Development of Novel Low-Oxidation State Main Group Catalysis – Gallium & Aluminium

by

Bo Qin

Doctor of Philosophy

EaStCHEM, School of Chemistry
College of Science and Engineering
The University of Edinburgh

2016
DECLARATION

I hereby declare that, except where specific reference is made to other resources, the work presented in this thesis is the original work of my own research since the start of my PhD degree in October 2012. This thesis has been composed by myself and has not been submitted, in whole or part, for any other degree, diploma or other qualification.

20/05/2016
ACKNOWLEDGEMENTS

First of all I would like to thank my supervisor, Dr Uwe Schneider, for giving me the opportunity to work in this group. His advice in organic chemistry and solving synthetic challenges is invaluable and he has been always patient to answer my questions in my study and research.

Also, I would like to thank my funding sponsor – School of Chemistry, University of Edinburgh – for the supporting of my three-year’s Ph.D study.

Thanks to all of the group members in the Schneider group, Xun Lu, JR, Wei, Hanno, and Alex. Whenever I have problems in both study and life, they were always ready to give me advice and helps. Also, I would like to thank my project students’ hard working, especially Aliim who contributed to this thesis. I would like to thank the NMR and mass services in School of Chemistry, University of Edinburgh for providing a smooth and high quality services. Without them this work would not have been possible.

Last, but not the least, I want to thank my parents and my fiancé, Zilei, for supporting me as always.
ABSTRACT

This PhD thesis is focused on the development of novel catalysis with low-oxidation main group species, mainly based on the group 13 element gallium, a relatively abundant, inexpensive, and low-toxic metal. Gallium in its stable high-oxidation state ‘+III’ is a commonly used Lewis acid catalyst in organic synthesis. In contrast, gallium in its less stable low-oxidation state ‘+I’ is under-explored, but may display both acceptor and donor properties at a single site (ambiphilicity). Based on the hypothesis that potentially ambiphilic gallium(I) – oxidatively generated in situ from gallium(0) using a silver salt – may activate both basic and acidic reagents, various gallium(I)-catalyzed carbon–carbon bond formations have been developed. These include catalytic C–O and C–B bond activations of electrophiles (acetals and aminals) and pro-nucleophiles (allyl and allenyl boronates), respectively. Gallium(III) and other metal Lewis acids have proved to be ineffective. These results represent the first catalytic use of gallium(0) in organic synthesis and a rare example of gallium(I) catalysis. The identity of the gallium(I) catalyst and its regeneration have been confirmed by $^{71}$Ga NMR analysis, and a reactive allyl–Ga(I) intermediate has been detected for the first time. In combination with $^{11}$B NMR and HRMS analyses, an $S_N1$ reaction mechanism has been proposed. Importantly, the potential for asymmetric gallium(I) catalysis has been demonstrated using a chiral silver co-catalyst (40% ee). This gallium(I) chemistry has proved to be applicable to the catalytic activation of other electrophiles, including ethers or aldehydes, and pro-nucleophiles such as boranes, silanes, or tin-based reagents. Finally, the potential of a related low-oxidation aluminium catalyst has been explored for C–C bond formation.
LAY SUMMARY

A catalyst is a molecule that is able to increase the rate of a chemical reaction while remaining unchanged after the reaction, i.e., a catalyst is not incorporated in the reaction product. This methodology is termed ‘catalysis’. Catalysis has been well developed in the past fifty years, and plays a particularly important role in today’s chemistry world. Currently, catalysts have been widely used in different industries including the production of food, pharmaceuticals, and materials, to name but a few. Unfortunately, however, most catalysts may contain precious and / or toxic metals, such as gold and / or mercury, which may be a major concern for both human health and the environment in general. As a consequence, the development of inexpensive and environmentally benign catalysts is a hot topic in nowadays chemistry research. This PhD thesis has focused on the exploration of a conceptually novel catalyst system based on the relatively inexpensive and low-toxic metal gallium. It has been shown that this new metal catalyst is able to efficiently catalyze a variety of chemical reactions under mild conditions. Importantly, the precise identity of the novel catalyst system and its mode of functioning have been elucidated using a variety of specific analytical laboratory instruments. Finally, the novel concept of the developed gallium catalysis has been transferred to the catalytic use of the metal aluminum, which is one of the most abundant elements in the Earth’s crust.
# LIST OF ABBREVIATIONS

<table>
<thead>
<tr>
<th>Abbreviation</th>
<th>Symbol</th>
<th>Definition</th>
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<tbody>
<tr>
<td>Ar</td>
<td>Aryl</td>
<td>LOMO</td>
</tr>
<tr>
<td>bp</td>
<td>Boiling point</td>
<td>MB</td>
</tr>
<tr>
<td>BTF</td>
<td>Trifluoromethylbenzene</td>
<td>MeCN</td>
</tr>
<tr>
<td>Cat</td>
<td>Catalyst</td>
<td>Me</td>
</tr>
<tr>
<td>Cp</td>
<td>C₂H₅</td>
<td>Mes</td>
</tr>
<tr>
<td>Cp*</td>
<td>C₂Me₅</td>
<td>mp</td>
</tr>
<tr>
<td>Cy</td>
<td>Cyclohexyl</td>
<td>NHC</td>
</tr>
<tr>
<td>DBE</td>
<td>Dibenzyl ether</td>
<td>NMR</td>
</tr>
<tr>
<td>DCE</td>
<td>Dichloroethene</td>
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<tr>
<td>DCM</td>
<td>Dichloromethane</td>
<td>OTf</td>
</tr>
<tr>
<td>DME</td>
<td>Dimethoxy ethane</td>
<td>pin</td>
</tr>
<tr>
<td>DNBA</td>
<td>Dinitrobenzene sulfonic acid</td>
<td>Ph</td>
</tr>
<tr>
<td>Dipp</td>
<td>2,6-Diisopropylphenyl</td>
<td>PhH</td>
</tr>
<tr>
<td>Et₂O</td>
<td>Diethyl ether</td>
<td>PhMe</td>
</tr>
<tr>
<td>equiv</td>
<td>Equivalent</td>
<td>ppm</td>
</tr>
<tr>
<td>HOMO</td>
<td>Highest occupied molecular orbital</td>
<td>PTLC</td>
</tr>
<tr>
<td>HOTf</td>
<td>Triflic acid</td>
<td>PTSA</td>
</tr>
<tr>
<td>HRMS</td>
<td>high-resolution mass spectrometry</td>
<td>rt</td>
</tr>
<tr>
<td>HSAB theory</td>
<td>Hard Soft Acid Base theory</td>
<td>TBME</td>
</tr>
<tr>
<td>iPr</td>
<td>Isopropyl</td>
<td>TMEDA</td>
</tr>
<tr>
<td>IR</td>
<td>Infrared spectroscopy</td>
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<tr>
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<tr>
<td>LB</td>
<td>Lewis base</td>
<td>))))</td>
</tr>
</tbody>
</table>
# TABLE OF CONTENTS

DECLARATION ......................................................................................................................... I

ACKNOWLEDGEMENTS .......................................................................................................... II

ABSTRACT ................................................................................................................................. III

LAY SUMMARY ........................................................................................................................ IV

LIST OF ABBREVIATIONS ....................................................................................................... V

CHAPTER 1: DEVELOPMENT OF GALLIUM(I) CATALYSIS ............................................. 1

1.1 INTRODUCTION .................................................................................................................. 1

   1.1.1 Physical and Chemical Properties of Gallium .............................................................. 1
   1.1.2 Gallium(III) Complexes in Medicinal Chemistry ........................................................ 3
   1.1.3 Gallium(III) Lewis Acid Catalysis ............................................................................. 4
   1.1.4 ‘Gallium(I)’ Halides – Mixed-Valent Gallium Salts ..................................................... 8
   1.1.5 Monomeric Gallium(I) Complexes – Potential Lewis Bases (LBs) ............................ 13
       1.1.5.1 Early Examples of True Gallium(I) Species ......................................................... 13
       1.1.5.2 Gallium(I) Species as Metallic NHC Analogue ................................................ 18
   1.1.6 Univalent Gallium(I) Salts – Potential Lewis Acids (LAs) ........................................ 24
   1.1.7 Ambiphilic Properties of Gallium(I) in a Stoichiometric Context ............................ 31
   1.1.8 Stoichiometric Applications in Organic Synthesis .................................................... 34
       1.1.8.1 Stoichiometric Use of ‘GaI’ ............................................................................... 34
       1.1.8.2 Stoichiometric Use of Ga(0) ............................................................................. 35

1.2 AIMS .................................................................................................................................. 38

1.3 RESULTS AND DISCUSSION .......................................................................................... 41

   1.3.1 Initial Catalysis Results with the Combination Ga(0)/Ag(I) ........................................ 41
       1.3.1.1 Proof of Concept .............................................................................................. 42
       1.3.1.2 Optimization of Reaction Parameters .............................................................. 45
       1.3.1.3 Ligand Effect on the Catalytic System .............................................................. 48
   1.3.2 Towards a Ga(0)/Ag(I) Catalytic System under Ultrasonication ............................. 51
       1.3.2.1 Initial Experiments ............................................................................................. 52
       1.3.2.2 Reaction Conditions Re-Visited ....................................................................... 53
       1.3.2.3 Control Experiments ......................................................................................... 59
       1.3.2.4 Substrate Scope for the Catalytic Allylation of Acetals and Ketals ................. 64
       1.3.2.5 Experiment at Low Catalyst Loading ................................................................ 66
       1.3.2.6 Catalytic Regiospecific Propargylation of Acetals ........................................ 67
CHAPTER 2: TOWARDS ASYMMETRIC GALLIUM (I) CATALYSIS ..........88

2.1 INTRODUCTION: HOSOMI–SAKURAI ALYLLATIONS USING C(sp³) ELECTROPHILES ...88

2.1.1 Use of an Allyl Silane .................................................................90
  2.1.1.1 Transition Metal Catalysis ......................................................90
  2.1.1.2 Main Group Catalysis ............................................................91
  2.1.1.3 Brønsted Acid Catalysis ........................................................93

2.1.2 Use of Boron-Based Allyl Pro-Nucleophiles ....................................95
  2.1.2.1 Indium(I) Catalysis Using a Boronic Ester ...............................95
  2.1.2.2 Indium(I) Catalysis Using a Borane .........................................97

2.1.3 Developments in Asymmetric Catalysis .........................................99

2.2 AIMS ..............................................................................................106

2.3 RESULTS AND DISCUSSION ............................................................108

2.3.1 Gallium(I) Catalysis Using an Allyl Silane ........................................108
  2.3.1.1 Initial and Control Experiments .............................................108
  2.3.1.2 Solvent Screening .................................................................111
  2.3.1.3 Stoichiometric 71Ga NMR Studies ........................................112

2.3.2 Gallium(I) Catalysis Using a Unique Reagent: Boron vs. Silicon ..........118
  2.3.2.1 Preparation of an α-Silyl Allyl Boronic Ester98 ................................120
  2.3.2.2 Initial Experiment with an Acetal ............................................122
  2.3.2.3 Preliminary Scope for C(sp³) Electrophiles .............................126

2.3.3 Gallium(I) Catalysis Using an Allyl Borane ....................................127
  2.3.3.1 Preparation of an Allyl Borane98 .............................................127
  2.3.3.2 Initial Experiments with an Acetal ........................................129
  2.3.3.3 Preliminary Scope for C(sp³) Electrophiles .............................130

2.3.4 Towards Asymmetric Gallium(I) Catalysis ....................................131
  2.3.4.1 Synthesis of Enantiomerically Enriched BINOL-Phosphate Derivatives ..132
  2.3.5.2 Attempted Enantioselective Allylation of Cyclic Acetals ..............135

2.4 SUMMARY .......................................................................................152

CHAPTER 3: TOWARDS ALUMINIUM(I) CATALYSIS ....................................154
3.1 INTRODUCTION ........................................................................................................154
  3.1.1 Physical and Chemical Properties of Aluminium ..............................................154
  3.1.2 Aluminium(III) Lewis Acid Catalysis ..............................................................155
  3.1.3 Dimeric Aluminium(II) Complexes .................................................................156
  3.1.4 Monomeric Aluminium(I) Complexes ..............................................................159
  3.1.5 Stoichiometric Use of Monomeric Aluminium(I) Species ...............................164
    3.1.5.1 Stoichiometric Lewis Basicity ..................................................................165
    3.1.5.2 Stoichiometric Lewis Acidity ..................................................................167
    3.1.5.3 Stoichiometric Ambiphilicity ..................................................................168
  3.1.6 Stoichiometric Use of Aluminium(0) in Organic Synthesis ............................169
  3.2 AIMS ....................................................................................................................171
  3.3 RESULTS AND DISCUSSION ..............................................................................173
    3.3.1 Preliminary Results with the Combination Al(0)/Ag(I) .................................173
      3.3.1.1 Initial Experiments Under Ultrasonication ............................................173
      3.3.1.2 Initial Experiments with Conventional Heating and Stirring ................175
      3.3.1.3 Control Experiments ............................................................................176
      3.3.1.4 Silver Salt Screening ............................................................................179
      3.3.1.5 The Combination of Al(0)/AgOTf.........................................................180
      3.3.1.6 The Combination of Al(0)/AgClO₄ .........................................................183
    3.3.2 Catalytic Allylation Using an Allyl Silane .....................................................185
  3.4 SUMMARY ...........................................................................................................190

CHAPTER 4: EXPERIMENTAL ......................................................................................195
  4.1 GENERAL EXPERIMENTAL ..............................................................................195
  4.2 SYNTHESIS AND ANALYSIS OF ELECTROPHILES .......................................198
    4.2.2 Analytical Data of Electrophiles ..................................................................202
  4.3 SYNTHESIS AND ANALYSIS OF ALKYL REAGENTS .....................................216
  4.4 DEVELOPMENT OF GALLIUM(I) AND ALUMINUM(I) CATALYSIS ............220
    4.4.1 General Procedures ....................................................................................220
    4.4.2 Analytical Data .........................................................................................223
  4.5 MECHANISTIC STUDIES ....................................................................................251
  4.6 SYNTHESIS OF ENANTIOMERICALLY ENRICHED SILVER BINOL-PHOSPHATE
    DERIVATIVES .......................................................................................................253
  4.7 TOWARDS ASYMMETRIC GALLIUM(I) CATALYSIS .......................................260
    4.7.1 General Procedures ....................................................................................260
    4.7.2 Analytical Data .........................................................................................262

REFERENCES ............................................................................................................267
CHAPTER 1: DEVELOPMENT OF GALLIUM(I)

CATALYSIS

1.1 Introduction

1.1.1 Physical and Chemical Properties of Gallium

Group XIII of the periodic table includes boron (B), aluminium (Al), gallium (Ga), indium (In), and thallium (Tl). In this main group, boron is defined as a hard metalloid, whereas all heavier homologues are classified as ‘typical’ metals. The boiling point of these elements in the oxidation state ‘0’ decreases from up-to-down with the increase of molecular weight, while the trend of density change is opposite.\(^1\) All of these elements may be reactive under fairly mild conditions. Due to the three valence electrons, ‘+III’ is the most stable and common oxidation state for the upper elements. However, with increasing atomic number the lower oxidation state ‘+I’ becomes increasingly stable. For instance, thallium(I) is actually more stable than thallium(III).\(^2\)

Gallium attracts more and more interest in both chemistry and biology. This soft metal with the atomic number 31 was discovered spectroscopically in 1875.\(^3\) Gallium is fairly abundant in the Earth's crust (~ 19 ppm).\(^4\) However, gallium(0) does not exist in its ‘free’ form in nature. Pure gallium metal has a silvery color, is fairly stable in air, and is not attached to water in the absence of oxygen. Quite uniquely, gallium has a very low melting point of 29.8 °C. Thus, it exists as a solid at or below room temperature (Figure 1-1, left photo),\(^5\) and can melt in the hand (Figure 1-1, right photo). Metallic gallium is not considered toxic, while most of the commercially available gallium salts are described as being low-toxicity.\(^4\)
Three different oxidation states of gallium have been observed: ‘+III’, ‘+II’ and ‘+I’, which indicate its special properties and unique potential for various applications. The different oxidation states of gallium are visualized in Figure 1-2.

The highest oxidation state ‘+III’ was reported to be the most stable under ambient conditions. Here, the gallium center is bound to three ligands and has a vacant low-energy p orbital. In turn, gallium(III) may act as a hard, strong Lewis acid. ‘Monomeric’ gallium(II) species were reported to be substantially less stable, but adducts may be formed fairly easily leading to more stable ‘dimeric’ Ga(II)–Ga(II) species, which may act as relatively soft, two-center Lewis acids. Gallium in its low oxidation state ‘+I’ may display
ambiphilic properties. On one hand, due to a vacant low-energy p orbital it may act as soft Lewis acid. On the other hand, due to an sp-type lone pair of electrons it may act as a Lewis base. This potentially ambiphilic character, or “switchable” acid–base feature, represents a potentially interesting area of research that is worth being thoroughly explored. Gallium(I) species were reported to be unstable under certain conditions, e.g. in the presence of water. The decomposition is supposed to involve electron-transfer processes, and proceeds through a redox-disproportionation to form gallium(0) and gallium(III) in a 2:1 molar ratio.

In the following chapters, the chemistry of gallium in its various oxidation states will be covered including: applications of stable Ga(III) compounds; synthesis and properties of gallium(II) and gallium(I) species; stoichiometric applications of the low-oxidation states ‘+I’ and ‘0’.

1.1.2 Gallium(III) Complexes in Medicinal Chemistry

As one potential surrogate of platinum-based anticancer agents, gallium(III) complexes have attracted an increasing attention in both biochemistry and medicine. Compared to platinum compounds, gallium(III) species are supposed to display better antitumor activity and lower toxicity for two reasons. First, Ga(III) complexes have been known for their decreased propensity to be hydrolyzed or to participate in redox transformations under physiological conditions. In turn, their bioavailability may be increased. Second, due to the similarity to Fe(III), Ga(III) may attach easily to serum proteins resulting in a decreased toxicity. There have been various studies to unravel the mechanism of the anticancer activity of gallium(III). For instance, it has been reported that gallium(III) could be up-taken by competitive binding to transferrin glycoproteins. After entering the cells, it may inhibit the enzyme ribonucleotide reductase, which is considered vital for DNA synthesis. Alternatively, it was reported that apoptosis may be induced through activation of the pro-apoptotic factor Bax and caspase-3.
As early as in the 1970s, a series of gallium(III) compounds were synthesized as anticancer candidates. One simple salt, gallium nitrate (1), was confirmed to display antitumor activity although strong side effects were observed (Figure 1-3, left structure).\textsuperscript{15} To mimic the Fe(III)–maltol complex, a specific gallium(III) complex, KP46 (2), was designed (Figure 1-3, right structure).\textsuperscript{11b} In phase I studies, this compound was shown to display outstanding metabolic features in patients and low levels of toxicity. Although the biological activity and the modes of delivery of KP46 (2) are still not clear, it has been considered as a lead-drug candidate with promising results.

![Figure 1-3 Gallium(III) nitrate (1) and KP46 (2)](image)

### 1.1.3 Gallium(III) Lewis Acid Catalysis

Gallium(III) salts have been commonly used as a Lewis acid catalyst in organic synthesis.\textsuperscript{6} For instance, gallium trifluoromethane sulfonate, Ga(OTf)\textsubscript{3}, has been considered as inexpensive, low-toxic, and water-tolerant. It can be prepared in a straightforward manner through oxidation of gallium(0), or through ligand exchange with GaCl\textsubscript{3}, using an excess of trifluoromethane sulfonic acid at reflux.\textsuperscript{16} Ga(OTf)\textsubscript{3} was found to display a better solubility in strongly coordinating solvents, such as nitromethane. In turn, it has been used as a potent Lewis acid catalyst in Friedel–Crafts alkylations, hydroxylalkylations, and acylations, affording the corresponding products in high yields and with high chemo- and regioselectivity.\textsuperscript{16,17}

Ga(OTf)\textsubscript{3} was also used to catalyze one-pot epoxide ring-opening reactions to form β-hydroxy sulfides 5 with high chemo- and regioselectivity under solvent-free conditions.
Although other metal triflates, such as Bi(OTf)$_3$ and Sc(OTf)$_3$, proved to catalyze these types of reactions, significantly longer reaction times were required under the same conditions.

\[ \text{Scheme 1-1 Ga(III)-catalyzed epoxide ring-opening reaction}^{18} \]

Gallium(III) trihalides have been reported to be largely covalent in nature when anhydrous. The bridged dimeric formula may be obtained if the gallium halides are dissolved in apolar solvents, such as benzene, dichloromethane etc. Solid gallium(III) chloride, GaCl$_3$, was shown to exist as a dimer with the molecular formula Ga$_2$Cl$_6$. It has been considered to be a weaker Lewis acid catalyst compared to AlCl$_3$, and was successfully used in Lewis acid-catalyzed C–C bond formations in the last decade,$^{19}$ including arylation.$^{20}$ Interestingly, GaCl$_3$ may act as a $\pi$ Lewis acid to activate $\pi$ Lewis bases such as C–C triple bonds (Scheme 1-2).$^{21}$ It was proposed that, in the presence of a catalytic amount of gallium(III), the alkynyl indene substrate 6 was converted to a non-classic zwitterion intermediate. The latter may undergo isomerization via a transient cyclopropane species to finally afford the tricyclic cycloisomerization product 7 in 90% yield.

\[ \text{Scheme 1-2 Ga(III)-catalyzed cycloisomerization}^{21} \]
Another interesting example of gallium(III) Lewis acid catalysis represents the reaction between α,β-unsaturated cyclic ketones of type 8 and isocyanides of type 9 to generate products of type 10 (Scheme 1-3).\textsuperscript{22} When boron(III) or aluminium(III) Lewis acids were employed, the yields of 10 proved to be rather low (<50\%).\textsuperscript{23} In contrast, Ga(III) was found to be a significantly better catalyst for this [4+1] cycloaddition.\textsuperscript{22} This success may be ascribed to the relatively lower oxophilicity of Ga(III), one of its advantages as a catalyst compared to its lighter homologues.

Both reaction scope and mechanism were reported by the same group in 2005.\textsuperscript{24} It was found that only aromatic isocyanides could be used. Interestingly, substrates with a higher degree of steric demand led to the formation of the corresponding products in higher yields. The proposed mechanism is detailed in Scheme 1-4. The Michael acceptor 11 may be activated through coordination of the gallium(III) center to the carbonyl oxygen atom. In turn, conjugate addition of the isocyanide may be greatly facilitated thus potentially resulting in the formation of two geometric isomers. Cyclization of the Z isomer 12 would lead to the desired product 13. The formation of the E isomer 12’ may be reversible so that so that its conversion to the corresponding Z isomer 12 is conceivable. Although a coordination of the gallium center to the isocyanide may be possible, the corresponding Ga–isocyanide complex was not considered as a viable reaction intermediate.
Scheme 1-4 Proposed mechanism for the Ga(III)-catalyzed [4+1] cycloaddition.24

Compared to common gallium(III) compounds, the ‘+II’ oxidation state of gallium has been much less explored. Typically, Ga(II)X2 compounds were considered to be rather mixed-valent species, i.e., Ga(I)[Ga(III)X4].7b Only limited examples of dimeric gallium(II) compounds, featuring a Ga(II)-Ga(II) bond, have been reported.25,26 Simple monomeric gallium(II) species were thought to be highly reactive intermediates with short life times.7b Remarkably, during the course of our studies Aldridge et al. accomplished the synthesis of the first thermally robust, monomeric Ga(II)(boryl)2 radical 15 (Scheme 1-5).27 This bis(boryl) species was obtained in 64% yield by reacting Ga(I) precursor 14, Ga(I)[N(SiMe3)Dipp*], with two equivalents of (THF)2Li[B(NDippCH)]2 at −78 °C, followed by addition of two equivalents of [12]crown-4 at room temperature [Dipp* = 2,6-(PH2CH)2-4-Me-C6H2]. The structure of the monomeric radical 15 was determined by X-ray crystallography, which contrasted the previously reported multi-metallic gallium(II) species (Figure 1-4). Electron paramagnetic resonance (EPR) spectroscopy confirmed the radical character of the Ga(II) center. It was suggested that the dimerization of 15 was impeded by the steric demand of the boryl substituent.
Regarding their relative Lewis acidities, Ga(I) has been considered substantially weaker than Ga(III) or Ga(II) species, but it should also display a ‘softer’ character, which may be an interesting property to explore in catalysis.

1.1.4 ‘Gallium(I)’ Halides – Mixed-Valent Gallium Salts

Due to the thermodynamic instability, ‘true’ Ga(I) monohalides cannot be prepared at room temperature. Redox-disproportionation to generate gallium metal and Ga(III) trihalides in
a 2:1 molar ratio can be frequently observed at a low temperature, which is one major challenge for the efficient synthesis of Ga(I) compounds. Although the mechanism is unknown, the ‘formal’ electron transfer for this ‘internal’ redox-reaction is shown in Scheme 1-6. In order to prepare sub-valent gallium halides, several synthetic routes have been developed.

Since gallium(I) halides have been reported to be very stable at high temperature, the first synthetic route to prepare Ga(I)X species was carried out at 800–1000 °C (Scheme 1-7). Indeed, this redox-reaction between liquid Ga(0) and gaseous H–X afforded Ga(I)X and hydrogen gas. Subsequently, the gaseous Ga(I)X was dissolved in a suitable solvent at a low temperature to provide a Ga(I)X solution. The advantage of this method is that the amount of Ga(I)X can be easily controlled by the amount of H–X. However, since the solvent should be able to prevent redox-disproportionation, while not being too reactive towards Ga(I), it proved difficult to find an appropriate solvent for this low-oxidation state gallium chemistry.

Schnöckel’s study has proved that there was a proportional relationship between the stability
and the atomic numbers of Ga and X. For instance, the synthesis of ‘Ga\textsubscript{1,05}’ (16) was first reported by Corbett and McMullan in 1955 by heating gallium metal and molecular iodine under vacuum at 350–500 °C for 72 h (Scheme 1-8, upper scheme).\textsuperscript{29} ‘Ga\textsubscript{1,05}’ (16) was isolated by washing the mixture with benzene. In the following decades, this approach was optimized to overcome its harsh conditions. In 1990, an improved synthesis of ‘Gal’ (17) was reported by Green \textit{et al.}\textsuperscript{30} The pale-green powder ‘Gal’ (17) was obtained through reaction between gallium metal and 0.5 equiv of iodine in toluene at >30 °C under ultrasonication (Scheme 1-8, lower scheme). The initially deep-purple solution of iodine in toluene (Scheme 1-8, left photo) changed to a light-greenish suspension when the reaction was completed (Scheme 1-8, right photo). This light-greenish powder was shown to be thermally stable under an inert atmosphere, but has proved to be very air- and moisture-sensitive. Although its accurate formulation remained to be a puzzle, it has been confirmed by Raman spectroscopy that this type of ‘Gal’ existed as a mixed-oxidation state salt, Ga(I)\textsubscript{2}Ga(II)\textsubscript{2}I\textsubscript{6}, with an average gallium oxidation state between ‘+I’ and ‘+II’.\textsuperscript{31} This salt proved to be insoluble in non-coordinating solvents, and was shown to decompose through redox-disproportionation to form Ga(II) or Ga(III) adducts alongside gallium(0). Nevertheless, due to its simple preparation and its thermal stability, 17 has been widely used as a precursor for ‘real’ gallium(I) species.

![Scheme 1-8 Synthesis of ‘Ga\textsubscript{1,05}’ (16) and ‘Gal’ (17)\textsuperscript{29,30}](image-url)
‘GaI’ (17) has been used as a Lewis acid towards a variety of Lewis bases, including monodentate imines, phosphines, or ethers to form through redox-disproportionation Ga(II), Ga(III) or mixed-valent products with gallium(0) formation.\textsuperscript{30,32} For example, mixing ‘GaI’ (17) with tetrahydrofuran (THF) or PPh\textsubscript{3} in a toluene solution provided THF•Ga(II) and Ph\textsubscript{3}P•Ga(III) adducts, respectively.\textsuperscript{30} Another simple preparation of donor–acceptor adducts was realised by reacting ‘GaI’ (17) with triethyl phosphine (18) in toluene at –78 °C (Scheme 1-9).\textsuperscript{32a}

\[
\begin{array}{ccc}
\text{‘GaI’} & + & \text{PEt}_3 \\
17 & & 18 \\
\text{PhMe, } –78^\circ\text{C} & \rightarrow & \text{(GaI}_2\text{PEt}_3)_2 & + & \text{Ga}_3\text{I}_5(\text{PET}_3)_3 \\
\text{19 colorless crystals} & & & & \text{20 yellow crystals} \\
\text{22\% y} & & & & \text{33\% y} \\
\end{array}
\]

\textbf{31P NMR (ppm): –19}  

\textbf{–24}  

\textbf{–8.4}  

\textbf{Scheme 1-9 Synthesis of donor–acceptor adducts by reacting ‘GaI’ (17) with PEt\textsubscript{3} (18)}\textsuperscript{30}

This transformation was monitored by \textsuperscript{31}P NMR analysis. The \textsuperscript{31}P NMR signal at $\delta = –19$ ppm of the starting material 18, PEt\textsubscript{3}, disappeared with time. Instead, the appearance of two new resonances at $\delta = –24$ ppm (d) and at $\delta = –8$ ppm (t) suggested the formation of two novel species. The latter signal was shown to correspond to a peculiar stucture, I\textsubscript{3}Ga\textsubscript{3}•(PEt\textsubscript{3})\textsubscript{3} (20; Figure 1-5). Interestingly, this compound turned out to be the first neutral species containing a Ga–Ga–Ga unit. Here, the central ‘Ga(I)’ atom was connected to two ‘Ga(II)’ atoms with Ga–Ga distances between 245.1 pm and 246.0 pm. The Ga–I distances within the two GaI\textsubscript{2} units (261.0 pm) proved to be shorter than the central Ga–I distance (262.7 pm), which may be ascribed to the fact that the size of Ga(I) is bigger than Ga(II). Based on the \textsuperscript{31}P NMR shifts, Ga(I) was considered a stronger donor towards ‘P’ than Ga(II). Similarly, the I\textsubscript{3}Ga\textsubscript{2}•2 PPh\textsubscript{3} adduct was prepared by the same procedure.
More recently, Jones et al. reported the preparation of a novel salt 22, [Ga$_2$I$_5$(IPr)][IPrH], by reacting a sterically demanding $N$-heterocyclic carbene, 1,3-bis(2,6-diisopropylphenyl)imidazol-2-ylidene (IPr; 21) and ‘GaI’ (17) in toluene (Scheme 1-10).$^{32b}$ This anion was shown to contain only one coordinated carbene ligand, which may be ascribed to the sterically demanding structure of IPr (21). The structure of this novel salt has been confirmed by X-ray diffraction (Figure 1-6).$^{32b}$

![Figure 1-5 The unique structure of Ga$_3$I$_4$(PEt$_3$)$_3$ [20; figure directly copied from the original source]](image)

**Scheme 1-10** Synthesis of the novel salt [Ga$_2$I$_5$(IPr)][IPrH] (22)$^{32b}$
1.1.5 Monomeric Gallium(I) Complexes – Potential Lewis Bases (LBs)

1.1.5.1 Early Examples of True Gallium(I) Species

In 1992, Schnöckel et al. reported the first organogallium(I) compound, cyclopentadienyl gallium(I) [25, Ga(I)Cp; Scheme 1-11]. This colorless and air-sensitive Ga(I) species was obtained by reacting MgCp$_2$ (24), or LiCp (27), with Ga(I)Cl (23) at low temperature for 7 days. The structure of Ga(I)Cp (25) was confirmed by $^1$H, $^{13}$C, and $^{71}$Ga NMR analysis at $-196$ °C, resulting in characteristic signals at $\delta = 5.71$ ppm, $\delta = 106.8$ ppm, and $\delta = -714$ ppm, respectively. These data suggested the formation of a Ga(I)–arene complex, whereas the analysis of the starting material, Ga(I)Cl (23), did not show any signal. Ga(I)Cp (25) was also detected by mass spectroscopy in the gas phase, where signals of the highest mass were obtained at m/z = 134 and 136 at $-70$ °C, corresponding to the natural $^{69}$Ga/$^{71}$Ga isotope distribution. It is noted that Ga(I)Cp (25) could not be isolated in a solvent-free state.
In 1993, Schnöckel et al. reported pentamethylcyclopentadienyl gallium(I), Ga(I)Cp* (30), as the first monomeric gallium(I) compound (Scheme 1-12). This species was prepared by reacting Ga(I)Cl (23) with MgCp*₂ (29), or LiCp* (32), in toluene/diethyl ether at −30 °C. While the yield was not mentioned, the structure of Ga(I)Cp* (30) was elucidated by gas-phase electron diffraction in 1994 (Figure 1-7). The $^{71}$Ga NMR analysis of Ga(I)Cp* (30) resulted a singlet resonance at $\delta = –653$ ppm, whereas the downfield shift comparing with Ga(I)Cp (25). The $C_{5v}$ structure with $\eta^5$ bonding between gallium and the Cp* ring showed nearly equal Ga–C bond distances, which confirmed that gallium was monohapto-bonded to the aromatic ring.

**Scheme 1-11** Synthesis of Ga(I)Cp (25) by Schnöckel and co-workers

**Scheme 1-12** Synthesis of Ga(I)Cp* (30) by Schnöckel and co-workers
Ga(I)Cp* (30) has been used as the starting material for new Ga(I) chemistry.\textsuperscript{35} For example, it was converted to mixed-valent gallium triflates and [Ga₂Cp*]⁺ [B(ArF)₄]⁻.\textsuperscript{36} Importantly, Ga(I)Cp* (30) was shown to act as a Lewis base when reacted with the Lewis acid B(C₆F₅)₃ (33) thereby forming a gallium(I)–boron(III) donor–acceptor complex (34; Scheme 1-13 and Figure 1-8).\textsuperscript{37} The $^{11}$B NMR analysis revealed a new broad signal at $\delta = -17.9$ ppm, consistent with a tetra-coordinated boron species. Based on the X-ray structure of this complex, the C₅Me₅ group was attached to the gallium center in a $\eta^5$ fashion and the ring-centroid Ga–B moiety proved to be linear. In addition, the $^{19}$F NMR analysis showed the expected up-field shift relative to the starting Lewis acid.\textsuperscript{38}

\begin{equation}
\text{Cp'}\text{Ga}^1 + \text{B(C}_6\text{F}_5)_3 \quad \text{PhMe, } -78^\circ\text{C, 1 h, warm to rt, 4 h} \quad \text{colorless crystals 78% y}
\end{equation}

\textbf{Scheme 1-13} Synthesis of Cp'Ga(I)B(C₆F₅)₃ (34) by Cowley \textit{et al.}\textsuperscript{37}
In 1996, Parkin et al. reported the synthesis of a new mono-valent gallium(I) complex, \([\text{Tp}^\text{tBu}_2\text{Ga(I)} (36)]\), by reacting \([\text{Tp}^\text{tBu}_2\text{Na}] (35)\) with an excess of ‘\text{Gal}’ (17) (Scheme 1-14). An alternative pathway proved to be the reduction of the corresponding gallium(III) iodide complex. The targeted Ga(I) complex was characterized by X-ray diffraction (Figure 1-9), which confirmed that the tris(pyrazolyl)hydroborato ligand, \([\text{TpRR}^\text{t}]\), could indeed stabilize the gallium(I) center. This Lewis basic complex was shown to react with the Lewis acid gallium(III) iodide to generate a Ga(I)–Ga(III) donor–acceptor complex, \([\text{Tp}^\text{tBu}_2\text{Ga(I)}\cdot\text{GaI}_3]\), the structure of which was confirmed by X-ray crystallography.

Scheme 1-14 Synthesis of \([\text{Tp}^\text{tBu}_2\text{Ga(I)} (36)]\) by Parkin et al.
Similarly, \([\text{TpMe}_2]\text{Ga}(\text{I})\cdot\text{GaX}_3\) (40; \(X = \text{Cl, I}\)) was successfully prepared by reacting \([\text{TpMe}_2]\text{M}\) with ‘\(\text{Gal}\)’ [17; \(\text{M} = \text{K}\) (38), \(\text{Tl}\) (39); Scheme 1-15 and Figure 1-10, left structure).\(^40\) Although the novel \(\text{Ga}(\text{I})\) species, \([\text{TpMe}_2]\text{Ga}(\text{I})\), has not been isolated, the subsequent formation of a \(\text{Ga}(\text{I})\)–\(\text{Ga}(\text{III})\) donor–acceptor complex suggested that \([\text{TpMe}_2]\text{Ga}(\text{I})\) should be at least a transient species. Based on this assumption, the \(\text{Ga}(\text{I})\)–\(\text{B}(\text{III})\) donor–acceptor complex \([\text{TpMe}_2]\text{Ga}\cdot\text{B}(\text{C}_6\text{F}_5)_3\) (41) was synthesized through an anion metathesis between \([\text{TpMe}_2]\text{K}\) (38) and ‘\(\text{Gal}\)’ (17), followed by the addition of the boron Lewis acid (Scheme 1-15 and Figure 1-10, right structure).

![Molecular structure of \([\text{Tp'Bu}_2]\text{Ga}(\text{I})\) (36; figure directly copied from the original source)\(^39\)](image)

**Figure 1-9** Molecular structure of \([\text{Tp'Bu}_2]\text{Ga}(\text{I})\) (36; figure directly copied from the original source)\(^39\)

\[
\begin{align*}
\text{Ga}(\text{Cl})_4 & \quad \xrightarrow{[\text{TpMe}_2]\text{M} (\text{M} = \text{K} \quad \text{38, Tl} \quad \text{39})} [\text{TpMe}_2]\text{Ga}^+ : \xrightarrow{\text{GaCl}_3} \quad \text{Ga}(\text{Cl})_3 \\
[\text{TpMe}_2]\text{K} & \quad \xrightarrow{1. [\text{TpMe}_2]\text{K} \quad \text{38}} [\text{TpMe}_2]\text{Ga}^+ : \xrightarrow{2. \text{B}(\text{C}_6\text{F}_5)_3 \quad \text{33}} [\text{TpMe}_2]\text{Ga}^+ : \xrightarrow{\text{B}(\text{C}_6\text{F}_5)_3 \quad \text{33}} \text{Ga}(\text{Cl})_3
\end{align*}
\]

**Scheme 1-15** Synthesis of \([\text{TpMe}_2]\text{Ga}(\text{I})\cdot\text{GaI}_3\) (40) and \([\text{TpMe}_2]\text{Ga}(\text{I})\cdot\text{B}(\text{C}_6\text{F}_5)_3\) (41)\(^40\)
1.1.5.2 Gallium(I) Species as Metallic NHC Analogues

Later on, several neutral and anionic Ga(I) compounds were reported and their potential as ‘metallic’ NHC analogues was discussed. Indeed, four-, five-, and six-membered ring systems of Ga(I) N-heterocycles have been well studied in recent years. Generally, they can be classified within two categories, neutral and anionic gallium(I) analogues of NHCs (Figure 1-11).

**Figure 1-10** Structures of the donor-acceptor complexes 40 and 41 [figures directly copied from the original source]^{40}

**Figure 1-11** Examples of neutral and anionic Ga(I) compounds as metallic NHC analogues

![Diagram showing structures of Ga(I) compounds as metallic NHC analogues]
Regarding the neutral species, only two structures have been confirmed to date. Indeed, the Ga(I) analogue bearing a six-membered ring, Ga(I)[(NDippCMe)₂CH] or Ga(I)[nacnac] (43), was synthesized by Power et al. in 2000 (Scheme 1-16). Ga(I)[nacnac] (43) was obtained as yellow crystals in 39% yield by reacting Li[nacnac] (42) with ‘Gal’ (17) under reducing conditions. This Ga(I) complex may be considered analogous to a singlet carbene, as it features two substituents on the six-electron gallium(I) center. Ga(I)[nacnac] (43) proved to be thermally stable (mp 202–204 °C), and the X-ray crystallographic analysis proved that this molecule was a mono-valent complex (Figure 1-12). The average Ga–N distance was shown to be 2.054 Å, which suggested a Ga–N single bond rather than the presence of a significant multiple bond character. This fact may be ascribed to a delocalization of the p electrons of the C₃N₂ unit. The N–Ga–N bond angle was measured to be 87.6 °. Finally, DFT calculations measured the HOMO–LUMO gap to be of 102.9 kcal mol⁻¹. In turn, the gallium center may be a good σ donor and a weak π acceptor, i.e., this Ga(I) species may be used predominantly as a Lewis base.

![Scheme 1-16 Synthesis of Ga(I)[nacnac] (43) by Power et al.](image)

**Scheme 1-16** Synthesis of Ga(I)[nacnac] (43) by Power et al.⁴²
Accordingly, a gallium(I)–boron(III) donor–acceptor complex 44 has been prepared by reacting the monomeric Lewis base Ga(I)[nacnac] (43) with the Lewis acid B(C₆F₅)₃ (33; Scheme 1-17).³⁷ The $^{11}$B NMR analysis of this product 44 showed a new broad singlet at $\delta = -20.3$ ppm, consistent with a tetra-coordinate boron species. In addition, the $^{19}$F NMR analysis data matched those of literature reports.³⁸,⁴³ Finally, this novel complex 44 was characterized as well by X-ray diffraction (Figure 1-13).
In 2006, Jones et al. reported the first example of a gallium(I) species bearing a four-membered ring, Ga(I)[(DippN)₂CNCy₂] or Ga(I)[giso] (46; Scheme 1-18). This new compound was prepared through an anion metathesis between the lithium guanidinate salt, Li[giso] (45), and ‘Gal’ (17). Although Ga(I)[giso] (46) has proved to be air-sensitive, it was shown to be very stable below 150 °C under an inert atmosphere. Compared to the six-membered analogue, the Ga–N distance of Ga(I)[giso] (46) proved to be longer with a more acute N–Ga–N angle (Figure 1-14). DFT calculations measured the HOMO–LUMO gap to be of 67.4 kcal·mol⁻¹, which proved to be less compared to the six-membered analogue. These data suggested as well that Ga(I)[giso] (46) may be a good σ donor and a good π acceptor.

\[\text{Dipp} = 2,6-	ext{Pr}_2-	ext{C}_6	ext{H}_3 \]
\[\text{Cy = cyclohexyl} \]

Scheme 1-18 Synthesis of Ga(I)[giso] (46) by Jones et al.⁴³
The nucleophilicity of Ga(I)[giso] (46) was exploited using transition metal precursors to form homo- and heteroleptic complexes.\textsuperscript{41, 44} Indeed, the thermally stable platinum complex, Pt[Ga(I)[giso]]\textsubscript{3} (48), was synthesized by reacting Ga(I)[giso] (46) with [Pt(norbornene)]\textsubscript{3} (47) in a 3:1 or 4:1 molar ratio (Scheme 1-19). The structural analysis revealed the complex to be homoleptic with a trigonal-planar Pt center and particularly short Pt–Ga bonds (2.309 Å; Figure 1-15).

\begin{center}
\textbf{Figure 1-14} Molecular structure of Ga(I)[giso] [46; figure directly copied from the original source]\textsuperscript{43}
\end{center}

\begin{center}
\textbf{Scheme 1-19} Synthesis of Pt–Ga complex 48\textsuperscript{44}
\end{center}
The most commonly used $N$-heterocyclic carbene in coordination chemistry has been 1,3-bis(2,6-diisopropylphenyl)imidazol-2-ylidene (21, IPr; Figure 1-16).

Due to its sterically demanding structure, it has proved to stabilize kinetically meta-stable low-valent metal centers. The first anionic Ga(I) species 52, reported by Hubert Schmidbaur in 1999, was described as a five-membered ring system (Scheme 1-20).\(^\text{45}\) GaCl$_3$ was used as the starting material and the dimeric gallium intermediate 51 was reduced with an excess of potassium metal in the final step. Since the gallium(I) cation is coordinated by a double-negatively charged ligand, this new complex, Ga(I)[(‘BuNCH)$_2]$ (52), must have overall a negative charge.
According to the crystal structure, compound 52 proved to contain complex cations and disordered anions (Figure 1-17). The heterocycle was shown to be almost planar with an N−Ga−N angle of 81.8 ° and Ga−N distances of 1.985 Å; earlier DFT calculations had predicted a planar heterocycle with a N−Ga−N angle of 80.7 ° and Ga−N distances of 1.983 Å. The gallium atom was confirmed to be two-coordinate with a formal oxidation state of ‘+I’. Thanks to the lone pair of electrons at the Ga(I) center and the electron-rich ligand, this monomeric Ga(I) species 52 may be a promising metallic Lewis base.

**Figure 1-17** Molecular structure of Ga(I)((tBuNCH)2]− (52; figure directly copied from the original source)45

### 1.1.6 Univalent Gallium(I) Salts – Potential Lewis Acids (LAs)

Typically, gallium(I) salts have been prepared through an anion metathesis reaction using ‘GaI’ (17) as a starting material. However, this approach may yield product mixtures. In 2010, a simple and novel route for the preparation of Ga(I) salts with weakly coordinating anions was reported by Krossing and Slattery et al. (Scheme 1-21). The key to the
success of this seminal method may be the excessive use of gallium metal as a starting material. The required oxidant, $\text{Ag}^+\{\text{Al(OR}_3)_4\}_4^-$ (53), had been synthesized and characterized by Krossing et al.\(^\text{47}\) In the event, a solution of $\text{Ag}^+\{\text{Al(OR}_3)_4\}_4^-$ (53) in $\text{o-F}_2\text{C}_6\text{H}_4$/toluene was reacted with an excess of gallium(0) under ultrasonication resulting in the formation of an off-white powder, $\text{[Ga(C}_6\text{H}_3\text{Me)}_2]^+\{\text{Al(OR}_3)_4\}_4^-\text{ (54)}$, in 99% isolated yield. The $^{19}\text{F NMR}$ analysis of Ga(I) salt 54 in $\text{o-F}_2\text{C}_6\text{H}_4$ showed a signal at $\delta = -75.6$ ppm for the perfluorinated counter anion and no evidence for anion decomposition products.

$$
\begin{align*}
\text{Ga}^0 & + \text{Ag}^+\{\text{Al(OR}_3)_4\}_4^- \rightarrow \text{Ga}^+\{\text{Al(OR}_3)_4\}_4^- + \text{Ag}^0
\end{align*}
$$

Scheme 1-21 Synthesis of the univalent gallium(I) salt 54 in $\text{o-F}_2\text{C}_6\text{H}_4$ by Krossing and Slattery et al.\(^\text{9a}\)

Similarly, when switching to fluorobenzene ($\text{C}_6\text{H}_5\text{F}$) as a solvent under the same conditions several species of the type $[\text{Ga(C}_6\text{H}_5\text{F}_n)_3]^+\{\text{Al(OR}_3)_4\}_4^-\text{ (n = 2, 2.5, 3; 54)}$ were generated in high yields. The crystal structures of these gallium(I) species were obtained (Figure 1-18). In the $[\text{Ga(C}_6\text{H}_5\text{F}_3)_3]^+$ ion (54a), gallium(I) was coordinated by three arene moieties, which was thought to be the first gallium(I) cation bearing three independent arene molecules. The Ga(I) oxidation state was confirmed by $^{71}\text{Ga NMR}$ analysis because a specific oxidation state of gallium typically displays a characteristic chemical shift. Expectedly, the resonance of $\text{Ga}^+\{\text{Al(OR}_3}_4\}_4^-\text{ (54)}$ in the $^{71}\text{Ga NMR}$ analysis was shown to be solvent-dependent: $\delta = -448$ ppm (THF), $\delta = -520$ ppm (toluene), $\delta = -630$ ppm (CD$_2$Cl$_2$), $\delta = -750$ ppm (1,2-fluorobenzene), $\delta = -756$ ppm (fluorobenzene). While this new Ga(I) complex proved to be stable in aromatic solvents, interesting phenomena were obtained in
THF and CD$_2$Cl$_2$. Indeed, in the presence of Ga(I) complex 54, THF was found to undergo ring-opening polymerization at room temperature within 24 h. In CD$_2$Cl$_2$ at room temperature, the new Ga(I) complex was shown to be stable for only several hours before the material decomposed with formation of a Ga(III) species, as confirmed by a new $^{71}$Ga NMR resonance at $\delta = +190$ ppm.

A similar grayish solid, [Ga(1,3,5-Me$_3$–C$_6$H$_3$)]$^+\{\text{Al[OC(CF}_3)_3]\}^-$ (54b), was also synthesized through a ligand exchange reaction using two equivalents of mesitylene (55; 1,3,5-Me$_3$–C$_6$H$_3$; Scheme 1-22). The molecular structure of this novel gallium(I) species 54b was determined as well (Figure 1-19). Here, the gallium(I) cation displayed a stronger interaction with the more electron-rich ligand, mesitylene, and a weaker ‘Ga–F contact’ interaction with the less electron-rich ligand, C$_6$H$_5$F. The $^{71}$Ga NMR analysis of this compound revealed two distinct Ga(I) resonances; the signals at $\delta = -758$ ppm and $\delta = -739$ ppm were ascribed to [Ga(C$_6$H$_5$F)$_2$]$^+$ and [Ga(1,3,5-Me$_3$C$_6$H$_3$)$_2$]$^+$, respectively.

![Molecular structure of 54a](image) 

**Figure 1-18 Molecular structure of 54a [figure directly copied from the original source]**

```
Scheme 1-22 Synthesis of the univalent gallium(I) salt 54b through a ligand-exchange reaction
```

\[
\text{Ga(C}_6\text{H}_5\text{F})_2\{\text{Al(OR}_3\text{F})_3\}^+ + 1,3,5\text{-Me}_3\text{--C}_6\text{H}_3 \xrightarrow{\text{C}_6\text{H}_5\text{F}} \text{Ga(1,3,5-Me}_3\text{C}_6\text{H}_3)_2\{\text{Al(OR}_3\text{F})_3\}^+
\]

$^{71}$Ga NMR (ppm): 
- 54a: 2.0 equiv at $-756$
- 54b: 83% yield at $-739$
The synthesis of these types of gallium(I) salts has proved to be very simple and straightforward. Surprisingly, there was no evidence for decomposition products. Thus, this mild access to pure Ga(I) species seemed to hold promise for applications in catalysis; it certainly displays a variety of significant advantages over the ‘reductive’ approach using ‘Gal’. Additionally, it is possible to easily separate Ga\(^+\){Al[OC(CF\(_3\)]\(_3\)}\(_4\)\(^-\) (54) from excessive Ga(0) and Ag(0) generated in situ.

Crown ethers have been widely used in coordination chemistry, particularly with low-oxidation state metal species, such as indium(I) salts. Crown ethers were first synthesized by Pedersen who was awarded the Nobel price in Chemistry for this discovery. It is well established that [18]crown-6 ([18]c-6; 56) has a predominant affinity for the potassium cation (K\(^+\)) over other alkali metal cations. In 2012, Krossing et al. examined the effect of crown ethers on gallium(I) species. It was found that a colorless solution was obtained when Ga\(^+\){Al[OC(CF\(_3\)]\(_3\)}\(_4\)\(^-\) (54) was reacted with one equivalent of [18]crown-6 in fluorobenzene (Scheme 1-23). The coordination of the Ga(I) center by the crown ether was confirmed by \(^1\)H and \(^{71}\)Ga NMR analyses. In the \(^1\)H NMR spectrum, the resonance of [18]crown-6 was found to be at \(\delta = 3.32\) ppm vs. \(\delta = 3.56\) ppm for the signal of non-coordinated [18]crown-6. In the \(^{71}\)Ga NMR analysis, a substantial down-field shift
was observed from $\delta = -756$ ppm for the native Ga(I) salt to $\delta = -643$ ppm for the Ga(I) salt coordinated by [18]crown-6.

\[
\text{Ga}^+\text{[Al(OR$_3$)$_3$]$^-$} \xrightarrow{\text{PhF}} \text{[Ga(C$_7$H$_5$F)$_2$]$^+$} + \text{R$_F$ = C(CF$_3$)$_3$}
\]

54 54a 56 54c

1.0 equiv 1.0 equiv

54c >99% y

$^{71}\text{Ga NMR (ppm):}$ –756 –643

Scheme 1-23 Synthesis of [18]-6–Ga$^+$[Al(OC(CF$_3$)$_3$)$_4$]$^-$ (54c) by Krossing et al.$^9b$

The crystal structure of this gallium(I)–crown ether complex 54c highlighted that two solvent molecules, one each above and below the coordination plane, coordinated to the Ga(I) center (Figure 1-20). It was shown that the HOMO and the LUMO were the s orbital and the p orbital –perpendicular to the coordination plane– at gallium, respectively. The crown ether coordination to gallium resulted in a HOMO–LUMO gap, which was increased by 6.9 kcal·mol$^{-1}$ suggesting that the stability of the molecular ion slightly increased.
In 2013, Krossing et al. reported a gallium(I)–bis(carbene) complex, [Ga(IPr)₂]⁺{Al[OC(CF₃)₃]₄}⁻•PhF (54d). Compound 54d was prepared as yellow crystals in quantitative yield by reacting Ga(I) salt 54a and IPr carbene (21) in a 2:1 molar ratio [IPr = 1,3-bis(2,6-diisopropylphenyl)imidazol-2-ylidene; Scheme 1-24]. Similarly, another Ga(I)–carbene complex, [Ga(IMes)₂]⁺{Al[OC(CF₃)₃]₄}⁻•0.5 PhF (54e), was obtained as orange crystals in 85% yield employing the same method [IMes: 1,3-bis(2,4,6-trimethylphenyl)imidazol-2-ylidene]. It is noted that in both cases the ⁷¹Ga NMR analysis proved to be ‘silent’.

![Scheme 1-24 Synthesis of [Ga(IPr)₂]⁺{Al[OC(CF₃)₃]₄}⁻ (54d) by Krossing et al.](image)

The molecular structures of [Ga(IPr)₂]⁺ (54d) and [Ga(IMes)₂]⁺ (54e) are shown in Figure 1-21. Accordingly, Ga(NHC)₂⁺ was shown to have a lone pair of electrons available at the gallium center for back-donation thus increasing the population of p orbitals and decreasing the s orbital population concomitantly.

![Figure 1-21 Structures of [Ga(IPr)₂]⁺ (54d) and [Ga(IMes)₂]⁺ (54e; figures directly copied from the original source)](image)
In 2015, Krossing et al. reported bis- and tris-\(\eta^6\)-coordinated gallium(I)–arene complexes of \(p\)-xylene (1,4-Me\(_2\)-C\(_6\)H\(_4\)), hexamethylbenzene (C\(_6\)Me\(_6\)), diphenylethane (PhH\(_2\)C–CH\(_2\)Ph) and \(m\)-terphenyl (1,3-Ph\(_2\)C\(_6\)H\(_4\)); Scheme 1-25.\(^{51}\) The [Ga(PhH\(_2\)C–CH\(_2\)Ph)]\(^+\) cation (54f) turned out to be first structurally characterized \(ansa\)-like bent sandwich chelate of gallium(I). Remarkably, the [(C\(_6\)H\(_5\)F)Ga(\(\mu\)–1,3-Ph\(_2\)C\(_6\)H\(_4\))\(_2\)Ga(C\(_6\)H\(_5\)F)]\(^2+\) cation (54g) was the first binuclear gallium(I) complex without a Ga–Ga bond (Figure 1-22).\(^{51}\) The \(^{71}\)Ga NMR analysis featured resonances at \(\delta = -746\) ppm and \(\delta = -751\) ppm for [Ga(PhH\(_2\)C–CH\(_2\)Ph)]\(^+\) (54f) and for [(C\(_6\)H\(_5\)F)Ga(\(\mu\)–1,3-Ph\(_2\)C\(_6\)H\(_4\))\(_2\)Ga(C\(_6\)H\(_5\)F)]\(^2+\) (54g), respectively. These data proved the successful ligand exchange for gallium(I). In the di-Ga(I) cation, each gallium(I) center was shown to be coordinated by two bridging 1,3-Ph\(_2\)–C\(_6\)H\(_4\) ligands (58).

\[
\begin{align*}
\text{Ga(C}_6\text{H}_5\text{F)}_2^+ [\text{Al(OR}_2\text{F)}_3]^+ & \quad \text{PhH}_2\text{C–CH}_2\text{Ph} \quad \text{Ga(PhH}_2\text{C–CH}_2\text{Ph)}^+ [\text{Al(OR}_2\text{F)}_3]^+ \\
\begin{array}{c}
54a \\
\text{R}_2 = \text{C(C}_3\text{F)}_3
\end{array} & \quad \begin{array}{c}
0.88 \text{ equiv} \\
57
\end{array} & \quad \begin{array}{c}
\text{C}_6\text{H}_4 \text{F} \\
54f
\end{array} \\
\hline
\text{Ga(C}_6\text{H}_5\text{F)}_2^+ [\text{Al(OR}_2\text{F)}_3]^+ & \quad 1,3\text{-Ph}_2\text{–C}_6\text{H}_4 \quad \text{[(C}_6\text{H}_5\text{F)}\text{Ga(µ–1,3-Ph}_2\text{–C}_6\text{H}_4),\text{Ga(C}_6\text{H}_5\text{F)})]^2+ \\
\begin{array}{c}
54a \\
\text{R}_2 = \text{C(C}_3\text{F)}_3
\end{array} & \quad \begin{array}{c}
1.0 \text{ equiv} \\
58
\end{array} & \quad \begin{array}{c}
\text{C}_6\text{H}_4 \text{F} \\
[(\text{C}_6\text{H}_5\text{F)}\text{Ga(µ–1,3-Ph}_2\text{–C}_6\text{H}_4),\text{Ga(C}_6\text{H}_5\text{F)})]^2+ & \quad [\text{Al(OR}_2\text{F)}_3]^2
\end{array} \\
\text{54g}
\end{align*}
\]

**Scheme 1-25** Synthesis of [Ga(PhH\(_2\)C–CH\(_2\)Ph)]\(^+\) (54f) and [(C\(_6\)H\(_5\)F)Ga(\(\mu\)–1,3-Ph\(_2\)C\(_6\)H\(_4\))\(_2\)Ga(C\(_6\)H\(_5\)F)]\(^2+\) (54g)\(^{51}\)

![Figure 1-22](https://example.com/final_image.png)

**Figure 1-22** Structure of 54f and 54g [figure directly copied from the original source]\(^{51}\)
In summary, Krossing and Slattery et al. provided a novel, convenient route for the preparation of univalent gallium(I) salts. Various gallium(I) complexes were prepared through ligand exchange reactions. *Since our laboratory investigates low-valant or low-oxidation state elements for applications in catalysis, we became interested in exploring the potential of low-oxidation state gallium catalysis. We were intrigued by a recent seminal report, in which ambiphilic properties of gallium(I) were exploited in a stoichiometric context.*

### 1.1.7 Ambiphilic Properties of Gallium(I) in a Stoichiometric Context

In 2009, a seminal report by Fischer and Frenking et al. confirmed that the metallic NHC analogue Ga(I)[nacnac] (43) could act as both a strong σ donor ligand and π acceptor [nacnac = (NDippCMe)₂CH].³⁷, ⁵² Indeed, an unusual compound bearing a Bi=Bi double bond was found to be accessible with the support of the above-mentioned electron-rich Ga(I) species. This Ga(I)–Bi=Bi–Ga(I) complex (54) was prepared as purple crystals by reacting bismuth triflate [Bi(OTf)₃] with two equivalents of Ga(I)[nacnac] (43; Scheme 1-26).⁸ Interestingly, metallic bismuth was obtained when Ga(I)[nacnac] (43) was reacted with other commercially available bismuth salts such as BiX₃ (X = Cl, Br, I). In this new compound, the Ga(I)–Bi=Bi–Ga(I) (60) backbone was shown to be planar with the two Ga(I)[nacnac] (43) ligands trans to each other, and the Ga–Bi–Bi bond angles were measured to be close to 90 ° (Figure 1-23). Bismuth was proposed to be in its formal ‘+I’ oxidation state. ⁷¹Ga NMR data were not reported for this new complex (60).
Importantly, the structure displayed a monomeric molecule with an unprecedented Bi=Bi double bond, in which each bismuth center was stabilized by a neutral Ga(I)[nacnac] (43) ligand through a gallium(I)–bismuth donor–acceptor bond. Such an interaction would render the corresponding gallium(I) center more electrophilic. In turn, a triflate counter anion was proposed to coordinate to each gallium(I) center thereby further stabilizing this unusual complex. The hypothesis of such an ambiphilic gallium(I) species was indirectly supported by the fact that the use of NHCs –instead of Ga(I)[nacnac]– failed to give the
corresponding NHC-stabilized complex, \( (\text{NHC})\text{Bi} = \text{Bi}(\text{NHC}) \). This result was explained by the lower \( \pi \) acceptor ability of the carbon center in an NHC compared to the gallium center in Ga(I)[nacnac].\(^{53}\)

In 2013, Krossing et al. reported the preparation and characterization of gallium(I)–bis(carbene) complexes of the type \( \{\text{Ga(I)[NHC]}_2\}^+ \) (54d; cf. Figure 1-21).\(^{9c}\) As an intrinsic Lewis acid, the gallium(I) center was suggested to be coordinated by the carbene. After such a coordination, the gallium(I) center was shown to act as a Lewis base, i.e., electron density from the gallium s-type lone pair of electrons was transferred back into the vacant p orbital of the carbene center (Figure 1-24). Based on the definition of an ambiphilic species, this gallium(I) center might be considered having an ambiphilic character, i.e., it formally displays acidic and basic properties at a single site.

![Figure 1-24](figure) The postulated \( \sigma \)-back-bonding interaction [figure directly copied from the original source]\(^{9c}\)

In contrast to the Lewis acid gallium(III), a gallium(I) center may be considered potentially ambiphilic because both vacant orbitals and a lone pair of electrons do exist at a single element site (Figure 1-25). Through coordination with different types of counteranions or ligands, a gallium(I) center may be tuned to act as a Lewis acid or a Lewis base, respectively. Indeed, gallium(I) was shown to act as a Lewis acid in the presence of weakly coordinating anions.\(^{9a}\) On the other hand, Lewis basicity was enfolded when the gallium(I) center was coordinated by an electron-rich ligand.\(^{41,42,45,54}\) These intriguing properties represent an extremely interesting area to be explored for novel catalysis.
1.1.8 Stoichiometric Applications in Organic Synthesis

1.1.8.1 Stoichiometric Use of ‘GaI’

‘GaI’ was occasionally used to facilitate C–C bond formations. For instance, Jones et al. have investigated the reactivity of ‘GaI’ as a reducing agent for substrates such as α-alkoxy ketones, α-halo ketones and α-diketones (Scheme 1-27). Several interesting properties of this metal reagent were uncovered during these initial studies. Indeed, the use four equivalents of ‘GaI’ (17) for the reduction of benzoin methyl ether 61 resulted in the formation of a new trifunctional aldol adduct 63 in high yield. A six-membered chelated cyclic transition state 62 was proposed to explain the generation of a single diastereomer.

![Scheme 1-27 Proposed mechanism for the reaction of ‘GaI’ with α-alkoxy ketones](image)

Since ‘GaI’ (17) was reported to exist as a mixed-valent multi-nuclear gallium species, it proved to be difficult to determine which of the gallium centers was responsible for the obtained reactivity and selectivity. In the same line, Ga(I) has been known to undergo redox-disproportionation under certain conditions to form Ga(0) and Ga(III) in a 2:1 molar ratio. Gallium(0) may act as a reducing agent, while gallium(III) may act as a Lewis acid.
In turn, the interpretation of this stoichiometric low-oxidation state gallium chemistry may be challenging. In order to explore, which component facilitated the reductive C–C bond formation, Ga₂Cl₄, GaCl₃, GaI₃, and Ga(0) were examined separately under otherwise identical conditions. The use of GaCl₃, GaI₃, or Ga(0) failed to give the expected aldol adduct. In the case of Ga₂Cl₄, the desired product was detected, albeit in a very low yield. These results may suggest that the Ga(I) or Ga(III) cations should play a significant role in facilitating the aldol-like reaction above. Similarly, ‘GaI’ plays a ‘Grignard reagent’-like role in α-halo ketones and other α-functionalized ketones. To date however, the use of a catalytic amount of ‘Gal’ has been not reported.

1.1.8.2 Stoichiometric Use of Ga(0)

Gallium metal exhibits interesting features such as a low first ionization potential of 5.99 eV, which may exploited in single electron transfer (SET) reactions. In 1988, Butsugan et al. reported gallium metal could be used in Barbier-type reactions involving aldehydes or ketones and allyl iodide (65; Scheme 1-28). The use of ultrasonication and DMF as a solvent proved to be critical to obtain the desired homoallylic alcohols 66 in high yield. It is noted that 1,2-addition products were observed exclusively when α,β-unsaturated carbonyl compounds were used.

![Scheme 1-28](image)

Scheme 1-28 Stoichiometric use of gallium(0) for a Barbier-type reaction

In 2002, Wang et al. showed that water could be used as a solvent and mediator for the gallium(0)-facilitated allylation of aldehydes and ketones using allyl bromide (67) at 45 °C (Scheme 1-29). Here, acidic additives or ultrasonication were not required anymore. In
Acid-sensitive functional group groups such as acetics were tolerated under these new conditions.

\[
\begin{align*}
\text{O} & \quad \text{R}' \quad \text{Br} \\
\text{R} = \text{Ar, HetAr, alkyl} & \\
\text{R}' = \text{H, Me} \\
67 & \\
\text{Ga}^0 (2.0 \text{ equiv}) & \\
\text{H}_2\text{O}, 45 \degree \text{C}, 6 \text{ h} & \\
\text{OH} & \\
11 \text{ examples} & \\
42-82\% \text{ y} & \\
\end{align*}
\]

**Scheme 1-29 Gallium(0)-mediated allylation of aldehydes and ketones**

In the same context, Andrews *et al.* examined gallium(0)-mediated Barbier-type chemistry under solvent-free conditions. The use of ultrasonication proved to be critical in order to obtain the products in high yields. Both carbonyl compounds and imines were converted to the corresponding homoallylic alcohols and amines, respectively.

In 2002, Takai *et al.* reported a seminal discovery: it was found that a catalytic amount of indium(0) could facilitate the gallium(0)-mediated Barbier-type allylation of ketones under particularly mild conditions (Scheme 1-30). Typically, gallium-mediated Barbier-type allylations require reflux conditions, whereas Takai demonstrated smooth reactivity at 10 °C. The key to this reactivity has proved to be the presence of a catalytic amount of indium and the stronger reducing character of gallium compared to indium: \(E^\circ [\text{Ga(III)/Ga(0)}] = -0.549\) V vs. \(E^\circ [\text{In(III)/In(0)}] = -0.338\) V. In turn, the consumed indium metal was proposed to be regenerated *in situ* through reduction of a transient indium(III) species by gallium(0), which was employed in stoichiometric quantities.
Overall, indium(0) may first activate allyl bromide through single electron transfer and subsequent oxidative addition into the C–Br bond of allyl bromide (67). The resulting allyl–In(III) may then undergo transmetallation with in situ generated Ga(III), thus forming allyl–Ga(III), which was considered to be the real nucleophile to react with the electrophilic ketone 68. Indium(III) would then be reconverted to indium(0) through reduction by gallium(0).

In summary, at the outset of this project only stoichiometric applications of ‘GaI’ and Ga(0) were reported in synthetic organic chemistry. In turn, our aim was to explore low-oxidation state gallium catalysis for various C–C bond-forming reactions.
1.2 Aims

As outlined above, gallium is a fairly abundant, inexpensive, and low-toxic metal. Ga(0) has been commonly used as a stoichiometric reagent in Barbier-type organic chemistry. Stable Ga(III) species have been frequently employed as a Lewis acid catalyst in organic synthesis, including asymmetric versions thereof. In contrast, only few reports have been published on the less stable Ga(I) compounds. Intriguingly however, Ga(I) has vacant p orbitals and a lone pair of electrons in an sp-type orbital, and may therefore trigger the activation of both basic and acidic reagents at a single metal site. At the start of this project, the catalytic use of Ga(0) or Ga(I) was unprecedented in organic synthesis.

According to the Krossing–Slattery protocol, monomeric electron-poor Ga(I) species were obtained through a redox-reaction between Ga(0) and a perfluorinated Ag(I) salt. We aimed at exploring this approach using a cheap and commercially available silver salt in order to obtain in situ a Ga(I) species, which could be exploited in Lewis acid or dual catalysis (Figure 1-26). Indeed, the Lewis acidic Ga(I) center may activate an electrophile E, which could then undergo direct C–C bond formation with a reactive nucleophile (simple Lewis acid catalysis). Alternatively, after coordination of the electrophile E to the Ga(I) center, the latter may be sufficiently electron-rich to facilitate the Lewis base activation of a less reactive pro-nucleophile in view of C–C bond formation (dual catalysis).

Figure 1-26 Generic scheme for the use of gallium(I) in Lewis acid or dual catalysis
Coordinated by an electron-rich ligand, Ga(I) could enfold potential Lewis basicity or trigger transition metal-like redox catalysis (Figure 1-27). Indeed, an electron-rich Ga(I) species may activate the Lewis acidic center of a pro-nucleophile in order to facilitate direct addition to a reactive electrophile \( E \) (simple Lewis base catalysis). Alternatively, after such an activation Ga(I) may be sufficiently electron-poor to allow coordination by a less reactive electrophile in view of C–C bond formation (dual catalysis).

Finally, such an electron-rich Ga(I) species may be also exploited in transition metal-like redox catalysis. It is conceivable that Ga(I) may insert into the C–X bond of an electrophilic reagent to form the corresponding Ga(III) intermediate (oxidative addition). The latter may undergo transmetallation with the C–Y bond of a nucleophilic reagent to generate a tri-coordinate Ga(III) intermediate bearing two organic rests \( cis \) to each other. This intermediate would have to undergo reductive elimination to form the intended cross-coupling product, \( R^1_R^2 \), with concomitant regeneration of Ga(I). This reductive elimination is considered the most challenging step because Ga(III) is known to be thermodynamically more stable than Ga(I). This key issue of the proposed redox catalysis cycle may be addressed with the use of a sterically demanding ligand, such as a carbene (NHC, CAAC), a phosphine, or a \( \beta \)-diketiminate.
Overall, the aims of this project were to explore: (i) the first catalytic use of gallium metal, and (ii) the catalysis potential of gallium(I) in organic synthesis.
1.3 Results and Discussion

1.3.1 Initial Catalysis Results with the Combination Ga(0)/Ag(I)

Initially, we were interested in examining the outlined Lewis acid or dual catalysis using a gallium(I) species. Since gallium(I) compounds are not commercially available, we anticipated that a gallium(I) species could be generated in situ through a Krossing–Slattery redox-reaction between gallium metal and a commercially available silver salt to see whether this concept was transferable to catalysis (proof of principle). We selected a borono variant of the Hosomi–Sakurai reaction as a model transformation, which does not proceed in the absence of a catalyst even at higher temperature (Scheme 1-31). Indeed, a Lewis acid would be required to activate a C(sp³) electrophile, e.g. an acetal, through abstraction of an alkoxy group to form an intermediary oxocarbenium ion. On the other hand, an allyl boron pro-nucleophile would require a Lewis base for C–B bond activation in view of ultimate C–C bond formation with the in situ generated oxonium ion. We envisioned that gallium(I) as a potentially ambiphilic species may facilitate this transformation as a single acid–base dual catalyst.

There has been precedence for this type of transformation in the context of indium(I) catalysis regarding the borono variant of the Hosomi–Sakurai reaction. In 2010, Kobayashi et al. reported the use of allyl boronic ester 71 as a pro-nucleophile in the C–C
bond formation with C(sp³) electrophiles (Scheme 1-32). Indium(I) triflate, In(I)OTf, was used as a dual catalyst resulting in the formation of the corresponding homoallylic ethers in 57–95% yields. The reactions proceeded smoothly with acyclic or cyclic aromatic, heteroaromatic, and aliphatic acetals, or ketals. It is noted that other metal triflates, including Ga(OTf)₃, In(OTf)₃, Sc(OTf)₃, Cu(OTf)₂, AgOTf, and Zn(OTf)₂ failed to catalyze this transformation.

**Scheme 1-32** In(I)OTf-catalyzed allylation of acetals and ketals

### 1.3.1.1 Proof of Concept

We used commercially available benzaldehyde-derived dimethyl acetal (70a) and allyl boronic ester 71 as model substrates and examined a variety of potential catalyst systems (Scheme 1-33). The latter included: combined use of gallium(0) and silver(I); separate use of gallium(0), silver(I), and gallium(III). Considering that gallium(I) was generated *in situ* from gallium(0) and silver(I), a mixture of gallium species may exist in the reaction mixture. Therefore, we had to carry out several control experiments with respect to the employed catalyst system Ga(0)/Ag(I). Allyl boronic ester 71 was prepared according to a literature-known procedure (pin = pinacolato).

**Scheme 1-33** Initial study using various potential catalysts
Boron has been shown to be a highly sensitive nucleus with two naturally occurring NMR-active nuclei, $^{10}\text{B}$ and $^{11}\text{B}$. The natural abundance of the $^{11}\text{B}$ isotope is higher than that of the $^{10}\text{B}$ isotope (80.1% vs. 19.9%). Both nuclei have spins greater than $I=1/2$ and are therefore quadrupolar. $^{11}\text{B}$ has proved to be the more NMR-sensitive nucleus giving narrower signals in NMR analysis, because it has a lower quadrupolar moment, $4.1 \times 10^{-30}$ m$^2$ (vs. $8.5 \times 10^{-30}$ m$^2$ for $^{10}\text{B}$). The reactions were monitored with $^{11}\text{B}$ NMR analysis because boron reagents can be used as an efficient probe to detect the progression of a reaction (through consumption of the boron reagent 71 and formation of the stoichiometric boron by-product 73). Indeed, the chemical shift of the signal of allyl–B(pin) (71) has a resonance at $\delta = 33$ ppm, whereas the signal of MeO–B(pin) (73) displays a signal at $\delta = 22$ ppm.$^{53,65}$ Examples of $^{11}\text{B}$ NMR spectra for the boron reagent (left) and a successful reaction mixture (right) are shown in Figure 1-28.

![Figure 1-28](image.png)

**Figure 1-28** $^{11}\text{B}$ NMR spectra of allyl–B(pin) (71) and MeO–B(pin) (73)

Meanwhile, a variety of side-products may theoretically be observed in this type of low-oxidation state metal catalysis, an overview is displayed in Figure 1-28. $^1\text{H}$ NMR analysis may reveal the true identity of the obtained products. The allylic proton of the desired product, homoallylic ether 72a, shows a signal for the benzylic hydrogen at $\delta = 4.2$ ppm (dd).$^{66}$ Dibenzyl ether (DBE, 25 mol% in mesitylene) was used as an internal standard in order to quantitatively determine both the conversion of 70a and the NMR yield of 72a.
(Scheme 1-33). Potential intermediates and side-products may be identified by carefully comparing the characteristic chemical shift of specific hydrogen atoms in the \(^1\)H NMR analysis.\(^{67}\)

Figure 1-28 Potential side-products for the use of acetal 70a in low-oxidation state metal catalysis

Initial experiments were carried out using 100 mol% of gallium(0) and 20 mol% of silver triflate in toluene at 30 °C (Table 1-1). Indeed, due to the low melting point of gallium metal (29.8 °C), literature-known Barbier-type reactions using gallium(0) as a reagent have been typically conducted at 30–35 °C.\(^{30}\)

Table 1-1 Initial screening of catalysts

<table>
<thead>
<tr>
<th>Entry</th>
<th>Cat (mol%)</th>
<th>NMR yield(^a) (MB(^b)) (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Ga(^0) (100) / AgOTf (20)</td>
<td>38 (49)</td>
</tr>
<tr>
<td>2</td>
<td>– / –</td>
<td>NR(^c) (93)</td>
</tr>
<tr>
<td>3</td>
<td>Ga(^0) (100) / –</td>
<td>NR(^c) (93)</td>
</tr>
<tr>
<td>4</td>
<td>– / AgOTf (20)</td>
<td>NR(^c) (87)</td>
</tr>
</tbody>
</table>
The yield was determined by $^1$H NMR analysis of a reaction aliquot: IS = dibenzyl ether (25 mol%).

Mass balance (MB, %) = percentage of (product + remaining acetal).

NR = no reaction; the desired product was not detected ($^1$H NMR analysis of a reaction aliquot).

Gratifyingly, the combined use of gallium(0) and silver triflate afforded the desired product 72a in 38% NMR yield (Table 1-1, entry 1). Since maximal 20 mol% of Ga(I)OTf should have been formed in theory, this yield indicated that a catalyst turnover might have occurred (TON ~ 2). Unfortunately though, the mass balance (MB) at this stage was not satisfactory (49%). Several pinacol-type coupling products may have been formed, however, the detection of these side-products proved to be challenging in the $^1$H NMR analysis of the reaction aliquot. Importantly, in the absence of a catalyst the reaction did not proceed (entry 2). In the same line, when gallium(0) and silver triflate were used separately, a reaction product was not detectable in either case (entries 3 and 4); both starting materials were fully recovered. The results of these control experiments suggested that an in situ formed low-oxidation gallium species was substantially more effective than each catalyst component itself. Overall, these preliminary data constituted a proof of principle for our conceptual approach, and suggested that a low-oxidation gallium species might be a good catalyst for this C–C bond formation. It is noted that the mixed-valent ‘GaI’ was not used for comparison purposes – the lack of information regarding the accurate composition of this potential catalyst prevented us from employing such an undefined species in catalysis.

1.3.1.2 Optimization of Reaction Parameters

Screening of Silver Co-Catalysts

In order to determine the most suitable counter anion for this gallium-catalyzed transformation, we screened various commercially available silver salts at 10 mol% catalyst loading [Ga(0)/AgX = 1:1] under slightly more concentrated conditions (Table 1-2).
Several important trends were observed (Table 1-2). The use of AgOTf, AgBF₄, and AgNTf₂ afforded 72a in significant yields (31–38%; entries 1, 2, and 5), whereas all other silver salts proved to be ineffective (0–12%; entries 3, 4, 6–11). In case of the AgPF₆ co-catalyst, a side-product (76) was detected (entry 7). This ether may be derived from in situ dimerization of the initial product. Extending the reaction time to 72 h did not substantially increase the yields, and the overall mass balance remained a serious issue at this stage (entries 1–11). Silver triflate is the least expensive silver salt and commercialized with the highest purity (99.995%). Thus, we continued our investigations with this most...
promising co-catalyst.

**Effect of the Ga(0)/Ag(I) Ratio**

In order to examine the importance of the Ga(0)/Ag(I) ratio on the reaction outcome, we carried out a set of experiments at 10 mol% Ga(0) catalyst loading using variable amounts of silver triflate (10–50 mol%; Table 1-3). Product 72a was obtained in 24–33% yields in all cases (entries 1–7). Unfortunately, the observed results were mainly inconclusive as there was no significant effect of the silver loading on the reaction outcome, i.e., the yield and the mass balance.

**Table 1-3 Effect of the Ga(0)/Ag(I) ratio**

<table>
<thead>
<tr>
<th>Entry</th>
<th>AgOTf (X mol%)</th>
<th>Yield[a] (MB[b]) (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>10</td>
<td>30 (68)</td>
</tr>
<tr>
<td>2</td>
<td>15</td>
<td>24 (62)</td>
</tr>
<tr>
<td>3</td>
<td>20</td>
<td>33 (65)</td>
</tr>
<tr>
<td>4</td>
<td>25</td>
<td>24 (37)</td>
</tr>
<tr>
<td>5</td>
<td>30</td>
<td>26 (60)</td>
</tr>
<tr>
<td>6</td>
<td>40</td>
<td>28 (48)</td>
</tr>
<tr>
<td>7</td>
<td>50</td>
<td>31 (43)</td>
</tr>
</tbody>
</table>

[a] The yield was determined by $^1$H NMR analysis of a reaction aliquot: IS = dibenzyl ether (25 mol%).  
[b] Mass balance (MB, %) = percentage of (product + remaining acetal).

**Solvent Screening**

Next, we examined the solvent effect for this transformation at 10 mol% catalyst loading at 30 °C by using various apolar and polar solvents (Table 1-4).
Apolar solvents proved to be more effective than polar solvents (Table 1-4, entries 1–8 vs. entries 9 and 10). Furthermore, two interesting trends were identified. The best yield of 72a was obtained in benzene (28%), but the mass balance for this reaction remained poor (60%; entry 2). While overall there is no outstanding result, reactions in ether-type solvents seemed to proceed slowly, but provided a higher mass balances (e.g. THF: up to 91%; entry 8).

### 1.3.1.3 Ligand Effect on the Catalytic System

Next, we turned our attention to the use of a crown ether ligand in order to stabilize the in situ formed gallium(I) species, and thereby improve the yield and the mass balance for our model reaction. Indeed, Krossing et al. reported both Ga(I) and In(I) species were coordinated and stabilized by a specific crown ether, [18]crown-6 (Scheme 1-23). In turn, a catalytic amount of [18]crown-6 was used in our subsequent studies.
In the first series of experiments, we re-visited the silver salt screening at 10 mol% catalyst loading in toluene, in the presence or absence of [18]crown-6 (Table 1-5).

### Table 1-5 Screening of silver salts – in the presence or absence of [18]crown-6 – in toluene

<table>
<thead>
<tr>
<th>Entry</th>
<th>AgX</th>
<th>[18]crown-6</th>
<th>Yield[a] (MB[b]) (%)</th>
<th>18 h</th>
<th>96 h</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>AgOTf</td>
<td>–</td>
<td>25 (33)</td>
<td>35</td>
<td>35</td>
</tr>
<tr>
<td>2</td>
<td>AgOTf</td>
<td>+</td>
<td>24 (74)</td>
<td>63</td>
<td>63</td>
</tr>
<tr>
<td>3</td>
<td>AgBF₄</td>
<td>+</td>
<td>6 (53)</td>
<td>20</td>
<td>69</td>
</tr>
<tr>
<td>4</td>
<td>AgNTf₂</td>
<td>+</td>
<td>4 (75)</td>
<td>12</td>
<td>50</td>
</tr>
<tr>
<td>5</td>
<td>AgPF₆</td>
<td>+</td>
<td>7[c] (88)</td>
<td>28[d] (100)</td>
<td></td>
</tr>
<tr>
<td>6</td>
<td>AgSbF₆</td>
<td>+</td>
<td>NR[d] (83)</td>
<td>NR[d] (89)</td>
<td></td>
</tr>
<tr>
<td>7</td>
<td>AgI</td>
<td>+</td>
<td>NR[d] (85)</td>
<td>NR[d] (88)</td>
<td></td>
</tr>
<tr>
<td>8</td>
<td></td>
<td>+</td>
<td>1 (91)</td>
<td>90</td>
<td>90</td>
</tr>
</tbody>
</table>

[a] The yield was determined by ¹H NMR analysis of a reaction aliquot: IS = dibenzyl ether (25 mol%).  
[b] Mass balance (MB, %) = percentage of (product + remaining acetal).  
[c] NR = no reaction.  

The beneficial effect of the crown ether was clearly demonstrated using AgOTf as a co-catalyst (Table 1-5, entries 1 and 2). In the absence of [18]crown-6, 72a was formed in maximal 35% yield (mass balance = 35%; entry 1). In contrast, in the presence of [18]crown-6, 72a was obtained in 63% yield corresponding to a turnover number of 6 (mass balance = 63%; entry 2). Most of the other silver co-catalysts proved to be ineffective in the presence of [18]crown-6 affording 72a in low yields (0–20%; entries 3–7). Interestingly however, the use of silver iodide provided substantially better results than all
other silver salts tested, although the reaction was extremely slow. Indeed, only trace amounts of 72a were detected after 18 h, whereas after the yield increased to 90% after 96 h (mass balance = 90%; entry 8). This reaction proceeded also remarkably cleanly, as highlighted with the 1H NMR spectrum of a reaction aliquot, doped with dibenzyl ether (DBE) as the internal standard (Figure 1-30).

A similar trend was observed when the experiments were carried out in diethyl ether as a reaction solvent (Table 1-6). The catalytic reaction in the absence of [18]crown-6 afforded 72a in 42% yield (entry 1), whereas the use of this ligand resulted in 81% yield equaling a turnover number of 8 (mass balance = 81%; entry 2). Other silver co-catalysts proved to be ineffective (entries 3–7). Here again, the slow catalysis using the combination Ga(0)/AgI/[18]crown-6 offered the best compromise between yield (64%) and mass balance (92%; entry 8).
Table 1-6 Screening of silver salts – in the presence or absence of [18]crown-6 – in ether

<table>
<thead>
<tr>
<th>Entry</th>
<th>AgX</th>
<th>[18]crown-6</th>
<th>Yield[a] (MB[b]) (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>18 h</td>
</tr>
<tr>
<td>1</td>
<td>AgOTf</td>
<td>–</td>
<td>23 (47)</td>
</tr>
<tr>
<td>2</td>
<td>AgOTf</td>
<td>+</td>
<td>45 (77)</td>
</tr>
<tr>
<td>3</td>
<td>AgBF₄</td>
<td>+</td>
<td>1 (84)</td>
</tr>
<tr>
<td>4</td>
<td>AgNTf₂</td>
<td>+</td>
<td>10 (76)</td>
</tr>
<tr>
<td>5</td>
<td>AgPF₆</td>
<td>+</td>
<td>6 (78)</td>
</tr>
<tr>
<td>6</td>
<td>AgSbF₆</td>
<td>+</td>
<td>3 (75)</td>
</tr>
<tr>
<td>7</td>
<td>AgF</td>
<td>+</td>
<td>4 (86)</td>
</tr>
<tr>
<td>8</td>
<td>AgI</td>
<td>+</td>
<td>6 (87)</td>
</tr>
</tbody>
</table>

[a] The yield was determined by ¹H NMR analysis of a reaction aliquot: IS = dibenzyl ether (25 mol%).  [b] Mass balance (MB, %) = percentage of (product + remaining acetal).

1.3.2 Towards a Ga(0)/Ag(I) Catalytic System under Ultrasonication

Based on the promising results we obtained, the proof of principle for the catalytic use of gallium(0) was established. At the same time, this chemistry was considered the first ‘gallium(I)’ catalysis. However, the reaction was not efficient enough because the mass balance proved to be substantially below 100%. The Krossing–Slattery method used ultrasonication conditions for the preparation of the perfluorinated gallium(I) salts (cf. Scheme 1-21).⁹a Similarly, ‘GaI’ was obtained through a redox-reaction between gallium metal and iodine under ultrasonication.³⁰ Clearly, ultrasonication may be used to activate the gallium metal surface more efficiently compared to conventional heating and stirring. In turn, it may be an efficient tool to improve the results for this low-oxidation state gallium.
catalysis. To the best of our knowledge, ultrasonication has not been used directly in catalysis, only in the pre-formation of metal catalysts prior to the real catalytic reaction.\textsuperscript{58,69}

1.3.2.1 Initial Experiments

The ultrasonicator bath FB15049 from Fisherbrand was used (power level: 37 kHz). The first set of reactions was carried out in dioxane, diethyl ether, and toluene at 10 mol% catalyst loading regarding Ga(0), Ag(I)OTf, and [18]crown-6 (Table 1-7). Importantly, it was found that the reactions proceeded much faster, i.e., the reaction time could be decreased from 96 h to 8 h while maintaining or slightly increasing the yields of 72a. Since the temperature of the ultrasonicator bath was slightly more difficult to control than a sand bath, the minimum temperature range (40–45 °C) was employed for these experiments. Under these conditions, we did not observe a very pronounced solvent effect on the product yields (76–89%; entries 1–3).\textsuperscript{68}

Table 1-7 Initial experiments under ultrasonication

<table>
<thead>
<tr>
<th>Entry</th>
<th>Solvent ((\epsilon))</th>
<th>NMR Yield\textsuperscript{[a]} (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>dioxane (2.3)</td>
<td>80</td>
</tr>
<tr>
<td>2</td>
<td>PhMe (2.4)</td>
<td>76</td>
</tr>
<tr>
<td>3</td>
<td>Et(_2)O (4.3)</td>
<td>89</td>
</tr>
</tbody>
</table>

\textsuperscript{[a]} The yield was determined by \(^1\)H NMR analysis of a reaction aliquot: IS = dibenzyl ether (25 mol%).

The boiling point of diethyl ether is 34.6 °C, which is lower than the temperature of the ultrasonicator bath. Thus, diethyl ether might not be the most suitable solvent. Instead, as an alternative ether solvent, dioxane was selected as it has a much higher boiling point, 101.1
However, the characteristic hydrogen signal of product 72a (δ = 4.15 ppm) proved to be slightly hidden by the hydrogen signal of dioxane (in the $^1$H NMR spectrum of the corresponding reaction aliquot). Thus, in order to obtain sufficiently baseline-separated signals, the amount of dioxane was decreased; a substrate concentration of 1.0 M in dioxane proved to be the best compromise regarding reactivity and ease of analysis (NMR yields).

In addition, the position of the catalysis reaction vials inside the ultrasonicator proved to be very important. Fully reproducible results were obtained with the vial-holder being in a fixed position on the ultrasonicator – the nine central positions were used exclusively (Figure 1-31). This reaction set-up proved to be convenient for up to 9 experiments in parallel while maintaining the bath temperature in a constant range.

![Figure 1-31 Photo of vial-holder on the top of the ultrasonicator](image)

### 1.3.2.2 Reaction Conditions Re-Visited

**Effect of the Ratio of Catalyst Compounds**

Based on the promising initial results obtained under ultrasonication, the relative ratio of the three catalyst components had to be investigated – the reactions were carried out in dioxane at 40–45 °C for 8 hours (Table 1-8). At 10 mol% catalyst loading for Ga(0) and AgOTf, the amount of [18]crown-6 was varied (10–20 mol%). Unfortunately, the obtained results were inconclusive as there was no significant effect of the crown ether loading on the
product yields (83–85%; entries 1–3). In turn, the use of mol% of [18]crown-6 was fixed for future experiments.

**Table 1-8** Optimization of the [18]crown-6 loading

![Chemical structure](image)

<table>
<thead>
<tr>
<th>Entry</th>
<th>[18]crown-6 (mol%)</th>
<th>NMR Yield (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>10</td>
<td>83</td>
</tr>
<tr>
<td>2</td>
<td>15</td>
<td>85</td>
</tr>
<tr>
<td>3</td>
<td>20</td>
<td>85</td>
</tr>
</tbody>
</table>

[a] The yield was determined by $^1$H NMR analysis of a reaction aliquot: IS = dibenzyl ether (25 mol%).

Next, at 10 mol% catalyst loading for Ga(0) and [18]crown-6, the amount of AgOTf was varied (2.5–20 mol%) under otherwise identical reaction conditions (Table 1-9).

**Table 1-9** Effect of the Ga/Ag ratio

![Chemical structure](image)

<table>
<thead>
<tr>
<th>Entry</th>
<th>AgOTf (mol%)</th>
<th>NMR Yield (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>2.5</td>
<td>89</td>
</tr>
<tr>
<td>2</td>
<td>5.0</td>
<td>95</td>
</tr>
<tr>
<td>3</td>
<td>7.5</td>
<td>94</td>
</tr>
<tr>
<td>4</td>
<td>10</td>
<td>80</td>
</tr>
<tr>
<td>5</td>
<td>15</td>
<td>79</td>
</tr>
<tr>
<td>6</td>
<td>20</td>
<td>62</td>
</tr>
</tbody>
</table>
The yield was determined by $^1$H NMR analysis of a reaction aliquot: IS = dibenzyl ether (25 mol%).

The use of 2.5 mol% of Ag(I) afforded $72\text{a}$ in 89% yield (Table 1-9, entry 1). A slight increase to 5–7.5 mol% led to slightly improved yields (94–95%; entries 2 and 3). However, increasing the amount of Ag(I) further to 10–20 mol% resulted in lower yields of $72\text{a}$ (62–80%; entries 4–6). This phenomenon may be ascribed to an over-oxidation of Ga(I) to less efficient gallium species in higher oxidation states, i.e., Ga(II), Ga(III), or mixed-valent gallium salts. Alternatively, a low-oxidation state gallium cluster may be formed in the presence of an excess of the oxidant; such a cluster may be substantially less reactive that the monomeric gallium(I) species. In turn, a loading of 5 mol% was fixed for the silver triflate co-catalyst, i.e., the optimal Ga(0)/Ag(I) ratio was found to be 2:1.

**Solvent Screening**

Next, we examined the solvent effect for this reaction under ultrasonication conditions in more detail (Table 1-10).

<table>
<thead>
<tr>
<th>Entry</th>
<th>Solvent ($\varepsilon$)</th>
<th>NMR Yield$^\text{[b]}$ (%)</th>
<th>Entry</th>
<th>Solvent ($\varepsilon$)</th>
<th>NMR Yield$^\text{[b]}$ (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>dioxane (2.3)</td>
<td>95</td>
<td>6</td>
<td>THF (7.5)</td>
<td>39</td>
</tr>
<tr>
<td>2</td>
<td>C$_6$D$_6$ (2.3)</td>
<td>48</td>
<td>7</td>
<td>DCM (8.9)</td>
<td>51</td>
</tr>
<tr>
<td>3</td>
<td>PhMe (2.4)</td>
<td>82</td>
<td>8</td>
<td>BTF (9.2)</td>
<td>57</td>
</tr>
<tr>
<td>4</td>
<td>Mes (3.4)</td>
<td>57</td>
<td>9</td>
<td>MeCN (37.5)</td>
<td>4</td>
</tr>
<tr>
<td>5</td>
<td>Et$_2$O (4.3)</td>
<td>73</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

[a] The yield was determined by $^1$H NMR analysis of a reaction aliquot: IS = dibenzyl ether (25 mol%).
Most of the solvents – deuterated benzene, mesitylene (mes), diethyl ether, THF, DCM, benzotrifluoride (BTF) – proved to be moderately effective in terms of product yields (39–73%; entries 2 and 4–8). The use of toluene provided a substantially better result (82%; entry 3), but here again dioxane displayed the highest catalyst acativity (95%; entry 1). Interestingly, the most polar solvent – acetonitrile – proved to be least efficient (4%; entry 9). This poor result may be ascribed to a less effective catalyst pre-formation in acetonitrile. The Ga(I) species may be coordinated by a strong donor ligand, or it may be decomposed through redox-disproportionation to form Ga(II), Ga(III), or other catalytically inactive species. In turn, dioxane was selected as the solvent of choice for future experiments.

**Screening of Silver Co-Catalysts**

In order to determine the most suitable counter anion for this gallium-catalyzed transformation, various commercially available silver salts were screened at 5 mol% loading under otherwise identical conditions (Table 1-11).

**Table 1-11** Screening of silver salts in dioxane under ultrasonication

\[
\text{OMe} \quad \text{OMe} \\
\text{Ph} \quad \text{OMe} \\
\text{Ph} \\
\text{70a} \\
1.1 \text{ equiv} \\
\]

\[
\text{Me} \quad \text{B(pin)} \\
\text{71} \\
\]

\[
\xrightarrow{\text{Ga}^0 \ (10 \text{ mol})} \\
\text{AgX} \ (5 \text{ mol}) \\
\text{[18]crown-6} \ (10 \text{ mol}) \\
\text{dioxane (1.0 M), } 40–45 ^\circ\text{C, 8 h} \\
\]

\[
\text{OMe} \\
\text{Ph} \\
\text{72a} \\
\]
The yield was determined by $^1$H NMR analysis of a reaction aliquot: IS = dibenzyl ether (25 mol%). [b] NR = no reaction.

The use of AgOTf once again proved to be the most effective co-catalyst (99%; entry 1). Most other silver salts displayed poor catalytic activity (0–22%; entries 2–11 and 14–15). Interestingly, silver fluoride and chloride afforded 72a in 60–63% yields (entries 12 and 13). Overall, these data may be explained by the differences in solubility and oxidation potential of these silver species, which may be strongly affected by the corresponding counter anion. Silver triflate was selected as the co-oxidant of choice for further optimizations.

**Ligand Screening**

Next, different types of ligands were screened in order to protect the presumably sensitive low-oxidation gallium catalyst, and thereby potentially improve the product yields under milder conditions (Table 1-12). Examined ligands included a variety of commercially available crown ethers, carbenes, and triphenyl phosphine.
Table 1-12 Effect of the ligand under ultrasonication

<table>
<thead>
<tr>
<th>Ligand</th>
<th>Yield (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>No ligand</td>
<td>53%</td>
</tr>
<tr>
<td>[18]crown-6</td>
<td>95%</td>
</tr>
<tr>
<td>Di-Ph</td>
<td>67%</td>
</tr>
<tr>
<td>NR</td>
<td>17%</td>
</tr>
<tr>
<td>NR</td>
<td>73%</td>
</tr>
<tr>
<td>PPh₃</td>
<td>NR</td>
</tr>
</tbody>
</table>

[a] The yield was determined by ¹H NMR analysis of a reaction aliquot: IS = dibenzyl ether (25 mol%).  
[b] NR = no reaction.

Two important trends were observed. Under the optimized conditions, crown ether ligands proved to be substantially more effective than the ligand-free experiment as well as reactions using carbenes and triphenyl phosphine. Indeed, the use of σ donors such as N-heterocyclic carbenes and PPh₃ did not allow the detection of 72a, which may be ascribed to the poor Lewis acidity of a gallium(I) center when coordinated by such an electron-rich ligand. In the absence of a ligand, product 72a was obtained in 53% yield, significant for an increased Lewis acidity and a decreased stability of the postulated Ga(I) center. The catalytic use of [18]crown-6 provided the best result (95%) – other crown ethers proved to be less efficient (17–73%). In conclusion, [18]crown-6 was found to be the optimal ligand for this Ga(0)/AgOTf catalyst system in dioxane under ultrasonication.
1.3.2.3 Control Experiments

**Proof of Principle Control Reactions**

Next, control experiments were carried out under the optimized conditions in order to confirm that the use of both metal components of the Ga(0)/Ag(I) catalyst system was critical (Table 1-13). Silver metal powder (-35+45 mesh) was used.

**Table 1-13** Control reactions under ultrasonication

<table>
<thead>
<tr>
<th>Entry</th>
<th>Cat</th>
<th>NMR Yield[a] (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Ga&lt;sup&gt;0&lt;/sup&gt; / AgOTf</td>
<td>95</td>
</tr>
<tr>
<td>2</td>
<td>Ga&lt;sup&gt;0&lt;/sup&gt; / –</td>
<td>NR&lt;sup&gt;[b]&lt;/sup&gt;</td>
</tr>
<tr>
<td>3</td>
<td>– / AgOTf</td>
<td>NR&lt;sup&gt;[b]&lt;/sup&gt;</td>
</tr>
<tr>
<td>4</td>
<td>Ag&lt;sup&gt;0&lt;/sup&gt;</td>
<td>NR&lt;sup&gt;[b]&lt;/sup&gt;</td>
</tr>
<tr>
<td>5</td>
<td>Ga(OTf)&lt;sub&gt;3&lt;/sub&gt;</td>
<td>3</td>
</tr>
</tbody>
</table>

[a] The yield was determined by <sup>1</sup>H NMR analysis of a reaction aliquot: IS = dibenzyl ether (25 mol%).  [b] NR = no reaction.

Bearing in mind the benchmark result obtained with the Ga(0)/Ag(I) system (95%; Table 1-13, entry 1), several important conclusions could be obtained from these experiments. When gallium(0) and silver triflate were used separately, the reaction did not proceed at all (entries 2 and 3). The same result was observed for the use of Ag(0), the by-product formed during the redox-reaction between Ga(0) and Ag(I) (entry 4). These experiments confirmed that a metal in its ‘0’ oxidation state does not display a catalytic activity under normal conditions, i.e., such a species is not a Lewis acid or base. In the same line, Ag(I) may not be Lewis acidic enough to trigger the required C–O bond activation of 70a. Significantly, the result using gallium(III) triflate—as a simple Lewis acid in a high-oxidation
state– proved to be poor (3%; entry 5). These results highlighted the fact that both catalyst components, Ga(0) and Ag(I), had to be present for high catalyst activity. Moreover, the low-oxidation state gallium catalyst proved to be substantially more effective than gallium(III), although the latter must be considered much more Lewis acidic. These data indicated that this C–C bond formation was not simply triggered by a strong Lewis acid, but rather by a catalyst with different or additional properties, i.e., a Lewis acid and Lewis base dual character.

**Use of Other Metal Triflates as a Potential Catalyst**

In the same line, we screened various other commercially available metal triflate Lewis acids in order to get more mechanistic insight and to highlight the unique feature of the discovered *in situ* low-oxidation gallium catalyst (Table 1-14).

**Table 1-14 Control reactions using various metal triflates under ultrasonication**

<table>
<thead>
<tr>
<th>Entry</th>
<th>M(OTf)$_x$</th>
<th>NMR Yield$^a$ (%)</th>
<th>Entry</th>
<th>M(OTf)$_x$</th>
<th>NMR Yield$^a$ (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>LiOTf</td>
<td>NR$^b$</td>
<td>11</td>
<td>Bi(OTf)$_3$</td>
<td>8</td>
</tr>
<tr>
<td>2</td>
<td>NaOTf</td>
<td>NR$^b$</td>
<td>12</td>
<td>Sc(OTf)$_3$</td>
<td>NR$^b$</td>
</tr>
<tr>
<td>3</td>
<td>KOTf</td>
<td>NR$^b$</td>
<td>13</td>
<td>Mn(OTf)$_2$</td>
<td>NR$^b$</td>
</tr>
<tr>
<td>4</td>
<td>Mg(OTf)$_2$</td>
<td>NR$^b$</td>
<td>14</td>
<td>Fe(OTf)$_2$</td>
<td>NR$^b$</td>
</tr>
<tr>
<td>5</td>
<td>Ba(OTf)$_2$</td>
<td>NR$^b$</td>
<td>15</td>
<td>Ni(OTf)$_2$</td>
<td>NR$^b$</td>
</tr>
<tr>
<td>6</td>
<td>Ca(OTf)$_2$</td>
<td>NR$^b$</td>
<td>16</td>
<td>Cu(OTf)$_2$</td>
<td>NR$^b$</td>
</tr>
<tr>
<td>7</td>
<td>Al(OTf)$_3$</td>
<td>NR$^b$</td>
<td>17</td>
<td>CuOTf</td>
<td>6</td>
</tr>
<tr>
<td>8</td>
<td>Ga(OTf)$_3$</td>
<td>3</td>
<td>18</td>
<td>AgOTf</td>
<td>NR$^b$</td>
</tr>
<tr>
<td>9</td>
<td>In(OTf)$_3$</td>
<td>7</td>
<td>19</td>
<td>Zn(OTf)$_2$</td>
<td>NR$^b$</td>
</tr>
<tr>
<td>10</td>
<td>Sn(OTf)$_2$</td>
<td>NR$^b$</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
The yield was determined by $^1$H NMR analysis of a reaction aliquot: IS = dibenzyl ether (25 mol%).

Overall, 19 different metal triflates were examined (s-, p-, and d-block metals; Table 1-14). Among these, the vast majority led to the recovery of starting materials with no formation of product 72a being detectable (entries 1–7, 10, 12–16, and 18–19). There were only very few exceptions where traces of 72a were detected: Ga(III), In(III), Bi(III), and Cu(I) [3–8%; entries 8–9, 11, and 17].

**Control Experiments with Conventional Heating and Stirring**

In order to confirm the necessity of ultrasonication, control experiments were carried out with conventional heating and stirring, i.e., using a sand bath and a magnetic stirrer (Table 1-15). The initial reactions in dioxane proved to be much less effective; in turn, toluene was used as an alternative solvent.

**Table 1-15 Control reactions using a sand bath and a magnetic stirrer**

<table>
<thead>
<tr>
<th>Entry</th>
<th>[18]crown-6$^{[a]}$</th>
<th>NMR Yield$^{[b]}$ (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>8 h</td>
<td>24 h</td>
</tr>
<tr>
<td>1</td>
<td>–</td>
<td>23</td>
</tr>
<tr>
<td>2</td>
<td>–</td>
<td>31</td>
</tr>
<tr>
<td>3</td>
<td>+</td>
<td>34</td>
</tr>
<tr>
<td>4</td>
<td>+</td>
<td>34</td>
</tr>
</tbody>
</table>

[a] 10 mol% of Ga(0) and 5 mol% of AgOTf were used to all reactions; [18]crown-6 was only used in the reactions of entries 3 and 4.  [b] The yield was determined by $^1$H NMR analysis of a reaction aliquot: IS = dibenzyl ether (25 mol%).
The results confirmed that this C–C bond formation proceeded sluggishly under non-ultrasonication conditions resulting in 23–34% yields after 8 h (Table 1-15, entries 1-4). It is therefore conceivable that ultrasonication is substantially more efficient to activate the surface of gallium(0), which would affect the amount of the active gallium(I) catalyst formed in situ. Furthermore, it is remarkable that only the use of [18]crown-6 as a ligand could increase the product yields to an acceptable level after a reaction time of 96 h (without ligand: 43–44%; entries 1 and 2 – with ligand: 83–89%; entries 3 and 4). In summary, this C–C bond formation proceeded slowly under conventional conditions, but high yields were obtained when a suitable ligand for gallium(I) was used.

**Is Ultrasonication a Requirement for the Reaction?**

The low-oxidation state gallium catalyst was pre-formed in situ under the typical ultrasonication conditions, prior to the addition of the two reagents and subsequent reaction with conventional heating and stirring (Table 1-16).

**Table 1-16** Results using a pre-formed low-oxidation state gallium catalyst

<table>
<thead>
<tr>
<th>Entry</th>
<th>Time (h)</th>
<th>Reaction Time (h)</th>
<th>NMR Yield(^{(a)}) (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>2</td>
<td>8</td>
<td>51</td>
</tr>
<tr>
<td>2</td>
<td>12</td>
<td>8</td>
<td>86</td>
</tr>
<tr>
<td>3</td>
<td>17</td>
<td></td>
<td>87</td>
</tr>
</tbody>
</table>

[a] The yield was determined by \(^1\)H NMR analysis of a reaction aliquot: IS = dibenzyl ether (25 mol%).
The results confirmed that ultrasonication was very important for the pre-formation of the active catalyst species (Table 1-16). If this pre-formation was conducted for 2 h only, the yield of 72a proved to be moderate after a ‘conventional’ reaction time of 8 h (51%; entry 1). On the other hand, if the catalyst pre-formation was carried out for 12 h, the yield of 72a increased to 86% under otherwise identical conditions (entry 2). Likewise, the same efficiency was observed when conducting the pre-formation for 4 h followed by a ‘conventional’ reaction time of 17 h (87%; entry 3). In turn, ultrasonication proved to be a very important parameter for the activation of the gallium surface, i.e., the generation of a larger quantity of the presumed Ga(I) catalyst was anticipated. However, if a sufficient quantity of the low-oxidation state gallium catalyst was pre-formed, the subsequent C–C bond formation could proceed smoothly under conventional conditions.

**Do Other Allyl Reagents Work for the Catalyst System?**

In order to confirm the necessity of an allyl boronic ester, a Lewis acidic tri-coordinated boron species, control experiments were carried out with four commercially available allyl reagents. These included two tetra-coordinated boron species –potassium allyl trifluoroborate and a MIDA-type allyl boronic ester– as well as allyl tributyl stannane and allyl magnesium bromide. Model substrate 70a was reacted with these allyl reagents in the presence of 10 mol% of gallium(0), 5 mol% of AgOTf, and 10 mol% [18]crown-6 in dioxane at 40–45 °C for 8 h under ultrasonication (Table 1-17).

**Table 1-17 Reactions with commercially available allyl reagents**
NR = no reaction; the desired product was not detected in the corresponding reaction aliquot (\( ^1 \text{H NMR} \) spectroscopy).

As anticipated based on the initial ‘ambiphilic catalysis’ concept, the desired product 72 was not observed. Indeed, we had envisioned that the in situ generated gallium(I) species may act as a potentially ambiphilic catalyst: a Lewis acid is required to activate the C(sp\(^3\)) electrophile 70a –through abstraction of an alkoxy group– and a Lewis base is required to activate the C–B bond of the tri-coordinated allyl boron pro-nucleophile 71. In Table 1-16 however, the boron center of both tetra-coordinated boron reagents is ‘saturated’ and can therefore not react with a Lewis base. In addition, as the solubility of these reagents proved to be poor in dioxane the reactions were re-conducted at 50 °C and/or in toluene; a similar reaction outcome was observed. In turn, tetra-coordinated boron reagents were shown to be substantially less reactive in this transformation, thereby confirming our initial hypothesis. Furthermore, the two other allyl reagents turned out to be entirely unreactive, likely due to the lower Lewis acidity of the corresponding metal center (tin and magnesium).

1.3.2.4 Substrate Scope for the Catalytic Allylation of Acetals and Ketals

With the optimized conditions in hand, we examined acetals and ketals as electrophilic substrates using the allyl or allenyl boronic ester as a pro-nucleophile. A few electrophiles are commercially available, others had to be synthesized according to literature procedures. Overall, 27 examples have been successfully converted to the corresponding homoallylic ethers 72 in 72–94% isolated yields (Table 1-18). Substrates comprised acyclic and cyclic aromatic, heteroaromatic, and aliphatic acetals or ketals. Typically, silver triflate was employed as the co-catalyst, but occasionally silver fluoride proved to be the better choice. It is noted again that in the absence of Ga(0) the C–C bond-forming reactions did not proceed at all. Tolerated functionalities on the electrophilic substrates included trifluoromethyl, ester, fluoro, chloro, bromo, hydroxy, amino, ether, and keto groups. The
C–C bond formations proceeded with exclusive regioselectivity (propargylic and allylic acetals) and chemoselectivity (ketal vs. ketone). Furthermore, interesting heteroaromatic motifs (indole, benzofuran, benzothiophene) proved to be accessible substrates. Finally, primary, secondary, and tertiary acetals were shown to undergo smooth transformations. This broad substrate scope confirmed that the uncovered gallium catalyst displayed excellent structural and functional tolerance among these electrophiles.
Table 1-18 Substrate scope for acetals and ketals

\[
\begin{array}{cccc}
\text{R}^1 & \text{R}^2 & \text{OR} & \text{B(pin)} \\
\text{70} & 1.1-1.5 \text{ equiv} & \text{71} & \text{72} \\
\end{array}
\]

\[
\begin{align*}
\text{Ga}^0 (10 \text{ mol\%}) & \\
\text{AgX} (5 \text{ mol\%}) & \\
[18\text{crown-6} (10 \text{ mol\%}) & \\
\text{dioxane or PhMe (0.25-1.0 M), & }
\text{40-50} \degree \text{C, 8-78 h} & \\
(\text{X = OTf, F}) & \\
\end{align*}
\]

<table>
<thead>
<tr>
<th>Substrate scope for acetals and ketals[a]</th>
<th>Isolated yields of homoallyl ethers 72a-z’ after purification on silica gel (PTLC).</th>
</tr>
</thead>
<tbody>
<tr>
<td>72a: R = H: 91%</td>
<td>72k: 91%</td>
</tr>
<tr>
<td>72b: R = CF3: 92%</td>
<td>72l: 90%</td>
</tr>
<tr>
<td>72c: R = CO2Me: 92%</td>
<td>72m: 91%</td>
</tr>
<tr>
<td>72d: R = F: 89%</td>
<td>72n: 91%</td>
</tr>
<tr>
<td>72e: R = Cl: 92%</td>
<td>72o: 87%</td>
</tr>
<tr>
<td>72f: R = Br: 92%</td>
<td>72p: 88%</td>
</tr>
<tr>
<td>72g: R = Me (AgF): 94%</td>
<td>72q: 90%</td>
</tr>
<tr>
<td>72h: R = CH2OH: 57%</td>
<td>72r: 80% (AgF)</td>
</tr>
<tr>
<td>72i: R = NMe2: 54%</td>
<td></td>
</tr>
<tr>
<td>72j: R = OMe (AgF): 93%</td>
<td></td>
</tr>
<tr>
<td>72k: 91%</td>
<td></td>
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<tr>
<td>72l: 90%</td>
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<tr>
<td>72m: 91%</td>
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<td>72n: 91%</td>
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<tr>
<td>72o: 87%</td>
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</tr>
<tr>
<td>72p: 88%</td>
<td></td>
</tr>
<tr>
<td>72q: 90%</td>
<td></td>
</tr>
<tr>
<td>72r: 80% (AgF)</td>
<td></td>
</tr>
<tr>
<td>72s: 84% (AgF)</td>
<td>72t: 90% (AgF)</td>
</tr>
<tr>
<td>72u: 80% (AgF)</td>
<td>72w: 72% (AgF)</td>
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<tr>
<td>72v: 85%</td>
<td>72x: 84% (AgF)</td>
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<tr>
<td>72y: 80%</td>
<td></td>
</tr>
<tr>
<td>72z: 91%</td>
<td></td>
</tr>
<tr>
<td>72z’: 82% (AgF)</td>
<td></td>
</tr>
</tbody>
</table>

[a] Isolated yields of homoallyl ethers 72a-z’ after purification on silica gel (PTLC).

### 1.3.2.5 Experiment at Low Catalyst Loading

In order to proof the high efficiency of this novel catalyst system, we also carried out an experiment at a very low catalyst loading. Indeed, the combined use of 0.2 mol\% of gallium(0), 0.1 mol\% of silver triflate, and 0.2 mol\% of [18]crown-6 –under otherwise
optimized ultrasonication conditions—resulted in the formation of product 72a in 80% yield (Scheme 1-34). This experiment corresponded to an effective catalyst loading of 0.1 mol% in gallium(I), which was assumed to be the catalytically active species. In turn, it was confirmed that this C–C bond formation proceeded smoothly at very low catalyst loading, and at a gram-scale, leading to a fairly high catalyst turnover number (TON = 800).

![Scheme 1-34 Model reaction with low catalyst loading](image)

1.3.2.6 Catalytic Regiospecific Propargylation of Acetals

We also wanted to demonstrate that pro-nucleophiles other than allyl species could be activated (Scheme 1-35). Indeed, the use of allenyl boronic ester 86 was shown to be very effective when silver fluoride was employed as a co-catalyst. This regiospecific C–C bond formation proceeded smoothly with an aromatic and an aliphatic acetal to afford the corresponding homopropargylic ethers 87a and 87x in 91% and 82% yields, respectively. Most notably, these rare C–C bond formations proceeded with high regioselectivity, 49:1 and >30:1, respectively. Importantly, in the absence of Ga(0) only the starting materials were recovered, i.e., silver fluoride has proved not to be an active catalyst.
Next, we turned our attention to the identity of the assumed low-oxidation state gallium catalyst and the mechanism of these catalytic C–C bond formations.

### 1.3.3 Mechanistic Studies

#### 1.3.3.1 Stoichiometric $^{71}$Ga NMR and $^{11}$B NMR Studies

Although the natural abundance of the $^{71}$Ga isotope is lower than that of the $^{69}$Ga isotope (39.6% vs. 60.1%), the $^{71}$Ga isotope has proved to be the more NMR-sensitive nucleus giving additionally more narrow signals in the NMR analysis.$^{70}$ Both nuclei have a spin $I = \frac{3}{2}$ and are therefore quadrupolar. The quadrupolar moments of $^{69}$Ga and $^{71}$Ga are $17.1 \times 10^{-30}$ m$^2$ and $10.7 \times 10^{-30}$ m$^2$, respectively. An external standard, such as Ga(D$_2$O)$_6^{3+}$ in aqueous solution, has been used.

In the presence of aromatic hydrocarbons, Ga(I) complexes have been found to exist as arene complexes, which have been characterized as $\eta^6$ coordination of the gallium centre to either one, two, or three arene ligands (Figure 1-32, cf. Figure 1-7, 1-18, 1-19, 1-22).$^{88, 89}$ The coordination of Ga(I) species by arene ligands was described by Schmidbaur in the 1980s as donor–acceptor adducts.$^{71a}$ Ga(I) has the electronic configuration 3d$^{10}$4s$^2$ and the filled d shell requires the bonding to an arene ligand. With a filled s orbital, Ga(I) has vacant p
orbitals as acceptor orbitals (LUMO's), which determine the strength and orientation of the arene interaction. The simple explanation is that the six electrons of the aromatic π system fill the three vacant p orbitals of Ga(I).

This theory was firstly confirmed using Ga(III)[Ga(I)X₄] by Schmidbaur (X = Cl, Br). When the arene-free Ga(III)[Ga(I)Cl₄] was melted at 200 °C, two separate resonances were observed in ⁷¹Ga NMR spectroscopy. A sharp high-field resonance at δ = −750 ppm was consistent with a Ga(I) species, whereas a resonance at δ = −60 ppm was ascribed to Ga(III). In the presence of an arene, such as toluene, a down-field shift to δ = −668 ppm was observed with a larger line-width. These NMR results suggested a symmetrical environment of the Ga(I) centre under these molten conditions, and a strong shielding due to decreased paramagnetic effects (presence of the 4s² lone pair of electrons). However, the ⁷¹Ga NMR spectra gave no indication of the simultaneous presence of mono(arene), bis(arene), and tris(arene) complexes of Ga(I) in solution. Normally, only a single Ga(I) signal was detected in mixed arene solvents.

Krossing and Slattery et al. have characterized various monomeric gallium(I) species by ⁷¹Ga NMR analysis. Relative chemical shifts of these and other gallium species in the oxidation states ‘I’ and ‘III’ are listed below (Figure 1-33). It was shown that gallium(I) species displayed signals in the range from δ = −500 ppm to δ = −800 ppm; the chemical shift was demonstrated to be solvent-dependent. Furthermore, the presence of [18]crown-6 as a ligand for coordination to the Ga(I) center resulted in a down-field shift of >100 ppm. If the univalent Ga(I) salt was decomposed to generate the corresponding Ga(III) species, a
new signal was observed at $\delta \sim 200$ ppm. Overall, $^{71}$Ga NMR analysis has proved a straightforward tool to identify the oxidation state of a gallium species.

**$^{71}$Ga NMR**

<table>
<thead>
<tr>
<th>$^{71}$Ga NMR (ppm)</th>
<th>$^{71}$Ga NMR (ppm):</th>
</tr>
</thead>
<tbody>
<tr>
<td>247</td>
<td>–448 (THF)</td>
</tr>
<tr>
<td>190</td>
<td>–520 (PhMe)</td>
</tr>
<tr>
<td>0</td>
<td>–630 (DCM)</td>
</tr>
<tr>
<td>–520</td>
<td>–750 (o-F$_2$C$_6$H$_4$)</td>
</tr>
<tr>
<td>–643</td>
<td>–756 (C$_6$H$_5$F)</td>
</tr>
</tbody>
</table>

**Detection of the Gallium Catalyst Species**

The initial $^{71}$Ga NMR experiments have been set up to detect a novel gallium species potentially formed in C$_6$D$_6$ under ultrasonication at 40–45 °C for 15 h (Scheme 1-36). In the absence of [18]crown-6, the use of Ga(0) and AgOTf in a 2:1 molar ratio resulted in the formation of a grayish suspension, and the appearance of a single signal at $\delta = –688$ ppm in the $^{71}$Ga NMR spectrum. Based on the literature data, this signal has been ascribed to the presence of the newly generated Ga(I)(C$_6$D$_6$)$_n$OTf ($^{89}$a, $n = 1, 2, 3$). When one equivalent of [18]crown-6 was added relative to Ga(I), a clear solution was observed together with a clean down-field shift to $\delta = –567$ ppm in the $^{71}$Ga NMR analysis (Scheme 1-36 and Figure 1-34). Based on the $^{71}$Ga NMR spectrum we obtained, the large line-width suggested coordination of Ga(I) by the arene. This signal has been ascribed to the presence of the new gallium(I) species [18]crown-6–Ga(I)(C$_6$D$_6$)$_n$OTf ($^{89}$b, $n = 1, 2, 3$). On the basis of literature reports, these chemical shifts in the $^{71}$Ga NMR spectrums confirmed the generation

---

Figure 1-33 $^{71}$Ga NMR reference data for various Ga(I) and Ga(III) species
of the novel gallium(I) species 89b, which proved to be stable for several days in the NMR solvent when stored in a sealed Young NMR tube. Unfortunately however, efforts to crystallize these new compounds 89, or to detect these reactive species by HRMS analysis failed to give any positive result.

![Scheme 1-36 Generation and 71Ga NMR analysis of 89a and 89b in C₆D₆](image)

**Figure 1-34** ⁷¹Ga NMR spectrum of [18]crown-6–Ga(I)(C₆D₆)₃OTf (89b)

With these promising initial data obtained through ⁷¹Ga NMR analysis in C₆D₆, we were encouraged to monitor the *in situ* generated gallium(I) catalyst 89b in a different solvent. According to the employed catalysis conditions, the gallium catalyst was pre-formed one-pot in dioxane (1.0 M) under ultrasonication for 36 h (Scheme 1-37). Pleasingly, a single resonance at δ = −565 ppm was detected by ⁷¹Ga NMR analysis in C₆D₆, which was ascribed
again to the generation of $[18]$crown-$6$–Ga(I)(dioxane)$_n$OTf ($89b$, $n = 1, 2, 3$).

\[
\begin{align*}
\text{Ga}^0 & \quad + \quad \text{AgOTf} & \quad + \quad [18]\text{crown-6} & \quad \xrightarrow{\text{dioxane (1.0 M), } 40-45^\circ \text{C, } 36\text{ h}} [18]\text{crown-6–Ga(dioxane)}_{n}\text{OTf} \\
0.5\text{ equiv} & \quad 1.0\text{ equiv} & & 89b
\end{align*}
\]

\[\text{Scheme 1-37 Formation of } [18]\text{crown-6–Ga(I)(dioxane)}_{n}\text{OTf} (89b) \text{ in dioxane}\]

Next, in order to confirm these results, toluene was re-used as a comparison solvent for the preparation of $[18]$crown-$6$–Ga(I)(PhMe)$_n$OTf ($89b$) according to the one-pot procedure (Scheme 1-37). Similarly to the result in dioxane ($\delta = -565$ ppm; Figure 1-35, left spectrum), a single resonance at $\delta = -561$ ppm was detected in toluene (Figure 1-35, right spectrum). Gratifyingly, it was confirmed that the employed catalysis conditions resulted in the clean generation of a gallium(I) salt coordinated by a crown ether ligand.

\[\text{Figure 1-35 } ^{71}\text{Ga NMR spectrums of } [18]\text{crown-6–Ga(I)}\text{OTf} (89b) \text{ in dioxane (left spectrum) and toluene (right spectrum)}\]

By comparison, two solutions of commercially available Ga(OTf)$_3$ were analyzed by $^{71}$Ga NMR spectroscopy in dioxane and toluene, respectively. Due to the poor solubility, a resonance was not observed in dioxane, whereas a singlet resonance at $\delta = -39$ ppm was detected in toluene (suspension). After the addition of two drops of water, a clear
two-phase solution was obtained in both cases. $^{71}$Ga NMR analysis of these samples showed a singlet resonance at $\delta = 0.75$ ppm and 0.30 ppm, respectively. These data may suggest that under our gallium catalysis conditions the in situ redox-reaction between Ga(0) and Ag(I) did not result in the formation of a Ga(III) species; rather, the generation of the novel gallium(I) species $^{89b}$ was confirmed ($\delta = -561 \sim -567$ ppm).

Detection of the Gallium(I) Catalyst in the Model Reaction

After the confirmation of the in situ generation of gallium(I) species $^{89b}$ under the employed catalysis conditions, further experiments were carried out in order to gain insight into the reaction mechanism and to confirm the recovery of the gallium(I) catalyst after the C–C bond formation. For instance, it was important to confirm which reagent, $^{70a}$ or $^{71}$, may be activated first by the gallium(I) catalyst. In turn, three identical catalyst pre-formations were set up in order to generate [18]crown-6–Ga(I)OTf ($^{89b}$) in dioxane (cf. Scheme 1-37). Identical results were confirmed by $^{71}$Ga NMR analysis: a singlet resonance was detected at $\delta = -565$ ppm, consistent with the expected gallium(I) species $^{89b}$ (cf. Figure 1-34, left spectrum). These three catalyst solutions were then reacted in additional experiments with: (i) allyl–B(pin) ($^{71}$); (ii) acetal $^{70a}$; (iii) acetal $^{70a}$ and allyl–B(pin) ($^{71}$) (Scheme 1-38).

![Scheme 1-38 Which reagent may be activated first by the gallium(I) species $^{89b}$?](image)

In the first experiment, allyl–B(pin) ($^{71}$; 1.1 equiv) was added directly to the solution of the
catalyst L–Ga(I)OTf (89b) in a Young NMR tube in order to see whether the Ga(I) catalyst was able to activate the Lewis acidic boronic ester. Indeed, the formation of an allyl boron–ate complex 91 or an allyl–Ga(I) (93) species may be anticipated if the coordinated Ga(I) center is sufficiently Lewis basic. This sample was then analyzed by $^{71}$Ga NMR and $^{11}$B NMR spectroscopy in C₆D₆ (Figure 1-36).

![Figure 1-36 $^{71}$Ga NMR and $^{11}$B NMR spectra of [18]crown-6–Ga(I)OTf (89b) in the presence of allyl boronic ester 71](image)

The $^{11}$B NMR analysis of this sample displayed a single resonance at $\delta = 33$ ppm, indicative of the initially used allyl–B(pin) (71); a new signal did not appear. This result suggested that [18]crown-6–Ga(I)OTf (89b) was not apt to activate the Lewis acidic boronic ester reagent 71. This conclusion was confirmed by the $^{71}$Ga NMR analysis of this sample: the same resonance at $\delta = -566$ ppm, indicative of the initially used gallium(I) species 89b, was detected.

In the second experiment, acetal 70a (1.1 equiv) was added directly to the pre-formed solution of L–Ga(I)OTf (89b) in a Young NMR tube in order to see whether the Ga(I) catalyst was able to activate the Lewis basic acetal. Indeed, the formation of an oxocarbenium ion 80 and L–Ga(I)OMe (90) may be conceivable if the coordinated Ga(I)
center is sufficiently Lewis acidic. This sample was kept at 40 °C for 2 h prior to \(^1\)H NMR, \(^{13}\)C NMR and \(^{71}\)Ga NMR analyses in C\(_6\)D\(_6\) (Scheme 1-39).

In the \(^{71}\)Ga NMR spectrum, the initial signal disappeared without the detection of a new resonance. The newly formed gallium(I) species \([[[18]crown-6\text{–}Ga(I)\text{–}OMe]^-]\) may be simply ‘NMR-silent’, which would be consistent with Krossing’s observation of an ‘NMR-silent’ gallium(I) species, in which the gallium center was coordinated by an NHC (cf. Scheme 1-24).\(^{9c}\) Unfortunately, the detection of the anticipated oxocarbenium ion by \(^1\)H NMR and \(^{13}\)C NMR spectroscopy did not give any conclusive results. However, careful analysis of this sample by HRMS (ESI) resulted in the detection of the corresponding oxocarbenium ion (80) of acetal 70a: calculated for C\(_8\)H\(_9\)O\(^+\): m/z = 121.0679; found: m/z = 121.0671. In this context, it is noted that the same experiment in the absence of Ga(0) under otherwise identical conditions did not lead to the detection of this oxocarbenium ion (80) by HRMS (ESI). These experiments suggested that in the first step of the catalytic cycle the gallium(I) catalyst, [18]crown-8\text{–}Ga(I)OTf (89b), may act as a Lewis acid to activate the C–O bond of acetal 70a, rather than as a Lewis base to activate the C–B bond of boronic ester 71.

In the third experiment, both acetal 70a (1.0 equiv) and allyl–B(pin) (71; 1.1 equiv) were
added to the pre-formed L–Ga(I)OTf solution in a Young NMR tube, which was subsequently kept at 40 °C for 4 h in order to simulate a stoichiometric C–C bond formation (Scheme 1-40).

Scheme 1-40 Detection of the gallium(I) catalyst after completed stoichiometric C–C bond formation?

Next, this sample was analyzed by $^1$H NMR, $^{11}$B NMR and $^{71}$Ga NMR spectroscopy in $C_6D_6$.

As expected, 70a and 71 were fully converted to product 72a, as indicated by the $^1$H NMR analysis. This result was supported by the $^{11}$B NMR analysis, which confirmed the
complete disappearance of the allyl–B(pin) signal (δ = 33 ppm), i.e., 71 was fully consumed. At the same time, the $^{11}$B NMR spectrum revealed a new signal at δ = 22 ppm, indicative of the generation of the stoichiometric by-product of the C–C bond formation, MeO–B(pin) (73). Most significantly, a singlet resonance at δ = -586 ppm was observed in the $^{71}$Ga NMR spectrum, which strongly suggested that the gallium(I) catalyst was regenerated after completed C–C bond formation (Figure 1-37).

**Detection of an Allyl–Gallium(I) Species**

Based on these encouraging results obtained by $^{71}$Ga NMR analysis, we attempted to detect the anticipated catalytically active nucleophile, allyl–Ga(I)–L (93). To date, only allyl–Ga(III) species have been reported by Takai et al. in 2002. Since we used allyl–B(pin) (71) as the pro-nucleophile, $^{11}$B NMR analysis was considered as a very useful tool to monitor a potential boron-to-gallium transmetalation. We basically considered three different boron species to be involved in our borono-Hosomi–Sakurai chemistry (Figure 1-38). Allyl boronic ester 71 was shown to display a signal at δ = 33 ppm in $^{11}$B NMR analysis (left). If a boron-to-gallium transmetalation occurred, the *allyl group would be stripped-off* the boron atom and replaced by a methoxide group (from 70a), thus leading to a signal at δ = 22 ppm [MeO–B(pin) (73); middle]. However, if a methoxide group or another basic entity, i.e., an electron-rich Ga(I) intermediate, was transferred to the Lewis acidic boron atom of 71 without 'loss' of the *allyl group*, a boron–ate complex (91) would be generated, which should provide a signal at δ = 0–10 ppm (right).

![Figure 1-38][1]

Figure 1-38  $^{11}$B NMR data of relevant boron reagents or intermediates in the borono-Hosomi–Sakurai reaction
In this context, a specific set of experiments was carried out (Scheme 1-41). The gallium(I) catalyst, L–Ga(I)OTf (89b), was pre-formed in dioxane as outlined in Scheme 1-37 (Scheme 1-41, first equation). In parallel, allyl boron–ate complex 91a was pre-formed by reacting allyl–B(pin) (71) with a stoichiometric amount of KOMe (92) in dioxane (Scheme 1-41, second equation). After confirmation of the successful generation of L–Ga(I)OTf (89b; $^{71}$Ga NMR analysis: $\delta = -565$ ppm) and allyl boron–ate complex 91a ($^{11}$B NMR analysis: $\delta = 7$ ppm), both reaction mixtures were combined and heated at 40 °C for 2 h (Scheme 1-41, third equation).

**Pre-formation of L–Ga(I)OTf:**

$$
Ga^0 + AgOTf + \text{[18]crown-6} + \text{dioxane (1.0 M)}, 40-45 °C, 32 h \rightarrow L–Ga(I)OTf
$$

$^{71}$Ga NMR (ppm): $-565$

**Pre-formation of ate complex:**

$$
KOMe + \text{dioxane (1.0 M), 40 °C, 18 h} \rightarrow \text{MeO–B(pin)} + \text{MeO–B(pin)}
$$

$^{11}$B NMR (ppm): $33$

**Preparation of allyl–Ga I:**

$$
L–Ga(I)OTf + 91a + \text{MeO–B(pin)} \rightarrow \text{40 °C, 2 h} \rightarrow L–Ga(I)OTf + \text{MeO–B(pin)}
$$

$^{71}$Ga NMR (ppm): $-624$

$^{11}$B NMR (ppm): $22$

**Scheme 1-41** Preparation of allyl–Ga(I)–L (93) from L–Ga(I)OTf (89b) and boron–ate complex 91a

Pleasingly, the $^{11}$B NMR analysis of this reaction mixture revealed a new signal at $\delta = 22$ ppm, indicative of the formation of a tri-coordinate boron–oxygen species, MeO–B(pin) (73).
This result corresponded to an indirect proof for a boron-to-gallium transmetalation because the allyl group must have been stripped-off the boron atom. Most importantly, the $^{71}$Ga NMR analysis of the same reaction mixture revealed that the initial signal of L–Ga(I)OTf ($\delta = -566$ ppm) disappeared and a single new resonance was detected at $\delta = -624$ ppm (Figure 1-39). Based on the literature data and the observed up-field shift, this new signal at $\delta = -624$ ppm was ascribed to an allyl–Ga(I) species (93) where the Ga(I) center may be coordinated by [18]crown-6. Unfortunately, efforts to isolate or analyze this highly reactive species by HRMS or $^1$H NMR and $^{13}$C NMR spectroscopy failed to give conclusive results.

![Figure 1-39 $^{71}$Ga NMR spectrum of allyl–Ga(I)–L (93) in dioxane](image)

### 1.3.3.2 Deuterium Labeling Experiment

In order to further support the boron-to-gallium transmetalation hypothesis, the $\alpha$-deuterated allyl boronic ester \{71–[d$_2$]\} was prepared and used under the optimized catalysis conditions (Scheme 1-42). If the in situ formed [18]crown-6–Ga(I)OTf (89b) species acts exclusively as a Lewis acid catalyst, i.e., no transmetalation occurs, homoallylic ether product 72’a–[d$_2$]...
should be obtained exclusively should be obtained (γ addition). In the event however, the formation of two regioisomers, 72a–[d2] and 72'a–[d2], in a 1:1 molar ratio was observed. In turn, this result supported the hypothesis of a boron-to-gallium transmetalation, which must have occurred prior to C–C bond formation. Since the C–Ga bond is known to be longer than a C–B bond, such a B/Ga exchange would lead to a rapid equilibrium between two the deuterated allyl–Ga(I) isomers, i.e., a scrambling of the deuterium label would occur. As both nucleophilic allyl–Ga(I) species are expected to display similar stability and reactivity, a 1:1 molar ratio of the two regioisomeric products would be a logical result. The obtained 1H NMR and 2H NMR data for the product mixture were shown to be consistent with the literature-reported data.

Scheme 1-42 Deuterium labeling experiment

Next, several additional mechanistic control experiments were carried out.

1.3.3.3 Miscellaneous Experiments

Mercury(0) Poisoning Test

This first test was carried out to distinguish between homogeneous and heterogeneous catalysis. When metallic mercury is used as an additive in metal catalysis, it would impede the reaction in the case of heterogeneous catalysis. In contrast, in the case of homogeneous catalysis, the reaction outcome would not be affected. Under the typical ultrasonication
conditions, the gallium(I) catalyst was pre-formed separately in three reaction vials prior to the addition of substrates 70a and 71 (Table 1-19). One of these reactions was conducted as a blank experiment in the absence of mercury (entry 1), while Hg(0) was used as an additive in the two other experiments (entries 2 and 3). The reactions were stirred at 40 °C for 8 h, and product 72a was obtained in 83–86% yields. Since the use of the Hg(0) additive did not affect the outcome, it was assumed that the gallium(I) catalysis should be homogeneous in nature.

**Table 1-19 Mercury(0) poisoning test**

<table>
<thead>
<tr>
<th>Entry</th>
<th>Hg(0)</th>
<th>NMR yield (%)[a]</th>
</tr>
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<tbody>
<tr>
<td>1</td>
<td>–</td>
<td>86</td>
</tr>
<tr>
<td>2</td>
<td>+</td>
<td>83</td>
</tr>
<tr>
<td>3</td>
<td>+</td>
<td>84</td>
</tr>
</tbody>
</table>

[a] The yield was determined by $^1$H NMR analysis of a reaction aliquot: IS = dibenzyl ether (25 mol%).

*‘Hot’ Filtration Test*³

This second test was conducted again to distinguish between homogeneous and heterogeneous catalysis. When a hot metal catalyst mixture is filtered and the obtained solution is used in catalysis, it would impede the reaction in the case of heterogeneous catalysis. In contrast, in the case of homogeneous catalysis, the reaction outcome would not be affected. Under the typical ultrasonication conditions at 40–45 °C, the gallium(I) catalyst was pre-formed separately in three reaction vials prior to the addition of substrates
70a and 71 (Table 1-20). One of these reactions was conducted as a blank experiment without filtration of the ‘hot’ pre-formed catalyst mixture (entry 1), while the pre-formed catalyst mixture was filtered ‘hot’ in the two other experiments (entries 2 and 3). The reactions were stirred at 40 °C for 8 h, and product 72a was obtained in 80–90% yields. The fact that this ‘hot’ filtration did not have any effect, supported the assumption that the gallium(I) catalysis should be homogeneous in nature.

Table 1-20 ‘Hot’ filtration test

<table>
<thead>
<tr>
<th>Entry</th>
<th>Hot Filtration</th>
<th>NMR yield (%)&lt;sup&gt;[a]&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>–</td>
<td>86</td>
</tr>
<tr>
<td>2</td>
<td>+</td>
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</tr>
<tr>
<td>3</td>
<td>+</td>
<td>80</td>
</tr>
</tbody>
</table>

[a] The yield was determined by <sup>1</sup>H NMR analysis of a reaction aliquot: IS = dibenzyl ether (25 mol%).

**Radical Trapping Experiments**

This third test was conducted in order to determine whether a radical reaction pathway was viable or not. When a suitable radical trapping agent is used as an additive in a reaction, it would impede the reaction in case radical intermediates are of importance. In contrast, if a reaction does not proceed through a radical pathway, the reaction outcome would not be affected. Under the typical ultrasonication conditions, the gallium(I) catalyst was pre-formed separately in three reaction vials prior to the addition of the corresponding radical trapping agent and substrates 70a and 71 (Table 1-21). Three different radical
traps were employed: TEMPO®, 2,2-diphenyl-1-picrylhydrazyl, and 3-carbamoyl-PROXYL. The corresponding reactions were stirred at 40 °C for 8 h, and product 72a was not obtained, or only in trace amounts. These results may suggest that radical intermediates are of importance in this novel gallium(I) catalysis. However, it is difficult to exclude the potentially impeding effect of the specific functional groups in the used radical traps (amide, nitro, …). Further experimentation, potentially with other radical traps, will be required for a firm conclusion.

**Table 1-21 Radical trapping experiments[^a^][^b^]**

<table>
<thead>
<tr>
<th>Radical trap</th>
<th>Yield</th>
<th>Remarks</th>
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<tbody>
<tr>
<td>TEMPO®</td>
<td>6% NMR y</td>
<td>NR</td>
</tr>
<tr>
<td>2,2-diphenyl-1-picrylhydrazyl</td>
<td>NR</td>
<td>NR</td>
</tr>
<tr>
<td>3-carbamoyl-PROXYL</td>
<td>NR</td>
<td>NR</td>
</tr>
</tbody>
</table>

[^a^]: The yield was determined by 1H NMR analysis of a reaction aliquot: IS = dibenzyl ether (25 mol%).
[^b^]: NR = no reaction.

### 1.3.3.4 Proposed Catalytic Cycle for Gallium(I) Catalysis

Based on the results obtained in our preliminary mechanistic study, a transmetalative S_N1-type mechanism is proposed (Figure 1-40). First, L–Ga(I)X – and Ag(0) – will be formed in situ through a redox-reaction between Ga(0) and Ag(I)X in the presence of [18]crown-6 as a ligand. The L–Ga(I)X species was confirmed by ^71^Ga NMR analysis. It may act as a Lewis acid catalyst to activate the C–O bond of the electrophile (acetal or ketal),
in order to generate a more reactive electrophile (oxocarbenium ion) and L–Ga(I)–OMe (90). The formation of an oxocarbenium ion was confirmed by HRMS (ESI) analysis. This new gallium(I) species may act as a Lewis base to trigger transmetalation of pro-nucleophile 71 [allyl–B(pin)] in order to form a more reactive nucleophile, allyl–Ga(I)–L (93), and MeO–B(pin) (73) as the stoichiometric by-product. The formation of allyl–Ga(I)–L (93) was confirmed by $^{71}$Ga NMR analysis. The C–C bond formation may then occur between the nucleophilic allyl–Ga(I)–L and the electrophilic oxocarbenium ion, with concomitant regeneration of the catalyst, L–Ga(I)X, which was confirmed by $^{71}$Ga NMR analysis.

Figure 1-40 Proposed catalytic cycle for the novel gallium(I) catalysis
1.4 Summary

In this first project we developed the first catalytic use of gallium(0) in organic synthesis through a novel in situ gallium(I) catalysis. This approach was applied to catalytic C–C bond formations using allyl and allenyl boron pro-nucleophiles together with C(sp³) electrophiles of type 71, such as acetals and ketals (borono-Hosomi–Sakurai reaction; Scheme 1-43). Key features of the in situ catalyst formation are the effective oxidation of gallium metal with a commercially available silver salt in the presence of a suitable ligand, [18]crown-6, under ultrasonication. Control experiments using separately Ga(0), Ag(I), and Ag(0) failed to catalyze this C–C bond formation. In the same line, Ga(III) and other metal triflates proved to be ineffective. This Ga(I) catalysis displayed a broad substrate scope, an excellent functional group tolerance, complete regio- and chemoselectivities, and a very high regioselectivity. A catalyst TON as high as 800 was achieved in a gram-scale experiment.

![Scheme 1-43 Novel gallium(I) catalysis](image)

Importantly, we were able to detect three novel catalytically active species by ⁷¹Ga NMR analysis: Ga(I)OTf (89a), [18]crown-6–Ga(I)OTf (89b; Scheme 1-44), and allyl–Ga(I)–L (93). It is noted that the catalyst regeneration after completed C–C bond formation was confirmed by ⁷¹Ga NMR analysis. It was shown that [18]crown-6–Ga(I)OTf (89b) was able to activate the acetal [HRMS (ESI)] rather than the boron reagent (¹¹B NMR). Our transmetalation hypothesis was supported by ¹¹B NMR, ¹H NMR, and ²H NMR spectroscopy. Based on these data, a transmetalative S_N1-type mechanism was proposed for the catalytic cycle.
Scheme 1: Detection of [18]-crown-6–Ga(III)OTf (89b) in dioxane solution

Ga⁰ + AgOTf + [18]crown-6
0.5 equiv 1.0 equiv

Dioxane (1.0 M), 40–45 °C, 36 h

[18]-crown-6–Ga(III)OTf

⁷¹Ga NMR (ppm): –565

Scheme 1-44 Detection of [18]crown-6–Ga(III)OTf (89b) in dioxane
During the Course of our Studies – Report on Gallium-Initiated Polymerization

During the course of our studies, Krossing et al. reported the use of univalent gallium salts bearing weakly coordinating counter anions as initiator or catalyst for the industrially relevant polymerization of isobutylene (Scheme 1-45). More recently, the same group applied more complex gallium(I) species to this type of polymerization.

![Scheme 1-45 Gallium(I)-initiated polymerization of isobutylene](image-url)
CHAPTER 2: TOWARDS ASYMMETRIC GALLIUM (I)

CATALYSIS

2.1 Introduction: Hosomi–Sakurai Allylations Using C(sp\textsuperscript{3}) Electrophiles

The Hosomi–Sakurai reaction is a fundamentally important, acid-mediated C–C bond formation developed by Hosomi and Sakurai.\textsuperscript{74} Generally, carbon-based electrophiles – such as aldehydes, ketones, imines, O,O-acetals, N,O-aminals, ethers, and alcohols – have been used in combination with silicon-based nucleophiles.

The first catalytic example using C(sp\textsuperscript{3}) electrophiles was reported by Hosomi and Sakurai in 1976, when titanium(IV) chloride was used as a strong, oxophilic Lewis acid (Scheme 2-1).\textsuperscript{74} A highly electrophilic oxocarbenium ion was proposed as a key intermediate, which could undergo direct C–C bond formation with allyl trimethylsilane (94). The corresponding homoallylic alcohols were obtained in 44–96% yields.

![Scheme 2-1 Hosomi–Sakurai reaction using carbonyl electrophiles catalyzed by TiCl\textsubscript{4}].

In 1978, the first example of a Hosomi–Sakurai reaction with C(sp\textsuperscript{3}) electrophiles was reported by the same group (Scheme 2-2).\textsuperscript{75} The use of a stoichiometric amount of a Lewis acid proved to be effective for the regioselective allylation of allylic acetals. Here again, an oxocarbenium ion was postulated as a key intermediate, which could be trapped by allyl trimethylsilane. The corresponding homoallylic ethers were obtained in 21–100% yields.
The mechanism for these Hosomi–Sakurai reactions follows a similar principle (Scheme 2-3). A Lewis basic oxygen atom of the electrophile may be coordinated by a strong Lewis acid, which may result in the formation of an electrophilic oxocarbenium ion intermediate. An allyl silane, which typically does not require pre-activation, is considered sufficiently nucleophilic to add to the oxocarbenium ion. The key point in this context was shown to be the β-silicon effect displayed by silicon: the secondary carbocation, formed through C–C bond formation, may be stabilized by hyperconjugation \([\sigma(SiC) \rightarrow p_z(C^+)]\). Indeed, the C–Si σ bond may transfer electron density into the vacant p orbital of the β cation.\(^{76}\)

Catalytic intermolecular C(sp\(^3\))–C(sp\(^3\)) bond formation through Lewis acid activation was shown to be more challenging than C(sp\(^2\))–C(sp\(^3\)) bond formation. To date, only a limited number of catalysts have been investigated for the allylation of non-carbonyl electrophiles, including transition metal, main group element, and Brønsted acid catalysts.
2.1.1 Use of an Allyl Silane

2.1.1.1 Transition Metal Catalysis

In 2001, Yadav et al. reported scandium triflate, Sc(OTf)$_3$, to be an efficient catalyst for the allylation of acetals using allyl trimethyl silane (94; Scheme 2-4). The corresponding products were obtained from aromatic, heteroaromatic, and aliphatic acetals or gem-diacetates in 68–90% yields. The oxophilic transition metal catalyst was recovered after the reaction by aqueous extraction.

\[
\begin{align*}
\text{OR'} & \quad + \quad \text{SiMe}_3 & \text{Sc(OTf)}_3 (5 \text{ mol%}) & \quad \text{DCM (0.2 M), 25}^{\circ}\text{C, 5–8 h} & \quad \text{OR'} \\
R & = \text{Ar, HetAr, alkyl} & 94 & 1.2 \text{ equiv} & 14 \text{ examples} \\
R' & = \text{Me, Ac} & & & 68–90\% \text{ y}
\end{align*}
\]

Scheme 2-4 Sc(OTf)$_3$-catalyzed allylation of acetals and gem-diacetates

Many acetals are not commercially available, and have to be synthesized from the corresponding aldehydes. Therefore, the direct use of aldehydes to generate the corresponding acetals in situ would be a convenient approach. In 2003, Oriyama et al. reported that homoallylic ethers were obtained directly from the corresponding aldehydes through iron(III) catalysis (Scheme 2-5). Benzzyloxytrimethyl silane, BnOTMS (95), was used for the in situ formation of acetals, and the corresponding allylation products were obtained in 81–100% yields. A number of advantages of this system were highlighted: one-pot synthesis, mild conditions, non-toxic and cheap iron catalysis. In 2007, Mohan et al. used (TsO)$_3$Fe•6H$_2$O for the same strategy.

\[
\begin{align*}
\text{RCHO} & \quad + \quad \text{BnOSiMe}_3 & \text{FeCl}_3 (2–5 \text{ mol%}) & \quad \text{neat, 0}^{\circ}\text{C, 2 h} & \quad \text{OBn} \\
\text{R} & = \text{Ar, alkyl} & 95 & 1.2 \text{ equiv} & 6 \text{ examples,} \\
\text{OBn} & \quad & & & 81–100\% \text{ y}
\end{align*}
\]

Scheme 2-5 FeCl$_3$-catalyzed one-pot synthesis of homoallylic ethers
In 2014, less electrophilic ethers have been used as substrates in the iron(III)-catalyzed alkyl–allyl cross-coupling by Fan et al. (Scheme 2-6).\(^{80}\) The desired products were obtained at room temperature in 62–99% yields. The iron catalyst showed a very high ability to activate secondary benzylic C–O bonds (R ≠ H), whereas primary benzylic ethers (R = H) failed to react. The reaction was facilitated when electron-rich benzyl methyl ethers were employed, while a slower reaction was observed in the case of electron-withdrawing groups. Interestingly, reactions with other metal salts, such as FeCl\(_2\), Fe(acac)_3, CuI, Cu(acac)_2, Cu(OAc)_2 and ZnCl\(_2\) failed to give the desired products.

![Scheme 2-6](image)

**Scheme 2-6** FeCl\(_3\)-catalyzed allylation of benzylic ethers\(^{80}\)

### 2.1.1.2 Main Group Catalysis

Although main group element catalysis has been used for the Hosomi–Sakurai reaction decades ago, limited examples for the use of C(sp\(^3\)) electrophiles have been reported. In 1978, Hosomi and Sakurai reported the first main group element-mediated reactions using a stoichiometric amount of AlCl\(_3\) or F\(_3\)B•OEt\(_2\) (cf. Scheme 2-2).\(^{75}\) More recently, Woerpel et al. applied this chemistry to a F\(_3\)B•OEt\(_2\)-promoted allylation of mannose and other pyranoses (Scheme 2-7).\(^{81}\) The use of a stoichiometric amount of this Lewis acid resulted in highly diastereoselective C-glycosylation.
In 1980, the first catalytic use of a main group species, TMSOTf, for the allylation of acetals and ketals was reported by Noyori et al. (Scheme 2-8). The homoallylic ether products were obtained under mild conditions in 79–98% yields. In this context, the reaction using 4-t-butylcyclohexanone dimethyl acetal resulted in the predominant formation of the more stable ‘equatorial’ diastereomer 99 (equatorial:axial = 93:7).

One year later, TMSI was developed as a Lewis acid catalyst for this type of reaction by Hosomi and Sakurai, and the homoallylic ethers were obtained in high yields. It is noted that both TMSOTf and TMSI failed to catalyze the equivalent transformations with carbonyl compounds, such as aldehydes and ketones.

Bismuth salts are generally considered to have low-toxicity and to be inexpensive. In 2002,
Mohan et al. reported the Bi(OTf)$_3$-catalyzed allylation of acetals using an allyl silane (94; Scheme 2-9).$^{84}$ The desired products were obtained in 69–94% yields.

\[
\begin{array}{c}
\text{OMe} \\
R \quad \text{OMe}
\end{array}
\text{+} \quad \begin{array}{c}
\text{SiMe}_3
\end{array}
\xrightarrow{\text{Bi(OTf)$_3$ (1 mol%), DCM (0.5 M), 25 °C, 0.25–20 h}}
\begin{array}{c}
\text{OMe} \\
R \quad \text{O}
\end{array}
\]

R = Ar, alkyl

94 1.3 equiv

9 examples

69–94% y

Scheme 2-9 Bismuth triflate-catalyzed allylation of acetals$^{84}$

Bismuth halides had been investigated as efficient catalysts as well by Komatsu and Suzuki et al. in 1997.$^{85}$ In addition, the BiBr$_3$-catalyzed allylation of carbohydrates was studied (Scheme 2-10). The reaction with benzyl-protected 1-O-methoxy α-D-glucose (100) and allyl silane (94) afforded the allylated product 101 in 63% yield with good diastereoselection ($\alpha\beta = 89:11$).

\[
\begin{array}{c}
\text{BnO} \\
\text{BnO} \\
\text{BnO} \\
\text{OMe}
\end{array}
\text{+} \quad \begin{array}{c}
\text{SiMe}_3
\end{array}
\xrightarrow{\text{BiBr$_3$ (50 mol%), MeCN, 25 °C, 6 h}}
\begin{array}{c}
\text{BnO} \\
\text{BnO} \\
\text{BnO} \\
\text{O}
\end{array}
\]

100

94

101

63% y ($\alpha\beta = 89:11$)

Scheme 2-10 BiBr$_3$-catalyzed allylation of a carbohydrate$^{85}$

### 2.1.1.3 Brønsted Acid Catalysis

To date, only two Brønsted acid catalysts have been investigated in the allylation of C(sp$^3$) electrophiles. In 2006, dinitrobenzene sulfonic acid (DNBA, 102) was used as an efficient catalyst for the Hosomi–Sakurai reaction by List et al. (Scheme 2-11).$^{86}$ This inexpensive and non-toxic Brønsted acid 102 catalyst showed a very high functional group tolerance. The reactions proceeded smoothly with aromatic, unbranched or branched aliphatic acetals, and ketals bearing electron-rich or electron-poor substituents. The corresponding
homoallylic ethers were obtained in 53–99% yields.

Scheme 2-11 Dinitrobenzenesulfonic acid-catalyzed allylation of acetals

In 2008, the first Brønsted acid-catalyzed three-component Hosomi–Sakurai reaction was reported by the same group (Scheme 2-12). Conceptually speaking, this work was similar to Oriyama’s iron catalysis as commercially available aldehydes were used in a one-pot procedure (cf. Scheme 2-5). This transformation proceeded smoothly without applying strictly anhydrous conditions. The catalyst proved to be effective for aromatic aldehydes with electron-donating or electron-withdrawing substituents, as well as for heteroaromatic and aliphatic aldehydes. However, ketones failed to react under these mild conditions.

Scheme 2-12 DNBA-catalyzed three-component Hosomi–Sakurai reaction

To date, limited examples of the Hosomi–Sakurai reaction between C(sp³) electrophiles and an allyl silane have been developed. The generally accepted mechanism is the addition of the nucleophilic allyl silane to an in situ generated electrophilic oxocarbenium ion (Scheme 2-13, left side). In the same context, the use of intrinsically less nucleophilic allyl boron reagents has been explored recently (Scheme 2-13, right side).

Scheme 2-13 Proposed transition states in the Hosomi–Sakurai allylation: Si vs. B
2.1.2 Use of Boron-Based Allyl Pro-Nucleophiles

2.1.2.1 Indium(I) Catalysis Using a Boronic Ester

In 2010, Kobayashi et al. reported the use of allyl boronic ester (71) as a pro-nucleophile in C–C bond formation with C(sp³) electrophiles (Scheme 2-14).\textsuperscript{62} Indium(I) triflate, In(I)OTf, was used as a dual catalyst, and resulted in the formation of the corresponding homoallylic ethers in 57–95% yields. The reactions proceeded smoothly with acyclic or cyclic aromatic, heteroaromatic, and aliphatic acetals, or ketals. It is noted that other metal triflates, including Ga(OTf)\textsubscript{3}, In(OTf)\textsubscript{3}, Sc(OTf)\textsubscript{3}, Cu(OTf)\textsubscript{2}, AgOTf, and Zn(OTf)\textsubscript{2} failed to catalyze this transformation.

\[
\begin{array}{ccc}
\text{OMe} & + & \text{R}^1\text{B} (\text{pin}) \\
\text{R}^2\text{OMe} & & \text{In}^I\text{OTf} (1–10 \text{ mol%}) \\
\text{PhMe} (1.0 \text{ M}), 25–30 ^\circ \text{C}, 14–40 \text{ h} & & \text{OMe} \\
\text{R} & & \text{R}^1\text{OMe} \\
1.1 \text{ equiv} & & 21 \text{ examples} \\
\text{R} = \text{Ar, hetAr, alkyl} & & 57–95\% \text{ y}
\end{array}
\]

\textbf{Scheme 2-14} In(I)OTf-catalyzed allylation of acetals and ketals\textsuperscript{62}

The mechanism was examined by using \(\alpha\)-substituted allyl reagents, and a transmetalative \(S_N1\) pathway was proposed (Scheme 2-15). Indeed, In(I)OTf as a Lewis acid was proposed to activate the acetal or ketal to form a very electrophilic oxocarbenium ion. In contrast to silanes, an allyl boronic ester has to be activated with a Lewis base in order to enfold its nucleophilicity. Here, a nucleophilic allyl–In(I) species was postulated as an intermediate. In turn, the classic \(\gamma\) product was obtained using an \(\alpha\)-methyl allyl silane, while an unusual \(\alpha\)-selectivity was obtained with an \(\alpha\)-methyl allyl boronic ester (boron-to-indium transmetalation).
In addition, the use of an allenyl boronic ester (86) as a pro-nucleophile was investigated, resulting in the highly regioselective formation of the homopropargyl ether product (ratio = 99:1, Scheme 2-16). The reactivity and selectivity observed in this transformation supported the boron-to-indium transmetalation hypothesis. It is believed that the more stable allenyl metal species 106 reacted as the real nucleophile with \( \gamma \)-selectivity.  

One year later, the same group developed an indium(I)/boron(III) co-catalyst system for the more challenging alkyl–allyl cross-coupling (Scheme 2-17). The highly Lewis acidic \( B\text{-methoxy-9-BBN (107) was used as a co-catalyst, and the corresponding products were obtained in 40–93\% yields. This In/B catalyst system was shown to have a very high ability to activate secondary ethers, whereas the primary ether failed to react. It is noted
that the sole use of In(I)OTf resulted in the formation of the desired products in low yields. Interestingly, its combination with commercially available metal salts, such as AlCl₃, Al(OTf)₃, and GaCl₃, failed to give the desired products.

![Scheme 2-17](image_url)

**Scheme 2-17** Catalytic allylation of ethers using an In/B dual catalyst system

It is believed that the activation of the ethereal C–O bond by In(I)OTf led to the *in situ* formation of an oxocarbenium ion and In(I)OMe, which may react with the highly Lewis acidic *B*-methoxy–9-BBN to afford boron–ate complex 108 (Scheme 2-18). The latter may act as an effective methoxide source to deliver a Lewis base (OMe) for the activation of allyl boronic ester (71). The reactivity observed in this transformation supported the B-to-In transmetalation hypothesis.

![Scheme 2-18](image_url)

**Scheme 2-18** Postulated boron-to-indium transmetalation

### 2.1.2.2 Indium(I) Catalysis Using a Borane

Next, Kobayashi *et al.* used the highly reactive allyl borane 110 as a pro-nucleophile in the same type of reaction (Scheme 2-19). Here, the use of In(I)OTf as a single catalyst resulted in the formation of the cross-coupling products in 25–95% yields. No reaction was observed in the absence of the catalyst. The substrate scope proved to be broad with
various primary, secondary and tertiary benzylic, allylic and propargylic ethers as viable substrates. However, non-benzylic ethers failed to react under these conditions.

Scheme 2-19 In(I)OTf-catalyzed alkyl–allyl cross-coupling

Other common allyl reagents failed to react in this challenging transformation (Scheme 2-20). These results demonstrated that an allyl borane 110—as a substantially more Lewis acidic reagent compared to allyl boronic ester (71)—also displayed a much higher nucleophilicity provided that the C–B bond was activated with a Lewis base.

Scheme 2-20 Alkyl–allyl cross-coupling: allyl borane vs. other allyl reagents

This reaction system was applied to the use of various carbohydrate substrates (Scheme 2-21). For instance, the In(I)-catalyzed reaction between benzyl-protected β-1-O-methoxy D-ribofuranose (118) and allyl borane (110) resulted in the formation of the corresponding product 119 in 75% yield with high diastereoselection (α:β = >94:6).
In conclusion, various types of catalysts have been investigated for the typical Hosomi–Sakurai allylation of C(sp³) electrophiles using allyl trimethyl silane. Recently, boron-based pro-nucleophiles were successfully employed in this chemistry using an indium(I) or an indium(I)/boron(III) dual catalyst system. However, this challenging and important area of organic synthesis remained to be under-explored, particularly in the context of asymmetric catalysis.

2.1.3 Developments in Asymmetric Catalysis

In 2004, a single report on highly asymmetric C–C bond formation between C(sp³) electrophiles and an allyl silane (94) was published by Braun and co-workers. In this seminal study, only six electrophiles proved to be activated by an enantiomerically enriched titanium(IV) Lewis acid catalyst (123). The use of an alcohol (120) and a silyl ether (121) as an electrophile resulted in the formation of the corresponding products 122 in 94% and 96% yields with 81% and 99% ee, respectively (Scheme 2-22).
In addition, this enantiomerically enriched titanium complex (123) was shown to catalyze the asymmetric allylation of two ethers, a cyclic $N,O$-aminal, and a cyclic $O,O$-acetal to afford the corresponding products in 62–96% yields with 54–93% ee (Scheme 2-23). However, a super-stoichiometric amount of the chiral catalyst (123) was required for the enantioselective allylation of cyclic $O,O$-acetal 128 (79% ee). Alternatively, the use of 10 mol% of the chiral catalyst (123) –combined with 90 mol% of titanium tetrafluoride (TiF$_4$)– proved to be an effective, although the observed asymmetric induction dropped significantly (54% ee). To the best of our knowledge, this is the best asymmetric catalysis result obtained for the allylation of a cyclic $O,O$-acetal.

The reaction mechanism was proposed to involve a dynamic kinetic resolution (DKR). Initial C–O bond activation of the racemic cyclic $O,O$-acetal 128 may lead to two enantiomeric oxocarbenium ion pairs (129) (Figure 2-1). These two ion pairs were proposed to be in equilibrium via the planar intermediate, and the $R$ enantiomer was believed to react faster than the $S$ enantiomer. The allyl silane was suggested to attack the oxocarbenium ion from the opposite face relative to the chiral titanium species.
Figure 2-1 Dynamic kinetic resolution: asymmetric allylation of a racemic cyclic O,O-acetal

Brønsted acid catalysis has been studied for this asymmetric allylation as well. In 2008, List et al. reported the first Brønsted acid-catalyzed three-component allylation (Scheme 2-24). The use of an enantiomerically enriched binaphthalenyl disulfonic acid (131) afforded the homoallylic benzyl ether product 130 in 80% yield with <5% ee (Scheme 2-24). To date, this unsatisfactory result has proved to be the only example of attempted asymmetric Brønsted acid catalysis for intermolecular C–C bond formation using a C(sp^3) electrophile.

Scheme 2-24 Attempted sulfonic acid-catalyzed asymmetric Hosomi–Sakurai allylation

Alternative pro-nucleophiles, such as allyl and allenyl boronic esters, were used in a similar context. The first highly enantioselective C(sp^3)–C(sp^3) bond formation using racemic
An enantiomerically enriched indium(I) catalyst was generated in situ from the corresponding silver BINOL-phosphate, (R)-132–Ag, and indium(I) chloride (anion metathesis). The use of this novel catalyst system resulted in the formation of the expected homoallylic amides in 88–99% yields with 72–96% ee. Interestingly, the obtained asymmetric induction with allyl boronic ester (71) was substantially higher compared to Braun’s study using allyl trimethyl silane (94) (56% ee).91

![Scheme 2-25 Indium(I)-catalyzed asymmetric allylation of N,O-aminals](image)

Importantly, the combined use of indium(I) chloride and (R)-132–Ag was demonstrated to be critical for both reactivity and asymmetric induction (96% yield, 95% ee; Table 2-1). Control experiments were carried out using the following catalyst systems: indium(I) chloride; (R)-132–Ag; (R)-132–H; combined use of indium(I) chloride and (R)-132–H. The results revealed a very low catalytic activity when indium(I) chloride, (R)-132–Ag, and the Brønsted acid (R)-132–H were employed separately (up to 5% yield; up to 14% ee). On the other hand, the combined use of indium(I) chloride and the Brønsted acid (R)-132–H in high activity, but poor asymmetric induction (88% yield, 25% ee). This result highlighted the importance of asymmetric Lewis acid catalysis vs. asymmetric Brønsted acid catalysis, the latter of which was reported for a similar iminium ion intermediate by Terada and co-workers.94
The reaction mechanism of this asymmetric indium(I) catalysis was investigated using an optically enriched aminal \((R)-133\) \((R; \text{er} = >99.9:0.1)\), allyl–B(pin), and a racemic indium catalyst \textit{in situ} generated from indium(I) chloride and a racemic silver phosphate 135 (Table 2-2). The experiment was monitored over time by determining the yields and optical purity of both the allylation product 134 and the remaining aminal 133 (\(^1\)H NMR and chiral HPLC analyses). Although the starting aminal and the recovered material were optically enriched at early stages (15–300 min), the corresponding product 134 was found to be racemic at all times. These results strongly suggested an S_N1-type mechanism, i.e., the \textit{in situ} formation of an iminium ion intermediate bearing a chiral counter anion, which would be trapped by a reactive allyl nucleophile.
Table 2-2 Use of an enantiomerically enriched N,O-aminal

<table>
<thead>
<tr>
<th>t (min)</th>
<th>Product</th>
<th>Starting Aminal</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>YIELD[a] (%)</td>
<td>ee[b] (%)</td>
</tr>
<tr>
<td>15</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>60</td>
<td>15</td>
<td>0</td>
</tr>
<tr>
<td>120</td>
<td>28</td>
<td>0</td>
</tr>
<tr>
<td>180</td>
<td>39</td>
<td>0</td>
</tr>
<tr>
<td>300</td>
<td>52</td>
<td>0</td>
</tr>
<tr>
<td>480</td>
<td>80</td>
<td>0</td>
</tr>
<tr>
<td>640</td>
<td>93</td>
<td>0</td>
</tr>
</tbody>
</table>

In the past few decades, reactions involving C(sp²) electrophiles have been well developed through efficient (asymmetric) Lewis or Brønsted acid catalysis (cyclic transition state). In contrast, limited catalysis examples were reported for C(sp³) electrophiles, especially in the context of asymmetric catalysis (Figure 2-2). The mechanism for the latter reactions follows a similar, but distinct principle. In the presence of a Lewis or Bronsted acid, an electrophilic carbenium ion may be formed as a key intermediate, which may be trapped by a nucleophilic allyl reagent in an acyclic transition state. Such a scenario renders asymmetric catalysis substantially more challenging.
Figure 2-2 Comparison of reactivity: electrophiles and nucleophiles in the literature
2.2 Aims

Following the initial study using a novel catalyst, [18]crown-6–Ga(I)OTf, for C–C bond formations between allyl or allenyl boronic esters and acetals or ketales (cf. Chapter 1, Table 1-17 and Scheme 1-35), we aimed to explore this novel approach using more reactive pro-nucleophiles in view of an improved electrophile scope. Pro-nucleophile candidates with an increased intrinsic nucleophilicty include an allyl silane (94), a mixed allyl B/Si reagent 136, and an allyl borane 110 (Scheme 2-26 and Figure 2-3).

Indeed, while the allyl boronic ester (71) seemed to require a boron-to-gallium transmetalation to enfold nucleophilicity, allyl silanes (94) have been known to be intrinsically nucleophile for direct C–C bond formation with very reactive electrophiles (Scheme 2-26, left scenario vs. middle and right scenarios). Moreover, in the case of the mixed B/Si reagent (136), chemoselectivity and geometric selectivity issues had to be addressed under catalysis conditions (Scheme 2-26, right scenario).
On the other hand, the highly Lewis acidic allyl borane may enfold boron–ate nucleophilicity –without a required transmetalation– through simple C–B bond activation by a suitable Lewis base (Figure 2-3).

Collection of these fundamentally important data in the context of the novel gallium(I) catalysis may allow the development of an efficient asymmetric version of this chemistry using C(sp³) electrophiles, which represents a long-standing problem in the context of asymmetric synthesis. We aimed to explore this potential asymmetric gallium(I) catalysis using: (i) a chiral counter anion; (ii) a chiral ligand; or (iii) a combination of both a chiral counter anion and a chiral ligand (Figure 2-4).

---

**Figure 2-3** Ga(I) catalysis – reactivity of a boronic ester vs. a borane

<table>
<thead>
<tr>
<th>Boron Lewis acidity</th>
<th>Reactivity</th>
<th>Catalyst</th>
</tr>
</thead>
<tbody>
<tr>
<td>moderate (32 ppm)</td>
<td>low</td>
<td>[18]crown-6–GaI OTf</td>
</tr>
<tr>
<td>very high (85 ppm)</td>
<td>very high</td>
<td>GaI cat?</td>
</tr>
</tbody>
</table>

---

**Figure 2-4** Two conceivable routes for asymmetric Ga(I) catalysis
2.3 Results and Discussion

2.3.1 Gallium(I) Catalysis Using an Allyl Silane

Based on the data obtained in the initial gallium(I) project (cf. Chapter 1, Scheme 1-42), we aimed to explore the novel gallium(I) catalysis using an allyl silane (Figure 2-5). An allyl boronic ester may be activated by a Lewis base, and through transmetalation an allyl–Ga(I) species may be generated in situ. The latter may then react with an electrophile, which may have been pre-activated by a gallium(I) species (Figure 2-5, left scenario). Alternatively, such a gallium(I) catalyst system may be used for other allyl reagents, which may not require a pre-activation, e.g. an allyl silane. The latter is an intrinsically better nucleophile, which may be sufficient for C–C bond formation with an electrophile pre-activated by a gallium(I) species (Figure 2-5, right scenario).

In this chapter, dibenzyl ether (DBE, 25 mol% in mesitylene) was used as an internal standard in order to quantitatively determine the NMR yield of the corresponding reaction products (\textsuperscript{1}H NMR spectroscopy using an aliquot of the corresponding reaction mixture).

2.3.1.1 Initial and Control Experiments

Initial Experiment

The initial experiment, between acetal 70a and allyl trimethyl silane, was carried out in dioxane at 40–45 °C for 8 h using catalytic amounts of gallium(0), silver triflate, and
[18]crown-6 in a 1:2:1 molar ratio under ultrasonication (Scheme 2-27). Pleasingly, product 72a was obtained in >99% NMR yield. This preliminary result suggested that this catalyst system was apt to catalyze this C–C bond formation using allyl trimethyl silane.

Based on the literature, an allyl silane has been considered nucleophilic enough to add to reactive electrophiles, which have been pre-activated by a Lewis acid catalyst. In the present catalysis, the use of a ligand, such as [18]crown-6, may decrease the Lewis acidity of the gallium(I) center and hence slow down the C–O bond activation of 70a. In addition, the use of ultrasonication cannot be considered as a particularly convenient method. Accordingly, we aimed to employ simpler reaction conditions for the low-oxidation state gallium catalysis using an allyl silane, i.e., conducting the C–C bond formation in the absence of a ligand and with conventional heating and stirring. In turn, the reaction conditions had to be optimized.

**Ligand Effect on the Catalyst System**

These experiments were carried out using 10 mol% of gallium(0) and 5 mol% of silver triflate, in the presence or absence of [18]crown-6 at 25 °C with conventional heating and stirring (Table 2-3).
Table 2-3 Initial experiments with conventional heating and stirring

![Chemical Reaction Diagram]

<table>
<thead>
<tr>
<th>Entry</th>
<th>Ligand</th>
<th>Time (h)</th>
<th>NMR Yield[a] (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>–</td>
<td>3</td>
<td>&gt;99</td>
</tr>
<tr>
<td>2</td>
<td>[18]crown-6</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>3</td>
<td>[18]crown-6</td>
<td>6</td>
<td>68</td>
</tr>
<tr>
<td>4</td>
<td>[18]crown-6</td>
<td>24</td>
<td>&gt;99</td>
</tr>
</tbody>
</table>

[a] The yield was determined by $^1$H NMR analysis of a reaction aliquot: IS = dibenzyl ether (25 mol%).

In the absence of the ligand, product 72a was obtained in >99% NMR yield in 3 h (Table 2-4, entry 1). In contrast, in the presence of [18]crown-6, 72a was formed in only 4% NMR yield under otherwise identical reaction conditions (entry 2). Higher yields of 72a were observed by extending the reaction time (6–24 h; entries 3 and 4). These experiments confirmed that the reaction proceeded smoothly with conventional heating and stirring, and even faster in the absence of a ligand.

**Control Experiments**

Next, control experiments were carried out in order to confirm that both catalyst components were required (Table 2-4).
Table 2-4 Control experiments using different catalyst systems

![Chemical structure diagram]

**Table 2-4** Control experiments using different catalyst systems

<table>
<thead>
<tr>
<th>Entry</th>
<th>Cat (mol%)</th>
<th>NMR Yield(^[a]) (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Ga(^0) (10) / AgOTf (5)</td>
<td>&gt;99</td>
</tr>
<tr>
<td>2</td>
<td>– / –</td>
<td>NR(^[b])</td>
</tr>
<tr>
<td>3</td>
<td>Ga(^0) (10) / –</td>
<td>NR(^[b])</td>
</tr>
<tr>
<td>4</td>
<td>– / AgOTf (5)</td>
<td>NR(^[b])</td>
</tr>
</tbody>
</table>

[a] The yield was determined by \(^1\)H NMR analysis of a reaction aliquot: IS = dibenzyl ether (25 mol%).  
[b] NR = no reaction.

The combined use of gallium(0) and AgOTf afforded 72a in >99% NMR yield (entry 1). In contrast, the non-catalyzed reaction did not proceed at all (entry 2). In the same line, the separate use of gallium(0) and AgOTf failed to give any conversion of 70a (entries 3 and 4). These data suggested that the combined use of gallium(0) and AgOTf was indeed necessary (proof of principle).

### 2.3.1.2 Solvent Screening

Next, various solvents, including alkanes, ethers, and aromatic solvents, were screened at 5 mol% catalyst loading (Table 2-5). All reactions were conducted at 25 °C for 30 min.
Table 2-5 Solvent screening for the model reaction

![Chemical structure]

<table>
<thead>
<tr>
<th>Entry</th>
<th>solvent (ε)</th>
<th>NMR Yield[a] (%)</th>
<th>Entry</th>
<th>solvent (ε)</th>
<th>NMR Yield[a] (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>pentane (1.8)</td>
<td>96</td>
<td>7</td>
<td>mesitylene (3.4)</td>
<td>97</td>
</tr>
<tr>
<td>2</td>
<td>PE (2.0)</td>
<td>86</td>
<td>8</td>
<td>Et₂O (4.3)</td>
<td>91</td>
</tr>
<tr>
<td>3</td>
<td>dioxane (2.3)</td>
<td>&gt;99</td>
<td>9</td>
<td>EtOAc (6.0)</td>
<td>&gt;99</td>
</tr>
<tr>
<td>4</td>
<td>PhMe (2.4)</td>
<td>99</td>
<td>10</td>
<td>DME (7.2)</td>
<td>93</td>
</tr>
<tr>
<td>5</td>
<td>m-xylene (2.4)</td>
<td>97</td>
<td>11</td>
<td>THF (7.5)</td>
<td>81</td>
</tr>
<tr>
<td>6</td>
<td>TBME (2.6)</td>
<td>91</td>
<td>12</td>
<td>BTF (9.2)</td>
<td>98</td>
</tr>
</tbody>
</table>

[a] The yield was determined by ¹H NMR analysis of a reaction aliquot: IS = dibenzyl ether (25 mol%).

Pleasingly, the desired product 72a was obtained in >90% NMR yields in most of the solvents (Table 2-5, except entries 2 and 11: PE and THF). With respect to our earlier study, we were particularly interested in the use of dioxane and toluene as a reaction solvent (entries 3 and 4). In order to confirm the formation of a potential low-oxidation state gallium species, its catalytic activity, and its regeneration after completed C–C bond formation, ⁷¹Ga NMR spectroscopy had to be employed to eventually detect the transient gallium intermediates.

2.3.1.3 Stoichiometric ⁷¹Ga NMR Studies

Although the natural abundance of the ⁷¹Ga isotope (39.6%) is lower than that of ⁶⁹Ga isotope (60.1%), ⁷¹Ga NMR spectroscopy proved to be more useful (cf. Chapter 1, Scheme 1-36). As outlined earlier, ⁷¹Ga NMR analysis has proved an important tool to identify the presence and the formal oxidation state of gallium species. An external standard, such as
Ga(D₂O)₆³⁺ in aqueous solution, has been used. The ⁷¹Ga NMR spectroscopic data mentioned in Chapter 1 have been summarized below (Figure 2-6). Generally, gallium(I) species have been shown to display a singlet resonance between δ = −500 ppm and δ = −800 ppm, whereas gallium(III) species typically give a pronounced down-field shift. According to our earlier gallium(I) study (cf. Chapter 1, Scheme 1-36), an in situ generated [18]crown-6–Ga¹OTf (89b) complex showed a singlet resonance at δ = −565 ppm in dioxane. To the best of our knowledge, gallium(II) species have not been analyzed by ⁷¹Ga NMR spectroscopy.

![Figure 2-6 ⁷¹Ga NMR spectroscopic data of reported gallium species](image)

**Attempted Detection of a Low-Oxidation Gallium Species in Dioxane**

On the basis of the solvent screening, 1,4-dioxane was used as a solvent. Gallium(0) and AgOTf were reacted in a 2:1 molar ratio – in the absence of [18]crown-6– in dioxane with conventional heating and stirring at 50 °C for 20 h (Scheme 2-28).

![Scheme 2-28 Detection of low-oxidation state gallium species in dioxane](image)
Unfortunately, a signal was not detectable in $^{71}$Ga NMR spectroscopy (Scheme 2-28, upper equation). This result may be ascribed to the rather slow redox-reaction if ultrasonication conditions were not employed, which may lead to insufficient quantities of soluble gallium species. It is conceivable that ultrasonication may be required to activate the surface of gallium(0). In addition, the absence of a ligand may be unfavorable regarding both the solubility and the stability of a potentially formed gallium(1) species in an ethereal solvent. For comparison, in our earlier study we were able to detect [18]crown-6–gallium(I) (89b) – in situ generated under ultrasonication – through a resonance at $\delta = -565$ ppm (Scheme 2-28, lower equation; cf. Chapter 1, Scheme 1-36).

**Detection of a Low-Oxidation Gallium Species in Toluene**

Next, based on the excellent result in the solvent screening, toluene was used as a solvent in order to detect the anticipated low-oxidation state gallium species. The experiment was carried out using gallium(0) and AgOTf in a 2:1 molar ratio in toluene at 40 °C or 50 °C for 16 h (Scheme 2-29).

![Scheme 2-29 Detection of Ga(I) species in toluene](image)

Pleasingly, under the employed conditions a single resonance at $\delta = -694$ ppm was detected by $^{71}$Ga NMR spectroscopy (Figure 2-7, left chart). This new signal suggested the clean formation of gallium(I) triflate (89a) in the absence of a coordinating ligand (non-ultrasonication conditions). For comparison, in our earlier study we were able to
detect [18]crown-6–gallium(I) \((89b)\) \(\textit{in situ}\) generated under ultrasonication through a resonance at \(\delta = -565\ ppm\) (cf. Chapter 1, Figure 1-35, \textit{left} chart). In agreement with our observation, Krossing and Slattery \textit{et al.} reported that the coordination of [18]crown-6 to a gallium(I) salt led a similar down-field shift (from \(\delta = -756\ ppm\) to \(\delta = -643\ ppm\)).\textsuperscript{9a,9b} In contrast, in a control experiment a solution of commercially available \(\text{Ga(OTf)}_3\) in toluene was analyzed by \(^{71}\text{Ga}\) NMR spectroscopy, resulting in a singlet resonance at \(\delta = -39\ ppm\) (suspension). After addition of two drops of water, a clear two-phase solution was obtained, which afforded a single resonance at \(\delta = 0.8\ ppm\). These \(^{71}\text{Ga}\) NMR data strongly suggested that our catalyst system was indeed an \(\textit{in situ}\) generated gallium(I) species, \(\text{Ga(I)OTf}\), rather than gallium(III) salt.

Next, the model substrates, acetal \(70a\) and allyl trimethyl silane, were added to the pre-formed \(\text{Ga(I)OTf}\) solution in toluene (Scheme 2-30). As expected, this C–C bond-forming reaction at 25 °C gave within 30 min \(>99\%\) conversion of \(70a\) to \(72a\) (\(^1\text{H}\) NMR spectroscopy). The \(^{71}\text{Ga}\) NMR analysis revealed that a signal was \textit{not} detectable after completed C–C bond formation (Figure 2-7, \textit{right} chart). A similar observation was reported by Krossing \textit{et al.},\textsuperscript{9c} where the signal of a gallium(I) salt disappeared in the \(^{71}\text{Ga}\) NMR spectrum after coordination by a carbene ligand (cf. Chapter 1, Scheme 1-24). In our present reaction, the ether product \(72a\) or the stoichiometric by-product, TMSOMe, may act as a ligand for \(\text{Ga(I)OTf}\) thereby impeding its detection by \(^{71}\text{Ga}\) NMR spectroscopy.

\begin{align*}
\text{Ga(I)(PhMe)}_n\text{OTf} & \quad \text{toluene solution} \quad 89a \\
\text{\(^{71}\text{Ga NMR: \(-694 ppm\)}\) & \\
+ \quad \text{OMe} \\
\text{70a} & \quad \text{25 °C, 0.5 h} \\
\text{no signal} \\
\text{94} & \quad 1.1 \text{ equiv} \\
\text{\(71\text{Ga NMR: \(-694 ppm\)}\) & \\
\text{OMe} + \text{MeOSiMe}_3 & \quad \text{72a} + 137 \\
\text{>99\% conv} & \end{align*}

\textit{Scheme 2-30} Attempted detection of gallium(I) before and after completed C–C bond formation
Although the use of dioxane did not afford a gallium(I) signal in $^{71}$Ga NMR spectroscopy, it was further used as a reaction solvent for the purpose of direct comparison with data obtained in Chapter 1.

2.3.1.4 Scope for C(sp$^3$) Electrophiles

Next, we examined the substrate scope using 10 mol% of gallium(0) and 5 mol% of AgOTf in dioxane at 25 °C with conventional heating and stirring (Table 2-6).
The combined use of gallium(0) and AgOTf resulted in the formation of the corresponding products in 71–99% NMR yields. The reactions proceeded smoothly with acyclic or cyclic aromatic, heteroaromatic, and aliphatic acetals. The reactions using propargylic and allylic substrates 70v and 70w resulted in completely regioselective C–C bond formations. In addition, ketal 70z reacted smoothly although a longer reactions time was required. Importantly, a reactive ketone group was chemoselectively preserved in product 72z'.

Encouraged by these results, we examined the possibility of using less reactive C(sp³) electrophiles and a C(sp³) electrophile (Scheme 2-31). This simple two-catalyst system was shown to successfully catalyze the allylation of an N,O-aminal (133), a benzylic secondary...
ether (138), and benzaldehyde (64). The corresponding products were obtained in 59–99% NMR yields. These results confirmed that a very simple gallium(I) catalyst was apt to catalyze a broad variety of C–C bond formations using allyl trimethyl silane under mild conditions.

![Scheme 2-31 Gallium(I)-catalyzed allylation of other electrophiles](image)

**2.3.2 Gallium(I) Catalysis Using a Unique Reagent: Boron vs. Silicon**

Initially, an in situ gallium(I) catalyst has been developed for C–C bond formation using allyl boronic ester 71 under ultrasonication conditions (Figure 2-8, left side). Subsequently, another in situ gallium(I) catalyst has been shown to facilitate C–C bond formation using the more nucleophilic allyl trimethyl silane 94 with conventional heating and stirring (Figure 2-8, middle). Next, we aimed to examine the use of a ‘mixed’ allyl reagent 136 containing both a boronic ester and a silane (Figure 2-8, right side). Here, the challenge was three-fold. First, it was interesting to see the intrinsic reactivity of this unique reagent under gallium(I) catalysis conditions. Second, the issue of chemoselectivity has to be addressed: allyl silane reactivity with loss of SiMe₃ (= bora-allylation) vs. allyl boron reactivity with loss of B(pin) (= sila-allylation). Third, the geometric selectivity in the product had to be optimized: E vs. Z.
An allyl boronic ester (71) was shown to react with aldehydes in the absence of a catalyst, while an allyl silane (94) typically requires a Lewis acid activation of the electrophile. In 2005, Hall et al. reported on the use of an α-silyl allyl boronic ester in the presence or absence of an acid catalyst (Scheme 2-32).\(^\text{95}\) Using an aldehyde as an electrophile, it was shown that the chemoselectivity and thus the type of product proved to be dependent on the reaction conditions. The allyl boronic ester component reacted \textit{in the absence} of a catalyst in a cyclic transition state (Scheme 2-32, \textit{left} side), resulting in the formation of the corresponding thermal, non-catalyzed product: a secondary alcohol 141 bearing a \(Z\) alkenyl silane moiety (\(Z:E = \text{up to 6.7}:1\)). In contrast, the allyl silane component reacted \textit{in the presence} of an acid catalyst in an acyclic transition state (Scheme 2-32, \textit{right} side), resulting in the formation of the corresponding catalyzed product, a secondary alcohol 142 bearing an \(E\) alkenyl boronic ester moiety (\(Z:E = \text{up to 1}:4\)). These transformations displayed good chemoselectivity, but low stereoselectivity. \textit{The reactivity of this reagent had not been investigated with C(\textit{sp}^3) electrophiles, and high geometric selectivity had not been reported neither.}
2.3.2.1 Preparation of an α-Silyl Allyl Boronic Ester

The so-called Matteson reagent, α-TMS–allyl–B(pin) (136), was prepared according to a modified procedure of a literature method (Scheme 2-33). It was formed through the treatment of vinyl–B(pin) (146) and (trimethylsilyl)chloromethyl lithium (145) via a so-called Matteson rearrangement (Figure 2-9). The crude product 136 was obtained in 80% yield as pale-yellow liquid. The obtained analytical data were identical with the literature-reported data, and the purity of this reagent proved to be sufficient for its use in catalysis.
Scheme 2-33 Preparation of α-TMS–allyl–B(pin) (136)\textsuperscript{96}

This reaction could be easily monitored by \textsuperscript{11}B NMR spectroscopy. The initial reagent, vinyl–B(pin) 146, showed a resonance at $\delta = 29$ ppm and the product showed a signal at $\delta = 33$ ppm (Figure 2-10). Although a tiny amount of vinyl–B(pin) (146) remained in 136, the latter proved to be sufficiently pure. Indeed, 146 was shown to be unreactive in catalysis.

Figure 2-9 \textsuperscript{1}H NMR spectrum of α-TMS–allyl–B(pin) (136)
2.3.2.2 Initial Experiment with an Acetal

Initial Experiment

In the initial experiment, model substrate 70a was reacted with α-TMS–allyl–B(pin) (136) in the presence of 10 mol% of gallium(0) and 5 mol% of AgOTf in dioxane at 25 °C for 30 min (non-ultrasonication conditions; Scheme 2-34). Based on our earlier study, the allyl silane may react faster that the allyl boronic ester in the presence of an in situ formed gallium(I) Lewis acid. In turn, we anticipated a borallylation with loss of the TMS group.

![Boron NMR Spectrum](image)

*Figure 2-10* $^{11}$B NMR spectrum of α-TMS–allyl–B(pin) (136)

Scheme 2-34 Initial experiment with acetal 1a and α-TMS–allyl–B(pin) (136)
Indeed, this catalyst system resulted in the exclusive formation of the more valuable boron-based product 148a in 82% yield with decent geometric selectivity, i.e., \( E:Z = 9:1 \) (\(^1\)H NMR spectroscopy). The formation of the stoichiometric by-product, TMSOMe 137, was confirmed as well (\(^1\)H NMR). Other potential products containing a boron or silicon moiety were not detected. The obtained analytical data fitted accurately with the literature data.\(^97\) The OMe group of the \( E \) isomer displayed a resonance at \( \delta = 3.21 \) ppm, while the \( Z \) isomer showed a signal at \( \delta = 3.24 \) ppm (\(^1\)H NMR). In addition, the coupling constants \( J \) for the two vinylic hydrogen atoms of each geometric isomer confirmed the product formation, including the indicated \( E:Z \) ratio (Figure 2-11). In this initial experiment, the geometric selectivity (9:1) proved to be substantially better than the one (4:1) reported by Hall and co-workers.\(^95\) In \(^{11}\)B NMR spectroscopy, a new singlet resonance was observed at \( \delta = 29.8 \) ppm, showing another evidence for the formation of the desired boron-containing product.

\[ \text{Figure 2-11 Coupling constants for the } E \text{ and } Z \text{ geometric isomers} \]

**Solvent Screening**

Next, we aimed to optimize the geometric selectivity in product 148a by performing a solvent screening. It is noted that several solvents, e.g. acetonitrile (MeCN), proved to be ineffective in the gallium(I)-catalyzed C–C bond formation between acetal 70a and allyl boronic ester 71 (cf. Chapter 1, Table 1-10). This lack of reactivity may be ascribed to an incomplete redox reaction between Ga(0) and AgOTf [for the \textit{in situ} formation of the gallium(I) catalyst], or the decomposition and/or the redox-disproportionation of Ga(I) in acetonitrile. In turn, the gallium catalyst was pre-formed in dioxane using 10 mo% of...
gallium(0) and 5 mol% AgOTf at 30 °C (5 h). Next, a solution of acetal \(70a\) and \(\alpha\)-TMS–allyl–B(pin) (136) in a specific solvent was added to the \textit{in situ} catalyst mixture in dioxane (Table 2-7). Three different solvents were examined for direct comparison.

**Table 2-7 Solvent screening**

<table>
<thead>
<tr>
<th>Entry</th>
<th>Solvent (ε)</th>
<th>NMR Yield[a] (%)</th>
<th>(E:Z) ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>dioxane (2.0)</td>
<td>90</td>
<td>9:1</td>
</tr>
<tr>
<td>2</td>
<td>PE (2.3)</td>
<td>96</td>
<td>13:1</td>
</tr>
<tr>
<td>3</td>
<td>PhMe (2.4)</td>
<td>97</td>
<td>12:1</td>
</tr>
<tr>
<td>4</td>
<td>MeCN (37.5)</td>
<td>97</td>
<td>17:1</td>
</tr>
</tbody>
</table>

[a] The yield was determined by \(^1\)H NMR analysis of a reaction aliquot; IS = dibenzyl ether (25 mol%).

Pleasingly, the desired product \(148a\) was obtained in >90% NMR yields for all examined solvents (entries 1–4). Petroleum ether and toluene proved to be more suitable solvents than dioxane (\(E:Z = 12:13:1\); entries 2 and 3 vs. \(E:Z = 9:1\); entry 1). The use of the most polar solvent, acetonitrile, afforded product \(148a\) with the best geometric selectivity (\(E:Z = 17:1\); entry 4). Product \(148a\) could be isolated by preparative thin-layer chromatography (PTLC) on silica gel, and resulted in 80% isolated yield with a ratio \(E:Z = 17:1\) (Figure 2-12). The coupling constants \(J\) of the two vinylic hydrogen atoms of each geometric isomer confirmed the indicated excellent \(E\) selectivity (Figure 2-13).
Encouraged by this result, we decided to apply these conditions to several electrophiles in order to examine a preliminary scope.
2.3.2.3 Preliminary Scope for C(sp\(^3\)) Electrophiles

We examined the generality of this reaction using Ga(I)OTf –pre-formed in dioxane– in acetonitrile at 25–30 °C with conventional heating and stirring (Table 2-8).

**Table 2-8** Substrate scope using α-TMS–allyl–B(pin) (136) under optimized conditions[^1]

<table>
<thead>
<tr>
<th>OR'</th>
<th>R' = Me, Et</th>
<th>B(pin)</th>
<th>[Ga/OTf] (10 mol% in dioxane)</th>
<th>MeCN (1 M), 25–30 °C, 0.5–1 h</th>
<th>OR'</th>
</tr>
</thead>
<tbody>
<tr>
<td>70a</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>148</td>
</tr>
<tr>
<td>136</td>
<td>1.1 equiv</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

[^1] The yield was determined by \(^1\)H NMR analysis of a reaction aliquot: IS = dibenzyl ether (25 mol%).

This *in situ* gallium(I) catalysis resulted in the efficient formation of the corresponding products 148 in 80–97% NMR yields; these functionalized products were isolated by PTLC on silica gel (73–80% isolated yield). High or complete geometric selectivities (E:Z = >17:1) were obtained using aromatic acetals. It is noted that in the case of compound 148o the geometric selectivity decreased from E:Z = 25:1 to E:Z = 5:1, which means that 148o underwent partial isomerization during the purification process. This issue may be addressed by using silica gel / \(\text{NEt}_3\) or neutral alumina for PTLC.

Next, a less reactive C(sp\(^3\)) electrophile, secondary ether 138, was examined in this bora-allylation under identical conditions, and the Ga(I) catalysis proved to be once more effective (Scheme 2-35). The corresponding product 151 was obtained in 94% NMR yield with a ratio E:Z = 18:1; purification of 151 by PTLC on silica gel afforded this compound in 84% isolated yield with exclusive E selectivity (95% chemical purity).
2.3.3 Gallium(I) Catalysis Using an Allyl Borane

We have successfully developed a gallium(I) catalyst system—in the presence of a ligand—for the use of allyl boronic ester (71) in Hosomi–Sakurai reactions under ultrasonication conditions (cf. Chapter 1, Table 1-17; Figure 2-14, left side). Compared to 71, an allyl borane of type 110 has been shown to be a substantially more Lewis acidic reagent, which was used in C–C bond formations using C(sp^3) electrophiles (Figure 2-14, right side). The high reactivity of such an allyl borane may be exploited in order to expand the scope for the developed gallium(I) catalysis.

![Scheme 2-35: Low-oxidation state gallium-catalyzed bora-allylation of a secondary ether (138)](image)

<table>
<thead>
<tr>
<th>Boron Lewis acidity:</th>
<th>moderate</th>
<th>very high</th>
</tr>
</thead>
<tbody>
<tr>
<td>^11B NMR (ppm):</td>
<td>32</td>
<td>85</td>
</tr>
<tr>
<td>Reactivity:</td>
<td>low</td>
<td>very high</td>
</tr>
<tr>
<td>Stability:</td>
<td>very stable</td>
<td>stable in solution (moisture-free)</td>
</tr>
</tbody>
</table>

Figure 2-14 Comparison between boron-based allyl reagents

2.3.2.1 Preparation of an Allyl Borane\textsuperscript{98}

The allyl–B(9-BBN) (110) reagent was synthesized based on the Aggarwal method (Scheme 2-36).\textsuperscript{98} A solution of MeO–B(9-BBN) (107) was first prepared \textit{in situ} using H–B(9-BBN)
(152) and methanol, showing a new singlet resonance at $\delta = 57$ ppm ($^{11}$B NMR spectroscopy). This signal was different from that of the starting material, H–B(9-BBN) (152), which displayed a doublet at $\delta = 28$ ppm ($^{11}$B NMR). After $\sigma$ bond metathesis of MeO–B(9-BBN) (107) with allyl magnesium bromide, the expected allyl borane 110 was obtained in a hexane solution, showing a signal at $\delta = 85$ ppm ($^{11}$B NMR; Figure 2-15). Trace amounts of impurities were observed at $\delta = 57$ ppm and 59 ppm ($^{11}$B NMR), suggesting the formation of XO–B(9-BBN) with $X = H, Me, 9$-BBN.

Scheme 2-36 Synthesis of allyl–B(9-BBN) (110)$^{98}$

Figure 2-15 $^{11}$B NMR spectrum of allyl–B(9-BBN) (110)
A solution of allyl–B(9-BBN) (110) in hexane proved to be stable at room temperature under an inert atmosphere. This more reactive allyl boron reagent 110—compared to 71—was examined under gallium(I) catalysis conditions.

2.3.3.2 Initial Experiments with an Acetal

Based on our earlier study, we initially used acetal 70a and allyl borane 110, as a solution in hexane (Table 2-9). The experiments were conducted using 10 mol% of gallium(0) and 5 mol% of AgOTf at 25–30 °C with conventional heating and stirring.

Table 2-9 Initial experiments with allyl–B(9–BBN) (110)

<table>
<thead>
<tr>
<th>Entry</th>
<th>Cat</th>
<th>T (°C)</th>
<th>Time (h)</th>
<th>NMR Yield[a] (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>+</td>
<td>25</td>
<td>3</td>
<td>96</td>
</tr>
<tr>
<td>2</td>
<td>+</td>
<td>30</td>
<td>3</td>
<td>98</td>
</tr>
<tr>
<td>3</td>
<td>–</td>
<td>30[b]</td>
<td>3</td>
<td>NR</td>
</tr>
<tr>
<td>4</td>
<td>+</td>
<td>25</td>
<td>0.5</td>
<td>93</td>
</tr>
</tbody>
</table>

[a] The yield was determined by 1H NMR analysis of a reaction aliquot: IS = dibenzyl ether (25 mol%). [b] A catalyst was not added.

The combined use of gallium(0) and AgOTf afforded product 72a in 96–98% NMR yields in 3 h (entries 1 and 2). In the absence of the catalyst system, the reaction of 70a and 110 under otherwise identical conditions failed to give product 72a (entry 3). It is noted that the reaction time could be shortened to 30 min while maintaining a high yield (93%; entry 4). Next, these conditions were applied to a variety of C(sp3) electrophiles.
2.3.3.3 Preliminary Scope for C(sp$^3$) Electrophiles

The generality of this reaction was investigated using 10 mol% of gallium(0) and 5 mol% of AgOTf at 25 °C with conventional heating and stirring (Table 2-10). Only one example from each type of electrophile was selected for this preliminary screening, including acyclic and cyclic aromatic and heteroaromatic acetals, and an ether.

Table 2-10 Preliminary substrate scope using allyl–B(9–BBN) (110) under optimized conditions$^{[a]}$

<table>
<thead>
<tr>
<th>Substrate</th>
<th>Yield (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>72a</td>
<td>93%</td>
</tr>
<tr>
<td>72r</td>
<td>88%</td>
</tr>
<tr>
<td>72u</td>
<td>87%</td>
</tr>
</tbody>
</table>

[a] The yield was determined by $^1$H NMR analysis of a reaction aliquot: IS = dibenzyl ether (25 mol%).

The reactions proceeded smoothly with acyclic and cyclic aromatic and heteroaromatic acetals resulting in the formation of the corresponding products 72 in 87–93% NMR yields. Similarly, this transformation using a secondary benzylic ether (138) afforded the corresponding product 139 in 70% NMR yield (Scheme 2-37).

Scheme 2-37 Gallium(I)-catalyzed allylation of an ether

At that stage, the gallium(0)/AgOTf catalyst system showed good to excellent reactivity towards different types of allyl reagents, i.e., boron- and silicon-based nucleophiles (Figure
In literature, only sporadic asymmetric metal catalysis with limited generality has been developed for C–C bond formations using C(sp³) electrophiles. To the best of our knowledge, asymmetric gallium(I) catalysis had not been reported yet. Accordingly, we aimed to develop an enantiomerically enriched gallium(I) catalyst for efficient asymmetric C–C bond formation with O,O-acetals and N,O-aminals.

![Figure 2-16 Direct comparison of the chemistry using different allyl reagents](image)

2.3.4 **Towards Asymmetric Gallium(I) Catalysis**

Based on the broad generality developed in the racemic C–C bond formation, we aimed to develop an asymmetric version of the *in situ* gallium(I) catalysis using C(sp³) electrophiles. Two conceivable strategies may be employed in this context: the use of a chiral counter anion (*left* scenario) or a chiral ligand (*right* scenario), or the combination of both approaches (Scheme 2-38).

![Scheme 2-38 Two conceivable routes to induce asymmetry in C–C bond formation using C(sp³) electrophiles](image)
2.3.4.1 Synthesis of Enantiomerically Enriched BINOL-Phosphate Derivatives

In 2007, Toste et al. reported a highly enantioselective gold(I)-catalyzed intramolecular C–O bond formation, where an enantiomerically enriched BINOL-phosphate anion – rather than a chiral ligand – was responsible for the asymmetric induction in the O-heterocyclic product. This seminal paper was the first report on this novel concept. To date, there have been few reports on the intermolecular C–C bond formation using this chiral counter anion concept in asymmetric metal catalysis.

![Scheme 2-39](image)

Scheme 2-39 The first use of a chiral counter anion in asymmetric metal catalysis

In 2011, this chiral counter anion concept was applied to the asymmetric borono variant of the Hosomi–Sakurai reaction using N,O-aminals and allyl or allenic boronic esters (Scheme 2-40). The combined use of indium(I) chloride and a chiral silver BINOL-phosphate (R)-132–Ag resulted in the formation of the corresponding amide products with 72–96% ee.

![Scheme 2-40](image)

Scheme 2-40 The use of a chiral counter anion in asymmetric indium(I) catalysis
Based on these examples that rely on the *chiral counter anion concept*, our initial plan was to prepare enantiomerically enriched silver BINOL-phosphates, which may be applied to the gallium(I) catalysis. In addition, we intended to use commercially available enantiomerically enriched ligands, such as crown ethers, in order to see whether these may display a similar asymmetric induction in the Hosomi–Sakurai chemistry.

**Synthesis of Enantiomerically Enriched Silver BINOL-Phosphates**

First, the preparation of enantiomerically enriched BINOL-phosphoric acids was executed according to Gong’s method using the corresponding enantiomerically enriched BINOL, pyridine, phosphorous oxychloride, water, and hydrochloric acid under the indicated conditions (Scheme 2-41). The crude products were purified by flash column chromatography, washed with aqueous hydrochloric acid, and dried carefully to give the expected chiral acids as colorless solids. The obtained analytical data proved to be consistent with the literature data. Specifically, the free phosphoric acids were unambiguously identified by $^{31}$P NMR spectroscopy as these compounds display a signal in the range $\delta = 2–4$ ppm (Scheme 2-41).

![Scheme 2-41 Synthesis of enantiomerically enriched BINOL-phosphoric acids according to Gong’s method](image-url)

**Scheme 2-41** Synthesis of enantiomerically enriched BINOL-phosphoric acids according to Gong’s method$^{101}$
Next, the synthesis of enantiomerically enriched silver BINOL-phosphates was carried out following Toste’s method using the corresponding free acid and silver carbonate under exclusion of light (Scheme 2-42). The crude products were purified by filtration through carefully dried celite to afford the desired silver salts as colorless solids. The obtained analytical data proved to be consistent with the literature data. Specifically, these silver phosphates were unambiguously identified by $^{31}$P NMR spectroscopy as these compounds display a resonance in the range $\delta = 10–13$ ppm. Overall, five optically enriched silver BINOL-phosphates were prepared and used in this project.

**Scheme 2-42** Synthesis of enantiomerically enriched silver BINOL-phosphates according to Toste’s method

**Figure 2-17** Overlay of $^{31}$P NMR spectrums: enantiomerically enriched phosphoric acid vs. silver salt
2.3.5.2 Attempted Enantioselective Allylation of Cyclic Acetals

We have reported that various types of acetals could react with allyl boronic ester 71 under gallium(I) catalysis to afford the corresponding homoallylic ethers 72 in high yields (cf. Chapter 1, Table 1-17). The best catalyst system was shown to comprise a combination of metallic gallium, a silver salt (AgOTf or AgF), and [18]crown-6 as a ligand for the in situ generated gallium(I) species. Two cyclic acetals, compounds 70q and 70r, were considered as promising candidates for asymmetric catalysis (Figure 2-18).

![Figure 2-18 Structure of the two cyclic acetals selected for asymmetric catalysis](image)

Racemic Experiments

1-Methoxyisochroman acetal (70q) was prepared according to Jacobsen’s method, whereas 2-ethoxy-2H-chromene acetal (70r) was synthesized following Schaus’ procedure. In the racemic gallium(I)-catalyzed allylation of these substrates, gallium metal (10 mol%) was used together with a silver salt (5 mol%) and [18]crown-6 (10 mol%) under optimized ultrasonication conditions (Scheme 2-43, cf. Chapter 1, Table 1-17). The isolated racemic products 72q and 72r were carefully analyzed by chiral HPLC in order to obtain a clean chart with two baseline-separated signals in a 1:1 ratio, respectively.
Next, in the attempted asymmetric gallium(I) catalysis the corresponding achiral silver oxidant was replaced by a chiral silver BINOL-phosphate oxidant. Theoretically, a chiral gallium(I) species may be formed in situ through a redox-reaction between gallium(0) and the chiral silver(I) co-catalyst.

**Attempted Asymmetric Catalysis with an Isochroman Acetal**

In the initial experiment, we used cyclic acetal 70q and allyl boronic ester 71 in toluene together with a catalyst system comprising gallium(0), silver BINOL-phosphate (R)-153–Ag, and [18]crown-6 under ultrasonication conditions (Scheme 2-44).

**Scheme 2-44** Initial asymmetric catalysis experiment using a chiral silver BINOL-phosphate co-catalyst
Under these conditions, the use of the chiral silver salt proved to be substantially less effective compared to silver triflate. Indeed, the expected product \( \text{72q} \) was obtained only in 21% isolated yield vs. 90% yield using AgOTf. Since the chiral silver salts proved to be very soluble in organic solvents, the lack of reactivity may be ascribed to the decreased oxidation ability of the chiral silver phosphate compared to silver triflate, which would lead to a lower ‘effective’ catalyst loading and thus a slower reaction. Unfortunately, the asymmetric induction with this chiral counter anion – in combination with [18]crown-6 – proved to be very low (4% ee). Thus, we examined the use of three commercially available chiral crown ether ligands – in combination with silver triflate – in order to see the effect on the enantioselectivity of product \( \text{72q} \) (Table 2-11).

Table 2-11 Asymmetric catalysis experiments using a chiral crown ether ligand

<table>
<thead>
<tr>
<th>Ligand</th>
<th>Yield</th>
<th>ee</th>
</tr>
</thead>
<tbody>
<tr>
<td>[18]crown-6[a]</td>
<td>56</td>
<td>90%</td>
</tr>
<tr>
<td>(S)-[20]crown-6</td>
<td>159</td>
<td>86% 0% ee</td>
</tr>
<tr>
<td>(R)-[17]crown-5</td>
<td>160</td>
<td>75% 0% ee</td>
</tr>
<tr>
<td>(S)-[14]crown-4</td>
<td>161</td>
<td>83% 0% ee</td>
</tr>
</tbody>
</table>

[a] Reaction conditions: \( \), 40–45 °C, 12 h.

An achiral ligand, [18]crown-6, was used in a racemic ‘background’ reaction for comparison. Interestingly, the use of the three chiral crown ether ligands afforded product \( \text{72q} \) in similar levels of yield. Unfortunately however, an asymmetric induction could not be observed under the employed conditions (0% ee in all cases). Based on the proposed mechanism, the reaction proceeded through an acyclic transition state (cf. Chapter 1, Figure 1-40). If coordinated to the gallium(I) center, the chiral crown ether ligand may be too far away from
the reaction center, an oxocarbenium ion intermediate. In turn, it may be conceivable that the use of a chiral ligand was less effective in the asymmetric induction.

**Attempted Asymmetric Catalysis with a 2H-Chromene Acetal**

In the first experiments, we used cyclic acetal 70r and allyl boronic ester 71 in the presence of a catalyst system comprising gallium(0), silver BINOL-phosphate (R)-153–Ag, and [18]crown-6 under ultrasonication conditions (Table 2-12). Here, dioxane and toluene were used as a solvent.

**Table 2-12** Initial asymmetric catalysis experiments using a chiral BINOL-phosphate counter anion

<table>
<thead>
<tr>
<th>Entry</th>
<th>Solvent (ε)</th>
<th>Time (h)</th>
<th>Yield[a] (%)</th>
<th>ee[b] (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>dioxane (2.0)</td>
<td>72</td>
<td>20</td>
<td>4</td>
</tr>
<tr>
<td>2</td>
<td>PhMe (2.4)</td>
<td>99</td>
<td>38</td>
<td>18</td>
</tr>
</tbody>
</table>

[a] Yield of isolated (R)-72r after purification by PTLC on silica gel. [b] The enantiomeric excess was determined by chiral HPLC analysis.

The employed chiral catalyst system proved to be moderately effective in terms of chemical reactivity (entries 1 and 2). Interestingly however, the use of toluene afforded product 72r in a substantially higher yield though compared to dioxane (38% vs. 20% yield). In addition, the C–C bond formation in toluene displayed for the first time a notable asymmetric induction for 72r (18% ee), whereas the transformation in dioxane proceeded essentially in a racemic fashion (4% ee). In turn, an aromatic solvent was considered to be favorable in these asymmetric reactions.
Next, we wanted to test whether the combined use of both a chiral silver salt and a chiral crown ether ligand may improve the asymmetric induction. Based on the two reactions above, toluene was selected as a solvent (Table 2-13).

**Table 2-13** Effect of enantiomerically enriched crown ethers

![Chemical structure](image)

<table>
<thead>
<tr>
<th>Crown Ether</th>
<th>Reaction Time (h)</th>
<th>Yield (%)</th>
<th>ee (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>[18]crown-6[a]</td>
<td>99</td>
<td>38</td>
<td>18</td>
</tr>
<tr>
<td>(S)-[20]crown-6</td>
<td>50–60</td>
<td>6</td>
<td>9</td>
</tr>
<tr>
<td>(R)-[17]crown-5</td>
<td>64</td>
<td>14</td>
<td>3</td>
</tr>
<tr>
<td>(S)-[14]crown-4</td>
<td>6</td>
<td>9</td>
<td>12</td>
</tr>
</tbody>
</table>

[a] Reaction time: 99 h.

Unfortunately, when the chiral crown ethers were used the yields proved to be much lower compared to the use of [18]crown-6 (6–14% vs. 38%). In addition, in these cases the enantioselectivity observed for product **72r** dropped (3–12% ee vs. 18% ee). It is conceivable that there was mismatched effect between the chiral counter anion and the corresponding chiral ligand. However, the asymmetric induction was too low to draw a definite conclusion. In order to improve the asymmetric induction, we next examined two different chiral counter anions.

*Screening of Chiral Silver BINOL-Phosphates*

In these experiments, a comparison was drawn between three distinct chiral silver
co-catalysts (Table 2-14). Reactions were carried out in the presence and absence of [18]crown-6 as a supporting ligand for the in situ generated low-oxidation gallium species.

Table 2-14 Screening of enantiomerically enriched silver BINOL-phosphates

<table>
<thead>
<tr>
<th>Entry</th>
<th>X</th>
<th>[18]crown-6</th>
<th>Conv[a] (%)</th>
<th>ee[b] (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>153</td>
<td>+</td>
<td>38</td>
<td>18</td>
</tr>
<tr>
<td>2</td>
<td>–</td>
<td>–</td>
<td>12</td>
<td>19</td>
</tr>
<tr>
<td>3</td>
<td>157</td>
<td>+</td>
<td>33[a]</td>
<td>2</td>
</tr>
<tr>
<td>4</td>
<td>–</td>
<td>–</td>
<td>6</td>
<td>19</td>
</tr>
<tr>
<td>5</td>
<td>+</td>
<td>23[a]</td>
<td>4</td>
<td></td>
</tr>
<tr>
<td>6</td>
<td>–</td>
<td>NR</td>
<td>–</td>
<td></td>
</tr>
</tbody>
</table>

[a] The conversion 1r-to-3r was determined by 1H NMR analysis of a reaction aliquot.  [b] The enantiomeric excess was determined by chiral HPLC analysis.  [c] Reaction conditions: 60 °C, 80 h.

Fortunately, all data obtained in these experiments proved to be disppointing. Indeed, the two alternative chiral phosphate counter anions induced very low enantioselectivity in product 72r (2–4% ee, entries 3 and 5 vs. 18% ee, entry 1). In addition, the reactions conducted in the absence of [18]crown-6 provided low to no reactivity (entries 2, 4, and 6), although the asymmetric induction was slightly improved (19% ee, entries 2 and 4). Based on these results, the use of a ligand resulted in the formation of the corresponding product 72r in lower yields, but relatively higher enantioselectivity. Potentially, even an achiral ligand may not be favorable for this asymmetric metal catalysis. Overall, the use of these cyclic acetals as substrates proved to be unsuccessful. Therefore, we turned our attention to the use of an N,O-aminal model substrate.
2.3.4.3 Towards Asymmetric Catalysis Using an N,O-Aminal

An N,O-aminal containing an N–H bond may be a more suitable pro-electrophilic substrate. Indeed, after C–O bond activation and removal of the alkoxy group, the resulting iminium ion 162 intermediate with the N–H bond may be involved in hydrogen bonding with the chiral BINOL-phosphate counter anion (Figure 2-19). Such a formation of a chiral ion pair may be good for the asymmetric induction in this challenging asymmetric metal catalysis (Figure 2-19). Indeed, N,O-aminals were successfully used as substrates in highly enantioselective Hosomi–Sakurai reactions. In turn, we used an N,O-aminal bearing an N–H bond as an electrophile in order to establish the proof of principle for an asymmetric version of the developed gallium(I) catalysis.

![Figure 2-19 Scenario for the chiral counter anion-induced enantioselectivity: formation of a chiral ion pair](H-bonding)

Racemic Experiments

Based on our earlier results, we opted for the use of benzaldehyde-derived N-benzoyl aminal (133) as model substrate under non-ultrasonication conditions (Table 2-15). Using allyl boronic ester 71, a catalyst system comprised of gallium(0), silver triflate, and [18]crown-6 was used in dioxane at 50 ºC to afford product 134 in 83% yield (24 h; entry 1). This result meant that N,O-aminal 133 was less reactive than the corresponding O,O-acetal 70a. The use of allyl silane (94) proved to be more efficient at 30 ºC and afforded product 134 in 95% yield without the use of [18]crown-6 (18 h; entry 2). Expectedly, allyl borane (110) turned out to be the most reactive pro-nucleophile at 25 ºC, resulting in the formation of product 11 in 89% yield (0.5 h; entry 3). In turn, we selected this most reactive allyl reagent for our
first experiments towards asymmetric catalysis.

**Table 2-15** Screening of potential allyl pro-nucleophiles in view of asymmetric catalysis

<table>
<thead>
<tr>
<th>Entry</th>
<th>allyl–X</th>
<th>Conditions</th>
<th>Yield (%)</th>
<th>Reactivity</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td><img src="image" alt="allyl-B(O)O" /></td>
<td>50 °C, 24 h (18-crown-6: 10 mol%)</td>
<td>83[^b]</td>
<td>low</td>
</tr>
<tr>
<td></td>
<td><img src="image" alt="allyl-SiMe3" /></td>
<td>30 °C, 18 h</td>
<td>95[^b]</td>
<td>intermediary</td>
</tr>
<tr>
<td>3</td>
<td><img src="image" alt="allyl-B(pin)" /></td>
<td>25 °C, 0.5 h</td>
<td>89[^a]</td>
<td>high</td>
</tr>
</tbody>
</table>

[^a]: Yield of isolated (R)-134 after purification by PTLC on silica gel.  
[^b]: The yield was determined by °[^H] NMR analysis of a reaction aliquot: IS = dibenzyl ether (25 mol%).

Here again, two conceivable scenarios may be considered for the asymmetric reaction using an \(N,O\)-aminal pro-electrophile. Assuming the formation of an electrophilic iminium ion intermediate, the chiral counter anion may generate a *chirally modified electrophile* (chiral ion pair; Figure 2-20). The latter may react with a suitable nucleophile. Allyl–Ga(I) or allyl–SiMe\(_3\) may be considered as a nucleophile (*left* scenario), or alternatively, an allyl boron–ate complex (*right* scenario).

**Figure 2-20** Two conceivable scenarios for the asymmetric induction postulating an iminium ion intermediate
Use of an Allyl Borane in Asymmetric Catalysis

Our initial experiments in asymmetric catalysis with the allyl borane (110) were conducted by pre-forming the corresponding chiral low-oxidation state gallium catalyst (Table 2-16).

Table 2-16 Initial asymmetric catalysis experiments using allyl-B(9-BBN) (110)

<table>
<thead>
<tr>
<th>Entry</th>
<th>Cat pre-formed</th>
<th>T (°C)</th>
<th>Conv[a] (%)</th>
<th>ee[b] (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>+</td>
<td>25</td>
<td>79</td>
<td>5</td>
</tr>
<tr>
<td>2</td>
<td>–</td>
<td>25</td>
<td>85</td>
<td>0</td>
</tr>
<tr>
<td>3</td>
<td>+</td>
<td>0</td>
<td>53</td>
<td>6</td>
</tr>
</tbody>
</table>

[a] The conversion of (R)-134 was determined by 1H NMR analysis of a reaction aliquot. [b] The enantiomeric excess was determined by chiral HPLC analysis.

Gallium(0) was reacted with the chiral silver salt (R)-154–Ag in dioxane at 50 °C for 17 h under ultrasonication conditions (entries 1 and 3). The in situ generated chiral catalyst was then used with the two reactants at 25 °C and 0 °C, respectively; it is noted that the allyl reagent 110 was added drop-wise over 15 minutes. The displayed reactivity was satisfactory (53–79% yield), while the asymmetric induction proved to be very low (5–6% ee; entries 1 and 3). When the reaction was carried out without pre-formation of the catalyst, product 134 was generated in its racemic form (0% ee, entry 3). These poor results in terms of asymmetric induction may be explained by a relatively fast racemic ‘background’ reaction between substrates 133 and 110, without an interference of the chiral in situ gallium(I) catalyst. In order to address this potential issue, the reaction was carried out at –
40 °C (Scheme 2-45). Toluene had to be used as a solvent because dioxane solidifies at 12 °C.

In the event, gallium(0) was reacted with chiral silver salt (R)-154–Ag in toluene at 50 °C for 13 h under ultrasonication conditions. The presumed *in situ* generated chiral catalyst was then used at −40 °C with drop-wise addition of allyl borane 110 over 24 h. Unfortunately, however, the conversion to product 134 was only 20%, and the asymmetric induction was not improved (5% *ee*). Since allyl borane 110 was considered to be too reactive for asymmetric C–C bond formation in this context, we turned our attention to the use of another, less reactive nucleophile, allyl trimethyl silane (94). As mentioned in the introduction (cf. Scheme 2-23), Braun *et al.* developed a chiral titanium catalyst system to efficiently catalyze the allylation of an *N*,*O*-aminal (54% *ee*). In light of this report, we attempted the use of allyl silane (94) in the next stage. In contrast to allyl borane 110 –where we assumed the formation of a reactive boron–ate complex intermediate– we anticipated that allyl silane (94) would react *without* ate complex formation or transmetalation. The envisioned scenario is shown in Figure 2-21.
Use of an Allyl Silane in Asymmetric Catalysis

Due to its lower reactivity, allyl silane (94) was used without pre-formation of the in situ chiral gallium(I) catalyst (Table 2-17). For comparison, allyl borane 110 was consumed at 25 °C within 2 h (85% conv, 0% ee; entry 1). In contrast, allyl silane (94) proved to be substantially less reactive under these conditions. The reaction was carried out at 30 °C for 18 h resulting in a poor conversion and low asymmetric induction (12% conv, 15% ee; entry 2).

Table 2-17 Comparison of asymmetric catalysis experiments using allyl borane (110) and allyl silane (94)

<table>
<thead>
<tr>
<th>Entry</th>
<th>Allyl–X</th>
<th>Conditions</th>
<th>Conv[a] (%)</th>
<th>ee[b] (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>110</td>
<td>25 °C, 2 h</td>
<td>85</td>
<td>0</td>
</tr>
<tr>
<td>2</td>
<td>94</td>
<td>30 °C, 18 h</td>
<td>12</td>
<td>15</td>
</tr>
</tbody>
</table>

[a] The conversion of (R)-134 was determined by 1H NMR analysis of a reaction aliquot. [b] The enantiomeric excess was determined by chiral HPLC analysis.

We considered this asymmetric induction (15% ee) obtained for the use of allyl silane (94).
not promising enough to further investigate this pathway. Rather, we opted for the use of the ‘last’ allyl reagent, allyl boronic ester (71). In this case, we anticipated that a boron-to-gallium transmetalation was required to convert 71 to a nucleophilic allyl reagent. This \textit{in situ} formed allyl–Ga(I) species may then add to the ‘chirally modified’ iminium ion pair.

\begin{figure}[h]
\centering
\includegraphics[width=\textwidth]{fig2-22.png}
\caption{Proposed scenario for the asymmetric induction using allyl boronic ester (71)}
\end{figure}

\textbf{Use of an Allyl Boronic Ester in Asymmetric Catalysis}

Allyl boronic ester (71) had been used as a pro-nucleophile in the racemic allylation under mild conditions (83\% yield; Table 2-15). In the initial asymmetric experiments using 71 and \textit{N,O}-aminal (133), a chiral catalyst system comprised of gallium(0), chiral silver salt (\textit{R})-132–Ag, and [18]crown-6, was used in diethyl ether and toluene at 30–50 °C (non-ultrasonication conditions; Table 2-18).

\begin{table}[h]
\centering
\begin{tabular}{|c|c|c|c|}
\hline
\textbf{Entry} & \textbf{Solvent} & \textbf{Conv\textsuperscript{[a]} (%)} & \textbf{ee \textsuperscript{[b]} (%)} \\
\hline
1 & \textit{Et}_2\text{O} & 20 & 14 \\
2 & \textit{PhMe} & 30 & 24 \\
\hline
\end{tabular}
\caption{Initial asymmetric catalysis experiments using allyl boronic ester}
\end{table}

\textsuperscript{[a]} The conversion of (\textit{R})-134 was determined by \textsuperscript{1}H NMR analysis of a reaction aliquot. \textsuperscript{[b]} The enantiomeric excess was determined by chiral HPLC analysis.
While the reactivity was relatively poor in both solvents (20–30% conv), the asymmetric induction in the aromatic solvent proved to be higher compared to ether (24% ee; entry 2 vs. 14% ee; entry 1). This level of enantioselectivity was fairly promising, and based on these data we further optimized the various reaction parameters.

**Optimization of Reaction Parameters**

The next set of asymmetric reactions using \((R)\)-154–Ag was conducted at 40 °C for 96 hours, with the intention to gain insight into important parameters such as the necessity of a ligand, the nature of the solvent, and the substrate concentration (Table 2-19).

**Table 2-19 Optimization of reaction parameters**

<table>
<thead>
<tr>
<th>Entry</th>
<th>Ligand</th>
<th>Solvent (M)</th>
<th>Conv(^{[a]}) (%)</th>
<th>ee(^{[b]}) (%)</th>
<th>Product</th>
<th>Aminal</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>[18]crown-6</td>
<td>PhMe (1.0)</td>
<td>22</td>
<td>14</td>
<td>7</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>–</td>
<td>PhMe (1.0)(^{[c]})</td>
<td>25</td>
<td>40</td>
<td>12</td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>–</td>
<td>dioxane (1.0)(^{[c]})</td>
<td>41</td>
<td>38</td>
<td>6</td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>–</td>
<td>PhMe/dioxane (1:1, 1.0)</td>
<td>37</td>
<td>27</td>
<td>4</td>
<td></td>
</tr>
<tr>
<td>5</td>
<td>–</td>
<td>PhMe/dioxane (1:1, 0.5)</td>
<td>38</td>
<td>39</td>
<td>9</td>
<td></td>
</tr>
</tbody>
</table>

[a] The conversion of \((R)\)-134 was determined by \(^1\)H NMR analysis of a reaction aliquot. [b] The enantiomeric excess was determined by chiral HPLC analysis. [c] Reaction time: 44 h.

In the presence of a catalytic amount of [18]crown-6 using toluene as a solvent, both the reactivity and the asymmetric induction proved to be very low (14% ee; entry 1). However, in the absence of this ligand the reaction time could be substantially shortened (44 h) and the
enantioselectivity was vastly improved (40% ee; entry 2). [18]Crown-6 may act as a Lewis basic ligand and coordinate to the silver(I) center. Therefore, it may potentially decrease the oxidation ability of the chiral silver(I) co-catalyst, which may lead to a low ‘effective’ loading of the presumed chiral gallium(I) catalyst and thus to a low yield and a low asymmetric induction. Alternatively, [18]crown-6 may coordinate to the gallium(I) center to decrease its Lewis acidity (slow C–O bond activation) and potentially hamper the facial approach of the postulated allyl–Ga(I) species to the iminium ion. The same reaction in dioxane afforded a higher yield with a similar level of asymmetric induction (38% ee; entry 3). The use of a toluene/dioxane mix (1:1) did not improve these results; however, it seemed that a lower substrate concentration was beneficial in terms of asymmetric induction (39% ee; entry 5 vs. 27% ee; entry 4). These results suggested that the aromatic solvent was slightly more favorable for the asymmetric induction. While the asymmetric induction looked promising (40% ee), the displayed reactivity was too low (25% conv), which may be ascribed to the potentially low oxidation ability of the chiral silver phosphate co-catalyst, and in turn a low ‘effective’ catalyst loading. Next, we examined the temperature effect on the asymmetric reaction.

**Temperature Effect**

In order to improve both the catalyst’s displayed activity and asymmetric induction, the reactions were conducted at variable temperatures at a higher catalyst loading, i.e., 15 mol% of gallium(0) and 7.5 mol% of (R)-154–Ag (Table 2-20).
Table 2-20 Temperature effect on yield and asymmetric induction

![Chemical structure of 133 and reaction scheme](image)

<table>
<thead>
<tr>
<th>Entry</th>
<th>T (°C)</th>
<th>Yield[a] (%)</th>
<th>ee[b] (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Product</td>
<td>Aminal</td>
</tr>
<tr>
<td>1</td>
<td>35</td>
<td>40</td>
<td>37</td>
</tr>
<tr>
<td>2</td>
<td>40</td>
<td>60</td>
<td>40</td>
</tr>
<tr>
<td>3</td>
<td>45</td>
<td>68</td>
<td>26</td>
</tr>
</tbody>
</table>

[a] Yield of isolated (R)-134 after purification by PTLC on silica gel.  [b] The enantiomeric excess was determined by chiral HPLC analysis.

When the reaction was carried out at 35 °C, product 134 was obtained in 40% yield with 37% ee (entry 1). The same experiment at 40 °C afforded product 134 in a much higher yield with a slightly increased asymmetric induction (60% yield, 40% ee; entry 2). Further increasing the temperature to 45 °C resulted in a drop of the observed enantioselectivity (26% ee; entry 3). To date, the optimized conditions in entry 2 represent our best result in asymmetric low-oxidation state gallium catalysis.

In order to demonstrate the significance of the in situ generated chiral gallium catalyst species regarding reactivity and selectivity, several control experiments had to be carried out (Table 2-21).
Table 2-21 Control reactions in asymmetric catalysis

<table>
<thead>
<tr>
<th>Entry</th>
<th>Cat (mol%)</th>
<th>Yield[a] (%)</th>
<th>ee[b] (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Ga^0 (15) / (R)-154–Ag (7.5)</td>
<td>60</td>
<td>40</td>
</tr>
<tr>
<td>2</td>
<td>Ga^0 (15) / -</td>
<td>NR[c]</td>
<td>-</td>
</tr>
<tr>
<td>3</td>
<td>- / (R)-154–Ag (7.5)</td>
<td>18</td>
<td>17</td>
</tr>
<tr>
<td>4</td>
<td>- / (R)-154–H (7.5)</td>
<td>NR[c]</td>
<td>-</td>
</tr>
<tr>
<td>5</td>
<td>Ga^0 (15) / (R)-154–H (7.5)</td>
<td>NR[c]</td>
<td>-</td>
</tr>
</tbody>
</table>

[a] Yield of isolated (R)-134 after purification by PTLC on silica gel.  [b] The enantiomeric excess was determined by chiral HPLC analysis.  [c] NR = no reaction.

Compared to the benchmark result with the optimized catalyst system (60% yield, 40% ee; entry 1), all other experimental conditions proved to be substantially less effective (entries 2–5). As expected, the separate use of gallium(0) as a potential catalyst failed to give any conversion of the starting materials (entry 2). The separate use of the chiral silver phosphate salt, (R)-154–Ag, afforded product 134 in 18% yield with 17% ee (entry 3). It is noted that the chiral BINOL-phosphate counter anion may be Lewis basic enough to add to the Lewis acidic boron atom of allyl boronic ester 71, which may trigger C–B bond activation and thus C–C bond formation. Interestingly, the separate use of the corresponding chiral phosphoric acid, (R)-154–H, failed to give any reactivity (entry 4). In turn, asymmetric Brønsted acid catalysis proved not to be a viable approach for this transformation; metal catalysis was found to be critical. Finally, the combined use of gallium(0) and (R)-154–H provided full recovery of both reactants as well (entry 5). This result meant that the chiral low-oxidation state gallium species was not formed in the
presence of the free acid. In summary, the combined use of gallium(0) and a chiral silver BINOL-phosphate, (R)-154–Ag, was found to be critical for both reactivity and asymmetric induction. The key for the reactivity may be the in situ oxidation of gallium(0) to form a catalytically active gallium species, e.g. gallium(I) (Scheme 2-46). The key for the asymmetric induction may be the use of a chiral counter anion, to generate a chirally modified iminium ion (electrophile; left scenario), rather than the use of a chiral ligand, to form a chirally modified allyl–Ga(I) species (nucleophile; right scenario). This is the first example of asymmetric induction for the catalytic use of gallium(0) and in situ gallium(I) catalysis, which is of fundamental importance. Further optimization of specific reaction parameters may allow to increase the asymmetric induction to a synthetically useful level.

Scheme 2-46 Summary of asymmetric catalysis: chiral counter anion vs. chiral ligand
2.4 Summary

In this second project, a simpler Ga(0)/Ag(I) catalyst system—ligand-free and without ultrasonication—was developed for C–C bond formations using various other boron- and silicon-based reagents. The combined use of Ga(0) and AgOTf afforded the desired products in up to 99% NMR yield using allyl trimethyl silane (94), α-TMS–allyl–B(pin) (136), and allyl–B(9-BBN) (110) as pro-nucleophiles under mild conditions (Figure 2-23). The electrophile scope was substantially extended to the use of aminals, ethers, and aldehydes—most reactions proceeded more smoothly under milder conditions compared to the initial catalyst system (cf. Chapter 1, Table 1-17). The use of the mixed B/Si reagent 136 under gallium(I) catalysis displayed complete chemoselectivity (Si >> B) and excellent geometric selectivity (E >> Z).

![Figure 2-23 Summary of Ga(I) catalysis using various types of allyl reagents](image)

Importantly, we were able to detect a ligand-free low-oxidation state gallium species, Ga(1)(PhMe)ₙOTf (89a, n = 1, 2 or 3), by ⁷¹Ga NMR spectroscopy (Scheme 2-47). The postulated gallium(I) species 89a displayed a resonance at δ = –694 ppm, whereas the corresponding Ga(III) compound showed a signal at δ = –39 ppm.

![Scheme 2-47 Detection of an unprecedented gallium(I) species in the absence of a crown ether ligand](image)
Most significantly, the catalytic use of Ga(0) and a chiral silver BINOL-phosphate, \((R)-154-Ag\), for the allylation of \(N,O\)-aminal (133) provided product 134 in 60% yield with 40% ee. This result constitutes the first example of asymmetric low-oxidation state gallium catalysis. Several control experiments confirmed that the presence of Ga(0) and \((R)-154-Ag\) were critical to both reactivity and selectivity.

**Scheme 2-48** Asymmetric low-oxidation state gallium catalysis
CHAPTER 3: TOWARDS ALUMINIUM(I) CATALYSIS

3.1 Introduction

3.1.1 Physical and Chemical Properties of Aluminium

Aluminium is located in the second row of main group XIII of the periodic table. It is the most abundant metal in the Earth’s crust and exists as aluminium(III) compounds in Nature (82,000 ppm). Indeed, aluminium accounts for as much as 8% of the Earth’s solid surface. However, this soft metal does not exist in its ‘0’ oxidation state in Nature. Aluminium(0) was first produced by Ørsted in 1825, and has been widely used in industrial production, which is deeply related to our daily life. Generally, aluminium metal is used to produce alloys with copper, zinc, magnesium, manganese etc. In addition to aluminium(0), three further oxidation states may be observed: ‘+III’, ‘+II’ and ‘+I’ (Figure 3-1), which indicates aluminium’s special properties and unique potential for a variety of applications. Generally, aluminium(III) features three substituents and a vacant low-energy p orbital (Figure 3-1). This most common high-oxidation state has proved to be thermodynamically stable at room temperature. Compared to the oxidation state ‘+III’, the synthesis of lower oxidation states of aluminium has proved to require sterically demanding substituents to prevent electron-transfer processes, which may lead to redox-disproportionation. Formally, aluminium(II) species have a vacant p orbital and an unpaired electron. In turn, this meta-stable species has been shown to exist rather as a dimeric two-centred Lewis acid (Figure 3-1). Finally, aluminium(I) has a vacant p orbitals and a lone pair of electrons in an sp-type orbital (Figure 3-1). In turn, this low-oxidation species may be considered as an ambiphilic compound, displaying acid–base characteristics at a single site. Overall, these trends closely parallel those of gallium. Interestingly, only few examples of monomeric low-oxidation state aluminium compounds have been reported.
3.1.2 Aluminium(III) Lewis Acid Catalysis

Several aluminium(III) salts are commercially available. Bearing three substituents and a vacant low-energy p orbital, aluminium(III) species have been shown to act as an efficient Lewis acid catalyst or initiator for various reactions, including asymmetric synthesis.

Aluminium trichloride, $\text{AlCl}_3$, is the most common Lewis acid reagent used in Friedel–Crafts reactions. It was first reported for this type of reaction by Friedel and Crafts in 1877 (Scheme 3-1).\textsuperscript{106} In the presence of a Lewis acid, an electrophile such as an alkyl or acyl halide was shown to react with an electron-rich aromatic compound through an electrophilic aromatic substitution to form a new C–C bond ($\text{S}_{\text{E}}\text{Ar}$). In 2012, Prieger et al. reported a Friedel–Crafts alkylation catalyzed by a microwave-assisted silica gel-bound aluminium chloride, Si–$\text{AlCl}_3$.\textsuperscript{107} This reaction proceeded smoothly at 750 W in only 5 min and provided the products in good yields.

\begin{align*}
\text{Scheme 3-1 Aluminium(III)-catalyzed Friedel–Crafts alkylation}^{106}
\end{align*}

Another commercially available salt, aluminium(III) trifluoromethanesulfonate [Al(OTf)$_3$], has been widely used as a Lewis acid catalyst in organic synthesis. In 2005, Williams et al. reported Al(OTf)$_3$-catalyzed epoxide ring-opening reactions using alcohols as a nucleophile (Scheme 3-2).\textsuperscript{108} Glycol ethers were obtained in 11–97% yields by employing an extremely low catalyst loading (0.001 mol%).
In 2001, Bolm et al. reported an enantiomerically enriched (S)-BINOL–aluminium(III) complex to mediate an asymmetric Baeyer–Villiger oxidation (Scheme 3-3). A substoichiometric amount of this chiral catalyst was formed in situ using Me₂AlCl and (S)-BINOL in a 1:1 molar ratio. The catalyst system afforded the corresponding products in 34–96% yields with moderate to high asymmetric induction. Other aluminium(III) species such as EtAlCl₂, AlCl₃, and Al(O'Bu)₃, in combination with (S)-BINOL, afforded the products only with low optical purity, whereas the combined use of Me₃Al and (S)-BINOL gave a racemic product.

### 3.1.3 Dimeric Aluminium(II) Complexes

Generally, there are two synthetic pathways to generate aluminium(II) compounds (Scheme 3-4). One method involves partial reduction of an aluminium(III) halide, while another one requires redox-disproportionation or redox-comproportionation involving aluminium(I) species.
In 1988, Uhl et al. reported the synthesis of the first stable dimeric aluminium(II) compound, \([\text{Me}_3\text{Si}]_2\text{CH}_2\text{Al(II)}-\text{Al(II)}[\text{CH}_2(\text{SiMe}_3)_2]_2\) \((167; \text{Scheme 3-5})\).\(^{110}\) The corresponding aluminium(III) monomer, \([\text{Me}_3\text{Si}]_2\text{CH}_2\text{AlCl}\), was reduced by a stoichiometric amount of metallic potassium. Further dimeric analogues, \(\text{Trip}_2\text{Al(II)}-\text{Al(II)}\text{Trip}_2\) and \((\text{tBu}_3\text{Si})_2\text{Al(II)}-\text{Al(II)}(\text{Si}^t\text{Bu}_3)_2\), were obtained using a similar strategy.\(^{111}\) It is noted that sterically demanding substituents were required to protect the aluminium center and prevent redox-disproportionation. However, the very large size substituent, \(\text{tBu}_3\text{Si}\), proved to weaken the Al–Al bond. Thus, the corresponding aluminium(II) dimer easily decomposed through a radical pathway.

\[\text{AlCl}_3 + \text{LiCH(SiMe}_3)_2 \rightarrow \text{ClAl}[\text{CH(SiMe}_3)_2]_2\]

\[\text{Et}_2\text{O} - 2\text{LiCl}\]

\[\text{K}^+ (1.0 \text{ equiv})\]

\[24\text{ h}\]

\[\text{KCl}\]

\[\text{[(Me}_3\text{Si})_2\text{CH}_2\text{Al(II)}-\text{Al(II)}[\text{CH}_2(\text{SiMe}_3)_2]_2(167)^{110}\]

In 1994, Schnöckel et al. reported the synthesis of an ether-stabilized aluminium(II) dimer, \(\text{Ph(Me)}\text{O}^+\text{Br}_2\text{Al(II)}-\text{Al(II)}\text{Br}_2^+\text{O(Me)}\text{Ph}\) \((170)\), through a redox-comproportionation using...
meta-stable aluminium(I) and aluminium(III) (Scheme 3-6). The dimeric structure of 170 was confirmed by X-ray crystallography (Figure 3-2). In the synthesis, a solution of aluminium(I) bromide (168) in PhOMe was prepared at −78 °C and warmed to room temperature, thereby partially undergoing redox-disproportionation to form metallic aluminium and aluminium(III) bromide. The latter was proposed to react with the aluminium(I) starting material in a redox-comproportionation to generate the corresponding dimeric aluminium(II) species 170. This adduct was obtained as yellow crystals and could be stored in toluene or C₆D₆ at room temperature for a few hours. The ²⁷Al NMR analysis of a freshly prepared sample displayed a broad signal at δ = 130 ppm together with another signal at δ = 95 ppm. These data proved to be consistent with the partial in situ formation of an aluminium(III) adduct, Br₂Al•O(Me)Ph.

**Scheme 3-6** Synthesis of Ph(Me)O•Br₂Al(II)–Al(II)Br₂•O(Me)Ph (170)⁻¹²
3.1.4 Monomeric Aluminium(I) Complexes

Compared to common aluminium(III) species, low-oxidation state aluminium compounds have proved to be much less explored. Interestingly however, compared to gallium(I) species, more aluminium(I) compounds have been reported, including Al(I)H, Al(I)₂O, Al(I)₂S and Al(I)X (X = F, Cl, Br, I). Similar to the meta-stable aluminium(II) chemistry, aluminium(I) species were shown to require bulky substituents to protect the aluminium center and prevent redox-disproportionation (Scheme 3-7).

![Scheme 3-7 Redox-disproportionation of aluminium(I)](image)
Generally, the preparation of simple aluminium(I) compounds required extremely high temperature or reduced pressure conditions. For example, Al(I)Cl \((171)\) was obtained through two different synthetic routes: aluminium metal reacted with elemental chlorine in an oxidation at 1000 °C, or underwent a redox-comproportionation with AlCl\(_3\) at high temperature under reduced pressure conditions (Scheme 3-8).\(^{113, 114}\) Al(I)Cl \((171)\) was reported to be meta-stable in coordinating solvents, but extremely unstable in weakly coordinating solvents.

\[
\begin{align*}
\text{Al}^0 + \text{Cl}_2 & \quad \xrightarrow{1000 \, ^\circ \text{C}} \quad \text{AlCl} \\
2 \text{ equiv} & \quad 171 \\
\text{Al}^0 + \text{AlCl}_3 & \quad \xrightarrow{1200 \, ^\circ \text{C}} \quad \text{AlCl} \\
2 \text{ equiv} & \quad 171 \\
\end{align*}
\]

Scheme 3-8 Synthesis of a solution of meta-stable Al(I)Cl \((171)\)\(^{113, 114}\)

Al(I)Cl \((171)\) was characterized as a solid and in an etheral solution by Schnöckel \textit{et al.} in 1988.\(^{115}\) In the \(^{27}\text{Al}\) NMR analysis at low temperature, a broad signal was observed at \(\delta = 15\) ppm, which was consistent with a monomeric aluminium(I) species (Scheme 3-9). When this solution was warmed to room temperature, the aluminium(I) species decomposed in a redox-disproportionation at \(-93^\circ\)C with a color change from dark-red to black. In addition, a new sharp signal was observed at \(\delta = 101\) ppm, which was ascribed to an aluminium(III) adduct, Cl\(_3\)Al•OEt\(_2\).

\[
\begin{align*}
\text{AlCl} & \quad \xrightarrow{-93 \, ^\circ \text{C}} \quad \text{Al}^0 + \text{AlCl}_3 \\
3 \text{ equiv} & \quad 171 \\
\text{Al}^0 + \text{AlCl}_3 & \quad \xrightarrow{600 \, ^\circ \text{C}} \quad \text{AlCl} \\
2 \text{ equiv} & \quad 171 \\
\end{align*}
\]

\(^{27}\text{Al NMR (ppm): 15}\)

Scheme 3-9 Redox-disproportionation of Al(I)Cl \(172\)\(^{115}\)
The first room temperature-stable aluminium(I) compound, [Cp*Al(I)]₄ (173a), was reported by Schnöckel et al. in 1991 (Cp* = C₅Me₅; Scheme 3-10). This tetrameric aluminium(I) species was obtained by treating an Al(I)Cl solution with Cp*₂Mg. The air- and moisture-sensitive [Cp*Al(I)]₄ (173a) was isolated as a yellow crystalline powder, and its structure was shown to be consistent with each aluminium(I) center being coordinated by one Cp* ring (Figure 3-3). In solution, [Cp*Al(I)]₄ (173a) proved to be in a temperature-dependent equilibrium with the monomer, Cp*Al(I) 173b (Scheme 3-10).

In the ²⁷Al NMR analysis at −80 °C ~ 25 °C, the existence of the monomeric species, Cp*Al(I) (173b), was confirmed by a sharp singlet resonance at δ = −81 ppm, whereas above 30 °C another singlet resonance at δ = −150 ppm was ascribed to tetramer, [Cp*Al(I)]₄ (173a).

Scheme 3-10 Synthesis of [Cp*Al(I)]₄ (173a)

\[
\text{ClAl}^+\text{OEt}_2 + \text{Cp*}_2\text{Mg} \rightarrow (\text{Cp*Al})_4, \text{Et}_2\text{O/PhMe (1:3, 0.05 M), −78 °C, 29 172 2.0 equiv} \\
\text{In solution:} (\text{Cp*Al})_4 \rightleftharpoons \text{Cp*Al}^+ 173b >30 °C 173a 4 equiv \rightarrow −80 °C to 25 °C
\]

In solution: (Cp*Al)₄

\[\begin{align*}
\text{ClAl}^+\text{OEt}_2 & + \text{Cp*}_2\text{Mg} \\
\text{(Cp*Al)}_4 & \text{Et}_2\text{O/PhMe (1:3, 0.05 M), −78 °C} \\
\text{In solution:} (\text{Cp*Al})_4 & \rightleftharpoons \text{Cp*Al}^+ 173b >30 °C 173a 4 equiv \rightarrow −80 °C to 25 °C
\end{align*}\]
In 2013, Frenking and Fischer et al. reported that monomeric Cp*Al(I) (173b) could be accessed from two different aluminium species, Cp*₂AlH or Cp*AlH₂, through reductive elimination (Scheme 3-11). For example, the reaction of AlCl₃ (172) with LiAlH₄ (174) in a 3:1 molar ratio afforded HAlCl₂ (175), which may undergo anion exchange with two equivalents of Cp*K to form Cp*₂AlH (176) in 82% yield; Cp*AlH₂ was prepared using a similar strategy. The structure of Cp*₂AlH (176) was confirmed by X-ray crystallography, which confirmed the cis relationship between the ‘Cp*’ and ‘H’ substituents (Figure 3-4). In toluene at 110 °C, Cp*₂AlH was shown to exist in an equilibration with Cp*Al(I) (173b) and Cp*H through reversible processes of reductive elimination and oxidative addition. However, this equilibrium was shown to be shifted to the right side because of the poor solubility of Cp*Al(I) (173b), which precipitated under these conditions. Alternatively, Cp*Al(I) (173b) was obtained in 93% yield by heating Cp*₂AlH (176) under solvent-free conditions to 110 °C in a high vacuum. Data regarding ²⁷Al NMR spectroscopy were not reported in this paper. This synthesis was an efficient way to access Cp*Al(I) (173b), which may prove to be critical for the development of transition metal-like redox catalysis.
using a suitable aluminium(I) species.

Scheme 3-11 Synthesis of Cp*Al(I) (173b) through reduction elimination of aluminium(III)\textsuperscript{119}

Figure 3-4 A substrate for reductive elimination, Cp*2AlH [176; figure was directly copied from the original source]\textsuperscript{119}

In 2000, another room temperature-stable monomeric aluminium(I) compound, Al(I)[nacnac] (179), was reported by Roesky \textit{et al.} (nacnac = HC[\(\text{C(NAr)}\)Me]$_2$, Ar = 2,6-\textit{Pr$_2$–C$_6$H$_3$}; Scheme 3-12).\textsuperscript{120} Here, the sterically demanding β-diketiminate ligand proved to be critical to protect the aluminium(I) center. Furthermore, thanks to the coordination of this electron-rich ligand, the lone pair of electrons at the aluminium(I) center was shown to display a singlet carbene character. In the synthesis, the reaction of a suitable
aluminium(III) precursor, Al(nacnac)Me₂ with I₂ in 1:2 molar ratio afforded Al(nacnac)I₂ as yellow crystals in 83% yield. This diiodide compound underwent partial reduction with two equivalents of potassium(0) to form Al(I)[nacnac] (179) as red crystals in 21% yield. The structure of 179 was confirmed by X-ray crystallography (Figure 3-5). According to the paper, this aluminium(I) species proved to be ‘silent’ in ²⁷Al NMR spectroscopy.

![Scheme 3-12 Synthesis of Al(I)[(nacnac)] (179)](image)

3.1.5 Stoichiometric Use of Monomeric Aluminium(I) Species

Similar to gallium(I), aluminium(I) displays both vacant low-energy p orbitals and a lone pair of electrons in an sp-type orbital. In turn, it may potentially display both acceptor and donor properties at a single site (ambiphilicity). This characteristic feature depends on the
ligand or the counter anion, by which the aluminium(I) center is coordinated.

### 3.1.5.1 Stoichiometric Lewis Basicity

In 2000, the first example of an aluminium(I)–boron(III) donor–acceptor complex, Cp*Al(I)•B(C₆F₅)₃ (180), was reported by Cowley et al. (Scheme 3-13). The reaction of monomeric Cp*Al(I) (173b) with B(C₆F₅)₃ in 1:1 molar ratio in toluene at room temperature afforded the donor–acceptor complex 180 as colorless crystals in 40% yield. The structure of 180 was confirmed by X-ray crystallography (Figure 3-6). The $^{27}$Al NMR analysis of 180 in solution revealed a new broad singlet resonance at $\delta = -59$ ppm, whereas the monomeric Cp*Al(I) (173b) displayed a singlet resonance at $\delta = -81$ ppm. The $^{11}$B NMR analysis of 180 in solution showed a new singlet resonance at $\delta = -33$ ppm, consistent with a tetracoordinate boron complex, whereas B(C₆F₅)₃ displayed a singlet resonance at $\delta = 60$ ppm. All these data supported a dative bond between the aluminium(I) and boron(III) centers, clearly indicating the Lewis basicity of Cp*Al(I) (173b).

![Scheme 3-13 Synthesis of the donor–acceptor complex Cp*Al(I)•B(C₆F₅)₃ (180)](image-url)
In 2000, an aluminium(I)–aluminium(III) donor–acceptor complex, Cp*Al(I)•Al(III)(C₆F₅)₃ (182), was reported by the same group (Scheme 3-14). The reaction of monomeric Cp*Al(I) (173b) with Al(C₆F₅)₃•PhMe in a 1:1 molar ratio in toluene afforded the aluminium(I)–aluminium(III) donor–acceptor complex as yellow crystals in 80% yield. The structure of 182 was confirmed by X-ray crystallography (Figure 3-7). The $^{27}$Al NMR analysis of 182 in solution showed a singlet resonances at $\delta = -116$ ppm and $\delta = 107$ ppm, which proved to be consistent with the presence of aluminium(I) and aluminium(III) centers, respectively.

![Figure 3-6 Structure of Cp*Al(I)•B(C₆F₅)₃, [180; figure was directly copied from the original source]](image)

Scheme 3-14 Synthesis of the donor–acceptor complex Cp*Al(I)•Al(III)(C₆F₅)₃ (182)
Both examples in this section proved that aluminium(I) species could act as a metallic Lewis base towards hard Lewis acids, such as boron(III) or aluminium(III). Such a feature may be exploited in metal Lewis base catalysis.

3.1.5.2 Stoichiometric Lewis Acidity

In 2004, Roesky et al. reported that a supposed Lewis acidic aluminium(I) complex, Al(I)[nacnac] (179), may be coordinated by a Lewis basic N-heterocyclic carbene ligand of type 183 or 184 (Scheme 3-15).\textsuperscript{124} To the best of our knowledge, this proposed NHC–aluminium(I) donor–acceptor complex proved to be the only claim indicating the Lewis acidity of an aluminium(I) center in the presence of a stronger donor. The reaction of Al(I)[nacnac] (179) and an NHC in a 1:1 molar ratio in toluene at 120 °C afforded the novel aluminium(III) complex 185 as colorless crystals in 48% yield. Indeed, under these harsh reaction conditions a formal proton migration –potentially triggered by the basic NHC–occurred from a lateral carbon atom of the nacnac ligand to the aluminium(I) center thus ‘oxidizing’ the latter to aluminium(III). The reaction product 185 was characterized by
X-ray crystallography, which confirmed that the generated aluminium(III) center was coordinated by the NHC ligand. Both the Al(I) precursor 179 and the Al(III) product 185 were shown to be ‘silent’ in $^{27}$Al NMR spectroscopy.

![Scheme 3-15 Reaction between Al(I)[nacnac] (179) and an NHC of type 183 or 184](image)

3.1.5.3 Stoichiometric Ambiphilicity

In 2005, Roesky et al. reported the only example of a stable aluminium(I) complex 186, in which the aluminium(I) center displayed an ambiphilic behaviour (Scheme 3-16 and Figure 3-8). The reaction of Al(I)[nacnac] (179) with B(C$_6$F$_5$)$_3$ (33) in a 1:1 molar ratio afforded the novel aluminium(I) species 186 as colorless crystals in 19% yield. Both Al(I)[nacnac] (179) and the novel Al(I) complex 186 proved to be ‘silent’ in $^{27}$Al NMR spectroscopy. The intrinsic feature of Al(I)[nacnac] (179) was proposed to be its strong Lewis basicity, i.e., the facile donation of its lone pair of electrons to the electrophilic boron center. As a consequence of the formation of this aluminium(I)–boron(III) donor–acceptor bond, the aluminium(I) center may become more electron-poor, i.e., it may accept electron density from an electron-rich fluorine atom in proximity (Scheme 3-16 and Figure 3-8). This unique example highlighted for the first time that an aluminium(I) center could unfold
both a Lewis basic and a Lewis acidic character at a single metallic site (ambiphilicity). Such an unusual feature may be exploited in dual catalysis.

Scheme 3-16 Synthesis of the ambiphilic aluminium(I) species [nacnac]Al(I)•B(C₆F₅)₃ (186)₁²⁶

![Scheme 3-16](image)

Figure 3-8 Structure of [nacnac]Al(I)•B(C₆F₅)₃ [186; figure was directly copied from the original source]₁²⁶

3.1.6 Stoichiometric Use of Aluminium(0) in Organic Synthesis

The Barbier reaction, developed by Barbier in 1899, has been well investigated. This important synthetic organic reaction was shown to be particularly useful for the efficient metal-mediated alkylation of carbonyl compounds. In this one-pot reaction, an electrophilic carbonyl derivative and an alkyl halide species may be used the presence of a
stoichiometric amount of a suitable metal, e.g. aluminium(0). In 1987, an aluminium(0)-promoted Barbier reaction was first reported by Torii et al. (Scheme 3-17).\textsuperscript{128} This allylation of carbonyl electrophiles proceeded smoothly with a catalytic amount of lead(II) bromide in the presence of a stoichiometric amount of aluminium foil. The role of aluminium(0) was proposed to be that of a reductant for the \textit{in situ} generation of lead(0).

\begin{center}
\textbf{Scheme 3-17} Lead-catalyzed Al(0)-mediated Barbier allylation of carbonyl compounds\textsuperscript{128}
\end{center}
3.2 Aims

Aluminium is the most abundant metal in the Earth’s crust. While Al(III) species proved to be established Lewis acid catalysts in organic synthesis, the chemistry of Al(I) remained under-explored. Similar to gallium, Al(I) features vacant p orbitals and a lone pair of electrons in an sp-type orbital, i.e., potential Lewis acidity and Lewis basicity at a single site (Figure 3-9). Moreover, compared to gallium, Al(0) displays similar first ionization and reduction potentials. In turn, a similar exploitation of these low-oxidation aluminium species in catalysis may be anticipated. At the outset of this project however, the catalytic use of Al(I) or Al(0) in organic synthesis had not been reported.

![Figure 3-9 General comparison: Ga(0) vs. Al(0) and Ga(I) vs. Al(I)](image)

We aimed to apply the Krossing–Slattery method to the in situ generation of an Al(I) species for use in catalysis, i.e., the activation of both basic and acidic reagents at a single site (Scheme 3-18).9a Based on the standard reduction potentials, Ag(I) may indeed be able to oxidize Al(0) to Al(I). Compared to gallium however, Al(I) has a smaller ionic radius, which may result in distinct properties and thus a different catalysis potential. Moreover, Al(I) species are considered less stable compared to gallium, thus adding to the challenge of novel catalysis development. On the other hand, the sensitive $^{27}$Al isotope may facilitate the detection of catalytically active Al(I) species by $^{27}$Al NMR spectroscopy.
Scheme 3-18 Generic scheme for the anticipated \textit{in situ} Al(I) catalysis

\[
\begin{align*}
\text{Al}^0 + \text{AgX} \quad &\xrightarrow{?} \quad \text{Al}^0 \quad \text{AgX} \\
\text{in situ Al}^0 \text{X catalyst} &\quad \xrightarrow{?} \quad Y \\
X = B, Si, ... &
\end{align*}
\]

reduction potential of Ag\textit{}/Ag\textit{0}: +0.799 V
3.3 Results and Discussion

As outlined above, the idea was to generate in situ an aluminium(I) species from aluminium(0) using a suitable oxidant under mild conditions. This potential catalyst was then examined in C–C bond formations with various reagents. All catalysis experiments using allyl boronic ester 71 were conducted by a visiting undergraduate student, Mohammad Aliim Bin Khamis, under my direct supervision in the laboratory. The catalysis experiments using allyl silane 94 and the stoichiometric $^{27}$Al NMR studies were carried out by myself.

Based on the data obtained in the gallium(I) project (cf. Chapters 1 and 2), we aimed to apply the same strategy to develop a potential low-oxidation state aluminium catalysis (Figure 3-10). Indeed, an allyl boronic ester may be activated by a Lewis base and, through transmetallation, an allyl–Al(I) species may be generated in situ. The latter may react with an electrophile pre-activated by an aluminium(I) Lewis acid species. Alternatively, such a catalyst system may be used for other allyl reagents, which may not require a pre-activation, i.e., an allyl silane.

![Figure 3-10](image)

**Figure 3-10** Anticipated activation of an allyl boronic ester and an allyl silane

3.3.1 Preliminary Results with the Combination Al(0)/Ag(I)

3.3.1.1 Initial Experiments Under Ultrasonication

Based on the gallium(I) study, we initially used acetal 70a and allyl boronic ester 71 in toluene at 40–45 °C for 16 h (Table 3-1). The potential catalyst was formed in situ using aluminium(0) and silver triflate, in the absence or presence of various ligands, under
ultrasonication conditions. Dibenzyl ether (DBE, 25 mol% in mesitylene) was used as an internal standard in order to quantitatively determine the NMR yield of the homoallylic ether product 72a.

Table 3-1 Initial experiments under ultrasonication

<table>
<thead>
<tr>
<th>Entry</th>
<th>Catalyst (mol%)</th>
<th>Ligand</th>
<th>NMR Yield (%)[a]</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Al(^0) (20) / AgOTf (10)</td>
<td>–</td>
<td>3</td>
</tr>
<tr>
<td>2</td>
<td>Al(^0) (20) / –</td>
<td>–</td>
<td>NR ([b])</td>
</tr>
<tr>
<td>3</td>
<td>–                / AgOTf (10)</td>
<td>–</td>
<td>NR ([b])</td>
</tr>
<tr>
<td>4</td>
<td>Al(^0) (20) / AgOTf (10)</td>
<td>[18]crown-6</td>
<td>NR ([b])</td>
</tr>
<tr>
<td>5</td>
<td>Al(^0) (20) / AgOTf (10)</td>
<td>[15]crown-5</td>
<td>NR ([b])</td>
</tr>
<tr>
<td>6</td>
<td>Al(^0) (20) / AgOTf (10)</td>
<td>PPh(_3)</td>
<td>NR ([b])</td>
</tr>
<tr>
<td>7</td>
<td>Al(^0) (20) / AgOTf (10)</td>
<td>[1]</td>
<td>NR ([b])</td>
</tr>
<tr>
<td>8</td>
<td>Al(^0) (20) / AgOTf (10)</td>
<td>[2]</td>
<td>NR ([b])</td>
</tr>
</tbody>
</table>

[a] The yield was determined by 1H NMR analysis of a reaction aliquot; IS: dibenzyl ether (25 mol%). [b] NR = no reaction; the desired product was not detected (\(^1\)H NMR analysis of a reaction aliquot).

The use of 20 mol% of aluminium(0) and 10 mol% of silver triflate – in the absence of a ligand – resulted in the formation of 3% of the desired product as detectable by \(^1\)H NMR analysis of an aliquot of the reaction mixture (Table 3-1, entry 1). While this yield was very low, we wanted to confirm that both catalyst components used separately were inactive. Indeed, the sole use of aluminium(0) or AgOTf as a potential catalyst did not give any
conversion of the starting materials (entries 2 and 3). In addition to these control experiments, we examined the effect of ligands – such as crown ethers, PPh₃, and NHCs – on the Al(0)/AgOTf catalyst system (entries 4–8). In all cases, the C–C bond formation did not proceed. These results could be ascribed to the decreased Lewis acidity of the in situ formed aluminium(I) center, which would be coordinated by a ligand. Alternatively, such a ligand may also coordinate to the electrophilic silver(I) center, which may potentially decrease its oxidation ability thereby suppressing the formation of aluminium(I). At that stage, we considered that ultrasonication may not be effective for the Ag-mediated oxidation of aluminium(0) to alumumium(I). In turn, it was decided to carry out the catalytic reactions with conventional heating and stirring.

3.3.1.2 Initial Experiments with Conventional Heating and Stirring

In order to facilitate both product formation and detection, the experiments were carried out using 40 mol% of aluminium(0) and 20 mol% of the corresponding silver salt (Table 3-2). Four different silver salts were examined as an oxidant, and the reactions were initially conducted in toluene at 40 °C, before moving on to 60 °C. The conversion of acetal 70a to product 72a was determined by ¹H NMR analysis of an aliquot of the reaction mixture through integration of remaining acetal 70a vs. integration of product 72a – an internal standard was not used.

Table 3-2 Initial experiments with conventional heating and stirring

<table>
<thead>
<tr>
<th>OMe</th>
<th>Ph</th>
<th>OMe</th>
</tr>
</thead>
<tbody>
<tr>
<td>70a</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

\[ \text{OMe} \quad \text{Ph} \quad \text{OMe} \]

\[
\begin{align*}
\text{OMe} & \quad \text{Ph} & \quad \text{OMe} \\
\text{70a} & \quad & \\
\text{1.1 equiv} & & \\
\end{align*}
\]

\[ \begin{align*}
& \text{OMe} \quad \text{Ph} \\
& \text{72a} \\
\end{align*} \]

\[ \begin{align*}
\text{OMe} & \quad \text{Ph} \\
\text{72a} & \\
\end{align*} \]

\[ \begin{align*}
\text{PhMe (1.0 M), 40–60 °C, 38 h} \\
\text{Al}^+ (40 \text{ mol%}) / \text{AgX (20 mol%)} \]

\[ \text{B(pin)} \]

\[ \text{71} \]

\[ \text{71} \]
The conversion of 1a to 3a was determined by $^1$H NMR analysis of a reaction aliquot. The desired product was not detected ($^1$H NMR analysis of a reaction aliquot).

Unfortunately, the use of aluminium(0) and AgOTf gave no reaction at 40 °C (Table 3-2, entry 1). However, increasing the reaction temperature to 60 °C led to complete conversion of electrophile 70a (entry 1). Interestingly, the use of AgBF$_4$ as a co-catalyst at 40 °C proved to be substantially more effective with >99% conversion of 70a (entry 2). In contrast, the use of AgF was shown to be much less efficient with a conversion of 20% at 40 °C and 57% at 60 °C, respectively (entry 3). Finally, under the same conditions, the use of AgI failed to give any conversion of the starting materials (entry 4). In order to confirm that a potentially generated low-oxidation state aluminium species was responsible for the reactivity, control experiments had to be carried out.

### 3.3.1.3 Control Experiments

We selected the most effective silver co-catalyst, AgBF$_4$, in order to confirm the full conversion of 70a to 72a and in order to conduct control experiments (Table 3-3). This time, dibenzyl ether (DBE, 25 mol% in mesitylene) was used as an internal standard in order to quantitatively determine the NMR yield of 72a.

<table>
<thead>
<tr>
<th>Entry</th>
<th>AgX</th>
<th>Conv (%)$^a$</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>40 °C, 18 h</td>
</tr>
<tr>
<td>1</td>
<td>AgOTf</td>
<td>NR$^b$</td>
</tr>
<tr>
<td>2</td>
<td>AgBF$_4$</td>
<td>&gt;99</td>
</tr>
<tr>
<td>3</td>
<td>AgF</td>
<td>20</td>
</tr>
<tr>
<td>4</td>
<td>AgI</td>
<td>NR$^b$</td>
</tr>
</tbody>
</table>

[a] The conversion of 1a to 3a was determined by $^1$H NMR analysis of a reaction aliquot. [b] NR = no reaction; the desired product was not detected ($^1$H NMR analysis of a reaction aliquot).

Table 3-3 Control experiments for the proof of principle of in situ Al(I) catalysis
The yield was determined by $^1$H NMR analysis of a reaction aliquot: IS = dibenzyl ether (25 mol%).  [b] NR = no reaction; the desired product was not detected ($^1$H NMR analysis of a reaction aliquot).

The combined use of aluminium(0) and AgBF$_4$ afforded the product in 48% NMR yield (entry 1). Expectedly, the use of aluminium(0) as a potential single catalyst proved to be ineffective (entry 2). Surprisingly however, the sole use of AgBF$_4$ provided product 72a in 22% NMR yield (entry 3). Typically, the BF$_4^-$ anion has been considered as a stable counter anion. However, under certain conditions the Lewis acid BF$_3$ and the Lewis base F$^-$ may be generated in situ (Scheme 3-19). Silver(I) has not been considered as a very strong, oxophilic Lewis acid. On the other hand, in the present context, BF$_3$ may be a suitable Lewis acid to activate acetal 70a (formation of an oxocarbenium ion; Scheme 3-19). In the same line, F$^-$ should be a suitable Lewis base for the activation of the allyl boronic ester 71. The boron–ate complex thus generated may add to the oxocarbenium ion, which may explain why the use of AgBF$_4$ generated product 72a to a certain extent (Scheme 3-19).

![Scheme 3-19 Postulated decomposition of AgBF$_4$ and subsequent bond activation of the reactants](image-url)
In order to prove or disprove this hypothesis, the reaction mixture – Table 3-3, entry 1 – was examined with $^{19}$F NMR spectroscopy. Three resonances were detected in the $^{19}$F NMR spectrum (Figure 3-11). Based on the literature, the resonances at $\delta = -151$ ppm and -133 ppm were ascribed to $\text{BF}_4^-$ and $\text{F}^-$, respectively. However, one unidentified signal was observed at $\delta = -155$ ppm. This signal may be ascribed to a new boron–ate complex, such as MeO–$\text{BF}_3^-$, or another boron center coordinated by $\text{F}^-$. Unfortunately, the $^{11}$B NMR analysis proved to be rather challenging because the corresponding chart was very messy.

At that stage, the combined use of aluminium(0) and AgBF$_4$ afforded product 72a in moderate yield (TON ~ 2–3). However, the sole use of AgBF$_4$ furnished as well product 72a, albeit in a lower yield. Therefore, AgBF$_4$ was considered not to be an ideal co-catalyst for this reaction system. In turn, other silver salts were considered in order to optimize the catalyst system.

![Figure 3-11 $^{19}$F NMR spectrum for the attempted catalysis using an Al(0)/AgBF$_4$ system (Table 3-3, Entry 1)](QinBo_BQ2212-2_120216_1H-11B-19F_pr500_FebVI-0705.012.001.1r.esp)
3.3.1.4 Silver Salt Screening

In order to find a more suitable silver salt as co-catalyst, several other commercially available silver(I) salts were screened under similar reaction conditions (Table 3-4).

Table 3-4 Silver salt screening

<table>
<thead>
<tr>
<th>Entry</th>
<th>Al(^0)</th>
<th>AgX</th>
<th>Conv (%)</th>
<th>Conv (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>40 °C, 20 h</td>
<td>60 °C, 38 h</td>
</tr>
<tr>
<td>1</td>
<td>+</td>
<td>AgOTf</td>
<td>7</td>
<td>24</td>
</tr>
<tr>
<td>2</td>
<td>−</td>
<td>AgOTf</td>
<td>NR</td>
<td>NR</td>
</tr>
<tr>
<td>3</td>
<td>+</td>
<td>Ag(_2)CO(_3)</td>
<td>NR</td>
<td>NR</td>
</tr>
<tr>
<td>4</td>
<td>+</td>
<td>AgNO(_3)</td>
<td>NR</td>
<td>NR</td>
</tr>
<tr>
<td>5</td>
<td>+</td>
<td>Ag(_3)PO(_4)</td>
<td>NR</td>
<td>NR</td>
</tr>
<tr>
<td>6</td>
<td>+</td>
<td>Ag(_2)O</td>
<td>NR</td>
<td>NR</td>
</tr>
<tr>
<td>7</td>
<td>+</td>
<td>AgOCN</td>
<td>NR</td>
<td>NR</td>
</tr>
<tr>
<td>8</td>
<td>+</td>
<td>AgCl</td>
<td>NR</td>
<td>NR</td>
</tr>
<tr>
<td>9</td>
<td>+</td>
<td>AgBr</td>
<td>NR</td>
<td>NR</td>
</tr>
<tr>
<td>10</td>
<td>+</td>
<td>AgClO(_4)</td>
<td>9</td>
<td>28</td>
</tr>
<tr>
<td>11</td>
<td>−</td>
<td>AgClO(_4)</td>
<td>NR</td>
<td>NR</td>
</tr>
</tbody>
</table>

[a] The conversion of 70a to 72a was determined by \(^1\)H NMR analysis of a reaction aliquot. [b] NR = no reaction; the desired product was not detected (\(^1\)H NMR analysis of a reaction aliquot). [c] The control experiment was carried out in the absence of Al(0).

Using 40 mol% of aluminium(0) and 20 mol% of silver triflate, the conversion of 70a to 72a was 7% based on the \(^1\)H NMR analysis of an aliquot of the reaction mixture (Table 3-4, entry 1). Increasing the reaction temperature to 60 °C led to 24% conversion (entry 1). While this conversion was very low, we confirmed that the use of AgOTf as a potential single catalyst proved to be ineffective (entry 2). Under the same conditions, the use of various other silver salts failed to give any conversion of the starting materials (entries 3–9).
Finally, the combined use of aluminium(0) and AgClO$_4$ showed similar reactivity, providing a conversion $70a$–$72a$ of 9% at 40 °C and 28% at 60 °C, respectively (entry 10). It is noted that the use of AgClO$_4$ as a potential single catalyst proved to be inefficient (entry 11). At that stage, only the combined use of aluminium(0) and AgOTf or AgClO$_4$ provided the desired product $72a$ in rather low yields (entries 1 and 10). In order to improve the catalyst activity, the reaction conditions had to be optimized for each silver co-catalyst.

### 3.3.1.5 The Combination of Al(0)/AgOTf

**Solvent Screening**

First, we used AgOTf as a co-catalyst in order to examine the effect of aromatic and etheral solvents. The experiments were conducted using 40 mol% of aluminium(0) and 20% mol% of AgOTf at 40 °C, before moving on to 60 °C (Table 3-5).

<table>
<thead>
<tr>
<th>Entry</th>
<th>Solvent ($\varepsilon_{\text{rel}}$)</th>
<th>Conv (%)$^[a]$</th>
<th>40 °C, 19 h</th>
<th>60 °C, 24 h</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>dioxane (2.3)</td>
<td>NR$^[[b]]$</td>
<td>23</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>PhMe (2.4)</td>
<td>7</td>
<td>24</td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>Et$_2$O (4.3)</td>
<td>4</td>
<td>12</td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>THF (7.5)</td>
<td>polymerized</td>
<td>polymerized</td>
<td></td>
</tr>
<tr>
<td>5</td>
<td>BTF (9.2)</td>
<td>7</td>
<td>65</td>
<td></td>
</tr>
</tbody>
</table>

[a] The conversion of $1a$ to $3a$ was determined by $^1$H NMR analysis of a reaction aliquot. [b] NR = no reaction; the desired product was not detected ($^1$H NMR analysis of a reaction aliquot).

Unfortunately, the use of dioxane as a solvent gave no reaction at 40 °C, and only 23%
conversion at 60 °C (Table 3-5, entry 1). The use of toluene and Et₂O showed similarly low reactivity at 40 °C; unfortunately, increasing the reaction temperature to 60 °C did not lead to a substantially higher yield (entries 2 and 3). It is noted that toluene was more effective than diethyl ether. Interestingly, the use of THF failed to give the desired product (entry 4). Instead, THF seemed to have polymerized with the in situ formed aluminium(I) Lewis acid, because the reaction mixture completely solidified. Typically, THF has been a commonly used, stable etheral solvent. However, under acidic conditions THF may undergo ring-opening polymerization (Figure 3-12).

![Figure 3-12 Proposed aluminium(I)-initiated THF ring-opening polymerization](image)

Finally, the use of benzotrifluoride (BTF) afforded a conversion 70a–to–72a of 7% at 40 °C and 65% at 60 °C, respectively (entry 5). We thought that the presence of a fluorine atom in the solvent structure may play an important role in both the stabilization and the activation of a potentially ambiphilic Al(I)OTf species through coordination an electron-rich fluorine atom to the postulated aluminium(I) center, i.e., BTF may act as a ligand (Figure 3-13). This scenario may be similar to the one proposed by Roesky et al. for the ambiphilic aluminium(I) complex 186 (cf. Scheme 3-16 and Figure 3-8). Such a coordination may afford an aluminium(I)–BTF complex, which may protect the aluminium(I) center from redox-disproportionation. It is noted that in our studies a redox-disproportionation of aluminium(I) was not detected. Next, the effect of BTF had to be confirmed.

![Figure 3-13 Anticipated ambiphilic coordination of Al(I) by benzotrifluoride](image)
**Toluene vs. BTF**

For direct comparison, the experiments were carried out in two aromatic solvents, toluene and BTF, at 50 °C for 68 h (Scheme 3-20).

![Scheme 3-20 Solvent effect: PhMe vs. BTF](image_url)

The use of toluene proved to be less efficient with a conversion of 70a to 72a of 41%, whereas BTF was shown to provide a conversion of 70a to 72a of 86%. Under the same conditions, the use of AgOTf as a potential single catalyst failed to give any conversion of the starting materials, which represented a proof-of-principle of our concept. At that stage, BTF was considered to be a more suitable solvent for this catalyst system. Next, the NMR yield of product 72a had to be confirmed.

**Control Experiments Re-Visited**

Control experiments were carried out in toluene and BTF at 50 °C for 70 h (Table 3-6). Dibenzyl ether (DBE, 25 mol% in mesitylene) was used as an internal standard in order to quantitatively determine the NMR yield of 72a.

| Table 3-6 Control experiments re-visited |  }
The yield was determined by $^1$H NMR analysis of a reaction aliquot: IS = dibenzyl ether (25 mol%).  

<table>
<thead>
<tr>
<th>Entry</th>
<th>Catalyst (mol%)</th>
<th>Solvent</th>
<th>NMR Yield (%)$^a$</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Al(0) (40) / AgOTf (20)</td>
<td>PhMe</td>
<td>9 (17)$^b$</td>
</tr>
<tr>
<td>2</td>
<td>– / AgOTf (20)</td>
<td>PhMe</td>
<td>NR$^c$</td>
</tr>
<tr>
<td>3</td>
<td>Al(0) (40) / –</td>
<td>PhMe</td>
<td>NR$^c$</td>
</tr>
<tr>
<td>4</td>
<td>Al(0) (40) / AgOTf (20)</td>
<td>BTF</td>
<td>15 (15)$^b$</td>
</tr>
<tr>
<td>5</td>
<td>– / AgOTf (20)</td>
<td>BTF</td>
<td>NR$^c$</td>
</tr>
<tr>
<td>6</td>
<td>Al(0) (40) / –</td>
<td>–</td>
<td>NR$^c$</td>
</tr>
</tbody>
</table>

$^a$ The yield was determined by $^1$H NMR analysis of a reaction aliquot: IS = dibenzyl ether (25 mol%).  

$^b$ Mass balance (MB, %) = percentage of (product + remaining acetal).  

$^c$ NR = no reaction; the desired product was not detected ($^1$H NMR analysis of a reaction aliquot).

Unfortunately, the combined use of 40 mol% of aluminium(0) and 20 mol% of AgOTf in toluene provided the desired product 72a in only 9% NMR yield (vs. 41% conversion of 70a; entry 1). Unfortunately, at that stage the mass balance of this reaction was not satisfactory (17%), which may be explained by the potential formation of side-products. The latter may include a transient oxocarbenium ion, which may undergo pinacol-type coupling reactions under the electron-transfer conditions, or bisallylation. The detection of these side-products by $^1$H NMR spectroscopy may be difficult. Although the NMR yield of 72a was low, we carried out control experiments and confirmed that aluminium(0) and AgOTf were catalytically inactive when used separately (entries 2 and 3). The use of BTF afforded the desired product 72a in a slightly higher yield compared to the use of toluene (15% vs. 9%; entry 4). However, here again the mass balance proved to be very low (15%), which may be the result of side-reactions. Control experiments confirmed the viability of our aluminium(I) concept although a catalyst turnover did not proceed (entries 5 and 6).

### 3.3.1.6 The Combination of Al(0)/AgClO$_4$

Next, we examined the solvent effect for the combined use of aluminium(0) and AgClO$_4$ under otherwise identical conditions (Table 3-7).
Table 3-7 Solvent screening

![Image of a reaction scheme]

<table>
<thead>
<tr>
<th>Entry</th>
<th>Solvent (ε)</th>
<th>Conv (%)&lt;sup&gt;[a]&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>40 °C, 16 h</td>
</tr>
<tr>
<td>1</td>
<td>dioxane (2.3)</td>
<td>NR&lt;sup&gt;[b]&lt;/sup&gt;</td>
</tr>
<tr>
<td>2</td>
<td>PhMe (2.4)</td>
<td>9</td>
</tr>
<tr>
<td>3</td>
<td>Et&lt;sub&gt;2&lt;/sub&gt;O (4.3)</td>
<td>NR&lt;sup&gt;[b]&lt;/sup&gt;</td>
</tr>
<tr>
<td>4</td>
<td>THF (7.5)</td>
<td>NR&lt;sup&gt;[b]&lt;/sup&gt;</td>
</tr>
<tr>
<td>5</td>
<td>BTF (9.2)</td>
<td>NR</td>
</tr>
</tbody>
</table>

[a] The conversion to 3a was determined by <sup>1</sup>H NMR analysis of a reaction aliquot.  [b] NR = no reaction; the desired product was not detected (<sup>1</sup>H NMR analysis of a reaction aliquot).

Similar to the combination of aluminium(0) and AgOTf, the use of dioxane as a solvent gave no reaction at 40 °C, whereas increasing the reaction at 60 °C led to 28% conversion of 70a to 72a (Table 3-7, entry 1). A similar tendency was observed when toluene was used as a solvent (entry 2). Unfortunately, the use of diethyl ether, THF, and BTF proved to be ineffective (entries 3–5). Interestingly, the use of THF as a solvent did not trigger any ring-opening polymerization.

In summary, our preliminary results for the use of allyl boronic ester 71 showed that the combination aluminium(0)/AgBF₄ afforded product 72a in up to 48% NMR yield (Figure 3-14). Although the efficiency proved to be rather low, control experiments confirmed that our concept of low-oxidation state aluminium catalysis was viable. Typically, an allyl silane has been considered to display a higher intrinsic nucleophilicity compared to an allyl boronic ester. Thus, the activation of an electrophile with an aluminium(I) Lewis acid may be sufficient to trigger C–C bond formation.
3.3.2 Catalytic Allylation Using an Allyl Silane

According to our earlier study, allyl trimethyl silane 94 proved to be a suitable nucleophilic reagent for C–C bond formation with C(sp³) electrophiles in the presence of a gallium(I) Lewis acid catalyst (cf. Chapter 2). Since the use of an allyl boronic ester 71 did provide satisfactory results in this aluminium(I) approach, we aimed to employ an allyl silane 94 in order to develop an efficient catalytic reaction.

In the initial experiment, we used acetal 70a and an allyl silane 94 in toluene in the presence of 20 mol% of aluminium(0) and 10 mol% of AgOTf at 25 °C for 2 h (Table 3-8).

Table 3-8 Catalytic allylation using an allyl silane

<table>
<thead>
<tr>
<th>Entry</th>
<th>Catalyst (mol%)</th>
<th>Time (h)</th>
<th>NMR yield (%)&lt;sup&gt;a&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Al&lt;sub&gt;0&lt;/sub&gt; (20) / AgOTf (10)</td>
<td>2</td>
<td>49</td>
</tr>
<tr>
<td>2</td>
<td>Al&lt;sub&gt;0&lt;/sub&gt; (20) / AgOTf (10)</td>
<td>5</td>
<td>82</td>
</tr>
<tr>
<td>3</td>
<td>Al&lt;sub&gt;0&lt;/sub&gt; (20) / –</td>
<td>2</td>
<td>NR&lt;sup&gt;b&lt;/sup&gt;</td>
</tr>
<tr>
<td>4</td>
<td>– / AgOTf (10)</td>
<td>2</td>
<td>NR&lt;sup&gt;b&lt;/sup&gt;</td>
</tr>
</tbody>
</table>

[a] The yield was determined by ¹H NMR analysis of a reaction aliquot: IS = dibenzyl ether (25 mol%). [b] NR = no reaction; the desired product was not detected (¹H NMR analysis of a reaction aliquot).

The combined use of aluminium (0) and AgOTf resulted in the formation of the desired
product 72a in 49% NMR yield, as detectable by 1H NMR analysis of an aliquot of a reaction mixture (TON ~ 5, entry 1). Pleasingly, it was found that after 5 h product 72a was obtained in 82% NMR yield (TON ~ 8, entry 2). While the yield was not perfect, we confirmed that the catalyst components separately used were inactive (entries 3 and 4). In all cases, a mass balance of >95% was detected, and side-products were seemingly not formed (entries 1–4). These results suggested that the new catalyst system was able to catalyze the C–C bond formation in the presence of an intrinsically stronger nucleophile under mild conditions. In order to confirm the formation of a potential low-oxidation state aluminium species, stoichiometric mechanistic studies were carried out.

3.3.3 Stoichiometric $^{27}$Al NMR Studies

$^{27}$Aluminium has been shown to be a highly sensitive nucleus with 100% natural abundance and a nuclear spin $I = 5/2$. In turn, $^{27}$Al NMR spectroscopy has been a useful tool to detect the presence and the oxidation state of various aluminium species. Typically, an external standard, such as Al(D$_2$O)$_6^{3+}$ in aqueous solution, has been used. The $^{27}$Al NMR spectroscopic data mentioned in the introduction part have been summarized below (Figure 3-15). To the best of our knowledge, $^{27}$Al NMR spectroscopic data for aluminium(II) species have not been reported.

![Figure 3-15 $^{27}$Al NMR spectroscopic data of reported aluminium species](Image)

Since toluene gave the most promising results in catalysis, we used this solvent in the present
NMR study in order to examine the aluminium species generated by the Krossing–Slattery method. The mechanistic experiment was carried out using aluminium(0) and AgOTf in a 2:1 molar ratio with conventional heating and stirring at 50 °C (Scheme 3-21).

\[
\text{Al}^0 + \text{AgOTf} \rightarrow \text{Al}^0(\text{PhMe})_n\text{OTf} \quad \text{toluene solution}
\]

\[\text{27}^{\text{Al}}\text{NMR (ppm): } -22\]

**Scheme 3-21** Detection of low-oxidation state aluminium species

The \(^{27}\text{Al}\) NMR spectrum showed a clear single resonance at \(\delta = -22\) ppm in toluene (Figure 3-16, left chart). Based on the literature-reported aluminium(I) NMR data (Figure 3-15), a low-oxidation state aluminium species generally displayed resonances in the range \(\delta = 0 \sim -150\) ppm. Compared with the Cp* anion, the triflate anion has been considered substantially less coordinating or basic, which may explain the pronounced down-field shift. This result proved to be also consistent with the fact that aluminium(I) triflate (187) was used as a Lewis acid in our catalysis. Similar to the formation of Ga(I) complexes in Chapter 1 (Figure 1-34, cf. Figure 1-7, 1-18, 1-19, 1-22), the in situ formed Al(I) complexes may exist as \(\eta^6\) arene complexes in the presence of aromatic hydrocarbons.\(^{9a, 71}\) For comparison, a solution of commercially available Al(OTf)_3 in toluene was analyzed by \(^{27}\text{Al}\) NMR spectroscopy, resulting in a singlet resonance at \(\delta = 0.4\) ppm (Figure 3-15). These \(^{27}\text{Al}\) NMR data proved that our catalyst system was an in situ generated low-oxidation state aluminium species, rather than aluminium(III).

Next, the model substrates were added to the pre-formed low-oxidation state aluminium solution (Scheme 3-22).
As expected, based on $^1$H NMR analysis the conversion of 70a to 72a in this Al(I)-mediated C–C bond formation proved to be >99% (25 °C, 2 h). Interestingly, in the $^{27}$Al NMR spectrum two singlet resonances were observed at $\delta = -11$ ppm and $\delta = -16$ ppm, respectively (Figure 3-16, right chart). This result corresponded to a down-field shift relative to the initially used aluminium(I) species (187) ($\delta = -22$ ppm), which may be explained by considering that this C–C bond formation proceeded with the generation of neutral oxygen Lewis bases, e.g. homoallylic ether 72a and MeO–SiMe$_3$ (136). Both species may act as a ligand for the proposed Lewis acidic aluminium(I) center. In turn, the observation of two distinct resonances in $^{27}$Al NMR spectroscopy may be conceivable. The down-field shift may be explained by the so-called Gutmann analysis (Scheme 3-23): the coordination of a neutral Lewis base to a Lewis acid may lead to a decreased electron density at the Lewis acidic site because electron density may be spilled out to the Lewis basic ligand. In turn, the partial positive charge of the coordinated atom may increase, and
thus its Lewis acid character as well. Projected to the present case of an aluminium(I) center being coordinated by neutral oxygen Lewis bases, it may be concluded that the Al(I) Lewis acidity may slightly increase. In turn, a down-field shift in $^{27}$Al NMR spectroscopy may be conceivable.

**Scheme 3-23** Postulated effect of a neutral Lewis base on the Lewis acidity of an aluminium(I) species
3.4 Summary

In this chapter, we successfully applied the Krossing–Slattery method to the \textit{in situ} formation of low-oxidation state aluminium species, which were examined in catalysis. Preliminary results using acetal 70a and allyl boronic ester 71 showed that the combined use of Al(0) and AgOTf afforded product 72a in 15% NMR yield (Scheme 3-24, \textit{upper} scheme). Unfortunately, the mass balance of this transformation proved to be not satisfactory. On the other hand, the use of an allyl silane 94 as a stronger nucleophile was shown to be substantially more effective: product 72a was obtained in 82% NMR yield (Scheme 3-24, \textit{lower} scheme). Control experiments confirmed that Al(0) and AgOTf separately used were not catalytically active (proof of principle of our concept).

We were able to detect a low-oxidation state aluminium species, presumably Al(I)OTf, by \textit{\textsuperscript{27}}Al NMR spectroscopy. Indeed, Al(0) and AgOTf in a 2:1 molar ratio were reacted under catalysis conditions (Scheme 3-25). The resulting solution showed a sharp singlet resonance at $\delta = -22$ ppm in the \textit{\textsuperscript{27}}Al NMR analysis, whereas Al(OTf)$_3$ displayed a resonance at $\delta = 0.4$ ppm. This pre-formed Al(I)OTf solution mediated the C–C bond formation between acetal 1a and allyl trimethylsilane to afford product 3a in >99% conversion. The regeneration of the Al(I) catalyst was confirmed by \textit{\textsuperscript{27}}Al NMR spectroscopy as well. To the best of our knowledge, this chemistry represents the first example of low-oxidation state aluminium catalysis, which is of fundamental importance.
Scheme 3-25 Detection of an aluminium(I) species by $^{27}$Al NMR spectroscopy

\[
\text{Al}^0 + \text{AgOTf} \quad \xrightarrow{\text{PhMe (1.0 M), 50 °C, 16 h}} \quad \text{Al}^0 \quad \xrightarrow{187} \quad \text{toluene solution} \quad \text{Al}^0 + \text{AgOTf} \\
0.5 \text{ equiv} \quad \xrightarrow{} \quad - \text{Ag}^0 \quad \text{27Al NMR (ppm): } -22
\]
**Future Work**

First, with the promising catalysis results in hand using the novel system Al(0)/Ag(I), the reaction various reaction parameters will be further optimized. These include: solvent, concentration, temperature, ligand, counter anion. Second, additional electrophiles – such as aminals, ethers, carbohydrates, and epoxides etc.— will be examined for both low-oxidation state metal catalyst systems (M = Al and Ga; Figure 3-17). In the same line, further nucleophiles will be explored using the proposed low-valent Lewis acid, Lewis base, or dual catalysis (Figure 3-17). In this context, an interesting result has been already obtained (Figure 3-17, bottom scheme). Indeed, the combined use of Ga(0) and AgOTf resulted in a catalytic C–C bond formation between benzaldehyde and stannanes. Third, an efficient asymmetric version of the developed Ga(I) and Al(I) catalyses will be investigated by employing a whole range of chiral counter anions and ligands.

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**Figure 3-17** Potential future substrates – preliminary results for the catalytic C–Sn bond activation
Additionally, electron-rich Ga(I) or Al(I) species will be explored in transition metal-like redox catalysis (Figure 3-18). As described in Chapter 1 (cf. Figure 1-27), the reductive elimination is expected to be the most challenging step because Ga(III) and Al(III) have been known to be thermodynamically more stable than the corresponding species in the low-oxidation state ‘+I’. In order to address this issue, the reaction conditions could be chosen to be ‘reductive’, i.e., use of electrochemistry. Alternatively, the use of a suitable sterically demanding ligand —such as a carbene (NHC, CAAC), a monophosphine, or a β-diketiminate— may force the unfavorable reductive elimination step (Figure 3-18).

![Figure 3-18 Exploiting Ga(I) and Al(I) in transition metal-like redox catalysis](image)

Finally, different types of oxidants will be investigated as co-catalysts. In this context, it is noted that the system Ag(I)/Ag(0) (+0.799) has a similar standard reduction potential compared to the system Fe(III)/Fe(II) (+0.771 V; Figure 3-19; upper scheme). In turn, Fe(III) species may be a suitable oxidant for the partial oxidation of Ga(0) or Al(0) species to Ga(I) or Al(I) catalysts, which may suggest the use of the soluble Fe(II) by-product as a co-catalyst in certain transformations. In a preliminary experiment, Fe(OTf)_3 has been used
in combination with Ga(0) (Figure 3-19; lower scheme). Pleasingly, we have been able to detect Ga(I)OTf by $^{71}$Ga NMR spectroscopy ($\delta = -699$ ppm). This approach may open up a whole variety of novel low-oxidation state metal catalysis in the future.

Figure 3-19 Fe(III) co-catalysis – preliminary result for the Fe(III)-mediated in situ generation of Ga(I)
CHAPTER 4: EXPERIMENTAL

4.1 General Experimental

Unless otherwise stated, all reagents purchased from commercial suppliers were used directly and all catalytic reactions were carried out in a nitrogen glove box with oven–dried apparatus and a magnetic stirrer bar. All the solvents were stored in a nitrogen glove box over 4 Å molecular sieves to prevent oxygen and moisture, including dioxane, benzene, toluene, mesitylene, diethyl ether, dimethoxyethane, THF, DCE and MeCN. THF, toluene, diethyl ether were distilled over Na\(^0\) with benzophenone indicator and stored over 4 Å molecular sieves. Solvent dryness was confirmed using the Karl-Fischer apparatus. Thin layer chromatography (TLC) was performed on Merck DFALufoilien 60F\(_{254}\) 0.2 mm pre-coated plates. Preparative thin-layer Chromatography (PTLC) was carried out on self-prepared plates prepared from Wakogel B-5F (particle size 45 µm). Product spots were visualized by UV light at 254 nm. Flash column chromatography was carried out using silica gel (Fisher Scientific 60 Å particle size 40–63 µm). Infrared spectra were recorded on a Shimadzu IRAffinity-1 instrument on isolated NMR sample in CDCl\(_3\) using the attenuated total reflectance sampling technique from teaching lab in School of Chemistry, University of Edinburgh. Nuclear Magnetic Resonance (NMR) spectra were recorded on a Bruker AVA400, Bruker AVA500, Bruker PRO500, or Bruker AVA600 spectrometer, operating at 400 MHz, 500 MHz, 500 MHz or 600 MHz for \(^1\)H NMR, and 100 MHz, 125 MHz, or 150 MHz for \(^13\)C NMR, and 77 MHz for \(^2\)D NMR, and 128 MHz, or 160 MHz for \(^11\)B NMR, and 128 MHz for \(^19\)F NMR and 162 MHz or 203 MHz \(^31\)P NMR. Chemical shifts (\(\delta\)) were quoted in parts per million (ppm) downfield of tetramethylsilane (TMS), or in the scale relative to the corresponding solvent used as an internal reference. Abbreviations used in the description of resonances are: s (singlet), d (doublet), t (triplet), q (quartet), m (multiplet) and br (broad). High-resolution mass spectra (HRMS) were recorded using electrospray ionization (ESI) technique on a Finnigan MAT 900 XLT spectrometer in School of Chemistry, University of Edinburgh. Chiral HPLC analyses were performed on a
Shimadzu LC-20AT with an SPD-20A detector using 4.6 x 250 mm columns from CHIRALPAK. Ultrasonicator bath FB15049 from Fisherbrand was used (power level: 37 kHz).

Acetals 70a (99%, ALDRICH), 70h (97%, ALDRICH), 70o (97%, TCI), 70v (98%, ALFA AESAR), as well as ketal 70z* (99%, ACROS ORGANICS), benzyl aldehyde (64, 99.5%, ALDRICH), allenyl boronic acid pinacol ester (86, 97%, ALDRICH), allyl trimethylsilane (94, 98%, ALDRICH), allyl boronic acid MIDA ester (ALDRICH) potassium allyl trifluoroborate (95%, ALDRICH), allyl tributylstannane (97%, ACROS ORGANICS) and allenyl tributylstannane (80%, ALFA AESAR) were commercially available and stored in a nitrogen glove box or a fridge. Other acetals,131,102,132,133 aminal 133134 and ether 138 are literature-known compounds and were prepared accordingly. Allyl reagents 71,63 71–[d2],135 11098, 13696 were prepared according to the reported methods; their analyses are in full agreement with the reported data. Trimethyl orthoformate (99%, ALDRICH), trimethyl borate (99%, ALDRICH), allylmagnesium bromide solution (1.0 M in diethyl ether, ALDRICH), pinacol (99%, ALFA AESAR), chloro(trimethyl)silane (143, 98%, ALDRICH), d2-chloriodomethane (OMX Laboratories), TMEDA (99%, ALDRICH), [H–B(9-BBN)]2 (152, 98%, ALDRICH), butyllithium (144, 1.3 M in cyclohexane/hexane, ACROS ORGANICS), vinyl boronic ester (146, 95%, ALDRICH) were commercially available.

Gallium metal (99.9999%) and gallium(III) triflate (98%) were purchased from STREM and stored in a nitrogen glove box. Silver triflate (99.95%), silver fluoride (99.9%), silver tetrafluoroborate (99.95%), silver tetrafluorophosphate (99.99%), silver bis(trifluoromethanesulfonyl)imide (97%), silver cyanate (99.995%), silver carbonate (99.999%), [12]crown-4 (83, 98%), Dipp-NHC (21, 97%), Mes-NHC (84, 97%) and mercury (99.9995%) were purchased from ALDRICH and stored in a nitrogen glove box or freezer. Silver chloride (99%) was purchased from ACROS ORGANICS. Silver metal (powder, 99.9%, -35+45 mesh), aluminum metal (powder, 99.97%), [18]crown-6 (56, 99%), dibenzo-[18]crown-6 (81, 98%), [15]crown-5 (82, 98%), triphenylphosphine (85, 99%) and the rest commercially available silver salts were purchased from ALFA AESAR, including
silver perchlorate (anhydrous), silver hexafluoroantimonate (99%), silver oxide (99.99%), silver phosphate (99%), silver nitrate (99.995%), silver bromide (99.9%) and silver iodide (99.999%). Chiral BINOL \(( R )-154-H\), \(( R )-155-H\), and \(( R )-156-H\) were purchased from APOLLO Scientific Support Research Library. All catalytic reactions were carried out in glove box under a nitrogen atmosphere in well-dried glassware.
4.2 Synthesis and Analysis of Electrophiles

4.2.1 General Procedures for Preparation

Acetals, aminal and ether are literature-known compounds and were prepared accordingly; 70p, 70q, 70r, 133, 134 and 138 their analysis are in full agreement with the reported data. All other non-commercially available acetals and ketals were prepared from the corresponding aldehydes or ketones. The electrophiles were all purified by distillation in vacuo or PTLC or flash column chromatography on silica gel.

General procedure A

Most of the acetals and ketals were prepared according to an improved Williams’s method. Aldehyde or ketone (20.0 mmol), trimethyl orthoformate (2.55–4.24 g, 24.0–40.0 mmol, 1.2–2.0 equiv) were added to a 50 mL round-bottle flask with a magnetic stirring bar under a nitrogen atmosphere. The reaction mixture was stirred at 25–50 °C overnight until the 1H NMR analysis of a reaction aliquot confirmed the consumption of the aldehyde or ketone. The reaction mixture was filtered through dried celite and directly purified by distillation under reduced pressure or PTLC or flash column chromatography on silica gel. The liquid products were stored in nitrogen-filled glove box over 4 Å molecular sieves.

Procedure B

The dibenzyl acetal 70p was prepared according to Madabhushi’s method. Benzaldehyde (1.59 g, 15.0 mmol), benzyl alcohol (3.57 g, 33.0 mmol, 2.2 equiv), InF₃ (210 mg, 1.20 mmol, 7.5 mol%), and toluene (15 mL) were added to a 50 mL round-bottomed flask with a magnetic stirring bar under a nitrogen atmosphere. The reaction mixture was refluxed with condensation overnight, at which point the 1H NMR analysis of a reaction aliquot confirmed the consumption of the aldehyde. The mixture was filtered, washed with toluene (10 mL). The toluene solution was concentrated in vacuo, and the crude product was purified by flash column chromatography on silica gel (EtOAc:hexane = 1:20) to afford
as pale yellow liquid. The product was stored in a nitrogen-filled glove box over 4 Å molecular sieves.

**Procedure C**

1-methoxyisochroman 70q was prepared according to Jacobsen’s method. Absolute methanol (380 µL, 9.30 mmol, 1.2 equiv) was added to a stirred solution of 2,3-dichloro-5,6-dicyano-1,4-benzoquinone (DDQ, 2.11 g, 9.30 mmol, 1.2 equiv) in DCM (50 mL). Next, isochroman (1.06 g, 7.91 mmol) was added to the reaction mixture and the resulting mixture was stirred vigorously for 24 h under a nitrogen atmosphere at room temperature, before the addition of aqueous NaHCO₃ (60 mL, saturated solution). The mixture was filtered through celite, washed with DCM (50 mL). The aqueous layer was separated and extracted with DCM (2 x 30 mL), and the combined organic phase was washed with aqueous NaHCO₃ (30 mL, saturated), and brine (30 mL), and dried over MgSO₄, and concentrated in vacuo. The crude product was purified by flash column chromatography on silica gel (Et₂O:hexane = 1:9) to afford 70q as a yellow liquid. The product was stored in a nitrogen-filled glove box over 4 Å molecular sieves.

**Procedure D**

2H-chromene acetal 70r was prepared according to Schaus’s method. Diisobutyl aluminum hydride (DIBAL-H, 1.0 M in PhCH₃; 52.5 mL, 52.5 mmol, 1.05 equiv) was added drop-wise to a stirred solution of coumarin (7.39 g, 50.0 mmol) in absolute DCM (75 mL) at −78 °C under a nitrogen atmosphere. After stirring at −78 °C for 1 h, the reaction mixture was warmed to 0 °C and stirred for 15 min, before being diluted with EtOAc (250 mL). The mixture was quenched with water (250 mL) and the two-phase mixture was stirred vigorously and was filtered through celite. The aqueous phase was extracted with EtOAc (2 x 250 mL) and the combined organic phase was washed with brine (250 mL), dried over
MgSO₄, and concentrated in vacuo. The residue was re-dissolved in EtOH (50 mL) and trifluoroacetic acid (TFA; 111 µL, 1.50 mmol, 3 mol%) was added to the reaction mixture at room temperature. After 3 h, the reaction mixture was quenched with K₂CO₃ (276 mg, 2.00 mmol), filtered and concentrated in vacuo. The crude product was purified by flash column chromatography on silica gel (EtOAc:hexane =1:20) to afford product 70r as a pale yellow liquid. The product was stored in a nitrogen-filled glove box over 4 Å molecular sieves.

Procedure E

N-(Methoxy(phenyl)methyl)benzamide 133 was prepared according to Pemak’s method. Benzaldehyde (2.12 g, 20.0 mmol), benzamide (2.42 g, 20.0 mmol), benzotriazole (2.38 g, 20.0 mmol), and p-toluenesulfonic acid (PTSA) were added to a mixture of water (20 mL) and methanol (10 mL). After stirring overnight at room temperature, the reaction mixture was cooled to 0 °C, filtered and the resulting solids were dissolved in DCM (10 mL). The organic phase was dried over MgSO₄ and concentrated in vacuo. Then, the crude was added to the stirred solution of sodium methoxide, which was pre-prepared from sodium (0.69 g, 30.0 mmol, 3.0 equiv) and methanol (10 mL). The reaction was stirred overnight before the addition of water (10 mL). The resulting participate was filtered, dissolved in DCM (10 mL), dried over MgSO₄ and concentrated in vacuo. Product was stored in a nitrogen-filled glove box as a colorless solid.

Procedure F

Diphenylmethyl methyl ether 138 was prepared using diphenylmethanol (1.84 g, 10.0 mmol), trimethyl orthoformate (2.12 g, 20.0 mmol, 2.0 equiv) and p-toluenesulfonic acid (PTSA, 1.70 g, 1.0 equiv) under a nitrogen atmosphere. The reaction mixture was stirred at room temperature overnight until the ¹H NMR analysis of a reaction aliquot confirmed the consumption of alcohol. The reaction mixture was filtered through celite and directly
purified by flash column chromatography on silica gel (heptane:EtOAc = 9:1). The colorless liquid was stored in a nitrogen-filled glove box over 4Å molecular sieves.
4.2.2 Analytical Data of Electrophiles

(Dimethoxymethyl)benzene (70a)

70a is commercially available and stored in a nitrogen-filled glove box over 4Å molecular sieves. The obtained analytical data fitted accurately with the reported data.\textsuperscript{67a} Colorless liquid.

\textbf{\textsuperscript{1}H NMR} (CDCl\textsubscript{3}, 500 MHz): δ = 3.33 (s, 6H), 5.40 (s, 1H), 7.32–7.46 (m, 5H) ppm.

\textbf{\textsuperscript{13}C NMR} (CDCl\textsubscript{3}, 150 MHz): δ = 51.6 (2C), 103.1, 126.6 (2C), 127.1 (2C), 128.4, 138.1 ppm.

1-(Dimethoxymethyl)-4-(trifluoromethyl)benzene (70b)

70b was prepared according to \textit{general procedure} A and the obtained analytical data fitted accurately with the reported data.\textsuperscript{137} Pale yellow liquid.

Yield: 42%.

\textbf{\textsuperscript{1}H NMR} (CDCl\textsubscript{3}, 600 MHz): δ = 3.36 (s, 6H), 5.47 (s, 1H), 7.61 (d, J = 8.1 Hz, 2H), 7.66 (d, J = 8.1 Hz, 2H) ppm.

\textbf{\textsuperscript{13}C NMR} (CDCl\textsubscript{3}, 125 MHz): δ = 52.6 (2C), 102.1, 124.0 (q, J = 272.3 Hz), 125.1 (q, J = 3.5 Hz, 2C), 127.2 (2C), 130.6 (q, J = 32.4 Hz), 142.0 ppm.

\textbf{\textsuperscript{19}F NMR} (CDCl\textsubscript{3}, 128 MHz): δ = –62.7 ppm.
Methyl 4-(dimethoxymethyl)benzoate (70c)

70c was prepared according to general procedure A and the obtained analytical data fitted accurately with the reported data.\textsuperscript{138}

Colorless liquid.
Yield: 40%.

\textsuperscript{1}H NMR (CDCl\textsubscript{3}, 600 MHz): $\delta = 3.35$ (s, 6H), 3.94 (s, 3H), 5.45 (s, 1H), 7.55 (d, $J = 8.1$ Hz, 2H), 8.06 (d, $J = 8.1$ Hz, 2H) ppm.

\textsuperscript{13}C NMR (CDCl\textsubscript{3}, 150 MHz): $\delta = 52.1$, 52.6 (2C), 102.3, 126.8 (2C), 129.5 (2C), 130.2, 142.9, 166.8 ppm.

1-(Dimethoxymethyl)-4-fluorobenzene (70d)

70d was prepared according to general procedure A and the obtained analytical data fitted accurately with the reported data.\textsuperscript{139}

Colorless liquid.
Yield: 67%.

\textsuperscript{1}H NMR (CDCl\textsubscript{3}, 600 MHz): $\delta = 3.31$ (s, 6H), 5.37 (s, 1H), 7.03–7.06 (m, 2H), 7.41–7.43 (m, 2H) ppm.

\textsuperscript{13}C NMR (CDCl\textsubscript{3}, 150 MHz): $\delta = 52.6$ (2C), 102.5, 115.0 (d, $J = 21.5$ Hz, 2C), 128.5 (d, $J = 8.3$ Hz, 2C), 134.0 (d, $J = 3.3$ Hz), 162.0 (d, $J = 246.0$ Hz) ppm.

\textsuperscript{19}F NMR (CDCl\textsubscript{3}, 128 MHz): $\delta = −113.8$ $\sim −113.9$ (m) ppm.
1-Chloro-4-(dimethoxymethyl)benzene (70e)

![70e]

70e was prepared according to general procedure A and the obtained analytical data fitted accurately with the reported data.\textsuperscript{67a}

Colorless liquid.

Yield: 54%.

\textsuperscript{1}H NMR (CDCl\textsubscript{3}, 600 MHz): $\delta = 3.30$ (s, 6H), 5.37 (s, 1H), 7.32–7.39 (m, 4H) ppm.

\textsuperscript{13}C NMR (CDCl\textsubscript{3}, 150 MHz): $\delta = 52.6$ (2C), 102.3, 128.2 (2C), 128.4 (2C), 134.3, 136.7 ppm.

1-Bromo-4-(dimethoxymethyl)benzene (70f)

![70f]

70f was prepared according to general procedure A and the obtained analytical data fitted accurately with the reported data.\textsuperscript{67a}

Colorless liquid.

Yield: 46%.

\textsuperscript{1}H NMR (CDCl\textsubscript{3}, 600 MHz): $\delta = 3.31$ (s, 6H), 5.35 (s, 1H), 7.33 (d, $J = 6.0$ Hz, 2H), 7.50 (d, $J = 6.0$ Hz, 2H) ppm.

\textsuperscript{13}C NMR (CDCl\textsubscript{3}, 150 MHz): $\delta = 52.5$ (2C), 102.3, 122.5, 128.5 (2C), 131.3 (2C), 137.1 ppm.
1-(Dimethoxymethyl)-4-methylbenzene (70g)

![70g]

70g was prepared according to general procedure A and the obtained analytical data fitted accurately with the reported data.\textsuperscript{67a}

Colorless liquid.

Yield: 53%.

\begin{align*}
\text{\textsuperscript{1}H NMR} \hspace{1em} & \text{CDCl}_3, 500 \text{ MHz}: \delta = 2.32 \text{ (s, 3H), 3.24 (s, 6H), 5.34 (s, 1H), 7.15 (d, J = 8.0 Hz, 2H), 7.32 (d, J = 8.0 Hz, 2H) ppm.} \\
\text{\textsuperscript{13}C NMR} \hspace{1em} & \text{CDCl}_3, 150 \text{ MHz}: \delta = 21.2, 52.6 (2\text{C}), 103.2, 126.6 (2\text{C}), 128.9 (2\text{C}), 135.2, 138.2 \text{ ppm.}
\end{align*}

(4-(Dimethoxymethyl)phenyl)methanol (70h)

![70h]

70h was commercially available and the obtained analytical data fitted accurately with the reported data.\textsuperscript{140}

Colorless solid.

\begin{align*}
\text{\textsuperscript{1}H NMR} \hspace{1em} & \text{CDCl}_3, 600 \text{ MHz}: \delta = 1.71 \text{ (t, J = 6.0 Hz, 1H), 3.35 (s, 6H), 4.73 (d, J = 6.0 Hz, 2H), 5.42 (s, 1H), 7.40 (d, J = 8.3 Hz, 2H), 7.47 (d, J = 8.3 Hz, 2H) ppm.} \\
\text{\textsuperscript{13}C NMR} \hspace{1em} & \text{CDCl}_3, 150 \text{ MHz}: \delta = 52.5 (2\text{C}), 65.1, 103.0, 126.8 (2\text{C}), 126.9 (2\text{C}), 137.6, 141.1 \text{ ppm.}
\end{align*}
4-(Dimethoxymethyl)-N,N-dimethylaniline (70i)

![Chemical Structure of 70i](image)

70i was prepared according to general procedure A and the obtained analytical data fitted accurately with the reported data.\textsuperscript{141}

Yellow liquid.

Yield: 54%.

\textsuperscript{1}H NMR (CDCl\textsubscript{3}, 600 MHz): \(\delta = 2.97\) (s, 6H), 3.33 (s, 6H), 5.34 (s, 1H), 6.72–6.74 (m, 2H), 7.31–7.32 (m, 2H) ppm.

\textsuperscript{13}C NMR (CDCl\textsubscript{3}, 150 MHz): \(\delta = 40.5\) (2C), 52.6 (2C), 103.6, 112.0 (2C), 125.9, 127.5 (2C), 150.7 ppm.

1-(Dimethoxymethyl)-4-methoxybenzene (70j)

![Chemical Structure of 70j](image)

70j was prepared according to general procedure A and the obtained analytical data fitted accurately with the reported data.\textsuperscript{67a}

Colorless liquid.

Yield: 37%.

\textsuperscript{1}H NMR (CDCl\textsubscript{3}, 600 MHz): \(\delta = 3.31\) (s, 6H), 3.81 (s, 3H), 5.35 (s, 1H), 6.89 (d, \(J = 12.0\) Hz, 2H), 7.36 (d, \(J = 12.0\) Hz, 2H) ppm.

\textsuperscript{13}C NMR (CDCl\textsubscript{3}, 150 MHz): \(\delta = 52.5\) (2C), 55.2, 103.0, 113.5 (2C), 127.9 (2C), 130.4, 159.7 ppm.
1-(Dimethoxymethyl)-3-methylbenzene (70k)

![structure_70k]

70k was prepared according to *general procedure A* and the obtained analytical data fitted accurately with the reported data.\textsuperscript{67a}

Colorless liquid.

Yield: 40%.

\textbf{H NMR} (CDCl\textsubscript{3}, 400 MHz): \( \delta = 2.34\) (s, 3H), 3.32 (s, 6H), 5.34 (s, 1H), 7.12–7.26 (m, 4H) ppm.

\textbf{C NMR} (CDCl\textsubscript{3}, 150 MHz): \( \delta = 21.4, 52.8\) (2C), 103.4, 123.8, 127.3, 128.1, 129.2, 137.9, 138.0 ppm.

1-(Dimethoxymethyl)-2-methylbenzene (70l)

![structure_70l]

70l was prepared according to *general procedure A* and the obtained analytical data fitted accurately with the reported data.\textsuperscript{67a}

Colorless liquid.

Yield: 57%.

\textbf{H NMR} (CDCl\textsubscript{3}, 500 MHz): \( \delta = 2.35\) (s, 3H), 3.39 (s, 6H), 5.44 (s, 1H), 7.11–7.54 (m, 4H) ppm.

\textbf{C NMR} (CDCl\textsubscript{3}, 150 MHz): \( \delta = 18.9, 53.0\) (2C), 101.8, 125.4, 126.6, 128.4, 130.5, 135.7, 136.3 ppm.
1-(Dimethoxymethyl)naphthalene (70m)

70m was prepared according to *general procedure* A and the obtained analytical data fitted accurately with the reported data.\(^{67a}\)

Colorless liquid.

Yield: 87%.

\(^1\)H NMR (CDCl\(_3\), 400 MHz): δ = 3.37 (s, 6H), 5.91 (s, 1H), 7.43–7.53 (m, 3H), 7.75–7.79 (m, 1H), 7.88–7.92 (m, 2H), 8.83–8.35 (m, 1H) ppm.

\(^{13}\)C NMR (CDCl\(_3\), 125 MHz): δ = 53.1 (2C), 102.4, 124.2, 124.8, 124.9, 125.6, 126.2, 128.5, 129.2, 130.8, 133.1, 133.8 ppm.

2-(Dimethoxymethyl)naphthalene (70n)

70n was prepared according to *general procedure* A and the obtained analytical data fitted accurately with the reported data.\(^{67a}\)

Colorless liquid.

Yield: 70%.

\(^1\)H NMR (CDCl\(_3\), 600 MHz): δ = 3.36 (s, 6H), 5.54 (s, 1H), 7.45–7.93 (m, 7H) ppm.

\(^{13}\)C NMR (CDCl\(_3\), 150 MHz): δ = 52.7 (2C), 103.2, 124.4, 126.0, 126.1, 126.2, 127.6, 128.0, 128.3, 133.0, 133.4, 135.5 ppm.
(Diethoxymethyl)benzene (70o)

70o is commercially available and stored in a nitrogen-filled glove box over 4Å molecular sieves. The obtained analytical data fitted accurately with the reported data.67a

Colorless liquid.

\[ \text{\textsuperscript{1}H NMR (CDCl}_3, 600 MHz): \delta = 1.28 (t, J = 6.0 \text{ Hz}, 6H), 3.56–3.69 (m, 4H), 5.55 (s, 1H), 7.33–7.53 (m, 5H) \text{ ppm.} \]

\[ \text{\textsuperscript{13}C NMR (CDCl}_3, 150 MHz): \delta = 15.2 (2C), 61.0 (2C), 110.5, 126.6 (2C), 128.1 (2C), 128.2, 139.1 \text{ ppm.} \]

(((Phenylmethylene)bis(oxy))bis(methylene))dibenzene (70p)

70p was prepared according to procedure B and the obtained analytical data fitted accurately with the reported data.131

Pale yellow liquid.

Yield: 27%.

\[ \text{\textsuperscript{1}H NMR (CDCl}_3, 600 MHz): \delta = 4.61 (d, J = 1.5 \text{ Hz}, 4H), 5.77 (s, 1H), 7.31–7.62 (m, 15H) \text{ ppm.} \]

\[ \text{\textsuperscript{13}C NMR (CDCl}_3, 150 MHz): \delta = 67.0 (2C), 100.4, 126.9 (2C), 127.6 (2C), 127.8 (4C), 128.3 (2C), 128.4 (4C), 128.5, 138.1 (2C), 138.3 \text{ ppm.} \]

1-Methoxyisochromane (70q)
70q was prepared according to procedure C and the obtained analytical data fitted accurately with the reported data.\textsuperscript{102}

Colorless liquid.

Yield: 54%

\textsuperscript{1}H NMR (CDCl\textsubscript{3}, 600 MHz): δ = 2.65 (ddd, J = 1.6, 3.4, 16.5 Hz, 1H), 3.06 (ddd, J = 6.1, 12.0, 16.5 Hz, 1H), 3.58 (s, 3H), 3.94 (ddd, J = 1.6, 6.1, 11.2 Hz, 1H), 4.12 (ddd, J = 3.4, 11.2, 12.0 Hz, 1H), 5.48 (s, 1H), 7.14–7.29 (m, 4H) ppm.

\textsuperscript{13}C NMR (CDCl\textsubscript{3}, 150 MHz): δ = 28.0, 55.3, 57.7, 97.8, 126.3, 127.4, 128.2, 128.4, 134.0, 134.1 ppm.

2-Ethoxy-2H-chromene (70r)

70r was prepared according to procedure D and the obtained analytical data fitted accurately with the reported data.\textsuperscript{132}

Colorless liquid.

Yield: 70%

\textsuperscript{1}H NMR (CDCl\textsubscript{3}, 600 MHz): δ = 1.25 (t, J = 7.1 Hz, 3H), 3.71 (dq, J = 7.1, 9.7 Hz, 1H), 3.98 (dq, J = 7.1, 9.7 Hz, 1H), 5.74 (d, J = 3.7 Hz, 1H), 5.90 (dd, J = 3.4, 9.7 Hz, 1H), 6.76 (d, J = 9.7 Hz, 1H), 6.97–7.10 (m, 2H), 7.17 (dd, J = 1.4, 7.5 Hz, 1H), 7.23–7.26 (m, 1H) ppm.

\textsuperscript{13}C NMR (CDCl\textsubscript{3}, 150 MHz): δ = 15.3, 63.5, 94.9, 116.5, 120.0, 120.7, 121.4, 126.5, 127.0, 129.3, 151.5 ppm.

\textit{tert}-Butyl 3-(dimethoxymethyl)-1H-indole-1-carboxylate (70s)

70s was prepared according to procedure A and the obtained analytical data fitted accurately
with the reported data.\textsuperscript{62}

Beige solid.

Yield: 17%.

$^1$H NMR (CDCl$_3$, 500 MHz): $\delta = 1.67$ (s, 9H), 3.36 (s, 6H), 5.70 (d, $J = 1.1$ Hz, 1H), 7.24 (ddd, $J = 1.1, 7.3, 8.4$ Hz, 1H), 7.32 (dd, $J = 1.1, 7.3, 8.4$ Hz, 1H), 7.63 (br s, 1H), 7.71 (ddd, $J = 1.1, 2.0, 8.0$ Hz, 1H), 8.19 (d, $J = 8.0$ Hz, 1H) ppm.

$^{13}$C NMR (CDCl$_3$, 150 MHz): $\delta = 28.2$ (3C), 52.3 (2C), 83.8, 99.2, 115.2, 118.2, 120.2, 122.8, 124.5, 124.8, 128.2, 135.8, 149.6 ppm.

2-(Dimethoxymethyl)benzofuran (70t)

70t was prepared according to \textit{general procedure} A and the obtained analytical data fitted accurately with the reported data.\textsuperscript{62}

Pale yellow liquid.

Yield: 33%.

$^1$H NMR (CDCl$_3$, 500 MHz): $\delta = 3.41$ (s, 6H), 5.57 (d, $J = 0.8$ Hz, 1H), 6.81 (dd, $J = 0.8, 0.9$ Hz, 1H), 7.23 (ddd, $J = 1.0, 7.3, 8.4$ Hz, 1H), 7.28 (ddd, $J = 1.4, 7.3, 8.4$ Hz, 1H), 7.50 (dd, $J = 1.0, 8.2$ Hz, 1H), 7.57 (ddd, $J = 0.9, 1.4, 8.2$ Hz, 1H) ppm.

$^{13}$C NMR (CDCl$_3$, 150 MHz): 53.0 (2C), 98.0, 105.4, 111.5, 121.3, 122.9, 124.6, 127.7, 153.1, 154.9 ppm.

2-(Dimethyloxymethyl)benzothiophene (70u)

70u was prepared according to \textit{general procedure} A.

Pale yellow liquid.
Yield: 36%.

$^1$H NMR (CDCl$_3$, 600 MHz): $\delta = 3.41$ (s, 6H), 5.71 (s, 1H), 7.29–7.37 (m, 3H), 7.75 (d, $J = 7.2$ Hz, 1H), 7.82 (d, $J = 7.2$ Hz, 1H) ppm.

$^{13}$C NMR (CDCl$_3$, 150 MHz): $\delta = 52.7$ (2C), 100.2, 122.3, 122.5, 123.8, 124.3, 124.4, 139.4, 140.0, 142.3 ppm.

IR (neat): $\nu = 2933, 1458, 1435, 1346, 1186, 1139, 1042, 977, 744, 725$ cm$^{-1}$.

HRMS (ESI): calculated for C$_{11}$H$_{12}$NaO$_2$S$^+$ = [M+Na]$^+$: $m/z = 231.0450$, found: $m/z = 231.0453$.

Phenylpropargyl aldehyde diethyl acetal (70v)

![Phenylpropargyl aldehyde diethyl acetal (70v)](image)

70v is commercially available and stored in fridge over 4 Å molecular sieves.

Pale yellow liquid.

$^1$H NMR (CDCl$_3$, 500 MHz): $\delta = 1.25$ (t, $J = 8.5$ Hz, 6H), 3.45–3.60 (m, 2H), 3.79–3.93 (m, 2H), 5.49 (s, 1H), 7.27–7.34 (m, 3H), 7.40–7.51 (m, 2H) ppm.

$^{13}$C NMR (CDCl$_3$, 150 MHz): $\delta = 15.2$ (2C), 61.0 (2C), 84.4, 85.2, 91.8, 121.9 (2C), 128.3, 128.8 (2C), 132.0 ppm.

IR (neat): $\nu = 2927, 2237, 1489, 1354, 1327, 1093, 1042, 1006, 754, 680$ cm$^{-1}$.

HRMS (ESI): calculated for C$_{13}$H$_{16}$NaO$_2$ = [M+Na]$^+$: $m/z = 227.1043$, found: $m/z = 227.1057$.

(\textit{E})-(3,3-Dimethoxyprop-1-en-1-yl)benzene (70w)

![\textit{E})-(3,3-Dimethoxyprop-1-en-1-yl)benzene (70w)](image)

70w was prepared according to general procedure A and the obtained analytical data fitted accurately with the reported data.$^{67a}$
Pale yellow liquid.

Yield: 37%.

$^1$H NMR (CDCl$_3$, 600 MHz): $\delta = 3.42$ (s, 6H), 4.96 (dd, $J = 1.2$, 4.9 Hz, 1H), 6.15 (dd, $J = 4.9$, 16.0 Hz, 1H), 6.73 (d, $J = 16.0$ Hz, 1H), 7.28–7.46 (m, 5H) ppm.

$^{13}$C NMR (CDCl$_3$, 150 MHz): 52.7 (2C), 102.9, 125.7, 126.7 (2C), 128.1, 128.6 (2C), 133.6, 136.1 ppm.

(3,3-Dimethoxypropyl)benzene (70x)

70x was prepared according to general procedure A and the obtained analytical data fitted accurately with the reported data.$^{67a}$

Colorless liquid.

Yield: 34%.

$^1$H NMR (CDCl$_3$, 600 MHz): $\delta = 1.90–1.95$ (m, 2H), 2.68 (t, $J = 8.0$ Hz, 2H), 3.33 (s, 6H), 4.37 (t, $J = 5.8$ Hz, 1H), 7.19–7.30 (m, 5H) ppm.

$^{13}$C NMR (CDCl$_3$, 150 MHz): $\delta = 30.8$, 34.1, 52.7 (2C), 103.8, 125.8 (2C), 128.4 (2C), 141.6 ppm.

(Dimethoxymethyl)cyclohexane (70y)

70y was prepared according to general procedure A and the obtained analytical data fitted accurately with the reported data.$^{67a}$

Colorless liquid.

Yield: 62%.

$^1$H NMR (CDCl$_3$, 600 MHz): $\delta = 0.93–1.21$ (m, 5H), 1.54–1.76 (m, 6H), 3.31 (s, 6H), 3.97
(d, J = 12.0 Hz, 1H) ppm.

$^{13}$C NMR (CDCl$_3$, 150 MHz): $\delta = 25.8$ (2C), 26.4, 28.0 (2C), 40.1, 53.5 (2C), 108.6 ppm.

(1,1-Dimethoxy-2,2-dimethylpropyl)benzene ($70z$)

$70z$ was prepared according to general procedure A and the obtained analytical data fitted accurately with the reported data.\textsuperscript{142}

Pale yellow liquid.

Yield: 38%.

$^1$H NMR (CDCl$_3$, 600 MHz): $\delta = 0.94$ (s, 9H), 3.33 (s, 6H), 7.41–7.24 (m, 5H) ppm.

$^{13}$C NMR (CDCl$_3$, 150 MHz): $\delta = 27.0$ (3C), 40.5, 51.9 (2C), 102.5, 126.8 (2C), 127.1, 129.3 (2C), 139.3 ppm.

2,2-Dimethoxy-2-phenylacetophenone ($70z'$)

$70z'$ is commercially available and stored in fridge.

Colorless solid.

$^1$H NMR (CDCl$_3$, 500 MHz): $\delta = 3.22$ (s, 6H), 7.27–7.33 (m, 3H), 7.33–7.38 (m, 2H), 7.38–7.45 (m, 1H), 7.59–7.65 (m, 2H), 8.03–8.08 (m, 2H) ppm.

$^{13}$C NMR (CDCl$_3$, 150 MHz): $\delta = 50.1$ (2C), 103.6, 127.0 (2C), 128.1 (2C), 128.5 (2C), 128.9, 130.0 (2C), 132.9, 134.3, 136.9, 195.2 ppm.

IR (neat): $\nu = 2974, 1689, 1448, 1234, 1040, 1018, 866, 758, 688, 659$ cm$^{-1}$.

HRMS: Mass spectroscopic analyses failed to give the desired molecular signal, resulting only in fragmentation.
**N-(Methoxy(phenyl)methyl)benzamide (133)**

![Chemical Structure](image)

133 was prepared according to procedure E and the obtained analytical data fitted accurately with the reported data.\(^{134}\)

Colorless solid.

Yield: 72%.

\(^1\)H NMR (CDCl\(_3\), 400 MHz): \(\delta = 3.58\) (s, 3H), 6.41 (d, \(J = 9.2\) Hz, 1H), 6.61 (d, \(J = 9.2\) Hz, 1H), 7.35–7.69 (m, 10H) ppm.

\(^13\)C NMR (CDCl\(_3\), 150 MHz): 56.2, 81.9, 125.9 (2C), 127.1 (2C), 128.6, 128.7 (4C), 132.0, 133.8, 139.4, 167.3 ppm.

**(Methoxymethylene)dibenzene (138)**

![Chemical Structure](image)

138 was prepared according to procedure F and the obtained analytical data fitted accurately with the reported data.\(^{143}\)

Colorless liquid.

Yield: 52%.

\(^1\)H NMR (CDCl\(_3\), 600 MHz): \(\delta = 3.45\) (s, 3H), 5.31 (s, 1H), 7.29–7.43 (m, 10H) ppm.

\(^13\)C NMR (CDCl\(_3\), 150 MHz): \(\delta = 57.0, 85.5, 127.0\) (4C), 127.5 (2C), 128.4 (4C), 142.1 (2C) ppm.
4.3 Synthesis and Analysis of Allyl Reagents

2-Allyl-4,4,5,5-tetramethyl-1,3,2-dionaborolane (71)

[Chemical structure image]

Allyl boronic ester was synthesized according to Roush’s method. Allylmagnesium bromide (1.0 M solution in ether, 110 mL, 110 mmol) and trimethyl borate (13.4 g, 120 mmol, 1.1 equiv) were dissolved in ether (78 mL) and the solution was added through an addition funnel to stirred diethyl ether (81 mL) in a three-neck flask at −78 °C under nitrogen (over 1.5 h). The reaction mixture was stirred at −78 °C for another 2.5 h, and then warmed to 0 °C before the addition of HCl (2.0 M aqueous HCl, 100 mL) at 0 °C. The two-phase mixture was stirred vigorously at room temperature for 1 h. The aqueous layer was extracted with ether and DCM (ratio = 5:1; 150 mL). The combined organic layers were dried with Na$_2$SO$_4$, filtered, and concentrated in vacuo to obtain a residue, which was diluted with diethyl ether up to a volume of 250 mL. Anhydrous pinacol (10.5 g, 89.0 mmol) was added to the solution. The reaction mixture was stirred overnight under nitrogen at room temperature. The reaction mixture was dried over Na$_2$SO$_4$, concentrated in vacuo. The resulting crude product was purified by distillation under reduced pressure to give a colorless liquid in 61% yield (10.3 g), which was stored in a nitrogen filled glove box over 4 Å molecular sieves. The obtained analytical data fitted accurately with the literature data.

Colorless liquid. Yield: 61%.

$^1$H NMR (CDCl$_3$, 400 MHz): δ = 1.28 (s, 12H), 1.72 (d, $J = 5.1$ Hz, 2H), 4.96 (dd, $J = 2.1, 10.1$ Hz, 1H), 5.03 (dd, $J = 2.1, 17.1$ Hz, 1H), 5.85–5.92 (m, 1H) ppm.

$^{11}$B NMR (CHCl$_3$, 160 MHz): δ = 32.8 ppm.

$^{13}$C NMR (CDCl$_3$, 150 MHz): δ = 24.4 (4C), (signal of the carbon connected to boron was
2-(Allyl-1,1-\text{d}_2)-4,4,5,5-tetramethyl-1,3,2-dionaborolane (71–[\text{d}_2])

![Chemical Structure](image)

The deuterio-allyl boronic ester was prepared according to improved Morken’s method.\textsuperscript{135}

\textsuperscript{6}Butyllithium (\textsuperscript{6}BuLi, 8.3 mL of 1.60 M solution in hexane, 5.18 mmol) was added drop-wise to a stirred solution of vinyl boronic ester (0.67 g, 4.32 mmol) and \textsuperscript{d}_2-chloroiodomethane (0.77 g, 4.32 mmol) in THF (17 mL) at \textsuperscript{–}78 °C. The reaction mixture was warmed to room temperature by increasing of 5 °C per 30 min and the mixture was stirred overnight at \textsuperscript{–}20 °C. The reaction was warmed to room temperature and concentrated \textit{in vacuo}. The resulting crude oil was diluted with hexane (10 mL) and then filtered through celite. NH\textsubscript{4}Cl (10 mL of saturated aqueous solution) was added and the two-phases mixture was then filtered through celite. The organic layer was washed with water (2 x 10 mL), dried over MgSO\textsubscript{4} and concentrated \textit{in vacuo}. The product was obtained as pale yellow liquid in 41% yield (298 mg), which was stored in a nitrogen filled glove box over 4 Å molecular sieves. The obtained analytical data fitted accurately with the literature data.\textsuperscript{135}

Pale yellow liquid.

Yield: 41%.

\textsuperscript{1}H NMR (CDCl\textsubscript{3}, 500 MHz): \(\delta = 1.28\) (s, 12H), 4.96 (dd, \(J = 2.1, 10.1\) Hz, 1H), 5.03 (dd, \(J = 2.1, 17.1\) Hz, 1H), 5.85–5.92 (m, 1H) ppm.

\textsuperscript{2}D NMR (CDCl\textsubscript{3}, 77 MHz): \(\delta = 1.72\) (d, \(J = 1.0\) Hz, 2D) ppm.

\textsuperscript{11}B NMR (CDCl\textsubscript{3}, 160 MHz): \(\delta = 32.8\) ppm.

\textsuperscript{13}C NMR (CDCl\textsubscript{3}, 125 MHz): \(\delta = 24.7\) (4C), (\textit{signal of the carbon connected to boron was not visible due to quadrupolar broadening}), 83.2 (2C), 114.8, 134.0 ppm.
Trimethyl(1-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)allylsilane (136)

The title compound was prepared according to a modified procedure of the “Matteson” method.^{96} Butyllithium (BuLi, 7.55 mL, 9.80 mmol, 1.30 M in cyclohexane/hexane, 1.40 equiv) was added drop-wise to a stirred solution of chloro(trimethyl)silane (1.15 mL, 9.10 mmol, 1.30 equiv) in absolute THF (12 mL) at –78 °C under a nitrogen atmosphere. Next, TMEDA (1.5 mL, 10.0 mmol, 1.43 equiv) was slowly added to the reaction mixture. After additional stirring for 30 min at –78 °C the reaction mixture was warmed up to –55 °C for 30 min, before cooling down again to –78 °C. A solution of the pinacolato vinyl boronic ester (1.08 g, 7.00 mmol) in absolute THF (2 mL) was then added in one portion to the reaction mixture at –78 °C. After 2 h the reaction mixture was warmed slowly to room temperature overnight (>8 h), before adding aqueous HCl (15 mL, 30.0 mmol, 2.0 M in H₂O, 4.70 equiv), which was kept at 0 °C. After phase separation, the organic phase was extracted with diethyl ether/DCM (5:1, 3 x 30 mL), dried over MgSO₄, and concentrated in vacuo. The product was obtained as a pale yellow oil in 80% yield (1.35 g), containing <5% unreacted vinyl boronic ester. The product was stored in a nitrogen-filled glove box over 4 Å molecular sieves. The obtained analytical data fitted accurately with the literature data.^{96}

Pale yellow liquid.

Yield: 80%.

^1H NMR (CDCl₃, 400 MHz): δ = 0.05 (s, 9H), 1.24 (s, 12 H), 1.53 (d, J = 10.7 Hz, 1H), 4.74–4.79 (m, 1H), 4.81 (br s, 1H), 5.83–5.92 (m, 1H) ppm.

^11B NMR (CDCl₃, 128 MHz): δ = 33.1 ppm.

^13C NMR (CDCl₃, 150 MHz): δ = 5.0 (3C), 26.7 (4C), (signal of the carbon connected to boron was not visible due to quadrupolar broadening), 84.7 (2C), 113.2, 137.9 ppm.
9-Allyl-9-Borabicyclo[3.3.1]nonane (110)

The allyl–B(9-BBN) was synthesized based on Aggarwal’s method. Absolute methanol (0.27 mL, 6.60 mmol) was added drop-wise to a stirred solution of 9-borabicyclo[3.3.1]nonane \([H-B(9-BBN)]_2\) (0.73 g, 3.00 mmol) in diethyl ether (6.6 mL) at 0 °C under a nitrogen atmosphere. The reaction mixture was warmed to room temperature and kept stirring until the hydroboration was finished. Allyl–MgBr solution (6.6 mL of 1.0 M solution in ether, 6.60 mmol) was added slowly to the reaction mixture at 0 °C and kept stirring for another hour. At that stage, the reaction mixture was concentrated in vacuo, and the residue was washed with hexane (2 × 6 mL) in a glove box, then filtered through celite and ready to use as a solution in hexane. The obtained analytical data fitted accurately with the literature data.

Colorless solution.

The \(^1\)H NMR is extremely complicated due to the “permanent migrating” nature of the allyl borane.

\[^{11}\text{B NMR (CDCl}_3, 128 \text{ MHz): } \delta = 85.7 \text{ ppm}\].
4.4 Development of Gallium(I) and Aluminum(I) Catalysis

4.4.1 General Procedures

**General procedure G (under ultrasonication)**

Gallium(0) (1.4 mg, 0.02 mmol, 10 mol%), silver triflate (2.8 mg, 0.01 mmol, 5 mol%) or silver fluoride (1.3 mg, 0.01 mmol, 5 mol%), [18]crown-6 (5.2 mg, 0.04 mmol, 10 mol%), the corresponding electrophile (0.20 mmol), allyl boronic ester (71, 37.0 mg, 0.22 mmol, 1.1 equiv) or deuterio-allyl boronic ester (71-[d2], 51.0 mg, 0.30 mmol, 1.5 equiv) or allenyl boronic ester (86, 39.9 mg, 0.24 mmol, 1.2 equiv), and dioxane (200 µL, 1.0 M) or toluene (400–800 µL, 0.25–0.5 M) were added to an oven-dried 2 mL-test tube in a nitrogen-filled glove box. The mixture was reacted under ultrasonication at 40–50 °C for 8–72 h, at which point the 1H NMR analysis indicated the complete consumption of the electrophile. The solvent was removed *in vacuo* and the residue was purified by PTLC on silica gel (0 to 10% heptane in EtOAc) to give the desired product as pale yellow liquid.

**General procedure H (low catalyst loading)**

Gallium(0) (1.4 mg, 0.02 mmol, 0.20 mol%), silver triflate (2.8 mg, 0.01 mmol, 0.10 mol%), the model acetal 70a (1.52 g, 10.0 mmol), allyl boronic ester (71, 1.85 g, 11.0 mmol, 1.1 equiv), and dioxane (10.0 mL, 1.0 M) were added to an oven-dried 50 mL round-bottom flask in a nitrogen-filled glove box. The mixture was reacted under ultrasonication at 40–45 °C for 96 h under a nitrogen atmosphere. The solvent was removed *in vacuo* and the residue was purified by a flash column chromatography on silica gel (heptane:EtOAc = 19:1) to give the desired product in 80% yield (1.3 g) as pale yellow liquid.

**General procedure I (using an allyl silane)**

Gallium(0) (1.4 mg, 0.02 mmol, 10 mol%), silver triflate (2.8 mg, 0.01 mmol, 5 mol%),
electrophile (0.20 mmol), allyl silane (94, 25.1 mg, 0.22 mmol, 1.1 equiv), and dioxane (200 µL, 1.0 M) were added to an oven-dried 2 mL-test tube with a magnetic stirring bar in a nitrogen-filled glove box. The reaction mixture was stirred at 25–30 °C for 0.5–18 h. Then the NMR yield of the corresponding product was analyzed by 1H NMR with dibenzyl ether (DBE, 25 mol% in mesitylene, 0.20 mmol) as an internal standard.

**General procedure J (using an α-silyl allyl boronic ester)**

Gallium(0) (1.4 mg, 0.02 mmol, 10 mol%), silver triflate (2.8 mg, 0.01 mmol, 5 mol%), and dioxane (100 µL) were added to an oven-dried 2 mL-test tube with a magnetic stirring bar in a nitrogen-filled glove box. The catalyst mixture was stirred at 30 °C for 5 h, at which point the corresponding electrophile (0.20 mmol), α-(trimethylsilyl)allyl boronic ester (136, 26.4 mg, 0.22 mmol, 1.1 equiv), and MeCN (100 µL) were added to the pre-formed catalyst mixture in a nitrogen-filled glove box. The reaction mixture was then stirred at 25 °C, at which point the 1H NMR analysis of a reaction aliquot confirmed the complete consumption of the electrophile. The solvents were then removed in vacuo, and the residue was purified by PTLC on silica gel (0–10% heptane in EtOAc) to give the desired product as a pale yellow liquid or a colorless solid.

**General procedure K (using an allyl borane)**

Gallium(0) (1.4 mg, 0.02 mmol, 10 mol%), silver triflate (2.8 mg, 0.01 mmol, 5 mol%), electrophile (0.20 mmol), allyl-9-BBN (110, 220 µL, 0.22 mmol, 0.5 M in heptane, 1.1 equiv), and dioxane (200 µL, 1.0 M) were added to an oven-dried 2 mL-test tube with a magnetic stirring bar in a nitrogen-filled glove box. The reaction mixture was stirred at 25 °C for 0.5–5 h. Then the NMR yield of the corresponding product was analyzed by 1H NMR with dibenzyl ether (DBE, 25 mol% in mesitylene, 0.20 mmol) as an internal standard.
**General procedure L (aluminum catalysis, using an allyl boronic ester)**

Aluminum(0) (2.2 mg, 0.08 mmol, 40 mol%), silver salt (0.04 mmol, 20 mol%), acetal 70a (30.4 mg, 0.20 mmol), allyl boronic ester (71, 37.0 mg, 0.22 mmol, 1.1 equiv), and solvent (200–400 µL, 0.5–1.0 M) were added to an oven-dried 2 mL-test tube with a magnetic stirring bar in a nitrogen-filled glove box. The reaction mixture was stirred at 40–60 °C for 16–70 h. Then the NMR yield of the corresponding product was analyzed by $^1$H NMR with dibenzyl ether (DBE, 25 mol% in mesitylene, 0.20 mmol) as an internal standard.

**General procedure M (aluminum catalysis, using an allyl silane)**

Aluminum(0) (1.1 mg, 0.04 mmol, 20 mol%), silver triflate (5.6 mg, 0.02 mmol, 10 mol%), acetal 70a (30.4 mg, 0.20 mmol), allyl silane (94, 25.1 mg, 0.22 mmol, 1.1 equiv), toluene (200 µL, 1.0 M) were added to an oven-dried 2 mL-test tube with a magnetic stirring bar in a nitrogen-filled glove box. The reaction mixture was stirred at 25 °C for 2–5 h. Then the NMR yield of the corresponding product was analyzed by $^1$H NMR with dibenzyl ether (DBE, 25 mol% in mesitylene, 0.20 mmol) as an internal standard.
4.4.2 Analytical Data

1-(1-Methoxybut-3-en-1-yl)benzene\textsuperscript{67a} (72a)

\[
\begin{array}{c}
\text{OMe} \\
\text{72a}
\end{array}
\]

72a was prepared according to:

*General procedure* G: using gallium metal (10 mol%), silver triflate (5 mol%), and [18]crown-6 (10 mol%) with acetal 70a and allyl boronic ester (71, 1.1 equiv) in dioxane (1.0 M) under ultrasonication at 40–45 °C for 8 h. 72a was purified by PTLC on silica gel (eluant: heptane:EtOAc = 19:1).

Yield: 91%.

*General procedure* H: using gallium metal (0.02 mol%), silver triflate (0.01 mol%) and [18]crown-6 (0.02 mol%) with acetal 70a and allyl boronic ester (71, 1.1 equiv) in dioxane (1.0 M) under ultrasonication at 40–45 °C for 96 h.

Yield: 80%.

*General procedure* I: using gallium metal (10 mol%), silver triflate (5 mol%) with acetal 70a and allyl silane (94, 1.1 equiv) in dioxane (1.0 M) at 25 °C for 0.5 h.

NMR yield: 99%.

*General procedure* K: using gallium metal (10 mol%), silver triflate (5 mol%) with acetal 70a and allyl borane (110, 1.1 equiv, 0.5 M solution in hexane) in dioxane (1.0 M) at 25 °C for 0.5 h.

NMR yield: 93%.

*General procedure* L: using aluminum metal (40 mol%), silver triflate (20 mol%) with acetal 70a and allyl boronic ester (71, 1.1 equiv) in toluene or BTF (0.5 M) at 50 °C for 70 h.

NMR yield: 9% in toluene and 15% in BTF.

*General procedure* M: using aluminum metal (20 mol%), silver triflate (10 mol%) with acetal 70a and allyl silane (94, 1.1 equiv) in toluene (1.0 M) at 25 °C for 5 h.

NMR yield: 82%.
The obtained analytical data fitted accurately with the reported data.\textsuperscript{67a}

Colorless liquid.

\textbf{\textsuperscript{1}H NMR} (CDCl\textsubscript{3}, 600 MHz): $\delta = 2.39$–2.43 (m, 1H), 2.54–2.59 (m, 1H), 3.22 (s, 3H), 4.16 (dd, $J = 5.9$, 7.4 Hz, 1H), 5.00–5.07 (m, 2H), 5.77 (dddd, $J = 6.9$, 6.9, 10.2, 17.1 Hz, 1H), 7.25–7.36 (m, 5H) ppm.

\textbf{\textsuperscript{13}C NMR} (CDCl\textsubscript{3}, 150 MHz): $\delta = 42.5$, 56.6, 83.7, 116.8, 126.7 (2C), 127.6, 128.3 (2C), 134.8, 141.7 ppm.

1-(1-Methoxybut-3-en-1-yl)-4-(trifluoromethyl)benzene (72b)

![Chemical structure](image)

72b was prepared according to:

\textit{General procedure G}: using gallium metal (10 mol\%), silver triflate (5 mol\%) and [18]crown-6 (10 mol\%) with acetal 70b and allyl boronic ester (71, 1.1 equiv) in dioxane (1.0 M) under ultrasonication at 40–45 °C for 12 h. 72b was purified by PTLC on silica gel (eluant: heptane:EtOAc = 19:1).

Yield: 92%.

\textit{General procedure I}: using gallium metal (10 mol\%), silver triflate (5 mol\%) with acetal 70b and allyl silane (94, 1.1 equiv) in dioxane (1.0 M) at 25 °C for 0.5 h.

NMR yield: 99%.

Colorless liquid.

\textbf{\textsuperscript{1}H NMR} (CDCl\textsubscript{3}, 500 MHz): $\delta = 2.39$–2.42 (m, 1H), 2.53–2.56 (m, 1H), 3.24 (s, 3H), 4.23 (dd, $J = 6.3$, 7.0 Hz, 1H), 5.03–5.06 (m, 2H), 5.74 (dddd, $J = 6.9$, 7.0, 9.7, 17.0 Hz, 1H), 7.41 (d, $J = 8.1$ Hz, 2H), 7.61 (d, $J = 8.1$ Hz, 2H) ppm.

\textbf{\textsuperscript{13}C NMR} (CDCl\textsubscript{3}, 125 MHz): $\delta = 42.3$, 56.9, 83.1, 117.5, 124.2 (q, $J = 271.8$ Hz), 125.4 (q, $J = 3.8$ Hz, 2C), 127.0 (2C), 129.9 (q, $J = 32.4$ Hz), 134.0, 145.9 ppm.

\textbf{\textsuperscript{19}F NMR} (CDCl\textsubscript{3}, 128 MHz): $\delta = -62.4$–$-62.5$ (m) ppm.
IR (neat): $\nu = 1320, 1163, 1122, 1097, 1064, 916, 837 \text{ cm}^{-1}$.

HRMS: Mass spectroscopic analyses failed to give the desired molecular signal, resulting only in fragmentation.

**Methyl 4-(1-methoxybut-3-en-1-yl)benzoate\textsuperscript{62} (72c)**

\[
\begin{array}{c}
\text{MeO} \\
\text{O} \\
\text{72c}
\end{array}
\]

72c was prepared according to:

*General procedure G:* using gallium metal (10 mol%), silver triflate (5 mol%) and [18]crown-6 (10 mol%) with acetal 70c and allyl boronic ester (71, 1.1 equiv) in dioxane (1.0 M) under ultrasonication at 40–45 °C for 8 h. 72c was purified by PTLC on silica gel (eluant: heptane:EtOAc = 19:1).

Yield: 92%.

*General procedure I:* using gallium metal (10 mol%), silver triflate (5 mol%) with acetal 70c and allyl silane (94, 1.1 equiv) in dioxane (1.0 M) at 25 °C for 0.5 h.

NMR yield: 99%.

The obtained analytical data fitted accurately with the reported data.\textsuperscript{62}

Colorless liquid.

\textsuperscript{1}H NMR (CDCl\textsubscript{3}, 500 MHz): $\delta = 2.38$–$2.43$ (m, 1H), $2.53$–$2.58$ (m, 1H), 3.23 (s, 3H), 3.91 (s, 3H), 4.23 (dd, $J = 6.3$, 6.9 Hz, 1H), 5.01–5.05 (m, 2H), 5.70–5.78 (m, 1H), 7.36 (d, $J = 8.1$ Hz, 2H), 8.03 (d, $J = 8.1$ Hz, 2H) ppm.

\textsuperscript{13}C NMR (CDCl\textsubscript{3}, 150 MHz): $\delta = 42.3$, 52.0, 56.9, 83.2, 117.3, 126.7 (2C), 129.5, 129.7 (2C), 134.1, 147.0, 166.9 ppm.
1-Fluoro-4-(1-methoxybut-3-en-1-yl)benzene (72d)

72d was prepared according to:

**General procedure G:** using gallium metal (10 mol%), silver triflate (5 mol%) and [18]crown-6 (10 mol%) with acetal 70d and allyl boronic ester (71, 1.1 equiv) in dioxane (1.0 M) under ultrasonication at 40–45 °C for 8 h. 72d was purified by PTLC on silica gel (eluant: heptane:EtOAc = 19:1).

Yield: 89%.

**General procedure I:** using gallium metal (10 mol%), silver triflate (5 mol%) with acetal 70d and allyl silane (94, 1.1 equiv) in dioxane (1.0 M) at 25 °C for 0.5 h.

NMR yield: 99%.

The obtained analytical data fitted accurately with the reported data.\textsuperscript{144}

Pale yellow liquid.

**$^1$H NMR** (CDCl\textsubscript{3}, 600 MHz): $\delta = 2.35–2.40$ (m, 1H), 2.52–2.57 (m, 1H), 3.20 (s, 3H), 4.15 (dd, $J = 6.4$, 7.0 Hz, 1H), 5.01–5.05 (m, 2H), 5.70–5.75 (m, 1H), 7.01–7.05 (m, 2H), 7.23–7.27 (m, 2H) ppm.

**$^{13}$C NMR** (CDCl\textsubscript{3}, 125 MHz): $\delta = 42.5$, 56.6, 83.0, 115.2 (d, $J = 21.4$ Hz, 2C), 117.1, 128.3 (d, $J = 8.0$ Hz, 2C), 134.5, 137.4 (d, $J = 3.0$ Hz), 162.3 (d, $J = 245$ Hz) ppm.

**$^{19}$F NMR** (CDCl\textsubscript{3}, 128 MHz): $\delta = -115.1$ ~ −115.2 (m) ppm.

1-Chloro-4-(1-methoxybut-3-en-1-yl)benzene (72e)

72e was prepared according to:

**General procedure G:** using gallium metal (10 mol%), silver triflate (5 mol%) and [18]crown-6 (10 mol%) with acetal 70e and allyl boronic ester (71, 1.1 equiv) in dioxane
(1.0 M) under ultrasonication at 40–45 °C for 12 h. **72e** was purified by PTLC on silica gel (eluant: heptane:EtOAc = 19:1).

Yield: 92%.

**General procedure** I: using gallium metal (10 mol%), silver triflate (5 mol%) with acetal **70e** and allyl silane (**94**, 1.1 equiv) in dioxane (1.0 M) at 25 °C for 0.5 h.

NMR yield: 97%.

The obtained analytical data fitted accurately with the reported data.\(^\text{67a}\)

Colorless liquid.

\(^1\text{H} \text{NMR} \text{ (CDCl}_3, 600 \text{ MHz}): \delta = 2.35–2.40 \text{ (m, 1H)}, 2.51–2.56 \text{ (m, 1H)}, 3.21 \text{ (s, 3H)}, 4.14 \text{ (dd, } J = 6.3, 6.9 \text{ Hz, 1H}), 5.01–5.05 \text{ (m, 2H)}, 5.69–5.76 \text{ (m, 1H)}, 7.21–7.23 \text{ (m, 2H)}, 7.31–7.34 \text{ (m, 2H) ppm.}

\(^{13}\text{C} \text{NMR} \text{ (CDCl}_3, 125 \text{ MHz}): \delta = 42.4, 56.7, 83.0, 117.2, 128.1 \text{ (2C)}, 128.5 \text{ (2C)}, 133.3, 134.3, 140.2 \text{ ppm.}

**1-Bromo-4-(1-methoxybut-3-en-1-yl)benzene\(^\text{67a}\) (72f)**

\[ \text{Br} \quad \text{OMe} \quad \text{72f} \]

**72f** was prepared according to:

**General procedure** G: using gallium metal (10 mol%), silver triflate (5 mol%) and [18]crown-6 (10 mol%) with acetal **70f** and allyl boronic ester (**71**, 1.1 equiv) in dioxane (1.0 M) under ultrasonication at 40–45 °C for 12 h. **72f** was purified by PTLC on silica gel (eluant: heptane:EtOAc = 19:1).

Yield: 92%.

**General procedure** I: using gallium metal (10 mol%), silver triflate (5 mol%) with acetal **70f** and allyl silane (**94**, 1.1 equiv) in dioxane (1.0 M) at 25 °C for 0.5 h.

NMR yield: 99%.

The obtained analytical data fitted accurately with the reported data.\(^\text{67a}\)

Colorless liquid.
$^1$H NMR (CDCl$_3$, 600 MHz): $\delta = 2.35$–2.39 (m, 1H), 2.51–2.55 (m, 1H), 3.21 (s, 3H), 4.13 (dd, $J = 6.3, 6.9$ Hz, 1H), 5.01–5.05 (m, 2H), 5.73 (dddd, $J = 6.9, 7.0, 10.3, 17.2$ Hz, 1H), 7.15–7.17 (m, 2H), 7.46–7.48 (m, 2H) ppm.

$^{13}$C NMR (CDCl$_3$, 150 MHz): $\delta =$ 42.3, 56.7, 83.0, 117.2, 121.4, 128.5 (2C), 131.5 (2C), 134.2, 140.8 ppm.

1-(1-Methoxybut-3-en-1-yl)-4-methylbenzene$^{67a}$ (72g)

72g was prepared according to:

*General procedure G*: using gallium metal (10 mol%), silver fluoride (5 mol%) and [18]crown-6 (10 mol%) with acetal 70g and allyl boronic ester (71, 1.1 equiv) in dioxane (1.0 M) under ultrasonication at 40–45 °C for 20 h. 72g was purified by PTLC on silica gel (eluant: heptane:EtOAc = 19:1).

Yield: 94%.

*General procedure I*: using gallium metal (10 mol%), silver triflate (5 mol%) with acetal 70g and allyl silane (94, 1.1 equiv) in dioxane (1.0 M) at 25 °C for 0.5 h.

NMR yield: 98%.

The obtained analytical data fitted accurately with the reported data.$^{67a}$

Colorless liquid.

$^1$H NMR (CDCl$_3$, 600 MHz): $\delta =$ 2.35 (s, 3H), 2.37–2.42 (m, 1H), 2.53–2.58 (m, 1H), 3.20 (s, 3H), 4.13 (dd, $J = 5.9, 7.4$ Hz, 1H), 5.03–5.10 (m, 2H), 5.76 (dddd, $J = 6.9, 7.0, 10.3, 17.2$ Hz, 1H), 7.14–7.19 (m, 4H) ppm.

$^{13}$C NMR (CDCl$_3$, 150 MHz): $\delta =$ 21.1, 42.5, 56.5, 83.5, 116.7, 128.7 (2C), 129.0 (2C), 135.0, 137.2, 138.6 ppm.

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228
(4-(1-Methoxybut-3-en-1-yl)phenyl)methanol (72h)

72h was prepared according to:

General procedure G: using gallium metal (10 mol%), silver triflate (5 mol%) and [18]crown-6 (10 mol%) with acetal 70h and allyl boronic ester (71, 1.1 equiv) in toluene (1.0 M) under ultrasonication at 50 °C for 20 h. 72h was purified by PTLC on silica gel (eluant: heptane:EtOAc = 9:1; eluted twice).

Yield: 57%.

^1H NMR (CDCl₃, 400 MHz): δ = 1.64 (br s, 1H), 2.38–2.42 (m, 1H), 2.54–2.59 (m, 1H), 3.22 (s, 3H), 4.17 (dd, J = 6.0, 7.3 Hz, 1H), 4.70 (s, 2H), 5.01–5.08 (m, 2H), 5.71–5.81 (m, 1H), 7.29 (d, J = 8.1 Hz, 2H), 7.36 (d, J = 8.1 Hz, 2H) ppm.

^13C NMR (CDCl₃, 150 MHz): δ = 42.5, 56.7, 65.2, 83.4, 117.0, 127.0 (2C), 127.1 (2C), 134.7, 140.2, 141.2 ppm.

IR (neat): ν = 3421, 2862, 2849, 1463, 1095, 1016, 914, 819 cm⁻¹.


4-(1-Methoxybut-3-en-1-yl)-N,N-dimethylaniline (72i)

72i was prepared according to:

General procedure G: using gallium metal (10 mol%), silver triflate (5 mol%) and [18]crown-6 (10 mol%) with acetal 70i and allyl boronic ester (71, 1.1 equiv) in toluene (0.25 M) under ultrasonication at 40–45 °C for 20 h. 72i was purified by PTLC on silica gel (eluant: heptane:EtOAc = 19:1).
Yield: 54%

Pale yellow liquid.

$^1$H NMR (CDCl$_3$, 600 MHz): $\delta$ = 2.37–2.42 (m, 1H), 2.54–2.59 (m, 1H), 2.95 (s, 6H), 3.18 (s, 3H), 4.07 (dd, $J$ = 6.2, 7.4 Hz, 1H), 5.00–5.07 (m, 2H), 5.75–5.80 (m, 1H), 6.71 (d, $J$ = 8.6 Hz, 2H), 7.16 (d, $J$ = 8.6 Hz, 2H) ppm.

$^{13}$C NMR (CDCl$_3$, 150 MHz): $\delta$ = 40.6 (2C), 42.4, 56.2, 83.3, 112.3 (2C), 116.5, 127.8 (2C), 129.3, 135.4, 150.2 ppm.

IR (neat): $\nu$ = 2918, 2828, 1614, 1521, 1346, 1274, 1261, 1093, 912, 756 cm$^{-1}$.

HRMS (ESI): calculated for C$_{13}$H$_{19}$NaNO$^+$ = [M+Na]$^+$: $m/z$ = 228.1359, found: $m/z$ = 228.1358.

1-Methoxy-4-(1-methoxybut-3-en-1-yl)benzene$^{67a}$ (72j)

![Chemical structure]

72j was prepared according to:

General procedure G: using gallium metal (10 mol%), silver fluoride (5 mol%) and [18]crown-6 (10 mol%) with acetal 70j and allyl boronic ester (71, 1.1 equiv) in dioxane (1.0 M) under ultrasonication at 40–45 °C for 20 h. 72j was purified by PTLC on silica gel (eluant: heptane:EtOAc = 19:1).

Yield: 93%.

General procedure I: using gallium metal (10 mol%), silver triflate (5 mol%) with acetal 70j and allyl silane (94, 1.1 equiv) in dioxane (1.0 M) at 25 °C for 0.5 h.

NMR yield: 99%.

The obtained analytical data fitted accurately with the reported data.$^{67a}$

Colorless liquid.

$^1$H NMR (CDCl$_3$, 600 MHz): $\delta$ = 2.37–2.41 (m, 1H), 2.54–2.59 (m, 1H), 3.19 (s, 3H), 3.81 (s, 3H), 4.14 (dd, $J$ = 6.3, 7.1 Hz, 1H), 5.00–5.06 (m, 2H), 5.75 (dddd, $J$ = 6.9, 6.9, 10.2, 17.1 Hz, 1H), 6.87–6.90 (m, 2H), 7.20–7.22 (m, 2H) ppm.
$^{13}$C NMR (CDCl$_3$, 150 MHz): $\delta = 42.5, 55.2, 56.4, 83.2, 113.7, 116.8, 127.9$ (2C), 133.7 (2C), 134.9, 159.1 ppm.

1-(1-Methoxybut-3-en-1-yl)-3-methylbenzene$^{67a}$ (72k)

[Diagram]

72k was prepared according to:

*General procedure G*: using gallium metal (10 mol%), silver triflate (5 mol%) and [18]crown-6 (10 mol%) with acetal 70k and allyl boronic ester (71, 1.1 equiv) in dioxane (1.0 M) under ultrasonication at 40–45 °C for 12 h. 72k was purified by PTLC on silica gel (eluant: heptane:EtOAc = 19:1).

Yield: 91%.

*General procedure I*: using gallium metal (10 mol%), silver triflate (5 mol%) with acetal 70k and allyl silane (94, 1.1 equiv) in dioxane (1.0 M) at 25 °C for 0.5 h.

NMR yield: 99%.

The obtained analytical data fitted accurately with the reported data.$^{67a}$

Colorless liquid.

$^1$H NMR (CDCl$_3$, 600 MHz): $\delta = 2.40$ (s, 3H), 2.41–2.46 (m, 1H), 2.57–2.62 (m, 1H), 3.26 (s, 3H), 4.16 (dd, $J = 5.8, 7.6$ Hz, 1H), 5.04–5.11 (m, 2H), 5.81 (dddd, $J = 6.9, 6.9, 10.2, 17.1$ Hz, 1H), 7.11–7.14 (m, 2H), 7.26–7.28 (m, 2H) ppm.

$^{13}$C NMR (CDCl$_3$, 150 MHz): $\delta = 21.5, 42.5, 56.7, 83.7, 116.8, 123.8, 127.4, 128.2, 128.3, 135.0, 138.0, 141.7$ ppm.

1-(1-Methoxybut-3-en-1-yl)-2-methylbenzene$^{67a}$ (72l)

[Diagram]
72l was prepared according to:

*General procedure G*: using gallium metal (10 mol%), silver triflate (5 mol%) and [18]crown-6 (10 mol%) with acetal 70l and allyl boronic ester (71, 1.1 equiv) in dioxane (1.0 M) under ultrasonication at 40–45 °C for 8 h. 72l was purified by PTLC on silica gel (eluant: heptane:EtOAc = 19:1).

Yield: 90%.

*General procedure I*: using gallium metal (10 mol%), silver triflate (5 mol%) with acetal 70l and allyl silane (94, 1.1 equiv) in dioxane (1.0 M) at 25 °C for 0.5 h.

NMR yield: 99%.

The obtained analytical data fitted accurately with the reported data.

Colorless liquid.

^1H NMR (CDCl₃, 600 MHz): δ = 2.32 (s, 3H), 2.37–2.41 (m, 1H), 2.47–2.52 (m, 1H), 3.21 (s, 3H), 4.46 (dd, J = 5.1, 7.9 Hz, 1H), 5.02–5.09 (m, 2H), 5.87 (dddd, J = 6.9, 6.9, 10.1, 17.1 Hz, 1H), 7.14 (dd, J = 1.4, 7.6 Hz, 1H) 7.16 (td, J = 1.4, 7.6 Hz, 1H), 7.22 (ddd, J = 1.1, 1.4, 7.6 Hz, 1H), 7.37 (dd, J = 1.1, 7.6 Hz, 1H) ppm.

^13C NMR (CDCl₃, 150 MHz): δ = 19.1, 41.6, 56.6, 80.0, 116.7, 125.9, 126.2, 127.1, 130.4, 135.0, 135.3, 139.7 ppm.

1-(1-Methoxybut-3-en-1-yl)naphthalene (72m)

![Chemical structure](image)

72m was prepared according to:

*General procedure G*: using gallium metal (10 mol%), silver triflate (5 mol%) and [18]crown-6 (10 mol%) with acetal 70m and allyl boronic ester (71, 1.1 equiv) in dioxane (1.0 M) under ultrasonication at 40–45 °C for 8 h. 72m was purified by PTLC on silica gel (eluant: heptane:EtOAc = 19:1).

Yield: 91%.

*General procedure I*: using gallium metal (10 mol%), silver triflate (5 mol%) with acetal
70m and allyl silane (94, 1.1 equiv) in dioxane (1.0 M) at 25 °C for 0.5 h.

NMR yield: 99%.

The obtained analytical data fitted accurately with the reported data. 67a

Colorless liquid.

$^1$H NMR (CDCl$_3$, 600 MHz): $\delta = 2.61$–2.72 (m, 2H), 3.29 (s, 3H), 4.94 (dd, $J = 5.1$, 7.8 Hz, 1H), 5.03–5.10 (m, 2H), 5.87 (dddd, $J = 6.9$, 6.9, 10.2, 17.0 Hz, 1H), 7.46–7.52 (m, 3H), 7.55 (br d, $J = 6.5$ Hz, 1H), 7.78 (d, $J = 8.1$ Hz, 1H), 7.91–7.93 (m, 1H), 8.17 (d, $J = 8.1$ Hz, 1H) ppm.

$^{13}$C NMR (CDCl$_3$, 150 MHz): $\delta = 41.9$, 56.9, 81.4, 116.7, 123.3, 124.1, 125.4, 125.5, 125.9, 128.0, 128.9, 131.1, 134.0, 135.2, 137.2 ppm.

2-(1-Methoxybut-3-en-1-yl)naphthalene 67a (72n)

72n was prepared according to:

General procedure G: using gallium metal (10 mol%), silver triflate (5 mol%) and [18]crown-6 (10 mol%) with acetal 70n and allyl boronic ester (71, 1.1 equiv) in dioxane (1.0 M) under ultrasonication at 40–45 °C for 8 h. 72n was purified by PTLC on silica gel (eluant: heptane:EtOAc = 19:1).

Yield: 91%.

General procedure I: using gallium metal (10 mol%), silver triflate (5 mol%) with acetal 70n and allyl silane (94, 1.1 equiv) in dioxane (1.0 M) at 25 °C for 0.5 h.

NMR yield: 99%.

The obtained analytical data fitted accurately with the reported data. 67a

Colorless liquid.

$^1$H NMR (CDCl$_3$, 600 MHz): $\delta = 2.47$–2.52 (m, 1H), 2.63–2.68 (m, 1H), 3.25 (s, 3H), 4.38 (dd, $J = 6.3$, 7.0 Hz, 1H), 5.01–5.08 (m, 2H), 5.79 (dddd, $J = 6.9$, 7.0, 10.2, 17.1 Hz, 1H), 7.49–7.54 (m, 3H), 7.77 (s, 1H), 7.86–7.90 (m, 3H) ppm.
\[^{13}\text{C} \text{NMR (CDCl}_3, 150 \text{ MHz)}: \delta = 42.4, 56.8, 83.8, 117.0, 124.5, 125.8, 126.0, 126.1, 127.7, 127.9, 128.3, 133.1, 133.2, 134.7, 139.1 \text{ ppm.}\]

(1-Ethoxybut-3-en-1-yl)benzene\(^{145}\) (72o)

72o was prepared according to:

*General procedure G:* using gallium metal (10 mol%), silver triflate (5 mol%) and \[^{[18]}\text{crown-6} (10 \text{ mol%})\] with acetal 70o and allyl boronic ester (71, 1.1 equiv) in dioxane (1.0 M) under ultrasonication at 40–45 °C for 12 h. 72o was purified by PTLC on silica gel (eluant: heptane:EtOAc = 19:1).

Yield: 87%.

*General procedure I:* using gallium metal (10 mol%), silver triflate (5 mol%) with acetal 70o and allyl silane (94, 1.1 equiv) in dioxane (1.0 M) at 25 °C for 0.5 h.

NMR yield: 97%.

The obtained analytical data fitted accurately with the reported data.\(^{145}\)

Colorless liquid.

\[^{1}\text{H} \text{NMR (CDCl}_3, 600 \text{ MHz)}: \delta = 1.17 (t, J = 6.9 \text{ Hz}, 3\text{H}), 2.37–2.42 (m, 1\text{H}), 2.55–2.60 (m, 1\text{H}), 3.30–3.41 (m, 2\text{H}), 4.26 (dd, J = 6.2, 7.4 \text{ Hz}, 1\text{H}), 4.99–5.05 (m, 2\text{H}), 5.78(dddd, J = 6.9, 6.9, 10.2, 17.1 \text{ Hz}, 1\text{H}), 7.25–7.34 (m, 5\text{H}) \text{ ppm.}\]

\[^{13}\text{C} \text{NMR (CDCl}_3, 150 \text{ MHz)}: \delta = 15.3, 42.7, 64.1, 81.8, 116.7, 126.7 (2\text{C}), 127.4, 128.3 (2\text{C}), 135.0, 142.5 \text{ ppm.}\]

(1-(Benzyloxy)but-3-en-1-yl)benzene\(^{146}\) (72p)

72p was prepared according to:
General procedure G: using gallium metal (10 mol%), silver triflate (5 mol%) and [18]crown-6 (10 mol%) with acetal 70p and allyl boronic ester (71, 1.1 equiv) in dioxane (1.0 M) under ultrasonication at 40–45 °C for 20 h. 72p was purified by PTLC on silica gel (eluant: heptane:EtOAc = 19:1). Yield: 88%.

General procedure I: using gallium metal (10 mol%), silver triflate (5 mol%) with acetal 70p and allyl silane (94, 1.1 equiv) in dioxane (1.0 M) at 25 °C for 1 h.
NMR yield: 65%.
The obtained analytical data fitted accurately with the reported data.\textsuperscript{146}

Colorless liquid.

\textsuperscript{1}H NMR (CDCl\textsubscript{3}, 600 MHz): \(\delta = 2.42–2.48\) (m, 1H), \(2.61–2.66\) (m, 1H), \(4.28\) (d, \(J = 11.8\) Hz, 1H), \(4.36\) (dd, \(J = 5.9, 7.6\) Hz, 1H), \(4.47\) (d, \(J = 11.8\) Hz, 1H), \(4.99–5.05\) (m, 2H), \(5.75–5.82\) (ddt, \(J = 6.9, 10.2, 17.1\) Hz, 1H), \(7.25–7.37\) (m, 10H) ppm.

\textsuperscript{13}C NMR (CDCl\textsubscript{3}, 150 MHz): \(\delta = 42.7, 70.4, 81.2, 116.8, 126.9\) (2C), \(127.5, 127.6, 127.7\) (2C), \(128.3\) (2C), \(128.4\) (2C), \(134.9, 138.5, 141.9\) ppm.

1-Allylisochromane\textsuperscript{62} (72q)

72q was prepared according to:

General procedure G: using gallium metal (10 mol%), silver triflate (5 mol%) and [18]crown-6 (10 mol%) with acetal 70q and allyl boronic ester (71, 1.1 equiv) in dioxane (1.0 M) under ultrasonication at 40–45 °C for 12 h. 72q was purified by PTLC on silica gel (eluant: heptane:EtOAc = 19:1). Yield: 90%.

General procedure I: using gallium metal (10 mol%), silver triflate (5 mol%) with acetal 70q and allyl silane (94, 1.1 equiv) in dioxane (1.0 M) at 25 °C for 1 h.
NMR yield: 99%.
The obtained analytical data fitted accurately with the reported data.\textsuperscript{62}

Colorless liquid.

\textbf{\textsuperscript{1}H NMR} (CDCl\textsubscript{3}, 600 MHz): $\delta = 2.56$–$2.61$ (m, 1H), $2.66$–$2.73$ (m, 2H), $2.99$ (ddd, $J = 5.4$, $9.7$, $15.5$ Hz, 1H), $3.82$ (ddd, $J = 3.8$, $9.7$, $11.3$ Hz, 1H), $4.20$ (ddd, $J = 3.8$, $5.4$, $11.3$ Hz, 1H), $4.84$ (dd, $J = 3.4$, $8.0$ Hz, 1H), $5.08$ (ddd, $J = 1.2$, $3.4$, $10.3$ Hz, 1H), $5.14$ (ddd, $J = 1.2$, $3.4$, $17.1$ Hz, 1H), $5.91$ (ddt, $J = 6.8$, $10.3$, $17.1$ Hz, 1H), $7.09$–$7.19$ (m, 4H) ppm.

\textbf{\textsuperscript{13}C NMR} (CDCl\textsubscript{3}, 150 MHz): $\delta = 29.1$, $40.4$, $63.4$, $75.6$, $117.0$, $124.8$, $126.1$, $126.3$, $128.9$, $134.1$, $135.0$, $137.8$ ppm.

\textbf{2-Allyl-2H-chromene}\textsuperscript{147} (72r)

72r was prepared according to:

\textit{General procedure G}: using gallium metal (10 mol\%), silver fluoride (5 mol\%) and \textsuperscript{[18]}crown-6 (10 mol\%) with acetal 70r and allyl boronic ester (71, 1.1 equiv) in dioxane (1.0 M) under ultrasonication at 40–45 °C for 52 h. 72r was purified by PTLC on silica gel (eluant: heptane:EtOAc = 19:1).

Yield: 80%.

\textit{General procedure K}: using gallium metal (10 mol\%), silver triflate (5 mol\%) with acetal 70r and allyl borane (110, 1.1 equiv, 0.5 M solution in hexane) in dioxane (1.0 M) at 25 °C for 0.5 h.

NMR yield: 88%.

The obtained analytical data fitted accurately with the reported data.\textsuperscript{147}

Colorless liquid.

\textbf{\textsuperscript{1}H NMR} (CDCl\textsubscript{3}, 600 MHz): $\delta = 2.43$–$2.48$ (m, 1H), $2.56$–$2.60$ (m, 1H), $4.90$–$4.92$ (m, 1H), $5.11$–$5.16$ (m, 2H), $5.69$ (dd, $J = 3.3$, $9.8$ Hz, 1H), $5.90$ (dddd, $J = 7.0$, $7.0$, $10.2$, $17.1$ Hz, 1H), $6.41$ (dd, $J = 1.2$, $9.8$ Hz, 1H), $6.77$ (d, $J = 8.1$ Hz, 1H), $6.87$ (td, $J = 1.2$, $7.4$ Hz, 1H), $6.99$ (dd, $J = 1.6$, $7.4$ Hz, 1H), $7.13$ (td, $J = 1.6$, $7.8$ Hz, 1H) ppm.
$^{13}$C NMR (CDCl$_3$, 125 MHz): $\delta = 39.7$, 74.7, 115.9, 117.7, 121.0, 121.7, 124.2, 125.1, 126.3, 129.1, 133.3, 153.2 ppm.

**Tert-butyl-3-(1-methoxybut-3-enyl)-1H-indole-1-carboxylate**$^{62}$ (72s)

![72s](image)

72s was prepared according to:

*General procedure G:* using gallium metal (10 mol%), silver fluoride (5 mol%) and [18]crown-6 (10 mol%) with acetal 70s and allyl boronic ester (71, 1.1 equiv) in toluene (0.5 M) under ultrasonication at 50°C for 16 h. 72s was purified by PTLC on silica gel (eluant: heptane:EtOAc = 19:1).

Yield: 84%.

The obtained analytical data fitted accurately with the reported data.$^{62}$

Pale yellow liquid.

$^1$H NMR (CDCl$_3$, 600 MHz): $\delta = 1.67$ (s, 9H), 2.60–2.65 (m, 1H), 2.74–2.79 (m, 1H), 3.29 (s, 3H), 4.47 (dd, $J = 6.6$, 6.8 Hz, 1H), 5.03–5.11 (m, 2H), 5.81 (dddd, $J = 6.9$, 6.9, 10.2, 17.1 Hz, 1H), 7.21–7.25 (m, 1H), 7.30–7.33 (m, 1H), 7.51 (s, 1H), 7.71 (d, $J = 7.8$ Hz, 1H), 8.14 (br s, 1H) ppm.

$^{13}$C NMR (CDCl$_3$, 150 MHz): $\delta = 28.2$ (3C), 40.4, 56.4, 77.1, 83.7, 115.3, 117.0, 120.2, 120.7, 122.5 (2C), 123.7, 124.5, 128.8, 134.8, 149.7 ppm.

**2-(1-Methoxybut-3-enyl)benzofuran**$^{62}$ (72t)

![72t](image)

72t was prepared according to:

*General procedure G:* using gallium metal (10 mol%), silver fluoride (5 mol%) and [18]crown-6 (10 mol%) with acetal 70t and allyl boronic ester (71, 1.1 equiv) in dioxane (1.0
M) under ultrasonication at 40–45 °C for 20 h. **72t** was purified by PTLC on silica gel (eluant: heptane:EtOAc = 19:1).

Yield: 90%.

**General procedure I:** using gallium metal (10 mol%), silver triflate (5 mol%) with acetal **70t** and allyl silane (94, 1.1 equiv) in dioxane (1.0 M) at 30 °C for 1 h.

NMR yield: 71%.

The obtained analytical data fitted accurately with the reported data.62

Pale yellow liquid.

1H NMR (CDCl3, 500 MHz): δ = 2.65–2.74 (m, 2H), 3.34 (s, 3H), 4.35 (dd, J = 6.8, 6.8 Hz, 1H), 5.03–5.13 (m, 2H), 5.81 (dddd, J = 6.8, 6.9, 10.2, 17.1 Hz, 1H), 6.63 (s, 1H), 7.22 (dddd, J = 1.1, 7.3, 8.4, 15.4 Hz, 2H), 7.45–7.47 (m, 1H), 7.52–7.54 (m, 1H) ppm.

13C NMR (CDCl3, 125 MHz): δ = 38.6, 56.9, 76.9, 104.8, 111.4, 117.6, 121.0, 122.7, 124.2, 128.0, 133.7, 155.0, 156.5 ppm.

2-(1-Methoxybut-3-enyl)benzo[b]thiophene (72u)

![Structure of 72u](image)

**72u** was prepared according to:

**General procedure G:** using gallium metal (10 mol%), silver fluoride (5 mol%) and [18]crown-6 (10 mol%) with acetal **70u** and allyl boronic ester (71, 1.1 equiv) in toluene (1.0 M) under ultrasonication at 40–45 °C for 20 h. **72u** was purified by PTLC on silica gel (eluant: heptane:EtOAc = 19:1).

Yield: 80%.

**General procedure I:** using gallium metal (10 mol%), silver triflate (5 mol%) with acetal **70u** and allyl silane (94, 1.1 equiv) in dioxane (1.0 M) at 25 °C for 1 h.

NMR yield: 95%.

**General procedure K:** using gallium metal (10 mol%), silver triflate (5 mol%) with acetal **70u** and allyl borane (110, 1.1 equiv) in dioxane (1.0 M) at 25 °C for 1 h.
NMR yield: 87%.
Pale yellow liquid.

\(^1\)H NMR (CDCl\(_3\), 500 MHz): \(\delta = 2.54–2.60\) (m, 1H), 2.68–2.75 (m, 1H), 3.32 (s, 3H), 4.49 (dd, \(J = 6.7, 6.8\) Hz, 1H), 5.04–5.13 (m, 2H), 5.80 (dddd, \(J = 6.9, 7.0, 10.3, 17.2\) Hz, 1H), 7.18 (s, 1H), 7.27–7.35 (m, 2H), 7.72 (d, \(J = 7.8\) Hz, 1H), 7.82 (d, \(J = 7.8\) Hz, 1H) ppm.

\(^13\)C NMR (CDCl\(_3\), 150 MHz): \(\delta = 42.3, 56.8, 79.7, 117.6, 122.0, 122.6, 123.4, 124.2\) (2C), 133.9, 139.3, 139.7, 146.5 ppm.

IR (neat): \(\nu = 2924, 1458, 1436, 1350, 1193, 1110, 916, 827, 746, 727\) cm\(^{-1}\).

HRMS (ESI): calculated for C\(_{13}\)H\(_{14}\)NaOS\(^+\): \([\text{M+Na}]^+: m/z = 241.0658\), found: \(m/z = 241.0667\).

(3-Ethoxyhex-5-en-1-yn-1-yl)benzene (72v)

72v was prepared according to:

General procedure G: using gallium metal (10 mol%), silver triflate (5 mol%) and [18]crown-6 (10 mol%) with acetal 70v and allyl boronic ester (71, 1.1 equiv) in dioxane (1.0 M) under ultrasonication at 40–45 °C for 78 h. 72v was purified by PTLC on silica gel (eluant: heptane:EtOAc = 19:1).

Yield: 85%.

General procedure I: using gallium metal (10 mol%), silver triflate (5 mol%) with acetal 70v and allyl silane (94, 1.1 equiv) in dioxane (1.0 M) at 25 °C for 3 h.

NMR yield: 88%.

Colorless liquid.

\(^1\)H NMR (CDCl\(_3\), 500 MHz): \(\delta = 1.25\) (t, \(J = 7.0\) Hz, 3H), 2.53–2.61 (m, 2H), 3.50–3.56 (m, 1H), 3.84–3.90 (m, 1H), 4.29 (dd, \(J = 6.5, 6.6\) Hz, 1H), 5.12–5.21 (m, 2H), 5.95 (dddd, \(J = 6.9, 7.0, 10.2, 17.2\) Hz, 1H), 7.28–7.31 (m, 3H), 7.42–7.44 (m, 2H) ppm.

\(^13\)C NMR (CDCl\(_3\), 150 MHz): \(\delta = 15.1, 40.3, 64.3, 69.5, 85.9, 88.1, 117.6, 122.8, 128.2\) (2C),
128.3, 131.8 (2C), 133.8 ppm.

**IR (neat):** \( \nu = 2976, 2358, 2339, 1489, 1334, 1089, 914, 760, 690 \) cm\(^{-1}\).

**HRMS (ESI):** calculated for C\(_{14}\)H\(_{16}\)NaO\(^+\) = [M+Na]\(^+\): \( m/z = 223.1093 \), found: \( m/z = 223.1118 \).

(3-Methoxyhexa-1,5-dien-1-yl)benzene\(^{67a}\) (72w)

72w was prepared according to:

**General procedure G:** using gallium metal (10 mol%), silver fluoride (5 mol%) and [18]crown-6 (10 mol%) with acetal 70w and allyl boronic ester (71, 1.1 equiv) in dioxane (1.0 M) under ultrasonication at 50 °C for 20 h. 72w was purified by PTLC on silica gel (eluant: heptane:EtOAc = 19:1).

Yield: 72%.

**General procedure I:** using gallium metal (10 mol%), silver triflate (5 mol%) with acetal 70w and allyl silane (94, 1.1 equiv) in dioxane (1.0 M) at 30 °C for 1 h.

NMR yield: 95%.

The obtained analytical data fitted accurately with the reported data.\(^{67a}\)

Pale yellow liquid.

**\(^1\)H NMR** (CDCl\(_3\), 500 MHz): \( \delta = 2.35–2.39 \) (m, 1H), 2.43–2.49 (m, 1H), 3.33 (s, 3H), 3.78 (dd, \( J = 6.5, 6.9 \) Hz, 1H), 5.06–5.13 (m, 2H), 5.88 (ddddd, \( J = 6.9, 7.0, 10.2, 17.1 \) Hz, 1H), 6.08 (dd, \( J = 7.9, 16.0 \) Hz, 1H), 6.58 (d, \( J = 16.0 \) Hz, 1H), 7.26–7.44 (m, 5H) ppm.

**\(^{13}\)C NMR** (CDCl\(_3\), 125 MHz): \( \delta = 40.2, 56.3, 82.0, 117.1, 126.5 \) (2C), 127.7, 128.6 (2C), 129.7, 132.5, 134.4, 136.6 ppm.
(3-Methoxyhex-5-en-1-yl)benzene$^{67a}$ (72x)

72x was prepared according to:

*General procedure G:* using gallium metal (10 mol%), silver fluoride (5 mol%) and [18]crown-6 (10 mol%) with acetal 70x and allyl boronic ester (71, 1.1 equiv) in dioxane (1.0 M) under ultrasonication at 50 °C for 24 h. 72x was purified by PTLC on silica gel (eluant: heptane:EtOAc = 19:1).
Yield: 84%.

*General procedure I:* using gallium metal (10 mol%), silver triflate (5 mol%) with acetal 70x and allyl silane (94, 1.1 equiv) in dioxane (1.0 M) at 30 °C for 16 h.
NMR yield: 94%.
The obtained analytical data fitted accurately with the reported data.$^{67a}$
Pale yellow liquid.

$^1$H NMR (CDCl$_3$, 600 MHz): $\delta = 1.77$–1.83 (m, 2H), 2.26–2.35 (m, 2H), 2.61–2.66 (m, 1H), 2.72–2.76 (m, 1H), 3.24 (ddd, $J = 5.8, 6.2, 12.1$ Hz, 1H), 3.36 (s, 3H), 5.05–5.10 (m, 2H), 5.81 (ddd, $J = 7.1, 7.1, 10.1, 17.1$ Hz, 1H), 7.16–7.29 (m, 5H) ppm.

$^{13}$C NMR (CDCl$_3$, 125 MHz): $\delta = 31.6, 35.3, 37.7, 56.5, 79.6, 117.0, 125.7, 128.3$ (2C), 128.4 (2C), 134.6, 142.4 ppm.

(1-Methoxybut-3-en-1-yl)cyclohexane$^{67a}$ (72y)

72y was prepared according to:

*General procedure G:* using gallium metal (10 mol%), silver triflate (5 mol%) and [18]crown-6 (10 mol%) with acetal 70y and allyl boronic ester (71, 1.1 equiv) in dioxane (1.0 M) under ultrasonication at 50 °C for 20 h. 72y was purified by PTLC on silica gel...
Yield: 80%.

The obtained analytical data fitted accurately with the reported data.\textsuperscript{67a}

Colorless liquid.

\textbf{H NMR} (CDCl\textsubscript{3}, 500 MHz): $\delta = 0.98$–$1.10$ (m, 2H), 1.12–$1.26$ (m, 4H), 1.45–$1.51$ (m, 1H), 1.60–$1.67$ (m, 2H), 1.72–$1.81$ (m, 2H), 2.21–$2.31$ (m, 2H), 2.94 (ddd, $J = 5.8$, 11.4 Hz, 1H), 3.35 (s, 3H), 5.03–$5.09$ (m, 2H), 5.81–$5.89$ (m, 1H) ppm.

\textbf{C NMR} (CDCl\textsubscript{3}, 100 MHz): $\delta = 26.2$, 26.3, 26.6, 28.6, 28.8, 34.9, 40.9, 57.7, 85.3, 116.3, 135.7 ppm.

\textbf{IR} (neat): $\nu = 2958$, 1483, 1444, 1392, 1363, 1097, 1074, 748, 705 cm\textsuperscript{$-1$}.

\textbf{HRMS} (ESI): calculated for $\text{C}_{15}\text{H}_{22}\text{NaO}^{+} = [\text{M}+\text{Na}^{+}]$: $m/z = 241.1563$, found: $m/z = 241.1557$.

\(72z\) was prepared according to:

\textit{General procedure} G: using gallium metal (10 mol\%), silver triflate (5 mol\%) and [18]crown-6 (10 mol\%) with acetal \(70z\) and allyl boronic ester (\(71\), 1.1 equiv) in dioxane (1.0 M) under ultrasonication at 50 °C for 40 h. \(72z\) was purified by PTLC on silica gel (eluant: heptane:EtOAc = 19:1).

Yield: 91%.

Colorless liquid.

\textbf{H NMR} (CDCl\textsubscript{3}, 500 MHz): $\delta = 0.88$ (s, 9H), 2.94–$3.03$ (m, 2H), 3.22 (s, 3H), 4.97 (ddd, $J = 2.2$, 3.4, 10.2 Hz, 1H), 5.13 (ddd, $J = 2.2$, 3.4, 17.2 Hz, 1H), 5.93–$6.00$ (m, 1H), 7.21–$7.32$ (m, 5H) ppm.

\textbf{C NMR} (CDCl\textsubscript{3}, 150 MHz): $\delta = 26.5$ (3C), 37.0, 39.5, 52.6, 85.3, 115.3, 126.2, 126.8 (2C), 129.3 (2C), 137.3, 140.8 ppm.

\textbf{IR} (neat): $\nu = 2958$, 1483, 1444, 1392, 1363, 1097, 1074, 906, 748, 705 cm\textsuperscript{$-1$}.

\textbf{HRMS} (ESI): calculated for $\text{C}_{15}\text{H}_{22}\text{NaO}^{+} = [\text{M}+\text{Na}^{+}]$: $m/z = 241.1563$, found: $m/z = 241.1557$. 

(3-Methoxy-2,2-dimethylhex-5-en-3-yl)benzene (\(72z\))

\begin{figure}[h]
\centering
\includegraphics[width=0.2\textwidth]{72z.png}
\caption{Structure of \(72z\).}
\end{figure}
2-Methoxy-1,2-diphenylpent-4-en-1-one (72z')

72z' was prepared according to:

**General procedure G**: using gallium metal (10 mol%), silver fluoride (5 mol%) and [18]crown-6 (10 mol%) with acetal 70z' and allyl boronic ester (71, 1.1 equiv) in dioxane (1.0 M) under ultrasonication at 40–45 °C for 60 h. 72z' was purified by PTLC on silica gel (eluant: heptane:EtOAc = 19:1).

Yield: 82%.

**General procedure I**: using gallium metal (10 mol%), silver triflate (5 mol%) with acetal 70z' and allyl silane (94, 1.1 equiv) in dioxane (1.0 M) at 30 °C for 18 h.

NMR yield: 98%.

Colorless liquid.

$^1$H NMR (CDCl$_3$, 500 MHz): $\delta = 3.08$ (s, 3H), 3.42 (ddd, $J = 1.6, 2.8, 6.9$ Hz, 2H), 5.00 (ddd, $J = 1.6, 3.1, 17.2$ Hz, 1H), 5.08 (ddd, $J = 1.6, 3.1, 10.2$ Hz, 1H), 5.83 (dddd, $J = 6.8, 6.9, 10.2, 17.1$ Hz, 1H), 7.26–7.42 (m, 10H) ppm.

$^{13}$C NMR (CDCl$_3$, 150 MHz): $\delta = 42.4, 53.0, 91.4, 118.2, 128.0, 128.1$ (6C), 129.0 (4C), 131.1, 138.7, 208.3 ppm.

IR (neat): $\nu = 2916, 2356, 2341, 1718, 1490, 1446, 1066, 914, 738, 680$ cm$^{-1}$.

HRMS (ESI): calculated for C$_{18}$H$_{18}$NaO$_2$ $^+ = [M+Na]^+$: $m/z = 289.1199$, found: $m/z = 289.1212$.

Ethers 72a–[d$_2$], 72’a–[d$_2$]$^{62}$

2-(1-Methoxybut-3-en-1-yl-4,4-d2)cyclohexa-1,3-diene (72a–[d$_2$])

(1-Methoxybut-3-en-1-yl-2,2-d$_2$)benzene (72’a–[d$_2$])
72a–[d_2] and 72’a–[d_2] were prepared according to:

*General procedure* G: using gallium metal (10 mol%), silver triflate (5 mol%) and [18]crown-6 (10 mol%) with acetal 70a and deuterio-allyl boronic ester (71–[d_2], 1.5 equiv) in dioxane (1.0 M) under ultrasonication at 40–45 °C for 8 h. 72a–[d_2] and 72’a–[d_2] were purified by PTLC on silica gel (eluant: heptane:EtOAc = 19:1).

Yield: 80% (72a–[d_2]:72’a–[d_2] = 1:1).

The obtained analytical data fitted accurately with the reported data.\(^6^2\)

Pale yellow liquid.

3a–[d_2]: \(^1\)H NMR (CDCl\(_3\), 500 MHz): \(\delta = 2.39–2.43\) (m, 1H), 2.54–2.60 (m, 1H), 3.22 (s, 3H), 4.19–4.21 (m, 1H), 5.73–5.78 (m, 1H), 7.25–7.36 (m, 5H) ppm.

\(^2\)H NMR (CDCl\(_3\), 77 MHz): \(\delta = 5.15–5.18\) (m, 2D) ppm.

\(^{13}\)C NMR (CDCl\(_3\), 125 MHz): \(\delta = 42.4, 56.6, 83.6, 116.9, 126.7, 128.8, 134.7, 141.7\) ppm.

3’a–[d_2]: \(^1\)H NMR (CDCl\(_3\), 500 MHz): \(\delta = 3.22\) (s, 3H), 4.19–4.21 (m, 1H), 5.01–5.06 (m, 1H), 5.73–5.78 (m, 1H), 7.25–7.36 (m, 5H) ppm.

\(^2\)H NMR (CDCl\(_3\), 77 MHz): \(\delta = 2.56\) (d, \(J = 11.9\) Hz, 2D) ppm.

\(^{13}\)C NMR (CDCl\(_3\), 125 MHz): \(\delta = 42.4, 56.6, 83.7, 116.9, 126.7, 128.8, 134.6, 141.7\) ppm.

(1-Methoxybut-3-yn-1-yl)benzene\(^{148}\) (87a)

87a was prepared according to:

*General procedure* G: using gallium metal (10 mol%), silver fluoride (5 mol%) and [18]crown-6 (10 mol%) with acetal 70a and allenyl boronic ester (86, 1.2 equiv) in dioxane (1.0 M) under ultrasonication at 40–45 °C for 52 h. 87a was purified by PTLC on silica gel (eluant: heptane:EtOAc = 19:1).

Yield: 91% (major:minor = 49:1).

The obtained analytical data fitted accurately with the reported data.\(^{148}\)

Pale yellow liquid.
Major product 87a: \(^1\)H NMR (CDCl\(_3\), 500 MHz): \(\delta = 1.97\) (t, \(J = 2.7\) Hz, 1H), 2.56 (ddd, \(J = 2.7, 6.5, 16.8\) Hz, 1H), 2.68 (ddd, \(J = 2.7, 6.5, 16.8\) Hz, 1H), 3.27 (s, 3H), 4.31 (dd, \(J = 6.5\) Hz, 1H), 7.34–7.41 (m, 5H) ppm.

\(^{13}\)C NMR (CDCl\(_3\), 125 MHz): \(\delta = 27.9, 57.0, 69.9, 80.9, 82.0, 126.7\) (2C), 128.1, 128.4 (2C), 140.5 ppm.

Minor product 88a: \(^1\)H NMR (CDCl\(_3\), 500 MHz): \(\delta = 3.37\) (s, 3H), 4.73 (dt, \(J = 1.5, 7.7\) Hz, 1H), 4.79–4.87 (m, 2H), 5.29 (dt, \(J = 6.5, 7.7\) Hz, 1H), 7.34–7.41 (m, 5H) ppm.

(3-Methoxyhex-5-yn-1-yl)benzene\(^{149}\) (87x)

87x was prepared according to:

*General procedure G*: using gallium metal (10 mol\%), silver fluoride (5 mol\%) and [18]crown-6 (10 mol\%) with acetal 70x and allenyl boronic ester (86, 1.2 equiv) in dioxane (1.0 M) under ultrasonication at 40–45 °C for 72 h. 87a was purified by PTLC on silica gel (eluant: heptane:EtOAc = 19:1).

Yield: 82% (major:minor = 30:1).

The obtained analytical data fitted accurately with the reported data.

Colorless liquid.

Major product 87x: \(^1\)H NMR (CDCl\(_3\), 500 MHz): \(\delta = 1.92–1.96\) (m, 2H), 2.00 (dd, \(J = 2.6, 2.7\) Hz, 1H), 2.41–2.51 (m, 2H), 2.64–2.70 (m, 1H), 2.74–2.80 (m, 1H), 3.35 (quint, \(J = 5.7\) Hz, 1H), 3.40 (s, 3H), 7.17–7.30 (m, 5H) ppm.

\(^{13}\)C NMR (CDCl\(_3\), 125 MHz): \(\delta = 23.0, 31.4, 35.3, 57.0, 70.1, 78.3, 80.8, 125.8, 128.3\) (2C), 128.4 (2C), 142.0 ppm.

Minor product 88x: \(^1\)H NMR (CDCl\(_3\), 500 MHz): \(\delta = 1.81–1.88\) (m, 1H), 1.93–2.00 (m, 1H), 2.67–2.75 (m, 2H), 3.33 (s, 3H), 3.66 (dd, \(J = 6.4, 13.5\) Hz, 1H), 4.78–4.80 (m, 2H), 5.00–5.10 (m, 1H), 7.19–7.29 (m, 5H) ppm.
**N-(1-phenylbut-3-en-1-yl)benzamide (134)**

![Structure of 134](image)

134 was prepared according to:

*General procedure G*: using gallium metal (10 mol%), silver triflate (5 mol%) and [18]crown-6 (10 mol%) with aminal 133 and allyl boronic ester (71, 1.1 equiv) in dioxane (1.0 M) at 50 °C for 24 h. 134 was purified by PTLC on silica gel [eluant: diethyl ether:petrol ether (40-60) = 1:4; eluted three times].

Yield: 83%.

*General procedure I*: using gallium metal (10 mol%), silver triflate (5 mol%) with aminal 133 and allyl silane (94, 1.1 equiv) in dioxane (1.0 M) at 30 °C for 18 h.

NMR yield: 95%.

*General procedure K*: using gallium metal (10 mol%), silver triflate (5 mol%) with aminal 133 and allyl borane (110, 1.1 equiv, 0.5 M solution in hexane) in dioxane (1.0 M) at 25 °C for 0.5 h.

NMR yield: 89%.

The obtained analytical data fitted accurately with the reported data.93

Colorless solid.

\[ ^1H \text{ NMR (CDCl}_3, 500 MHz): \delta = 2.72 (dd, J = 6.9, 6.9 Hz, 2H), 5.11–5.20 (m, 2H), 5.30 (dt, J = 6.9, 7.5 Hz, 1H), 5.77 (ddt, J = 7.1, 10.2, 17.2 Hz, 1H), 6.45 (d, J = 6.9 Hz, 1H), 7.26–7.29 (m, 1H), 7.35 (d, J = 4.2 Hz, 4H), 7.42–7.54 (m, 3H), 7.79–7.81 (m, 2H) ppm. \]

\[ ^13C \text{ NMR (CDCl}_3, 125 MHz): \delta = 40.6, 52.8, 118.4, 126.4 (2C), 126.9 (2C), 127.4, 128.6 (2C), 128.7 (2C), 131.5, 134.1, 134.6, 141.6, 166.7 \text{ ppm.} \]
But-3-ene-1,1-diyl dibenzene (139)

139 was prepared according to:

*General procedure* I: using gallium metal (10 mol%), silver triflate (5 mol%) with aminal 138 and allyl silane 94 (1.1 equiv) in dioxane (1.0 M) at 25 °C for 16 h. 139 was purified by PTLC on silica gel (eluant: heptane:EtOAc = 19:1).

NMR yield: 99%.

*General procedure* K: using gallium metal (10.0 mol%), silver triflate (5.00 mol%) with aminal 138 and allyl borane 110 (1.10 equiv, 0.50 M solution in hexane) in dioxane (1.00 M) at 25 °C for 5 h.

NMR yield: 70%.

The obtained analytical data fitted accurately with the reported data.\(^93\)

\(^1\)H NMR (CDCl\(_3\), 600 MHz): \(\delta = 2.84–2.87\) (m, 2H), 4.05 (t, \(J = 7.9\) Hz, 1H), 4.97–4.99 (m, 1H), 5.05–5.08 (m, 1H), 5.76 (ddt, \(J = 7.0\), 10.2, 17.2 Hz, 1H), 7.19–7.42 (m, 10H) ppm.

\(^13\)C NMR (CDCl\(_3\), 150 MHz): \(\delta = 41.4, 54.7, 116.4, 126.2\) (2C), 128.2 (4C), 129.2 (4C), 134.3, 143.8 (2C) ppm.

\((E)-2-(4-methoxy-4-phenylbut-1-en-1-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane\) (148a)

148a was prepared according to:

*General procedure* I: using pre-formed solution of gallium metal (10 mol%), silver triflate (5 mol%) in dioxane (1.0 M) with acetal 70a and α-silyl allyl boronic ester 136 (1.1 equiv) in MeCN (1.0 M) at 25 °C for 0.5 h. 148a was purified by PTLC on silica gel (eluant: heptane:EtOAc = 19:1).
NMR yield: 97% \((E:Z = 17:1)\).

Yield: 80% \((E:Z = 17:1)\).

The obtained analytical data fitted accurately with the reported data.\(^7\)

Pale yellow liquid.

\(^1\)H NMR (CDCl\(_3\), 500 MHz): \(\delta = 1.25\) (s, 12H), 2.45–2.51 (m, 1H), 2.63–2.69 (m, 1H), 3.20 (s, 3H, \(E\) isomer), 3.24 (s, 3H, \(Z\) isomer), 4.23 (dd, \(J = 5.0, 8.1\) Hz, 1H), 5.41 (ddd, \(J = 1.3, 1.3, 13.6\) Hz, 1H, \(Z\) isomer), 5.50 (ddd, \(J = 1.5, 1.5, 18.0\) Hz, 1H, \(E\) isomer), 6.62 (ddd, \(J = 6.4, 6.5, 18.0\) Hz, 1H), 7.25–7.35 (m, 5H) ppm.

\(^{13}\)C NMR (CDCl\(_3\), 125 MHz): \(\delta = 24.7\) (4C), 44.6, 56.6, 81.5, 83.0 (2C), the signal of the carbon connected to boron was not visible due to quadrupolar broadening, 126.6 (2C), 127.6, 128.4 (2C), 141.8, 150.2 ppm.

\(^{11}\)B NMR (CDCl\(_3\), 160 MHz): \(\delta = 29.8\) ppm.

\((E)-2-(4\text{-ethoxy-4-phenylbut-1-en-1-yl})-4,4,5,5\text{-tetramethyl-1,3,2-dioxaborolane (148o)}\)

\(17o\) was prepared according to:

General procedure I: using pre-formed solution of gallium metal (10 mol%), silver triflate (5 mol%) in dioxane (1.0 M) with acetal \(70o\) and \(\alpha\)-silyl allyl boronic ester \(136\) (1.1 equiv) in MeCN (1.0 M) at 25 °C for 1 h. \(148o\) was purified by PTLC on silica gel (eluant: heptane:EtOAc = 19:1).

NMR yield: 80% \((E:Z = 25:1)\).

Yield: 73% \((E:Z = 5:1)\).

Pale yellow liquid.

\(^1\)H NMR (CDCl\(_3\), 500 MHz): \(\delta = 1.16\) (dd, \(J = 7.0, 7.0\) Hz, 3H, \(E\) isomer), 1.24 (dd, \(J = 5.0, 5.0\) Hz, 3H, \(Z\) isomer), 1.25 (s, 12H), 2.46–2.59 (m, 1H, \(E\) isomer), 2.66–2.69 (m, 1H, \(E\) isomer), 2.80–2.89 (m, 2H, \(Z\) isomer), 3.30–3.42 (m, 2H, \(E\) isomer), 3.42–3.45 (m, 2H, \(Z\) isomer), 4.30–4.33 (m, 1H, \(Z\) isomer), 4.34 (dd, \(J = 5.2, 8.0\) Hz, 1H, \(E\) isomer), 5.40 (ddd, \(J = 5.0, 5.0, 7.0\) Hz, 3H, \(E\) isomer).
= 1.1, 1.1, 13.5 Hz, 1H, Z isomer), 5.49 (ddd, J = 1.4, 1.4, 18.0 Hz, 1H, E isomer), 6.43–6.49 (m, 1H, Z isomer) 6.62 (ddd, J = 6.4, 6.5, 18.0 Hz, 1H, E isomer), 7.26–7.34 (m, 5H) ppm.

$^{13}$C NMR (CDCl$_3$, 125 MHz): δ = 15.3, 24.7 (4C), 44.7, 64.1, 81.1, 83.0 (2C), the signal of the carbon connected to boron was not visible due to quadrupolar broadening, 126.6 (2C), 127.5, 128.3 (2C), 142.5, 150.3 ppm; the signals of the Z isomer were not visible due to a too low concentration of the NMR sample).

$^{11}$B NMR (CDCl$_3$, 160 MHz): δ = 29.8 ppm.

IR (neat): ν = 2970, 1638, 1361, 1319, 1261, 1144, 1096, 1006, 742, 650 cm$^{-1}$.

HRMS (ESI): calculated for C$_{18}$H$_{27}$BNaO$_3$ $^+$ = [M+Na]$^+$: m/z = 325.1945, found: m/z = 325.1971.

(E)-2-(3-(isochroman-1-yl)prop-1-en-1-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane

(148q)

148q was prepared according to:

General procedure I: using pre-formed solution of gallium metal (10 mol%), silver triflate (5 mol%) in dioxane (1.0 M) with acetal 70q and α-silyl allyl boronic ester 136 (1.1 equiv) in MeCN (1.0 M) at 25 °C for 1 h. 148q was purified by PTLC on silica gel (eluant: heptane:EtOAc = 19:1).

NMR yield: 84% (E isomer only).

Yield: 78% (E isomer only).

Pale yellow liquid.

$^1$H NMR (CDCl$_3$, 500 MHz): δ = 1.26 (s, 12H), 2.66–2.71 (m, 2H), 2.77–2.81 (m, 1H), 2.96–3.01 (m, 1H), 3.77 (ddd, J = 4.0, 9.3, 11.3 Hz, 1H), 4.14 (ddd, J = 4.0, 5.3, 11.3 Hz, 1H), 4.87 (dd, J = 3.2, 8.7 Hz, 1H), 5.59 (ddd, J = 1.5, 1.5, 18.0 Hz, 1H), 6.75 (ddd, J = 6.4, 6.5, 18.0 Hz, 1H), 7.07–7.11 (m, 2H), 7.14–7.18 (m, 2H) ppm.

$^{13}$C NMR (CDCl$_3$, 125 MHz): δ = 24.8, 29.0 (4C), 42.5, 63.2, 75.1, 83.1 (2C), the signal of
the carbon connected to boron was not visible due to quadrupolar broadening, 124.8, 126.1, 126.3, 128.9, 134.0, 137.8, 150.5 ppm.

$^{11}$B NMR (CDCl$_3$, 160 MHz): $\delta = 29.7$ ppm.

IR (neat): $\nu =$ 2976, 2926, 1637, 1352, 1319, 1146, 1107, 970, 849, 749, 635 cm$^{-1}$.

HRMS (ESI): calculated for C$_{18}$H$_{25}$BNaO$_3^+$ = [M+Na]$^+$: $m/z =$ 323.1789, found: $m/z =$ 323.1797.

$(E)$-2-(4,4-diphenylbut-1-en-1-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (151)

151 was prepared according to:

*General procedure I:* using pre-formed solution of gallium metal (10 mol%), silver triflate (5 mol%) in dioxane (1.0 M) with ether 138 and $\alpha$-silyl allyl boronic ester 136 (1.1 equiv) in MeCN (1.0 M) at 30 °C for 1 h. 151 was purified by PTLC on silica gel (eluant: heptane:EtOAc = 19:1).

NMR yield: 94% ($E$:Z = 18:1);

Yield: 84% (95% chemical purity; $E$ isomer only).

Pale yellow liquid.

$^1$H NMR (CDCl$_3$, 500 MHz): $\delta =$ 1.22 (s, 12H), 2.92 (ddd, $J =$ 1.5, 6.5, 7.8 Hz, 2H), 4.08 (t, $J =$ 7.8 Hz, 1H), 5.46 (br dt, $J =$ 1.5, 17.9 Hz, 1H), 6.54 (dt, $J =$ 6.5, 17.9 Hz, 1H), 7.14–7.29 (m, 10H) ppm.

$^{13}$C NMR (CDCl$_3$, 125 MHz): $\delta =$ 24.7 (4C), 42.0, 50.4, 83.0 (2C), the signal of the carbon connected to boron was not visible due to quadrupolar broadening, 128.2 (2C), 127.9 (4C), 128.4 (4C), 144.5 (2C), 151.9 ppm.

$^{11}$B NMR (CDCl$_3$, 160 MHz): $\delta =$ 29.8 ppm.

IR (neat): $\nu =$ 2978, 1638, 1274, 1323, 1144, 970, 849, 735, 690 cm$^{-1}$.

HRMS (ESI): calculated for C$_{22}$H$_{27}$BNaO$_2^+$ = [M+Na]$^+$: $m/z =$ 357.1996, found: $m/z =$ 357.1996.
4.5 Mechanistic Studies

General procedure N (with crown ether)

Gallium(0) (27.9 mg, 0.40 mmol), silver triflate (51.4 mg, 0.20 mmol, 0.5 equiv), [18]crown-6 (106 mg, 0.40 mmol), and dioxane or toluene (400 µL, 1.0 M) were added to an oven-dried 2 mL-test tube in a nitrogen-filled glove box. The catalyst mixture was reacted under ultrasonication at 40–45 °C for 16–36 h, at which point the $^{71}$Ga NMR analysis indicated the formation of new gallium species. Then the model acetal 70a and allyl boronic ester 71 were added directly into the pre-formed gallium(I) solution and kept at 40 °C for 4 h, at which point the resulting mixture was analyzed by $^{71}$Ga NMR ($\text{C}_6\text{D}_6$, 100 µL).

$^{71}$Ga NMR ($\text{C}_6\text{D}_6$, 152 MHz): $\delta = -565$ ppm (dioxane); $\delta = -561$ ppm (toluene).

General procedure O (without crown ether)

Gallium(0) (27.9 mg, 0.40 mmol), silver triflate (51.4 mg, 0.20 mmol, 0.5 equiv), and dioxane or toluene (400 µL, 1.0 M) were added to an oven-dried 2 mL-test tube with a magnetic stirring bar in a nitrogen-filled glove box. The catalyst mixture was stirred at 40–50 °C for 16–20 h, at which point the $^{71}$Ga NMR analysis indicated the formation of new gallium species. Then the model acetal 70a and allyl silane 94 were added directly to the pre-formed gallium(I) solution and kept at 25 °C for 0.5 h, at which point the resulting mixture was analyzed by $^{71}$Ga NMR ($\text{C}_6\text{D}_6$, 100 µL).

$^{71}$Ga NMR ($\text{C}_6\text{D}_6$, 152 MHz): $\delta = -694$ ppm (toluene).

General procedure P (with crown ether)

Aluminum(0) (10.4 mg, 0.40 mmol), silver triflate (51.4 mg, 0.20 mmol, 0.5 equiv), and toluene (400 µL, 1.0 M) were added to an oven-dried 2 mL-test tube with a magnetic stirring bar in a nitrogen-filled glove box. The catalyst mixture was stirred at 40 or 50 °C for 16 h, at which point the $^{27}$Al NMR analysis indicated the formation of new gallium species. Then the model acetal 70a and allyl silane 94 were added directly into the preformed
aluminum(I) solution and kept at 25 °C for 2 h, at which point the resulting mixture was analyzed by $^{27}$Al NMR (C$_6$D$_6$, 100 µL).

$^{27}$Al NMR (C$_6$D$_6$, 130 MHz): δ = –22 ppm.
4.6 Synthesis of Enantiomerically Enriched Silver BINOL-Phosphate Derivatives

Enantiomerically Enriched BINOL-Phosphoric Acids

![Scheme 4-1](image)

The chiral phosphoric acid was prepared according to Gong’s method.\textsuperscript{101} Phosphorus oxychloride (0.23 g, 1.50 mmol, 5.0 equiv) was added to a stirred solution of (R)-BINOL (200 mg) in pyridine (5 mL) at room temperature under a nitrogen atmosphere. The reaction mixture was stirred at 60 °C for overnight, before cooling down to room temperature. Deionized water (2 mL) was then added to the reaction mixture and warmed to 60 °C for an additional 4 h. After cooling to room temperature, aqueous HCl (20 mL, 6.0 M in deionized water) was added to the mixture and extracted with DCM (3 x 10 mL). The combined organic phase was washed with aqueous HCl (20 mL, 6.0 M in deionized water), dried over Na\textsubscript{2}SO\textsubscript{4}, and concentrated in vacuo. The crude product was purified by PTLC on silica gel (MeOH:DCM = 1:50) to afford the corresponding acid. The product was dissolved in DCM (20 mL), washed with aqueous HCl (20 mL, 6.0 M in deionized water), dried over Na\textsubscript{2}SO\textsubscript{4}, and then concentrated in vacuo. The product was obtained as colorless solid.
(R)-3,3′-bis(3,5-di-tert-butylphenyl)-[1,1′-binaphthalene]-2,2′-diol [(R)-154–H]

Enriched BINOL-Phosphoric Acid (R)-154–H is literature known and the obtained analytical data fitted accurately with the reported data.\(^9\)

Pale yellow solid.

Yield: 91%.

\(^1\)H NMR (CDCl\(_3\), 500 MHz): \(\delta = 1.16 \text{ (s, 36H), 7.28–7.40 (m, 10H), 7.49 (t, } J = 7.4 \text{ Hz, 2H), 7.96–7.97 (m, 4H)} \text{ ppm.}\)

\(^{13}\)C NMR (CDCl\(_3\), 125 MHz): \(\delta = 31.4 \text{ (12C), 34.7 (4C), 121.7 (2C), 122.3 (2C), 124.1 (2C), 125.7 (2C), 126.2 (2C), 127.2 (2C), 128.2 (2C), 131.5 (2C), 131.7 (2C), 131.9 (2C), 135.5 (2C), 136.1 (2C), 145.0 (d, } J = 10.1 \text{ Hz, 2C), 150.3 (2C)} \text{ ppm.}\)

\(^{31}\)P NMR (CDCl\(_3\), 203 MHz): \(\delta = 3.5 \text{ ppm.}\)

(R)-3,3′-bis(3,5-diisopropylphenyl)-[1,1′-binaphthalene]-2,2′-diol [(R)-153–H]

Enriched BINOL-Phosphoric Acid (R)-153–H is literature known and the obtained analytical data fitted accurately with the reported data.
Off-white solid.

Yield: 71%.

$^1$H NMR (CDCl$_3$, 500 MHz): $\delta = 1.11$ (dd, $J = 7.0$, 8.7 Hz, 12H), 2.82 (quint, $J = 7.0$ Hz, 4H), 6.98 (br s, 1H), 7.28–7.33 (m, 6H), 7.39 (d, $J = 8.43$ Hz, 2H), 7.51 (t, $J = 7.5$ Hz, 2H), 7.98 (d, $J = 8.2$ Hz, 2H), 8.01 (s, 2H) ppm.

$^{31}$P NMR (CDCl$_3$, 203 MHz): $\delta = 2.1$ ppm.

$(R)$-3,3’-bis(3,5-dimethylphenyl)-[1,1’-binaphthalene]-2,2’-diol [$(R)$-156–H]

Enriched BINOL-Phosphoric Acid $(R)$-156–H is literature known and the obtained analytical data fitted accurately with the reported data.$^{150}$

Off-white solid.

Yield: 53%.

$^1$H NMR (CDCl$_3$, 500 MHz): $\delta = 2.21$ (s, 12H), 7.27–7.37 (m, 10H), 7.51 (t, $J = 6.8$ Hz, 2H), 7.97 (d, $J = 8.2$ Hz, 2H), 8.00 (s, 2H) ppm.

$^{31}$P NMR (CDCl$_3$, 203 MHz): $\delta = 2.6$ ppm.
Scheme 4-2 Synthesis of enantiomerically enriched silver BINOL-phosphates according to Toste's method93,100 Chiral silver phosphate was obtained from the corresponding chiral phosphoric acid and silver carbonate (Ag₂CO₃) according to a literature report.100 Ag₂CO₃ (19.3 mg, 0.07 mmol, 0.5 equiv) was added to a stirred solution of chiral phosphoric acid (100 mg) in DCM (1 mL) in the dark. At that stage deionized water (1 mL) was added and the two-phase mixture was stirred vigorously for 1 h. After this time, the mixture was diluted with DCM (2 mL) and deionized water (2 mL). The aqueous phase was extracted with DCM (3 x 5 mL), and then the combined organic phase was filtered through celite and concentrated in vacuo. The corresponding chiral silver phosphate was obtained as colorless or gray solid.

(((6R,11bR)-4-oxido-2,6-bis(2,4,6-triisopropylphenyl)dinaphtho[2,1-d:1',2'-f][1,3,2]dioxaphosphepin-4-yl)oxy)silver [(R)-153–Ag]

Chiral phosphate (R)-153–Ag is literature known and the obtained analytical data fitted accurately with the reported data.100 Off-white solid. Yield: 70%.

1H NMR (CDCl₃, 500 MHz): δ = 0.97 (d, J = 6.8 Hz, 6H), 1.19 (d, J = 6.8 Hz, 12H), 1.20 (d,
$J = 5.2 \text{ Hz, 12H}$, 1.25 (d, $J = 6.8 \text{ Hz, 6H}$), 6.99 (d, $J = 1.5 \text{ Hz, 3H}$), 7.06 (d, $J = 1.5 \text{ Hz, 3H}$), 7.31 (dd, $J = 1.2$, 6.8, 8.1 Hz, 2H), 7.38 (d, $J = 8.1 \text{ Hz, 2H}$), 7.48 (m, 2H), 7.87 (s, 2H), 7.90 (d, $J = 8.2 \text{ Hz, 2H}$) ppm.

$^{31}\text{P NMR (CDCl}_3$, 203 MHz): $\delta = 12.7 \text{ ppm}$.

$((2,6$-Bis(3,5-bis(trifluoromethyl)phenyl)-4-oxidodinaphtho[2,1$-d$:1',2$-'f][1,3,2]$dioxaphosphepin-4-yl)oxy)silver \((R)-157$–Ag\)

Chiral phosphate \((R)-157$–Ag\) is literature known and the obtained analytical data fitted accurately with the reported data.

Off-white solid.

Yield: 67%.

$^1\text{H NMR (CDCl}_3$, 500 MHz): $\delta = 7.17$ (dt, $J = 7.5$, 38.5 Hz, 1H), 7.31–8.20 (m, 15H) ppm.

$^{31}\text{P NMR (CDCl}_3$, 203 MHz): $\delta = 11.3 \text{ ppm}$.

$(((11b$R)-4-oxido-2,6-bis(triphenylsilyl)dinaphtho[2,1$-d$:1',2$-'f][1,3,2]$dioxaphosphepin-4$-yl)oxy)silver \((R)-158$–Ag\)

Chiral phosphate \((R)-158$–Ag\) is literature known and the obtained analytical data fitted accurately with the reported data.\(^93\)
Off-white solid.

Yield: 53%.

$^1$H NMR (CDCl$_3$, 500 MHz): $\delta = 6.9$ (ddd, $J = 1.2$, 6.9, 8.5 Hz, 2H), 7.00 (ddd, $J = 0.9$, 7.8, 8.0 Hz, 2H), 7.06–7.15 (m, 20H), 7.28 (d, $J = 9.3$ Hz, 4H), 7.79–7.82 (m, 12H) ppm.

$^{31}$P NMR (CDCl$_3$, 203 MHz): $\delta = 10.6$ ppm.

((2,6-Bis(3,5-di-tert-butylphenyl)-4-oxidinaphtho[2,1-\textit{d}:1',2'-\textit{f}][1,3,2]dioxaphosphepin -4-yl)oxy)silver [(\textit{R})-154–Ag]

Chiral phosphate (\textit{R})-154–Ag is literature known and the obtained analytical data fitted accurately with the reported data.$^{93}$

Off-white solid.

Yield: 87%.

$^1$H NMR (CDCl$_3$, 400 MHz): $\delta = 1.25$ (s, 36H), 7.27–7.31 (m, 2H), 7.37 (t, $J = 1.7$ Hz, 2H), 7.38 (t, $J = 8.5$ Hz, 2H), 7.48 (t, $J = 7.2$ Hz, 2H), 7.60 (s, $J = 9.3$ Hz, 4H), 7.95–7.97 (m, 4H) ppm.

$^{31}$P NMR (CDCl$_3$, 162 MHz): $\delta = 12.0$ ppm.
((11bR)-2,6-bis(3,5-di-tert-butyl-4-methoxyphenyl)-4-oxidodinaphtho[2,1-d:1',2'-f][1,3,2]dioxaphosphepin-4-yl)oxy)silver [(R)-132–Ag]

![Chemical structure of (R)-132–Ag](image)

Chiral phosphate (R)-132–Ag is literature known and the obtained analytical data fitted accurately with the reported data.\(^9^3\)

Off-white solid.

\(^1\)H NMR (CDCl\(_3\), 600 MHz): \(\delta = 1.27\) (s, 36H), 7.22 (dd, \(J = 6.8, 7.6\) Hz, 2H), 7.27 (br s, 2H), 7.32 (d, \(J = 7.6\) Hz, 2H), 7.39 (dd, \(J = 6.8, 7.6\) Hz, 2H), 7.50 (br s, 4H), 7.84–7.99 (m, 4H) ppm.

\(^31\)P NMR (CDCl\(_3\), 203 MHz): \(\delta = 12.5\) ppm.
4.7 Towards Asymmetric Gallium(I) Catalysis

4.7.1 General Procedures

**General procedure Q (under ultrasonication)**

Gallium(0) (1.4 mg, 0.02 mmol, 10 mol%), chiral silver phosphate (0.01–0.02 mmol, 5–10 mol%), or silver triflate (2.6 mg, 0.01 mmol, 5 mol%), ligand (0.02 mmol, 10 mol%), cyclic acetal (0.20 mmol), allyl boronic ester (71, 37.0 mg, 0.22 mmol, 1.1 equiv) and dioxane (200 µL, 1.0 M) or toluene (200 µL, 1.0 M) were added to an oven-dried 2 mL-test tube in a nitrogen-filled glove box. The mixture was reacted under ultrasonication at 50–60 °C for 12–100 h, at which point the $^1$H NMR analysis indicated the complete consumption of the electrophile. The solvent was removed *in vacuo* and the residue was purified by PTLC on silica gel (heptane:EtOAc = 19:1) to give the desired product as pale yellow liquid. The products were then analyzed by chiral HPLC (CHIRALPAK IA).

**General procedure R (conventional heating and stirring)**

Gallium(0) (1.4–2.1 mg, 0.02–0.03 mmol, 10–15 mol%), chiral silver phosphate (0.01–0.015 mmol, 5–7.5 mol%), aminal (50.2 mg, 0.20 mmol), allyl reagent (0.22 mmol, 1.1 equiv), and solvent (0.2–2.0 mL, 0.1–1.0 M) were added to an oven-dried 2 mL-test tube with a magnetic stirring bar in a nitrogen-filled glove box. The reaction mixture was then stirred at various temperatures, at which point the $^1$H NMR analysis of a reaction aliquot confirmed the complete consumption of the aminal. The solvents were then removed *in vacuo*, and the residue was purified by PTLC on silica gel [diethyl ether:petrol ether (40-60) = 1:5] to give the desired product as a colorless solid. The products were then analyzed by chiral HPLC (CHIRALPAK IF).
General procedure S (pre-formation of chiral catalyst)

Gallium(0) (1.4 mg, 0.02 mmol, 10 mol%), chiral silver phosphate (0.01 mmol, 5 mol%), and dioxane or toluene (100 µL) were added to an oven-dried 2 mL-test tube in a nitrogen-filled glove box. The catalyst mixture was reacted under ultrasonication at 40–50 °C for 13–24 h, at which point the aminal (0.20 mmol), and dioxane or toluene (100 µL were added to the pre-formed catalyst mixture with a magnetic stirring bar in a nitrogen-filled glove box. The reaction mixture was then stirred at various low temperatures with slow addition of allyl reagents (0.22 mmol, 1.1 equiv), at which point the 1H NMR analysis of a reaction aliquot confirmed the complete consumption of the aminal. The solvents were then removed in vacuo, and the residue was purified by PTLC on silica gel [diethyl ether:petrol ether (40-60) = 1:5] to give the desired product as a colorless solid. The products were then analyzed by chiral HPLC (CHIRALPAK IF).
4.7.2 Analytical Data

1-Allylisochromane\textsuperscript{62} (72q)

\begin{center}
\begin{tikzpicture}
\node (a) at (0,0) {\textsuperscript{72q}};
\node (b) at (-0.55,0) {\textsuperscript{72q}};
\end{tikzpicture}
\end{center}

72q was prepared according to:

{}\textit{General procedure Q:} using gallium metal (10 mol\%), chiral silver phosphate (R)-153–Ag (5 mol\%), [18]crown-6 (10 mol\%) with acetal 70q and allyl boronic ester (71, 1.1 equiv) in toluene (1.0 M) under ultrasonication at 50–60 °C for 60 h. 72q was purified by PTLC on silica gel (eluant: heptane:EtOAc = 19:1). The obtained analytical data fitted accurately with the reported data.\textsuperscript{62}

HPLC analysis was done immediately after isolation.

Yield: 21%; 4% \textit{ee}.

Pale yellow liquid.

\textsuperscript{1}H NMR (CDCl\textsubscript{3}, 500 MHz): \(\delta = 2.56–2.60\) (m, 1H), 2.69–2.74 (m, 1H), 2.99–3.02 (m, 1H), 3.77 (ddd, \(J = 3.8, 9.8, 11.3\) Hz, 1H), 4.14 (ddd, \(J = 3.8, 5.4, 11.3\) Hz, 1H), 4.83 (dd, \(J = 3.4, 8.0\) Hz, 1H), 5.10 (ddt, \(J = 1.2, 2.0, 10.3\) Hz, 1H), 5.16 (dq, \(J = 1.8, 17.1\) Hz, 1H), 5.90 (ddt, \(J = 6.8, 10.3, 17.1\) Hz, 1H), 7.09–7.18 (m, 10H) ppm.

\textsuperscript{13}C NMR (CDCl\textsubscript{3}, 125 MHz): \(\delta = 29.1, 40.4, 63.4, 75.6, 117.0, 124.8, 126.1, 126.3, 128.9, 134.1, 135.0, 137.8\) ppm.

HPLC (DAICEL CHIRALPAK IA; hexane:i-propanol = 99:1; flow rate: 1.0 mL/min): \(t_r = 4.48, 4.98\) min.

(R)-2-Allyl-2H-chromene\textsuperscript{147} [(R)-72r]

\begin{center}
\begin{tikzpicture}
\node (a) at (0,0) {\textsuperscript{(R)}-72r};
\node (b) at (-0.55,0) {\textsuperscript{(R)}-72r};
\end{tikzpicture}
\end{center}

(R)-72r was prepared according to:
General procedure Q: using gallium metal (10 mol%), chiral silver phosphate (R)-153–Ag (5 mol%) with acetal 70r and allyl boronic ester (71, 1.1 equiv) in toluene (1.0 M) at 50 °C for 99 h. (R)-72r was purified by PTLC on silica gel (eluant: heptane:EtOAc = 19:1). The obtained analytical data fitted accurately with the reported data.147
HPLC analysis was done immediately after isolation. The absolute configuration of homoallylic ether was assigned to the corresponding literature report.151
Yield: 38%; 18% ee.

Pale yellow liquid.

1H NMR (CDCl3, 600 MHz): δ = 2.47–2.52 (m, 1H), 2.58–2.63 (m, 1H), 4.93–4.96 (m, 1H), 5.15–5.19 (m, 2H), 5.73 (dd, J = 3.3, 9.8 Hz, 1H), 5.94 (ddt, J = 7.0, 10.2, 17.2 Hz, 1H), 6.44 (dd, J = 1.2, 9.8 Hz, 1H), 6.81 (d, J = 8.1 Hz, 1H), 6.87 (td, J = 1.2, 7.4 Hz, 1H), 6.99 (dd, J = 1.6, 7.4 Hz, 1H), 7.13 (td, J = 1.6, 7.8 Hz, 1H) ppm.

13C NMR (CDCl3, 150 MHz): δ = 39.7, 74.7, 115.9, 117.7, 121.0, 121.7, 124.2, 125.1, 126.3, 129.1, 133.3, 153.2 ppm.

HPLC (DAICEL CHIRALPAK IA; THF:hexane = 2:98; flow rate: 0.3 mL/min): t_r = 14.5 (S), 15.1 (R) min.

N-[(R)-1-Phenylbut-3-enyl]benzamide [(R)-134]

(R)-134 was prepared according to:

General procedure R: using gallium metal (15 mol%), chiral silver phosphate (R)-134–Ag (7.5 mol%) with aminal 133 and allyl boronic ester (71, 1.5 equiv) in toluene (1.0 M) at 40 °C for 120 h. (R)-134 was purified by PTLC on silica gel [eluant: diethyl ether:petrol ether (40-60) = 1:4; eluted four times].

The obtained analytical data fitted accurately with the reported data.93
HPLC analysis was done immediately after isolation. The absolute configuration of homoallylic amide was assigned to the corresponding literature report.93

263
Yield: 60%; 40% ee.

Colorless solid.

$^1$H NMR (CDCl$_3$, 500 MHz): $\delta = 2.70$ (dd, $J = 6.9, 6.9$ Hz, 2H), 5.11–5.20 (m, 2H), 5.30 (dt, $J = 6.8, 7.7$ Hz, 1H), 5.78 (dddd, $J = 7.0, 7.1, 10.2, 17.2$ Hz, 1H), 6.41 (d, $J = 6.5$ Hz, 1H), 7.25–7.29 (m, 1H), 7.34 (d, $J = 4.41$ Hz, 4H), 7.41–7.44 (m, 2H), 7.48–7.51 (m, 1H), 7.76–7.77 (m, 2H) ppm.

$^{13}$C NMR (CDCl$_3$, 500 MHz): $\delta = 40.6, 52.7, 118.5, 126.4$ (2C), 126.9 (2C), 127.4, 128.6 (2C), 128.7 (2C), 131.5 (2C), 134.0, 134.6, 141.6, 166.6 ppm.

HPLC (DAICEL CHIRALPAK IF; hexane:i-propanol = 90:10; flow rate: 1.0 mL/min): $t_r = 15.4$ (R), 21.0 (S) min.
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271