

Dissertation zur Erlangung des Doktorgrades  
der Fakultät für Chemie und Pharmazie  
der Ludwig-Maximilians-Universität München

# **Chiral Diphosphine Ligands and New Reactions of Organozinc Compounds**

von

**Andrey Gavryushin**

aus

Ruzaewka, Russland

München 2006

## **Erklärung**

Diese Dissertation wurde im Sinne von § 13 Abs. 3 bzw. 4 der Promotionsordnung vom 29. Januar 1998 von Herrn Prof. Dr. Paul Knochel betreut.

## **Ehrenwörtliche Versicherung**

Diese Dissertation wurde selbständig, und ohne unerlaubte Hilfe erarbeitet.

München, am 09. 01. 2007.

Andrey Gavryushin

Dissertation eingereicht am 11. 01. 2007

1. Gutachter: Prof. Dr. Paul Knochel

2. Gutachter: Prof. Dr. Hans Rudolf Pfaendler

Mündliche Prüfung am 09. 02. 2007

This work was carried out from August 2001 to July 2006 under the guidance of Prof. Knochel at the Fakultät für Chemie und Pharmazie der Ludwig-Maximilians-Universität, Munich.



I would like to thank Prof. Dr. Paul Knochel for giving me the opportunity of doing my Ph.D. in his group, for his invaluable support through this time.

I am also very grateful to Prof. Dr. H. R. Pfaendler for agreeing to be my “Zweitgutachter”, as well as Prof. Dr. K. Karaghiosoff, Prof. Dr. T. Lindel, Prof. Dr. H. Zipse and Dr. L. Ackermann for the interest shown in this manuscript by accepting to be referees.

I thank Dr. Darunee Soorukram, Tobias Thaler and Dr. Vicente del Amo for the careful correction of this manuscript.

I would like to thank the Ludwig-Maximilians-Universität and Saltigo GmbH for the financial support.

My special thanks to Vladimir Malakhov for his immense and patient help in everyday life as well as in scientific work.

My thanks to all the students, diplomants and postdocs that came and went during this time for their friendship that made these years such an enjoyable experience. I would like to thank my labmates Katja Tappe, Tanasri Bunlaksananusorn, Viet-Anh Vu, Ching-Yuan Liu, Georg Manolikakes, Vicente del Amo and all others for the excellent time and friendly atmosphere during the working hours.

I would also like to thank Beatrix Cammelade, Yulia Tsvik and Simon Matthe for their help in organizing everyday life in the lab, as well as the analytical team, Dr. D. Stephenson, Dr. C. Dubler, B. Tschuk, and P. Maier for their help.

I would like to thank my family, my wife and my parents for their love and great support, as well as all my friends for their kindness through these years.

Thank you very much!

## Parts of this Ph. D. thesis have been published:

1. Gavryushin, Andrei; Polborn, Kurt; Knochel, Paul. „Novel chiral diphosphine ligands with a pinene core obtained via an allylphosphinite-allylphosphine oxide rearrangement”. *Tetrahedron: Asymmetry* **2004**, *15*, 2279-2288.
2. Gavryushin, Andrei; Kofink, Christiane; Manolikakes, Georg; Knochel, Paul. “Efficient Cross-Coupling of Functionalized Arylzinc Halides Catalyzed by a Nickel Chloride-Diethyl Phosphite System.” *Organic Letters* **2005**, *7*, 4871-4874.
3. Krasovskiy, Arkady; Gavryushin, Andrey; Knochel, Paul. “A general thiolation of magnesium organometallics using tetramethylthiuram disulfide.” *Synlett* **2005**, 2691-2693.
4. Krasovskiy, Arkady; Malakhov, Vladimir; Gavryushin, Andrei; Knochel, Paul. „Efficient synthesis of functionalized organozinc compounds by the direct insertion of zinc into organic iodides and bromides.” *Angewandte Chemie, International Edition* **2006**, *45*, 6040-6044.
5. Krasovskiy, Arkady; Gavryushin, Andrey; Knochel, Paul. “Highly stereoselective access to sulfur derivatives starting from zinc organometallics.” *Synlett* **2006**, 792-794.
6. Gavryushin, Andrei; Kofink, Christiane; Manolikakes, Georg; Knochel, Paul. “An efficient Negishi cross-coupling reaction catalyzed by nickel(II) and diethyl phosphite.” *Tetrahedron* **2006**, *62*, 7521-7533.

## Patents:

1. Knochel, Paul; Bunlaksananusorn, Tanasari; Gavryushin, Andrei. “Chiral diphosphinoterpenes and transition metal complexes thereof.” U.S. Pat. Appl. Publ. (2005), US 2005267316.
2. Knochel, Paul; Bunlaksananusorn, Tanasari; Gavryushin, Andrei. “Chiral diphosphines with cyclic diterpene backbone as ligands for transition metal-catalyzed asymmetric hydrogenation, addition and substitution reactions and process for preparation thereof.” Eur. Pat. Appl. (2005), EP 1595886 .
3. Knochel, Paul; Bunlaksananusorn, Tanasari; Gavryushin, Andrei. “An improved process for preparation of chiral diphosphines with cyclopentane backbone as ligands for asymmetric transition metal-catalyzed hydroboration, hydrogenation and allylic substitution.” Eur. Pat. Appl. (2005), EP 1595885.
4. Knochel, Paul; Gavryushin, Andrey; Kofink, Christiane C. “An iron-, nickel- and cobalt-catalyzed cross-coupling reactions of organozinc compounds.” *Patent pending*.
5. Knochel, Paul; Gavryushin, Andrey; Malakhov, Vladimir; Krasovskiy, Arkady. “New preparation of organometallic compounds in the presence of lithium salts.” *Patent pending*.

*To Victoria, with love.*

***And I gave my heart to seek and search out by wisdom concerning all things that are done under heaven: this sore travail hath God given to the sons of man to be exercised therewith.***

***Ecclesiastes, 1:13***

## ABBREVIATIONS

|                                 |  |
|---------------------------------|--|
| Ac                              | acetyl                                   |
| AcOH                            | acetic acid                              |
| Ar                              | aryl                                     |
| Bn                              | benzyl                                   |
| Boc                             | <i>tert</i> -butoxycarbonyl              |
| br.                             | broad                                    |
| calcd.                          | calculated                               |
| CH <sub>2</sub> Cl <sub>2</sub> | dichloromethane                          |
| Cy                              | cyclohexyl                               |
| d                               | double                                   |
| dba                             | <i>trans,trans</i> -dibenzylideneacetone |
| dec.                            | decomposition                            |
| DMAP                            | 4-dimethylaminopyridine                  |
| DME                             | 1,2-dimethoxyethane                      |
| DMF                             | <i>N,N</i> -dimethylformamide            |
| DMSO                            | dimethyl sulfoxide                       |
| equiv.                          | equivalent                               |
| EI                              | electron-impact                          |
| Et                              | ethyl                                    |
| FAB                             | fast-atom bombardment                    |
| FG                              | functional group                         |
| GC                              | gas chromatography                       |
| h                               | hour                                     |
| HMPT                            | hexamethylphosphorous triamide           |
| HRMS                            | high resolution mass spectroscopy        |
| <i>n</i> -Bu                    | <i>n</i> -butyl                          |
| <i>i</i> -Pr                    | isopropyl                                |
| IR                              | infra-red                                |
| <i>J</i>                        | coupling constant (NMR)                  |
| LG                              | leaving group                            |
| M                               | molarity                                 |
| <i>m</i>                        | meta                                     |
| m                               | multiplet                                |

|              |  |
|--------------|--|
| Me           | methyl                                       |
| Met          | metal  |
| min          | minute                                       |
| mol.         | mole   |
| mp.          | melting point                                |
| MS           | mass spectroscopy                            |
| NBS          | <i>N</i> -bromosuccinimide                   |
| NMR          | nuclear magnetic resonance                   |
| Nu           | nucleophile                                  |
| <i>o</i>     | ortho  |
| <i>p</i>     | para   |
| Pent         | pentyl                                       |
| PG           | protecting group                             |
| Ph           | phenyl                                       |
| Piv          | pivaloyl                                     |
| q            | quartet                                      |
| rt           | room temperature                             |
| s            | singlet                                      |
| t            | triplet                                      |
| <i>t</i> -Bu | <i>tert</i> -butyl                           |
| TBS          | <i>tert</i> -butyldimethylsilyl              |
| TES          | triethylsilyl                                |
| Tf           | triflate                                     |
| TFA          | trifluoroacetic acid                         |
| tfp          | <i>tri</i> -(2-furyl)phosphine               |
| THF          | tetrahydrofuran                              |
| TLC          | thin layer chromatography                    |
| TMEDA        | <i>N,N,N',N'</i> -tetramethylethylenediamine |
| TMS          | trimethylsilyl                               |
| TMP          | 2,2,6,6-tetramethylpiperidyl                 |
| TP           | typical procedure                            |
| Ts           | 4-toluenesulfonyl                            |



# Table of contents

## Theoretical Part

|   |           |
|---|-----------|
| <b>Part I.</b> -----  | <b>13</b> |
| <b>Synthesis of chiral diphosphine ligands</b> -----  | <b>13</b> |
| <b>1. Overview and objectives</b> -----   | <b>13</b> |
| 1.1 <i>General overview</i> -----   | 13        |
| 1.2 <i>Objectives</i> -----   | 14        |
| <b>2. Allylphosphinite-allylphosphine oxide [2,3]-sigmatropic rearrangement on exocyclic systems and its application to the synthesis of new phosphorus ligands for asymmetric catalysis.</b> ----- | <b>15</b> |
| 2.1 <i>Chiral diphosphines with a saturated cyclic core and their applications in asymmetric catalysis.</i> -----   | 15        |
| 2.2 <i>[2,3]-sigmatropic rearrangement as a method for preparation of novel phosphine ligands</i> -----   | 19        |
| 2.2.1. <i>Preliminary studies of [2,3]-sigmatropic rearrangement on exocyclic systems</i> -----   | 22        |
| 2.2.2. <i>Studies on the allylic double bond functionalization in allylphosphine oxides</i> -----   | 24        |
| 2.3 <i>Preparation of optically pure diphosphine ligands with a cyclopentane core</i> -----   | 29        |
| 2.3.1. <i>Enzymatic resolution of 2-alkylidenecyclopentanols</i> -----  | 30        |
| 2.3.2. <i>Enantioselective synthesis of alkyl-substituted analogs of PCPP</i> -----   | 34        |
| 2.4 <i>Synthesis of new chiral diphosphines with a natural terpene framework</i> -----  | 37        |
| 2.4.1. <i>Preparation of diphosphine ligands starting from (-)-myrtenol</i> -----   | 38        |
| 2.4.2. <i>Preparation of diphosphine ligands from trans-pinocarveol (47)</i> -----  | 41        |
| <b>3. Novel approaches to the synthesis of chiral diphosphine ligands with a cyclopentane scaffold.</b> -----   | <b>47</b> |
| 3.1 <i>Enzymatic kinetic resolution for the preparation of optically pure 2-substituted cyclopentanols.</i> -----   | 47        |
| 3.2 <i>Modular enantioselective synthesis of PCPP ligand</i> -----  | 51        |
| 3.3 <i>Enantioselective synthesis of a new 1,4-diphosphine ligand with a cyclopentane scaffold</i> -----  | 58        |
| <b>4. Applications of the new ligands in the transition metal-catalyzed asymmetric reactions.</b> -----   | <b>64</b> |
| 4.1. <i>Rh-catalyzed asymmetric hydrogenation of acetamidocinnamates and acetamidoacrylates.</i> -----  | 64        |
| 4.2. <i>Rh-catalyzed asymmetric hydrogenation of dimethyl itaconate.</i> -----  | 69        |
| 4.3 <i>Rh-catalyzed asymmetric 1,4-addition of phenylboronic acid to cyclohexenone.</i> -----   | 71        |
| 4.4. <i>Rh-catalyzed asymmetric hydroboration of styrene.</i> -----   | 74        |
| 4.5 <i>Rh- and Ru-catalyzed asymmetric hydrogenation of C=N and C=O bonds and Pd-catalyzed allylic substitution reactions.</i> -----  | 75        |
| <b>Part II.</b> -----   | <b>78</b> |
| <b>New reactions of organozinc compounds</b> -----  | <b>78</b> |
| <b>5. New cross-coupling reaction of triorganosilylzinc compounds with aryl triflates.</b> -----  | <b>79</b> |
| 6.1 <i>Reaction optimization</i> -----  | 81        |
| 6.2 <i>Cross-coupling reaction of silylzinc and silylaluminium compounds</i> -----  | 84        |
| 6.3 <i>Conversion of phenols into aryl iodides and arylboronic esters.</i> -----  | 90        |
| <b>6. Novel method of thiolation of organozinc and organomagnesium compounds.</b> -----   | <b>94</b> |

|   |            |
|---|------------|
| 6.1 New thiolation reaction of organomagnesium compounds. -----   | 94         |
| 6.2 New thiolation reaction of organozinc compounds-----  | 97         |
| 6.3 Synthesis of thiols and sulfides from dithiocarbamates -----  | 99         |
| <b>7. New efficient Ni-catalyzed cross-coupling of arylzinc compounds-----</b>  | <b>100</b> |
| 7.1. Optimization of the reaction conditions and the catalytic system. -----  | 102        |
| 7.2 Ni-catalyzed cross-coupling of arylzinc compounds with aryl- and alkenyl halides and triflates. -----                                     | 107        |
| <b>8. Direct preparation of organozinc compounds from alkyl bromides in the presence of LiCl. -----</b>                                       | <b>112</b> |
| <b>9. Summary and outlook -----</b>   | <b>117</b> |
| <b><u>Experimental Part</u></b>   |            |
| <b>10. General considerations-----</b>  | <b>126</b> |
| <b>11. Typical procedures (TP) -----</b>  | <b>127</b> |
| 11.1. Typical procedure for the condensation of cycloalkanones with aliphatic aldehydes (TP1). -----  | 128        |
| 11.2 Typical procedure for the Luche reduction of enones (TP2). -----   | 128        |
| 11.3 Typical procedure for the enzymatic kinetic resolution of cyclic allylic alcohols with Amano lipase (PS-A) (TP3). -----                  | 128        |
| 11.4 Typical procedure for the preparation and in situ rearrangement of allyl diphenylphosphinites (TP4). -----                               | 128        |
| 11.5 Typical procedure for the hydroboration of allyldiphenylphosphine oxides with 9-BBN and oxidation with <i>m</i> -CPBA (TP5). -----       | 128        |
| 11.6 Typical procedure for the reduction of phosphine oxides by Ti(IV)-PMHS (TP6). -----  | 129        |
| 11.7 Typical procedure for the synthesis of bis-phosphine boranes from phosphine-borane alcohols (TP7). -----                                 | 129        |
| 11.8 Typical procedure for the deprotection of a phosphine borane with <i>N,N'</i> -bis-(3-aminopropyl)piperazine (TP8). -----                | 129        |
| 11.9 Typical procedure for the hydrogenation of a diphenylphosphine oxide over Raney Ni (TP9). -----  | 130        |
| 11.10 Typical procedure for the cross-coupling of silylzinc reagents with aryl triflates (TP10). -----  | 130        |
| 11.11 Typical procedure for the cross-coupling of tris-(trimethylsilyl)aluminium with aryl triflates (TP11). -----                            | 130        |
| 11.12 Typical procedure for the conversion of aryl(dimethyl)phenylsilanes into aryl iodides (TP12). -----                                     | 130        |
| 11.13 Typical procedure for the conversion of aryl(dimethyl)phenylsilanes into arylboronic esters (TP13). -----                               | 131        |
| 11.14 Typical procedure for the halogen-magnesium exchange reaction in the presence of LiCl (TP14). -----                                     | 131        |
| 11.15 Typical procedure for the preparation of <i>S</i> -aryl- <i>N,N</i> -dimethyldithiocarbamates from arylmagnesium halides (TP15). -----  | 131        |
| 11.16 Typical procedure for the preparation of <i>N,N</i> -dimethyldithiocarbamates from organozinc compounds (TP16). -----                   | 131        |
| 11.17 Typical procedure for the Ni-catalyzed cross-coupling reaction of arylzinc halides with aryl electrophiles (TP17). -----                | 131        |
| 11.18 Typical procedure for the Ni-catalyzed cross-coupling reaction of arylzinc halides with alkenyl electrophiles (TP18). -----             | 132        |
| 11.19 Typical procedure for the insertion of Zn into alkyl bromides in the presence of LiCl and reaction with an electrophile (TP19). -----   | 132        |
| 11.20 Typical procedure for the asymmetric Rh-catalyzed hydrogenation of methyl acetamidocinnamate and methyl acetamidoacrylate (TP20). ----- | 132        |
| 11.21 Typical procedure for the asymmetric Rh-catalyzed hydrogenation of dimethyl itaconate (TP21). -----                                     | 132        |

|  |            |
|--|------------|
| 11.22 Typical procedure for the asymmetric Rh-catalyzed 1,4-addition of phenylboronic acid to cyclohexen-2-one (TP22). ----- | 133        |
| 11.23 Typical procedure for the asymmetric Rh-catalyzed hydroboration of styrene with catecholborane (TP23).-----            | 133        |
| 11.24 Typical procedure for the asymmetric Rh-catalyzed hydrogenation of acetophenone semicarbazone (TP24).-----             | 133        |
| 11.25 Typical procedure for the asymmetric Ru-catalyzed hydrogenation of ethyl benzoylacetate (TP25). -----                  | 134        |
| 11.26 Typical procedure for the asymmetric Pd-catalyzed allylic substitution reaction (TP26). -----                          | 134        |
| <b>12. Syntheses of new alkyl analogs of PCPP-----</b>   | <b>135</b> |
| <b>13. Syntheses of chiral phosphine ligands with a pinene scaffold. -----</b>   | <b>149</b> |
| <b>14. Syntheses of new chiral diphosphines with cyclopentane scaffold-----</b>  | <b>159</b> |
| <b>15. Syntheses of arylsilanes from aryl triflates.-----</b>  | <b>168</b> |
| <b>16. New thiolation reaction of organomagnesium and organozinc compounds. -----</b>  | <b>179</b> |
| <b>17. Ni-catalyzed cross-coupling reaction of arylzinc halides. -----</b>   | <b>188</b> |
| <b>18. Direct preparation of organozinc compounds from alkyl bromides in the presence of LiCl.-----</b>                      | <b>193</b> |

# Theoretical Part

## Part I.

### Synthesis of chiral diphosphine ligands

#### 1. Overview and objectives

##### *1.1 General overview*

The application of organometallic compounds or complexes as catalysts or reagents in organic synthesis is nowadays an extremely fast growing field of scientific research. An immense number of novel organometallic transformations which were impossible to perform by conventional synthetic methods were discovered in the last two decades. They are currently employed practically in all areas of preparative organic chemistry. Much shorter syntheses of complex organic molecules, not possible only ten years ago, were successfully performed recently, using the powerful methodology of organometallic chemistry. New applications and methodologies in organometallic chemistry are now intensively investigated, and indeed, these reagents and catalysts have revolutionized organic synthesis in the last twenty years.

Among the organometallic reagents, organozinc compounds possess outstanding properties from the point of view of the synthetic versatility, compatibility with various functionalities in complex organic molecules, easiness of tuning of the reactivity by the addition of a catalyst and the lack of environmental hazard. The chemistry of organozinc reagents has recently become a rapidly and dynamically growing field of organic synthesis. Design of new synthetic methods in this branch of organometallic chemistry is a quite important and challenging synthetic task.

Another challenging research topic in organometallic chemistry is the development of novel chiral phosphine ligands for transition metal-catalyzed reactions. Such ligands play an extremely important role in the industrial production of enantiomerically enriched compounds. The worldwide sales of artificial enantiopure products achieved \$123 billion several years ago, and this value keeps on growing constantly. The discovery of novel reactions in the field of new ligand synthesis is an interesting target for an organic chemist.

## 1.2. Objectives

The discovery of the diastereoselective [2,3]-sigmatropic allylphosphinite-allylphosphine oxide rearrangement more than 50 years ago has opened an interesting synthetic pathway to the creation of a new chiral carbon center, bearing a phosphorus atom. Recently, this reaction was applied in our group for the synthesis of several new diphosphine ligands having a carbocyclic scaffold. They displayed promising properties in several industrially important transition metal-catalyzed reactions. However, the synthetic potential of this interesting method has not yet been fully investigated. As the first goal, we planned to use this approach in the synthesis of new diphosphine ligands with the carbocyclic core, using as starting materials the allylic alcohols with an exocyclic double bond, either prepared synthetically or naturally occurring. It was planned to perform the evaluation of these ligands in several important asymmetric metal-catalyzed reactions.

The development of the chemoenzymatic methods for the resolution of various substituted cycloalkanols during the study of the [2,3]-allylphosphinite rearrangement gave us a possibility to design several novel routes towards some perspective classes of diphosphine ligands. One of the target of the following investigation was the design of a modular asymmetric synthesis of the diphosphines with the cyclopentane core from a common chiral precursor, using the newly developed chemoenzymatic techniques.

Studies in the field of transition metal catalysis led us to the search for new synthetic methods for the transformation of aryl functional groups. The aim of the next project was the development of a versatile method for the conversion of a phenolic hydroxyl into an aryl iodide, using the methodology of organometallic chemistry. The lack of a mild and general method for the conversion of organozinc and -magnesium compounds into the corresponding thiols brought about the discovery of a broadly useful synthetic protocol for this transformation. Several observations of the catalytic activity of nickel complexes in the reactions of organozinc compounds led to the development of a highly versatile and robust method for the Ni-catalyzed cross-coupling reaction of organozinc species. This became the objective of the next research project. The outstanding enhancing effect of lithium chloride on the reactivity of various main-group organometallic reagents, which led to the recent discovery of several extremely useful synthetic methods in organomagnesium chemistry in our group, made very promising the investigation of this reagent in the field of organozinc chemistry. It was the main target of the last part of this work.

## 2. Allylphosphinite-allylphosphine oxide [2,3]-sigmatropic rearrangement on exocyclic systems and its application to the synthesis of new phosphorus ligands for asymmetric catalysis.

### 2.1 Chiral diphosphines with a saturated cyclic core and their applications in asymmetric catalysis.

One of the main purposes of contemporary organic synthesis is the preparation of compounds in optically pure form. Among the methods developed to achieve this goal, the transition metal-catalyzed reactions using chiral ligands now play undoubtedly the most important role, especially for large-scale industrial applications.<sup>1</sup> In 2001, the pioneers of the metal-catalyzed asymmetric synthesis *Knowles*<sup>2</sup>, *Noyori*<sup>3</sup> and *Sharpless* were awarded the Nobel Prize. This emphasized the exceptional industrial significance of this branch of modern organic chemistry. The number of new metal-catalyzed asymmetric reactions and discovered ligands has been increasing from year to year. The chiral *bis*-phosphine ligands are the most important class of ligands for the transition metal catalysis. The first important ligand of this type, DIPAMP, discovered by *Knowles* and *Horner*,<sup>4</sup> enabled the first industrial asymmetric synthesis of an amino acid L-DOPA, an extremely important pharmacological agent in the treatment of the Parkinson's disease.<sup>5</sup> The preparation of chiral diphosphine ligands which are rather complex molecules, bearing multiple chiral centers, is often expensive and lengthy. Therefore, the search for new promising structures of this class as well as the novel methods for their synthesis is an important and challenging task for organic chemists.

Diphosphine ligands with a rigid cyclic scaffold are one of the most important classes of currently used chiral phosphine ligands. Such compounds as *Brunner's* NORPHOS (**2**)<sup>6</sup> *Nagel's* DEGUPHOS (**4**),<sup>7</sup> BICP (**3**),<sup>8</sup> developed by *Zhang*, PCPP (**1**),<sup>9</sup> designed by *Achiwa*, NOPAPHOS (**5**)<sup>10</sup> and PHELLANPHOS (**6**)<sup>11</sup> from *Kagan* and CAMPHORPHOS (**7**)<sup>12</sup> from *Helmchen* (Scheme 1) are excellent ligands for the Rh-catalyzed asymmetric reduction of

---

<sup>1</sup> a) R. Noyori, *Asymmetric Catalysis in Organic Synthesis*, Wiley, New York, **1994**; b) I. Ojima, *Catalytic Asymmetric Synthesis*, 2. Ed., Wiley, New York, **2000**.

<sup>2</sup> W. S. Knowles, *Adv. Synth. Cat.* **2003**, *345*, 3.

<sup>3</sup> R. Noyori, *Adv. Synth. Cat.* **2003**, *345*, 15.

<sup>4</sup> W. S. Knowles, *Acc. Chem. Res.* **1983**, *16*, 106.

<sup>5</sup> B. D. Vineyard, W. S. Knowles, M. J. Sabacky, G. L. Bachman, D. J. Weinkauff, *J. Am. Chem. Soc.* **1977**, *99*, 5946.

<sup>6</sup> H. Brunner, W. Pieronczyk, *Angew. Chem. Int. Ed.* **1979**, *18*, 620.

<sup>7</sup> a) U. Nagel, *Angew. Chem. Int. Ed.* **1985**, *23*, 435. b) U. Nagel, T. Krink, *Chem. Ber.* **1993**, *126*, 1091.

<sup>8</sup> G. Zhu, P. Cao, Q. Jiang, X. Zhang, *J. Am. Chem. Soc.* **1997**, *119*, 1799.

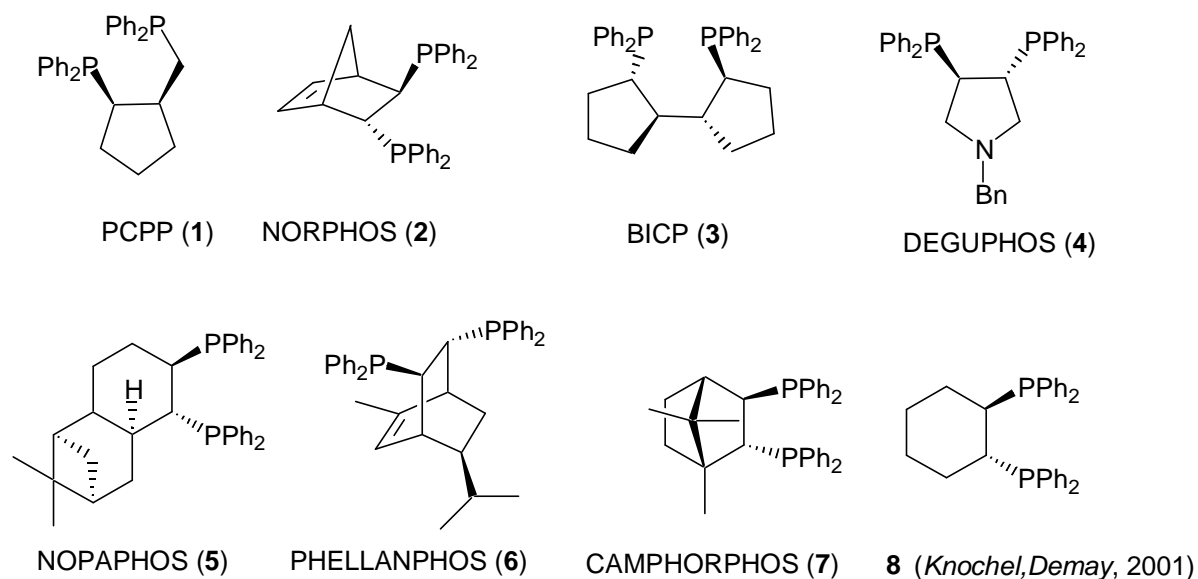
<sup>9</sup> K. Inoguchi, K. Achiwa, *Synlett*, **1991**, 49.

<sup>10</sup> O. Samuel, R. Couffignal, M. Lauer, S. Y. Zhang, H. B. Kagan, *Nouv. J. Chem.* **1981**, *5*, 15.

<sup>11</sup> M. Lauer, O. Samuel, H. B. Kagan, *J. Organomet. Chem.* **1979**, *177*, 309.

<sup>12</sup> A. Krotz, *Dissertation*, Universität Heidelberg, **1999**.

C=C double bonds in acetamidocinnamic esters and their analogs, itaconic esters and similar unsaturated compounds. Similarly, C=O and C=N bonds can be enantioselectively hydrogenated, using complexes of this ligand types with Ru or Ir.<sup>13</sup>



**Scheme 1.** Chiral diphosphine ligands with carbocyclic frameworks.

Beside the asymmetric hydrogenation, the most common application fields of such ligands are Rh-catalyzed hydroboration of alkenes,<sup>14</sup> Rh-catalyzed 1,4-addition of arylboronic acids to enones<sup>15</sup> and Pd-catalyzed allylic alkylation and allylic amination.<sup>16</sup> Several examples of the asymmetric hydrogenation, one of the most widely used asymmetric transition metal-catalyzed reactions, are given below (Scheme 2).<sup>17</sup>

<sup>13</sup> a) W. Tang, X. Zhang, *Chem. Rev.* **2003**, *103*, 3029. b) S. Kobayashi, H. Ishitani, *Chem. Rev.* **1999**, *99*, 1069. c) M. J. Burk, J. E. Feaster, *J. Am. Chem. Soc.* **1992**, *114*, 6266.

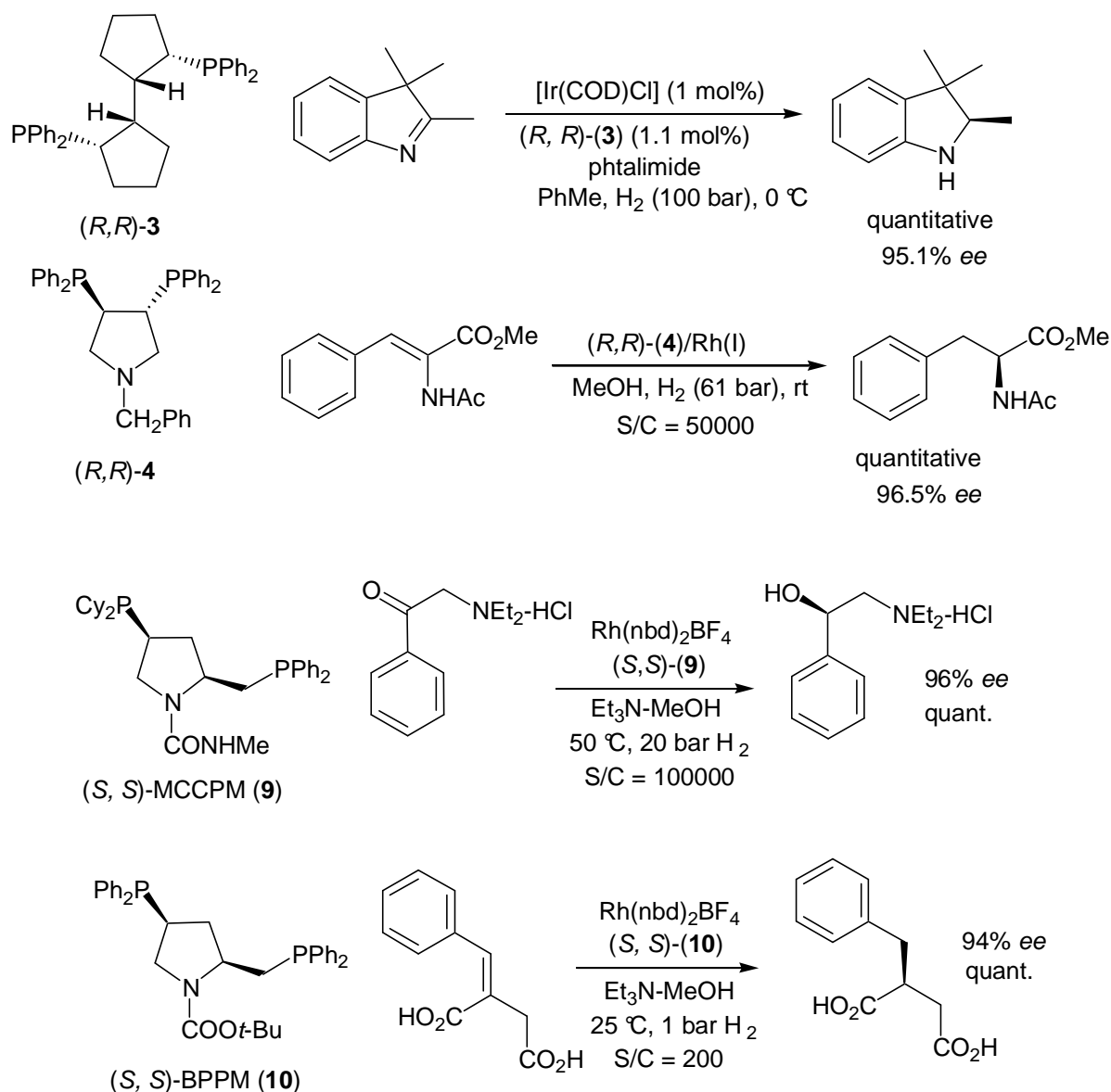
<sup>14</sup> a) T. Hayashi, Y. Matsumoto, Y. Ito, *J. Am. Chem. Soc.* **1989**, *111*, 3426. b) A. Schnyder, L. Hintermann, A. Togni, *Angew. Chem. Int. Ed.* **1995**, *34*, 931.

<sup>15</sup> a) Y. Takaya, M. Ogasawara, T. Hayashi, *J. Am. Chem. Soc.* **1998**, *120*, 5579. b) M. T. Reetz, D. Moulin, A. Gosberg

<sup>16</sup> a) B. M. Trost, D. L. Van Vranken, *Chem. Rev.* **1996**, *96*, 395. b) A. Heumann, M. Réglér, *Tetrahedron* **1995**, *51*, 975.

<sup>17</sup> a) G. Zhu, X. Zhang, *Tetrahedron: Asymmetry* **1998**, *9*, 2415. b) U. Nagel, E. Kinzel, J. Andrade, G. Prescher *Chem. Ber.* **1986**, *119*, 3326. c) H. Takeda, T. Tachinami, M. Aburatani, H. Takahashi, T. Morimoto, K. Achiwa *Tetrahedron Lett.* **1989**, *30*, 363. d) H. Jendralla, R. Henning, B. Seuring, J. Herchen, B. Kulitzscher, I. Wunner *Synlett*, **1993**, 155.



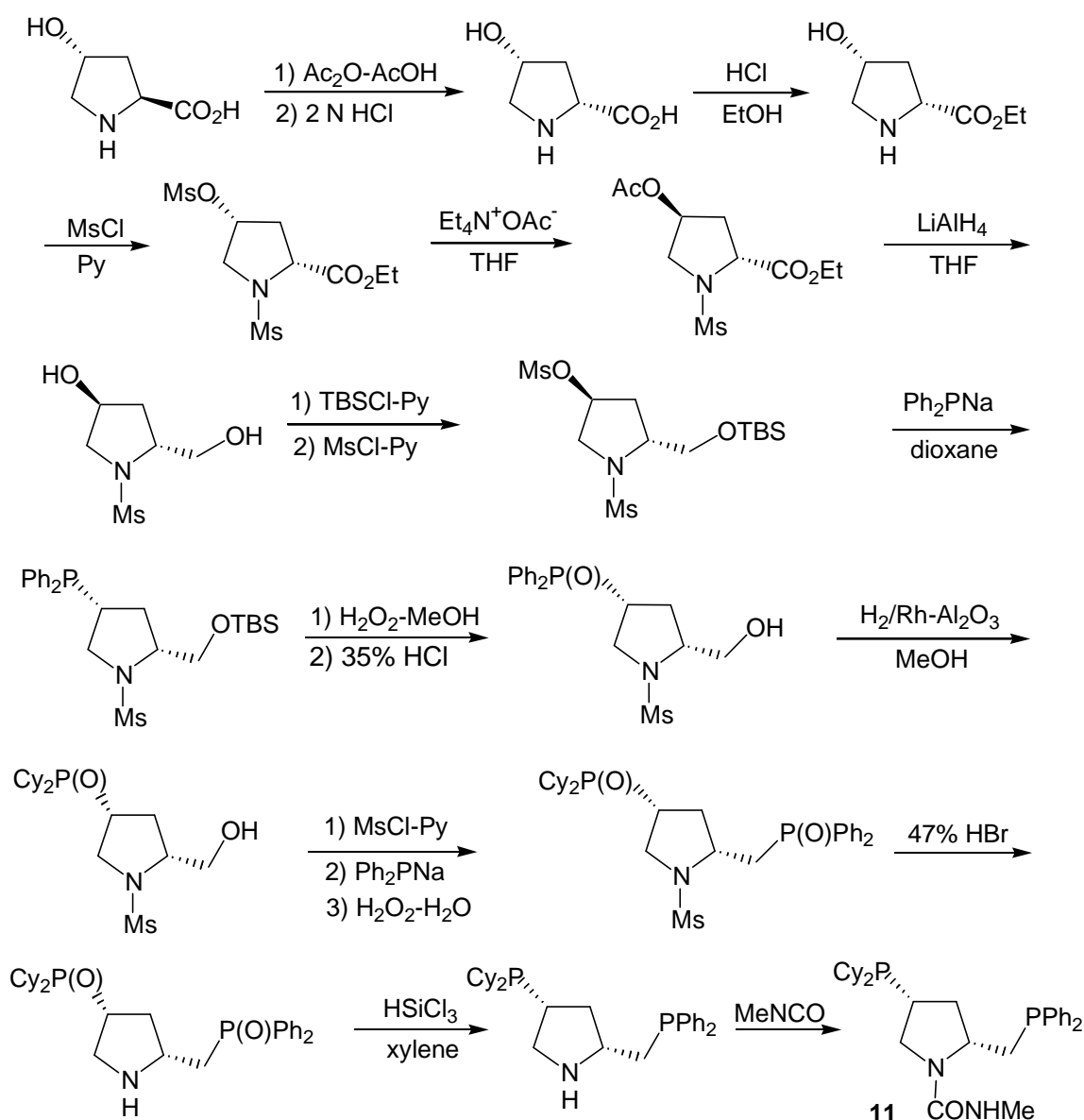


**Scheme 2.** Asymmetric reactions, catalyzed by the diphosphines with cyclic scaffolds.

Ligands of this kind form extremely reactive catalysts for many industrially important reaction. These catalysts demonstrate excellent substrate-to-catalyst ratios and enantioselectivities, therefore the search for new ligands with a saturated cyclic core is a perspective task for an organic chemist.

This type of chiral ligands share the same common feature, namely, a tertiary carbon stereocenter, bearing a phosphorus atom. With only few exceptions, the only method used for the creation of such stereocenter is the substitution of an activated sulfonate ester of the corresponding alcohol with a phosphorous nucleophile like lithium or potassium

diphenylphosphide.<sup>18</sup> The starting chiral alcohols can be prepared by various conventional methods, besides, the starting materials from the natural chiral pool can be applied. This approach usually requires a tedious preparation of secondary phosphines, which are air-sensitive and therefore difficult to handle, which often results in low yields. Besides, the formed phosphines are usually air-sensitive and often need to be protected before isolation.<sup>19</sup> Some common features of the synthesis of a phosphine ligand are illustrated below (Scheme 3) by the 16-step synthesis of ligand (*R,R*)-MCCPM (**11**):<sup>20</sup>



**Scheme 3.** Synthesis of (*R,R*)-MCCPM (**11**) by Achiwa.

<sup>18</sup> a) N. V. Dubrovina, V. I. Tatarov, A. Spannenberg, I. D. Kostas, A. Boemer *Tetrahedron: Asymmetry* **2005**, *16*, 3640. b) D. G. Genov, *Phosphorus, Sulfur, Silicon Rel. Elements* **2004**, *179*, 1949. c) Z. Herseczki, I. Gergely, S. Hegedues, A. Szoellozy, J. Bakos, *Tetrahedron: Asymmetry* **2004**, *15*, 1673.

<sup>19</sup> L. McKinsty, T. Livinghouse, *Tetrahedron*, **1995**, *51*, 7655.

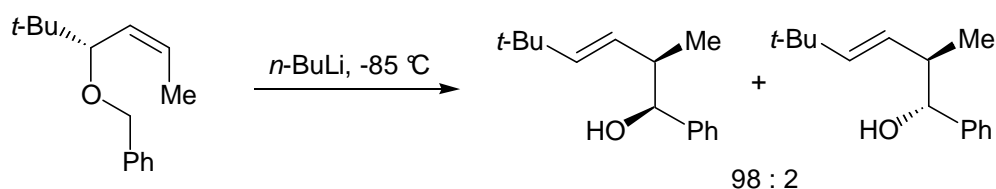
<sup>20</sup> K. Achiwa, *Eur. Pat. Appl.* EP 251164, **1988**.

Thus, the development of new, original methods for making of carbon stereogenic centers, bearing phosphorus atoms, is an important task in organic chemistry.

In 1999, *Knochel* and *Demay* developed a novel method for the synthesis of chiral phosphorus ligands, based on the diastereoselective [2,3]-sigmatropic rearrangement of allyl phosphinites into allyl phosphine oxides.<sup>21</sup> It offers a simple method for the formation of a carbon chiral center bearing a phosphorus substituent, starting from various chiral allylic alcohols. A number of novel chiral diphosphines were prepared in this way. They demonstrated high regio- and enantioselectivity in the Rh-catalyzed asymmetric hydroboration of styrenes.<sup>22</sup> Further applications of this rearrangement reaction to the synthesis of chiral phosphine ligands was the objective of the first part of this work.

## 2.2 [2,3]-sigmatropic rearrangement as a method for preparation of novel phosphine ligands

The [2,3]-sigmatropic rearrangement is a well-known reaction in organic chemistry, although its synthetic use was limited until now mostly by the Wittig rearrangement of allyl ethers.<sup>23</sup> *Baldwin* and *Patrick* demonstrated in 1971 that this process occurs with a high degree of chirality transfer (Scheme 4):<sup>24</sup>



**Scheme 4.** Diastereoselective [2,3]-Wittig rearrangement.

In 1948, *Arbuzov* discovered the thermal rearrangement of allyl diphenylphosphinite to allyldiphenylphosphine oxide.<sup>25</sup> This reaction during the following decades attracted little attention. *Mislow* (Scheme 5) demonstrated that this rearrangement occurs without racemization if a chiral phosphorus atom is involved:<sup>26</sup>

<sup>21</sup> S. Demay, K. Harms, P. Knochel, *Tetrahedron Lett.* **1999**, 40, 4981.

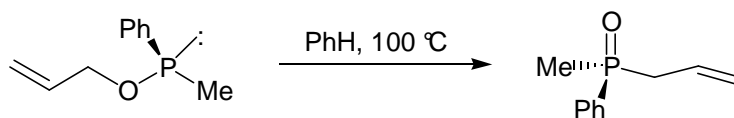
<sup>22</sup> S. Demay, F. Volant, P. Knochel, *Angew. Chem. Int. Ed.* **2001**, 40, 1235.

<sup>23</sup> a) T. Nakai, K. Tomooka, *Pure Appl. Chem.* **1997**, 69, 595. b) T. Nakai, K. Mikami, *Chem. Rev.* **1986**, 86, 885.

<sup>24</sup> a) J. E. Baldwin, J. E. Patrick, *J. Am. Chem. Soc.* **1971**, 93, 3556. b) N. Sayo, E. Kitahara, T. Nakai, *Chem. Lett.* **1985**, 259.

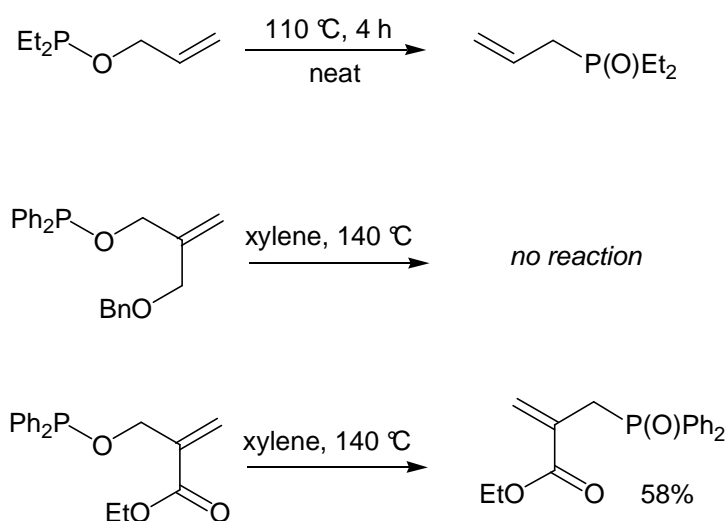
<sup>25</sup> A. E. Arbuzov, K. V. Nikonorov, *Zh. Obshch. Khim.* **1948**, 18, 2008.

<sup>26</sup> A. W. Herriott, K. Mislow, *Tetrahedron Lett.* **1968**, 25, 3013.



**Scheme 5.** Diastereoselective rearrangement of a *P*-chiral diallylphosphinite.

This reaction was later applied by *Pudovik* to the rearrangement of allyl dialkyl phosphinites to allyldialkylphosphine oxides.<sup>27</sup> The success of the reaction for functionalized allylphosphinites significantly depends on the substituents in the molecule (Scheme 6). The same reaction with propargylic phosphinites proceeds under very mild conditions.<sup>28</sup>



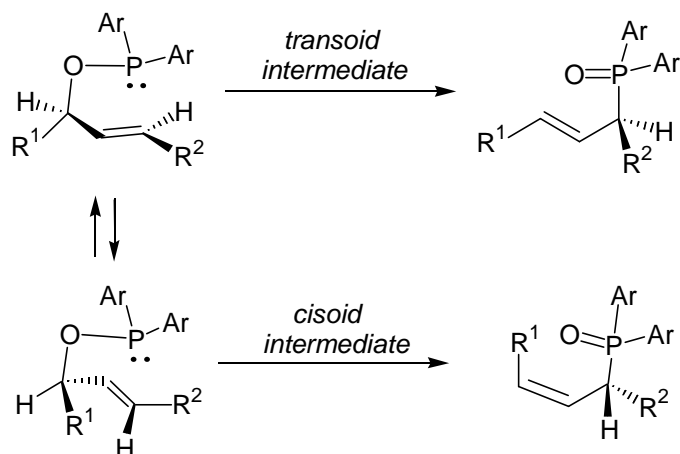
**Scheme 6.** [2,3]-sigmatropic rearrangement of various allylphosphinites.

The [2,3]-sigmatropic rearrangement of allylphosphinites includes the attack of the electron pair of the phosphorus atom on the double bond. A low electron density on the double bond facilitates this process. The overall enthalpy of the reaction is quite favorable (about  $-170 \text{ kJ mol}^{-1}$ ) due to the formation of a highly energetic  $\text{P}=\text{O}$  bond. The cyclic transition state ensures a high degree of the chirality transfer from the carbon atom, connected to the oxygen, to the carbon that forms a new bond with the phosphine moiety. For the rearrangement of the diarylphosphinites derived from 1,3-disubstituted allylic alcohols, two routes are possible (Scheme 7), leading to two different products:<sup>29</sup>

<sup>27</sup> A. I. Pudovik, I. M. Aladzheva, L. V. Spirina, *Zh. Obshch. Khim.* **1967**, 37, 700.

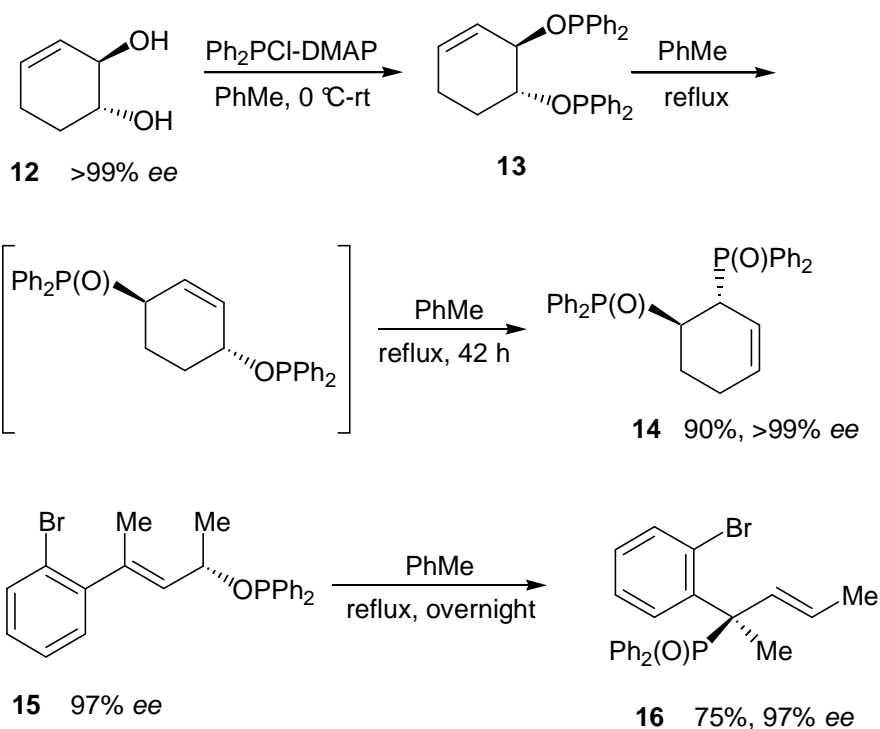
<sup>28</sup> T. Pollok, H. Schmidbaur, *Tetrahedron Lett.* **1987**, 28, 1085.

<sup>29</sup> P. Bickart, F. W. Carson, J. Jacobus, E. G. Miller, K. Mislow, *J. Am. Chem. Soc.* **1968**, 90, 4869.



**Scheme 7.** Possible transition states of the allylphosphinite-allylphosphine oxide rearrangement reaction.

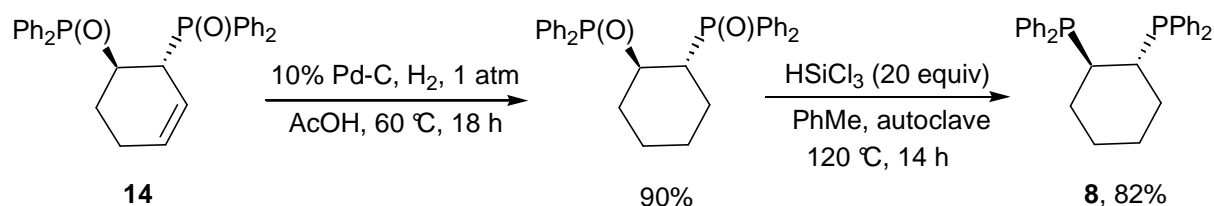
In the case of cyclic systems, the rotation around the C1-C2 bond is impossible and the rearrangement should proceed completely stereoselectively. In 2001, *Demay* proved that the rearrangement of enantiopure cyclic allylic diarylphosphinites takes place with the complete retention of the chiral information.<sup>22</sup> Shortly later, *Liron* demonstrated that this reaction proceeds with the complete transfer of chirality even in the case of flexible acyclic systems like **15**, giving enantiopure product **16** (Scheme 8):<sup>30</sup>



**Scheme 8.** Diastereoselective rearrangement of enantiopure allylic diphenylphosphinites.

<sup>30</sup> F. Liron, P. Knochel, *Chem. Comm.* **2004**, 304.

Bis-phosphine oxide **14**, derived from enantiopure 2,3-cyclohexendiol (**12**) can be further transformed into chiral diphosphine ligand **8** (Scheme 9):<sup>22</sup>



**Scheme 9.** Synthesis of ligand **8** by *Demay*.

This method allowed *Demay* preparing a number of similar ligands with a cyclohexane framework, starting from the same chiral diol **12** and several readily available diarylchlorophosphines. This showed the feasibility of this novel approach to the synthesis of libraries of ligands from the same chiral precursor, which permits their fast and easy tuning for a desired catalytic process.

The target of our investigation was to study the [2,3]-sigmatropic rearrangement reaction on chiral exocyclic allylic alcohols and apply this reaction to the synthesis of new perspective P-P ligands.

### 2.2.1. Preliminary studies of [2,3]-sigmatropic rearrangement on exocyclic systems

In the realization of this synthetic approach, three main problems have to be encountered:

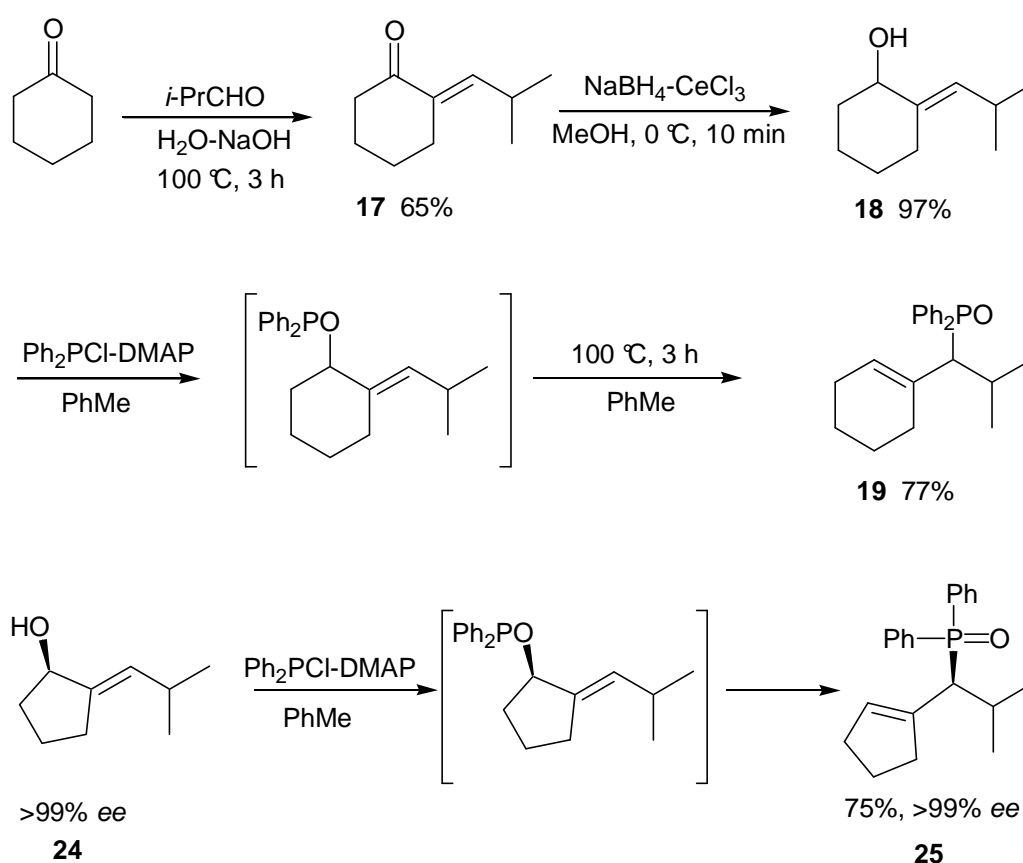
- 1) the development of a robust synthetic method for the preparation of starting allylic alcohols;
- 2) the optimization of reaction conditions for the rearrangement of allylphosphinites to the corresponding allyl phosphine oxides;
- 3) the development of pathways for the further elaboration of the prepared chiral allyl phosphine oxides into the target ligands.

The conception of the preparation of diarylphosphine oxides by the rearrangement method from exocyclic precursors was proved on a readily available model substrate. Condensation of cyclohexanone with isobutanal in a basic aqueous emulsion<sup>31</sup> gave enone **17** in a moderate yield. It was subjected to the Luche reduction<sup>32</sup> with NaBH<sub>4</sub> in the presence of 1 equiv. of CeCl<sub>3</sub> in aqueous methanol at 0 °C to obtain quantitatively the racemic allylic alcohol **18**. The corresponding diphenylphosphinite **18a** was prepared as described by *Demay* by treatment

<sup>31</sup> a) S. V. Kelkar, A. A. Arbale, G. S. Joshi, G. H. Kulkarni, *Synth. Comm.* **1990**, *20*, 839. b) R. Baltzly, E. Lorz, P. B. Russell, F. M. Smith, *J. Am. Chem. Soc.* **1955**, *77*, 624.

<sup>32</sup> a) A. L. Gemal, J.-L. Luche, *J. Am. Chem. Soc.* **1981**, *103*, 5454. b) C. Dupuy, J.-L. Luche, *Tetrahedron* **1989**, *45*, 3437.

with  $\text{Ph}_2\text{PCI}$  (1.05 equiv) and DMAP (1.05 equiv) in dry toluene,<sup>21</sup> and *in situ* rearranged into the phosphine oxide **19** in 77% yield by the heating of the reaction mixture at 100 °C for 3 h. This reaction can be conveniently monitored by  $^{31}\text{P}$  NMR. The chemical shifts of  $^{31}\text{P}$  in diphenylphosphinites lay in the region of 100-120 ppm, while for the corresponding diphenylphosphine oxides they appear between 20 and 40 ppm. Thus, the rearrangement conditions could be easily optimized in terms of time and temperature. It is noteworthy that for the exocyclic substrates the rearrangement occurs under significantly milder conditions than are usually required for this process. The anticipated complete diastereoselectivity of the process was proved by using enantiomerically pure alcohol **24** (obtained by the enzymatic resolution of the racemate, see Chapter 2.3.1) in the same reaction. The corresponding diphenylphosphine oxide was obtained after the rearrangement under the same conditions (100 °C for 3 h) in 75% yield and >99% *ee*, as was determined by chiral HPLC (Scheme 10).

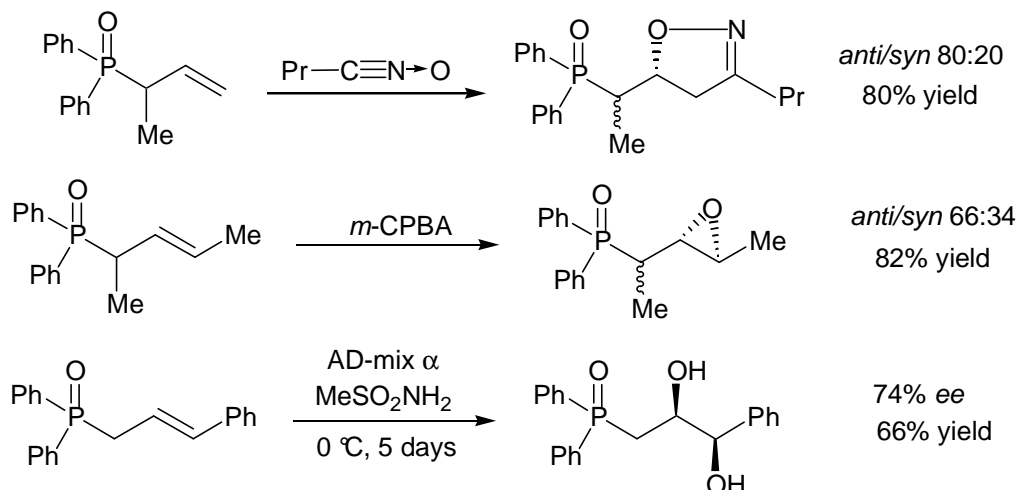


**Scheme 10.** [2,3]-Sigmatropic rearrangement on exocyclic systems.

One asymmetric carbon center bearing a phosphorus atom could be easily created in a ligand molecule by using this reaction. To prepare a bidentate phosphine ligand, another phosphorus atom has to be introduced into the same molecule.

### 2.2.2. Studies on the allylic double bond functionalization in allylphosphine oxides

The functionalization of the double bond in allylic diphenylphosphine oxides has been studied previously. *Warren* investigated several reactions of non-hindered, mostly open-chained, allyldiphenylphosphine oxides like the nitrile oxide cycloaddition, osmium-catalyzed dihydroxylation and peracid-mediated epoxidation (Scheme 11).<sup>33</sup> The halogenation of allylic diphenylphosphine oxides was shown to proceed with the migration of the diphenylphosphinoyl moiety.<sup>34</sup>



**Scheme 11.** Functionalization of the allylic double bond in allylphosphine oxides by *Warren*.

We investigated the functionalization of the allylic double bond in allyl phosphine oxides formed after the Arbuzov rearrangement on a simple model substrate. For this purpose compound **19** was chosen, which is easily available in a 3-step synthetic sequence.

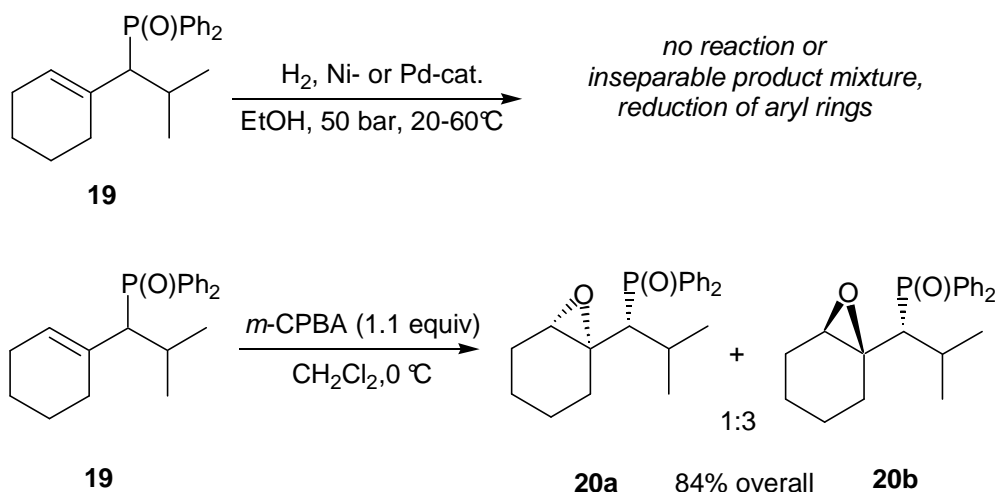
The catalytic hydrogenation of **19** did not give the desired product of the double bond reduction under all the tested conditions. In some cases the aryl rings were reduced to the corresponding cyclohexyls. This gives an easy method for the preparation of the dicyclohexylphosphine derivatives. Epoxidation of **19** with *m*-CPBA proceeded smoothly, giving an inseparable mixture of epoxides **20a** and **20b** in a 1:3 ratio, as shown by <sup>31</sup>P and <sup>1</sup>H-NMR, in 84% overall yield. According to *Warren*, mainly the *anti*-isomer should be formed in this reaction (Scheme 12):<sup>35</sup>

<sup>33</sup> a) M. J. Doyle, D. Hall, P. R. Raithby, N. Skelton, S. Warren, *J. Chem. Soc. Perkin Trans. 1* **1993**, 517. b) S. K. Armstrong, E. W. Collington, J. G. Knoght, A. Naylor, S. Warren, *J. Chem. Soc. Perkin Trans. 1* **1993**, 1433. c) P. O'Brien, S. Warren, *J. Chem. Soc. Perkin Trans. 1* **1996**, 2129. d) A. Nelson, S. Warren, *J. Chem. Soc. Perkin Trans. 1* **1997**, 2645.

<sup>34</sup> D. Howells, S. Warren, *J. Chem. Soc. Perkin Trans. 2* **1973**, 1472.

<sup>35</sup> J. Clayden, E. W. Collington, E. Egert, A. B. McElroy, S. Warren, *J. Chem. Soc. Perkin Trans. 1* **1994**, 2801.

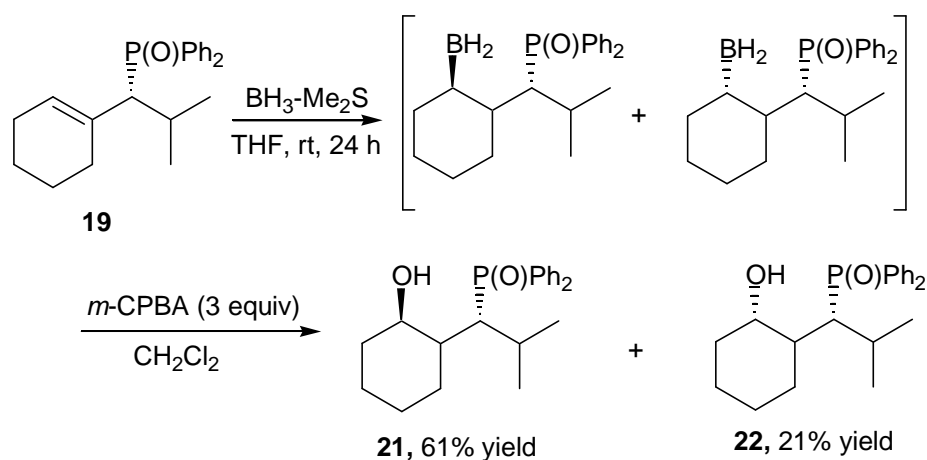




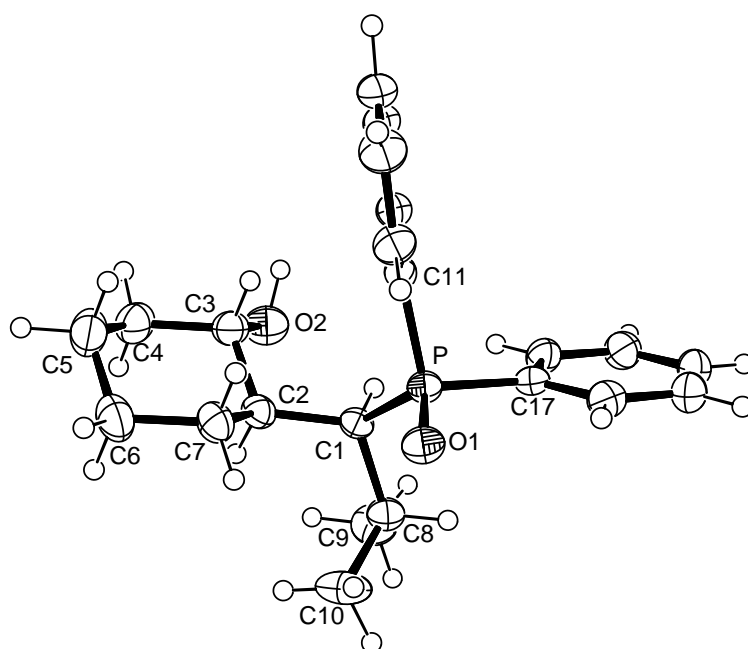
**Scheme 12.** Reduction and epoxidation of allylphosphine oxide **19**.

The epoxides **20a** and **20b** are quite resistant to a nucleophilic attack. The attempts to derivatize them by the reaction with nucleophiles (amines, potassium diphenylphosphide) were not successful. Hydroboration turned out to be more a useful reaction for this purpose.

When compound **19** was treated with 3 equiv. of  $\text{BH}_3\text{-Me}_2\text{S}$  in THF at room temperature,  $^{31}\text{P}$ -NMR analysis of the reaction mixture revealed the complete consumption of the starting material after 24 h with the formation of two new compounds in a ratio of 3:1. Addition of MeOH in order to destroy the excess of  $\text{BH}_3$ , followed by treatment with *m*-CPBA in  $\text{CH}_2\text{Cl}_2$  afforded two diastereomeric alcohols **21** and **22** in high yield and the same ratio of 3:1. The alcohols were separated by column chromatography, and the structure of the major, more polar diastereomer was confirmed by X-ray analysis (Scheme 13, Fig. 2):

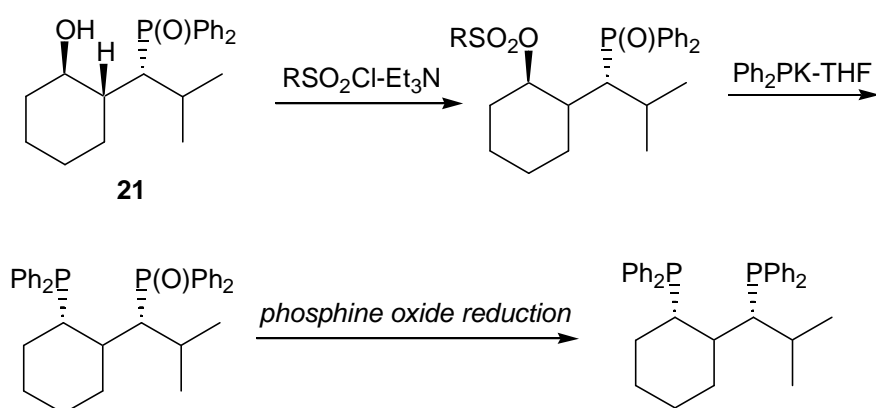


**Scheme 13.** Synthesis of diphenylphosphinoyl alcohols **21** and **22**.



**Fig. 2.** ORTEP diagram of 2-[1-(diphenylphosphinoyl)-2-methylpropyl]-cyclohexanol (**21**)

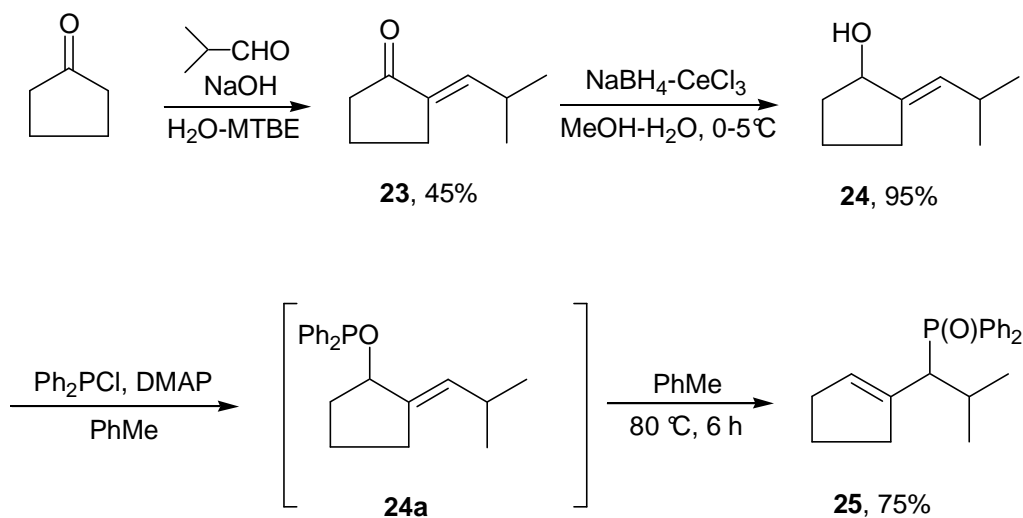
This result demonstrated the good perspectives of the hydroboration reaction in the functionalization of allyl phosphine oxides. A simple synthetic sequence could be envisioned for the synthesis of a *bis*-phosphine from compound **21** (Scheme 14).



**Scheme 14.** Possible synthetic route to the preparation of a diphosphine ligand from **21**.

Further investigation of the hydroboration of **19** revealed that changing the hydroborating agent to diethylborane increased the diastereoselectivity to 9:1. The reaction in this case required 20 h at 70 °C. Further increase of the size of the hydroborating agent (using dicyclohexylborane, 9-BBN and (-)-isopinocampheylborane) made the reaction too sluggish

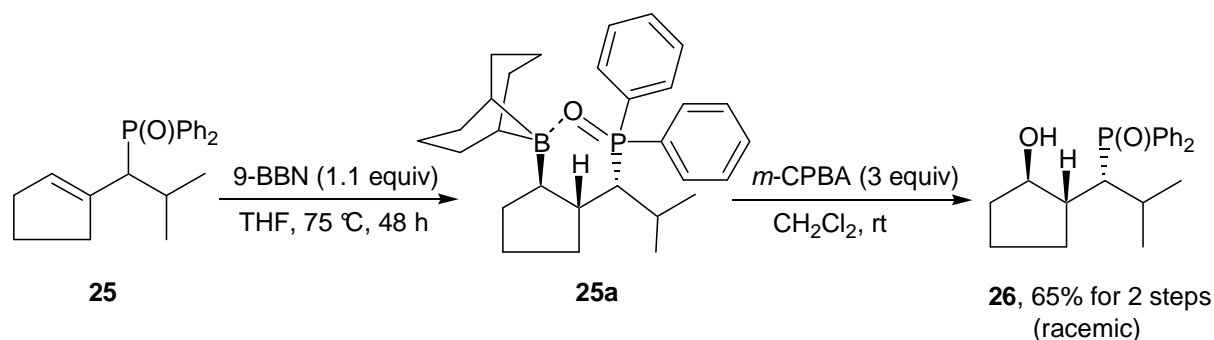
even at 90 °C. Therefore, we changed the attention to cyclopentane derivatives, presuming that a rigid 5-membered ring would offer a better side differentiation and a less steric hindrance during the hydroboration reaction. The substrate **25** was prepared according to a method which is similar to the one used for compound **19** (Scheme 15):



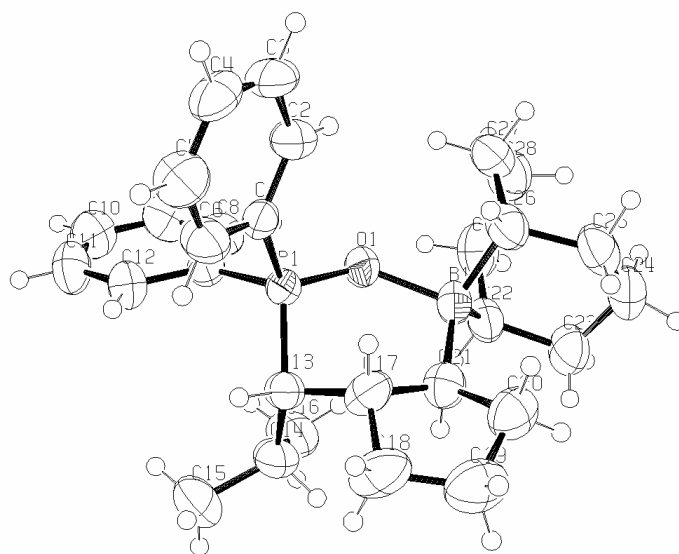
**Scheme 15.** Synthesis of allyldiphenylphosphine oxide **25**.

The reaction of **25** with  $\text{BH}_3\text{-Me}_2\text{S}$  at room temperature gave two diastereomers in a 85:15 ratio as was observed by  $^{31}\text{P}$ -NMR. The reaction with 9-borabicyclo[3.3.1]borane (9-BBN) in THF at 75 °C within 48 h led to a single diastereomer of product **25a**. Interestingly, this compound turned out to be a relatively air-stable crystalline solid. Its structure was determined by X-ray analysis (Fig. 3). The length of the donor-acceptor B-O bond in this molecule is close to the length of the P-O bond, demonstrating a strong intramolecular interaction responsible for the high stability toward air oxidation, unusual for a trialkylborane. Due to this interaction, the chemical shift of the phosphorus atom in  $^{31}\text{P}$  NMR spectra of this compound is about 60 ppm, while usual values for alkylidiphenylphosphine oxides are in the range of 30-40 ppm.

Treatment of the hydroboration adduct **25a** with *m*-CPBA in  $\text{CH}_2\text{Cl}_2$  afforded the desired alcohol **26** as a single diastereomer in a 65% overall yield.

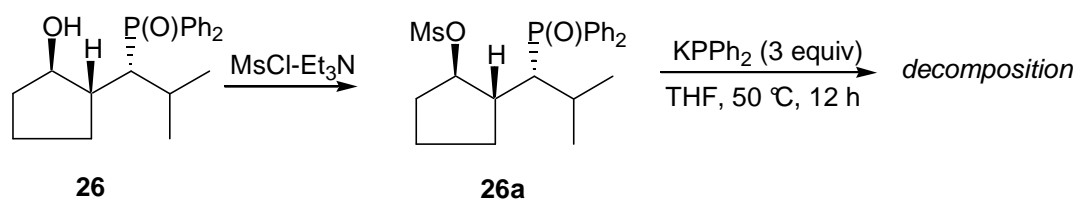


**Scheme 16.** Diastereoselective hydroboration-oxidation of compound **25**.



**Fig. 3.** ORTEP diagram of 9-{2-[1-(diphenylphosphino)propyl]-cyclopentyl}-9-bora-bicyclo[3.3.1]nonane (**25a**).

In the next steps, the hydroxyl moiety had to be substituted by a diphenylphosphinyl group. Conversion of the alcohol **26** into the corresponding mesylate **26a** (MsCl, Et<sub>3</sub>N, CH<sub>2</sub>Cl<sub>2</sub>, 0 °C) required a 2-3-fold excess of MsCl and the base. Treatment of **26a** with commercial solution of Ph<sub>2</sub>PK in THF (3 equiv, RT) gave no desired product (Scheme 17). We assumed that the diphenylphosphinoyl group has to be reduced and protected<sup>36</sup> before the nucleophilic substitution of the alcohol becomes possible.



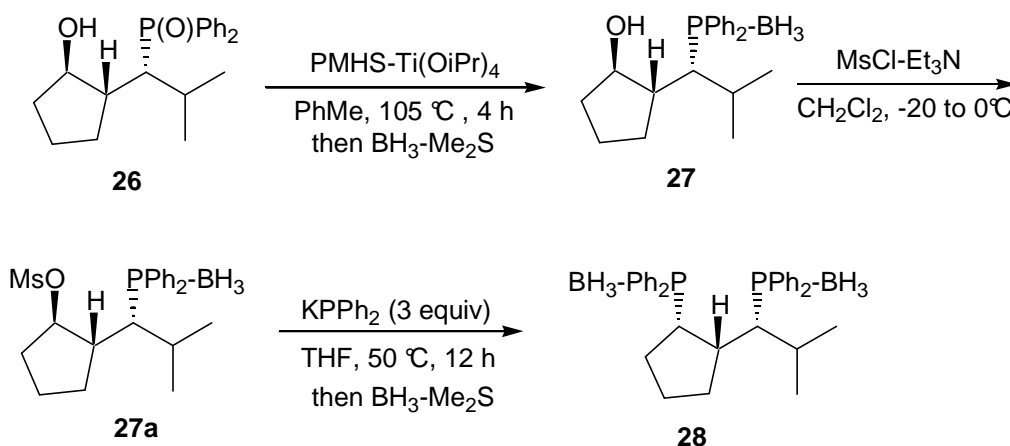
**Scheme 17.** Substitution of alcohol **26**.

<sup>36</sup> P. Pellon, *Tetrahedron Lett.* **1992**, *33*, 4451.

After several experiments we have found the reduction with  $\text{Ti}(\text{OiPr})_4$  and polymethylhydrosiloxane (PMHS)<sup>37</sup> the most efficient. This reaction proceeds *via* the formation of a Ti(II) species, responsible for the smooth reduction of a P=O bond. The published method was optimized in order to simplify the isolation of the product. The reaction mixture, after the protection with borane, was treated with an excess of 20% aq. HF for several hours at room temperature. This treatment converts all the silicon, titanium and boron compounds into the highly hydrophilic complex anions, and thus leaves the organic phase free from inorganic materials. Thus, the phosphine oxide **26** was heated for 2 h in toluene at 105 °C in the presence of 4 equiv. of PMHS and 1 equiv. of  $\text{Ti}(\text{OiPr})_4$ , until <sup>31</sup>P-NMR showed complete conversion. Borane-dimethylsulfide (1.5 equiv) was added to the mixture and it was stirred with an excess of 20% HF in a PTFE vessel at room temperature for 12 h. The yields of the phosphine-borane complexes usually exceeded 95% (Scheme 18). The borane protection remains intact during this procedure. This convenient protocol was later used for the reduction of all the phosphinoyl groups in our ligand syntheses.

### 2.3 Preparation of optically pure diphosphine ligands with a cyclopentane core

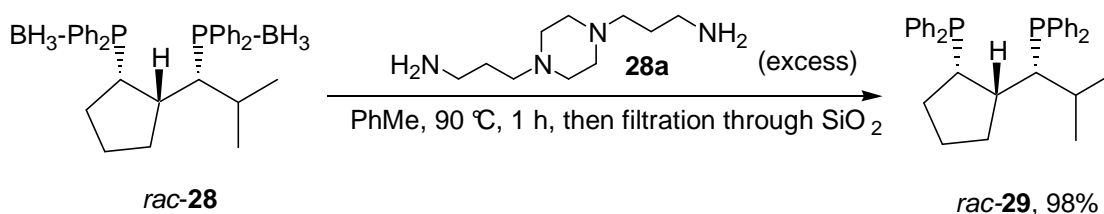
The phosphine-borane **27** was further transformed into the corresponding mesylate **27a** as described above, and reacted with an excess of commercial  $\text{KPh}_2$  in THF from 0 to 50 °C for 12 h. Instead of  $\text{KPh}_2$ , a mixture of  $\text{Ph}_2\text{PH}$  and *t*-BuOK in THF can be used. After mixing of these compounds the solution immediately turns orange, which indicates the formation of the diphenylphosphide anion. Excess of  $\text{BH}_3\text{-Me}_2\text{S}$  was added to protect the introduced phosphine group, and *bis*-phosphine-borane **28** was isolated by crystallization from hexanes in 52% yield (Scheme 18).



**Scheme 18.** Synthesis of racemic *bis*-phosphine-borane **28**.

<sup>37</sup> T. Coumbe, N. J. Lawrence, F. Muhammad, *Tetrahedron Lett.* **1994**, 35, 625.

The deprotection of phosphine-borane complexes to form phosphines is usually performed by several heating-evaporation cycles with a volatile amine, removing the formed amine-borane complex *in vacuo*. While this method works well for monophosphine-boranes, the complete deprotection of *bis*-phosphines by this procedure is quite difficult.<sup>38</sup> Therefore, we designed a new, more convenient deprotection method for *bis*-phosphine-boranes. The substrate was heated with commercially available inexpensive *bis-N,N'*-(3-aminopropyl)-piperazine in toluene at 100 °C for 1-2 h. The borane migrates to a more basic nitrogen atom of the polyamine. Since the resulting amine-borane still possesses free highly polar amino groups, it can be easily removed from the reaction mixture by passing it in an ethereal solution through a short pad of dry degassed silica gel. The resulting phosphine was obtained in nearly quantitative yield. These simple operations can be easily performed in an inert atmosphere, using standard Schlenk techniques. This new method turned out to be very convenient for the deprotection of various *bis*-phosphine-boranes. Using this technique, the free racemic phosphine **29** was obtained in 98% yield (Scheme 19).



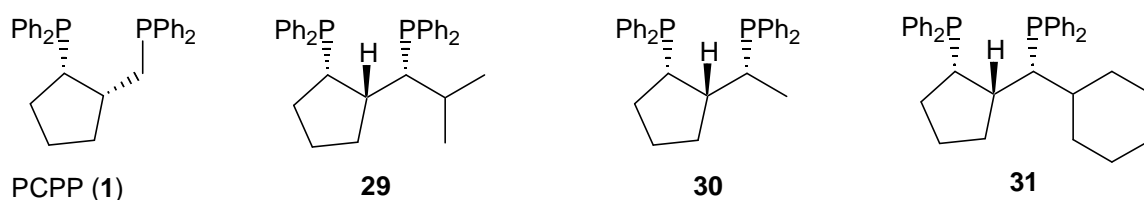
**Scheme 19.** New method for the deprotection of *bis*-phosphine-boranes.

By this synthetic sequence the problem of the functionalization of the allylic double bond and the diastereoselective introduction of a second phosphine moiety was solved. It opened the way to the preparation of a number of new chiral *bis*-phosphine ligands having a good potential for transition metal catalysis.

### 2.3.1. Enzymatic resolution of 2-alkylidenecyclopentanols

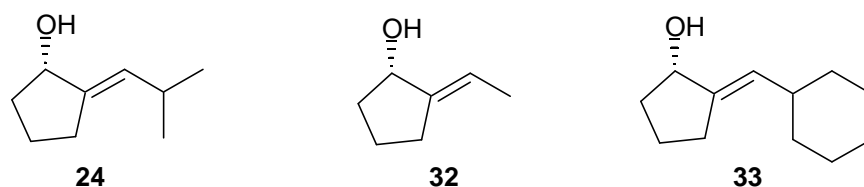
The preparation of novel chiral phosphines according to the method described above required the development of a robust procedure for the synthesis the allylic alcohols as starting materials. We chose three analogs of the known ligand BCPP (**1**)<sup>9</sup> as synthetic targets (Scheme 20):

<sup>38</sup> a) D. Williams, G. Bradley, H. Lombard, M. van Nierkerk, P. P. Goetze, C. W. Holzapfel, *Phosphorus, Sulfur, Silicon and Rel. El.* **2002**, 177, 2799. b) D. Williams, G. Bradley, H. Lombard, M. van Nierkerk, P. P. Goetze, *Phosphorus, Sulfur, Silicon and Rel. El.* **2002**, 177, 2115.



**Scheme 20.** The alkyl analogs of ligand PCPP (**1**).

Ligand **1** affords 96% *ee* in the Rh-catalyzed hydrogenation of acetamidocinnamic ester. The preparation and screening of ligands **29-31** would be interesting in order to reveal the influence of the introduction of an alkyl group of different sizes on the enantioselectivity of the transition metal catalysis. The enantiopure starting allylic alcohols for the synthesis of ligands **29-31** will have the following structures (Scheme 21):



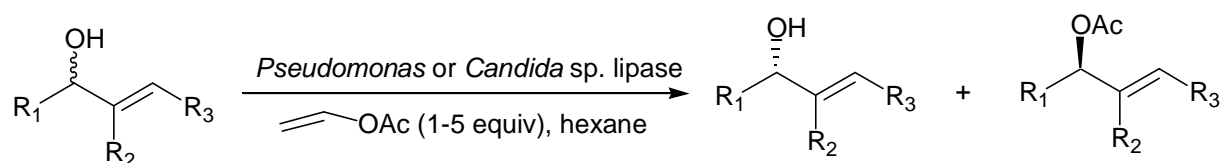
**Scheme 21.** Chiral allylic alcohols as starting materials for the synthesis of ligands **29-31**.

Since the racemates of those alcohols are readily available in sufficient amounts by a 2-step sequence, we checked the possibility to perform the resolution of enantiomers. One of the most practical ways for secondary alcohols is enzymatic kinetic resolution, which is based on the enzyme-catalyzed transfer of an acyl moiety from an ester onto a single enantiomer of the substrate.<sup>39</sup> This method, sometimes with simultaneous epimerization of the undesired enantiomer, has been used for the preparation of a variety of enantiomerically pure amines and alcohols.<sup>40</sup> The procedure of the enantioselective transesterification is exceptionally simple. It is performed by the stirring of the alcohol with 0.6-5 equiv of an acyl donor (usually vinyl acetate to ensure the irreversibility of the reaction) in the presence of a suitable enzyme in an unpolar solvent. After the reaction completion, the enzyme is filtered off and the

<sup>39</sup> a) J. M. J. Williams, R. J. Parker, C. Neri, in: *Enzyme Catalysis in Organic Synthesis*, 2<sup>nd</sup> Ed., Wiley-Weinheim, **2002**, 287. b) Z. Wimmer, V. Skoridou, M. Zarevucka, D. Saman, F. N. Kolisis, *Tetrahedron: Asymmetry* **2004**, *15*, 3911. c) V. Bodai, O. Orovecz, G. Szakacs, L. Novak, L. Poppe *Tetrahedron: Asymmetry* **2003** *14*, 2605.

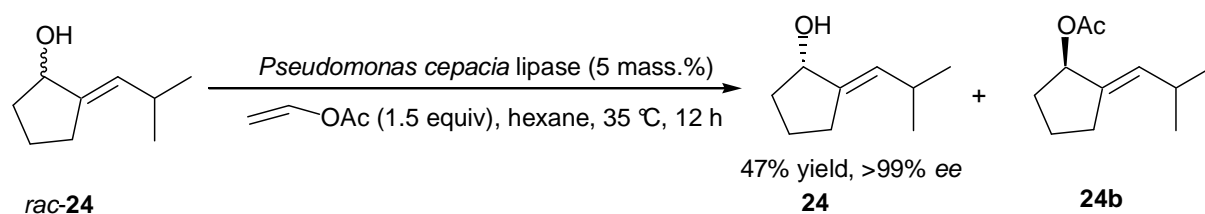
<sup>40</sup> S. Akai, K. Tanimoto, Y. Kanao, M. Egi, T. Yamamoto, Y. Kita, *Angew. Chem. Int. Ed.* **2006**, *45*, 2592 and refs. therein.

enantiomerically enriched alcohol and the acetate of the opposite enantiomer are separated by any suitable way like column chromatography. The choice of the enzyme is dictated by the substrate structure and normally requires a screening procedure. For allylic alcohols, the lipases from *Pseudomonas* sp. and the lipase from *Candida antarctica* (Novozym 435®) have been successfully used (Scheme 22).<sup>40</sup>



**Scheme 22.** Enantioselective enzymatic kinetic resolution of allylic alcohols.

The lipase from *Pseudomonas cepacia* (PS-A, Aldrich) showed excellent results in the screening of the kinetic resolution of alcohol **24**. Hexane was used as a solvent in the presence of 1.5 equiv. of vinyl acetate and 5 mass. % of the enzyme. The reaction conversion was monitored by GC analysis. After the reaction completion, the enzyme was removed by filtration and the optical purity of the remained alcohol was measured by chiral HPLC. The single enantiomer (>99.5% *ee*) of **24** was obtained in 47% yield (94% from theory) after 12 h at 35 °C (Scheme 23). The enantiopure alcohol **24** and the acetate **24b** were readily separated by column chromatography. This simple technique was also successfully applied to the preparation of enantiopure alcohols **32** and **33**, affording nearly quantitative yields of the products with excellent enantioselectivities. The enzymatic resolution with PS-A proved to be a straightforward way to prepare enantiopure allylic alcohols **24**, **32-33** in a multigram scale.

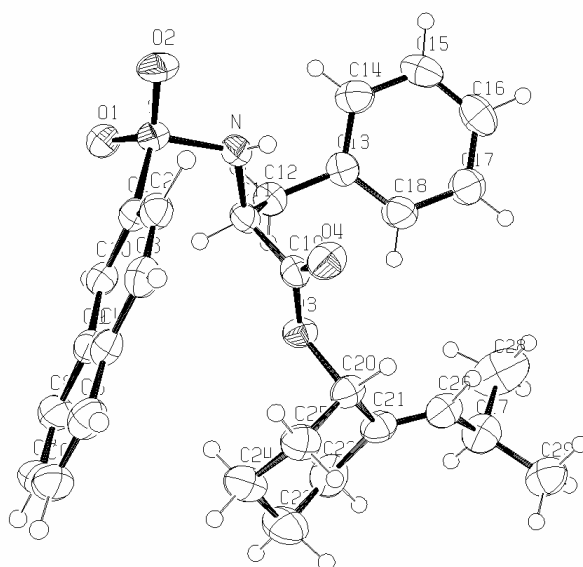


**Scheme 23.** Enzymatic kinetic resolution of alcohol **24**.

The same conditions were applied to the enzymatic kinetic resolution of 2-isopropylidencyclohexanol (**18**). In this case the enantioselectivity was slightly lower and the reaction significantly slower. The desired alcohol was obtained after 3 days with 92% *ee* in 45% yield. Despite many efforts, we were not able to obtain from any derivatives of alcohols

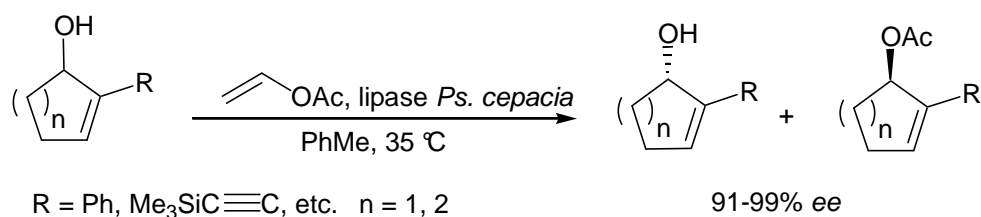


**24, 32-33** (esters with *O*-acetylmandelic and Mosher acids, 1-phenylethylcarbamate) a crystal, suitable for the X-ray analysis in order to establish their absolute configuration. We assigned to them the (*S*)-configuration, based on the following facts. First, the enantioselective transesterification of alcohol **18**, catalyzed by the *Pseudomonas cepacia* lipase, gives enantioenriched **18** with the (*S*)-configuration (92% ee) as was proven by the X-ray structure of its ester with *N*-(2-naphthylsulfonyl)-(*S*)-phenylalanine (Fig. 4).



**Fig. 4.** ORTEP diagram of (*S,S*)-2-(naphthalene-2-sulfonylamino)-3-phenyl-propionic acid 2-isobutyridene-cyclohexyl ester.

Then, the enantioselective acylation of 2-substituted cyclohexen-2-ols and cyclopenten-2-ols catalyzed by the *Pseudomonas cepacia* lipase gives (*R*)-acetates and (*S*)-alcohols with high enantioselectivities independently on the size and structure of the substituent:<sup>50</sup>

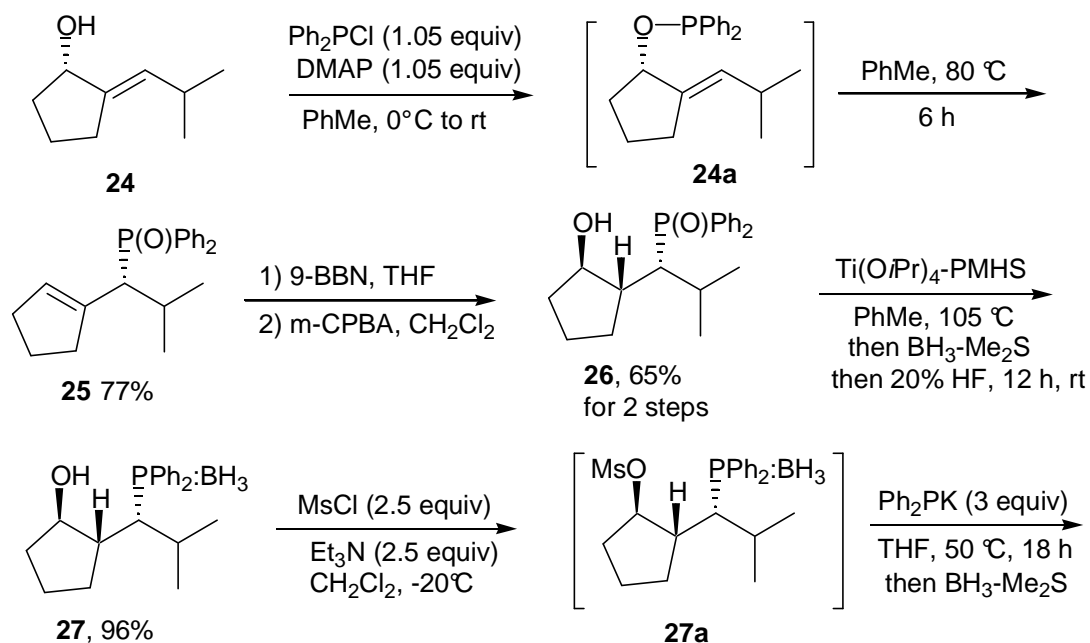


**Scheme 24.** Enzymatic kinetic resolution of 2-substituted cyclopentenols.

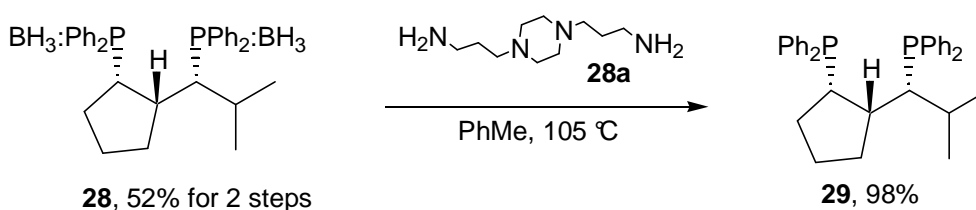
According to the commonly accepted mechanism of the enzyme-catalyzed acylation, for similar substrates the absolute selectivity of an enzyme-catalyzed reaction should be the same, as it is determined only by the spatial structure of the enzyme “chiral pocket”, where the catalytic center is placed.<sup>41</sup>

### 2.3.2. Enantioselective synthesis of alkyl-substituted analogs of PCPP

Using the enantiopure alcohol **24**, we performed the same synthetic sequence that was formerly used for the racemic compound. The [2,3]-sigmatropic rearrangement of the corresponding diphenylphosphinite **24a** gave enantiomerically pure allyldiphenylphosphine oxide **25**, as was proved by chiral HPLC analysis. Its hydroboration with 9-BBN gave a single diastereomer of the product, which was directly oxidized by *m*-CPBA into the corresponding alcohol **26**. Its reduction with  $\text{Ti}(\text{O}i\text{Pr})_4$ -PMHS<sup>37</sup> and *in situ* protection with  $\text{BH}_3$ - $\text{Me}_2\text{S}$  gave phosphine-borane **27** in almost quantitative yield. Compound **27** was converted into the mesylate **27a** (2.5 equiv.  $\text{MsCl}$ , 2.5 equiv.  $\text{Et}_3\text{N}$ ,  $\text{CH}_2\text{Cl}_2$ , -20 to 0 °C, 2 h), which was reacted with the excess of 1 M  $\text{Ph}_2\text{PK}$  in THF. After 18 h, the resulted phosphine was protected with the excess of  $\text{BH}_3$ - $\text{Me}_2\text{S}$ . Recrystallization from hexanes afforded the *bis*-phosphine-borane complex **28** as a white crystalline solid. It was deprotected using *bis*-(3-aminopropyl)-piperazine (**28a**) in PhMe (105 °C, 1 h). The resulting enantiopure ligand **29** was obtained as an air-sensitive foam in nearly quantitative yield (Scheme 25).

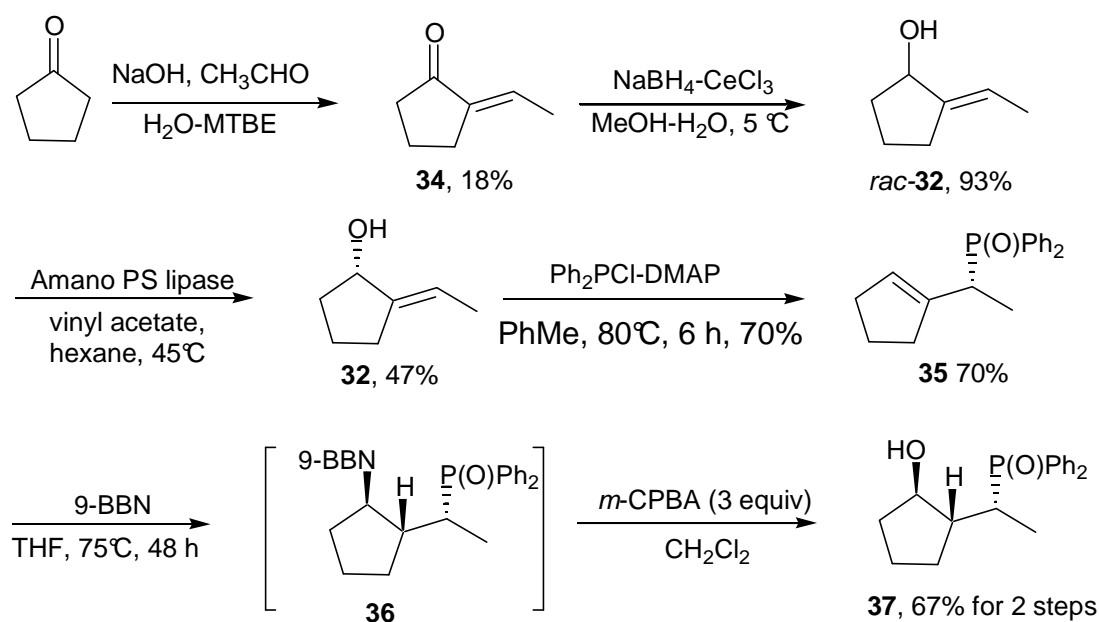


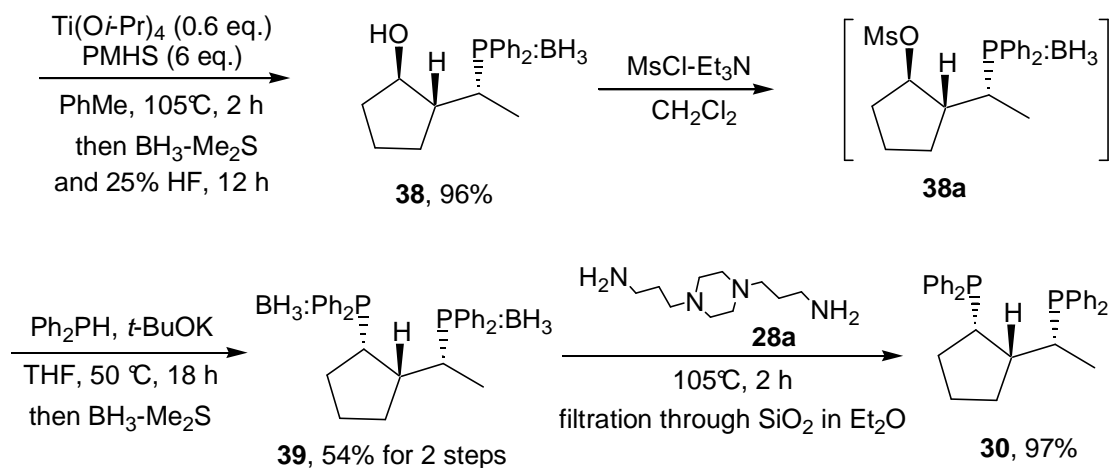
<sup>41</sup> K. Faber, *Biotransformations in Organic Synthesis*, 3<sup>rd</sup> Ed. Springer: Heidelberg, 1997.



**Scheme 25.** Enantioselective synthesis of diphosphine ligand **29**.

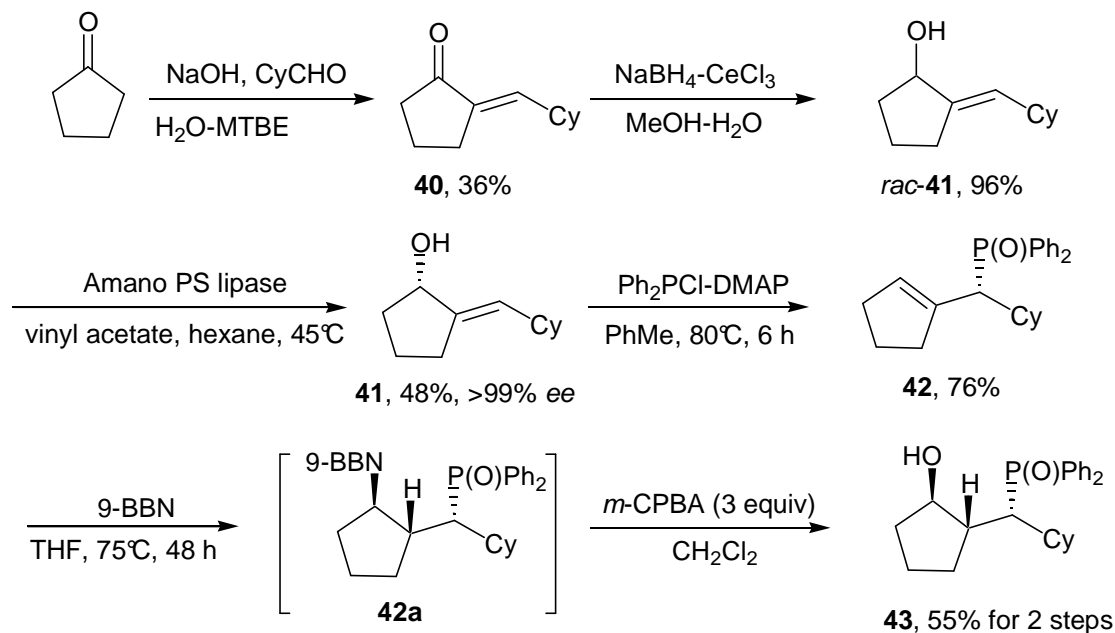
In a similar way, the analogs of **29** with the methyl and cyclohexyl side chains were prepared. Condensation of cyclopentanone with acetaldehyde gave 18% yield of enone **34**. Despite the low yield, it afforded 200 mmol of this product in a single batch, which was subjected to the Luche reduction.<sup>32</sup> The enantiomers of alcohol **32** were resolved using the chemoenzymatic method described above with excellent results. The rearrangement of its diphenylphosphinite into compound **35**, the hydroboration-oxidation sequence, the reduction of phosphine oxide **37** and the nucleophilic substitution of the alcohol group in **38** furnished *bis*-phosphine-borane **39**. It was deprotected by heating with *bis*-(3-aminopropyl)-piperazine (**28a**), what gave diphosphine **30** in almost quantitative yield (Scheme 26):

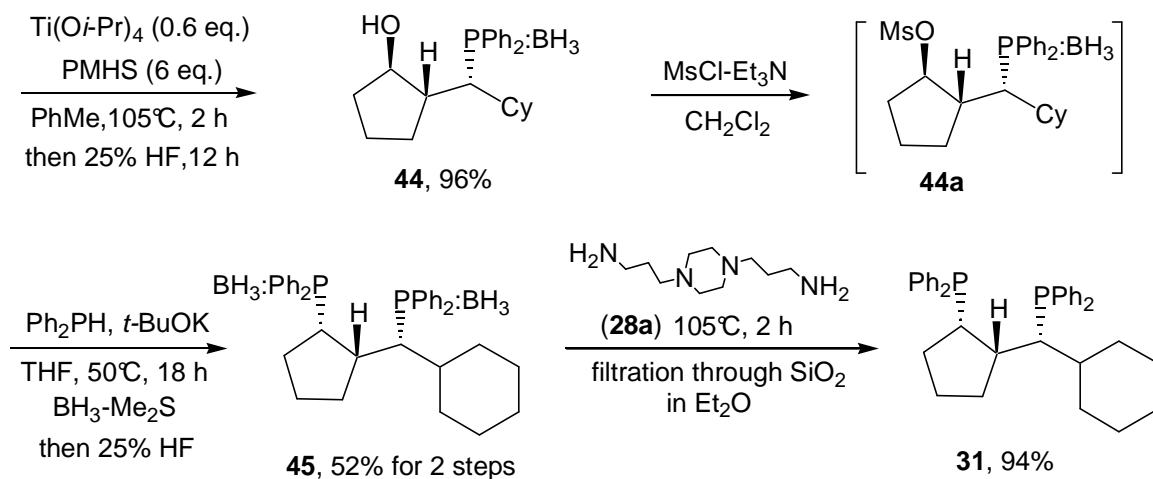




**Scheme 26.** Enantioselective synthesis of diphosphine ligand **30**.

Starting from enone **40**, the same sequence was performed *via* phosphine oxide **42**, alcohols **43** and **44** and *bis*-phosphine-borane **45** to yield the cyclohexyl analog **31** (Scheme 27). All the previously developed synthetic steps worked excellent on this substrate despite the greater steric hindrances, caused by the cyclohexyl group.





**Scheme 27.** Enantioselective synthesis of diphosphine **31**.

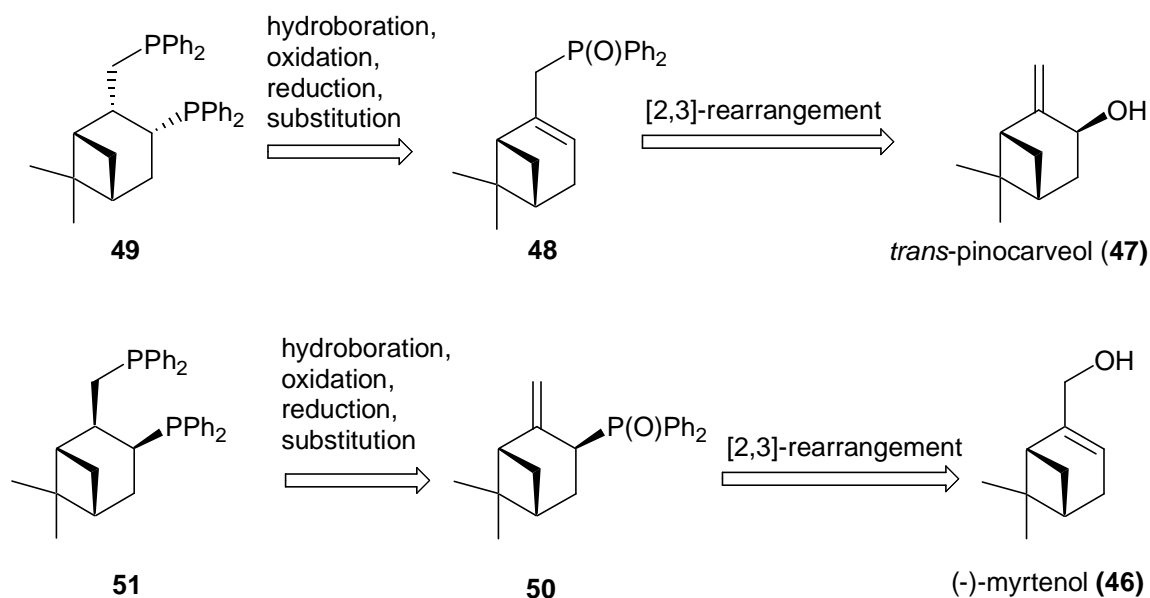
In summary, we successfully applied the allylphosphinite-allylphosphine oxide [2,3]-sigmatropic rearrangement to the preparation of several new chiral diphosphine ligands with a cyclopentane scaffold. The starting enantiopure allylic alcohols were prepared by enzyme-catalyzed kinetic resolution of the corresponding racemates. The diastereoselective functionalization of the double bond in the resulted allyldiphenylphosphine oxides was achieved by the hydroboration with 9-BBN. The diphenylphosphinoalcohols, obtained after the oxidation of the boron adducts, were reduced into the corresponding phosphine-boranes, transformed into the mesylates and reacted with potassium diphenylphosphinide to obtain the diphosphines. The borane protection of the air-sensitive phosphine groups was applied during the synthesis. The was removed on the last step by a new method, especially suitable for the deprotection of *bis*-phosphines.

#### 2.4 Synthesis of new chiral diphosphines with a terpene framework

A number of readily available compounds derived from the chiral pool possess an allylic alcohol function. Such compounds can be quite interesting starting materials for the studies on the allylphosphinite [2,3]-sigmatropic rearrangement and the further elaboration of chiral phosphorus ligands. The methods, formerly developed for the transformation of allylphosphine oxides into the corresponding diphosphines could also be applied in this case. We have chosen two naturally occurring pinene-derived compounds, (-)-myrtenol (**46**) and *trans*-pinocarveol (**47**) (Scheme 28) for the study of the allylphosphinite-allylphosphine oxide rearrangement in the application to the synthesis of new chiral ligands. Both of them are

available from commercial sources, and *trans*-pinocarveol can be prepared in large amounts from cheap  $\beta$ -pinene, the main component of turpentine oil.<sup>42</sup>

The reaction sequence, similar to the described above for the synthesis of the diphosphine ligands with the cyclopentane framework, while starting from these alcohols, should give two diastereomeric ligands **49** and **51** (Scheme 28).

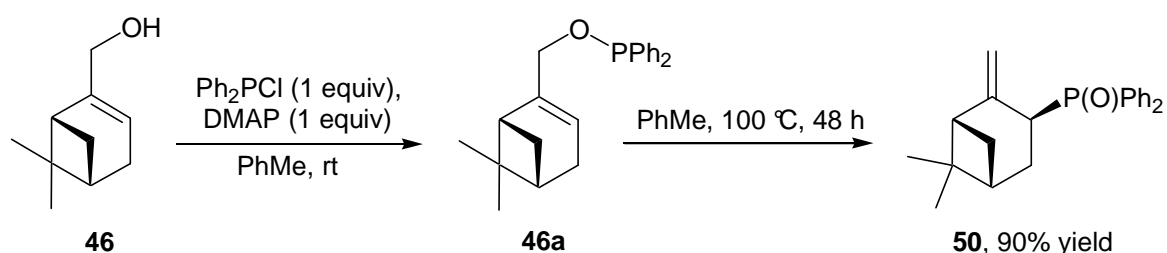


**Scheme 28.** Retrosynthetic analysis of the diphosphines **49** and **51**.

#### 2.4.1. Preparation of diphosphine ligands starting from (-)-myrtenol

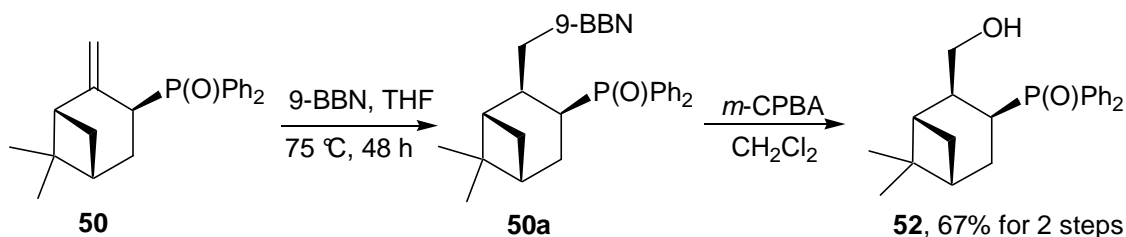
Both enantiomers of myrtenol are widely occurring in nature as components of essential oils and tree resins. (-)-Myrtenol is commercially available and relatively cheap (1.20 Euro per gram, *Aldrich*). Since the rearrangement reaction of the corresponding phosphinite would proceed with the formation of an exocyclic double bond, this process should be more sluggish than the similar rearrangement on exocyclic systems. The myrtenyl diphenylphosphinite **46a** was obtained by usual way from  $\text{Ph}_2\text{PCl}$  and DMAP in toluene at room temperature and subjected *in situ* to the thermal rearrangement. Indeed, the reaction took 48 h at 100 °C to complete as was displayed by  $^{31}\text{P}$  NMR, and furnished 90% yield of a single diastereomer of **50** (Scheme 29). The electrophilic attack at the pinene double bond usually occurs diastereoselectively due to the significant steric hindrance caused by the methyl groups.<sup>43</sup>

<sup>42</sup> J. M. Coxon, E. Dansted, M. P. Hartshorn, *Org. Synth.* **1977**, *56*, 25.

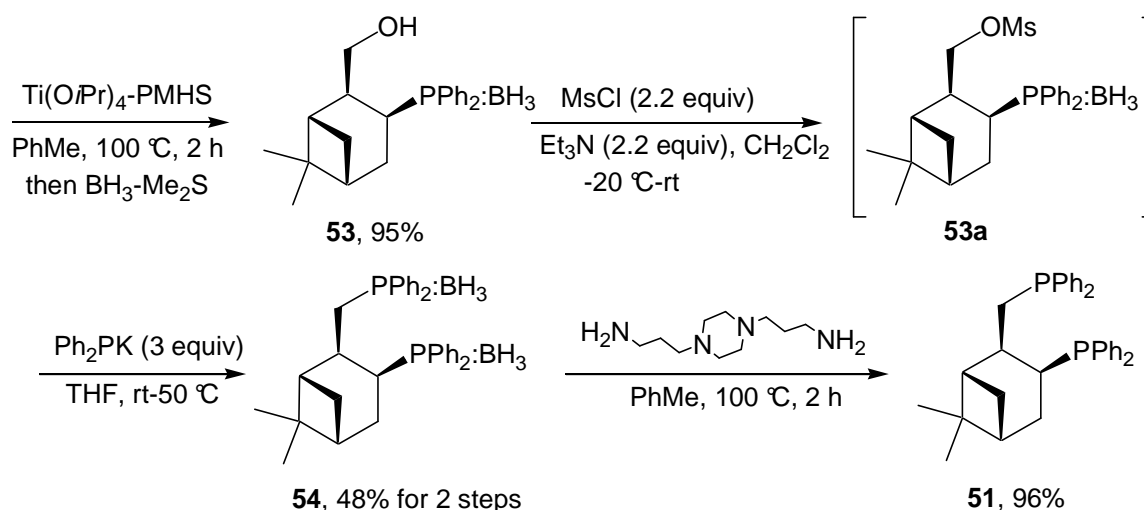


**Scheme 29.** [2,3]-Sigmatropic rearrangement of myrtenyl diphenylphosphinite (**46a**).

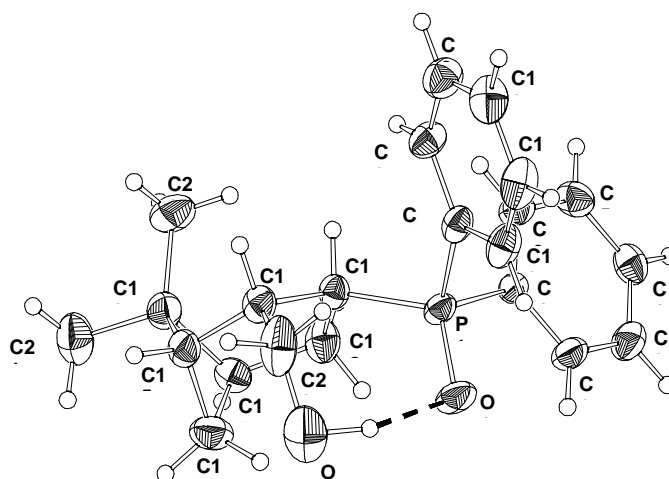
While for  $\beta$ -pinene the hydroboration occurs with a high diastereoselectivity,<sup>43</sup> the reaction of **50** with  $\text{BH}_3\text{-Me}_2\text{S}$  gave a 3:1 mixture of diastereomers. In this case, two methyl groups and the diphenylphosphinoyl moiety direct the borane attack to the double bond in an opposite way. The observed stereoselectivity for the relatively small borane is not sufficient. The use of more bulky 9-BBN-H, however, gave a single crystalline product **50a**, which appeared to be fairly stable in air. Its oxidation with *m*-CPBA in  $\text{CH}_2\text{Cl}_2$  led to a single diastereomer of the diphenylphosphinoyl alcohol **52**. Its structure was confirmed by X-ray analysis (Fig. 5). Alcohol **52** was reduced as described above by  $\text{Ti}(\text{O}i\text{Pr})_4\text{-PMHS}$  in toluene to the corresponding phosphine and protected *in situ* with  $\text{BH}_3\text{-Me}_2\text{S}$ . The product **53** was isolated from thereaction mixture as a glassy foam in 95% yield after the work-up with 20% HF. It was converted into the corresponding mesylate **53a** and reacted with  $\text{Ph}_2\text{PK}$  in THF. The resulted diphosphine was protected *in situ* with borane. The *bis*-phosphine-borane complex **54** was crystallized from hexane in 48% overall yield. It was deprotected by heating with *bis*-(3-aminopropyl)-piperazine in PhMe (100 °C, 2 h) and the *bis*-phosphine ligand **51** was isolated after filtration in ether through a pad of dry silica under argon as a wax-like air-sensitive mass (Scheme 30).



<sup>43</sup> H. C. Brown, N. N. Joshi, *J. Org. Chem.* **1988**, *53*, 4059.



**Scheme 30.** Synthesis of diphosphine ligand **51**.



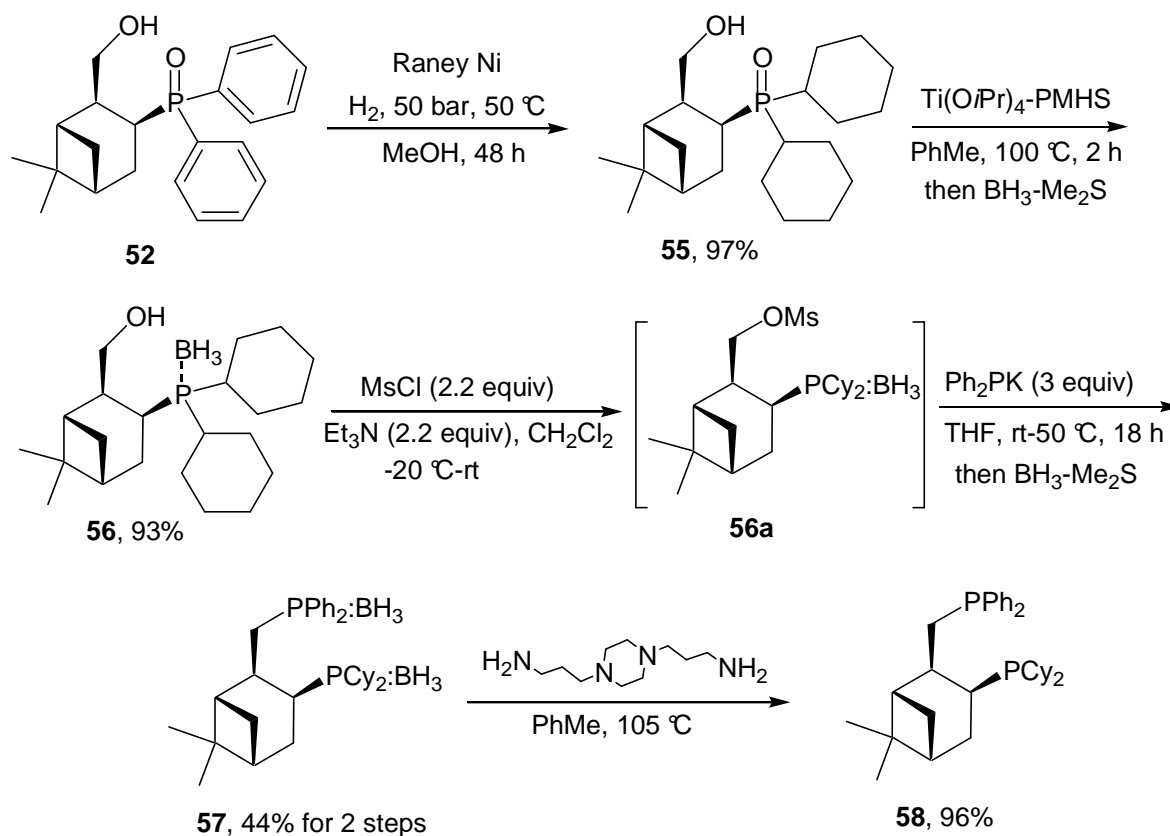
**Fig. 5.** ORTEP diagram of alcohol **52**.

“Mixed” *bis*-phosphine ligands with different substituents on the phosphorus atoms often possess the more interesting and useful properties than their “symmetrical” analogs.<sup>13</sup> In our case, we could convert one diphenylphosphinoyl group into the dicyclohexylphosphinoyl moiety by simple hydrogenation and then, continuing the general synthetic sequence, obtain “mixed” dicyclohexyl-diphenyl phosphine ligand. The reduction of alcohol **52** (200% mass of Raney Ni, 50 bar, 50 °C, 48 h in MeOH) proceeded smoothly and gives quantitatively the corresponding cyclohexyl analog **55**.<sup>44</sup> The reduction of the P=O bond of the dicyclohexylphosphinoyl group by the previously used method (PMHS-Ti(OiPr)<sub>4</sub>, 2 h at 100

<sup>44</sup> a) Krause, H.; Doebler, C. *Catalysis Letters* **1991**, *8*, 23-6. b) Yamamoto, K.; Saeed R. *Chem. Lett.* **1984**, *9*, 1603-6.



°C) and protection gave phosphine-borane **56** in an excellent yield. The conversion of alcohol **56** into the mesylate **56a** proceeded smoothly, and after nucleophilic substitution with Ph<sub>2</sub>PK and *in situ* protection, the *bis*-borane complex **57** was isolated by crystallization in 44% yield. The deprotection with *bis*-(3-aminopropyl)-piperazine in PhMe (100 °C, 12 h) afforded the pure diphosphine **58** (Scheme 31):



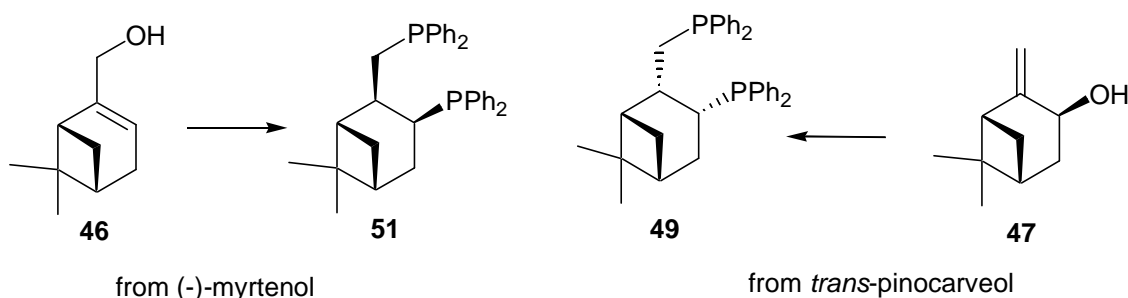
**Scheme 31.** Synthesis of the “mixed” diphosphine ligand **58**.

Attempts to prepare *bis*-dicyclohexylphosphine derivatives by the reaction of the mesylate **56a** with the *in situ* prepared Cy<sub>2</sub>PLi or with a Cy<sub>2</sub>PH-*t*-BuOK mixture failed. In both cases, the compound decomposed, giving a complex mixture of products.

#### 2.4.2. Preparation of diphosphine ligands from *trans*-pinocarveol (**47**)

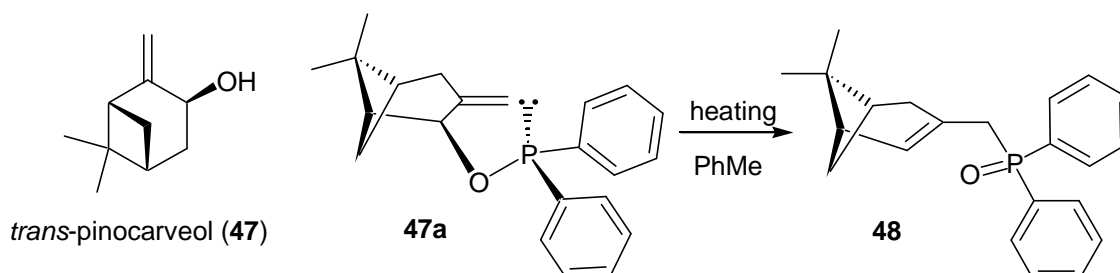
Similarly to myrtenol, *trans*-pinocarveol is widely spread in nature, mostly in essential oils and as a component of insect pheromones. It can be prepared in large amounts from β-pinene, the main component of turpentine oil, by a single-step SeO<sub>2</sub>-promoted diastereoselective hydroxylation.<sup>42</sup> The synthetic sequence, used for the preparation of **51**, starting from *trans*-

pinocarveol, should give its diastereoisomer **49**, where the diphenylphosphine and methylenediphenylphosphine groups are directed in the opposite way (Scheme 32). The comparison of both compounds as ligands for asymmetric catalysis would be interesting and could give an insight on the structure-activity relations in this class of compounds.



**Scheme 32.** Diposphine ligands, prepared from myrtenol and pinocarveol.

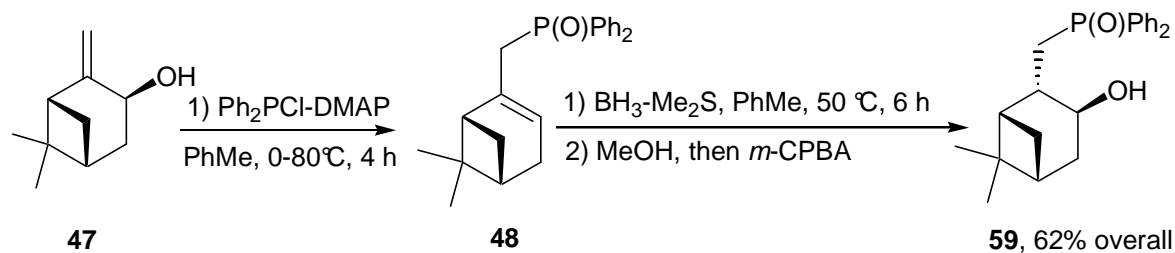
The thermal rearrangement of the diphenylphosphinite **47a** should proceed easily, due to a relatively little sterical hindrance for the attack of the terminal double bond. Only a single diastereomer of the rearranged product can form in this case (Scheme 33):



**Scheme 33.** Rearrangement reaction of pinocarveol diphenylphosphinite (**47a**).

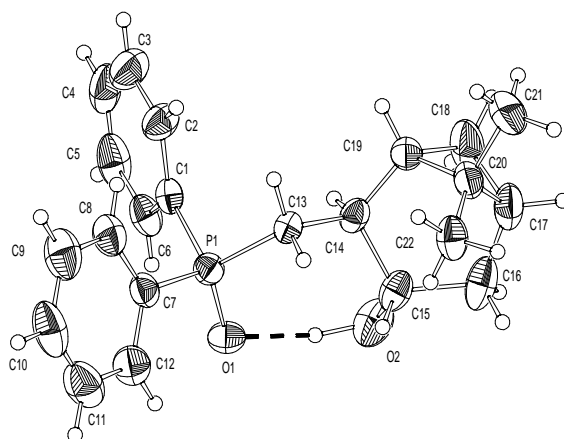
*trans*-Pinocarveol diphenylphosphinite (**47a**) was prepared by usual way from **47**, Ph<sub>2</sub>PCl and DMAP in toluene. Its rearrangement required unusually mild conditions and proceeded with significant rate even at 65 °C. It was completed at 80 °C within 4 h and afforded the myrtenyl diphenylphosphine oxide **48** in 75% yield. The product has a relatively low melting point and could be isolated in crystalline form only after careful chromatographical separation. The next steps were carried out similarly to those previously described for the ligand synthesis starting from (-)-myrtenol. The diphenylphosphine oxide **48** in PhMe solution was hydroborated with BH<sub>3</sub>-Me<sub>2</sub>S directly after the rearrangement reaction. As for  $\alpha$ -pinene,<sup>43</sup> the hydroboration

reaction proceeds stereoselectively. The oxidation of the intermediate borane adduct with *m*-CPBA (6 equiv) gave the corresponding alcohol **59** as a single diastereomer (Scheme 34):



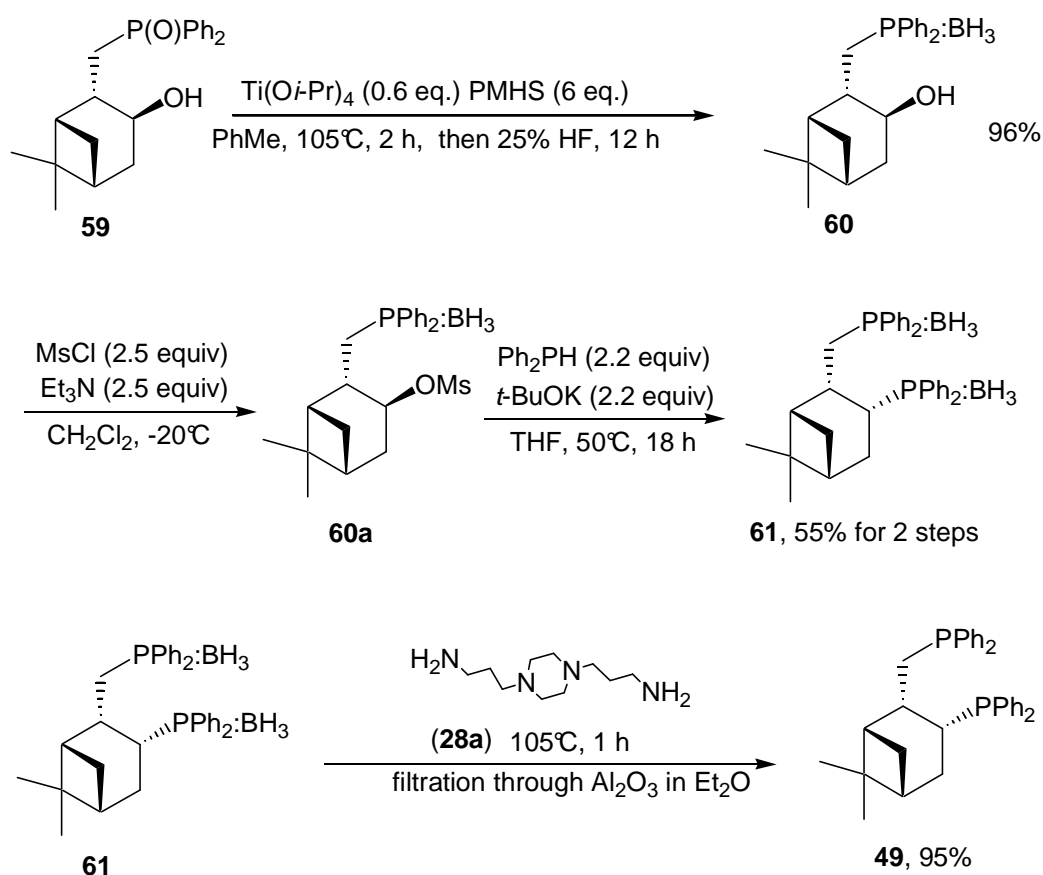
**Scheme 34.** One-pot preparation of alcohol **102** from *trans*-pinocarveol.

Compound **59** was obtained in 62% yield from *trans*-pinocarveol in a pure form without the need of a chromatographical purification. Its structure was proved by X-ray analysis (Fig. 6):



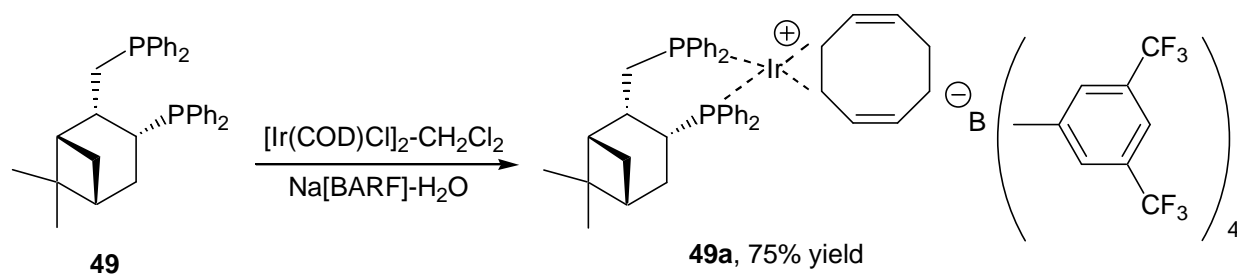
**Fig. 6.** ORTEP diagram of alcohol **59**.

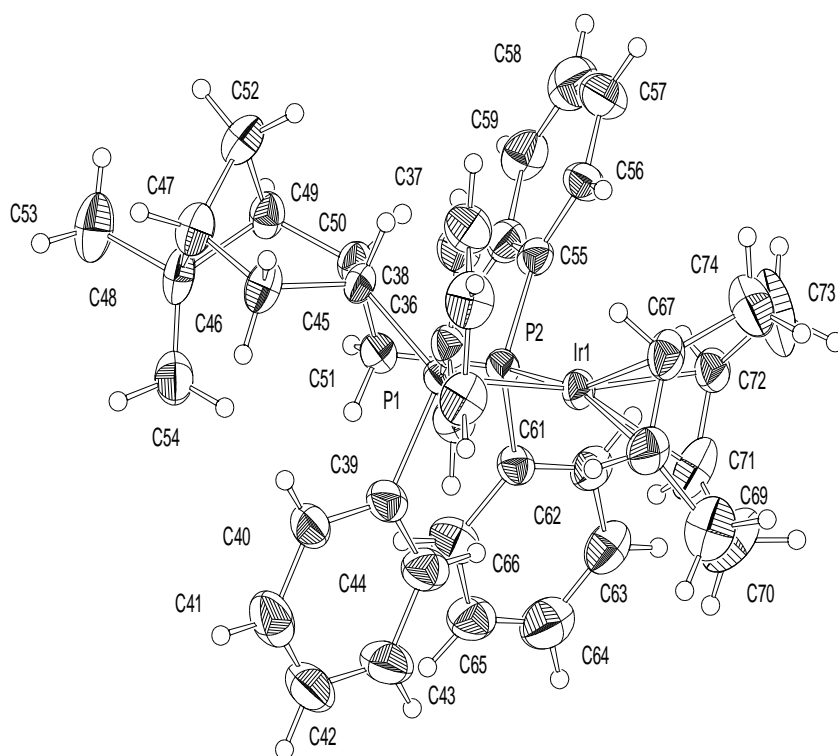
Compound **59** was reduced according to the usual procedure by PMHS and  $\text{Ti}(\text{O}i\text{Pr})_4$  in toluene followed by the protection with  $\text{BH}_3\text{-Me}_2\text{S}$ , affording the alcohol **60**. The phosphine-borane **60** was converted into the corresponding mesylate **60b** and reacted with  $\text{HPPH}_2\text{-}t\text{-BuOK}$  in THF at 50 °C, followed by the protection with  $\text{BH}_3\text{-Me}_2\text{S}$ . The *bis*-borane complex **61** was isolated by crystallization from ether in overall 55% yield for 2 steps. The deprotection with the previously used amine **28a** and filtration through alumina furnished ligand **49** in an excellent yield (Scheme 35):



**Scheme 35.** Synthesis of ligand **49**.

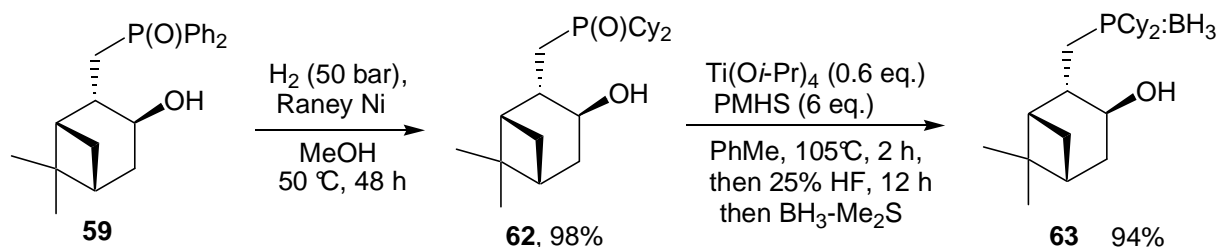
Several complexes of this ligand with transition metals were prepared and screened in asymmetric catalytic reactions like hydrogenation, 1,4-addition and allylic substitution (see Chapter 3). Among others, an iridium complex **49a** was prepared, having tetra-(3,5-bis-trifluoromethylphenyl)-borate ([BARF]<sup>-</sup>) as a counteranion. This counteranion provides an unusual stability to the metallic complexes of this type, so that they can be purified by standard chromatography on silica. The structure of this complex was determined by X-ray analysis. This also proved the alleged structure of diphosphine **49** (Fig. 7).

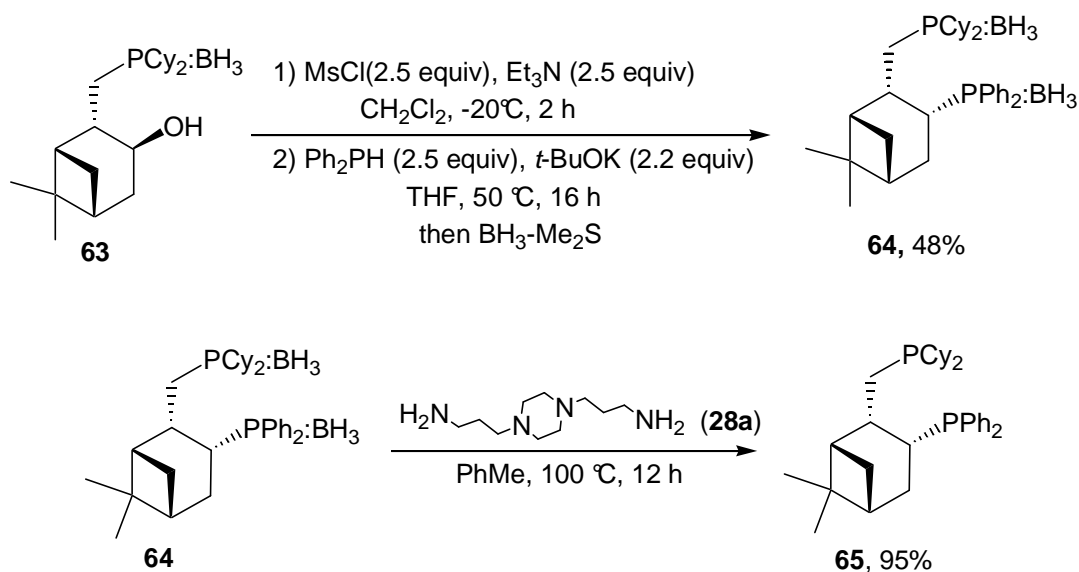




**Fig. 7.** ORTEP diagram of Ir complex **49a** (the counteranion [BARF]<sup>-</sup> is not shown).

Having completed the synthetic sequence that gave *bis*-diphenylphosphine ligand **49**, we applied the hydrogenation of the diphenylphosphinoyl group to compound **59** in order to synthesize the corresponding dicyclohexylphosphine ligand. Compound **59** was hydrogenated in MeOH in an autoclave at 50 °C and 50 bar for 12 h over 200 mass. % of Raney Ni. The product **62** was further transformed into the mixed diphosphine-borane complex **64** by the usual synthetic sequence (Scheme 36):





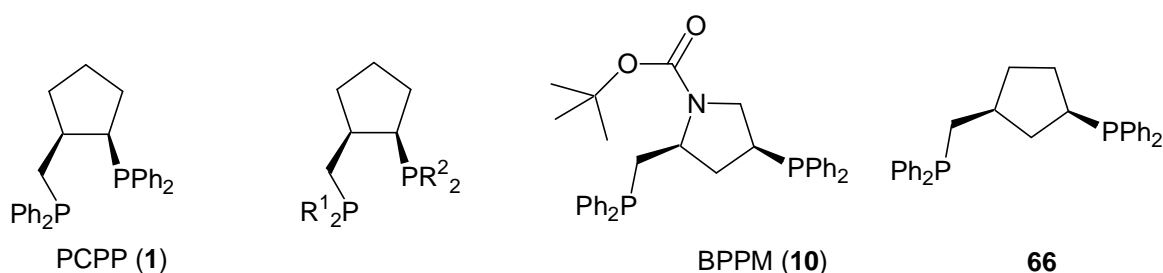
**Scheme 36.** Synthesis of the “mixed” ligand **65**.

The final deprotection of this complex required 12 h of heating at 100 °C with *bis*-(3-aminopropyl)-piperazine (**28a**) in toluene. The resulted dicyclohexyl-diphenyl-substituted *bis*-phosphine **65** was isolated in 95% yield.

In conclusion, we applied the [2,3]-sigmatropic allylphosphinite-allylphosphine oxide rearrangement to the synthesis of new chiral diphosphine ligands with a cyclic terpene scaffold. Chiral precursors from the chiral pool were used as starting materials. The resulting allyldiphenylphosphine oxides were converted by the diastereoselective hydroboration-oxidation protocol into the corresponding alcohols. After the reduction of the diphenylphosphinoyl group, the alcohols were transformed *via* mesylates into the protected *bis*-phosphines. The latter were deprotected by a novel convenient method, yielding the corresponding diphosphines. The aryl moieties of the intermediate diphenylphosphinoyl alcohols could be quantitatively reduced by H<sub>2</sub> in the presence of Raney Ni into cyclohexyl groups, thus giving the corresponding dicyclohexylphosphinoyl analogs. These can be successively subjected to the same transformations leading to the mixed dicyclohexyl-diphenyl phosphine ligands. The whole sequence did not require the use of chromatographical methods and can be readily scaled up. The newly synthesized ligands were screened in several transition metal-catalyzed asymmetric reaction (see Chapter 3).

### 3. Novel approaches to the synthesis of chiral diphosphine ligands with a cyclopentane scaffold.

Diphosphines with a rigid 5-membered cyclic core represent an important class of chiral ligands for asymmetric catalysis. Several compounds of this kind, like PCPP (**1**) and BPPM (**10**) have found a broad use in various industrial processes as ligands for the asymmetric hydrogenation of C=C or C=N bonds (Scheme 37). New methods for their synthesis as well as the development of new ligands of this type are therefore of significant interest for synthetic chemists. Using the methods, developed during the studies of the applications of [2,3]-sigmatropic rearrangement to the synthesis of chiral diphosphines, we continued the investigation in this field in order to design some novel approaches to the preparation of *bis*-phosphine ligands of the PCPP(**1**) type. One of the goals of this study was the development of a simple, scalable and combinatorial-like synthetic pathway to the preparation of analogs of **1** with various substituents on the phosphorus atoms. Another target of this investigation was the design of a synthetic method for the preparation of the previously unknown enantiopure compound **109**, a simplified analog of the valuable and broadly applied ligand BPPM (**10**).

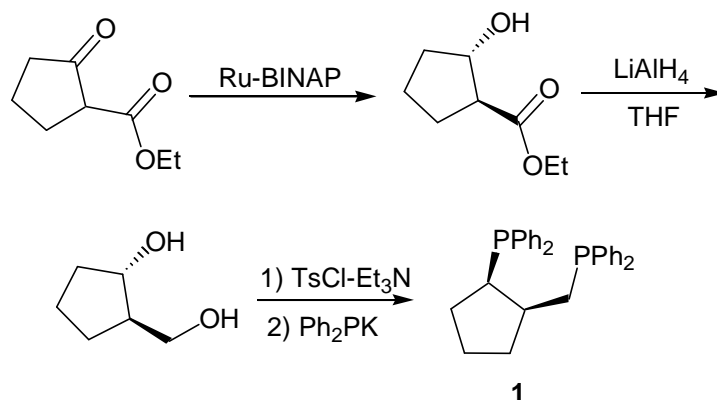


**Scheme 37.** Diphosphine ligands with a cyclopentane scaffold.

#### 3.1 Enzymatic kinetic resolution for the preparation of optically pure 2-substituted cyclopentanols.

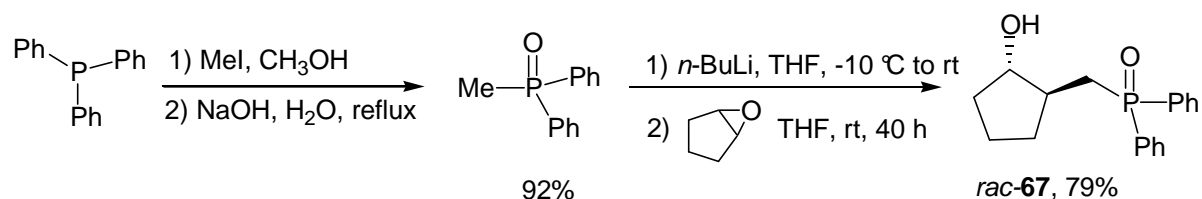
During the investigation of synthetic methods for chiral exocyclic allylic alcohols, we found that 2-substituted cyclopentanols are excellent substrates for the enzymatic kinetic resolution (EKR) process. The racemates of such alcohols can be easily resolved by enantioselective transesterification, using vinyl acetate as an acyl donor and a suitable bacterial lipase as a catalyst. It seemed promising to apply this method to the resolution of an intermediate, which then can be converted directly into ligand **1** or its analogs. The original synthesis of PCPP (**1**)

by *Achiwa* (Scheme 38) does not permit the preparation of mixed-type phosphines, and thus such a method can overcome this disadvantage.



**Scheme 38.** Synthesis of PCPP (**1**) by *Achiwa*.

A good candidate for the enzyme-catalyzed kinetic resolution is *trans*-2-(diphenylphosphinoylmethyl)cyclopentanol (**67**), which after the separation of enantiomers can be transformed into PCPP using the synthetic procedures, described above. We based our first approach on the known acidity of methyl diarylphosphine oxides, which can be cleanly deprotonated by bases like *n*-BuLi or LDA. The resulting anions are good nucleophiles and should attack cyclopentene epoxide to give the desired substituted cyclopentanols. The starting methyl diarylphosphine oxides can be easily prepared from commercially available triarylphosphines by a one-pot alkylation-hydrolysis sequence. The ring-opening product **67** (racemic) was obtained in this way in 79% yield (Scheme 39):

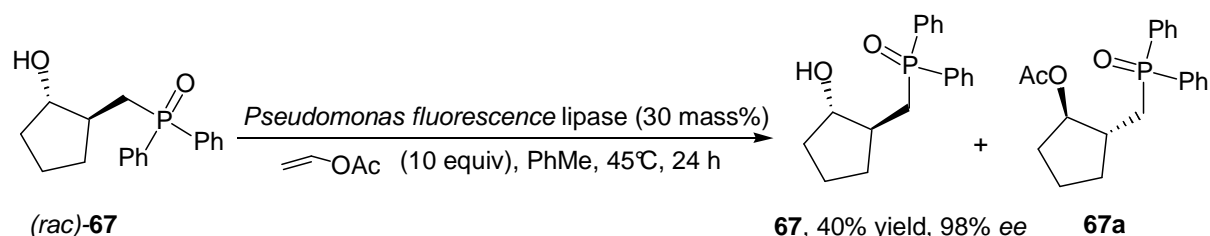


**Scheme 39.** Ring-opening of cyclopentene oxide with the methyldiphenylphosphine oxide anion.

With this compound as a substrate, we screened six different enzymes as catalysts for EKR, using vinyl acetate as an acyl donor in toluene at 45 °C: the *Pseudomonas fluorescens* lipase, *Pseudomonas cepacia* lipase, immobilized on ceramic particles (PS-D), the protease from *Aspergillus melleus*, pig pancreatic lipase (Sigma, Type II), pig pancreatic lipase (Fluka) and

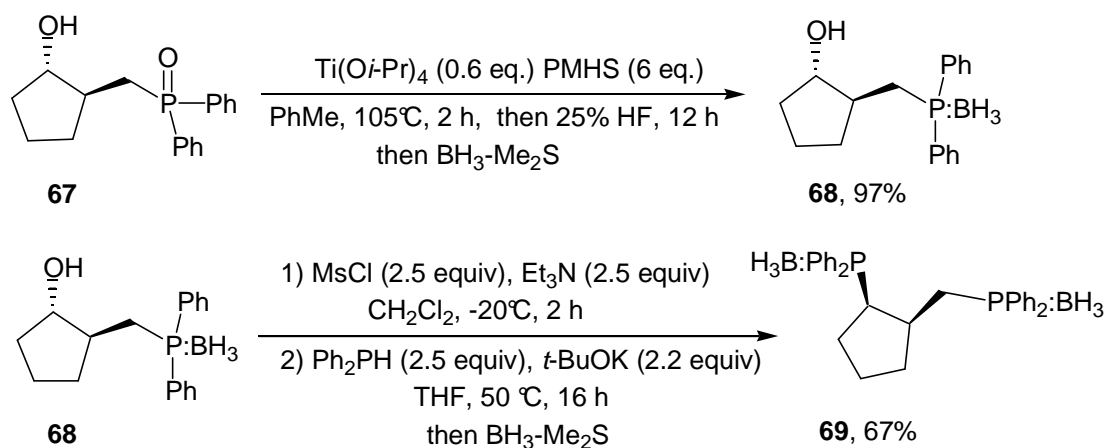


pig liver esterase. The reactions were monitored by  $^{31}\text{P}$  NMR. Among all the screened enzymes only immobilized *Pseudomonas cepacia* lipase (PS-D) provided a sufficient reaction rate and selectivity (Scheme 40). After 24 h of the reaction the enantiopure product **67** was isolated in 40% yield (80% from theory) and 98% *ee* after recrystallization:

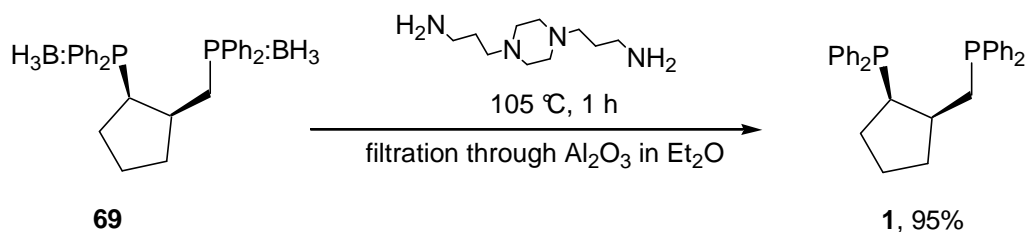


**Scheme 40.** Enzymatic kinetic resolution of alcohol **67**.

The enantioenriched phosphinoyl **67** was reduced according to the previously developed protocol with PMHS-Ti(*Oi*Pr) $_4$  in toluene and protected as borane complex **68**, which was isolated in 97% yield. The completion of the synthesis of **1** was performed via *bis*-phosphine-borane **69** following the methods, developed earlier (Scheme 41). The sign and the value of the optical rotation of the prepared ligand **1** ( $\alpha_D^{20} +111$ , *c* 0.67, PhMe compared with +114 from the literature) corresponds to the (*R,R*)-enantiomer of **1**, synthesized for the first time by Achiwa.<sup>45</sup>

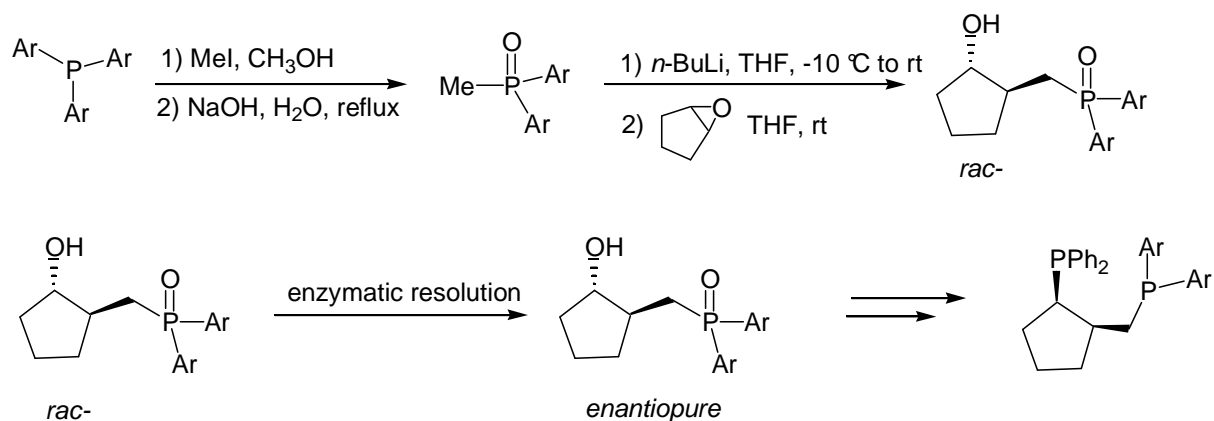


<sup>45</sup> K. Inoguchi, N. Fujie, K. Yoshikawa, K. Achiwa, *Chem. Pharm. Bull.* **1992**, *40*, 2921.



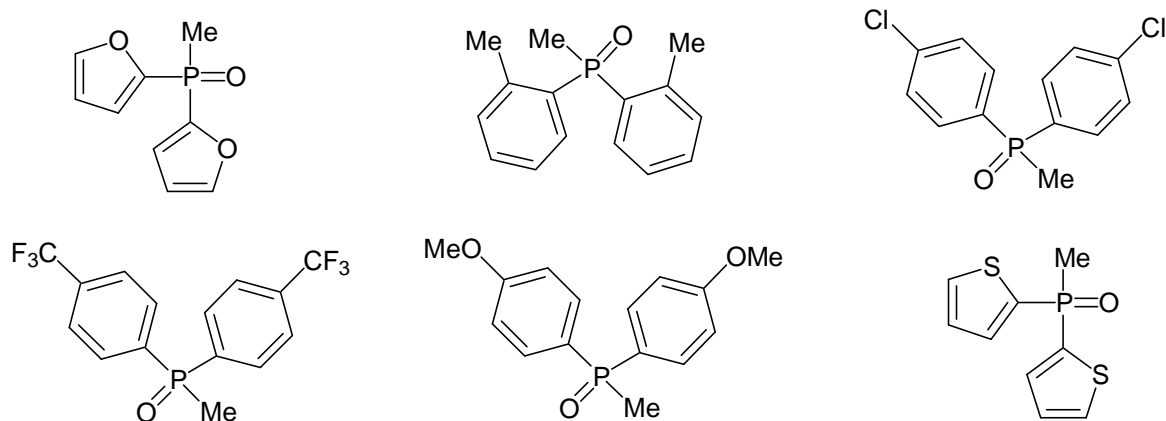
**Scheme 41.** Chemoenzymatic preparation of PCPP (**1**).

Thus, the enzymatic resolution turned out to be a useful method for the enantioselective preparation of  $\gamma$ -diarylphosphinoyl alcohols, which may allow a simple, practical synthesis of chiral analogs of **1** with various aryl substituents (Scheme 42).



**Scheme 42.** Synthetic route for the chemoenzymatic preparation of PCPP analogs.

To reach this goal, six different methyldiarylphosphine oxides (Scheme 43) were prepared from commercially available triaryl phosphines by the alkylation with  $\text{MeI}$  followed by basic hydrolysis. In all cases, yields about 90% were achieved.



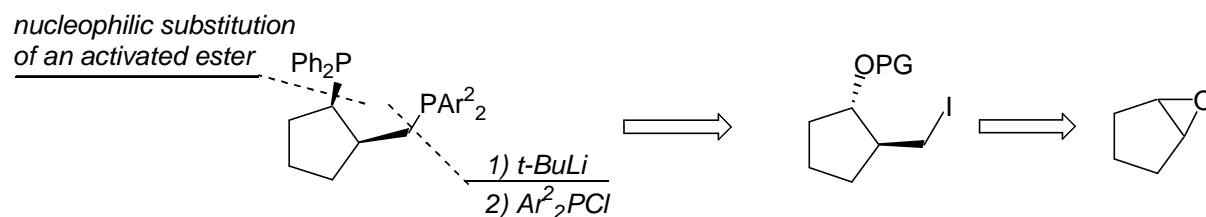
**Scheme 43.** Diarylphosphine oxides, tested in the ring-opening reaction with cyclopentene oxide.

However, attempts to involve the prepared methyl-diarylphosphinoxides in the reaction with cyclopentene oxide unexpectedly failed. Despite many experiments we were not able to develop a protocol, giving any of the desired cyclopentyl alcohols in more than 20% yield. Attempts to promote the reaction by addition of Lewis acids, Cu salts or switching to organomagnesium anions constantly gave either unreacted starting materials or complex mixtures of products with a low content of the desired alcohol.

It seemed reasonable therefore to design a chiral common intermediate, which would not require the resolution of enantiomers for every synthesized phosphine. Such a precursor should be easily available in relatively large amounts. We considered enzymatic resolution as the method of choice for the preparation of chiral cyclopentanols. Besides, the formation of *trans*-2-substituted cyclopentanols by the ring-opening of cyclopentene oxide seemed to be the most convenient way to access them.

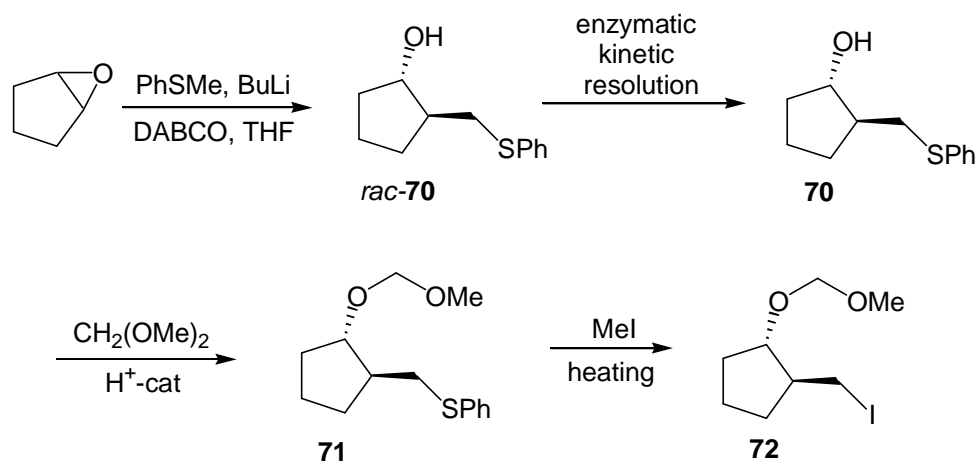
### 3.2 Modular enantioselective synthesis of PCPP ligand

The retrosynthetic analysis of chiral 1,3-diphosphine ligands with a cyclopentane scaffold, taking into account the above-mentioned considerations, is shown in Scheme 44:



**Scheme 44.** Retrosynthetic analysis of PCPP-type ligands.

The protecting group (PG) in Scheme 44 should be stable towards organolithium reagents, and MOM-protection meets this requirement. The iodine leaving group should be introduced in the last steps. The group which may serve as the precursor to this iodine has to impart some acidity to the neighboring carbon, so that it can be transformed into an anion in order to simplify the nucleophilic attack on cyclopentene oxide. With this in mind, we developed the following synthetic route to the common precursor **72** (Scheme 45):



**Scheme 45.** Chemoenzymatic synthesis of intermediate **72**.

Cyclopentene oxide was supposed to react with the anion of thioanisole obtained by its reaction with *n*-BuLi in THF in the presence of TMEDA or DABCO, as it has been described for cyclohexene oxide.<sup>46</sup> The resulting *trans*-alcohol **70** should be subjected to enzymatic kinetic resolution. The protection of the enantiomerically pure **70** as a MOM-ether had to be performed by the acid-catalyzed reaction with cheap and non-toxic dimethoxymethane,<sup>47</sup> in contrast to commonly used harmful MOM-Cl.<sup>48</sup> The last step should include the known transformation of alkyl phenyl sulfides into the corresponding alkyl iodides by the alkylation with MeI followed by nucleophilic substitution of the sulfonium salt.<sup>49</sup>

Cyclopentene oxide, which is a relatively expensive substance, was prepared by the epoxidation of cyclopentene. Among several methods known for this reaction, MeReO<sub>3</sub>-catalyzed epoxidation was the simplest. Pyrazole serves as a stabilizing ligand for the rhenium

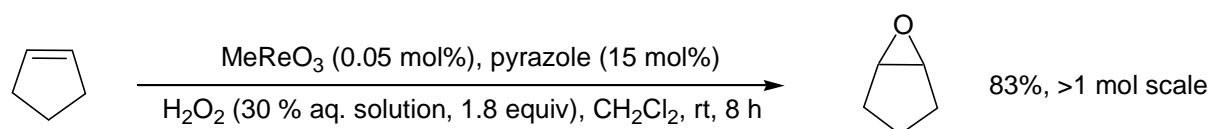
<sup>46</sup> a) H. A. Khan, I. Paterson, *Tetr. Lett.* **1982**, 23, 5083. b) C. Rücker, *J. Organomet. Chem.* **1986**, 310, 135.

<sup>47</sup> a) E. Vedejs, S. D. Larsen, *J. Am. Chem. Soc.* **1984**, 106, 3030. b) M. P. Groziak, A. Koohang, *J. Org. Chem.* **1992**, 57, 940.

<sup>48</sup> G. Stork, T. Takahashi, *J. Am. Chem. Soc.* **1977**, 99, 1275.

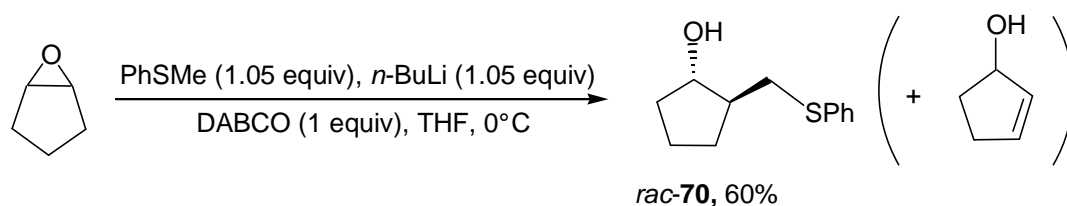
<sup>49</sup> S.Sagannathan, T. P. Forsyth, C. A. Kettner, *J. Org. Chem.* **2001**, 66, 6375.

species.<sup>50</sup> In the original publication, 0.5 mol% of MeReO<sub>3</sub> was used, and the reaction was completed within 15 min. We found that if the rhenium catalyst was added in 5 small portions after each 1.5 h, its overall amount can be decreased to 0.05 mol% still with a good yield of the product (Scheme 46). Using this protocol, 75 g of cyclopentene oxide was obtained in a single batch in 83% yield:



**Scheme 46.** Scaled-up synthesis of cyclopentene oxide.

The known reaction between the metalated thioanisole and cyclohexene oxide afforded 55% yield of the product.<sup>46</sup> The same reaction with cyclopentene oxide in the presence of DABCO gave 60% yield. The competing process is a base-induced isomerisation of the epoxide into the corresponding allylic alcohol, which was detected by GC-MS (Scheme 47):<sup>51</sup>



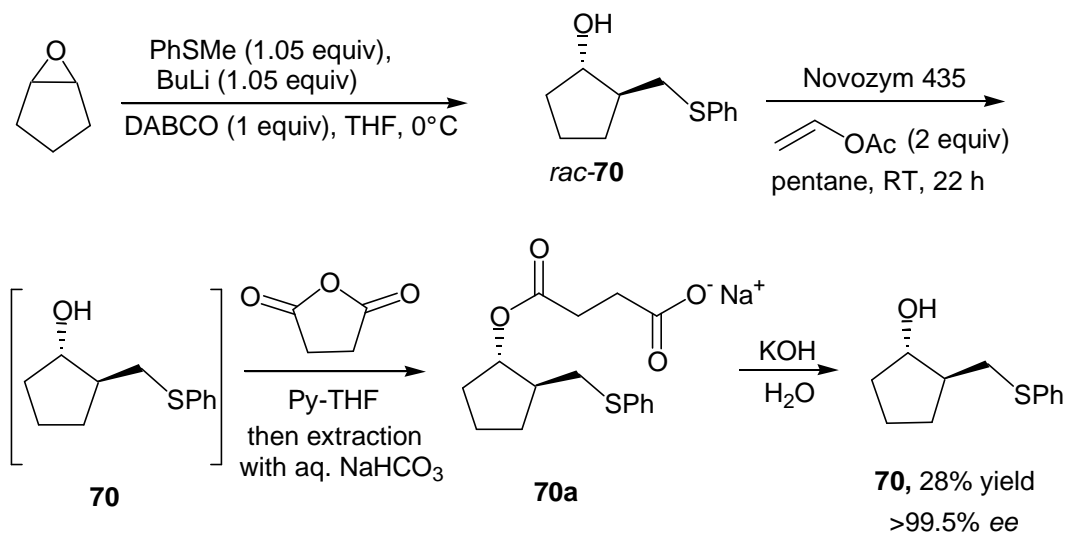
**Scheme 50.** Ring-opening of cyclopentene oxide with metalated thioanisole.

From the reaction mixture the desired product can be isolated after work-up by column chromatography or vacuum distillation. However, due to the strong unpleasant smell of thioanisole we decided to use the reaction mixture directly after the removal of the strongly basic components in the following enzymatic resolution step, and perform the isolation of the enantiomerically pure alcohol later. Screening of several enzymes for the enantioselective transesterification reaction of alcohol **70** revealed that the lipase from *Candida antarctica*, immobilized on ceramic particles (Novozym 435®) possesses an outstanding catalytic activity in this reaction. Only 0.2 g of this catalyst was enough to completely resolve within several hours at ambient temperature the amount of alcohol **70**, prepared from 0.4 mol of

<sup>50</sup> W. A. Herrmann, R. M. Kratzer, H. Ding, W. R. Thiel, H. Glas, *J. Organomet. Chem.* **1998**, 555, 293.

<sup>51</sup> a) S. J. Oxenford, P. O'Brien, M. R. Shipton, *Tetrahedron Lett.* **2004**, 45, 9053. b) P. Saravanan, A. Bisai, S. Baktharaman, M. Chandrasekhar, V. K. Singh, *Tetrahedron* **2002**, 58, 4693.

cyclopentene oxide. The product was obtained with more than 99.5% *ee*. It was isolated from the mixture by the method, described by *Marshall* for the enzymatic kinetic resolution of 4-trimethylsilyl-3-butin-2-ol.<sup>52</sup> The enzyme after the EKR step was filtered off and all the volatile compounds were removed *in vacuo*. The residue was dissolved in THF, and 0.7 equiv of succinic anhydride together with 1 equiv. of pyridine (to the starting alcohol) were added. After 2 h the mixture was extracted twice with 10% aqueous NaHCO<sub>3</sub>. Careful acidification of the aqueous solution and extraction with ether gave the succinic monoester **70a**, which was reextracted from the organic phase by 15% aq. KOH and hydrolyzed in this solution within 6 h at room temperature. The pure alcohol **70**, formed after the hydrolysis, was isolated in 28% overall yield from cyclopentene oxide and >99.5% *ee* (Scheme 48).



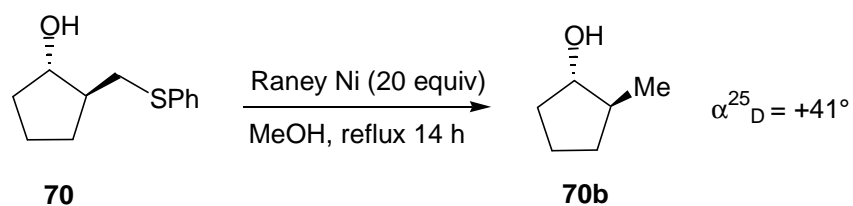
**Scheme 48.** Enzymatic kinetic resolution and isolation of alcohol **70**.

The absolute configuration of alcohol **70** was determined by its reduction into known optically pure *trans*-2-methylcyclopentanol **70b** by the excess of Raney Ni (Scheme 49)<sup>53</sup> and the comparison of the optical rotation sign of obtained **70b** with the literature value.<sup>54</sup> According to the positive sign of the optical rotation of the product (+41° against +43° of literature value), it possesses the (1*S*, 2*S*) absolute configuration, as well as the starting *trans*-(2-thiophenylmethyl)-cyclopentanol (**70**).

<sup>52</sup> J. A. Marshall, H. Chobanian, P. Wipf, J. Pierce, *Org. Synth.* **2005**, 82, 43.

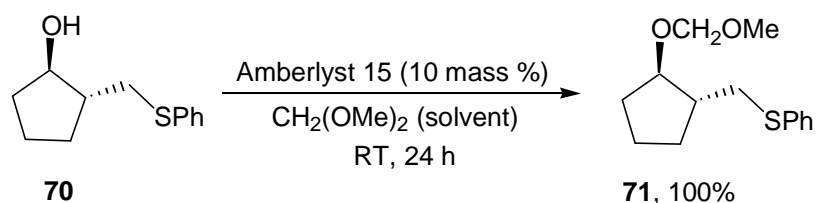
<sup>53</sup> O. Tamura, T. Yanagimachi, H. Ishibashi, *Tetrahedron: Asymmetry* **2003**, 14, 3033

<sup>54</sup> J. J. Partridge, N. K. Chadha, M. R. Uskoković, *J. Am. Chem. Soc.* **1973**, 95, 532.



**Scheme 49.** Determination of the absolute configuration of alcohol **70**.

The protection of alcohols by the acid-catalyzed reaction with  $(\text{MeO})_2\text{CH}_2$  has been described.<sup>45, 55</sup> However, the soluble acid catalysts usually used require a special work-up step for their removal after completion of the reaction. We tested cationite resin Amberlyst 15® as a catalyst for this reaction and found that the protection in dimethoxymethane as a solvent takes place quantitatively at ambient temperature within 24 h (Scheme 50):



**Scheme 50.** MOM-protection of alcohol **70**.

The isolation of the product **71** is simple and includes only filtering off the catalyst and evaporation of the excess of  $\text{CH}_2(\text{OMe})_2$ .

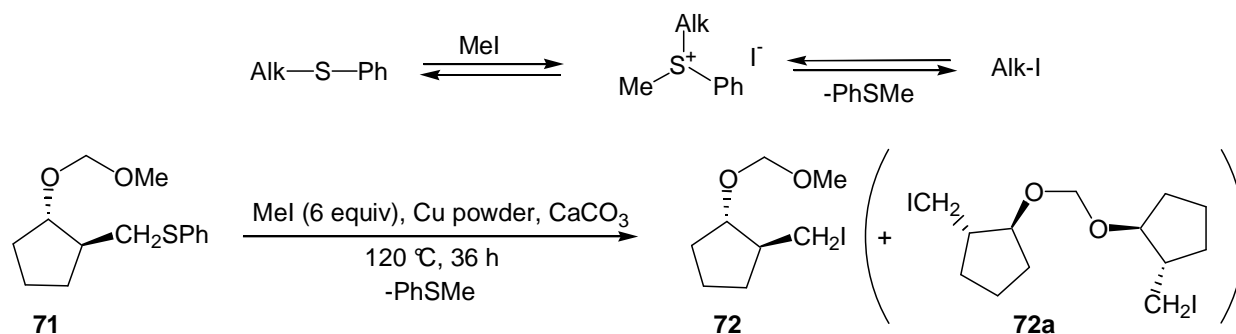
The direct conversion of phenylthiomethyl derivatives into the corresponding alkyllithium species by the reaction with Li in the presence of 4,4'-di-tert-butylbiphenyl (DBB) or naphthalene is well-known.<sup>56</sup> However, our attempts to apply this reaction to the synthesis of organophosphorus compounds were not successful. While the formation of the alkyllithium species from acetal **71** and Li in the presence of DBB or 1-dimethylaminonaphthalene proceeded rather smoothly, the addition of  $\text{Ph}_2\text{PCl}$  led to complex product mixtures, mostly because the reaction of  $\text{Ph}_2\text{PCl}$  with the thiolate species, presenting in the mixture, is quite fast even at low temperatures. Therefore, this route was abandoned and we turned our attention to the transformation of the arylthiolate group into the iodide.

<sup>55</sup> a) J.-L. Gras, Y.-Y. Chang, L. Chang, A. Guerin *Synthesis* **1985**, 74. b) K. Fuji, S. Nakano, E. Fujita *Synthesis* **1975**, 276.

<sup>56</sup> T. Cohen, M. Bhupathy, *Acc. Chem. Res.* **1989**, 22, 152.

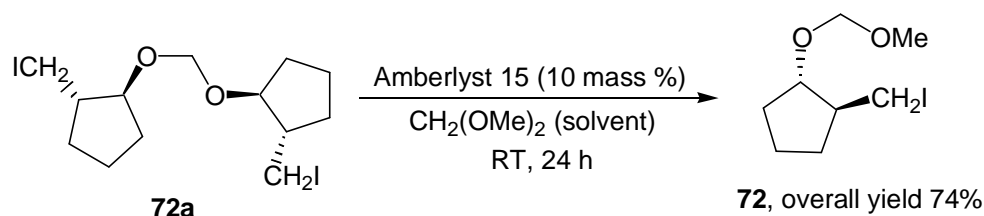
This synthetic step was based on the known substitution of a thiophenyl group on primary alkyls by an iodine.<sup>49</sup> Heating of the sulfide with an excess of MeI leads to the alkylation of the sulfur atom. The sulfonium salt is then attacked by I<sup>-</sup>, forming either starting methyl iodide or the desired alkyl iodide. The excess of MeI shifts the equilibrium to the right side.

The optimal conditions were found as follows: 6 equiv MeI, 120 °C, 36 h in an autoclave in the presence of Cu powder and CaCO<sub>3</sub>, preventing the accumulation of free iodine and acids in the reaction mixture. During this reaction, however, a substantial amounts of a side product was formed, which was identified by the mass-spectra as the formaldehyde *bis*-acetal **72a**, which is formed by the scrambling of the alcohol moieties (Scheme 51):



**Scheme 51.** Conversion of a thiophenyl group into an iodide.

We found, however, that compound **72a** can be quantitatively transformed into the desired MOM-ether **72** by the simple stirring of the filtered reaction mixture after the evaporation of MeI in (MeO)<sub>2</sub>CH<sub>2</sub> in the presence of Amberlyst 15®, under the conditions that served for the protection of alcohol **70** (Scheme 52). After this treatment, PhSMe and acetal **72** were separated by short-path flash chromatography and vacuum distillation. The overall yield of the iodide **72** from alcohol **70** was 74% .

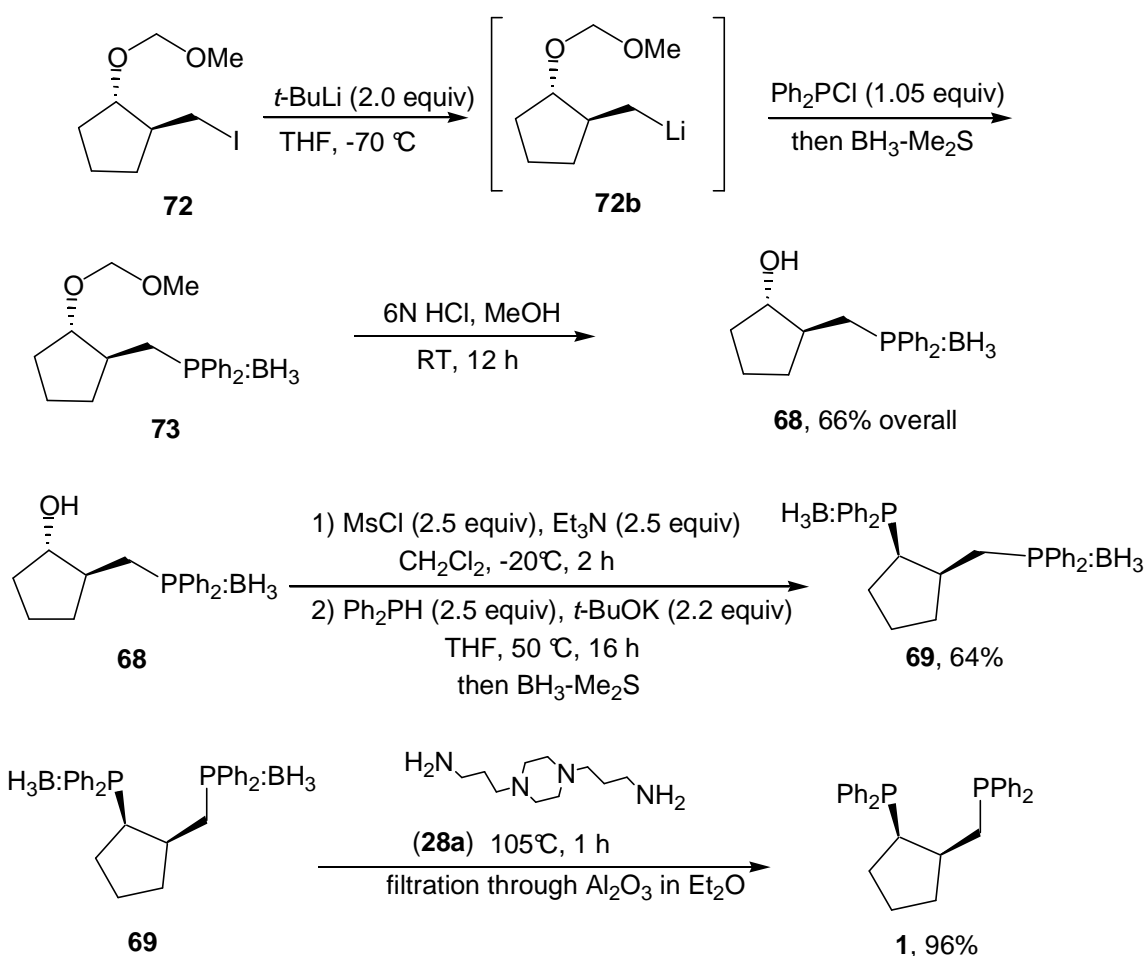


**Scheme 52.** Conversion of compound **72a** into acetal **72**.



Following this protocol, compound **72** was prepared in a 35 g single batch with purity >98% by GC analysis and >99% *ee*.

The parent ligand PCPP (**1**) was prepared from iodide **72**. The iodine-lithium exchange with *t*-BuLi led to the corresponding lithium species, which were trapped by the addition of Ph<sub>2</sub>PCl. The resulting phosphine was protected *in situ* as a borane complex. Without purification of the intermediate, the MOM-protection was cleaved by stirring **73** overnight with 6 N HCl in MeOH, and the phosphine-borane **68** was isolated by column chromatography in 66% overall yield. It was converted into the same enantiomer of ligand PCPP (**1**) which has previously been synthesized by a chemoenzymatic route (Scheme 53, see Chapter 2.1):



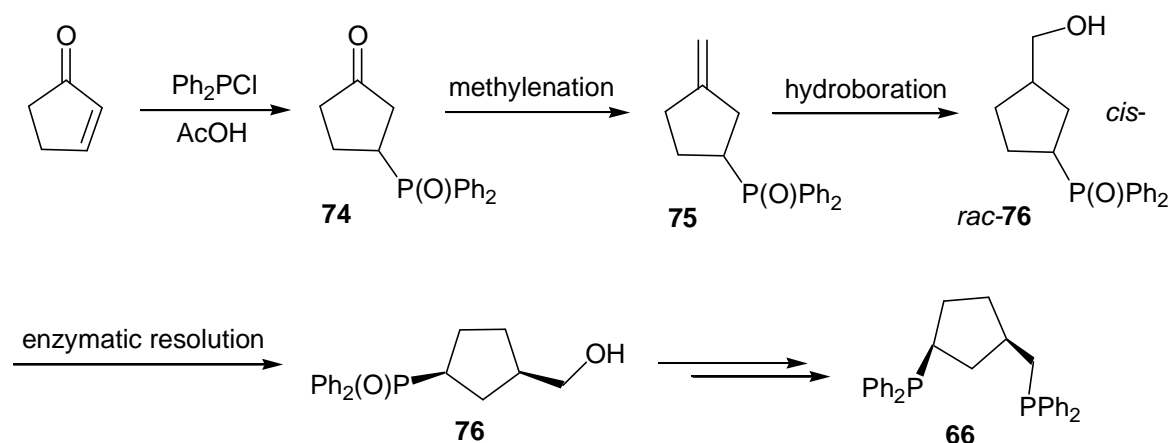
**Scheme 53.** Synthesis of **1** from chiral intermediate **72**.

This proved the concept of the synthesis of a single chiral precursor for the preparation of various diphosphine ligands. This approach can be readily used for the preparation of various ligands of the same type, if different diarylchlorophosphines are used in the reaction. The

preparation of the intermediate **72** can be readily upscaled. Therefore, the desired ligands can be obtained in sufficient amounts.

### 3.3 Enantioselective synthesis of a new 1,4-diphosphine ligand with a cyclopentane scaffold

Having successfully prepared several chiral 1,3-diphosphine ligands, we turned our attention to the preparation of novel 1,4-diphosphine ligands, using the already developed synthetic methods. The 1,4-diphosphines with a rigid 5-membered ring are promising widely used ligands for several transition metal-catalyzed enantioselective reactions. The closest analog of PCPP, compound **66** has not yet been prepared in enantiomerically pure form, despite the relative simplicity of its structure and the reasonable efforts undertaken in this direction.<sup>57</sup> We planned to apply the aforementioned enzymatic resolution of diphenylphosphinoyl alcohols to the synthesis of this compound at the key step. The sequence, designed for the synthesis of the target 1,4-diphosphine, is shown in Scheme 54.

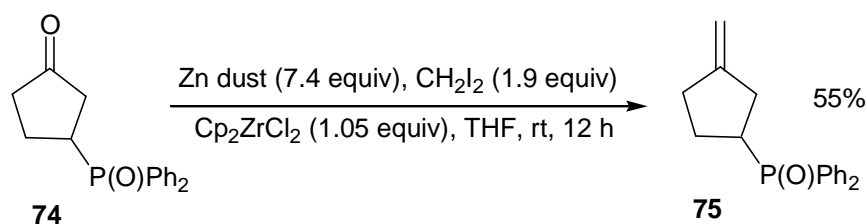


**Scheme 54.** Retrosynthetic analysis of the diphosphine ligand **66**.

The first step, the 1,4-addition of diphenylphosphinic acid to cyclopentenone, gives 3-diphenylphosphinoylcyclopentanone in a very high yield.<sup>57</sup> Having received the addition product **74**, we investigated the methylenation of the keto-group. Common Wittig olefination was not feasible here, since compound **75** can hardly be separated from triphenylphosphine oxide.

<sup>57</sup> a) P. Camps, G. Colet, S. Vazquez, *ARKIVOC*, **2003**, *10*, 16. b) P. Camps, G. Colet, M. Font-Bardia, V. Muñoz-Torrero, X. Solans, S. Vazquez, *Tetrahedron: Asymmetry* **2002**, *13*, 759.

One of the modern methods for methylenation of ketones is the Tebbe reaction, which employs a titanocene-based complex  $\text{Cp}_2\text{TiCl}_2\text{-AlMe}_3$  as a methylene equivalent.<sup>58</sup> The more recent version of this process described by *Eisch* uses Zn,  $\text{Cp}_2\text{TiCl}_2$  and  $\text{CH}_2\text{I}_2$  for the same transformation.<sup>59</sup> We chose this method for its simplicity and safety compared to the use of flammable  $\text{AlMe}_3$ . By substituting titanocene dichloride by zirconocene dichloride, we achieved much better results than with the original protocol and finally obtained the desired product **75** in 55% yield (Scheme 55). The product was isolated as white crystalline solid after column chromatography.

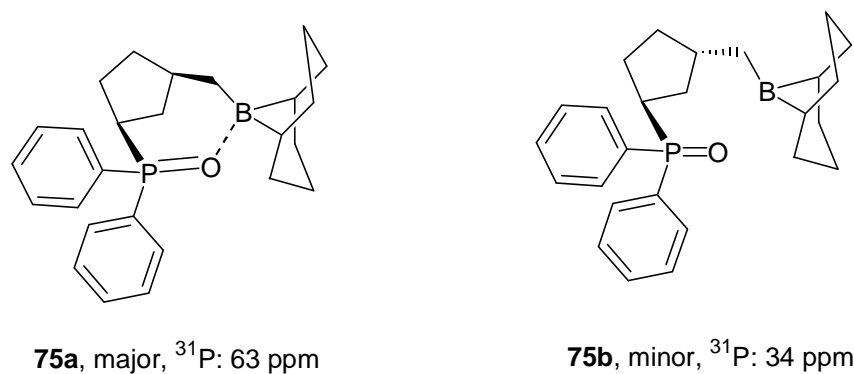


**Scheme 55.** Methylenation of ketone **74** according to the modified method of *Eisch*.

We used 9-BBN-H for the stereoselective hydroboration of the exocyclic double bond of **75**. The difference in the steric requirements of the diastereotopic sides in this substrate is obviously not high. To get the *cis*-product with the highest possible selectivity, a sterically hindered borane has to be employed. Monitoring of the reaction with  $^{31}\text{P}$  NMR revealed the formation of two products in an approximate ratio of 85:15. The chemical shift of the phosphorus in the  $^{31}\text{P}$  spectra of the major product **75a** was in the range of 62-63 ppm, pointing out a strong intramolecular coordination of the phosphinoyl group, corresponding to the *cis*-isomer of the hydroboration product (see Chapter 1.2.4). We have previously observed a similar unusual chemical shift in  $^{31}\text{P}$  NMR spectra of compound **25a**, for which the X-ray structure demonstrates a very strong donor-acceptor interaction between the oxygen and the boron atoms. In contrast, in the minor hydroboration product **75b** the chemical shift of the phosphorus atom is around 34 ppm, which is common for non-complexed diphenylphosphine oxides (Fig. 8). On this basis, we concluded that the selectivity of the hydroboration with 9-BBN is 85:15 in favor of the desired *cis*-stereoisomer:

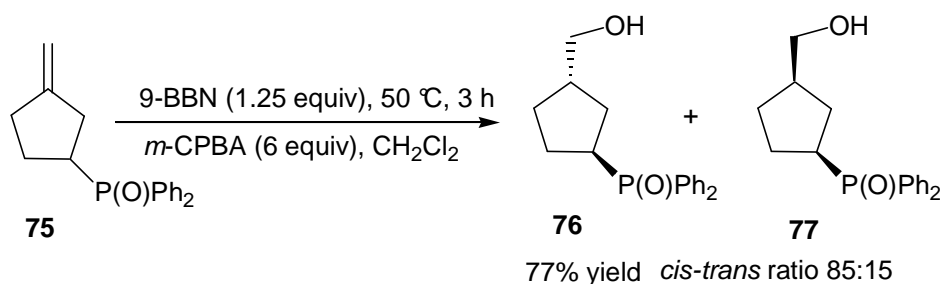
<sup>58</sup> F. N. Tebbe, G. W. Parshall, G. S. Reddy *J. Am. Chem. Soc.* **1978**, *100*, 3611.

<sup>59</sup> J. J. Eisch, A. Piotrowski, *Tetrahedron Lett.* **1983**, *24*, 2043.



**Fig. 8.** Structures of the major and minor products of the hydroboration of **75** with 9-BBN.

The oxidation of **75a** and **75b** with *m*-CPBA furnished the resulting mixture of alcohols **76** and **77** in 77% overall yield, which, however, were not possible to separate by chromatography or crystallization. The major *cis*-isomer **77** could be isolated from the mixture in a low yield after three recrystallizations from acetonitrile-chloroform.

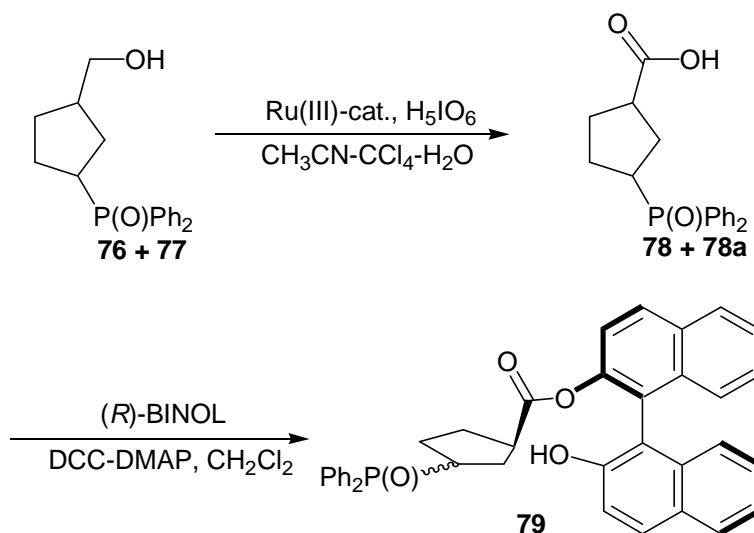


**Scheme 56.** Hydroboration-oxidation of alkene **75**.

Despite the numerous examples of successful enzymatic kinetic resolution of primary alcohols<sup>41</sup> existing in the literature, the extensive screening of enzymes and acyl donors for the resolution of alcohol mixture **76+77** did not lead to any success. Mostly, the acetates of both alcohols were obtained relatively fast, but without significant enantioselectivity. In all cases the resolution was not practical. These disappointing results made us turn the attention to other methods of enantiomer resolution.

The preparation of some esters of chiral acids and alcohols **76+77** in order to separate the resulting diastereomers did not meet much success either. The products with the Mosher acid and the monoester of *O,O*-dibenzoyltartaric acid were hygroscopic low-melting foams and their diastereomers were not separable by TLC. A 2,2'-binaphthol derivative could be a good choice, as large naphthyl rings and  $C_2$ -symmetry should offer sufficient structural

differentiation of the diastereomers. It required, however, the transformation of the alcohol into the corresponding acid followed by the formation of a binaphthol monoester. We chose to apply the Ru-catalyzed oxidation of **76+77** to acids **78** and **78a** with  $\text{H}_5\text{IO}_6$  as the reoxidant. The solvent has a quite strong influence on the output of this reaction, and the use of the two-phase system  $\text{MeCN-CCl}_4\text{-H}_2\text{O}$  was shown to be essential.<sup>60</sup> The esterification method, developed by *Steglich*,<sup>61</sup> was used for the formation of the BINOL ester **79** (Scheme 57).

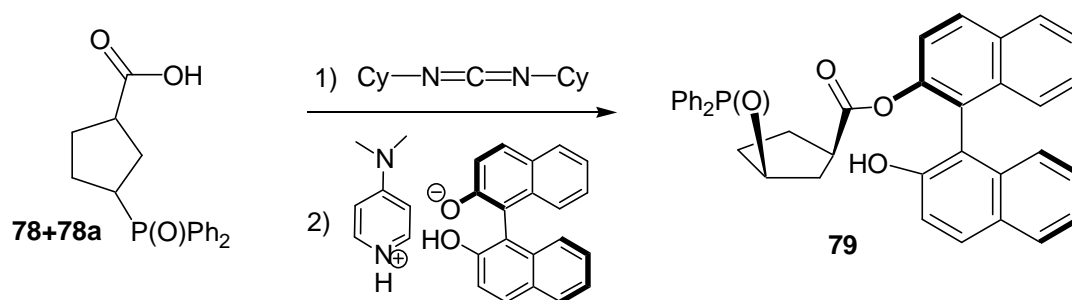


**Scheme 57.** Synthesis of ester **79**.

By the Ru-catalyzed oxidation of the diastereomeric mixture of alcohols **76+77**, the mixture of the corresponding acids **78+78a** with the same diastereomeric ratio was obtained in 85% yield. The NMR data suggested the presence of about 5 molecules of water per molecule of the acid after the recrystallization from  $\text{CH}_3\text{CN}$ . The prolonged stirring of  $\text{CHCl}_3$ -solution of **78+78a** over molecular sieves (MS 4Å) reduced the amount of water only to nearly 2 molecules per acid molecule. Therefore, we decided to use the compound in the next step in a hydrate form for the ester formation. The basicity of DMAP is sufficient to transform BINOL into the highly nucleophilic phenolate anion, which has to react with the activated ester of the acid preferentially even in the presence of water (Scheme 58):

<sup>60</sup> H. S. Carlsen, T. Katsuki, V. S. Martin, K. B. Sharpless, *J. Org. Chem.* **1981**, *46*, 3936.

<sup>61</sup> B. Neises, W. Steglich, *Angew. Chem.* **1978**, *90*, 556.

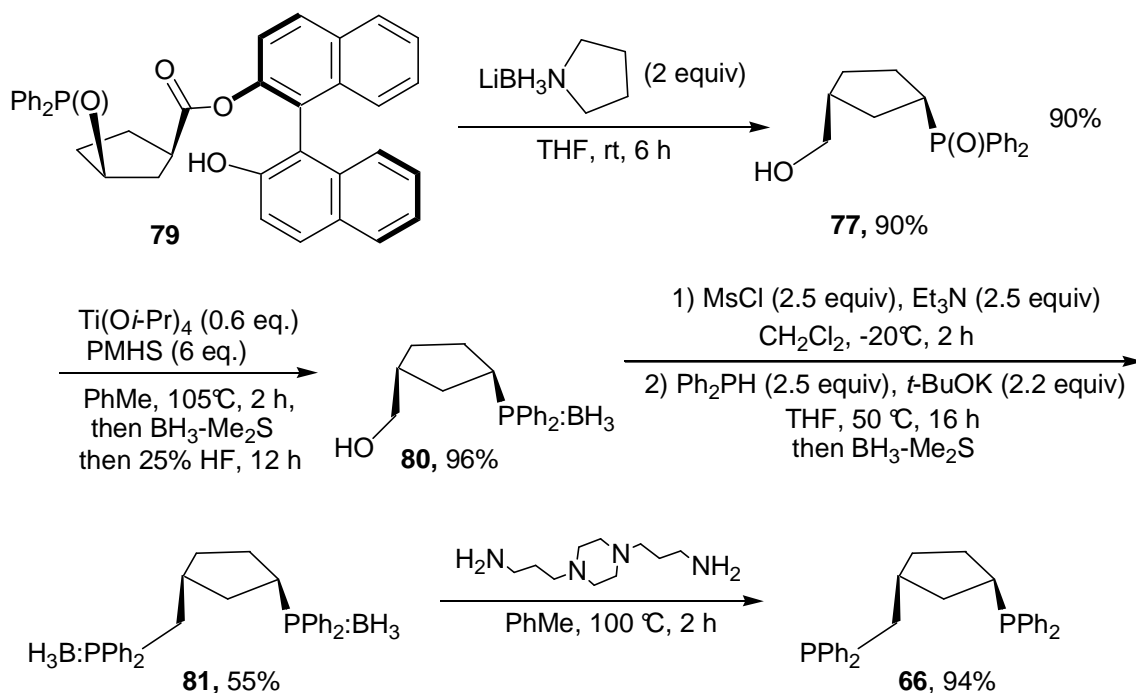


**Scheme 58.** Preparation of enantiopure ester **79**.

The desired ester **79** was isolated in 34% yield. To our delight, it turned out to be a single diastereomer, according to  $^1\text{H}$ ,  $^{13}\text{C}$  and  $^{31}\text{P}$  NMR data. Interestingly, we could not detect any diastereomer of **79** in the reaction mixture, and the rest of it consisted of the mixture of the starting *cis*-acid **78** and its *trans*-isomer **78a**, presenting in the mixture before the esterification. Obviously, for steric or other reasons they do not react with (*R*)-BINOL under the applied conditions. In this way, we could serendipitously perform the resolution of the enantiomers of the acid **78** as well as get rid of the undesirable admixture of its *trans*-isomer in a single step. Unfortunately, we were not able to prepare a crystal, suitable for X-ray analysis, neither from compound **79** nor from its *p*-bromobenzoate ester in order to establish its absolute configuration. So far, the absolute configuration of the alcohol **77** also remains unknown.

Ester **79** was further reduced into the enantiopure alcohol **77** using lithium trihydropyrrolidinoborate reagent.<sup>62</sup> It was chosen because of its high reducing ability (similar to  $\text{LiAlH}_4$ ) together with the ease and safety of handling and work-up. The resulting alcohol **77** was isolated in 90% yield in an enantiopure state, as was proved by chiral HPLC.

<sup>62</sup> G. B. Fisher, J. C. Fuller, J. Harrison, S. G. Alvarez, E. R. Burkhardt, C. T. Goralski, B. Singaram *J. Org. Chem.* **1994**, *59*, 6378.



**Scheme 59.** Synthesis of enantiopure ligand **66**.

Further transformations were performed according to the previously developed techniques. The reduction and protection of the diphenylphosphinoyl group gave the phosphine-borane **80** in 96% yield. It was converted into the corresponding mesylate, that was treated without purification with  $\text{Ph}_2\text{PH-}t\text{BuOK}$  (3 equiv.) in THF to obtain after the *in situ* protection bis-phosphine borane **81** in 54% yield. Finally, **81** was deprotected according to the previously used protocol to furnish diphosphine **66** in 94% yield (Scheme 59).

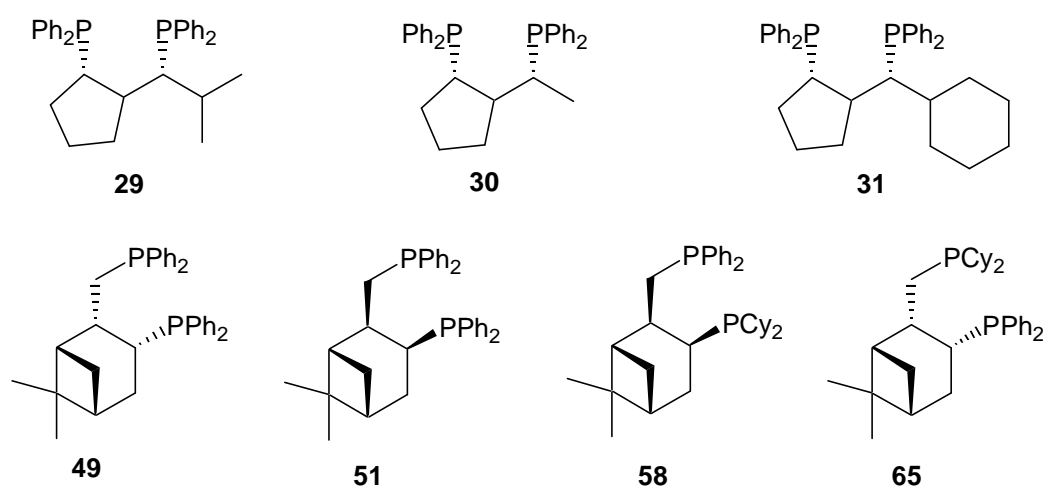
In conclusion, we prepared a new chiral cyclopentane-derived 1,4-diphosphine ligand, starting from readily available cyclopentenone, using originally designed synthetic sequence. In the key step, the enantiomers were resolved by the selective preparation of a single diastereomer of 3-diphenylphosphinoylcyclopentanecarboxylic acid (*R*)-2,2'-binaphthol ester (**79**). The overall sequence offers an easy pathway for the preparation of various representatives of a new class of chiral 1,4-diphosphine ligands with a cyclopentane scaffold.

## 4. Applications of the new ligands in the transition metal-catalyzed asymmetric reactions.

The reason for the synthesis of new chiral ligands is their application in enantioselective transition metal-catalyzed reactions. We screened our new ligands in several Rh-catalyzed hydrogenation reactions of prochiral unsaturated compounds, Rh-catalyzed 1,4-addition of phenylboronic acid to cyclohexenone, Rh-catalyzed hydroboration of styrene, and Rh- and Ru-catalyzed hydrogenation of C=N and C=O double bonds.

### 4.1. Rh-catalyzed asymmetric hydrogenation of acetamidocinnamates and acetamidoacrylates.

The Rh-catalyzed asymmetric hydrogenation of enamides is one of the most important enantioselective methods for the synthesis of chiral aminoacids.<sup>63</sup> These compounds are important intermediates for the synthesis of a great number of pharmaceuticals, agrochemicals and other compounds of industrial interest. We examined the performance of the newly synthesized ligands (Fig. 9) in the Rh-catalyzed asymmetric reduction of three substrates: methyl acetamidocinnamate, dimethyl itaconate, and methyl acetamidoacrylate.<sup>64</sup>



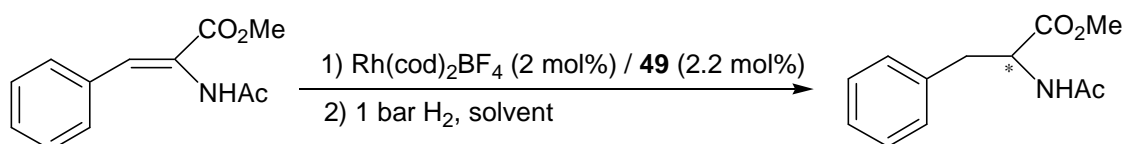
**Fig. 9.** New chiral diphosphine ligands, tested in transition metal-catalyzed asymmetric reactions.

<sup>63</sup> a) I. Ojima, *Catalytic Asymmetric Synthesis*, 2<sup>nd</sup> Ed., VCH, Weinheim, **2000**. b) R. Noyori, *Asymmetric Catalysis in Organic Synthesis*, Wiley, New York, **1994**.

<sup>64</sup> For mechanistic studies of Rh- and Ru-catalyzed hydrogenations, see: K. Rossen, *Angew. Chem. Int. Ed.* **2001**, *40*, 4611.



Since the enantiomeric excess of the hydrogenation reaction is strongly dependent on the solvent, we performed the optimization of the solvent system for these reactions using ligand **49**. The hydrogenation of methyl (*Z*)-acetamidocinnamate was conducted at room temperature and 1 bar pressure, with Rh(COD)<sub>2</sub>BF<sub>4</sub> as a metal source, using 2 mol% of the preformed catalyst. The highest enantioselectivities were achieved in the mixture of toluene and methanol (10:1) (Table 1). This mixture was used for testing all other ligands in the Rh-catalyzed hydrogenation of acetamidocinnamic and acetamidoacrylic esters.

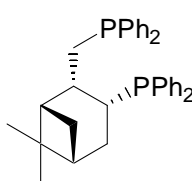
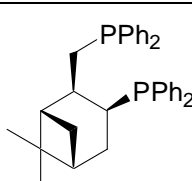
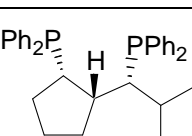
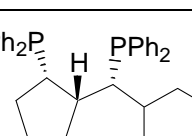
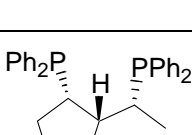
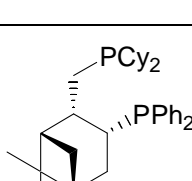


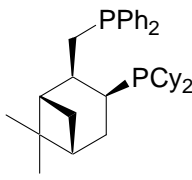
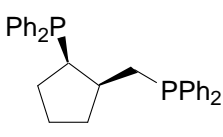
**Table 1.** Influence of the solvent mixture on the enantiomeric excess of the Rh-catalyzed asymmetric hydrogenation of acetamidocinnamic acid in the presence of ligand **89**.

| Entry    | Solvent system                             | Enantiomeric excess, % |
|----------|--|------------------------|
| 1        | MeOH                                       | 38                     |
| 2        | CH <sub>2</sub> Cl <sub>2</sub> -MeOH 10:1 | 29                     |
| 3        | THF-MeOH 10:1                              | 47                     |
| 4        | PhMe-MeOH 1:1                              | 52                     |
| 5        | PhMe-THF 5:1                               | 49                     |
| <b>6</b> | <b>PhMe-MeOH 10:1</b>                      | <b>78</b>              |

Ligand screening was carried out using 0.5 mmol of the substrate with 2 mol% of Rh(COD)<sub>2</sub>BF<sub>4</sub> and 2.2 mol% of the chiral ligand under the same conditions. In all cases, full conversion was achieved. The enantiomeric excess of the product was measured by chiral GC and compared to the authentic commercial compounds. The results of the hydrogenation tests are presented in Table 2.

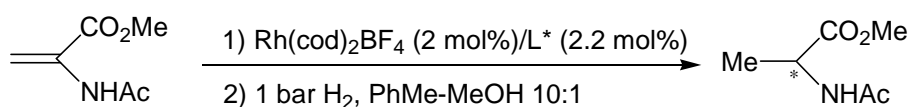
**Table 2.** Rh-catalyzed asymmetric hydrogenation of methyl (*Z*)-acetamidocinnamate.

| Entry | L*   | [T, h]        | % <i>ee</i>         | Conv.      |
|-------|--|---------------|---------------------|------------|
| 1     | <br><b>49</b>   | 20, 12        | 78( <i>S</i> )      | 100        |
| 2     | <br><b>51</b>   | <u>20, 12</u> | <u>84(<i>R</i>)</u> | <u>100</u> |
| 3     | <br><b>29</b>  | 20, 12        | 31( <i>R</i> )      | 100        |
| 4     | <br><b>31</b> | 20, 12        | 10( <i>R</i> )      | 100        |
| 5     | <br><b>30</b> | 20, 12        | 78( <i>R</i> )      | 100        |
| 6     | <br><b>65</b> | 20, 12        | 46( <i>S</i> )      | 100        |

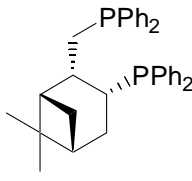
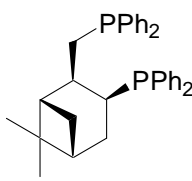
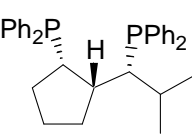
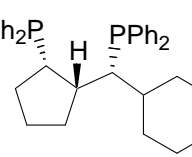
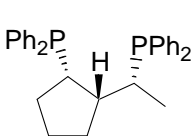
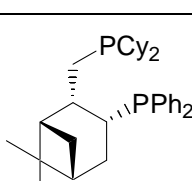
|   |  |        |                 |     |
|---|--|--------|-----------------|-----|
| 7 |  <p style="text-align: center;"><b>58</b></p> | 20, 12 | 51( <i>R</i> )  | 100 |
| 8 |  <p style="text-align: center;"><b>1</b></p>  | 20, 12 | 94 ( <i>R</i> ) | 100 |

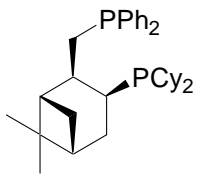
As it can be seen from the data, the additional steric hindrance, created by the methyl groups of the pinene core forces the phosphorus atom to take a more advantageous position resulting in a higher enantioselectivity for the tested reactions. The introduction of cyclohexyl instead of phenyl rings impairs the enantioselectivity of the reaction in both cases. The ligands with a cyclopentane framework displayed only modest enantioselectivity in this hydrogenation reaction. We also tested the parent ligand PCPP (**1**) (entry 8). The obtained results are in good correlation with the data, reported by *Achiwa*.<sup>9</sup> The introduction of an additional alkyl in the side chain of the ligand molecule gives compounds which are inferior ligands for the enantioselective hydrogenation reaction.

For the hydrogenation of acetamidoacrylic ester (Table 3, the same reaction conditions) the situation changes significantly: both ligands **49** and **51** give essentially the same enantioselectivity (Entries 1 and 2), while the introduction of cyclohexyl rings leads to an improvement of *ee* in one case (ligand **58**, Entry 7), and a dramatic drop in another (ligand **65**, Entry 6). Contrarily to the reaction with acetamidocinnamic ester, all the ligands gave the same enantiomer of the product. Again, the ligands with a cyclopentane core demonstrated modest results in this reaction.



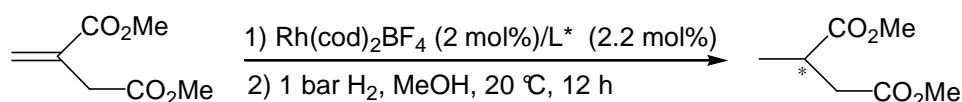
**Table 3.** Rh-catalyzed enantioselective hydrogenation of methyl acetamidoacrylate.

| Entry | L*   | [T, h] | % <i>ee</i>     | Conv. |
|-------|--|--------|-----------------|-------|
| 1     | <br><b>49</b>   | 20, 12 | 61 ( <i>R</i> ) | 100   |
| 2     | <br><b>51</b>   | 20, 12 | 60 ( <i>R</i> ) | 100   |
| 3     | <br><b>29</b>  | 20, 12 | 34 ( <i>R</i> ) | 100   |
| 4     | <br><b>31</b> | 20, 12 | 10 ( <i>R</i> ) | 100   |
| 5     | <br><b>30</b> | 20, 12 | 63 ( <i>R</i> ) | 100   |
| 6     | <br><b>65</b> | 20, 12 | 7 ( <i>R</i> )  | 100   |

|   |  |                      |                      |                   |
|---|--|----------------------|----------------------|-------------------|
| 7 |  <p><b>58</b></p> | <u><b>20, 12</b></u> | <u><b>79 (R)</b></u> | <u><b>100</b></u> |
|---|--|----------------------|----------------------|-------------------|

#### 4.2. Rh-catalyzed asymmetric hydrogenation of dimethyl itaconate.

Dimethyl itaconate is the common model compound for studies in asymmetric hydrogenation of substituted acrylates, leading to valuable chiral synthons for fine organic synthesis.



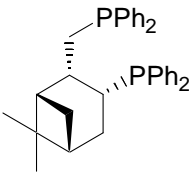
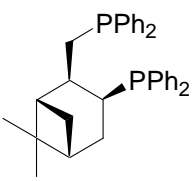
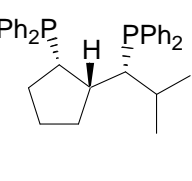
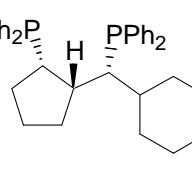
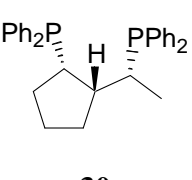
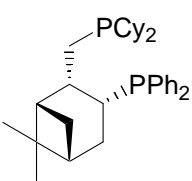
The solvent optimization for the hydrogenation of dimethyl itaconate, using ligand **49**, showed that methanol and a toluene-THF mixture give in this case similar results (Table 4). Further test reactions for this substrate with other ligands were performed in methanol.

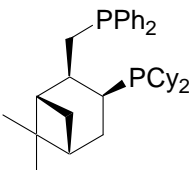
**Table 4.** Solvent screening in Rh/**49**-catalyzed enantioselective hydrogenation of dimethyl itaconate.

| Entry    | Solvent system | Enantiomeric excess, % |
|----------|----------------|------------------------|
| 1        | PhMe           | 58                     |
| 2        | PhMe-MeOH 10:1 | 66                     |
| 3        | PhMe-THF 10:1  | 78                     |
| <b>4</b> | <b>MeOH</b>    | <b>81</b>              |

The reactions were performed under the same conditions as for the hydrogenation of acetamidoacrylic and -cinnamic esters. The test results of the prepared ligands are given in Table 5.

**Table 5.** Rh-catalyzed asymmetric hydrogenation of dimethyl itaconate.

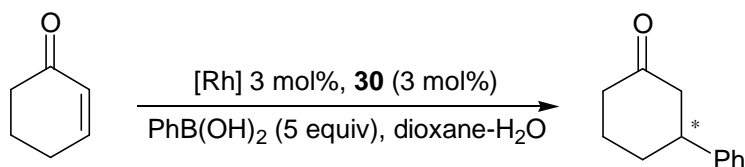
| Entry | L*   | Solvent     | % <i>ee</i>   | Conv.      |
|-------|--|-------------|---------------|------------|
| 1     | <br><b>49</b>   | <b>MeOH</b> | <b>81 (S)</b> | <b>100</b> |
| 2     | <br><b>51</b>   | MeOH        | 18 (S)        | 100        |
| 3     | <br><b>29</b>  | MeOH        | 19 (S)        | 100        |
| 4     | <br><b>31</b> | MeOH        | 8 (S)         | 100        |
| 5     | <br><b>30</b> | MeOH        | 14 (S)        | 100        |
| 6     | <br><b>65</b> | MeOH        | 54 (S)        | 100        |

|   |  |      |                 |     |
|---|--|------|-----------------|-----|
| 7 | <br><b>58</b> | MeOH | 17 ( <i>R</i> ) | 100 |
|---|--|------|-----------------|-----|

Interestingly, in this hydrogenation reaction the structure of the rigid ligand core played a significant role in the reaction outcome. The substitution of the phenyl groups of the phosphine moiety by cyclohexyls rings led to an inferior selectivity (Entries 1-2 and 6-7). The ligands with a cyclopentane framework gave poor enantioselectivity.

### **4.3 Rh-catalyzed asymmetric 1,4-addition of phenylboronic acid to cyclohexenone.**

The 1,4-conjugate addition of organometallic reagents to enones is a widely used process for the asymmetric carbon-carbon bond formation, leading to  $\beta$ -substituted carbonyl compounds which are versatile synthons to further organic transformations. We examined the applications of our newly synthesized ligands in the Rh-catalyzed 1,4-addition of phenylboronic acid to 2-cyclohexenone, employing the *Hayashi's* procedure<sup>65</sup> (3 mol % of Rh source and 3 mol% of a chiral ligand in the presence of H<sub>2</sub>O in dioxane at 100 °C). However, the source of Rh, temperature and the reaction time significantly influenced the enantioselectivity. We used ligand **30** for screening and found the optimal conditions for high enantioselectivity in this reaction.



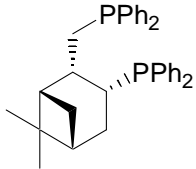
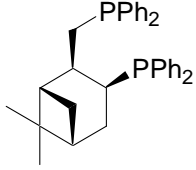
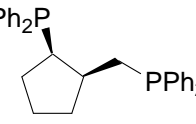
<sup>65</sup> Y. Takaya, M. Ogasawara, T. Hayashi, M. Sakai, N. Miyaura, *J. Am. Chem. Soc.* **1998**, *120*, 5579.

**Table 6.** Influence of the reaction conditions and the rhodium source in the Rh-catalyzed 1,4-addition of phenylboronic acid to cyclohexenone.

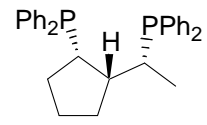
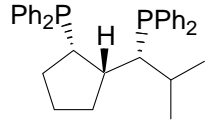
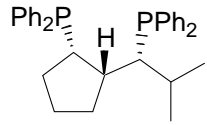
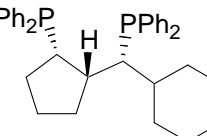
| Entry | [Rh]   | [T,h]           | % <i>ee</i> <sup>a</sup> | % conv     | % yield <sup>b</sup> |
|-------|--|-----------------|--------------------------|------------|----------------------|
| 1     | <b>Rh(cod)acac</b>                                   | <b>100, 2.5</b> | <b>88 (R)</b>            | <b>100</b> | <b>86</b>            |
| 2     | Rh(C <sub>2</sub> H <sub>4</sub> ) <sub>2</sub> acac | 100, 2.5        | 63 (R)                   | 100        | 88                   |
| 3     | Rh(C <sub>2</sub> H <sub>4</sub> ) <sub>2</sub> acac | 70, 5           | 35 (R)                   | 100        | 88                   |
| 4     | Rh(cod)acac  | 70, 5           | 10 (R)                   | 100        | 92                   |
| 5     | Rh(cod)acac  | 110, 1          | 36 (R)                   | 100        | 99                   |

These conditions were further used for screening other new ligands. Rh(cod)(acac) was found to be the best Rh source in terms of the reaction enantioselectivity. The prolonged reaction times, required for the ligands with a pinene core, negatively influenced the enantioselectivity, leading to an almost racemic product. The results of the ligand testing are given in Table 7.

**Table 7.** Rh-catalyzed 1,4-addition of phenylboronic acid to cyclohexenone.

| Entry | Ligand   | [T,h]    | % <i>ee</i> | % conv | % yield |
|-------|--|----------|-------------|--------|---------|
| 1     | <br><b>49</b> | 100, 16  | <i>rac</i>  | 100    | 85      |
| 2     | <br><b>51</b> | 100, 16  | 8 (R)       | 100    | 87      |
| 3     | <br><b>1</b>  | 100, 2.5 | 31 (R)      | 100    | 83      |

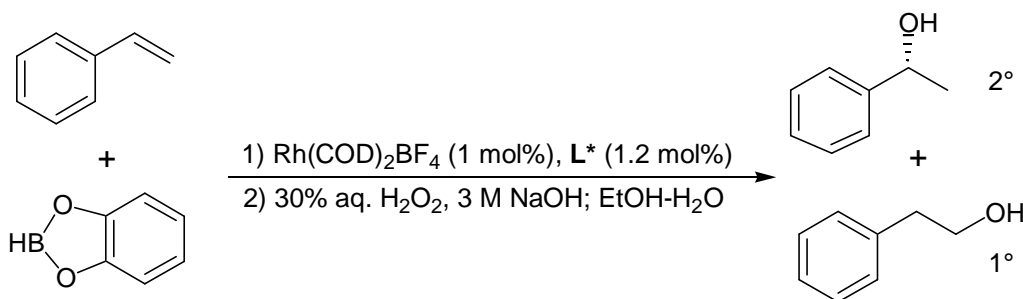


|   |   |                 |               |            |           |
|---|---|-----------------|---------------|------------|-----------|
| 4 |  <p style="text-align: center;"><b>30</b></p>  | <u>100, 2.5</u> | <u>88 (R)</u> | <u>100</u> | <u>86</u> |
| 5 |  <p style="text-align: center;"><b>29</b></p>  | 100, 16         | 45 (R)        | 100        | 88        |
| 6 |  <p style="text-align: center;"><b>29</b></p>  | 100, 2.5        | 57 (R)        | 100        | 87        |
| 7 |  <p style="text-align: center;"><b>31</b></p> | 100, 2.5        | 68 (R)        | 100        | 88        |

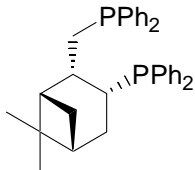
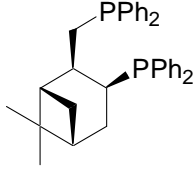
Interestingly, PCPP ligand (**1**) from *Achiwa* with the opposite configuration gives 31% *ee* of the same enantiomer of the product, in contrast to almost 90% *ee* for  $\alpha$ -methylated compound **30**. The increase in size of the alkyl substituent in the chain from Me to *i*Pr causes a big drop of enantioselectivity, although a further increase to the cyclohexyl group improves it again. In this reaction, the pinene-derived ligands performed relatively poorly. In all cases, the reaction was carried out at 100 °C, leading to 3-phenylcyclohexanone in high yields (Table 7, entries 1-6). A high enantioselectivity was achieved using the ligand **30** (88 % *ee*, entry 4). The increase of steric hindrance next to the phosphine group leads to a decrease in enantioselectivity (entry 4 and entries 6-7). The enantiomeric excess of the product increased from 45 % to 57 % when we reduced the time from 16 h at 100 °C to 2.5 h (entries 5 and 6). With Rh(C<sub>2</sub>H<sub>4</sub>)<sub>2</sub>(acac) as the rhodium source the enantioselectivity dropped from 88 % to 63 % (Entries 1 and 2). The reaction temperature is also important for enantioselectivity. Decrease of the temperature from 100 °C to 70 °C with the same catalyst led a the lower enantioselectivity (10 % *ee*, entry 4). When the temperature was increased to 110 °C, again only poor enantioselectivity was observed (entry 5).

#### 4.4. Rh-catalyzed asymmetric hydroboration of styrene.

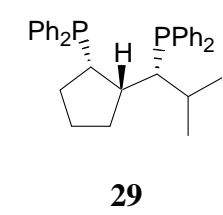
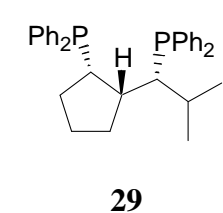
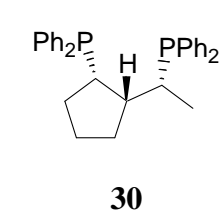
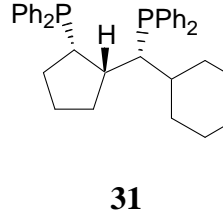
The hydroboration of alkenes is a valuable reaction in organic synthesis. The asymmetric hydroboration of styrene with catecholborane using chiral BINAP as a ligand gave high enantioselectivity, as was shown by Hayashi.<sup>66</sup> We have applied our novel chiral P,P-ligands in the Rh-catalyzed asymmetric hydroboration of styrene and have revealed a complete regioselectivity of hydroboration, which gave exclusively branched  $\alpha$ -phenylethanol after the oxidation (30 % H<sub>2</sub>O<sub>2</sub>, 2 M NaOH, entries 1-6, Table 8). The ligands with cyclopentane scaffolds gave better enantioselectivity in comparison with those with pinene-derived structures. The increase of steric hindrance in the side chain of the cyclopentane-derived ligands led to higher enantioselectivity which reached 80 % under optimized conditions (-20 °C, 16 h) (Table 8, entry 6).



**Table 8.** Rh-catalyzed asymmetric hydroboration of styrene.

| Entry | L*   | [T, h] | Solvent | 2°:1° | % ee       | Conv. | % yield |
|-------|--|--------|---------|-------|------------|-------|---------|
| 1     | <br><b>49</b> | 0, 6   | THF     | 100:0 | <i>rac</i> | 100   | 67      |
| 2     | <br><b>51</b> | 0, 6   | THF     | 100:0 | <i>rac</i> | 100   | 55      |

<sup>66</sup> a) T. Hayashi, Y. Matsumoto, Y. Ito, *J. Am. Chem. Soc.* **1989**, *111*, 3426. b) T. Hayashi, Y. Matsumoto, *Tetrahedron: Asymmetry* **1991**, *2*, 601.

|   |  |                |            |              |                      |            |           |
|---|--|----------------|------------|--------------|----------------------|------------|-----------|
| 3 |  <p style="text-align: center;"><b>29</b></p>   | 0, 6           | THF        | 100:0        | 73 ( <i>R</i> )      | 100        | 75        |
| 4 |  <p style="text-align: center;"><b>29</b></p>   | -20, 16        | THF        | 100:0        | 73 ( <i>R</i> )      | 85         | 65        |
|   |  | -10, 16        | THF        | 100:0        | 70 ( <i>R</i> )      | 100        | 64        |
| 5 |  <p style="text-align: center;"><b>30</b></p>  | -20, 16        | THF        | 100:0        | 55 ( <i>R</i> )      | 48         | 67        |
|   |  | -10, 16        | THF        | 100:0        | 57 ( <i>R</i> )      | 46         | 65        |
| 6 |  <p style="text-align: center;"><b>31</b></p> | -20, 16        | THF        | 100:0        | 80 ( <i>R</i> )      | 83         | 71        |
|   |  | <b>-10, 16</b> | <b>THF</b> | <b>100:0</b> | <b>80 (<i>R</i>)</b> | <b>100</b> | <b>69</b> |

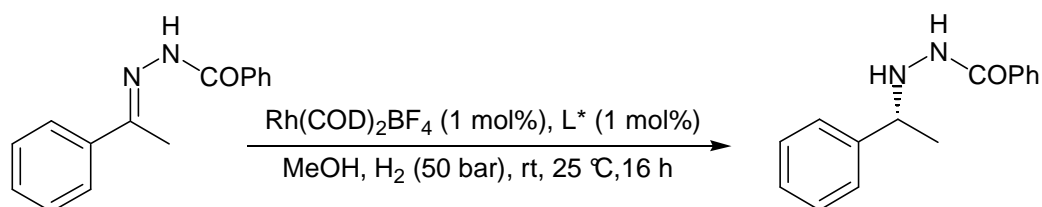
#### 4.5 Rh- and Ru-catalyzed asymmetric hydrogenation of C=N and C=O bonds and Pd-catalyzed allylic substitution reactions.

We tested several of our chiral diphosphine ligands for the Rh-catalyzed hydrogenation of C=N double bonds,<sup>67</sup> Ru-catalyzed hydrogenation of a keto ester,<sup>68</sup> and Pd-catalyzed

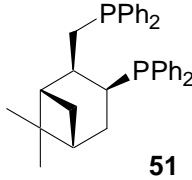
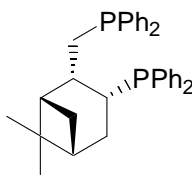
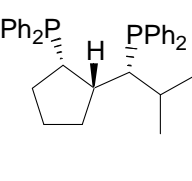
<sup>67</sup> (a) Burk, M. J.; Feaster, J. E. *J. Am. Chem. Soc.* **1992**, *114*, 6266; (b) Burk, M. J.; Martinez, J. P. *Tetrahedron* **1994**, *50*, 4399.

<sup>68</sup> (a) Ireland, T.; Grossheimann, G.; Wieser-Jeunesse, C.; Knochel, P. *Angew. Chem.* **1999**, *111*, 3397; *Angew. Chem. Int. Ed.* **1999**, *38*, 3212; (b) Ireland, T.; Tappe, K.; Grossheimann, G.; Knochel, P. *Chem. Eur. J.* **2002**, *8*, 843. (c) Lotz, M.; Polborn, K.; Knochel, P. *Angew. Chem.* **2002**, *114*, 4902; *Angew. Chem. Int. Ed.* **2002**, *41*, 4708. (d) Tappe, K.; Knochel, P. *Tetrahedron: Asymmetry* **2004**, in press.

asymmetric allylic substitution.<sup>69</sup> The results of these tests are presented in Tables 9-11. Acetophenone semicarbazone was chosen for screening of the ligands in C=N bond reduction.<sup>67</sup> In two out of three cases a full conversion was obtained with the tested ligands, although the enantioselectivity was poor.



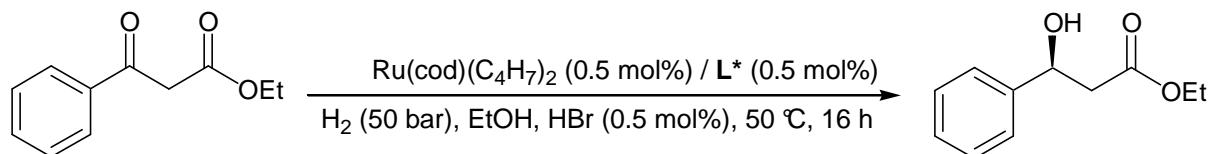
**Table 9.** Ru-catalyzed asymmetric hydrogenation of acetophenone semicarbazone.

| Entry | L*   | % ee <sup>a</sup> | Conv. | yield <sup>b</sup> |
|-------|--|-------------------|-------|--------------------|
| 1     | <br><b>51</b> | 30 ( <i>R</i> )   | 100   | 88%                |
| 2     | <br><b>49</b> | -                 | 0     | -                  |
| 3     | <br><b>29</b> | 19 ( <i>R</i> )   | 100   | 92%                |

The enantioselective hydrogenation of  $\beta$ -ketoesters, catalyzed by Ru-diphosphine catalysts is a well-known and industrially important reaction, broadly used for the preparation of chiral hydroxyesters.<sup>68</sup> We tested two of our novel chiral diphosphines in this reaction (one pinene-

<sup>69</sup> (a) Trost, B.M.; Van Vranken, D. L. *Chem. Rev.* **1996**, *96*, 395. (b) Heumann, A.; Réglie, M. *Tetrahedron* **1995**, *51*, 975. (c) Trost, B. M.; Murphy, D. J. *Organometallics* **1985**, *4*, 1143.

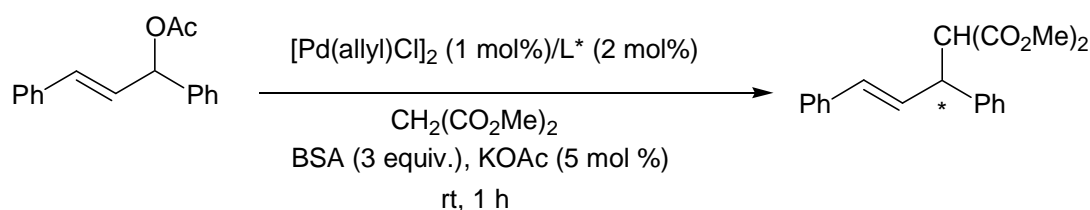
derived and one cyclopentane-derived compound), using benzoylacetate as a substrate. The catalysts were prepared *in situ* from Ru(cod)(C<sub>4</sub>H<sub>7</sub>)<sub>2</sub>, the ligands and HBr in MeOH (0.5 mol% of each component). In both cases, despite the good yields, the enantioselectivity was too low to be practical (Table 10).



**Table 10.** Ru-catalyzed hydrogenation of benzoylacetate.

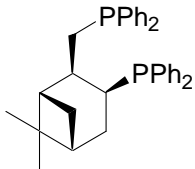
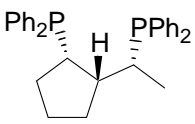
| Entry | L*   | H <sub>2</sub> (bar) | % ee   | Conv. | % yield |
|-------|--|----------------------|--------|-------|---------|
| 1     | <p style="text-align: center;"><b>30</b></p> | 50                   | 7 (R)  | 100   | 98      |
| 2     | <p style="text-align: center;"><b>49</b></p> | 50                   | 37 (R) | 100   | 98      |

We examined the new ligands in the Pd(0)-catalyzed allylic substitution of racemic 1,3-diphenylpropen-2-yl acetate with dimethyl malonate, according to the procedure of Trost.<sup>70</sup> [Pd(C<sub>3</sub>H<sub>5</sub>)Cl]<sub>2</sub> was used as the catalyst precursor in the presence of potassium acetate, *N,O*-bis(trimethylsilyl)acetamide (BSA), the *bis*-phosphine ligand, and the substrate in dry degassed CH<sub>2</sub>Cl<sub>2</sub>. Despite a good conversion, the yield and the enantiomeric excess of the product were low (Table 11).



<sup>70</sup> B. M. Trost, D. J. Murphy, *Organometallics*, **1985**, *4*, 1143.

**Table 11.** Pd-catalyzed enantioselective allylic substitution.

| Entry | L*   | % ee            | Conv. | % yield |
|-------|--|-----------------|-------|---------|
| 1     | <br><b>51</b> | 33 ( <i>S</i> ) | 100   | 78      |
| 2     | <br><b>30</b> | 28 ( <i>S</i> ) | 100   | 75      |

## Part II

### New reactions of organozinc compounds

Organozinc compounds were among the first organometallic species prepared. While some types of organozinc compounds like Reformatsky<sup>71</sup> and iodomethylzinc iodide (Simmons-Smith)<sup>72</sup> reagents found since long a broad application in organic synthesis, the synthetic potential of the organozinc species in general has been recognized only recently.<sup>73</sup> The reasons for that are their lower reactivity in comparison with Grignard reagents and the lack of general methods for their preparation until recently. Due to its highly covalent character, the carbon-zinc bond is inert to the majority of electrophiles like aldehydes, ketones, esters or nitriles. However, the presence of empty low-lying *p*-orbitals at the zinc atom allows transmetalation with a number of transition metal complexes. The availability of *d*-orbitals at the metal center in those compounds allows for new reaction pathways with electrophiles, which are not available for the corresponding zinc reagents. Such a mode of reactivity has

<sup>71</sup> a) F. Reformatsky, *Chem. Ber.* **1887**, 20, 1210. b) A. Fürstner, *Angew. Chem. Int. Ed. Engl.* **1993**, 32, 164.

<sup>72</sup> a) H. E. Simmons, R. D. Smith, *J. Am. Chem. Soc.* **1959**, 81, 4256. b) G. Wittig, F. Wingler, *Chem. Ber.* **1964**, 97, 2146.

<sup>73</sup> a) P. Knochel, R. D. Singer, *Chem. Rev.* **1993**, 93, 2117. b) P. Knochel, J. Almena, P. Jones, *Tetrahedron* **1998**, 54, 8275. c) P. Knochel, P. Jones, *Organozinc Reagents. A Practical Approach*. Oxford University Press. **1999**. d) P. Knochel, N. Millot, A. L. Rodriguez, C. E. Tucker *Org. React.* **2001**, 58, 417.

been broadly exploited for the formation of new carbon-carbon bonds and efficient cross-coupling reactions between  $sp^3$  and  $sp^2$  centers, as was demonstrated, for instance, by Negishi using catalytic amounts of Pd salts.<sup>74</sup> Similar catalytic reactions were reported in large amounts for Cu(I)<sup>75</sup> and Ti(IV)<sup>76</sup> complexes, which were found to promote numerous reactions of organozinc reagents with organic electrophiles.

The synthetic applications of organozinc compounds greatly increased when it was noticed that these reagents tolerate a wide range of functional groups. Therefore, they perfectly fit for the construction of complex functionalized organic molecules without the need in special protection-deprotection steps. The chemistry of organozinc compounds is now a rapidly growing branch of organometallic chemistry with great perspectives and high potential for numerous industrial applications.

## 5. New cross-coupling reaction of triorganosilylzinc compounds with aryl triflates.

During the studies of the halogen-magnesium exchange reaction for the preparation of functionalized organomagnesium reagents, we noticed the lack of a synthetically useful, mild and general method for the transformation of a phenolic hydroxyl into a halogen moiety like iodine and bromine. Such transformation would allow further functionalization of molecules, containing phenolic groups, by methods of organomagnesium or organozinc chemistry, including the novel ones, recently developed in our group.<sup>77</sup> Several methods can be considered to perform such transformation:

- 1) reaction of a phenol with  $Ph_3PBr_2$  at 320 °C<sup>78</sup>
- 2) reaction of an aryl triflate with hexabutylditin,<sup>79</sup> followed by the iodolysis of the C-Sn bond;
- 3) reaction of a phenyl triflate with diboron reagents (*bis*-(pinacolato)diboron<sup>80</sup> or pinacolborane<sup>81</sup>) and the subsequent iodolysis of the formed C-B bond.

<sup>74</sup> E. Negishi, L. F. Valente, M. Kobayashi, *J. Am. Chem. Soc.* **1980**, *102*, 3289.

<sup>75</sup> B. H. Lipshutz, S. Sengupta, *Org. React.* **1992**, *41*, 135.

<sup>76</sup> D. Seebach, A. K. Beck, B. Schmidt, Y. M. Wang, *Tetrahedron*, **1994**, *50*, 4363.

<sup>77</sup> a) A. Krasovsky, P. Knochel, *Angew. Chem. Int. Ed.* **2004**, *45*, 3333. b) A. Krasovsky, V. Malakhov, A. Gavryushin, P. Knochel, *Angew. Chem. Int. Ed.* **2006**, *47*, 6040.

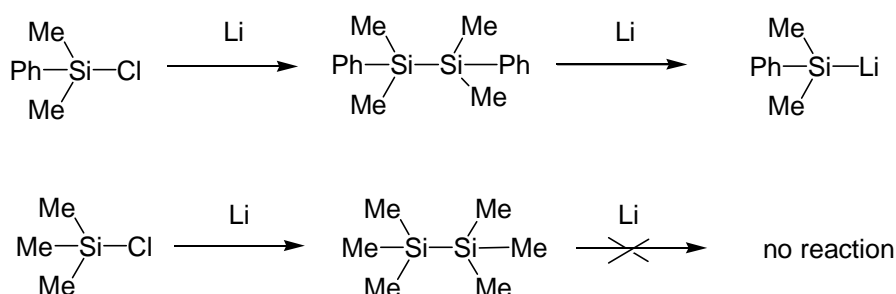
<sup>78</sup> H. Takaya, S. Akutagawa, R. Noyori, *Org. Synth.* **1989**, *67*, 20.

<sup>79</sup> H. Azizian, C. Eaborn, A. Pidcock, *J. Organomet. Chem.* **1981**, *215*, 49.

<sup>80</sup> T. Ishiyama, K. Ishida, N. Miyaura, *Tetrahedron* **2001**, *57*, 9813.

<sup>81</sup> M. Murata, T. Oyama, S. Watanabe, Y. Masuda, *J. Org. Chem.* **2000**, *65*, 164.

All these methods have certain drawbacks, and mostly are not sufficiently general. One of the convenient precursors for aryl iodides are the corresponding arylsilanes, since an Ar-Si bond can be readily subjected to iodolysis under relatively mild conditions. The preparation of arylsilanes from phenols required a new synthetic pathway from an activated phenyl ester to the corresponding arylsilane. Although several publications described Pd-catalyzed cross-coupling of hydro- and disilanes with aryl halides, this reaction proceeds only for a limited number of substrates and is less useful for aryl triflates.<sup>82</sup> The silane partner should be a nucleophile in this coupling reaction, therefore an anionic silicon species has to be taken as starting material. Literature research revealed that known compounds of such type are relatively few in number and their syntheses are difficult and not practical. A notable exception is the phenyldimethylsilyllithium species, whose chemistry has been profoundly investigated by *Fleming*.<sup>83</sup> Phenyldimethylsilyllithium can be readily prepared by the stirring of PhMe<sub>2</sub>SiCl with 2 equiv. of Li in THF at 0 °C.<sup>83b</sup> During the stepwise formation of this compound, tetramethyldiphenylsilane is formed first. It is cleaved by the excess of Li, finally giving the silyllithium species. Such splitting is selective for disilanes, bearing at least one aryl group on each silicon atom. In the case of Me<sub>3</sub>SiCl the reaction stops after the formation of hexamethyldisilane (Scheme 60).



**Scheme 60.** Reactions of chlorosilanes with Li metal.

The solution of PhMe<sub>2</sub>SiLi can be titrated after the preparation and is sufficiently stable for storage at least for a week at 0 °C without a decrease in concentration. Thus, it may serve as a precursor for the nucleophilic silicon species in the planned cross-coupling reaction.

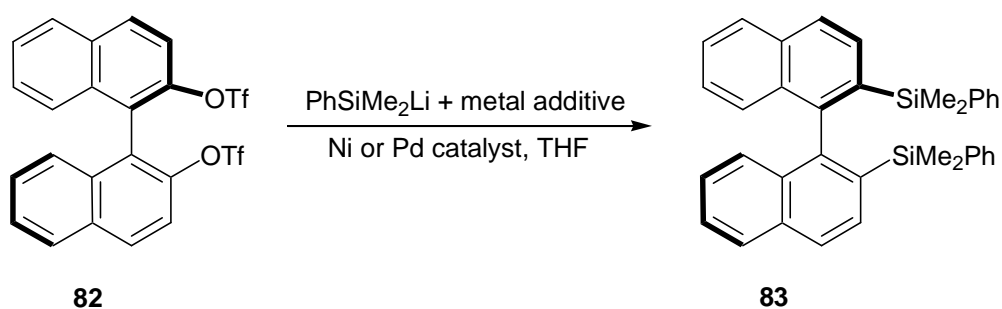
<sup>82</sup> a) M. Murata, H. Ohara, R. Oiwa, S. Watanabe, Y. Masuda, *Synthesis* **2006**, *11*, 1771. b) M. Murata, K. Suzuki, S. Watanabe, Y. Masuda, *J. Org. Chem.* **1997**, *62*, 8569. c) M. Murata, M. Ishikira, M. Nagata, S. Watanabe, Y. Masuda, *Org. Lett.* **2002**, *4*, 1843. d) Y. Yamanoi, *J. Org. Chem.* **2005**, *70*, 9607.

<sup>83</sup> a) I. Fleming, R. S. Roberts, S. C. Smith, *Tetrahedron Lett.* **1996**, *37*, 9395. b) I. Fleming, R. S. Roberts, S. C. Smith, *J. Chem. Soc. Perkin Trans. 1* **1998**, *7*, 1209.



## 6.1 Reaction optimization

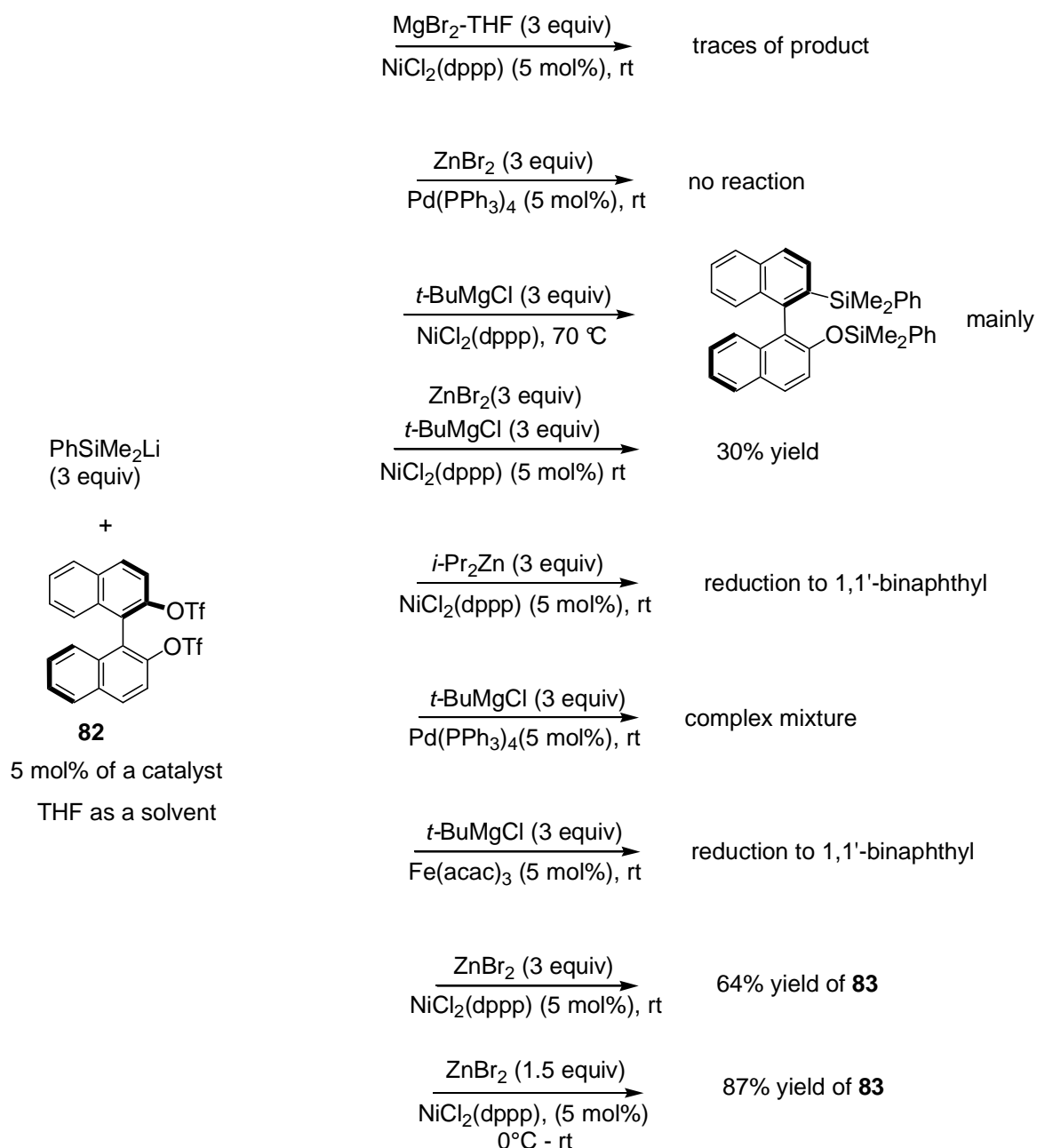
One of the goals of our investigation was the preparation of enantiopure binaphthyl halides from chiral 1,1'-bi-(2-naphthol) (BINOL), and we chose (*R*)-binaphthyl-*bis*-triflate as a model compound for the development of the new cross-coupling reaction with silyl species (Scheme 61). The silyllithium reagent, prepared according to the published protocol,<sup>83</sup> was transmetalated with 0.5 or 1 equiv. of ZnBr<sub>2</sub>, MgBr<sub>2</sub>, *t*-BuMgCl or *i*Pr<sub>2</sub>Zn. The resulted reagents were reacted with (*R*)-binaphthyl-*bis*-triflate in the presence of various Pd- and Ni-containing catalysts.



**Scheme 61.** Synthetic plan for the new cross-coupling reaction of aryl triflates.

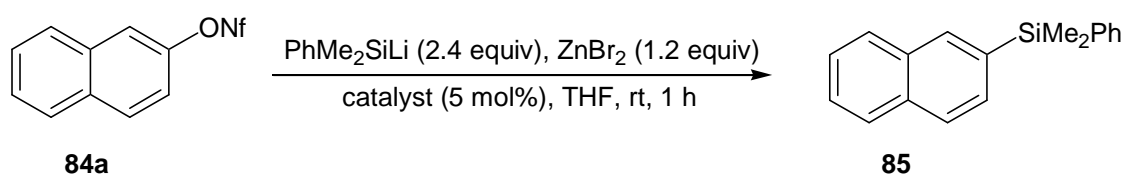
Neither of the several screened Pd catalysts gave *bis*-silane **83**. We then turned our attention to nickel catalysis, since the cross-coupling reaction of sterically hindered BINOL-*bis*-triflate usually perform well with Ni catalysts.<sup>84</sup> Several reaction conditions tested for the test cross-coupling reaction are described below (Scheme 62):

<sup>84</sup> P. Kasak, M. Putala, *Tetrahedron Lett.* **2004**, *45*, 5279 and refs. therein.



**Scheme 62.** Screening of the reaction condition for the Ni-catalyzed cross-coupling reaction of aryl triflates with silylmetal reagents.

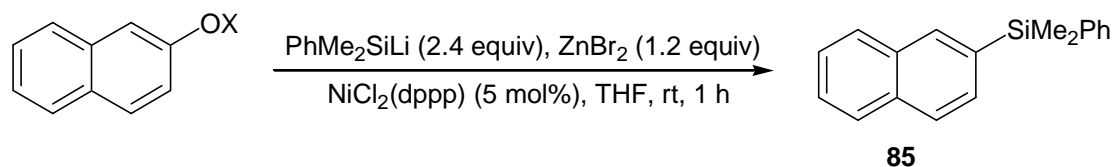
The optimal conditions were established finally as following: 1.2 equiv of  $(\text{PhMe}_2\text{Si})_2\text{Zn}$  (prepared *in situ* from 2.4 equiv.  $\text{PhMe}_2\text{SiLi}$  and 1.2 equiv.  $\text{ZnBr}_2$ ), 5 mol% of  $\text{NiCl}_2(\text{dppp})$  as a catalyst, THF, 1 h at room temperature. The yield of compound **83** in this reaction was 87%. In order to determine the scope of the process and to optimize the ligand for the nickel catalysis, we continued the investigation of this reaction, using 2-naphthyl nonaflate as a substrate. The catalyst  $\text{NiCl}_2(\text{dppp})$  turned out to be the best among the several Ni complexes screened.



**Table 12.** Optimization of the catalyst.

| Entry | Catalyst   | Yield (GC), % |
|-------|--|---------------|
| 1     | <b>NiCl<sub>2</sub>(dppp)</b>                      | <b>73</b>     |
| 2     | NiCl <sub>2</sub> (dppe)                           | 70            |
| 3     | NiCl <sub>2</sub> (PPh <sub>3</sub> ) <sub>2</sub> | 41            |
| 4     | NiCl <sub>2</sub> (PBu <sub>3</sub> ) <sub>2</sub> | 0             |
| 5     | PdCl <sub>2</sub> (PPh <sub>3</sub> ) <sub>2</sub> | 0             |

Various leaving groups were also tested, using the sulfonate esters of  $\beta$ -naphthol as models. From the four sulfonate esters tested,  $\beta$ -naphthyl triflate (**84**) turned out to be the best concerning the yield of the arylsilane **85** (Table 13).

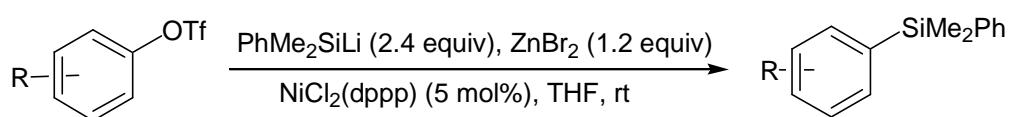


**Table 13.** Optimization of the leaving group.

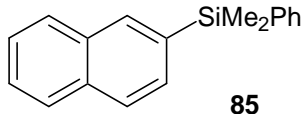
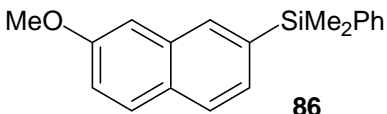
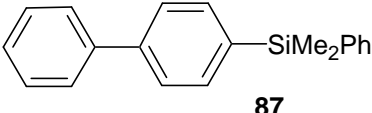
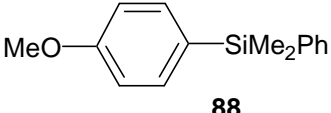
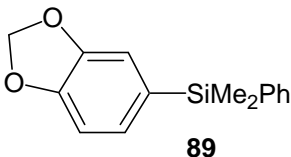
| Entry | Leaving group X | Yield, % |
|-------|-----------------|----------|
| 1     | Nf              | 73       |
| 2     | Tf              | 88       |
| 3     | Ts              | 82       |
| 4     | Ms              | 51       |

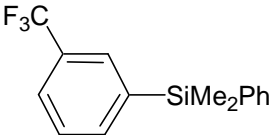
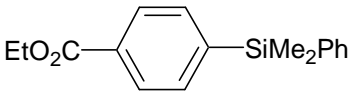
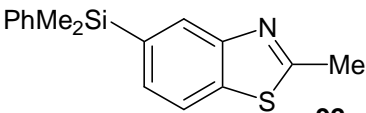
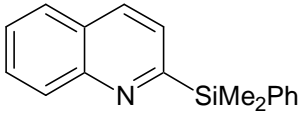
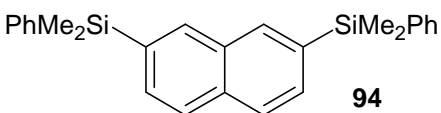
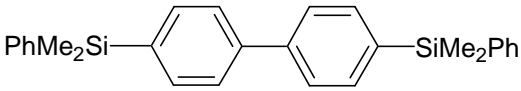
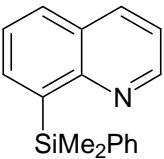
## 6.2 Cross-coupling reaction of silylzinc and silylaluminium compounds

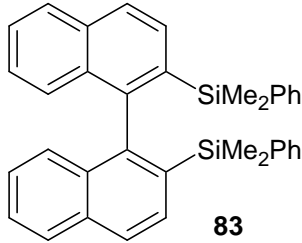
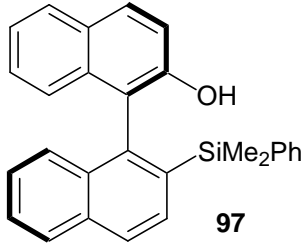
Based on the results of these experiments, we chose the triflate group as the leaving group for this cross-coupling reaction. A number of arylsilanes was prepared starting from the corresponding triflates in good to excellent yields. The results are presented in Table 14.



**Table 14.** Ni-catalyzed cross-coupling reaction of aryl triflates with silylzinc reagents.

| Entry | Product  | Reaction time (h) | Yield, % |
|-------|--|-------------------|----------|
| 1     | <br><b>85</b>   | 1                 | 88       |
| 2     | <br><b>86</b>   | 1                 | 71       |
| 3     | <br><b>87</b> | 3                 | 80       |
| 4     | <br><b>88</b> | 3                 | 64       |
| 5     | <br><b>89</b> | 6                 | 63       |

|    |  |    |    |
|----|--|----|----|
| 6  |  <p style="text-align: center;"><b>90</b></p>   | 1  | 54 |
| 7  |  <p style="text-align: center;"><b>91</b></p>   | 1  | 71 |
| 8  |  <p style="text-align: center;"><b>92</b></p>   | 8  | 71 |
| 9  |  <p style="text-align: center;"><b>93</b></p> | 8  | 72 |
| 10 |  <p style="text-align: center;"><b>94</b></p> | 3  | 65 |
| 11 |  <p style="text-align: center;"><b>95</b></p> | 24 | 64 |
| 12 |  <p style="text-align: center;"><b>96</b></p> | 1  | 75 |

|    |  |   |                   |
|----|--|---|-------------------|
| 13 |  <p style="text-align: center;"><b>83</b></p> | 6 | 77 <sup>a,b</sup> |
| 14 |  <p style="text-align: center;"><b>97</b></p> | 6 | 79 <sup>a</sup>   |

<sup>a</sup> Double amount of the silylzinc reagent was used    <sup>b</sup> Racemic product was obtained

Despite the good yields of products in many cases, the reaction was found to have several limitations, which were revealed during further investigations. No reaction or low yields are observed for sterically hindered substrates like mesityl triflate. The *bis*-silyl product **83**, obtained from enantiopure (*R*)-BINOL-bitriflate, turned out to be racemic. While for the enantiopure material the optical rotation is  $-46.7$  (c 1.12, cyclohexane),<sup>85</sup> for the synthesized compound **83** it was equal to zero. Attempts to adjust the reaction conditions in order to avoid racemization failed. Supposedly, the reaction in our case takes place *via* formation of an intermediate nickelacycle, which is planar or possesses a very low epimerization barrier. The formation of similar metallacycles during the cross-coupling reactions of 2,2'-diiodobinaphthyls in the presence of Pd has been demonstrated.<sup>86</sup> Moreover, it is known that 2,2'-bimetallic derivatives of 1,1'-binaphthyls possess a relatively low epimerization barrier, so that 2,2'-dilithio-1,1'-binaphthyl epimerizes above  $-40$  °C.<sup>87</sup> On the other hand, the Ni-catalyzed cross-coupling of the chiral binaphthol-bitriflate with diphenylphosphine proceeds with complete retention of configuration,<sup>88</sup> which shows a possibility to achieve this result in our case.

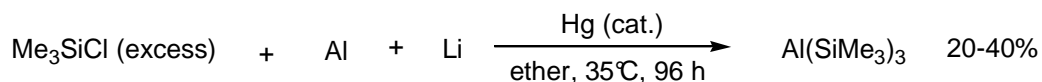
<sup>85</sup> T. Hoshi, H. Shionori, T. Suzuki, M. Ando, H. Hagiwara, *Chem. Lett.* **1999**, 1245.

<sup>86</sup> P. Kasák, P. Mikláš, M. Putala, *J. Organomet. Chem.* **2001**, 637-639, 318.

<sup>87</sup> K. J. Brown, R. J. Murdoch, *J. Am. Chem. Soc.* **1984**, 106, 7843.

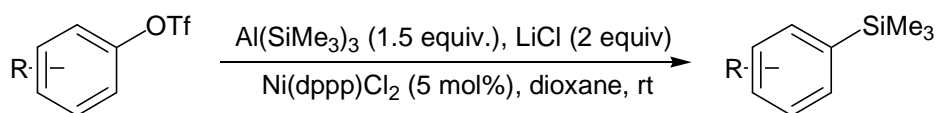
<sup>88</sup> D. Cai, J. F. Payack, D. R. Beuder, D. L. Hughes, T. R. Verhoeven, P. J. Reider, *Org. Synth.* **1999**, 76, 6.

In order to overcome the above-mentioned limitations of this reaction, we investigated briefly the possibility to use other silylmetal reagents. A viable substitution for the  $(\text{PhMe}_2\text{Si})_2\text{Zn}$  can be *tris*-(trimethylsilyl)aluminium which can be obtained, although in low yield, by the reaction between  $\text{Me}_3\text{SiCl}$ , Al and Li metals in refluxing ether in the presence of catalytic amounts of metallic mercury (Scheme 63)<sup>89</sup>



**Scheme 63.** Preparation of *tris*-(trimethylsilyl)aluminium.

This reagent can be isolated after filtration and evaporation of the reaction mixture and crystallization from pentane at  $-78^\circ\text{C}$ . The neat compound at room temperature is a highly pyrophoric liquid, forming big colourless needles below  $0^\circ\text{C}$ . First attempts demonstrated that the cross-coupling reaction with 1-naphthyltriflate in THF can be successfully catalyzed by  $\text{NiCl}_2(\text{dppp})$ , but the reaction is too sluggish at room temperature. It was found to proceed optimally at room temperature in dioxane in the presence of 2 equiv. of LiCl, using 5 mol% of  $\text{NiCl}_2(\text{dppp})$  as catalyst, leading to 1-trimethylsilylnaphthalene in 79% yield. Earlier, the reaction of  $(\text{Me}_3\text{Si})_3\text{Al}$  with aryl bromides was described by *Trost*.<sup>90</sup> Interestingly, the reaction between 1-naphthyl triflate and  $(\text{PhMe}_2\text{Si})_2\text{Zn}$  gives mixture of products, probably, due to a higher steric hindrances. However, the aluminium reagent was found incompatible with the most functional groups like esters or halides. Only one trimethylsilyl group out of three could be transferred during the reaction. The difficulties in the preparation and handling of this reagent as well as the toxicity of mercury, required for its preparation, make its use less advantageous. Several products, obtained from the Ni-catalyzed cross-coupling reaction of *tris*-(trimethylsilyl)aluminium and aryltriflates, are shown below (Table 15):

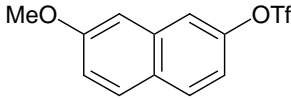
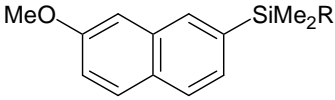
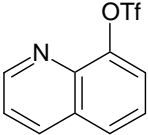
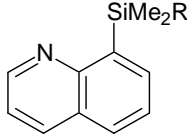
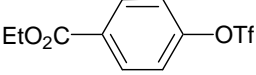
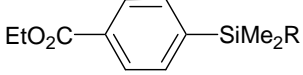
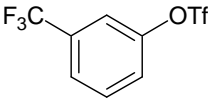
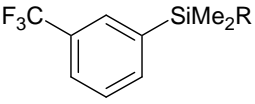


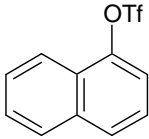
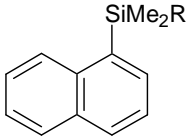
<sup>89</sup> L. Roesch, G. Altnau, *J. Organomet. Chem.* **1980**, *195*, 47.

<sup>90</sup> a) B. Trost, J. Yoshida, *Tetrahedron Lett.* **1983**, *24*, 4895. Reactions of  $\text{Al}(\text{SiMe}_3)_3$  with allylic acetates and alkynes have been described: b) B. M. Trost, J. Yoshida, M. Lautens, *J. Am. Chem. Soc.* **1983**, *105*, 4494; c) L. Roesch, G. Altnau, G. Jas, *Chemiker-Zeitung* **1983**, *107*, 128.



**Table 15.** Comparison of Ni-catalyzed cross-coupling reactions of  $(\text{Me}_3\text{Si})_3\text{Al}$  and  $(\text{PhMe}_2\text{Si})_2\text{Zn}$  with aryl triflates.

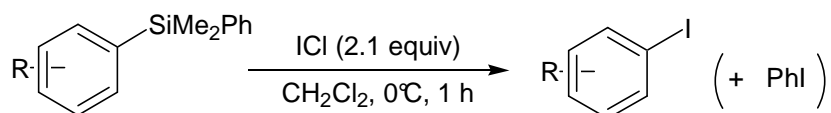
| Entry | Starting material   | Product   | Yield and reaction time with $(\text{PhMe}_2\text{Si})_2\text{Zn}$ (R=Ph) | Yield and reaction time with $(\text{Me}_3\text{Si})_3\text{Al}$ (R=Me) |
|-------|---|---|---|---|
| 1     |  <p><b>98</b></p>    |    | <p><b>86</b></p> <p>71%, 1 h</p>  | <p><b>86a</b></p> <p>52%, 19 h</p>                                      |
| 2     |  <p><b>96a</b></p> |  | <p><b>96</b></p> <p>75%, 1 h</p>  | <p><b>96b</b></p> <p>71%, 19 h</p>                                      |
| 3     |  <p><b>91a</b></p> |  | <p><b>91</b></p> <p>71%, 1 h</p>  | <p>complex mixture</p>  |
| 4     |  <p><b>90a</b></p> |  | <p><b>90</b></p> <p>54%, 1 h</p>  | <p><b>90b</b></p> <p>57%, 1 h</p>                                       |

|   |   |   |                    |                         |
|---|---|---|--------------------|-------------------------|
| 5 | <br><b>96c</b> | <br> | Complex<br>mixture | <b>96d</b><br>79%, 19 h |
|---|---|---|--------------------|-------------------------|

This method in some cases can be considered as complementary to the coupling with *bis*-(phenyldimethylsilyl)zinc.

### 6.3 Conversion of phenols into aryl iodides and arylboronic esters.

Initially, we considered the cross-coupling reaction of silylmetal reagents as a part of a synthetic method for the conversion of phenols into aryl iodides. A commonly used synthetic protocol for the conversion of arylsilanes into the corresponding iodides includes their treatment with an excess of ICl.<sup>91</sup> Several arylphenyldimethylsilanes, prepared from the corresponding triflates as described above, could be easily transformed into the aryl iodides with this reagent in CH<sub>2</sub>Cl<sub>2</sub> at 0 °C (Scheme 64).

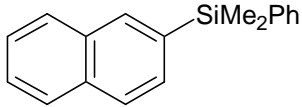
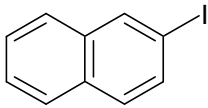
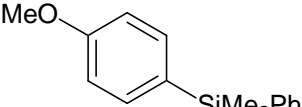
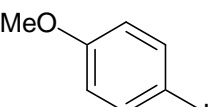

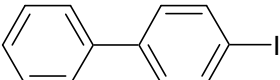
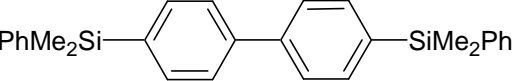
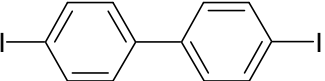
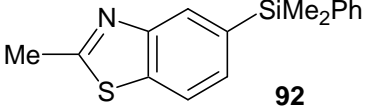
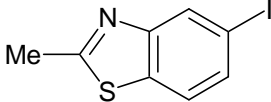


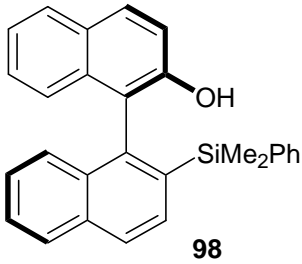
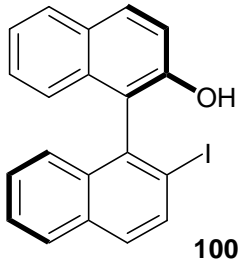
**Scheme 64.** Conversion of arylphenyldimethylsilanes into aryl iodides.

The structures and the yields of the iodoarenes, synthesized according to this method, are given in Table 16:

<sup>91</sup> B. C. Berris, G. H. Hovakeemian, Y.-H. Lai, H. Mestdagh, K. P. C. Vollhardt, *J. Am. Chem. Soc.* **1985**, *107*, 5670.

**Table 16.** Conversion of arylphenyldimethylsilanes into aryl iodides.

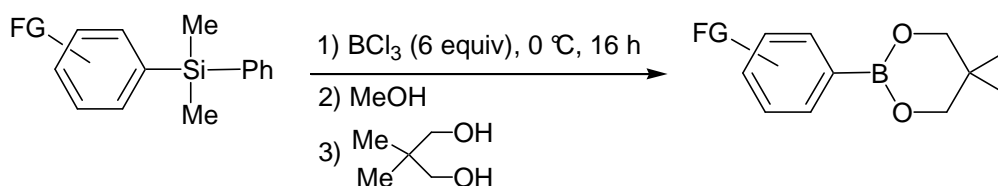
| Entry | Starting material  | Product  | Yield |
|-------|--|--|-------|
| 1     | <br><b>85</b>   |                  | 90%   |
| 2     | <br><b>88</b>   |                  | 89%   |
| 3     | <br><b>87</b> |                | 90%   |
| 4     | <br><b>95</b> |                | 75%   |
| 5     | <br><b>92</b> | <br><b>101</b> | 56%   |

|   |  |  |                  |
|---|--|--|------------------|
| 6 |  <p><b>98</b></p> |  <p><b>100</b></p> | 78% <sup>a</sup> |
|---|--|--|------------------|

<sup>a</sup>5 equiv of TMSCl was added.

An interesting behaviour was demonstrated by 2-phenyldimethylsilyl-2'-hydroxy-1,1'-binaphthyl **98** (entry 6). The reaction with ICl in CH<sub>2</sub>Cl<sub>2</sub> led exclusively to the product, identified by mass-spectra as a *mono*-chlorinated iodobinaphthol. The exact position of the chlorine atom in this molecule was difficult to establish. The mechanism of the formation of this compound is not clear. We supposed that PhMe<sub>2</sub>SiCl, formed on the first step, might react with the free phenolic group, giving the corresponding silyl ether. The reaction of this silyl ether with the second molecule of ICl occurs as the electrophilic attack, leading to an intermediate arenonium cation. Due to the steric hindrance of this substrate, the addition of chlorine tends to proceed abnormally. The attack of chlorine may occur, obviously, on several positions of the naphthalene ring, thus leading to a different substitution pattern. In order to avoid this side reaction, according to this hypothesis, it should be sufficient to protect the phenol hydroxyl. We performed the iodination reaction in the presence of 10 equiv of Me<sub>3</sub>SiCl, which was added before the iodinating reagent. Indeed, in this case the single reaction product was the desired iodophenol **100** (entry 6).

Beside the synthesis of aryl iodides, the arylsilanes may serve as precursors for the preparation of several other classes of substituted arenes. Arylsilanes react with the excess of BCl<sub>3</sub> in CH<sub>2</sub>Cl<sub>2</sub> at 0 °C, giving arylchloroboranes.<sup>92</sup> Those can be transformed into stable arylboronic esters, which might be further involved into numerous transition metal-catalyzed reactions (Scheme 65):

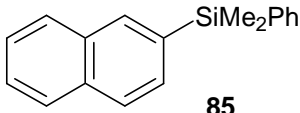
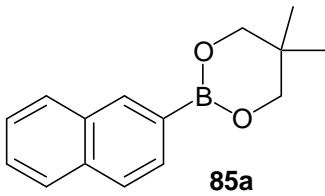
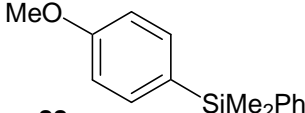
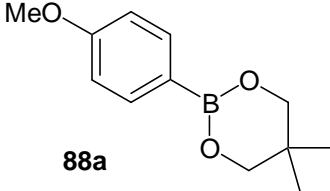
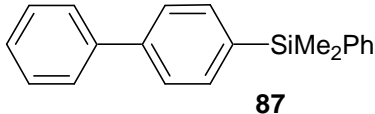
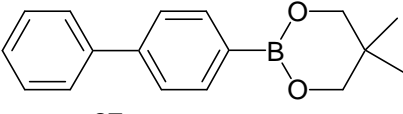


**Scheme 65.** Conversion of aryl(dimethyl)phenylsilanes into arylboronic esters.

<sup>92</sup> D. Kaufmann, *Chem. Ber.* **1987**, *120*, 853.

The attack of  $\text{BCl}_3$  on the aryldimethylsilyl chloride under the reaction condition does not take place, as we have never observed the formation of two different boronic esters in this reaction. Three different arylboron 2,2-dimethylpropanediolates were obtained from the aryldimethylphenylsilanes prepared before, as shown in the Table 17.

**Table 17.** Conversion of aryldimethylphenylsilanes into arylboronic esters.

| Entry | Starting material  | Product  | Yield |
|-------|--|--|-------|
| 1     |  <p style="text-align: center;"><b>85</b></p>   |  <p style="text-align: center;"><b>85a</b></p>   | 71%   |
| 2     |  <p style="text-align: center;"><b>88</b></p> |  <p style="text-align: center;"><b>88a</b></p> | 68%   |
| 3     |  <p style="text-align: center;"><b>87</b></p> |  <p style="text-align: center;"><b>87a</b></p> | 62%   |

In general, we developed a new synthetic method for the transformation of phenols into the corresponding aryl iodides and arylboronic esters *via* the intermediate formation of arylsilanes. The key step of this method is an unprecedented Ni-catalyzed cross-coupling reaction of silylmetallic species *bis*-(phenyldimethylsilyl)zinc or *tris*-(trimethylsilyl)aluminium with aryl triflates. The scope and limitations of this method have been investigated.

## 6. Novel method of thiolation of organozinc and organomagnesium compounds.

Many aromatic and heteroaromatic thio-derivatives have biological activities and their synthesis attracts a lot of attention. A great number of new copper and palladium catalyzed aryl-sulfur bond formation reactions have been recently described.<sup>93</sup> The preparation of arylthiols and their derivatives from the corresponding halides is synthetically highly advantageous, since aryl halides are among the most common aryl derivatives. In one variant, it can be performed *via* the conversion of a halide to the corresponding aryllithium, followed by the reaction with elemental sulfur. This reaction, however, is strictly limited in scope, as most of functional groups are incompatible with organolithium chemistry. On the other hand, the use of less reactive (and more tolerant to functionalities) organometallic species like organomagnesium or organozinc reagents is not convenient for the introduction of a thiol group due to the lack of sufficiently reactive sulfur electrophiles and is limited by the synthesis of substituted sulfides. Recently, in our group a simple and extremely versatile methods for the preparation of Grignard and zinc reagents from the corresponding aryl and alkyl bromides were developed.<sup>77</sup> It looked reasonable, therefore, to design a general synthetic method for the introduction of a thiol group using organozinc or organomagnesium reagents, which would tolerate a broad variety of functional groups.

### 6.1 New thiolation reaction of organomagnesium compounds.

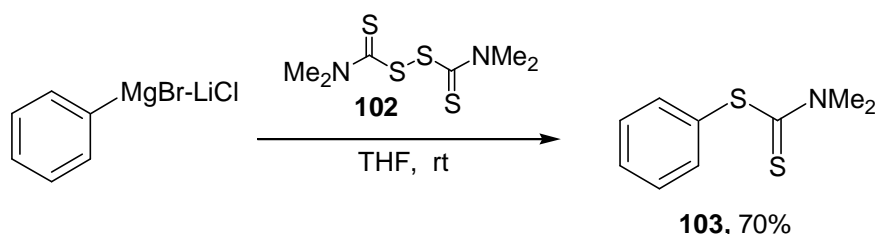
In our search for a suitable sulfur-containing electrophile, we turned our attention to alkylthiuram disulfides. Their reaction with organometallic reagents should give *N,N'*-dialkyldithiocarbamates, which can be easily hydrolysed to the corresponding thiols. On the other hand, thiuram disulfides are cheap, easy to handle, non-hygroscopic and non-toxic solids. Tetramethylthiuram disulfide (TMTD, **102**) is the best available representative of that class of compounds and a multiton industrial product. The reaction between TMTD and phenylmagnesium bromide has been reported, but gave only 26% yield of the product.<sup>94</sup> A possible explanation of this poor result can be the low solubility of TMTD and the reaction product - magnesium dimethyl dithiocarbamate, which makes the reaction mixture heterogeneous and causes the formation of by-products. We anticipated that the increase in

---

<sup>93</sup> a) G. Solladié, in: *Comprehensive Organic Synthesis* B. M. Trost, I. Fleming, E. Winterfeld (Eds.) Vol. 6, Pergamon Press, **1991**, 133. b) C. G. Bates, R. K. Gujadjur, D. Venkataraman *Org. Lett.* **2002**, *4*, 2803. c) F. Y. Kwang, S. L. Buchwald, *Org. Lett.* **2002**, *4*, 3517. C. Savarin, J. Srogl, L. S. Liebeskind, *Org. Lett.* **2002**, *4*, 4309. d) Y.-J. Chen, H.-H. Chen, *Org. Lett.* **2006**, *8*, 5609.

<sup>94</sup> J. R. Greenwell, *J. Org. Chem.* **1970**, *35*, 1500.

the reactivity of the Grignard reagents as well as the increase in the solubility of the resulting magnesium salts, acquired by the addition of LiCl to the mixture<sup>77a</sup> should positively influence the yield of this reaction. The first reaction attempt between phenylmagnesium chloride-lithium chloride and solid TMTD in THF led to encouraging 70% yield of the *S*-phenyl *N,N*-dimethyldithiocarbamate (Scheme 66):

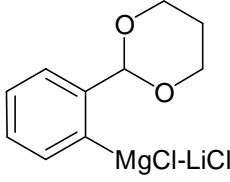
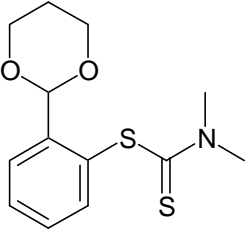
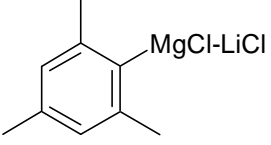
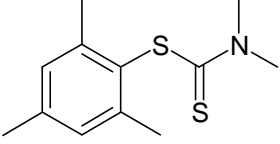
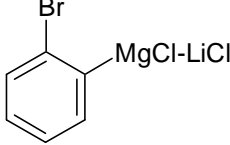
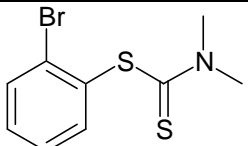
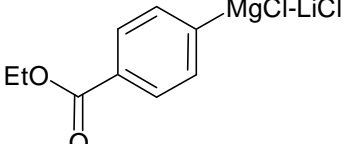
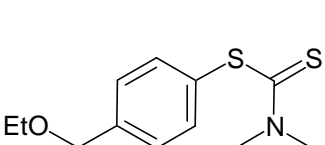
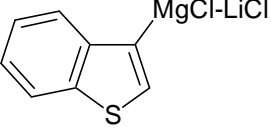
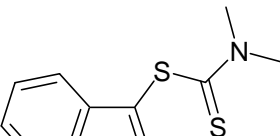
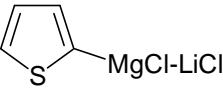
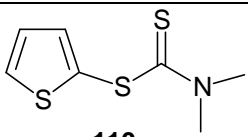
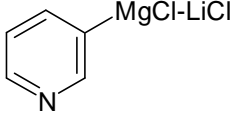
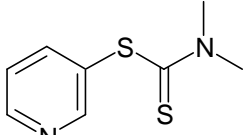
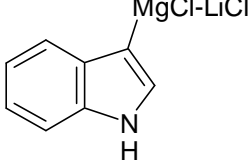
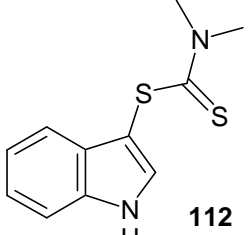


**Scheme 66.** Reaction of PhMgBr-LiCl with TMTD (**102**).

We found that the preliminary dissolution of TMTD in CH<sub>2</sub>Cl<sub>2</sub> significantly facilitates the process, as TMTD is insoluble in neat THF. This solution was added to the 1 M solution of PhMgBr-LiCl in THF at 0 °C within several minutes and allowed to reach room temperature within 2 h. Under these conditions, the yield of product **103** reached 94%. Using this protocol, a number of various aryl *N,N*-dimethyldithiocarbamates were prepared in excellent yields (Table 18). The method of the preparation of the Grignard reagent did not influence the reaction output. Equally good results were demonstrated by aryl- and hetarylmagnesium compounds, obtained by the direct Mg insertion in THF in the presence of LiCl, bromine- or iodine-magnesium exchange with *i*PrMgCl-LiCl or, as in the case of indol (Table 18, entry 9) by the direct metalation with *i*PrMgCl-LiCl in THF (RT, 12 h).

**Table 18.** Synthesis of *S*-aryl-*N,N*-dimethyldithiocarbamates from arylmagnesium chlorides in the presence of LiCl.

| Entry | Grignard reagent | Product of type <b>4</b> | Yield, % |
|-------|------------------|--------------------------|----------|
| 1     |                  |                          | 84       |

|   |   |  |                 |
|---|---|--|-----------------|
| 2 |    |  <p><b>105</b></p>   | 91              |
| 3 |    |  <p><b>106</b></p>   | 83 <sup>a</sup> |
| 4 |    |  <p><b>107</b></p>   | 89              |
| 5 |   |  <p><b>108</b></p>  | 95 <sup>b</sup> |
| 6 |  |  <p><b>109</b></p> | 93              |
| 7 |  |  <p><b>110</b></p> | 96              |
| 8 |  |  <p><b>111</b></p> | 92              |
| 9 |  |  <p><b>112</b></p> | 92 <sup>c</sup> |



|    |  |                   |
|----|--|-------------------|
| 10 |  | 78 <sup>b,d</sup> |
| 11 |  | 90%               |

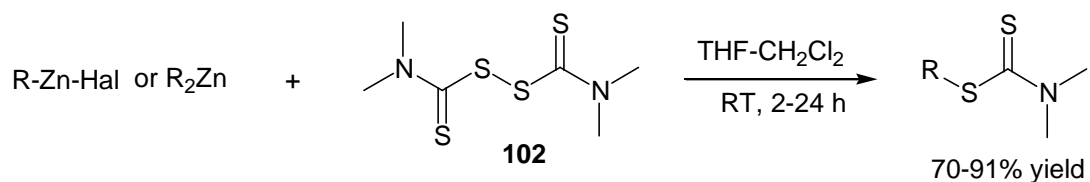
<sup>a</sup>Prepared by the direct insertion of Mg into the aryl bromide; <sup>b</sup>prepared by the exchange reaction from the corresponding iodide; <sup>c</sup> prepared by the metalation of indole with *i*PrMgCl-LiCl; <sup>d</sup> complete retention of the chirality observed during the reaction.

We applied our method to the synthesis of chiral binaphthol **113** (entry 10), starting from the 2-iodo-2'-hydroxybinaphthyl **100** (prepared from (*R*)-BINOL monotriflate *via* the corresponding phenyldimethylsilyl derivative **98**, as described in section 5.3). The product was obtained with complete retention of chirality. Compound **113** was previously used as a ligand for Cu-catalyzed asymmetric addition of alkylzinc and alkylaluminium species to linear conjugated enones.<sup>95</sup>

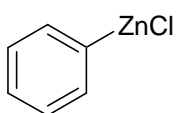
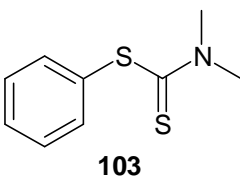
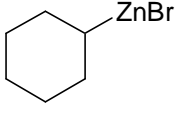
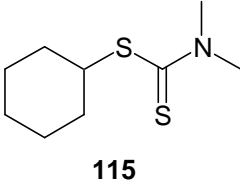
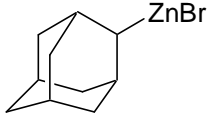
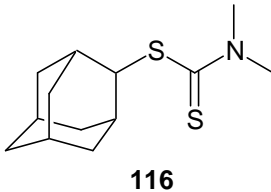
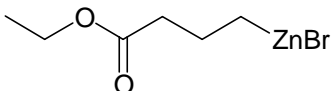
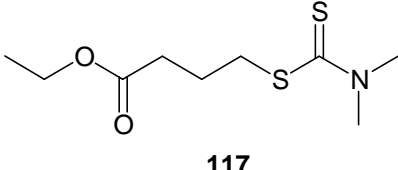
## 6.2 New thiolation reaction of organozinc compounds

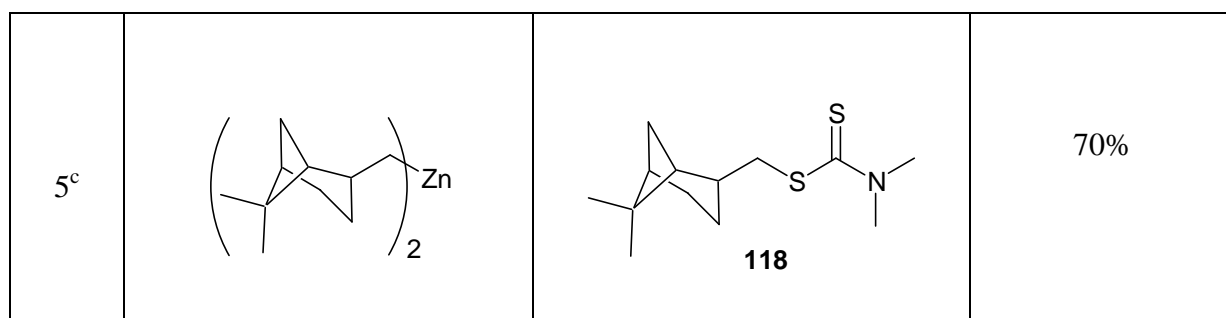
Despite the many advantages of Grignard reagents, they are poorly compatible with some functional groups. From this point of view, organozinc reagents are preferable, because they demonstrate a much broader range of compatibility. So far, no direct methods for the transformation of organozinc reagents into thiols have been described, and a protocol for such synthetic transformation would be highly desirable. Our further studies on the thiolation reaction revealed that organozinc compounds are equally effective in the reaction with tetramethylthiuram disulfide as Grignard reagents. In this case, the addition of LiCl is not necessary. The reaction proceeds at room temperature within several hours, affording *S*-aryl- and *S*-alkyldimethyldithiocarbamates in good to excellent yields. Aryl, primary and secondary alkyl and benzylzinc chlorides and bromides react smoothly, as shown in Table 19.

<sup>95</sup> S. M. W. Bennett, S. M. Brown, A. Cunningham, M. R. Dennis, J. P. Muxworthy, M. A. Oakley, S. Woodward, *Tetrahedron* **2000**, *56*, 2847.



**Table 19.** Synthesis of *S*-phenyl and *S*-alkyl-*N,N*-dimethyldithiocarbamates from organozinc compounds.

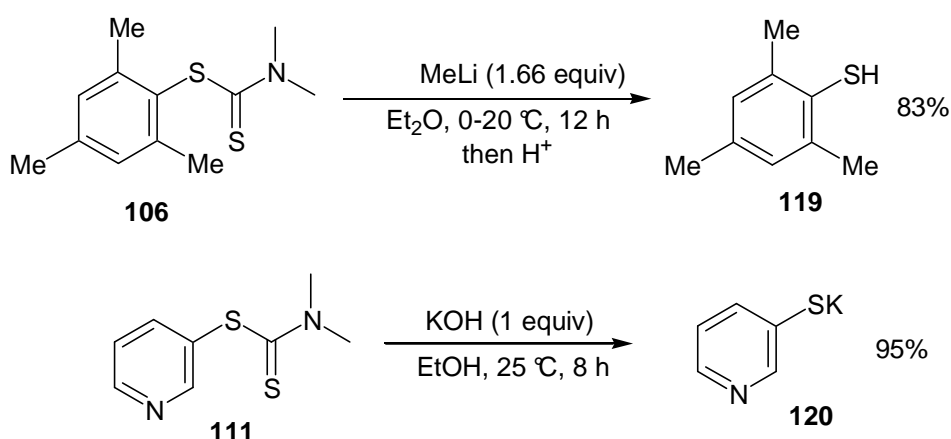
| Entry          | Organozinc derivative   | Product  | Yield |
|----------------|---|--|-------|
| 1 <sup>a</sup> |    |    | 88%   |
| 2 <sup>b</sup> |  |  | 91%   |
| 3 <sup>b</sup> |  |  | 79%   |
| 4 <sup>b</sup> |  |  | 87%   |



<sup>a</sup> obtained by the transmetalation of PhMgCl with ZnCl<sub>2</sub> in THF; <sup>b</sup> obtained by the direct insertion of Zn into the alkyl bromide in the presence of LiCl (see Part 8); <sup>c</sup> obtained from β-pinene *via* the hydroboration and the B-Zn exchange reaction.

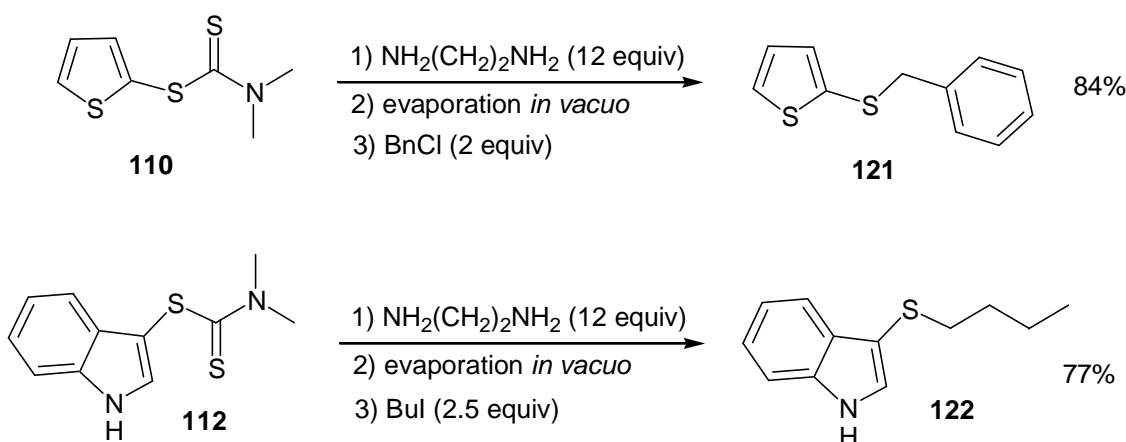
### 6.3 Synthesis of thiols and sulfides from dithiocarbamates

For the compounds, bearing no groups which are sensitive to organolithium reagents, the cleavage of the dithiocarbamate group can be achieved by the treatment with MeLi in ether, followed by aqueous workup. Noteworthy, most of the arylthiols are highly sensitive toward the oxidation by atmospheric oxygen, which requires their handling under inert atmosphere and makes their chromatographic purification difficult. Mesitylthiol (**119**), less prone to such oxidation, was obtained in this way in 83% yield. Another route includes the treatment of a dithiocarbamate with KOH (1 equiv) in absolute EtOH. As an example, product **120** (the potassium salt) was precipitated by the addition of pentane and isolated in 95% yield (Scheme 67).



**Scheme 67.** Base-promoted cleavage of *S*-aryl-*N,N*-dimethyldithiocarbamates.

In order to develop a one-pot method for the transformation of dimethyldithiocarbamates into unsymmetric sulfides, we checked a cleaving agent that can be readily removed after the reaction. Ethylenediamine (EDA) turned out to be an excellent reagent for this purpose. Heating of a dimethyldithiocarbamate with an excess of EDA (12 equiv), followed by its removal *in vacuo* and the treatment with an alkylation reagent provided a direct route for the synthesis of unsymmetric sulfides from dimethyldithiocarbamates (Scheme 68). Following this protocol, 2-thienylbenzylsulfide (**121**) and 3-indolylbutylsulfide (**122**) were obtained in 84% and 77% yields, correspondingly.



**Scheme 68.** One-pot transformation of *S*-aryl-*N,N*-dimethyldithiocarbamates into arylalkylsulfides.

In summary, we developed a highly versatile protocol for the transformation of organozinc and organomagnesium compounds into the corresponding dimethyldithiocarbamates. The resulting dimethyldithiocarbamates can be readily transformed into the corresponding thiols by several methods and by *in situ* alkylation of the formed thiols converted into sulfides. This synthetic transformations are simple, practical and give high yields for different types of organozinc and organomagnesium reagents. A broad variety of functional groups tolerates this new method, especially in the case of organozinc reagents.

## 7. New efficient Ni-catalyzed cross-coupling of arylzinc compounds

The transition metal catalyzed cross-coupling reactions between aryl organometallics and aryl or heteroaryl halides are quite important in modern organic chemistry. A number of the

resulting biaryl products are of great industrial use.<sup>96</sup> Although arylboronic acids and their derivatives are preferred nucleophiles for these reactions due to their availability and excellent stability,<sup>97</sup> in many cases polyfunctional aryl or heteroaryl zinc reagents are an attractive alternative.<sup>98</sup> The required arylzinc compounds can be prepared by the transmetalation from the corresponding magnesium or lithium organometallics,<sup>99</sup> by the direct zinc insertion into aryl halides<sup>100</sup> or by an I/Zn-exchange reaction.<sup>101</sup> Palladium-catalyzed cross-couplings require typically 1-3 mol% of a palladium phosphine complex. Both catalyst components (palladium and the phosphine) are expensive which hinders large-scale applications. In light of this, we have turned our attention to the use of nickel, an intrinsically more active metal. Various Ni-catalyzed Suzuki cross-coupling reactions have been described,<sup>102</sup> whereas only few nickel-catalyzed cross-couplings of organozinc derivatives are known.<sup>103</sup>

While studying the cross-coupling reactions of arylzinc compounds, we noticed that the reaction between 4-methoxyphenylzinc bromide, prepared by the transmetalation of 4-methoxyphenylmagnesium bromide with ZnBr<sub>2</sub> and some reactive electrophiles like ethyl 4-bromobenzoate in a THF-NMP mixture gave traces of product at room temperature even in the absence of any added catalyst (Scheme 69):

---

<sup>96</sup> (a) *Metal-Catalyzed Cross-Coupling Reactions* (A. de Meijere, F. Diederich, Eds.) 2<sup>nd</sup> ed., Wiley-VCH, Weinheim, **2004**. (b) J. Tsuji, *Transition Metal Reagents and Catalysts: Innovations in Organic Synthesis* Wiley, Chichester, **1995**. (c) *Top. Curr. Chem.* **2002**, 219. (d) *Transition Metals for Organic Synthesis* (M. Beller, C. Bolm, Eds.) Wiley-VCH, Weinheim, **1998**.

<sup>97</sup> a) N. Miyaura, A. Suzuki, *Chem. Rev.* **1995**, 95, 2457. (b) G. A. Molander, B. Biolatto, *J. Org. Chem.* **2003**, 68, 4302.

<sup>98</sup> (a) E. Negishi, L. F. Valente, M. Kobayashi, *J. Am. Chem. Soc.* **1980**, 102, 3298. (b) M. Kobayashi, E. Negishi, *J. Org. Chem.* **1980**, 45, 5223. (c) E. Negishi, *Acc. Chem. Res.* **1982**, 15, 340. (d) J. Tamaru, H. Ochiai, T. Nakamura, Z. Yoshida, *Tetrahedron Lett.* **1986**, 27, 955. (e) M. Qian, E. Negishi, *Tetrahedron Lett.* **2005**, 46, 2927. (f) X. Zeng, F. Zeng, E. Negishi, *Org. Lett.* **2004**, 6, 3245. (g) X. Zeng, M. Qian, Q. Hu, E. Negishi, *Angew. Chem., Int. Ed.* **2004**, 43, 2259. (h) M. Qian, Z. Huang, E. Negishi, *Org. Lett.* **2004**, 6, 1531.

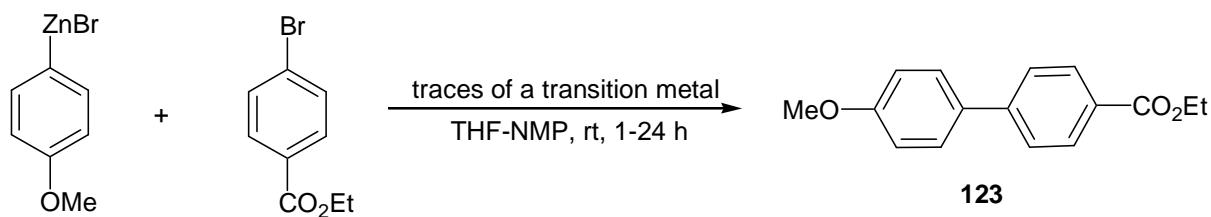
<sup>99</sup> P. Knochel, W. Dohle, N. Gommermann, F. F. Kneisel, F. Kopp, T. Korn, I. Sapountzis, V. A. Vu, *Angew. Chem., Int. Ed.* **2003**, 42, 4302.

<sup>100</sup> (a) R. D. Rieke *Science* **1989**, 246, 1260. (b) T. P. Burns, R. D. Rieke, *J. Org. Chem.* **1987**, 52, 3674. (c) J. Lee, R. Velarde-Ortiz, A. Guijarro, J. R. Wurst, R. D. Rieke, *J. Org. Chem.* **2000**, 65, 5428. (d) A. Krasovskiy, V. Malakhov, A. Gavryushin, P. Knochel, *Angew. Chem., Int. Ed.* **2006**, 45, 6040, see also Chapter 8.

<sup>101</sup> (a) F. F. Kneisel, M. Dochnahl, P. Knochel, *Angew. Chem., Int. Ed.* **2004**, 43, 1017. (b) L.-Z. Gong, P. Knochel, *Synlett* **2005**, 267.

<sup>102</sup> (a) V. Percec, J.-Y. Bac, D. H. Hill, *J. Org. Chem.* **1995**, 60, 1060. (b) S. Saito, S. Oh-tani, N. Miyaura, *J. Org. Chem.* **1997**, 62, 8024. (c) A. F. Indolese, *Tetrahedron Lett.* **1997**, 38, 3513. (d) J.-C. Galland, H. Savignac, J.-P. Genet, *Tetrahedron Lett.* **1999**, 40, 2323. (e) K. Inada, N. Miyara, *Tetrahedron* **2000**, 56, 8657. (f) V. Percec, G. M. Golding, J. Smidrkal, O. Weihold, *J. Org. Chem.* **2004**, 69, 3447.

<sup>103</sup> (a) B. H. Lipshutz, P. A. Blomgren, *J. Am. Chem. Soc.* **1999**, 121, 5819. (b) V. P. W. Böhm, T. Weskamp, C. W. K. Gstöttmayr, W. A. Herrmann, *Angew. Chem., Int. Ed.* **2000**, 39, 1602. (c) C. A. Quesnelle, O. B. FAMILONI, V. Snieckus, *Synlett* **1994**, 349. (d) C. E. Tucker, J. G. de Vries, *Topics in Catalysis* **2002**, 19, 111.



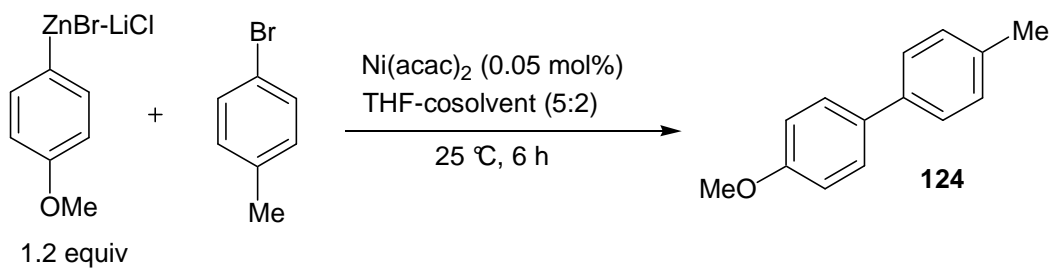
**Scheme 69.** Cross-coupling reaction of an arylzinc halide and an aryl bromide in the presence of the traces of transition metals.

This could be ascribed to the presence of Pd or Ni traces in commercial  $\text{ZnBr}_2$ . Indeed, no product was formed, when extra pure  $\text{ZnBr}_2$  (Aldrich, 99.999% purity) was used for the reaction. Further experiments excluded the influence of Pd traces, whereas Ni salts were found to promote the coupling reaction under these conditions even at the level of  $10^{-4}$  mol%, and 0.01 mol% was sufficient to achieve full conversion for some substrates.<sup>104</sup> However, a substantial amount of the product of the arylzinc homocoupling was observed. Other transition metals like Fe or Mn were not active as catalysts under the same conditions. This process could have good perspective for industrial use. Therefore, we started optimization studies of this cross-coupling reaction. Two issues had to be addressed during the reaction optimization: the low reactivity of the electron-rich aryl halides and the observed extensive homocoupling of the organozinc reagents.

### 7.1. Optimization of the reaction conditions and the catalytic system.

For the optimization of the solvent mixture, we chose the test reaction between 4-methoxyphenylzinc bromide (made by the transmetalation of 4-methoxyphenylmagnesium bromide-lithium chloride with 1 equiv. of  $\text{ZnBr}_2$ ) and 4-bromotoluene (0.05 mol%  $\text{Ni}(\text{acac})_2$ , 1.2 equiv. of the zinc reagent, THF-cosolvent 5:2, room temperature, 6 h). The conversion of 4-bromotoluene was determined by GC-analysis with *n*-octadecane as internal standard. The effect of different cosolvents on the conversion is summarized in Table 20.

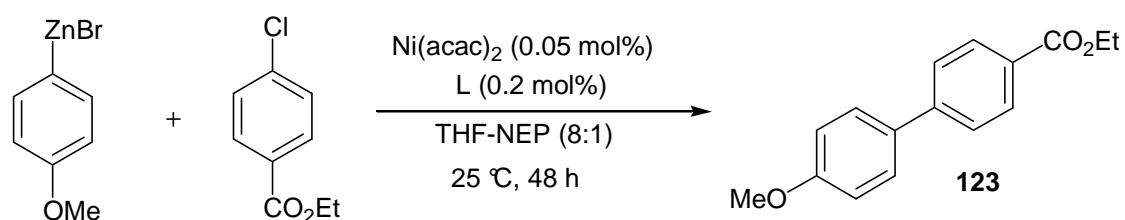
<sup>104</sup> For Ni-catalyzed cross-coupling reactions, using other organometallics, see: (a) J. W. Han, N. Tokunaga, T. Hayashi, *Synlett* **2002**, 871. (b) E. Shirakawa, K. Yamasaki, T. Hiyama, *Synthesis* **1998**, 1544. (c) J. Terao, H. Watanabe, A. Ikumi, H. Kuniyasu, N. Kambe, *J. Am. Chem. Soc.* **2002**, *124*, 4222. (d) J. Terao, S. Nii, F. A. Chowdhury, A. Nakamura, N. Kambe, *Adv. Synth. Cat.* **2004**, *346*, 905. (e) V. Percec, J.-Y. Bae, D. H. Hill, *J. Org. Chem.* **1995**, *60*, 6895.



**Table 20.** Influence of co-solvents on the cross-coupling reaction of 4-methoxyphenylzinc bromide and 4-bromotoluene in THF.

| Co-solvent                                | Conversion |  | Co-solvent                               | Conversion |
|---|------------|--|--|------------|
| THF                                       | <5%        |  | DMF                                      | <5%        |
| <i>N</i> -methylpyrrolidinone (NMP)       | 44%        |  | DMSO                                     | <5%        |
| <i>N,N</i> -dimethylacetamide (DMAC)      | <5%        |  | Et <sub>3</sub> N                        | 11%        |
| <i>N,N'</i> -dimethylpropyleneurea (DMPU) | <5%        |  | <i>N</i> -(2-methoxyethyl)-pyrrolidinone | 68%        |
| Tetramethylurea (TMU)                     | <5%        |  | <i>N</i> -ethylpyrrolidinone (NEP)       | 88%        |

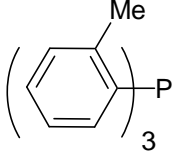
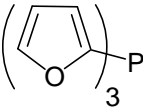
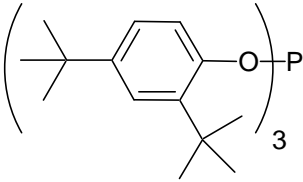
None of the tested solvents afforded the coupling product except *N*-alkylpyrrolidinones, among which *N*-ethylpyrrolidinone (NEP) was the most efficient. The optimal ratio THF-NEP after further optimization was found as 8:1. With a higher concentration of NEP in the reaction mixture the conversion decreased. In most of the cases, the complete conversion was observed within 1 h and a significant amount of 4,4'-dimethoxybiphenyl as a by-product was formed. Trying to inhibit this side reaction, we have investigated the influence of different ligands on this cross-coupling reaction, using 4-methoxyphenylzinc bromide and ethyl 4-chlorobenzoate as reactants (0.05 mol% Ni(acac)<sub>2</sub>, 0.2 mol% of ligand, 1.3 equiv of 4-MeOC<sub>6</sub>H<sub>4</sub>ZnBr, THF-NEP (8:1), 25 °C, 48 h). The yield of the coupling product **123** was determined by GC-analysis, using *n*-octadecane as an internal standard and the comparison with an authentic sample of the product. The results of the ligand optimizations are given in Table 21.

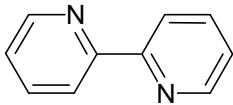
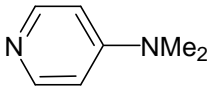


**Table 21.** Ligand optimization for the Ni-catalyzed Negishi cross-coupling reaction.

| Entry | Ligand | Yield (GC) |
|-------|--------|------------|
| 1     |        | 61%        |



|   |   |     |
|---|---|-----|
| 2 | $\text{Ph}_2\text{P}-\text{CH}_2-\text{CH}_2-\text{PPh}_2$                          | 51% |
| 3 |    | 53% |
| 4 |    | <5% |
| 5 | $\text{Ph}_3\text{P}$   | 47% |
| 6 | $\text{Cy}_3\text{P}$   | 14% |
| 7 | $(\text{Me}_2\text{N})_3\text{P}$   | 62% |
| 8 |  | 9%  |

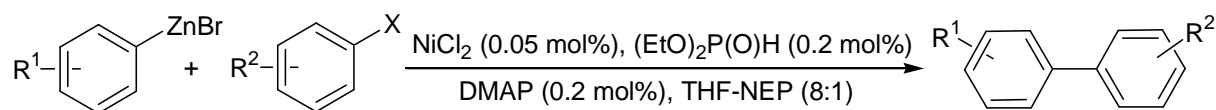
|    |  |     |
|----|--|-----|
| 9  |   | 50% |
| 10 | (EtO) <sub>2</sub> P(O)H   | 71% |
| 11 |  | 18% |
| 12 | (EtO) <sub>2</sub> P(O)H-DMAP  | 81% |
| 13 | no ligand  | <5% |

Without a ligand, this reaction is very sluggish and gives only traces of the desired product (entry 13). Surprisingly, diethyl phosphite (entry 12) appeared to be the best ligand for this reaction, affording 71% yield of compound **123** along with only a small amount of the homocoupled side product. Among other ligands, DPPP (entry 1) and *tris*-(dimethylamino)phosphine (entry 7) showed a good performance. Triphenylphosphine (entry 5) was less active and, interestingly, did not influence the product yield even in a large excess

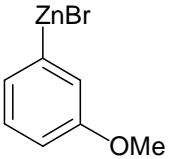
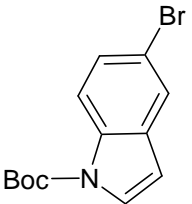
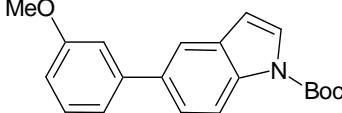
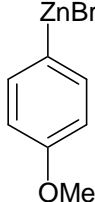
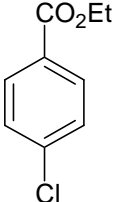
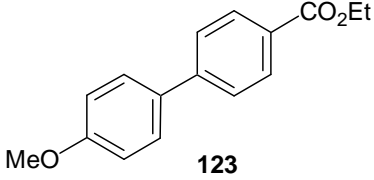
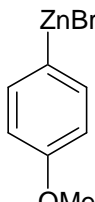
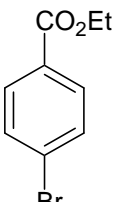
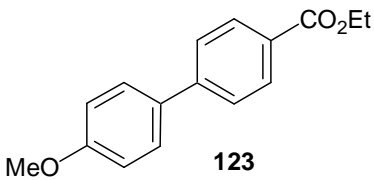
(up to 1 mol%, ratio 20:1 to Ni). Noteworthy, the exact order of the reagent mixing significantly influenced the reaction rate. The optimal method was the addition of the arylmagnesium reagent to the solution of ZnBr<sub>2</sub>, premixed with NEP. If the Grignard reagent solution is first mixed with ZnBr<sub>2</sub>, a precipitate quickly forms, and the following coupling reaction proceeds much slower. This observation can be explained by the fast formation of polymeric zinc-halide associates in the arylzinc halide solution, which possess a lower reactivity. The precomplexation with NEP seems to suppress this undesirable process, and then significantly increases the reactivity. Some aza-heterocycles were also found to be active as ligands in this reaction. Thus, 2,2'-bipyridine (entry 9) afforded 50% yield of the target compound, although along with a large amount of the homocoupling product. Furthermore, we used the same reaction for screening several ligand mixtures. Diethyl phosphite - triphenyl phosphine and especially diethyl phosphite - DMAP (1:1) were found superior as additives to Ni (entry 12) and the last mixture yielded 81% of the coupling product. The optimal ratio Ni:diethyl phosphite turned out to be 1:4. Other phosphites like (*i*PrO)<sub>3</sub>P, (MeO)<sub>2</sub>P(O)H, (*i*PrO)<sub>2</sub>P(O)H, (BuO)<sub>3</sub>P or (PhO)<sub>3</sub>P were by far less active as ligands.


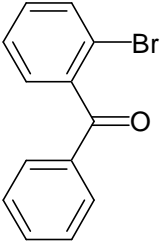
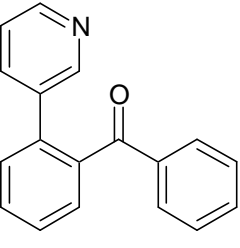
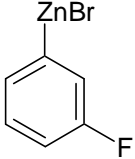
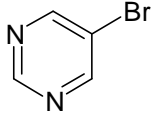
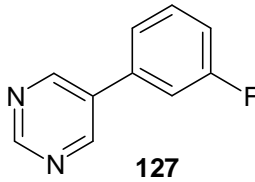
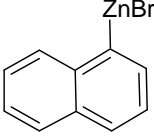
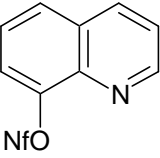
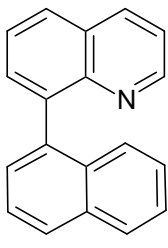
### 7.2 Ni-catalyzed cross-coupling of arylzinc compounds with aryl- and alkenyl halides and triflates

Several results of the aryl-aryl cross-coupling reaction with this optimized catalytic system (0.05 mol% of NiCl<sub>2</sub>, 0.2 mol% (EtO)<sub>2</sub>P(O)H and 0.2 mol% of DMAP, THF-NEP (8:1)) are shown in Table 22.



**Table 22.** An efficient Ni-catalyzed cross-coupling reaction of arylzinc halides with aryl halides and sulfonates.

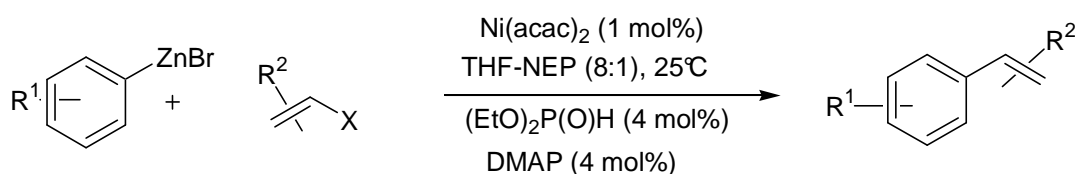
| Entry | Ar <sup>1</sup> -ZnX  | Ar <sup>2</sup> -X  | Product  | T °C, h   | Yield |
|-------|---|---|--|-----------|-------|
| 1     |    |    | <br><b>125</b>   | 50 °C, 6  | 47%   |
| 2     |  |  | <br><b>123</b> | 25 °C, 48 | 81%   |
| 3     |  |  | <br><b>123</b> | 25 °C, 1  | 87%   |

|   |   |   |  |           |     |
|---|---|---|--|-----------|-----|
| 4 |    |                  | <br><b>126</b>   | 50 °C, 18 | 76% |
| 5 |    |                  | <br><b>127</b>   | 25 °C, 1  | 82% |
| 6 |  | <br><b>128</b> | <br><b>129</b> | 25 °C, 24 | 81% |

As shown in Table 22, a broad range of substrates can be involved into this reaction. Electron-rich, electron-poor and heterocyclic zinc compounds can be coupled with aryl and heteroaryl bromides, chlorides and nonaflates. Electron-rich arylzinc halides react with aryl bromides to give the desired products within several hours at room temperature in good to excellent yields (entries 2, 3, 6). With heteroaryl electrophiles, sometimes prolonged reaction time or elevated temperature (entries 1 and 6) is required. Aryl chlorides also react, but in comparison to the corresponding bromides the reaction times are longer and the yields lower (entry 2). The electron-poor 3-pyridylzinc bromide, which is often a problematic substrate for cross-coupling reactions, affords a good yield of the product (entry 4). We also attempted to employ some aryl tosylates, mesylates and phosphates in this reaction, but could not achieve acceptable yields of products under our conditions.

The required organozinc reagents were obtained mostly from the corresponding bromides or iodides *via* halogen-magnesium exchange with *i*-PrMgCl-LiCl,<sup>77a</sup> or by the direct insertion of Mg, followed by the transmetalation with 1 equiv. of ZnBr<sub>2</sub>.

Beside the aryl-aryl cross-coupling, we have found that arylzinc halides can also react with alkenyl halides and triflates in the presence of our catalytic system, although it required a higher amount of the catalyst (1 mol% Ni(acac)<sub>2</sub>, 4 mol% (EtO)<sub>2</sub>P(O)H, 4 mol% DMAP, 1.3 equiv. of ArZnBr, THF-NEP (8:1)) (Scheme 70).

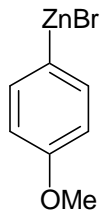
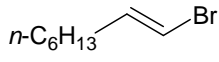
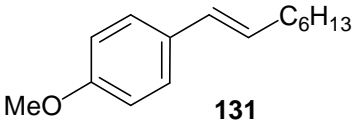
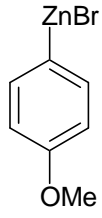
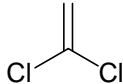
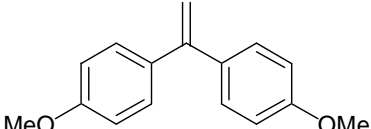
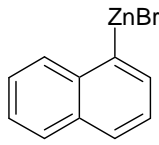
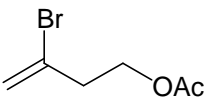
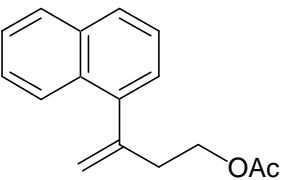
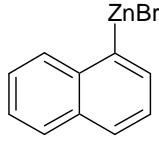
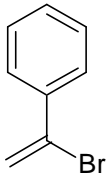
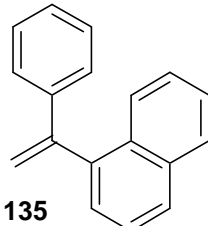


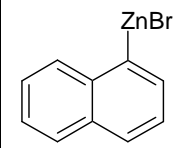
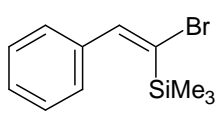
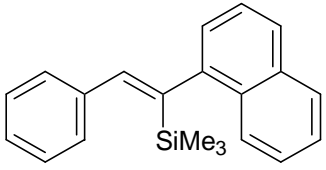
**Scheme 70.** Ni-catalyzed cross-coupling reaction of arylzinc halides with vinyl electrophiles.

The reactions were complete at room temperature within a period between 15 minutes and some hours and gave the desired products **130-136** in 71-88% yield. The results of the aryl-alkenyl cross-coupling reaction in the presence of a Ni catalyst are summarized in Table 23.

**Table 23.** Ni-catalyzed cross-coupling reaction of arylzinc halides with vinyl electrophiles.

| Entry | Ar-ZnBr | Electrophile | Product | Conditions    | Yield |
|-------|---------|--------------|---------|---------------|-------|
| 1     |         |              |         | 25 °C, 15 min | 85%   |

|                |   |  |  |               |     |
|----------------|---|--|--|---------------|-----|
| 2              |    | <br><b>131a</b>   | <br><b>131</b>   | 25 °C, 30 min | 79% |
| 3 <sup>a</sup> |    | <br><b>132a</b>   | <br><b>132</b>   | 25 °C, 6 h    | 88% |
| 4              |  | <br><b>133</b>  | <br><b>134</b> | 25 °C, 12 h   | 81% |
| 5              |  | <br><b>135a</b> | <br><b>135</b> | 25 °C, 6 h    | 77% |

|   |   |  |  |             |     |
|---|---|--|--|-------------|-----|
| 6 |  | <br><b>136a</b> | <br><b>136</b> | 25 °C, 24 h | 67% |
|---|---|--|--|-------------|-----|

In summary, we have developed a very efficient catalytic system, based on NiCl<sub>2</sub>, (EtO)<sub>2</sub>P(O)H and DMAP for the cross-coupling reaction between arylzinc halides and aryl and alkenyl bromides, triflates, nonaflates and activated chlorides. An extremely small amount of a transition-metal catalyst (0.05 mol% Ni) is usually required and a broad range of highly functionalized substrates react at room temperature, giving the cross-coupling products in good to excellent yields.

## 8. Direct preparation of organozinc compounds from alkyl bromides in the presence of LiCl.

Organozinc compounds are important intermediates in organic chemistry due to their compatibility with many functional groups.<sup>71</sup> The direct insertion of zinc into organic halides is the most attractive and simple method for the preparation of functionalized organozinc halides. Whereas several polar solvents such as DMAC, HMPA, DMF, DMSO or TMU can be used,<sup>105</sup> the most common and convenient one for industrial application is THF.<sup>106</sup> The preparation of unactivated alkylzinc bromides in THF from alkyl bromides can be achieved only by using highly activated zinc powder (Rieke Zn)<sup>107</sup> or requires the presence of coordinating groups as well as high temperatures.<sup>106</sup> The use of Rieke Zn also allows the preparation of arylzinc reagents starting from aryl iodides.<sup>108</sup> The stability of Rieke Zn is not

<sup>105</sup> a) K. Tagaki, N. Hayama, S. Inokawa, *Bull. Chem. Soc. Jpn.* **1980**, 53, 3691; b) K. Tagaki, *Chem. Lett.* **1993**, 469; c) K. Tagaki, Y. Shimoishi, K. Sasaki, *Chem. Lett.* **1994**, 2055; d) T. N. Majid, P. Knochel, *Tetrahedron Lett.* **1990**, 31, 4413.

<sup>106</sup> R. Ikegami, A. Koresawa, T. Shibata, K. Takagi, *J. Org. Chem.* **2003**, 68, 2195.

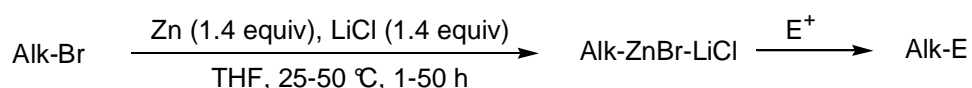
<sup>107</sup> a) R. D. Rieke, P. T. Li, T. P. Burns, S. T. Uhm, *J. Org. Chem.* **1981**, 46, 4323. b) R. T. Arnold, S. T. Kulenovic, *Synth. Commun.* **1977**, 7, 223.

<sup>108</sup> a) L. Zhu, R. M. Wehmeyer, R. D. Rieke, *J. Org. Chem.* **1991**, 56, 1445; b) R. D. Rieke, M. V. Hanson, J. D. Brown, Q. J. Niu, *J. Org. Chem.* **1996**, 61, 2726; c) P. Knochel, M. C. P. Yeh, S. C. Berk, J. Talbert, *J. Org. Chem.* **1988**, 53, 2390.



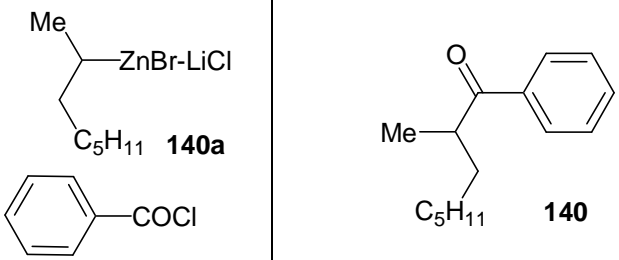
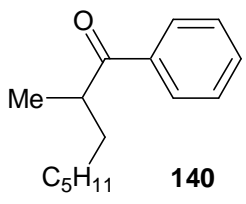
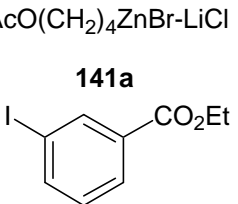
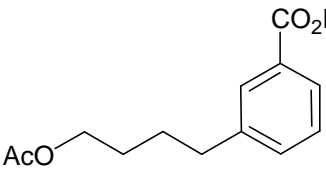
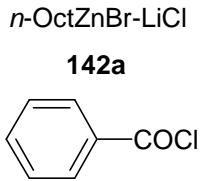
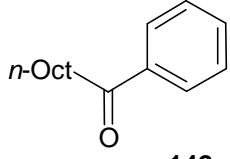
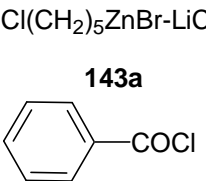
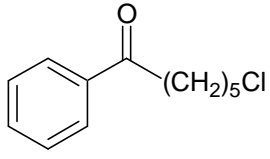
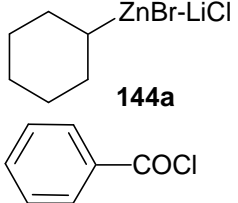
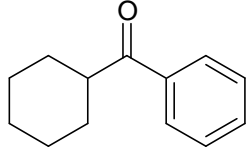
sufficiently good and its price is quite high. Therefore, the development of a practical zinc insertion procedure using a commercial zinc powder would be highly desirable.

Recently, in our laboratory it was found that the Br/Mg-exchange reaction can be dramatically accelerated by the addition of LiCl.<sup>77a</sup> Based on this result, we have examined the effect of LiCl on the zinc insertion reaction in the case of alkyl bromides, using ethyl 4-bromobutyrate as a model compound. Practically no insertion reaction of zinc powder, activated by addition of a little amount Me<sub>3</sub>SiCl, took place in neat THF in the absence of LiCl. However, we found that the addition of LiCl (1-1.3 equiv.) into the reaction mixture leads to a relatively fast reaction. Primary and secondary alkyl bromides gave high yields of the corresponding organozinc derivatives after 1-50 h at temperatures between 25 and 50 °C. The concentrations of the resulted Zn reagents were determined by the titration with a standard I<sub>2</sub> solution in THF. Then, the reagent solution was treated with an electrophile, if needed, in the presence of a catalyst. Various electrophiles like acyl chlorides, allyl halides or thiuram disulfides react smoothly with the resulting alkylzinc bromides, giving the products in excellent yields. The yields of the alkylzinc reagents and the products (based on the exact amount of the alkylzinc reagent used) are given in Table 24.



**Table 24.** Insertion of zinc into alkyl bromides in the presence of LiCl and the reactions with electrophiles.

| Entry | Alk-ZnBr·LiCl<br>and electrophile   | Product        | Conditions<br>of insertion<br>reaction | Yield of<br>Zn reagent<br>/ product,<br>% |
|-------|---|----------------|--|---|
| 1     | $(\text{CH}_2)_3\text{ZnBr}\cdot\text{LiCl}$<br><br><b>137a</b><br>                 | <br><b>137</b> | 50 °C, 3 h                             | 85(71)                                    |
| 2     | $\text{CN}(\text{CH}_2)_4\text{ZnBr}\cdot\text{LiCl}$<br><b>138a</b><br>            | <br><b>138</b> | 50 °C, 8 h                             | 87(80)                                    |
| 3     | $\text{EtO}_2\text{C}(\text{CH}_2)_3\text{ZnBr}\cdot\text{LiCl}$<br><b>139a</b><br> | <br><b>139</b> | 50 °C, 1 h                             | 95(93)                                    |

|   |  |  |             |        |
|---|--|--|-------------|--------|
| 4 |  <p>Me<br/>ZnBr-LiCl<br/>C<sub>5</sub>H<sub>11</sub> <b>140a</b><br/>COCl</p>           |  <p><b>140</b></p>                                      | 50 °C, 1 h  | 88(77) |
| 5 |  <p>AcO(CH<sub>2</sub>)<sub>4</sub>ZnBr-LiCl<br/><b>141a</b><br/>I CO<sub>2</sub>Et</p> |  <p>AcO CO<sub>2</sub>Et<br/><b>141</b></p>             | 25 °C, 6 h  | 96(83) |
| 6 |  <p><i>n</i>-OctZnBr-LiCl<br/><b>142a</b><br/>COCl</p>                                |  <p><i>n</i>-Oct<br/><b>142</b></p>                   | 50 °C, 24 h | 92(89) |
| 7 |  <p>Cl(CH<sub>2</sub>)<sub>5</sub>ZnBr-LiCl<br/><b>143a</b><br/>COCl</p>              |  <p>(CH<sub>2</sub>)<sub>5</sub>Cl<br/><b>143</b></p> | 50 °C, 12 h | 93(89) |
| 8 |  <p>ZnBr-LiCl<br/><b>144a</b><br/>COCl</p>  |  <p><b>144</b></p>                                    | 50 °C, 6 h  | 96(91) |

|    |  |                   |             |        |
|----|--|-------------------|-------------|--------|
| 9  | <p> <chem>C1CCC1CC[Zn]Br.[Li]Cl</chem><br/> <b>145a</b><br/> <chem>CCOC(=C)CCBr</chem> </p>                            | <p><b>145</b></p> | 50 °C, 50 h | 86(82) |
| 10 | <p> <chem>C12CC3CC4CC5C1CC2C3(C4)C5[Zn]Br.[Li]Cl</chem><br/> <b>116a</b><br/> <chem>CN(C)C(=S)SSC(=S)N(C)C</chem> </p> | <p><b>116</b></p> | 50 °C, 24 h | 83(79) |

The use of Zn powder in the presence of LiCl allows an expedient preparation of functionalized alkylzinc reagents starting from primary alkyl bromides. Thus, unactivated *n*-OctBr and 1-bromo-5-chloropentane react cleanly with Zn in the presence of LiCl affording the corresponding alkylzinc reagents in >90% yields. The reaction with PhCOCl in the presence of 20 mol% of CuCN-LiCl provides ketones **140**, **142** and **143** in high yields (Table 24, entries 4, 6, 8). The formation of cyclobutylmethylzinc bromide **145a** proceeds without ring-opening side reactions (entry 9), leading after allylation to unsaturated ester **145**. Pd-catalyzed coupling of the formed alkylzinc reagents with ethyl 3-iodobenzoate lead to bifunctionalized arenes **139** and **141** in good yields (entries 3 and 5). The insertion reaction is also efficient in the case of secondary alkyl bromides. Adamantylzinc bromide (**117a**) was obtained by the direct insertion of Zn in the presence of LiCl in 83 % yield, giving after treatment with tetramethylthiuramdisulfide dithiocarbamate **117** in 79% yield (entry 10).

The nature of the activation of zinc dust with LiCl is speculative. However, it can be envisioned that the role of LiCl may be to remove rapidly the formed organozinc reagent from the metal surface by leading to highly soluble RZnX·LiCl complexes and allowing thus a rapid reaction of a further molecule of R-X avoiding the competitive deactivation of an active metal site. Beside, the formation of the zinc complexes with Cl<sup>-</sup> instead of usual alkylzinc species should increase the free energy of the insertion reaction, thus facilitating the single

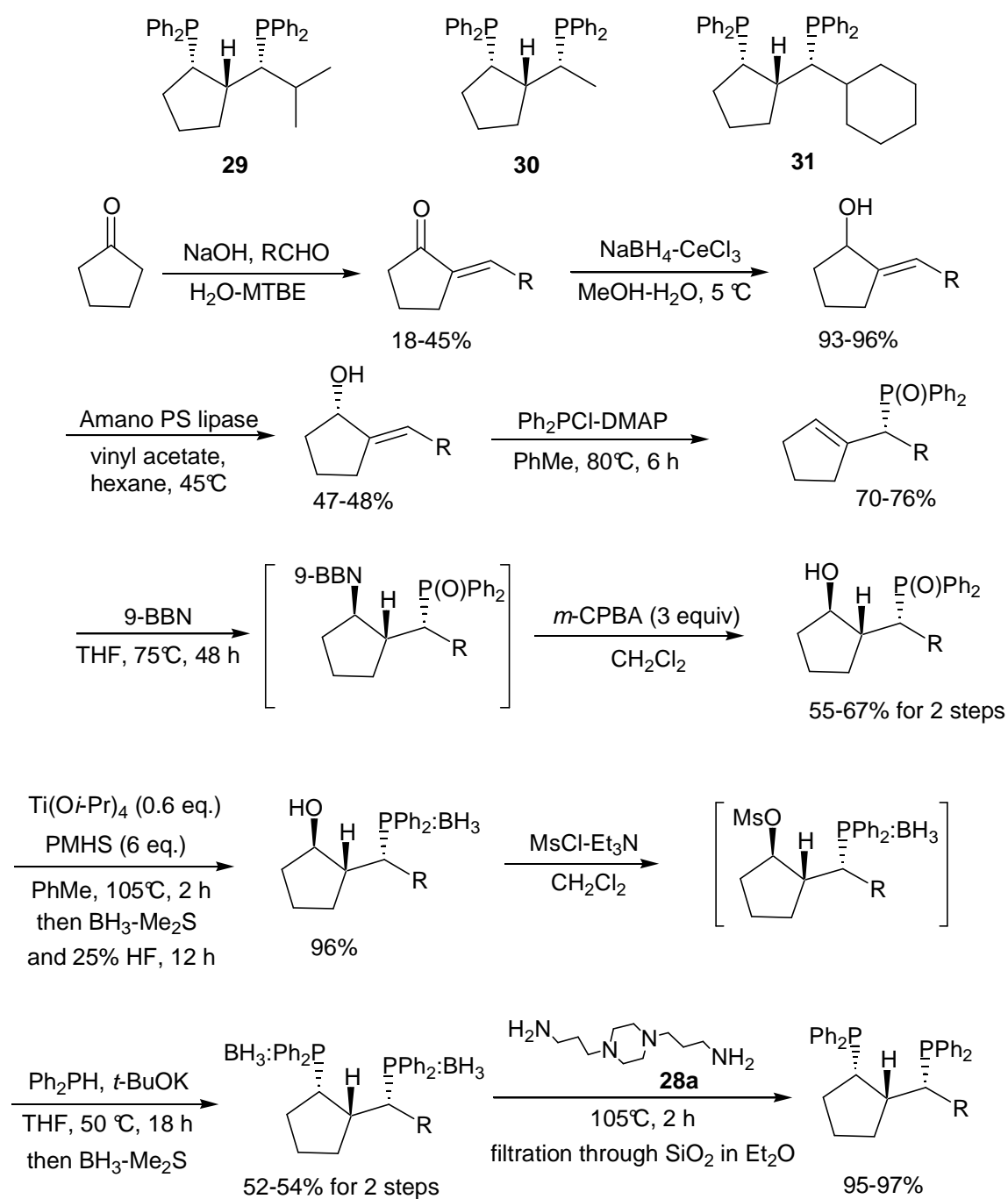
electron transfer from the zinc surface onto the halide molecule. Indeed, this effect is general for zinc insertion reaction, as it was also found that LiCl greatly promotes formation of arylzinc iodides from aryl iodides and Zn dust.

In conclusion, we have shown that the use of Zn powder in the presence of LiCl in THF allows a simple, highly efficient preparation of a broad range of functionalized alkylzinc reagents. Syntheses of alkylzinc reagents were performed from cheap and readily available alkyl bromides. All reactions proceed within a convenient temperatures range (25°C – 50°C), and can be readily extended to the large scale preparation.

In summary, we discovered a novel, very simple and practical method for the preparation of alkylzinc reagents from the corresponding primary and secondary alkyl bromides. This method allows using relatively cheap alkyl bromides and the conventional solvent THF for the preparation of highly synthetically valuable alkylzinc bromides from a very broad range of substrates. This method can be expected to find an industrial application for the scaled preparation of alkylzinc reagents.

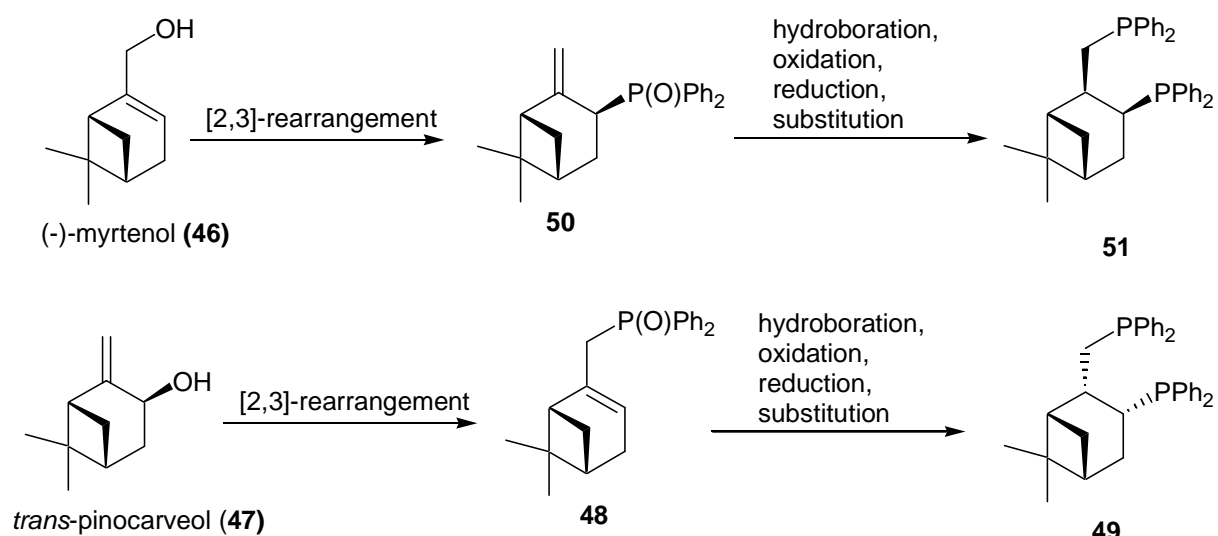
## 9. Summary and outlook

In the first part of this work we described the preparation and the testing results of several new chiral diphosphines, suitable as ligands for transition metal-catalyzed enantioselective reactions. The diphosphines were prepared applying the originally designed synthetic sequence, based on the sigmatropic [2,3]-allylphosphinite-allylphosphine oxide rearrangement reaction as a key step. Initially, the sequence started from 2-alkylidenecyclopentanones, prepared by the condensation of several aliphatic aldehydes with cyclopentanone. The resulting enones were reduced to the corresponding allylic alcohols, which were subjected to enzymatic kinetic resolution leading to the single enantiomers of the alcohols. The stereoselective rearrangement of the corresponding diphenylphosphinites gave enantiopure allyldiphenylphosphine oxides. They were subjected to hydroboration-oxidation sequence to obtain the corresponding  $\gamma$ -hydroxy-diphenylphosphine oxides. The diphenylphosphinoyl group was reduced to the corresponding diphenylphosphine and protected as a borane complex, the hydroxyl moiety was converted to the mesylate and substituted by the diphenylphosphinide anion, followed by a protection with borane. Finally, the *bis*-phosphine-boranes were deprotected according to the newly designed protocol, using the highly nucleophilic polyamine *N,N'*-*bis*-(3-aminopropyl)-piperazine to afford the corresponding enantiopure diphosphine ligands. According to this sequence, three different diphosphine ligands were synthesized (R = Me, *i*-Pr, cyclohexyl):



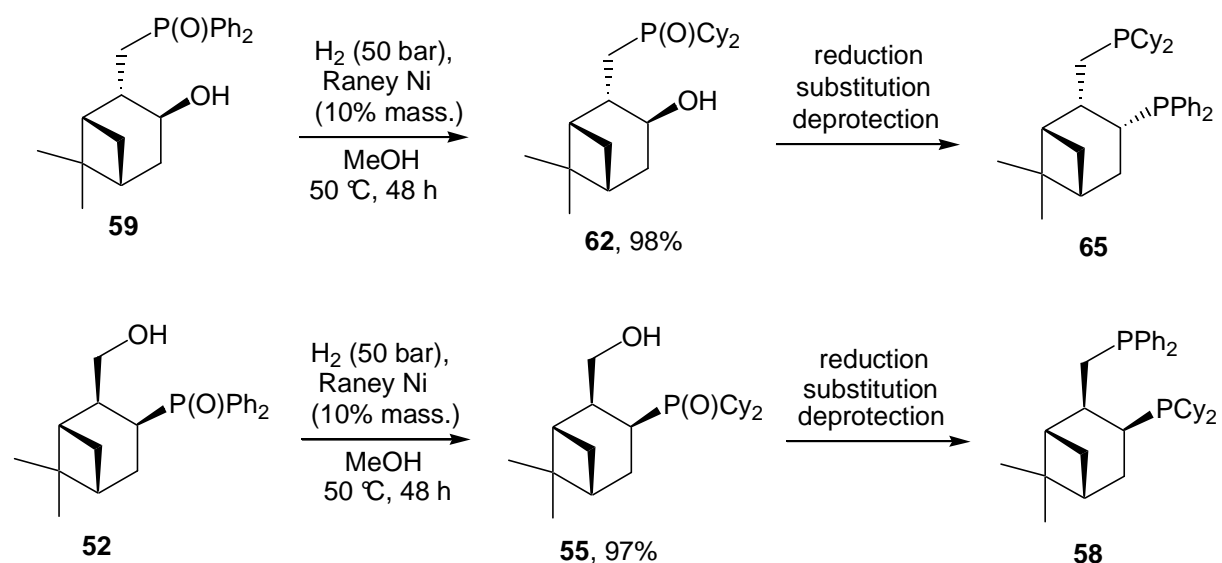
**Scheme 71.** Synthesis of chiral diphosphines with a cyclopentane scaffold.

The allylphosphinite-allylphosphine oxide rearrangement reaction was successfully performed using allylic alcohols from natural chiral pool: (-)-myrtenol and *trans*-pinocarveol. The previously developed synthetic methods were used to transform the resulting allylphosphine oxides into *bis*-phosphine ligands (**49** and **51**):



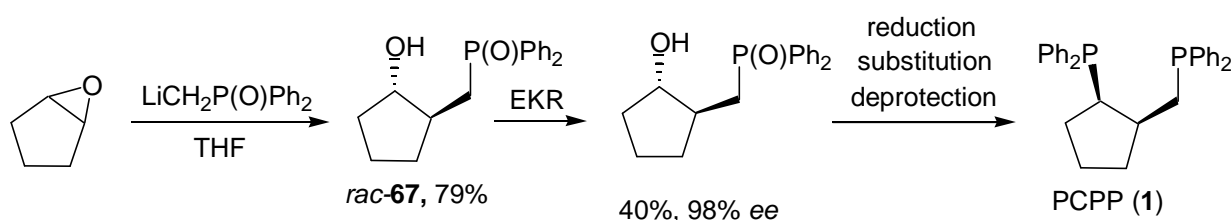
**Scheme 72.** Synthesis of diphosphine ligands from natural terpenic allylic alcohols.

$\gamma$ -Hydroxydiphenylphosphine oxides could be smoothly reduced on Raney Ni into the corresponding dicyclohexylphosphine derivatives. They were transformed into “mixed” dicyclohexyl-diphenyl phosphine ligands (**58** and **65**), using the previously developed synthetic transformations:



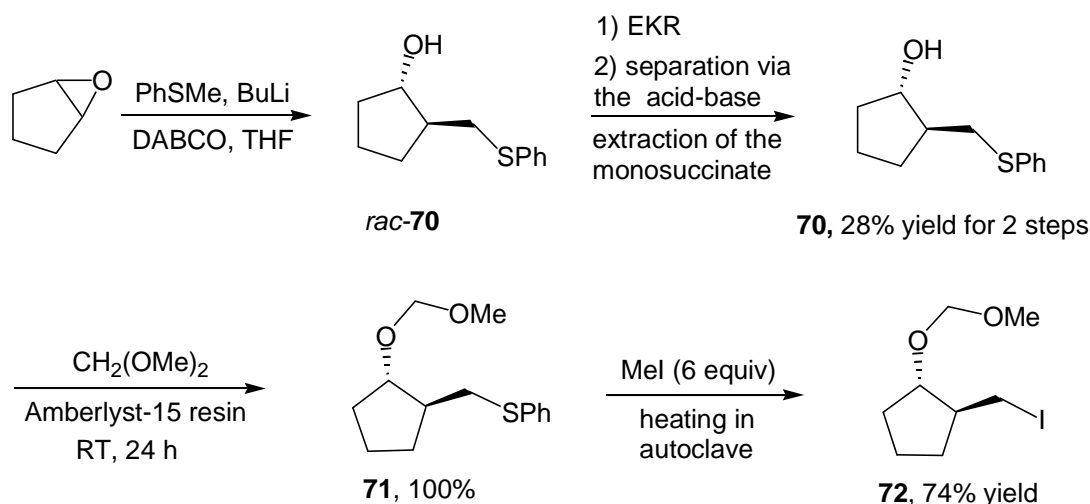
**Scheme 73.** Synthesis of „mixed“ diphosphine ligands.

Enzymatic kinetic resolution was successfully applied to other substituted cyclopentanol. Using this method, *trans*-2-(diphenylphosphinoymethyl)-cyclopentanol was obtained in enantiopure form and transformed into chiral diphosphine ligand PCPP (**1**), using similar to the previously developed synthetic procedures:



**Scheme 74.** Chemoenzymatic synthesis of PCPP.

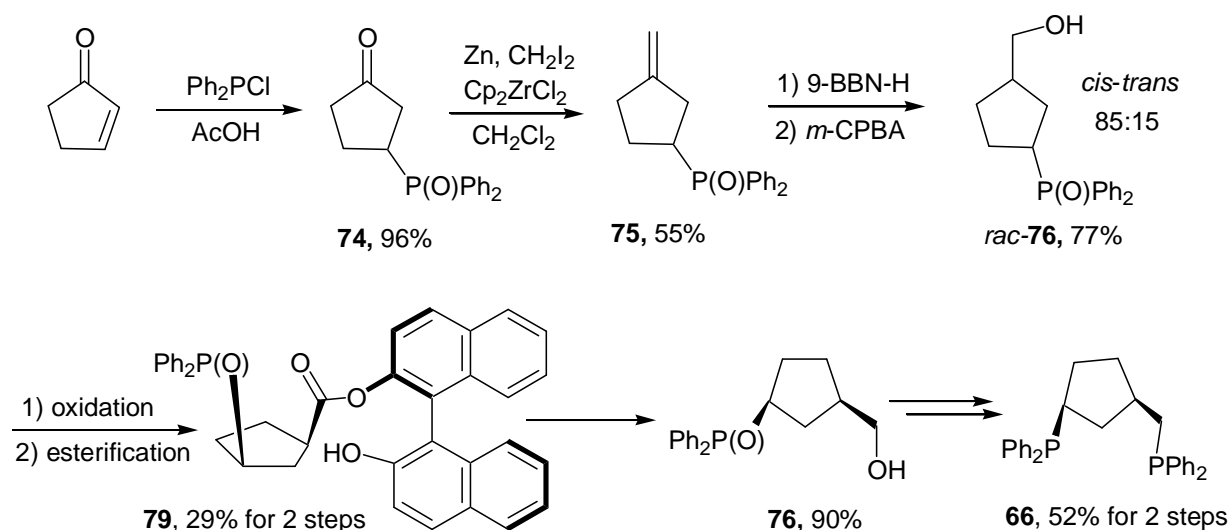
In order to develop a modular approach to the chiral phosphorus ligands of this type, a synthetic method for a common chiral precursor **72** was elaborated. The method is based on the highly efficient enzymatic kinetic resolution of *trans*-2-(phenylthiomethyl)cyclopentanol followed by the conversion of the thiophenyl moiety into the iodide. It allowed to obtain 35 g of the chiral precursor **72** with >99.5% *ee* in a single batch, using only one simple chromatographic separation during the synthesis. From the iodide **72**, the ligand **1** was obtained in enantiopure form in 3 simple steps. Besides, the use of allylic iodide **72** allows preparing the whole family of the PCPP analogs with various substituents on the phosphorus atoms, using quite simple synthetic protocol.



**Scheme 75.** Synthesis of chiral intermediate **72**.

Some of the methods, developed during the investigation of the 1,3-diphosphines, were applied in the synthesis of a new 1,4-diphosphine ligand **66**, starting from cyclopentenone. Since in this case the enzymatic methods were not fruitful, the resolution was performed by the preparation of a diastereomeric ester with (*R*)-BINOL (**79**). Following this sequence, the ligand **66** was obtained for the first time in enantiomerically pure form.

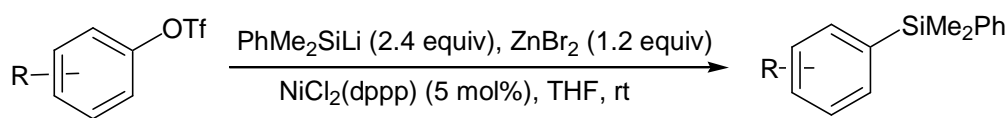




**Scheme 76.** Synthesis of chiral diphosphine ligand **66**.

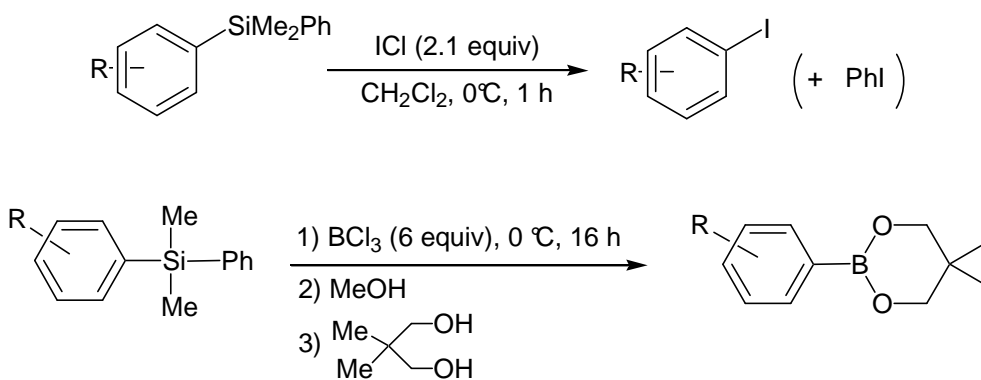
Finally, the new ligands were tested in several Rh-, Ru- and Pd-catalyzed enantioselective reactions. Enantioselectivities in the range of 80-88% were achieved for the Rh-catalyzed 1,4-addition of phenylboronic acid to cyclohexenone, the hydrogenation of acetamidocinnamic acid and the hydroboration of styrene. The developed synthetic methods can be readily applied for the synthesis of other new diphosphines of various kinds.

In the second part of this work, several new reactions of organozinc compounds were investigated. *Bis*-(phenyldimethylsilyl)zinc species, prepared *in situ* from the corresponding silyllithium compound, was found to react with various aryl triflates in the presence of Ni(dppp)Cl<sub>2</sub> as a catalyst, giving corresponding aryl silanes.



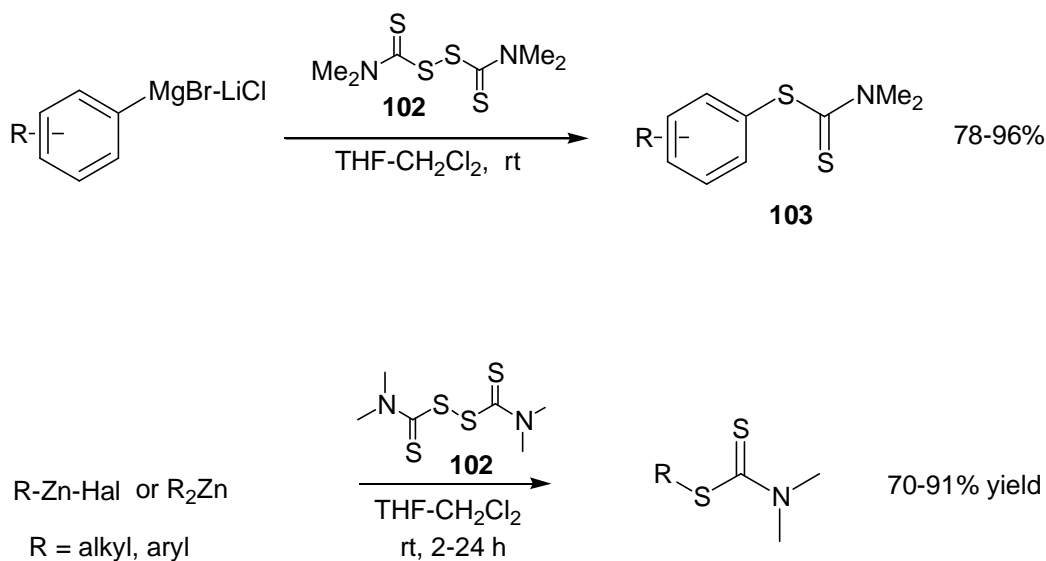
**Scheme 77.** Cross-coupling of aryl triflates with silylzinc compounds.

Using this method, 14 various arylsilanes were conveniently prepared from the corresponding triflates in 54-88% yield. Similarly, *tris*-(trimethylsilyl)aluminium reacted with several aryl triflates with Ni catalysis, affording aryltrimethyl silanes. The products of these new coupling reactions could be readily transformed into corresponding aryl iodides and arylboronic esters. Therefore, the developed method presents a new simple technique for the transformation of a phenol into the corresponding aryl iodide or arylboronic ester.



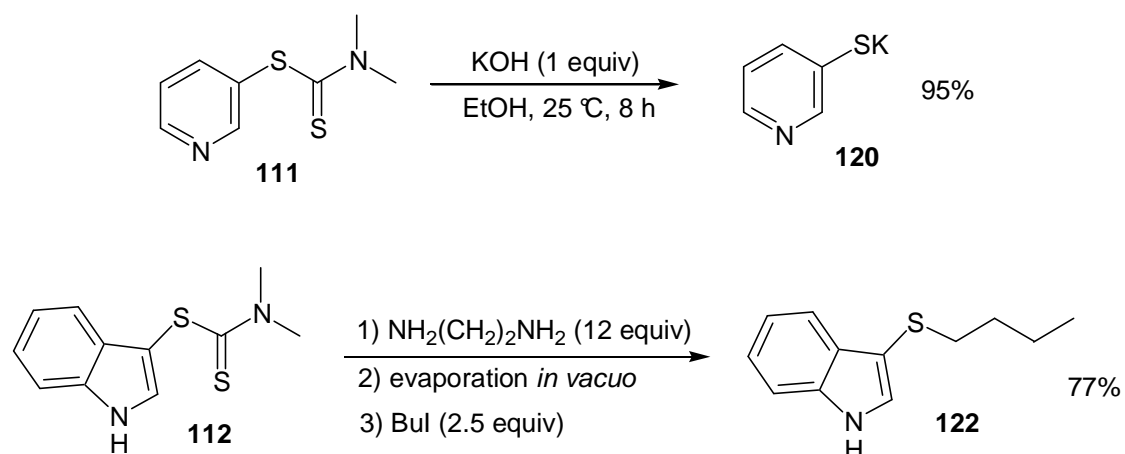
**Scheme 78.** Conversion of aryl silanes into aryl iodides and arylboronic esters.

During the studies of the influence of LiCl on the reactivity of organometallic compounds, a new method for the thiolation of organomagnesium and organozinc compounds by the reaction with tetramethylthiuram disulfide was elaborated. The resulting dithiocarbamates were obtained in excellent yields from a broad variety of functionalized organozinc and organomagnesium compounds.



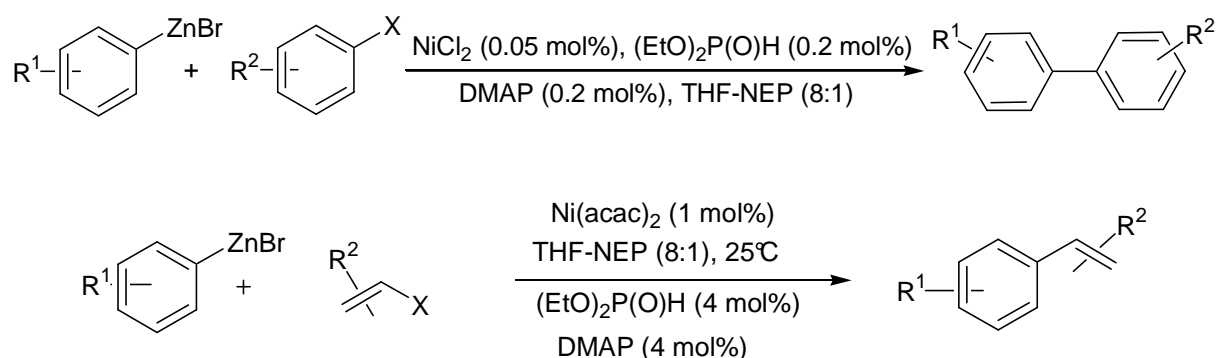
**Scheme 79.** New method for thiolation of organomagnesium and organozinc compounds.

The resulting dithiocarbamates can be readily converted into corresponding thiols, or after the cleavage in situ alkylated into unsymmetrical sulfides.



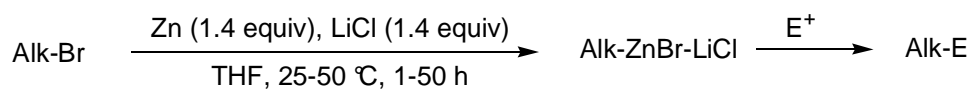
**Scheme 80.** Conversion of dithiocarbamates into thiols and sulfides.

Further studies on the reactivity of organozinc compounds revealed the high activity of Ni salt in the presence of N-alkylpyrrolidinones as cosolvents in the cross-coupling reaction with aryl halides and sulfonates. The thoroughful screening of cosolvents, ligands and additives allowed elaboration of a highly efficient and versatile method for the cross-coupling of arylzinc compounds with various aryl and alkenyl electrophiles in the presence of small amounts of Ni as a catalyst.



**Scheme 81.** New Ni-catalyzed cross-coupling reaction of arylzinc compounds.

Finally, a new highly versatile method for the preparation of primary and secondary alkylzinc compounds from the corresponding alkyl bromides was developed. It was discovered that the commercial zinc powder readily reacts with alkyl bromides in the presence of 1.0-1.4 equiv. of LiCl in THF at temperatures 25-50 °C, giving corresponding alkylzinc species.



**Scheme 82.** Synthesis of organozinc compounds from alkyl bromides.

Formerly, such insertion reaction was known only for alkyl iodides, which were not suitable for the large-scale industrial applications due to their high prices. The resulting alkylzinc compounds were reacted in situ with various electrophiles, affording the products in good to excellent yields. This newly developed method will open new horizons in the industrial application of organozinc compounds.

# Experimental Part

## 10. General considerations

Unless otherwise stated, all reactions were carried out with magnetic stirring and, if air or moisture sensitive, in flame-dried glassware under argon. Syringes used to transfer reagents and solvents were purged with argon prior to use.

### Solvents

Solvents were dried according to standard methods by distillation over drying agents as follows: dichloromethane, DMF, NMP and pentane (CaH<sub>2</sub>), THF, diethyl ether and DME (Na/benzophenone), toluene (Na), methanol, ethanol and isopropanol (Mg), pyridine and triethylamine (KOH).

### Reagents

Reagents of > 98% purity were used without further purification. The following reagent were prepared according to literature procedure:

CuCN·2LiCl<sup>109</sup> solution (1.0 M) was prepared by drying CuCN (896 mg, 10 mmol) and LiCl (848 mg, 20 mmol) in a Schlenk-flask under vacuum for 5 h at 140°C. After cooling to RT, dry THF (10 mL) was added and stirring was continued until the salts were dissolved.

#### *Organolithium reagents:*

*n*-Butyllithium was used as approx. 1.5 M solution in hexanes (Chemetall) and titrated prior to use.

*t*-Butyllithium was used as approx. 1.5 M solution in pentane (Chemetall) and titrated prior to use.

Phenyldimethylsilyllithium was prepared and titrated as described by *Fleming*.<sup>83b</sup>

#### *Content determination of organometallic reagent:*

Organolithium and organomagnesium solutions were titrated according to the literature procedures.<sup>110</sup> The concentration of organozinc solutions were determined by back titration of iodine in THF.

### Chromatography

Thin layer chromatography (TLC) was performed using aluminium plates, coated with SiO<sub>2</sub> (Merck 60, F-254). The spots were visualized by UV light and by treating the plate with different solutions:

- KMnO<sub>4</sub> (3 g), K<sub>2</sub>CO<sub>3</sub> (20 g), KOH (0.3 g) in water (300 mL)
- Phosphomolybdic acid (10 g) in absolute ethanol (100 mL)
- Cerium molybdate: phosphomolybdic acid (5 g), Ce(SO<sub>4</sub>)<sub>2</sub> (2 g), conc. H<sub>2</sub>SO<sub>4</sub> (12 mL) in water (230 mL).

<sup>109</sup> P. Knochel, M. C. P. Yeh, S. C. Berk, J. Talbert, *J. Org. Chem.* **1988**, *53*, 2390.

<sup>110</sup> (a) H. S. Lin, L. A. Paquette, *Synth. Commun.* **1994**, *24*, 2503. (b) A. Krasovskiy, P. Knochel, *Synthesis* **2006**, *5*, 890.

Flash column chromatography was performed using SiO<sub>2</sub> 60 (0.040-0.063 mm; 230-400 mesh ASTM) from Merck. The amount of silica gel was calculated according to the recommendations of *Still*.<sup>111</sup>

## Analytical data

**Melting points** were measured on a Büchi B-540 apparatus.

**NMR** spectra were recorded on a Varian Mercury 200, VXR 400S and on a Bruker ARX 300, AMX 600 instruments. Chemical shifts ( $\delta$ /ppm) were given relative to CDCl<sub>3</sub> (7.26 ppm, for <sup>1</sup>H-NMR, 77.0 ppm for <sup>13</sup>C-NMR).

For the characterization of the observed signal multiplicities the following abbreviations were applied: s (singlet), d (doublet), dd (doublet doublet), dt (doublet triplet), t (triplet), q (quartet), m (multiplet) and br (broad).

**Infrared** spectra were recorded from 4000-400 cm<sup>-1</sup> on a Nicolet 510 FT-IR or a Perkin-Elmer 281 IR spectrometer or BX FT-IR System with a Smith Durasampl IR II, ATR unit in substance. Samples were measured either as neat or as a film between sodium glass plates for liquids and as potassium bromide tablets for solids. The absorption bands were reported in wave numbers (v/cm<sup>-1</sup>).

**Optical rotations** were measured on a Perkin-Elmer 241 polarimeter.

**Mass spectroscopy:** mass spectra were recorded on a Finnigan MAT 95Q or a Finnigan 90 instrument for electro impact ionization (EI). High resolution mass spectra (HRMS) were recorded on the same instruments. Fast atom bombardment (FAB) samples were recorded in either a 2-nitrobenzyl alcohol or a glycerine-matrix.

## Determination of the enantiomeric excess

**Gas chromatography** (GC) was performed on the following columns:

- Chirasil-L-Val, Varian, CP7495 (25.0 m x 250  $\mu$ m x 0.12  $\mu$ m),
- Chirasil-Dex CB, Varian, CP7502 (25.0 m x 250  $\mu$ m x 0.25  $\mu$ m), 12.10 psi, 2.8 mL/min, H<sub>2</sub>-flux.
- TFA- $\gamma$ -Cyclodextrin, Astec, G 9105-18 (30.0 m x 250  $\mu$ m x 0.00  $\mu$ m), 10.86 psi, 2.1 mL/min, H<sub>2</sub>-flux.

**High Performance Liquid Chromatography** (HPLC) was performed on a Dionex instrument with a UV/vis diode array detector on the following columns (eluent: *i*-PrOH/*n*-hexane, isocratic):

- Chiralcel OD-H
- Chiralcel OD
- Chiralcel AD
- Chiralcel OJ.

## 11. Typical procedures (TP)

---

<sup>111</sup> W. C. Still, M. Khan, A. Mitra, *J. Org. Chem.* **1978**, *43*, 2923.

### **11.1. Typical procedure for the condensation of cycloalkanones with aliphatic aldehydes (TP1).**

To aqueous KOH solution (0.5 M, 500 mL) was added the cycloalkanone (500 mM) and methyl *tert*-butyl ether (MTBE, 200 mL). With stirring, the aldehyde (400 mM) was slowly added and the mixture was refluxed with vigorous stirring for 3 h. The phases were separated and the organic layer washed with aq. KHSO<sub>4</sub> (10%, 100 mL), dried (Na<sub>2</sub>SO<sub>4</sub>), concentrated and distilled *in vacuo* using 40-cm silver-plated Vigreux column. The products were obtained as colourless liquids.

### **11.2 Typical procedure for the Luche reduction of enones (TP2).**

The enone (100 mmol) was added to the solution of CeCl<sub>3</sub> in MeOH (0.4 M, 250 mL, 1 equiv.) and the mixture was cooled to 0 °C. NaBH<sub>4</sub> (3.90 g, 1 equiv.) was added slowly in portions so that the temperature did not exceed 5 °C. The mixture was stirred 15 min at 0 °C quenched with aq. KHSO<sub>4</sub> (5%, 200 mL) and extracted three times with Et<sub>2</sub>O. The organic phase was dried over Na<sub>2</sub>SO<sub>4</sub>, evaporated and the residue distilled *in vacuo*.

### **11.3 Typical procedure for the enzymatic kinetic resolution of cyclic allylic alcohols with Amano lipase (PS-A) (TP3).**

The allylic alcohol (100 mmol) was dissolved in hexane (200 mL) and vinyl acetate (12.6 g, 150 mmol, 1.5 equiv.) was added, followed by the Amano PS lipase (from *Pseudomonas cepacia*, 5 mass.% to the substrate). The mixture was slightly stirred at 35 °C for 12 h and filtered. The solvent was removed *in vacuo* and the residue chromatographed on silica (pentane-ether 3:1).

### **11.4 Typical procedure for the preparation and *in situ* rearrangement of allyl diphenylphosphinites (TP4).**

A 250 ml Schlenk-flask was charged with toluene (60 ml), the allylic alcohol (15 mmol) and DMAP (1.93 g, 15.8 mmol, 1.05 equiv). The solution was cooled to 0 °C and neat Ph<sub>2</sub>PCl (3.50 g, 15.8 mmol, 1.05 equiv.) was added slowly. The mixture was heated at the specified temperature and time and the rearrangement was monitored by <sup>31</sup>P spectra. After the reaction completion, the mixture was filtered while still hot through a pad of Celite and evaporated *in vacuo*. The residue was recrystallized from CH<sub>2</sub>Cl<sub>2</sub>-heptane mixture.

### **11.5 Typical procedure for the hydroboration of allyldiphenylphosphine oxides with 9-BBN and oxidation with *m*-CPBA (TP5).**

The allyldiphenylphosphine oxide (10 mmol) was dissolved in a dry argon-flushed Schlenk-flask in 9-BBN solution in THF (25 mL of 0.5 M solution, 12.5 mmol, 1.25 equiv.). The mixture was heated at 50 °C for the specified time. The slow evaporation of THF usually leads to the crystallization of the hydroboration product. In a separate flask, *m*-CPBA (15 g of the 70% prepartate, 60 mmol, 6 equiv.) was dissolved in CH<sub>2</sub>Cl<sub>2</sub> (150 mL) and the solution was dried over Na<sub>2</sub>SO<sub>4</sub>. To this solution, cooled to 10 °C, the reaction mixture in THF was added slowly, keeping the same temperature. The mixture was stirring for 30 min at RT,



added slowly to aq.  $\text{Na}_2\text{S}_2\text{O}_5$  (25% in  $\text{H}_2\text{O}$ , 100 mL) and stirred for 1 h more. The organic phase was washed twice with 10% aq. ammonia, then saturated brine, dried ( $\text{Na}_2\text{SO}_4$ ) and evaporated *in vacuo*. To the residue, ether was added (30 mL) and the mixture was stirred for 12 h. The white precipitate of the diphenylphosphinoyl alcohol was filtered and dried *in vacuo*.

### **11.6 Typical procedure for the reduction of phosphine oxides by Ti(IV)-PMHS (TP6).**

The phosphine oxide (7 mmol) was dissolved in toluene (15 mL) and  $\text{Ti}(\text{O}i\text{Pr})_4$  (2.1 mL, 4.2 mmol, 0.6 equiv.) was added. To this mixture, polymethylhydrosiloxane (PMHS, 2.5 mL, 42 mmol, 6 equiv.) was added and the mixture was heated at 105 °C for 2 h, until  $^{31}\text{P}$  showed complete conversion. The black solution was cooled down and  $\text{BH}_3\text{-Me}_2\text{S}$  (0.85 mL, 8 mmol, 1.1 equiv) was added. After 10 min, MeOH (5 mL) was added carefully. When the gas evolution ceased, the mixture was poured into a plastic bottle, containing aq. HF (24%, 20 mL) and stirred for 12 h. The organic layer was separated, washed with 10% aq.  $\text{NH}_3$ , dried ( $\text{Na}_2\text{SO}_4$ ) and passed through a short column of silica. The column was washed with ether. The combined filtrates were evaporated *in vacuo* to give the phosphine-borane as a viscous mass in nearly quantitative yield.

### **11.7 Typical procedure for the synthesis of bis-phosphine boranes from phosphine-borane alcohols (TP7).**

Into a 100 mL Schlenk-flask was placed a phosphine-borane alcohol (5 mmol) and dry dichloromethane (40 mL). Cooled to  $-20^\circ\text{C}$  and dry triethylamine (1.7 mL, 12 mmol) was added. Methanesulfonyl chloride (0.78 mL, 11 mmol) was added at this temperature dropwise with a good stirring. The mixture was left at  $-20^\circ$  for 2 h and, still cold, poured into dry ether (200 mL). After 5 min, the white precipitate was filtered off through a pad of silica gel, the filter cake washed with ether (100 mL) and the filtrate concentrated on rotary evaporator to about 10 mL. The residual solvents and the excess of MsCl were removed in oil pump vacuum during 5 h. The mesylate was used in the next step without purification.

In a 100 mL Schlenk-flask, *t*BuOK (1.68 g, 15 mmol) was dissolved in THF (25 mL) and neat diphenylphosphine (2.80 g, 15 mmol) was added. The orange solution was cooled to  $-20^\circ\text{C}$  and the solution of the mesylate in THF (10 mL) was slowly added. The mixture was heated at 50°C for 18 h.  $\text{BH}_3\text{-Me}_2\text{S}$  (2.0 mL, 20 mmol) was added and the reaction mixture was transferred into a 250 mL erlenmeyer flask with methanol (10 mL). When gas evolution ceased, saturated  $\text{NH}_4\text{Cl}$  (50 mL) was added, the aqueous layer extracted twice with dichloromethane (20 mL portions). Combined organic extracts washed with saturated brine, dried ( $\text{MgSO}_4$ ) and evaporated. The residue was dissolved in small amount of dichloromethane - pentane mixture (1:1) and passed through silica. The filtrate was concentrated to dryness and to the oily residue hexane (20 mL) was quickly added. In several minutes, crystallization of the product starts. After 12 h, the product was filtered off and dried *in vacuo*.

### **11.8 Typical procedure for the deprotection of a phosphine borane with *N,N'*-bis-(3-aminopropyl)piperazine (TP8).**

A phosphine-borane (1 mmol) was placed into a 10 mL Schlenk-tube and dissolved in toluene (2 mL). To the solution, of *N,N'*-bis-(3-aminopropyl)-piperazine (0.5 mL, excess) was added. The mixture was heated at 100°C for 2 h in the case of diarylphosphine boranes and 12 h for dicyclohexylphosphine boranes, cooled down and diluted with ether (10 mL). The solution was filtered in argon atmosphere through a pad of previously dried silica and the filtrate was

evaporated. The resulting phosphine was obtained as a white foam or very viscous oil and stored under argon.

### **11.9 Typical procedure for the hydrogenation of a diphenylphosphine oxide over Raney Ni (TP9).**

6.0 g of Raney Ni (50% in water, Acros) was washed three times with 20 mL portions of methanol and transferred in methanol into a 200 mL stainless steel autoclave. The diphenylphosphine oxide (8 mmol) was added, and the autoclave was charged with hydrogen to 50 bar pressure. Hydrogenation was performed at 50 °C for 48 h. The autoclave was depressurized, the contents were filtered through a pad of Celite and the precipitate was washed successively with methanol. The filtrate was evaporated to give the product as a colourless solid in quantitative yield.

### **11.10 Typical procedure for the cross-coupling of silylzinc reagents with aryl triflates (TP10).**

A solution of  $\text{PhMe}_2\text{SiLi}$  (0.65 M in THF, 3 mL, 2 mmol) was cooled to -20 °C.  $\text{ZnBr}_2$  (1.0 M solution in THF, 1 mL, 1 mmol) was added dropwise, the mixture was warmed up to RT and stirred for 15 min. An aryl triflate (0.8 mmol, 0.4 mmol in the case of a *bis*-triflate or a hydroxy-triflate) and  $\text{NiCl}_2(\text{dppp})$  (22 mg, 0.04 mmol, 5 mol%) was added, and the resulting solution was stirred at RT. After 1 h, sat.  $\text{NH}_4\text{Cl}$  (20 mL) was added and the mixture was extracted with  $\text{CH}_2\text{Cl}_2$  (2×15 mL). The organic phase was washed with brine, dried ( $\text{Na}_2\text{SO}_4$ ) and concentrated *in vacuo*. The residue was purified by column chromatography (pentane- $\text{CH}_2\text{Cl}_2$ ).

### **11.11 Typical procedure for the cross-coupling of tris-(trimethylsilyl)aluminium with aryl triflates (TP11).**

In a 25 mL Schlenk-flask was placed  $\text{LiCl}$  (70 mg, 1.6 mmol) and dried *in vacuo* at 120 °C for 1 h. On cooling, dry dioxane (5 mL) was added. Into the flask,  $\text{Al}(\text{Me}_3\text{Si})_3$  (300 mg, 1.2 mmol) was carefully added by a syringe and the mixture was stirred until it becomes homogeneous. An aryl triflate (0.8 mmol) and  $\text{NiCl}_2(\text{dppp})$  (22 mg, 0.04 mmol, 5 mol%) was added, and the resulting solution was stirred at RT for the specified time. Sat.  $\text{NH}_4\text{Cl}$  (20 mL) was carefully added and the mixture was extracted with  $\text{CH}_2\text{Cl}_2$  (2×15 mL). The organic phase was washed with brine, dried ( $\text{Na}_2\text{SO}_4$ ) and concentrated *in vacuo*. The residue was purified by column chromatography (pentane- $\text{CH}_2\text{Cl}_2$ ).

### **11.12 Typical procedure for the conversion of aryldimethylphenylsilanes into aryl iodides (TP12).**

An aryl silane (0.5 mmol) was dissolved in  $\text{CH}_2\text{Cl}_2$  (1 mL) and to this solution was added  $\text{ICl}$  (0.5 M solution in  $\text{CH}_2\text{Cl}_2$ , 2.2 mL, 1.1 mmol, 2.2 equiv.) at 0 °C. The mixture was stirred 1 h at 0 °C, diluted with  $\text{CH}_2\text{Cl}_2$  and washed with aq.  $\text{Na}_2\text{S}_2\text{O}_3$  (10%, 20 mL). The organic phase was washed with brine, dried ( $\text{Na}_2\text{SO}_4$ ) and concentrated *in vacuo*. The residue was purified by column chromatography (pentane- $\text{CH}_2\text{Cl}_2$ ).

### **11.13 Typical procedure for the conversion of aryldimethylphenylsilanes into arylboronic esters (TP13).**

An arylsilane (0.5 mmol) was dissolved in CH<sub>2</sub>Cl<sub>2</sub> (1 mL) and to this solution at 0 °C was added BCl<sub>3</sub> (1.0 M solution in CH<sub>2</sub>Cl<sub>2</sub>, 3.0 mL, 3 mmol, 6 equiv.). The mixture was stirred 16 h at RT. The volatiles were removed *in vacuo* and to the residue was added MeOH (3 mL), followed by 2,2-dimethyl-1,3-propanediol (0.26 g, 2.5 mmol, excess). The mixture was stirred 1 h at RT, the solvents were removed *in vacuo* and the residue was purified by column chromatography (pentane- CH<sub>2</sub>Cl<sub>2</sub>).

### **11.14 Typical procedure for the halogene-magnesium exchange reaction in the presence of LiCl (TP14).**

A dry and argon flushed 10 mL flask, equipped with a magnetic stirrer and a septum, was charged with *i*-PrMgCl·LiCl (1.5 mL, 1.4 M in THF, 2.1 mmol, 1.05 equiv). Neat aryl bromide or aryl iodide (2 mmol, 1 equiv.) was added at the specified temperature. The reaction mixture was stirred, and the completion of the halogene-magnesium exchange was checked by GC-analysis using tetradecane as internal standard.

### **11.15 Typical procedure for the preparation of S-aryl-N,N-dimethylditiocarbamates from arylmagnesium halides (TP15).**

The freshly prepared as specified magnesium reagent was cooled to 0 °C and the solution of tetramethylthiuram disulfide (TMTD, 2.28 g, 9.5 mmol) in CH<sub>2</sub>Cl<sub>2</sub> (7 mL) was added at this temperature. The mixture was allowed to reach rt within 1-2 h. After the reaction was completed, sat. NH<sub>4</sub>Cl solution (25 mL) was added and the mixture was extracted with CH<sub>2</sub>Cl<sub>2</sub>. The solvent was evaporated and the product was purified by recrystallization (CH<sub>2</sub>Cl<sub>2</sub>-heptane) or flash chromatography (SiO<sub>2</sub>, CH<sub>2</sub>Cl<sub>2</sub>-pentane).

### **11.16 Typical procedure for the preparation of N,N-dimethylditiocarbamates from organozinc compounds (TP16).**

A 25 mL Schlenk-flask containing a solution of TMTD (1.00 g, 4.16 mmol) in CH<sub>2</sub>Cl<sub>2</sub> (5 mL) was cooled to 0°C, and the organozinc compound prepared as specified was added slowly at this temperature. The reaction mixture was stirred 20 h at RT (a white precipitate of zinc dimethyldithiocarbamate formed), then was diluted with ether (30 ml) and filtered. The precipitate was washed with ether, the filtrate evaporated and the residue was purified by column chromatography (SiO<sub>2</sub>, CH<sub>2</sub>Cl<sub>2</sub>-pentane).

### **11.17 Typical procedure for the Ni-catalyzed cross-coupling reaction of arylzinc halides with aryl electrophiles (TP17).**

In a dry and argon flushed 25 mL flask, equipped with a magnetic stirrer and a septum, to the ZnBr<sub>2</sub> solution (0.67 mL, 1.5 M in THF) and *N*-ethylpyrrolidinone (NEP, 0.17 mL) was added dropwise the arylmagnesium halide, prepared as specified (1.57 mL, 0.83 M in THF), then the catalyst solution (0.08 mL in NEP, corresponding to 0.05 mol% NiCl<sub>2</sub>, 0.2 mol% (EtO)<sub>2</sub>P(O)H and 0.2 mol% DMAP), and the aryl electrophile (1.0 mmol). The mixture was stirred at the specified temperature and time, until the GC of an aliquot showed the reaction completion, quenched with sat. NH<sub>4</sub>Cl solution, extracted twice with ether, and the product was purified by column chromatography.

### **11.18 Typical procedure for the Ni-catalyzed cross-coupling reaction of arylzinc halides with alkenyl electrophiles (TP18).**

In a dry and argon flushed 25 mL flask, equipped with a magnetic stirrer and a septum, to the ZnBr<sub>2</sub> solution (0.67 mL, 1.5 M in THF) and *N*-ethylpyrrolidinone (NEP, 0.17 mL) was added dropwise the arylmagnesium halide, prepared as specified (1.57 mL, 0.83 M in THF), then the catalyst solution (0.08 mL in NEP, corresponding to 1 mol% NiCl<sub>2</sub>, 4 mol% (EtO)<sub>2</sub>P(O)H and 0.2 mol% DMAP), and the alkenyl electrophile (1.0 mmol). The mixture was stirred at the specified temperature and time, until the GC of an aliquot showed the reaction completion, quenched with sat. NH<sub>4</sub>Cl solution, extracted twice with ether, and the product was purified by column chromatography.

### **11.19 Typical procedure for the insertion of Zn into alkyl bromides in the presence of LiCl and reaction with an electrophile (TP19).**

Anhydrous LiCl (7 mmol) was placed in a Schlenk-flask and dried for 20 min at 130-140 °C on high vacuum (1 mbar). Zinc powder (7 mmol) was added and the heterogeneous mixture of Zn and LiCl was dried again 10-20 min at 130-140 °C. THF (5 mL) was added and Zn was activated by the addition of BrCH<sub>2</sub>CH<sub>2</sub>Br (5 mol %) and Me<sub>3</sub>SiCl (2 mol %). The alkyl bromide (5 mmol) was added neat at room temperature. The reaction heated and stirred for the specified time and temperature (checked by GC analysis of reaction aliquots, until the conversion was higher than 98%). The organozinc reagent was titrated using 1 mmol of iodine, carefully separated from the remaining zinc powder using a syringe, and transferred into another Schlenk-flask. The specified electrophile and the catalyst were added. The reaction mixture was stirred for the specified time and then quenched with sat. aq. NH<sub>4</sub>Cl (15 mL). The aqueous phase was extracted with ethyl acetate (3 x 5 mL), the organic phase was dried (Na<sub>2</sub>SO<sub>4</sub>) and concentrated *in vacuo*. The crude residue was purified by flash chromatography.

### **11.20 Typical procedure for the asymmetric Rh-catalyzed hydrogenation of methyl acetamidocinnamate and methyl acetamidoacrylate (TP20).**

In a dried 50-mL Schlenk-flask under argon was placed PhMe (9 mL) and MeOH (1 mL). The ligand (0.011 mmol, 2.2 mol%) and Rh(COD)<sub>2</sub>BF<sub>4</sub> (4.1 mg, 2 mol%) was added, followed by the substrate (0.5 mmol). The flask was flushed with H<sub>2</sub> and then the contents were stirred under a slightly positive pressure of H<sub>2</sub> for 12 h at RT. The reaction mixture was evaporated and the product purified by a short column chromatography (CH<sub>2</sub>Cl<sub>2</sub>-pentane). The enantiomeric excess was determined by chiral GC using the comparison with an authentic product sample.

Methyl *N*-acetylphenylalaninate: column Chiralsil *L*-Val (Chrompak, 25 m×0.12 μm×0.22 μm); 140 °C const. Retention time: (*R*)-enantiomer 10.5 min, (*S*)-enantiomer 11.3 min.

Methyl *N*-acetylalaninate: column Chiralsil *L*-Val, 120 °C const., (*R*)-enantiomer 1.94 min, (*S*)-enantiomer 2.06 min.

### **11.21 Typical procedure for the asymmetric Rh-catalyzed hydrogenation of dimethyl itaconate (TP21).**

In a dried 50-mL Schlenk-flask under argon was placed and MeOH (10 mL). The ligand (0.011 mmol, 2.2 mol%) and Rh(COD)<sub>2</sub>BF<sub>4</sub> (4.1 mg, 2 mol%) was added, followed by dimethyl itaconate (0.5 mmol). The flask was flushed with H<sub>2</sub> and then the contents were stirred under a slightly positive pressure of H<sub>2</sub> for 12 h at RT. The reaction mixture was

evaporated and the product purified by a short column chromatography (pentane-ether). The enantiomeric excess was determined by chiral GC (comparison with commercial dimethyl (*R*)- $\alpha$ -methylsuccinate):

column TFA-cyclodextrine; 60°C for 3 min, then ramp 2°C/min to 100°C, (*R*)-enantiomer 19.0 min, (*S*)-enantiomer 19.6 min.

### **11.22 Typical procedure for the asymmetric Rh-catalyzed 1,4-addition of phenylboronic acid to cyclohexen-2-one (TP22).**

Into a 10 mL Schlenk-tube under argon was placed dioxane (2.5 mL), water (0.25 mL), cyclohexen-2-one (96 mg, 1 mmol) and PhB(OH)<sub>2</sub> (170 mg, 1.4 mmol). To this mixture, Rh(COD)(acac) (9.3 mg, 0.03 mmol, 3 mol%) and the ligand (0.03 mmol, 3 mol%) was added. The mixture was stirred for 2.5 h at 100 °C. Water (5 mL) was added and the mixture was extracted with Et<sub>2</sub>O. The organic phase was washed with brine, dried (MgSO<sub>4</sub>) and concentrated in vacuo. Flash chromatography (pentane-ether 3:1) gave 3-phenylcyclohexanone as colourless oil.

**Chiral HPLC** (Chiralcel OD-H, *n*-heptane/*i*-PrOH 98:2, 0.3 mL/min): (*S*)-enantiomer 44.0 min, (*R*)- enantiomer 47.0 min.

**<sup>1</sup>H NMR** (300 MHz, CDCl<sub>3</sub>):  $\delta$  7.30-7.20 (m, 5H), 3.01 (m, 1H), 2.60-2.30 (m, 4H), 2.10-2.00 (m, 2H), 1.89-1.70 (m, 2H) ppm.

**<sup>13</sup>C NMR** (75 MHz, CDCl<sub>3</sub>):  $\delta$  211.0, 144.3, 128.6, 126.6, 126.5, 48.9, 44.7, 41.1, 32.7, 25.5 ppm.

### **11.23 Typical procedure for the asymmetric Rh-catalyzed hydroboration of styrene with catecholborane (TP23).**

A mixture of [Rh(cod<sub>2</sub>)]BF<sub>4</sub> (8.2 mg, 0.020 mmol, 1 mol %) and a ligand (0.48 mL in 0.05 M in Et<sub>2</sub>O, 0.020 mmol, 1 mol%) in dry THF (2 mL) was stirred for 10 min at RT in a 10 mL Schlenk-tube under argon. Styrene (2 mmol, 0.23 mL) was added to the resulting orange solution. The homogeneous mixture was cooled to -20 °C and stirred at this temperature for 15 min before the addition of freshly distilled catecholborane (2.4 mmol, 0.26 mL). The reaction was stirred at -10 °C for 16 h and then quenched by the addition of EtOH (2 mL). Aq. NaOH (2 M, 2 mL) and 30 % H<sub>2</sub>O<sub>2</sub> (1 mL) were added subsequently and the mixture was warmed up to RT, over a period of 2 h under vigorous stirring. The mixture was extracted with Et<sub>2</sub>O, the organic phase was washed with NaOH (1 M), brine and dried (MgSO<sub>4</sub>). The residue was purified by flash chromatography (pentane-ether 4:1) to give 2-phenylethanol as a colourless liquid.

**HPLC** (Chiralcel OD-H, *n*-heptane/*i*-PrOH 98/2, 0.4 mL/min, 215 nm): (*R*)-enantiomer 35.5 min, (*S*)-enantiomer 43.7 min.

**<sup>1</sup>H NMR** (300 MHz, CDCl<sub>3</sub>):  $\delta$  7.20-7.09 (m, 5H), 4.66 (q, *J* = 6.5 Hz, 1H), 2.80 (br s, 1H), 1.30 (d, *J* = 6.5 Hz, 3H) ppm.

**<sup>13</sup>C NMR** (75 MHz, CDCl<sub>3</sub>):  $\delta$  146.4, 128.8, 127.7, 125.9, 70.6, 25.6 ppm.

### **11.24 Typical procedure for the asymmetric Rh-catalyzed hydrogenation of acetophenone semicarbazone (TP24).**

Into a dry 50 mL Schlenk-flask was placed MeOH (5 mL), [Rh(cod<sub>2</sub>)]BF<sub>4</sub> (4.1 mg, 0.020 mmol, 1 mol %) and a ligand (0.02 mmol, 1 mol%). The solution of acetophenone semicarbazone (238 mg, 1 mmol) in MeOH (5 mL) was added. The mixture was transferred into a steel autoclave under argon, and it was flushed with hydrogen. The mixture was stirred

at RT under 50 bar H<sub>2</sub> for 16 h. The volatiles were removed *in vacuo* and the product was purified by chromatography (silica, ether).

**Chiral HPLC** (Chiralcel OJ, *n*-heptane/*i*-PrOH 90/10, 0.6 mL/min): (*R*)-enantiomer 13.3 min, (*S*)-enantiomer 15.7 min.

**<sup>1</sup>H NMR** (300 MHz, CDCl<sub>3</sub>): δ 7.75 (s, 1H), 7.56-7.53 (m, 2H), 7.30-7.25 (m, 2H), 4.37 (q, *J* = 6.7 Hz, 1H), 1.34-1.32 (m, 3H).

**<sup>13</sup>C NMR** (75 MHz, CDCl<sub>3</sub>): δ 166.4, 142.1, 131.9, 130.7, 127.6-125.9 (m), 59.0, 20.1.

### 11.25 Typical procedure for the asymmetric Ru-catalyzed hydrogenation of ethyl benzoylacetate (TP25).

Into a dry 50 mL Schlenk-flask was placed acetone (3 mL), Ru(cod) (C<sub>4</sub>H<sub>7</sub>)<sub>2</sub> (3.2 mg, 0.010 mmol, 0.5 mol %) and the ligand (0.01 mmol, 0.5 mol%). When the complex is dissolved, HBr (0.2 mL, 0.3 M in MeOH) was added and the solution was stirred 30 min at RT. The solvents were removed *in vacuo* and the residue was dissolved in EtOH (12 mL) and benzoylacetate (384 mg, 2 mmol) was added. The mixture was transferred into an autoclav under argon and stirred at 50 °C and 50 bar H<sub>2</sub> pressure for 16 h. The solvent was removed *in vacuo* and the residue purified by chromatography (silica, ether). The product (ethyl 3-hydroxy-3-phenylpropionate) was obtained as a colourless oil.

**HPLC** (Chiralcel OD, *n*-heptane/*i*-PrOH 95/5, 0.9 mL/min): (*R*)-enantiomer 13.9 min, (*S*)-enantiomer 11.1 min.

**<sup>1</sup>H NMR** (300 MHz, CDCl<sub>3</sub>): δ 7.31-7.18 (m, 5H), 5.07-5.02 (m, 1H), 4.09 (q, *J* = 8.1 Hz, 2H), 3.25 (d, *J* = 3.6 Hz, 1H), 2.72-2.57 (m, 2H), 1.18 (t, *J* = 6.9 Hz, 3H).

**<sup>13</sup>C NMR** (75 MHz, CDCl<sub>3</sub>): δ 172.5, 143.4, 128.8, 128.0, 126.1, 70.7, 61.1, 44.0, 14.4.

### 11.26 Typical procedure for the asymmetric Pd-catalyzed allylic substitution reaction (TP26).

In a 10 mL Schlenk-tube, [Pd(allyl)Cl]<sub>2</sub> (3.7 mg, 0.01 mmol), KOAc (5.0 mg, 0.05 mmol, 5 mol%) and the ligand (0.02 mmol, 2 mol%) were dissolved in CH<sub>2</sub>Cl<sub>2</sub> (4 mL). 3-Acetoxy-1,3-diphenylpropene (252 mg, 1 mmol) in CH<sub>2</sub>Cl<sub>2</sub> (2 mL), *N,O*-bis-trimethylsilylacetamide (610 mg, 2 mmol, 2 equiv.) and dimethyl malonate (0.4 mL, 3 mmol, 3 equiv) were added. The mixture was stirred 2 h at RT, then quenched with sat. NH<sub>4</sub>Cl and extracted with ether (3×15 mL). The organic phases were washed with water, brine, dried and concentrated. The residue was purified by column chromatography (pentane-ether) and *trans*-methyl 2-carbomethoxy-3,5-diphenylpent-4-enolate was obtained as a white solid.

**Mp.:** 93-94.5 °C

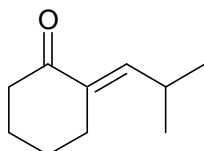
**HPLC** (Chiralcel OD-H, *n*-heptane/*i*-PrOH 98/2, 0.4 mL/min): (*R*)-enantiomer 25.0 min, (*S*)-enantiomer 27.1 min.

**<sup>1</sup>H NMR** (300 MHz, CDCl<sub>3</sub>): δ 7.27-7.06 (m, 10 H), 6.40 (d, *J* = 15.8 Hz, 1 H), 6.25 (dd, *J*<sub>1</sub> = 15.8 Hz, *J*<sub>2</sub> = 8.4 Hz, 1H), 4.19 (dd, *J*<sub>1</sub> = 10.8 Hz, *J*<sub>2</sub> = 8.4 Hz, 1H), 3.88 (d, *J* = 8.4 Hz, 1H), 3.61 (s, 3H), 3.43 (s, 3H).

**<sup>13</sup>C NMR** (75 MHz, CDCl<sub>3</sub>): δ 168.1, 167.7, 140.2, 136.8, 131.8, 129.1, 128.7, 128.4, 127.8, 127.4, 127.0, 126.4, 57.5, 52.5, 52.3, 49.0.

## 12. Syntheses of new alkyl analogs of PCPP

### Synthesis of 2-isobutylidenecyclohexanone (17)



Prepared according to the **TP1** from cyclohexanone (49.0 g, 500 mmol) and isobutyraldehyde (28.8 g, 400 mmol). Colourless liquid, yield 39.5 g (65%). The analytical data corresponds to those given in the literature.<sup>112</sup>

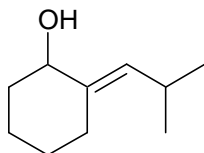
**Bp.:** 90-92 °C (10 mbar).

**<sup>1</sup>H NMR** (300 MHz, CDCl<sub>3</sub>): δ 6.05 (*J* = 10.0 Hz, 1H), 3.00-2.85 (m, 1H), 2.57-2.49 (m, 1H), 2.48-2.40 (m, 1H), 2.38-2.20 (m, 2H), 1.89-1.72 (m, 4H), 0.99 (d, *J* = 11.8 Hz, 6H).

**<sup>13</sup>C NMR** (75 MHz, CDCl<sub>3</sub>): δ 201.8, 145.3, 138.8, 40.4, 27.1, 25.6, 24.7, 23.9, 22.1, 22.0.

**IR** (KBr, cm<sup>-1</sup>): 2958 (s), 2866 (m), 1717 (vs), 1653 (s), 1471 (w), 1198 (m), 831 (w), 549 (w).

### Synthesis of 2-isobutylidenecyclohexanol (18)



Prepared according to the **TP2** from 2-isobutylidenecyclohexanone (15.2 g, 100 mmol). Colourless liquid, yield 14.9 g (97%). The analytical data corresponds to those given in the literature.<sup>113</sup>

**Bp.:** 66-69 °C (1 mbar).

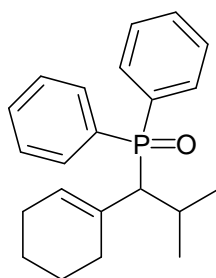
**<sup>1</sup>H NMR** (300 MHz, CDCl<sub>3</sub>): δ 4.77 (d, *J* = 9.6 Hz, 1H), 3.98-3.95 (m, 1H), 2.97-2.94 (m, 1H), 2.80-2.60 (m, 1H), 2.03-1.60 (m, 4H), 1.45-1.36 (m, 2H), 0.92 (d, *J* = 6.7 Hz, 6H).

**<sup>13</sup>C NMR** (75 MHz, CDCl<sub>3</sub>): δ 133.5, 127.8, 72.8, 34.2, 27.5, 27.4, 23.5, 23.3, 21.9.

### Synthesis of 1-(1-diphenylphosphinoyl-2-methyl-propyl)cyclohexene (19)

<sup>112</sup> I. Paterson, *Tetrahedron*, **1988**, *44*, 4207.

<sup>113</sup> Kelkar, S. V.; Arbale, A. A.; Joshi, G. S.; Kulkarni, G. H., *Synth. Comm.* **1990**, *20*, 839.



Prepared according to the **TP4** from 2-isobutylidenecyclohexanol (2.31 g, 15 mmol), reaction time 3 h, reaction temperature 100 °C. Yield 3.90 g (77%).

**Mp.:** 160-161 °C.

**<sup>1</sup>H NMR** (300 MHz, CDCl<sub>3</sub>): δ 7.92-7.86 (m, 2H), 7.69-7.65 (m, 2H), 7.45-7.42 (m, 3H), 7.33-7.26 (m, 3H), 5.69 (s, 1H), 2.58 (dd, J<sub>1</sub> = 8.6 Hz, J<sub>2</sub> = 6.8 Hz, 1H), 2.40-2.32 (m, 1H), 1.95-1.56 (m, 4H), 1.25-1.16 (m, 4H), 0.97 (d, J = 6.7 Hz, 3H), 0.81 (d, J = 6.7 Hz, 3H).

**<sup>13</sup>C NMR** (75 MHz, CDCl<sub>3</sub>): δ 134.6, 133.7, 132.7, 131.3, 131.0 (m), 130.5 (m), 128.5, 127.5 (m), 54.5 (d, J = 71.4 Hz), 39.7, 29.8, 28.2, 25.3, 23.3, 22.5, 21.7.

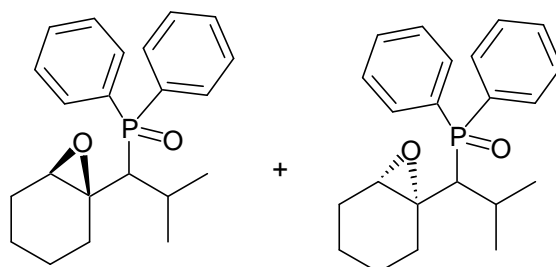
**<sup>31</sup>P NMR** (81 MHz, CDCl<sub>3</sub>): δ 31.9.

**IR** (KBr, cm<sup>-1</sup>): 2925 (w), 1436 (m), 1172 (s), 1098 (m), 698 (vs), 715 (vs).

**MS** (EI, 70 eV): 339 (17), 338 (27), 295 (48), 203 (31), 202 (100), 201 (36), 77 (10).

**HRMS:** calcd. 338.1800 (C<sub>22</sub>H<sub>27</sub>OP), found: 338.1776.

### Synthesis of 1-(1-diphenylphosphinoyl-2-methyl-propyl)cyclohexene epoxide (mixture **20a** and **20b**)



To the solution of *m*-CPBA (70%, 0.81 g, 3.3 mmol, 1.1 equiv) in CH<sub>2</sub>Cl<sub>2</sub> (20 mL), **19** (1.01 g, 3 mmol) was added at 0 °C. After 3 h, the reaction was quenched with aq. Na<sub>2</sub>S<sub>2</sub>O<sub>5</sub> (10%, 25 mL), the organic phase washed with aq. NH<sub>3</sub>, brine, dried (Na<sub>2</sub>SO<sub>4</sub>), evaporated *in vacuo* and recrystallized from CH<sub>2</sub>Cl<sub>2</sub>-hexane. The mixture of **20a** and **20b** was obtained as white solid, overall yield 0.89 g (84%).

**Mp.:** 188-189 °C.

**<sup>31</sup>P NMR** (81 MHz, CDCl<sub>3</sub>): δ 31.44 (major), 31.67 (minor).

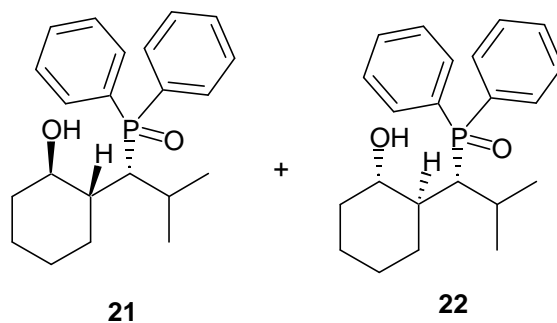
**IR** (KBr, cm<sup>-1</sup>): 2934 (w), 1437 (m), 1177 (s), 1115 (m), 746 (m), 722 (s), 695 (vs).

**MS** (EI, 70 eV): 311 (17), 203 (24), 202 (100), 201 (29), 77 (8).

**HRMS:** calcd. 354.1749 (C<sub>22</sub>H<sub>27</sub>O<sub>2</sub>P), found: 355.1814.

### Synthesis of 2-(1-diphenylphosphinoyl-2-methylpropyl)cyclohexanols (**21** and **22**)





In a 25 mL Schlenk-flask, **19** (1.01 g, 3 mmol) was dissolved in THF (5 mL) and  $\text{BH}_3\text{-Me}_2\text{S}$  (0.36 mL, 3.6 mmol, 1.2 equiv) was added. The mixture was stirred 24 h at RT and quenched with MeOH (2 mL). This solution was slowly added to the solution of *m*-CPBA (70%, 2.2 g, 9 mmol, 3 equiv.) in  $\text{CH}_2\text{Cl}_2$  (20 mL) and stirred for 6 h. The mixture was quenched with aq.  $\text{Na}_2\text{S}_2\text{O}_5$  (10%, 25 mL), the organic phase washed with aq.  $\text{NH}_3$ , brine, dried ( $\text{Na}_2\text{SO}_4$ ), and evaporated *in vacuo*. The residue was subjected to column chromatography on silica (ether- $\text{CH}_2\text{Cl}_2$ -MeOH 50:50:1) which afforded compounds **21** (653 mg, 61%, more polar) and **22** (216 mg, 21%, less polar) as white crystalline solids.

#### Compound 21:

**Mp.:** 199-200 °C.

**$^1\text{H}$  NMR** (300 MHz,  $\text{CDCl}_3$ ):  $\delta$  7.92-7.83 (m, 4H), 7.48-7.40 (m, 6H), 3.30 (bs, 1H), 2.52 (d,  $J = 10.8$  Hz, 1H), 2.33-2.25 (m, 1H), 1.99-1.95 (m, 1H), 1.76-1.67 (m, 2H), 1.58-1.47 (m, 3H), 1.17 (d,  $J = 7.0$  Hz, 3H), 1.20-0.95 (m, 3H), 0.88 (d,  $J = 7.0$  Hz, 3H).

**$^{13}\text{C}$  NMR** (75 MHz,  $\text{CDCl}_3$ ):  $\delta$  134.6 (d,  $J = 32.0$  Hz), 133.6 (d,  $J = 32.0$  Hz), 131.6 (dd,  $J_1 = 4.1$  Hz,  $J_2 = 2.6$  Hz), 131.4 (d,  $J = 8.8$  Hz), 130.8 (d,  $J = 8.5$  Hz), 128.8 (dd,  $J_1 = 19.3$  Hz,  $J_2 = 11.2$  Hz), 69.4, 45.1, 42.9 (d,  $J = 49.3$  Hz), 35.9, 32.7, 27.0, 26.0, 24.4, 21.8 (d,  $J = 10.3$  Hz).

**$^{31}\text{P}$  NMR** (81 MHz,  $\text{CDCl}_3$ ):  $\delta$  37.3.

**IR** (KBr,  $\text{cm}^{-1}$ ): 3282 (w), 2921 (m), 1436 (m), 1168 (s), 1067 (s), 818 (w), 716 (vs), 700 (vs).

**MS** (EI, 70 eV): 258 (18), 243 (48), 203 (24), 202 (100), 201 (18).

**HRMS**: calcd. 356.1905 ( $\text{C}_{22}\text{H}_{29}\text{O}_2\text{P}$ ), found: 357.1984 ( $[\text{M}+\text{H}]^+$ ).

#### Compound 22:

**Mp.:** 193-194 °C.

**$^1\text{H}$  NMR** (300 MHz,  $\text{CDCl}_3$ ):  $\delta$  7.82-7.70 (m, 4H), 7.49-7.37 (m, 6H), 4.79 (s, 1H), 2.66 (d,  $J = 12.9$  Hz, 1H), 2.32-2.22 (m, 1H), 2.17-2.13 (m, 1H), 1.80-1.26 (m, 8H), 1.20 (d,  $J = 7.3$  Hz, 3H), 1.16-0.95 (m, 1H), 0.88 (d,  $J = 7.3$  Hz, 3H).

**$^{13}\text{C}$  NMR** (75 MHz,  $\text{CDCl}_3$ ):  $\delta$  137.4, 136.5, 134.7, 133.8, 132.3 (d,  $J = 9.2$  Hz), 131.5 (dd,  $J_1 = 9.2$  Hz,  $J_2 = 2.6$  Hz), 130.1 (d,  $J = 8.5$  Hz), 128.9 (d,  $J = 11.1$  Hz), 128.4 (d,  $J = 11.4$  Hz), 76.7, 52.6 (d,  $J = 63.3$  Hz), 40.3 (d,  $J = 7.0$  Hz), 36.7 (d,  $J = 7.4$  Hz), 27.3, 25.5, 23.4, 23.3, 21.9, 21.4.

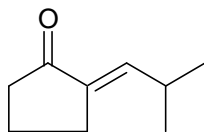
**$^{31}\text{P}$  NMR** (81 MHz,  $\text{CDCl}_3$ ):  $\delta$  40.8.

**IR** (KBr,  $\text{cm}^{-1}$ ): 3350 (w), 2930 (w), 1438 (m), 1167 (s), 1102 (m), 715 (m), 698 (vs).

**MS** (EI, 70 eV): 313 (21), 295 (12), 258 (24), 244 (16), 243 (100), 203 (17), 202 (56), 201 (39).

**HRMS**: calcd. 356.1905 ( $\text{C}_{22}\text{H}_{27}\text{O}_2\text{P}$ ), found: 356.1908.

### Synthesis of 2-isobutylidenecyclopentanone (23)



Prepared according to the **TP1** from cyclopentanone (42.0 g, 500 mmol) and isobutyraldehyde (28.8 g, 400 mmol). Colourless liquid, yield 24.8 g (45%).

**Bp.:** 62-64 °C (2 mbar).

**<sup>1</sup>H NMR** (300 MHz, CDCl<sub>3</sub>): δ 6.31-6.22 (m, 1H), 2.54-2.22 (m, 2H), 2.27-2.21 (m, 2H), 1.89-1.83 (m, 2H), 0.96 (d, *J* = 6.7 Hz, 6H).

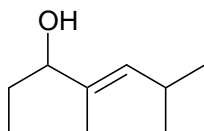
**<sup>13</sup>C NMR** (75 MHz, CDCl<sub>3</sub>): δ 208.0, 142.7, 135.3, 38.8, 29.4, 26.9, 22.8, 20.2, 19.4.

**IR** (KBr, cm<sup>-1</sup>): 2963 (s), 2871 (m), 1720 (vs), 1649 (s), 1466 (w), 1203 (m), 826 (w).

**MS** (EI, 70 eV): 138 (100), 123 (28), 95 (14), 82 (23), 67 (20).

**HRMS:** calcd. 138.1045 (C<sub>9</sub>H<sub>14</sub>O), found: 138.1037

### Synthesis of 2-isobutylidenecyclopentanol (*rac*-24)



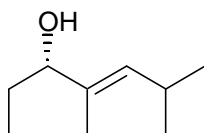
Prepared according to the **TP2** from 2-isobutylidenecyclopentanone (13.8 g, 100 mmol). Colourless liquid, yield 13.3 g (95%). The analytical data corresponds to those reported in the literature.<sup>114</sup>

**Bp.:** 90-93 °C (10 mbar).

**<sup>1</sup>H NMR** (300 MHz, CDCl<sub>3</sub>): δ 5.32-5.24 (m, 1H), 4.30-4.27 (m, 1H), 2.40-2.26 (m, 2H), 2.18-2.03 (m, 1H), 1.83-1.66 (m, 2H), 1.62-1.48 (m, 2H), 0.91 (d, *J* = 1.7 Hz, 3H), 0.89 (d, *J* = 1.7 Hz, 3H).

**<sup>13</sup>C NMR** (75 MHz, CDCl<sub>3</sub>): δ 143.8, 132.0, 76.0, 35.9, 29.1, 27.0, 23.1, 22.9, 22.5.

### Synthesis of (*S*)-2-isobutylidenecyclopentanol (24)



Prepared according to the **TP3** by the resolution of racemic 2-isobutylidenecyclopentanol (*rac*-24, 14.0 g, 100 mmol), reaction time 12 h, reaction temperature 35 °C. The mixture after the enzymatic kinetic resolution was separated by column chromatography on silica (pentane-ether 3:1). Colourless liquid, yield 6.58 g (47%), >99% *ee*.

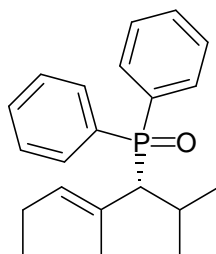
**Chiral GC:** column TFA-cyclodextrine; 65°C const. (*R*)-enantiomer 37.1 min, (*S*)-enantiomer 39.0 min.

<sup>114</sup> A. F. Simpson, C. D. Bodkin, C. P. Butts, M. A. Armitage, T. Gallagher, *J. Chem. Soc. Perkin 1* **2000**, 18, 3047.

$[\alpha]_D^{20}$ : -69.2 (c 2.00, CH<sub>2</sub>Cl<sub>2</sub>).

The spectral data are identical to those of the racemic compound.

### Synthesis of 1-[(1*R*)-1-diphenylphosphinoyl-2-methylpropyl]cyclopentene (**25**)



Prepared according to the **TP4** from 2-isobutylidenecyclopentanol (**24**, 2.1 g, 15 mmol), reaction time 6 h, reaction temperature 80 °C. Yield 3.74 g (77%), >99% *ee*.

**Chiral HPLC** (Chiralcel OD, *n*-heptane/*i*-PrOH 99/1, 0.6 mL/min): (*R*)-enantiomer 34.8 min, (*S*)-enantiomer 29.9 min.

**<sup>1</sup>H NMR** (300 MHz, CDCl<sub>3</sub>): δ 7.85-7.82 (m, 2H), 7.66-7.60 (m, 2H), 7.42-7.39 (m, 3H), 7.31-7.19 (m, 3H), 5.63-5.60 (m, 1H), 2.98-2.93 (m, 1H), 2.30-1.85 (m, 7H), 0.96 (d, *J* = 6.6 Hz, 3H), 0.79 (d, *J* = 6.6 Hz, 3H).

**<sup>13</sup>C NMR** (75 MHz, CDCl<sub>3</sub>): δ 138.0 (d, *J* = 6.5 Hz), 135.4 (d, *J* = 21.0 Hz), 134.2 (d, *J* = 22.5 Hz), 132.8, 132.1 (d, *J* = 14.8 Hz), 131.9, 131.6 (d, *J* = 7.8 Hz), 131.2, 129.0, 128.8, 128.3, 128.2, 114.0, 48.5 (d, *J* = 63.2 Hz), 37.4, 37.3, 32.8, 28.8, 23.8, 21.4, 21.3 (d, *J* = 7.5 Hz).

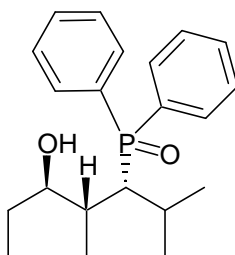
**<sup>31</sup>P NMR** (81 MHz, CDCl<sub>3</sub>): δ 31.6.

**IR** (KBr, cm<sup>-1</sup>): 2957 (m), 1438 (s), 1179 (vs), 116 (w), 700 (m), 553 (s).

**MS** (EI, 70 eV): 324 (11), 203 (24), 202 (100), 77 (29), 51 (13), 47 (21).

**HRMS**: calcd. 324.1643 (C<sub>21</sub>H<sub>25</sub>OP), found: 324.1624.

### Synthesis of (1*R*,2*R*)-2-[(1*R*)-1-diphenylphosphinoyl-2-methylpropyl]cyclopentanol (**26**)



Prepared from **25** (3.24 g, 10 mmol) according to the **TP5**. White solid, yield 2.22 g (65%).

**Mp.**: 220-220.5 °C

$[\alpha]_D^{20}$ : -65.5 (c 0.88, CH<sub>2</sub>Cl<sub>2</sub>).

**<sup>1</sup>H NMR** (300 MHz, CDCl<sub>3</sub>): δ 7.85-7.76 (m, 4H), 7.41-7.20 (m, 6H), 5.72 (s, 1H), 4.05 (m, 1H), 2.48 (d, *J* = 9.3 Hz, 1H), 2.12-2.05 (m, 2H), 1.93-1.91 (m, 1H), 1.56-1.53 (m, 1H), 1.50-1.43 (m, 4H), 1.14 (d, *J* = 7.8 Hz, 3H), 0.82 (d, *J* = 7.8 Hz, 3H).

$^{13}\text{C}$  NMR (75 MHz,  $\text{CDCl}_3$ ):  $\delta$  134.8 (d,  $J = 15.0$  Hz), 133.5 (d,  $J = 15.0$  Hz), 132.0, 131.8 (d,  $J = 8.5$  Hz), 131.7 (d,  $J = 8.5$  Hz), 131.6 (d,  $J = 10.9$  Hz), 131.2, 129.8 (d,  $J = 11.3$  Hz), 129.3, 129.2, 129.0, 128.0, 72.7, 47.9, 44.7 (d,  $J = 67.1$  Hz), 34.4, 32.5, 30.8, 26.9, 25.9, 21.7 (d,  $J = 7.8$  Hz).

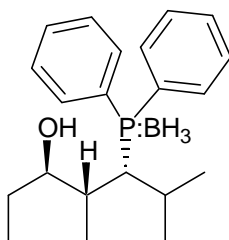
$^{31}\text{P}$  NMR (81 MHz,  $\text{CDCl}_3$ ):  $\delta$  38.2

IR (KBr,  $\text{cm}^{-1}$ ): 3367 (s), 2958 (s), 1438 (s), 1164 (s), 1089 (s), 718 (s), 545 (vs).

MS (EI, 70 eV): 258 (12), 243 (37), 203 (23), 202 (100), 201 (18).

HRMS: calcd. 342.1749 ( $\text{C}_{21}\text{H}_{27}\text{O}_2\text{P}$ ), found: 342.1752.

### Synthesis of (1*R*,2*R*)-2-[(1*R*)-1-diphenylphosphinyl-2-methylpropyl]cyclopentanol-borane complex (27)



Prepared from **26** (2.40 g, 7 mmol) according to the **TP6**. White solid, yield 2.28 g (96%).

**Mp.:** 110-112 °C

$[\alpha]_{\text{D}}^{20}$ : 14.6 (c 0.9,  $\text{CH}_2\text{Cl}_2$ ).

$^1\text{H}$  NMR (300 MHz,  $\text{CDCl}_3$ ):  $\delta$  7.85-7.17 (m, 4H), 7.36-7.29 (m, 6H), 3.49-3.47 (m, 1H), 3.00 (d,  $J = 21.7$  Hz, 1H), 1.78-1.70 (m, 2H), 1.49-1.43 (m, 2H), 1.30-1.21 (m, 3H), 0.97 (d,  $J = 11.4$  Hz, 3H), 0.92 (d,  $J = 11.4$  Hz, 3H).

$^{13}\text{C}$  NMR (75 MHz,  $\text{CDCl}_3$ ):  $\delta$  132.9, 131.7 (d,  $J = 7.8$  Hz), 131.6 (d,  $J = 8.5$  Hz), 130.3 (d,  $J = 5.0$  Hz), 130.2, 129.8 (d,  $J = 8.5$  Hz), 129.6, 129.1, 127.7, 127.6 (d,  $J = 5.0$  Hz), 127.5, 127.3, 87.6, 47.2, 43.5 (d,  $J = 52.3$  Hz), 43.2, 33.6, 32.7, 31.9, 27.4, 20.6, 19.1.

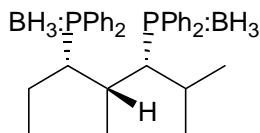
$^{31}\text{P}$  NMR (81 MHz,  $\text{CDCl}_3$ ):  $\delta$  18.4 (bs).

IR (KBr,  $\text{cm}^{-1}$ ): 3436 (s), 2961 (vs), 2402 (s), 1436 (vs), 1102 (s), 738 (vs).

MS (EI, 70 eV): 339 (50), 242 (28), 227 (48), 183 (45), 136 (100), 107 (52).

HRMS: calcd. 340.2127 ( $\text{C}_{21}\text{H}_{30}\text{BOP}$ ), found: 340.2136.

### Synthesis of [(1*S*,2*R*)-2-[(1*R*)-1-diphenylphosphinyl-2-methylpropyl]-cyclopentyl]-diphenylphosphine-bis-borane complex (28)



Prepared from **27** (1.70 g, 5 mmol) according to the **TP7**. White crystals, yield 1.36 g (52%).

**Mp.:** 205-206 °C

$[\alpha]_{\text{D}}^{20}$ : -149.4 (c 0.70,  $\text{CH}_2\text{Cl}_2$ ).

$^1\text{H}$  NMR (300 MHz,  $\text{CDCl}_3$ ):  $\delta$  8.38-8.33 (m, 2H), 8.14-8.11 (m, 2H), 8.00-7.94 (m, 4H), 7.73-7.46 (m, 12H), 3.74-3.62 (m, 2H), 3.10-2.95 (m, 1H), 2.15-1.95 (m, 1H), 1.90-1.40 (m, 12H), 1.20 (d,  $J = 16.1$  Hz, 3H), 1.01 (d,  $J = 14.2$  Hz, 3H).

$^{13}\text{C}$  NMR (75 MHz,  $\text{CDCl}_3$ ):  $\delta$  134.2, 34.1, 133.3, 133.2, 133.1, 133.0, 132.9, 131.6, 131.5, 131.3, 131.1, 129.3, 129.2, 129.0, 128.9, 128.7, 128.6, 47.7, 47.6, 39.9, 38.5, 31.1, 30.8, 29.0, 23.0, 22.5, 22.0, 20.8, 19.2, 19.1.

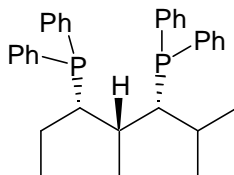
$^{31}\text{P}$  NMR (81 MHz,  $\text{CDCl}_3$ ):  $\delta$  17.3 (bs).

IR (KBr,  $\text{cm}^{-1}$ ): 2390 (s), 1436 (s), 1064 (s), 732 (vs), 697 (vs), 513 (m).

MS (EI, 70 eV): 508 (12), 419 (31), 418 (100), 310 (60), 185 (23), 183 (29), 108 (12).

HRMS: calcd. 522.2948 ( $\text{C}_{33}\text{H}_{42}\text{B}_2\text{P}_2$ ), found: 522.2962.

### Synthesis of [(1*S*,2*R*)-2-[(1*R*)-1-diphenylphosphinyl-2-methylpropyl]-cyclopentyl]-diphenylphosphine (29)



Prepared from **28** (522 mg, 1 mmol) according to the **TP8**. White foam, yield 484 mg (98%).

$[\alpha]_{\text{D}}^{20}$ : -4.8 (c 1.05,  $\text{CH}_2\text{Cl}_2$ ).

$^1\text{H}$  NMR (300 MHz,  $\text{CDCl}_3$ ):  $\delta$  7.51-7.13 (m, 20 H), 3.00-2.82 (m, 2H), 2.75-2.55 (m, 1H), 2.05-1.95 (m, 1H), 1.92-1.52 (m, 4H), 1.45-1.30 (m, 2H), 0.59 (d,  $J = 16.5$  Hz, 3H), 0.28 (d,  $J = 16.5$  Hz, 3H).

$^{13}\text{C}$  NMR (75 MHz,  $\text{CDCl}_3$ ):  $\delta$  139.3, 139.0, 138.6, 138.3, 138.2, 138.0, 135.4, 135.2, 134.3, 134.0, 133.6, 133.3, 133.1, 129.0, 128.5, 128.4, 128.2, 128.0, 127.9, 127.5, 41.4, 41.0 (d,  $J = 38$  Hz), 40.6 (d,  $J = 32$  Hz), 31.7, 31.5, 29.4, 24.5, 21.1, 18.4.

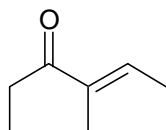
$^{31}\text{P}$  NMR (81 MHz,  $\text{CDCl}_3$ ):  $\delta$  1.09 (d,  $J = 1.5$  Hz), -15.3 (d,  $J = 1.5$  Hz).

IR (KBr,  $\text{cm}^{-1}$ ): 2954 (s), 1433 (s), 741 (s), 696 (vs), 506 (m).

MS (EI, 70 eV): 495 (4), 418 (25), 417 (100), 309 (59), 185 (15), 183 (14).

HRMS: calcd. 494.2292 ( $\text{C}_{33}\text{H}_{36}\text{P}_2$ ), found: 494.2275.

### Synthesis of 2-ethylidenecyclopentanone (34)



Prepared according to the **TP1** from cyclopentanone (126.0 g, 1.5 mol) and acetaldehyde (52.8 g, 1.2 mol). Colourless liquid, yield 23.7 g (18%).

**Bp.:** 65 °C (12 mbar).

$^1\text{H}$  NMR (300 MHz,  $\text{CDCl}_3$ ):  $\delta$  6.33-6.30 (m, 1H), 2.33-2.27 (m, 2H), 2.06-2.00 (m, 2H), 1.70-1.62 (m, 2H), 1.51 (dt,  $J_1 = 13.2$  Hz,  $J_2 = 2.1$  Hz, 3H).

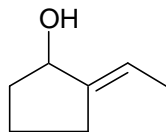
$^{13}\text{C}$  NMR (75 MHz,  $\text{CDCl}_3$ ):  $\delta$  207.1, 138.7, 132.4, 38.9, 26.8, 20.0, 14.5.

IR (KBr,  $\text{cm}^{-1}$ ): 2967 (s), 1721 (vs), 1656 (vs), 1230 (m), 1206 (s), 840 (w).

MS (EI, 70 eV): 110 (100), 95 (42), 82 (11), 67 (28), 54 (43), 53 (11).

HRMS: calcd. 110.0732 ( $\text{C}_7\text{H}_{10}\text{O}$ ), found: 110.0746.

### Synthesis of 2-ethylidenecyclopentanol (*rac*-32)



Prepared according to the **TP2** from 2-ethylidenecyclopentanone (**34**, 11.0 g, 100 mmol). Colourless liquid, yield 10.4 g (93%).

**Bp.:** 40-42 °C (0.8 mbar).

**<sup>1</sup>H NMR** (300 MHz, CDCl<sub>3</sub>): δ 5.53-5.45 (m, 1H), 4.30-4.27 (m, 1H), 2.45-2.20 (m, 2H), 2.15-2.03 (m, 2H), 1.95-1.76 (m, 2H), 1.58-1.52 (m, 3H).

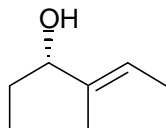
**<sup>13</sup>C NMR** (75 MHz, CDCl<sub>3</sub>): δ 146.8, 118.1, 75.7, 36.0, 27.2, 22.3, 14.9.

**IR** (KBr, cm<sup>-1</sup>): 3351 (s), 2960 (vs), 1713 (w), 1433 (m), 1084 (m).

**MS** (EI, 70 eV): 112 (62), 97 (100), 84 (32), 83 (37), 79 (31), 69 (30), 41 (25).

**HRMS:** calcd. 112.0888 (C<sub>7</sub>H<sub>12</sub>O), found: 112.0892.

### Synthesis of (*S*)-2-ethylidenecyclopentanol (**32**)



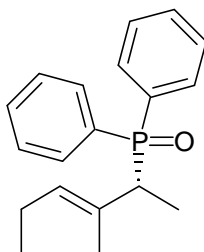
Prepared according to the **TP3** by the enzymatic kinetic resolution of racemic 2-ethylidenecyclopentanone (*rac*-**34**, 100 mmol), reaction time 3 h, reaction temperature 45 °C. The mixture after the reaction was separated by column chromatography on silica (pentane-ether 3:2). Colourless liquid, yield 5.26 g (47%), >99% *ee*.

**Chiral GC:** column TFA-cyclodextrine; 65 °C const. (*R*)-enantiomer 22.1 min, (*S*)-enantiomer 24.0 min.

**[α]<sub>D</sub><sup>20</sup>:** +231 (c 1.41, CH<sub>2</sub>Cl<sub>2</sub>).

The spectral data are identical to those from the racemic compound.

### Synthesis of 1-[(1*R*)-1-diphenylphosphinoethyl]cyclopentene (**35**)



Prepared according to the **TP4** from (*S*)-2-ethylidenecyclopentanol (**34**, 1.68 g, 15 mmol), reaction time 6 h, reaction temperature 80 °C. Yield 3.11 g (70%).

**Mp.:** 133-134 °C.

**$[\alpha]_D^{20}$ :** +276 (c 1.2, CH<sub>2</sub>Cl<sub>2</sub>).

**<sup>1</sup>H NMR** (300 MHz, CDCl<sub>3</sub>): δ 7.76-7.62 (m, 4H), 7.41-7.31 (m, 6H), 5.40 (s, 1H), 3.25-3.20 (m, 1H), 2.30-1.90 (m, 4H), 1.70-1.50 (m, 2H), 1.24 (dd,  $J_1 = 16.5$  Hz,  $J_2 = 14.4$  Hz, 3H).

**<sup>13</sup>C NMR** (75 MHz, CDCl<sub>3</sub>): δ 140.5, 140.4, 133.6, 133.4, 132.3, 132.2, 131.9, 131.8, 131.7-131.4 (m), 131.2, 129.6, 129.4, 129.2, 128.8, 128.4, 37.2 (d,  $J = 65.8$  Hz), 36.5, 32.7, 23.7, 23.5, 13.8.

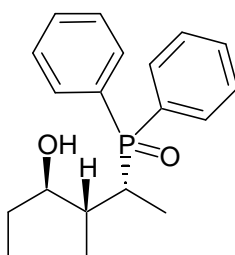
**<sup>31</sup>P NMR** (81 MHz, CDCl<sub>3</sub>): δ 34.0.

**IR** (KBr, cm<sup>-1</sup>): 3432 (m), 3056 (m), 1438 (s), 1181 (vs), 1118 (s), 720 (vs), 550 (vs), 537 (vs).

**MS** (EI, 70 eV): 296 (30), 203 (25), 202 (100), 201 (69), 171 (18), 155 (16), 77 (15).

**HRMS:** calcd. 296.1330 (C<sub>19</sub>H<sub>21</sub>OP), found: 296.1305.

### Synthesis of (1*R*,2*R*)-2-[(1*R*)-1-diphenylphosphinoyl-ethyl]cyclopentanol (37)



Prepared from **35** (2.96 g, 10 mmol) according to the **TP5**. White solid, yield 2.10 g (67%).

**Mp.:** 173-174 °C.

**$[\alpha]_D^{20}$ :** -31 (c 1.1, CH<sub>2</sub>Cl<sub>2</sub>).

**<sup>1</sup>H NMR** (300 MHz, CDCl<sub>3</sub>): δ 7.79-7.68 (m, 4H), 7.50-7.26 (m, 6H), 4.06-4.01 (m, 1H), 2.55-2.51 (m, 1H), 2.10-1.80 (m, 2H), 1.73-1.30 (m, 5H), 1.08 (dd,  $J_1 = 16.8$  Hz,  $J_2 = 7.5$  Hz, 3H).

**<sup>13</sup>C NMR** (75 MHz, CDCl<sub>3</sub>): δ 132.7, 132.1, 131.7-131.2 (m), 129.4-129.1 (m), 128.8, 128.7, 71, 4, 46.4 (d,  $J = 37.2$  Hz), 38.3, 34.0, 33.1, 21.7, 11.1.

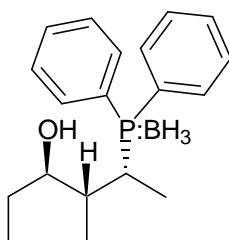
**<sup>31</sup>P NMR** (81 MHz, CDCl<sub>3</sub>): δ 41.7.

**IR** (KBr, cm<sup>-1</sup>): 3376 (s), 2959 (m), 1437 (s), 1159 (vs), 1119 (s), 722 (vs), 546 (vs).

**MS** (EI, 70 eV): 203 (8), 202 (100), 155 (4), 77 (2).

**HRMS:** calcd. 314.1436 (C<sub>19</sub>H<sub>23</sub>O<sub>2</sub>P), found: 314.1442.

### Synthesis of (1*R*,2*R*)-2-[(1*R*)-1-diphenylphosphinyl-ethyl]cyclopentanol-borane complex (38)



Prepared from **37** (2.20 g, 7 mmol) according to the **TP6**. White crystalline solid, yield 2.10 g (96%).

**Mp.:** 173-174 °C.

$[\alpha]_D^{20}$ : -42 (c 1.4, CH<sub>2</sub>Cl<sub>2</sub>).

**<sup>1</sup>H NMR** (300 MHz, CDCl<sub>3</sub>): δ 7.75-7.67 (m, 4H), 7.39-7.18 (m, 6H), 4.21-4.17 (m, 1H), 2.67-2.64 (m, 1H), 2.10-1.95 (m, 1H), 1.85-1.70 (m, 1H), 1.56-1.42 (m, 4H), 1.31-1.16 (m, 1H), 1.02 (dd,  $J_1 = 18$  Hz,  $J_2 = 8.5$  Hz, 3H).

**<sup>13</sup>C NMR** (75 MHz, CDCl<sub>3</sub>): δ 132.9, 132.8, 131.8-131.5 (m), 131.2, 131.0, 129.6, 129.4-129.1 (m), 128.9, 128.6, 74.0, 49.3, , 41.7 (d,  $J = 34.0$  Hz), 36.4, 33.2, 23.9, 11.0.

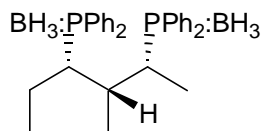
**<sup>31</sup>P NMR** (81 MHz, CDCl<sub>3</sub>): δ 22.6 (bs), 21.6 (bs).

**IR** (KBr, cm<sup>-1</sup>): 3413 (vs), 2951 (s), 2381 (vs), 1436 (vs), 1067 (s), 734 (s), 696 (vs).

**MS** (EI, 70 eV): 311 (100), 310 (29), 309 (27), 291 (22), 214 (30), 185 (61), 183 (35).

**HRMS**: calcd. 312.1814 (C<sub>21</sub>H<sub>26</sub>BOP), found: 312.1833.

**Synthesis of [(1S,2R)-2-[(1R)-1-diphenylphosphinyl-ethyl]-cyclopentyl]-diphenylphosphine-bis-borane complex (39)**



Prepared from **38** (1.56 g, 5 mmol) according to the **TP7**. White crystals, yield 1.33 g (54%).

**Mp.:** 206-207 °C

$[\alpha]_D^{20}$ : -183 (c 1.0, CH<sub>2</sub>Cl<sub>2</sub>).

**<sup>1</sup>H NMR** (300 MHz, CDCl<sub>3</sub>): δ 7.89-7.68 (m, 6H), 7.45-7.39 (m, 2H), 7.25-7.12 (m, 12H), 3.40-3.15 (m, 1H), 2.40-2.22 (m, 1H), 2.10-1.85 (m, 1H), 1.81-0.83 (m, 6H), 0.26 (dd,  $J_1 = 17.1$  Hz,  $J_2 = 6.3$  Hz, 3H).

**<sup>13</sup>C NMR** (75 MHz, CDCl<sub>3</sub>): δ 133.5, 133.1, 133.0, 132.9, 132.7-132.3, 131.6-131.1 (m), 130.7, 130.5, 129.3-128.9 (m), 50.1, 37.9 (d,  $J = 35.2$  Hz), 30.9, 29.2, 28.7 (d,  $J = 7.6$  Hz), 24.2, 16.3.

**<sup>31</sup>P NMR** (81 MHz, CDCl<sub>3</sub>): δ 24.0 (bs), 17.2 (bs).

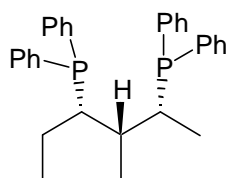
**IR** (KBr, cm<sup>-1</sup>): 2388 (vs), 2350 (s), 1437 (s), 1070 (s), 738 (vs), 697 (vs), 511 (s).

**MS** (EI, 70 eV): 479 (5), 389 (30), 281 (3), 185 (4), 183 (9).

**HRMS**: calcd. 494.2635 (C<sub>31</sub>H<sub>38</sub>B<sub>2</sub>P<sub>2</sub>), found: 479.2252 ([M-BH<sub>4</sub>]<sup>+</sup>).

**Synthesis of [(1S,2R)-2-[(1R)-1-diphenylphosphinyl-ethyl]cyclopentyl]diphenylphosphine (30).**





Prepared from **39** (495 mg, 1 mmol) according to the **TP8**. White foam, yield 452 mg (97%).

$[\alpha]_D^{20}$ : +3.8 (c 1.1, CH<sub>2</sub>Cl<sub>2</sub>).

<sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>): δ 7.53-7.19 (m, 20H), 2.94-2.92 (m, 1H), 2.90-2.87 (m, 1H), 2.05-1.95 (m, 1H), 1.78-1.71 (m, 2H), 1.50-1.05 (m, 4H), 0.68 (dd,  $J_1 = 9$  Hz,  $J_2 = 6.8$  Hz, 3H).

<sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>): δ 137.9, 137.8, 137.5, 137.3, 135.8, 135.6, 133.9, 133.7, 133.4, 132.6, 132.4, 131.7, 131.5, 127.7, 127.3, 127.2, 127.1-126.8 (m), 49.6 (d,  $J = 31.3$  Hz), 39.3 (d,  $J = 33.7$  Hz), 31.1, 30.5, 28.2, 22.0, 15.9.

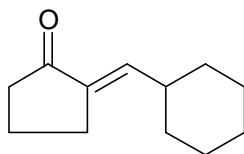
<sup>31</sup>P NMR (81 MHz, CDCl<sub>3</sub>): δ 1.45 (d,  $J = 8.1$  Hz), -15.0 (d,  $J = 8.1$  Hz).

IR (KBr, cm<sup>-1</sup>): 2957 (m), 1480 (m), 1433 (s), 740 (s), 697 (vs).

MS (EI, 70 eV): 390 (22), 389 (100), 281 (10), 185 (10), 183 (18).

HRMS: calcd. 466.1979 (C<sub>31</sub>H<sub>32</sub>P<sub>2</sub>), found: 466.1969.

### Synthesis of 2-cyclohexylmethylidenecyclopentanone (**40**)



Prepared according to the **TP1** from cyclopentanone (42.0 g, 500 mmol) and cyclohexanecarbaldehyde (44.8 g, 400 mmol). Colourless liquid, yield 25.6 g (36%).

**Bp.:** 72 °C (0.3 mbar).

<sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>): δ 6.31 (dt,  $J_1 = 9.6$  Hz,  $J_2 = 2.4$  Hz, 1H), 2.56-2.50 (m, 2H), 2.27-2.21 (m, 2H), 2.18-2.02 (m, 1H), 1.88-1.83 (m, 2H), 1.66-1.55 (m, 4H), 1.21-1.07 (m, 6H).

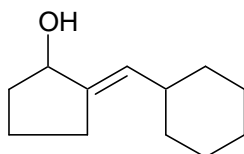
<sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>): δ 208.1, 141.2, 135.6, 41.0, 39.1, 36.0, 32.9, 32.1, 26.0, 25.9, 20.9, 20.2.

IR (KBr, cm<sup>-1</sup>): 2926 (vs), 2851 (s), 1720 (vs), 1650 (s), 1449 (m), 1193 (m).

MS (EI, 70 eV): 178 (65), 121 (10), 97 (100), 95 (26), 79 (30), 67 (31), 41 (21).

HRMS: calcd. 178.1358 (C<sub>12</sub>H<sub>18</sub>O), found: 178.1356.

### Synthesis of 2-cyclohexylmethylidenecyclopentanol (*rac*-**33**)



Prepared according to the **TP2** from 2-cyclohexylmethylidenecyclopentanone (**40**, 17.8 g, 100 mmol). Colourless liquid, yield 17.3 g (96%).

**Bp.:** 102-106 °C (0.8 mbar).

**<sup>1</sup>H NMR** (300 MHz, CDCl<sub>3</sub>): δ 5.33-5.28 (m, 1H), 4.30-4.27 (m, 1H), 2.29-2.27 (m, 1H), 1.96-1.53 (m, 10H), 1.18-1.14 (m, 6H).

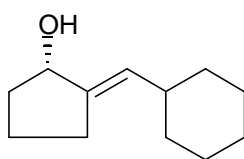
**<sup>13</sup>C NMR** (75 MHz, CDCl<sub>3</sub>): δ 144.3, 133.4, 76.0, 39.0, 35.8, 34.1, 33.1, 32.0, 29.0, 26.7, 25.7, 24.0.

**IR** (KBr, cm<sup>-1</sup>): 3400 (s), 2925 (vs), 2851 (s), 1713 (s), 1644 (m), 1448 (s), 1243 (m).

**MS** (EI, 70 eV): 162 (43), 119 (29), 98 (11), 97 (100), 91 (22), 80 (52).

**HRMS**: calcd. 180.1514 (C<sub>12</sub>H<sub>20</sub>O), found: 180.1520.

### Synthesis of (*S*)-2-cyclohexylmethylidenecyclopentanol (**33**)



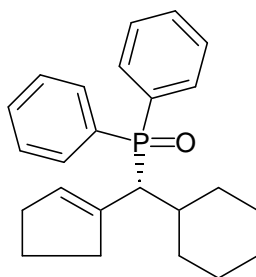
Prepared according to the **TP3** by the resolution of racemic 2-cyclohexylidenecyclopentanol (*rac*-**33**, 18.0 g, 100 mmol), reaction time 12 h, reaction temperature 45 °C. The mixture after the enzymatic kinetic resolution was separated by column chromatography on silica (pentane-ether 3:1). Colourless liquid, yield 8.64 g (48%), >99% *ee*.

**Chiral GC**: column TFA-cyclodextrine; 75°C const. (*R*)-enantiomer 36.1 min, (*S*)-enantiomer 31.4 min.

**[α]<sub>D</sub><sup>20</sup>**: +157 (c 1.4, CH<sub>2</sub>Cl<sub>2</sub>).

Spectral data are identical to those from the racemic compound.

### Synthesis of 1-[(*R*)-diphenylphosphinoyl-cyclohexyl-methyl]cyclopentene (**41**)



Prepared according to the **TP4** from (*S*)-2-cyclohexylidenecyclopentanol (**33**, 2.70 g, 15 mmol), reaction time 12 h, reaction temperature 80 °C. Yield 3.82 g (70%).

**Mp.:** 214-215 °C.

**[α]<sub>D</sub><sup>20</sup>**: +391 (c 1.6, CH<sub>2</sub>Cl<sub>2</sub>).

**<sup>1</sup>H NMR** (300 MHz, CDCl<sub>3</sub>): δ 7.81-7.78 (m, 2H), 7.63-7.57 (m, 2H), 7.40-7.31 (m, 3H), 7.27-7.24 (m, 3H), 5.57-5.54 (m, 1H), 3.02-2.96 (m, 1H), 2.30-1.88 (m, 5H), 1.58-1.54 (m, 6H), 1.05-0.95 (m, 6H).

$^{13}\text{C}$  NMR (75 MHz,  $\text{CDCl}_3$ ):  $\delta$  138.4, 135.7 (d,  $J = 37.5$  Hz), 134.5 (d,  $J = 32.5$  Hz), 132.4, 131.7, 131.5, 131.0 (d,  $J = 27.2$  Hz), 129.0, 128.8, 128.2, 128.1, 48.3 (d,  $J = 66.7$  Hz), 38.5, 38.4, 38.4, 37.1, 34.0, 32.7, 26.9, 25.8, 22.8.

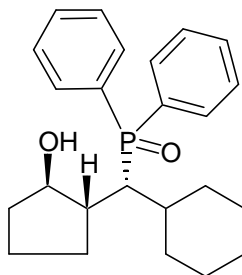
$^{31}\text{P}$  NMR (81 MHz,  $\text{CDCl}_3$ ):  $\delta$  31.3

IR (KBr,  $\text{cm}^{-1}$ ): 3436 (m), 2927 (s), 2851 (m), 1436 (m), 1182 (s), 698 (s), 550 (vs).

MS (EI, 70 eV): 364 (23), 282 (49), 281 (22), 203 (40), 202 (100), 201 (31).

HRMS: calcd. 364.1956 ( $\text{C}_{24}\text{H}_{29}\text{OP}$ ), found: 364.1953.

### Synthesis of (1*R*,2*R*)-2-[(*R*)-diphenylphosphinoyl-cyclohexylmethyl]cyclopentanol (43).



Prepared from **41** (3.64 g, 10 mmol) according to the **TP5**. White solid, yield 2.87 g (75%).

**Mp.:** 248-249 °C

$[\alpha]_{\text{D}}^{20}$ : -51.6 (c 0.76,  $\text{CH}_2\text{Cl}_2$ ).

$^1\text{H}$  NMR (300 MHz,  $\text{CDCl}_3$ ):  $\delta$  7.84-7.73 (m, 4H), 7.43-7.20 (m, 6H), 5.82 (s, 1H), 4.02-3.96 (m, 1H), 2.39-2.35 (m, 1H), 2.13-0.89 (m, 18H).

$^{13}\text{C}$  NMR (75 MHz,  $\text{CDCl}_3$ ):  $\delta$  133.4 (d,  $J = 38.1$  Hz), 132.2 (d,  $J = 38.3$  Hz), 130.6-130.3 (m), 130.1, 129.8, 129.6, 129.4, 127.9, 127.6-127.4 (m), 71.3, 46.5, 43.5 (d,  $J = 67.2$  Hz), 38.0, 36.6, 33.4, 32.1, 29.4, 27.7, 26.3, 25.4, 20.0.

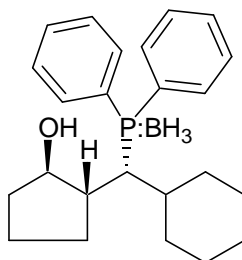
$^{31}\text{P}$  NMR (81 MHz,  $\text{CDCl}_3$ ):  $\delta$  39.3.

IR (KBr,  $\text{cm}^{-1}$ ): 3402 (s), 2929 (vs), 2853 (s), 1438 (s), 1166 (s), 720 (vs), 699 (vs), 546 (s).

MS (EI, 70 eV): 300 (17), 299 (26), 298 (100), 203 (11), 202 (58).

HRMS: calcd. 382.2062 ( $\text{C}_{24}\text{H}_{31}\text{O}_2\text{P}$ ), found: 383.2187 ( $[\text{M}+\text{H}]^+$ ).

### Synthesis of (1*R*,2*R*)-2-[(*R*)-diphenylphosphinyl-cyclohexylmethyl]cyclopentanol-borane complex (44).



Prepared from **43** (2.67 g, 7 mmol) according to the **TP6**. White solid, yield 2.55 g (96%).

**Mp.:** 261-262 °C (dec.).

$[\alpha]_{\text{D}}^{20}$ : +4.0 (c 0.90,  $\text{CH}_2\text{Cl}_2$ ).

$^1\text{H}$  NMR (300 MHz,  $\text{CDCl}_3$ ):  $\delta$  7.88-7.74 (m, 4H), 7.39-7.20 (m, 6H), 3.52-3.04 (m, 1H), 3.02 (d,  $J = 18.1$  Hz, 1H), 2.10-0.92 (m, 19H).

$^{13}\text{C}$  NMR (75 MHz,  $\text{CDCl}_3$ ):  $\delta$  133.2-133.0 (m), 131.3, 129.1-129.0 (m), 128.9, 76.3, 47.2, 40.0 (d,  $J = 37.2$  Hz), 34.2, 29.8, 29.7, 29.2, 29.1, 23.8, 23.6, 22.0, 20.5.

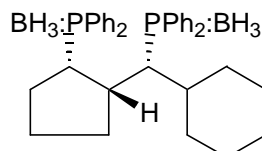
$^{31}\text{P}$  NMR (81 MHz,  $\text{CDCl}_3$ ):  $\delta$  17.6 (bs).

IR (KBr,  $\text{cm}^{-1}$ ): 3475 (vs), 3410 (vs), 2960 (vs), 2390 (vs), 2390 (s), 1437 (s), 1067 (s), 739 (vs).

MS (EI, 70 eV): 339 (100), 319 (28), 227 (59), 185 (89), 149 (99), 41 (40).

HRMS: calcd. 380.2440 ( $\text{C}_{24}\text{H}_{34}\text{BOP}$ ), found: 380.2452.

### Synthesis of [(1*S*,2*R*)-2-[(*R*)-diphenylphosphinyl-cyclohexylmethyl]-cyclopentyl]-diphenylphosphine-bis-borane complex (**45**)



Prepared from **44** (1.90 g, 5 mmol) according to the **TP7**. White crystals, yield 1.46 g (52%).

**Mp.**: 188-189 °C

$[\alpha]_{\text{D}}^{20}$ : -146 (c 0.95,  $\text{CH}_2\text{Cl}_2$ ).

$^1\text{H}$  NMR (300 MHz,  $\text{CDCl}_3$ ):  $\delta$  8.22-7.83 (m, 8H), 7.75-7.27 (m, 12H), 4.03-3.85 (m, 1H), 3.27-3.14 (m, 1H), 2.88-2.67 (m, 1H), 2.20-1.83 (m, 2H), 1.60-0.75 (m, 15H).

$^{13}\text{C}$  NMR (75 MHz,  $\text{CDCl}_3$ ):  $\delta$  133.7, 133.6, 133.3, 133.2, 132.7, 132.6, 132.5, 132.4, 131.8, 131.5, 131.4, 131.1, 130.7-130.4 (m), 129.3, 129.0, 128.8, 128.7, 44.7, 40.4, 40.2, 39.9, 39.3, 37.0, 36.5, 31.4, 30.4, 22.8, 21.7.

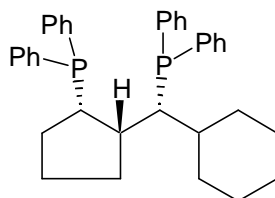
$^{31}\text{P}$  NMR (81 MHz,  $\text{CDCl}_3$ ):  $\delta$  16.4 (bs), 15.6 (bs).

IR (KBr,  $\text{cm}^{-1}$ ): 2400 (s), 1436 (s), 1101 (m), 1064 (s), 740 (s), 698 (vs), 516 (m).

MS (EI, 70 eV): 490 (39), 469 (100), 201 (25), 154 (36), 136 (34).

HRMS: calcd. 562.3261 ( $\text{C}_{36}\text{H}_{46}\text{B}_2\text{P}_2$ ), found: 562.3282.

### Synthesis of [(1*S*,2*R*)-2-[(*R*)-diphenylphosphinyl-cyclohexylmethyl]-cyclopentyl]-diphenylphosphine (**31**)



Prepared from **45** (560 mg, 1 mmol) according to the **TP8**. White foam, yield 502 mg (94%).

$[\alpha]_{\text{D}}^{20}$ : -11 (c 0.89,  $\text{CH}_2\text{Cl}_2$ ).

$^1\text{H}$  NMR (300 MHz,  $\text{CDCl}_3$ ):  $\delta$  7.24-7.12 (m, 20H), 2.93-2.78 (m, 2H), 2.67-2.55 (m, 1H), 2.06-0.60 (m, 17H).

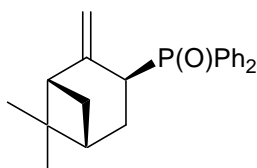
$^{13}\text{C}$  NMR (75 MHz,  $\text{CDCl}_3$ ):  $\delta$  138.2, 138.0, 137.7-137.4 (m), 137.0, 134.4, 134.1, 133.3, 133.0, 132.6, 132.3, 132.0, 131.8, 129.9, 127.5, 127.4, 127.0, 126.5, 41.3 (d,  $J = 34.5$  Hz), 40.6, 31.6 (d,  $J = 38.3$  Hz), 31.4, 29.3, 29.2, 28.7, 24.6, 24.5, 21.2, 21.1, 18.4.

$^{31}\text{P}$  NMR (81 MHz,  $\text{CDCl}_3$ ):  $\delta$  -3.4 (d,  $J = 12.9$  Hz), -17.3 (d,  $J = 12.9$  Hz).

**IR** (KBr,  $\text{cm}^{-1}$ ): 2956 (s), 1433 (s), 1092 (s), 1026 (s), 740 (s), 696 (vs).  
**MS** (EI, 70 eV): 418 (23), 417 (100), 309 (30), 185 (9), 183 (13).  
**HRMS**: calcd. 534.2605 ( $\text{C}_{36}\text{H}_{40}\text{P}_2$ ), found: 534.2593.

### 13. Syntheses of chiral phosphine ligands with a pinene scaffold.

**Synthesis of [(1*R*,3*S*,5*R*)-6,6-dimethyl-2-methylenebicyclo-[3.1.1]hept-3-yl](diphenyl)-phosphine oxide (50).**



Into a 250 mL Schlenk-flask under argon was placed 4-dimethylaminopyridine (7.60 g, 62 mmol) in dry toluene (120 mL). (-)-Myrtenol (9.50 g, 62 mmol) (Dragoco, >99% *ee*) was added and the solution cooled down to  $-30^\circ\text{C}$ . At this temperature, diphenylchlorophosphine (11.2 mL, 62 mmol) was added dropwise in 5 min. The mixture was allowed to reach room temperature and heated at  $100^\circ\text{C}$  for 48 h, then filtered hot through a pad of Celite, and the solid was washed with hot toluene (50 mL). The filtrate evaporated *in vacuo*, the residue filtered off and washed with ether. Yield 20.8 g (90%), white crystalline solid.

**Mp.:** 189.5-190°C.

$[\alpha]_{\text{D}}^{20}$ : -35.0 (c 1.05,  $\text{CH}_2\text{Cl}_2$ ).

**$^1\text{H}$  NMR** (300 MHz,  $\text{CDCl}_3$ ):  $\delta$  7.88-7.82 (m, 4 H), 7.50-7.43 (m, 6 H), 4.56 (d,  $J = 3.4\text{ Hz}$ , 1 H), 3.91 (s, 1 H), 3.64 (bs, 1 H), 2.41-1.94 (m, 6 H), 1.24 (s, 3 H), 0.77 (s, 3 H).

**$^{13}\text{C}$  NMR** (75 MHz,  $\text{CDCl}_3$ ):  $\delta$  145.4 (d,  $J = 8.5\text{ Hz}$ ), 134.5 (d,  $J = 10.0\text{ Hz}$ ), 133.2 (d,  $J = 13.2\text{ Hz}$ ), 132.2 (d,  $J = 8.5\text{ Hz}$ ), 131.7 (m), 131.5 (d,  $J = 8.5\text{ Hz}$ ), 129.1 (d,  $J = 11.2\text{ Hz}$ ), 128.6 (d,  $J = 11.2\text{ Hz}$ ), 112.3 (d,  $J = 7.6\text{ Hz}$ ), 52.0, 41.0, 39.9, 34.9 (d,  $J = 67.1\text{ Hz}$ ), 26.9, 26.5, 26.1, 21.7.

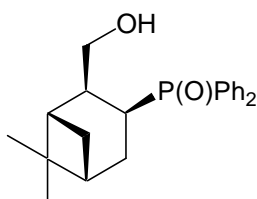
**$^{31}\text{P}$  NMR** (81 MHz,  $\text{CDCl}_3$ ):  $\delta$  37.0.

**IR** (KBr,  $\text{cm}^{-1}$ ):  $\tilde{\nu}$  3435 (bs), 3054 (w), 2981 (m), 2920 (s), 1631 (w), 1437 (s), 1174 (s), 1116 (s), 720 (s), 701 (vs), 538 (s), 606 (m).

**MS** (EI, 70 eV) *m/z* (%): 155 (19), 201 (68), 202 (100), 203 (76), 267 (33), 293 (22), 335 (29), 336 (28).

**HRMS**: calcd. 336.1643 ( $\text{C}_{22}\text{H}_{25}\text{OP}$ ), found: 336.1647.

**Synthesis of (1*S*,2*S*,3*S*,5*R*)[3-(Diphenyl-phosphinoyl)-6,6-dimethyl-bicyclo[3.1.1]hept-2-yl]-methanol (52).**



The phosphine oxide **50** (8.0 g, 20 mmol) was dissolved under argon in 0.5 M THF solution of 9-BBN (Aldrich, 50 mL, 25 mmol) and the mixture was heated at  $70^\circ\text{C}$  in a sealed tube for

12 h. Into a 0.5 L 3-necked flask was placed the dried solution of *meta*-chloroperbenzoic acid (25 g, 106 mmol, 70-75% Acros) in CH<sub>2</sub>Cl<sub>2</sub> (250 mL), the flask was cooled to 15°C in an acetone-dry ice cooling bath and the solution of the hydroborated phosphine oxide was added there at such a rate that the temperature did not exceed 20°C. After the end of the addition, the mixture was stirred for 1 h and filtered. The filtrate was stirred for 15 min with the solution of 80 g Na<sub>2</sub>S<sub>2</sub>O<sub>5</sub> in 200 mL H<sub>2</sub>O, the layers separated and the organic phase washed twice with 100 mL portions of 2 M NaOH, then with saturated brine, dried (Na<sub>2</sub>SO<sub>4</sub>) and evaporated. The semi-solid residue was stirred 24 h with ether (100 mL), the precipitate was filtered off, washed with ether and dried *in vacuo*. Yield 5.65 g (67%), white solid.

**Mp.:** 185.5-186 °C

**[α]<sub>D</sub><sup>20</sup>:** 56.6 (c 0.66, CH<sub>2</sub>Cl<sub>2</sub>).

**<sup>1</sup>H NMR** (300 MHz, CDCl<sub>3</sub>): 7.94-7.82 (m, 2 H), 7.80-7.67 (m, 2 H), 7.50-7.23 (m, 6 H), 4.81 (bs, 1 H), 3.83 (bs, 1 H), 3.52-3.25 (m, 2H), 2.58 (bs, 1 H), 2.27 (bs, 1 H), 2.12-1.90 (m, 2 H), 1.87-1.65 (m, 3 H), 1.19 (s, 3 H), 0.98 (s, 3 H).

**<sup>13</sup>C NMR** (75 MHz, CDCl<sub>3</sub>): δ 135.9, 134.6, 134.2, 132.9, 132.0, 131.7, 131.1 (d, *J* = 8.7 Hz), 130.4 (d, *J* = 8.7 Hz), 129.5 (d, *J* = 11.0 Hz), 129.1 (d, *J* = 11.0 Hz), 89.0, 65.4 (d, *J* = 12.0 Hz), 46.1, 41.5 (d, *J* = 3.8 Hz), 40.0 (d, *J* = 55.0 Hz), 39.5, 29.4, 29.0, 28.7, 28.5, 27.0, 21.3.

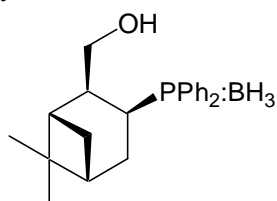
**<sup>31</sup>P NMR** (81 MHz, CDCl<sub>3</sub>): δ 39.1.

**IR** (KBr, cm<sup>-1</sup>):  $\tilde{\nu}$  3370 (bs), 2882 (s), 1437 (s), 1162 (s), 720 (s), 700 (s), 538 (vs), 1117 (m).

**MS** (EI, 70 eV) *m/z* (%): 155 (19), 201 (68), 202 (100), 203 (76), 267 (33), 293 (22), 335 (29), 336 (28).

**HRMS:** calcd. 354.1749 (C<sub>22</sub>H<sub>27</sub>O<sub>2</sub>P), found: 355.1825 [M+H]<sup>+</sup>.

### Synthesis of (1*S*,2*S*,3*S*,5*R*)[3-(Diphenylphosphanyl)-6,6-dimethyl-bicyclo[3.1.1]hept-2-yl]-methanol-borane complex (53).



Prepared from compound **52** (3.54 g, 10 mmol) according to the **TP6**. Yield 3.34 g (95%), white viscous foam.

**[α]<sub>D</sub><sup>20</sup>:** +86.8 (c 1.15, CH<sub>2</sub>Cl<sub>2</sub>).

**<sup>1</sup>H NMR** (300 MHz, CDCl<sub>3</sub>): 7.82-7.72 (m, 2 H), 7.61-7.52 (m, 2 H), 7.41-7.32 (m, 3 H), 7.27-7.18 (m, 3 H), 3.55-3.35 (m, 2 H), 2.61 (bs, 1 H), 2.17-2.00 (m, 2 H), 1.94-1.77 (m, 2 H), 1.43-0.99 (m, 4 H), 1.12 (s, 3 H), 0.95 (s, 3 H).

**<sup>13</sup>C NMR** (75 MHz, CDCl<sub>3</sub>): δ 132.8 (d, *J* = 8.8 Hz), 132.3 (d, *J* = 8.8 Hz), 131.8, 131.6, 131.1, 129.3 (d, *J* = 4.7 Hz), 129.2 (d, *J* = 4.7 Hz), 128.8, 71.1 (d, *J* = 5.6 Hz), 48.5, 48.4, 41.1, 38.1, 33.8, 33.3, 32.5, 27.4, 24.1.

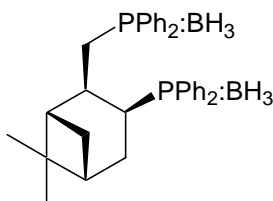
**<sup>31</sup>P NMR** (81 MHz, CDCl<sub>3</sub>): δ 21.0 (bs).

**IR** (KBr, cm<sup>-1</sup>):  $\tilde{\nu}$  3434 (s, bs), 2932 (s), 2387 (m), 1437 (s), 1105 (vs), 1070 (vs), 1027 (s), 740 (m), 695 (vs).

**MS** (EI, 70 eV) *m/z* (%): 40 (48), 108 (55), 183 (100), 185 (41), 186 (69), 213 (80), 267 (85).

**HRMS:** calcd. 352.2127 (C<sub>22</sub>H<sub>30</sub>O<sub>2</sub>P), found: 351.2047 ([M-H]<sup>+</sup>).

### Synthesis of (1*S*,2*S*,3*S*,5*R*)-3-(diphenylphosphino)-6,6-dimethylbicyclo[3.1.1]hept-2-yl]-methyl}(diphenyl)-phosphine bis-borane complex (54).



Bis-phosphine borane **54** was synthesized from **53** (1.76 g, 5 mmol) according to the Typical Procedure **TP7**. The residue after the solvent evaporation was quickly dissolved in ether (25 mL). In some minutes, crystallization of the product started, after 12 h the crystals were filtered off, washed with small amount of ether and dried *in vacuo*. Yield 1.28 g (48%), colorless crystals.

**Mp.:** 195.5-196 °C.

$[\alpha]_D^{20}$ : -47.3 (c 0.69, CH<sub>2</sub>Cl<sub>2</sub>).

**<sup>1</sup>H NMR** (300 MHz, CDCl<sub>3</sub>): δ 7.90-7.80 (m, 2H), 7.62-7.53 (m, 2H), 7.52-7.44 (m, 2H), 7.33-7.09 (m, 10H), 7.10-6.98 (m, 2H), 6.86-6.73 (m, 2H), 3.58-3.35 (m, 1H), 3.13-2.81 (m, 2H), 2.25-2.00 (m, 1H), 1.99-1.86 (m, 1H), 1.77 (bs, 1H), 1.64 (bs, 1H), 1.20 (d, *J* = 10.3 Hz), 1.09 (s, 1H), 0.87 (s, 3H), 0.71 (s, 1H), 0.50 (s, 3H).

**<sup>13</sup>C NMR** (75 MHz, CDCl<sub>3</sub>): δ 133.5 (d, *J* = 9.4 Hz), 133.0, 132.9, 132.8, 132.7, 132.1, 131.8, 131.7, 131.6, 131.3, 131.0, 130.9-130.7 (m), 130.2 (d, *J* = 10.3 Hz), 129.9 (d, *J* = 9.7 Hz), 129.5, 129.1, 129.0, 128.2, 44.2, 40.7 (d, *J* = 8.5 Hz), 39.1, 37.4, 29.0, 28.5, 27.9, 27.5, 27.2, 23.0.

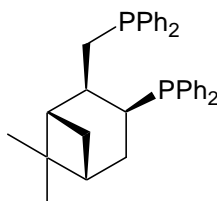
**<sup>31</sup>P NMR** (81 MHz, CDCl<sub>3</sub>): δ 17.4 (bs), 19.0 (bs).

**IR** (KBr, cm<sup>-1</sup>):  $\tilde{\nu}$  2919 (m), 2383 (s), 2401 (s), 1437 (s), 1106 (m), 1054 (m), 739 (s), 698 (vs), 500 (m).

**MS** (EI, 70 eV) *m/z* (%): 183 (24), 185 (14), 262 (10), 429 (100), 430 (30), 519 (17).

**HRMS**: calcd. 534.2948 (C<sub>34</sub>H<sub>42</sub>B<sub>2</sub>P<sub>2</sub>), found: 534.2926.

#### Synthesis of (1*S*,2*S*,3*S*,5*R*)-3-(diphenylphosphino)-6,6-dimethylbicyclo[3.1.1]hept-2-yl]-methyl}(diphenyl)-phosphine (**51**).



Bis-phosphine borane **54** (535 mg, 1 mmol) was deprotected to furnish **51** according to the Typical Procedure **TP8** (heating at 105 °C for 2 h). Yield 487 mg (96%), glassy foam.

$[\alpha]_D^{20}$ : 4.0 (c 0.75, CH<sub>2</sub>Cl<sub>2</sub>).

**<sup>1</sup>H NMR** (300 MHz, CDCl<sub>3</sub>): δ 7.55-7.47 (m, 2H), 7.45-7.35 (m, 2H), 7.33-7.23 (m, 2H), 7.22-7.10 (m, 10H), 7.10-7.00 (m, 2H), 6.84-6.74 (m, 2H), 3.22 (t, *J* = 9.1 Hz, 1H), 2.65 (t, *J* = 13.1 Hz, 1H), 2.54-2.40 (m, 2H), 2.32-2.21 (m, 1H), 2.14-2.03 (m, 1H), 1.82-1.71 (m, 1H), 1.69-1.58 (m, 1H), 1.28 (d, *J* = 9.8 Hz, 1H), 1.08 (s, 3H), 1.04 (s, 3H).

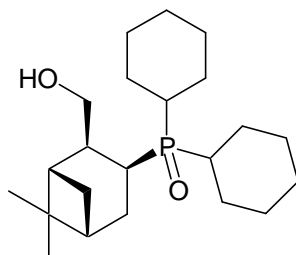
**<sup>13</sup>C NMR** (75 MHz, CDCl<sub>3</sub>): δ 138.8 (d, *J* = 12.9 Hz), 137.9 (d, *J* = 12.6 Hz), 137.1 (d, *J* = 13.5 Hz), 136.7 (d, *J* = 14.7 Hz), 133.3 (d, *J* = 20.8 Hz), 132.1, 131.8, 131.6, 128.1-126.7 (m), 43.6 (d, *J* = 13.5 Hz), 40.1, 38.6-38.3 (m), 38.2, 30.3-29.2 (m), 27.1-26.6 (m), 26.6 (d, *J* = 31.7 Hz), 22.2.

**<sup>31</sup>P NMR** (81 MHz, CDCl<sub>3</sub>): δ 15.7 (d, *J* = 3.2 Hz), -16.3 (d, *J* = 3.2 Hz).

**IR** (KBr, cm<sup>-1</sup>):  $\tilde{\nu}$  2929 (vs), 2854 (m), 2371 (w), 1448 (w), 1064 (w).

**MS** (EI, 70 eV)  $m/z$  (%): 201 (29), 262 (24), 276 (20), 321 (21), 429 (100), 430 (29).  
**HRMS**: calcd. 506.2292 (C<sub>34</sub>H<sub>36</sub>P<sub>2</sub>), found: 506.2288.

**Synthesis of [(1*S*,2*S*,3*S*,5*R*)-3-(dicyclohexylphosphinoyl)-6,6-dimethyl-bicyclo[3.1.1]hept-2-yl]-methanol (55).**



According to the Typical Procedure **TP9**, compound **52** (2.83 g, 8 mmol) was reduced into the cyclohexyl adduct **55**. Yield 2.87 g (98%), white solid.

**Mp.**: 164-165°C

$[\alpha]_D^{20}$ : 12.9 (c 1.35, CH<sub>2</sub>Cl<sub>2</sub>).

**<sup>1</sup>H NMR** (300 MHz, CDCl<sub>3</sub>): δ 6.05 (bs, 1H), 3.92 (bs, 1H), 3.66-3.48 (m, 1H), 3.00-2.78 (m, 1H), 2.59 (bs, 1H), 2.31-1.05 (m, 36H), 0.94 (s, 3H).

**<sup>13</sup>C NMR** (75 MHz, CDCl<sub>3</sub>): δ 65.8, 46.3, 42.7, 39.7, 39.1, 37.8, 37.0, 35.6, 34.8, 28.3, 27.3, 27.2-24.9 (m), 20.5.

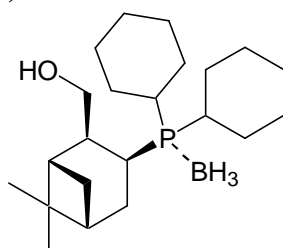
**<sup>31</sup>P NMR** (81 MHz, CDCl<sub>3</sub>): δ 62.0

**IR** (KBr, cm<sup>-1</sup>):  $\tilde{\nu}$  3436 (m, bs), 2929 (vs), 2854 (m), 2371 (w), 1448 (w), 1064 (w).

**MS** (EI, 70 eV)  $m/z$  (%): 214 (45), 241 (30), 267 (31), 335 (22), 283 (32), 336 (100), 337 (33).

**HRMS**: calcd. 366.2688 (C<sub>22</sub>H<sub>40</sub>PO<sub>2</sub>), found: 367.2767([M+H]<sup>+</sup>).

**Synthesis of [(1*S*,2*S*,3*S*,5*R*)-3-(dicyclohexylphosphoryl)-6,6-dimethylbicyclo[3.1.1]hept-2-yl]methanol borane complex (56).**



Prepared from compound **55** (2.58 g, 7 mmol) according to the **TP6**. Yield 2.40 g (94%), white viscous foam.

$[\alpha]_D^{20}$ : 2.6 (c 0.91, CH<sub>2</sub>Cl<sub>2</sub>).

**<sup>1</sup>H NMR** (300 MHz, CDCl<sub>3</sub>): δ 4.01-3.92 (m, 1H), 3.80-3.70 (m, 1H), 3.00-2.80 (m, 1H), 2.55-2.37 (m, 1H), 2.31-1.06 (m, 33H), 1.01 (s, 3H).

**<sup>13</sup>C NMR** (75 MHz, CDCl<sub>3</sub>): δ 63.3, 49.3, 43.5, 41.3, 40.0, 37.1, 33.2, 32.8, 32.4, 28.8, 28.0, 27.7, 27.2-27.0 (m), 25.2, 21.3, 21.0, 20.4.

**<sup>31</sup>P NMR** (81 MHz, CDCl<sub>3</sub>): δ 17.2 (bs).

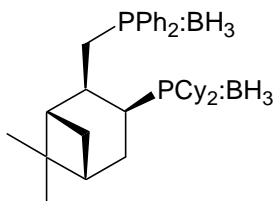
**IR** (KBr, cm<sup>-1</sup>):  $\tilde{\nu}$  3435 (s, bs), 2930 (vs), 2380 (m), 1634 (w, bs), 1449 (m), 1070 (m).

**MS** (EI, 70 eV)  $m/z$  (%): 117 (31), 170 (35), 198 (47), 225 (35), 279 (39), 319 (49), 333 (58), 334 (53), 361 (100), 377 (77).

**HRMS**: calcd. 364.3066 (C<sub>22</sub>H<sub>41</sub>BOP), found: 363.3014 ([M-H]<sup>+</sup>).

**Synthesis of (1*S*,2*S*,3*S*,5*R*)-dicyclohexyl{(2-[(diphenyl-phosphino)-methyl]-6,6-dimethylbicyclo-[3.1.1]hept-3-yl)}phosphine bis-borane complex (57).**





Bis-phosphine borane **57** was synthesized from **56** (1.83 g, 5 mmol) according to the Typical Procedure **TP7**. The residue after evaporation of the filtrate was dissolved in dichloromethane (10 mL). Methanol (50 mL) was added and the solution was concentrated on rotary evaporator to a half volume and left at 0°C. After 12 h, the precipitate was filtered off, washed with small amount of ether and dried *in vacuo*. Yield 1.20 g (44%), colorless crystals.

**Mp.**: 204-205°C (dec.).

**[ $\alpha$ ]<sub>D</sub><sup>20</sup>**: 14.4 (c 0.73, CH<sub>2</sub>Cl<sub>2</sub>).

**<sup>1</sup>H NMR** (300 MHz, CDCl<sub>3</sub>):  $\delta$  7.98-7.88 (m, 2H), 7.68-7.58 (m, 2H), 7.51-7.42 (m, 3H), 7.35-7.23 (m, 3H), 3.68-3.42 (m, 1H), 3.09-2.91 (m, 1H), 2.43-2.14 (m, 4H), 1.91-0.57 (m, 31H), 0.53-0.29 (m, 1H).

**<sup>13</sup>C NMR** (75 MHz, CDCl<sub>3</sub>):  $\delta$  132.7 (d,  $J = 8.3$  Hz), 131.9, 131.2, 131.1, 130.4, 129.9 (d,  $J = 9.6$  Hz), 129.7, 129.0, 129.0 (d,  $J = 9.6$  Hz), 44.8, 41.0, 39.3, 37.4, 34.7 (d,  $J = 32.0$  Hz), 32.7 (d,  $J = 32.0$  Hz), 28.2-25.8 (m), 23.4, 22.0-21.3 (m).

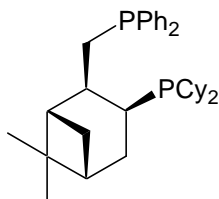
**<sup>31</sup>P NMR** (81 MHz, CDCl<sub>3</sub>):  $\delta$  16.8 (bs), 28.7 (bs).

**IR** (KBr, cm<sup>-1</sup>):  $\tilde{\nu}$  2930 (vs), 2853 (m), 2378 (s), 1437 (m), 1070 (m), 738 (m), 695 (m)

**MS** (EI, 70 eV)  $m/z$  (%): 183 (7), 435 (100), 436 (27), 530 (14), 531 (42), 532 (19).

**HRMS**: calcd. 546.8887 (C<sub>34</sub>H<sub>54</sub>B<sub>2</sub>P<sub>2</sub>), found: 531.3467 ([M-BH<sub>4</sub>]<sup>+</sup>).

### Synthesis of (*1S,2S,3S,5R*)-dicyclohexyl{(2-[(diphenyl-phosphino)-methyl]-6,6-dimethylbicyclo-[3.1.1]hept-3-yl}phosphine (**58**).



Bis-phosphine borane **57** (550 mg, 1 mmol) was deprotected to **58** according to the Typical Procedure **TP8** (heating at 105 °C for 2 h). Yield 497 mg (96%), viscous foam.

**[ $\alpha$ ]<sub>D</sub><sup>20</sup>**: 4.5 (c 0.93, CH<sub>2</sub>Cl<sub>2</sub>).

**<sup>1</sup>H NMR** (300 MHz, CDCl<sub>3</sub>):  $\delta$  7.64-7.52 (m, 2H), 7.47-7.35 (m, 2H), 7.35-7.21 (m, 3H), 7.20-7.10 (m, 3H), 3.40-3.20 (m, 1H), 2.60-2.23 (m, 3H), 2.22-2.08 (m, 1H), 1.98-1.81 (m, 1H), 1.80-0.46 (m, 32H).

**<sup>13</sup>C NMR** (75 MHz, CDCl<sub>3</sub>):  $\delta$  138.8 (d,  $J = 12.3$  Hz), 137.4 (d,  $J = 13.8$  Hz), 133.3 (d,  $J = 20.8$  Hz), 131.7 (d,  $J = 18.8$  Hz), 128.2-126.8 (m), 43.4 (d,  $J = 12.3$  Hz), 40.8-39.7 (m), 38.0, 32.8-32.1 (m), 29.7 (d,  $J = 17.6$  Hz), 29.0 (d,  $J = 12.3$  Hz), 28.9-28.4 (m), 28.0 (d,  $J = 10.3$  Hz), 27.1, 27.0-26.0 (m), 25.4 (d,  $J = 17.0$  Hz).

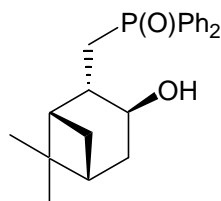
**<sup>31</sup>P NMR** (81 MHz, CDCl<sub>3</sub>):  $\delta$  -3.4 (s), -17.4 (s).

**IR** (KBr, cm<sup>-1</sup>):  $\tilde{\nu}$  2923 (vs), 2849 (s), 1447 (m), 1434 (m), 1262 (m), 1096 (m), 1027 (m), 738 (s), 696 (s).

**MS** (EI, 70 eV)  $m/z$  (%): 41(5), 55 (7), 183 (6), 185 (5), 435 (100), 436 (26), 437 (4), 451 (8).

**HRMS**: calcd. 518.3231 (C<sub>34</sub>H<sub>48</sub>P<sub>2</sub>), found: 518.3222.

### Synthesis of (1*S*,2*R*,3*S*,5*R*)-2-(diphenyl-phosphinoylmethyl)-6,6-dimethyl-bicyclo[3.1.1]-heptan-3-ol (59).



4-Dimethylaminopyridine (10.2 g, 84 mmol) was placed into a 250 mL Schlenk-flask and dissolved under argon in dry toluene (100 mL). *Trans*-pinocarveol (**47**) (12.7 g, 84 mmol) was added, mixture cooled to  $-30\text{ }^{\circ}\text{C}$ , and at this temperature diphenyl chlorophosphine (15.2 mL, 84 mmol) was added dropwise in 5 min. The mixture was allowed to reach ambient temperature and heated at  $80\text{ }^{\circ}\text{C}$  for 4 h.  $^{31}\text{P}$  NMR showed complete rearrangement (diphenylphosphinite: 126 ppm, diphenylphosphine oxide: 29 ppm). The hot mixture was filtered through a pad of Celite and the filter cake washed with toluene. The filtrate was concentrated to about 70 mL and borane-dimethyl sulfide complex (12 mL, 120 mmol) was added carefully. The solution was heated at  $50\text{ }^{\circ}\text{C}$  for 6 h, cooled down and carefully poured into a 1 L Erlenmeyer flask with methanol (70 mL). After 4 h, the solution was evaporated *in vacuo* and the residue redissolved in dichloromethane (80 mL). *m*-Chloroperbenzoic acid (70%, 25 g, 106 mmol) was dissolved separately in dichloromethane (200 mL), the solution was dried over  $\text{MgSO}_4$  and placed into 0.5 L 2-necked flask with a dropping funnel and a thermometer. The flask was immersed into acetone-dry ice cooling bath, and the solution of the hydroborated adduct was added slowly so that the temperature did not exceed  $15\text{ }^{\circ}\text{C}$ . After the completion of the addition, the mixture was stirred for 1 h and filtered. The filtrate was stirred with the solution of  $\text{Na}_2\text{S}_2\text{O}_5$  (80 g in 200 mL)  $\text{H}_2\text{O}$  for 10 min, the layers separated and the organic phase washed twice with 2 M NaOH (100 mL), then with saturated brine, dried and evaporated. The semi-solid residue was stirred 24 h with ether (200 mL), the precipitate was filtered off, washed with ether and dried *in vacuo*. Yield 18.4 g (62%), white solid.

**Mp.:** 200-200.5 $^{\circ}\text{C}$ .

**$[\alpha]_{\text{D}}^{20}$ :**  $-4.2$  (c 0.75,  $\text{CHCl}_3$ ).

**$^1\text{H}$  NMR** (300 MHz,  $\text{CDCl}_3$ ):  $\delta$  7.71-7.63 (m, 4H), 7.50-7.36 (m, 6H), 5.56 (bs, 1H), 4.34-4.24 (m, 1H), 3.64 (bs, 1H), 2.56-2.38 (m, 2H), 2.29-2.13 (m, 2H), 1.94-1.86 (m, 1H), 1.14 (s, 3H), 0.99 (s, 1H), 0.96 (s, 1H), 0.91 (s, 3H).

**$^{13}\text{C}$  NMR** (75 MHz,  $\text{CDCl}_3$ ):  $\delta$  134.6, 133.2, 132.7, 132.4-132.3 (m), 131.5 (d,  $J = 9.2$  Hz), 130.8 (d,  $J = 9.2$  Hz), 129.3 (m), 129.1 (m), 70.2, 51.3 (d,  $J = 14.4$  Hz), 48.3, 41.8, 38.7, 38.0 (d,  $J = 69.2$  Hz), 37.0, 34.5, 27.9, 24.2.

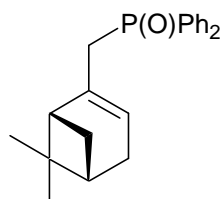
**$^{31}\text{P}$  NMR** (81 MHz,  $\text{CDCl}_3$ ):  $\delta$  36.0.

**IR** (KBr,  $\text{cm}^{-1}$ ):  $\tilde{\nu}$  3351 (bs), 1438 (s), 1173 (vs), 1120 (s), 740 (vs), 546 (s).

**MS** (EI, 70 eV)  $m/z$  (%): 155 (20), 201 (78), 202 (100), 215 (32), 311 (57).

**HRMS:** calcd. 354.1749 ( $\text{C}_{22}\text{H}_{28}\text{O}_2\text{P}$ ), found: 355.1809 ( $[\text{M}+\text{H}]^+$ ).

### Synthesis of {[(1*R*,5*S*)-6,6-dimethylbicyclo[3.1.1]hept-2-en-2-yl]methyl}-(diphenyl)-phosphine oxide (48).



The synthesis and the rearrangement of diphenylphosphinite **47a** was performed as described for the synthesis of **59** using one-tenth of the amounts of the reagents. The mixture after the rearrangement reaction was filtered and the solvent was evaporated *in vacuo*. The residue was purified by column chromatography (CH<sub>2</sub>Cl<sub>2</sub>-Et<sub>2</sub>O 1:1). White highly hygroscopic solid, yield 2.06 g (73%).

**Mp.**: 50-52°C.

**[α]<sub>D</sub><sup>20</sup>**: -10.1 (c 0.85, CH<sub>2</sub>Cl<sub>2</sub>).

**<sup>1</sup>H NMR** (300 MHz, CDCl<sub>3</sub>): δ 7.73-7.63 (m, 4H), 7.43-7.30 (m, 6H), 5.30-5.25 (m, 1H), 3.07-2.95 (m, 2H), 2.15-2.02 (m, 2H), 1.90-1.82 (m, 1H), 1.08 (s, 3H), 0.86 (s, 1H), 0.83 (s, 1H), 0.62 (s, 3H).

**<sup>13</sup>C NMR** (75 MHz, CDCl<sub>3</sub>): δ 138.6 (d, *J* = 11.0 Hz), 134.5 (d, *J* = 28.2 Hz), 133.2 (d, *J* = 28.2 Hz), 131.8, 131.4, 131.3, 131.2, 128.9-128.6 (m), 122.3 (d, *J* = 11.0 Hz), 47.4, 40.5, 39.8, 38.9, 38.4, 31.9 (d, *J* = 9.1 Hz), 26.5, 21.4, 134.6, 133.2, 132.7, 132.4-132.3 (m), 131.5 (d, *J* = 9.2 Hz), 130.8 (d, *J* = 9.2 Hz), 129.3 (m), 129.1 (m), 70.2, 51.3 (d, *J* = 14.4 Hz), 48.3, 41.8, 38.7, 38.0 (d, *J* = 68.8 Hz), 37.0, 34.5, 27.9, 24.2.

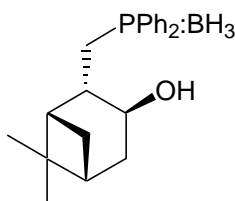
**<sup>31</sup>P NMR** (81 MHz, CDCl<sub>3</sub>): δ 29.4

**IR** (KBr, cm<sup>-1</sup>):  $\tilde{\nu}$  2984 (s), 2914 (s), 1437 (s), 1194 (vs), 1119 (s), 735 (m), 719 (s), 696 (s), 533 (m).

**MS** (EI, 70 eV) *m/z* (%): 155 (20), 201 (78), 202 (100), 215 (32), 311 (57).

**HRMS**: calcd. 336.1643 (C<sub>22</sub>H<sub>25</sub>OP), found: 336.1660.

### Synthesis of (1*S*,2*R*,3*S*,5*R*)-2-(diphenyl-phosphanylmethyl)-6,6-dimethyl-bicyclo[3.1.1]-heptan-3-ol borane complex (**60**).



Prepared from compound **59** (3.36 g, 10 mmol) according to the **TP6**. Yield 3,37 g (96%), white solid.

**Mp.**: 107-107.5°C.

**[α]<sub>D</sub><sup>20</sup>**: 13.0 (c 0.75, CH<sub>2</sub>Cl<sub>2</sub>).

**<sup>1</sup>H NMR** (300 MHz, CDCl<sub>3</sub>): δ 7.78-7.62 (m, 4H), 7.56-7.40 (m, 6H), 4.20-4.10 (bs, 1H), 2.70-2.40 (m, 1H), 2.48 (bs, 1H), 2.33-2.20 (m, 2H), 1.93 (s, 1H), 1.86 (s, 1H), 1.79 (s, 1H), 1.75 (s, 1H), 1.17 (s, 3H), 1.15 (s, 1H), 1.11 (s, 1H), 0.96 (s, 3H).

**<sup>13</sup>C NMR** (75 MHz, CDCl<sub>3</sub>): δ 132.8 (d, *J* = 8.8 Hz), 132.3 (d, *J* = 8.8 Hz), 131.8, 131.6, 131.1, 129.3 (d, *J* = 4.7 Hz), 129.2 (d, *J* = 4.7 Hz), 128.8, 71.1 (d, *J* = 5.6 Hz), 48.5, 48.4, 41.1, 38.1, 33.8, 33.3, 32.5, 27.4, 24.1. 38.6 (d, *J* = 11.3 Hz).

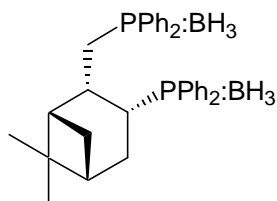
**<sup>31</sup>P NMR** (81 MHz, CDCl<sub>3</sub>): δ 15.4 (bs).

**IR** (KBr, cm<sup>-1</sup>):  $\tilde{\nu}$  3432 (bs), 3255 (bs), 2922 (s), 2386 (s), 1436 (vs), 1105 (m), 1062 (m), 1031 (m), 736 (vs), 691 (s).

**MS** (EI, 70 eV) *m/z* (%): 108 (16), 183 (34), 185 (17), 186 (11), 199 (100), 200 (82), 338 (11).

**HRMS**: calcd. 352.2127 (C<sub>22</sub>H<sub>30</sub>BOP), found: 351.2051 ([M-H]<sup>+</sup>).

### Synthesis of (1*S*,2*R*,3*R*,5*R*)-3-Diphenylphosphanyl-2-[(diphenylphosphanyl)-methyl]-6,6-dimethyl-bicyclo[3.1.1]heptane bis-borane complex (**61**).



Bis-phosphine borane **61** was synthesized from **60** (1.76 g, 5 mmol) according to the Typical Procedure **TP7**. The residue after the solvent evaporation was quickly dissolved in ether (25 mL). In some minutes, crystallization of the product started, after 12 h the crystals were filtered off, washed with small amount of ether and dried *in vacuo*. Yield 1.47 g (55%), white crystals.

**Mp.:** 195-196°C.

**[ $\alpha$ ]<sub>D</sub><sup>20</sup>:** 17.9 (c 0.48, CH<sub>2</sub>Cl<sub>2</sub>).

**<sup>1</sup>H NMR** (300 MHz, CDCl<sub>3</sub>):  $\delta$  7.93-7.79 (m, 2H), 7.71-7.50 (m, 4H), 7.47-7.21 (m, 8H), 7.22-7.00 (m, 4H), 6.90-6.77 (m, 2H), 3.70-3.45 (m, 1H), 3.26 (bs, 1H), 3.10-2.85 (m, 1H), 2.16-1.90 (m, 1H), 1.80-0.73 (m, 6H), 0.91 (s, 3H), 0.87 (s, 3H).

**<sup>13</sup>C NMR** (75 MHz, CDCl<sub>3</sub>):  $\delta$  131.5, 131.4, 131.2, 131.1, 130.7, 130.4, 130.2, 130.0 (d,  $J$  = 8.8 Hz), 129.8, 129.6 (m), 129.4, 129.3, 129.3, 129.2, 129.0, 128.8, 128.5 (d,  $J$  = 9.4 Hz), 128.1, 127.6 (d,  $J$  = 10.0 Hz), 127.3 (d,  $J$  = 10.0 Hz), 44.5, 38.9, 37.2, 33.9, 32.7, 28.1, 27.2 (d,  $J$  = 10.6 Hz), 26.8 (d,  $J$  = 10.6 Hz), 25.6 (d,  $J$  = 8.5 Hz), 19.9.

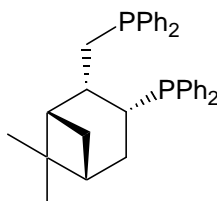
**<sup>31</sup>P NMR** (81 MHz, CDCl<sub>3</sub>):  $\delta$  17.5 (bs), 19.0 (bs).

**IR** (KBr, cm<sup>-1</sup>):  $\tilde{\nu}$  2919 (w), 2401 (s), 2383 (s), 1436 (s), 1106 (m), 1054 (m), 739 (s), 698 (vs), 500 (m).

**MS** (EI, 70 eV)  $m/z$  (%): 183 (24), 185 (14), 262 (11), 429 (100), 430 (30), 519 (17).

**HRMS:** calcd. 534.2948 (C<sub>34</sub>H<sub>42</sub>B<sub>2</sub>P<sub>2</sub>), found: 534.2953.

### Synthesis of (1*S*,2*R*,3*R*,5*R*)-3-Diphenylphosphanyl-2-[(diphenylphosphanyl)-methyl]-6,6-dimethyl-bicyclo[3.1.1]heptane (**49**).



Compound **49** was obtained from **61** (535 mg, 1 mmol) according to the Typical Procedure **TP8**. Yield 481 mg (95%), colorless, very viscous foam.

**[ $\alpha$ ]<sub>D</sub><sup>20</sup>:** 19.8 (c 1.25, CH<sub>2</sub>Cl<sub>2</sub>).

**<sup>1</sup>H NMR** (300 MHz, CDCl<sub>3</sub>):  $\delta$  7.49-7.36 (m, 4H), 7.25-7.00 (m, 16H), 6.85-6.78 (m, 2H), 3.24-3.10 (m, 1H), 2.53-2.37 (m, 3H), 2.36-2.32 (m, 1H), 2.10-2.00 (m, 1H), 1.76 (bs, 1H), 1.58-1.40 (m, 2H), 1.27 (d,  $J$  = 10.1 Hz, 1H), 1.10 (s, 3H), 0.91 (s, 3H).

**<sup>13</sup>C NMR** (75 MHz, CDCl<sub>3</sub>):  $\delta$  139.3 (d,  $J$  = 14.1 Hz), 138.2 (d,  $J$  = 11.8 Hz), 137.4 (d,  $J$  = 13.5 Hz), 137.0 (d,  $J$  = 14.7 Hz), 133.4 (d,  $J$  = 20.8 Hz), 132.1 (d,  $J$  = 19.4 Hz), 131.4 (d,  $J$  = 18.5 Hz), 127.9-127.0 (m), 124.3, 45.3 (d,  $J$  = 14.4 Hz), 40.1, 37.2, 35.1-34.8 (m), 31.7 (d,  $J$  = 17.0 Hz), 29.8-29.3 (m), 27.2-27.0 (m), 26.6, 26.1, 20.0.

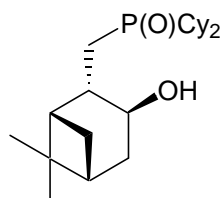
**<sup>31</sup>P NMR** (81 MHz, CDCl<sub>3</sub>):  $\delta$  -15.6 (d,  $J$  = 3.4 Hz), -16.2 (d,  $J$  = 3.4 Hz).

**IR** (KBr, cm<sup>-1</sup>):  $\tilde{\nu}$  2912 (s), 1479 (w), 1433 (s), 696 (s), 741 (vs), 513 (m).

**MS** (EI, 70 eV)  $m/z$  (%): 183 (25), 185 (11), 262 (9), 429 (100), 431 (27).

**HRMS:** calcd. 506.2292 (C<sub>34</sub>H<sub>36</sub>P<sub>2</sub>), found: 506.2288.

**Synthesis of (1*S*,2*R*,3*S*,5*R*)-2-[(dicyclohexylphosphinoyl)methyl]-6,6-dimethylbicyclo[3.1.1]heptan-3-ol (62).**



According to the Typical Procedure **TP9**, compound **59** (2.83 g, 8 mmol) was hydrogenated over Ni into adduct **19**. Yield 2.87 g (98%), white solid.

**Mp.:** 160-161°C.

$[\alpha]_D^{20}$ : -20.8 (c 0.85, CH<sub>2</sub>Cl<sub>2</sub>).

<sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>): δ 5.94 (s, 1H), 4.05 (bs, 1H), 2.49-2.19 (m, 3H), 2.08-1.54 (m, 17H), 1.52-1.06 (m, 14H), 1.16 (s, 3H), 0.90 (s, 3H).

<sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>): δ 70.9, 51.0, 50.2, 42.9, 39.8, 38.7, 38.1, 37.7 (d, *J* = 14.7 Hz), 36.8, 35.2, 31.7 (d, *J* = 57.5 Hz), 28.9, 28.3-26.7 (m), 26.3, 25.3.

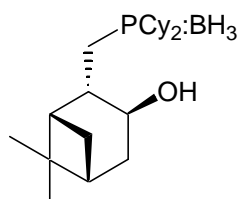
<sup>31</sup>P NMR (81 MHz, CDCl<sub>3</sub>): δ 61.0.

IR (KBr, cm<sup>-1</sup>):  $\tilde{\nu}$  3435 (m, bs), 3231 (m, bs), 2927 (vs), 2854 (s), 1450 (m), 1147 (s), 1028 (m).

MS (EI, 70 eV) *m/z* (%): 39 (6), 55 (10), 146 (9), 214 (18), 268 (6), 323 (100), 324 (23).

HRMS: calcd. 366.2688 (C<sub>22</sub>H<sub>39</sub>PO<sub>2</sub>), found: 367.2728 ([M+H]<sup>+</sup>).

**Synthesis of (1*S*,2*R*,3*S*,5*R*)-2-[(dicyclohexylphosphoryl)methyl]-6,6-dimethylbicyclo[3.1.1]-heptan-3-ol-borane complex (63).**



Prepared from phosphine oxide **62** (2.56 g, 7 mmol) according to the **TP6**. Yield 2.37 g (93%), white solid.

**Mp.:** 103-104°C

$[\alpha]_D^{20}$ : -13.6 (c 1.03, CH<sub>2</sub>Cl<sub>2</sub>).

<sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>): δ 4.01-3.92 (m, 1H), 2.50-2.08 (m, 4H), 1.97-1.47 (m, 19H), 1.42-1.05 (m, 18H), 0.84 (s, 3H).

<sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>): δ 69.4, 47.7, 47.4, 39.7, 36.5 (d, *J* = 24.3 Hz), 32.1-30.3 (m), 26.6-24.3 (m), 22.8.

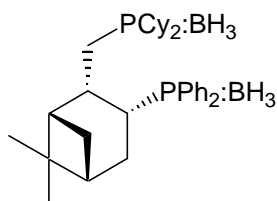
<sup>31</sup>P NMR (81 MHz, CDCl<sub>3</sub>): δ 34.0 (bs).

**IR** (KBr,  $\text{cm}^{-1}$ ):  $\tilde{\nu}$  3435 (m, bs), 1435 (vs, bs), 2915 (m, bs), 1637 (w, bs), 1435 (m), 1183 (w, bs), 695 (s).

**MS** (EI, 70 eV)  $m/z$  (%): 55 (33), 130 (76), 131 (47), 212 (100), 251 (26), 323 (27), 350 (31).

**HRMS**: calcd. 364.3066 ( $\text{C}_{22}\text{H}_{42}\text{BOP}$ ), found: 363.2978 ( $[\text{M}-\text{H}]^+$ ).

**Synthesis of (1*S*,2*R*,3*R*,5*R*)-dicyclohexyl{[3-(diphenylphosphino)-6,6-dimethylbicyclo[3.1.1]hept-2-yl]methyl}phosphine bis-borane complex (64).**



Prepared from compound **63** (1.82 g, 5 mmol) according to the **TP7**. Yield 1.31 g (48%), white solid.

**Mp.**: 228-229 °C.

$[\alpha]_{\text{D}}^{20}$ : 206.6 (c 0.49,  $\text{CH}_2\text{Cl}_2$ ).

**$^1\text{H}$  NMR** (300 MHz,  $\text{CDCl}_3$ ):  $\delta$  7.79-7.69 (m, 4H), 7.48-7.37 (m, 6H), 3.29-3.00 (m, 3H), 2.60-2.45 (m, 1H), 2.28-2.08 (m, 2H), 2.07-1.79 (m, 8H), 1.78-1.56 (m, 6H), 1.55-1.05 (m, 18H), 1.02 (s, 3H), 1.00 (s, 3H).

**$^{13}\text{C}$  NMR** (75 MHz,  $\text{CDCl}_3$ ):  $\delta$  132.5 (d,  $J = 9.4$  Hz), 132.2, 132.0 (d,  $J = 8.8$  Hz), 131.5, 131.2, 131.0, 130.3, 129.1 (d,  $J = 10.0$  Hz), 128.9 (d,  $J = 10.0$  Hz), 46.9, 40.8, 38.4, 35.9, 34.6 (d,  $J = 30.8$  Hz), 33.9 (d,  $J = 27.8$  Hz), 30.2, 29.7, 29.4, 29.2, 28.8, 28.4-27.5 (m), 26.4 (d,  $J = 22.0$  Hz), 24.6-24.0 (m), 21.5.

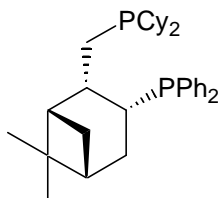
**$^{31}\text{P}$  NMR** (81 MHz,  $\text{CDCl}_3$ ):  $\delta$  16.0 (bs), 33.5 (bs).

**IR** (KBr,  $\text{cm}^{-1}$ ):  $\tilde{\nu}$  2930 (vs), 2852 (m), 2380 (s), 1436 (m), 1069 (w), 1056 (w), 742 (w), 695 (m).

**MS** (EI, 70 eV)  $m/z$  (%): 185 (5), 435 (100), 436 (33), 531 (25), 532 (9).

**HRMS**: calcd. 546.3887 ( $\text{C}_{34}\text{H}_{54}\text{B}_2\text{P}_2$ ), found: 531.3499 ( $[\text{M}-\text{BH}_4]^+$ ).

**Synthesis of (1*S*,2*R*,3*R*,5*R*)-dicyclohexyl{[3-(diphenylphosphino)-6,6-dimethylbicyclo[3.1.1]hept-2-yl]methyl}phosphine (65).**



Prepared from compound **64** (550 mg, 1 mmol) according to the **TP8**. Heating time 12 h. Yield 492 mg (95%), viscous foam.

$[\alpha]_{\text{D}}^{20}$ : 26.5 (c 1.8,  $\text{CH}_2\text{Cl}_2$ ).

**$^1\text{H}$  NMR** (300 MHz,  $\text{CDCl}_3$ ):  $\delta$  7.42-7.32 (m, 4H), 7.26-7.17 (m, 6H), 2.73-2.60 (m, 3H), 2.49-2.20 (m, 7H), 2.07-1.37 (m, 16H), 1.29-0.98 (m, 15H), 0.94 (s, 3H).

**$^{13}\text{C}$  NMR** (75 MHz,  $\text{CDCl}_3$ ):  $\delta$  138.4 (d,  $J = 11.5$  Hz), 137.8 (d,  $J = 14.1$  Hz), 132.4 (d,  $J = 19.1$  Hz), 131.8 (d,  $J = 18.2$  Hz), 127.5, 127.4-126.8 (m), 55.5, 52.4, 46.3, 40.4, 39.9, 37.2, 36.4, 32.7-30.3 (m), 29.6, 29.3, 28.2, 27.7, 27.4-26.3 (m), 25.5 (d,  $J = 23.8$  Hz), 24.4-23.7 (m), 20.3.

**<sup>31</sup>P NMR** (81 MHz, CDCl<sub>3</sub>): δ -3.8 (s), -17.5(s).

**IR** (KBr, cm<sup>-1</sup>):  $\tilde{\nu}$  2921 (vs), 2850 (s), 1446 (m), 1433 (m), 737 (m), 696 (s), 511 (w).

**MS** (EI, 70 eV) *m/z* (%): 41(6), 55 (8), 183 (6), 185 (5), 435 (100), 436 (25).

**HRMS**: calcd. 518.3231 (C<sub>34</sub>H<sub>48</sub>P<sub>2</sub>), found: 518.3240.

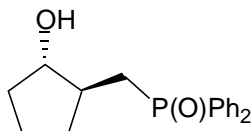
## 14. Syntheses of new chiral diphosphines with cyclopentane scaffold

### Synthesis of cyclopentene oxide.



Into a 2 L Erlenmeyer flask was placed CH<sub>2</sub>Cl<sub>2</sub> (400 mL), 35% H<sub>2</sub>O<sub>2</sub> (180 mL), pyrazole (10.0 g) and CH<sub>3</sub>ReO<sub>3</sub> (25 mg). Cyclopentene was added (100 mL), the flask was immersed in a cold water bath and the contents were vigorously stirred. After each 1.5 h, new 25 mg portions of CH<sub>3</sub>ReO<sub>3</sub> were added, overall 125 mg. The mixture was stirred overnight, layers separated and the organic phase was stirred with H<sub>2</sub>O (50 mL) and MnO<sub>2</sub> (200 mg) for 3 h. The organic layer was separated, dried (Na<sub>2</sub>SO<sub>4</sub>), filtered and fractionated at a normal pressure using a 40-cm Vigreux column. Cyclopentene oxide was obtained as colourless liquid, purity >98% by GC and <sup>1</sup>H NMR, yield 75 g (83%), bp 102-105 °C.

### Synthesis of racemic *trans*-2-diphenylphosphinoylmethyl-cyclopentanol (*rac*-67).



In a 250 mL Schlenk-flask, MeP(O)Ph<sub>2</sub> (6.50 g, 30 mmol) was dissolved in dry THF (80 mL). The solution was cooled to 0 °C and *n*-BuLi in hexanes (23 mL of 1.4 M solution, 32 mmol, 1.07 equiv) was slowly added. The mixture was warmed to RT and stirred for 3 h. Cooled to 0 °C and cyclopentene oxide (3.40 mL, 37.5 mmol, 1.25 equiv) was added. The mixture was again allowed to warm to RT and stirred for 40 h, then quenched with sat. NH<sub>4</sub>Cl (20 mL) with solid NH<sub>4</sub>Cl (5 g) added. The organic phase was dried, evaporated *in vacuo*, redissolved in ether (150 mL) and concentrated to a half-volume. After 72 h of stirring, white precipitate was filtered off, washed with small amount of ether and dried *in vacuo*. Yield 7.11 g (79%), white solid.

**Mp.:** 132-133 °C.

**<sup>1</sup>H NMR** (300 MHz, CDCl<sub>3</sub>): δ 7.72-7.62 (m, 4H), 7.45-7.20 (m, 6H), 5.72 (s, 1H), 3.91-3.84 (m, 1H), 2.52-2.44 (m, 1H), 2.52-2.12 (m, 1H), 2.02-1.98 (m, 2H), 1.95-1.75 (m, 4H), 1.56-1.50 (m, 1H).

**<sup>13</sup>C NMR** (75 MHz, CDCl<sub>3</sub>): δ 134.2, 133.9, 132.9, 132.5-132.3 (m), 131.6, 131.4, 131.2, 130.9, 129.2, 129.1, 79.1, 43.3, 35.2 (d, *J* = 74.3 Hz), 34.0, 33.7, 21.8.

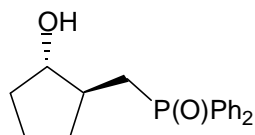
**<sup>31</sup>P NMR** (81 MHz, CDCl<sub>3</sub>): δ 39.1.

**IR** (KBr, cm<sup>-1</sup>):  $\tilde{\nu}$  3375 (s), 2961 (m), 1436 (s), 1159 (vs), 1121 (s), 721 (vs), 544 (vs).

**MS** (EI, 70 eV) *m/z* (%): 301 (25), 216 (22), 215 (41), 202 (100), 201 (27), 155 (13).

**HRMS**: calcd. 300.1279 (C<sub>18</sub>H<sub>21</sub>O<sub>2</sub>P), found: 301.1363 ([M+H<sup>+</sup>]).

### Synthesis of (*S*)-*trans*-2-diphenylphosphinoylmethyl-cyclopentanol (**67**).



Racemic **67** (4.5 g, 15 mmol) was dissolved in dry toluene (45 mL) and vinyl acetate (8.3 mL, 6 equiv) was added followed by the immobilized lipase from *Pseudomonas cepacia* (Fluka PS-D, immobilized on ceramic particles, 250 mg). The mixture was stirred at 45 °C for 24 h, filtered and evaporated. The volatiles were removed *in vacuo*. The oily residue was dissolved in ether and stirred for 36 h. The precipitate was filtered off and recrystallized (dioxane-ether). Yield 1.8 g (40%), 98.1% *ee*.

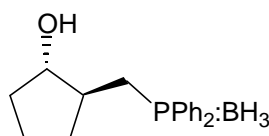
**HPLC** (Chiralcel OD-H, *n*-heptane/*i*-PrOH 90/10, 0.6 mL/min): (*R*)-enantiomer 17.9 min, (*S*)-enantiomer 19.9 min.

**Mp.:** 133-134 °C.

$[\alpha]_{\text{D}}^{20}$ : + 26 (c 0.9, CH<sub>2</sub>Cl<sub>2</sub>)

The spectral data are identical to those from the racemic compound.

### Synthesis of (*S*)-*trans*-2-(diphenylphosphanylmethyl)-cyclopentanol-borane complex (**68**).



Prepared from phosphine oxide **67** (2.10 g, 7 mmol) according to the **TP6**. Yield 2.02 g (97%), viscous foam.

$[\alpha]_{\text{D}}^{20}$ : + 17.5 (c 0.45, CH<sub>2</sub>Cl<sub>2</sub>)

**<sup>1</sup>H NMR** (300 MHz, CDCl<sub>3</sub>): δ 7.63-7.57 (m, 4H), 7.38-7.17 (m, 6H), 3.79-3.74 (m, 1H), 2.49-2.43 (m, 1H), 2.19-2.07 (m, 2H), 1.83-1.75 (m, 3H), 1.51-1.39 (m, 3H).

**<sup>13</sup>C NMR** (75 MHz, CDCl<sub>3</sub>): δ 132.1, 131.3-131.1 (m), 130.9, 130.2, 129.3-129.0 (m), 128.6, 128.4, 127.9-127.7 (m), 124.3, 78.8, 42.5, 32.5, 30.5, 28.9 (d, *J* = 30.9 Hz), 20.4.

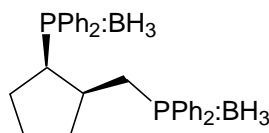
**<sup>31</sup>P NMR** (81 MHz, CDCl<sub>3</sub>): δ 15.3 (bs).

**IR** (KBr, cm<sup>-1</sup>):  $\tilde{\nu}$  3391 (m), 2960 (s), 2383 (vs), 1436 (vs), 1106 (vs), 1061 (vs), 737 (s).

**MS** (EI, 70 eV) *m/z* (%): 284 (21), 200 (79), 199 (100), 185 (15), 183 (36), 108 (13).

**HRMS**: calcd. 298.1658 (C<sub>18</sub>H<sub>24</sub>BOP), found: 298.1670.

### Synthesis of (*1R,2R*)-[2-(diphenylphosphanylmethyl)-cyclopentyl]-(diphenyl)phosphine-bis-borane complex (**69**).





Prepared from alcohol **68** (1.49 g, 5 mmol) according to the **TP7**. Yield 1.61 g (67%), white crystalline solid.

**Mp.:** 147-148 °C.

$[\alpha]_D^{20}$ : + 11.3 (c 0.75, CH<sub>2</sub>Cl<sub>2</sub>)

<sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>): δ 7.72-7.64 (m, 2H), 7.48-7.43 (m, 4H), 7.26-7.15 (m, 10H), 7.02-6.95 (m, 4H), 3.01-2.80 (m, 1H), 2.60-2.42 (m, 1H), 2.32-2.10 (m, 2H), 1.88-1.65 (m, 1H), 1.57-1.16 (m, 5H).

<sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>): δ 132.9-132.7 (m), 132.5, 132.4, 132.0, 131.9, 131.8, 131.6-131.5 (m), 131.3, 131.0, 130.8, 129.6-129.5 (m), 129.0-128.9 (m), 40.0 (d, *J* = 45.0 Hz), 38.5, 33.2, 28.0, 27.4 (d, *J* = 22.7 Hz), 24.4, 15.7.

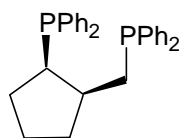
<sup>31</sup>P NMR (81 MHz, CDCl<sub>3</sub>): δ 15.9 (bs).

**IR** (KBr, cm<sup>-1</sup>):  $\tilde{\nu}$  3436 (m), 2390 (vs), 1436 (s), 1105 (m), 1063 (m), 739 (s), 694 (s), 505 (m).

**MS** (EI, 70 eV) *m/z* (%): 465 (18), 376 (26), 375 (100), 185 (12), 183 (25), 108 (18).

**HRMS**: calcd. 480.2478 (C<sub>30</sub>H<sub>36</sub>B<sub>2</sub>P<sub>2</sub>), found: 480.2456.

### Synthesis of (*1R,2R*)-[2-(diphenylphosphanylmethyl)-cyclopentyl]-(diphenyl)phosphine (**PCPP, 1**).



Prepared from compound **69** (500 mg, 1.04 mmol) according to the **TP8**. Yield 445 mg (95%), white solid. The analytical data correspond to those given in the literature.<sup>45</sup>

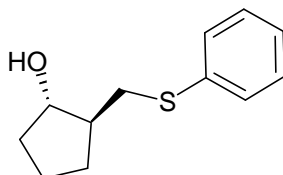
**Mp.:** 83-85 °C.

$[\alpha]_D^{20}$ : +111 (c 0.67, PhMe).

<sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>): δ 7.56-7.17 (m, 20H), 2.77-2.56 (m, 2H), 2.26-2.08 (m, 1H), 2.01-1.53 (m, 7H).

<sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>): δ 139.1, 138.2, 137.0, 135.0, 134.6, 134.3, 133.9, 128.8-128.2 (m), 53.0, 44.2 (d, *J* = 39.5 Hz), 35.5 (d, *J* = 29.1 Hz), 34.8, 30.3, 26.6.

### Synthesis of (*S*)-*trans*-2-(phenylthiomethyl)-cyclopentanol (**70**).



Into a 2 L 3-necked flask, immersed into an ice-water cooling bath, was placed DABCO (51 g, 0.45 mol), thioanisole (56 g, 0.45 mol) and dry THF (800 mL). The mixture was cooled to 0 °C and *n*-BuLi in hexanes (1.6 M, 280 mL, 0.45 mol) was slowly added. The mixture was stirred 3 h at 0 °C, and cyclopentene oxide (40 mL, 0.45 mol) was added within 10 min. Stirred at 0 °C for 24 h and quenched with sat. NH<sub>4</sub>Cl (300 mL). The organic phase was separated, the aqueous extracted with ether (150 mL), combined organic phases were washed with sat. brine, dried (MgSO<sub>4</sub>) and concentrated *in vacuo*. To the oily residue, vinyl acetate (75 mL, excess), pentane (200 mL) and the lipase from *Candida antarctica* (Novozym 435®, 200 mg, immobilized on ceramics) were added. The mixture was shaken at RT for 22 h,

filtered and concentrated *in vacuo*. The residue was dissolved in THF (150 mL) and pyridine (25 mL), and succinic anhydride (30 g, 0.3 mol) was added. Stirred for 24 h, volatiles removed *in vacuo* and the residue was diluted with ether (200 mL). This solution was vigorously stirred for 30 min with aq. solution of  $\text{KHCO}_3$  (70 g in 200 mL  $\text{H}_2\text{O}$ ). The aqueous phase was washed twice with ether ( $2 \times 100$  mL), carefully acidified with conc. HCl to pH 1 and extracted with ether ( $3 \times 100$  mL). The organic phase were reextracted with aq. KOH (100 mL of 2.5 M solution) and the aqueous phase was stirred 6 h at RT. The separated oil was extracted with ether ( $3 \times 100$  mL), org. phase washed with water, brine, dried ( $\text{MgSO}_4$ ) and evaporated *in vacuo* to furnish the product as pale yellow oil. Yield 26.4 g (28%), >99.5% *ee*. HPLC (Chiralcel AD, *n*-heptane/*i*-PrOH 95/5, 0.5 mL/min): (*R*)-enantiomer 28.3 min, (*S*)-enantiomer 26.5 min.

$[\alpha]_{\text{D}}^{20}$ : +121 (c 0.82,  $\text{CH}_2\text{Cl}_2$ )

$^1\text{H NMR}$  (300 MHz,  $\text{CDCl}_3$ ):  $\delta$  7.41-7.20 (m, 5H), 4.03-3.93 (m, 1H), 3.00-2.88 (m, 2H), 2.14-1.85 (m, 3H), 1.91-1.52 (m, 3H), 1.48-1.28 (m, 1H).

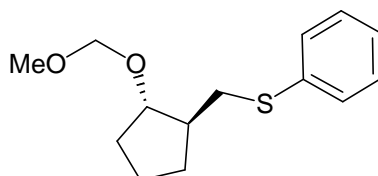
$^{13}\text{C NMR}$  (75 MHz,  $\text{CDCl}_3$ ):  $\delta$  136.7, 136.1, 129.6, 129.3, 126.4, 78.9, 47.5, 38.2, 34.8, 30.6, 22.1.

IR (KBr,  $\text{cm}^{-1}$ ):  $\tilde{\nu}$  3368 (s), 2956 (s), 1480 (s), 1438 (m), 1090 (m), 738 (vs), 691 (s).

MS (EI, 70 eV)  $m/z$  (%): 208 (40), 123 (14), 110 (100), 98 (73), 97 (16).

HRMS: calcd. 208.0922 ( $\text{C}_{12}\text{H}_{16}\text{OS}$ ), found: 208.0936.

#### Synthesis of (*S*)-*trans*-1-(methoxymethyl)-2-(phenylthiomethyl)-cyclopentane (71).



Alcohol **70** (10.4 g, 50 mmol) was dissolved in dimethoxymethane (100 mL), Amberlyst 15® (1 g) was added, the mixture was stirred at RT for 24 h, then filtered and concentrated *in vacuo*. The product was obtained in quantitative yield (12.6 g, 100%) as a pale yellow oil.

$[\alpha]_{\text{D}}^{20}$ : +67 (c 0.90,  $\text{CH}_2\text{Cl}_2$ )

$^1\text{H NMR}$  (300 MHz,  $\text{CDCl}_3$ ):  $\delta$  7.20-7.05 (m, 5H), 4.63-4.57 (m, 2H), 3.97-3.92 (m, 1H), 3.18 (s, 3H), 3.10-3.04 (m, 1H), 2.96-2.90 (m, 1H), 2.16-2.07 (m, 1H), 2.07-1.92 (m, 2H), 1.90-1.78 (m, 3H), 1.50-1.32 (m, 1H).

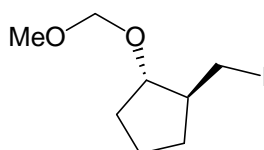
$^{13}\text{C NMR}$  (75 MHz,  $\text{CDCl}_3$ ): 137.3, 129.4, 129.2, 129.1, 129.0, 95.8, 83.2, 55.6, 45.6, 37.8, 32.3, 30.0, 22.6.

IR (KBr,  $\text{cm}^{-1}$ ):  $\tilde{\nu}$  2948 (w), 1480 (w), 1438 (w), 1147 (m), 1034 (vs), 915 (m), 736 (s), 689 (s).

MS (EI, 70 eV)  $m/z$  (%): 252 (11), 190 (30), 123 (30), 110 (15), 81 (13), 45 (100), 41 (13).

HRMS: calcd. 252.1184 ( $\text{C}_{14}\text{H}_{20}\text{O}_2\text{S}$ ), found: 252.1161.

#### Synthesis of (*S*)-*trans*-2-(iodomethyl)-cyclopentane (72).



Acetal **71** (44.0 g, 175 mmol) was mixed in a stainless steel autoclave with MeI (65 mL, 6 equiv.), 3 g of Cu powder and 3 g CaCO<sub>3</sub>. The mixture was stirred at 120 °C for 36 h and filtered through a pad of Celite. The volatile products were removed under reduced pressure, the residue redissolved in dimethoxymethane (400 mL), Amberlyst 15® (5 g) was added, and the mixture was stirred at RT. After 24 h, it was filtered and concentrated *in vacuo*. The remained oil was subjected to column chromatography on silica (200 g). Thioanisol was removed by washing with pentane, and product was eluted with pentane-ether (1:1). The eluate was concentrated and distilled *in vacuo*, yielding **72** as a yellowish liquid (35.0 g, 74%) with >98% purity by GC.

**Bp.:** 69-72 °C (0.9 mbar).

**[α]<sub>D</sub><sup>20</sup>:** +49 (c 0.90, CH<sub>2</sub>Cl<sub>2</sub>).

**<sup>1</sup>H NMR** (300 MHz, CDCl<sub>3</sub>): δ 4.58 (s, 2H), 3.95-3.87 (m, 1H), 3.30 (s, 3H), 3.31-3.25 (m, 1H), 3.18-3.13 (m, 1H), 2.07-1.95 (m, 1H), 1.94-1.81 (m, 3H), 1.70-1.57 (m, 3H), 1.45-1.28 (m, 1H).

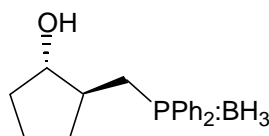
**<sup>13</sup>C NMR** (75 MHz, CDCl<sub>3</sub>): δ 95.5, 82.8, 55.3, 47.7, 32.0, 30.7, 21.7, 11.4.

**IR** (KBr, cm<sup>-1</sup>):  $\tilde{\nu}$  2953 (15), 111 (35), 93 (31), 85 (20), 81 (24).

**MS** (EI, 70 eV) *m/z* (%): 209 (15), 111 (35), 93 (31), 85 (20), 81 (24),

**HRMS:** calcd. 270.0117 (C<sub>8</sub>H<sub>15</sub>IO<sub>2</sub>), found: 270.0122.

### Synthesis of (*S*)-*trans*-2-(diphenylphosphanylmethyl)-cyclopentanol-borane complex (**68**) from **72**.



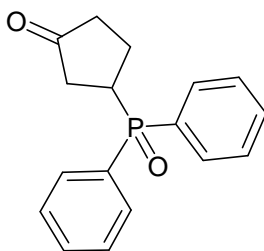
Into a 25 mL Schlenk-flask under argon was placed THF (5 mL), cooled to -78 °C and *t*-BuLi in pentane (3.2 mL of 1.3 M solution, 4.2 mmol, 2.1 equiv) was added. To this solution, iodide **72** (540 mg, 2 mmol) in THF (2 mL) was slowly added at -78 °C. After 10 min at this temperature, Ph<sub>2</sub>PCl (660 mg, 3 mmol, 1.5 equiv.) in THF (2 mL) was added. The mixture was allowed to reach RT and BH<sub>3</sub>-Me<sub>2</sub>S (0.5 mL, 5 mmol) was added. The mixture was separated between ether (25 mL) and sat. NH<sub>4</sub>Cl (25 mL), the aqueous phase was reextracted with ether, combined organic phases were washed with water and concentrated *in vacuo*. The residue was redissolved in MeOH (5 mL) and conc. HCl (5 mL) was added. After 12 h at RT, the mixture was carefully neutralized with solid Na<sub>2</sub>CO<sub>3</sub>, diluted with water and extracted with ether (3×25 mL), the organic phase was dried and evaporated. The residue was purified by chromatography (pentane-ether 1:1). Compound **68** was obtained as a white solid, 393 mg (66%). The analytical data are identical to those from the previously synthesized substance.

**[α]<sub>D</sub><sup>20</sup>:** +16.3 (c 0.45, CH<sub>2</sub>Cl<sub>2</sub>).

**<sup>1</sup>H NMR** (300 MHz, CDCl<sub>3</sub>): δ 7.63-7.57 (m, 4H), 7.38-7.17 (m, 6H), 3.79-3.74 (m, 1H), 2.49-2.43 (m, 1H), 2.19-2.07 (m, 2H), 1.83-1.75 (m, 3H), 1.51-1.39 (m, 3H).

**<sup>13</sup>C NMR** (75 MHz, CDCl<sub>3</sub>): δ 132.1, 131.3-131.1 (m), 130.9, 130.2, 129.3-129.0 (m), 128.6, 128.4, 127.9-127.7 (m), 124.3, 78.8, 42.5, 32.5, 30.5, 28.9 (d, *J* = 30.7 Hz), 20.4.

### Synthesis of 3-(diphenylphosphinoyl)cyclopentanone (**74**).



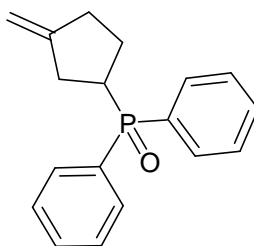
A mixture of cyclopentanone (10.0 g, 122 mmol), acetic acid (10 mL, 175 mmol) and molecular sieves 4Å (2 g) was stirred for 1 h at RT. The mixture was cooled in an ice bath and Ph<sub>2</sub>PCl (22.5 mL, 120 mmol) was added slowly with good stirring. The mixture was stirred for 2 h at RT, quenched with water (100 mL) and extracted with CH<sub>2</sub>Cl<sub>2</sub> (4×50 mL). The organic phase was washed with sat. NaHCO<sub>3</sub>, dried and concentrated in vacuo to furnish **74** as a viscous oil (32.2 g, 96% yield). The analytical data corresponds to those given in the literature.<sup>57b</sup>

<sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>): δ 7.80-7.70 (m, 4H), 7.54-7.42 (m, 6H), 3.08-3.00 (m, 1H), 2.58 (m, 1H), 2.45-2.38 (m, 1H), 2.32-2.21 (m, 2H), 2.19 (dd, *J*<sub>1</sub> = 18.1 Hz, *J*<sub>2</sub> = 8.5 Hz, 1H), 2.03-1.95 (m, 1H).

<sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>): δ 216.5 (d, *J* = 13.3 Hz), 132.0, 131.6, 131.2, 130.8, 130.5, 128.9, 38.1, 37.8, 35.3 (d, *J* = 75.3 Hz), 22.7.

<sup>31</sup>P NMR (81 MHz, CDCl<sub>3</sub>): δ 30.2.

#### Synthesis of 3-(diphenylphosphino)-methylenecyclopentane (**75**).



Into a 500 mL Schlenk-flask under argon was placed dry THF (180 mL), ketone **74** (28.4 g, 100 mmol), Zn powder (48.0 g, 740 mmol, 7.4 equiv.), and Cp<sub>2</sub>ZrCl<sub>2</sub> (30.6 g, 105 mmol, 1.05 equiv.). Dibromoethane (0.7 mL) and Me<sub>3</sub>SiCl (0.7 mL) were added to activate Zn, the mixture was stirred for 1 h at RT and placed into a cooling bath. Diiodomethane (15.3 mL, 190 mmol, 1.9 equiv.) was added within 1 h with a good stirring and the stirring continued for 12 h at RT. The mixture was filtered through Celite and the solids were washed with CH<sub>2</sub>Cl<sub>2</sub>. To the filtrate, MeOH was added (50 mL) and volatiles were removed in vacuo. The residue was redissolved in CH<sub>2</sub>Cl<sub>2</sub> (300 mL) and washed consequently with 1 N HCl (400 mL), 20% aq. NH<sub>4</sub>OAc (3×100 mL), 2 N aq. NH<sub>3</sub> (100 mL), dried (Na<sub>2</sub>SO<sub>4</sub>) and evaporated. The brown residue was purified by column chromatography on silica (EtOAc-*i*-PrOH 30:1). Compound **75** was obtained as white solid, yield 15.5 g (55%).

**Mp.:** 128-129 °C.

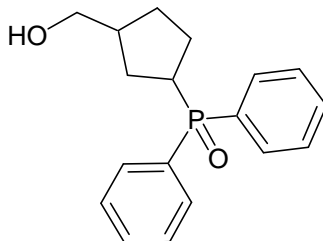
<sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>): δ 7.75-7.65 (m, 4H), 7.46-7.35 (m, 6H), 4.80-4.76 (m, 2H), 2.82-2.55 (m, 2H), 2.51-2.20 (m, 3H), 2.07-1.86 (m, 1H), 1.75-1.60 (m, 1H).

<sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>): δ 150.7, 134.1, 134.0, 132.7, 132.0, 131.2, 129.0, 106.5, 38.7 (d, *J* = 71.0 Hz), 33.4, 33.3, 26.6.

<sup>31</sup>P NMR (81 MHz, CDCl<sub>3</sub>): δ 33.9.

**IR** (KBr,  $\text{cm}^{-1}$ ):  $\tilde{\nu}$  3053 (m), 1437 (s), 1180 (vs), 1120 (s), 722 (s), 702 (s), 552 (vs), 540 (vs).  
**MS** (EI, 70 eV)  $m/z$  (%): 282 (10), 203 (13), 202 (100), 201 (20), 155 (17).  
**HRMS**: calcd. 282.1174 ( $\text{C}_{18}\text{H}_{19}\text{OP}$ ), found: 282.1169.

**Synthesis of [3-(hydroxymethyl)-cyclopentyl](diphenyl)phosphine oxide (racemic *cis*- and *trans*-mixture, 76+77).**



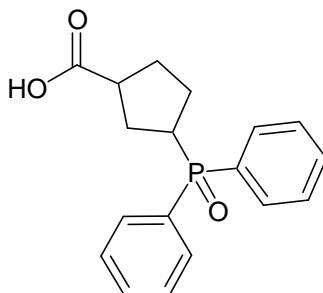
Prepared from compound **75** (3.38 g, 12 mmol) according to the **TP5**. The reaction mixture was heated for 3 h at 50 °C. The mixture of *cis*- and *trans*-alcohols (85:15 ratio) was obtained as a white solid, 2.77 g (77% yield).

**Mp.**: 116-119 °C.

**$^{31}\text{P}$  NMR** (81 MHz,  $\text{CDCl}_3$ ):  $\delta$  36.43 (*cis*-isomer), 36.33 (*trans*-isomer).

The spectral data of the main stereoisomer are identical to those given below for enantiopure **77**.

**Synthesis of [3-(carboxy)-cyclopentyl](diphenyl)phosphine oxide (racemic *cis*- and *trans*-mixture, 78+78a).**



The mixture of alcohols **76** and **77**, obtained in the previous step (2.30 g, 7.67 mmol),  $\text{CCl}_4$  (15 mL) and  $\text{CH}_3\text{CN}$  (15 mL) were placed in a 100 mL flask and  $\text{RuCl}_3$  (15 mg, 1 mol%) was added. Separately,  $\text{H}_5\text{IO}_6$  (3.5 g, 15.3 mmol, 2 equiv.) was dissolved in  $\text{H}_2\text{O}$  (15 mL) and this solution was added at a rate about 0.2 mL/min to the first solution with vigorous stirring, until the dark-green colour of the mixture changed to a persisting orange. The mixture was stirred for 6 h more and concentrated *in vacuo* to remove the organic solvents. The precipitate was filtered and washed with cold water. The solid was redissolved in mixture  $\text{CH}_2\text{Cl}_2$ -MeOH (50 mL, 9:1), the solution was dried overnight ( $\text{Na}_2\text{SO}_4$ ) and evaporated almost to dryness. The residue was stirred 1 h in ether (100 mL), filtered and dried *in vacuo*. A sample of the product was recrystallized from acetonitrile. According to the NMR data, this substance contains five molecules of  $\text{H}_2\text{O}$  per one molecule of the acid. White solid, yield 2.63 g (pentahydrate, 85%), a mixture of *cis*- and *trans*-isomers (85:15).

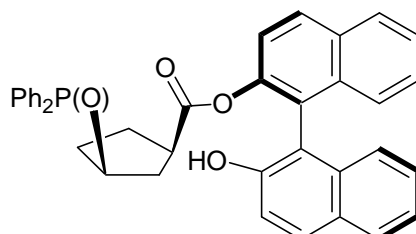
**Mp.**: 219-220 °C (decomp.)

**$^{31}\text{P}$  NMR** (81 MHz,  $\text{CDCl}_3$ ):  $\delta$  38.40 (major), 38.05 (minor).

**IR** (KBr,  $\text{cm}^{-1}$ ):  $\tilde{\nu}$  2921 (w), 1714 (m), 1144 (vs), 1120 (s), 1097 (m), 725 (m), 698 (vs).

**HRMS**: calcd. 314.1072 ( $\text{C}_{18}\text{H}_{19}\text{O}_3\text{P}$ ), found: 314.1047.

**Synthesis of enantiopure *cis*-(3-diphenylphosphinoyl)-cyclopentanecarboxylic acid (*R*)-2,2'-dihydroxy-1,1'-binaphthyl ester (**79**).**



In dry  $\text{CH}_2\text{Cl}_2$  (150 mL) was dissolved **78** (pentahydrate, 9.0 g, 22 mmol), dicyclohexylcarbodiimide (DCC, 6.8 g, 33 mmol, 1.5 equiv.), 4-dimethylaminopyridine (DMAP, 3.7 g, 30 mmol, 1.36 equiv.) and (*R*)-BINOL (8.0 g, 28 mmol, 1.27 equiv.). The mixture was stirred for 14 h at RT, filtered and the solids were washed with  $\text{CH}_2\text{Cl}_2$ . The filtrate was concentrated *in vacuo* and the residue chromatographed on silica (acetonitrile). Yield 4.35 g (34%), pale yellow solid.

**Mp.:** 139-140 °C.

$[\alpha]_{\text{D}}^{20}$ : -483 (c 0.40,  $\text{CH}_2\text{Cl}_2$ )

$^1\text{H NMR}$  (300 MHz,  $\text{CDCl}_3$ ):  $\delta$  8.05-7.90 (m, 2H), 7.80-7.05 (m, 22H), 2.85-2.67 (m, 2H), 2.65-2.53 (m, 1H), 2.15-1.83 (m, 3H), 1.72-1.54 (m, 2H).

$^{13}\text{C NMR}$  (75 MHz,  $\text{CDCl}_3$ ):  $\delta$  132.3-132.1 (m), 131.5, 131.3, 131.2-129.9 (m), 129.2-129.0 (m), 128.5, 128.2, 127.1, 126.7, 126.1, 125.3, 123.3, 122.3, 119.4, 44.7 (d,  $J = 14.7$  Hz), 38.3 (d,  $J = 72.3$  Hz), 29.9, 29.7, 26.5.

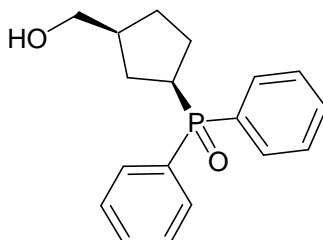
$^{31}\text{P NMR}$  (81 MHz,  $\text{CDCl}_3$ ):  $\delta$  35.1.

**IR** (KBr,  $\text{cm}^{-1}$ ):  $\tilde{\nu}$  3430 (s), 1753 (s), 1437 (s), 1166 (vs), 1212 (vs), 1122 (vs), 748 (m), 723 (m), 698 (m), 537 (m).

**MS** (EI, 70 eV)  $m/z$  (%): 298 (19), 297 (100), 286 (45), 269 (42), 268 (41), 229 (36), 202 (42), 201 (64), 77 (11).

**HRMS**: calcd. 582.1960 ( $\text{C}_{38}\text{H}_{31}\text{O}_4\text{P}$ ), found: 582.1979.

**Synthesis of enantiopure *cis*-[3-(hydroxymethyl)-cyclopentyl](diphenyl)phosphine oxide (**77**).**



Solution of lithium pyrrolidinoborohydride (0.8 M in THF-hexane) was prepared from *n*-BuLi and borane-pyrrolidine complex according to the literature procedure.<sup>62</sup> To this solution (30 mL, 24 mmol, 3.5 equiv.) in a 100 mL Schlenk-flask under argon was added the solution of ester **79** (4.0 g, 6.9 mmol) in THF (15 mL). The solution was stirred for 24 h, MeOH was added (5 mL) and the mixture was carefully neutralized with 6 N HCl to slightly acidic reaction. Organic solvents were removed *in vacuo* and the residue was extracted several times

with CH<sub>2</sub>Cl<sub>2</sub>. The extracts were dried (Na<sub>2</sub>SO<sub>4</sub>), evaporated and the residual oil chromatographed on silica (gradient MeOH in CH<sub>2</sub>Cl<sub>2</sub> from 50:1 to 5:1). Compound **77** was obtained as a white solid, yield 1.86 g (90%), >99.5% *ee*.

**Chiral HPLC** (Chiralcel AD, *n*-heptane/*i*-PrOH 75/25, 0.6 mL/min): the obtained enantiomer: 12.9 min, the second enantiomer: 17.9 min.

**Mp.:** 135-136 °C.

**[α]<sub>D</sub><sup>20</sup>:** +56 (c 0.90, CH<sub>2</sub>Cl<sub>2</sub>)

**<sup>1</sup>H NMR** (300 MHz, CDCl<sub>3</sub>): δ 7.70-7.63 (m, 4H), 7.41-7.20 (m, 6H), 3.72 (bs, 1H), 3.55-3.38 (m, 2H), 2.82-2.63 (m, 1H), 2.29-2.08 (m, 1H), 2.05-1.35 (m, 6H).

**<sup>13</sup>C NMR** (75 MHz, CDCl<sub>3</sub>): 134.0, 132.8, 131.9 (m), 131.3, 131.2 (m), 130.5, 129.1, 128.9, 128.4, 127.0, 66.3, 43.0, 37.5 (d, *J* = 74.5 Hz), 30.6, 29.8, 26.1.

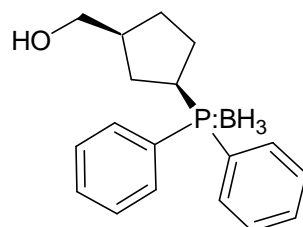
**<sup>31</sup>P NMR** (81 MHz, CDCl<sub>3</sub>): δ 36.4.

**IR** (KBr, cm<sup>-1</sup>):  $\tilde{\nu}$  3331 (w), 2932 (w), 1438 (w), 1167 (m), 1119 (m), 724 (m), 698 (vs).

**MS** (EI, 70 eV) *m/z* (%): 270(15), 269 (27), 229 (39), 203 (16), 202 (100), 201 (39), 155 (13).

**HRMS:** calcd. 300.1279 (C<sub>18</sub>H<sub>21</sub>O<sub>2</sub>P), found: 300.1269.

### Synthesis of *cis*-[3-(hydroxymethyl)-cyclopentyl](diphenyl)phosphine-borane complex (**80**).



Prepared from phosphine oxide **77** (2.10 g, 7 mmol) according to the **TP6**. The chemical shift of the unprotected phosphine -2.4 ppm (PhMe, unlocked). Yield 2.00 g (96%), viscous foam.

**[α]<sub>D</sub><sup>20</sup>:** +44 (c 1.1, CH<sub>2</sub>Cl<sub>2</sub>)

**<sup>1</sup>H NMR** (300 MHz, CDCl<sub>3</sub>): δ 7.74-7.60 (m, 4H), 7.50-7.28 (m, 6H), 3.58-3.40 (m, 2H), 3.00-2.82 (m, 1H), 2.27-2.05 (m, 1H), 1.92-1.60 (m, 4H), 1.57-1.30 (m, 2H).

**<sup>13</sup>C NMR** (75 MHz, CDCl<sub>3</sub>): δ 132.5, 132.4, 132.3 (m), 131.0 (m), 128.7, 128.6, 66.4, 43.2, 32.7 (d, *J* = 36.2 Hz), 30.6, 28.5, 26.1.

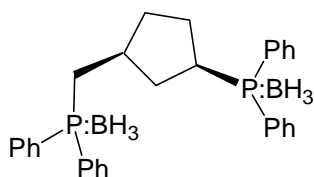
**<sup>31</sup>P NMR** (81 MHz, CDCl<sub>3</sub>): δ 23.5 (bs).

**IR** (KBr, cm<sup>-1</sup>):  $\tilde{\nu}$  3345 (w), 2378 (m), 1436 (s), 1106 (s), 1059 (s), 736 (vs), 660 (vs).

**MS** (EI, 70 eV) *m/z* (%): 284 (77), 267 (22), 213 (14), 187 (19), 186 (100), 183 (55), 109 (15), 108 (69).

**HRMS:** calcd. 298.1658 (C<sub>18</sub>H<sub>24</sub>BOP), found: 297.1553 ([M-H]<sup>+</sup>).

### Synthesis of enantiopure *cis*-[3-(diphenylphosphanylmethyl)-cyclopentyl](diphenyl)-phosphine-*bis*-borane complex (**81**).



Prepared from alcohol **80** (1.49 g, 5 mmol) according to the **TP7**. The product was recrystallized from ether. Yield 1.32 g (55%), white crystalline solid.

**Mp.:** 196-197 °C.

$[\alpha]_D^{20}$ : +8.4 (c 0.60, CH<sub>2</sub>Cl<sub>2</sub>)

<sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>): δ 7.78-7.34 (m, 20H), 2.87-2.80 (m, 1H), 2.37 (d, *J* = 7.3 Hz, 2H), 1.90-1.65 (m, 2H), 1.32-1.17 (m, 5H).

<sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>): δ 133.2 (d, *J* = 9.6 Hz), 132.6, 132.5, 132.3-132.0 (m), 131.9, 131.4, 131.1 (dd, *J*<sub>1</sub> = 5.9 Hz, *J*<sub>2</sub> = 3.0 Hz), 130.9, 130.7, 130.6, 130.1, 130.0, 129.9, 129.6, 129.5, 129.3, 129.0, 128.7-128.5 (m), 36.3 (m), 34.2, 32.5 (d, *J* = 38.0 Hz), 31.0 (d, *J* = 36.1 Hz), 26.7 (d, *J* = 3.7 Hz), 23.6.

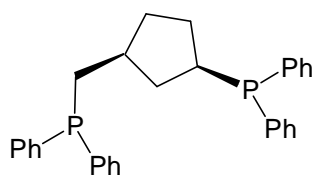
<sup>31</sup>P NMR (81 MHz, CDCl<sub>3</sub>): δ 18.3 (bs).

IR (KBr, cm<sup>-1</sup>):  $\tilde{\nu}$  2416 (s), 2350 (vs), 1436 (vs) 1105 (m), 1056 (m), 738 (s), 692 (vs).

MS (EI, 70 eV) *m/z* (%): 465 (33), 375 (42), 268 (18), 267 (100), 185 (13), 183 (27).

HRMS: calcd. 480.2478 (C<sub>30</sub>H<sub>36</sub>B<sub>2</sub>P<sub>2</sub>), found: 480.2501.

**Synthesis of enantiopure *cis*-[3-(diphenylphosphanylmethyl)-cyclopentyl](diphenyl)-phosphine (66).**



Prepared by the deprotection of *bis*-phosphine-borane **81** (480 mg, 1 mmol) according to the **TP8**. Yield 425 mg (94%), viscous foam.

$[\alpha]_D^{20}$ : + 6.0 (c, 0.62 CH<sub>2</sub>Cl<sub>2</sub>)

<sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>): δ 7.38-7.30 (m, 8H), 7.26-7.21 (m, 12H), 2.56-2.47 (m, 1H), 2.12-2.03 (m, 2H), 1.95-1.79 (m, 3H), 1.80-1.68 (m, 1H), 1.63-1.50 (m, 1H), 1.42-1.33 (m, 1H), 1.25-1.10 (m, 1H).

<sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>): 139.5, 138.8, 138.7, 133.2-133.0 (m), 132.8, 132.6, 128.6-128.1 (m), 40.2 (d, *J* = 21.0 Hz), 38.7, 35.7, 35.0, 34.3, 30.1 (d, *J* = 23.0 Hz).

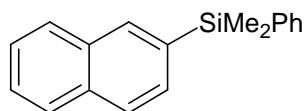
<sup>31</sup>P NMR (81 MHz, CDCl<sub>3</sub>): δ -4.4 (s), -20.3 (s).

IR (KBr, cm<sup>-1</sup>):  $\tilde{\nu}$  2955 (m), 1477 (m), 1431 (s), 732 (s), 694 (vs).

HRMS: calcd. 452.1823 (C<sub>30</sub>H<sub>30</sub>P<sub>2</sub>), found: 452.1818.

## 15. Syntheses of arylsilanes from aryl triflates.

**Synthesis of dimethylnaphthalen-2-yl-phenylsilane (85).**



Prepared from 2-naphthyl triflate (221 mg, 0.8 mmol) according to the **TP10**. Reaction time 1 h, purification by chromatography (SiO<sub>2</sub>, *n*-pentane). Yield 184 mg (88%), colourless oil.

<sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>): δ 7.82 (s, 1H), 7.63-7.58 (m, 3H), 7.40-7.34 (m, 3H), 7.29-7.24 (m, 2H), 7.19-7.13 (m, 3H), 0.43 (s, 6H).

<sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>): δ 140.6, 138.0, 137.2, 136.6, 136.1, 135.2, 132.7, 131.5, 130.4, 130.2, 130.0, 129.4, 128.7, 128.2, -1.5.

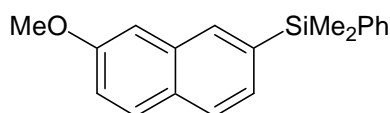


**IR** (KBr,  $\text{cm}^{-1}$ ):  $\tilde{\nu}$  3051 (m), 2956 (m), 1428 (m), 1248 (m), 1113 (m), 1086 (m), 856 (s), 806 (vs), 777 (s), 700 (s).

**MS** (EI, 70 eV)  $m/z$  (%): 262 (12) [ $\text{M}^+$ ], 247 (100), 215 (5), 169 (7).

**HRMS**: calcd. 262.1178 ( $\text{C}_{18}\text{H}_{18}\text{Si}$ ), found: 262.1154.

### Synthesis of (7-methoxynaphthalen-2-yl)dimethylphenylsilane (86).



Prepared from 7-methoxy-2-naphthyl triflate (245 mg, 0.8 mmol) according to the **TP10**. Reaction time 1 h, purification by chromatography ( $\text{SiO}_2$ ,  $n$ -pentane- $\text{CH}_2\text{Cl}_2$  = 2:1). Yield 166 mg (71%), colourless oil.

**$^1\text{H}$  NMR** (300 MHz,  $\text{CDCl}_3$ ):  $\delta$  7.84 (s, 1H), 7.65 (d,  $J$  = 8.0 Hz, 1H), 7.62 (d,  $J$  = 8.0 Hz, 1H), 7.50-7.46 (m, 2H), 7.37 (d,  $J$  = 8.0 Hz, 1H), 7.30-7.24 (m, 3H), 7.09-7.03 (m, 2H), 3.82 (s, 3H), 0.54 (s, 6H).

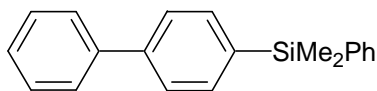
**$^{13}\text{C}$  NMR** (75 MHz,  $\text{CDCl}_3$ ):  $\delta$  160.0, 140.6, 138.5, 136.6, 136.3, 136.0, 131.6, 131.4, 130.6, 130.1, 129.1, 121.6, 108.2, 57.6, -1.9.

**IR** (KBr,  $\text{cm}^{-1}$ ):  $\tilde{\nu}$  3067 (w), 2955 (m), 1627 (m), 1505 (m), 1393 (m), 1254 (s), 1214 (vs), 1089 (m), 1032 (m), 812 (s), 833 (vs), 700 (m).

**MS** (EI, 70 eV)  $m/z$  (%): 292 (47) [ $\text{M}^+$ ], 277 (100), 234 (9), 215 (4), 138 (7).

**HRMS**: calcd. 292.1283 ( $\text{C}_{19}\text{H}_{20}\text{OSi}$ ), found: 292.1254.

### Synthesis of biphenyl-4-yl-dimethylphenylsilane (87).



Prepared from 4-biphenyl triflate (242 mg, 0.8 mmol) according to the **TP10**. Reaction time 3 h, purification by chromatography ( $\text{SiO}_2$ ,  $n$ -pentane- $\text{CH}_2\text{Cl}_2$  = 9:1). Yield 184 mg (80%), white solid.

**Mp.**: 55.5-57.0 °C.

**$^1\text{H}$  NMR** (300 MHz,  $\text{CDCl}_3$ ):  $\delta$  7.57-7.52 (m, 9H), 7.37-7.32 (m, 5H), 0.56 (s, 6H).

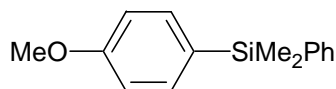
**$^{13}\text{C}$  NMR** (75 MHz,  $\text{CDCl}_3$ ):  $\delta$  144.2, 143.4, 140.5, 139.3, 137.0, 136.5, 131.5, 131.1, 130.2, 129.7, 129.5, 128.9, -2.7.

**IR** (KBr,  $\text{cm}^{-1}$ ):  $\tilde{\nu}$  3049 (w), 2955 (w), 1428 (m), 1249 (m), 1115 (s), 829 (s), 814 (vs), 731 (m), 698 (s).

**MS** (EI, 70 eV)  $m/z$  (%): 430 (1) [ $\text{M}^+$ ], 288 (20), 273 (100).

**HRMS**: calcd. 288.1334 ( $\text{C}_{20}\text{H}_{20}\text{Si}$ ), found: 288.1336.

### Synthesis of (4-methoxyphenyl)dimethylphenylsilane (88).



Prepared from 4-methoxyphenyl triflate (205 mg, 0.8 mmol) according to the **TP10**. Reaction time 3 h, purification by chromatography ( $\text{SiO}_2$ ,  $n$ -pentane- $\text{CH}_2\text{Cl}_2$  = 4:1). Yield 124 mg (64%), colourless oil.

**$^1\text{H}$  NMR** (300 MHz,  $\text{CDCl}_3$ ):  $\delta$  7.45-7.42 (m, 2H), 7.36 (d,  $J$  = 8.8 Hz, 2H), 7.29-7.24 (m, 3H), 6.83 (d,  $J$  = 8.8 Hz, 2H), 3.73 (s, 3H), 0.45 (s, 6H).

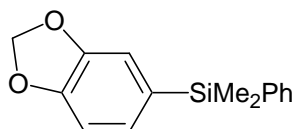
**$^{13}\text{C}$  NMR** (75 MHz,  $\text{CDCl}_3$ ):  $\delta$  162.7, 140.9, 137.8, 136.3, 131.2, 130.0, 115.8, 57.2, -2.0.

**IR** (KBr,  $\text{cm}^{-1}$ ):  $\tilde{\nu}$  3050 (w), 2956 (m), 1594 (vs), 1503 (s), 1428 (m), 1279 (vs), 1249 (vs), 1182 (s), 1112 (vs), 1033 (m), 818 (vs), 774 (m), 700 (m).

**MS** (EI, 70 eV)  $m/z$  (%): 242 (10) [ $\text{M}^+$ ], 227 (100), 184 (2).

**HRMS**: calcd. 242.1127 ( $\text{C}_{15}\text{H}_{18}\text{OSi}$ ), found: 242.1117.

### Synthesis of benzo[1,3]dioxol-5-yl-dimethylphenylsilane (89).



Prepared from 3,4-methylenedioxyphenyl triflate (216 mg, 0.8 mmol) according to the **TP10**. Reaction time 6 h, purification by chromatography ( $\text{SiO}_2$ ,  $n$ -pentane- $\text{CH}_2\text{Cl}_2$  = 4:1). Yield 130 mg (63%), colourless oil.

**$^1\text{H}$  NMR** (300 MHz,  $\text{CDCl}_3$ ):  $\delta$  7.45-7.40 (m, 2H), 7.30-7.25 (m, 3H), 6.92 (d,  $J$  = 7.5 Hz, 1H), 6.88 (s, 1H), 6.75 (d,  $J$  = 7.5, 1H), 5.84 (s, 2H), 0.44 (s, 6H).

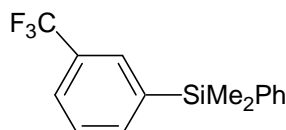
**$^{13}\text{C}$  NMR** (75 MHz,  $\text{CDCl}_3$ ):  $\delta$  150.7, 149.6, 140.5, 136.3, 133.4, 131.3, 130.5, 130.0, 123.8, 115.7, 110.8, 102.7, -2.0.

**IR** (KBr,  $\text{cm}^{-1}$ ):  $\tilde{\nu}$  3068 (m), 2956 (m), 1502 (m), 1483 (vs), 1417 (m), 1233 (vs), 1111 (m), 1059 (m), 1041 (s), 804 (s), 701 (m).

**MS** (EI, 70 eV)  $m/z$  (%): 241 (100), 211 (4), 120 (4).

**HRMS**: calcd. 256.0920 ( $\text{C}_{15}\text{H}_{16}\text{O}_2\text{Si}$ ), found: 256.0911.

### Synthesis of dimethylphenyl-(3-trifluoromethylphenyl)silane (90).



Prepared from 3-trifluoromethylphenyl triflate (235 mg, 0.8 mmol) according to the **TP10**. Reaction time 1 h, purification by chromatography (SiO<sub>2</sub>, *n*-pentane). Yield 120 mg (54%), colourless oil.

**<sup>1</sup>H NMR** (300 MHz, CDCl<sub>3</sub>): δ 7.69 (s, 1H), 7.60 (d, *J* = 7.5 Hz, 1H), 7.53 (d, *J* = 7.5 Hz, 1H), 7.46-7.42 (m, 2H), 7.38 (t, *J* = 7.5 Hz, 1H), 7.33-7.28 (m, 3H), 0.51 (s, 6H).

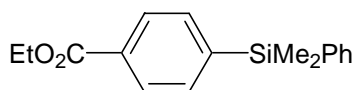
**<sup>13</sup>C NMR** (75 MHz, CDCl<sub>3</sub>): δ 142.4, 140.1, 139.6, 136.7, 132.9 (q, *J* = 565 Hz), 132.4, 132.0, 130.8, 130.6 (q, *J* = 52 Hz), 128.4, 126.2 (q, *J* = 13.5 Hz), 125.1, -2.6.

**IR** (KBr, cm<sup>-1</sup>):  $\tilde{\nu}$  3070 (w), 2959 (w), 1429 (m), 1326 (vs), 1252 (m), 1166 (s), 1119 (vs), 1074 (s), 839 (m), 776 (m), 701 (m).

**MS** (EI, 70 eV) *m/z* (%): 280 (0.8) [M<sup>+</sup>], 265 (100), 184 (4).

**HRMS**: calcd. 280.0895 (C<sub>15</sub>H<sub>15</sub>F<sub>3</sub>Si), found: 280.0870.

### Synthesis of dimethylphenyl-(4-carbomethoxyphenyl)silane (**91**).



Prepared from 4-carboethoxyphenyl triflate (238 mg, 0.8 mmol) according to the **TP10**. Reaction time 1 h, purification by chromatography (SiO<sub>2</sub>, *n*-pentane-CH<sub>2</sub>Cl<sub>2</sub> 3:2). Yield 160 mg (71%), pale yellow oil.

**<sup>1</sup>H NMR** (300 MHz, CDCl<sub>3</sub>): δ 7.78 (d, *J* = 8.3 Hz, 2H), 7.37 (d, *J* = 8.3 Hz, 2H), 7.31-7.27 (m, 2H), 7.16-7.11 (m, 3H), 4.16 (q, *J* = 7.1 Hz, 2H), 1.17 (t, *J* = 7.1 Hz, 3H), 0.36 (s, 6H).

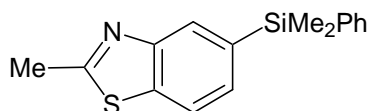
**<sup>13</sup>C NMR** (75 MHz, CDCl<sub>3</sub>): δ 169.3, 147.1, 140.0, 136.7, 133.5, 131.9, 131.1, 130.5, 63.5, 16.9, -4.7.

**IR** (KBr, cm<sup>-1</sup>):  $\tilde{\nu}$  3070 (w), 2959 (m), 1717 (vs), 1389 (m), 1279 (vs), 1113 (m), 1094 (s), 833 (s), 815 (s), 780 (m), 700 (m).

**MS** (EI, 70 eV) *m/z* (%): 283 (8) [M-H<sup>+</sup>], 269 (100), 241 (20), 135 (4).

**HRMS**: calcd. 283.1154 (C<sub>17</sub>H<sub>19</sub>O<sub>2</sub>Si), found: 283.1127.

### Synthesis of 5-(dimethylphenylsilyl)-2-methylbenzothiazole (**92**).



Prepared from 2-methyl-5-(trifluoromethanesulfonyloxy)benzothiazole (238 mg, 0.8 mmol) according to the **TP10**. Reaction time 8 h, purification by chromatography (SiO<sub>2</sub>, *n*-pentane-CH<sub>2</sub>Cl<sub>2</sub> 2:1). Yield 160 mg (71%), pale yellow oil.

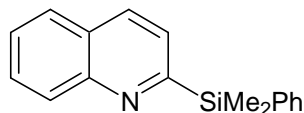
**<sup>1</sup>H NMR** (300 MHz, CDCl<sub>3</sub>): δ 8.00 (s, 1H), 7.67 (d, *J* = 8.0 Hz, 1H), 7.44-7.40 (m, 2H), 7.32 (d, *J* = 8.0 Hz, 1H), 7.24-7.20 (m, 3H), 2.69 (s, 3H), 0.48 (s, 6H).

**<sup>13</sup>C NMR** (75 MHz, CDCl<sub>3</sub>): δ 169.0, 155.4, 140.2, 139.0, 138.3, 136.5, 132.3, 131.5, 130.6, 130.2, 123.3, 22.4, -2.7.

**IR** (KBr, cm<sup>-1</sup>):  $\tilde{\nu}$  3067 (w), 2955 (m), 1525 (m), 1427 (m), 1248 (s), 1170 (m), 1113 (s), 1053 (s), 833 (vs), 814 (vs), 732(m), 701 (m).

**MS** (EI, 70 eV)  $m/z$  (%): 283 (16)  $[M^+]$ , 268 (100), 135 (6).  
**HRMS**: calcd. 283.0851 ( $C_{16}H_{17}NSSi$ ), found: 283.0826.

### Synthesis of 2-(dimethylphenylsilyl)quinoline (93).



Prepared from 2-(trifluoromethanesulfonyloxy)quinoline (222 mg, 0.8 mmol) according to the **TP10**. Reaction time 8 h, purification by chromatography ( $Al_2O_3$ , *n*-pentane-ether 9:1). Yield 150 mg (72%), yellowish oil.

**$^1H$  NMR** (300 MHz,  $CDCl_3$ ):  $\delta$  8.00 (d,  $J = 8.4$  Hz, 1H), 7.80 (d,  $J = 8.4$  Hz, 1H), 7.55 (d,  $J = 7.9$  Hz, 1H), 7.52-7.40 (m, 2H), 7.33-7.28 (m, 2H), 7.18-7.14 (m, 4H), 0.51 (s, 6H).

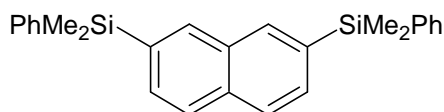
**$^{13}C$  NMR** (75 MHz,  $CDCl_3$ ):  $\delta$  136.9, 135.7, 132.6, 131.8, 131.5, 130.4, 130.3, 130.2, 129.9, 129.0, 128.3, -3.1.

**IR** (KBr,  $cm^{-1}$ ):  $\tilde{\nu}$  3068 (w), 2956 (w), 1428 (m), 1249 (m), 1114 (m), 829 (vs), 808 (vs), 779 (s), 700 (m).

**MS** (EI, 70 eV)  $m/z$  (%): 262 (100)  $[M-H^+]$ , 248 (20), 232 (12), 170 (6).

**HRMS**: calcd. 263.1130 ( $C_{17}H_{17}NSi$ ), found: 262.1051  $[M-H^+]$ .

### Synthesis of 2,7-bis(dimethylphenylsilyl)naphthalene (94).



Prepared from 2,7-naphthyl bitriflate (167 mg, 0.4 mmol) according to the **TP10**. Reaction time 3 h, purification by chromatography ( $SiO_2$ , *n*-pentane- $CH_2Cl_2 = 10:1$ ). Yield 103 mg (65%), colourless oil.

**$^1H$  NMR** (300 MHz,  $CDCl_3$ ):  $\delta$  7.81 (s, 2H), 7.57 (d,  $J = 8.4$  Hz, 2H), 7.38 (d,  $J = 8.4$  Hz, 2H), 7.31-7.33 (m, 4H), 7.16-7.19 (m, 6H), 0.42 (s, 12H).

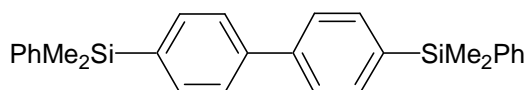
**$^{13}C$  NMR** (75 MHz,  $CDCl_3$ ):  $\delta$  140.6, 138.1, 137.5, 136.6, 135.8, 134.7, 133.3, 131.5, 130.2, 129.2, -1.9.

**IR** (KBr,  $cm^{-1}$ ):  $\tilde{\nu}$  3047 (w), 2955 (w), 1428 (m), 1249 (m), 1112 (m), 1095 (m), 832 (vs), 811 (vs), 730 (m), 700 (m), 472 (m).

**MS** (EI, 70 eV)  $m/z$  (%): 396 (36)  $[M^+]$ , 381 (100), 183 (20), 135 (41).

**HRMS**: calcd. 396.1730 ( $C_{26}H_{28}Si_2$ ), found: 396.1702.

### Synthesis of 4,4'-bis-(dimethylphenylsilyl)biphenyl (95).



Prepared from 4,4'-biphenyl bitriflate according (180 mg, 0.4 mmol) to the **TP10**. Reaction time 24 h, purification by chromatography (SiO<sub>2</sub>, *n*-pentane-CH<sub>2</sub>Cl<sub>2</sub> = 9:1). Yield 108 mg (64%), white solid.

**Mp.:** 37.0-39.5 °C.

**<sup>1</sup>H NMR** (300 MHz, CDCl<sub>3</sub>): δ 7.59-7.54 (m, 12H), 7.39-7.36 (m, 6H), 0.59 (s, 12H).

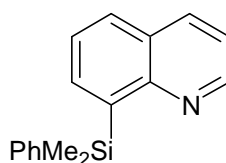
**<sup>13</sup>C NMR** (75 MHz, CDCl<sub>3</sub>): δ 144.1, 140.5, 139.5, 137.0, 136.5, 131.5, 130.2, 128.9, -2.3.

**IR** (KBr, cm<sup>-1</sup>):  $\tilde{\nu}$  3065 (w), 2955 (w), 1594 (m), 1427 (m), 1248 (m), 1116 (vs), 833 (s), 813 (vs), 804 (vs), 777 (s), 732 (s), 512 (m).

**MS** (EI, 70 eV) *m/z* (%): 422 (29) [M<sup>+</sup>], 407 (100), 269 (7), 196 (30), 135 (31).

**HRMS:** calcd. 422.1886 (C<sub>28</sub>H<sub>30</sub>Si<sub>2</sub>), found: 422.1918.

### Synthesis of 8-(dimethylphenylsilyl)quinoline (**96**).



Prepared from 8-(trifluoromethanesulfonyloxy)quinoline (222 mg, 0.8 mmol) according to the **TP10**. Reaction time 8 h, purification by chromatography (SiO<sub>2</sub>, *n*-pentane-CH<sub>2</sub>Cl<sub>2</sub> 9:1). Yield 158 mg (75%), yellow solid.

**Mp.:** 49.0-49.5 °C.

**<sup>1</sup>H NMR** (300 MHz, CDCl<sub>3</sub>): δ 8.80 (dd, *J* = 7.6 Hz, 1.8 Hz, 1H), 8.01 (dd, *J* = 8.3 Hz, 1.8 Hz, 1H), 7.72 (dd, *J* = 7.5 Hz, 1.8 Hz, 1H), 7.63-7.60 (m, 3H), 7.36 (dd, *J* = 7.8 Hz, 1.8 Hz, 1H), 7.29-7.24 (m, 4H), 0.68 (s, 6H).

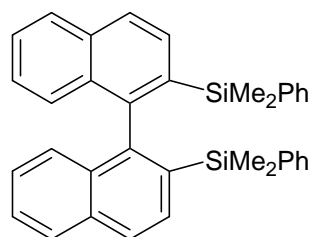
**<sup>13</sup>C NMR** (75 MHz, CDCl<sub>3</sub>): δ 154.0, 150.4, 141.3, 140.9, 139.4, 137.3, 136.0, 130.7, 130.0, 129.1, 128.9, 127.3, 122.1, -1.6.

**IR** (KBr, cm<sup>-1</sup>):  $\tilde{\nu}$  3436 (w), 2953 (w), 1602 (m), 1489 (m), 1427 (m), 1241 (m), 1111 (m), 848 (s), 790 (vs), 735 (s), 701 (s), 473(m).

**MS** (EI, 70 eV) *m/z* (%): 263 (4) [M<sup>+</sup>], 248 (100), 232 (5), 186 (22), 156 (5).

**HRMS:** calcd. 263.1130 (C<sub>17</sub>H<sub>17</sub>NSi), found: 263.1116.

### Synthesis of *rac*-2,2'-bis-(dimethylphenylsilyl)-1,1'-binaphthyl (**83**).



Prepared from 2,2'-bis-(trifluoromethanesulfonyloxy)-1,1'-binaphthyl (220 mg, 0.4 mmol) according to the **TP10**. Reaction time 6 h, purification by chromatography (SiO<sub>2</sub>, *n*-pentane-CH<sub>2</sub>Cl<sub>2</sub> 5:1). Yield 160 mg (77%), yellow solid.

**Mp.:** 83-84 °C.

**<sup>1</sup>H NMR** (300 MHz, CDCl<sub>3</sub>): δ 7.96-7.75 (m, 6H), 7.55-7.27 (m, 4H), 7.32-7.08 (m, 12H), 0.07 (s, 6H), -0.08 (s, 6H).

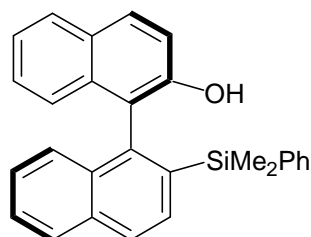
$^{13}\text{C}$  NMR (75 MHz,  $\text{CDCl}_3$ ):  $\delta$  145.4, 139.2, 138.6, 135.4, 133.7 (m), 133.5, 133.1, 131.4, 128.6, 128.4, 127.9, 127.8, 127.6, 127.3, 126.8, 126.7, 126.6, 126.2, 125.8, 125.6, 125.0, -1.0, -1.9.

IR (KBr,  $\text{cm}^{-1}$ ):  $\tilde{\nu}$  3045 (s), 1500 (w), 1427 (m), 1248 (m), 1113 (m), 874 (s), 852 (s), 834 (vs), 701 (vs).

MS (EI, 70 eV)  $m/z$  (%): 522 (22), 357 (31), 295 (56), 252 (33), 197 (32), 135 (100).

HRMS: calcd. 522.2199 ( $\text{C}_{36}\text{H}_{34}\text{Si}_2$ ), found: 522.2212.

### Synthesis of (*R*)-2-hydroxy-2'-(dimethylphenylsilyl)-1,1'-binaphthyl (97).



Prepared from 2-(trifluoromethanesulfonyloxy)-2-hydroxy-1,1'-binaphthyl (167 mg, 0.4 mmol) according to the **TP10** (with a double amount of the silylzinc reagent). Reaction time 6 h, purification by chromatography ( $\text{SiO}_2$ , *n*-pentane- $\text{CH}_2\text{Cl}_2$  1:1). Yield 128 mg (79%), pale yellow solid.

Chiral HPLC (Chiralcel OD, *n*-heptane/*i*-PrOH 95/5, 0.5 mL/min): (*R*)-enantiomer 14.3 min, (*S*)-enantiomer 21.8 min.

Mp.: 142-143 °C.

$[\alpha]_{\text{D}}^{20}$ : -267 (c 0.50,  $\text{CHCl}_3$ )

$^1\text{H}$  NMR (300 MHz,  $\text{CDCl}_3$ ):  $\delta$  7.93-7.75 (m, 5H), 7.55-7.46 (m, 1H), 7.20-7.02 (m, 10H), 4.56 (s, 1H), 0.09 (s, 3H), 0.04 (s, 3H).

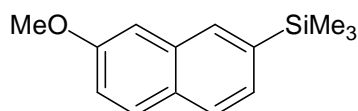
$^{13}\text{C}$  NMR (75 MHz,  $\text{CDCl}_3$ ):  $\delta$  135.7, 134.1, 132.0, 131.8, 130.7, 130.6, 130.0-129.8 (m), 129.6-129.5 (m), 128.9, 128.8, 128.5, 128.3, 127.8, 127.2, 125.2, 119.3, -0.5.

IR (KBr,  $\text{cm}^{-1}$ ):  $\tilde{\nu}$  3537 (s), 1620 (m), 1595 (m), 869 (m), 775 (vs), 737 (s).

MS (EI, 70 eV)  $m/z$  (%): 404 (43), 389 (21), 326 (60), 311 (100), 252 (813), 135 (50).

HRMS: calcd. 404.1596 ( $\text{C}_{28}\text{H}_{24}\text{OSi}$ ), found 404.1584.

### Synthesis of 2-trimethylsilyl-7-methoxynaphthalene (86a).



Prepared from 7-methoxy-2-naphthyl triflate (245 mg, 0.8 mmol) according to the **TP11**. Reaction time 19 h, purification by chromatography ( $\text{SiO}_2$ , *n*-pentane- $\text{CH}_2\text{Cl}_2$  = 6:1). Yield 96 mg (52%), colourless oil.

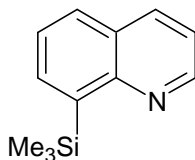
$^1\text{H}$  NMR (300 MHz,  $\text{CDCl}_3$ ):  $\delta$  7.91-7.86 (m, 1H), 7.70-7.58 (m, 2H), 7.40-7.36 (m, 1H), 7.10-7.02 (m, 2H), 3.84 (s, 3H), 0.26 (s, 9H).

$^{13}\text{C}$  NMR (75 MHz,  $\text{CDCl}_3$ ):  $\delta$  157.7, 138.5, 132.6, 129.5, 129.3, 128.4, 127.7, 126.4, 119.2, 105.9, 55.4, -1.4.

IR (KBr,  $\text{cm}^{-1}$ ):  $\tilde{\nu}$  2954 (m), 1628 (m), 1253 (m), 1214 (s), 1089 (m), 1034 (m), 838 (vs).

MS (EI, 70 eV)  $m/z$  (%): 230 (32), 216 (17), 215 (100), 185 (8), 172 (6).  
HRMS: calcd. 230.1127 (C<sub>14</sub>H<sub>18</sub>OSi), found: 230.1102.

### Synthesis of 8-(trimethylsilyl)quinoline (96b).



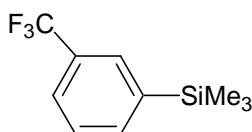
Prepared from 8-(trifluoromethanesulfonyloxy)quinoline (222 mg, 0.8 mmol) according to the **TP11**. Reaction time 19 h, purification by chromatography (SiO<sub>2</sub>, *n*-pentane-CH<sub>2</sub>Cl<sub>2</sub> 3:1). Yield 114 mg (71%), pale yellow oil. The analytical data correspond to those given in the literature.<sup>115</sup>

<sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>): δ 8.91 (dd,  $J_1 = 4.2$  Hz,  $J_2 = 1.8$  Hz, 1H), 8.11 (dd,  $J_1 = 8.0$  Hz,  $J_2 = 1.8$  Hz, 1H), 7.90-7.77 (m, 2H), 7.51 (t,  $J = 7.2$  Hz, 1H), 7.36 (q,  $J = 4.0$  Hz), 0.52 (s, 9H).

<sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>) 152.5, 148.7, 141.5, 135.8, 135.4, 128.7, 126.4, 125.6, 120.4, -0.3.

MS (EI, 70 eV)  $m/z$  (%): 200 (33), 186 (100), 170 (11), 156 (35).

### Synthesis of (3-trifluoromethylphenyl)trimethylsilane (90b).



Prepared from 3-trifluoromethylphenyl triflate (235 mg, 0.8 mmol) according to the **TP11**. Reaction time 1 h, purification by chromatography (SiO<sub>2</sub>, *n*-pentane). Yield 100 mg (57%), colourless oil.

<sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>): δ 7.66-7.62 (m, 2H), 7.52-7.47 (m, 1H), 7.40-7.34 (m, 1H), 0.23 (s, 9H).

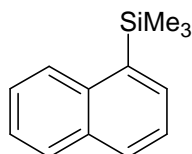
<sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>): δ 141.4 (m), 135.5, 131.1 (q,  $J = 15.2$  Hz), 130.3 (q,  $J = 37.7$  Hz), 126.1 (q,  $J = 16.0$  Hz), 125.1 (q,  $J = 52.2$  Hz), 123.0, -1.3.

IR (KBr, cm<sup>-1</sup>):  $\tilde{\nu}$  2958 (m), 2926 (m), 1326 (vs), 1263 (m), 1129 (s), 1167 (vs), 1076 (s), 800 (s).

MS (EI, 70 eV)  $m/z$  (%): 218 (3), 205 (5), 204 (18), 203 (100), 135 (5).

HRMS: calcd. 218.0739 (C<sub>10</sub>H<sub>13</sub>F<sub>3</sub>Si), found: 218.0740.

### Synthesis of 1-trimethylsilylnaphthalene (96d).



<sup>115</sup> E. Lukevics, E. Liepins, I. Segal, M. Fleisher, *J. Organomet. Chem.* **1991**, 406, 283.

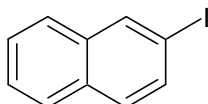
Prepared from 1-naphthyl triflate (221 mg, 0.8 mmol) according to the **TP11**. Reaction time 19 h, purification by chromatography (SiO<sub>2</sub>, *n*-pentane). Yield 126 mg (79%), colourless oil. The analytical data corresponds those given in literature.<sup>116</sup>

<sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>): δ 8.12 (d, *J* = 7.1 Hz, 1H), 7.88 (d, *J* = 3.8 Hz, 2H), 7.70 (d, *J* = 6.9 Hz, 1H), 7.55-7.43 (m, 3H), 0.49 (s, 9H).

<sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>): δ 138.1, 136.8, 133.4, 133.1, 129.7, 129.0, 128.0, 125.5, 125.2, 125.0, 0.4.

MS (EI, 70 eV) *m/z* (%): 200 (42), 186 (100), 43 (18).

#### Synthesis of 2-iodonaphthalene.



Prepared from **85** (131 mg, 0.5 mmol) according to the **TP12**. Purification by chromatography (SiO<sub>2</sub>, *n*-pentane). Yellowish oil, yield 114 mg (90%).

<sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>): δ 8.14 (s, 1H), 7.71-7.67 (m, 1H), 7.63-7.60 (m, 2H), 7.48-7.36 (m, 3H).

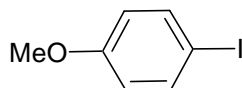
<sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>): δ 137.0, 135.4, 134.8, 132.5, 129.9, 128.2, 127.2, 127.1, 126.9, 114.2.

IR (KBr, cm<sup>-1</sup>):  $\tilde{\nu}$  3052 (m), 1579 (s), 1498 (m), 813 (vs), 712 (s), 476 (s).

MS (EI, 70 eV) *m/z* (%): 254 (100), 127 (54).

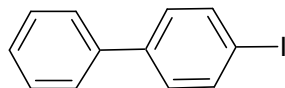
HRMS: calcd. 253.9592 (C<sub>10</sub>H<sub>7</sub>I), found: 253.9574.

#### Synthesis of 4-iodoanisole.



Prepared from **88** (85 mg, 0.35 mmol) according to the **TP12**. Purification by chromatography (SiO<sub>2</sub>, *n*-pentane-CH<sub>2</sub>Cl<sub>2</sub> 10:1). Colourless oil, yield 73 mg (89%). The analytical data corresponds to those from an authentic sample.

#### Synthesis of 4-iodobiphenyl.



Prepared from **87** (114 mg, 0.5 mmol) according to the **TP12**. Purification by chromatography (SiO<sub>2</sub>, *n*-pentane-CH<sub>2</sub>Cl<sub>2</sub> 20:1). Pale yellow solid, yield 126 mg (90%). The analytical data corresponds to those from an authentic sample.

**Mp.:** 110-112 °C.

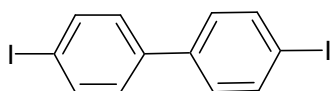
<sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>): δ

MS (EI, 70 eV) *m/z* (%): 280 (100), 153 (58), 127 (14).

#### Synthesis of 4, 4'-diiodobiphenyl.

<sup>116</sup> M. Tobisu, Y. Kita, N. Chatani, *J. Am. Chem. Soc.* **2006**, *128*, 8152.





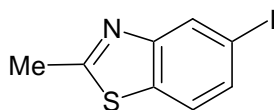
Prepared from **95** (84 mg, 0.2 mmol) according to the **TP12**. Purification by chromatography (SiO<sub>2</sub>, *n*-pentane-CH<sub>2</sub>Cl<sub>2</sub> 20:1). Pale yellow solid, yield 61 mg (75%). The analytical data corresponds to those reported in the literature.<sup>117</sup>

**Mp.:** 201-204 °C.

<sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>): δ 7.71 (d, *J* = 8.4 Hz, 4H), 7.22 (d, *J* = 8.6 Hz, 4H).

<sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>): δ 139.5, 137.9, 128.7, 93.4.

#### Synthesis of 5-iodo-2-methylbenzothiazole (101).



Prepared from **92** (85 mg, 0.3 mmol) according to the **TP12**. Purification by chromatography (SiO<sub>2</sub>, *n*-pentane-CH<sub>2</sub>Cl<sub>2</sub> 1:2). Yield 46 mg (56%), white solid.

**Mp.:** 85.0-85.5 °C.

<sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>): 8.20 (d, *J* = 1.4 Hz, 1H), 7.54 (dd, *J* = 8.4 Hz, *J* = 1.4 Hz, 1H), 7.47 (d, *J* = 8.4 Hz, 1H), 2.76 (s, 3H).

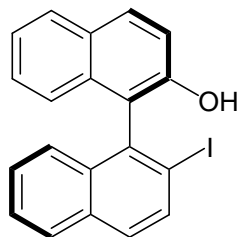
<sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>): δ 168.6, 155.3, 135.6, 133.7, 131.9, 123.1, 90.5, 20.5

**IR** (KBr, cm<sup>-1</sup>):  $\tilde{\nu}$  3041 (w), 1519 (m), 1434 (m), 1169 (m), 1152 (m), 1066 (s), 883 (m), 795 (s), 644 (m).

**MS** (EI, 70 eV) *m/z* (%): 274 (100) [M<sup>+</sup>], 148 (32), 107 (12), 63 (14).

**HRMS**: calcd. 274.9266 (C<sub>8</sub>H<sub>6</sub>INS), found: 274.9270.

#### Synthesis of (*R*)-2-iodo-2'-hydroxy-1,1'-binaphthyl (100).



Into a 100 ml Schlenk-flask under Ar was placed (*R*)-2-phenyldimethylsilyl-2'-hydroxy-1,1'-binaphthyl (**98**, 1.60 g, 4.0 mmol) in dry CH<sub>2</sub>Cl<sub>2</sub> (20 mL). The mixture was cooled to 0 °C and TMSCl (2.1 mL, 20 mmol) was added at this temperature. The solution of ICl (1.37 g, 8.4 mmol) in dry CH<sub>2</sub>Cl<sub>2</sub> (20 mL) was added dropwise at 0 °C during 15 min. The mixture was stirred for 30 min at RT and then poured into vigorously stirred 20% aqueous Na<sub>2</sub>S<sub>2</sub>O<sub>3</sub> (100 mL). The organic layer was separated and the aqueous phase was extracted twice with CH<sub>2</sub>Cl<sub>2</sub>. The combined organic layers were dried over MgSO<sub>4</sub>, evaporated and the product was isolated by column chromatography (CH<sub>2</sub>Cl<sub>2</sub>-pentane 1:1, then CH<sub>2</sub>Cl<sub>2</sub>). Yield 1.22 g (78%), >99% *ee*.

<sup>117</sup> Z. H. Li, M. S. Wong, Y. Tao, M. D'Iorio, *J. Org. Chem.* **2004**, *69*, 921.

**Chiral HPLC:** (Chiralsel OD-H, heptane-*i*-PrOH 99/1, flow 0.5 mL/min. (*R*)-enantiomer 88.5 min; (*S*)-enantiomer 104.0 min).

**Mp.:** 116-117 °C.

$[\alpha]_D^{20}$ : -26.3° (*c* = 0.30, CHCl<sub>3</sub>).

**<sup>1</sup>H NMR** (300 MHz, CDCl<sub>3</sub>): δ 8.01 (d, *J* = 8.6 Hz, 1H); 7.89-7.80 (m, 3H); 7.65 (d, *J* = 8.7 Hz, 1H); 7.47-7.42 (m, 1H); 7.30-7.17 (m, 5H); 6.87 (d, *J* = 8.4 Hz, 1H); 4.66 (s, 1H).

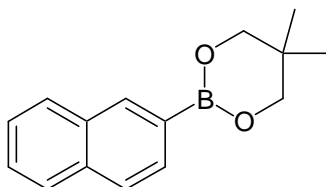
**<sup>13</sup>C NMR** (75 MHz, CDCl<sub>3</sub>): δ 150.8; 137.1; 136.4; 134.4; 133.7; 133.1; 130.9; 130.8; 129.5; 128.7; 128.6; 128.2; 127.5; 127.4; 126.9; 124.7; 124.1; 122.3; 118.1; 102.2.

**IR** (KBr, cm<sup>-1</sup>):  $\tilde{\nu}$  3501 (s); 3434 (s); 3056 (w); 1620 (w); 1596 (w); 1206 (w); 1143 (w); 826 (s); 811 (s).

**MS** (EI, 70 eV) *m/z* (%): 396 (M<sup>+</sup>, 76); 270 (17); 268 (32); 251 (15); 241 (19); 239 (53); 207 (39); 125 (22); 97 (17); 78 (26); 49 (14); 41 (14).

**HRMS:** calcd. 396.0011 (C<sub>20</sub>H<sub>13</sub>IO), found: 396.0001.

### Synthesis of 5,5-dimethyl-2-naphthalen-2-yl-[1,3,2]dioxaborinane (85a).



Prepared from **85** (131 mg, 0.5 mmol) according to the **TP13**. Purification by chromatography (SiO<sub>2</sub>, *n*-pentane-CH<sub>2</sub>Cl<sub>2</sub> 1:1). Yield 86 mg (71%), white solid.

**Mp.:** 103-105 °C.

**<sup>1</sup>H NMR** (300 MHz, CDCl<sub>3</sub>): δ 8.26 (s, 1H), 7.80-7.70 (m, 4H), 7.42-7.33 (m, 2H), 3.74 (s, 4H), 0.96 (s, 6H).

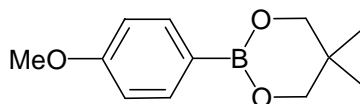
**<sup>13</sup>C NMR** (75 MHz, CDCl<sub>3</sub>): δ 135.4, 134.2, 133.3, 130.3, 129.1, 128.6, 128.0, 127.2, 127.0, 126.0, 72.8, 32.3, 22.3.

**IR** (KBr, cm<sup>-1</sup>):  $\tilde{\nu}$  3436 (m), 2957 (w), 1479 (m), 1417 (m), 1329 (vs), 1309 (vs), 1253 (m), 1136 (m), 747 (m).

**MS** (EI, 70 eV) *m/z* (%): 240 (100) [M<sup>+</sup>], 197 (5), 154 (80).

**HRMS:** calcd. 240.1322 (C<sub>15</sub>H<sub>17</sub>BO<sub>2</sub>), found: 240.1315.

### Synthesis of 2-(4-methoxyphenyl)-5,5-dimethyl-[1,3,2]dioxaborinane (88a).



Prepared from **88** (242 mg, 1 mmol) according to the **TP13**. Purification by chromatography (SiO<sub>2</sub>, CH<sub>2</sub>Cl<sub>2</sub>). Yield 150 mg (68%), white solid.

**Mp.:** 63.0-64.5 °C.

**<sup>1</sup>H NMR** (300 MHz, CDCl<sub>3</sub>): δ 7.65 (d, *J* = 8.8 Hz, 1H), 6.79 (d, *J* = 8.8 Hz, 1H), 3.73 (s, 3H), 3.66 (s, 4H), 0.93 (s, 6H).

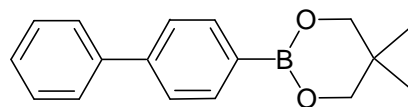
**<sup>13</sup>C NMR** (75 MHz, CDCl<sub>3</sub>): δ 161.8, 135.5, 129.6, 113.2, 72.3, 55.1, 31.9, 21.9.

**IR** (KBr, cm<sup>-1</sup>):  $\tilde{\nu}$  2957 (w), 1722 (w), 1604 (m), 1477 (m), 1318 (vs), 1307(s), 1246 (s), 1174 (m), 1132 (m), 827 (m).

**MS** (EI, 70 eV) *m/z* (%): 220 (100) [M<sup>+</sup>], 177 (10), 134 (87).

**HRMS:** calcd. 220.1271 (C<sub>12</sub>H<sub>17</sub>BO<sub>3</sub>), found: 220.1281.

### Synthesis of 2-(4-biphenyl)-5,5-dimethyl-[1,3,2]dioxaborinane (**87a**).



Prepared from **87** (183 mg, 0.8 mmol) according to the **TP13**. Purification by chromatography (SiO<sub>2</sub>, *n*-pentane-CH<sub>2</sub>Cl<sub>2</sub> 1:1). Yield 132 mg (62%), white solid.

**Mp.:** 108-109 °C.

**<sup>1</sup>H NMR** (300 MHz, CDCl<sub>3</sub>): δ 7.82-7.77 (m, 2H), 7.54-7.50 (m, 3H), 7.38-7.17 (m, 4H), 3.71 (s, 4H), 0.95 (s, 6H).

**<sup>13</sup>C NMR** (75 MHz, CDCl<sub>3</sub>): δ 143.7, 141.6, 134.7, 131.1, 129.1, 128.0, 127.8, 127.6, 126.7, 72.7, 32.3, 22.3.

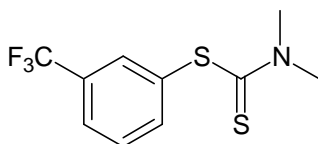
**IR** (KBr, cm<sup>-1</sup>):  $\tilde{\nu}$  2932 (w), 1478 (w), 1379 (m), 1318 (vs), 1134 (s), 642 (m).

**MS** (EI, 70 eV) *m/z* (%): 266 (100), 265 (24), 180 (79), 179 (29), 152 (11).

**HRMS:** calcd. 266.1478 (C<sub>17</sub>H<sub>19</sub>BO<sub>2</sub>), found: 266.1491.

## 16. Thiolation reaction of organomagnesium and organozinc compounds.

### Synthesis of 3-trifluoromethylphenyl dimethyldithiocarbamate (**104**).



The Grignard reagent was prepared from 3-bromotrifluoromethylbenzene (2.25 g, 10 mmol) according to the **TP14** (RT, 1.5 h). It was converted into **104** according to the **TP15**. The product was recrystallized from CH<sub>2</sub>Cl<sub>2</sub>-heptane. Yield 2.11 g (84%), white solid.

**Mp.:** 83-84 °C.

**<sup>1</sup>H NMR** (300 MHz, CDCl<sub>3</sub>): δ 7.71-7.61 (m, 3H); 7.51 (t, *J* = 7.7 Hz, 1H); 3.47 (d, *J* = 16.9 Hz, 6H).

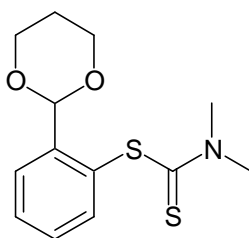
**<sup>13</sup>C NMR** (75 MHz, CDCl<sub>3</sub>): δ 196.3; 140.8; 134.1 (q, *J* = 3.6 Hz); 131.7 (q, *J* = 32.6 Hz); 129.8; 127.1 (q, *J* = 3.6 Hz); 124.0 (q, *J* = 272 Hz), 46.1, 42.4.

**IR** (KBr, cm<sup>-1</sup>):  $\tilde{\nu}$  3436 (w); 1507 (w); 1327 (s); 1304 (s); 1249 (s); 1114 (s); 1067 (s); 974 (s); 799 (s); 694 (s).

**MS** (EI, 70 eV) *m/z* (%): 265 (26); 246 (5); 177 (4); 157 (4); 145 (9); 88 (100); 73 (6); 42 (5).

**HRMS:** calcd. 265.0207 (C<sub>10</sub>H<sub>10</sub>NS<sub>2</sub>F<sub>3</sub>), found: 265.0194.

### Synthesis of 2-(1,3-dioxan-2-yl)phenyl dimethyldithiocarbamate (**105**).



The Grignard reagent was prepared from 2-(2-bromophenyl)-1,3-dioxane (2.42 g, 10 mmol) according to the **TP14** (RT, 36 h). It was converted into **105** according to the **TP15**. The product recrystallized from CH<sub>2</sub>Cl<sub>2</sub>-heptane. Yield 2.45 g (91%), white solid.

**Mp.:** 125-126 °C.

**<sup>1</sup>H NMR** (300 MHz, CDCl<sub>3</sub>): δ 7.76 (dd, *J*<sub>1</sub> = 7.8 Hz, *J*<sub>2</sub> = 1.4 Hz, 1H), 7.44 (m, 1H); 7.35-7.31 (m, 2 H); 5.64 (s, 1H); 4.15 (dd, *J*<sub>1</sub> = 10.6 Hz, *J*<sub>2</sub> = 5.1 Hz, 2H); 3.91 (dt, *J*<sub>1</sub> = 12.2 Hz, *J*<sub>2</sub> = 2.5 Hz, 2H); 3.52 (s, 3H); 3.47 (s, 3H), 2.15-2.10 (m, 1H); 1.36 (d, *J* = 13.5 Hz, 1H).

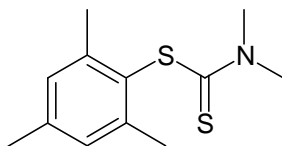
**<sup>13</sup>C NMR** (75 MHz, CDCl<sub>3</sub>): δ 197.1; 143.0; 138.4; 130.6; 129.8; 127.4; 100.1; 67.8; 46.0; 42.6; 26.2.

**IR** (KBr, cm<sup>-1</sup>):  $\tilde{\nu}$  3435 (w); 2857 (s); 1503 (s); 1376 (s); 1232 (s); 1145 (s); 1101 (s); 1010 (s); 983 (s); 772 (s).

**MS** (EI, 70 eV) *m/z* (%): 282 ([M-H]<sup>+</sup>, 0.6); 196 (22); 164 (11); 163 (100); 137 (14); 109 (7); 105 (16); 88 (84); 73 (7).

**HRMS**: calcd. 283.0701 (C<sub>13</sub>H<sub>17</sub>NO<sub>2</sub>S<sub>2</sub>), found: 282.0608 [M-H]<sup>+</sup>.

#### Synthesis of 2-(1,3-dioxan-2-yl)phenyl dimethylthiocarbamate (**106**).



The Grignard reagent was prepared from mesityl bromide (2.57 g, 13 mmol) by insertion of Mg metal in THF in the presence of 1.1 equiv. of LiCl. Yield 82%. It was converted into **106** according to the **TP15** (10 mmol of the reagent used). The product was purified by chromatography (SiO<sub>2</sub>, CH<sub>2</sub>Cl<sub>2</sub>-heptane). Yield 1.86 g (83%), white solid.

**Mp.:** 84-85 °C.

**<sup>1</sup>H NMR** (300 MHz, CDCl<sub>3</sub>): δ 6.93 (s, 2H); 3.45 (s, 6H); 2.27 (s, 6H); 2.23 (s, 3H).

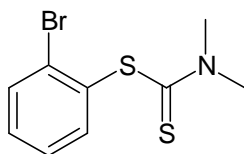
**<sup>13</sup>C NMR** (75 MHz, CDCl<sub>3</sub>): δ 196.4; 144.2; 140.8; 129.7; 128.0; 46.0; 42.4; 22.2; 21.8.

**IR** (KBr, cm<sup>-1</sup>):  $\tilde{\nu}$  2920 (w); 1600 (w); 1490 (s); 1369 (s); 1250 (s); 1143 (s); 979 (s); 854 (s); 846 (s).

**MS** (EI, 70 eV) *m/z* (%): 239 (M<sup>+</sup>, 18); 206 (5); 119 (6); 91(4); 90 (4); 89 (5); 88 (100); 73 (4).

**HRMS**: calcd. 239.0802 (C<sub>12</sub>H<sub>17</sub>NS<sub>2</sub>), found: 239.0787.

#### Synthesis of 2-bromophenyl dimethylthiocarbamate (**107**).



The Grignard reagent was prepared from *o*-dibromobenzene (2.36 g, 10 mmol) according to the **TP14** (RT, 6 h). It was converted into **107** according to the **TP15**. The product recrystallized from CH<sub>2</sub>Cl<sub>2</sub>-heptane. Yield 2.33 g (89%), white solid.

**Mp.:** 103.5-104.5 °C.

**<sup>1</sup>H NMR** (300 MHz, CDCl<sub>3</sub>): δ 7.75 (dd, *J*<sub>1</sub> = 7.8 Hz, *J*<sub>2</sub> = 1.5 Hz, 1H); 7.61 (dd, *J*<sub>1</sub> = 7.5 Hz, *J*<sub>2</sub> = 1.9 Hz, 1H); 7.41 (td, *J*<sub>1</sub> = 7.5 Hz, *J*<sub>2</sub> = 1.6 Hz, 1H); 7.41 (td, *J*<sub>1</sub> = 7.6 Hz, *J*<sub>2</sub> = 1.9 Hz, 1H); 3.57 (s, 3H); 3.54 (s, 3H).

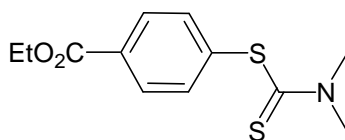
**<sup>13</sup>C NMR** (75 MHz, CDCl<sub>3</sub>): δ 195.4; 139.6; 134.0; 133.6; 132.3; 132.1; 128.5; 42.6; 42.4.

**IR** (KBr, cm<sup>-1</sup>):  $\tilde{\nu}$  2924 (w); 1494 (s); 1371 (s); 1251 (s); 983 (s); 759 (s).

**MS** (EI, 70 eV) *m/z* (%): 196 (100); 140 (5); 108 (5); 88 (15); 73(3).

**HRMS**: calcd. 274.9438 (C<sub>9</sub>H<sub>10</sub>BrNS<sub>2</sub>), found: 275.9543 ([M+H]<sup>+</sup>).

### Synthesis of 4-carbethoxyphenyl dimethyldithiocarbamate (**108**).



The Grignard reagent was prepared from ethyl 4-iodobenzoate (3.04 g, 11 mmol) according to the **TP14** (-20 °C, 30 min). It was converted into **108** according to the **TP15**. Yield 2.43 g (95%), white solid.

**Mp.:** 95-96 °C.

**<sup>1</sup>H NMR** (300 MHz, CDCl<sub>3</sub>): δ 8.03 (d, *J* = 8.5 Hz, 2H), 7.47 (d, *J* = 8.5 Hz, 2H), 4.32 (q, *J* = 7.5 Hz, 2H); 3.48 (s, 3H); 3.43 (s, 3H), 1.32 (t, *J* = 7.5 Hz, 3H).

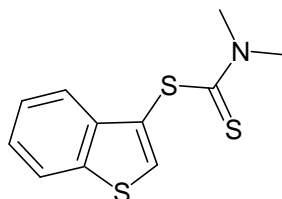
**<sup>13</sup>C NMR** (75 MHz, CDCl<sub>3</sub>): δ 196.5; 166.3; 137.3; 137.1; 132.1; 126.4; 61.6; 46.0; 42.5; 14.7.

**IR** (KBr, cm<sup>-1</sup>):  $\tilde{\nu}$  2974 (w); 1710 (s); 1474 (s); 1372 (s); 1275 (s); 1249 (s); 1105 (s); 977 (s), 760 (s).

**MS** (EI, 70 eV) *m/z* (%): 269 (M<sup>+</sup>, 32); 224 (10); 136 (5); 108 (4); 88 (100);

**HRMS**: calcd. 269.0544 (C<sub>12</sub>H<sub>15</sub>NO<sub>2</sub>S<sub>2</sub>), found: 269.0547.

### Synthesis of 3-benzothienyl dimethyldithiocarbamate (**109**).



The Grignard reagent was prepared from 3-bromobenzothiophene (2.12 g, 10 mmol) according to the **TP14** (0 °C-RT, 1.5 h). It was converted into **109** according to the **TP15**. The product recrystallized from CH<sub>2</sub>Cl<sub>2</sub>-heptane. Yield 2.11 g (93%), pink solid.

**Mp.:** 144-145 °C.

**<sup>1</sup>H NMR** (300 MHz, CDCl<sub>3</sub>) δ 7.78 (d, *J* = 7.1 Hz, 1H); 7.71 (d, *J* = 8.7 Hz, 1H); 7.07 (s, 1H); 7.33-7.28 (m, 1H); 3.41 (s, 6H).

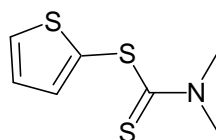
**<sup>13</sup>C NMR** (75 MHz, CDCl<sub>3</sub>): δ 195.9; 139.9; 139.8; 136.9; 125.3; 125.2; 123.4; 46.1; 42.5.

**IR** (KBr, cm<sup>-1</sup>):  $\tilde{\nu}$  3436 (w); 1498 (s); 1420 (s); 1248 (s); 985 (s); 960 (s); 756 (s).

**MS** (EI, 70 eV) *m/z* (%): 253 (M<sup>+</sup>, 14); 165 (5); 121 (7); 89(6); 88(100); 73(5); 43(4).

**HRMS:** calcd. 239.0054 (C<sub>11</sub>H<sub>11</sub>NS<sub>3</sub>), found: 253.0059.

### Synthesis of 2-thienyl dimethyldithiocarbamate (**110**).



The Grignard reagent was prepared from 2-bromothiophene (1.64 g, 10 mmol) according to the **TP14** (0 °C-RT, 1.5 h). It was converted into **110** according to the **TP15**. Yield 1.85 g (96%), pink solid. The analytical data corresponds to those reported in literature.<sup>118</sup>

**Mp.:** 83-84 °C.

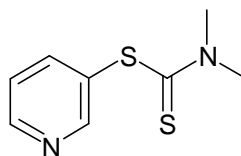
**<sup>1</sup>H NMR** (300 MHz, CDCl<sub>3</sub>) δ 7.54-7.52 (m, 1H), 7.43-7.40 (m, 1H), 7.15-7.12 (m, 1H), 3.55 (s, 3H), 3.48 (s, 3H).

**<sup>13</sup>C NMR** (75 MHz, CDCl<sub>3</sub>): δ 197.7, 139.2, 133.9, 129.6, 128.3, 46.5, 42.2.

**MS** (EI, 70 eV) *m/z* (%): 203 (3), 88 (100), 73 (4).

**HRMS:** calcd. 202.9897 (C<sub>9</sub>H<sub>7</sub>NS<sub>3</sub>), found: 202.9891.

### Synthesis of 3-pyridyl dimethyldithiocarbamate (**111**).



The Grignard reagent was prepared from 3-bromopyridine (1.90 g, 12 mmol) according to the **TP14** (0 °C-RT, 1.5 h). It was converted into **111** according to the **TP15**. The product recrystallized from CH<sub>2</sub>Cl<sub>2</sub>-heptane. Yield 1.73 g (92%), yellowish solid. The analytical data corresponds to those reported in literature.<sup>118</sup>

**Mp.:** 85-87 °C.

<sup>118</sup> S. Gronowitz, A.-B. Hörnfeldt, M. Temciuc, *Synthesis* **1993**, 483.

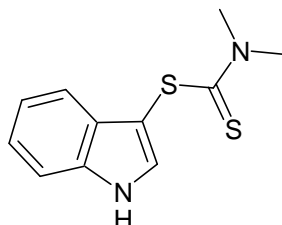
**<sup>1</sup>H NMR** (300 MHz, CDCl<sub>3</sub>) δ 8.68-8.61 (m, 1H), 8.40-8.38 (m, 1H), 7.80-7.76 (m, 1H), 7.40-7.28 (m, 1H), 3.55 (s, 3H), 3.52 (s, 3H).

**<sup>13</sup>C NMR** (75 MHz, CDCl<sub>3</sub>): δ 196.2, 156.9, 150.9, 144.8, 129.7, 124.2, 46.2, 42.4.

**MS** (EI, 70 eV) *m/z* (%): 198 (7), 90 (4), 88 (100), 73 (9).

**HRMS**: calcd. 198.0285 (C<sub>8</sub>H<sub>10</sub>N<sub>2</sub>S<sub>2</sub>), found 198.0284.

### Synthesis of 3-indolyl dimethyldithiocarbamate (**112**).



In a 25 ml Schlenk-flask, *i*-PrMgCl-LiCl solution (10.5 mmol, 5.25 mL of 2.00 M solution in THF) was cooled to 0 °C, and indole (10.0 mmol, 1.17 g) in dry THF (6 mL) was added at this temperature. The mixture was allowed to reach RT within 3 h, and then stirred overnight. The mixture was cooled to 0 °C and tetramethylthiuram disulfide (**102**, 9.5 mmol, 2.28 g) in dry CH<sub>2</sub>Cl<sub>2</sub> (8 mL) was added at this temperature. After 24 h of stirring at RT the mixture was poured into sat. NH<sub>4</sub>Cl solution (50 mL), the aqueous phase was extracted with CH<sub>2</sub>Cl<sub>2</sub>, the combined organic layers were dried over MgSO<sub>4</sub>, evaporated *in vacuo* and the residue was recrystallized from CH<sub>2</sub>Cl<sub>2</sub>-heptane. Yield 2.04 g (91%).

**Mp.**: 187-188 °C (dec.).

**<sup>1</sup>H NMR** (300 MHz, CDCl<sub>3</sub>) δ 7.48 (d, *J* = 8.1 Hz, 1H); 7.40 (d, *J* = 7.6 Hz, 1H); 7.17 (t, *J* = 6.9 Hz, 1H); 7.08 (t, *J* = 7.0 Hz, 1H); 3.54 (s, 3H); 3.46 (s, 3H).

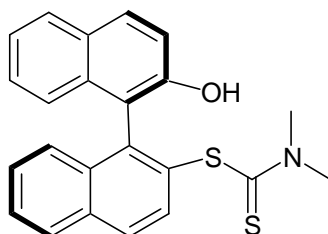
**<sup>13</sup>C NMR** (75 MHz, CDCl<sub>3</sub>): δ 197.3; 136.8; 134.3; 129.6; 122.1; 120.3; 118.9; 112.5; 100.9; 45.9; 41.9.

**IR** (KBr, cm<sup>-1</sup>):  $\tilde{\nu}$  3323 (s); 1504 (s); 1457 (s); 1370 (s); 1252 (s); 1147 (s); 978 (s); 739 (s); 486 (w).

**MS** (EI, 70 eV) *m/z* (%): 236 (M<sup>+</sup>, 31); 148 (12); 121 (6); 117 (3); 90 (5); 89 (6); 88 (100); 77 (4).

**HRMS**: calcd. 236.0442 (C<sub>11</sub>H<sub>12</sub>N<sub>2</sub>S<sub>2</sub>), found: 236.0429.

### Synthesis of (*R*)-2-hydroxy-2'-(*N,N'*-dimethyldithiocarbamoyl)-1,1'-binaphthyl (**113**).



Into a 10 mL Schlenk-flask was placed *i*-PrMgCl-LiCl (0.33 mL of 2.05 M in THF, 2.5 equiv.), cooled to 0° C and (*R*)-2-iodo-2'-hydroxy-1,1'-binaphthyl (**100**) (0.099 g, 0.25 mmol) was added at this temperature in one portion. The mixture was stirred at rt for 3 h and again cooled to 0° C. The solution of TMTD (**102**) (0.25 g, 1.04 mmol) in CH<sub>2</sub>Cl<sub>2</sub> (2 mL) was

added in one portion, the mixture was stirred overnight and poured into sat.  $\text{NH}_4\text{Cl}$  (10 mL). The aqueous phase was extracted with  $\text{CH}_2\text{Cl}_2$ , combined organic phases dried ( $\text{MgSO}_4$ ), evaporated and the residue purified by column chromatography ( $\text{Et}_2\text{O}-\text{CH}_2\text{Cl}_2$  2:1). Yield 0.075 g (78%), >99% *ee*.

**Chiral HPLC:** Chiralsel OJ, heptane-*i*-PrOH 90/10, 0.6 mL/min. (*R*)-enantiomer 19.0 min; (*S*)-enantiomer 21.3 min.

$[\alpha]_{\text{D}}^{20}$ : +658 (c 2.6  $\text{CHCl}_3$ ).

**Mp.:** 208-209 °C.

**$^1\text{H}$  NMR** (300 MHz,  $\text{CDCl}_3$ )  $\delta$  8.07 (d,  $J$  = 9.0 Hz, 1H), 7.98 (d,  $J$  = 8.2 Hz, 1H), 7.89-7.86 (m, 1H), 7.68 (d,  $J$  = 9.0 Hz, 1H), 7.55-7.52 (m, 1H), 7.26-7.35 (m, 3H), 7.21-7.17 (m, 1H), 7.14 (d,  $J$  = 8.3 Hz, 1H), 6.89 (d,  $J$  = 8.0 Hz, 1H), 6.31 (s, 1H), 3.42 (s, 3H), 3.19 (s, 3H).

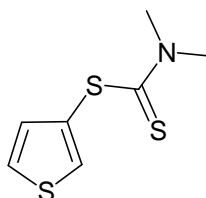
**$^{13}\text{C}$  NMR** (75 MHz,  $\text{CDCl}_3$ ):  $\delta$  198.2, 153.0, 139.3, 134.4 (m), 134.1, 133.7, 132.4, 130.0, 128.5, 128.2, 128.0, 127.8, 127.2, 127.0, 126.4, 124.2, 123.2, 119.7, 117.8, 45.6, 42.4.

**IR** (KBr,  $\text{cm}^{-1}$ ):  $\tilde{\nu}$  3435 (s), 2926 (w), 1619 (m), 1504 (m), 1380 (m), 1146 (w), 815 (m).

**MS** (EI, 70 eV)  $m/z$  (%): 389 (28), 284 (23), 283 (15), 282 (15), 239 (14), 88 (100).

**HRMS:** calcd. 389.0908 ( $\text{C}_{23}\text{H}_{19}\text{NOS}_2$ ), found: 389.0883.

### Synthesis of 3-thienyl dimethyldithiocarbamate (114).



The Grignard reagent was prepared from 3-bromothiophene (1.64 g, 10 mmol) according to the **TP14** (0 °C-RT, 3 h). It was converted into **114** according to the **TP15**. The product recrystallized from  $\text{CH}_2\text{Cl}_2$ -heptane. Yield 1.74 g (90%), pink solid. The analytical data corresponds to those reported in literature.<sup>118</sup>

**Mp.:** 82-83 °C.

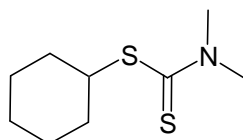
**$^1\text{H}$  NMR** (300 MHz,  $\text{CDCl}_3$ )  $\delta$  7.56-7.54 (m, 1H), 7.18-7.16 (m, 1H), 7.08-7.05 (m, 1H), 3.46 (s, 3H), 3.40 (s, 3H).

**$^{13}\text{C}$  NMR** (75 MHz,  $\text{CDCl}_3$ ):  $\delta$  197.1, 139.2, 133.9, 129.6, 128.3, 46.2, 42.2.

**MS** (EI, 70 eV)  $m/z$  (%): 203 (13), 88 (100), 73 (7).

**HRMS:** calcd. 202.9897 ( $\text{C}_7\text{H}_9\text{NS}_3$ ), found: 202.9869.

### Synthesis of *S*-cyclohexyl-*N,N*-dimethyldithiocarbamate (115).



Cyclohexylzinc bromide-lithium chloride was prepared from bromocyclohexane (815 mg, 5 mmol) according to **TP19** (50 °C, 6 h, 96% yield). It was converted into compound **115** according to the **TP16**. The product was purified by chromatography (pentane- $\text{CH}_2\text{Cl}_2$ ). Yield 768 mg (91%), white crystalline solid.



**Mp.:** 61-63 °C.

**<sup>1</sup>H NMR** (300 MHz, CDCl<sub>3</sub>) δ 3.92-3.88 (m, 1H), 3.54 (s, 3H), 3.35 (s, 3H), 2.16-2.10 (m, 2H), 1.77-1.28 (m, 8H).

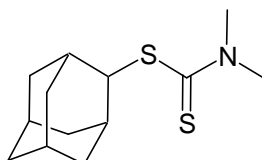
**<sup>13</sup>C NMR** (75 MHz, CDCl<sub>3</sub>): δ 197.3, 51.1, 45.3, 41.8, 33.2, 26.6, 26.0.

**IR** (KBr, cm<sup>-1</sup>):  $\tilde{\nu}$  2927 (vs), 2846 (s), 1490 (s), 1370 (vs), 1254 (s), 1119 (s), 983 (vs).

**MS** (EI, 70 eV) *m/z* (%): 203 (7), 123 (8), 122 (48), 121 (83), 88 (100), 41 (9).

**HRMS:** calcd. 203.0802 (C<sub>9</sub>H<sub>17</sub>NS<sub>2</sub>), found: 203.0812.

### Synthesis of *S*-(2-adamantyl)-*N,N*-dimethyldithiocarbamate (**116**).



2-Adamantylzinc bromide-lithium chloride was prepared from 2-bromoadamantane (1.08 g, 5 mmol) according to the **TP19** (50 °C, 24 h). It was converted into compound **116** according to the **TP16**. The product was purified by chromatography (pentane-CH<sub>2</sub>Cl<sub>2</sub>). Yield 838 mg (79%), white needles.

**Mp.:** 110.5-111 °C.

**<sup>1</sup>H NMR** (300 MHz, CDCl<sub>3</sub>) δ 4.26 (s, 1H), 3.47 (s, 3H), 3.32 (s, 3H), 2.09 (s, 2H), 1.89-1.60 (m, 12H).

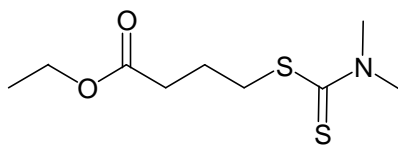
**<sup>13</sup>C NMR** (75 MHz, CDCl<sub>3</sub>): δ 197.7, 59.3, 45.5, 41.9, 39.0, 38.0, 34.2, 33.6, 30.1, 27.8, 27.5.

**IR** (KBr, cm<sup>-1</sup>):  $\tilde{\nu}$  2912 (s), 2853 (m), 1374 (m), 1254 (m), 986 (m), 909 (vs), 733 (vs).

**MS** (EI, 70 eV) *m/z* (%): 255 (35), 135 (100), 121 (33), 93 (35), 88 (81), 79 (31), 67 (31).

**HRMS:** calcd. 255.1115 (C<sub>13</sub>H<sub>21</sub>NS<sub>2</sub>), found: 255.1090.

### Synthesis of *S*-(3-carboethoxypropyl)-*N,N*-dimethyldithiocarbamate (**117**).



3-Carboethoxypropylzinc bromide-lithium chloride was prepared from ethyl 4-bromobutyrate (975 mg, 5 mmol) according to the **TP19** (50 °C, 1 h). It was converted into compound **117** according to the **TP16**. The product was purified by chromatography (pentane-CH<sub>2</sub>Cl<sub>2</sub>). Yield 850 mg (87%), colourless oil.

**<sup>1</sup>H NMR** (300 MHz, CDCl<sub>3</sub>) δ 4.07 (q, *J* = 10.2 Hz, 2H), 3.48 (s, 3H), 3.30-3.26 (m, 2H), 3.28 (s, 3H), 2.40-2.35 (m, 2H), 2.00-1.95 (m, 2H), 1.19 (t, *J* = 10.2 Hz, 3H).

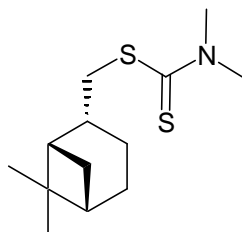
**<sup>13</sup>C NMR** (75 MHz, CDCl<sub>3</sub>): δ 197.4, 173.3, 60.8, 45.7, 41.8, 37.0, 33.6, 24.6, 14.6.

**IR** (KBr, cm<sup>-1</sup>):  $\tilde{\nu}$  2979 (m), 2930 (m), 1732 (vs), 1497 (s), 1374 (s), 1253 (s).

**MS** (EI, 70 eV) *m/z* (%): 121 (36), 115 (13), 88 (100), 73 (7).

**HRMS:** calcd. 235.0701 (C<sub>9</sub>H<sub>17</sub>NO<sub>2</sub>S<sub>2</sub>), found: 235.0675.

### Synthesis of *S*-myrtanyl-*N,N*-dimethyldithiocarbamate (**118**).



Bis-myrtanyl zinc was prepared from  $\beta$ -pinene (1.09 g, 8 mmol) by hydroboration and boron-zinc exchange sequence as was previously described.<sup>119</sup> It was converted into compound **118** according to the **TP16**. The product was purified by chromatography (pentane-CH<sub>2</sub>Cl<sub>2</sub>). Yield 800 mg (70%), colourless low-melting solid.

**Mp.:** 33-35 °C.

**[ $\alpha$ ]<sub>D</sub><sup>20</sup>:** 9.9 (c 0.76 CHCl<sub>3</sub>).

**<sup>1</sup>H NMR** (300 MHz, CDCl<sub>3</sub>)  $\delta$  3.27 (bs, 3H); 3.18-3.02 (m, 2H), 3.09 (bs, 3H); 2.18-2.04 (m, 2H); 1.84-1.52 (m, 5H); 1.41-1.25 (m, 1H); 0.94 (s, 3H); 0.81 (s, 3H); 0.62 (d,  $J$  = 9.6 Hz, 1H).

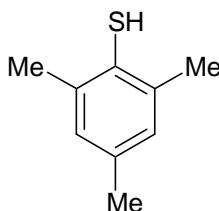
**<sup>13</sup>C NMR** (75 MHz, CDCl<sub>3</sub>):  $\delta$  197.6; 45.5; 45.1; 41.3; 41.1; 40.1; 38.5; 33.2; 27.8; 26.0; 23.2; 21.9.

**IR** (KBr, cm<sup>-1</sup>):  $\tilde{\nu}$  3435 (w); 2857 (s); 1503 (s); 1376 (s); 1232 (s); 1145 (s); 1101 (s); 1010 (s); 983 (s); 772 (s).

**MS** (EI, 70 eV)  $m/z$  (%): 265 (M<sup>+</sup>, 26); 246 (5); 177 (4); 157 (4); 145(9); 88 (100); 73 (6); 42 (5).

**HRMS:** calcd. 257.1272 (C<sub>13</sub>H<sub>23</sub>NS<sub>2</sub>), found: 257.1274.

### Synthesis of 2,4,6-trimethylthiophenol (**119**).



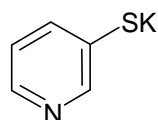
The dithiocarbamate **106** (0.580 g, 2 mmol) was dissolved at 0 °C under Ar in ethereal MeLi (10 ml of 0.33 M) and the mixture was left at RT overnight. After quenching with water and separation of the phases, the product was isolated by column chromatography (pentane-ether). Yield 251 mg (83%), colourless, heavily smelling oil.

**<sup>1</sup>H NMR** (300 MHz, CDCl<sub>3</sub>)  $\delta$  6.78 (s, 2H), 3.01 (s, 1H), 2.24 (s, 6H), 2.12 (s, 3H).

<sup>119</sup> F. Langer, L. Schwink, A. Devasagaray, P.-Y. Chavant, P. Knochel *J. Org. Chem.* **1996**, *61*, 8229.

$^{13}\text{C}$  NMR (75 MHz,  $\text{CDCl}_3$ ):  $\delta$  136.7, 135.1, 129.6, 127.5, 21.8, 21.1.

### Synthesis of potassium 3-pyridylthiolate (**120**).



Pyridin-3-yl dimethyldithiocarbamate (**111**) (398 mg, 2 mmol) was dissolved in the solution of 2 mmol KOH in 2 ml degassed EtOH. The mixture was stirred for 12 h at RT and dry pentane (10 ml) was added. The precipitate formed was filtered off under Ar, washed with additional 10 ml of pentane and dried in high vacuum. Yield 284 mg (95%). The compound is hygroscopic and air-sensitive and was characterized after quantitative conversion to the corresponding thiol. Analytical data for the thiol are given below.

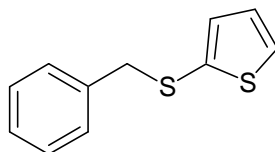
$^1\text{H}$  NMR (300 MHz,  $\text{CDCl}_3$ )  $\delta$

$^{13}\text{C}$  NMR (75 MHz,  $\text{CDCl}_3$ ):  $\delta$  149.8, 144.2, 138.5, 131.0, 124.8.

MS (EI, 70 eV)  $m/z$  (%): 111 (100), 84 (19), 64 (17), 58 (8), 51 (11).

HRMS: calcd. 111.0143 ( $\text{C}_5\text{H}_5\text{NS}$ ), found: 111.0155

### Synthesis of 2-thienylbenzylsulfide (**121**).



The dithiocarbamate **110** (0.210 g, 1 mmol) was dissolved at 0 °C under argon in ethylenediamine (1.0 ml, 12 equiv.) and the mixture was stirred at rt for 24 h. The volatiles were removed in vacuo and the residue redissolved in dry degassed MeOH. Benzyl chloride (0.250 g, 2 equiv.) was added and the mixture was stirred for 1 h at rt. The product was isolated by column chromatography (pentane-ether). Yield 173 mg (84%), colourless smelling oil.

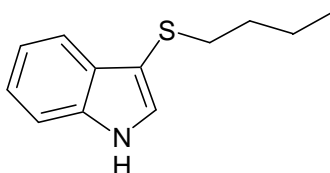
$^1\text{H}$  NMR (300 MHz,  $\text{CDCl}_3$ )  $\delta$  7.36-7.18 (m, 6H), 6.98-6.91 (m, 2H), 4.00 (s, 2H).

$^{13}\text{C}$  NMR (75 MHz,  $\text{CDCl}_3$ ):  $\delta$  138.1, 134.8, 134.0, 133.2, 129.9, 129.4, 129.0, 128.7, 127.7, 126.6, 44.5.

MS (EI, 70 eV)  $m/z$  (%): 206 (100), 91 (100), 71 (9), 65 (12).

HRMS: calcd. 206.0224 ( $\text{C}_{11}\text{H}_{10}\text{S}_2$ ), found: 206.0215.

### Synthesis of 3-indolyl butyl sulfide (**122**).



The dithiocarbamate **112** (0.250 g, 1 mmol) was heated under Ar with ethylenediamine (1.0 ml, 12 equiv.) at 50 °C for 2 h. The excess of the amine was removed in vacuo (40 °C, 0.2 mbar, 1 h), the residue was diluted with MeOH and BuI (460 mg, 2.5 equiv.) was added. The mixture was stirred overnight at RT, the volatiles removed *in vacuo* and the product was isolated by column chromatography (pentane-ether). Yield 170 mg (77%), colourless oil.

**<sup>1</sup>H NMR** (300 MHz, CDCl<sub>3</sub>) δ 8.20 (bs, 1H), 7.84-7.80 (m, 1H), 7.36-7.23 (m, 4H), 2.61 (t, *J* = 7.6 Hz, 2H), 1.47-1.27 (m, 4H), 0.77 (t, *J* = 7.9 Hz, 3H).

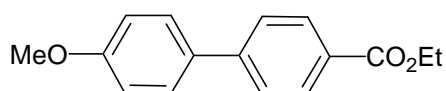
**<sup>13</sup>C NMR** (75 MHz, CDCl<sub>3</sub>): δ 136.7, 129.8, 123.0, 121.4, 120.8, 120.2, 111.9, 106.6, 36.0, 32.4, 31.1, 22.1, 14.1.

**MS** (EI, 70 eV) *m/z* (%): 205 (71), 149 (100), 148 (69), 121 (813), 117 (23), 77 (10).

**HRMS**: calcd. 205.0925 (C<sub>12</sub>H<sub>15</sub>NS), found: 205.0920.

## 17. Ni-catalyzed cross-coupling reaction of arylzinc halides.

### Synthesis of ethyl 4'-methoxybiphenyl-2-carboxylate (**123**).



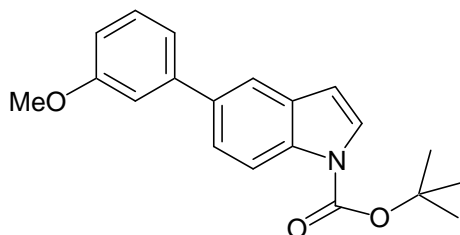
4-Methoxyphenylmagnesium bromide was obtained by insertion of Mg in 4-bromoanisole in THF in the presence of LiCl (1.1 equiv.). The cross-coupling reaction with ethyl 4-bromobenzoate (228 mg, 1.0 mmol) was performed according to the **TP18** at RT within 1 h and furnished compound **123** (223 mg, 87% yield). The same reaction with ethyl 4-chlorobenzoate (184 mg, 1.0 mmol) gave compound **123** in slightly lower yield (207 mg, 81% yield, reaction time 48 h). The products were purified by chromatography on silica (pentane-ether 9:1).

**Mp.:** 100.5-101 °C.

**<sup>1</sup>H NMR** (300 MHz, CDCl<sub>3</sub>) δ 8.09 (d, *J* = 8.7 Hz, 2H), 7.62-7.55 (m, 4H), 6.99 (d, *J* = 8.7 Hz, 2H), 4.39 (q, *J* = 7.1 Hz, 2H), 3.84 (s, 3H), 1.41 (t, *J* = 7.1 Hz, 3H).

**<sup>13</sup>C NMR** (75 MHz, CDCl<sub>3</sub>): δ 166.5, 159.8, 145.0, 132.4, 130.0, 128.6, 128.3, 126.4, 114.3, 60.8, 55.3, 14.3.

### Synthesis of 5-(3-methoxyphenyl)-1-(*tert*-butoxycarbonyl)-indole (125).



3-Methoxyphenylmagnesium bromide was obtained by insertion of Mg in 3-bromoanisole in THF in the presence of LiCl (1.1 equiv.). The cross-coupling reaction with 5-brom-1-(*tert*-butoxycarbonyl)indole (296 mg, 1.0 mmol) was accomplished according to the **TP18** at RT within 24 h and furnished compound **125** as a yellow solid (194 mg, 60% yield). The product was purified by chromatography on silica (CH<sub>2</sub>Cl<sub>2</sub>-ether 1:1).

**Mp.:** 109.5-110 °C.

**<sup>1</sup>H NMR** (300 MHz, CDCl<sub>3</sub>): δ 8.11 (d, *J* = 8.6 Hz, 1 H), 7.69 (d, *J* = 1.4 Hz, 1 H), 7.55 (d, *J* = 3.6 Hz, 1 H), 7.48 (dd, *J* = 8.6, *J* = 1.8 Hz, 1 H), 7.31-7.25 (m, 1H), 7.18-7.10 (m, 2 H), 6.81 (ddd, *J* = 8.2 Hz, *J* = 2.5, *J* = 0.8 Hz, 1H), 6.54 (d, *J* = 3.7 Hz, 1 H), 3.80 (s, 3 H), 1.62 (s, 9 H).

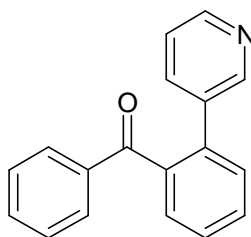
**<sup>13</sup>C NMR** (75 MHz, CDCl<sub>3</sub>): δ 159.9, 149.7, 143.2, 135.9, 134.7, 131.0, 129.7, 126.5, 123.7, 119.9, 119.4, 115.3, 113.1, 112.3, 107.5, 83.8, 55.3, 28.2

**IR** (KBr, cm<sup>-1</sup>):  $\tilde{\nu}$  2968 (w), 1721 (vs), 1607 (m), 1471 (s), 1369 (vs), 1164 (s), 781 (m), 713 (m).

**MS** (EI, 70 eV) *m/z* (%): 223 (100), 180 (30), 152 (16), 111 (8), 77 (7)

**HRMS**: calcd. 323.1521 (C<sub>20</sub>H<sub>21</sub>NO<sub>3</sub>), found: 323.1512.

### Synthesis of 2-(3-pyridyl)-benzophenone (126).



3-Pyridylmagnesium bromide was obtained from 3-bromopyridine (235 mg, 1.5 mmol) according to the **TP14** (0 °C-RT, 1 h). The cross-coupling reaction with 2-bromobenzophenone (261 mg, 1.0 mmol) was performed according to the **TP18** (50 °C, reaction time 18 h). The product was obtained after chromatography on silica (pentane-CH<sub>2</sub>Cl<sub>2</sub>, 1:1) as a white solid (197 mg, yield 76%).

**Mp.:** 106-106.5 °C.

**<sup>1</sup>H NMR** (300 MHz, CDCl<sub>3</sub>): δ 8.01 (d, *J* = 8.6 Hz, 1H); 7.89-7.80 (m, 3H); 7.65 (d, *J* = 8.7 Hz, 1H); 7.47-7.42 (m, 1H); 7.30-7.17 (m, 5H); 6.87 (d, *J* = 8.4 Hz, 1H); 4.66 (s, 1H).

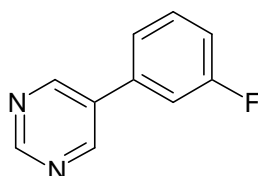
**<sup>13</sup>C NMR** (75 MHz, CDCl<sub>3</sub>): δ 150.8; 137.1; 136.4; 134.4; 133.7; 133.1; 130.9; 130.8; 129.5; 128.7; 128.6; 128.2; 127.5; 127.4; 126.9; 124.7; 124.1; 122.3; 118.1; 102.2.

**IR** (KBr,  $\text{cm}^{-1}$ ):  $\tilde{\nu}$  3501 (s); 3434 (s); 3056 (w); 1620 (w); 1596 (w); 1206 (w); 1143 (w); 826 (s); 811 (s).

**MS** (EI, 70 eV)  $m/z$  (%): 396 ( $\text{M}^+$ , 76); 270 (17); 268 (32); 251 (15); 241 (19); 239 (53); 207 (39); 125 (22); 97 (17); 78 (26); 49 (14); 41 (14).

**HRMS**: calcd. 259.0997 ( $\text{C}_{18}\text{H}_{13}\text{NO}$ ), found: 259.0996.

### Synthesis of 5-(3-fluorophenyl)-pyrimidine (127).



3-Fluorophenylmagnesium bromide was obtained from 3-fluorobromobenzene (228 mg, 1.3 mmol) according to the **TP14** (RT, 12 h). The cross-coupling reaction with 5-bromopyrimidine (159 mg, 1 mmol) was performed according to the **TP18** (25 °C, reaction time 1 h). The product was obtained after chromatography on silica (pentane-ether) as a white solid, yield 142 mg (82%).

**Mp.:** 63-63.5 °C.

**$^1\text{H}$  NMR** (300 MHz,  $\text{CDCl}_3$ ):  $\delta$  9.13 (s, 1H), 8.85 (s, 2H), 7.44-7.23 (m, 1H), 7.29-7.26 (m, 1H), 7.22-7.17 (m, 1H), 7.10-7.03 (m, 1H).

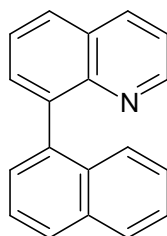
**$^{13}\text{C}$  NMR** (75 MHz,  $\text{CDCl}_3$ ):  $\delta$  160.7 (d,  $J = 248$  Hz), 158.3, 155.2, 136.8 (d,  $J = 7.9$  Hz), 133.5, 131.5 (d,  $J = 8.5$  Hz), 123.0, 116.3 (d,  $J = 21.1$  Hz), 114.3 (d,  $J = 21.1$  Hz).

**IR** (KBr,  $\text{cm}^{-1}$ ):  $\tilde{\nu}$  2239 (w), 1591 (s), 1416 (s), 909 (vs), 734 (vs)

**MS** (EI, 70 eV)  $m/z$  (%): 259 (12), 105 (25), 120 (100), 173 (21), 174 (96).

**HRMS**: calcd. 174.0593 ( $\text{C}_{10}\text{H}_7\text{N}_2\text{F}$ ), found: 174.0577.

### Synthesis of 8-(1-naphthyl)-quinoline (129).



1-Naphthylmagnesium bromide was obtained from 1-bromonaphthalene (270 mg, 1.3 mmol) according to the **TP14** (RT, 24 h). The cross-coupling reaction with quinoline-8-nonaflate<sup>120</sup> (**128**, 427 mg, 1 mmol) was performed according to the **TP18** (25 °C, reaction time 24 h). The

<sup>120</sup> L. R. Subramanian, A. Garcia Martinez, A. Herrera Fernandez, R. Martinez Alvarez, *Synthesis*, **1984**, 481.

product was obtained after chromatography on silica (pentane-ether) as a white solid, yield 206 mg (81%).

**Mp.:** 163-164 °C.

**<sup>1</sup>H NMR** (300 MHz, CDCl<sub>3</sub>): δ 8.76-8.74 (m, 1H); 8.16-8.13 (m, 1H); 7.89-7.82 (m, 3H); 7.69-7.66 (m, 1H), 7.60-7.46 (m, 3H), 7.41-7.18 (m, 4H).

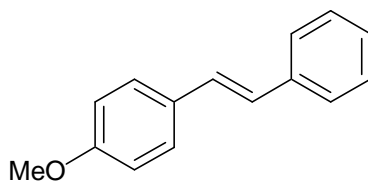
**<sup>13</sup>C NMR** (75 MHz, CDCl<sub>3</sub>): δ 150.9, 147.7, 140.6, 138.5, 136.6, 134.1, 133.3, 132.0, 128.9, 128.7, 128.5, 128.4, 128.3, 127.1, 126.6, 126.1, 126.0, 125.8, 121.5

**IR** (KBr, cm<sup>-1</sup>):  $\tilde{\nu}$  3042 (w), 1593 (w), 1492 (s), 829 (s), 797 (vs), 782 (vs), 773 (vs)

**MS** (EI, 70 eV) *m/z* (%): 127 (9), 226 (9), 252 (14), 254 (100), 255 (47)

**HRMS:** calcd. 255.1048 (C<sub>19</sub>H<sub>13</sub>N), found: 255.1020.

### Synthesis of (*E*)-4-methoxystilbene (**130**).



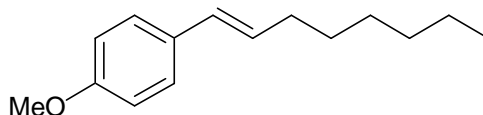
4-Methoxyphenylmagnesium bromide was obtained by insertion of Mg in 4-bromoanisole in THF in the presence of LiCl (1.1 equiv.). The cross-coupling reaction with  $\beta$ -bromostyrene (183 mg, 1.0 mmol) was performed according to the **TP19** at RT within 15 min and furnished compound **130** (179 mg, 85% yield). The product was purified by chromatography on silica (pentane-ether 20:1). Pale yellow solid.

**Mp.:** 136-138 °C.

**<sup>1</sup>H NMR** (300 MHz, CDCl<sub>3</sub>): δ 7.52-7.48 (m, 4H), 7.45-7.32 (m, 3H), 7.31-6.96 (m, 4H), 3.90 (s, 3H).

**<sup>13</sup>C NMR** (75 MHz, CDCl<sub>3</sub>): δ 159.2, 137.6, 130.1, 128.6, 128.1, 127.7, 127.2, 126.5, 16.2, 114.1, 55.3.

### Synthesis of (*E*)-1-(4-methoxyphenyl)octene (**131**).



4-Methoxyphenylmagnesium bromide was obtained by insertion of Mg in 4-bromoanisole in THF in the presence of LiCl (1.1 equiv.). The cross-coupling reaction with (*E*)-1-bromooctene (190 mg, 1 mmol) was performed according to the **TP19** at RT within 30 min and furnished compound **131** as a pale yellow oil (172 mg, 79% yield). The product was purified by chromatography on silica (pentane-ether 20:1).

**<sup>1</sup>H NMR** (300 MHz, CDCl<sub>3</sub>): δ 7.28 (d, *J* = 8.8 Hz, 2H), 6.86 (d, *J* = 8.8 Hz, 2H), 6.33 (d, *J* = 16.0 Hz, 2H), 6.09 (dt, *J*<sub>1</sub> = 15.7 Hz, *J*<sub>2</sub> = 7.0 Hz, 1H), 3.81 (s, 3H), 2.19 (q, *J* = 7.5 Hz, 2H), 1.51-1.43 (m, 2H), 1.40-1.26 (m, 6H), 0.91-0.85 (m, 3H).

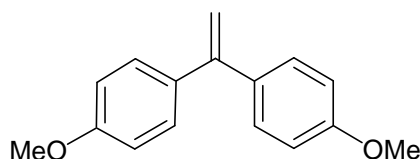
**<sup>13</sup>C NMR** (75 MHz, CDCl<sub>3</sub>): δ 158.6, 130.8, 129.1, 129.0, 126.9, 113.9, 55.2, 33.0, 31.8, 29.5, 28.9, 22.6, 14.1.

**IR** (KBr, cm<sup>-1</sup>):  $\tilde{\nu}$  2955 (w), 2921 (m), 1609 (s), 1175 (s), 965 (vs).

**MS** (EI, 70 eV) *m/z* (%): 218 (30), 147 (100), 134 (10), 121 (10).

**HRMS**: calcd. 218.1671 (C<sub>15</sub>H<sub>22</sub>O), found: 218.1572

### Synthesis of 1,1-di-(4-methoxyphenyl)ethylene (**132**).



4-Methoxyphenylmagnesium bromide was obtained by insertion of Mg in 4-bromoanisole in THF in the presence of LiCl (1.1 equiv.). The cross-coupling reaction with 1,1-dichloroethylene (96 mg, 1.0 mmol) was performed according to the **TP19**, using 2.6 equiv. of the arylzinc reagent at RT within 6 h, and furnished compound **132** as a yellow solid (211 mg, 88% yield). The product was purified by chromatography on silica (pentane-ether).

**Mp.**: 142-144 °C.

**<sup>1</sup>H NMR** (300 MHz, CDCl<sub>3</sub>): δ 7.19 (d, *J* = 9.0 Hz, 4H), 6.77 (d, *J* = 9.0 Hz, 4H), 5.21 (s, 2H), 3.73 (s, 6H).

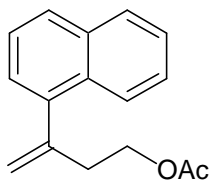
**<sup>13</sup>C NMR** (75 MHz, CDCl<sub>3</sub>): δ 159.7, 149.4, 134.7, 130.2, 113.9, 112.1, 55.7.

**IR** (KBr, cm<sup>-1</sup>):  $\tilde{\nu}$  2960 (w), 2911 (m), 1613 (s), 1186 (s), 971 (vs).

**MS** (EI, 70 eV) *m/z* (%):

**HRMS**: calcd. 240.1150 (C<sub>16</sub>H<sub>16</sub>O<sub>2</sub>), found: 240.1145.

### Synthesis of $\gamma$ -methylene-2-naphthalene-propyl acetate (**134**).



1-Naphthylmagnesium bromide was obtained from 1-bromonaphthalene (270 mg, 1.3 mmol) according to the **TP14** (RT, 24 h). The cross-coupling reaction with 3-bromo-3-buten-1-yl acetate (**133**, 193 mg, 1 mmol) was performed according to the **TP19** at RT within 12 h and furnished compound **134** as a colourless oil (194 mg, 81% yield). The product was purified by chromatography on silica (pentane-ether).



**<sup>1</sup>H NMR** (300 MHz, CDCl<sub>3</sub>): δ 7.86 (dd, *J*<sub>1</sub> = 9.5 Hz, *J*<sub>2</sub> = 3.6 Hz, 1H), 7.70 (dd, *J*<sub>1</sub> = 9.5 Hz, *J*<sub>2</sub> = 3.6 Hz, 1H), 7.62 (d, *J* = 8.3 Hz, 1H), 7.34-7.25 (m, 3H), 7.11 (t, *J* = 8.0 Hz, 1H), 5.32 (s, 1H), 5.04 (s, 1H), 3.97 (t, *J* = 6.7 Hz, 2H), 2.70 (t, *J* = 6.7 Hz, 2H), 1.81 (s, 3H).

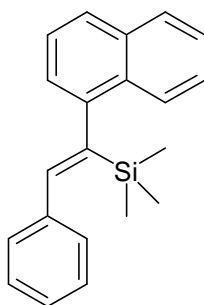
**<sup>13</sup>C NMR** (75 MHz, CDCl<sub>3</sub>): δ 170.9, 144.7, 140.1, 133.7, 131.1, 128.3, 127.5, 125.9-125.1 (m), 117.6, 62.7, 37.4, 20.8.

**IR** (KBr, cm<sup>-1</sup>):  $\tilde{\nu}$  2960 (w), 2911 (m), 1613 (s), 1186 (s), 971 (vs).

**MS** (EI, 70 eV) *m/z* (%): 240 (11, M<sup>+</sup>), 180 (46), 179 (52), 167 (19), 165 (100), 153 (20), 152 (37).

**HRMS**: calcd. 240.1150 (C<sub>16</sub>H<sub>16</sub>O<sub>2</sub>), found: 240.1127.

### Synthesis of 1-( $\alpha$ -naphthyl)-1-trimethylsilyl-2-phenylethylene (**136**).



1-Naphthylmagnesium bromide was obtained from 1-bromonaphthalene (270 mg, 1.3 mmol) according to the **TP14** (RT, 24 h). The cross-coupling reaction with 2-bromo-2-trimethylsilylstyrene<sup>121</sup> (255 mg, 1.0 mmol) was performed according to the **TP19** at RT within 24 h and furnished compound **136** (202 mg, 67% yield). The product was purified by chromatography on silica (pentane). Pale yellow oil.

**<sup>1</sup>H NMR** (300 MHz, CDCl<sub>3</sub>): δ 7.76 (d, *J* = 3.1 Hz, 2H), 7.73 (d, *J* = 2.9 Hz, 1H), 7.62-7.32 (m, 4H), 7.23-7.14 (m, 2H), 6.99-6.90 (m, 1H), 6.86-6.75 (m, 3H), -0.01 (s, 9H).

**<sup>13</sup>C NMR** (75 MHz, CDCl<sub>3</sub>): δ 145.0, 140.4, 138.9, 137.2, 133.8, 130.7, 129.0, 128.6, 128.2, 127.9, 127.4, 127.1, 126.4, 126.1, 126.0, 125.8, 125.7, 125.5, 125.3, 125.1, 124.8, -1.1.

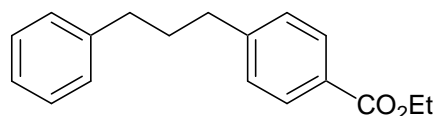
**MS** (EI, 70 eV) *m/z* (%): 302 (29), 229 (20), 228 (63), 135 (33), 73 (100), 59 (15).

**HRMS**: calcd. 302.1491 (C<sub>21</sub>H<sub>22</sub>Si), found: 302.1499.

## 18. Direct preparation of organozinc compounds from alkyl bromides in the presence of LiCl.

<sup>121</sup> M.-Z. Cai, J.-D. Huang, C.-S. Song, *J. Chem. Res. Synopses*, **2003**, 12, 770.

### Synthesis of ethyl 4-(3-phenylpropyl)benzoate (**137**).



3-Bromopropylbenzene (1.00 g, 5 mmol) reacted with zinc dust (455 mg, 7 mmol) in the presence of LiCl (300 mg, 7 mmol) according to the **TP19** at 50 °C for 3 h. The corresponding zinc reagent was obtained in 85% yield as shown by iodometric titration. Ethyl 4-iodobenzoate (1.66 g, 6 mmol) and Pd(PPh<sub>3</sub>)<sub>4</sub> (1 mol%) as a catalyst were added. The reaction was stirred for 6 h at RT, quenched with sat.

NH<sub>4</sub>Cl and the product was isolated by column chromatography (silica, pentane-ether) as a colourless oil (808 mg, 71% yield).

**<sup>1</sup>H NMR** (300 MHz, CDCl<sub>3</sub>): δ 8.01 (d, *J* = 12.1 Hz, 2H), 7.32-7.19 (m, 7H), 4.27 (q, *J* = 10.8 Hz, 2H), 2.70 (q, *J* = 11.4 Hz, 4H), 2.02 (q, *J* = 11.4 Hz, 2H), 1.41 (t, *J* = 10.8 Hz, 3H).

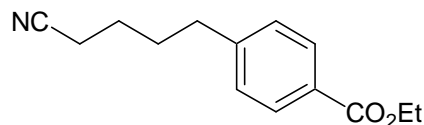
**<sup>13</sup>C NMR** (75 MHz, CDCl<sub>3</sub>): δ 166.6, 147.6, 141.9, 129.6, 129.3, 128.4, 128.3, 128.1, 128.0, 127.9, 126.3, 125.8, 60.7, 35.4, 32.6, 14.4.

**IR** (KBr, cm<sup>-1</sup>):  $\tilde{\nu}$  2936 (m), 1716 (s), 1275 (vs), 1177 (m), 1106 (s), 1022 (m), 700 (m).

**MS** (EI, 70 eV) *m/z* (%): 268 (76), 223 (39), 177 (52), 164 (39), 105 (52), 92 (59), 91 (100).

**HRMS**: calcd. 268.1463 (C<sub>18</sub>H<sub>20</sub>O<sub>2</sub>), found: 268.1470.

### Synthesis of ethyl 4-(4-cyanobutyl)benzoate (**138**).



$\omega$ -Bromovaleronitrile (805 mg, 5 mmol) reacted with zinc dust (455 mg, 7 mmol) in the presence of LiCl (300 mg, 7 mmol) according to the **TP19** at 50 °C for 8 h. The corresponding zinc reagent was obtained in 87% yield as shown by iodometric titration. Ethyl 4-iodobenzoate (1.66 g, 6 mmol, 1.2 equiv.) and Pd(PPh<sub>3</sub>)<sub>4</sub> (1 mol%) as a catalyst were added. The reaction was stirred for 6 h at RT, quenched with sat. NH<sub>4</sub>Cl and the product **138** was isolated by column chromatography (silica, pentane-ether) as a colourless oil (802 mg, 80% yield).

**<sup>1</sup>H NMR** (300 MHz, CDCl<sub>3</sub>): δ 7.95 (d, *J* = 12.0 Hz, 2H), 7.22 (d, *J* = 12.0 Hz, 2H), 4.34 (q, *J* = 10.5 Hz, 2H), 2.69 (t, *J* = 10.8 Hz, 2H), 2.33 (t, *J* = 10.8 Hz, 2H), 1.87-1.55 (m, 4H), 1.37 (t, *J* = 10.5 Hz, 3H).

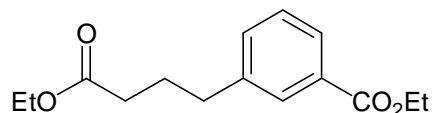
**<sup>13</sup>C NMR** (75 MHz, CDCl<sub>3</sub>): δ 166.9, 147.0, 138.2, 131.4, 130.5, 129.9, 127.6, 120.0, 64.3, 35.4, 30.3, 28.1, 17.4, 14.7.

**IR** (KBr, cm<sup>-1</sup>):  $\tilde{\nu}$  2937 (m), 1715 (s), 1278 (vs), 1179 (m), 1104 (s), 1022 (m), 763 (m).

**MS** (EI, 70 eV) *m/z* (%): 231 (12), 187 (13), 186 (100), 185 (44), 163 (33).

**HRMS**: calcd. 231.1259 (C<sub>14</sub>H<sub>17</sub>NO<sub>2</sub>), found: 231.1260.

### Synthesis of ethyl 3-(3-(carboethoxy)propyl)benzoate (**139**).



Ethyl  $\omega$ -bromobutyrate (970 mg, 5 mmol) reacted with zinc dust (455 mg, 7 mmol) in the presence of LiCl (300 mg, 7 mmol) according to the **TP19** at 50 °C for 1 h. The corresponding zinc reagent was obtained in 85% yield as shown by iodometric titration. Ethyl 3-iodobenzoate (1.66 g, 6 mmol, 1.2 equiv) and Pd(PPh<sub>3</sub>)<sub>4</sub> (1 mol%) as a catalyst were added. The reaction was stirred for 6 h at RT, quenched with sat. NH<sub>4</sub>Cl and the product **139** was isolated by column chromatography (silica, pentane-ether) as a colourless oil (1.04 g, 93% yield).

<sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>):  $\delta$  7.87-7.84 (m, 2H), 7.37-7.26 (m, 2H), 4.36-4.04 (m, 2H), 4.05 (q,  $J = 7.2$  Hz, 2H), 2.63 (t,  $J = 7.5$  Hz, 2H), 2.24 (t,  $J = 7.2$  Hz, 2H), 1.92-1.87 (m, 2H), 1.37-1.29 (m, 3H), 1.78 (t,  $J = 7.2$  Hz, 3H).

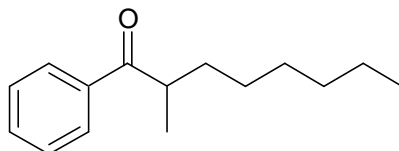
<sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>):  $\delta$  173.3, 166.7, 141.7, 140.4, 133.0, 129.5, 128.4, 127.3, 60.8, 60.3, 34.9, 33.5, 26.4, 14.3, 14.2.

IR (KBr, cm<sup>-1</sup>):  $\tilde{\nu}$  2981 (w), 1721 (vs), 1280 (vs), 1197 (m), 1107 (m), 749 (m).

MS (EI, 70 eV)  $m/z$  (%): 219 (57), 218 (96), 190 (100), 177 (59), 149 (75), 117 (55), 105 (47), 90 (29).

HRMS: calcd. 264.1362 (C<sub>15</sub>H<sub>20</sub>O<sub>4</sub>), found: 264.1333.

#### Synthesis of 2-methyl-1-phenyloctan-1-one (**140**).



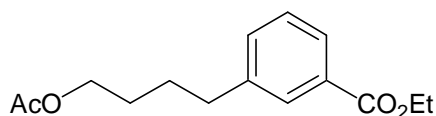
2-Bromooctane (960 mg, 5 mmol) reacted with zinc dust (455 mg, 7 mmol) in the presence of LiCl (300 mg, 7 mmol) according to the **TP19** at 50 °C for 1 h. The corresponding zinc reagent was obtained in 88% yield as shown by iodometric titration. Benzoyl chloride (840 mg, 6 mmol, 1.2 equiv.) and CuCN·2LiCl (1 mL of 1 M solution in THF, 20 mol%) as a catalyst were added at -20 °C. The reaction was stirred for 6 h at RT, quenched with sat. NH<sub>4</sub>Cl and the product **140** was isolated by column chromatography (silica, pentane-ether) as a colourless oil (740 mg, 77% yield).

<sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>):  $\delta$  7.88-7.47 (m, 2H), 7.44-7.18 (m, 3H), 3.21-3.14 (m, 1H), 1.90-1.57 (m, 8H), 1.50-1.04 (m, 8H).

<sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>):  $\delta$  204.2, 136.8, 129.4, 129.1, 128.8, 46.0, 29.8 (m), 26.3 (m).

MS (EI, 70 eV)  $m/z$  (%): 218 (3), 134 (42), 105 (100), 77 (34).

#### Synthesis of ethyl 3-(4-acetoxybutyl)benzoate (**141**).



4-Bromobutyl acetate (975 mg, 5 mmol) reacted with zinc dust (455 mg, 7 mmol) in the presence of LiCl (300 mg, 7 mmol) according to the **TP19** at 25 °C for 6 h. The corresponding zinc reagent was obtained in 96% yield as shown by iodometric titration. Ethyl 3-iodobenzoate (1.66 g, 6 mmol, 1.2 equiv.) and Pd(PPh<sub>3</sub>)<sub>4</sub> (1 mol%) as a catalyst were added. The reaction was stirred for 6 h at RT, quenched with sat. NH<sub>4</sub>Cl and the product **141** was isolated by column chromatography (silica, pentane-ether) as a colourless oil (1.05 g, 83% yield).

<sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>): δ 7.93-7.85 (m, 2H), 7.22-7.10 (m, 2H), 4.40 (m, 2H), 4.06 (m, 2H), 2.66 (q, *J* = 7.1 Hz, 2H), 2.10 (s, 3H), 1.68-1.60 (m, 4H), 1.40 (t, *J* = 7.1 Hz, 3H).

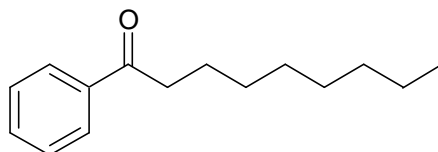
<sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>): δ 173.0, 166.8, 141.2, 133.3, 130.6, 129.1, 129.0, 127.3, 61.7, 60.7, 36.2, 30.1, 28.7, 20.4, 13.8.

IR (KBr, cm<sup>-1</sup>):  $\tilde{\nu}$  2935 (w), 1719 (vs), 1279 (vs), 1257 (s), 1109 (m), 745 (s).

MS (EI, 70 eV) *m/z* (%): 264 (12), 219 (40), 176 (43), 158 (37), 148 (41), 131 (47).

HRMS: calcd. 264.1362 (C<sub>15</sub>H<sub>20</sub>O<sub>4</sub>), found: 264.1381.

#### Synthesis of 1-phenylnonan-1-one (**142**).



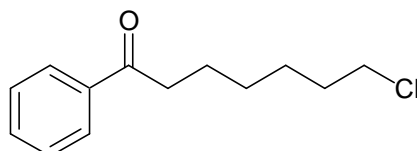
1-Bromooctane (960 mg, 5 mmol) reacted with zinc dust (455 mg, 7 mmol) in the presence of LiCl (300 mg, 7 mmol) according to the **TP19** at 50 °C for 24 h. The corresponding zinc reagent was obtained in 92% yield as shown by iodometric titration. Benzoyl chloride (840 mg, 6 mmol, 1.2 equiv.) and CuCN·2LiCl (1 mL of 1 M solution in THF, 20 mol%) as a catalyst were added at -20 °C. The reaction was stirred for 6 h at RT, quenched with sat. NH<sub>4</sub>Cl and the product **142** was isolated by column chromatography (silica, pentane-ether) as a colourless oil (890 mg, 89% yield).

<sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>): δ 7.87-7.85 (m, 2H), 7.48-7.33 (m, 3H), 2.87 (t, *J* = 7.2 Hz, 2H), 1.67-1.63 (m, 2H), 1.31-1.20 (m, 8H), 0.86-0.77 (m, 5H).

<sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>): δ 200.9, 137.5, 130.9, 130.6, 129.2, 128.7, 39.0, 31.2, 29.8-29.6 (m), 28.2, 27.2, 14.5.

MS (EI, 70 eV) *m/z* (%): 218 (14), 133 (17), 120 (94), 105 (100), 77 (36).

#### Synthesis of 7-chloro-1-phenylheptan-1-one (**143**).



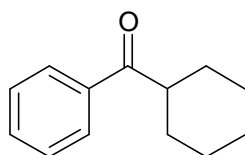
6-Chloro-1-bromohexane (1.00 g, 5 mmol) reacted with zinc dust (455 mg, 7 mmol) in the presence of LiCl (300 mg, 7 mmol) according to the **TP19** at 50 °C for 12 h. The corresponding zinc reagent was obtained in 93% yield as shown by iodometric titration. Benzoyl chloride (840 mg, 6 mmol, 1.2 equiv.) and CuCN·2LiCl (1 mL of 1 M solution in THF, 20 mol%) as a catalyst were added at -20 °C. The reaction was stirred for 6 h at RT, quenched with sat. NH<sub>4</sub>Cl and the product **143** was isolated by column chromatography (silica, pentane-ether) as a colourless oil (925 mg, 89% yield).

<sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>): δ 7.88-7.85 (m, 2H), 7.46-7.33 (m, 3H), 3.44 (t, *J* = 6.6 Hz, 2H), 2.88 (t, *J* = 7.1 Hz, 2H), 1.73-1.65 (m, 4H), 1.41-1.32 (m, 4H).

<sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>): δ 199.2, 136.0, 131.9, 128.5, 127.0, 44.0, 37.3, 31.4, 28.2, 25.2, 23.0.

MS (EI, 70 eV) *m/z* (%): 224 (4), 133 (6), 120 (82), 105 (100), 77 (47), 51 (11).

#### Synthesis of phenylcyclohexylketone (**144**).



Bromocyclohexane (806 mg, 5 mmol) reacted with zinc dust (455 mg, 7 mmol) in the presence of LiCl (300 mg, 7 mmol) according to the **TP19** at 50 °C for 6 h. The corresponding zinc reagent was obtained in 96% yield as shown by iodometric titration. Benzoyl chloride (840 mg, 6 mmol, 1.2 equiv.) and CuCN·2LiCl (1 mL of 1 M solution in THF, 20 mol%) as a catalyst were added at -20 °C. The reaction was stirred for 6 h at RT, quenched with sat. NH<sub>4</sub>Cl and the product **144** was isolated by column chromatography (silica, pentane-ether) as pale yellow solid (820 mg, 91% yield).

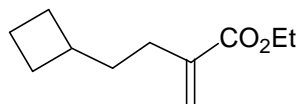
**Mp.:** 55-57 °C.

<sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>): δ 7.97-7.88 (m, 2H), 7.56-7.40 (m, 3H), 3.36-3.17 (m, 1H), 1.93-1.32 (m, 10H).

<sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>): δ 204.3, 136.8, 133.1, 129.0-128.6 (m), 46.0, 29.8, 26.4 (m).

MS (EI, 70 eV) *m/z* (%): 188 (25), 133 (16), 120 (11), 105 (100), 77 (31), 55 (12).

#### Synthesis of ethyl 2-(2-cyclobutylethyl)acrylate (**145**).



2-(Cyclobutyl)-1-bromoethane (810 mg, 5 mmol) reacted with zinc dust (455 mg, 7 mmol) in the presence of LiCl (300 mg, 7 mmol) according to the **TP19** at 50 °C for 50 h. The corresponding zinc reagent was obtained in 86% yield as shown by iodometric titration. Ethyl α-(bromomethyl)acrylate (830 mg, 4.3 mmol, 1.0 equiv.) and CuCN·2LiCl (0.02 mL of 1 M solution in THF, 0.4 mol%) as a catalyst were added. The reaction was stirred for 1 h at RT, quenched with sat. NH<sub>4</sub>Cl and the product **141** was isolated by column chromatography (silica, pentane-ether) as a colourless oil (640 mg, 82% yield).

**<sup>1</sup>H NMR** (300 MHz, CDCl<sub>3</sub>): δ 7.39 (d, *J* = 2.66 Hz, 1 H); 6.64 (s, 1 H); 6.33 (dd, *J*<sub>1</sub> = 3.10 Hz, *J*<sub>2</sub> = 1.77 Hz, 1 H); 6.25 (m, 1 H); 6.14 (d, *J* = 6.19 Hz, 1 H); 4.43 (d, *J* = 6.19 Hz, 1 H); 4.38 (q, *J* = 7.08 Hz, 2 H); 1.38 (t, *J* = 7.08 Hz, 3 H)

**<sup>13</sup>C NMR** (75 MHz, CDCl<sub>3</sub>): δ 159.2; 154.1; 143.0; 141.8; 138.6; 127.3; 114.9; 110.7; 107.7; 63.1; 62.2; 14.6.

**IR** (KBr, cm<sup>-1</sup>):  $\tilde{\nu}$  3408 (w); 1704 (vs); 1476 (vs); 1400 (m); 1384 (m); 1370 (m); 1314 (s); 1302 (s); 1172 (s); 1148 (vs); 1092 (m); 1078 (m); 1008 (s); 934 (s); 910 (m); 758 (m); 728 (vs).

**MS** (EI, 70 eV) *m/z* (%): 153 (100); 119 (63); 117 (66); 95 (31); 45 (14).

**HRMS**: calcd. 182,1307 (C<sub>11</sub>H<sub>18</sub>O<sub>2</sub>), found: 182,1305.

## Curriculum Vitae

Name: Gavryushin Andrei

Date of birth: February 2, 1973

Place of birth: Ruzaewka, Russian Federation

Sitizenship: Russian Federation

Marital status: married, two children

### **Educational background:**

2001-2006: Ph. D. student, Ludwig-Maximilians-University, Munich, group Prof. Dr. Paul Knochel.

1998-2001: Graduate student, Department of Chemistry, Moscow State University, Moscow, Russian Federation.

1990-1993: Undergraduate student, Department of Chemistry, Moscow State University, Moscow, Russian Federation.

### **Publications:**

1. Nenajdenko, V. G.; Gavryushin, A. E.; Balenkova, E. S. „A facile route to thiophene-1,1-dioxides bearing electron-withdrawing groups.“ *Tetrahedron Letters* **2001**, *42*, 4397-4399.

2. Gavryushin, A.; Polborn, K.; Knochel, P. „Novel chiral diphosphine ligands with a pinene core obtained via an allylphosphinite-allylphosphine oxide rearrangement“. *Tetrahedron: Asymmetry* **2004**, *15*, 2279-2288.

3. Gavryushin, A.; Kofink, C.; Manolikakes, G.; Knochel, P. “Efficient Cross-Coupling of Functionalized Arylzinc Halides Catalyzed by a Nickel Chloride-Diethyl Phosphite System.” *Organic Letters* **2005**, *7*, 4871-4874.

4. Krasovskiy, A.; Gavryushin, A.; Knochel, P. “A general thiolation of magnesium organometallics using tetramethylthiuram disulfide.” *Synlett* **2005**, 2691-2693.

5. Yasuike, S.; Kofink, C. C.; Kloetzing, R. J.; Gommermann, N., Tappe, K.; Gavryushin, A.; Knochel, P. “Synthesis of JOSIPHOS-type ligands via a diastereoselective three-component reaction and their application in asymmetric rhodium-catalyzed hydroboration.” *Tetrahedron: Asymmetry* **2005**, *16*, 3385-3393.

6. Krasovskiy, A.; Malakhov, V.; Gavryushin, A.; Knochel, P. „Efficient synthesis of functionalized organozinc compounds by the direct insertion of zinc into organic iodides and bromides.“ *Angew. Chem. Int. Ed.* **2006**, *45*, 6040-6044.

7. Krasovskiy, A.; Gavryushin, A.; Knochel, P. “Highly stereoselective access to sulfur derivatives starting from zinc organometallics.“ *Synlett* **2006**, 792-794.

8. Gavryushin, A.; Kofink, C.; Manolikakes, G.; Knochel, P. “An efficient Negishi cross-coupling reaction catalyzed by nickel(II) and diethyl phosphite.” *Tetrahedron* **2006**, *62*, 7521-7533.

### **Poster presentations:**

1. V. Nenajdenko, A. Gavryushin, E. Balenkova “New thiophene-1,1-dioxides Bearing Electron-Withdrawing Groups” International Conference on Organic Synthesis (ICOS-13), Warsaw, Poland, **2000**.

2. P. Knochel, F. Liron, A. Gavryushin “Enantioselective [2,3]-Sigmatropic Rearrangement of Allylic Phosphinites” Annual Congress of GDCh, Munich, **2003**.

3. L. Melzig, A. Gavryushin, P. Knochel „Direct Introduction of Aminoalkyl Pharmacophores by a Cross-Coupling Reaction” 4th Industrie Tag, Munich, Germany, **2006**.

### **Books:**

1. P. Knochel, A. Gavryushin, A. Krasovskiy, H. Leuser “Magnesium”, in *Comprehensive Organometallic Chemistry III*, Vol. 9, Chapter 3. Ed.: P. Knochel, Elsevier, **2006**.

2. A. Gavryushin, P. Knochel “Vinylmagnesium Bromide”, in *Electronic Encyclopedia of Reagents for Organic Synthesis (E-Eros)*, **2006**.

**Patents:**

1. Knochel, P.; Bunlaksananusorn, T.; Gavryushin, A. "Chiral diphosphinoterpenes and transition metal complexes thereof." US 2005267316 A1.
2. Knochel, P.; Bunlaksananusorn, T.; Gavryushin, A. "Chiral diphosphines with cyclic diterpene backbone as ligands for transition metal-catalyzed asymmetric hydrogenation, addition and substitution reactions and process for preparation thereof." Eur. Pat. Appl. (2005), EP 1595886 A1.
3. Knochel, P.; Bunlaksananusorn, T.; Gavryushin, A. "An improved process for preparation of chiral diphosphines with cyclopentane backbone as ligands for asymmetric transition metal-catalyzed hydroboration, hydrogenation and allylic substitution." Eur. Pat. Appl. (2005), EP 1595885 A2.
4. Knochel, P.; Gavryushin, A.; Kofink, C. C. "An iron-, nickel- and cobalt-catalyzed cross-coupling reactions of organozinc compounds." *Patent pending*.
5. Knochel, P.; Gavryushin, A.; Malakhov, V.; Krasovskiy, A. "New preparation of organometallic compounds in the presence of lithium salts." *Patent pending*.