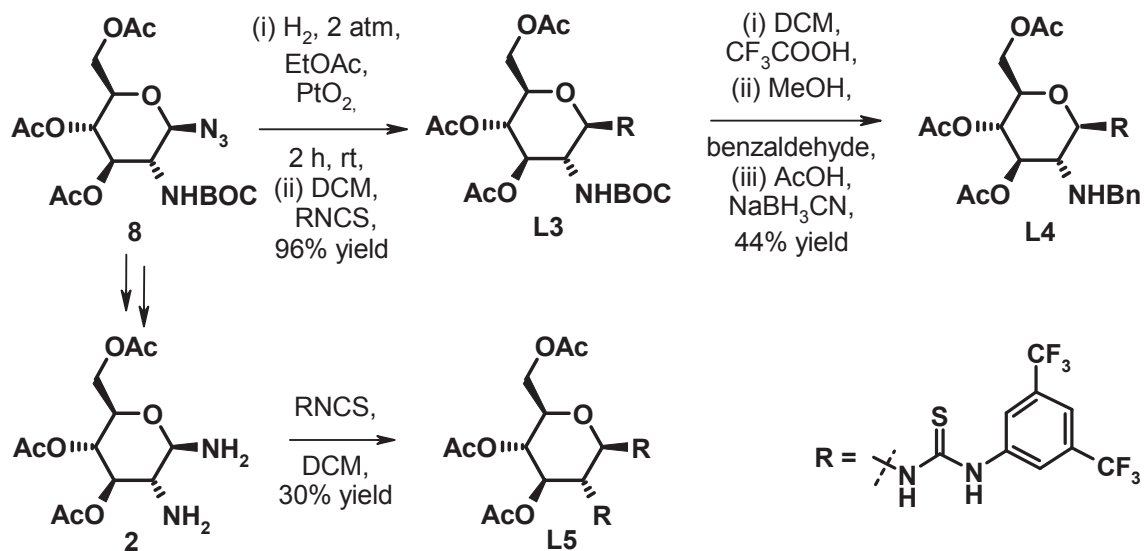
⁶⁵ M. S. Sigman, E. N. Jacobsen, *J. Am. Chem. Soc.*, **1998**, 120, 4901-4902.

⁶⁶ T. Okino, Y. Hoashi, Y. Takemoto, *J. Am. Chem. Soc.*, **2003**, 125, 12672-12673.

⁶⁷ Y. Sohtome, A. Tanatani, Y. Hashimoto, K. Nagasawa, *Tetrahedron Lett.*, **2004**, 45, 5589-5592.

⁶⁸ Other examples: (a) D. E. Fuerst, E. N. Jacobsen, *J. Am. Chem. Soc.*, **2005**, 127, 8964-8965, (b) M. S. Taylor, N. Tokunaga, E. N. Jacobsen, *Angew. Chem. Int. Ed.*, **2005**, 44, 6700-6704, (c) T. Okino, S. Nakamura, T. Furukawa, Y. Takemoto, *Org. Lett.*, **2004**, 6, 625-627, (d) X. Xu, T. Furukawa, T. Okino, H. Miyabe, Y. Takemoto, *Chem. Eur. J.*, **2006**, 12, 466-476.

preparation another catalyst **L4**. Deprotection of amino function followed by condensation with benzaldehyde and reduction of created imine to amine using thiocyanoborohydride in acidic conditions gave catalyst **L4** containing thiourea moiety and benzyl function in neighboring amino functions.



Scheme 2.13 Preparation of thiourea organocatalysts.

Last compound from series of thiourea organocatalysts is product of condensation of 1 equivalent of diamine **2** with two equivalents of dicyano compound to give catalyst **L5** with 30% of yield after purification (Scheme 2.13).

Ligands **L3-L5** were characterized by many techniques: ^1H NMR, ^1H - ^1H COSY, ^{13}C NMR, ^1H - ^{13}C HSQC, ESI-MS (See experimental part).

In Table 2.4 we can observe how protons H-1, H-2, and carbons C-1, C-2 shifts for the particular compounds.

Entry	Ligand	H-1 δ (ppm)	C-1 δ (ppm)	H-2 δ (ppm)	C-2 δ (ppm)
1	L3	5.61	85.1	4.40	54.4
2	L4	5.20	84.3	3.04	61.5
3	L5	6.01	85.0	5.52	58.6

Table 2.4 Chemical shifts of H-1, H-2, C-1, C-2 for Ligands **L3-L5**.

Spectra analysis allows to confirm the ligands structure and to check his purity. The sugar identity was confirmed by the typical pattern of glucosamine (Figure 2.13).

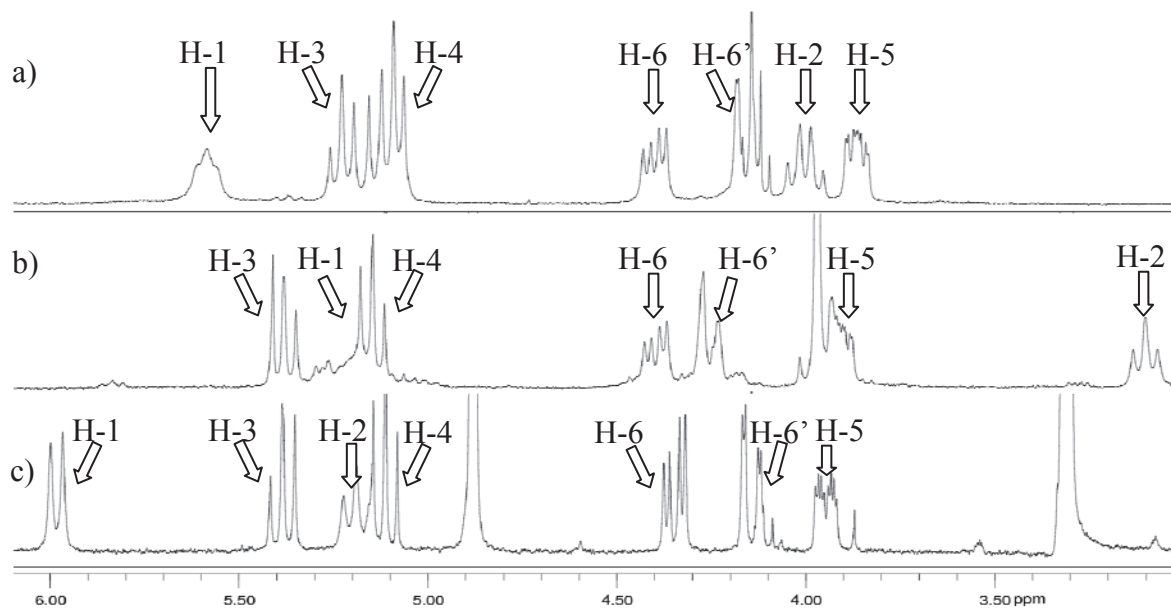


Figure 2.13 ^1H NMR from 3.0 to 6.1 ppm of ligands: a) L3, b) L4, c) L5.

Using ESI-MS technique we definitely confirmed presence of expected compounds (Figure 2.14).

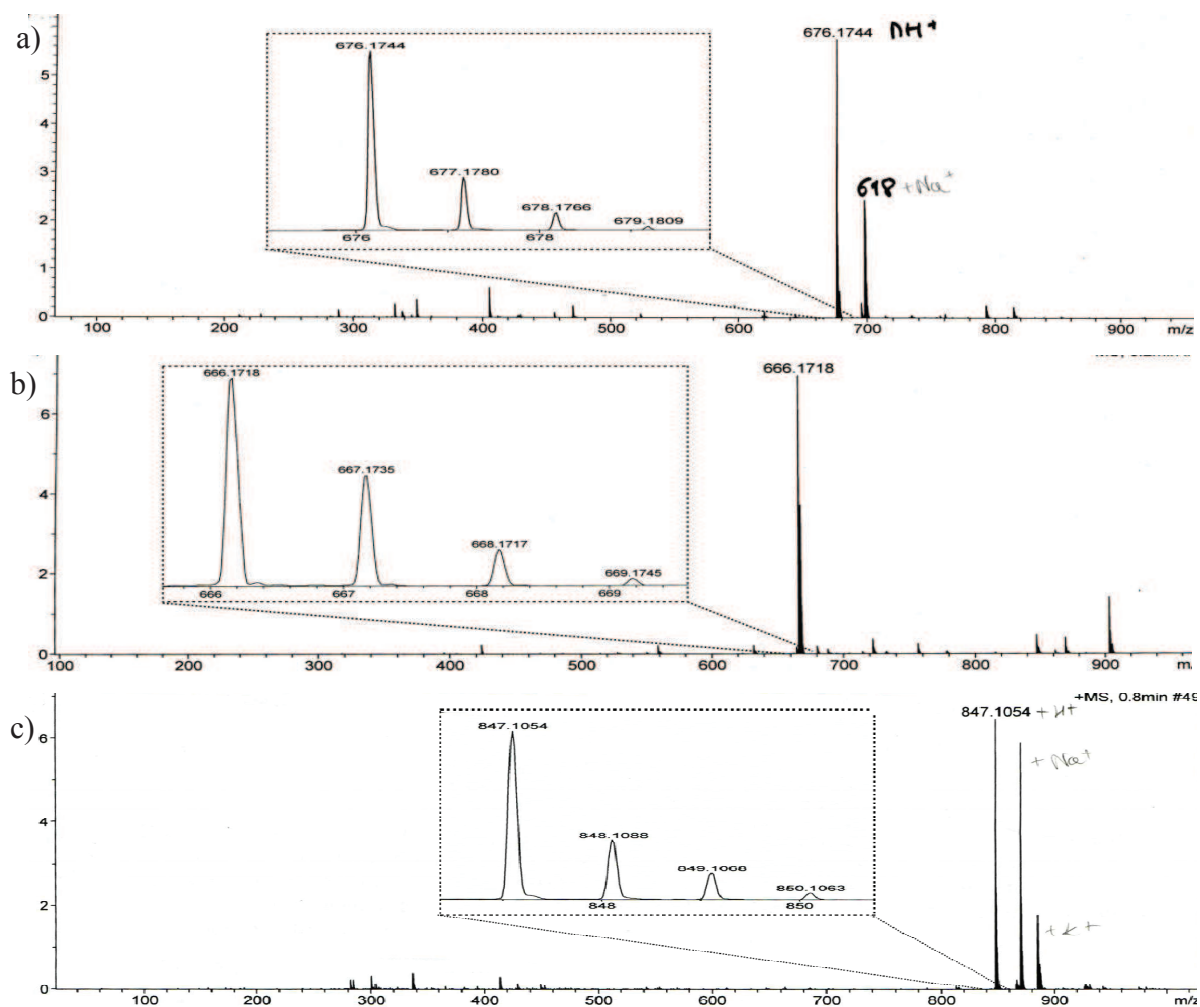


Figure 2.14 ESI-MS spectra for ligands: a) L3, b) L4, c) L5.

2.4.2 Michael addition with thiourea organocatalysts

Asymmetric Michael addition is one of the most useful methods in formation of C-C bonds, which provides easy access to important chiral building blocks and intermediates in synthesis. Thiourea compounds bearing 3,5-bis(trifluoromethyl)benzene and different substituted amino groups were revealed to be highly efficient catalysts in this kind of reactions⁶⁹.

Two different models are proposed in literature for hydrogen bonding activation of unsaturated ketone and nitronate anion by thiourea moiety.

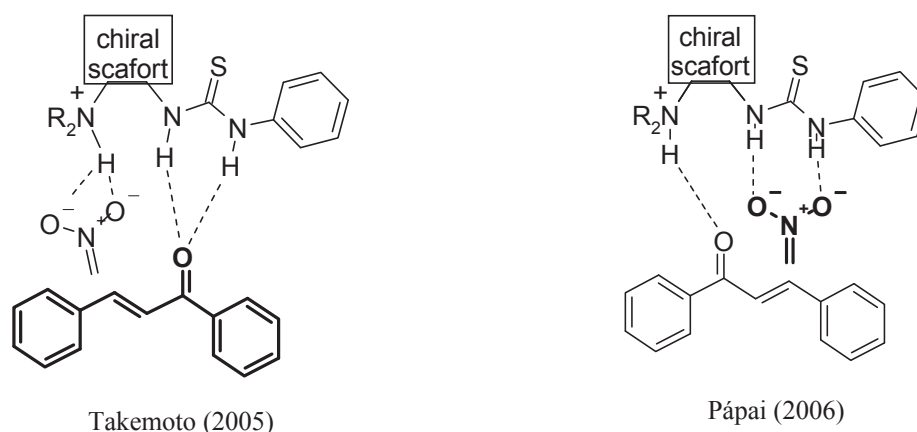


Figure 2.15 Proposed hydrogen-bonding activation models used in the computational study of the Michael addition of nitronate anion to chalcone.

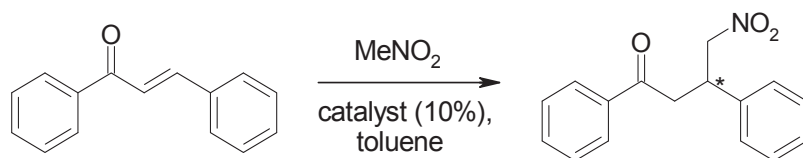
First mechanism correspond to dual activation model of Takemoto⁷⁰, nitronate interacts with the protonated amine while the ketone binds the thiourea. Pápai⁷¹ proposed other system: thiourea stabilized the nitronate and ketone is activated by the protonated amine of the organocatalyst.

In order to evaluate D-glucosamine based bifunctional thiourea as organocatalysts, compounds **L3-L5** were used in the Michael addition between nitromethane and chalcone (Table 2.5).

⁶⁹ For review on use thiourea organocatalyst in organocatalysis see (a) W. Y. Siau, J. Wang, *Catal. Sci. Technol.*, **2011**, 1, 1298-1310, (b) S. J. Connon, *Synlett*, **2009**, 354-376.

⁷⁰ T. Okino, Y. Hoashi, T. Furukuwa, X. Xu, Y. Takemoto, *J. Am. Chem. Soc.*, **2005**, 127, 119-125.

⁷¹ A. Hamza, G. Schubert, T. Soós, I. Pápai, *J. Am. Chem. Soc.*, **2006**, 128, 13151-13160.



Entry	Catalyst	Time (h)	Others	Temp. (°C)	Conv. (%)	ee (%)
1	K ₂ CO ₃	5	sonication	25	96	-
2	quinine	96	-	110	4	50
3	quinine	45	sonication	25	18	55
4	L3	36	sonication	25	<0.1	-
5	L4	36	sonication	25	<0.1	-
6	L5	36	sonication	25	<0.1	-

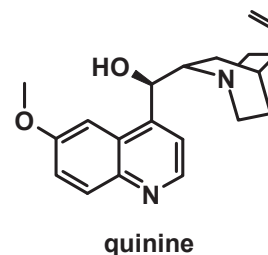


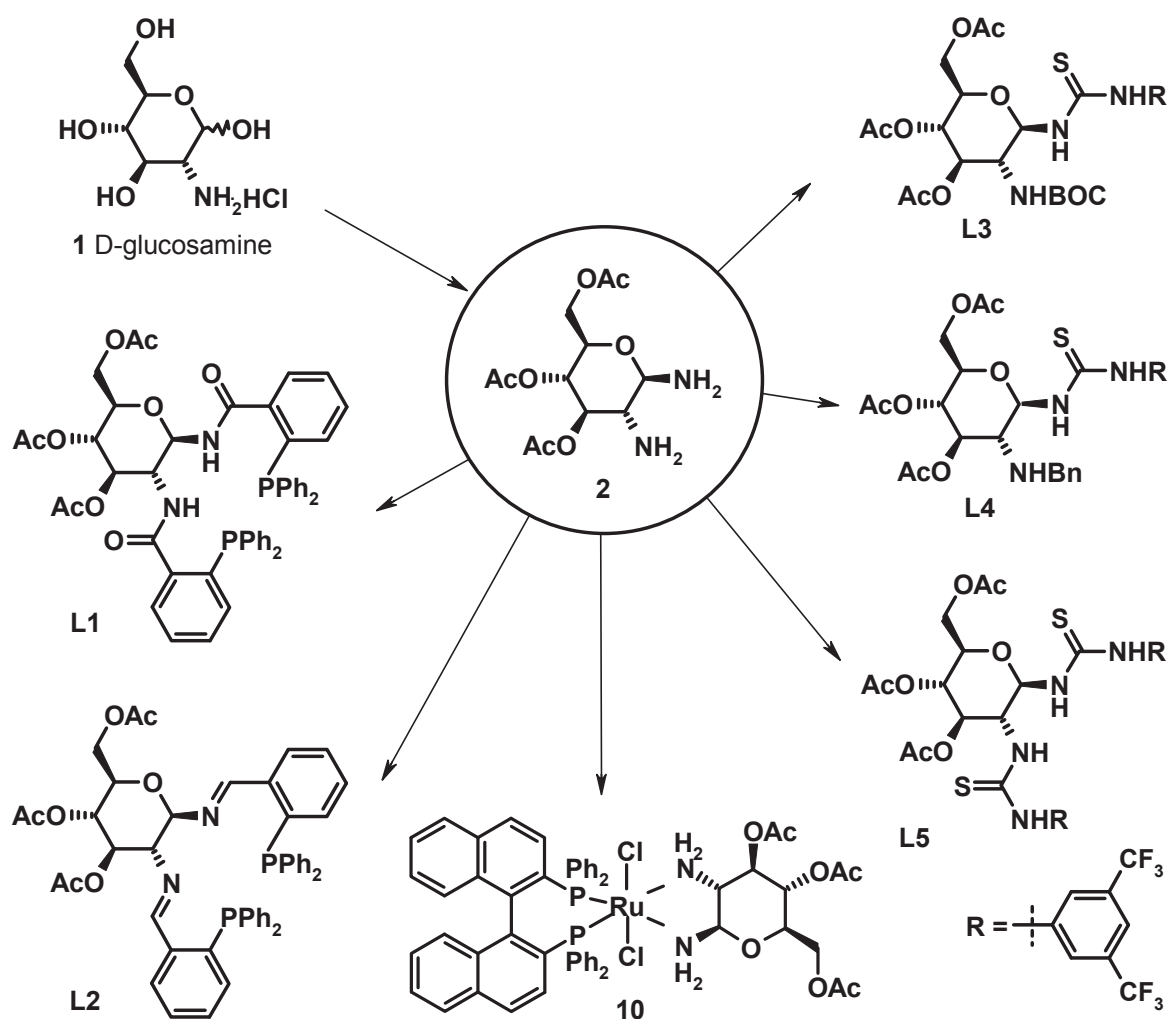
Table 2.5 Results of Michael addition of nitromethane to chalcone

Reaction of addition works very well with inorganic base (Table 2.5, entry 1), nevertheless conditions to obtain chiral product were investigated. Due to the privileged role in asymmetric organic synthesis, alkaloid-based compound-quinine was employed in reaction in these Michael reactions as catalyst to give up to 55% enantiomeric excess. The best conditions established for quinine: room temperature and sonification (Table 2.5, entry 3) were applied for carbohydrate based thiourea organocatalysts. However in any case conversion didn't exceed 0.1% (Table 2.5, entry 4, 5, 6).

Conclusions

Presently chemistry of carbohydrates is well known and developed. Attention of chemists all over the world is focused on those molecules, because of their biological activity and synthetic utility. They are easy available from biomass and are excellent natural chiral building blocks. The strategy of this work has involved the synthesis of carbohydrate-based ligands, which can reproduce the structural and stereochemical motifs of already known and use in asymmetric catalysis ligands.

In the first place was established synthesis of *trans*-1,2- β -glucodiamine which with its structure is similar to one of the widely used building blocks in synthesis of chiral ligands: *trans*-1,2-cyclohexanediamine. This newly synthesized molecule been used to prepare ligands and catalysts designed for asymmetric reactions:



Scheme 2.14 Ligands obtained for homogeneous catalysis.

Amido- and imino- ligands were synthesized and tested in reaction of allylic alkylation with two different substrates. Also attempts have been made to prepare diamino carbohydrate complex with Ruthenium and BINAP which was tested in reaction of hydrogenation of acetophenone. Finally considering increasing interest in organocatalysis in last few years synthesis of new thiourea organocatalysts was developed, and obtained compounds were used in catalytic reaction of addition of nitromethane to chalcone.

Although there has been well developed synthesis of ligands for asymmetric catalysis there still remain great challenges including using natural sources like carbohydrates. The main objective of such studies have been to replace known ligands with ligands derived from D-glucosamine. The results obtained so far have been somewhat disappointing, but further development considering advantages of those catalysts is necessary.

Experimental part

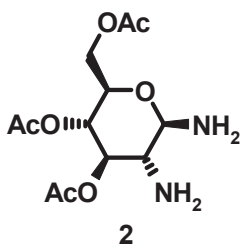
All experiments involving organometallic catalysis were carried out in a Schlenk tube under inert atmosphere. Solvents were dried and distilled under argon before use. The reagents were purchased from commercial suppliers and used without further purification. Conversion was determined by GC using Shimadzu GC-14B apparatus with flame ionization detector (FID) and integrator Shimadzu C-R6A. The capillary column Quadrex OV1 (30cm x 0.25mm) was used and helium as a carrier gas. The temperature of detector and the cell of injector was 250 °C. The inject volume was 1 µL.

Enantiomeric excesses were determined by HPLC method, with Chiralpack AD column (25 cm x 4.6 mm) with amylose tris(3,5-dimethoxyphenylcarbamate) coated on silica as a support, in companion of Shimadzu SPD-6A pump and integrator Shimadzu C-R6A pump and integrator Shimadzu C-R6A. The mobile phase was ratio of hexane / *i*-propanol. The analyses were performed at room temperature with inject volume of 20 µL.

2.5 Experiments dealing with synthesis of 1,2-β-glucodiamine

Synthesis of 3,4,6-tri-O-acetyl-β-1,2-D-diamineglucopyranose **2**

A mixture of azide compound **8** (0.46 g, 1.5 mmol) in degassed ethyl acetate (30 mL) was hydrogenated at room temperature under 2.5 atm pressure for 3 hours in the presence of Pt₂O (0.045 g, 0.20 mmol). The catalyst was removed by filtration through celite and washed with ethyl acetate. Solution was evaporated under reduced pressure producing a white solid

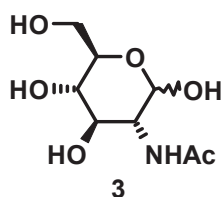


- Yield 90%
- White solid
- R_f = 0.29 (dichloromethane : methanol 20 : 1)
- m.p. 90-91 °C
- [α]_D²⁰ = +59.7 (c = 0.68, chloroform)
- ¹H NMR (CDCl₃): δ (ppm) = 1.62 (bs, 4H, 2 x NH₂), 2.01 (s, 3H, CH₃), 2.06 (s, 3H, CH₃), 2.08 (s, 3H, CH₃), 2.67-2.72 (m, 1H, H-2), 3.68 (ddd, 1H, J=2.3, J=4.9, J=9.7Hz, H-5), 3.98 (d, 1H, J=8.8Hz, H-1), 4.07 (dd, 1H, J=2.3, J=12.0Hz, H-6), 4.24 (dd, 1H, J=4.9, J=12.0Hz, H-6), 4.95-5.00 (m, 2H, H-3, H-4).

- ^{13}C NMR (CDCl_3): δ (ppm) = 21.1 (COCH_3), 21.2 (2 x COCH_3), 57.8 (C-2), 63.0 (C-6), 69.4 (C-4), 73.3 (C-5), 77.0 (C-3), 87.9 (C-1), 170.38 (COCH_3), 171.1 (COCH_3), 171.2 (COCH_3).
- IR: ν (thin film, cm^{-1}) = 3402 (ν_{NH}), 3364 (ν_{NH}), 3262 (ν_{NH}), 2891, 2842, 1736 ($\nu_{\text{C=O}}$), 1594 (ν_{NH}), 1421, 1366, 1218, 1174, 1100, 1042, 1006, 957, 912, 881, 837, 732.
- ESI full ms calcd. for $\text{C}_{12}\text{H}_{20}\text{N}_2\text{NaO}_7$ ($\text{M} + \text{Na}^+$): 327.1163, found 327.1167.

Synthesis of 2-acetamido-2-deoxy-6-D-glucopyranose 3⁷²

In Schlenk tube under argon atmosphere D-glucosamine hydrochloride (3 g, 13.9 mmol) was added to solution of sodium (0.64 g, 27.8 mmol) in methanol (25 mL). After 30 minutes solution was filtrated and solid was washed by methanol anhydride. Mixture was cooled to 0 °C and acetic anhydride (2 mL, 20.9 mmol) was added drop wise. Solution was stirred overnight in room temperature. Solution was filtrated and wash with methanol : diethyl ether 1 : 3. Solid was recrystallized from mixture water : ethanol and dry on vacuum pump.



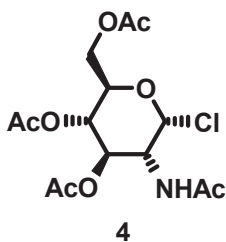
- Yield 68%
- White solid
- R_f = 0.68 (chloroform : methanol 1:1)
- m.p. 209-211 °C lit.⁷² 203-205 °C
- ^1H NMR (DMSO-d_6): δ (ppm) = 1.82 (s, 3H, CH_3) 3.10 (dd, 1H, $J=9.5\text{Hz}$, $J=13.6\text{Hz}$, H-4) 3.38 (s, 2H) 3.47 (dd, 2H, $J=5.9\text{Hz}$, $J=11.4\text{Hz}$) 3.52-3.65 (m, 3H) 4.41 (t, 1H, $J=5.4\text{Hz}$) 4.52 (d, 0.13H, $J=5.6\text{Hz}$) 4.62 (d, 0.87H, $J=4.3\text{Hz}$) 4.91 (s, 2H) 6.41 (d, 0.87H, $J=3.9\text{Hz}$) 6.49 (d, 0.13H, $J=6.3\text{Hz}$) 7.63 (d, 0.87H, $J=7.9\text{Hz}$) 7.73 (d, 0.13H, $J=8.1\text{Hz}$), according to the literature⁷².

Synthesis of 2-acetamido-3,4,6-tri-O-acetyl-1-chloro-2-deoxy- α -D-glucopyranse 4

Solution of 2-acetamido-2-deoxy-6-D-glucopyranose (1.5 g, 6.80 mmol) in acetyl chloride (5 mL, 81,5 mmol) was stirred at room temperature under argon atmosphere for 48 hours. Chloroform (12 mL), ice (10 g) and water (10 mL) were added to this solution. The organic phase was separated and washed with an aqueous solution of NaHCO_3 (15 mL).

⁷² A. Babič, S. Pečar, *Syn. Comm.*, **2008**, 38, 3052-3061.

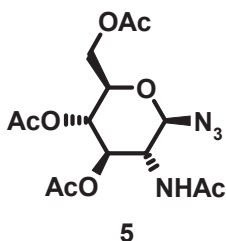
After drying over anhydrous sodium sulfate, the solvent was removed under reduced pressure. The residue was purified by crystallization from ether diethyl.



- Yield 70%
 - White solid
 - $R_f = 0.52$ (cyclohexane : ethyl acetate 1 : 2)
 - m.p. 118-119 °C, lit.⁵² 119 °C
 - $[\alpha]_D^{20} = +109.0$ (c = 0.99, chloroform)
- **¹H NMR (CDCl₃):** δ (ppm) = 1.98 (s, 3H, CH₃), 2.04 (s, 6H, 2xCH₃), 2.09 (s, 3H, CH₃), 4.02-4.13 (m, 1H, H-6), 4.21-4.30 (m, 2H, H-6, H-5), 4.53 (ddd, 1H, J=3.7, J=8.8, J=10.3Hz, H-2), 5.20 (dd, 1H, J=9.8, J=9.6Hz, H-4), 5.31 (dd, 1H, J=10.3, J=9.6Hz, H-3), 5.86 (d, 1H, J=8.8Hz, NHAc), 6.18 (d, 1H, J=3.7Hz, H-1), according to the literature⁵².
 - **¹³C NMR (CDCl₃):** δ (ppm) = 20.9 (COCH₃), 21.0 (COCH₃), 21.3 (COCH₃), 23.3 (COCH₃), 53.7 (C-2), 61.5 (C-6), 67.4 (C-4), 70.4 (C-3), 71.2 (C-5), 94.0 (C-1), 169.5 (COCH₃), 170.7 (COCH₃), 170.9 (COCH₃), 171.7 (COCH₃), according to the literature⁵².

Synthesis of 2-acetamido-3,4,6-tri-O-acetyl-1-azido-2-deoxy- β -D-glucopyranose **5**

After being stirred, a solution of 2-acetamido-3,4,6-tri-O-acetyl-1-chloro-2-deoxy- α -D-glucopyranose (2.23 g, 6.0 mmol) and sodium azide (0.39 g, 6.0 mmol) in dry DMF (15 mL) was heated under argon atmosphere at 75 - 80 °C for 4 hours. To the mixture, ice was added and then extracted with ethyl acetate (4 x 15 mL). The combined organic phases were dried over anhydrous sodium sulfate and concentrated under reduced pressure. The residue was purified by column chromatography on silica gel using a gradient from pure cyclohexane to cyclohexane : ethyl acetate 1 : 2.



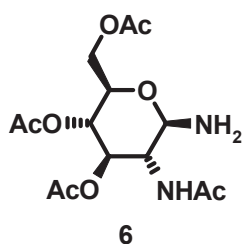
- Yield 84%
 - White solid
 - $R_f = 0.52$ (cyclohexane : ethyl acetate 1 : 2)
 - $[\alpha]_D^{20} = -22.4$ (c = 1.00, chloroform)
 - m.p. 156-157 °C, lit.⁵² 166-167 °C
- **¹H NMR (CDCl₃):** δ (ppm) = 1.98 (s, 3H, CH₃), 2.03 (s, 3H, CH₃), 2.04 (s, 3H, CH₃), 2.10 (s, 3H, CH₃), 3.78 (ddd, 1H, J=2.4, J=4.7, J=9.9Hz, H-5), 3.92 (dd, 1H, J=9.3, J=10.2Hz, H-2), 4.16 (dd, 1H, J=2.4, J=12.5Hz, H-6), 4.27 (dd, 1H, J=4.7,

$J=12.5\text{Hz}$, H-6'), 4.74 (d, 1H, $J=9.3\text{Hz}$, H-1), 5.10 (dd, 1H, $J=9.3$, $J=9.9\text{Hz}$, H-4), 5.23 (dd, 1H, $J=9.3$, $J=10.2\text{Hz}$, H-3), 5.63-5.89 (m, 1H, NH), according to the literature⁵².

- **^{13}C NMR (CDCl_3):** δ (ppm) = 20.9 (COCH₃), 21.0 (COCH₃), 21.1 (COCH₃), 23.6 (COCH₃), 54.5 (C-2), 62.3 (C-6), 68.5 (C-4), 72.5 (C-3), 74.3 (C-5), 88.8 (C-1), 169.7 (COCH₃), 170.9 (COCH₃), 171.1 (COCH₃), 171.3 (COCH₃), according to the literature⁵².

Synthesis of 2-acetamido-3,4,6-tri-*O*-acetyl-1-amino-2-deoxy- β -D-glucopyranose 6

A mixture of azide compound (1.0 g, 2.6 mmol) in degassed methanol (30 mL) was hydrogenated at room temperature under 2.5 atm pressure for 15 hours in the presence of Pd/C 10% (0.30 g). The catalyst was removed by filtration through celite and washed with ethanol. Solution was evaporated under reduced pressure producing a white solid.



- Yield 96%
- White solid
- $R_f = 0.62$ (chloroform : methanol 10 : 1)
- m.p. 215 °C, lit.⁵² 220-221 °C
- $[\alpha]_D^{20} = -0,82$ ($c = 0.97$, chloroform).
- **^1H NMR (CDCl_3):** δ (ppm) = 0.97 (m, 2H, NH₂), 1.97 (s, 3H, CH₃), 2.02 (s, 3H, CH₃), 2.04 (s, 3H, CH₃), 2.09 (s, 3H, CH₃), 3.63 (ddd, 1H, $J=2.3$, $J=4.8$, $J=9.5\text{Hz}$, H-5), 4.00 (dd, 1H, $J=9.2$, $J=9.6\text{Hz}$, H-2), 4.11 (dd, 1H, $J=2.4$, $J=12.3\text{Hz}$, H-6), 4.13 (d, 1H, $J=9.2\text{Hz}$, H-1), 4.22 (dd, 1H, $J=4.8$, $J=12.3\text{Hz}$, H-6), 5.04 (dd, 1H, $J=9.6$, $J=9.6\text{Hz}$, H-4), 5.09 (dd, 1H, $J=9.6$, $J=9.6\text{Hz}$, H-3), 5.68 (d, 1H, $J=9.1\text{Hz}$, NHAc), according to the literature⁵².
- **^{13}C NMR (CDCl_3):** δ (ppm) = 21.0 (COCH₃), 21.1 (COCH₃), 21.2 (COCH₃), 23.7 (COCH₃), 55.3 (C-2), 62.8 (C-6), 68.8 (C-4), 73.2 (C-3), 73.8 (C-5), 86.9 (C-1), 169.7 (COCH₃), 171.1 (COCH₃), 171.2 (COCH₃), 172.0 (COCH₃), according to the literature⁵².

Synthesis of 2-Amino-3,4,6-tri-*O*-acetyl-1-azido-2-deoxy- β -D-glucopyranose 7⁵⁵

Method A

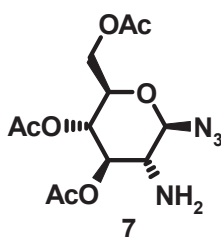
Azide compound **5** (1,00 g, 2.89 mmol, 1.0 equiv) and *N,N*-dimethyl-4-aminopyridine (0.10 g, 0.87 mmol, 0.3 equiv) were dissolved in THF (20 mL). Di-*tert*-butyl dicarbonate

Ligands for homogeneous catalysis

(1.89 g, 8.67 mmol, 3.0 equiv) was added, and the mixture was heated to reflux overnight. After the solution was cooled to room temperature, methanol (20 mL) and hydrazine (0.62 mL, 12.7 mmol, 4.4 equiv) were added and the mixture was stirred at room temperature for 4 h. The reaction mixture was poured into dichloromethane, washed with 1N HCl, $\text{CuSO}_{4\text{sat}}$, and $\text{NaHCO}_{3\text{sat}}$, dried (Na_2SO_4), and concentrated. Chromatography on silica using dichloromethane : methanol 20 : 1 gave 0.33 g (38%) of pure **7**.

Method B

3,4,6-tri-*O*-acetyl-1-azido-2-[(*tert*-butoxycarbonyl)amino]-2-deoxy- β -D-glucopyranose **8** (2.66 g, 6.2 mmol) was dissolved in dichloromethane (6.5 mL) and trifluoroacetic acid (2.6 mL) was added. Mixture was stirred overnight in room temperature. After that time solution was diluted with dichloromethane and washed with $\text{NaHCO}_{3\text{sat}}$, dried (Na_2SO_4) and evaporated. Filtration through pad of silica gave 1.80 g (88%) of pure **7**.

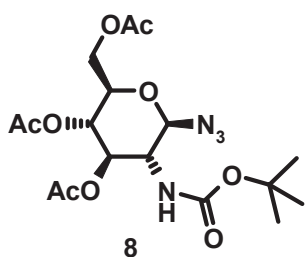


- White solid
- $R_f = 0.63$ (chloroform : methanol 10 : 1)
- m.p. 120-121 °C
- $[\alpha]_D^{20} = -24.05$ ($c = 1.01$, chloroform)
- $^1\text{H NMR}$ (CDCl_3): δ (ppm) = 1.39 (bs, 2H, NH_2), 2.01 (s, 3H, CH_3), 2.06 (s, 3H, CH_3), 2.07 (s, 3H, CH_3), 2.80 (dd, 1H, $J=9.0$, $J=9.7\text{Hz}$, H-2), 3.76 (ddd, 1H, $J=2.3$, $J=4.8$, $J=9.6\text{Hz}$, H-5), 4.12 (dd, 1H, $J=2.3$, $J=12.4\text{Hz}$, H-6), 4.28 (dd, 1H, $J=4.8$, $J=12.4\text{Hz}$, H-6'), 4.52 (d, 1H, $J=9.0\text{Hz}$, H-1), 4.94 (dd, 1H, $J=9.7$, $J=9.0\text{Hz}$, H-3), 5.01 (dd, 1H, $J=9.0$, $J=9.6\text{Hz}$, H-4).
- $^{13}\text{C NMR}$ (CDCl_3): δ (ppm) = 21.0 (COCH_3), 21.1 (COCH_3), 21.2 (COCH_3), 56.2 (C-2), 62.4 (C-6), 68.7 (C-4), 74.4, 75.57, 92.3 (C-1), 170.1 (COCH_3), 171.1 (COCH_3), 171.1 (COCH_3).
- **IR**: ν (thin film, cm^{-1}) = 3379 (ν_{NH}), 3324, 2110 (ν_{N_3}), 1746 ($\nu_{\text{C=O}}$), 1736, 1602, 1451, 1434, 1364, 1311, 1234, 1216, 1136, 1104, 10867, 1039, 951, 907, 861.
- **ESI full ms** calcd. for $\text{C}_{12}\text{H}_{18}\text{N}_4\text{NaO}_7$ ($\text{M} + \text{Na}^+$): 353.1068, found 353.1072.

Synthesis of 3,4,6-tri-*O*-acetyl-1-azido-2-[(*tert*-butoxycarbonyl)amino]-2-deoxy- β -D-glucopyranose **8**⁵⁶

Azide compound **5** (5.40 g, 14.5 mmol, 1.0 equiv) and *N,N*-dimethyl-4-aminopyridine (0.52 g, 4.7 mmol, 0.3 equiv) were dissolved in THF (20 mL). Di-*tert*-butyl dicarbonate

(10.2 g, 48.8 mmol, 3.0 equiv) was added, and the mixture was heated to reflux for 4 h. After the solution was cooled to room temperature, solvents were evaporated, mixture was dissolved in methanol (20 mL) added to solution of freshly prepared sodium metanolate. After 2 hours in room temperature methanol was evaporated and mixture was drying in vacuum pump for another 3 hours. In 0 °C crude was dissolved in mixture of pyridine (17 mL) and acetic anhydride (11.1 mL) After overnight solvents were removed under vacuum pressure and solid coevaporated three times with toluene. Chromatography on silica using dichloromethane : methanol 20 : 1 gave 4.57 g of pure **8**.



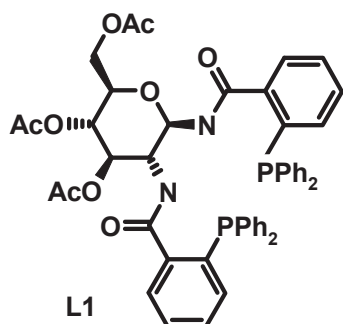
- Yield 73%
- White solid
- R_f = 0.81 (dichloromethane : methanol 20 : 1)
- m.p. 163-164 °C
- [α]_D²⁰ = -18.91 (c = 1.01, chloroform)
- ¹H NMR (CDCl₃): δ (ppm) = 1.40 (s, 9H *tert*-butyl), 1.99 (s, 3H, CH₃), 2.01 (s, 3H, CH₃), 2.06 (s, 3H, CH₃), 3.51 (ddd, 1H, J=9.3, J=9.3, J=9.3Hz, H-2), 3.76 (ddd, 1H, J=2.2, J=4.8, J=9.6Hz, H-5), 4.12 (dd, 1H, J=2.2, J=12.4Hz, H-6), 4.23 (dd, 1H, J=4.8, J=12.4Hz, H-6), 4.78 (bd, 1H, NH), 4.86 (d, 1H, J=9.3Hz, H-1), 5.02 (dd, 1H, J=9.6, J=9.6Hz, H-4), 5.23 (bm, 1H, H-3).
- ¹³C NMR (CDCl₃): δ (ppm) = 20.9 (COCH₃), 28.5 (2 x COCH₃), 21.0 (C(CH₃)₃), 55.8 (C-2), 62.2 (C-6), 68.5 (C-4), 72.4 (C-3), 74.2 (C-5), 80.9 (C(CH₃)₃), 88.9 (C-1), 155.2 (NHC=O), 169.7 (COCH₃), 170.8 (COCH₃), 170.9 (COCH₃).
- IR: ν (thin film, cm⁻¹) = 3400 (ν_{NH}), 2115 (ν_{N₃}), 1744 (ν_{C=O}), 1684, 1527 (ν_{NH}), 1371, 1320, 1294, 1211, 1162, 1106, 1080, 1033, 1008, 966, 897, 862.
- ESI full ms calcd. for C₁₇H₂₆N₄NaO₉ (M + Na⁺):453.1592, found 453.1601.

2.6 Experiments dealing with synthesis of ligands for allylic alkylation.

Synthesis of 3,4,6-tri-*O*-acetyl-1,2-di-{[2-(diphenylphosphino)benzoyl]amino} -β-D-glucopyranose **L1**

3,4,6-tri-*O*-acetyl-1,2-diamino-1,2-deoxy-β-D-glucopyranose **2** (100 mg, 0.33 mmol), 2-diphenylphosphinobenzoic acid (202 mg, 0.66 mmol), EDC (122 mg, 0.79 mmol), and HOBT (97 mg, 0.79 mmol) were dissolved in a mixture of dichloromethane (2 mL) and THF (4 mL) in a Schlenk tube under argon. After being stirred for 5 h at room temperature,

the solvents were evaporated. The residue was washed with 5% NaOH (10 mL), and 0.5 M HCl (5 mL). Product was purified with column chromatography using cyclohexane : ethyl acetate 3 : 1 as eluent.

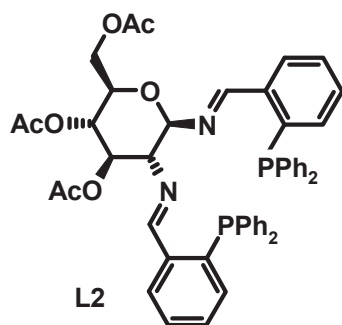


- Yield 23%
- White solid
- $R_f = 0.47$ (ethyl acetate : cyclohexane 1 : 1)
- m.p. 129-132 °C
- $[\alpha]_D^{20} = +4.7$ (c = 1, chloroform)

- $^1\text{H NMR}$ (CDCl_3): δ (ppm) = 1.96 (s, 3H, CH_3), 1.98 (s, 3H, CH_3), 2.01 (s, 3H, CH_3), 3.66 (ddd, 1H, $J=1.9$, $J=3.9$, $J=9.8\text{Hz}$ H-5), 3.96 (dd, 1H, $J=1.9$, $J=12.3\text{Hz}$ H-6), 4.20 (dd, 1H, $J=3.9$, $J=12.3\text{Hz}$ H-6), 4.37 (ddd, 1H, $J=8.7$, $J=9.6$, $J=9.8\text{Hz}$ H-2), 4.94 (dd, 1H, $J=9.6$, $J=9.8\text{Hz}$ H-3), 5.08 (dd, 1H, $J=9.6$, $J=9.8\text{Hz}$ H-4), 5.20 (dd, 1H, $J=8.4$, $J=9.6\text{Hz}$, H-1), 6.28 (d, 1H, $J=8.7\text{Hz}$, H-N2), 6.82-7.30 (m, 26H H_{arom}), 7.35-7.41 (m, 1H, H_{arom}), 7.45 (d, 1H, $J=8.4\text{Hz}$, H-N1), 7.75 (dd, 1H, $J=3.7$, $J=6.5\text{Hz}$, H_{arom}).
- $^{13}\text{C NMR}$ (CDCl_3): δ (ppm) = 21.1 (COCH_3), 21.2 (COCH_3), 21.4 (COCH_3), 53.9 (C-2), 62.2 (C-6), 68.2 (C-4), 73.4 (C-5), 73.9 (C-3), 80.9 (C-1), 127.2-135.5 (28 x C_{arom}), 137.3-141.1 (8 x C_{arom}), 168.8 (CONH), 169.7 (CONH), 170.7 (COCH_3), 171.2 (COCH_3), 172.3 (COCH_3).
- $^{31}\text{P NMR}$ (CDCl_3): δ (ppm) = -10.17, -6.29.
- **IR:** ν (thin film, cm^{-1}) = 3304 (ν_{NH}), 3051, 2925, 1741 ($\nu_{\text{C=O}}$), 1655, 1585, 1525 (ν_{NH}), 1479, 1462, 1433, 1366, 1303, 1228, 1082, 1029, 908, 847, 795, 741.
- **ESI full ms** calcd. for $\text{C}_{50}\text{H}_{47}\text{N}_2\text{O}_9\text{P}_2$ ($\text{M} + \text{H}^+$): 881.2783, found 881.2751.

Synthesis of 3,4,6-tri-O-acetyl-1,2-di-{[2-(diphenylphosphino)benzoyl]imino}- β -D-glucopyranose **L2**.

In a Schlenk tube under argon atmosphere, diamino compound **2** (125 mg, 0.41 mmol), and 2-diphenylphosphinobenzoic aldehyde (802 mg, 0.82 mmol), were stirring with MgSO_4 in dry, degassed toluene in 60 °C. After being stirred for overnight, the solvent was evaporated, mixture dissolved in dichloromethane and filtrated through celite. Product was purified with flash column chromatography using cyclohexane : ethyl acetate : NEt_3 80 : 10 : 1 as eluent.



- Yield 28%
- Light yellow solid
- $R_f = 0.64$ (ethyl acetate : cyclohexane 1 : 1)
- m.p. 97-98 °C
- $[\alpha]_D^{20} = +10.7$ (c = 1.03, chloroform)

- $^1\text{H NMR}$ (CDCl_3): δ (ppm) = 1.59 (s, 3H, CH_3), 1.94 (s, 3H, CH_3), 2.01 (s, 3H, CH_3), 3.26 (ddd, 1H, $J=8.2, J=9.0, J=9.0\text{Hz}$, H-2), 3.81 (ddd, 1H, $J=2.0, J=4.6, J=10.2\text{Hz}$, H-5), 4.07 (dd, 1H, $J=2.0, J=12.3\text{Hz}$, H-6), 4.23 (dd, 1H, $J=4.6, J=12.3\text{Hz}$, H-6), 4.80 (d, 1H, $J=8.2\text{Hz}$, H-1), 5.06 (dd, 1H, $J=9.6, J=10.2\text{Hz}$, H-4), 5.31 (dd, 1H, $J=9.0, J=9.6\text{Hz}$, H-3), 6.81 (m, 2H, H_{arom}), 7.15 (m, 28H, H_{arom}), 7.93 (m, 2H, H_{arom}), 8.76 (d, 1H, $J=4.9\text{Hz}$, $\text{N}=\text{CH}$), 8.99 (d, 1H, $J=5.6\text{Hz}$, $\text{N}=\text{CH}$).
- $^{13}\text{C NMR}$ (CDCl_3): δ (ppm) = 20.31 (COCH_3), 20.7 (COCH_3), 20.8 (COCH_3), 62.5 (C-6), 68.7 (C-4), 73.4 (C-3), 73.7 (C-5), 73.9 (C-2), 95.4 (C-1), 127.7-139.6 (36 x C_{arom}), 161.5 ($\text{N}=\text{CH}$), 163.7 ($\text{N}=\text{CH}$), 170.7 (COCH_3), 169.8 (2 x COCH_3).
- $^{31}\text{P NMR}$ (CDCl_3): δ (ppm) = -15.3, -14.9.
- **IR**: ν (thin film, cm^{-1}) = 3051, 2923, 2866, 2280, 2160, 1980, 1746 ($\nu_{\text{C}=\text{O}}$), 1636, 1584, 1478, 1461, 1433, 1364, 1224, 1068, 1027, 903, 743.
- **ESI full ms** calcd. for $\text{C}_{50}\text{H}_{47}\text{N}_2\text{O}_7\text{P}_2$ ($\text{M} + \text{H}^+$): 849.2853, found 849.2813.

General procedure for the asymmetric allylic alkylation with NaH / THF

A THF (1 mL) solution of $[\text{Pd}(\eta^3\text{-C}_3\text{H}_5)\text{Cl}]_2$ (2 mol%) and ligand (4 mol%) were stirred for 0.5 hour under an argon atmosphere and then substrate (1 equiv) in THF (1 mL) was added. The mixture was stirred for 10 min and a solution of sodium dimethyl malonate, prepared from dimethyl malonate (3.0 equiv) and sodium hydride (3.0 equiv) in THF (2 mL), was cannulated to Schlenk at room temperature. The reaction mixture was then stirred for 24 h at room temperature. After this time, solution was diluted with diethyl ether (5 mL) and wash with water (5 mL) and brine (5 mL). The combined organic layers were dried with MgSO_4 , the solvent was evaporated and the crude product was purified by chromatography eluting with hexane : ethyl acetate (10 : 1). For Dimethyl (1,3-Diphenylprop-2-en-1-yl)malonate conversions were determined by GC and $^1\text{H NMR}$ analysis. Enantiomeric excess was determined by chiral HPLC (Cellulose 3 column). For (E)-dimethyl (1-methyl-2-butenyl)propanedioate conversions were determined by GC and $^1\text{H NMR}$ analysis.

General procedure for the asymmetric allylic alkylation with Cs₂CO₃ / DCM

A solution of [Pd(η^3 -C₃H₅)Cl]₂ (2 mol%) and ligand (4 mol%) in dichloromethane (1 mL) were stirred for 30 min under an argon atmosphere and then 4-acetoxy-2-pentene (1 equiv) in dichloromethane (1 mL) was added. The mixture was stirred for 10 min at this temperature and dimethyl malonate (3.0 equiv), and cesium carbonate (3.0 equiv) were sequentially added. The reaction mixture was then stirred for 24 h at room temperature. After this time, solution was diluted with diethyl ether (5 mL) and wash with water (5 mL) and brine (5 mL). The combined organic layers were dried with MgSO₄, the solvent was evaporated. Conversions were determined by GC and ¹H NMR analysis. Differentiation of enantiomers of racemic mixture was visible using ¹H NMR technique by addition Europium tris[3-(heptafluoropropylhydroxymethylene)-(+)-camphorate].

Analysis of substrates and products of catalysis were made using conditions:

GC:

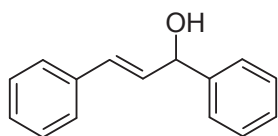
200°C (0 min) $\xrightarrow{5^\circ\text{C} / \text{min}}$ 250°C (60 min)

HPLC:

0.5 mL/min, heptane / 2-propanol 95 : 5, 254 nm

Synthesis of 1,3-Diphenyl-3-hydroxyprop-1-ene⁷³

Chalcone (5.12 g, 24.6 mmol) was dissolved in methanol (50 mL). At room temperature cerium (III) chloride heptahydrate (9.15 g, 24.6 mmol) was added in one portion. Then at 0 °C sodium borohydride (1.18 g, 31.2 mmol) was added spatula-wise and mixture was stirred in room temperature for 3 hours. Water (50 mL) was added and the aqueous layer was extracted with ether (3 × 40 mL). Organic phase was dried with sodium sulfate, filtered and concentrated. The resulting oil was purified by chromatography on silica. Elution with cyclohexane : EtOAc (10 : 1) gave the product (3.90 g, 76%) as a yellow oil, with crystallized in 0 °C overnight.



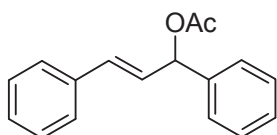
- Yield 76%
- White needles
- R_f = 0.36 (ethyl acetate : cyclohexane 1 : 10)
- m.p. 56 °C

⁷³ W. Leung, S. Cosway, R. H. V. Jones, H. McCann, M. Wills, *J. Chem. Soc., Perkin Trans. 1*, **2001**, 2588-2594.

- $^1\text{H NMR}$ (CDCl_3): δ (ppm) = 2.10 (s, 3H, CH_3), 5.28 (d, 1H, $J=6.4\text{Hz}$), 6.29 (dd, 1H, $J=6.4$, $J=15.8\text{Hz}$), 6.59 (d, 1H, $J=15.8\text{Hz}$), 7.11-7.37 (m, 10H, H_{arom}), according to the literature⁷³.

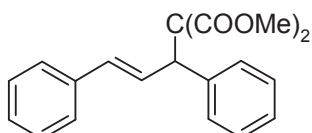
Synthesis of *rac*-(*E*)-1,3-Diphenyl-3-acetoxyprop-1-ene⁷³

1,3-Diphenyl-3-hydroxyprop-1-ene (3,9 g, 18.57 mmol) was dissolved in pyridine (10 mL). DMAP (2 crystals, catalytic) were added. At 0 °C acetic anhydride (5.3 mL, 55.6 mmol) was added dropwise. The solution was gradually allowed up to room temperature where it was stirred overnight. Ether (200 mL) was added and the solution washed with sat. CuSO_4 solution, sat. NaHCO_3 solution and water. The organic phase was dried with Na_2SO_4 , filtered and concentrated. Resulting yellow oil was purified by chromatography on silica. Elution with cyclohexane : EtOAc (20 : 1) gave the product **20** (2.55 g, 53%) as a pale yellow oil.



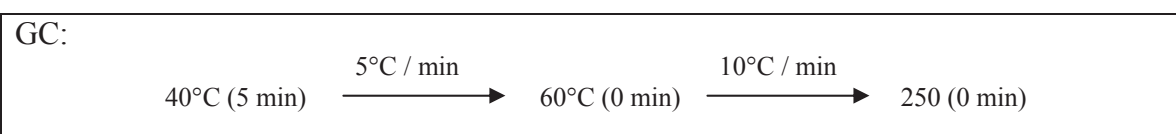
- Yield 53%
- Colorless oil
- $R_f = 0.78$ (ethyl acetate : cyclohexane 1 : 10).
- GC $t_R = 4.65$ min
- $^1\text{H NMR}$ (CDCl_3): δ (ppm) = 2.17 (s, 3H), 6.38 (dd, 1H, $J=6.9$, $J=15.7\text{Hz}$), 6.48 (d, 1H, $J=6.9\text{Hz}$), 6.67 (d, 1H, $J=15.7\text{Hz}$), 7.23-7.47 (m, 10H, H_{arom}).

Dimethyl (1,3-Diphenylprop-2-en-1-yl)malonate



- Colorless oil
- $R_f = 0.40$ (ethyl acetate : cyclohexane 1 : 10)
- GC $t_R = 8.55$ min
- HPLC (*R*) $t_R = 26.8$ min, (*S*) $t_R = 32.15$ min.
- $^1\text{H NMR}$ (CDCl_3): δ (ppm) = 3.43 (s, 3H, CH_3), 3.61 (s, 3H, CH_3), 3.88 (d, 1H, $J=10.9\text{Hz}$), 4.19 (dd, 1H, $J=8.4$, $J=10.9\text{Hz}$), 6.25 (dd, 1H, $J=8.4$, $J=15.7\text{Hz}$), 6.40 (d, 1H, $J=15.7\text{Hz}$), 7.07-7.26 (m, 10H, H_{arom}), according to the literature⁷⁴.

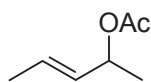
Analysis of substrates and products of catalysis were made using conditions:



⁷⁴ Š. Vyskočil, M. Smrčina, V. Hanuš, M. Polášek, P. Kočovský, *J. Org. Chem.*, **1998**, 63, 7738-7748.

Synthesis of *rac*-(E)-4-Acetoxy-2-pentene⁷⁵

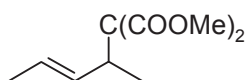
(E)-3-Penten-2-ol(1.00 g, 11.6 mmol) was dissolved in 25 mL of Et₂O and treated with DMAP (1.7 g, 13.9 mmol) and acetic anhydride (2.85 g, 13.9 mmol). After being stirred for 4 h, the reaction mixture was washed successively with 25 mL water, 3 x 25 mL of 10% HCl, and 3 x 25 mL of saturated NaHCO₃. Drying with sodium sulfate and concentration provided (E)-4-acetoxy-2-pentene (2.1 g, 16.4 mmol, 70%) as a colorless oil.



- Colorless oil
- R_f = 0.57 (ethyl acetate : cyclohexane 1 : 10)
- GC t_R = 3.8 min

- ¹H NMR (CDCl₃): δ (ppm) = 1.27 (d, 3H, J=6.4Hz, CH₃), 1.68 (ddd, 3H, J=0.6, J=1.5, J=6.4Hz, CH₃), 2.02 (s, 3H, COCH₃), 5.29 (p, 1H, J=6.5Hz), 5.47 (dddd, 1H, J=1.5, J=3.1, J=6.8, J=15.3Hz), 5.71 (dq, 1H, J=0.7, J=6.4, J=15.1Hz).

Dimethyl (1-methyl-2-butenyl)propanedioate



- Colorless oil
- R_f = 0.15 (ethyl acetate : cyclohexane 1 : 10)
- GC t_R = 14.93 min

- ¹H-NMR (300 MHz) ppm 1.05 (d, 3H, J=6.8Hz), 1.63 (d, 3H, J=6.3Hz), 2.89 (m, 1H), 3.26 (d, 1H, J=9.1Hz), 3.69 (s, 3H), 3.72 (s, 3H), 5.34 (m, 1H), 5.52 (m, 1H) according to the literature⁷⁶.

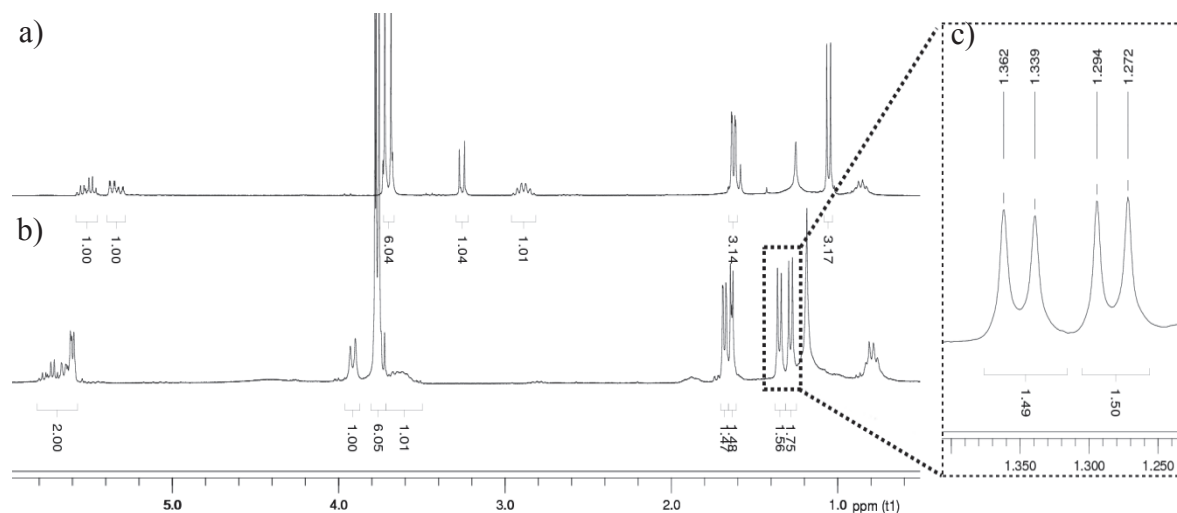


Figure 2.16 ¹H NMR spectra of racemic dimethyl (1-methyl-2-butenyl)propanedioate, b) with addition of europium tris[3-(heptafluoropropylhydroxymethylene)-(+)-camphorate], c) zoom in area of methyl group and visible differentiation of signals from enantiomers.

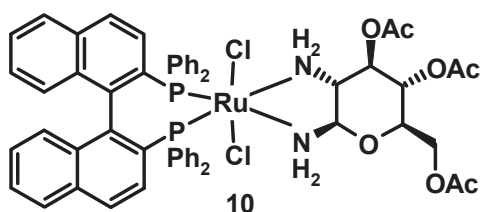
⁷⁵ Y. D. Ward, L. A. Villanueva, G. D. Allred, S. C. Payne, M. A. Semones, L. S. Liebeskind, *Organometallics*, **1995**, 14, 4132-4156.

⁷⁶ M. Widhalm, P. Wimmer, G. Klintschar, *J. Organometallic Chem.*, **1996**, 523, 167-178.

2.7 Experiments dealing with synthesis catalyst for hydrogenation.

Synthesis of (R),(R,R)-10:

[RuCl₂(C₆H₆)₂] (15.5 mg, 0.031 mmol) and (R)-BINAP (41 mg, 0.066 mmol) were placed in a dry 50-mL Schlenk flask. DMF (1 mL) was added, the mixture was degassed by three vacuum argon cycles and stirred under argon at 100 °C for 10 min to form a reddish brown solution. After the solution was cooled to 25 °C, 1,2-diamino-D-glucosamine **2** (20 mg, 0.066 mmol) was added and the mixture was stirred for 3 h. The solvent was removed under reduced pressure for 30 min in 25 °C and then in 50 °C for one hour. The residue was dissolved in dichloromethane (1 mL) and turbidity was removed by filtration. The filtrate was concentrated to about 1 mL, then ether (2 mL) was added and a light brown powder was obtained. The supernatant was removed and the resulting solid was dried under reduced pressure to give 63 mg of **10** quantitative.



- Yield quantitative
- Brown solid

- ¹H NMR (CDCl₃): δ (ppm) = 1.83 (s, 3H, CH₃), 1.87 (s, 3H, CH₃), 1.94 (s, 3H, CH₃), 2.06 (m, 1H, NH), 2.73 (m, 2H, H-1, H-3), 3.19 (m, 1H, NH), 3.51 (ddd, 1H, J=2.1, J=3.2, J=9.9Hz, H-5), 3.67 (t, 1H, J=8.3Hz, NH), 3.88 (dd, 1H, J=1.5, J=12.5Hz, H-6), 4.07 (dd, 1H, J=3.6, J=12.4Hz, H-6), 4.68 (dd, 1H, J=9.4, J=9.4Hz), 4.76 (dd, 1H, J=9.4, J=9.4Hz), 6.05 (d, 1H, J=8.7Hz, H_{arom}), 6.19 (d, 1H, J=8.6Hz, H_{arom}), 6.41 (m, 6H, H_{arom}), 6.59 (m, 2H, H_{arom}), 7.42 (m, 18H), 8.05 (t, 1H, J=8.4Hz, H_{arom}), 8.22 (t, 1H, J=8.2Hz, H_{arom})
- ESI full ms calcd. for C₅₆H₅₂C₁₁N₂O₇P₂Ru (M + H⁺): 1063.1989, found 1063.1891.

General procedure for the hydrogenation reaction of acetophenone to 1-phenylethanol.

2-Propanol (5 mL) charged into a Schlenk flask and was degassed by three vacuum argon replacement cycles. Solid trans **10** (0.2 mol%) was dissolved in the 2-propanol and used as a catalyst stock solution. Acetophenone (1.0 equiv) and solid (CH₃)₃COK (1 mol%) were placed in argoned steel autoclave. 2-Propanol (5 mL) and an aliquot of the catalyst solution were added to the autoclave under a stream of nitrogen. Hydrogen was introduced initially

Ligands for homogeneous catalysis

into the autoclave at a pressure of 10 atm and then reduced to 1 atm by carefully releasing the stop valve. After this procedure was repeated three times, the vessel was pressurized to desired pressure. The reaction mixture was vigorously stirred at room temperature to give 1-phenylethanol. After the hydrogen gas was carefully vented, the solvent was removed under reduced pressure. The conversions were determined by GC analysis, yields by isolation from reaction mixture using column chromatography (cyclohexane : ethyl acetate 20 : 1) and *ee* value were determined by HPLC (Cellulose 3 column)

Analysis of substrates and products of catalysis were made using conditions:

GC:

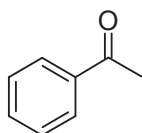
50°C (3 min) $\xrightarrow{5^\circ\text{C} / \text{min}}$ 250°C (60 min)

HPLC:

0.5 mL/min, heptane / 2-propanol 95 : 5, 254 nm

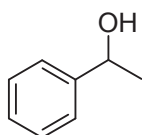
Acetophenone

Commercially available acetophenone was used for reaction. Compound was distilled before use as a substrate.



- Colorless oil (room temperature)
 - $R_f = 0.48$ (ethyl acetate : cyclohexane 1 : 10)
 - GC $t_R = 8.13$ min
 - HPLC $t_R = 9.09$ min.
- $^1\text{H NMR}$ (CDCl_3): δ (ppm) = 2.61 (s, 3H, CH_3), 7.42-7.60 (m, 3H, H_{arom}), 7.93-7.97 (m, 3H, H_{arom}).

1-Phenylethanol

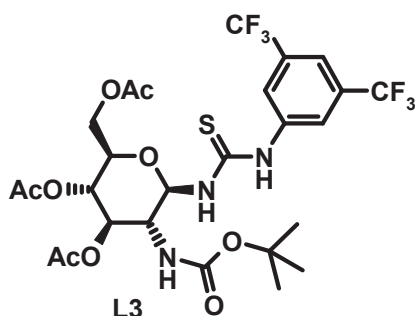


- Colorless oil
 - $R_f = 0.24$ (ethyl acetate : cyclohexane 1 : 10)
 - GC $t_R = 8.98$ min
 - HPLC (*R*) $t_R = 13.63$ min, (*S*) $t_R = 15.52$ min.
- $^1\text{H NMR}$ (CDCl_3): δ (ppm) = 1.42 (d, 3H, $J=6.4\text{Hz}$, CH_3), 1.80 (s, 1H, OH), 4.82 (q, 1H, $J=6.4\text{Hz}$), 7.25 (m, 5H, H_{arom}).

2.8 Experiments dealing with synthesis of d-glucosamine based organocatalysts.

Synthesis of Thiourea, N-[3,5-bis(trifluoromethyl)phenyl]-N'-{3,4,6-tri-O-acetyl-2-[(*tert*-butoxycarbonyl)amino]-2-deoxy- β -D-glucopyranose} L3

A mixture of azide compound **8** (0.300 g, 0.69 mmol) in degassed ethyl acetate (10 mL) was hydrogenated at room temperature under 2.5 atm pressure for 2 hours in the presence of PtO₂ (0.016 g, 0.069 mmol). The catalyst was removed by filtration through celite and washed with ethyl acetate. Solution was evaporated under reduced pressure. Obtained white solid was placed in argoned Schlenk tube, dissolved in dry dichloromethane, and then thiocyanato compound was added. Mixture was stirred overnight in room temperature. TLC show full conversion of starting material, solvent was evaporated, compound was crystallized from mixture of solvents dichloromethane : pentane in low temperature to gave 0.445 g of pure **L3**.

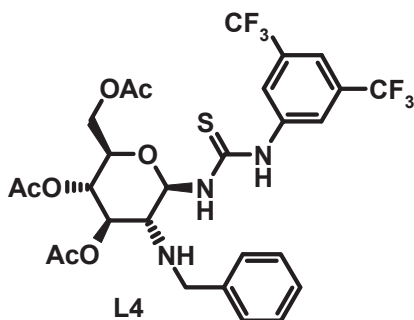


- Yield 95%
- White solid
- R_f = 0.66 (dichloromethane : methanol 20 : 1)
- $[\alpha]_D^{20} = +23,5$ (c = 1.02, chloroform)

- ¹H NMR (CDCl₃): δ (ppm) = 1.35 (s, 9H *tert*-butyl), 1.89 (s, 3H, CH₃), 2.05 (s, 3H, CH₃), 2.10 (s, 3H, CH₃), 3.85 (ddd, 1H, J=2.0, J=6.2, J=9.9Hz, H-5), 4.00 (dd, 1H, J=9.9, J=12.3Hz, H-6), 4.14 (dd, 1H, J=2.0, J=12.3Hz, H-6), 4.40 (ddd, 1H, J=7.5, J=9.3, J=9.3Hz, H-2), 5.06-5.26 (m, 3H, H-3, H-4, NH), 5.61 (bdd, 1H, J=6.5, J=7.5Hz, H-1), 7.63 (bs, 1H, H_{arom}), 7.93 (bs, 2H, H_{arom}), 8.00 (bd, 1H, J=7.5Hz, NH), 8.64 (bs, 1H, NH).
- ¹³C NMR (CDCl₃): δ (ppm) = 20.5 (COCH₃), 20.6 (COCH₃), 20.7 (COCH₃), 28.0 (C(CH₃)₃), 54.4 (C-2), 62.2 (C-6), 68.2 (C-4), 72.8 (C-3), 74.2 (C-5), 81.4 (C(CH₃)₃), 85.1 (C-1), 119.3 (C_{arom}), 121.1 (CF₃), 124.7 (CF₃), 124.8 (C_{arom}), 124.9 (C_{arom}), 131.3-132.7 (q, 2C, J=33.3Hz, 2 x C_{arom}-CF₃), 139.3 (N-C_{arom}), 157.0 (NHC=O), 169.4(COCH₃), 170.8 (COCH₃), 171.5 (COCH₃), 182.9 (C=S).
- ESI full ms calcd. for C₂₆H₃₂N₃O₉S (M + H⁺):676.1758, found 676.1744.

Synthesis of Thiourea, N-[3,5-bis(trifluoromethyl)phenyl]-N'-[3,4,6-tri-O-acetyl-2-amino-benzyl -2-deoxy- β -D-glucopyranose] **L4**

Thiourea compound **L3** (0.28 g, 0.42 mmol) was dissolved in dichloromethane (5 mL) and trifluoroacetic acid (0.25 mL) was added. Mixture was stirred overnight in room temperature. After that time solution was diluted with dichloromethane and washed with NaHCO₃, dried (Na₂SO₄) and evaporated. Solid was dissolved in methanol anhydride (4 mL), and benzaldehyde was added. Mixture was stirred overnight in room temperature. TLC show full conversion of starting material. Acetic acid (2.5 mL) and sodium cyanoborohydride (0.197 g, 3.1 mmol) were added. Reaction was monitored by TLC. After 1 hour reaction was quenched with water and extracted with dichloromethane. Organic phase was wash with NaHCO₃sat and brine, dried using Na₂SO₄, evaporated. Compound was purified by column chromatography using Cyclohexane : Ethyl acetate 1 : 1 as eluent.

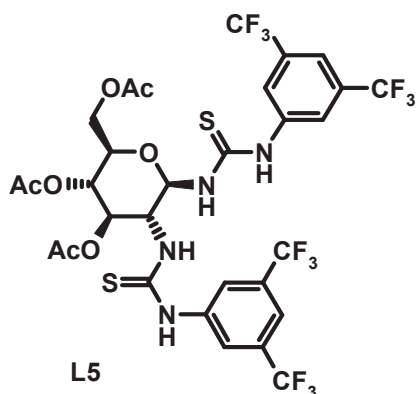


- Yield 44 %
- White solid
- R_f = 0.32 (dichloromethane : methanol 20 : 1)
- [α]_D²⁰ = +80.4 (c = 0.95, chloroform)

- ¹H NMR (CDCl₃): δ (ppm) = 2.08 (s, 6H, 2 x CH₃), 2.13 (s, 3H, CH₃), 3.04 (ddd, 1H, J=9.8, J=9.8, J=9.8Hz, H-2), 3.79 (ddd, 1H, J=1.6, J=5.8, J=8.5Hz, H-5), 3.86 (d, 2H, J=2.1Hz, CH₂), 4.09 (dd, 1H, J=1.6, J=12.3Hz, H-6), 4.36 (dd, 1H, J=5.8, J=12.3Hz, H-6), 5.04 (dd, 1H, J=8.5, J=9.8Hz, H-4), 5.20 (bd, 1H, J=8.2Hz, H-1), 5.32 (dd, 1H, J=9.8Hz, J=9.8Hz, H-3), 7.02 (s, 1H, NH), 7.23-7.37 (m, 5H, H_{arom}), 7.60 (s, 1H, H_{arom}), 7.90 (s, 2H, H_{arom}).
- ¹³C NMR (CDCl₃): δ (ppm) = 20.6 (COCH₃), 20.7 (COCH₃), 20.8 (COCH₃), 51.2 (CH₂), 61.5 (C-2), 62.2 (C-6), 68.8 (C-4), 73.7 (C-3), 74.5 (C-5), 84.3 (C-1), 118.6 (C_{arom}), 121.1 (CF₃), 123.4 (C_{arom}), 123.5 (C_{arom}), 124.7 (q, 2C, J=33.7Hz, 2 x CF₃), 127.8 (C_{arom}), 128.3 (2 x C_{arom}), 128.8 (2 x C_{arom}), 131.8 (m, 2 x C_{arom}-CF₃), 138.5 (CH₂-C_{arom}), 139.3 (N-C_{arom}), 169.7(COCH₃), 171.0 (COCH₃), 171.3 (COCH₃), 182.6 (C=S).
- ESI full ms calcd. for C₂₈H₃₀F₆N₃O₇S (M + H⁺): 666.1718, found 666.1703.

Synthesis of 3,4,6-tri-*O*-acetyl-1,2-di- $\{N,N'$ -dithiourea, N,N' -[3,5-bis(trifluoromethyl)phenyl]}- β -D-glucopyranose. **L5**

Diamino compound **2** (0.10 g, 0.33 mmol) was dissolved in dichloromethane (3 mL) and solution of 3,5-Di(trifluoromethyl)phenyl isothiocyanate (0.178 g, 0.66 mmol) in dichloromethane (1 mL) was added. Mixture was stirred overnight in room temperature. Solution was concentrated. Compound was purified by column chromatography using Cyclohexane : Ethyl acetate 2 : 1 as eluent. 0.085 g.



- Yield 30%
- White solid
- $R_f = 0.45$ (cyclohexane ethyl : acetate 2 : 1)
- m.p. 174 °C
- $[\alpha]_D^{20} = +78.2$ ($c = 1.00$, chloroform)

- $^1\text{H NMR}$ (CD_3OD): δ (ppm) = 2.07 (s, 3H, CH_3), 2.08 (s, 3H, CH_3), 2.10 (s, 3H, CH_3), 3.98 (ddd, 1H, $J=2.2$, $J=4.7$, $J=10.1\text{Hz}$, H-5), 4.17 (dd, 1H, $J=2.2$, $J=12.4\text{Hz}$, H-6), 4.38 (dd, 1H, $J=4.7$, $J=12.4\text{Hz}$, H-6), 5.14 (dd, 1H, $J=9.4$, $J=10.1$, H-4), 5.22 (ddd, 1H, $J=9.7$, $J=9.7$, $J=9.9\text{Hz}$, H-2), 5.41 (dd, 1H, $J=9.4$, $J=9.9\text{Hz}$, H-3), 6.01 (d, 1H, $J=9.7\text{Hz}$, H-1), 7.70 (s, 2H, 2 x H_{arom}), 8.12 (s, 2H, 2 x H_{arom}), 8.19 (s, 2H, 2 x H_{arom}).
- $^{13}\text{C NMR}$ (CD_3OD): δ (ppm) = 20.6 (COCH_3), 20.8 (2 x COCH_3), 58.6 (C-2), 63.3 (C-6), 70.1 (C-4), 74.7 (C-3), 74.8 (C-5), 85.0 (C-1), 118.9 (2 x C_{arom}), 122.8 (2 x CF_3), 124.7 (4 x C_{arom}), 126.4 (2 x CF_3), 132.1-133.6 (dq, 4C, $J=3.8$, $J=33.5$, 4 x $\text{C}_{\text{arom}}-\text{CF}_3$), 142.4 (2 x $\text{N}-\text{C}_{\text{arom}}$), 171.4(COCH_3), 172.2 (COCH_3), 172.5 (COCH_3), 184.0 (C=S), 184.3 (C=S).
- ESI full ms calcd. for $\text{C}_{30}\text{H}_{27}\text{F}_{12}\text{N}_4\text{O}_7\text{S}_2$ ($\text{M} + \text{H}^+$):847.1124, found 847.1054.

CHAPTER 3

Ligands for heterogeneous catalysis

Introduction

Research on heterogenisation of homogeneous catalysts is extensively explored⁷⁷. Many issues is discussing with included insuring high activity and selectivity in immobilization with avoid leaching of catalyst, improving enantioselectivity or increasing availability of cheaper chiral ligands. Immobilized catalysts have many advantages like easy separation and recover of the catalyst, or stabilization of highly reactive species that cannot exist in solution. Furthermore multifunctional catalysts can be obtained in which more than one active component is bound to a support. However using immobilized catalysts have also disadvantages. A common phenomenon is leaching of the metal and/or ligand and inhomogeneity due to different linkages between support matrix and complex. Also problematic features of homogeneous catalysts, such as corrosion, catalyst recovery and catalyst recycling, have so far not been overcome satisfactorily. Besides heterogeneous catalysts have lower catalytic activity comparing to their homogeneous counterparts caused by incapability of solvent and support, steric effects of the matrix with decreased accessibility of the active sites for the substrate, and deactivation of the active centers.

Although, high activity and better control of stereoselectivity are generally easier to achieve with homogeneous systems, they create major problems in terms of product purification and separation of expensive metal catalyst that leads to toxic wastes. These problems are particularly important when dealing with large scale-synthesis for environmental and economic concerns.

To reach high activity of catalyst and minimize obstacles many immobilization techniques have been used:

- **Covalent binding** is the most frequently used strategy. It is carried out with polymeric organic matrix or inorganic matrices, both by copolymerization of functionalized ligand with suitable monomer or by grafting functionalized ligands with reactive groups on surface of the support.

⁷⁷ For review see: (a) Volume 242 devoted to “Immobilized Catalysts Solid Phases, Immobilization and Applications” from *Top. Curr. Chem.*, **2004**, (b) L. Alaerts, J. Wahlen, P. A. Jacobs, D. E. De Vos. *Chem. Commun.*, **2008**, 1727-1737, (c) B.Pugin, H.-U. Blaser, “Immobilized Complexes for Enantioselective Catalysis: the Industrial Perspective”, from *Catalysis by Metal Complexes*, **2010**, 33, 231-245. F. Zaera, (d) Q.-H. Fan, K. Ding “Enantioselective Catalysis with Structurally Tunable Immobilized Catalysts” from *Top. Organomet. Chem.*, **2011**, 36, 207-245 (e) *Catal Lett.*, **2012**, 142, 501-516.

- **Ionic binding** is useful for anionic or cationic catalysts. Various supports with ion exchange capabilities can be used (standard organic and inorganic exchange resins, inorganic materials with polarized groups, zeolites).
- **Adsorption** is easy to perform very often even without need to previously functionalize of the ligand, however applicability is restricted due to possible competition with solvents or substrates.
- **Physisorption** or **entrapment** for big sizes of metal complexes and strict control of porosity of support is required. Catalyst is building up in well defined cages of porous support or polymer build up network around a preformed catalyst.
- **Supported aqueous phase catalysts (SAPC)** can be seen as special case of adsorption where a water soluble catalysts dissolve in water is adsorbed on a hydrophilic support forming a thin film on the inert surface of the support.
- **Supported liquid phase catalyst (SLPC)** is similar system to SAPC where water film is replaced by a solvent of low vapor pressure
- **Biphasic catalysts.** Aqueous (Phase Transfer Catalyst) or non aqueous catalysts containing two immiscible liquids without any additional additive.

The search for better performing and more reliable systems is ongoing, this situation favors the advanced state of immobilization techniques and commercial availability of sufficient number of potential supports and carriers, both organic and inorganic. In this chapter we will focus on three of the systems: SAPC, biphasic catalysis and covalent binding.

Covalent binding. Ligands supported on silica matrix

In the last several years, many efforts have been devoted to the use of mesoporous materials as a support for immobilization⁷⁸. Also the large surface areas of mesoporous materials make these materials very attractive as support for homogeneous ligands. In this study silica was used as the support material. Silica matrix is a nanostructured mesoporous material composed of siloxane groups (Si-O-Si) with silanol groups (Si-OH) distributed on the surface.

⁷⁸ Review: C. E. Song, S. Lee, *Chem. Rev.*, **2002**, 102, 3495-3524 Some selected application of silica matrix supported catalysts: (a) R. Sayah, E. Framery, V. Dufaud *Green Chem.*, **2009**, 11, 1694-1702, (b) R. Sayah, M. Le Floch, E. Framery, V. Dufaud, *J. Mol. Cat. A: Chemical*, **2010**, 315, 51-59, (c) R. Sayah, K. Glegola E. Framery, V. Dufaud, *Adv. Synt. Cat.* **2007**, 349, 373-381.

References

The systematic use of immobilization of organofunctional groups in silica has increased in the past four decades, because this support offers pronounced advantages over other organic/inorganic supports:

- Immobilization on silica results in great variety of silylating agents.
- Attachment is easier on silica surface than on organic polymeric supports.
- It is the first commercially available high specific surface area substrate with constant composition, enabling easy analysis and interpretation of results.
- Silica gel has no swelling.
- Great resistance to organic solvents.
- Very high thermal resistance.

However irreversible binding of metal ions and lack of selectivity are the main disadvantages of silica bound ligands in their repeated cyclic use.

The modification of silica gel using organic functional groups has been a subject of considerable interest, and it can be made by silanization which involves the covalent binding of a silane reagent molecule, either a chlorosilane or an alkyloxysilane (Figure 3.1), to the surface through a siloxane bond.

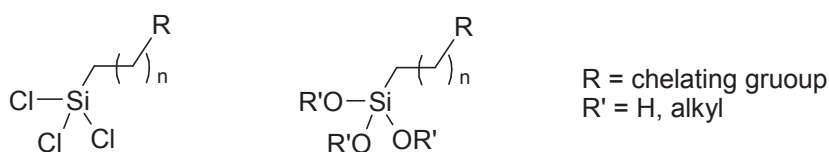


Figure 3.1 Silane molecules used in silanization.

In this study surface modification was performed by using triethoxysilane. Attachment of the chelating molecule to silica surface ongoing via sequences of reaction to have the chelating molecule at the free end of the linking group (Figure 3.2).

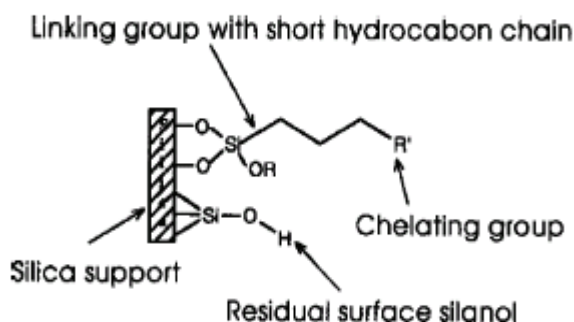


Figure 3.2 Product of silization

Biphasic catalysis. Ligands supported with poly(ethylene glycol).

The linear polymer of ethylene oxide: poly(ethylene glycol) (PEG) is inexpensive, nonvolatile, nontoxic, and is becoming attractive reaction media in organic synthesis. PEG has been also used as soluble polymer support. It can be dissolved in various organic solvents specially protic like water or alcohols. Moreover, PEG-supported catalysts have exhibited high catalytic activity and can be recovered conveniently.

The advantages of soluble polymers such as poly(ethylene glycol) (PEG) and its mono methyl ether (MPEG) have been explored as supports for catalyst immobilization and have led to a steadily increasing number of applications⁷⁹.

Supported Aqueous Phase Catalyst (SAPC)⁸⁰ is an elegant method of immobilization, where the hydrophilic catalyst system is placed in thin water phase in the surface of hydrophilic carrier while substrates and products stay in organic phase while catalytic reaction taking place efficiently at the aqueous-organic interface (Figure 3.3).

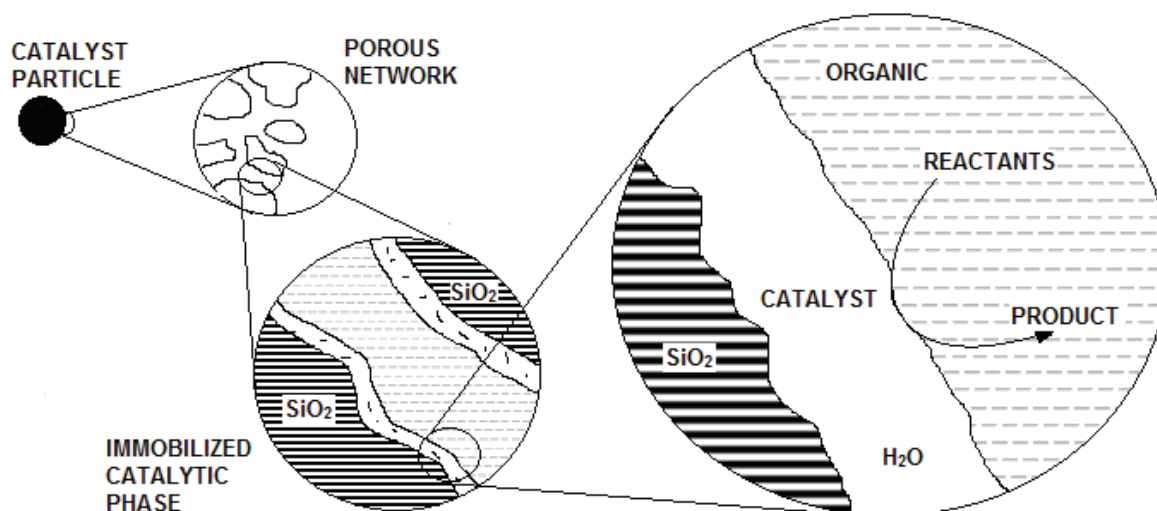


Figure 3.3 Schematic illustration of a supported aqueous-phase catalyst.

SAPC system is promising due to its high capacity in the conversion, the selectivity and also the easy recovery of the catalyst from the organic phase, and thus is economically and

⁷⁹ Review: P. H. Toy, K. D. Janda, *Acc. Chem. Res.*, **2000**, 33, 546–554. Some selected application of poly(ethylene glycol)-supported catalysts: (a) M. Bandini, M. Benaglia, R. Sinisi, S. Tommasi, A. Umani-Ronchi, *Org. Lett.*, **2007**, 9, 2151-2153, (b) H.-X. Li, C. Xie, M.-W. Ding, Z.-M. Liu, G.-F. Yang, *Synlett.*, **2007**, 14, 2280-2282, (c) S. H. Hong, R. H. Grubbs, *Organic Lett.*, **2007**, 9, 1955-1957, (d) X. Wang, L. Yin, T. Yang, Y. Wang, *Tetrahedron: Asymm.*, **2007**, 18, 108-114.

⁸⁰ For review see: (a) B. Cornils, *Supported aqueous-phase catalysis as the alternative method from Multiphase Homogeneous Catalysis* (Eds.: H. Delmas, U. Jauregui-Haza, A. M. Wilhelm), Wiley-VCH, Weinheim **2005**, 297-304, (b) M. E. Davis *Transitions to Heterogeneous Techniques (SAPC and Variations)*, from *Aqueous-Phase Organometallic Catalysis* (Eds.: B. Cornils, W. A. Herrmann), Wiley-VCH, Weinheim **1998**, 241-251.

References

ecologically advantageous. Large interfacial area makes metal easily available even for highly hydrophobic substrates, and metal losses can be reduced by convenient selection of hydrophilic supports and water-soluble ligands. However SAPC is strongly dependent on the water content of the solid support⁸¹.

Three types of water content effects have been reported: first at very low water content catalytic complex is strongly absorbed to the surface, what caused with lack of mobility and make it very stable, so low catalytic activity is observed. Secondly, at intermediate water contents activity reaches maximum, usually SAPC is efficient over a very restricted hydration range. Thirdly at high water loading the SAPC loose both activity and stability, leaching of catalyst is observed.

It has been proven that SAPC can perform a broad spectrum of reactions such as hydroformylation⁸¹, hydrogenation^{81d}, and oxidation^{81e} for the synthesis of the fine chemicals or pharmaceuticals. Although rhodium complexes are the most extensively used in SAPC few examples with Pd complexes are described in allylic substitution of allyl acetates⁸² or in alkoxy-carbonylation of alkenes⁸³. To our knowledge, no example of Suzuki-Miyaura cross-coupling reaction using SAPC methodology is already described in literature.

Organization of Chapter 3

In this chapter we will focus on three topics. Firstly Supported aqueous phase catalysts (SAPC) based on D-glucosamine will be presented and its use in Suzuki Myaura cross-coupling reaction. In the next subchapter synthesis of ligands containing poly (ethylene glycol) moiety for biphasic catalysis will be presented. Finally catalysts immobilized by covalent binding on silica matrix will be discussed.

⁸¹ (a) J. P. Arhancet, M. E. Davis, S. S. Merola, B. E. Hanson, *Nature* **1989**, 339, 454-455 (a) J. P. Arhancet, M. E. Davis, S. S. Merola, B. E. Hanson, *J. Catal.* **1990**, 121, 327-339, (b) J. P. Arhancet, M. E. Davis, B. E. Hanson, *J. Catal.* **1991**, 129, 94-99, (c) J. P. Arhancet, M. E. Davis, S. S. Merola, B. E. Hanson, *J. Catal.* **1991**, 129, 100-105, (d) I. Tóth, I. Guo, B. E. Hanson, *J. Mol. Catal.* **1997**, 116, 217-229, (e) S. C. Tsang, N. Zhang, L. Fellas, A. M. Steele, *Catal. Today* **2000**, 61, 29-36.

⁸² (a) P. Schneider, F. Quignard, A. Choplin, D. Sinou, *New J. Chem.*, **1996**, 20, 545-547, (b) S. Dos Santos, Y. Tong, F. Quignard, A. Choplin, D. Sinou, J. P. Dutatsta, *Organometallics*, **1998**, 17, 78-89, (c) A. Choplin, S. Dos Santos, F. Quignard, S. Sigismondi, D. Sinou, *Catal. Today*, **1998**, 42, 471-478, (d) S. Dos Santos, F. Quignard, D. Sinou, A. Choplin, *Top.Catal.*, **2000**, 13, 311-318.

⁸³ J. Seayed, A. M. Seayed, B. R. Sarkar, R. V. Chaudhari, US 20020137964 **2002**.

Results and discussion

3.1 Supported Aqueous Phase Catalyst (SAPC) for Suzuki-Miyaura cross coupling reaction.

In 2002 our team described the synthesis of the D-glucosamine-based phosphine, called 2-deoxy-2- {[4-(diphenylphosphino)benzoyl]amino}-D-glucopyranose **L6** (Figure 3.4) and its use in the cross-coupling reaction of aryl iodides or bromides with arylboronic acids (Chapter 1 Table 1.9)^{25a}.

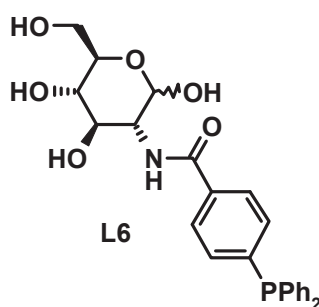
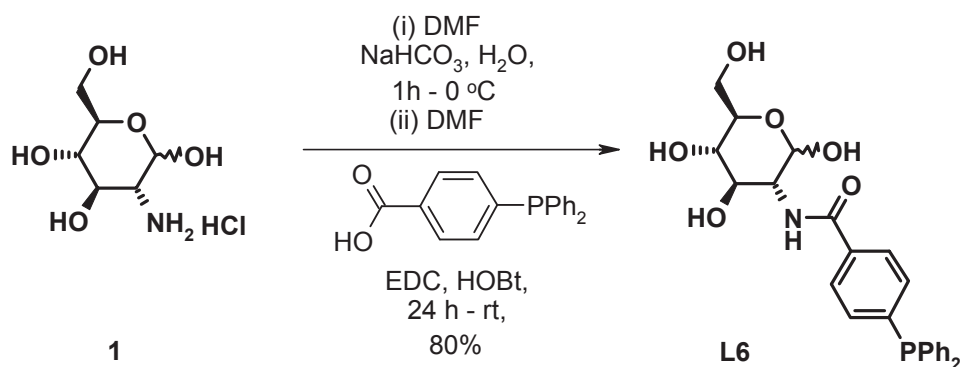


Figure 3.4 Polyhydroxylated ligand prepared by our team.

In a second study^{25b}, it has been demonstrated that a medium conversion is obtained when water is used as solvent, whereas when a mixture of toluene / ethanol / water (3/2/2), where ethanol plays the role of transfer agent, is used as solvent excellent yields have been obtained, with TON up to 97000. Unfortunately, no recoverable has been possible. In this context, we decided to immobilized the Pd-complex obtained from the same D-glucosamine-based phosphine and Pd(OAc)₂ in aqueous layer of the SAPC system in order to recycle the catalyst.

3.1.1 Synthesis of ligand

Synthesis of 2-deoxy-2- {[4-(diphenylphosphino)benzoyl]amino}-D-glucopyranose **L6** is shown in Scheme 3.1, and it was prepared using previously described procedure^{25a}. First D-glucosamine hydrochloride was hydrolyzed in cold solution of sodium bicarbonate in mixture of water / DMF and next simple coupling with 4-(diphenylphosphino)benzoic acid was performed using EDC (or 1-[3-dimethylaminopropyl]-3-ethylcarbodiimide) and HOBt (or 1-hydroxybenzotriazole) as coupling reagents, to give product in 75% of yield as a mixture of anomers α and β (in ratio 15 / 85) (Scheme 3.1).



Scheme 3.1 Synthesis of hydrophilic ligand for grafting in SAPC system

3.1.2 Impregnation of catalyst

The synthesis of the SAP catalyst was achieved by simple incipient wetness impregnation of silica (0.035-0.070 mm, 60 $\mu\text{\AA}$) by an aqueous solution of $\text{Pd}(\text{OAc})_2$ and 3 equivalents of **L6**, using method described by Sinou^{82b} (Figure 3.5).

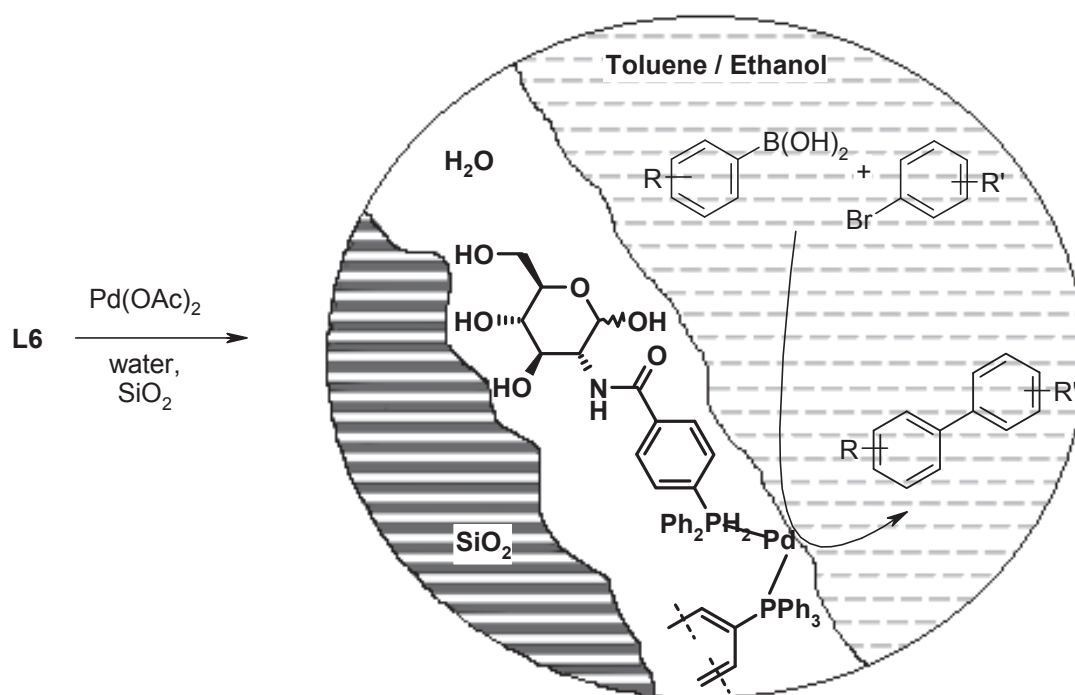


Figure 3.5 Schematic illustration of a supported aqueous-phase catalyst (SAPC).

According to author this procedure allows to obtain in a reproducible way, a solid with a water content close to 3%. Similarly like in above case to ensure a fast diffusion of the liquid into the porous system and thus a good dispersion of the catalytic active species, the silica was evacuated at 150 °C in vacuum pump prior to impregnation and the final solid was dried under vacuum (25 °C) for 16 hours.

3.1.3 Suzuki Miyaura cross coupling

Suzuki Miyaura cross coupling reaction⁸⁴ is probably one of the most studied [Pd]-catalyzed reactions. Its catalytic system provides simple and practical method for creating C-C and C-N bonds under sustainable conditions with excellent yields.

The cross-coupling reaction of organoboron compounds involving oxidative addition of organic halides or other electrophiles to a Pd(0) complex, transmetalation between Pd-X and R', and reductive elimination of R-R' to regenerate the "Pd⁽⁰⁾L₂".

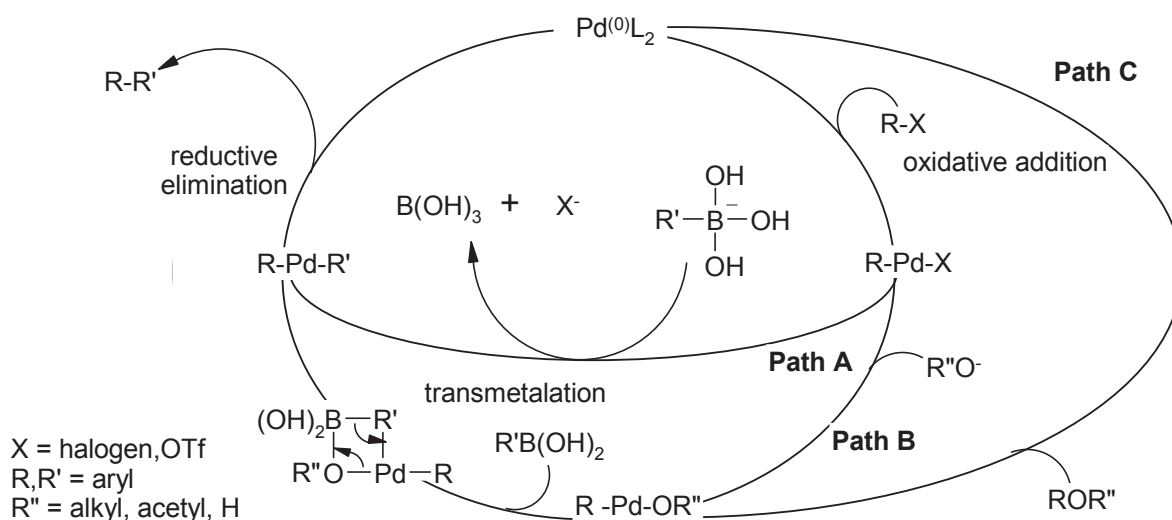


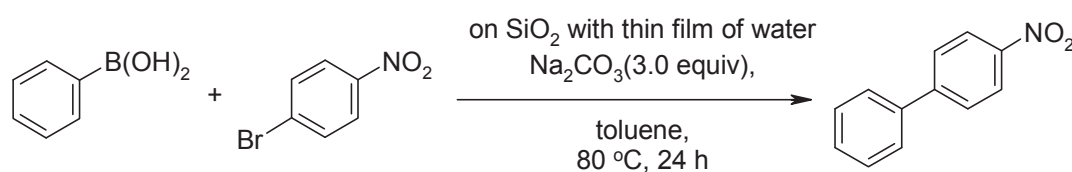
Figure 3.6 Catalytic cycle of cross-coupling.

There are three possible processes, path A-C, for preparing R-Pd-R' complex (Figure 3.6). Path A usually required presence of base for quarternization the boron atom to enhance the nucleophilicity of the organic group R'. An alternative process (path B) is transmetalation to an (oxo)palladium(II) complexes [R-Pd(0)-R''] *in situ* generated by the ligand exchange between R-Pd-X and a base (R''O⁻). For organic electrophiles reaction often proceeds under neutral conditions directly yielding an (oxo)palladium(II) intermediate from the "Pd⁽⁰⁾L₂". (path C). The reaction may involve coordination of the R-Pd(0)-R to the B(OH)₃ and as a result formation of complex and transfer of an activated organic group from boron to palladium (paths B,C). Last step reductive elimination is common for all path and involves creation of product R-R' and regeneration of Pd(0) complex.

⁸⁴ For selected reviews see: (a) N. Miyaura and A. Suzuki, *Chem. Rev.*, **1995**, 95, 2457-2483, (b) Volume 219 devoted to "Cross-Coupling Reactions A Practical Guide" from *Top. Curr. Chem.*, **2002**, (c) V. Farina, *Adv. Synth. Catal.*, **2004**, 346, 1553-1582, (d) N. T. S. Phan, M. Van Der Sluys, C. W. Jones, *Adv. Synth. Catal.*, **2006**, 348, 609-679, (e) C. Torborg, M. Beller, *Adv. Synth. Catal.*, **2009**, 351, 3027-3043.

Because of its excellent performance, economic and environmental concerns, numerous efforts have been devoted to the development of Suzuki-Miyaura reaction under benign conditions. Among them, the use of water as solvent is one possibility, however many substrates is not suitable with hydrophilic environment. For this reason, the immobilization of the catalyst could be good solution. And in the case of the Pd catalysts derived from mono- or diphosphine ligand, for the Suzuki-Miyaura reaction, numerous examples on organic⁸⁵ or inorganic⁸⁶ supports have been used

Before to evaluate our SAPC system, blank experiments were made (Table 3.1). We test the effect of the alone silica, dried before under vacuum at 150°C during 4 hours. The reaction was carried out in toluene in the presence of SiO₂, Na₂CO₃ (3 equiv) as the base, with a 4-bromonitrobenzene / phenylboronic acid ratio of 1 / 1.1, for 24 hours at 80°C. No reaction took place. (Table 3.1, entry 1).



Entry	Pd(OAc) ₂ (%mol)	Run	Conv. (%)
1	0.0	1	no reaction
2	1.0	1	74
3	1.0	2	15

Table 3.1 Influence of ligand and palladium for reaction of Suzuki-Miyaura.

Similarly to explain the role of our ligand in the SAPC, a catalyst (Pd SAPC) was prepared by impregnating a dried silica with a solution of Pd(OAc)₂ in a mixture of ethanol and water (ratio 2/1), following by concentration and drying under vacuum at room temperature for 16 hours.

Indeed, it is well known that ligand-free Pd(OAc)₂ is able to catalyze the coupling reaction of aryl iodides and activated or deactivated aryl bromides^{84b,e,87}. Using the same conditions

⁸⁵ For selected examples see: (a) Y. Uozumi, H. Danjo, T. Hayashi, *J. Org. Chem.*, **1999**, 64, 3384-3384, (b) K. Inada, N. Miyaura, *Tetrahedron*, **2000**, 56, 8661-8664, (c) A. Datta, F. Ebert, H. Plenio, *Organometallics*, **2003**, 22, 4685-4691, (d) K. Glegoła, E. Framery, K. M. Pietrusiewicz, D. Sinou, *Adv. Synth. Catal.*, **2006**, 348, 1728-1733.

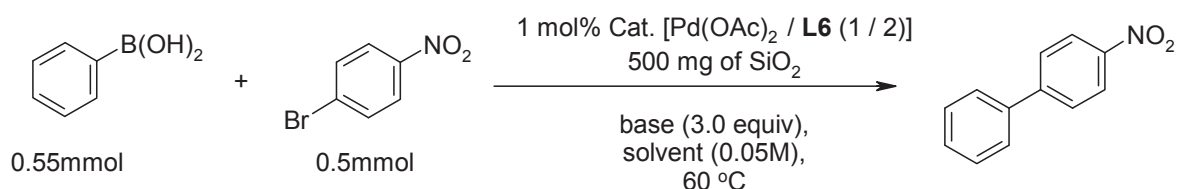
⁸⁶ For selected examples see: (a) E. Paetzold, I. Jovel, G. Oehme, *J. Mol. Catal. A: Chem.*, **2004**, 214, 241-247 (b) R. Sayah, K. Glegoła, E. Framery, V. Dufaud, *Adv. Synth. Catal.*, **2007**, 349, 373-381, (c) N. J. S. Costa, P. K. Kiyohara, A. L. Monteiro, Y. Coppel, K. Philippot, L. M. Rossi, *J. Catal.*, **2010**, 276, 382-389, (d) W. Chen, P. Li, L. Wang, *Tetrahedron*, **2011**, 67, 318-325.

⁸⁷ Examples: (a) D. Badone, M. Baroni, R. Cardamone, A. Ielmini, U. Guzzi, *J. Org. Chem.*, **1997**, 62, 7170-7173 (b) N. A. Bumagin, V. V. Bykov, *Tetrahedron*, **1997**, 53, 14437-14450, (c) J. C. Bussolari, D. C.

References

as reported before and changing SiO₂ by Pd SAPC (1 molar% of Pd loading), after the first run, the Pd SAPC was filtered, washed with toluene and dried under vacuum at room temperature for 16 hours, before to be used in a second run without any addition of Pd(OAc)₂ (Table 1.1, entries 2, 3). The yield of the coupling product of 4-bromonitrobenzene and phenylboronic acid decreased from 74% to 15%. This drop in performance was explained by the leaching of the metal when the catalyst was filtered and washed with toluene.

We then studied the influence of the solvent on the coupling reaction between 4-bromonitrobenzene and phenylboronic acid using 1 molar% Pd(OAc)₂ and L6 as the catalyst, at 60 °C. We noticed that the highest conversions were obtained using toluene and ethanol in ratio 7.5 / 1 (Table 3.2, entries 5, 6) or toluene and ethanol in ratio 10 / 1 (Table 3.2, entry 4) as the solvent. The use of toluene alone resulted in poor conversions (Table 3.2, entries 1-3).



Entry	Solvent	Base	Time	Conv. (%)
1	Toluene	K ₃ PO ₄	4 h	8
2	Toluene	Na ₂ CO ₃	4 h	4
3	Toluene	Na ₂ CO ₃	4days	38
4	Toluene / Ethanol (10/1)	Na ₂ CO ₃	18 h	68
5	Toluene / Ethanol (7.5/1)	K ₃ PO ₄	18 h	63
6	Toluene / Ethanol (7.5/1)	Na ₂ CO ₃	18 h	96

Table 3.2 Optimisation of conditions for solvent and base.

Other tested factor was influence of base. When reaction was carried out in toluene as solvent better results were obtained with potassium phosphate (Table 3.2, entry 1), however using ratio toluene / ethanol (7.5/1) almost full conversion was obtained with sodium carbonate (Table 3.2, entry 6) while in the same conditions K₃PO₄ gave only 63% of conversion (Table 3.2, entry 5).

Recyclability of catalyst (L/Pd SAPC) was also estimated by repeatedly carrying out Suzuki coupling reactions at 80°C in toluene / ethanol (7.5 / 1) with model reaction using

two different amounts of molar Pd loading 1% and 0.1% respectively. After the first run of the reaction, the Pd SAPC was filtered, washed with toluene and dried under vacuum at room temperature for 16 hours, and then recharged with the same substrates, base and solvents for the next run, without any addition of catalyst.

Under the same conditions and with the Pd loading of 1% molar of, the conversions of products remained the same (99-91%) during three runs, and decreased slightly in the fourth (85%), before to decrease in the fifth and sixth run to 40 and 20%, respectively (Figure 3.7).

We also tried to reduce the Pd loading to 0.1% molar, nevertheless application of smaller amounts of catalyst led to poorer results. The conversion of the two first run (93 and 86%) were almost similar to the two first runs with a Pd load ten times higher. But from the third cycle, the conversions decreased drastically from 88% to 44%, 32% and 18% (due to bad decantation and lost of supported silica catalyst).

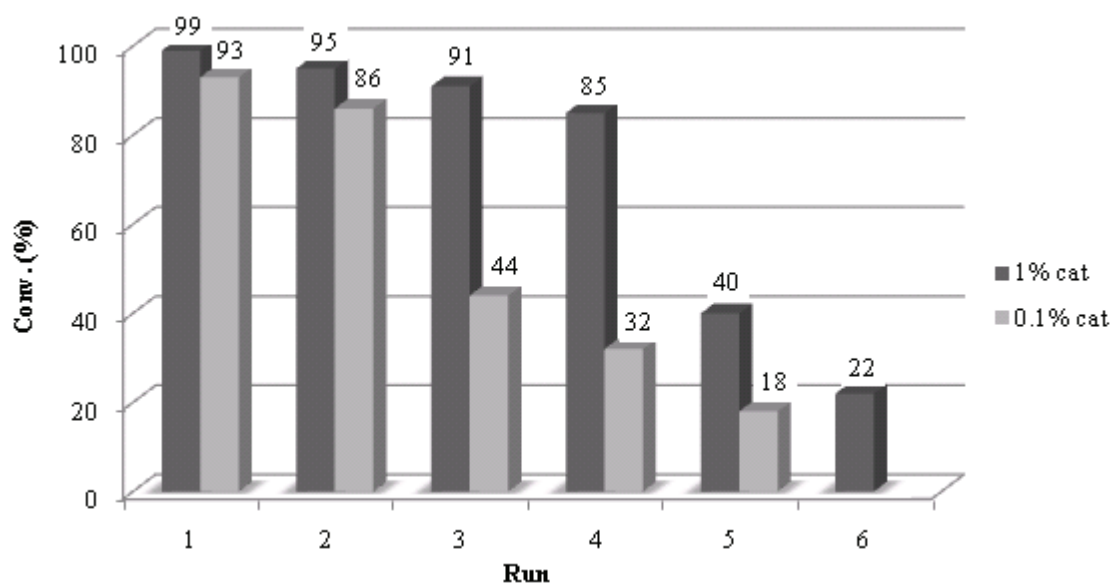


Figure 3.7 Influence of amount of catalyst for conversion during recycling.

Reaction conditions: 0.5 mmol of 4-bromonitrobenzene, 0.55 mmol of phenylboronic acid, 500 mg of silica, 1 mL ethanol, 7.5 mL toluene, 80°C, 24 h.

Despite the average yields obtained from the fifth or the third run, in the case of a 1.0% or 0.1% molar Pd loading respectively, we demonstrated the positive effect of the D-glucosamine-based phosphine to prevent the leaching of the catalyst.

Having these results in hand, we then investigated the scope and limitations of the method. As shown in Table 3.3, many acyclic activated or deactivated aryl bromides with various arylboronic acids were effectively transformed into their corresponding biaryls with yields

References

up to 99%. The reactions were carried out in the same conditions as described above with 1% molar of Pd.

The yields in biaryl coupling of aryl bromides bearing electron withdrawing group with phenylboronic acid were good between 88% and 99% (Table 3.3, entries 1, 5 and 6), except in the case of 4-vinylbromobenzene where the yield was 65% with a conversion of 76% (Table 3.3, entry 7). In the case of coupling of aryl bromides bearing electron donating group with phenylboronic acid, the conversions were over 90% (Table 3.3, entries 9, 10), except in the case of 4-bromomethoxybenzene where a poor conversion of 30% was observed (Table 3.3, entry 8).

Ar-B(OH) ₂ 0.55mmol	+	Ar'-Br 0.5mmol	$\xrightarrow[\text{Na}_2\text{CO}_3(3.0 \text{ equiv.}), \text{ toluene / ethanol } 7.5 / 1, 80 \text{ }^\circ\text{C}, 24 \text{ h}]{1 \text{ mol\% } [\text{Pd}(\text{OAc})_2 / \text{L6} (1 / 2)], 500 \text{ mg of SiO}_2}$	Ar-Ar'
-----------------------------------	---	-------------------	--	--------

Entry	Ar	Ar'	Conv. (%) ^a	Yield (%) ^b
1	C ₆ H ₅	4-NO ₂ C ₆ H ₄	100	99
2	3-MeCOC ₆ H ₄		92	75
3	4-MeC ₆ H ₄		97	95
4	2,6-Me ₂ C ₆ H ₃		50	45 ^c
5	C ₆ H ₅	4-MeCOC ₆ H ₄	99	88
6		4-MeCO ₂ C ₆ H ₄	96	95
7		4-VinylC ₆ H ₄	76	65 ^c
8		4-MeOC ₆ H ₄	30	n.d. ^d
9		2-MeC ₆ H ₄	100	96
10		4-MeC ₆ H ₄	93	85
11		2-Bromonaphtalene	85	83 ^a
12		2-Bromopyridine	100	75 ^a

Table 3.3 Suzuki-Miyaura cross-coupling of various aryl bromides and arylboronic acids.

^a Determined by GC. ^b Isolated chemical yield after column chromatography. ^c Determined by ¹H NMR and ¹³C NMR. ^d Not determined.

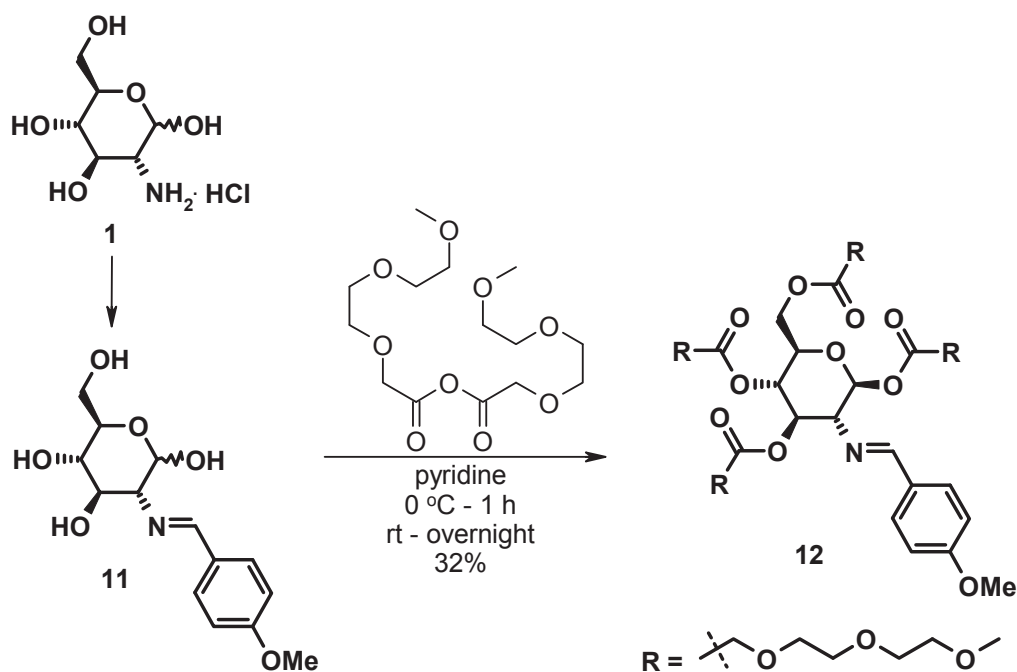
Biaryl coupling of 4-bromonitrobenzene with 4 arylboronic acids was also studied (Table 3.3, entries 1-4). 4-Bromonitrobenzene reacted efficiently with phenylboronic-, 3-acetylphenylboronic- or 4-tolylboronic acid to give with good yields the corresponding biaryl compounds (Table 3.3, entries 1-3). The sterically hindered 2,6-dimethylphenylboronic acid reacted also affording the coupling product in 45% yield (Table 3.3, entry 4).

Finally, when 2-bromonaphthalene in homogeneous conditions gave very low conversion (20%) of coupling product with phenylboronic acid with the same Pd loading in a mixture of Toluene/Ethanol/Water as solvent^{25b} the same cross-coupling reaction performed under SABC conditions gave the biaryl compound with a conversion of 85% (Table 3.3, entry 11). And the condensation of the heterocyclic 2-bromopyridine with phenylboronic acid occurred with a total conversion and a isolated chemical yield of 75% (Table 3.3, entry 12).

3.2 PEG-supported ligands

3.2.1 Ligand containing 4-polyethylene arms

Starting from D-glucosamine **1**, through carbohydrate **11** we are interested in synthesis new hydrosoluble ligand containing PEG moiety (Scheme 3.2). Compound **11** was prepared according to procedure described for synthesis of *tetra*-acetylated D-glucosamine⁸⁸ in two steps starting from D-glucosamine **1**. First step was protection of amino function using *p*-anisaldehyde, second step was reaction acetylation of hydroxyl groups in solution of pyridine in the presence of [(methoxy)ethoxy]ethoxyacetic anhydride prepared according to literature⁸⁹ starting from [(methoxy)ethoxy]ethoxyacetic acid and DCC as coupling agent. After 15 hours in room temperature 1,3,4,6-*tetra*-O-[(methoxy)ethoxy]ethoxyacetyl-2-(*p*-methoxybenzylidene)amino-2-deoxy- β -D-glucopyranose **12** was isolated using column chromatography with yield 32%.

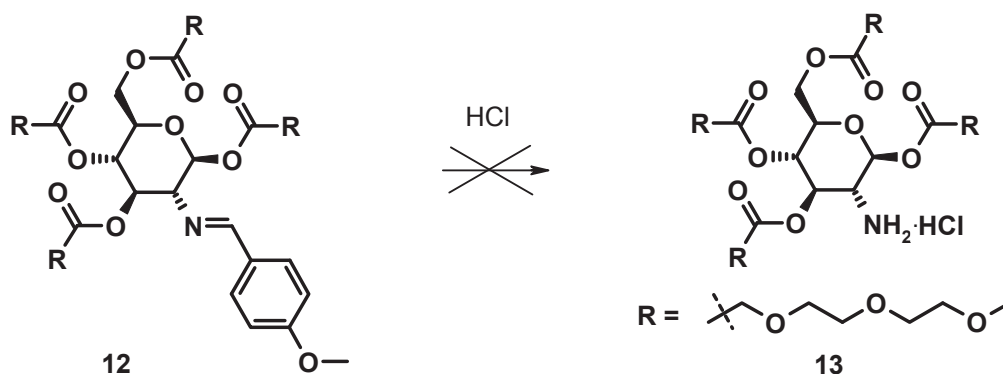


Scheme 3.2 Esterification with polyethylene anhydride.

However starting from **12** it was impossible for us to continue. We try to hydrolyze imino function using hydrochloric acid to obtain amine hydrochloride (Scheme 3.3).

⁸⁸ H. Myszka, D. Bednarczyk, M. Najder, W. Kaca, *Carbohydrate Research*, **2003**, 338, 133-141.

⁸⁹ P. A. Wender, J. L. Baryza, *Org. Lett.*, **2005**, 7, 1177-1180.



Scheme 3.3 Attempts for deprotecting amino function.

Unfortunately every time we had problems with isolation of product. Explanation can be to big solubility in solvents use for hydrolysis, as already mentioned⁹⁰.

3.2.2 Ligands containing 1- polyethylene arm

Preparation of ligand based on D-glucosamine containing four PEG arms was impossible for us and one for reasons could be spherical effect. We decided to prepare ligand containing only one PEG arm. In our group was already prepared that kind of ligand containing PEG arm in anomeric position (Figure 3.8)⁹⁰.

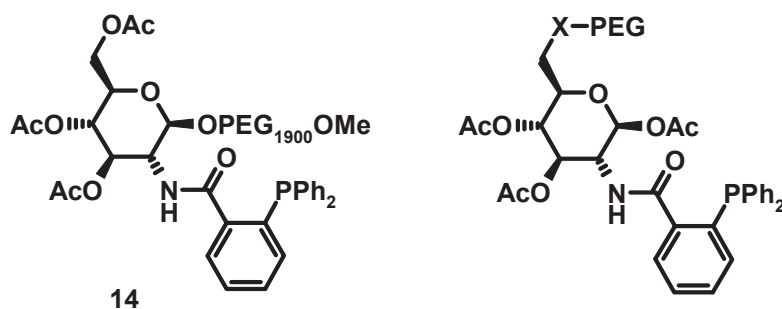


Figure 3.8 Ligands containing 1-polyethylene arm.

That ligand was used in asymmetric allylation type Tsuji-Trost. With different kinds of nucleophiles compound **14** catalyzed reactions with yield up to 98%, unfortunately with not very high enantiomeric excesses. Explanation could be effect of ether function which creates with palladium less stable complexes than ester function. It was known before that in order to obtain high enantiomeric excess it is necessary to have an ester group at the anomeric center in a β -position^{24a}.

⁹⁰ Ouisam Adidou, Claude Bernard University Lyon 1, thesis 2009.

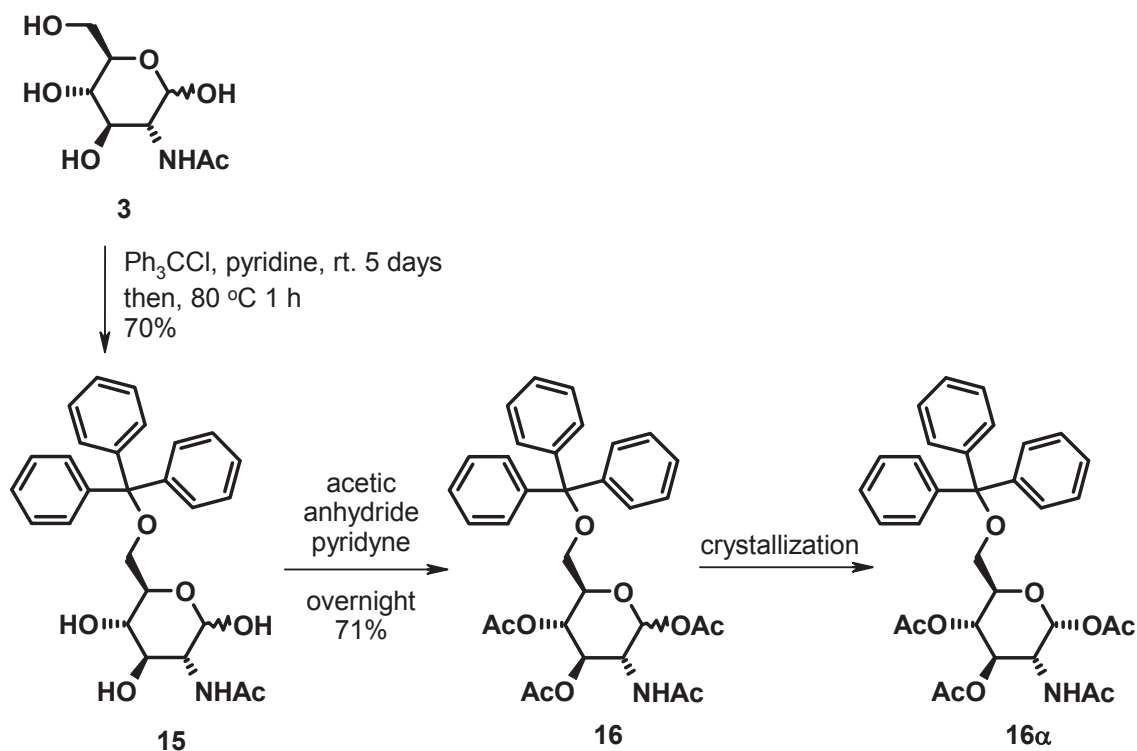
References

Collect that information we decide to prepare hydrosoluble ligand containing one PEG arm in primary carbon in carbohydrate skeleton and with ester function on anomeric carbon in β -position (Figure 3.8).

For establish protocol for synthesis new ligand we decide to use different reagents for protecting primary alcohol.

3.2.2.1 Using trityl protecting group.

Our first choice was to use trityl chloride (Scheme 3.4). Starting from 2-acetamido-2-deoxy-6-D-glucopyranose **3** we obtained 2-acetamido-2-deoxy-6-O-trityl-D-glucopyranose **15** using protocol described by Sharama *et al.*⁹¹ with yield 70%. Acetylation in pyridine overnight gave mixture of α and β anomers with ratio: 85:15 and with yield 71%. Crystallization was prepared as described by Anderson and Percival⁹². Unfortunately from mixture we obtained only α -anomer **16 α** , in opposite to describe by authors postulated β -anomer.



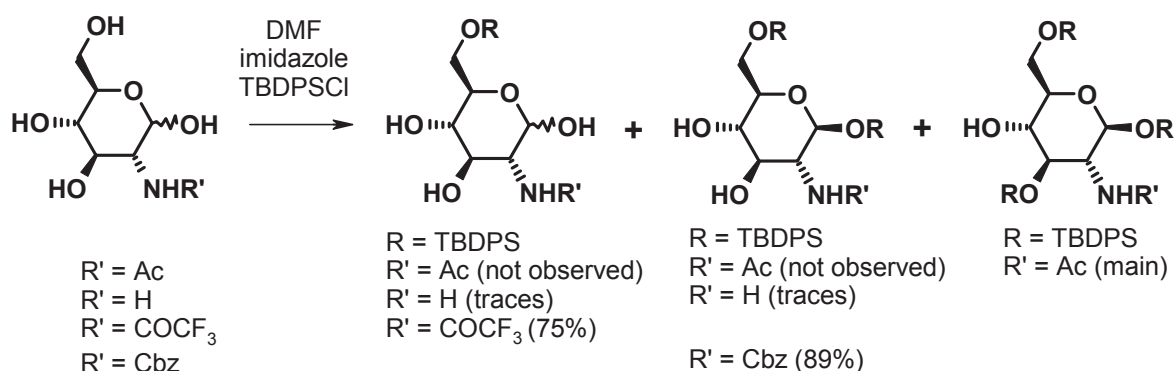
Scheme 3.4 Attempts for employed of trityl group as protection for primary hydroxyl function.

⁹¹ M. Sharama, G. G. Potti, O. D. Simmons, W. Korytnyk, *Carbohydrate Research*, **1987**, 163, 41-51.

⁹² J. M. Anderson; E. Percival, *J. Chem. Soc.*, **1956**, 814-819.

3.2.2.2 Using silyl protecting group.

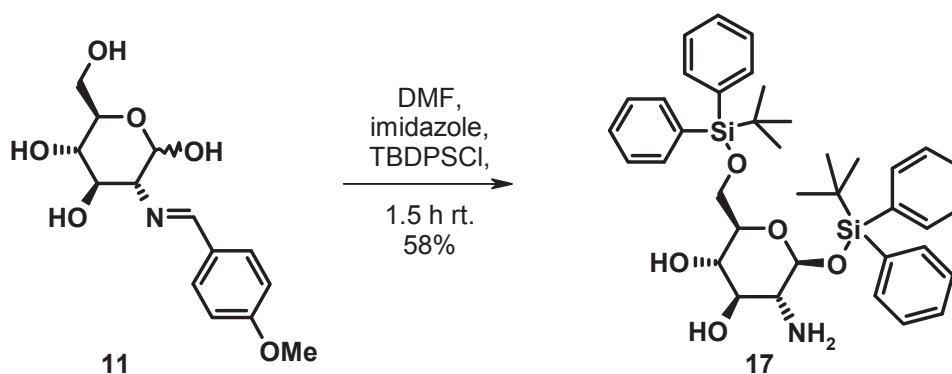
Protection of primary hydroxyl function by silyl compounds in glucosamine scaffold was tested by Sugai *et al.*⁹³ (Scheme 3.5). When *N*-acetyl glucosamine was used as starting material tri-TBDPS ether was the major product of reaction. In case of D-glucosamine authors obtain complex mixture and silylated products were only observed in traces amounts. Introduction of strongly electron withdrawing trifluoroacetyl group on nitrogen atom resulted in obtaining monoprotected compound in 75% of yield.



Scheme 3.5 Effect of silyl protecting group for D-glucosamine derivatives.

Last tested group was less electronwithdrawing Cbz, reaction proceeded with silylation of C-1, C-6 positions with 71% of yield (Scheme 3.5).

In order to prepare β -anomer we decide to use D-glucosamine derivative with nitrogen group protected with sterically demanding *p*-anisylbenzylidene function, which is known in literature that during acetylation direct substituent in β position⁸⁸.



Scheme 3.6 Effect of protection D-glucosamine derivative with silyl group

Standard conditions for preparation of silyl ethers were tested with *tert*-butyl diphenylsilyl chloride as source of silicon, however starting from

⁹³ Y. Nagai, N. Ito, Y. Tokuda, S. Ohba, T. Sugai, *Bull. Chem. Soc. Jpn.*, **2004**, 1181-1186.

References

2-deoxy-2-[*p*-methoxybenzylidene(amino)]-*D*-glucopyranose **11** it was impossible for us to protect selectively six position in carbohydrate ring (Scheme 3.6)⁹⁴.

Base on NMR and MS analysis we observed as a main compound product in which reaction occurred in primary hydroxyl group, but also with hydroxyl group of anomeric carbon in carbohydrate skeleton. Also during reaction nitrogen protecting group was removed, what was probably caused by forming hydrochloric acid.

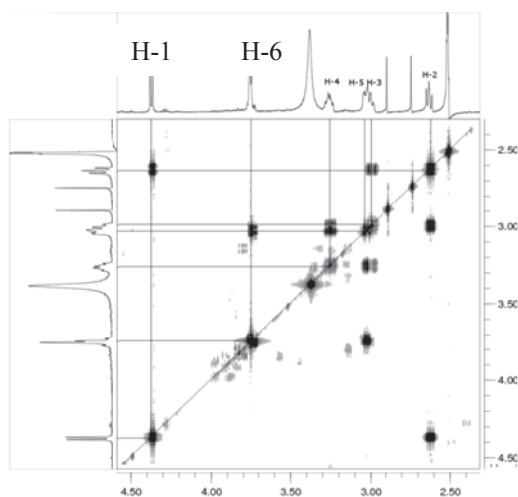


Figure 3.9 COSY ^1H - ^1H (DMSO- d_6) from 2.3 to 4.6 ppm for compound **17**

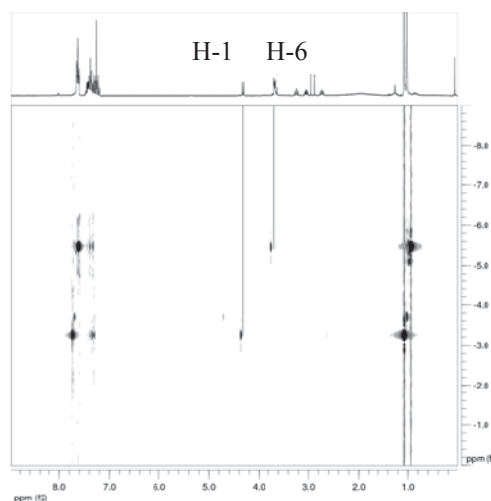


Figure 3.10 HSQC ^1H - ^{29}Si (DMSO- d_6) for compound **17**

3.2.2.3 Using tosyl protecting group.

Other method to protect selectively six position is by introducing in carbohydrate skeleton tosyl function. There is not many examples in literature where tosyl function was introduced into carbohydrate skeleton with free hydroxyl group in anomeric position. In mostly cases *N*-acetyl-*D*-glucosamine was used as starting material⁹⁵, but there is also one example of use *N*-allyloxycarbonyl-*D*-glucosamine^{95a}, and carboxybenzyl protecting group⁹⁶. However in all of those cases product of the reaction in mixture of anomers. Tosyl group was also introduced into carbohydrate using tosylation and *in situ* acylation^{97,98}.

⁹⁴ W. Muramatsu, K. Mishiro, Y. Ueda, T. Furuta, T. Kawabata, *Eur. J. Org. Chem.*, **2010**, 827-831.

⁹⁵ (a) D. Lafont, P. Boullanger, O. Cadas, G. Descotes, *Synthesis*, **1989**, 191-194, (b) R. Thomson, M. von Itzstein, *Carbohydrate Research*, **1995**, 274, 29-44.

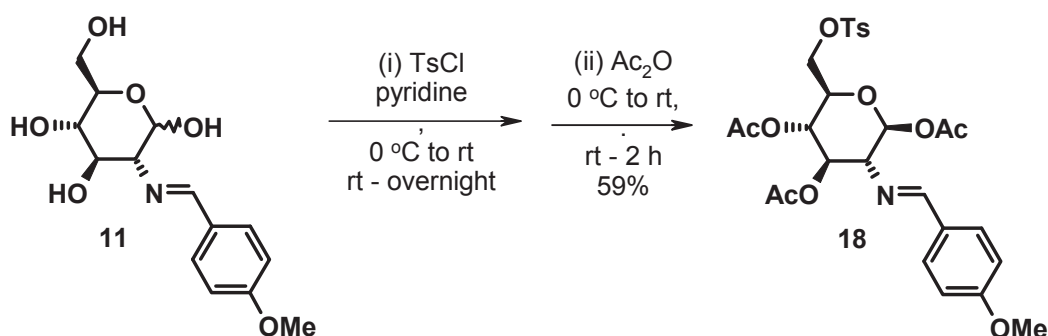
⁹⁶ U. Zehavi, N. Sharon, *J. Org. Chem.*, **1964**, 29, 3654-3658.

⁹⁷ (a) M. Murakami, K. Ikeda, K. Achiwa, *Carbohydrate Research*, **1996**, 280, 101-110, (b) P. R. Sridhar, V. Saravanan, S. Chandrasekaran, *Pure Appl. Chem.*, **2005**, 77, 145-153, (c) S. Buchini, A. Buschiazzi, S. G. Withers, *Angew. Chem. Int. Ed.*, **2008**, 47, 2700-2703, (d) Y. Horita, T. Takii, T. Chiba, R. Kuroishi, Y. Maeda, Y. Kuroono, E. Inagaki, K. Nishimura, Y. Yamamoto, C. Abe, M. Mori, K. Onozaki, *Bioorg. Med. Chem. Lett.*, **2009**, 19, 6313-6316.

⁹⁸ C. J. Morel, *Helv. Chim. Acta*, **1958**, 1501-1503.

When *N*-acetylglucosamine is used as starting material similarly like in previous cases mixture of anomers was obtained, but when sterically demanded group *p*-anisyl was used⁹⁸ only product of reaction was β -anomer.

It was impossible for us to repeat reaction using harsh conditions described by Morel⁹⁸ but changing temperature reaction from -15 to 0 °C allow us to get tosyl protected carbohydrate **18** starting from compound **11** in two steps: by tosylation using tosyl chloride in pyridine in 0 °C and room temperature overnight and following that acylation in 0 °C and two hours in room temperature using acetic anhydride.



Scheme 3.7 Preparation of carbohydrate containing azido function in 6-position

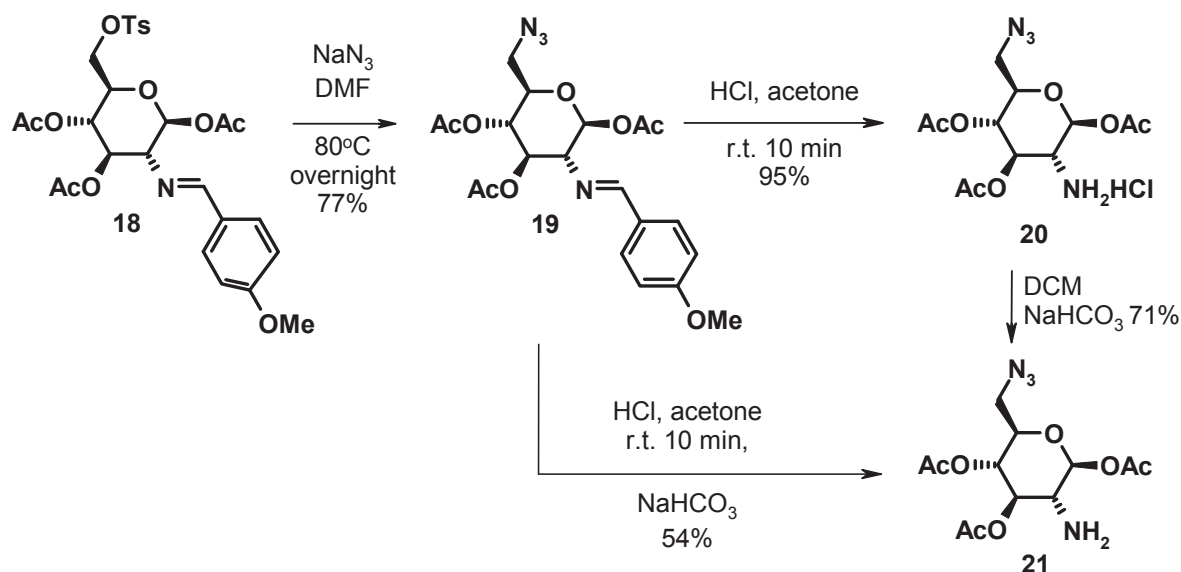
Tosyl compound **18** was obtained with tosyl function exclusively in six position and only β -anomer was observed (Scheme 3.7).

3.2.2.4 Introducing azido function

Our first choice to replace tosyl function was to prepare azido derivative, with can be easily attached to PEG using reaction of “click chemistry”. Substitution with sodium azide in DMF give compound **19** in 77% of yield. (Scheme 3.8)⁹⁹. Hydrolysis with hydrochloric acid in warm acetone allow to obtain compound **20** with 95% of yield and washing it with sodium bicarbonate gave carbohydrate **21** containing amino and azido functions with 71% of yield. It was also possible to obtain **21** directly from **19** without isolation of **20** with 54% of yield, however purification **21** is much more easier when organic residue from protecting *p*-anisyl group is removed during washing insoluble solid **20** with organic solvents. This avoids a long and tedious purification by column chromatography as in the case of direct deprotection of **21** from **19**.

⁹⁹ S. Ogawa, H. Fujimori, T. Suami, *Bull. Chem. Soc. Jpn.*, **1976**, 2585-2586.

References



Scheme 3.8 Preparation of azido carbohydrate **21**

Starting from compound **21** using reaction of “click chemistry” we prepared derivative with polyethylene glycol arm placed in C-6 position. Reaction took part in THF with using catalytic amount of copper iodide and after one hour product was obtained quantitatively (Scheme 3.9).

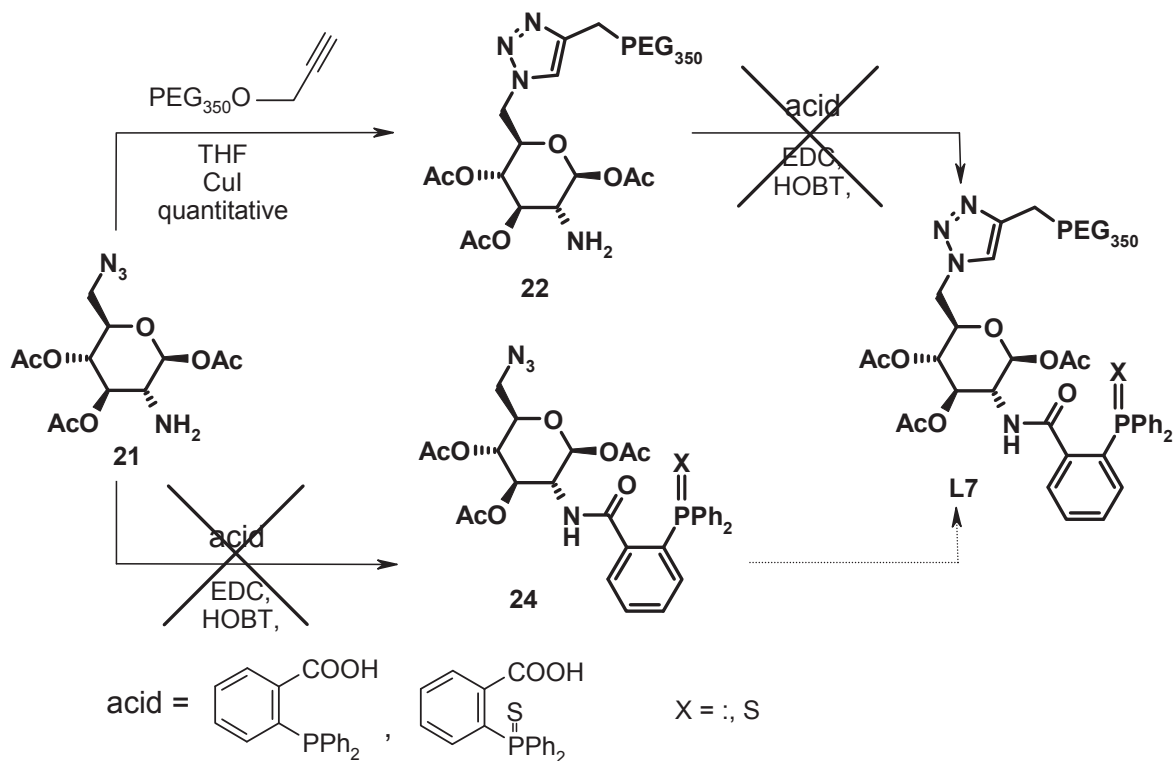
It is known that salts of Cu(I) can catalyze Huisgen 1,3-dipolar cycloaddition¹⁰⁰, however, the iodide and bromide Cu salts require either the presence of amine base or higher temperatures. In our case no addition of base was required, probably amino function present substrate structure played role of base in reaction.

Unfortunately it was impossible for us to couple PEG derivative **21** with 2-diphenylphosphino benzoic acid, no conversion of starting material was observed. We tried to explain failure of reaction by similarity of triazol ring with coupling reagents, however there are examples of creation of amido bonds when in structure of starting material is present triazol ring¹⁰¹. However to our knowledge no example of coupling reaction using EDC, HOBt when starting material containing both triazol ring and phosphorus function is present in literature.

¹⁰⁰ For review of Huisgen 1,3-dipolar cycloaddition see: M. Meldal, C. W. Tornøe, *Chem. Rev.*, **2008**, 108, 2952-3015.

¹⁰¹ (a) T. Wang, J. F. Kadow, Z. Zhang, Z. Yin, N. A. Meanwell, A. Regueiro-Ren, J. Swidorski, Y. Han, D. J. Carini, US 20070249579, **2007**. (b) K. Thede, I. Flamme, F. Oehme, J.-K. Ergueden, F. Stoll, J. Schhmacher, H. Wild, P. Kolkhof, H. Beck, J. Keldenich, M. Akaba, M. Jeske, WO2008067871, **2008**, (c) F. Stieber, O. Schadt, D. Dorsch, A. Blaukat, WO 2008145243, (d) T. Wang, J. F. Kadow, Z. Zhang, Z. Yin, N. A. Meanwell, A. Regueiro-Ren, J. Swidorski, Y. Han, D. J. Carini, L. Hamann, US 20080139572, **2008**, (e) I. Akritopoulou-Zanze, B. D. Wakefield, H. Mack, S. C. Turner, A. F. Gasielki, V. J. Gracias, K. Sarris, D. M. Kalvin, M. J. Michmerhuizen, Q. Shuai, J. R. Patel, M. Bakker, N. Teusch, E. T. Johnson, P. Kovar, S. W. Djuric, A. J. Long, A. Vasudevan, A. Hobson, N. St John Moore, L. Wang, D. George, B. Li, K. Frank, WO 2008154241 (f) R. Mueller, L. J. Street, S. Rachwal, K. Alisala, Kashinatham, WO 2009038752, **2009**.

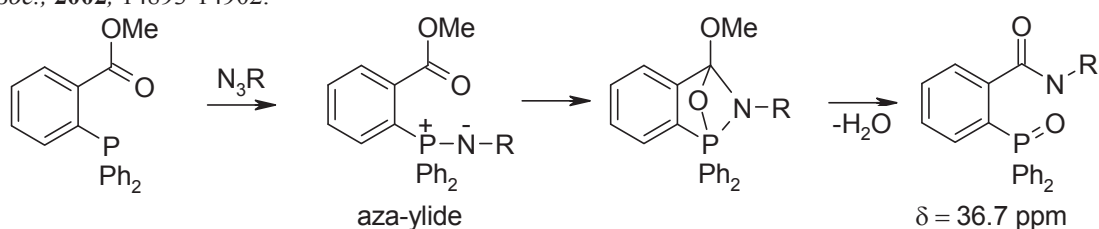
Other way to prepare ligand **L7** is to prepare first amide compound **24** and after “click” it with PEG containing propargyl function but also in this case coupling was unsuccessful in our hands (Scheme 3.9). Using mixture EDC, HOBT as coupling reagents, five different signals from phosphorus atoms were observed on spectrum ($\delta = 30.1$ to 35.8 ppm), changing reagents for DCC, DMAP, we obtained complex mixture, using ^{31}P NMR as analysis method we were able to observe nine different signals from phosphorus atoms with similar shifts ($\delta = 31.0$ to 35.7 ppm).



Scheme 3.9 Preparation of Ligand **L7** containing PEG function

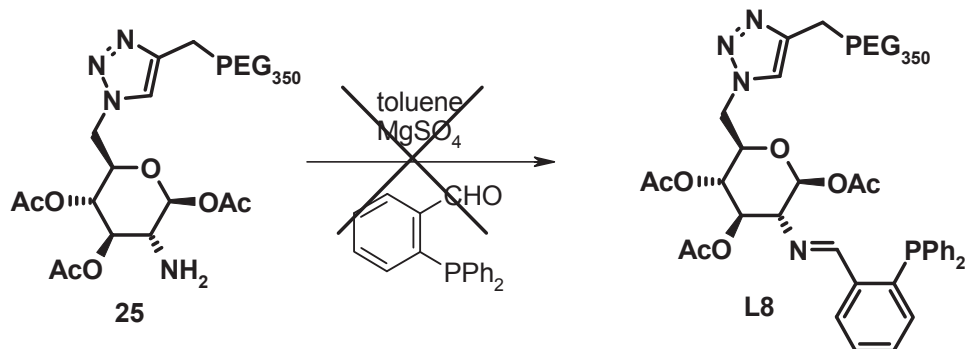
Probably reaction of phosphorus atom with azido group occurring in first place to give aza-ylide, and presence complex reaction mixture can be explained by interactions of situated in *ortho* position carboxylic function. Products of reaction had not been examined¹⁰². To avoid interaction of phosphorus with azido function, 2-diphenylphosphino benzoic acid was protected with sulfur, unfortunately also in this

¹⁰² Possible pathway of Strodinger ligation with methyl ester of 2-(diphenylphosphino)benzoic acid was proposed before: E. Saxon, S. J. Luchansky, H. C. Hang, C. Yu, S. C. Lee, C. R. Bertozzi, *J. Am. Chem. Soc.*, **2002**, 14893-14902.



References

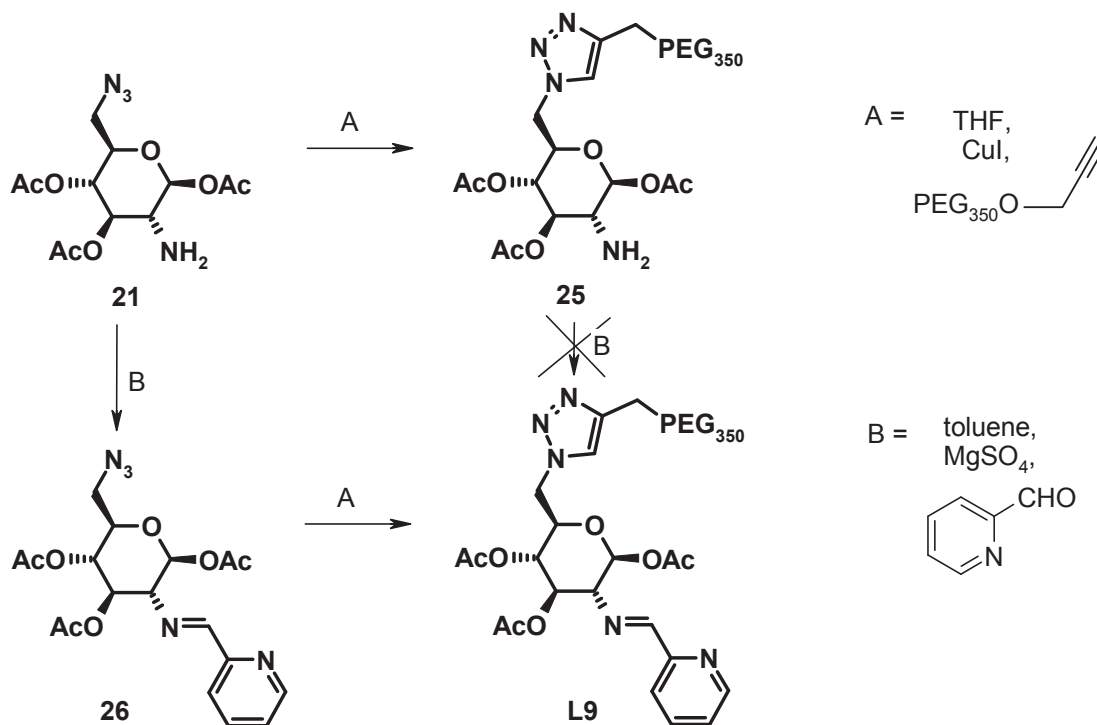
case the main product of reaction was compound with shift characteristic for aza-ylide ($\delta = 34.9$ ppm), which after column chromatography decomposed to its oxide ($\delta = 37$ ppm). We decide to prepare analogous compound containing instead of amido bond imino function. In this case reaction also did not occurred (Scheme 3.10).



Scheme 3.10

Because it was possible for us to prepare before imino function containing phosphorus group and triazol ring (Subchapter 3.3.3.4, Scheme 3.19) we have suspected that maybe cause of not working of reaction was presence of water in polyethylene arm. Unfortunately even liofilisation of starting material before reaction did not leaded reaction to work.

Reaction do not work also with aldehyde without phosphorus function. When pyridine aldehyde was used in reaction only starting materials were observed even after 4 days of reaction (Scheme 3.11).



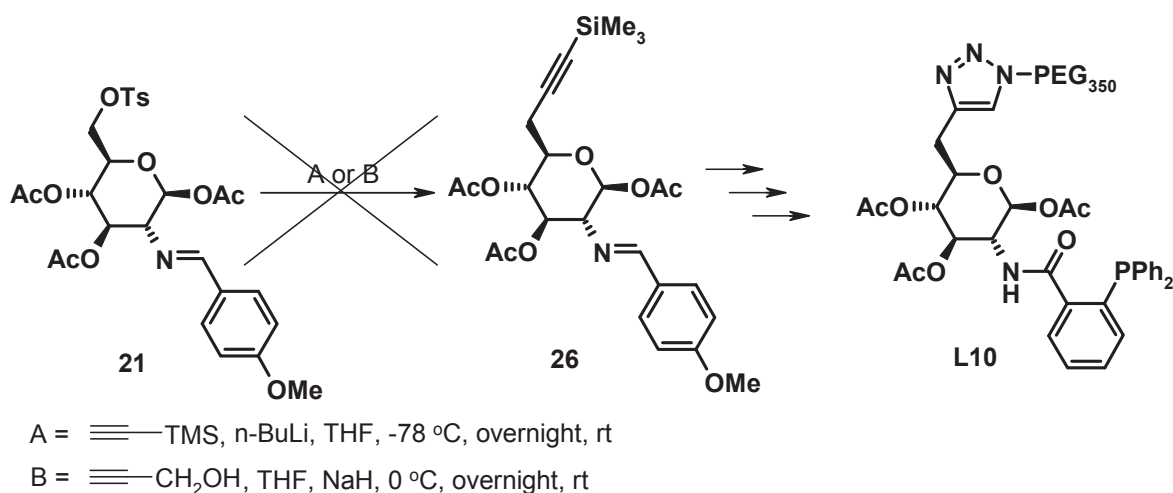
Scheme 3.11 Preparation of ligand L9

Other possible way was first to prepare imino derivative **26** and after make reaction of cycloaddition. Condensation of **21** with pyridine aldehyde proceed quantitatively. In future we plan to prepare ligand **L9** and test it in catalytic reactions of allylic alkylation in water.

3.2.2.5 Introducing alkynyl function

Other way to graft ligands on hydrosoluble matrix by using azide-alkyne Huisgen cycloaddition is by introducing alkynyl function in carbohydrate skeleton.

In literature there is not report mentioned transformation of tosyl carbohydrate into alkynyl compound. However we decided to try replace good leaving group: tosyl with alkynyl chain using standard conditions.



Scheme 3.12

Two different bases were tested, in both cases using one equivalent of base for one tosyl function caused appearing small amount of compound in Thin Layer Chromatography confirmed presence of compound in NMR spectra, however increasing time of reaction or increasing amount of base to three equivalents caused with degradation of carbohydrate starting material. We expected that cause of this could be not very stable protection function of nitrogen atom, surprisingly using acetyl as very stable protecting group did not lead to increasing conversion of product. Similarly like in case of *p*-anisyl protecting group using one equivalent of base give small conversion of product, using three equivalents of base causes with degradation of starting material. We think the reasons for failure is in the nature of the sugar. Because of small amounts products were not isolated.

3.3 Silica immobilized ligands

This subchapter deals with a stepwise synthesis of two unsymmetrical silica supported D-glucosamine based phosphorus containing ligands.

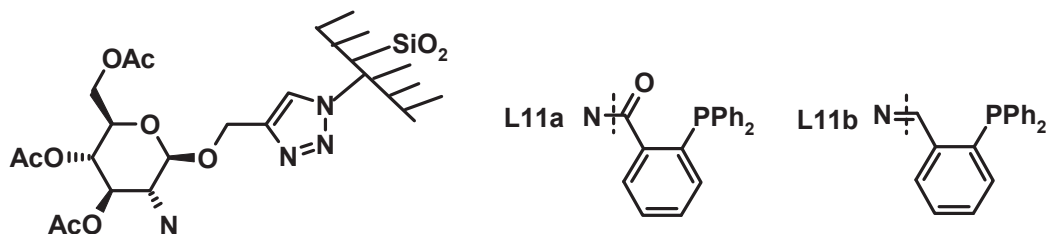


Figure 3.11 Structure of ligands supported on silica.

We decided to prepare two types of ligands. Ligands **L11** connected with silica by anomeric position, with two different kind of linkers with phosphorus function: amido linker for ligand **L11a** and imino linker for ligand **L11b** (Figure 3.11).

Project was made in collaboration with Doctor Chloe Thieuleux and Doctor Reine Sayah from LCOMS team of University Lyon 1, who provided mesoporous silica materials (SBA-15) and carried out analysis of supported products.

3.3.1 Silica materials

Among provided materials containing azido function were silica SBA-15 with free hydroxyl groups on surface (Figure 3.12a), and passivated silica SBA-15 with trimethylsilyl groups (Figure 3.12b).

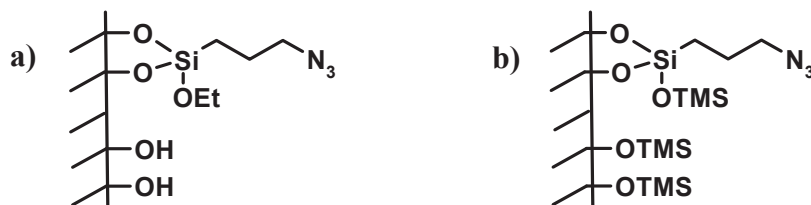


Figure 3.12 Silica materials.

Materials were analyzed using IR technique (Figure 3.13). In both spectra there are signals with high intensity in area from 500 to 1400 cm^{-1} corresponding to stretching and deformation vibrations of Si-O-Si groups, and also sharp signal around 2150 cm^{-1} corresponding to azido function.

Comparing spectra of both of them we observed disappearance of broad signal in area from 3000 to 3800 cm^{-1} and sharp signal around 1630 cm^{-1} which are assigned, respectively, to the stretching and deformation vibrations of adsorbed water molecules¹⁰³.

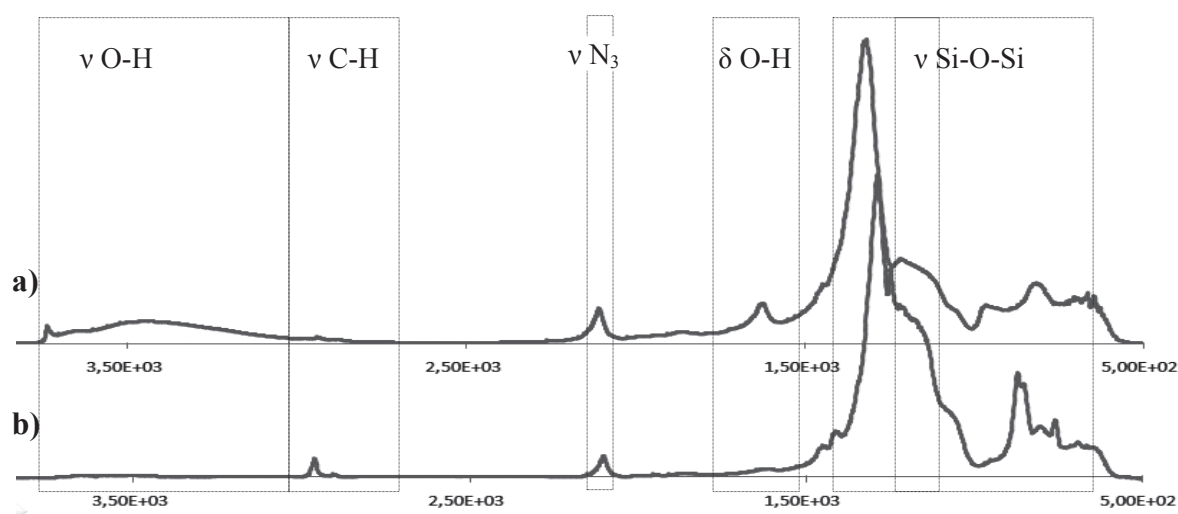


Figure 3.13 IR spectra from 700 to 3800 cm^{-1} of azido functionalized silica a) SBA-15, b) passivated SBA-15.

In Figure 3.14, isotherm of adsorption and desorption of nitrogen for both SBA-15 materials is presented. Shape of isotherm is typical for mesoporous materials. The upper plateau correspond to maximum volume of adsorbed nitrogen and determine surface area, which is 1226 m^2/g and 583 m^2/g for SBA-15 and passivated SBA-15 respectively. Surface area after protection of hydroxyl groups with TMS decreased what is caused by hindered effect of protecting groups.

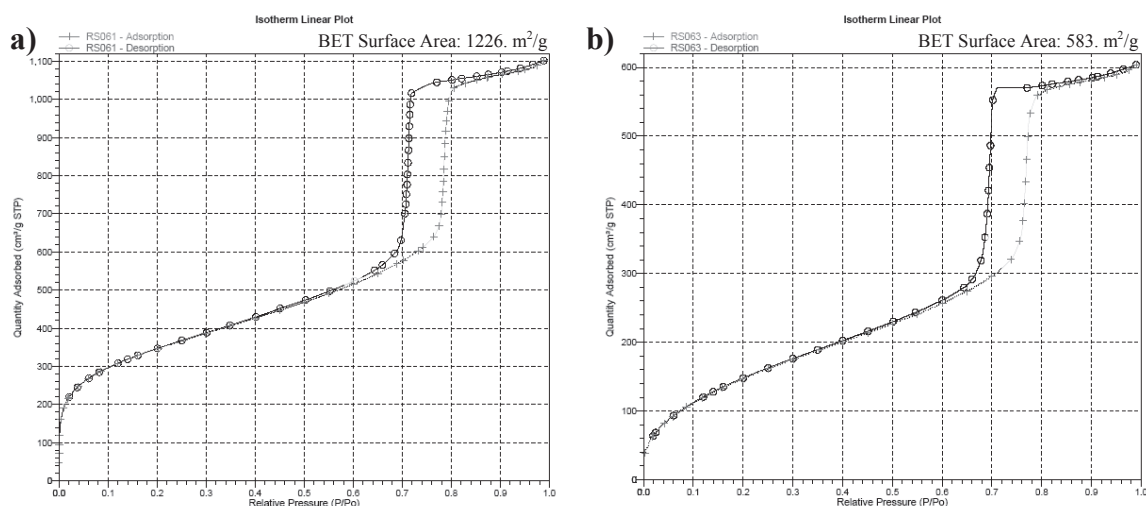


Figure 3.14 BET analysis for a) SBA-15: BET Surface Area (1226.7584 m^2/g), b) passivated SBA-15: BET Surface Area (583 m^2/g),

¹⁰³ G. D. Chukin, V. I. Malevich, *Appl. Spectrosc.*, **1977**, 26, 223-229.

References

Moreover it is possible to calculate size of the pores. Figure 3.15 presenting distribution of pores diameters for adsorption and desorption of nitrogen, where maximum of Gaussian curve determine value of pores diameters.

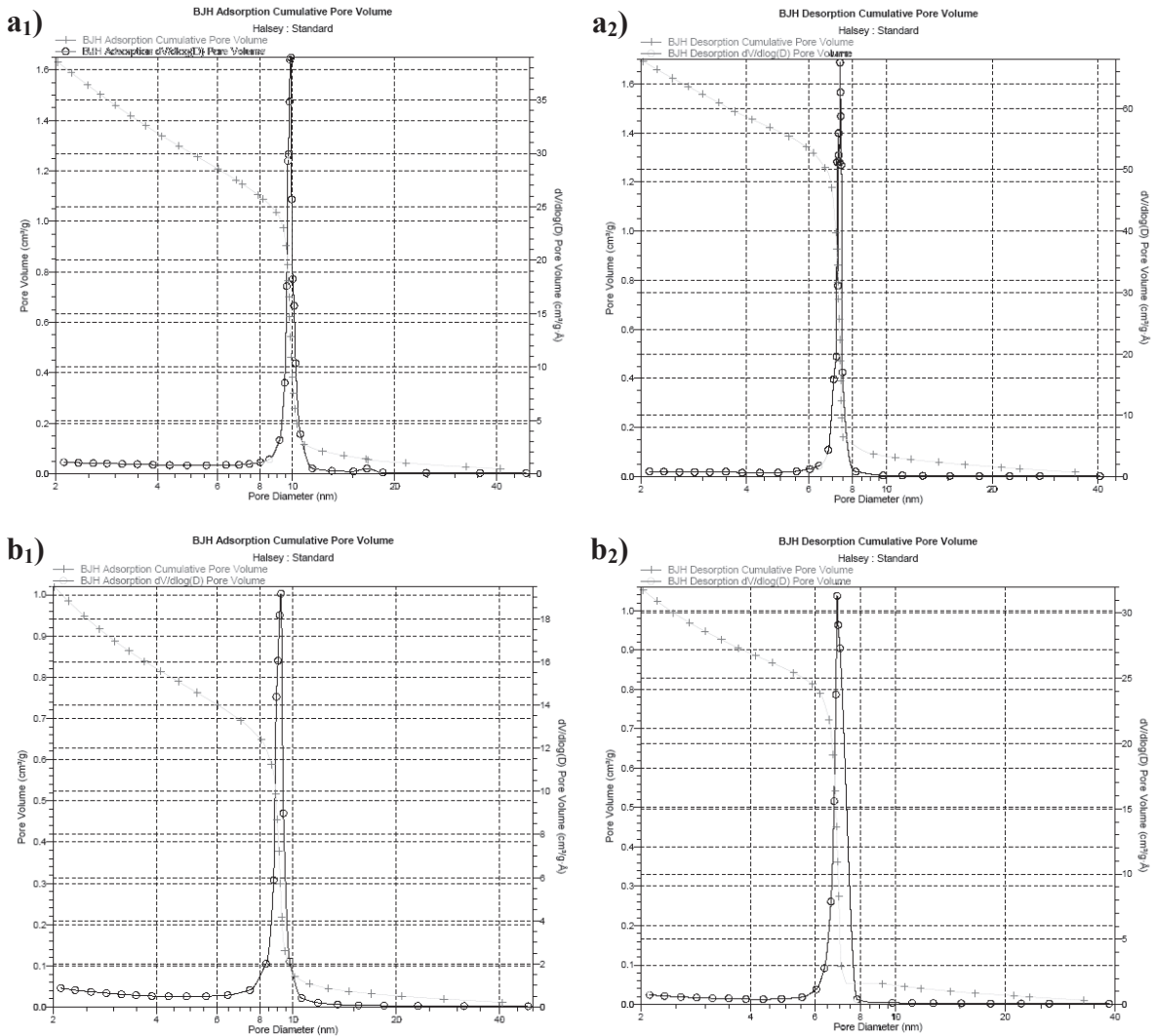


Figure 3.15 BET analysis: Pore Diameter for a) SBA-15 b) passivated SBA-15.

In Table 3.4 are featured values of pores determined from isotherms of adsorption and desorption of nitrogen.

	Adsorption (Å)	Desorption (Å)
SBA-15	99	71
Passivated SBA-15	94	68

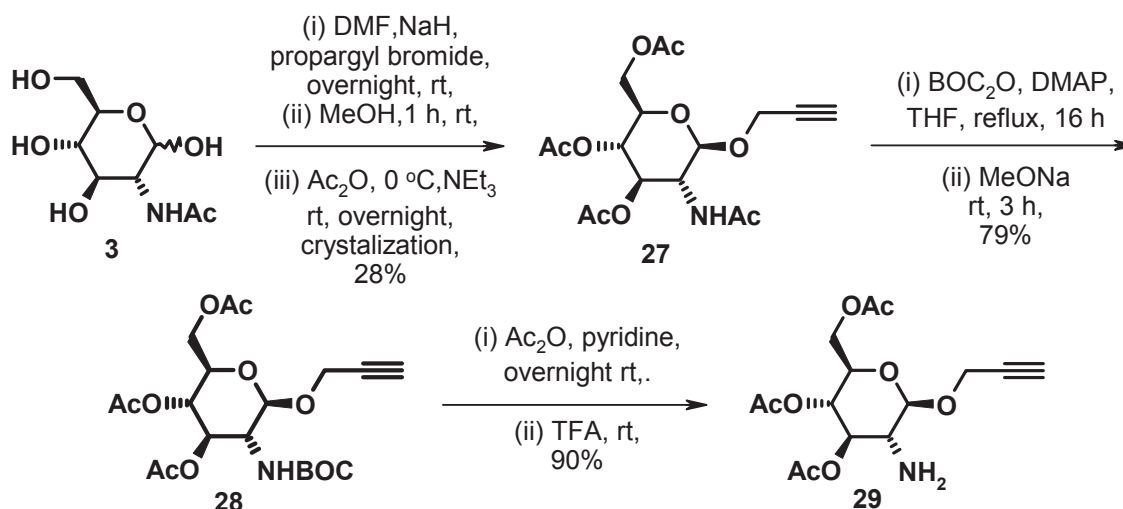
Table 3.4 Values of pore size for SBA-15 and passivated SBA-15 determined from isotherms of adsorption and desorption of nitrogen.

Similarly like in case of surface area in case of pore volume decreasing of size is observed caused by hindered effect of TMS groups.

3.3.2 Synthesis of carbohydrate with alkynyl function in β -anomeric position

Starting from *N*-acetyl-D-glucosamine **3** using procedure described by Brimble *et al.*¹⁰⁴ glucosylation with propargyl bromide was made and followed it acetylation of free hydroxyl functions (Scheme 3.13).

Carbohydrate **27** was obtained after crystallization as exclusively β -anomer in 28% of yield while authors claimed that only product of reaction was α -anomer. High coupling constant of H-1 ($\delta = 8.4\text{Hz}$) and opposite sign of specific rotation ($[\alpha]_D$) led us declare that in our case obtained anomer was different than postulated.



Scheme 3.13 Synthesis of carbohydrate **28** containing alkynyl function in β -anomeric position.

To deprotect acetyl from amino function procedure described by Lafont⁵⁶ was used and compound **29** was obtained with 65% of yield after two steps (Scheme 3.13).

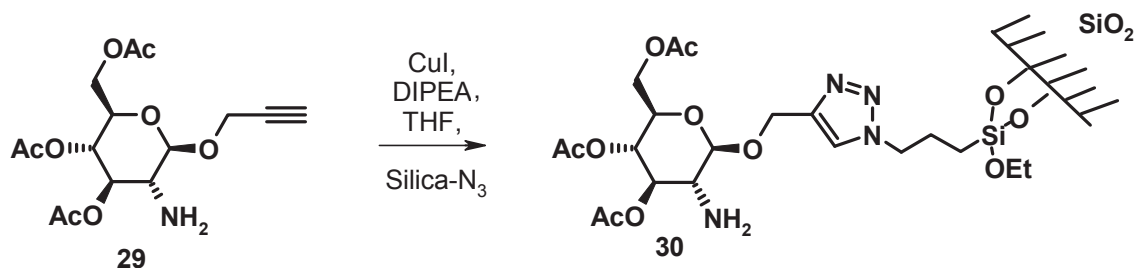
3.3.3 Immobilization of silica with carbohydrate *via* anomeric position

3.3.3.1 Amido type ligand

Compound **29** was immobilized on surface of porous of silica SBA-15 functionalized with azido functions, using so-called “click reaction” of the Huisgen [3+2]-cycloaddition between terminal alkyne and azide (Scheme 3.14). Because of its high efficiency, simple procedure, absence of side products and mild reaction conditions, this reaction attracted attention for catalyst immobilization¹⁰⁵.

¹⁰⁴ N. Miller, G. M. Williams, M. A. Brimble, *Org. Lett.*, **2009**, 11, 2409-2412.

¹⁰⁵ For selected examples, see: (a) A. Gissibl, M. G. Finn, O. Reiser, *Org. Lett.*, **2005**, 7, 2325-2328, (b) A. Gheorghe, A. Matsuno, O. Reiser, *Adv. Synth. Catal.*, **2006**, 348, 1016-1020, (c) S. L. Jain, A. Modak, A.



Scheme 3.14 Preparation of ligand L11a

Reaction was followed by IR study, till disappearance of characteristic signal from azido function of starting material. which, can be identified by the strong $\text{N}\equiv\text{N}$ asymmetric stretching absorption which occurs with great consistency close to 2130 cm^{-1} (Figure 3.16b,c). On IR spectra of product we can also observe signals characteristic for absorption of $\text{C}=\text{O}$ bond close to 1740 cm^{-1} coming from acetyl groups of carbohydrate skeleton (Figure 3.16c).

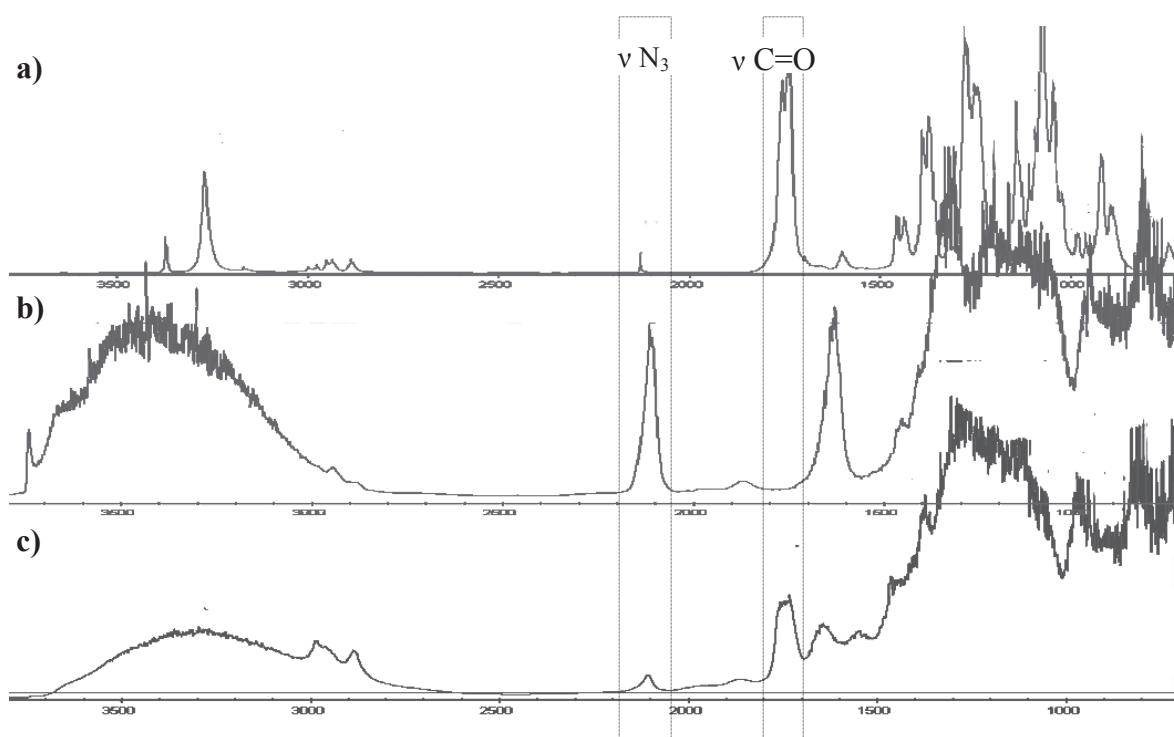
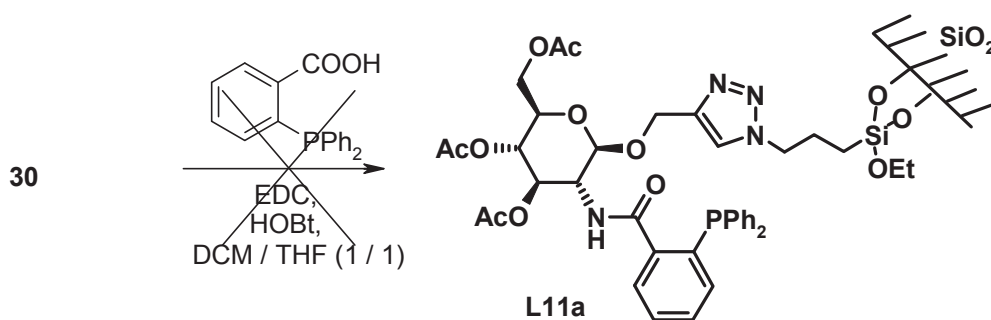


Figure 3.16 DRIFT IR spectra from 700 to 3800 cm^{-1} of a) compound **28**, b) silica containing azido function c) product **29**.

In next step coupling with 2-diphenylphosphino acid was performed using EDC and HOBt as coupling reagents (Scheme 3.15).



Scheme 3.15 Coupling reaction

Two different materials SBA-15 and passivated SBA-15 were used for reaction. In both cases in solid ^{31}P NMR (Figure 3.17) we can observe large signal close to $\delta = 35$ ppm which probably correspond to product of oxidation of phosphorus¹⁰⁶. Additionally when SBA-15 was used as a material smaller peak around $\delta = 18$ ppm is observed. For second case SBA-15 passivated when silanoxo groups in silica surface were protected with TMS groups broad signal from $\delta = -30$ to 20 ppm is present in phosphorus spectrum (Figure 3.17).

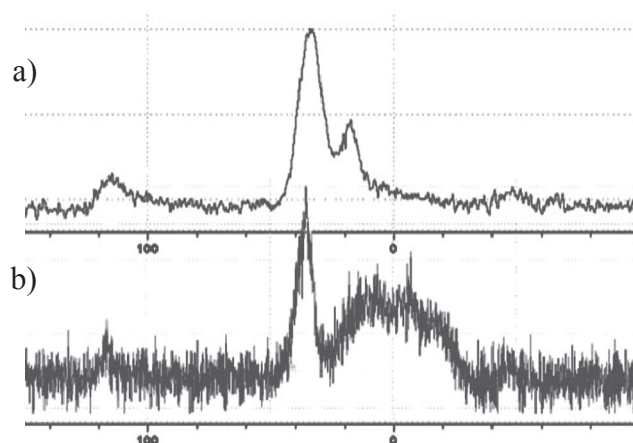


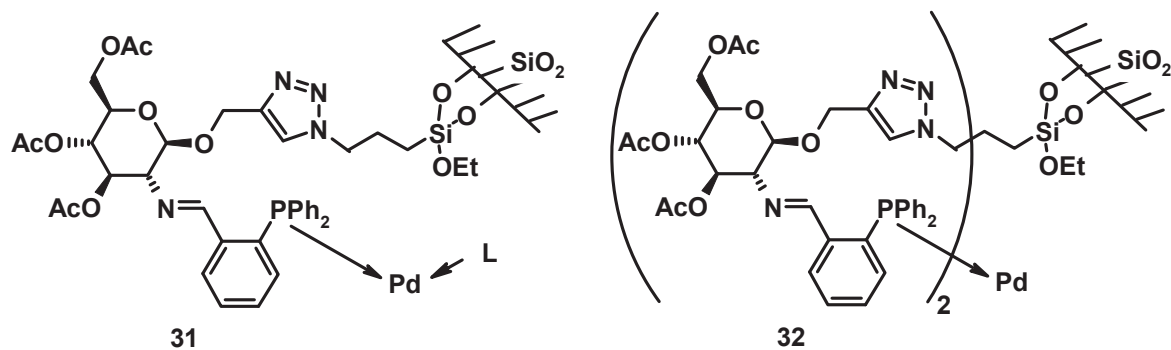
Figure 3.17 MAS ^{31}P NMR from -100 to 150 ppm for reaction of **29** with 2-diphenylphosphino benzoic acid, a) without protection of surface b) with protected surface

Despite of that solvents were distilled and degassed before use and reactions were carried out under argon atmosphere it was impossible for us to avoid oxidation process, even when surface of silica was protected, probably because of the high affinity of the trivalent phosphorus to oxygen from silica material.

¹⁰⁶ In literature for o-diphenylphosphonylbenzoic acid $\delta = 28$ ppm (in DMF) see: N. A. Bondarenko, E. N. Tsvetkov, E. I. Matrosov, M. I. Kabachnik, *Russian Chemical Bulletin*, **1981**, 30, 1289-1293.

3.3.3.2 Imino type ligand

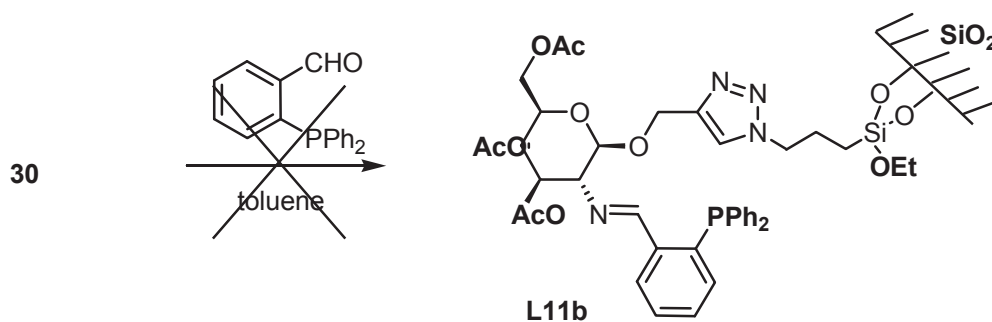
In previous study made by our team different types of complexation were investigated for carbohydrate based imino type ligands in homogeneous catalysis (Chapter 1, Figure 1.14 and Scheme 1.7). Also in this case we decide to prepare two type of complexes where palladium with phosphorus will be in ratio 1 / 1 (complex **31**) and when palladium with phosphorus will be in ratio 1 / 2 (complex **32**) (Scheme 3.16).



Scheme 3.16 Imino type ligand with two different types of complexation.

3.3.3.3 Complex L-Pd (1 / 1)

Previously prepared compound **30** was condensed with 2-diphenylphosphino benzaldehyde in toluene as solvent.



Scheme 3.17 Condensation reaction.

MAS ^{31}P NMR spectra show that main product of coupling was oxide ($\delta = 28.7$) of ligand **L11b** (Figure 3.18).

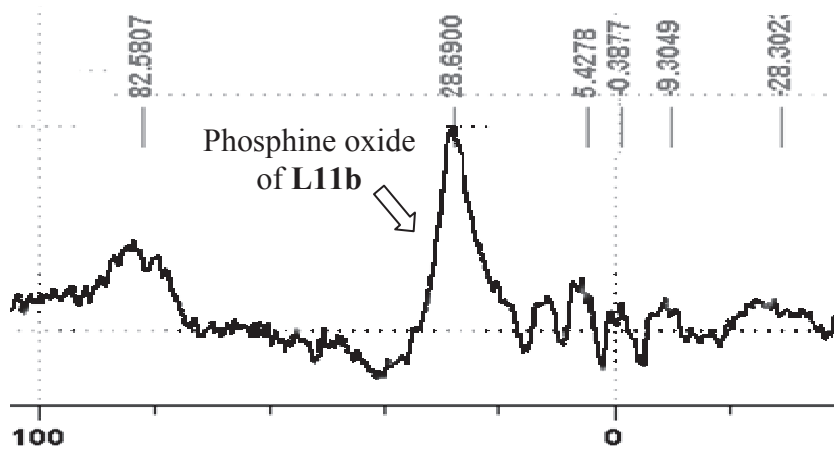
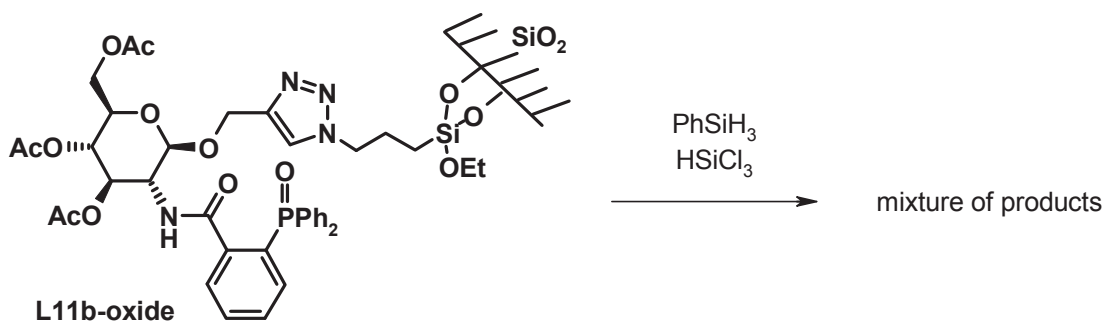


Figure 3.18 MAS ^{31}P NMR spectra from -40 to 100 ppm for grafted ligand **L11b**.

In order to remove oxygen from phosphorus atom reduction of oxide of ligand **L11b** was made using trichlorosilane as reducing agent in phenylsilane as solvent (Scheme 3.18).



Scheme 3.18 Reduction of **32**.

Unfortunately product was reduced only partially ($\delta = -17.7$), and in spectra were present also other compounds (Figure 3.19).

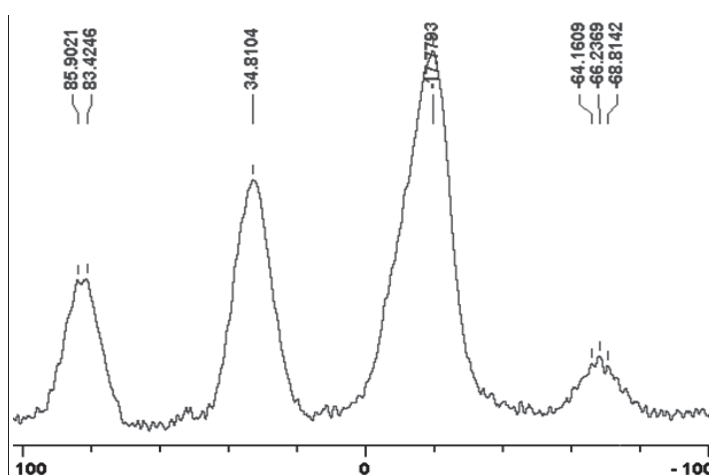
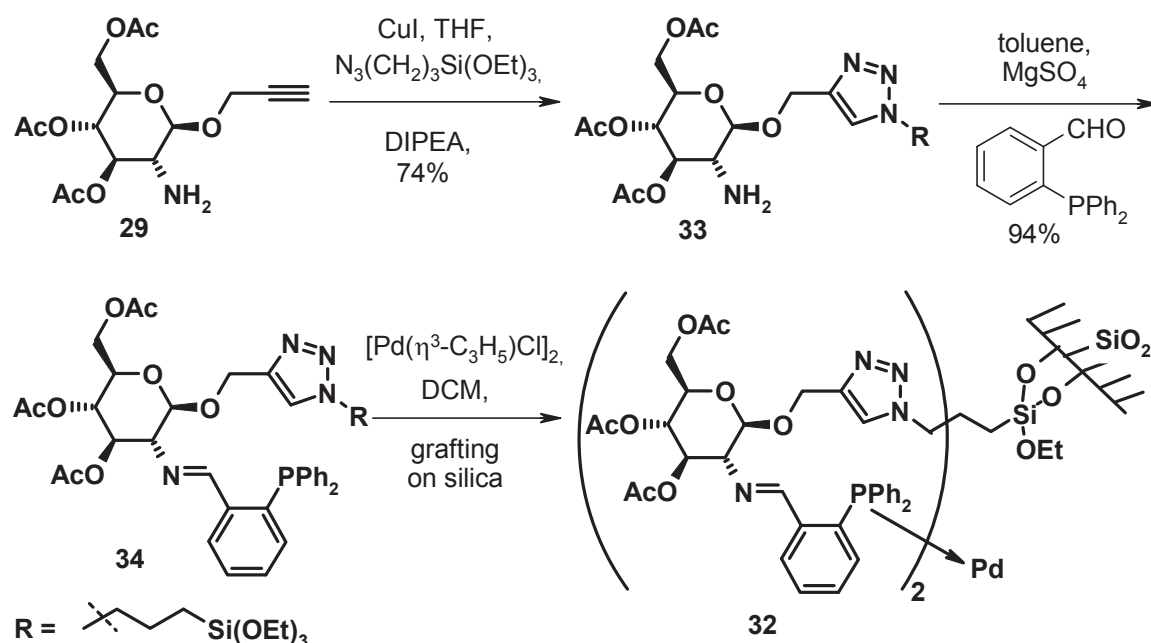


Figure 3.19 MAS ^{31}P NMR spectra from -100 to 100 ppm after reduction of phosphine oxide of ligand **L11b**.

It was impossible for us to obtain ligand **L11b** without oxidation of phosphorus atom.

3.3.3.4 Complex L-Pd (2 / 1)

It was shown before that the best results in catalysis were obtained when one palladium was complexed with two phosphorus atoms (Chapter 1, Figure 1.14 and Scheme 1.7). For this reason we decided to prepare palladium complex and after graft it into structure of silica matrix in order to obtain complex **32**. Direct grafting on silica matrix and after complexation does not guarantee that two phosphorus atoms will be connected with one palladium atom.

Scheme 3.19 Synthesis of palladium complex **32**.

Compound **33** was prepared using reaction of “click chemistry” between **29** and 3-azidopropyltriethoxysilane¹⁰⁷ with 74% of yield after purification, followed that condensation with 2-(diphenylphosphino)benzaldehyde yielded compound **33** (Scheme 3.19).

Next step complexation with allylpalladium chloride dimer was difficult for us to carry out. Each time when reaction was made small traces of oxidation occurred (Figure 3.20).

¹⁰⁷ M. Ortega-Muñoz, J. Lopez-Jaramillo, F. Hernandez-Mateo, F. Santoyo-Gonzalez, *Adv. Synth. Catal.*, **2006**, 348, 2410-2420.

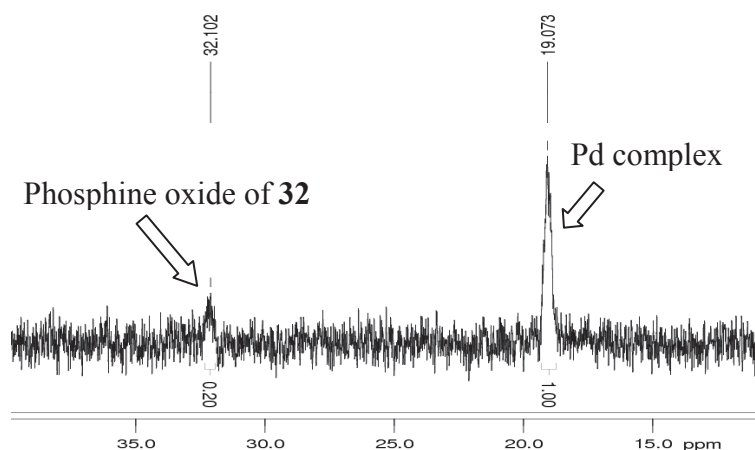


Figure 3.20 ^{31}P NMR spectra from 10 to 40 ppm after reaction of complexation.,

However we decide to continue on partially oxidized material, and compound was grafted on passivated SBA-15.

To investigate the products of the solid state reactions DRIFT IR spectroscopy and MAS ^{31}P NMR were used. Presence of imino bond was confirmed by appearance in IR spectra signal in area $1615\text{-}1715\text{ cm}^{-1}$ characteristic for this bond (Figure 3.21a). Unfortunately on MAS ^{31}P NMR spectra main product was compound with shift $\delta = 41.2$ instead of expected compound with $\delta = 19.1$ (Figure 3.21b).

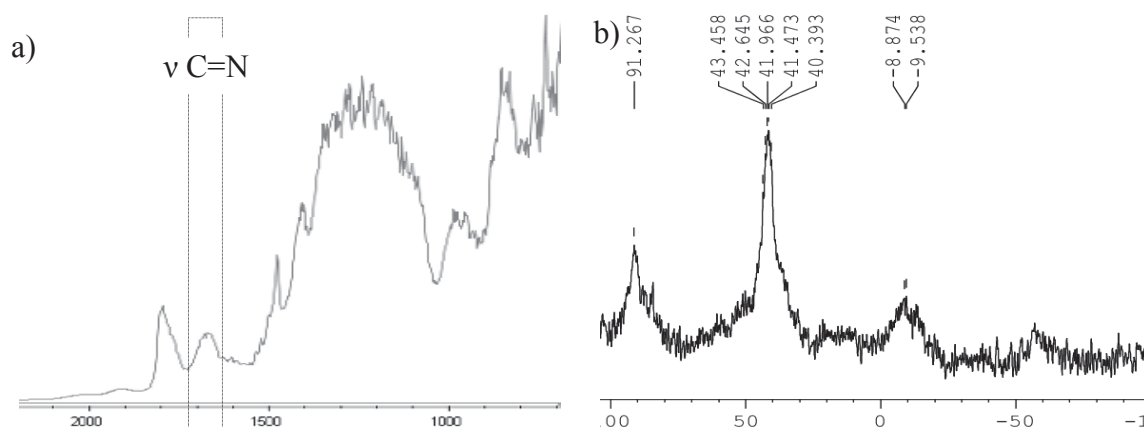


Figure 3.21 a) Drift IR spectra from 800 to 2200 cm^{-1} of complex after grafting of complex **31**,
b) MAS ^{31}P NMR spectra from -40 to 100 ppm after grafting of complex **31**.

Because of difficulties in preparation silica grafted ligands caused by oxidation of phosphorus atom we decide to stop project.

Conclusions

An important task of today's chemistry is to design new products prepared from renewable starting materials and produced using green processes. This chapter we can find many reactions that follow these concepts.

Using Supported Aqueous Phase Catalyst system D-glucosamine based catalyst was prepared and immobilized on silica matrix without the use of tedious protecting and deprotecting steps that allows time-, money- and atom-economies. First time SAPC system was applied to Suzuki coupling reactions. Its efficiency was demonstrated in catalytic reactions with various of substrates, moreover catalyst can be easily isolated and reused four times without loss of activity. And to compare with the coupling reaction perform from the same Pd complex in a mixture of Toluene/Ethanol/Water as solvent, we observed in some cases a positive effect of silica support.

Attempt to obtain D-glucosamine ligand containing 4-polyethylene arms was made and in order to protect selectively primary hydroxide function in D-glucosamine skeleton different reagents were tested. Works on preparation ligands containing polyethylene glycol arm catalysts are ongoing.

Immobilization of unsymmetrical silica supported D-glucosamine based phosphorus containing ligands. on the silica surface was studied. For this purpose reaction of "click chemistry" known from its high efficiency, simple procedure, absence of side products and mild reaction conditions was used.

Unfortunately, because of the high oxygen affinity of the trivalent phosphorus it was impossible to succeed in the synthesis of amido and imino types ligands supported in silica matrix.

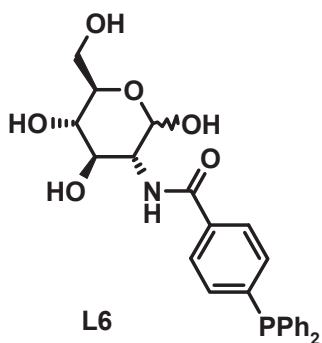
Experimental part

Solvents were purified and dried by standard methods. The reagents were purchased from commercial suppliers and used without further purification. All manipulations involving palladium catalyst were performed under usual inert atmosphere techniques in Schlenk tube. Conversion was determined by GC using Shimadzu GC-14B apparatus with flame ionization detector (FID) and integrator Shimadzu C-R6A. the capillary column Quadrex OV1 (30cm x 0.25mm) was used and helium as a carried gas. The temperature of detector and the cell of injector was 250 °C. The inject volume was 1 μ L.

3.4 Experiments dealing with SAPC system.

Synthesis of 2-Deoxy-2- $\{[4-(\text{diphenylphosphino})\text{benzoyl}]\text{amino}\}$ -D-glucopyranose **L6**^{25a}

In Schlenk tube 4-diphenylphosphino benzoic acid (500.0 mg, 1.63 mmol, 0.5 equiv), EDC (375.5 mg, 1.96 mmol, 0.6 equiv), and HOBT (264.6 mg, 1.96 mmol, 0.6 equiv), were dissolved in degassed DMF (13 mL). In second Schlenk tube D-glucosamine (704.2 mg, 3.27 mmol, 1.0 equiv), and NaHCO₃ (658.8 mg, 7.84 mmol, 2.4 equiv), were stirred in water (6.5 mL) in 0 °C during 1 hour, and after this time transferred using canula to the first Schlenk. Solutions were stirred 20 hours in room temperature. Solvents were evaporated on vacuum pump and crude was purified using flash chromatography under argon atmosphere using chloroform : ethanol 3 : 1 as eluent.



- Yield 80%
- White solid
- R_f = 0.63 (chloroform : ethanol 3:1)
- m.p. 119-124 °C , lit.^{25a} 120-124 °C

- ¹H NMR (C₅D₅N): δ (ppm) = 4.02 (m, 0.25H, H-5 β) 4.24 (dd, 0.25H, J=8.7, J=9.3, H-4 β) 4.32 (dd, 0.75H, J=8.8, J=9.8Hz, H-4 α) 4.41 (dd, 1H, J=5.6, J=11.6Hz, H-6' α) 4.56 (dd, 0.75H, J=2.5, J=11.6Hz, H-6 α) 4.76-4.87 (m, 1.5H, H-3 α /H-5 α) 5.12 (ddd, 0.75H, J=3.4, J=8.5, J=11.8Hz, H-2 α) 5.59 (d, 0.25H, J=8.4Hz, H-1 β) 6.09

(d, 0.75H, J=3.4Hz, H-1 α) 7.23-7.45 (m, 14H, H_{arom}) 9.03 (d, 0.75H, J=8.5Hz, NH) 9.45 (d, 0.25H, J=8.8Hz, NH) according to the literature^{25a}.

- ³¹P NMR (C₅D₅N): δ (ppm) = -4.4

Preparation of SAPC

Silica (500.0 mg) was dried under vacuum for 4 hours at 150°C. In another Schlenk tube, Pd(OAc)₂ (1.1 mg, 5.0 μ mol), D-glucosamine based phosphine (6.6 mg, 15.0 μ mol), ethanol (2 mL), water (1 mL) were added. The mixture was stirred for 1 hour at room temperature, and then using canula, was transferred to silica. After stirring for 2 hours at room temperature, solvents were evacuated under vacuum and the solid was dried under vacuum for 16 hours at room temperature, and then kept under Argon atmosphere prior to be used

General procedure for the Suzuki-Miyaura reaction with 1% molar of Pd catalyst

Case of 1.0% molar of Pd: Na₂CO₃ (156.0 mg, 1.5 mmol), aryl bromide (0.5 mmol) and arylboronic acid (0.55 mmol) were placed in the Schlenk tube containing the SAPC prepared as described above. After to add ethanol (1 mL) and toluene (7.5 mL), the mixture was stirred at 80°C for 24 hours. After cooling down and filtration, silica support was washed with dichloromethane (3 x 8 mL). The combined organic phases were concentrated and filtrated through thin pad of silica before to be analyzed in GC. Purification of the crude product by flash chromatography on silica gel gave the coupling product.

Recycling cross-coupling reaction of 4-bromonitrobenzene with phenylboronic acid

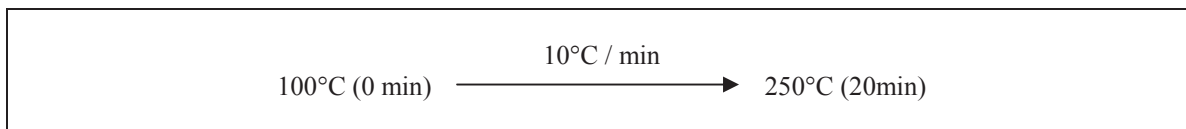
In the case of 1% molar of Pd catalyst: for the first run, the same experimental condition than described above was used. After decantation and filtration, the SAPC was washed with toluene (5 mL), and was dried under vacuum for 16 hours. After, a mixture of 4-bromonitrobenzene (0.5 mmol), phenylboronic acid (0.55 mmol) and Na₂CO₃ (156.0 mg, 1.5 mmol) were added to the solid. After that the new cycle was performed following the general procedure for the Suzuki-Miyaura reaction. In the case of 0.1% molar of Pd catalyst: the same protocol as described above was used increasing per ten the amount of base, 4-bromonitrobenzene, phenylboronic acid and solvents.

For different substrates two conditions were used during GC analysis. Below retention time for compounds use in catalytic reactions and characteristics for isolated biaryls are

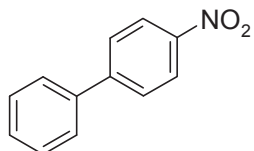
References

presented.

Analysis of products were made using conditions:

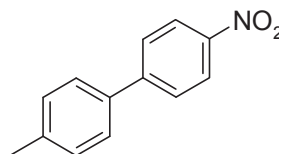


4-Nitrobiphenyl (Table 3.3, Entry 1)¹⁰⁸



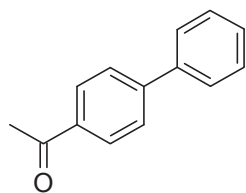
- Yellow solid
- GC t_R = 7.57 min.
- $^1\text{H NMR}$ (CDCl_3): δ (ppm) = 7.42-7.54 (m, 3H), 7.60-7.66 (m, 2H), 7.71-7.78 (m, 2H), 8.28-8.32 (m, 2H).

4'-Methyl-4-nitro-biphenyl (Table 3.3, Entry 3)¹⁰⁸



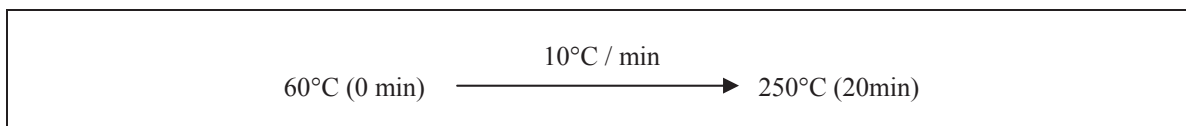
- Yellow solid
- GC t_R = 8.88 min.
- $^1\text{H NMR}$ (CDCl_3): δ (ppm) = 2.32 (s, 3H), 7.20 (d, 2H, $J=7.9\text{Hz}$), 7.42 (d, 2H, $J=7.9\text{Hz}$), 7.60 (d, 1H, $J=8.9\text{Hz}$), 8.16 (d, 1H, $J=8.9\text{Hz}$)

4-Phenyl-acetophenone (Table 3.3, Entry 1)¹⁰⁹



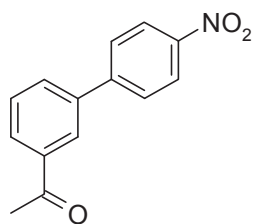
- White solid
- GC t_R = 7.48 min.
- $^1\text{H NMR}$ (CDCl_3): δ (ppm) = 2.64 (s, 3H), 7.34 – 7.55 (m, 3H), 7.63 (d, 2H, $J=7.3\text{Hz}$), 7.69 (d, 2H, $J=8.2\text{Hz}$), 8.04 (d, 2H, $J=8.2\text{Hz}$)

Analysis of products were made using conditions:

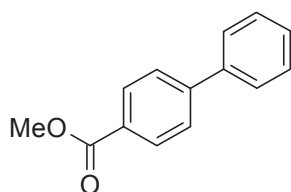


¹⁰⁸ Y. Kitamura, A. Sakurai, T. Udzu, T. Maegawa, Y. Monguchi, Hironao Sajiki, *Tetrahedron*, **2007**, 63, 10596-10602.

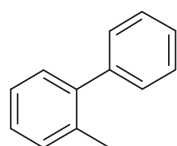
¹⁰⁹ B. Sreedhar, D. Yada, P. S. Reddy, *Adv. Synth. Catal.*, **2011**, 353, 2823-2836.

3-Acetyl-4'-nitrobiphenyl (Table 3.3, Entry 2)¹⁰⁸

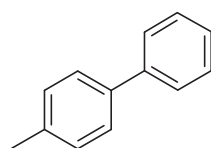
- Yellow solid
- GC t_R = 11.6 min.
- $^1\text{H NMR (CDCl}_3\text{)}$: δ (ppm) = 2.66 (s, 3H), 7.60 (t, 1H, $J=7.8\text{Hz}$), 7.75 (d, $J=8.8\text{Hz}$, 2H), 7.81 (d, 1H, $J=7.8\text{Hz}$), 8.01 (d, 1H, $J=7.8\text{Hz}$), 8.20 (s, 1H), 8.29 (d, 2H, $J=8.8\text{Hz}$).

Methyl 4-phenylbenzoate (Table 3.3, Entry 6)¹¹⁰

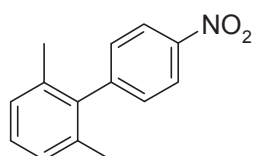
- Yellow solid
- GC t_R = 11.5 min.
- $^1\text{H NMR (CDCl}_3\text{)}$: δ (ppm) = 3.95 (s, 3H), 7.36-7.50 (m, 3H), 7.60-7.69 (m, 4H), 8.09-8.14 (m, 2H).

2-Methylbiphenyl (Table 3.3, Entry 9)¹⁰⁹

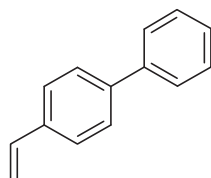
- Yellow solid
- GC t_R = 6.43 min.
- $^1\text{H NMR (CDCl}_3\text{)}$: δ (ppm) = 3.95 (s, 3H), 7.15-7.28 (m, 3H), 7.32-7.45 (m, 4H), 7.48-7.54 (m, 2H).

4-Methylbiphenyl (Table 3.3, Entry 10)¹¹¹

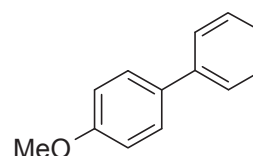
- GC t_R = 6.43 min.
- $^1\text{H NMR (CDCl}_3\text{)}$: δ (ppm) = 2.40 (s, 3H), 7.23-7.36 (m, 3H), 7.39-7.53 (m, 4H), 7.55-7.61 (m, 2H).

4-nitro-2',6'-dimethylbiphenyl
(Table 3.3, Entry 4)

- GC t_R = 5,53 min.

4-vinylbiphenyl
(Table 3.3, Entry 7)

- GC t_R = 9,23 min.

4-Methoxybiphenyl
(Table 3.3, Entry 8)

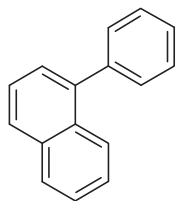
- GC t_R = 9,38 min

¹¹⁰ G. Bing-Tao, W. Yang, L. Bi-Jie, Y. Da-Gang, S. Zhang-Jie, *J. Am. Chem. Soc.*, **2008**, 130, 14468-14470.

¹¹¹ L. Lin, L. Yanchun, Z. Suobo, L. Shenghai, *Synlett*, **2011**, 12, 1779-1783.

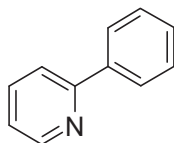
References

1-Phenylnaphthalene (Table 3.3, Entry 11)



- GC t_R = 12.83 min.

1-Phenylpyridine (Table 3.3, Entry 12)

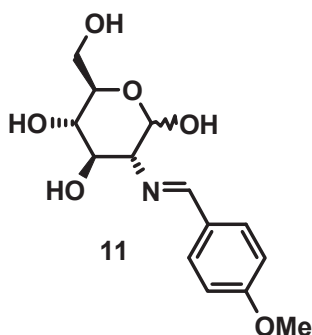


- GC t_R = 6.90 min.

3.5 Experiments dealing with synthesis of poly(ethylene) based ligands.

Synthesis of 2-deoxy-2-[*p*-methoxybenzylidene(amino)]-*D*-glucopyranose **11**⁸⁸

p-Anisylaldehyde (3.5 mL, 28.8 mmol) was added, in a round bottom flask to a solution of *D*-glucosamine hydrochloride (5 g, 23.0 mmol) in 1M NaOH (24 mL). After short time crystallization began. The mixture was stirred for 2 h and then the precipitated product was filtered off and washed with cold water, followed by mixture of EtOH : Et₂O 1 : 1.



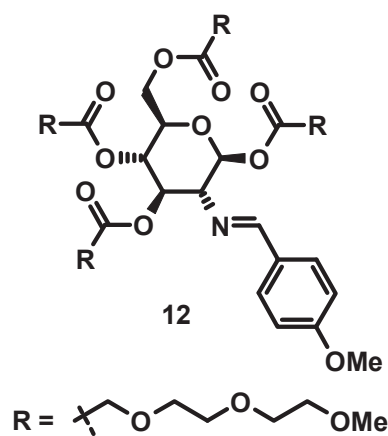
- Yield 75%
- White solid
- m.p. 159-161 °C , lit. 165-166 °C

- ¹H NMR (C₅D₅N): δ (ppm) = 3.70 (s, 3H, CH₃O), 3.88 (dd, 1H, J=7.8, J=9.0Hz, H-2), 4.24 (ddd, 1H, J=2.5, J=5.6, J=9.2Hz, H-5), 4.45 (dd, 1H, J=9.2, J=9.2Hz, H-4), 4.54 (m, 1H, H-6), 4.61 (dd, 1H, J=9.0, J=9.2Hz, H-3), 4.73 (dd, 1H, J=11.8, J=2.5Hz, H-6), 5.82 (dd, 1H, J=4.7, J=7.3Hz, H-1), 6.66 (s, 1H, O-H), 7.03 (d, 2H, J=8.8Hz, H_{arom}), 7.63 (s, 1H, O-H), 7.94 (d, 2H, J=8.8Hz, H_{arom}), 8.74 (s, 1H, O-H), 8.78 (s, 1H, O-H), 8.96 (d, 1H, J=5.6Hz, NCH) according to literature⁸⁸.

Synthesis of 1,3,4,6-tetra-*O*-[(methoxy)etoxy]ethoacyetyl-2-(*p*-methoxybenzylidene)amino-2-deoxy- β -*D*-glucopyranose **12**

In Schlenk flask with argon balloon was dissolve (0.30 g, 1.0 mmol) 2-desoxy-2-[*p*-methoxybenzylidene(amino)]-*D*-glucopyranose **10** in 10 mL of dry pyridine. Mixture was cooled to 0 °C and anhydride (3.43 g, 10.15 mmol) dissolved in 10 mL pyridine was added. After 1 h ice bath was removed and solution was stirred in room temperature overnight.

Mixture was evaporated, and chromatographed on silica gel column using gradient from dichloromethane : methanol 40 : 1 to dichloromethane : methanol 20 : 1.

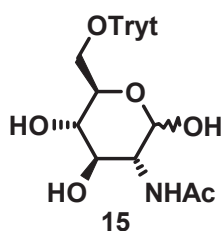


- Yield 32%
- Yellow oil
- $R_f = 0.24$ (dichloromethane : methanol 20:1)
- $[\alpha]_D^{20} = +34.5$ ($c = 0.85$, chloroform)

- $^1\text{H NMR}$ (CDCl_3): δ (ppm) = 3.29-4.22 (m, 58H, H-2, H-5, H-6, 20 x CH_2PEG , 4 x CH_3PEG , 4 x OCH₃), 4.37 (dd, 1H, $J=4.6$, $J=12.4\text{Hz}$, H-6), 5.13 (dd, 1H, $J=9.6$, $J=9.9\text{Hz}$, H-4), 5.45 (dd, 1H, $J=9.6$, $J=9.6\text{Hz}$, H-3), 5.95 (d, 1H, $J=8.3\text{Hz}$, H-1), 6.86 (d, 2H, $J=8.8\text{Hz}$, H_{arom}), 7.59 (d, 2H, $J=8.8\text{Hz}$, H_{arom}), 8.11 (s, 1H, NCH).

Synthesis of 2-acetamido-2-deoxy-6-*O*-trityl-D-glucopyranose **15**¹¹²

A solution of 2-acetamido-2-deoxy-6-*O*-trityl-D-glucopyranose (2.0 g, 9.0 mmol) and chlorotriphenylmethane (2.52 g, 9.0 mmol) in dry pyridine was stirred at room temperature for 5 days. The reaction mixture was heated at 80 °C for 1 h, cooled, and poured into ice-water. After 30 min, chloroform was added and solutions were extracted, dried (Na_2SO_4), and evaporated. The residue was freed from pyridine by addition and evaporation of toluene, and chromatographed on a silica gel column. Chloroform eluted the fast moving triphenylmethanol and the product was eluted with methanol-chloroform 1:9.



- Yield 66%
 - White solid
 - $R_f = 0.32$ (dichloromethane / methanol 20:1)
 - m.p. 124 °C, lit.¹¹² 130 °C
- $^1\text{H NMR}$ (DMSO-d_6): δ (ppm) = 1.85 (s, 3H, CH₃), 3.11 (dd, 1H, $J=5.1$, $J=9.8\text{Hz}$, H-6), 3.23 (m, 1H, H-6), 3.64 (ddd, 1H, $J=3.2$, $J=6.3$, $J=11.1\text{Hz}$, H-2), 3.83 (ddd, 1H, $J=1.5$, $J=5.1$, $J=10.8\text{Hz}$, H-5), 4.67 (d, 1H, $J=6.3\text{Hz}$, H-1), 4.89 (dd, 1H, $J=5.1$, $J=10.8\text{Hz}$, H-4), 4.99 (dd, 1H, $J=3.2$, $J=5.1\text{Hz}$, H-3), 6.52 (d, 0.8H, $J=4.5\text{Hz}$), 6.62

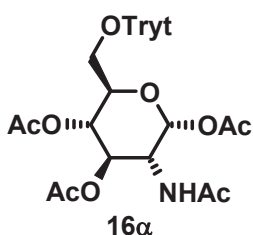
¹¹² A. B. Foster, D. Horton, N. Salim, M. Stacey, J. M. Webber, *J. Chem. Soc.*, **1960**, 2587-2796.

References

(d, 0.2H, J=6.3Hz), 7.29 (m, 9H), 7.43 (m, 6H), 7.68 (d, 0.8H, J=8.2Hz), 7.74 (d, 0.2H, J=8.4Hz).

Synthesis of 2-acetamido-1,3,4-tri-O-acetyl-2-deoxy-6-O-trityl-D-glucopyranose **16a**¹¹³

The trityl compound (2.5 g, 5.4 mmol) was acetylated with acetic anhydride (10 mL, 0.1 mol) and dry pyridine (20 mL) overnight. It was poured into ice-water, and extracted with chloroform, and solution washed with water dried (Na₂SO₄) and evaporated. The residue was freed from pyridine by addition and evaporation of toluene and passed through a column of silica gel. The product was eluted with chloroform and crystallized from hot carbon tetrachloride. After 4 days first part of compound **16a** was filtrated.

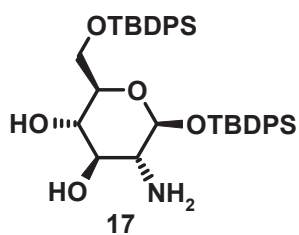


- White crystals
- R_f = 0.22 (chloroform)
- m.p. 119-124, lit.¹⁴ 111-112°C
- [α]_D²⁰ = +96.9 (c = 1, chloroform), lit¹¹³. +90.0 (c = 1,2 chloroform).
- ¹H NMR (CDCl₃): δ (ppm) = 1.72 (s, 3H, CH₃), 1.95 (s, 3H, CH₃), 2.04 (s, 3H, CH₃), 2.17 (s, 3H, CH₃), 3.02 (dd, 1H, J=4.1, J=10.5Hz, H-6), 3.28 (dd, 1H, J=2.2, J=10.7Hz, H-6), 3.88 (ddd, 1H, J=2.0, J=3.8, J=10.1Hz, H-5), 4.54 (ddd, 1H, J=3.7, J=9.0, J=10.8Hz, H-2), 5.17 (dd, 1H, J=9.7, J=10.7Hz, H-3), 5.35 (dd, 1H, J=9.9, J=9.9Hz, H-4), 5.53 (d, 1H, J=9.0Hz, NH), 6.29 (d, 1H, J=3.6Hz, H-1), 7.18-7.32 (m, 9H), 7.39-7.45 (m, 6H) according to literature¹¹³.
- ¹³C NMR (CDCl₃): δ (ppm) = 20.8 (COCH₃), 21.2 (COCH₃), 21.4 (COCH₃), 23.5 (COCH₃), 51.7 (C-2), 61.9 (C-6), 68.3 (C-4), 71.6 (C-3), 71.7 (C-5), 86.9 (CPh₃), 91.3 (C-1), 127.4 (3 x C_{arom}), 128.2 (6 x C_{arom}), 129.1 (6 x C_{arom}), 143.9 (3 x C_{arom}), 168.9 (COCH₃), 169.1 (COCH₃), 170.4 (COCH₃), 172.4 (COCH₃).

Synthesis of 2-amino-1,6-di-O-(tert-butylidiphenylsilyl)-2-deoxy-β-D-glucopyranose **17**

Solution of 2-deoxy-2-[p-methoxybenzylidene(amino)]-D-glucopyranose (0.20 g, 0.67 mmol), imidazole (0.11 g, 1.69 mmol), and diphenyl tert-butyl silyl chloride (157.7μL, 0.61 mmol) was stirred in dry DMF in a Schlenk tube under argon for 1.5 hour. After that time solution was quenched with ethanol, chloroform was added, and mixture was washed 3 times with water, drying with Na₂SO₄ and evaporated. Mixture was purified by column chromatography using eluent DCM : methanol 20 : 1.

¹¹³ H. Homiyama, N. Ueyama, M. Yanagiya, Y. Ohkur, US6858724 B2, **2002**.

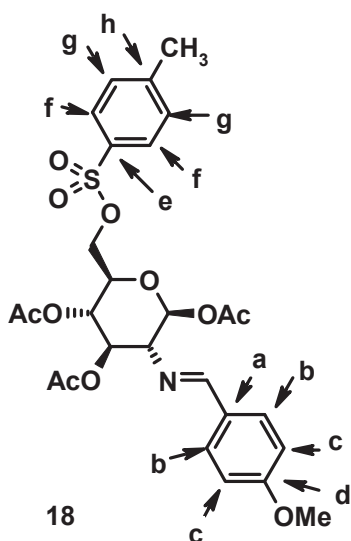


- Yield 58%
- Colorless oil
- $R_f = 0.22$ (dichloromethane : methanol 20:1)

- $^1\text{H NMR}$ (CDCl_3): δ (ppm) = 1.02 (s, 9H, *tert*-butyl), 1.08 (s, 9H, *tert*-butyl), 1.96 (bs, 2H, NH_2), 2.73 (dd, 1H, $J=7.6$, $J=9.4\text{Hz}$, H-2), 3.04 (ddd, 1H, $J=1.0$, $J=5.1$, $J=9.8\text{Hz}$, H-5), 3.24 (dd, 1H, $J=9.4$, $J=9.4\text{Hz}$, H-3), 3.68 (m, 3H, H-4, H-6, H-6'), 4.32 (d, 1H, $J=7.6\text{Hz}$, H-1), 7.45 (m, 20H, 4 x H_{arom}).
- $^{13}\text{C NMR}$ (DMSO-d_6): δ (ppm) = 19.4 ($\text{C}-(\text{CH}_3)_3$), 19.5 ($\text{C}-(\text{CH}_3)_3$), 27.1 ($\text{C}-(\text{CH}_3)_3$), 27.5 ($\text{C}-(\text{CH}_3)_3$), 59.9 (C-2), 63.9 (C-6), 70.12, 76.9, 77.61, 99.5 (C-1), 114.7 (s, 1H), 128.0 (2 x C_{arom}), 128.1 (2 x C_{arom}), 128.3 (2 x C_{arom}), 128.3 (2 x C_{arom}), 130.2 (C_{arom}), 130.3 (C_{arom}), 130.3 (C_{arom}), 130.3 (C_{arom}), 133.6 ($\text{C}_{\text{arom-Si}}$), 133.7 ($\text{C}_{\text{arom-Si}}$), 133.7 ($\text{C}_{\text{arom-Si}}$), 133.8 ($\text{C}_{\text{arom-Si}}$), 135.7 (2 x C_{arom}), 135.7 (2 x C_{arom}), 136.0 (4 x C_{arom}).

Synthesis of 1,3,4-tri-*O*-acetyl-2-deoxy-2-(*p*-methoxybenzylideneamino)-6-*O*-tosyl- β -D-glucopyranose **18**⁹⁸

Carbohydrate compound **11** (4.00 g, 13.4 mmol) was suspended in pyridine (30 mL) and cooled to 0 °C. Under vigorous stirring tosyl chloride (2.56 g, 13.4 mmol) dissolved in 10 mL of pyridine was added dropwise. Mixture was stirred in -5 °C overnight. After this time mixture was cooled to 0 °C and acetic anhydride was added, mixture was left to warm to room temperature and stirred 2 h. Mixture was poured into ice water, and precipitate filtered off to give 1.74 g of **18**.



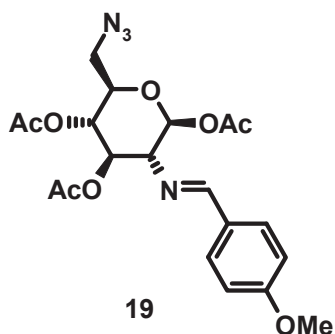
- Yield 23%
- Yellow solid
- $R_f = 0.51$ (cyclohexane ethyl acetate 1:1)
- m.p. 194-195 °C, lit.⁹⁸. 203-204 °C
- $[\alpha]_D^{20} = +96.8$ (c = 1.00, chloroform),
lit.⁹⁸ $[\alpha]_D^{20} = +99.3$ (c = 1.00, chloroform)

References

- **¹H NMR (CDCl₃):** δ (ppm) = 1.87 (s, 3H, CH₃), 1.96 (s, 3H, CH₃), 2.00 (s, 3H, CH₃), 2.45 (s, 3H, CH₃), 3.44 (dd, 1H, J=8.1, J=9.6Hz, H-2), 3.85 (s, 3H, OCH₃), 3.94 (bdd, 1H, J=9.6Hz, H-5), 4.09-4.23 (m, 2H, H-6, H-6'), 5.10 (dd, 1H, J=9.6, J=9.6Hz, H-4), 5.41 (dd, 1H, J=9.6 J=9.6Hz, H-3), 5.93 (d, 1H, J=8.1Hz, H-1), 6.92 (d, 2H, J=8.5Hz, H_{aromc}), 7.35 (d, 2H, J=8.1Hz, H_{aromg}), 7.72 (d, 2H, J=8.5Hz, H_{aromb}), 7.79 (d, 2H, J=8.1Hz, H_{aromf}), 8.11 (s, 1H, N=CH).
- **¹³C NMR (CDCl₃):** δ (ppm) = 20.4 (COCH₃), 20.5 (COCH₃), 20.7 (COCH₃), 21.6 (CH₃), 55.3 (OCH₃), 67.0 (C-6), 68.0 (C-3), 72.1 (C-5), 72.6 (C-2), 73.1 (C-4), 93.0 (C-1), 114.0 (2 x C_{aromc}), 128.1 (2 x C_{aromf}), 128.2 (C_{aroma}), 129.8 (2 x C_{aromg}), 130.2 (2 x C_{aromb}), 132.4 (C_{arome}), 144.9 (C_{aromh}), 162.3 (C_{aromd}), 157.0 (N=CH), 168.6 (COCH₃), 169.5 (2 x COCH₃).

Synthesis of 1,3,4-tri-O-acetyl-6-azido-2,6-dideoxy-2-(p-methoxybenzylideneamino)-β-D-glucopyranose **19**⁹⁹

A mixture of tosyl compound **18** (1.74 g, 3.10 mmol), sodium azide (0.20 g, 3.10 mmol), and N,N-dimethylformamide (15 mL) was heated at 80-90 °C under stirring for 4 h. The reaction mixture was evaporated and the residue was extracted with chloroform (200 mL). The extract was washed with water, dried over anhydrous sodium sulfate and evaporated to give syrup, which was recrystallized from ethanol to give 1.08 g of **19**.

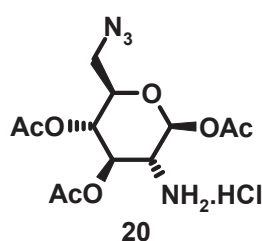


- Yield 77%
- Yellow solid
- R_f = 0.58 (cyclohexane ethyl acetate 1:1)
- m.p. 119-121 °C, lit. 123.5-124 °C
- [α]_D²⁰ = +114.6 (c = 1.02 chloroform), lit.⁹⁹, [α]_D²⁰ = +127 (c = 1.00 chloroform)
- **¹H NMR (CDCl₃):** δ (ppm) = 1.88 (s, 3H, CH₃), 2.02 (s, 3H, CH₃), 2.05 (s, 3H, CH₃), 3.37 (dd, 1H, J=5.3Hz, J=13.3Hz, H-6), 3.41-3.49 (m, 2H, H-2, H-6'), 3.85 (s, 3H, OCH₃), 3.94 (ddd, 1H, J=2.7Hz, J=5.3Hz, J=9.9Hz, H-5), 5.11 (dd, 1H, J=9.7, J=9.9Hz, H-4), 5.43 (dd, 1H, J=9.7, J=9.7Hz, H-3), 5.95 (d, 1H, J=8.4Hz, H-1), 6.92 (d, 2H, J=8.7Hz, H_{arom}), 7.67 (d, 2H, J=8.7Hz, H_{arom}), 8.15 (s, 1H, N=CH), according to the literature⁹⁹.
- **¹³C NMR (CDCl₃):** δ (ppm) = 20.4 (COCH₃), 20.6 (2 x COCH₃), 50.6 (C-6), 55.3 (OCH₃), 69.1 (C-4), 72.7 (C-2), 73.06 (C-3), 73.6 (C-5), 92.9 (C-1), 113.9 (2 x

C_{arom}), 128.2 (C_{arom}), 130.1 (2 x C_{arom}), 162.2 ($C_{\text{arom}}\text{-OCH}_3$), 164.2 ($\text{N}=\text{CH}$), 168.6 (COCH_3), 169.4 (COCH_3), 169.7 (COCH_3), according to the literature⁹⁹.

Synthesis of 1,3,4-tri-*O*-acetyl-2-amino-6-azido-2,6-dideoxy- β -D-glucopyranose hydrochloride **20**⁹⁹

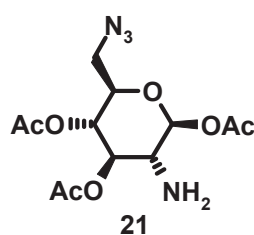
To a warm solution of **19** (0.89 g, 1.986 mmol) in acetone (3 mL) was added dropwise 6M aqueous hydrochloric acid (0.331 mL, 1.986 mmol) under vigorous agitation. After few minutes precipitate was observed. The product was collected by filtration and washed with ether to give 0.69 g of **20**.



- Yield 95%
- Yellow solid
- m.p. 152-161 °C (decomp.) , lit. 147-154 °C (decomp.)
- $[\alpha]_{\text{D}}^{20} = +41.1$ (c = 0.50 methanol), lit.⁹⁹, $[\alpha]_{\text{D}}^{20} = +43$ (c = 0.50, methanol)
- ¹H NMR (DMSO-*d*₆): δ (ppm) = 1.98 (s, 3H, CH₃), 2.02 (s, 3H, CH₃), 2.16 (s, 3H, CH₃), 3.34-3.59 (m, 3H, H-2, H-6, H-6'), 3.92-4.02 (m, 1H, H-5), 4.88 (dd, 1H, J=9.5, J=9.5Hz, H-4), 5.35 (dd, 1H, J=9.7, J=9.7Hz, H-3), 5.95 (d, 1H, J=8.6Hz, H-1), 8.94 (s, 3H, NH₃Cl), according to the literature⁹⁹.
- ¹³C NMR (DMSO-*d*₆): δ (ppm) = 20.4 (COCH₃), 20.7 (COCH₃), 20.9 (COCH₃), 49.7 (C-2), 52.0 (C-6), 68.6 (C-4), 70.3 (C-3), 72.7 (C-5), 89.9 (C-1), 168.4 (COCH₃), 169.3 (COCH₃), 169.7 (COCH₃), according to the literature⁹⁹.

Synthesis of 1,3,4-tri-*O*-acetyl-2-amino-6-azido-2,6-dideoxy- β -D-glucopyranose **21**

Compound **20** (0.69 g, 1.88 mmol) was suspended in 5 mL of dichloromethane, and saturated solution of NaHCO₃ (5 mL) was added, mixture stirred for one hour till starting material was completely dissolved. Mixture was transferred to separatory funnel, organic phase separated, and water phase washed two times with dichloromethane. Organic phases were collected, dried over Na₂SO₄ and solvent were evaporated. Colorless oil was flirtd through pad of silica to gave 0.439 g of white solid.



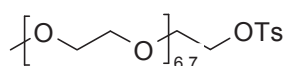
- Yield 71%
- White solid
- $R_f = 0.16$ (dichloromethane : methanol 20:1)
- m.p. 79-80 °C
- $[\alpha]_{\text{D}}^{20} = 22,8$ (c = 1.01 chloroform)

References

- **¹H NMR (CDCl₃):** δ (ppm) = 1.63 (bs, 2H, NH₂), 2.04 (s, 3H, CH₃), 2.09 (s, 3H, CH₃), 2.17 (s, 3H, CH₃), 2.98-3.09 (m, 1H, H-2), 3.27-3.41 (m, 2H, H-6, H-6'), 3.76-3.82 (m, 1H, H-5), 4.96-5.07 (m, 2H, H-3, H-4), 5.47 (d, 1H, J=8.5Hz, H-1).
- **¹³C NMR (CDCl₃):** δ (ppm) = 20.6 (COCH₃), 20.7 (COCH₃), 20.8 (COCH₃), 50.6 (C-2), 54.8 (C-6), 69.2 (C-4), 73.6 (C-3), 74.7 (C-5), 94.8 (C-1), 169.1 (COCH₃), 170.6 (COCH₃).

Synthesis of O-tosyl polyethylene glycol monomethyl ether¹¹⁴

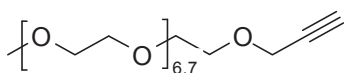
p-Toluenesulfonic acid chloride (3.20 g, 16.8 mmol) and NEt₃ (2.3 mL, 16.8 mmol) were added to a solution of polyethylene glycol monomethyl ether (3.00g 8.57mmol) in DCM (10 mL) while stirring. The reaction mixture was stirred for 16 h, precipitate filtered off and solution concentrated in vacuum. The crude product was purified by column chromatography (dichloromethane : methanol 100 : 1 to 9 : 1) (3.26 g, 74%).



- Yield 74%
- Colorless oil
- R_f = 0.65 (dichloromethane : methanol 20:1)
- **¹H NMR (CDCl₃):** δ (ppm) = 2.40 (s, 3H, CH₃), 3.24 (s, 2H), 3.32 (s, 3H, OCH₃), 3.47-3.66 (m, 33H), 4.10 (t, 2H, J=4.7Hz), 7.30 (d, 2H, J=8.2Hz, H_{arom}), 7.74 (d, 2H, J=8.2Hz, H_{arom}) according to literature¹¹⁴.
- **¹³C NMR (CDCl₃):** δ (ppm) = 21.5 (CH₃), 58.8 (OCH₃), 68.5 (CH₂), 69.1 (CH₂), 70.3 (14 x CH₂), 70.5 (CH₂), 71.7 (CH₂), 127.8 (2 x C_{arom}), 127.8 (2 x C_{arom}), 132.8 (C_{arom}), 144.6 (C_{arom}) according to literature¹¹⁴.

Synthesis of O-propargyl polyethylene glycol monomethyl ether¹¹⁴

Propargyl alcohol (0.271 mL, 4.57 mmol) was added to a suspension of NaH (0.110 g, 4.57 mmol) in THF (1.7 mL) at 0 °C. After 30 min, a solution of O-tosyl polyethylene glycol monomethyl ether (0.231 g, 0.45 mmol) in THF (4 mL) was added and the mixture was allowed to warm to room temperature and stirred for 16 h. Precipitate was filtered off and solvents were evaporated. The crude product was purified by column chromatography (dichloromethane : methanol 100 : 1 to 20 : 1) (0.121 g, 68%).



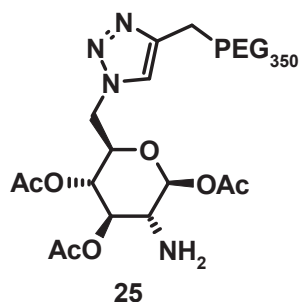
- Yield 68%
- Pale yellow oil
- R_f = 0.62 (dichloromethane : methanol 9 : 1)

¹¹⁴ A. Baccaro, A. Marx, *Chem. Eur. J.*, **2010**, 16, 218-226.

- $^1\text{H NMR}$ (CDCl_3): δ (ppm) = 2.41 (t, 1H, $J=2.2\text{Hz}$, $\text{CH}_2\text{C}\equiv\text{CH}$), 3.33 (s, 3H, OCH_3), 3.48-3.53 (m, 2H), 3.56-3.68 (m, 30H), 4.15 (d, 2H, $J=2.4\text{Hz}$, $\text{CH}_2\text{C}\equiv\text{CH}$) according to literature¹¹⁴.
- $^{13}\text{C NMR}$ (CDCl_3): δ (ppm) = 57.9 ($\text{CH}_2\text{C}\equiv\text{CH}$), 58.6 (OCH_3), 68.7 (CH_2), 69.9 (CH_2), 70.1 (CH_2), 70.1 (12 x CH_2), 71.5 (CH_2OCH_3), 74.4 ($\text{CH}_2\text{C}\equiv\text{CH}$), 79.3 ($\text{CH}_2\text{C}\equiv\text{CH}$) according to literature¹¹⁴.

Synthesis of 1,3,4-tri-*O*-acetyl-2-amino-2-deoxy- β -D-glucofuranose,6-[(1H-1,2,3-triazol-4-yl)methyl]-1-(polyethylen glycol) **22**

MPEG containing alkynyl function (0.059 g, 0.15 mmol) was dissolved in tetrahydrofuran (2 mL) and transferred to solution of **21** (0.050 g, 0.15 mmol) in tetrahydrofuran (1 mL). After copper iodide (1.7 mg, 0.9 μmol) was added under stream of argon. Mixture was stirred overnight in room temperature. Solution was concentrated, and dried on vacuum pump to give 0.95 g of triazol compound **22**.



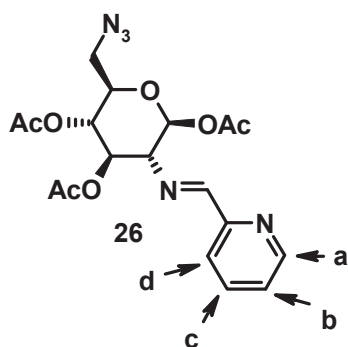
- Yield 89%
- Brown oil

$^1\text{H NMR}$ ($\text{DMSO-}d_6$): δ (ppm) = 1.22 (bs, 2H, NH_2), 2.05 (s, 6H 2 x CH_3), 2.15 (s, 3H, CH_3), 3.34 (d, 4H, $J=1.5\text{Hz}$ $\text{CH}_2\text{CH}_2\text{OCH}_3$), 3.52 (m, 3H $\text{CH}_2\text{CH}_2\text{OCH}_3$), 3.65-3.68 (m, 40H), 3.95 (m, 1H, H-5), 4.36 (dd, 1H, $J=7.0$, $J=14.4\text{Hz}$, H-6), 4.58 (dd, 1H, $J=6.8$, $J=7.7\text{Hz}$, H-6'), 4.65 (s, 2H, CH_2), 4.75 (dd, 1H, $J=8.6$, $J=8.6\text{Hz}$, H-4), 4.94 (m, 1H, H-3), 5.35 (d, 1H, $J=3.9\text{Hz}$, H-1), 7.66 (s, 1H).

Synthesis of 1,3,4-tri-*O*-acetyl-6-azido-2-[(*E*)-(2-pyridinylmethylene)amino]-2,6-dideoxy- β -D-glucofuranose **26**

Amino compound **21** (150 mg, 0.45 mmol), and 2-pyridine benzaldehyde (43.2 μl , 0.45 mmol), were stirred with MgSO_4 in dry, toluene in 60°C . After being stirred for 8 hours, the solvent was evaporated, mixture dissolved in dichloromethane and filtrated through celite. Product was filtered through pad of silica using dichloromethane : NEt_3 99 : 1 as eluent. To give product **26** with 100% of yield.

References



- Yield quantitative%
- White solid
- R_f = 0.67 (dichloromethane : methanol 20 : 1)
- [α]_D²⁰ = +84.4 (c = 0.10 chloroform),

- ¹H NMR (CDCl₃): δ (ppm) = 1.90 (s, 3H, CH₃), 2.04 (s, 1H, CH₃), 2.05 (s, 3H, CH₃), 3.39 (dd, 1H, J=5.3, J=13.5Hz, H-6), 3.45 (dd, 1H, J=3.0, J=13.5Hz, H-6'), 3.58 (dd, 1H, J=8.3, J=9.7Hz, H-2), 3.95 (ddd, 1H, J=3.0, J=5.3, J=9.7Hz, H-5), 5.13 (dd, 1H, J=9.7Hz, H-4), 5.46 (dd, 1H, J=9.7, J=9.7Hz, H-3), 5.99 (d, 1H, J=8.3Hz, H-1), 7.36 (ddd, 1H, J=1.1, J=4.8, J=7.5Hz, H_{arom}b), 7.75 (ddd, 1H, J=1.6, J=7.5, J=7.8Hz, H_{arom}c), 7.98 (ddd, 1H, J=0.8, J=1.1, J=7.8Hz, H_{arom}d), 8.35 (s, 1H, N=CH), 8.65 (ddd, 1H, J=0.8, J=1.6, J=4.8Hz, H_{arom}a).
- ¹³C NMR (CDCl₃): δ (ppm) = 20.4 (COCH₃), 20.5 (COCH₃), 20.6 (COCH₃), 50.6 (C-6), 68.9 (C-3), 72.4, 72.6, 73.7, 92.5 (C-1), 121.7 (C_{arom}d), 125.4 (C_{arom}b), 136.8 (C_{arom}c), 149.3 (C_{arom}a), 153.5 (C_{arom}), 166.2 (N=CH), 166.2 (COCH₃), 168.6 (COCH₃), 169.5 (COCH₃), 169.6 (COCH₃).

3.6 Experiments dealing with silica grafted ligands.

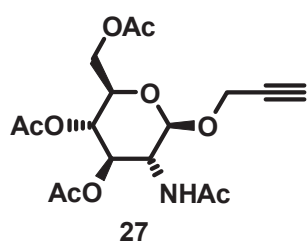
General procedure for grafting compounds in silica matrix

Compound for grafting was dissolved in toluene (distilled over CaH₂ and degassed with three freeze-pump cycles) and solution was cannulated to Schlenk tube containing SBA-15 (dried under vacuum in 140 °C for 16 hours, and degassed five times with argon-vacuum cycles). Mixture was stirred in room temperature for 2 hours and after in 60 °C for 24 hours. Stirring was stopped and solid decanted over 1 hour, after this time under stream of nitrogen liquid was removed using syringe and dry, degassed toluene was added. Mixture was stirred for 0.5 hour, and after stopped for decantation. Washing with toluene was repeated for 4 times. Solid was dried on vacuum pump for 16 hours.

Synthesis of propargyl 2-acetamido-3,4,6-tri-O-acetyl-2-deoxy-β-D-glucopyranoside 27¹⁰⁴

N-acetyl-D-glucosamine **3** (4.42 g, 20 mmol) was suspended in dry DMF (60 mL) and successively treated with sodium hydride (1.04 g, 26 mmol) and propargyl bromide

(6.68 mL, 60 mmol). After overnight stirring at room temperature methanol (2.5 mL) was added and stirring continued for 1 h. Methanol and DMF were removed under vacuum and the residue dissolved in Ac₂O (25 mL). At 0 °C NEt₃ (50 mL) was slowly added and the mixture allowed to warm to room temperature. After stirring overnight the mixture was diluted with ethyl acetate (100 mL) and treated with 1 M HCl (80 mL). The aqueous phase was extracted with ethyl acetate (2 × 100 mL) and the organic phase washed with brine (80 mL). The combined organic extracts were dried over MgSO₄, filtered and concentrated. Purification by flash column chromatography (EtOAc : cyclohexane 1 : 1 to 3 : 1) afforded 2.1 g (27%) of the **27** as a white solid.



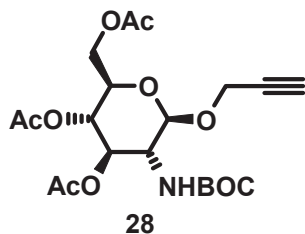
- Yield 28%
- White solid
- R_f = 0.32 (ethyl acetate : cyclohexane 2 : 1)
- m.p. 189-190 °C
- [α]_D²⁰ = -48.6 (c = 1.02, chloroform)
- ¹H NMR (CDCl₃): δ (ppm) = 1.95 (s, 3H, CH₃), 2.02 (s, 3H, CH₃), 2.02 (s, 3H, CH₃), 2.08 (s, 3H, CH₃), 2.47 (t, 1H, J=2.2Hz, CH), 3.72 (ddd, 1H, J=2.2, J=4.4, J=9.8Hz, H-5), 3.94 (ddd, 1H, J=8.4, J=8.8, J=10.2Hz, H-2), 4.13 (dd, 1H, J=2.2, J=12.2Hz, H-6), 4.26 (dd, 1H, J=4.4, J=12.2Hz, H-6), 4.37 (d, 2H, J=2.2Hz, CH₂), 4.85 (d, 1H, J=8.4Hz, H-1), 5.08 (dd, 1H, J=9.6, J=9.8Hz, H-4), 5.27 (dd, 1H, J=10.2, J=9.6Hz, H-3), 5.61 (d, 1H, J=8.8Hz, NH).
- ¹³C NMR (CDCl₃): δ (ppm) = 21.0 (COCH₃), 21.1 (COCH₃), 21.1 (COCH₃), 23.7 (COCH₃), 54.6 (CH₂C≡CH), 56.3 (C-2), 62.4 (C-6), 68.9 (C-4), 72.3 (C-5), 72.8 (C-3), 75.8 (CH₂C≡CH), 78.9 (CH₂C≡CH), 98.7 (C-1), 169.8 (COCH₃), 170.8 (COCH₃), 171.1 (COCH₃), 171.3 (COCH₃).
- IR: ν (thin film, cm⁻¹) = 3267, 3090, 1738, h, 1566, 1432, 1367, 1308, 1202, 1217, 1161, 1113, 1079, 1031, 1015, 974, 942, 928, 902, 699.
- ESI full ms calcd. for C₁₇H₂₃NNaO₉ (M + Na⁺): 408.1265, found 408.1270.

Synthesis of propargyl 3,4,6-tri-O-acetyl-2-[(*tert*-butoxycarbonyl)amino]-2-deoxy-β-D-glucopyranose⁵⁶

Propargyl compound **27** (1.22 g, 3.16 mmol) and *N,N*-dimethyl-4-aminopyridine (0.10 g, 0.95 mmol) was dissolved in THF (65 mL). Di-*tert*-butyl dicarbonate (1.38 g, 6. mmol) was added, and the mixture was heated to reflux overnight. After the solution was cooled

References

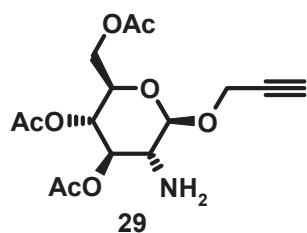
to room temperature, evaporate and methanol (20 mL) and catalytic amount of Na were added and the mixture was stirred at room temperature for 6 h. mixture was evaporated, dissolved in mixture acetic anhydride : pyridine 2 : 3, and stirred overnight. Solvents were removed under vacuum, DCM was added and mixture was filtrated through silica gel, evaporated, and crystallized from mixture DCM / pentane.



- Yield 79%
- White solid
- $R_f = 0.76$ (ethyl acetate : cyclohexane 2 : 1)
- m.p. 152-153 °C
- $[\alpha]_D^{20} = -23.5$ (c = 0.98, chloroform)
- $^1\text{H NMR}$ (CDCl_3): δ (ppm) = 1.42 (s, 9H *tert*-butyl), 2.01 (s, 3H, CH_3), 2.03 (s, 3H, CH_3), 2.07 (s, 3H, CH_3), 2.45 (t, 1H, $J=2.4\text{Hz}$, CH), 3.52 (dd, 1H, $J=7.0$, $J=7.3$, $J=9.9\text{Hz}$, H-2), 3.70 (ddd, 1H, $J=2.4$, $J=4.7$, $J=9.9\text{Hz}$, H-5), 4.12 (dd, 1H, $J=2.4$, $J=12.4\text{Hz}$, H-6), 4.27 (dd, 1H, $J=4.7$, $J=12.4\text{Hz}$, H-6), 4.38 (d, 2H, $J=2.2\text{Hz}$, CH_2), 4.62 (d, 1H, $J=7.3\text{Hz}$, H-1), 4.85 (d, 1H, $J=7.0\text{Hz}$, NH), 5.04 (dd, 1H, $J=9.6$, $J=9.9\text{Hz}$, H-4), 5.31 (dd, 1H, $J=9.6$, $J=9.9\text{Hz}$, H-3).
- $^{13}\text{C NMR}$ (CDCl_3): δ (ppm) = 21.0 (COCH_3), 21.1 (COCH_3), 21.1 (COCH_3), 28.6 ($\text{C}(\text{CH}_3)_3$), 56.0 (C-2), 56.3 ($\text{CH}_2\text{C}\equiv\text{CH}$), 62.4 (C-6), 69.1 (C-4), 72.2 (C-5), 72.6 (C-3), 75.8 ($\text{CH}_2\text{C}\equiv\text{CH}$), 78.8 ($\text{CH}_2\text{C}\equiv\text{CH}$), 80.4 ($\text{C}(\text{CH}_3)_3$), 98.8 (C-1), 155.5 (COCH_3), 169.9 (COCH_3), 170.9 (COCH_3), 171.1 (COCH_3).
- **IR:** ν (thin film, cm^{-1}) = 3319, 1739, 1679, 1537, 1365, 1332, 1298, 1219, 1161, 1115, 1087, 1066, 1042, 1016, 962, 906.
- **ESI full ms** calcd. for $\text{C}_{20}\text{H}_{30}\text{NO}_{10}$ ($\text{M} + \text{H}^+$): 444.1864, found 444.1882.

Synthesis of propargyl 2-amino-3,4,6-tri-*O*-acetyl-2-deoxy- β -D-glucopyranoside **29**⁵⁶

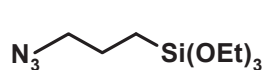
Propargyl 3,4,6-tri-*O*-acetyl-2-[(*tert*-butoxycarbonyl)amino]-2-deoxy- β -D-glucopyranose **28** (1.1 g) was dissolved in dichloromethane (4 mL) and trifluoroacetic acid (1 mL) was added. Mixture was stirred overnight in room temperature. After that time solution was diluted with dichloromethane and washed with NaHCO_3 , dried (Na_2SO_4) and evaporated. Crystallization from pentane gave 0.77 g of pure **29**.



- Yield 90%
- White solid
- $R_f = 0.22$ (ethyl acetate : cyclohexane 2 : 1)
- m. p. 127 °C
- $[\alpha]_D^{20} = +41.2$ (c = 0.68, chloroform)
- **$^1\text{H NMR}$ (CDCl_3):** δ (ppm) = 1.45 (s, 2H, NH_2), 2.01 (s, 3H, CH_3), 2.06 (s, 3H, CH_3), 2.07 (s, 3H, CH_3), 2.48 (t, 1H, $J=2.4\text{Hz}$, $\text{C}\equiv\text{CH}$), 2.92 (ddd, 1H, $J=8.4$, $J=8.8$, $J=10.2\text{Hz}$, H-2), 3.69 (ddd, 1H, $J=2.3$, $J=4.6$, $J=9.5\text{Hz}$, H-5), 4.10 (dd, 1H, $J=2.3$, $J=12.3\text{Hz}$), 4.28 (dd, 1H, $J=4.7$, $J=12.3\text{Hz}$), 4.39 (dd, 2H, $J=2.4$, $J=4.1\text{Hz}$, CH_2), 4.47 (d, 1H, $J=8.0\text{Hz}$, H-1), 4.94-5.06 (m, 2H).
- **$^{13}\text{C NMR}$ (CDCl_3):** δ (ppm) = 21.1 (COCH_3), 21.2 (COCH_3), 21.2 (COCH_3), 56.1 (C-2), 56.5 ($\text{CH}_2\text{C}\equiv\text{CH}$), 62.5 (C-6), 69.1 (C-4), 72.4 (C-5), 75.6 (C-3), 76.0 ($\text{CH}_2\text{C}\equiv\text{CH}$), 78.8 ($\text{CH}_2\text{C}\equiv\text{CH}$), 102.0 (C-1), 170.1 (COCH_3), 171.1 (COCH_3), 171.1 (COCH_3).
- **IR:** ν (thin film, cm^{-1}) = 3268, 3090, 1739, 1655, 1566, 1431, 1367, 1231, 1218, 1161, 1112, 1079, 1031, 1014, 975, 942, 928, 902, 801.
- **ESI full ms** calcd. for $\text{C}_{15}\text{H}_{22}\text{NO}_8$ ($\text{M} + \text{H}^+$): 344.1340, found 344.1346.

Synthesis of 3-azidopropyltriethoxysilane¹⁰⁷

To a solution of 3-chloropropyltriethoxysilane (2.00 g, 8.3 mmol) and tetrabutylammonium bromide (0.64 g, 2.0 mmol) in acetonitrile (50 mL) was added sodium azide (1.08 g, 16.6 mmol) and the reaction mixture heated under reflux for 50 h. After this time, filtration over celite was followed by evaporation of the solvent under vacuum. to give product (1.57 g) as a syrup that was directly used without further purification.

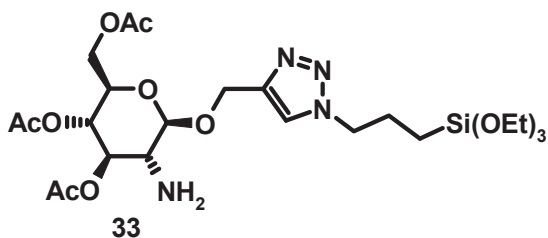


- Yield 76%
- Colorless oil
- **$^1\text{H NMR}$ (CD_3Cl_3):** δ (ppm) = 0.67 (m, 2H, CH_2Si), 1.22 (t, 9H, $J=7.0\text{Hz}$, OCH_2CH_3), 1.70 (m, 2H, $\text{CH}_2\text{CH}_2\text{N}_3$), 3.27 (t, 2H, $J=7.0\text{Hz}$, CH_2N_3), 3.82 (q, 6H, $J=7.0\text{Hz}$, OCH_2) according to literature¹⁰⁷.
- **$^{13}\text{C NMR}$ (DMSO-d_6):** δ (ppm) = 7.58 ($\text{N}_3\text{CH}_2\text{CH}_2\text{CH}_2\text{Si}$), 18.25 ($\text{SiOCH}_2\text{CH}_3\text{Si}$), 22.63 ($\text{N}_3\text{CH}_2\text{CH}_2\text{CH}_2$), 53.80 ($\text{N}_3\text{CH}_2\text{CH}_2\text{CH}_2$), 58.42 ($\text{SiOCH}_2\text{CH}_3$).
- **IR:** ν (thin film, cm^{-1}) = 2974, 2927, 2885, 2358, 2093, 1443, 1390, 1365, 1344, 1276, 1242, 1166, 1100, 1074, 945, 831, 774, 703, 687, 681.

References

Synthesis of 3,4,6-tri-O-acetyl-2-amino-2-deoxy- β -D-glucopyranose,1-[(1H-1,2,3-triazol-4-yl)methyl]-1-(3-propyltriethoxysilane)] **33**

Alkynyl compound **29** (0.100 g, 0.29 mmol) was dissolved in tetrahydrofuran (3 mL) and solution of 3-Azidopropyltriethoxysilane (0.072 g, 0.29 mmol) in tetrahydrofuran (1 mL) was added, and after copper iodide (3.2 mg, 0.0174 μ mol). Mixture was stirred overnight in room temperature. Solution was concentrated, and dried on vacuum pump to give 0.126 g of triazole compound.

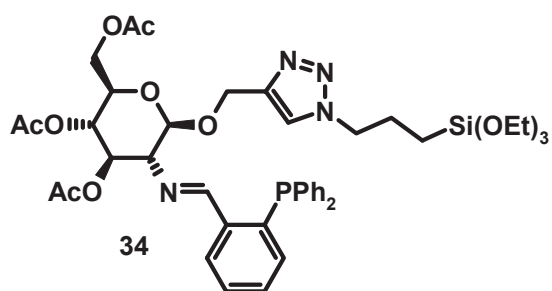


- Yield 74%
- Green solid
- m.p. 64-65 °C
- $[\alpha]_D^{20} = -15.6$ (c = 1.06 chloroform)

- $^1\text{H NMR}$ (CDCl_3): δ (ppm) = 0.59 (m, 2H, CH_2Si), 1.20 (t, 9H, $J=7.0\text{Hz}$, OCH_2CH_3), 1.97-2.10 (m, 2H, $\text{CH}_2\text{CH}_2\text{N}_3$, 9H, COCH_3), 3.68-3.75 (m, 1H), 3.80 (q, 6H, $J=7.0\text{Hz}$, OCH_2), 4.13 (d, 1H, $J=12.3\text{Hz}$), 4.23-4.53 (m, 4H), 4.79-5.13 (m, 4H), 7.61 (s, 1H).
- $^{13}\text{C NMR}$ (CDCl_3): δ (ppm) = 7.4 (CH_2Si), 18.2 ($\text{Si}(\text{OCH}_2\text{CH}_3)_3$), 20.5 (COCH_3), 20.6 (COCH_3), 20.7 (COCH_3), 24.1 ($\text{CH}_2\text{CH}_2\text{Si}$), 52.4 (OCH_2), 58.4 ($\text{Si}(\text{OCH}_2\text{CH}_3)_3$), 62.1 (C-6), 63.1 (C-2), 64.4 (C-5), 68.6 (C-4), 71.7 ($\text{CH}_2\text{CH}_2\text{CH}_2\text{Si}$), 74.2 (C-3), 101.6 (C-1), 122.5 (C=CH-“triazole ring”), 169.4 (COCH_3), 169.6 (COCH_3), 169.8 (COCH_3), 170.5 (C=CH-“triazole ring”).
- **IR**: ν (thin film, cm^{-1}) = 2975, 2929, 2889, 1744, 1599, 1444, 1366, 1322, 1295, 1232, 1216, 1167, 1146, 1099, 1068, 1026, 985, 948, 922, 899, 884, 846, 790, 766, 724, 681.
- **ESI full ms** calcd. for $\text{C}_{24}\text{H}_{43}\text{N}_4\text{O}_{11}\text{Si}$ ($\text{M} + \text{H}^+$): 591.2698, found 591.2692.

Synthesis of 3,4,6-tri-O-acetyl-2-deoxy-2-{[2-(diphenylphosphino)benzoyl]imino}- β -D-glucopyranose,1-[(1H-1,2,3-triazol-4-yl)methyl]-1-(3-propyltriethoxysilane)] **34**

In a Schlenk tube under argon atmosphere, triazole compound **33** (0.728 g, 1.23 mmol), and 2-diphenylphosphinobenzoic aldehyde (0.322 g, 1.11 mmol), were stirring with MgSO_4 in dry, degassed toluene in 60 °C. After being stirred for 5 hours in 60 °C, solution was filtered under argon, MgSO_4 washed with deglazed toluene and the solvents were evaporated, mixture was dried on vacuum pump (m = 0.969g).



- Yield 94%
- Orange solid
- $[\alpha]_D^{20} = -11.04$ ($c = 1.06$, chloroform)

- $^1\text{H NMR}$ (CDCl_3): δ (ppm) = 0.46 (m, 2H, CH_2Si), 1.13 (t, 9H, $\text{J}=7.0\text{Hz}$, $\text{Si}(\text{OCH}_2\text{CH}_3)_3$), 1.59 (s, 3H, CH_3), 1.82 (m, 2H, $\text{CH}_2\text{CH}_2\text{Si}$), 1.93 (s, 3H, CH_3), 2.01 (s, 3H, CH_3), 3.27 (dd, 1H, $\text{J}=8.0\text{Hz}$, $\text{J}=9.6\text{Hz}$, H-2), 3.72 (q, 6H, $\text{J}=7.0\text{Hz}$, $\text{Si}(\text{OCH}_2\text{CH}_3)_3$), 3.77-3.79 (m, 1H, H-5), 3.98-4.16 (m, 3H, $\text{CH}_2\text{CH}_2\text{CH}_2\text{Si}$, H-6), 4.25 (dd, 1H, $\text{J}=4.8\text{Hz}$, $\text{J}=12.3\text{Hz}$, H-6'), 4.63 (d, 1H, $\text{J}=6.6\text{Hz}$, H-1), 4.71 (s, 2H, CH_2), 4.98 (dd, 1H, $\text{J}=9.6$, Hz, $\text{J}=9.6\text{Hz}$, H-4), 5.21 (dd, 1H, $\text{J}=9.6\text{Hz}$, $\text{J}=9.6\text{Hz}$, H-3), 6.88 (dd, 1H, $\text{J}=4.8\text{Hz}$, $\text{J}=6.6\text{Hz}$, H_{arom}), 7.04-7.59 (m, 14H, H_{arom}), 7.85 (bs, 1H, NCH), 8.90 (d, 1H, $\text{J}=3.8\text{Hz}$, $\text{C}=\text{CH}$).
- $^{13}\text{C NMR}$ (CDCl_3): δ (ppm) = 7.4 (CH_2Si), 18.2 ($\text{Si}(\text{OCH}_2\text{CH}_3)_3$), 20.2 (COCH_3), 20.6 (COCH_3), 20.7 (COCH_3), 24.1 ($\text{CH}_2\text{CH}_2\text{Si}$), 52.4 ($\text{CH}_2\text{CH}_2\text{CH}_2\text{Si}$), 58.4 ($\text{Si}(\text{OCH}_2\text{CH}_3)_3$), 62.1 (C-6), 63.3 (OCH_2), 68.4 (C-4), 71.8 (C-5), 73.1 (C-3), 73.1 (C-2), 100.6 (C-1), 122.6 ($\text{C}=\text{CH}$ -“triazole ring”), 125.1-144.5 (18 x C_{arom}), 166.5 (NCH), 169.6 (COCH_3), 169.7 (COCH_3), 169.8 (COCH_3), 170.6 ($\text{C}=\text{CH}$ -“triazole ring”).
- $^{31}\text{P NMR}$ (CDCl_3): δ (ppm) = -15.17
- **IR:** ν (thin film, cm^{-1}) = 3054, 2974, 2927, 2883, 2323, 2109, 1980, 1745, 1638, 1585, 1560, 1480, 1435, 1365, 1223, 1163, 1099, 1069, 1028, 956, 784, 746, 696, 695, 678.
- **ESI full ms** calcd. for $\text{C}_{43}\text{H}_{56}\text{N}_4\text{O}_{11}\text{PSi}$ ($\text{M} + \text{H}^+$): 863.3447, found 863.3420.

References

References

1. P. T. Anastas, J. C. Warner, *Green Chemistry: Theory and Practice*, Oxford University Press, USA, **1998**.
2. P. T. Anastas, M. M. Kirchhoff, T. C. Williamson, *Appl. Catal. A: General*, **2001**, 221, 3-13.
3. "Collection of Emil Fischer Papers" (Bancroft Library, University of California, Berkeley), were summarized by Professor Frieder W. Lichtenthaler in his article (*Angew. Chem. Int. Ed.*, **1992**, 31, 1541-1556).
4. (a) H. D. K. Drew, W. N. Haworth, *J. Chem. Soc.*, 1926, 2303-2310 (b) W. N. Haworth, E. L. Hirst, A. Learner, *J. Chem. Soc.*, **1927**, 1040-1047.
5. Reviews: a) M. M. K. Boysen, *Chem. Eur. J.*, **2007**, 13, 8648-8659, (b) M. Diéguez, C. Claver, O. Pàmies, *Eur. J. Org. Chem.*, **2007**, 4621-4634; (c) M. Diéguez, O. Pàmies, C. Claver, *Chem. Rev.*, **2004**, 104, 3189-3215; (d) M. Diéguez, O. Pàmies, A. Ruiz, Y. Diaz, S. Castillon, C. Claver, *Coord. Chem. Rev.*, **2004**, 248, 2165-2192.
6. For recent reviews see: (a) R. K. Shukla, A. Tiwari, *Critical Reviews in Therapeutic Drug Carrier Systems*, **2011**, 28, 255-292. (b) H. M. I. Osborn, P. G. Evans, N. Gemmell, S. D. Osborne, *Molecular Pathomechanisms and New Trends in Drug Research*, **2003**, 178-190.
7. B. Brauckmann, *CLB Chemie in Labor und Biotechnik*, **2003**, 54, 292-295.
8. Examples: (a) K-H. Renz, B. Schleifenbaum, J. Uhlemann, F. Saleeb, DE 10219228 **2003**, (b) R. C. McIver, F. Vlad, R. A. Golding Jr, T. D. Leichssenring, D. Benczedi., WO 2002065858, **2002**, (c) O. Chmiel, R. T.-S. Liu, M. Furrer, D.F. Rushmore, WO 9623423 **1996**.
9. (a) M. Beller, J.G.E. Krauter, A. Zapf, *Angew. Chem. Int. Ed.*, **1997**, 36, 772-774, (b) M. Beller, J. G. E. Krauter, A. Zapf, S. Bogdanovic, *Catal. Today*, **1999**, 48, 279-290.
10. H. Park, T. V. RajanBabu, *J. Am. Chem. Soc.*, **2002**, 124, 734-735.
11. H. Park, R. Kumareswaran, T. V. RajanBabu, *Tetrahedron*, **2005**, 17, 6352-6367.
12. (a) R. Del Litto, A. De Roma, A. D'Errico, S. Magnolia, F. Ruffo, *Tetrahedron: Asymmetry*, **2006**, 17, 2265-2269, (b) V. Benessere, A. De Roma, F. Ruffo, *ChemSusChem.*, **2008**, 1, 425-430, (c) A. De Roma, F. Ruffo, S. Woodward, *Chem. Commun.*, **2008**, 5384-5386.
13. B. M. Trost D. L. Van Vranken, and C. Bingel, *J. Am. Chem. Soc.*, **1992**, 114, 9327-9343.
14. (a) T. V. RajanBabu, T. A. Ayers, A. L. Casalnuovo, *J. Am. Chem. Soc.*, **1994**, 116, 4101-4102. (b) T. V. RajanBabu, T. A. Ayers, G. A. Halliday, K. K. You, J. C. Calabrese, *J. Org. Chem.*, **1997**, 62, 6012-6028.
15. D. A. Holland, D. J. Laidler, D. A. Milner, *J. Mol. Catal.*, **1981**, 119-127.
16. (a) C. Borriello, M.E. Cucciolo, A. Panunzi, F. Ruffo, *Tetrahedron: Asymmetry*, **2001**, 12, 2467-2471, (b) C. Borriello, M. E. Cucciolo, A. Panunzi, F. Ruffo, A. Saporito, *Inorg. Chem. Commun.*, **2003**, 6, 1081-1085.
17. (a) M. Irmak, A. Groschner, M. M. K. Boysen, *Chem. Commun.*, **2007**, 177-179, (b) T. Minuth, M. Irmak, A. Groschner, T. Lehnert, M. M. K. Boysen, *Eur. J. Org. Chem.*, **2009**, 997-1008, (c) T. Minuth, M. M. K. Boysen, *Synlett.*, **2008**, 1483-1486.

18. B. V. Subba Reddy , Jimil George, *Tetrahedron: Asymmetry*, **2011**, 22, 1169-1175.
19. B. Gläser, H. Kunz, *Synlett*, **1998**, 53-54.
20. (a) K., Yonehara, T.; Hashizume, K.; Mori, K.; Ohe, S. Uemura, *Chem. Commun.* **1999**, 415-416, (b) K., Yonehara, T.; Hashizume, K.; Mori, K.; Ohe, S. Uemura, *J. Org. Chem.* **1999**, 64, 9374-9380, (c) K. Yonehara, K. Mori, T. Hashizume, K. G. Chung, K. Ohe, S. Uemura, *J. Organomet. Chem.*, **2000**, 40-49.
21. (a) Y. Mata, M. Diéguez, O. Pàmies, C. Claver, *Adv. Synth. Catal.* **2005**, 347, 1943-1947, (b) Y. Mata, M. Diéguez, O. Pàmies, C. Claver, *Org. Lett.* **2005**, 7, 5597-5599, (c) Y. Mata, O. Pàmies, M. Diéguez, *Chem. Eur. J.* **2007**, 13, 3296-3304, (d) M. Diéguez, J. Mazuela, O. Pàmies, J. J. Verendel, P. G. Andersson, *J. Am. Chem. Soc.* **2008**, 130, 7208-7209, (e) J. Mazuela, P. Norrby, P. G. Andersson, O. Pàmies, M. Diéguez, *J. Am. Chem. Soc.*, **2011**, 133, 13634-13645.
22. (a) C. Shen, H. Xia, H. Zheng, P. Zhang, X. Chen, *Tetrahedron: Asymmetry*, **2010**, 21, 1936-1941, (b) H. Xia, H. Yan , C. Shen, F. Shen, P. Zhang, *Catal. Commun.*, **2011**, 16, 155-158.
23. N. Khiar, R. Navas, I. Fernández, *Tetrahedron Lett.*, **2012**, 53, 395-398.
24. (a) M. Tollabi, E. Framery, C. Goux-Henry, D. Sinou *Tetrahedron: Asymmetry*, **2003**, 14, 3329-3333, (b) A. Konovets, K. Glegoła, A. Penciu, E. Framery, P. Jubault, C. Goux-Henry, K. M. Pietrusiewicz, J. C. Quirion, D. Sinou, *Tetrahedron: Asymmetry*, **2005**, 16, 3183-3187, (c) K. Glegoła, E. Framery, C. Goux-Henry, K. M. Pietrusiewicz, D. Sinou, *Tetrahedron*, **2007**, 63, 7133-7141.
25. (a) S. Parisot, R. Kolodziuk, C. Goux-Henry, A. Iourtchenko, D. Sinou, *Tetrahedron Lett.*, **2002**, 43, 7397-7400. (b) R. Kolodziuk, A. Penciu, M. Tollabi, E. Framery, C. Goux-Henry, A. Iourtchenko, D. Sinou, *J. Organomet. Chem.*, **2003**, 687, 348-391. (c) A. Konovets, A. Penciu, E. Framery, N. Percina, C. Goux-Henry, D. Sinou, *Tetrahedron Lett.*, **2005**, 46, 3205-3208.
26. (a) S. A. Johannesen, K. Glegoła, D. Sinou, E. Framery, T. Skrydstrup, *Tetrahedron Lett.*, **2007**, 48, 3569-3573, (b) K. Glegoła, S. A. Johannesen, L. Thim, C. Goux-Henry, T. Skrydstrup, E. Framery, *Tetrahedron Lett.*, **2008**, 49, 6635-6638.
27. (a) V. Benessere, F. Ruffo, *Tetrahedron: Asymmetry*, **2010**, 21, 171-176, (b) V. Benessere, M. Lega, A. Silipo, F. Ruffo, *Tetrahedron*, **2011**, 67, 4826-4831.
28. (a) T. Bauer, J. Tarasiuk, K. Paśniczek, *Tetrahedron: Asymmetry*, **2002**, 13, 77-82, (b) T. Bauer, S. Smoliński, *Appl. Catal. A: General*, **2010**, 375, 247-251, (c) T. Bauer, S. Smoliński, P. Gaweł, J. Jurczak, *Tetrahedron Lett.*, **2011**, 52, 4882-4884.
29. D. Cheng, F. Gan, W. Qian, W. Bao, *Green Chem.*, **2008**, 171-173.
30. K. G. Thakur, D. Ganapathy, G. Sekar, *Chem. Commun.*, **2011**, 5076-5078.
31. N. Khiar, B. Suárez, I. Fernández, *Inorg. Chim. Acta*, **2006**, 359, 3048-3053.
32. M. Irmak, T. Lehnert, M. M. K. Boysen, *Tetrahedron Lett.*, **2007**, 48, 7890-7893, (b) M. Irmak, M. M. K. Boysen, *Adv. Synth. Catal.*, **2008**, 350, 403-405.
33. V. Benessere, R. Del Litto, F. Ruffo, C. Moberg, *Eur. J. Org. Chem.*, **2009**, 1352-1356.
34. M. E. Cucciolito, R. Del Litto, G. Roviello, F. Ruffo, *J. Mol. Catal. A*, **2005**, 236, 176-181.

References

35. D. Chatterjee, S. Basak, A. Mitra, A. Sengupta, J. Le Bras, J. Muzart, *Inorg. Chim. Acta.*, **2006**, 359, 1325-1328.
36. D. Chatterjee, S. Basak, J. Muzart, *J. Mol. Catal. A: Chem.*, **2007**, 271, 270-276.
37. M. H. Lin, T.V. RajanBabu, *Org. Lett.*, **2002**, 4, 1607-1610.
38. (a) C. Borriello, R. Del Litto, A. Panunzi, F. Ruffo, *Tetrahedron: Asymmetry*, **2004**, 15, 681-686, (b) C. Borriello, R. Del Litto, A. Panunzi, F. Ruffo, *Inorg. Chem. Commun.*, **2005**, 8, 717-721.
39. A. Tsutsui, H. Takeda, M. Kimura, T. Fujimoto, T. Machinami, *Tetrahedron Lett.*, **2007**, 48, 5213-5217.
40. (a) J. Agarwal, R. K. Peddinti, *Tetrahedron: Asymmetry*, **2010**, 21, 1906-1909, (b) J. Agarwal, R. K. Peddinti, *Tetrahedron Lett.*, **2011**, 52, 117-121.
41. S. Pedatella, M. De Nisco, D. Mastroianni, D. Naviglio, A. Nucci, R. Caputo, *Adv. Synth. Catal.* **2011**, 353, 1443-1446.
42. J. Agarwal, R. K. Peddinti, *J. Org. Chem.* **2011**, 76, 3502-3505.
43. C. Becker, C. Hoben, H. Kunz, *Adv. Synth. Catal.* **2007**, 349, 417-424.
44. C. Shen, F. Shen, H. Xia, P. Zhang, X. Chen, *Tetrahedron: Asymmetry*, **2011**, 22, 708-712.
45. A. Puglisi, M. Benaglia, L. Raimondi, L. Lay, L. Poletti, *Org. Biomol. Chem.*, **2011**, 9, 3295-3302.
46. O. Boutureira, J. F. McGouran, R. L. Stafford, D. P. G. Emmerson, B. G. Davis, *Org. Biomol. Chem.*, **2009**, 7, 4285-4288.
47. C. Schöberl, V. Jäger, *Adv. Synth. Catal.*, **2012**, 354, 790-796.
48. (a) D. P. G. Emmerson, R. Villard, C. Mugnaini, A. Batsanov, J. A. K. Howard, W. P. Hems, R. P. Tooze, B. G. Davis, *Org. Biomol. Chem.*, **2003**, 3826-3838, (b) D. P. G. Emmerson, W. P. Hems, B. G. Davis, *Org. Lett.*, **2006**, 8, 207-210.
49. *Ionic Liquids in Synthesis* (Eds.: P. Wasserscheid, T. Welton), Wiley-VCH, Weinheim, **2003**.
50. T. Hashizume, K. Yonehara, K. Ohe, S. Uemura, *J. Org. Chem.*, **2000**, 65, 5197-5201.
51. D. Horton, *Org. Synth.*, **1973**, 5, 1-4.
52. A. C. Cunha, L. O. R. Pereira, R. O. P. de Souza, M. C. B. V. de Souza, V. F. Ferreira, *Nucleosides, Nucleocides & Nucleic Acids*, **2001**, 20, 1555-1569.
53. G. A. Dilbeck, L. Field, A. Gallo, R. J. Gargiulo, *J. Org. Chem.* **1978**, 43, 4593-4596.
54. X. Hu, W. Zhang, I. Carmichael, A. S. Serianni, *J. Am. Chem. Soc.*, **2010**, 132, 4641-4652.
55. M. J. Burk, J. G. Allen *J. Org. Chem.*, **1997**, 62, 7054-7057.
56. D. Lafont, P. Boullanger, *Tetrahedron: Asymmetry*, **2006**, 17, 3368-3379.
57. A. Bertho, A. Révész, *Justus Liebigs Annalen der Chemie*, **1953**, 581, 161-167.
58. V. Benessere, A. De Roma, R. Del Litto, M. Lega, F. Ruffo, *Eur. J. Org. Chem.*, **2011**, 5779-5782.

59. (a) B. M. Trost D. L. Van Vranken, and C. Bingel, *J. Am. Chem. Soc.*, **1992**, 114, 9327-9343, (b) B. M. Trost, D. L. Van Vranken, C. Bingel, *Angew. Chem., Int. Ed. Eng.*, **1992**, 31, 228-230.
60. Examples of using Trost ligand in asymmetric catalysis: (a) B. M. Trost, R. C. Bunt, *J. Am. Chem. Soc.*, **1994**, 116, 4089-4090, (b) B. M. Trost, C. B. Lee, J. M. Weiss, *J. Am. Chem. Soc.*, **1995**, 117, 7247-7248, (c) B. M. Trost, M. G. Organ, G. A. O'Doherty, *J. Am. Chem. Soc.*, **1995**, 117, 9662-9670, (d) B. M. Trost, S. R. Pulley, *J. Am. Chem. Soc.*, **1995**, 117, 10143-10144, (e) B. M. Trost, R. C. Lemoine, *Tetrahedron Lett.*, **1996**, 37, 9161-9164, (f) B. M. Trost, G. R. Cook, *Tetrahedron Lett.*, **1996**, 37, 7485-7488.
61. For review, see: B. M. Trost, M. L. Crawley, *Chem. Rev.*, **2003**, 103, 2921-2943.
62. B. M. Trost, A. C. Krueger, R. C. Bunt, J. Zambrano, *J. Am. Chem. Soc.*, **1996**, 118, 6520-6521.
63. (a) R. Noyori, T. Ohkuma, *Angew. Chem. Int. Ed.*, **2001**, 40, 40-73, (b) T. Ohkuma, H. Ooka, S. Hashiguchi, T. Ikariya, R. Noyori, *J. Am. Chem. Soc.*, **1995**, 117, 2675-2676, (c) H. Doucet, T. Ohkuma, K. Murata, T. Yokozawa, M. Kozawa, E. Katayama, A. F. England, T. Ikariya, R. Noyori, *Angew. Chem. Int. Ed.*, **1998**, 37, 1703-1707, (d) R. Noyori, T. Ohkuma, *Pure Appl. Chem.*, **1999**, 71, 1493-1501, (e) R. Noyori, M. Koizumi, D. Ishii, T. Ohkuma, *Pure Appl. Chem.*, **2001**, 73, 227-232, (f) T. Ohkuma, M. Koizumi, M. Yoshida, R. Noyori, *Org. Lett.*, **2000**, 2, 1749-1751, (g) P. Cao, X. Zhang, *J. Org. Chem.*, **1999**, 64, 2127-2129, (h) T. Ohkuma, M. Koizumi, H. Doucet, T. Pham, M. Kozawa, K. Murata, E. Katayama, T. Yokozawa, T. Ikariya, R. Noyori, *J. Am. Chem. Soc.*, **1998**, 120, 13529-13530, (i) M. Kitamura, T. Ohkuma, S. Inoue, N. Sayo, H. Kumobayashi, S. Akutagawa, T. Ohta, H. Takaya, R. Noyori, *J. Am. Chem. Soc.*, **1988**, 110, 629-631, (j) T. Ohkuma, D. Ishii, H. Takeno, R. Noyori, *J. Am. Chem. Soc.*, **2000**, 122, 6510-6511, (k) T. Ohkuma, H. Ooka, T. Ikariya, R. Noyori, *J. Am. Chem. Soc.*, **1995**, 117, 10417-10418, (l) T. Ohkuma, H. Ikehira, T. Ikariya, R. Noyori, *Synlett*, **1997**, 467-468.
64. For recent reviews on asymmetric organocatalysis, see: (a) F. Giacalone, M. Gruttadauria, P. Agrigento, R. Noto, *Chem. Soc. Rev.*, **2012**, 41, 2406-2447, (b) B. R. Buckley, M. M. Farah, *Annu. Rep. Prog. Chem., Sect. B: Org. Chem.*, **2011**, 107, 102-117, (c) The special issue devoted to 'Asymmetric Organocatalysis': *Chem. Rev.*, **2007**, 107, 5413-5883.
65. M. S. Sigman, E. N. Jacobsen, *J. Am. Chem. Soc.*, **1998**, 120, 4901-4902.
66. T. Okino, Y. Hoashi, Y. Takemoto, *J. Am. Chem. Soc.*, **2003**, 125, 12672-12673.
67. Y. Sohtome, A. Tanatani, Y. Hashimoto, K. Nagasawa, *Tetrahedron Lett.*, **2004**, 45, 5589-5592.
68. Other examples: (a) D. E. Fuerst, E. N. Jacobsen, *J. Am. Chem. Soc.*, **2005**, 127, 8964-8965, (b) M. S. Taylor, N. Tokunaga, E. N. Jacobsen, *Angew. Chem. Int. Ed.*, **2005**, 44, 6700-6704, (c) T. Okino, S. Nakamura, T. Furukawa, Y. Takemoto, *Org. Lett.*, **2004**, 6, 625-627, (d) X. Xu, T. Furukawa, T. Okino, H. Miyabe, Y. Takemoto, *Chem. Eur. J.*, **2006**, 12, 466-476.
69. For review on use thiourea organocatalyst in organocatalysis see (a) W. Y. Siau, J. Wang, *Catal. Sci. Technol.*, **2011**, 1, 1298-1310, (b) S. J. Connon, *Synlett*, **2009**, 354-376.

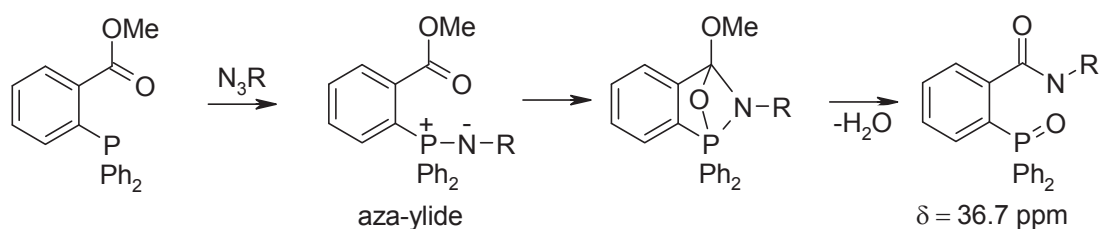
References

70. T. Okino, Y. Hoashi, T. Furukuwa, X. Xu, Y. Takemoto, *J. Am. Chem. Soc.*, **2005**, 127, 119-125.
71. A. Hamza, G. Schubert, T. Soós, I. Pápai, *J. Am. Chem. Soc.*, **2006**, 128, 13151-13160.
72. W. Leung, S. Cosway, R. H. V. Jones, H. McCann, M. Wills, *J. Chem. Soc., Perkin Trans. 1*, **2001**, 2588-2594.
73. Š. Vyskočil, M. Smrčina, V. Hanuš, M. Polášek, P. Kočovský, *J. Org. Chem.*, **1998**, 63, 7738-7748.
74. Y. D. Ward, L. A. Villanueva, G. D. Allred, S. C. Payne, M. A. Semones, L. S. Liebeskind, *Organometallics*, **1995**, 14, 4132-4156.
75. M. Widhalm, P. Wimmer, G. Klintschar, *J. Organometallic Chem.*, **1996**, 523, 167-178.
77. For review see: (a) Volume 242 devoted to “Immobilized Catalysts Solid Phases, Immobilization and Applications” from *Top. Curr. Chem.*, **2004**, (b) L. Alaerts, J. Wahlen, P. A. Jacobs, D. E. De Vos. *Chem. Commun.*, **2008**, 1727-1737, (c) B. Pugin, H.-U. Blaser, “Immobilized Complexes for Enantioselective Catalysis: the Industrial Perspective”, from *Catalysis by Metal Complexes*, **2010**, 33, 231-245. F. Zaera, (d) Q.-H. Fan, K. Ding “Enantioselective Catalysis with Structurally Tunable Immobilized Catalysts” from *Top. Organomet. Chem.*, **2011**, 36, 207-245 (e) *Catal Lett.*, **2012**, 142, 501-516.
78. Review: C. E. Song, S. Lee, *Chem. Rev.*, **2002**, 102, 3495-3524 Some selected application of silica matrix supported catalysts: (a) R. Sayah, E. Framery, V. Dufaud *Green Chem.*, **2009**, 11, 1694-1702, (b) R. Sayah, M. Le Floch, E. Framery, V. Dufaud, *J. Mol. Catal. A: Chemical*, **2010**, 315, 51-59, (c) R. Sayah, K. Glegoła E. Framery, V. Dufaud, *Adv. Synt. Cat.* **2007**, 349, 373-381.
79. Review: P. H. Toy, K. D. Janda, *Acc. Chem. Res.*, **2000**, 33, 546–554. Some selected application of poly(ethylene glycol)-supported catalysts: (a) M. Bandini, M. Benaglia, R. Sinisi, S. Tommasi, A. Umani-Ronchi, *Org. Lett.*, **2007**, 9, 2151-2153, (b) H.-X. Li, C. Xie, M.-W. Ding, Z.-M. Liu, G.-F. Yang, *Synlett.*, **2007**, 14, 2280-2282, (c) S. H. Hong, R. H. Grubbs, *Organic Lett.*, **2007**, 9, 1955-1957, (d) X. Wang, L. Yin, T. Yang, Y. Wang, *Tetrahedron: Asymm.*, **2007**, 18, 108-114.
80. For review see: (a) B. Cornils, *Supported aqueous-phase catalysis as the alternative method* from *Multiphase Homogeneous Catalysis* (Eds.: H. Delmas, U. Jauregui-Haza, A. M. Wilhelm), Wiley-VCH, Weinheim **2005**, 297-304, (b) M. E. Davis *Transitions to Heterogeneous Techniques (SAPC and Variations)*, from *Aqueous-Phase Organometallic Catalysis* (Eds.: B. Cornils, W. A. Herrmann), Wiley-VCH, Weinheim **1998**, 241-251.
81. (a) J. P. Arhancet, M. E. Davis, S. S. Merola, B. E. Hanson, *Nature* **1989**, 339, 454-455 (a) J. P. Arhancet, M. E. Davis, S. S. Merola, B. E. Hanson, *J. Catal.* **1990**, 121, 327-339, (b) J. P. Arhancet, M. E. Davis, B. E. Hanson, *J. Catal.* **1991**, 129, 94-99, (c) J. P. Arhancet, M. E. Davis, S. S. Merola, B. E. Hanson, *J. Catal.* **1991**, 129, 100-105, (d) I. Tóth, I. Guo, B. E. Hanson, *J. Mol. Catal.* **1997**, 116, 217-229, (e) S. C. Tsang, N. Zhang, L. Fellas, A. M. Steele, *Catal. Today* **2000**, 61, 29-36.
82. (a) P. Schneider, F. Quignard, A. Choplin, D. Sinou, *New J. Chem.*, **1996**, 20, 545-547, (b) S. Dos Santos, Y. Tong, F. Quignard, A. Choplin, D. Sinou, J. P. Dutasta, *Organometallics*, **1998**, 17, 78-89, (c) A. Choplin, S. Dos Santos, F. Quignard, S.

- Sigismondi, D. Sinou, *Catal. Today*, **1998**, 42, 471-478, (d) S. Dos Santos, F. Quignard, D. Sinou, A. Choplin, *Top.Catal.*, **2000**, 13, 311-318.
83. J. Seayed, A. M. Seayed, B. R. Sarkar, R. V. Chaudhari, US 20020137964 **2002**.
84. For selected reviews see: (a) N. Miyaura and A. Suzuki, *Chem. Rev.*, **1995**, 95, 2457-2483, (b) Volume 219 devoted to "Cross-Coupling Reactions A Practical Guide" from *Top. Curr. Chem.*, **2002**, (c) V. Farina, *Adv. Synth. Catal.*, **2004**, 346, 1553-1582, (d) N. T. S. Phan, M. Van Der Sluys, C. W. Jones, *Adv. Synth. Catal.*, **2006**, 348, 609-679, (e) C. Torborg, M. Beller, *Adv. Synth. Catal.*, **2009**, 351, 3027-3043.
85. For selected examples see: (a) Y. Uozumi, H. Danjo, T. Hayashi, *J. Org. Chem.*, **1999**, 64, 3384-3384, (b) K. Inada, N. Miyaura, *Tetrahedron*, **2000**, 56, 8661-8664, (c) A. Datta, F. Ebert, H. Plenio, *Organometallics*, **2003**, 22, 4685-4691, (d) K. Glegoła, E. Framery, K. M. Pietrusiewicz, D. Sinou, *Adv. Synth. Catal.*, **2006**, 348, 1728-1733.
86. For selected examples see:(a) E. Paetzold, I. Jovel, G. Oehme, *J. Mol. Catal. A: Chem.*, **2004**, 214, 241-247 (b) R. Sayah, K. Glegola, E. Framery, V. Dufaud, *Adv. Synth. Catal.*, **2007**, 349, 373-381, (c) N. J. S. Costa, P. K. Kiyohara, A. L. Monteiro, Y. Coppel, K. Philippot, L. M. Rossi, *J. Catal.*, **2010**, 276, 382-389, (d) W. Chen, P. Li, L. Wang, *Tetrahedron*, **2011**, 67, 318-325.
87. Examples: (a) D. Badone, M. Baroni, R. Cardamone, A. Ielmini, U. Guzzi, *J. Org. Chem.*, **1997**, 62, 7170-7173 (b) N. A. Bumagin, V. V. Bykov, *Tetrahedron*, **1997**, 53, 14437-14450, (c) J. C. Bussolari, D. C. Rehborn, *Org. Lett.*, **1999**, 1, 965-967, (d) L. M. Klingensmith, N. E. Leadbeater, *Tetrahedron Lett.*, **2003**, 44, 765-768; (e) X. Tao, Y. Zhao, D. Shen, *Synlett*, **2004**, 359-361.
88. H. Myszka, D. Bednarczyk, M. Najder, W. Kaca, *Carbohydrate Research*, **2003**, 338, 133-141.
89. P. A. Wender, J. L. Baryza, *Org. Lett.*, **2005**, 7, 1177-1180.
90. Ouisam Adidou, Cloude Bernard University Lyon 1, thesis 2009.
91. M. Sharama, G. G. Potti, O. D. Simmons, W. Korytnyk, *Carbohydrate Research*, **1987**, 163, 41-51.
92. J. M. Anderson; E. Percival, *J. Chem. Soc.*, **1956**, 814-819.
93. Y. Nagai, N. Ito, Y. Tokuda, S. Ohba, T. Sugai, *Bull. Chem. Soc. Jpn.*, **2004**, 1181-1186.
94. W. Muramatsu, K. Mishiro, Y. Ueda, T. Furuta, T. Kawabata, *Eur. J. Org. Chem.*, **2010**, 827-831.
95. (a) D. Lafont, P. Boullanger, O. Cadas, G. Descotes, *Synthesis*, **1989**, 191-194, (b) R. Thomson, M. von Itzstein, *Carbohydrate Research*, **1995**, 274, 29-44.
96. U. Zehavi, N. Sharon, *J. Org. Chem.*, **1964**, 29, 3654-3658.
97. (a) M. Murakami, K. Ikeda, K. Achiwa, *Carbohydrate Research*, **1996**, 280, 101-110, (b) P. R. Sridhar, V. Saravanan, S. Chandrasekaran, *Pure Appl. Chem.*, **2005**, 77, 145-153, (c) S. Buchini, A. Buschiazzo, S. G. Withers, *Angew. Chem. Int. Ed.*, **2008**, 47, 2700-2703, (d) Y. Horita, T. Takii, T. Chiba, R. Kuroishi, Y. Maeda, Y. Kurono, E. Inagaki, K. Nishimura, Y. Yamamoto, C. Abe, M. Mori, K. Onozaki, *Bioorg. Med. Chem. Lett.*, **2009**, 19, 6313-6316.
98. C. J. Morel, *Helv. Chim. Acta*, **1958**, 1501-1503.

References

99. S. Ogawa, H. Fujimori, T. Suami, *Bull. Chem. Soc. Jpn.*, **1976**, 2585-2586.
100. For review of Huisgen 1,3-dipolar cycloaddition see: M. Meldal, C. W. Tornøe, *Chem. Rev.*, **2008**, 108, 2952-3015.
101. (a) T. Wang, J. F. Kadow, Z. Zhang, Z. Yin, N. A. Meanwell, A. Regueiro-Ren, J. Swidorski, Y. Han, D. J. Carini, US 20070249579, **2007**. (b) K. Thede, I. Flamme, F. Oehme, J.-K. Ergueden, F. Stoll, J. Schhmacher, H. Wild, P. Kolkhof, H. Beck, J. Keldenich, M. Akaba, M. Jeske, WO2008067871, **2008**, (c) F. Stieber, O. Schadt, D. Dorsch, A. Blaukat, WO 2008145243, (d) T. Wang, J. F. Kadow, Z. Zhang, Z. Yin, N. A. Meanwell, A. A. Regueiro-Ren, J. Swidorski, Y. Han, D. J. Carini, L. Hamann US 20080139572, **2008**, (e) I. Akritopoulou-Zanze, B. D. Wakefield, H. Mack, S. C. Turner, A. F. Gasiiecki, V. J. Gracias, K. Sarris, D. M. Kalvin M. J. Michmerhuizen Q. Shuai, J. R. Patel, M. Bakker, N. Teusch, E. T. Johnson, P. Kovar, S. W. Djuric, A. J. Long, A. Vasudevan, A. Hobson, N. St John Moore, L. Wang, D. George, B. Li, K. Frank, WO 2008154241 (f) R. Mueller, L. J. Street, S. Rachwal, K. Alisala, Kashinatham, WO 2009038752, **2009**.
102. Possible pathway of Strodinger ligation with methyl ester of 2-diphenylphosphino benzoic acid was proposed before: E. Saxon, S. J. Luchansky, H. C. Hang, C. Yu, S. C. Lee, C. R. Bertozzi, *J. Am. Chem. Soc.*, **2002**, 14893-14902.



103. G. D. Chukin, V. I. Malevich, *Appl. Spectrosc.*, **1977**, 26, 223-229.
104. N. Miller, G. M. Williams, M. A. Brimble, *Org. Lett.*, **2009**, 11, 2409-2412.
105. For selected examples, see: (a) A. Gissibl, M. G. Finn, O. Reiser, *Org. Lett.*, **2005**, 7, 2325-2328, (b) A. Gheorghe, A. Matsuno, O. Reiser, *Adv. Synth. Catal.*, **2006**, 348, 1016-1020, (c) S. L. Jain, A. Modak, A. Bhaumik, *Green Chem.*, **2011**, 13, 586-590; (d) Y. He, C. Cai, *Chem. Commun.*, **2011**, 47, 12319-12321, (e) E. Alza, S. Sayalero, P. Kasaplar, D. Almas, M. A. Pericàs *Chem. Eur. J.*, **2011**, 17, 11585-11595.
106. In literature for o-diphenylphosphonylbenzoic acid $\delta = 28 \text{ ppm}$ (in DMF) see: N. A. Bondarenko, E. N. Tsvetkov, E. I. Matrosov, M. I. Kabachnik, *Russian Chemical Bulletin*, **1981**, 30, 1289-1293.
107. M. Ortega-Muñoz, J. Lopez-Jaramillo, F. Hernandez-Mateo, F. Santoyo-Gonzalez, *Adv. Synth. Catal.*, **2006**, 348, 2410-2420.
108. Y. Kitamura, A. Sakurai, T. Udzu, T. Maegawa, Y. Monguchi, Hironao Sajiki, *Tetrahedron*, **2007**, 63, 10596-10602.
109. B. Sreedhar, D. Yada, P. S. Reddy, *Adv. Synth. Catal.*, **2011**, 353, 2823-2836.
110. G. Bing-Tao, W. Yang, L. Bi-Jie, Y. Da-Gang, S. Zhang-Jie, *J. Am. Chem. Soc.*, **2008**, 130, 14468-14470.
111. L. Lin, L. Yanchun, Z. Suobo, L. Shenghai, *Synlett*, **2011**, 12, 1779-1783.
112. A. B. Foster, D. Horton, N. Salim, M. Stacey, J. M. Webber, *J. Chem. Soc.*, **1960**, 2587-2796.

113. H. Homiyama, N. Ueyama, M. Yanagiya, Y. Ohkur, US6858724 B2, **2002**.
114. A. Baccaro, A. Marx, *Chem. Eur. J.*, **2010**, 16, 218-226.

*General conclusions
and recommendations for future work*

General conclusions

Green chemistry constitutes a good theoretical framework for pollution prevention in the development of chemical products and processes. The 12 guiding principles offered by this framework are useful as fundamental approaches motivating and inspiring chemists and chemical engineers to design chemical products and processes that reduce or eliminate the use and generation of hazardous substances.

This work involved the synthesis and the application of the new ligands derived from D-glucosamine compound easy available from biomass. Compounds were designed especially for two kind of catalysis, homogeneous catalysis and heterogeneous catalysis.

Among ligands for homogeneous catalysis were compounds based on 1,2- β -glucodiamine which is structural analogous of 1,2-cyclohexdiamine. Various ligands and catalysts were prepared to perform a series of metal-catalyzed or organocatalyzed reactions such as allylic alkylation, hydrogenation and Michael addition.

Heterogeneous SAPC system was prepared without the use of tedious protecting and deprotecting steps that allows time-, money- and atom-economies. Its efficiency was demonstrated in catalytic reactions with various substrates, moreover catalyst can be easily isolated and reused four times without loss of activity.

Also attempts for preparing heterogeneous catalysts easily that could be easy separated after catalytic reactions by simple filtration were made. Unfortunately, because of the high oxygen affinity of the trivalent phosphorus, synthesis of ligands was not successful.

Taking care of environment and consider economic reasons use of water poly(ethylene) glycol can be good support for ligands and seems to be very interesting object because they are known to be inexpensive, thermally stable, and nontoxic. For this reason synthesis of poly(ethylene) glycol containing ligand was made and work are ongoing.

Annex A

Abstract of the PhD Thesis in English

Abstract of the PhD Thesis in French

(Résumé en Français)

Abstract in English

Several ligands derived from D-glucosamine, designed for different catalytic reactions have been synthesized. The ligands for homogeneous catalysis based on 1,2- β -glucodiamine were prepared, and used in reactions of allylic alkylation, hydrogenation and Michael addition.

Supported Aqueous Phase Catalyst (SAPC) system was prepared from D-glucosamine and use with very good results in Suzuki Miyaura cross coupling reactions. Catalyst was also recycled. Attempt to prepare ligands grafted on SBA-silica matrix were made as well as ligands containing poly(ethylene) glycol moiety.

Keywords:

D-glucosamine, „Green chemistry”, allylic alkylation, hydrogenation, organocatalysis, PEG, Silica supported catalysts, SAPC, homogeneous catalysis, heterogeneous catalysis.

Résumé en Français

Plusieurs ligands dérivés de la D-glucosamine, conçus pour différentes réactions catalytiques, ont été synthétisés. Les ligands pour la catalyse homogène basés sur 1,2- β -glucodiamine ont été préparés, et utilisés dans des réactions d'alkylation allylique, d'hydrogénation et d'addition de Michael.

La D-glucosamine a été utilisée pour la préparation de catalyseur type de SPAC (Supported Aqueous Phase Catalyst). Ce catalyseur hétérogène a été utilisé avec de très bons résultats dans les réactions de couplage croisé de Suzuki Miyaura. Le catalyseur a également été recyclé. Des essais de préparation de ligands greffés sur une matrice de silice de type SBA-15 ont été réalisés ainsi que des ligands à base de poly (éthylène) glycol.

Mots-clés:

D-glucosamine, „chimie verte”, alkylation allylique, hydrogénation, organocatalyse, PEG, les catalyseurs supportés sur silice, SAPC, catalyse homogène, catalyse hétérogène.

Annex B

Abstract of the PhD Thesis in Polish
(Streszczenie Dysertacji)

D-GLUKOZAMINA JAKO "ZIELONY" SUBSTRAT
W SYNTEZIE LIGANDÓW DLA POTRZEB
KATALIZY ASYMETRYCZNEJ

Wstęp

Tematyka pracy doktorskiej:

Tematyka pracy koncentruje się na syntezie i wykorzystaniu ligandów opartych na strukturze D-glukozaminy. Ten amino cukier otrzymywany jest poprzez hydrolizę polisacharydów takich jak chitozan czy chityna, które wchodzą w skład pancerzyków skorupiaków i innych stawonogów, ścian komórkowych grzybów i wielu innych organizmów. Łatwa dostępność biomasy wykorzystywanej w celu uzyskania glukozaminy sprawia, że jest ona również interesującym materiałem startowym, którego cena wynosi ok. 1 zł za 1 g związku (Acros Organics). Również ze względu na obecność pięciu centrów stereogennych jest cennym naturalnym źródłem chiralności.

Ze względu na to, że glukozamina może być łatwo zmodyfikowana i sfunkcjonalizowana w ciągu ostatnich dwóch dekad zainteresowanie tym węglowodanem znacznie wzrosło. D-glukozamina zaczęła być używana w syntezie chiralnych odczynników, ligandów a także organokatalizatorów.

Kluczowe hasła:

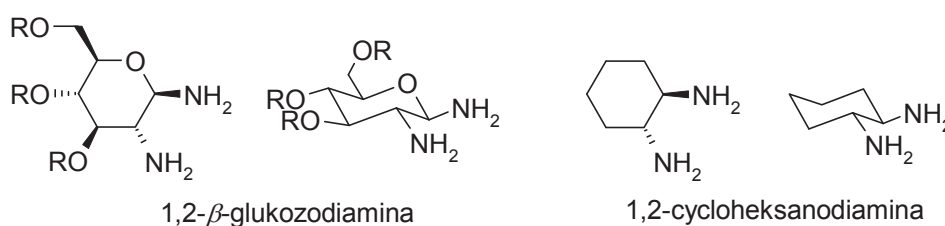
D-glukozamina, 1,2- β -glukodiamina, „Zielona chemia”, substytucja alkilowa, uwodornienie, organokataliza, PEG, katalizatory umieszczone na żelu krzemionkowym, SAPC, kataliza homogeniczna, kataliza heterogenna.

Cel projektu

Jednym z celów pracy było opracowanie strategii, która pozwoliłaby na umieszczenie w strukturze któregoś z węglowodanów istotnych funkcji znanych ligandów i przekształcanie jej w nowe ligandy wzbogacone o chiralność szkieletu węglowego i wykorzystanie tych ligandów w wybranych procesach asymetrycznej katalizy homogennej z udziałem kompleksów metali przejściowych jako katalizatorów.

Strukturą z wyboru stała się 1,2- β -glukozodiamina, którą można było otrzymać z łatwo dostępnej D-glukozaminy i która swą strukturą przypominała znany prekursor chiralnych ligandów jakim jest *trans*-1,2-cykloheksylo-diamina ze względu na występowanie w obu związkach sąsiadujących grup aminowych w *trans*-diekwatorialnej pozycji w pierścieniu sześciocłonowym (

Rysunek 1).



Rysunek 1 Struktury 1,2- β -glukozodiaminy i 1,2-cykloheksanodiaminy.

Kolejnym z celów pracy było przygotowanie katalizatorów także dla katalizy heterogenicznej. Pomimo, że w literaturze opisanych jest wiele przykładów użycia ligandów bazujących na wykorzystaniu D-glukozaminy w katalizie homogennej, ich produktywność wymaga jednak dalszego usprawnienia w celu osiągnięcia np. wysokiej liczby cykli katalitycznych (ang turnover number-TON). Oczekiwano, że zadanie takie mogłoby być zrealizowane poprzez heterogenizację katalizatorów otrzymanych przeze mnie wcześniej dla potrzeb procesów prowadzonych w środowisku homogennym.

Rozdział 1 Część literaturowa

Celem przeglądu literaturowego stanowiącego *Rozdział 1* dysertacji było przedstawienie aktualnego stanu wiedzy dotyczącej związków na bazie D-glukozaminy dla katalizy homogennej i heterogennej. Opisane zostały tylko te pochodne D-glukozaminy, które zawierały w swej strukturze pierścień piranozowy natomiast acykliczne i heterocykliczne pochodne D-glukozy zostały pominięte. Przedstawione zostały wszystkie przykłady użycia tego typu ligandów (*Rozdziały 1.1-1.2, 1.5-1.6*), organokatalizatorów (*Rozdział 1.3*) i reagentów (*Rozdział 1.4*), oraz omówione zostały najlepsze wyniki w reakcjach katalitycznych z poszczególnymi pochodnymi, opisane w literaturze do kwietnia 2012.

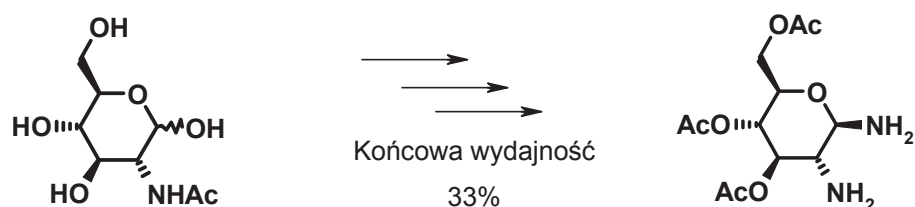
Ligandy homogeniczne podzielone zostały w zależności od typu grupy donorowej na homodonorowe (*Rozdział 1.1*) i heterodonorowe (*Rozdział 1.2*) i uszeregowane w pierwszej kolejności w zależności od atomu donora (P, N, S, O), a następnie od funkcjonalizacji liganda.

Ligandy heterogeniczne podzielone zostały w zależności od sposobu użycia na ligandy dla katalizy dwufazowej (*Rozdział 1.5*) i ligandy związane na matrycy organicznej (*Rozdział 1.6*).

Rozdział 2 Ligandy dla katalizy homogenicznej

1,2-Glukozodiamina (Rozdział 2.1)

W rozdziale drugim przedstawiona została synteza 1,2-glukozodiaminy z *N*-acetyloglukozaminy. Związek zsyntetowany został w pięciu etapach z sumaryczną wydajnością końcową 33% (Schemat 1).

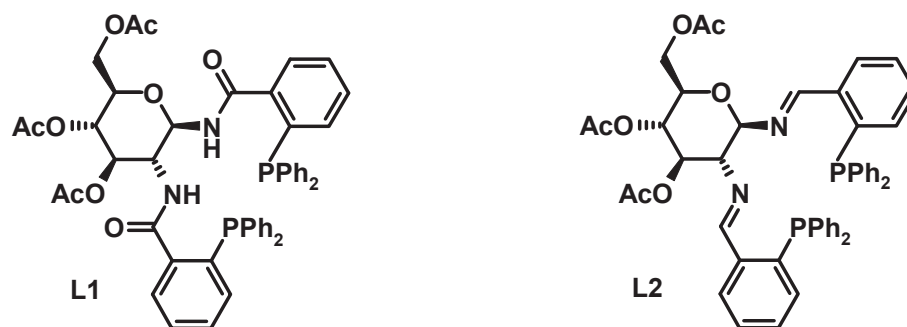


Schemat 1

Związek ten użyty został następnie jako materiał startowy do syntezy ligandów i katalizatorów przedstawionych w rozdziale 2.

Ligandy typu „Trosta” dla substytucji alkilowej (Rozdział 2.2)

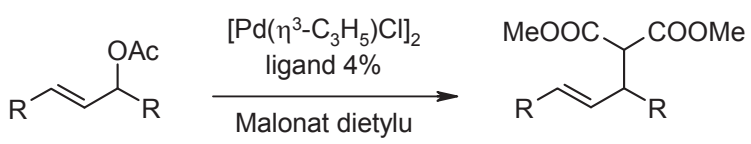
W tej części pracy opisana została synteza dwóch nowych ligandów wywodzących się ze struktury 1,2-β-glukozodiaminy t.j. liganda amidowego **L1** i liganda iminowego **L2** (Rysunek 2) o strukturze zbliżonej do struktury tzw. „liganda Trosta”

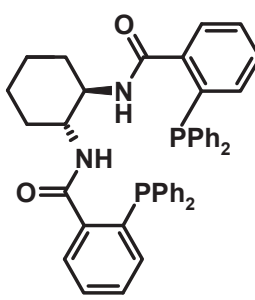


Rysunek 2

Ligand amidowy **L1** użyty został w kompleksie z palladem jako katalizator w reakcji substytucji alkilowej z dwoma różnymi substratami (Tabela 1). Najlepsze wydajność i nadmiary enancjomeryczne otrzymane zostały kiedy jako substrat użyty został octan 1,3-difenyloallilu. Wyniki te były nieco lepsze w porównaniu z wynikami otrzymanymi z ligandem Trosta, jednakże wciąż nie w pełni satysfakcjonujące bowiem wiele innych ligandów wywiedzionych z węglowodanów katalizuje taką reakcję z

wysokimi wydajnościami i nadmiarami enancjomerycznymi (patrz *Rozdział 1, Schematy 1.5-1.7*).



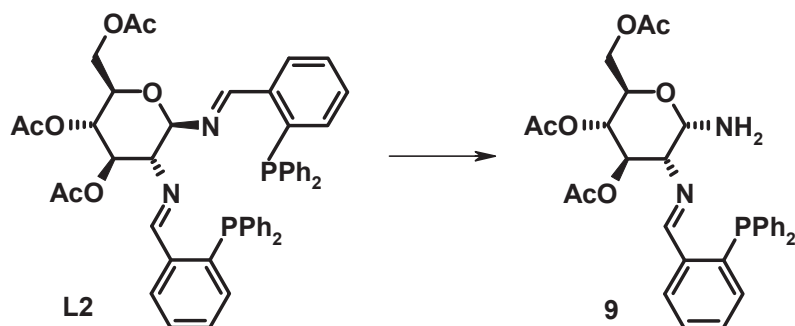


ligand Trosta

Nr	Ligand	R	Rozpu- szczalnik	Zasada	Wydaj- ność(%)	ee (%)
1	ligand Trosta	Ph	THF	NaH	24	12
2	L1	Ph	THF	NaH	39	42
3	ligand Trosta	Me	DCM	Cs ₂ CO ₃	98	92
4	L1	Me	DCM	Cs ₂ CO ₃	0	0
5	L1	Me	THF	NaH	0	0

Tabela 1

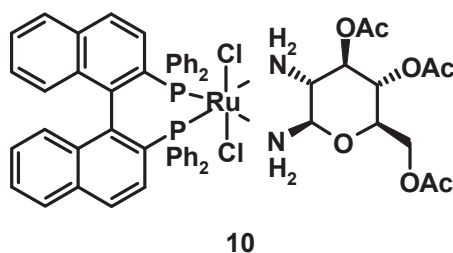
Aplikacja liganda iminowego w reakcji substytucji alkilowej okazała się być niemożliwa ze względu na jego niską stabilność i szybką degradację do monoiminy w środowisku reakcji (Schemat 2).



Schemat 2

Katalizator dla uwodornienia (*Rozdział 2.3*)

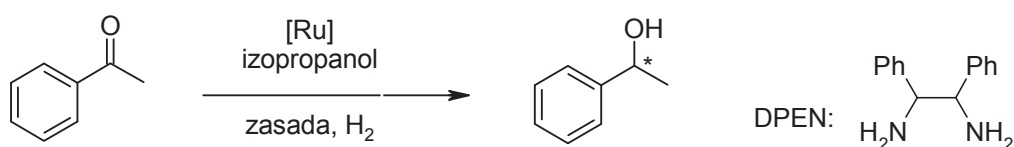
Bezpośrednio z 1,2-glukozodiaminy przygotowany został także kompleks z rutenem i BINAP-em (Rysunek 3).



10

Rysunek 3

Związek został użyty jako katalizator w reakcji uwodornienia acetofenonu:



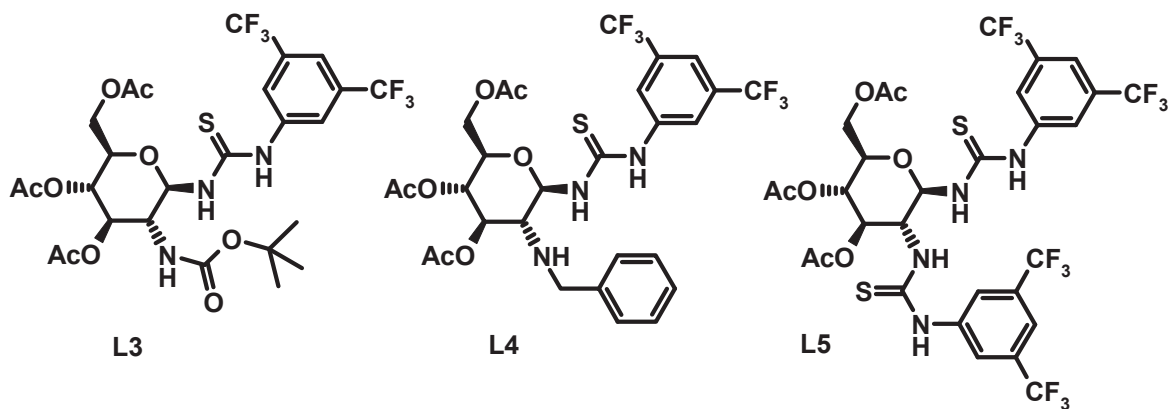
Amina	Zasada	Ciśnienie (hPa)	Katalizator (mol%)	Czas (godz.)	Konwersja (%)	Wydajność	ee (%)
1,2-glukodiamina	KOH	4	0.2	72	0	0	-
DPEN	<i>t</i> -BuOK	20	0.2	72	60	40	75
1,2-glukodiamina	<i>t</i> -BuOK	20	0.2	72	0	0	-

Tabela 2

Nadmiar enancjomeryczny 75% osiągnięty zostały jedynie w przypadku kiedy jako katalizator użyty został kompleks Noyori'ego zawierający zawierający chiralną 1,2-difenyloetylenodiaminę. Niestety, zupełnym niepowodzeniem zakończyły się próby zastosowania kompleksu **10** do tej reakcji. W żadnym z badanych przypadków produkt uwodornienia nie został zaobserwowany.

Organokatalizatory dla addycji Michaela (Rozdział 2.4)

Następnie opisana została synteza trzech związków **L3-L5** zawierających ugrupowanie tiomocznikowe dołączone do pierścienia węglowodanowego w oczekiwaniu na uzyskanie korzystnych właściwości takich związków jako organokatalizatorów (Rysunek 4).



Rysunek 4

W następnej części pracy, która realizowana była we współpracy z Profesorem Florence Popowycz i mgr Marciem Baronem z laboratorium CASYEN na Uniwersytecie Claude Bernard Lyon 1, którzy przeprowadzili testy katalityczne z wykorzystaniem związków **L3-L5** jako organokatalizatorów w reakcji addycji nitrometanu do chalkonu. Wyniki katalizy podane są w Tabeli 4



Nr	Katalizator	Czas (godz)	Inne	Temp. (°C)	Konwersja (%)	ee (%)
1	K ₂ CO ₃	5	ultradźwięki	T. pok	96	-
2	chinina	96	-	110	4	50
3	chinina	45	ultradźwięki	T. pok	18	55
4	L3	36	ultradźwięki	T. pok	<0.1	-
5	L4	36	ultradźwięki	T. pok	<0.1	-
6	L5	36	ultradźwięki	T. pok	<0.1	-

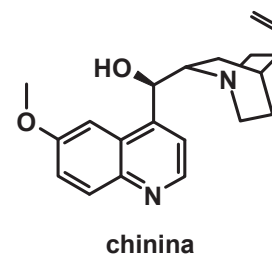


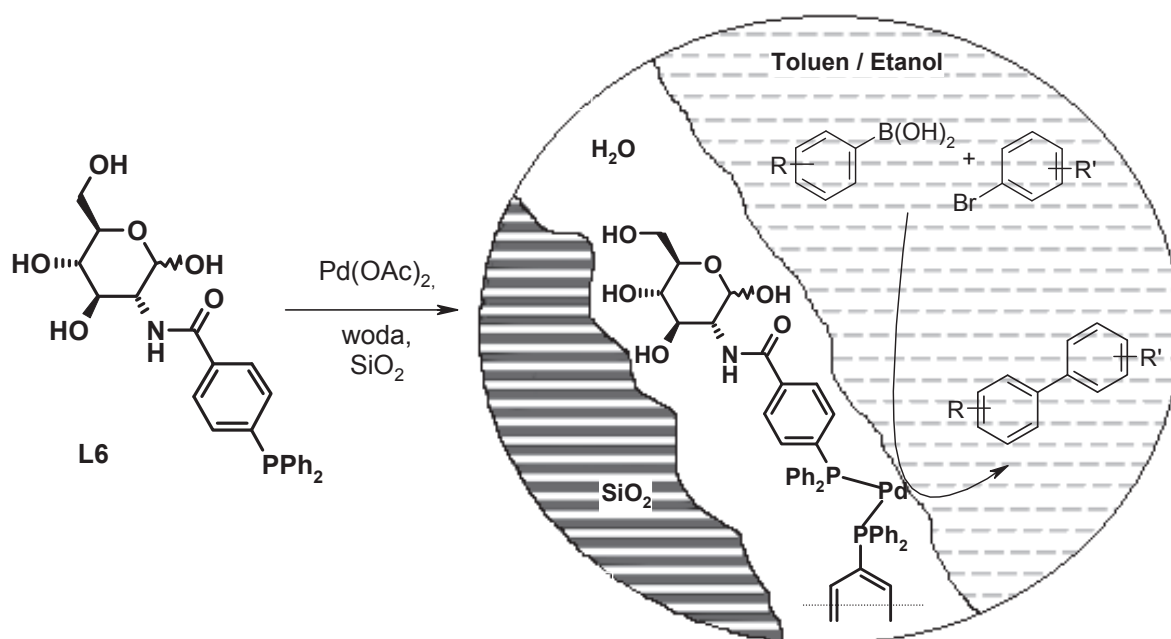
Tabela 3

Reakcja w obecności nieorganicznej zasady (K₂CO₃) przebiegała z prawie pełną konwersją 96%. W przypadku użycia chiralnej zasady organicznej (chinina) obserwowana była indukcja asymetryczna na poziomie 50-55% ale osiągnięte konwersje były bardzo niskie. Podjęte próby zastosowania chiralnych związków **L1-L3** zasady zakończyły się niestety niepowodzeniem. W warunkach ustalonych dla chininy związki **L3-L5** nie dały wyższych konwersji niż 0.1%.

Rozdział 3 Ligandy dla katalizy heterogennej

Katalizatory typu SAPC dla reakcji Suzuki-Miyaura (Rozdział 3.1)

Dla potrzeb tej fazy projektu na drodze jednoetapowej syntezy wychodzącej z D-glukozy otrzymany został najpierw ligand zawierający dodatkową funkcję fosfinową, który następnie został zaimpregnowany w cienkim filmie wody na powierzchni żelu krzemionkowego z wykorzystaniem wiązań niekowalencyjnych (Schemat 3).



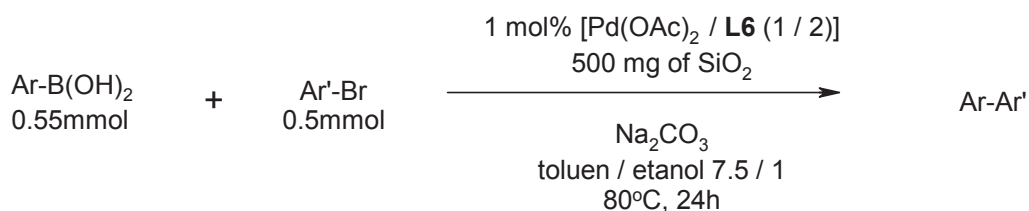
Schemat 3

Tak przygotowany katalizator, tzw. Supported Aqueous Phase Catalyst (SAPC), użyty został następnie w reakcjach sprzęgania Suzuki-Miyaura z wykorzystaniem aktywowanych i dezaktywowanych bromków arylowych oraz różnych kwasów boronowych. Podczas takiego procesu katalizy substraty i produkty pozostają w fazie organicznej zaś reakcja zachodzi na powierzchni pomiędzy fazami wodną i organiczną (Schemat 3).

Początkowo przeprowadzone zostały eksperymenty bez użycia katalizatora i w takich warunkach reakcja nie była obserwowana. Kiedy żel krzemionkowy zaimpregnowany był jedynie octanem palladu (bez liganda), konwersja substratów wyniosła 75% w pierwszym cyklu i 15% w drugim cyklu. Najwyraźniej kataliza miała tym

razem miejsce ale katalizator nie był związany z podłożem i następowało jego szybkie wypłukiwanie do fazy organicznej.

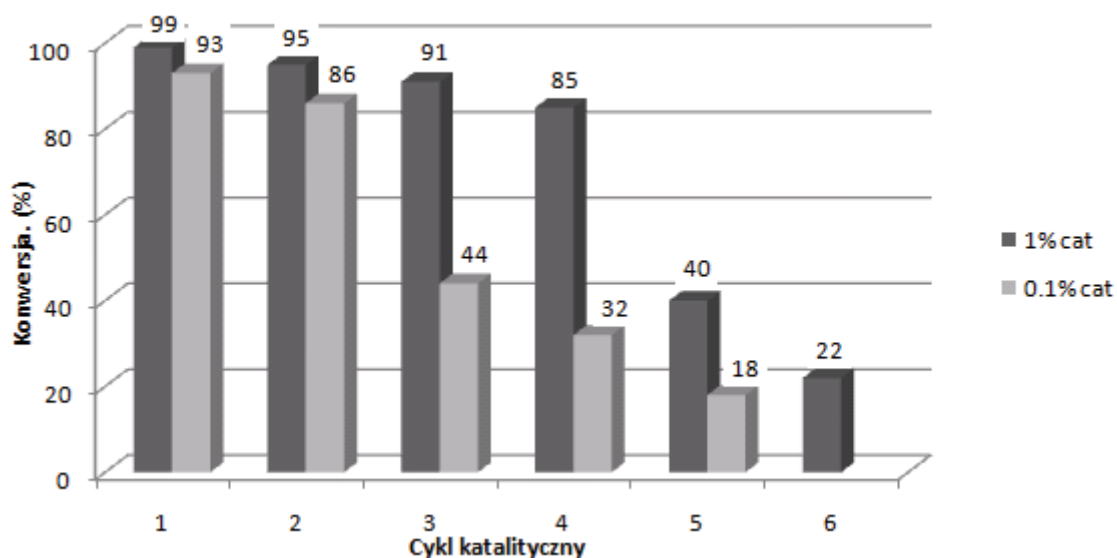
Zastosowanie przygotowanego katalizatora SAPC z wykorzystaniem liganda **L6** przyniosło natomiast bardzo dobre rezultaty. Tym razem różne bromki arylowe i kwasy boronowe ulegały konwersji do oczekiwanych produktów biarylowych z wydajnościami dochodzącymi do 99% (Tabela 4).



Nr	Ar	Ar'	Konwersja (%) ^a	Wydajność (%)
1	C ₆ H ₅	4-NO ₂ C ₆ H ₄	100	99
2	3-MeCOC ₆ H ₄		92	75
3	4-MeC ₆ H ₄		97	95
4	2,6-Me ₂ C ₆ H ₃		50	45
5	C ₆ H ₅	4-MeCOC ₆ H ₄	99	88
6		3-MeCO ₂ C ₆ H ₄	96	95
7		4-WinylC ₆ H ₄	76	65
8		4-MeOC ₆ H ₄	30	n.d.
9		2-MeC ₆ H ₄	100	96
10		4-MeC ₆ H ₄	93	85
11		2-Bromonaftalen	85	83
12		2-Bromopirydyna	100	75

Tabela 4

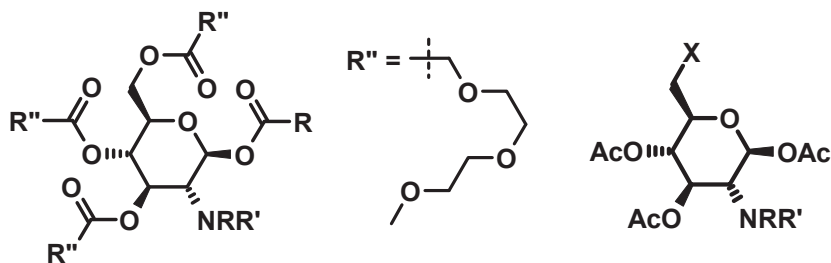
Możliwy okazał się także recykling katalizatora SAPC. Reakcje przeprowadzone zostały z dwoma różnymi ilościami katalizatora i w obydwu przypadkach okazało się możliwe jego łatwe odzyskanie i użycie w czterech kolejnych cyklach katalitycznych bez znaczącego spadku konwersji w przypadku (Wykres 1).



Wykres 1 Recykling katalizatora SAPC w reakcji sprzęgania p-bromonitrobenzenu i kwasu fenyloboronowego

Ligandy zawierające ugrupowanie polietylenowo glikolowe (Rozdział 3.2)

W celu sprawdzenia efektywności ligandów otrzymywanych z D-glokozaminy w procesach katalizy w środowisku difazowym z wodą jako jednym z rozpuszczalników podjęta została następnie synteza pochodnej glukozaminy zawierającej ugrupowania polietylenoglikolowe. Zaprojektowana wstępnie struktura zawierająca cztery takie ugrupowania polietylenoglikolowe okazała się zbyt trudna do otrzymania ze względu na zbyt dużą rozpuszczalność w rozpuszczalnikach użytych do ich otrzymania i niemożność ich wydzielenia w formie czystej. Lepszym rozwiązaniem okazało się być wprowadzenie do struktury glukozaminy tylko jednego ramienia polietylenowo glikolowego (Rysunek 5).



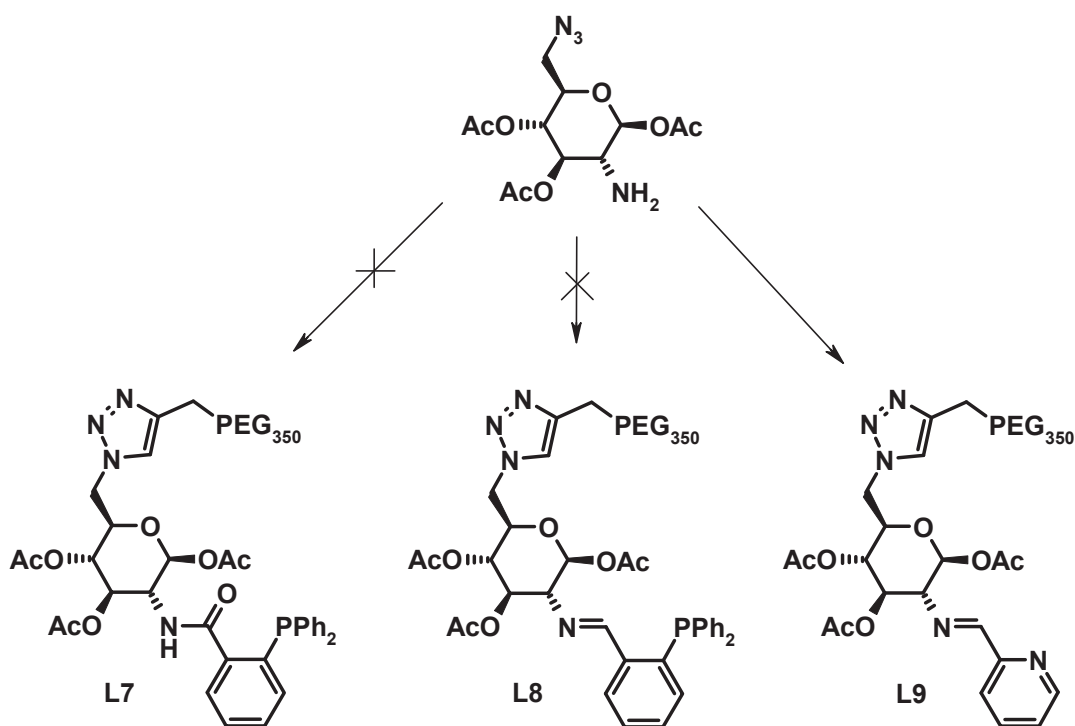
Rysunek 5

Przetestowane zostały warunki wprowadzenia różnych grup zabezpieczających w pozycję 6 pierścieni piranozowego i grupy acetylowej w pozycji β -anomerycznej.

Wprowadzenie grupy trotylowej okazało się możliwe ale otrzymywano w efekcie końcowym anomer przeciwny do pożądanego. Sprawdzone również grupę difenylo-*tert*-butylosililową służącą do zabezpieczania pierwszorzędowych grup hydroksylowych ale ze względu na wysoką aktywność grupy anomerycznej w przypadku D-glukozaminy zabezpieczenie takie nie zachodziło selektywnie.

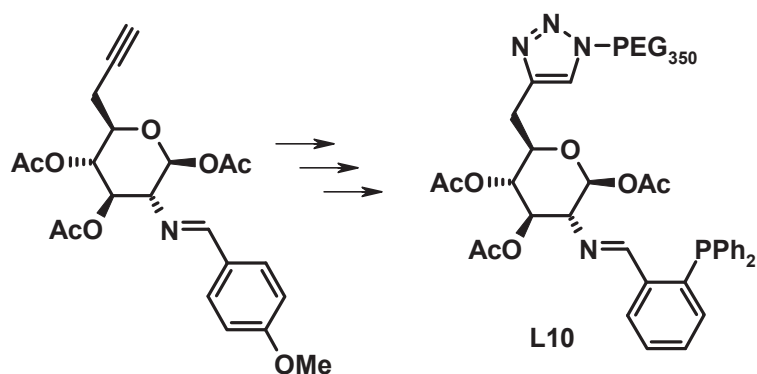
Najlepszym wyborem okazała się w końcu grupa tosyłowa, która selektywnie zabezpieczyła pozycję 6 w pierścieniu glukozaminy. Grupa tosyloksylowa w tej pozycji została następnie w prosty sposób podstawiona przez grupę azydową.

Umożliwiło to następnie zaplanowanie syntez trzech ligandów **L7-L8** poprzez wykorzystanie reakcji cykloaddycji 1,3-dipolarnej Huisgena (Schemat 4).



Schemat 4

Niepowodzeniem zakończyła się próba przygotowania wymaganych produktów przejściowych dla syntez ligandów **L7-L8** ze względu na obecność w związkach wyjściowych atomu fosforu, który w pierwszej kolejności reagował z grupą azydową w reakcji Staudingera. W celu uniknięcia niepożądanej reakcji Staudingera podjęta została próba syntezy pochodnej glukozaminy zawierającej ugrupowanie akinowe w pozycji 6 (Schemat 5) jednak ze względu na uzyskane niewielkie konwersje materiału startowego produkty nie były wydzielane.

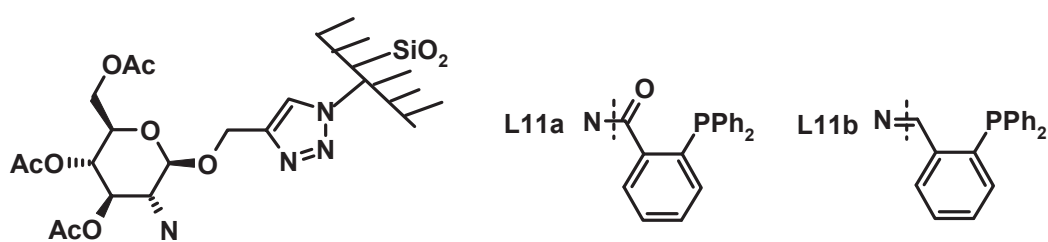


Schemat 5

W tej sytuacji, poprzez kondensację odpowiednio zablokowanej pochodnej glukozaminy z aldehydem 2-pirydylowym przygotowany został ligand **L9** (Schemat 4). Jego planowane użycie w reakcjach asymetrycznej substytucji allilowej w wodzie jako rozpuszczalniku będzie jednak możliwe już po złożeniu pracy doktorskiej.

Ligandy mocowane na żelu krzemionkowym poprzez wiązania kowalencyjne (Rozdział 3.3)

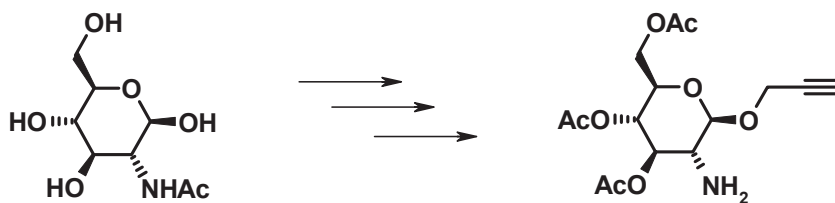
W ostatnim fragmencie pracy podjęta została próba syntezy dwóch glukozaminowych ligandów **L11a,b** zawierających funkcje fosfinowe osadzonych na żelu krzemionkowym (Rysunek 6).



Rysunek 6

Jednostki liganda miały być łączone z nieorganiczną matrycą poprzez reakcję cykloaddycji Huisgena pomiędzy grupami azydowymi odpowiednio sfunkcjonalizowanego SBA-15 a prekursorem węglowodanowym posiadającym ugrupowanie *O*-propargilowe w pozycji anomerycznej.

Po przeprowadzeniu niezbędnych analiz materiałów wyjściowych (Rozdział 3.3.1) zrealizowana została synteza pochodnej D-glukozy zawierającej ugrupowanie propargilowe w pozycji β -anomerycznej (Rozdział 3.3.2) (Schemat 6).

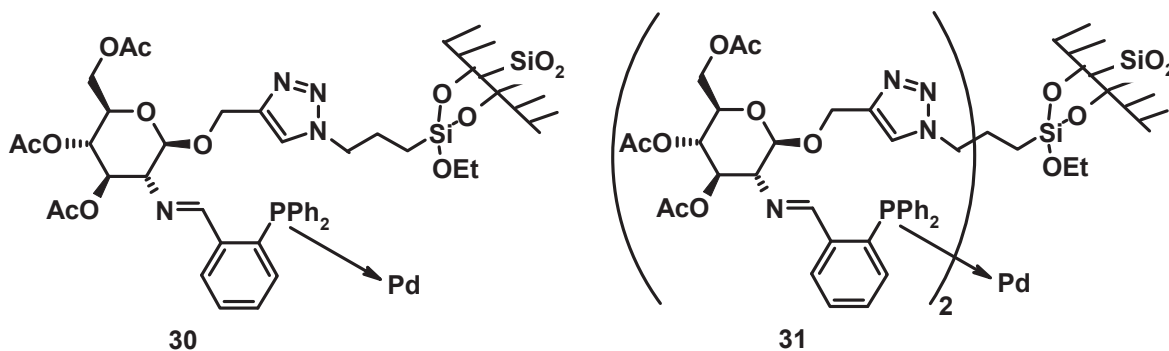


Schemat 6

Ten projekt był wykonywany we współpracy z Dr Chloe Thieuleux i Dr Reine Sayah z Laboratorium LCOMS z Uniwersytetu Claude Bernard Lyon 1. Dostarczyły one mezoporowate materiały SBA-15, oraz przeprowadziły analizy produktów metodami IR DRIFT, BET oraz MAS ^{31}P NMR.

Podjęte w następnej kolejności próby otrzymania heterogenizowanego liganda **L11a** niestety nie okazały się owocne. Przy próbach związania liganda z matrycą SBA-15 obserwowano utlenienie atomy fosforu i to nawet wtedy gdy wolne grupy hydroksylowe użytego SBA-15 zabezpieczone były grupami trimetylosililowymi.

Również w przypadku liganda **L11b** podjęte próby przygotowania dwóch kompleksów z palladem (Rysunek 7) nie zakończyły się powodzeniem..



Rysunek 7

Niestety, podobnie jak w przypadku liganda **L11a**, podczas prób łączenia liganda z matrycą nieorganiczną następowało utlenienie funkcji fosforowej.

Część eksperymentalna

Część eksperymentalna (*Rozdziały 2.5-2.8, 3.4-3.6*) pracy doktorskiej zawiera wyniki przeprowadzonych badań eksperymentalnych związanych z opracowaniem procedur syntetycznych wykorzystanych do syntezy i oczyszczania nowych związków i kompleksów, a także substratów i produktów reakcji katalitycznych. W tej części zostały również przedstawione szczegółowe dane z przeprowadzanych analiz z zastosowaniem metod analitycznych t.j. ^1H NMR, ^{13}C NMR, ^{31}P NMR, GC, HPLC, IR, ESI MS.

Podsumowanie i wnioski

- Opracowana została synteza *trans*-1,2-glukozodiaminy, której struktura zbliżona jest do struktury *trans*-1,2-cyklohexodiaminy, jednego z powszechnie używanych elementów konstrukcyjnych w syntezach chiralnych ligandów.
- Otrzymane zostały ligandy amidowe i iminowe o strukturze zbliżonej do struktury „liganda Trosta”. Ligand amidowy przetestowany został w reakcjach substytucji allilowej z użyciem dwóch różnych substratów.
- Kompleks 1,2-glukozodiaminy z rutenem i BINAP-em wykorzystany został w reakcji uwodornienia acetofenonu
- Przeprowadzona została synteza trzech ligandów glukozaminowych zawierających ugrupowania tiomocznikowe. Ligandy te wykorzystane zostały następnie w reakcjach addycji Michaela nitrometanu do chalkonu.
- Bez użycia żmudnych procesów protekcji i deprotekcji grup funkcyjnych, zwykle niezbędnych przy syntezie ligandów na bazie węglowodanów, otrzymany został z glukozaminy na drodze jednoetapowej syntezy nowy ligand fosfinowy dla katalizowanych palladem reakcji sprzęgania Suzuki-Miyaura. Ligand ten został następnie sheterogenizowany na żelu krzemionkowym za pomocą oddziaływań niekwalencyjnych (Supported Aqueous Phase Catalyst-SAPC)
- Uzyskany SAPC wykorzystany został w reakcjach sprzęgania Suzuki-Miyaura aktywowanych i dezaktywowanych bromoaryli z różnymi kwasami boronowymi. Odpowiednie biaryle otrzymane zostały z wydajnościami dochodzącymi do 99% a katalizator może być z łatwością oddzielony od mieszaniny reakcyjnej i użyty czterokrotnie bez znaczącego spadku aktywności

Streszczenie dysertacji

- W niektórych przypadkach wyniki otrzymane z użyciem systemu SAPC były lepsze niż wyniki katalizy przeprowadzone z tym samym ligandem w warunkach homogenicznych.
- Przebadane zostały różne warunki selektywnego zabezpieczania pierwszorzędowej grupy hydroksylowej w cząsteczce D-glukozaminy
- Podjęte zostały próby przygotowania liganda zawierającego ugrupowanie polietylenoglikolowe w celu jego użycia w reakcjach substytucji alkilowej w wodzie
- Próby przygotowania kompleksów zawierających funkcję fosfinową w jednostce glukozaminy osadzonych na mezoporowatym silika żelu za pomocą reakcji cykloaddycji Huisgena zakończone zostały niepowodzeniem ze względu na trudne do opanowania procesy utleniania funkcji fosfinowej.

Annex C

Supplementary work

Cite this: *Dalton Trans.*, 2011, **40**, 9090

www.rsc.org/dalton

COMMUNICATION

Dipyrinphenol–Mn(III) complex: synthesis, electrochemistry, spectroscopic characterisation and reactivity†

Sanae El Ghachtouli,^a Karolina Wójcik,^b Laurent Copey,^b Florence Szydło,^b Eric Framery,^b Catherine Goux-Henry,^b Laurianne Billon,^a Marie-France Charlot,^a Régis Guillot,^a Bruno Andrioletti^{*b} and Ally Aukauloo^{*a,c}

Received 9th May 2011, Accepted 5th July 2011

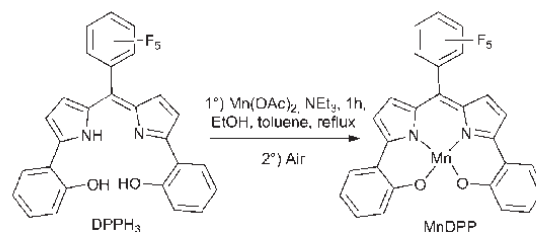
DOI: 10.1039/c1dt10868a

Herein, we report the manganese complex with a novel tri-anionic ligand, the pentafluorophenyldipyrinphenol ligand DPPH₃. The X-ray crystal structure reveals that the Mn^{III} complex exists in a dimeric form in the solid state. Electrochemical studies indicate two quasi-reversible one electron oxidation processes. EPR data on the one electron oxidised species in solution support the formation of a mononuclear Mn complex with an *S* = 3/2 spin system. Preliminary studies towards epoxidation reactions were tested in the presence of iodosylbenzene (PhIO) and are in favour of an oxygen-atom-transfer (OAT) reaction catalyzed by the Mn^{III} complex.

The development of robust molecular catalysts to drive oxidation reactions in environmentally benign conditions is an ongoing challenge and a priority for chemists. Prototypical metal complexes in this field are based on well-established porphyrin,¹ phthalocyanine,² corrole³ and salen⁴ derivatives. These molecular systems act as monooxygenase catalysts upon activation with oxygen containing oxidants to produce high valent metal–oxo species. TetraAmidoMacrocyclic Ligands (TAML) developed by Collins and collaborators are also known to give access to reactive high-valent metal–oxo derivatives that lead to degradation of persistent organic pollutants.⁵ The difference in reactivity between these families of complexes bearing the same metal ion evidences the primary importance of the ligand set surrounding the metal ion that shapes the electronic structure of the active species. In this communication, we describe the synthesis, spectroscopic and structural characterisation of a manganese(III) derivative of a new

ligand: pentafluorophenyldipyrinphenol (DPPH₃). Preliminary results concerning the epoxidation of cyclooctene using iodosylbenzene (PhIO) as terminal oxidant are also presented.⁶

The dipyrinphenol ligand can be seen as a combination of structural features from a porphyrin and a salen core. The synthesis of the ligand DPPH₃ was realised following the condensation of 2-orthoanisylpyrrole with pentafluorobenzaldehyde in acidic conditions followed by classical deprotection of the methoxy groups with BBr₃ according to Nabeshima's strategy.⁷ Insertion of manganese in the free base DPPH₃ was realised by refluxing with an excess of Mn(OAc)₂ in a toluene–EtOH mixture in the presence of NEt₃ as base under aerobic conditions (Scheme 1). Color changes from blue to green and usual analytical techniques probe the insertion of the metal ion in the N₂O₂ coordination environment.



Scheme 1

Single crystals of MnDPP of suitable quality for X-ray analysis, were produced by slow evaporation of acetonitrile in air.

The crystal structure shows that the complex exists as a dimer of [MnDPP] in the solid state (see Fig. 1). The lack of counter anions attests the presence of a manganese(III) ion in the trianionic N₂O₂ coordinating site. Each manganese ion adopts a square pyramidal geometry, with the DPP ligand as the basal plane and the oxygen atom of a phenolato group bridging two monomeric units.⁸ We note also a particularly short intradimer Mn–Mn distance at 3.146 Å.⁹ The oxygen atom of the bridging phenol is tilted towards the opposite manganese ion and departs from the N₂O₂ mean plane by 0.773 Å, while the Mn ion is found at 0.337 Å outside the basal plane.

Mass spectrometry of the isolated compound using ESI technique shows a major peak at 569 corresponding to [MnDPP + Na]⁺. A peak at 610 attributable to a monomeric manganese

^aInstitut de Chimie Moléculaire et des Matériaux d'Orsay, UMR-CNRS 8182, Université de Paris-Sud XI, F-91405, Orsay, France. E-mail: ally.aukauloo@u-psud.fr; Fax: +33 (0) 169 154 756; Tel: +33 (0) 169 154 755

^bInstitut de Chimie et Biochimie Moléculaire et Supramoléculaire (Equipe CASYEN), UMR-CNRS 5246, Université Claude Bernard Lyon1, Bâtiment Curien (CPE) 43 Boulevard du 11 novembre 1918, 69622, Villeurbanne Cedex, France. E-mail: bruno.andrioletti@univ-lyon1.fr; Fax: +33 (0) 472 448 160; Tel: +33 (0) 472 446 264

^cCEA, iBiTec-S, Service de Bioénergétique Biologie Structurale et Mécanismes (SB2SM), F-91191, Gif-sur-Yvette, France

† Electronic supplementary information (ESI) available: Electronic supplementary information (ESI) available: Synthesis, characterization of DPPMn, Cyclic voltammetry, DFT Calculations. CCDC reference numbers 811013. For ESI and crystallographic data in CIF or other electronic format see DOI: 10.1039/c1dt10868a

complex with an axial acetonitrile molecule to $[\text{MnDPP}(\text{CH}_3\text{CN}) + \text{Na}^+]^+$ was also detected under our experimental conditions.

Typically, Mn^{III} (d^4 , $S = 2$) is spectroscopically silent in the conventional EPR experiment (X-Band, 9 GHz) but transitions can be observed using parallel polarisation EPR. The parallel mode EPR spectrum of $[\text{MnDPP}(\text{CH}_3\text{CN})]$ in acetonitrile exhibits six well-resolved hyperfine lines centred at $g \approx 8.05$ that are split by 39.2 G. The morphology and field position of these signals are consistent with previously reported mononuclear Mn^{III} complexes in similar geometries.¹⁰ Although MnDPP was evidenced in the monomeric form in solution by mass spectrometry and EPR spectroscopy, attempts to crystallise the manganese monomer were unfruitful to date.

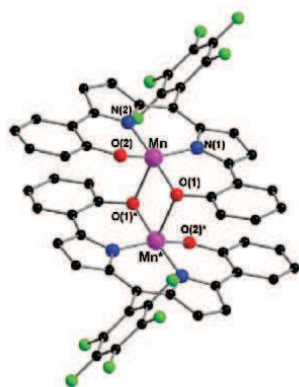


Fig. 1 Crystal structure of $[\text{MnDPP}]$. Hydrogen atoms are omitted for clarity. Selected metric distances (Å): Mn–N(1) 1.954(3), Mn–N(2) 1.942(3), Mn–O(1) 1.909(3), Mn–O(2) 1.854(3), Mn–O(1)* 2.206(3), Mn–Mn* 3.146(13). The asterisk indicates the symmetry operation $(1 - x, -y, -z)$.

Running the cyclic voltammogram of the manganese complex in acetonitrile, (Fig. 2) we observed two quasi-reversible anodic processes of equal intensity at 0.67 V and 1.23 V vs. SCE, that were attributed to the $\text{Mn}^{\text{IV}}/\text{Mn}^{\text{III}}$ couple and to a putative $\text{Mn}^{\text{V}}/\text{Mn}^{\text{IV}}$ couple, respectively. Upon addition of water, we noticed a shift of the redox potential of the $\text{Mn}^{\text{IV}}/\text{Mn}^{\text{III}}$ couple by 60 mV to

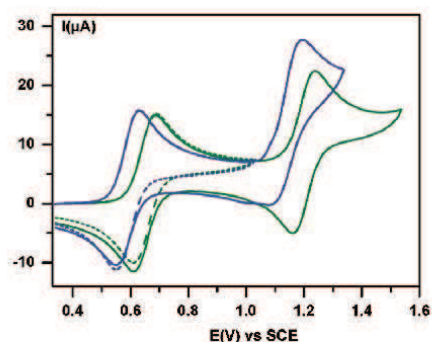


Fig. 2 Cyclic voltammetry of MnDPP (2 mM) at 0.1 V s^{-1} , $T = 253 \text{ K}$, on a glassy carbon electrode in acetonitrile (0.2 M NBu_4PF_6), (green line) and in acetonitrile containing 6% water (blue line). The corresponding dotted lines indicate the reversible nature of the first oxidation wave.

less positive values while the second oxidation process becomes irreversible. These effects on the electrochemical response in the presence of water imply the participation of water molecules in the coordination sphere of the manganese centre.¹¹

Exhaustive bulk electrolysis was performed both in pure and wet acetonitrile at 253 K, at + 0.8 V/SCE and coulometry confirmed a one-electron oxidation process. Furthermore, the chemical reversibility of the oxidation process was supported by the identical electrochemical response on the electrolysed solution in comparison with the initial one. This process is associated with a colour change from green to intense dark green. Monitoring this oxidation process by UV-Visible spectroscopy shows among other changes the appearance of two absorption bands at 870 and 970 nm (Fig. 3). These electronic features are reminiscent to the formation of a metalloradical type species. The electrochemical re-reduction of the oxidised species generated gave a spectrum corresponding to that initially observed for MnDPP, demonstrating the chemical reversibility of the one-electron electrochemical process.

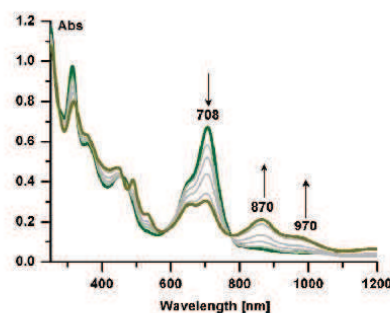


Fig. 3 UV-vis absorption spectra recorded in the course of the electrochemical oxidation of MnDPP at 0.8 V vs. SCE. Conditions: 0.2 M NBu_4PF_6 , 1 mM solution in acetonitrile, $T = 253 \text{ K}$, optical path: 0.5 mm.

Perpendicular mode X-band EPR data obtained at 5 K on the electrolysed solution in acetonitrile in the presence of water, indicate well-resolved (Fig. 4) signals with g_{off} at 4.9, 3.0 and 1.8 compatible with the one electron oxidation of the Mn^{III} complex

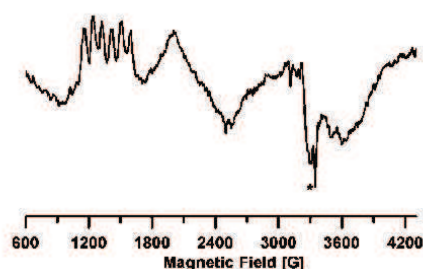


Fig. 4 Perpendicular mode EPR spectrum of a 2 mM solution of MnDPP in acetonitrile containing 6% water (0.2 M NBu_4PF_6) recorded after exhaustive reduction at 0.8 V vs. SCE; $T = 253 \text{ K}$; working electrode: glassy carbon crucible; auxiliary electrode: Pt grid separated from the rest of the solution with a fritted glass. EPR recording conditions: microwave frequency 9.38 GHz; modulation frequency 100 kHz; microwave power 2 mW; modulation amplitude 1 mT; $T = 5 \text{ K}$; time constant 160 ms. * trace of free $\text{Mn}(\text{II})$.

to a $S = 3/2$ spin system.^{10,12} Only Mn⁵⁵ hyperfine coupling was resolved for the $g = 4.9$ signal with an A value of 91 G.

Density functional theory (DFT) calculations were used to support this finding. The geometry optimisation of the penta-coordinated [Mn(DPP)(OH₂)] monomer with a water molecule in apical position places the water molecule at 2.27 Å from the manganese centre, while the Mulliken atomic spin on manganese and the map of the spin density distribution are characteristic of a high-spin Mn^{III} centre (see SI†). Theoretical data on the oxidised complex [Mn(DPP)(OH₂)]⁺ with a total spin state $S = 3/2$ lead to an optimised geometry with a Mn–O_w distance of 2.24 Å. Interestingly, we found that the Mulliken atomic spin on manganese is 3.87 (a value close to four unpaired electrons) and the map of the spin density distribution (Fig. 5) reveals a spin density of essentially negative sign developed on the whole DPP ligand. In such a configuration, the quartet state of the oxidised complex results from an antiferromagnetic coupling between an $S_{Mn} = 2$ Mn^{III} ion and an $S_L = 1/2$ ligand radical. Thus the electronic structure is best described as [Mn^{III}(DPP^{•+})(OH₂)]⁺.

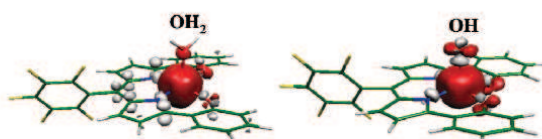


Fig. 5 Map of the spin density distribution for the quartet states of [Mn(DPP)(OH₂)]⁺ (left) evidencing the antiferromagnetic coupling between a high spin Mn^{III} ion and a ligand DPP^{•+} radical and of [Mn(DPP)(OH)] (right) showing a high spin Mn^{IV} ion.

As deprotonation of the water ligand may occur in the oxidised aqua complex under certain experimental conditions, a DFT study was also performed on the oxidised hydroxo monomer in the quartet state. A noticeable shrinking of the optimised Mn–O_w distance was found at 1.79 Å and the Mulliken atomic spin on manganese ρ_{Mn} falls to 2.99 corresponding to three unpaired spins. As shown in Fig. 5, the spin density map now reflects a metal centred oxidation. Kurahashi *et al.* have recently proposed such an electronic reshuffling in the case of a SalenMn complex.¹²

The preliminary catalytic performances of DPPMn were evaluated towards the epoxidation of cyclooctene in the presence of iodosylbenzene, a nucleophilic mono oxidizing species (Table 1).

Table 1 Catalytic activity

Entry	DPPMn (μmol)	PhIO (μmol)	Temp.	Epoxide (GC-yield) (%)
1 ^a	1	100	rt	38
2 ^a	1	10	rt	97
3 ^a	1	10	60 °C	78
4	0	100	rt	0

^a Reaction conditions: 1 μmol of MnDPP, ξ μmol PhIO, 1000 μmol alkene, 2 mL solvent.

In acetonitrile, at room temperature, MnDPP catalyzed efficiently the oxidation of the alkene to the corresponding epoxide. Indeed, in the presence of 10 equiv., the GC yield of the epoxide was 97%. This observation pertains to the formation of a high valent Mn(v)-oxo species. A recent report has indeed shown the formation of a genuine manganese(v)-oxo species within the same family of ligands upon treatment of the corresponding Mn(III) complex with peroxytriflate ions (ONOO⁻).¹³ However no reactivity towards organic substrates was reported.

These preliminary catalytic results clearly indicate that MnDPP constitutes an efficient catalyst for the epoxidation of alkene. Further work on the catalytic activities of this novel manganese complex using other oxidising agents are currently ongoing in our labs.

Conclusion

We described here the manganese complex of the pentafluorophenyl-dipyrromethene ligand, DPPH₃. We have shown the ability to transfer an oxygen atom to organic substrates. Collected spectroscopic and theoretical data converge towards a structure–reactivity relationship similar to those of Salen and Corrole. We believe that the synthetic versatility of the DDPH₃ core will allow us to efficiently tune the reactivity of the corresponding metal complexes. Furthermore, the participation of the ligand in the redox properties of the metal complex holds the promise of an intriguing non-innocent ligand.¹⁴ Work is underway in our labs to develop the coordination chemistry of the dipyrromethene ligand.

This work was supported by the EU/Energy SOLAR-H2 project (FP7 contract 212508) and by the EU/PERG-GA-2009-247924-ENCAT grant (FP7-PEOPLE-2009-RG) for Dr Florence Szydló.

Notes and references

- C.-M. Che and J.-S. Huang, *Chem. Commun.*, 2009, (27), 3996; J. T. Groves, K. Shalyaev, J. Lee, in *The Porphyrin Handbook*, ed. K. M. Kadish, K. M. Smith, R. Guilard, Academic Press, San Diego, CA and Burlington, MA, 1999, vol. 4, ch. 27, pp. 17–40.
- A. B. Sorokin and E. V. Kudrik, *Catal. Today*, 2011, **159**, 37.
- Z. Gross and H. B. Gray, *Adv. Synth. Catal.*, 2004, **346**, 165.
- (a) K. C. Gupta and A. K. Sutar, *Coord. Chem. Rev.*, 2008, **252**, 1420; (b) T. Katsuki, *Coord. Chem. Rev.*, 1995, **140**, 189; (c) W. Zhang, J. L. Leobach, S. R. Wilson and E. N. Jacobsen, *J. Am. Chem. Soc.*, 1990, **112**, 2801.
- (a) T. J. Collins, *Acc. Chem. Res.*, 2002, **35**, 782; (b) T. J. Collins, *Science*, 2001, **291**, 48.
- P. J. Stang and V. V. Zhdankin, *Chem. Rev.*, 1996, **96**, 1123.
- C. Ikeda, S. Ueda and T. Nabeshima, *Chem. Commun.*, 2009, (18), 2544.
- F. M. MacDonnell, N. L. P. Fackler, C. Stern and T. V. O'Halloran, *J. Am. Chem. Soc.*, 1994, **116**, 7431.
- Z. Lü, M. Yuan, F. Pan, S. Gao, D. Zhang and D. Zhu, *Inorg. Chem.*, 2006, **45**, 3538; H. Miyasaka, R. Clérac, W. Wernsdorfer, L. Lecren, C. Bonhomme, K. I. Sugiura and M. Yamashita, *Angew. Chem., Int. Ed.*, 2004, **43**, 2801.
- (a) K. A. Campbell, M. R. Lashley, J. K. Wyatt, M. H. Nantz and R. D. Britt, *J. Am. Chem. Soc.*, 2001, **123**, 5710; (b) C. S. Mullins and V. L. Pecoraro, *Coord. Chem. Rev.*, 2008, **252**, 416; (c) C. Herrero, J. L. Hughes, A. Quaranta, N. Cox, A. W. Rutherford, W. Leibl and A. Aukauloo, *Chem. Commun.*, 2010, **46**, 7605.
- (a) L. A. Berben and J. C. Peters, *Inorg. Chem.*, 2008, **47**, 11669; (b) P. Huang, A. Magnuson, R. Lomoth, M. Abrahamsson, M. Tamm, L. Sun, B. van Rotterdam, J. Park, L. Hammarström, B. Åkermark and S. Styring, *J. Inorg. Biochem.*, 2002, **91**, 159; (c) S. El Ghachtouli, B. L.

-
- Kaiser, P. Dorlet, R. Guillot, E. Anxolabéhère-Mallart, C. Costentin and A. Aukauloo, *Energy Environ. Sci.*, 2011, **4**, 2041.
- 12 (a) T. Kurahashi, A. Kikuchi, T. Tosha, Y. Shiro, T. Kitagawa and H. Fujii, *Inorg. Chem.*, 2008, **47**, 1674; (b) F. N. Penkert, T. Weyhermüller, E. Bill, P. Hildebrandt, S. Lecomte and K. Wieghardt, *J. Am. Chem. Soc.*, 2000, **122**, 9663.
- 13 S. Rausaria, A. Kamadulski, N. P. Rath, L. Bryant, Z. Chen, D. Salvemini and W. L. Neumann, *J. Am. Chem. Soc.*, 2011, **133**, 4200.
- 14 (a) O. Rotthaus, F. Thomas, O. Jarjayes, C. Philouze, E. Saint-Aman and J.-L. Pierre, *Chem.–Eur. J.*, 2006, **12**, 6953; (b) K. Ray, T. Petrenko, K. Wieghardt and F. Neese, *Dalton Trans.*, 2007, 1552; (c) T. Storr, E. C. Wasinger, R. C. Pratt and T. D. P. Stack, *Angew. Chem., Int. Ed.*, 2007, **46**, 5198; (d) S. Shaik, H. Hirao and D. Kumar, *Acc. Chem. Res.*, 2007, **40**, 532; (e) L. Cavallo and H. Jacobsen, *Angew. Chem., Int. Ed.*, 2000, **39**, 589.

Abstract in English

Several ligands derived from D-glucosamine, designed for different catalytic reactions have been synthesized. The ligands for homogeneous catalysis based on 1,2- β -glucodiamine were prepared, and used in reactions of allylic alkylation, hydrogenation and Michael addition.

Supported Aqueous Phase Catalyst (SAPC) system was prepared from D-glucosamine and use with very good results in Suzuki Miyaura cross coupling reactions. Catalyst was also recycled. Attempt to prepare ligands grafted on SBA-silica matrix were made as well as ligands containing poly(ethylene) glycol moiety.

Keywords:

D-glucosamine, „Green chemistry”, allylic alkylation, hydrogenation, organocatalysis, PEG, Silica supported catalysts, SAPC, homogeneous catalysis, heterogeneous catalysis.

Résumé en Français

Plusieurs ligands dérivés de la D-glucosamine, conçus pour différentes réactions catalytiques, ont été synthétisés. Les ligands pour la catalyse homogène basés sur 1,2- β -glucodiamine ont été préparés, et utilisés dans des réactions d'alkylation allylique, d'hydrogénation et d'addition de Michael.

La D-glucosamine a été utilisée pour la préparation de catalyseur type de SPAC (Supported Aqueous Phase Catalyst). Ce catalyseur hétérogène a été utilisé avec de très bons résultats dans les réactions de couplage croisé de Suzuki Miyaura. Le catalyseur a également été recyclé. Des essais de préparation de ligands greffés sur une matrice de silice de type SBA-15 ont été réalisés ainsi que des ligands à base de poly (éthylène) glycol.

Mots-clés:

D-glucosamine, „chimie verte”, alkylation allylique, hydrogénation, organocatalyse, PEG, les catalyseurs supportés sur silice, SAPC, catalyse homogène, catalyse hétérogène.