INFORMATION TO USERS

This manuscript has been reproduced from the microfilm master. UMI films the text directly from the original or copy submitted. Thus, some thesis and dissertation copies are in typewriter face, while others may be from any type of computer printer.

The quality of this reproduction is dependent upon the quality of the copy submitted. Broken or indistinct print, colored or poor quality illustrations and photographs, print bleedthrough, substandard margins, and improper alignment can adversely affect reproduction.

In the unlikely event that the author did not send UMI a complete manuscript and there are missing pages, these will be noted. Also, if unauthorized copyright material had to be removed, a note will indicate the deletion.

Oversize materials (e.g., maps, drawings, charts) are reproduced by sectioning the original, beginning at the upper left-hand corner and continuing from left to right in equal sections with small overlaps. Each original is also photographed in one exposure and is included in reduced form at the back of the book.

Photographs included in the original manuscript have been reproduced xerographically in this copy. Higher quality 6" x 9" black and white photographic prints are available for any photographs or illustrations appearing in this copy for an additional charge. Contact UMI directly to order.

UMI
A Bell & Howell Information Company
300 North Zeib Road, Ann Arbor, MI 48106-1346 USA
313/761-4700 800/521-0500
ARYL MESYLATES IN NICKEL (0) CATALYZED
HOMO- AND CROSS-COUPLING REACTIONS

by

JIN-YOUNG BAE

Submitted in partial fulfillment of the requirements
for the Degree of Doctor of Philosophy

Thesis Advisor: Professor Virgil Percec

Department of Macromolecular Science

CASE WESTERN RESERVE UNIVERSITY

May, 1995
CASE WESTERN RESERVE UNIVERSITY

GRADUATE STUDIES

We hereby approve the thesis of

Jin-Young Bae

candidate for the ph.D.
degree.*

(signed)

(chair)

(date) 3/26/95

*We also certify that written approval has been obtained for any proprietary material contained therein.
I grant to Case Western Reserve University the right to use this work, irrespective of any copyright, for the University's own purposes without cost to the University or to its students, agents and employees. I further agree that the University may reproduce and provide single copies of the work, in any format other than in or from microforms, to the public for the cost of reproduction.

[Signature]

Jim Young Bae
ARYL MESYLATES IN NICKEL (0) CATALYZED HOMO- AND CROSS-COUPLING REACTIONS

Abstract

by

JIN-YOUNG BAE

This dissertation is concerned with the synthetic utility of aryl mesylates derived from phenols in various nickel (0) catalyzed homo- and cross-coupling reactions and their application to the polymer synthesis.

In PART I, highly selective nickel (0) catalyzed homo-coupling reaction of aryl mesylates is described. This reaction provides a convenient method for the synthesis of many functional symmetrical biaryls and was applied to the preparation of both well known and novel $2,2'$-, $3,3'$- and $4,4'$-disubstituted biphenyls and other biaryls. In addition, the influence of the electronic and steric effects of substituents attached in the para, meta and ortho positions of phenols on the yield of homo-coupling of the corresponding mesylate is discussed.

The utility of this reaction is demonstrated by the efficient synthesis of four novel $2,2'$-disubstituted-$4,4'$-dihydroxybiphenyls (i.e., $2,2'$-dibenzoyl-$4,4'$-dihydroxybiphenyl, $2,2'$-di($p$-fluorobenzoyl)-$4,4'$-dihydroxybiphenyl, $2,2'$-di($p$-t-butylbenzoyl)-$4,4'$-dihydroxybiphenyl and $2,2'$-diphenyl-$4,4'$-dihydroxybiphenyl). In all cases, the nickel (0) catalyzed homo-coupling of the aryl mesylates of 4-protected-$2$-substituted hydroquinones was used as the key reaction step.

In PART II, various nickel (0) catalyzed cross-coupling reactions based on aryl mesylates are described. These experiments also demonstrate that nickel catalysts can be used in place of the more expensive palladium catalysts in already known palladium catalyzed cross-coupling reactions.
The Ni(0) catalyzed Suzuki-type cross-coupling reaction of aryl mesylates with aryloboronic acids in the presence of K₃PO₄ is described. This novel reaction which yields unsymmetrical biaryls in good yields under mild conditions, is highly regiospecific and tolerates various functional groups.

The Ni(0) catalyzed cyanation of aryl mesylates is also described. It is demonstrated that aryl mesylates are converted to nitriles in high yields by reaction with KCN in the presence of nickel (0) catalyst in DMF. The influence of the electronic effects of para-substituents upon the yields of cyanation product and side reaction products are described. In addition, the influence of solvent, polarity, the type of catalyst, and the amount of added ligand are discussed.

The Ni(0) catalyzed cross-coupling reactions of aryl mesylates with various organometallic carbanion synthons (organotin, -magnesium and -zinc compounds) are also described. It is demonstrated that Stille-type coupling reaction based on organotin compounds results in low yields. Good to high yields of cross-coupled products are obtained by using more reactive organomagnesium and -zinc compounds as coupling partners. The Ni(0) catalyzed aromatic nucleophilic substitution reaction of aryl mesylates with heteroatom-nucleophilie (phenylthiolate anion) is also presented.

In PART III, the synthesis and characterization of functional poly(p-phenylene)s and other polyarylenes based on Ni(0) catalyzed homo-coupling of bismesylates derived from substituted hydroquinones and other dihydroxy arylenes are described. In addition, the synthetic procedures which lead to regioregular and regioirregular substituted poly(p-phenylene)s with high molecular weight are discussed.
DEDICATION

This dissertation is dedicated to my wife, Jin-Suk, and to my daughter, Christina.
ACKNOWLEDGMENTS

The author would first like to acknowledge Prof. Virgil Percec for his guidance and support throughout this research.

Also, the author acknowledges the entire research group, particularly, Dr. Hill and Dr. Zhao who were co-workers on this research.

Finally, the author thanks the financial support provided by BP.
TABLE OF CONTENTS

ABSTRACT.......................................................................................................................... ii
DEDICATION......................................................................................................................... iv
ACKNOWLEDGMENTS........................................................................................................ v
TABLE OF CONTENTS.......................................................................................................... vi
LIST OF SCHEMES AND FIGURES.................................................................................... xii
LIST OF TABLES.................................................................................................................. xiv
CHAPTER 1. GENERAL INTRODUCTION......................................................................... 1

1.1.-TRANSITION METAL CATALYZED REACTIONS................................................. 1

1.2.-NICKEL(0) CATALYZED HOMO-COUPLING REACTION.............................. 3

1.3.-PALLADIUM (OR NICKEL) CATALYZED CROSS-COUPLING
    REACTION....................................................................................................................... 4
    1.3.1.-Cross-Coupling Reactions with Organoboronic Acids
    1.3.2.-Cross-Coupling Reactions with Organostannanes
    1.3.3.-Cross-Coupling Reactions with Organomagnesiums
    1.3.4.-Cross-Coupling Reactions with Organozincs
    1.3.5.-Heck-Type Olefination of Aromatic Electrophiles
    1.3.6.-Carbonylation of Aromatic Electrophiles
    1.3.7.-Transition Metal Catalyzed Aromatic Nucleophilic Substitution
        1.3.7.1.-Cyanation Reaction of Aromatic Electrophiles
        1.3.7.2.-Miscellaneous Reactions

1.4.-POLY(P-PHENYLENE)S......................................................................................... 14

1.5.-GENERAL EXPERIMENTAL.................................................................................... 19

REFERENCES..................................................................................................................... 21

PART I. ARYL MESYLATES IN NICKEL-CATALYZED HOMO-COUPLING
    REACTIONS.................................................................................................................... 27
CHAPTER 2. SYNTHESIS OF FUNCTIONAL SYMMETRICAL BIARYLS FROM PHENOLS VIA NICKEL-CATALYZED HOMO-COUPLING OF THEIR MESYLATES

2.1.-INTRODUCTION ................................................................. 28

2.2.-EXPERIMENTAL .................................................................. 30
   2.2.1.-Materials
   2.2.2.-Techniques
   2.2.3.-Synthesis of Aryl Triflates and Aryl Arenesulfonates
   2.2.4.-Synthesis of Aryl Mesylates
   2.2.5.-General Procedure for Homocoupling of Aryl Sulfonates

2.3.-RESULTS AND DISCUSSION .............................................. 41
   2.3.1.-Effects of Substituents and Leaving Groups on the
          Synthesis of 2,2'-, 3,3'- and 4,4'-Disubstituted Biphenyls
          and Biaryls
   2.3.2.-Solvent Effect
   2.3.3.-Halide Ion Effect
   2.3.4.-Effect of the Amount of Catalyst
   2.3.5.-Dried versus Wet Solvent
   2.3.6.-Ligand Effect
   2.3.7.-Comparison of THF Method with Dipolar Aprotic Solvent Method
   2.3.8.-Reaction Mechanism

2.4.-CONCLUSIONS .................................................................. 64

REFERENCES ............................................................................. 66

CHAPTER 3. SYNTHESIS OF 2,2'-DIAROYL-4,4'-DIHYDROXY-
BIPHENYLS ........................................................................... 70

3.1.-INTRODUCTION ................................................................. 70

3.2.-EXPERIMENTAL ............................................................... 71
   3.2.1.-Materials
   3.2.2.-Techniques
   3.2.3.-Synthesis of 2,2'-Diaryl-4,4'-Dihydroxybiphenyls
CHAPTER 4. SYNTHESIS OF 2,2'-DIPHENYL-4,4'-DIHYDROXY BIPHENYL

4.1.-INTRODUCTION ................................................................. 89
4.2.-EXPERIMENTAL ............................................................... 89
  4.2.1.-Materials
  4.2.2.-Techniques
  4.2.3.-Synthesis of 2,2'-Diphenyl-4,4'-dihydroxybiphenyl

4.3.-RESULTS AND DISCUSSION ............................................... 96
4.4.-CONCLUSIONS ............................................................... 99
REFERENCES ............................................................................ 101

PART II. ARYL MESYLATES IN NICKEL-CATALYZED CROSS-COUPLING REACTIONS ......................................................... 102

CHAPTER 5. SUZUKI-TYPE NICKEL-CATALYZED CROSS-COUPLING OF ARYL MESYLATES WITH ARYLBORONIC ACIDS .......................................................................... 103

5.1.-INTRODUCTION ..................................................................... 103
5.2.-EXPERIMENTAL .................................................................... 104
  5.2.1.-Materials
  5.2.2.-Techniques
  5.2.3.-Synthesis of Aryl Sulfonates
  5.2.4.-Synthesis of Arylboronic Acids
  5.2.5. General Procedure for Palladium-Catalyzed Cross-Coupling
5.2.6.-General Procedure for Nickel-Catalyzed Cross-Coupling

5.3.-RESULTS AND DISCUSSION.................................................. 108
5.3.1.-Palladium-Catalyzed Cross-Coupling
5.3.2.-Nickel-Catalyzed Cross-Coupling
5.3.3.-Reaction Mechanism

5.4.-CONCLUSIONS .................................................................. 124
REFERENCES........................................................................... 125

CHAPTER 6. NICKEL-CATALYZED CYANATION OF ARYL MESYLATES.127
6.1.-INTRODUCTION..................................................................127

6.2.-EXPERIMENTAL................................................................. 128
  6.2.1.-Materials
  6.2.2.-Techniques
  6.2.3.-Synthesis of Aryl Mesylates
  6.2.4.-General Procedure for Nickel-Catalyzed Cyanation

6.3.-RESULTS AND DISCUSSION...............................................130
6.4.-CONCLUSIONS..................................................................139
REFERENCES........................................................................... 141

CHAPTER 7. NICKEL CATALYZED CROSS-COUPLING REACTIONS OF
ARYL MESYLATES WITH VARIOUS ORGANOMETALLICS
(ORGANOTIN, -MAGNESIUM AND -ZINC COMPOUNDS) AND
SODIUM BENZENE-THIOLATE....................................................143

7.1.-INTRODUCTION..................................................................143

7.2.-EXPERIMENTAL................................................................. 144
  7.2.1.-Material
  7.2.2.-Synthesis of Aryl Sulfonates
  7.2.3.-General Procedure for Pd(0)-Catalyzed Cross-Coupling of
         Aryl Sulfonates with Tri-n-butylyphenylstannane
7.2.4.-General Procedure for Ni(0)-Catalyzed Cross-Coupling of Aryl Sulfonates with Tri-\textit{n}-butylphenylstannane
7.2.5.-General Procedure for Ni(0)-Catalyzed Cross-Coupling of Aryl Mesylates with Grignard- and Zinc Reagents
7.2.6.-General Procedure for Ni(0)-Catalyzed Cross-Coupling of Aryl Mesylates with Sodium Benzenethiolate

7.3.-RESULTS AND DISCUSSION..........................................................149
7.3.1.-Pd(0)- and Ni(0)-Catalyzed Cross-Coupling Reactions of Aryl Sulfonates with Tri-\textit{n}-butylphenylstannane
7.3.2.-Ni(0)-Catalyzed Cross-Couplings of Aryl Mesylates with Organomagnesium and -Zinc Compounds
7.3.3.-Cross-Coupling of Aryl Mesylates with Sodium Benzene-thiolate
7.3.4.-Attempt on Ni(0)-Catalyzed Heck-Type Olefination of Aryl Mesylate

REFERENCES..................................................................................161

PART III. SYNTHESIS OF FUNCTIONAL POLYARYLENES FROM SUBSTITUTED HYDROQUINONES AND BISPHENOLS VIA NICKEL CATALYZED HOMO-COUPLING OF THEIR BISMESYLATES........................................163

CHAPTER 8. SYNTHESIS OF FUNCTIONAL REGIOREGULAR AND REGIOIRREGULAR SUBSTITUTED POLY(\textit{p}-PHENYLENE)S FROM HYDROQUINONES VIA NICKEL(0) CATALYZED COUPLING OF THEIR BISMESYLATES..........................164

8.1.-INTRODUCTION.............................................................................164
8.2.-EXPERIMENTAL...........................................................................166
8.2.1.-Materials
8.2.2.-Synthesis of Monomers
8.2.3.-Polymerizations

8.3.-RESULTS AND DISCUSSION.......................................................177
8.4. CONCLUSIONS ................................................................. 204
REFERENCES ........................................................................ 206

CHAPTER 9. SYNTHESIS OF AROMATIC BIPHENYLENE POLYMERS BY 
NICKEL(0) CATALYZED HOMO-COUPLING OF ARYLENE 
BISMESYLATES DERIVED FROM BISPHENOLS .............. 209

9.1. INTRODUCTION ................................................................. 209

9.2. EXPERIMENTAL ............................................................... 209
  9.2.1. Techniques
  9.2.2. Materials
  9.2.3. Synthesis of Monomers
  9.2.4. Polymerization

9.3. RESULTS AND DISCUSSION ........................................... 213
REFERENCES ........................................................................ 221

BIBLIOGRAPHY .................................................................... 222
CHAPTER 1

Scheme I. General Mechanism of Pd(0)-Catalyzed Cross-Coupling Reaction........... 5

CHAPTER 2

Scheme I. Plausible Mechanism of Ni(0) Catalyzed Homo-Coupling of Aryl
Mesylate in the Presence of Excess Zn........................................... 60
Scheme II. Plausible Mechanism of Ni(0) Catalyzed Homo-Coupling of Aryl
Mesylate in the Absence of Excess Zn........................................... 61

CHAPTER 3

Scheme I. Synthesis of 2,2'-Diaroyl-4,4'-Dihydroxybiphenyls......................... 73
Figure 1. 200 MHz $^1$H-NMR Spectrum of 2,2'-Dibenzoyl-4,4'
   bis(methylsulfonyloxy)biphenyl (7a)........................................... 85
Figure 2. 200 MHz $^1$H-NMR Spectrum of 2,2'-Di(p-fluorobenzoyl)-4,4'
   bis(methylsulfonyloxy)biphenyl (7b).......................................... 86
Figure 3. 200 MHz $^1$H-NMR Spectrum of 2,2'-Di(p-t-butylbenzoyl)-4,4'
   bis(methylsulfonyloxy)biphenyl (7c).......................................... 87

CHAPTER 4

Scheme I. Synthesis of 2,2'-Diphenyl-4,4'-dihydroxybiphenyl from
Phenylhydroquinone............................................................... 91
Scheme II. Synthesis of 2,2'-Diphenyl-4,4'-dihydroxybiphenyl from
2-Phenylphenol............................................................................ 92
Figure 1. 200 MHz $^1$H-NMR Spectrum of 2,2'-Diphenyl-4,4'
   bis(methylsulfonyloxy)biphenyl (12).......................................... 100

CHAPTER 5
LIST OF TABLES

CHAPTER 1
Table I. 'Acceptor' and 'Donor' Groups in Various Pd(0)-Catalyzed Cross-Coupling Reactions.......................................................... 6

CHAPTER 2
Table I. Ni(0)-Catalyzed Homocoupling of Various p-Carbomethoxyphenyl Sulfonates................................................................. 43
Table II. Effect of Various Substituents on the Ni(0)-Catalyzed Homocoupling of Aryl Sulfonates....................................................... 45
Table III. Effect of Various Substituents on the Ni(0)-Catalyzed Homocoupling of Aryl Methanesulfonates............................................ 46
Table IV. Effect of Various Reaction Conditions on the Ni(0)-Catalyzed Homocoupling of Methyl 4-methylsulfonyloxy benzoate.................50
Table V. Effect of Various Reaction Conditions on the Ni(0)-Catalyzed Homocoupling of 4-Acetylphenyl methanesulfonate....................58

CHAPTER 5
Table I. Pd(0)-Catalyzed Cross-Coupling of Various Aryl Sulfonates with Phenylboronic Acid......................................................... 109
Table II. Ni(0)-Catalyzed Cross-Coupling of Various Aryl Sulfonates with Phenylboronic Acid.......................................................... 113
Table III. Effect of Various Reaction Conditions on the NiCl2(dppf)-Catalyzed Cross-Coupling of Methyl 4-(methylsulfonyloxy)benzoate with Phenylboronic Acid .......................................................... 117

CHAPTER 6
Table I. Nickel (0) Catalyzed Cyanation of Phenyl Mesylate...................... 132
Table II. Nickel (0) Catalyzed Cyanation of Various Aryl Mesylates........ 137
CHAPTER 7

Table I. Pd(0)- and Ni(0)-Catalyzed Cross-Coupling Reactions of Various Aryl Sulfonates with Tri-\(n\)-butylphenylstannane.............................. 150

Table II. Ni(0)-Catalyzed Cross-Coupling Reaction of Aryl Mesylates with Organomagnesium and -Zinc Compounds................................. 153

Table III. Ni(0)-Catalyzed Cross-Coupling of Phenyl Mesylate with Sodium Benzenethiolate................................................................. 156

Table IV. Ni(0)-Catalyzed Cross-Coupling of Substituted Aryl Mesylates with Sodium Benzenethiolate................................................................. 158

CHAPTER 8

Table I. Ni(0) Catalyzed Polymerization of Methyl 2,5-bis(methylsulfonyloxy)-benzoate......................................................................................... 179

Table II. Ni(0) Catalyzed Polymerization of (2-Ethylhexyl)-2,5-bis(methylsulfonyloxy) Benzoate.............................................................................. 183

Table III. Ni(0) Catalyzed Polymerization of 2-Ethylhexyloxycarbonyl Substituted Benzene Derivatives Containing Bromine, Chlorine, Trifluoromethanesulfonate, 4-Fluoro-benzenesulfonate, and Methanesulfonate Leaving Groups.............................................................. 186

Table IV. Ni(0) Catalyzed Copolymerization of Methyl 2,5-Bis(methylsulfonyloxy) benzoate With Various Comonomers........................................ 189

Table V. Ni(0) Catalyzed Homocoupling Polymerization of Various Aryl Bismesylates....................................................................................... 192

Table VI. Nickel(0) Catalyzed Copolymerization of 2,2'-Disubstituted-4,4'-bis(methylsulfonyloxy)biphenyl with 2-Substituted 1,4-Bis(methylsulfonyloxy)benzene............................................................... 199
CHAPTER 9

Table I. Ni (0) Catalyzed Polymerization of Aryl Bismesylates Derived from Various Bisphenols........................................................................................................214

Table II. Ni(0) Catalyzed Copolymerization of Various Aryl Bismesylates.....218
1.1.-TRANSITION METAL CATALYZED REACTIONS

The formation of new carbon-carbon bonds is a key step in many organic reactions. The use of transition-metal complexes as catalysts for these reactions has attracted the interest of synthetic chemists, as a variety of organic and organometallic substrates can be used. Among the Group 10 triad (Ni, Pd and Pt) of transition metals, palladium has been extensively used in numerous organic reactions. Pd(0) complexes are efficient catalysts for a large number of reactions such as carbonylation of aryl halides, arylation of olefins, and cross-coupling of aryl halides with various organometallic reagents (e.g., organomagnesium, -zinc, -tin, and -boron compounds) and with terminal acetylenes. In several cases, nickel based coupling reactions have been described. For example, the Ni(0) catalyzed cross-coupling reaction of aryl and alkenyl halides with Grignard reagents was reported. Another representative example for utilization of Ni(0) complexes is Ullmann-type homocoupling reaction.

Aryl halides are important substrates in transition metal (particularly palladium) catalyzed coupling reactions. Most reactions with aryl halides employ rather expensive aryl bromides and iodides. Unfortunately, application of inexpensive aryl chlorides for coupling reactions are somewhat limited due to the inertness of their C-Cl bonds. It was reported that the order of reactivity of aryl halides with Pd(0)(PPh₃)₄ is ArI>ArBr>ArCl. Aryl chlorides usually do not readily undergo palladium catalyzed coupling reactions even under drastic conditions, because oxidative addition of nonactivated aryl chlorides to the Pd(0) species is slow, and the premature decomposition of the catalyst is frequently encountered. So far, many research groups...
have tried to enhance the poor reactivity of aryl chlorides. One of the most popular approaches is the introduction of strong electron-withdrawing groups (e.g., -NO₂) to aryl chlorides, which increases the electrophilic nature of arenes making the substrates susceptible to the desired coupling reactions. However, most coupling reactions of nonactivated aryl chlorides require nickel complexes as the catalyst, because zerovalent nickel can readily undergo oxidative addition of the carbon-chlorine bond (i.e., C-Cl bond activation). The reactivity of zerovalent d¹⁰ transition metal-phosphine ligand complexes toward oxidative addition of aryl halides is known to decrease significantly in the order of Ni>Pd>Pt.⁹

**Aryl Triflates in Transition Metal Catalyzed Reactions**

Transition metal catalyzed homo- and cross-coupling reactions of aryl halides are certainly of great synthetic value (*vide supra*). The use of aryl trifluoromethanesulfonates (aryl triflates) instead of aryl halides in such reactions is particularly important in organic synthesis because it can provide an access of forming a carbon-carbon bond at a phenolic site, which is often useful when appropriate halides are unavailable.¹⁰ Since aryl triflates are readily available from phenols, the scope of the application of these compounds in transition metal catalyzed reactions has broadened enormously.

Aryl triflates undergo palladium catalyzed cross-coupling reactions with a variety of organometallic reagents (organotin,⁴ -zinc,¹⁰ -boron¹¹ and -magnesium¹² compounds) as coupling partners or addition reactions to alkenes and alkynes (i.e., Heck coupling¹³) under mild conditions. Palladium catalyzed carbon monoxide insertion of triflates providing the corresponding carboxylic acid derivatives (esters or amides) has been described.¹⁴ Recently nickel(0) catalyzed Ullmann-type homocoupling reaction of ary triflates was also reported.¹⁵
Although the triflates have been used extensively in organic synthesis, the main drawback of triflate methodology is the high price for the triflating agents (e.g., triflic anhydride), which prevent the wide utilization of aryl triflates in transition metal catalyzed reactions.

1.2.-NiCkEL(0) CATALYZED HOMO-COUPlING REACTION

In 1971, Semmelhack and coworkers first reported the synthesis of symmetrical biaryls from aryl halides and stoichiometric amounts of preformed Ni(COD)$_2$ (bis[1,5-cyclooctadiene]nickel(0)).$^7$ Unlike the classical Ullmann reaction,$^{16}$ this nickel(0) mediated reductive homocoupling reaction of aryl halides proceeds under exceedingly mild conditions. This original method, based on preformed nickel(0) complex, was then modified by Kende et al. using in situ generation of the stoichiometric amounts of Ni(0)-phosphine complexes from nickel(II) precursors with zinc as a reducing agent.$^{17}$ The reaction was rendered catalytic in the presence of the stoichiometric amounts of zinc and catalytic amounts of nickel(II)-phosphine complexes (eq 1)$^{18}$, and this catalytic reaction could also be conducted electrochemically.$^{19}$

\[
2\text{ArX} + \text{Zn} \xrightarrow{\text{NiCl}_2(\text{PPh}_3)_2} \text{Ar-Ar} + \text{ZnX}_2 \quad (1)
\]

$X=\text{Br, I}$

Recently the method has been extended to the use of aryl chlorides in the presence of an excess of reducing metal (e.g., Zn)$^{20}$

The Ni(0) catalyzed homocoupling of aryl triflates$^{15a}$, aryl tosylates$^{15b}$ and one example of an aryl mesylate$^{15b}$ to symmetrical biaryls were first reported to proceed under ultrasonication. Subsequently, our laboratory has shown that Ni(0) catalyzed homocoupling of bistriﬂates takes place in the absence of ultrasonication and this reaction yielded a convenient method for the synthesis of functional poly($p$-phenylene)s
and polyarylenes.\textsuperscript{15c-e} Pd catalyzed electrosynthesis of biaryls from aryl triflates was also reported.\textsuperscript{15g} Recently a communication reported the Ni(0) and Pd(0) catalyzed homocoupling of aryl triflates,\textsuperscript{15f} and a patent reported the Ni(0) mediated homocoupling of aryl sulfoxides including one example of an aryl mesylate.\textsuperscript{15h}

Mechanistic aspects of Ni(0) catalyzed homo-coupling will be discussed in chapter 2.

1.3.-PALLADIUM (OR NICKEL) CATALYZED CROSS-COUPLING REACTION

Palladium, and to a lesser extent nickel, are widely used to promote the various cross-coupling reactions.\textsuperscript{1} The process involves a generally accepted catalytic cycle\textsuperscript{21} in which the zerovalent palladium first undergoes oxidative addition, usually to an aryl-halogen bond, in the substrate (often referred to as the 'acceptor'). The new group ('Donor') is then added to the resulting intermediate (transmetallation), and the aryl and the substituent groups then combine to generate the product and regenerate the catalyst (reductive elimination, Scheme I). The R group can be a wide range of functional groups (e.g., alkyl, alkenyl, alkynyl or aryl groups). Some representative examples of 'donor' and 'acceptor' groups are shown in Table I.

Notable aspects of these palladium (or nickel) catalyzed reactions are the mild conditions, the tolerance of various functional groups and the high yields produced. The palladium catalyst is usually a palladium(II) salt, which is reduced \textit{in situ} to palladium(0) and complexed by added ligands. The ligands are usually triaryl phosphines and their structure can dramatically affect the yield and regioselectivity of the reaction.\textsuperscript{22}
Scheme I. General Mechanism of Pd(0)-Catalyzed Cross-Coupling Reaction
Table I. 'Acceptor' and 'Donor' Groups in Various Pd(0)-Catalyzed Cross-Coupling Reactions

<table>
<thead>
<tr>
<th>Acceptor</th>
<th>Donor$^a$</th>
<th>Coupling Type</th>
</tr>
</thead>
<tbody>
<tr>
<td>ArX (X=I, Br, Cl, OTf etc.)</td>
<td>R-B(OH)$_2$</td>
<td>Suzuki Coupling$^5$</td>
</tr>
<tr>
<td></td>
<td>R-ZnX</td>
<td>Negishi Coupling$^3$</td>
</tr>
<tr>
<td></td>
<td>R-Sn(n-Bu)$_3$</td>
<td>Stille Coupling$^4$</td>
</tr>
<tr>
<td></td>
<td>R-MgX</td>
<td>Grignard Coupling$^2$</td>
</tr>
<tr>
<td></td>
<td>Alkene or alkyne</td>
<td>Heck Coupling$^{1a}$</td>
</tr>
</tbody>
</table>

$^a$ R=aryl, alkenyl, etc.
1.3.1. Cross-Coupling Reactions with Organoboronic Acids

The palladium(0) catalyzed cross-coupling reaction of aryl halides (aryl iodides, aryl bromides or activated aryl chlorides)$^{1b,5}$ and aryl triflates$^{11}$ with arylboronic acids in the presence of a base, known as the "Suzuki reaction", is a versatile method for synthesizing unsymmetrically substituted biaryls (eq 2).

\[
\text{Ar-X} + \text{Ar'-B(OH)_2} \xrightarrow{\text{Pd(0) \ base}} \text{Ar-Ar'} \quad (2)
\]

\(X = I, Br, OTf\)

This coupling reaction, which is generally catalyzed by tetrakis-(triphenylphosphine)palladium(0) with biphasic mixture of benzene (or toluene) and water as the solvent, offers the advantages of high yields, clean products with less side reaction, tolerance of a variety of functional groups on either coupling partner, and no necessity for anhydrous conditions.

The most frequently employed aryl halides in Suzuki reactions are aryl iodides and bromides. In general, the reactivity of aryl halides toward organoboronic acids decreases in the order of ArI>ArBr>ArCl. Except for a few electron-deficient heteroaryl chlorides,$^{23}$ aryl chlorides usually do not participate in the cross-coupling. The discovery that aryl triflates can be used in this coupling reaction is of great synthetic value, since aryl triflates can be easily prepared from phenols.$^{11}$

Arylboronic acids are fairly stable towards air and moisture, heat resistant, and can be easily prepared from an aryl lithium or an aryl Grignard reagent by treatment with trimethylborate, followed by the hydrolysis of the borate ester with aqueous hydrochloric acid.

Because of the weak nucleophilic character of organoboronic acid, a base is essential to carry out a successful coupling. A relatively weak base such as aqueous carbonate is the most often used base.$^{5b}$ Recently it was demonstrated that both water
and base are required to activate the boronic acid toward Suzuki reaction.\textsuperscript{24} The function of the base in the coupling reaction is thought to be to form a boronate anion, which can facilitate the transmetallation of boron to palladium.\textsuperscript{5c}

It is note-worthy that anhydrous reaction conditions with thallium(I) carbonate or potassium phosphate as base also produce high yields of cross-coupled product.\textsuperscript{11}

1.3.2.-Cross-Coupling Reactions with Organostannanes

The "Stille reaction",\textsuperscript{4} known as the palladium catalyzed cross-coupling between organic electrophiles and organostannanes, has become a powerful synthetic tool for carbon-carbon bond formation (eq 3).

\[
\begin{align*}
R^1\cdot X + R^2\cdot SnR_3^3 & \xrightarrow{Pd(0)} R^1\cdot R^2 + XSnR_3^3 \\
R^1 &= \text{aryl, alkenyl} \\
R^2 &= \text{aryl, alkenyl, alkynyl, allyl, alkyl} \\
R^3 &= \text{Me, n-Bu} \\
X &= I, Br, OTf
\end{align*}
\] (3)

As indicated in eq 3, alkyl, alkenyl, allyl, alkynyl, and aryl groups can be transferred from tin to vinylic or acrylic carbon.

The Stille reaction has many attractive features: yields are high under mild conditions; various functional groups, including aldehydes and esters, are tolerated; and functionalized organostannanes are readily available and stable to air and moisture.\textsuperscript{4} The reaction is usually catalyzed by Pd(0)-phosphine complexes such as Pd(PPh\textsubscript{3})\textsubscript{4}.\textsuperscript{25} Large rate accelerations in the Stille reactions with tri-2-furylphosphine or triphenylarsine instead of triphenylphosphine as palladium ligands have been reported.\textsuperscript{25} It was also reported that the addition of copper(I) iodide as a co-catalyst promotes the cross-coupling of aryl halides or triflates with organostannanes.\textsuperscript{26}
Among the aryl halides as substrates, usually aryl iodides and bromides give high yields of coupled products under mild condition.\textsuperscript{27} Aryl chlorides are usually unreactive under the standard conditions, and require activation with electron-withdrawing substituents or by coordination of an electron-withdrawing Cr(CO)\textsubscript{3} to the arene moiety.\textsuperscript{28} Recently the cross-coupling reaction of arene-Cr(CO)\textsubscript{3} triflate complexes with organostannanes was reported.\textsuperscript{29}

The cross-coupling reaction with aryl triflates as substrates is especially important since these compounds can be easily prepared from readily available phenols.\textsuperscript{4} This reaction has been further extended to the use of aryl fluorosulfonates\textsuperscript{30} and aryl arenesulfonates\textsuperscript{31} as substrates, which are more stable and less expensive than the corresponding aryl triflates.

In the classical procedure for the cross-coupling of aryl triflates with organostannanes using Pd(PPh\textsubscript{3})\textsubscript{4} as a catalyst, LiCl has been reported to be essential for the success of the reaction, although the function of LiCl is not fully understood.\textsuperscript{4b} However, Stille reactions in the absence of LiCl have been reported.\textsuperscript{32}

\textbf{1.3.3.-Cross-Coupling Reactions with Organomagnesiums}

Organomagnesium compounds (i.e., Grignard reagents) are frequently used in the cross-coupling reactions with organic electrophiles catalyzed by transition metal complexes.\textsuperscript{2} In 1972, Corriu\textsuperscript{33} and Kumada\textsuperscript{34} first reported the cross-coupling reactions of aryl and alkenyl halides with Grignard reagents. This type of coupling reaction is usually catalyzed by nickel-phosphine complexes such as [dichloro(1.3-bis(diphenylphosphino)propane)Ni(II) (NiCl\textsubscript{2}(dppp))] (eq 4).\textsuperscript{33-35}
\[ \text{R-X} + \text{R'}\text{MgX} \xrightarrow{\text{Ni(0)}} \text{R-R'} \quad (4) \]

R=aryl, alkenyl
R'=aryl, alkenyl, alkyl
X=I, Br, Cl, OTf

Such coupling reactions of aryl halides with organomagnesium compounds in the presence of palladium complexes such as PdCl\(_2\)(dppf) have been described.\(^{36}\) It was recently reported that Grignard reagents undergo Ni(0)-catalyzed cross-coupling reactions with aryl triflates.\(^{12}\)

The major drawback of Grignard cross-coupling is that the reaction usually does not tolerate various sensitive functional groups such as aldehyde or ester on either coupling partner. In addition, Grignard reagents are air and moisture sensitive, and those involving alkyl groups containing \(\beta\)-hydrogen atom(s) do not always give satisfactory results due to \(\beta\)-elimination.

1.3.4.-Cross-Coupling Reactions with Organozincs

Organozinc compounds are useful organometallic reagents for organic synthesis.\(^{37}\) Since these compounds tolerate many functional groups such as ester and cyano groups and show enough nucleophilicity toward various organic electrophiles, palladium catalyzed cross-coupling reaction of zinc compounds with organic halides (especially iodides and bromides) is a versatile method for carbon-carbon bond formation (eq 5).\(^3\)

\[ \text{R-X} + \text{R'ZnX} \xrightarrow{\text{Pd(0)}} \text{R-R'} \quad (5) \]

R=aryl, alkenyl
R'=aryl, alkenyl, alkyl
X=halides
Negishi first reported that aryl iodides or bromides can be cross-coupled with arylzinc chlorides in the presence of Pd(PPh$_3$)$_4$ as catalyst (i.e., "Negishi coupling"). Palladium-catalyzed cross-coupling reactions of aryl fluoroalkanesulfonates including triflate with zinc reagents were also reported. Nickel-based cross-coupling of chlorobenzene with alkylzinc reagent was described.

In general, the zinc reagents are prepared by the transmetallation reaction of the corresponding lithium or magnesium reagents with zinc halides. Recently the direct synthesis of arylzinc halides by the oxidative addition of activated zinc with aryl halides was developed. More recently ultrasound-promoted oxidative addition of zinc to aryl iodide was also reported.

1.3.5.-Heck-Type Olefination of Aromatic Electrophiles

The palladium-catalyzed arylation of olefins, known as the "Heck reaction", is a unique and convenient method for carbon-carbon bond formation at unsubstituted vinylic positions (eq 6).

\[
\begin{align*}
  \text{Ar-X} & + \text{CH}_2=\text{CHR} & \xrightarrow{\text{Pd(0)}} & \text{Ar-CH}=\text{CHR} \\
  \text{base} & & \text{-HX} &
\end{align*}
\]

\( \text{X= I, Br, OTf} \)

This reaction is generally accomplished by the catalytic action of a zerovalent palladium-phosphine complexes \textit{in situ} generated by the reduction of a palladium (II) salt in the presence of a phosphine ligand. The regioselectivity in such reaction can be controlled by the proper choice of the phosphine ligands. A base is essential to neutralize the hydrogen halide generated in Heck reaction. Among bases, triethylamine is the most frequently used.

The most often used aryl halides in Heck reaction are aryl iodides and bromides. Aryl chlorides are usually unreactive under the standard conditions due to
the low reactivity of zerovalent palladium catalyst toward oxidative addition of the carbon-chlorine bond.\textsuperscript{16} However, several examples of palladium\textsuperscript{44} and nickel\textsuperscript{45}-catalyzed Heck reactions of aryl chlorides have been reported. Aryl triflates, readily prepared from phenols, are also useful substrates in Heck reaction.\textsuperscript{13}

1.3.6.-Carbonylation of Aromatic Electrophiles

The palladium-catalyzed carbonylation reaction of aromatic electrophiles in the presence of various nucleophiles is a versatile method to synthesize a variety of aromatic carbonyl compounds including arene carboxylic acids and their derivatives.\textsuperscript{46} This reaction can be run under mild conditions, tolerates a variety of substituents, and usually gives high yields of products.

Depending on the nucleophile added to the reaction mixture (e.g., water, alcohol or amine), the carbonylation of aryl halides (especially aryl iodides and bromides) and triflates can generate aromatic aldehydes,\textsuperscript{47} ketones,\textsuperscript{48} acids,\textsuperscript{49} esters,\textsuperscript{14,50} and amides\textsuperscript{14a,50a,50e} (eq 7).

\[
\begin{align*}
\text{ArX} & \quad \text{CO} \\
\quad \quad & \quad [\text{H}] \quad \text{ArCHO} \\
\quad \quad & \quad [R_1] \quad \text{ArCOR}_1 \\
\quad \quad & \quad [\text{OH}^-] \quad \text{ArCOOH} \quad \text{(7)} \\
\quad \quad & \quad [\text{OR}_2] \quad \text{ArCO}_2\text{R}_2 \\
\quad \quad & \quad [\text{NR}_1\text{R}_2] \quad \text{ArCONR}_1\text{R}_2
\end{align*}
\]
Recently palladium catalyzed carbonylation of aryl halides by using chloroform as a carbon monoxide precursor and aqueous alkali was reported.\textsuperscript{51} In several cases, nickel-\textsuperscript{52} and cobalt \textsuperscript{53} complexes based carbonylations have been described.

\textbf{1.3.7.-Transition Metal Catalyzed Aromatic Nucleophilic Substitution}

The classical aromatic nucleophilic substitution reaction normally involves the displacement of electronegative leaving groups (usually halogens) by electron-rich carbon- or heteroatom-nucleophiles. Enhancement of the reactivity of aromatic electrophiles toward nucleophiles has been successfully achieved by transition metal catalysis.\textsuperscript{1} Palladium (or nickel) catalyzed substitution reaction of aromatic electrophiles with various nucleophiles is an important method for the formation of new carbon-carbon (or carbon-heteroatom) bond. This reaction usually takes place at mild conditions, and is usually regiospecific.

\textbf{1.3.7.1.-Cyanation Reaction of Aromatic Electrophiles}

The nucleophilic displacement of an aromatic halogen with a cyano group is commonly carried out using stoichiometric amounts of CuCN.\textsuperscript{54} Such reaction with alkali metal cyanides (NaCN or KCN) does not take place under conventional conditions. However, palladium or nickel can induce this reaction through aromatic carbon-halogen bond activation.

The use of Pd(0) complex as catalyst in cyanation of aryl halides is well documented in the literature.\textsuperscript{55} The reactions usually employ aryl iodides or bromides as substrates. Aryl chlorides are known to be substantially less reactive toward Pd(0) catalyzed cyanation, unless the carbon-chlorine bond is activated.\textsuperscript{56} However, aryl chlorides could undergo cyanation in the presence of catalytic amounts of nickel-phosphine complex.\textsuperscript{57} Aryl triflates also participated in a nickel catalyzed cyanation,
thereby providing a convenient method for the conversion of phenolic oxygen into a cyano group.\textsuperscript{58}

One of the difficulties in transition metal catalyzed cyanation is that high concentrations of cyanide ions in solution are detrimental to the catalytic cycle.\textsuperscript{55a} The cyanide ion can bind to Pd(0) or Ni(0) too strongly to render the catalyst inactive. To circumvent this problem, slow addition of cyanide into reaction mixture is frequently carried out to promote the cyanation reaction.\textsuperscript{55a} Recently an efficient method for conversion of aryl bromides to aryl cyanides using zinc cyanide, which gives much lower cyanide concentration than sodium and potassium cyanides, is reported.\textsuperscript{59}

1.3.7.2.-Miscellaneous Reactions

Various heteroatom-nucleophiles such as thiolate anion,\textsuperscript{60} amine,\textsuperscript{61} and phosphorus\textsuperscript{62} were utilized in the Pd(0) or Ni(0) catalyzed aromatic nucleophilic displacement reaction. Ni(0) catalysts also promote the halogen exchange reaction with halide ions.\textsuperscript{63}

1.4.-Poly(p-Phenylene)s (PPPs)

Poly(p-phenylene)s are rigid rod-like materials which display good thermal and oxidative stability as well as electrical conductivity upon doping.\textsuperscript{64} Unfortunately, synthesis and characterization of this type of polymer is limited due to its insolubility and infusibility. Many attempts to synthesize PPPs by various synthetic routes have been described.\textsuperscript{64c-d} Kovacic first reported the direct synthesis of PPP by oxidative coupling of benzene using AlCl₃/CuCl as Lewis acid.\textsuperscript{65} However, the main disadvantage of this method is that the resulting polymer inevitably contains structural defects of irregularly linked phenylene units. The other direct route was developed by Yamamoto, which involved nickel catalyzed Grignard coupling of 1.4-
dihalobenzene. But both methods are limited by decreasing solubility of the polymer with increase in molecular weight. Since unsubstituted PPPs are insoluble and infusible below their decomposition temperatures, direct methods are expected to result in low molecular weight.

Soluble polyphenylenes could be obtained by introducing lateral substituents or backbone disorder through meta links in the phenylene unit (i.e., increasing the configurational entropy). This approach was used for the synthesis of soluble linear alkyl-substituted PPPs by a palladium catalyzed polymerization of benzene derivatives containing both bromo and boronic acid functional groups. Phenyl-substituted PPP was also synthesized by a nickel catalyzed Yamamoto coupling of 2,5-dibromobiphenyl.

Indirect methods for the preparation of unsubstituted PPPs by the use of a soluble precursor were also reported. A Li/HMPA-promoted polymerization of 1,4-dibromobenzene was recently reported.

Our laboratory reported two methods for the synthesis of soluble polyphenylenes. The first refers to the Ni(0) catalyzed homo-coupling of substituted 1,4-dihaloarylenes. The second is based on the Ni(0) catalyzed homo-coupling of the bistriflates of substituted hydroquinones and of other dihydroxyarenes.

As discussed above, palladium, and to a lesser extent nickel, catalyzed reactions are a powerful synthetic tool with their applications being widespread. However, aromatic substrates in these reactions are almost limited to the aryl halides and triflates. The use of aryl triflates in such reactions are of great synthetic value since they provide an access of forming carbon-carbon bond at the phenolic site. However, the main drawback of triflate-based methodology is the high price for the triflating agents, which
prevent the wide utilization of aryl triflates in transition metal catalyzed reactions. Therefore, we decided to expand the scope of these reactions using phenols as starting materials by seeking less expensive alternatives to aryl triflates. For this purpose, we have examined aryl mesylates, which have been generally considered to have a poor reactivity toward transition metal catalysts, as possible alternatives.

Our efforts have been also made directed at the development of nickel-based catalysis for the already known various palladium catalyzed reactions. Although palladium catalysis represents a well established methodology in organic synthesis, it is more preferable if inexpensive nickel catalyst could be used in place of the expensive palladium catalyst.

Inexpensive aryl mesylates are of interest as substrates but suffer from their relatively inert character of carbon-oxygen bond. Two approaches appeared possible for the C-O bond activation of aryl mesylate: a) palladium catalysis with strongly donating phosphine ligands and b) generally more reactive nickel catalysis. Our initial attempt was the activation of aryl mesylates using a palladium complex. Various efforts to develop synthetically useful palladium catalyzed reactions based on aryl mesylates have resulted in failure. The synthesis of new ligands and palladium complexes has not been explored. Thus, most attention has been focused on the reaction of aryl mesylates using the more reactive nickel catalyst. A catalyst system consisting of NiCl$_2$(PPh$_3$)$_2$ or NiCl$_2$(dppf) in the presence of Zn were proved to be efficient for various transformations of aryl mesylates.

This dissertation is concerned with the catalytic aspects of nickel complexes in various organic transformations of aryl mesylates and their application to the polymer synthesis.
In PART I, we have demonstrated that aryl sulfonates including mesylate derived from phenols are converted in high yields to biaryls by homo-coupling in the presence of catalytic amounts of Ni(0) catalysts generated in situ. The influence of the electronic and steric effects of substituents attached in the ortho, meta and para positions of aryl sulfonates, and the nature of the sulfonate leaving group on the yield of homo-coupled product as well as their influence on the extent of various side reactions were investigated. In addition, the influence of the effects of the polarity and dryness of solvent, halide ion source and concentration, and ratio of catalyst and ligand to aryl sulfonate are discussed.

The utility of this homo-coupling reaction was demonstrated by the synthesis of three novel 2,2′-diaroyl-4,4′-dihydroxybiphenyls (i.e., 2,2′-dibenzoyl-4,4′-dihydroxybiphenyl, 2,2′-di(p-fluorobenzoyl)-4,4′-dihydroxybiphenyl and 2,2′-di(p-t-butylbenzoyl)-4,4′-dihydroxybiphenyl). All three new compounds were synthesized in 20-40% overall yield by a five step procedure which consists of Friedel-Crafts aroylation of 1,4-dimethoxybenzene followed by regioselective demethylation of the 1-methoxy group, mesylation, Ni(0) catalyzed homo-coupling and demethylation.

The synthesis of novel 2,2′-diphenyl-4,4′-dihydroxybiphenyl is also described. This compound was synthesized by two synthetic routes. The first one starts from phenylhydroquinone (10% overall yield) in four steps, while the second one starts from 2-phenylphenol (13% overall yield) in five steps. In both cases, the nickel(0) catalyzed homo-coupling of the aryl mesylate of 4-protected-2-phenylhydroquinone was used as the key reaction step.

In PART II, it is demonstrated that under nickel catalysis, aryl mesylates can be cross-coupled with various organometallics (organoboron, -tin, -magnesium and -zinc compounds) and heteroatom-nucleophile (phenylthiolate anion). These experiments
also demonstrate that nickel catalysts can be used instead of the more expensive palladium catalysts for already known palladium catalyzed cross-coupling reactions.

The novel Ni(0) catalyzed Suzuki-type cross-coupling reaction of various aryl sulphonates including mesylate with arylboronic acids in the presence of K$_3$PO$_4$ is described. The Ni(0) catalyst is generated *in situ* from NiCl$_2$(dpdf) and Zn. The influence of the effects of the substituent of the aromatic substrates, the nature of the leaving group, solvent and type of catalyst, and base on the reaction yield are discussed. The reactivity of various Ni(0) catalysts is compared with that of the less reactive Pd(0) catalysts.

Facile synthesis of aryl cyanides from aryl mesylates is also described. Aryl mesylates were converted in high yields to nitriles by reaction with KCN in the presence of Ni(0) catalyst in DMF. The nickel catalyst was generated *in situ* from NiCl$_2$(PPh$_3$)$_2$, PPh$_3$ and Zn. Since phenols are readily converted to aryl mesylates, this procedure constitutes the most convenient method for the conversion of phenols to aryl nitriles.

It is also demonstrated that aryl mesylates undergo Ni(0) catalyzed cross-coupling reactions with organometallic carbanion synthons such as organotin, -magnesium and -zinc compounds. Although Stille-type coupling reactions based on organotin compounds result in low yields, good to high yields of cross-coupled products are obtained by using generally more reactive organomagnesium and -zinc compounds as coupling partners.

The nickel(0) catalyzed aromatic nucleophilic substitution reaction of aryl mesylates with phenylthiolate anion as nucleophile is also described.

PART III describes the synthesis and characterization of functional poly(p-phenylene)s and other polyarylenes based on nickel(0) catalyzed homo-coupling of bismesylates derived from substituted hydroquinones and other dihydroxyarylenes. In
addition, the synthetic procedures which leads to regioregular and regiorrregular substituted PPPs with high molecular weight are discussed.

1.5.-GENERAL EXPERIMENTAL

Melting points are uncorrected and were determined with a Thomas Hoover Uni-Melt capillary melting point apparatus. $^1$H-NMR (200-MHz) and $^{13}$C{$^1$H} (50-MHz) spectra were recorded on a Gemini-200 spectrometer, in CDCl$_3$ and with TMS as an internal standard except when reported. Electron Impact Mass Spectra (EIMS) were recorded at 20-50 eV ionizing energy. High Resolution Mass Spectra (HRMS) were obtained with a Kratos MS25RFA instrument. GC analyses were performed on a Hewlett Packard 5890 gas chromatograph using a flame ionization detector and a 3% SP-2250 column. Yields were determined by GC (diphenyl ether as an internal standard), and in some cases by $^1$H-NMR spectroscopy. TLC analyses were performed on polyester sheets precoated with 0.25 mm thick silica gel containing a 254-nm indicator (Kodak 13181). Column chromatographic purifications were performed with 32-63 mesh ICN silica gel or activated basic Brockmann I 150 mesh aluminum oxide. A Perkin-Elmer DSC-7 differential scanning calorimeter, equipped with a TAC 7/DX thermal analysis controller was used to determine the thermal transitions which were reported as the maxima and minima of their endothermic and exothermic peaks respectively. In all cases, heating and cooling rates were 20°C/min. Glass transition temperatures ($T_g$) were read at the middle of the change in the heat capacity. Molecular weights were determined by gel permeation chromatography (GPC) with a Perkin-Elmer series 10 LC instrument equipped with an LC-100 column oven, LC-600 autosampler and Nelson analytical 900 series integrator data station. The measurements were made at 40°C using the UV detector set at 254 nm. A set of Perkin-Elmer PL gel columns of $10^4$ and 500Å with THF as solvent (1ml/min) and a
calibration plot constructed with polystyrene standards was used to determine the molecular weights. Therefore, all molecular weights reported in this dissertation are relative to polystyrene. High pressure liquid chromatography (HPLC) experiments were performed with the same instrument.
REFERENCES


PART I. ARYL MESYLATES IN NICKEL-CATALYZED HOMO-COUPLING REACTIONS
SYNTHESIS OF FUNCTIONAL SYMMETRICAL BIARYLS FROM PHENOLS
VIA NICKEL-CATALYZED HOMO-COUPLING OF THEIR MESYLATES

2.1.-INTRODUCTION

Symmetrical biaryls were traditionally obtained by the Ullmann reaction.\textsuperscript{1} and more recently by Ni(0) catalyzed homocoupling of aryl halides.\textsuperscript{2} The original method for the homocoupling of aryl halides based on stoichiometric amounts of preformed Ni(0) catalysts\textsuperscript{2a-c} was first extended to the use of stoichiometric amounts of Ni(0) reagents generated \textit{in situ}.\textsuperscript{2d} and then adapted to catalytic amounts of Ni(0) species.\textsuperscript{2e-g} A Pd catalyzed desulfonative homocoupling of arylsulfonylchlorides was recently reported.\textsuperscript{3} Unsymmetrical biaryls are synthesized by Pd(0) catalyzed cross-coupling of aryl halides with aryl stannanes,\textsuperscript{4} aryl boronic acids,\textsuperscript{5} aryl boronic esters,\textsuperscript{6} and arylzinc derivatives.\textsuperscript{7} This last reaction can be also carried out in the presence of Ni(0) catalysts.\textsuperscript{7} As compared with the classic Ullmann reaction, both the Pd(0) and Ni(0) catalyzed coupling reactions proceed under very mild conditions and tolerate a large variety of functional groups.

Recently, it has been shown that aryl triflates behave analogously to enol triflates in a series of Pd(0) catalyzed cross-coupling reactions.\textsuperscript{8} Subsequently, unsymmetrical biaryls were prepared by the Pd(0) catalyzed cross-coupling of aryl triflates with aryl stannanes\textsuperscript{9} and aryl boronic acids\textsuperscript{10a} or esters.\textsuperscript{10b} Additional procedures for the synthesis of unsymmetrical biaryls are based on the cross-coupling of aryl triflates with organo copper reagents,\textsuperscript{11} on the Pd catalyzed cross-coupling of aryl fluorosilanes with aryl iodides,\textsuperscript{12} and of aryl acid chlorides with disilanes.\textsuperscript{13} Aryl triflates were also cyanoated\textsuperscript{14a,b} and have been cross-coupled with organocopper\textsuperscript{11} and Grignard\textsuperscript{15} reagents by Ni(0) catalyzed reactions. Aryl triflates have undergone
catalytic reduction in the presence of Ni(0)\textsuperscript{16a} and Pd(0)\textsuperscript{16b} catalysts. The palladium catalyzed carbylation of aryl triflates was also reported.\textsuperscript{17}

The Ni(0) catalyzed homocoupling of aryl triflates\textsuperscript{18a}, aryl tosylates\textsuperscript{18b} and one example of an aryl mesylate\textsuperscript{18b} to symmetrical biaryls were first reported to proceed under ultrasonication. A low yield (21\%) was reported for the coupling reaction of the aryl mesylate.\textsuperscript{18b} Subsequently, we have shown that Ni(0) catalyzed homocoupling of bistriflates takes place in the absence of ultrasonication and this reaction yielded a convenient method for the synthesis of functional poly(\textit{p}-phenylene)s and polyarylenes.\textsuperscript{18c-e} Pd catalyzed electrosynthesis of biaryls from aryl triflates was also reported.\textsuperscript{18g} Recently a communication reported the Ni(0) and Pd(0) catalyzed homocoupling of aryl triflates,\textsuperscript{18f} and a patent reported the Ni(0) mediated homocoupling of aryl sulfonates including one example of an aryl mesylate.\textsuperscript{18h}

Therefore, alternative sulfonate leaving groups on aromatic substrates besides triflates were only briefly investigated in Ni(0) and Pd(0) mediated reactions.\textsuperscript{19} Aryl mesylates and tosylates have been generally considered to have a poor reactivity toward transition metal catalysts, and only a few experiments have indicated the contrary. For example, reports have been made of the Pd(0) catalyzed reduction of aryl mesylate,\textsuperscript{20} the NaBH\textsubscript{4}-NiCl\textsubscript{2} mediated reduction of aryl tosylate\textsuperscript{21} and the cobalt catalyzed methoxycarbonylation of aryl tosylate.\textsuperscript{22} Two publications have mentioned the Pd(0) catalyzed cross-coupling of aryl fluorosulfonates\textsuperscript{23a}, aryl \textit{p}-fluorophenylsulfonates\textsuperscript{23b} and a few other sulfonates with aryl stannanes\textsuperscript{23b} and two very brief experiments on the Ni(0) catalyzed homocoupling of 1-naphthyltosylate.\textsuperscript{18f}

The use of aryl sulfonates in Ni(0) and Pd(0) catalyzed reactions are of interest since they provide access to biaryls starting from phenols. Recently we became interested in the evaluation of less expensive leaving groups than triflates for the transformation of phenols into symmetrical and unsymmetrical biaryls via various Ni(0)
and Pd(0) catalyzed homo- and cross-coupling reactions. The goal of this chapter is to report our results which demonstrate that the most common aryl sulfonates including aryl mesylates undergo Ni(0) catalyzed homocoupling reactions under mild conditions resulting in high yields of symmetrical biaryls. An investigation of the scope of this reaction using varying reaction conditions was undertaken. The application of this synthetic method to the facile preparation of well known functional biaryls from readily available phenols will be demonstrated. Because substituted phenols, hydroquinones and bisphenols are readily available and inexpensive, the use of mesylate leaving group in Ni(0) catalyzed homocoupling reactions provides the most convenient access to already known and to new functionalized symmetrical biaryls.

2.2.-EXPERIMENTAL

2.2.1.-Materials

All reagents, including phenols, were purchased from commercial sources (Aldrich or Lancaster) and used without further purification except when reported. Pyridine was dried over CaH₂ and distilled. THF and dioxane were distilled from sodium-benzophenone ketyl. Zinc dust was stirred in acetic acid, washed with water and dried in vacuo at 120°C. NiCl₂(PPh₃)₂ was prepared according to a literature procedure.³²

2.2.2.-Techniques

Unless otherwise noted, all compounds synthesized in this chapter were purified until their 200 MHz ¹H-NMR spectra corresponded to the expected structure and the purity was established by comparison with published mp or found to be higher than 99.5% by GC or HPLC.
2.2.3. - Synthesis of Aryl Triflates and Aryl Arenesulfonates

Aryl triflates\textsuperscript{10a} were synthesized by the reaction of triflic anhydride with the corresponding phenol in pyridine, and aryl arenesulfonates were synthesized by the reaction of the arenesulfonyl chloride with the corresponding phenol in pyridine, unless otherwise noted.

\textbf{Methyl 4-\textit{(trifluoromethyl)sulfonyloxy}benzoate}. (85\%): purified by column chromatography, (SiO\textsubscript{2}, Hexanes/E\textsubscript{t}O\textsubscript{2} 1:1), and vacuum distilled. colorless oil: bp 71-73\textdegree C/ 0.3 mmHg (lit.\textsuperscript{33} 93-95\textdegree C/1.4 mmHg); \textsuperscript{1}H NMR \textit{\delta} 8.14 (d, \textit{J}= 7.4 Hz, 2H, \textit{o} to -CO\textsubscript{2}CH\textsubscript{3}), 7.39 (d, \textit{J}= 7.4 Hz, 2H, \textit{m} to -CO\textsubscript{2}CH\textsubscript{3}), 3.95 (s, 3H, -CO\textsubscript{2}CH\textsubscript{3}).

\textbf{Methyl 4-\textit{((4-fluorophenyl)sulfonyloxy}benzoate}. (90\%): white crystals; mp 80-82\textdegree C (hexanes); \textsuperscript{1}H NMR \textit{\delta} 7.99 (d, \textit{J}= 8.5 Hz, 2H, \textit{o} to -CO\textsubscript{2}CH\textsubscript{3}), 7.87 (dd, \textit{J}= 9.0, 5.0 Hz, 2H, \textit{m} to fluorine), 7.22 (dd, \textit{J}= 8.5, 8.3 Hz, 2H, \textit{o} to fluorine), 7.10 (d, \textit{J}= 8.5 Hz, 2H, \textit{m} to -CO\textsubscript{2}CH\textsubscript{3}), 3.91 (s, 3H, -CO\textsubscript{2}CH\textsubscript{3}); \textsuperscript{13}C\{\textsuperscript{1}H\} NMR \textit{\delta} 166.00 (d, \textit{J}\textsubscript{CF}=258 Hz, \textit{ipso} to fluorine), 165.66 (-CO\textsubscript{2}CH\textsubscript{3}), 152.56 (p to -CO\textsubscript{2}CH\textsubscript{3}), 131.28 (m to -CO\textsubscript{2}CH\textsubscript{3}), 131.27 (d, \textit{J}\textsubscript{CF}=9.6 Hz, \textit{m} to fluorine), 130.89 (d, \textit{J}\textsubscript{CF}=3Hz, \textit{p} to fluorine), 129.04 (\textit{ipso} to -CO\textsubscript{2}CH\textsubscript{3}), 122.12 (\textit{o} to -CO\textsubscript{2}CH\textsubscript{3}), 116.61 (d, \textit{J}\textsubscript{CF}=23 Hz, \textit{o} to fluorine), 52.22 (-CO\textsubscript{2}CH\textsubscript{3}); EIMS \textit{m/e} (\%) 310 (M\textsuperscript{+}, 32), 279 (6), 175 (6), 159 (100), 123 (15), 95 (89); HRMS calcd for C\textsubscript{14}H\textsubscript{11}FO\textsubscript{5}S 310.0311, found 310.0323.

\textbf{Methyl 4-\textit{((4-chlorophenyl)sulfonyloxy}benzoate}. (83\%): white crystals; mp 95-96\textdegree C (hexanes); \textsuperscript{1}H NMR \textit{\delta} 7.99 (d, \textit{J}= 8.5 Hz, 2H, \textit{o} to -CO\textsubscript{2}CH\textsubscript{3}), 7.75 (d, \textit{J}= 8.8 Hz, 2H, \textit{m} to chlorine), 7.54 (d, \textit{J}= 8.8 Hz, 2H, \textit{o} to chlorine), 7.11 (d, \textit{J}= 8.8 Hz, 2H, \textit{m} to -CO\textsubscript{2}CH\textsubscript{3}), 3.92 (s, 3H, -CO\textsubscript{2}CH\textsubscript{3}); \textsuperscript{13}C\{\textsuperscript{1}H\} NMR \textit{\delta} 165.67 (-CO\textsubscript{2}CH\textsubscript{3}), 152.54
Methyl 4-\{(phenylsulfonyl)oxy\}benzoate. (79\%): white crystals; mp 63-64°C (hexanes); \(^1\)H NMR \(\delta\) 7.96 (d, \(J= 8.5\) Hz, 2H, \(\text{m to oxygen}\)), 7.82 (d, \(J= 7.2\) Hz, 2H, \(\sigma\) to sulfur), 7.73-7.66 (m, 1H, \(p\) to sulfur), 7.58-7.50 (m, 2H, \(\text{m to sulfur}\)), 7.09 (d, \(J= 8.5\) Hz, 2H, \(\sigma\) to oxygen), 3.90 (s, 3H, -CO\(_2\)CH\(_3\)); \(^{13}\)C\{\(^1\)H\} NMR \(\delta\) 165.69 (-CO\(_2\)CH\(_3\)), 152.65 (p to -CO\(_2\)CH\(_3\)), 134.82 (ipso to -CO\(_2\)CH\(_3\)), 134.40 (p to -OSO\(_2\)), 131.16 (m to -CO\(_2\)CH\(_3\)), 129.16 (\(\sigma\) to -OSO\(_2\)), 128.86 (ipso to -OSO\(_2\)), 128.26 (\(\sigma\) to -CO\(_2\)CH\(_3\)), 122.14 (m to -OSO\(_2\)), 52.18 (-CO\(_2\)CH\(_3\)); EIMS \(m/e\) (\%) 292 (M\(^+\), 28), 141 (72), 123 (9), 77 (100); HRMS calcd for C\(_{14}\)H\(_{11}\)ClO\(_5\)S 326.0016, found 326.0017.

Methyl 4-\{((4-Methylphenyl)sulfonyl)oxy\}benzoate. (75\%): white crystals; mp 85-86°C (hexanes) (lit.\(^{34}\) 84-85°C); \(^1\)H NMR \(\delta\) 7.96 (d, \(J= 8.8\) Hz, 2H, \(\text{m to oxygen}\)), 7.69 (d, \(J= 8.3\) Hz, 2H, \(\sigma\) to sulfur), 7.34 (d, \(J= 8.1\) Hz, 2H, \(\text{m to sulfur}\)), 7.09 (d, \(J= 8.7\) Hz, 2H, \(\sigma\) to oxygen), 3.90 (s, 3H, -CO\(_2\)CH\(_3\)), 2.45 (s, 3H, -CH\(_3\)).

4-Acetylphenyl \(p\)-fluorobenzenesulfonate. (85\%): white crystals; mp 77-79°C (hexanes) (lit.\(^{35}\) 75-77°C); \(^1\)H NMR \(\delta\) 7.95-7.84 (m, 4H, \(\text{m to oxygen and \(\sigma\) to fluorine}\)), 7.28-7.20 (m, 2H, \(\text{m to fluorine}\)), 7.13 (d, \(J= 8.7\) Hz, 2H, \(\sigma\) to oxygen), 2.59 (s, 3H, -COCH\(_3\)).
Methyl 2-(((4-fluorophenyl)sulfonyl)oxy)benzoate, (85%): white crystals; mp 87-88°C (hexanes); $^1$H NMR δ 7.93-7.86 (m, 3H, aromatic protons), 7.54-7.12 (m, 5H, aromatic protons), 3.82 (s, 3H, -CO$_2$CH$_3$); $^{13}$C{ $^1$H} NMR δ 165.86 (d, $^1$J$_{CF}$=258 Hz, ipso to fluorine), 164.59 (-CO$_2$CH$_3$), 147.44 (ipso to oxygen), 133.29 (p to -CO$_2$CH$_3$ and m to -OSO$_2$-), 131.84 (o to -CO$_2$CH$_3$), 131.39 (m to fluorine), 131.21 (ipso to sulfur), 127.12 (m to -CO$_2$CH$_3$), 125.10 (ipso to -CO$_2$CH$_3$), 123.62 (m to -CO$_2$CH$_3$ and o to -OSO$_2$-), 116.32 (d, $^2$J$_{CF}$=23 Hz, o to fluorine), 52.15 (-CO$_2$CH$_3$); EIMS m/e (%) 310 (M$^+$, 57), 279 (19), 205 (14), 159 (80) 120 (100). 95 (91); HRMS calcd for C$_{14}$H$_{11}$FO$_5$S 310.0311, found 310.0311.

4-Biphenyl p-fluorobenzenesulfonate, (64%): white crystals; mp 117-118°C (hexanes): $^1$H NMR δ 7.89 (dd, J= 7.4, 5.1 Hz, 2H, m to fluorine), 7.54-7.36 (m, 7H, aromatic protons on biphenyl), 7.22 (dd, J= 7.4, 7.0 Hz, 2H, o to fluorine), 7.08 (d, J= 8.4 Hz, 2H, o to oxygen on biphenyl); $^{13}$C{ $^1$H} NMR δ 165.96 (d, $^1$J$_{CF}$=257 Hz. ipso to fluorine), 148.71 (ipso to oxygen), 140.35 (p to oxygen), 139.52 (ipso to -PhOSO$_2$Ph-p-F on biphenyl), 131.45 (ipso to sulfur), 131.26 (o to oxygen), 128.83 (m to oxygen), 128.27 (o to sulfur), 127.69 (p to -PhOSO$_2$Ph-p-F on biphenyl), 126.98 (o to -PhOSO$_2$Ph-p-F on biphenyl), 122.51 (m to -PhOSO$_2$Ph-p-F on biphenyl), 116.53 (d, $^2$J$_{CF}$=23 Hz, o to fluorine); EIMS m/e (%) 328 (M$^+$, 32), 170 (16), 141 (25), 120 (7), 95 (8); HRMS calcd for C$_{18}$H$_{13}$FO$_3$S 328.0569, found 328.0559.

Phenyl p-fluorobenzenesulfonate, (71%): colorless oil, purified by column chromatography (SiO$_2$, hexanes/ether 1:1) and vacuum distilled; bp 123-125°C/0.36 mmHg (lit.$^{36}$ 95-96°C/0.08 mmHg); $^1$H NMR δ 7.85 (dd, J= 7.1, 5.0 Hz, 2H, m to
fluorine), 7.31-7.16 (m, 5H, o to fluorine, and m and p to oxygen), 7.00 (d, J= 7.8 Hz, 2H, o to oxygen).

4-Toly1 p-fluorobenzenesulfonate, (88%): white crystals; mp 83-84°C (hexanes) (lit.\textsuperscript{37} 85-86°C): \(^1\)H NMR δ 7.36 (dd, J= 8.9, 5.0 Hz, 2H, m to fluorine), 7.20 (dd, J= 8.9, 8.6 Hz, 2H, o to fluorine), 7.07 (d, J= 8.3 Hz, 2H, m to oxygen), 6.87 (d, J= 8.8 Hz, 2H, o to oxygen), 2.31 (s, 3H, -CH\textsubscript{3}).

2-Toly1 p-fluorobenzenesulfonate, (80%): white crystals: mp 64-65°C (hexanes): \(^1\)H NMR δ 7.88 (dd, J= 7.1, 5.1 Hz, 2H, m to fluorine), 7.26-7.01 (m, 6H, aromatic protons), 2.09 (s, 3H, -CH\textsubscript{3}); \(^13\)C\{\(^1\)H\} NMR δ 165.90 (d, \(^1\)JC\textsubscript{F}=257 Hz, ipso to fluorine), 148.06 (ipso to oxygen), 132.02 (d, \(^4\)JC\textsubscript{F}=2.7 Hz, p to fluorine), 131.60 (ipso to methyl), 131.35 (o to oxygen and m to methyl), 131.13 (d, \(^3\)JC\textsubscript{F}=9.8 Hz, m to fluorine), 127.09 (p to methyl), 126.91 (m to oxygen and o to methyl), 122.07 (m to methyl and p to oxygen), 116.47 (d, \(^2\)JC\textsubscript{F}=23 Hz, o to fluorine), 16.12 (-CH\textsubscript{3}); EIMS m/e (%): 266 (M\textsuperscript{+}, 62), 159 (97), 107 (100), 95 (67), 77 (39); HRMS calcd for C\textsubscript{13}H\textsubscript{11}FO\textsubscript{3}S 266.0413, found 266.0410.

4-Methoxyphenyl p-fluorobenzenesulfonate, (94%): white crystals; mp 66-67°C (hexanes): \(^1\)H NMR δ 7.84 (dd, J= 8.9, 5.0 Hz, 2H, m to fluorine), 7.20 (dd, J= 8.9, 8.5 Hz, 2H, o to fluorine), 6.87 (d, J= 9.3 Hz, 2H, m to methoxy), 6.81 (d, J= 9.3 Hz, 2H, o to methoxy), 3.77 (s, 3H, -OCH\textsubscript{3}); \(^13\)C\{\(^1\)H\} NMR δ 165.82 (d, \(^1\)JC\textsubscript{F}=257 Hz, ipso to fluorine), 158.20 (ipso to methoxy), 142.67 (ipso to oxygen and p to methoxy), 131.28 (d, \(^3\)JC\textsubscript{F}=9.7 Hz, m to fluorine), 131.03 (d, \(^4\)JC\textsubscript{F}=3.0 Hz, p to fluorine), 123.12 (o to oxygen), 116.39 (d, \(^2\)JC\textsubscript{F}=23 Hz, o to fluorine), 114.43 (o to
methoxy), 55.39 (-OCH₃); EIMS m/e (%) 282 (M⁺, 18), 123 (100), 95 (14); HRMS calcd for C₁₃H₁₁FO₄S 282.0362, found 282.0361.

4-Tolyl benzenesulfonate, (90%): white crystals; mp 50-51°C (hexanes) (lit. 38 48-49°C); ¹H NMR δ 7.82 (d, J = 7.5 Hz, 2H, o to sulfur), 7.71-7.63 (m, 1H, p to sulfur), 7.56-7.48 (m, 2H, m to sulfur) 7.05 (d, J = 8.6 Hz, 2H, o to methyl), 6.87 (d, J = 8.5 Hz, 2H, o to oxygen), 2.30 (s, 3H, -CH₃).

4-Methoxyphenyl benzenesulfonate, (73%): colorless oil, purified by column chromatography (SiO₂, hexanes/Et₂O 1:1) and vacuum distilled; bp 152-154°C/0.03 mmHg; ¹H NMR δ 7.80 (d, J = 7.7 Hz, 2H, o to sulfur), 7.70-7.63 (m, 1H, p to sulfur), 7.55-7.48 (m, 2H, m to sulfur), 6.85 (d, J = 9.2 Hz, 2H, m to methoxy), 6.78 (d, J = 9.2 Hz, 2H, o to methoxy), 3.74 (s, 3H, -OCH₃); ¹³C ¹H NMR δ 158.01 (ips to methoxy), 142.65 (p to methoxy), 134.89 (ips to sulfur), 134.04 (p to sulfur), 128.92 (o to methoxy), 128.19 (m to methoxy), 123.01 (o to sulfur), 114.25 (m to sulfur), 55.23 (-OCH₃); EIMS m/e (%) 264 (M⁺, 72), 123 (100), 95 (35), 77 (22); HRMS calcd for C₁₃H₁₂O₄S 264.0456, found 264.0450.

2.2.4.-Synthesis of Aryl Mesylates

Aryl mesylates were prepared by the reaction of methanesulfonyl chloride with the corresponding phenols in pyridine. 39

Methyl 4-methylsulfonyloxybenzoate, (92%): white crystals; mp 89-90°C (hexanes); ¹H NMR δ 8.10 (d, J = 8.8 Hz, 2H, m to oxygen), 7.39 (d, J = 8.8 Hz, 2H, o to oxygen), 3.94 (s, 3H, -CO₂CH₃), 3.19 (s, 3H, -OSO₂CH₃); ¹³C ¹H NMR δ 165.67
Methyl 3-methylsulfonyloxybenzoate. (81%): white crystals; mp 70-72°C (hexanes): 
$^1$H NMR δ 8.04–7.94 (m, 2H, aromatic protons), δ 7.54–7.51 (m, 2H, aromatic protons), 3.94 (s, 3H, -CO$_2$CH$_3$), 3.20 (s, 3H, -OSO$_2$CH$_3$); $^{13}$C{ $^1$H} NMR δ 165.37 (-CO$_2$CH$_3$), 148.88 (ipso to oxygen), 132.06 (ipso to -CO$_2$CH$_3$), 129.95 (o to oxygen and -CO$_2$CH$_3$), 128.25 (o to oxygen and p to-CO$_2$CH$_3$), 126.51 (p to oxygen and o to-CO$_2$CH$_3$), 122.83 (m to oxygen and -CO$_2$CH$_3$), 52.29 (-CO$_2$CH$_3$), 37.38 (-OSO$_2$CH$_3$); EIMS m/e (%) 230 (M$^+$, 53), 152 (100), 121 (64), 92 (24); HRMS calcd for C$_9$H$_{10}$O$_5$S 230.0249, found 230.0255.

Methyl 2-methylsulfonyloxybenzoate. (81%): colorless oil, purified by column chromatography (SiO$_2$, hexanes/Et$_2$O 1:1) and vacuum distilled; bp 120-123°C/0.004 mmHg; $^1$H NMR δ 7.97 (d, $J$= 7.6 Hz, 1H, o to -CO$_2$CH$_3$), 7.63–7.56 (m, 1H, aromatic proton), 7.47-7.36 (m, 2H, aromatic protons), 3.93 (s, 3H, -CO$_2$CH$_3$), 3.28 (s, 3H, -OSO$_2$CH$_3$); $^{13}$C{ $^1$H} NMR δ 164.51 (-CO$_2$CH$_3$), 147.53 (ipso to oxygen), 133.61 (o to oxygen), 131.84 (p to oxygen), 126.99 (p to -CO$_2$CH$_3$), 124.24 (ipso to -CO$_2$CH$_3$), 123.83 (o to -CO$_2$CH$_3$ and m to oxygen), 52.23 (-CO$_2$CH$_3$), 38.11 (-OSO$_2$CH$_3$); EIMS m/e (%) 230 (M$^+$, 26), 199 (14), 152 (54), 120 (100), 92 (31), 64 (16); HRMS calcd for C$_9$H$_{10}$O$_5$S 230.0249, Found 230.0014.
4-Acetylphenyl methanesulfonate. (83%): yellow crystals; mp 71-72°C (hexanes) (lit. 70-71°C); $^1$H NMR δ 8.02 (d, $J= 8.7$ Hz, 2H, $m$ to oxygen), 7.41 (d, $J= 8.7$ Hz, 2H, $o$ to oxygen), 3.20 (s, 3H, -OSO$_2$CH$_3$), 2.62 (s, 3H, CH$_3$(=O)-).  

4-Cyanophenyl methanesulfonate. (82%): white crystals; mp 89-90°C (hexanes); $^1$H NMR δ 7.73 (d, $J= 8.8$ Hz, 2H, $o$ to -CN), 7.45 (d, $J= 8.8$ Hz, 2H, $o$ to oxygen), 3.24 (s, 3H, -OSO$_2$CH$_3$); $^{13}$C($^1$H) NMR δ 151.77 (ipso to oxygen), 134.10 (m to oxygen), 122.90 (o to oxygen), 117.54 (-CN), 111.19 ($p$ to oxygen), 37.97 (-OSO$_2$CH$_3$); EIMS m/e (%) 197 (M+, 56), 133 (9), 120 (16), 90 (46), 79 (100), 64 (22); HRMS calcd for C$_8$H$_7$NO$_3$S 197.0147, found 197.0145.  

4-Fluorophenyl methanesulfonate. (58%): colorless oil, purified by column chromatography (SiO$_2$, hexanes/Et$_2$O 1:1) and vacuum distilled; $^1$H NMR δ 7.28 (dd, $J=9.3$, 3.9 Hz, 2H, $o$ to oxygen), 7.12 (dd, $J=9.3$, 8.6 Hz, 2H, $o$ to fluorine), 3.16 (s, 3H, -OSO$_2$CH$_3$); $^{13}$C($^1$H) NMR δ 160.97 (d, $J_{CF}=247$ Hz, ipso to fluorine), 144.80 (ipso to oxygen), 123.61 (d, $J_{CF}=8$ Hz, $o$ to oxygen), 116.55 (d, $J_{CF}=24$ Hz, $o$ to fluorine), 37.00 (-OSO$_2$CH$_3$); EIMS m/e (%) 190 (M+, 47), 119 (21), 112 (100), 83 (71), 57 (25); HRMS calcd for C$_7$H$_7$FO$_3$S 190.0100, found 190.0171.  

4-Nitrophenyl methanesulfonate. (91%): pale brown needles; mp 93-94°C (lit. 93-93.5°C); $^1$H NMR δ 8.33 (d, $J=9.1$ Hz, 2H, $m$ to oxygen), 7.48 (d, $J=9.1$ Hz, 2H, $o$ to oxygen), 3.26 (s, 3H, -OSO$_2$CH$_3$).  

Phenyl methanesulfonate. (91%): white crystals; mp 62-63°C (hexanes) (lit. 61.5°C); $^1$H NMR δ 7.44-7.28 (m, 5H, aromatic protons), 3.14 (s, 3H, -OSO$_2$CH$_3$).
4-Biphenyl methanesulfonate. (92%): white crystals; mp 146-148°C (Et₂O); ¹H NMR δ 7.64–7.41 (m, 7H, aromatic protons), 7.38 (d, J=8.0 Hz, 2H, o to oxygen), 3.18 (s, 3H, -OSO₂CH₃); ¹³C{¹H} NMR δ 148.51 (ipso to oxygen), 140.57 (p to oxygen), 139.66 (ipso to PhO₅SO₂CH₃), 128.86 (o to oxygen), 128.63 (p to PhO₅SO₂CH₃), 127.71 (m to oxygen), 127.07 (o to PhO₅SO₂CH₃), 122.24 (m to PhO₅SO₂CH₃), 37.32 (-OSO₂CH₃); EIMS m/e (%) 248 (M⁺, 80), 170 (55), 141 (100), 115 (28); HRMS calcd for C₁₃H₁₂O₃S 248.0507, found 248.0508.

4-Toly methanesulfonate. (75%): white crystals; mp 46-48°C (hexanes) (lit 43 44.5-46°C); ¹H NMR δ 7.20 (d, J=9.2 Hz, 2H, o to methyl), 7.19 (d, J=9.0 Hz, 2H, o to oxygen), 3.12 (s, 3H, -OSO₂CH₃), 2.36 (s, 3H, -CH₃).

4-Methoxyphenyl methanesulfonate. (77%): white crystals; mp 78-80°C (hexanes) (lit 42 77-79°C); ¹H NMR δ 7.19 (d, J=7.1 Hz, 2H, m to methoxy), 6.93 (d, J=7.1 Hz, 2H, o to methoxy), 3.81 (s, 3H, -OCH₃), 3.11 (s, 3H, -OSO₂CH₃).

Pentafluorophenyl methanesulfonate. (96%): colorless oil; ¹H NMR δ 3.10 (s, 3H, -OSO₂CH₃); ¹³C{¹H} NMR δ 142.18 (d, ¹JC⁻F=254 Hz, o to oxygen), 140.36 (d, ¹JC⁻F=257 Hz, p to oxygen), 137.93 (d, ¹JC⁻F=257 Hz, m to oxygen), 123.94 (ipso to oxygen), 39.18 (-OSO₂CH₃); EIMS m/e (%) 262 (M⁺, 74), 198 (27), 184 (82), 155 (53), 79 (100); HRMS calcd for C₇H₃F₅O₃S 261.9723, found 261.9632.

6-Carbomethoxy-2-naphthyl methanesulfonate. (84%): white crystals (benzene); mp 114°C (hexanes); ¹H NMR δ 8.58 (s, 1H, C₇⁻H), 8.06 (d, J=9.0 Hz, 1H, C₅⁻H), 7.95 (d, J=10 Hz, 1H, C₉⁻H), 7.87 (d, J=9.0Hz, 1H, C₄⁻H), 7.76 (s, 1H, C₂⁻H),
7.46 (d, J=10 Hz, 1H, C10–H), 3.98 (s, 3H, -CO2CH3), 3.22 (s, 3H, -OSO2CH3):
13C{1H} NMR δ 166.73 (-CO2CH3), 148.34 (C1), 135.76 (C6), 131.71 (C2), 131.02
(C3), 130.73 (C9), 128.10 (C10), 126.46 (C8), 121.64 (C7), 119.29 (C4), 52.34 (-
CO2CH3), 37.65 (-OSO2CH3); m/e (%) 280 (M+, 70), 201 (74), 173 (100), 142 (49),
114 (72); HRMS calcd for C13H12O5S 280.0405, found 280.0416.

2.2.5.-General Procedure for Homocoupling of Aryl Sulfonates

All reactions were carried out under nitrogen using oven-dried (110°C)
glassware. In a typical reaction a 125 mL Schlenk tube was charged with
NiCl2(PPh3)2 (0.10 mmol), Zn powder (1.7 mmol), Et4NI (1.5 mmol) and a magnetic
stirring bar. After sealing the tube with a rubber septum, the contents were dried at
22°C under reduced pressure (1 x 10⁻³ mmHg) for 10 hr. The contents of the tube
were then placed under an Ar atmosphere by filling with Ar followed by three
evacuation-filling cycles. Freshly distilled THF (0.50 ml) was added via a syringe
through the rubber septum. The mixture was stirred at room temperature for 5 min and
during this time the color of the mixture gradually changed deep red brown. Aryl
sulfonate (1.0 mmol) was dissolved in freshly distilled THF (0.50 ml) and added to the
catalyst mixture via a syringe through the rubber septum. The reaction mixture was
heated to the reflux temperature and stirred at this temperature for 5-10h. The reaction
mixture was then cooled, filtered, diluted with water, extracted with CHCl3, dried
(MgSO4) and the solvent evaporated in vacuo. The corresponding biaryl was obtained
after column chromatography (silica gel, n-hexane/ethyl acetate) and recrystallization
from CHCl3/hexanes.
4,4'-Di(carbomethoxy)biphenyl: white crystals; mp 214-216°C (benzene) (lit.44 215-217°C): $^1$H NMR δ 8.12 (d, J=8.4 Hz, 4H, o to -CO$_2$CH$_3$), 7.72 (d, J=8.4 Hz, 4H, m to -CO$_2$CH$_3$), 3.96 (s, 6H, -CO$_2$CH$_3$).

4,4'-Diacetyl biphenyl: pale yellow crystals; mp 190-193°C (benzene) (lit.45 191°C): $^1$H NMR δ 8.06 (d, J=8.3 Hz, 4H, o to acetyl), 7.76 (d, J=8.3 Hz, 4H, m to acetyl). 2.66 (s, 6H, -COCH$_3$).

2,2'-Di(carbomethoxy)biphenyl: white crystals: mp 69-71°C (hexanes) (lit.46 73-74°C); $^1$H NMR δ 8.00 (d, J=6.7 Hz, 2H, o to -CO$_2$CH$_3$), 7.55 (dd, J=7.5, 5.9 Hz, 2H, p to -CO$_2$CH$_3$), 7.43 (dd, J=7.5, 7.4 Hz, 2H, m to -CO$_2$CH$_3$), 7.24 (d, J=7.6 Hz, 2H, m to -CO$_2$CH$_3$ and o to phenyl), 3.62 (s, 6H, -CO$_2$CH$_3$).

p-Quaterphenyl: white crystals: mp 319°C (CHCl$_3$) (by DSC, lit.47 320°C).

Biphenyl: white solid; mp 70-71°C (hexanes) (lit.48 71°C); $^1$H NMR δ 7.58 (d, J=7.0 Hz, 4H, o to phenyl), 7.48-7.31 (m, 6H, aromatic protons).

4,4'-Dimethylbiphenyl: white crystals; mp 120-122°C (hexanes) (lit.49 121°C); $^1$H NMR δ 7.46 (d, J=8.0 Hz, 4H, m to methyl), 7.26 (d, J=8.0 Hz, 4H, o to methyl), 2.39 (s, 6H, -CH$_3$).

2,2'-Dimethylbiphenyl: colorless oil purified by column chromatography (SiO$_2$ hexanes) vacuum distilled: bp 80-83°C/0.8 mmHg (lit.50 69°C/0.5 mmHg); $^1$H NMR δ 7.38-7.05 (m, 8H, aromatic protons), 2.05 (s, 6H, -CH$_3$).
4,4'-Dimethoxybiphenyl: white crystals; mp 174-176°C (hexanes) (lit. 176.5-177°C): ¹H NMR δ 7.46 (d, J=8.8 Hz, 4H, m to methoxy), 6.99 (d, J=8.8 Hz, 4H, o to methoxy), 3.85 (s, 6H, -OCH₃).

3,3'-Di(carbomethoxy)biphenyl: white crystals; mp 100-102°C (hexanes) (lit. 103°C): ¹H NMR δ 8.32 (s, 2H, o to -CO₂CH₃ and phenyl), 8.04 (d, J=7.8 Hz, 2H, o to -CO₂CH₃ and p to phenyl), 7.81 (d, J=7.8 Hz, 2H, m to -CO₂CH₃), 7.74-7.64 (m, 2H, p to -CO₂CH₃), 3.96 (s, 6H, -CO₂CH₃).

4,4'-Dicyanobiphenyl: white crystals; mp 229-230°C (benzene) (lit. 232-234°C); ¹H NMR δ 7.78 (d, J=8.6 Hz, 4H, o to -CN), 7.72 (d, J=8.5 Hz, 4H, m to -CN).

4,4'-Difluorobiphenyl: white crystals; mp 88-89°C (hexanes) (lit. 87-89°C): ¹H NMR δ 7.49 (dd, J=8.8, 5.2 Hz, 4H, m to fluorine), 7.12 (dd, J=8.8, 8.7 Hz, 4H, o to fluorine).

6,6'-Bis(carbomethoxy)-2,2'-dinapthyl: white crystals; mp 275°C (CHCl₃); ¹H NMR δ: 8.65 (s, 2H, C₇-H), 8.23 (s, 2H, C₁-H), 8.17-8.09 (m, 4H, aromatic protons), 8.02-7.94 (m, 4H, aromatic protons), 4.03 (s, 6H, -CO₂CH₃); Anal. Calcd. for C₂₄H₁₈O₄: C, 77.82; H, 4.90. Found: C, 77.16; H, 4.81.

2.3.-RESULTS AND DISCUSSION
2.3.1.-Effects of Substituents and Leaving Groups on the Synthesis of 2,2'-, 3,3'- and 4,4'-Disubstituted Biphenyls and Biaryls
The homocoupling reactions of aryl sulfonates were mediated by a nickel catalyst generated from NiCl₂(PPh₃)₂ (0.10 equiv) in the presence of excess Zn (1.7 equiv) and Et₄NI (1.5 equiv) in THF (eq 1).

![Chemical reaction diagram]

\[ \text{CH}_3\text{O-C-C-OSO}_2\text{R} \xrightarrow{\text{NiCl}_2(\text{PPh}_3)_2, \text{Zn, Et}_4\text{NI}} \text{THF, 67°C, 10 h} \]

\[ \text{R=CH}_3, \text{C}_6\text{H}_5, \text{p-CH}_3\text{C}_6\text{H}_4, \text{p-FC}_6\text{H}_4 \]

\[ \text{CH}_3\text{O-C-} = \text{O-CH}_3 \]

>97%

(1)

This method of generating the Ni(0) catalyst in situ was first developed for the homocoupling of aryl halides in THF (vide infra). The reaction is regiospecific with no isomerization detected.

A series of the nickel-catalyzed homocoupling reactions was performed with various p-carboxymethoxyphenyl sulfonates, in order to evaluate the effectiveness of sulfonate leaving groups which could be used in place of triflate (Table I). The use of three sulfonate leaving groups, p-toluene sulfonate, p-fluorobenzene sulfonate and methane sulfonate, resulted in high yields (>99%) equal to those obtained with the triflate (entries 1, 2, 5, & 6 in Table I). The reactivity of the p-fluorobenzene sulfonate leaving group was similar to that of the triflate, as the reaction times were identical. The reaction time was doubled (10 h) when using the p-toluene sulfonate or methane sulfonate leaving groups. A slightly reduced yield (97%) was obtained after 5 h for the benzene sulfonate leaving group. A decreased yield (79% isolated) was obtained with the 4-chlorobenzene sulfonate leaving group. In this case the reduced yield was at least
Table I. Ni(0)-Catalyzed Homocoupling of Various $p$-Carbomethoxyphenyl Sulfonates$^a$

\[
\begin{array}{ccc}
\text{CH}_3\text{O} & \text{C} & \text{O} \\
\text{X} & \rightarrow & \text{NiCl}_2(\text{PPh}_3)_2, \text{Zn, Et}_4\text{Ni} \\
& & \text{THF, 67°C} \\
\text{CH}_3\text{O} & \text{C} & \text{O} \text{CH}_3
\end{array}
\]

<table>
<thead>
<tr>
<th>Entry</th>
<th>Leaving group</th>
<th>Reaction time (h)</th>
<th>GC yield$^b$(%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>CF$_3$SO$_2$O</td>
<td>5</td>
<td>&gt;99</td>
</tr>
<tr>
<td>2</td>
<td>$p$-FPhSO$_2$O</td>
<td>5</td>
<td>&gt;99(85)</td>
</tr>
<tr>
<td>3</td>
<td>$p$-ClPhSO$_2$O</td>
<td>10</td>
<td>(79)$^c$</td>
</tr>
<tr>
<td>4</td>
<td>PhSO$_2$O</td>
<td>5</td>
<td>97(83)</td>
</tr>
<tr>
<td>5</td>
<td>$p$-CH$_3$PhSO$_2$O</td>
<td>10</td>
<td>&gt;99</td>
</tr>
<tr>
<td>6</td>
<td>CH$_3$SO$_2$O</td>
<td>10</td>
<td>&gt;99</td>
</tr>
</tbody>
</table>

$^a$Reactions Conditions: 10 mol% NiCl$_2$(PPh$_3$)$_2$, 1.7 equiv Zn, 1.5 equiv Et$_4$NI. refluxing THF, N$_2$. $^b$Isolated yields in parenthesis. $^c$Chlorine of 4-chlorobenzenesulfonate moiety was also homo- and cross-coupled to give complicated byproducts.
partly due to the participation of the chloro group as a leaving group in the coupling reaction.

The effect of various substituents on the coupling reaction, when using benzene sulfonate or $p$-fluorobenzene sulfonate leaving groups was studied (Table II). High yields were obtained when benzene sulfonate was the leaving group (Table II, entries 1-4). The $p$-carbomethoxy substituted aryl benzene sulfonate was substantially more reactive than both the $p$-methyl and $p$-methoxy substituted aryl benzene sulfonates. A doubling of the reaction time was necessary in the latter two cases. The $p$-fluorobenzene sulfonate leaving group gave higher yields than the benzene sulfonate group when identical reaction times were used (Table II, entries 1 & 6 and entries 2 & 10). The ortho substituted substrates reacted more sluggishly than the para substituted substrates. This is reflected in the reduced yield obtained for o-methyl (Table II, entries 10 & 11) and the longer reaction time required for o-carbomethoxy (Table II, entries 6 & 7). Slightly lower reactivity was obtained when the aryl group had electron donating substituents (Table II, entries 9 & 12). This effect was less pronounced with better leaving groups (Table II, entries 2 & 10).

In regard to cost, the most important leaving group investigated was the mesylate group. Good to high coupling yields of a number of aryl mesylates were obtained (Table III). The reaction tolerates a wide range of functional groups: alkyl, ester, ether, fluoro, ketone, nitrile, and phenyl. No coupled product was detected when the nitro group was present, perhaps due to the generation of nitrosonickel (0) complexes$^{24}$ or the reduction of the aryl nitro group.

A general trend was apparent in regard to the electronic properties of the aryl substituents. Increased yields, relative to phenyl methane sulfonate, were obtained when the para substituents were electron-withdrawing groups (Table III, entries 1-6). The exception being the nitro group (Table III, entry 8) which could not tolerate the
Table II. Effect of Various Substituents on the Ni(0)-Catalyzed Homocoupling of Aryl Sulfonates\textsuperscript{a}

\[
\begin{array}{cccc}
\text{Entry} & \text{R} & \text{R'} & \text{Reaction time (h)} & \text{GC yield}\textsuperscript{b} (\%) \\
1 & p-\text{CO}_2\text{CH}_3 & \text{Ph} & 5 & 97 (83) \\
2 & p-\text{CH}_3 & \text{Ph} & 5 & 67 (48) \\
3 & p-\text{CH}_3 & \text{Ph} & 10 & 90 \\
4 & p-\text{OCH}_3 & \text{Ph} & 10 & 94 \\
5 & p-\text{COCH}_3 & p-\text{FPh} & 5 & 98\textsuperscript{c} \\
6 & p-\text{CO}_2\text{CH}_3 & p-\text{FPh} & 5 & >99 (85) \\
7 & o-\text{CO}_2\text{CH}_3 & p-\text{FPh} & 24 & >99 \\
8 & p-\text{Ph} & p-\text{FPh} & 5 & >99\textsuperscript{d} \\
9 & \text{H} & p-\text{FPh} & 5 & >99 \\
10 & p-\text{CH}_3 & p-\text{FPh} & 5 & 93 (80) \\
11 & o-\text{CH}_3 & p-\text{FPh} & 5 & 72 \\
12 & p-\text{OCH}_3 & p-\text{FPh} & 5 & 85 (71) \\
\end{array}
\]

\textsuperscript{a} Reaction conditions are identical to those in Table I. \textsuperscript{b} Isolated yields in parenthesis: Trace amounts of transarylation byproducts were found in most experiments. \textsuperscript{c} 2\% of 4-acetylbiphenyl was detected. \textsuperscript{d} Actual yield based on the disappearance of the substrate. The product was insoluble.
Table III. Effect of Various Substituents on the Ni(0)-Catalyzed Homocoupling of Aryl Methanesulfonates$^a$

<table>
<thead>
<tr>
<th>Entry</th>
<th>Ar</th>
<th>Reaction time (h)</th>
<th>GC yield$^b$(%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>$p$-C$_6$H$_4$CO$_2$CH$_3$</td>
<td>10</td>
<td>&gt;99</td>
</tr>
<tr>
<td>2</td>
<td>$m$-C$_6$H$_4$CO$_2$CH$_3$</td>
<td>10</td>
<td>93</td>
</tr>
<tr>
<td>3</td>
<td>$o$-C$_6$H$_4$CO$_2$CH$_3$</td>
<td>10</td>
<td>83</td>
</tr>
<tr>
<td>4</td>
<td>$o$-C$_6$H$_4$CO$_2$CH$_3$</td>
<td>24</td>
<td>&gt;99$^c$</td>
</tr>
<tr>
<td>5</td>
<td>$p$-C$_6$H$_4$COCH$_3$</td>
<td>10</td>
<td>73$^d$</td>
</tr>
<tr>
<td>6</td>
<td>$p$-C$_6$H$_4$CN</td>
<td>10</td>
<td>94$^e$</td>
</tr>
<tr>
<td>7</td>
<td>$p$-C$_6$H$_4$F</td>
<td>10</td>
<td>(54)</td>
</tr>
<tr>
<td>8</td>
<td>$p$-C$_6$F$_4$NO$_2$</td>
<td>10</td>
<td>0</td>
</tr>
<tr>
<td>9</td>
<td>Ph</td>
<td>10</td>
<td>91</td>
</tr>
<tr>
<td>10</td>
<td>$p$-C$_6$H$_4$Ph</td>
<td>10</td>
<td>(60)</td>
</tr>
<tr>
<td>11</td>
<td>$p$-C$_6$H$_4$CH$_3$</td>
<td>10</td>
<td>84</td>
</tr>
<tr>
<td>12</td>
<td>$p$-C$_6$H$_4$OCH$_3$</td>
<td>10</td>
<td>83</td>
</tr>
<tr>
<td>13</td>
<td>$p$-C$_6$H$_4$OCH$_3$</td>
<td>24</td>
<td>70$^c$</td>
</tr>
<tr>
<td>14</td>
<td>C$_6$F$_5$</td>
<td>10</td>
<td>0$^f$</td>
</tr>
<tr>
<td>15</td>
<td>![Aryl group]</td>
<td>10</td>
<td>(91)</td>
</tr>
</tbody>
</table>

$^a$ Reaction conditions are identical to those in Table 1. $^b$ Isolated yields in parentheses; Trace amounts of transarylation byproducts were found in most experiments. $^c$ Reaction run with additional 2 equiv of PPh$_3$ relative to NiCl$_2$(PPh$_3$)$_2$. $^d$ Also produced acetophenone (20%) and 4-acetyl biphenyl (7%). $^e$ 6% of 4-cyanobiphenyl was detected. $^f$ The remaining material isolated was a mixture of starting substrate and C$_6$F$_3$OH.
reaction conditions. Yields were reduced when the para substituent was an electron-donating group (Table III, entries 10-13). A reduced yield was obtained when the substituent was a fluoro group (Table III, entry 7). While this group is electron-withdrawing via inductive effects, it is electron-donating by resonance effects. Pentafluorophenyl methane sulfonate did not participate in the reaction to give coupled product (Table III, entry 14), instead, induced only a O-S bond cleavage. The general trend in reference to the electronic properties of the aryl substituents is that electron-withdrawing groups activate the aryl mesylate and electron-donating groups deactivate the aryl mesylate toward the Ni(0) promoted coupling reaction.

The position of the substituent also affects the reaction yield. The highest yield was obtained when a para carbomethoxy substituent was present. The order of reactivity for this group was para > meta > ortho (Table III, entries 1-3). When in the para position it can have an electron-withdrawing effect by resonance thus facilitating the oxidative addition step.\(^{25}\) When the group is in the ortho position steric effects apparently predominate over the electronic effects of the group. However, the yield was increased by lengthening the reaction time in the presence of extra PPh\(_3\) (Table III, entry 4). It is well known that Ni(0) catalyzed aryl-aryl coupling reactions are impeded by substituents in the ortho position.\(^{26}\)

The major side reactions in Ni(0) and Pd(0) catalyzed reactions involving aryl halides and aryl triflates are: reduction,\(^{2a-c,f}\) transarylation,\(^{2d,f}\) and phosphonium salt formation.\(^{27}\) Side reactions were more evident in cases involving the less reactive aryl sulfonates (Table II, entry 5 vs. Table III, entry 5). Trace amounts of transarylation byproducts were detected in most experiments. These products were formed by the coupling of the aryl mesylate with a phenyl group from PPh\(_3\). Phenyl group transfer from PPh\(_3\) is a common side reaction in Pd and Ni catalyzed reactions in the presence of PPh\(_3\).\(^{2f}\) The phenyl group transfer from PPh\(_3\) was further indicated by the detection
of trace amounts of biphenyl when the reaction was performed under identical reaction conditions except for the absence of aryl mesylate substrate. The other side reaction identified was the reduction of the aryl sulfonate. In other coupling reactions two general pathways for aryl reduction have been identified: (a) a reductive elimination process, involving a nickel-hydride species, prior to completion of the reaction steps which lead to the coupled product (vide infra) and (b) hydrogenolysis via the formation of an aryl radical.\textsuperscript{28} Aryl radicals readily abstract hydrogen from THF, enolizable ketones when available or adventitious protic sources such as water.\textsuperscript{2f} For example, in addition to the formation of 73% homocoupled product, the reaction of 4-acetylphenyl methanesulfonate resulted in 20% reduction to acetophenone, and 7% transarylation yielding 4-acetylbiphenyl (eq 2). Shorter reaction times decreased these side reactions, but also reduced the yield of the homocoupled product. This fairly large amount of reduction product might be rationalized by the lower reduction potential of the aryl mesylate due to the strong electron-withdrawing group. However, for more reactive aryl sulfonates, (i.e., aryl p-fluorobenzenesulfonates) the reduction product was negligible (Table II, entry 5).

\[
\begin{align*}
\text{CH}_3\text{C} & \text{O} \quad \text{NiCl}_2\text{(PPh}_3)_2 \quad \text{Zn, Et}_4\text{Ni} \\
\text{O} \quad \text{THF, 67°C, 10h} \\
\text{CH}_3\text{C} & \text{O} \quad \text{CH}_3 \\
\text{O} & \text{O} \quad \text{CH}_3 \quad \text{73%} \\
\text{O} & \text{O} \quad \text{20%} \\
\text{O} & \text{O} \quad \text{7%} \\
\end{align*}
\]

(eq 2)

2.3.2.- Solvent Effect
The generation of Ni(0) catalyst in situ from the reduction of NiCl₂(PPh₃)₂ with Zn, was used for the homocoupling of aryl halides in both dipolar aprotic solvents such as DMF or DMAc and in less polar solvents such as THF. However, THF was the best solvent in reference to the rate and selectivity of the homocoupling under our reaction conditions which employed coordinatively unsaturated Ni catalyst (i.e., NiCl₂(PPh₃)₂, Zn, and Et₄NI) (Table IV, entry 1). Typical dipolar aprotic solvents for Ni(0) homocoupling such as DMAc, which can increase the nucleophilicity of Ni(0) and also act as a donor ligand gave lower yields under the same reaction conditions (Table IV, entry 1 vs. 2). When DMAc was utilized, a significant amount of most probably colloidal nickel-black deposition occurred within minutes of initiation. Also, a significant amount of reduction side-product (20%) was detected. Early catalyst decomposition in DMAc was avoided by increasing the amount of PPh₃. However, this retarded the reaction as relatively low yields and recovered starting material were obtained (Table IV, entries 3 & 4). An attempt to circumvent the reduced reactivity, in the presence of excess PPh₃, by increasing the reaction temperature (100°C) resulted in lower yields (Table IV, entry 4 vs. 5). When using THF, no additional PPh₃ was required in the presence of halide source such as Et₄NI (Table IV, entry 1). Therefore, the in situ generated Ni(0)(PPh₃)₂ complexes were less stable in more polar and strongly dissociating solvents such as DMAc.

2.3.3.-Halide Ion Effect

It is known that halide ions, especially iodide, enhance the reaction rate of nickel catalyzed homocoupling reactions, although the exact role of halide is somewhat unclear. One role of halide is to function as a bridging ion between nickel and zinc in the electron transfer process. Under our typical reaction conditions which employ THF as solvent in the absence of additional PPh₃, the coupling reaction proceeded very
Table IV. Effect of Various Reaction Conditions on the Ni(0)-Catalyzed Homocoupling of Methyl 4-methylsulfonyloxy benzoate$^d$

![Chemical Structure](image_url)

<table>
<thead>
<tr>
<th>Entry</th>
<th>NiCl$_2$(PPh$_3$)$_2$ (mol %)</th>
<th>PPh$_3$ (mol %)</th>
<th>Halide</th>
<th>Solvent</th>
<th>Ar-H</th>
<th>Ar-OMs</th>
<th>Ar-Ph</th>
<th>Ar-Ar</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>10</td>
<td>-</td>
<td>Et$_4$NI / 1.5</td>
<td>THF</td>
<td>-</td>
<td>-</td>
<td>traces</td>
<td>&gt;99</td>
</tr>
<tr>
<td>2</td>
<td>10</td>
<td>-</td>
<td>Et$_4$NI / 1.5</td>
<td>DMAc</td>
<td>20</td>
<td>0</td>
<td>2</td>
<td>72$^b$</td>
</tr>
<tr>
<td>3</td>
<td>10</td>
<td>30</td>
<td>Et$_4$NI / 1.5</td>
<td>DMAc</td>
<td>22</td>
<td>2</td>
<td>1</td>
<td>73</td>
</tr>
<tr>
<td>4</td>
<td>10</td>
<td>60</td>
<td>Et$_4$NI / 1.5</td>
<td>DMAc</td>
<td>19</td>
<td>11</td>
<td>-</td>
<td>60</td>
</tr>
<tr>
<td>5</td>
<td>10</td>
<td>60</td>
<td>Et$_4$NI / 1.5</td>
<td>DMAc</td>
<td>15</td>
<td>-</td>
<td>6</td>
<td>47</td>
</tr>
<tr>
<td>6</td>
<td>10</td>
<td>-</td>
<td>Et$_4$NI / 0.8</td>
<td>THF</td>
<td>6</td>
<td>3</td>
<td>3</td>
<td>87</td>
</tr>
<tr>
<td>7</td>
<td>10</td>
<td>-</td>
<td>-</td>
<td>THF</td>
<td>-</td>
<td>29</td>
<td>2</td>
<td>64$^b$</td>
</tr>
<tr>
<td>8</td>
<td>5</td>
<td>-</td>
<td>Et$_4$NI / 1.5</td>
<td>THF</td>
<td>3</td>
<td>24</td>
<td>1</td>
<td>69$^b$</td>
</tr>
<tr>
<td>9</td>
<td>3</td>
<td>-</td>
<td>Et$_4$NI / 1.5</td>
<td>THF</td>
<td>3</td>
<td>43</td>
<td>traces</td>
<td>53$^b$</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>---</td>
<td>---</td>
<td>---</td>
<td>---</td>
<td>---</td>
<td>---</td>
<td>---</td>
<td></td>
<td></td>
</tr>
<tr>
<td>27</td>
<td>10</td>
<td>-</td>
<td>-</td>
<td>pyridine</td>
<td>14</td>
<td>25</td>
<td>traces</td>
<td>55</td>
</tr>
<tr>
<td>28</td>
<td>10</td>
<td>-</td>
<td>-</td>
<td>THT&lt;sup&gt;h&lt;/sup&gt;</td>
<td>-</td>
<td>100</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>29&lt;sup&gt;i&lt;/sup&gt;</td>
<td>10</td>
<td>-</td>
<td>-</td>
<td>pyridine</td>
<td>14</td>
<td>66</td>
<td>-</td>
<td>12</td>
</tr>
<tr>
<td>30&lt;sup&gt;i&lt;/sup&gt;</td>
<td>10</td>
<td>-</td>
<td>-</td>
<td>THT&lt;sup&gt;h&lt;/sup&gt;</td>
<td>-</td>
<td>100</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>31&lt;sup&gt;i,j&lt;/sup&gt;</td>
<td>10</td>
<td>-</td>
<td>-</td>
<td>THF&lt;sup&gt;d&lt;/sup&gt;</td>
<td>-</td>
<td>100</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>32&lt;sup&gt;k&lt;/sup&gt;</td>
<td>5.3</td>
<td>20</td>
<td>NaBr / 1.0</td>
<td>DMAc</td>
<td>5</td>
<td>-</td>
<td>2</td>
<td>78</td>
</tr>
<tr>
<td>33&lt;sup&gt;k&lt;/sup&gt;</td>
<td>5.3</td>
<td>20</td>
<td>KBr / 1.0</td>
<td>DMAc</td>
<td>4</td>
<td>-</td>
<td>2</td>
<td>79</td>
</tr>
</tbody>
</table>

<sup>a</sup> Reaction conditions: 1.7 equiv Zn, reaction temperature 67°C (except reaction temperature in DMAc was 100°C), and reaction time 10 h unless otherwise noted.  <sup>b</sup> Catalyst decomposed in the early stage of the reaction.  <sup>c</sup> 20 Mol % 18-crown-6 (based on substrate) was added to the reaction mixture.  <sup>d</sup> Wet THF.  <sup>e</sup> 5 Mol % H₂O (based on substrate) was added.  <sup>f</sup> 20 Mol % pyridine (based on substrate) was added.  <sup>g</sup> 20 Mol % tetrahydrothiophene (based on substrate) was added.  <sup>h</sup> Tetrahydrothiophene.  <sup>i</sup> NiCl₂ instead of NiCl₂(PPh₃)₂ was employed.  <sup>j</sup> 20 Mol % 2,2'-dipyridyl (based on substrate) instead of PPh₃ was employed.  <sup>k</sup> 1.0 equiv Zn, reaction time 3 h.
efficiently in the presence of Et₄NI. Relatively large amounts of Et₄NI (1.5 equivalents based on mesylate) were necessary in order to obtain high yields (in the absence of additional PPh₃). An increase in yield occurred as the relative amount of Et₄NI was increased (Table IV, entry 1, 6, & 7). In the absence of both additional PPh₃ and Et₄NI (Table IV, entry 7), premature catalyst decomposition resulted in low yield. However, addition of Et₄NI to the reaction significantly enhanced the stability of the Ni(0) catalyst. This may indicate that iodide can act as a donor ligand which can stabilize the Ni(0) catalyst, as well as facilitating the electron transfer process. It is important to note that Ni(0) PPh₃ complexes exist in solution entirely as the tris complex, i.e., Ni(0)(PPh₃)₃, in the presence of excess PPh₃ due to the bulkiness of the PPh₃ ligand. However, in the absence of added PPh₃, our catalyst system generates Ni(0)(PPh₃)₂. This highly coordinatively unsaturated Ni(0) complex might be stabilized by iodide coordination. Thus, iodide is essential for high yield in the absence of additional PPh₃. However, it was found that in the presence of additional PPh₃, the coupling reaction proceeded efficiently without iodide (91% yield, entry 17 in Table IV). This may indicate that an important role of the halide is to stabilize the aryl nickel species and/or to prevent the deactivation of the catalyst which would limit the yield.

Other halide sources were compared with Et₄NI. When Et₄NBr was employed, lower yield was observed (Table IV, entry 1 vs. 13). The utilization of KI, which has very low solubility in THF, resulted in yields which were similar to that obtained with no iodide present (Table IV, entry 7 vs. 14). The enhancement of the solubility of KI in THF by the addition of a catalytic amount (20 mol%) of 18-crown-6 resulted in high yield (Table IV, entry 14 vs. 15). When using KBr instead of KI together with 18-crown-6, a slightly lower yield was obtained (Table IV, entry 15 vs. 16).

2.3.4.-Effect of the Amount of Catalyst
Ni(0) catalyst is decomposed by the decoordination of ligand from metal center and by adventitious traces of water in reaction medium. The decomposition of the Ni(0) catalyst accelerates as the temperature is increased. Therefore, it is important to have enough catalyst initially present so that active catalyst is present at the end of the reaction and the last of the mesylate can be coupled. However, too much catalyst may also be harmful (see mechanistic discussion, *vide infra*). The yield of homocoupling decreased as the amount of Ni(0) catalyst decreased in the absence of additional PPh₃ (Table IV, entries 1, 8 & 9). Almost quantitative yield was obtained with 10 mol% Ni(0) catalyst (Table IV, entry 1). When using 5 & 3 mol% Ni(0) catalyst (Table IV, entries 8-9), premature catalyst decomposition was observed and the remaining material isolated was unreacted aryl mesylate. Addition of PPh₃ to the reaction mixture greatly enhanced the stability of the Ni(0) catalyst, resulting in increased yield (Table IV, entries 8 vs. 10 & 9 vs. 11). When using 1 mol% Ni(0) catalyst in the presence of 20 mol% PPh₃, 36% coupled product was obtained (Table IV, entry 12).

2.3.5.-Dried versus Wet Solvent

It has been generally accepted that water and oxygen in the reaction medium can result in premature decomposition of Ni(0) catalyst.² Water can also reduce aryl halides and aryl sulfonates to the corresponding arene in the presence of zerovalent nickel catalyst. For this reason, careful removal of water in the reaction medium has been a critical factor in Ni(0) mediated reactions. This is also the reason that most Ni(0) coupling reactions require relatively large amounts of ligands such as PPh₃ and/or bidentate ligands such as 2,2'-dipyridyl in order to strongly stabilize the Ni(0) catalyst. It was discussed that in the presence of additional PPh₃ (20 mol%), the coupling reaction proceeded efficiently without iodide (91% yield, entry 17 in Table IV), *vide supra*. Although some reaction rate retardation was expected, the active Ni(0)
catalyst lasted for the entire reaction time. The same reaction conditions employing 20 mol% PPh₃ except using wet THF (i.e., taken directly from a bottle without drying) instead of dried THF (freshly distilled from sodium-benzophenone ketyl) gave almost identical results (Table IV, entry 17 vs. 18). However, when the amount of PPh₃ was decreased from 20 mol% to 10 mol%, with wet THF the catalyst decomposed immediately resulting in very low yield (Table IV, entry 18 vs. 19). A slight increase in yield was detected in the presence of Et₄NI (Table IV, entry 19 vs. 20). In the absence of additional PPh₃, wet THF did not give any homocoupled product even in the presence of Et₄NI (Table IV, entries 21 & 22). Apparently, at least 20 mol% additional PPh₃ was essential for the high coupling yield when using wet THF. A further increase in yield by using 30 mol% PPh₃ was not obtained (entry 18 vs. 24). In order to confirm the efficiency of the coupling reaction in wet THF, H₂O (5 mol% based on aryl mesylate) was added to the reaction mixture in dried THF, with 20 mol% PPh₃ present. This resulted in a slightly decreased yield (83% yield, entry 23 in Table IV). This amount of H₂O was sufficient to deactivate the catalyst in the absence of added PPh₃.

2.3.6.-Ligand Effect

Ligands (such as PPh₃) are essential in Ni(0) homocoupling reaction in order to stabilize the in situ generated Ni(0) catalyst and aryl nickel species during the entire reaction sequence. The selection of the appropriate ligand can also increase the electron density on low valent transition metals, making the metal more nucleophilic, thus facilitating the oxidative addition step of the catalytic cycle. However, ligands also should have a proper tendency for dissociation from the metal to generate the coordinatively unsaturated species (i.e., generation of a vacant reacting site). It is well established that this dissociation is highly dependent on the polarity of the solvents and
the reaction temperature. When replacing THF with dipolar aprotic solvents such as DMF or DMAc, the ligand dissociation is much more favored. In the absence of added PPh₃ this sometimes results in premature catalyst decomposition and low yields. However, when using less dissociating solvents such as THF, decoordination of ligand from Ni(0) catalyst and/or aryl nickel species is less favored, and for this reason, reduced amounts of PPh₃ can be used. Since excess PPh₃ can retard the transition metal catalyzed coupling reaction and the difficulty of separating excess PPh₃ from the reaction can give lower isolated yield than the actual one, we employed THF as solvent for most studies in order to reduce the amount of excess PPh₃. However, using the coordinatively unsaturated Ni(0) catalyst generated from NiCl₂(PPh₃)₂, with no additional PPh₃, required the addition of a halide such as Et₄NI to obtain high yields. Et₄NI can function as a donor ligand stabilizing the Ni(0) catalyst and/or aryl nickel species, as well as facilitate the electron transfer process (vide supra). However, for successful coupling, severe anhydrous reaction conditions were essential with this system (Table IV, entry 1 vs. 22). We also demonstrated that iodide can be replaced by additional PPh₃, which might mean that the major role of iodide is stabilizing the Ni(0) catalyst and/or aryl nickel species (Table IV, entry 1 vs. 17), vide supra. The advantage of additional PPh₃ over iodide was that small amounts of water was tolerable in the coupling reaction (Table IV, entry 17 vs. 18). It is likely that in less polar solvents such as THF, small amounts of water do not impede the coupling reaction greatly. Further studies using wet THF as solvent in combination with other nucleophilic solvents such as pyridine and tetrahydrothiophene as ligand were performed. In the absence of additional PPh₃ or iodide, the coupling reaction did not proceed with wet THF (0% yield, entry 21 in Table IV) due to the immediate deactivation of the catalyst. However, addition of 20 mol% pyridine or tetrahydrothiophene (based on substrate) to the reaction substantially enhanced the
stability of the catalyst resulting in high yield (83% and 53% respectively, entries 25 & 26 in Table IV). Using pyridine as both solvent and ligand instead of THF gave moderate yield (55% yield, entry 27 in Table IV). On the other hand, straight tetrahydrothiophene did not give any homocoupled product, probably due to the poor solubility of nickel catalyst and Zn (Table IV, entry 28). Using NiCl₂ together with other ligands such as pyridine, tetrahydrothiophene and 2,2'-dipyridyl except PPh₃ failed to give homocoupled product (Table IV, entry 29-31).

2.3.7.-Comparison of THF Method with Dipolar Aprotic Solvent Method

In summary, the most efficient Ni(0) catalyst used was generated from NiCl₂(PPh₃)₂ (10 mol%), Et₄NI (1.5 equiv), and Zn (1.7 equiv) in THF at 67°C. These results need to be compared with those obtained using the system which was used in the reported Ni(0) catalyzed coupling of 4-acetylphenyl methanesulfonate.¹⁸h This system typically involved the generation of a Ni(0) catalyst from NiCl₂(PPh₃)₂ (5.3%), PPh₃ (20%), an alkaline metal halide salt (1.0 equiv), and Zn (1.0 equiv) in DMAc (or another dipolar aprotic solvent) at 100°C.¹⁸h The effect of various reaction conditions is summarized in Table V. The reaction time is much shorter in the DMAc system (3 h vs. 10 h in THF). The reaction yields in DMAc were virtually unchanged at 80°C (96% vs. 95%, entries 1 & 2 in Table V). Conversely, an increase in temperature to 120°C resulted in a significant decrease in yield (65% yield, entry 3 in Table V). The best results were obtained using NaBr as the halide source (96% yield, entry 1 in Table V). Lower yields were obtained with iodide ions. NaI and KI were much more effective iodide sources than Et₄NI (91%, 93%, & 85% yields respectively, entries 4, 5, & 6 in Table V). DMAc was a more effective solvent than DMF (69% yield, entry 7 in Table V). No coupled product was obtained in NMP (entry 8 in Table V). When the reaction was performed in the absence of a halide source a low yield of
Table V. Effect of Various Reaction Conditions on the Ni(0)-Catalyzed Homocoupling of 4-Acetylphenyl methanesulfonate

\[
\begin{align*}
\text{CH}_3\text{C} & \text{O} \quad \begin{array}{c} \text{O} \\ \text{[Ar-OMs]} \end{array} \\
& \xrightarrow{\text{Ni}(0)} \\
& \begin{array}{c} \text{CH}_3\text{C} \\ \text{O} \\ \text{[Ar-Ar]} \end{array}
\end{align*}
\]

<table>
<thead>
<tr>
<th>Entry</th>
<th>NiCl$_2$(PPh$_3$)$_2$ (mol %)</th>
<th>PPh$_3$ (mol %)</th>
<th>Halide / equiv</th>
<th>Solvent</th>
<th>Ar-H</th>
<th>Ar-OMs</th>
<th>Ar-Ph</th>
<th>Ar-Ar</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>5.3</td>
<td>20</td>
<td>NaBr / 1.0</td>
<td>DMAc</td>
<td>2</td>
<td>-</td>
<td>2</td>
<td>96</td>
</tr>
<tr>
<td>2</td>
<td>5.3</td>
<td>20</td>
<td>NaBr / 1.0</td>
<td>DMAc</td>
<td>3</td>
<td>-</td>
<td>1</td>
<td>95</td>
</tr>
<tr>
<td>3</td>
<td>5.3</td>
<td>20</td>
<td>NaBr / 1.0</td>
<td>DMAc</td>
<td>2</td>
<td>-</td>
<td>3</td>
<td>65</td>
</tr>
<tr>
<td>4</td>
<td>5.3</td>
<td>20</td>
<td>NaI / 1.0</td>
<td>DMAc</td>
<td>7</td>
<td>-</td>
<td>1</td>
<td>91</td>
</tr>
<tr>
<td>5</td>
<td>5.3</td>
<td>20</td>
<td>KI / 1.0</td>
<td>DMAc</td>
<td>6</td>
<td>-</td>
<td>1</td>
<td>93</td>
</tr>
<tr>
<td>6</td>
<td>5.3</td>
<td>20</td>
<td>Et$_4$NI / 1.0</td>
<td>DMAc</td>
<td>5</td>
<td>-</td>
<td>7</td>
<td>85</td>
</tr>
<tr>
<td>7</td>
<td>5.3</td>
<td>20</td>
<td>NaBr / 1.0</td>
<td>DMF</td>
<td>21</td>
<td>-</td>
<td>7</td>
<td>69</td>
</tr>
<tr>
<td>8</td>
<td>5.3</td>
<td>20</td>
<td>NaBr / 1.0</td>
<td>NMP</td>
<td>2</td>
<td>60</td>
<td>-</td>
<td>traces</td>
</tr>
<tr>
<td>9</td>
<td>5.3</td>
<td>20</td>
<td>-</td>
<td>DMAc</td>
<td>4</td>
<td>69</td>
<td>5</td>
<td>16</td>
</tr>
<tr>
<td>10</td>
<td>5.3</td>
<td>40</td>
<td>-</td>
<td>DMAc</td>
<td>8</td>
<td>-</td>
<td>8</td>
<td>55</td>
</tr>
<tr>
<td>11</td>
<td>5.3</td>
<td>20</td>
<td>KI / 1.0</td>
<td>DMAc$^b$</td>
<td>22</td>
<td>60</td>
<td>-</td>
<td>17</td>
</tr>
<tr>
<td>12</td>
<td>5.3</td>
<td>20</td>
<td>NaBr / 1.0</td>
<td>DMAc$^b$</td>
<td>19</td>
<td>40</td>
<td>-</td>
<td>40</td>
</tr>
<tr>
<td>13$^c$</td>
<td>10</td>
<td>-</td>
<td>Et$_4$NI / 1.5</td>
<td>THF</td>
<td>20</td>
<td>-</td>
<td>7</td>
<td>73</td>
</tr>
</tbody>
</table>

$^{a}$ Reaction conditions: 1.0 equiv Zn, 100°C, 3 h. $^{b}$ Wet DMAc. $^{c}$ 1.7 equiv Zn, 67°C, 10 h.
coupled product (16%, entry 9 in Table V) was obtained. This yield was increased when the amount of PPh₃ was doubled (55% yield, entry 10 in Table V). The coupling reaction in DMAC was very sensitive to the dryness of the solvent, as yields were dramatically reduced when wet (i.e. not dried over CaH₂) DMAC was used (40% yield with NaBr, 17% yield with KI, entries 11 & 12 in Table V respectively).

The selection of a general method (THF or DMAC methods) depends on the exact substrate undergoing the coupling reaction. For example, in the case of 4-acetylphenyl mesylate, the best results were obtained using the reaction conditions typically used with DMAC. The yield of coupled product was 96% in DMAC (entry 1 in Table V) versus 73% in THF (entry 13 in Table V). The DMAC system also has the advantage of a shorter reaction time and the use of a more readily available halide source. Alternatively, in the coupling reaction of methyl 4-methylsulfonyloxybenzoate the typical THF reaction conditions gave the best results. The yield of coupled product in this case was >99% (Table IV, entry 1) compared to yields of 78% & 79% obtained in DMAC (Table IV, entries 32 & 33). In this case, the THF system has the further advantage that no extra PPh₃ is necessary under anhydrous conditions and that the reaction can be performed in wet THF when PPh₃ is added (90% yield, Table IV, entry 24).

2.3.8.-Reaction Mechanism

Several different reaction mechanisms have been suggested for Ni(0) catalyzed homo-coupling reactions of aryl halides. The mechanism outlined in Scheme I has been proposed for the Ni(0) mediated coupling reaction of aryl chlorides in polar aprotic solvents in the presence of excess Zn. The mechanistic details have been supported by an comprehensive electrochemical study. The mechanism outlined in Scheme II has been proposed for the coupling reaction of ArX (X = halide) in nonpolar
Scheme I. Plausible Mechanism of Ni(0) Catalyzed Homo-Coupling of Aryl Mesylate in the Presence of Excess Zn.

X = Mesylate or other leaving groups
L = PPh₃ or THF
Scheme II. Plausible Mechanism of Ni(0) Catalyzed Homo-Coupling of Aryl Halides in the Absence of Excess Zn.
solvents in the absence of excess reducing metal.\textsuperscript{28} The primary mechanistic pathway followed is highly dependent on the reaction conditions.\textsuperscript{2c} Under the conditions utilized for the coupling of aryl mesylates, the most plausible mechanism is shown in Scheme I.\textsuperscript{2f,29}

The catalytic cycle shown in Scheme I can serve as a working model for a mechanistic discussion of the coupling reaction. The first step of the mechanism involves the reduction of Ni(II) to Ni(0) by Zn. This is followed by the oxidative addition of ArX (X = mesylate or other sulfonate leaving group) to the Ni(0) species. This Ni(II) species may have an ionic structure, i.e., $[\text{ArNi(PPh}_3)_2]^+\{\text{OMs}\}^-$. The oxidative addition of vinyl triflates to Pt(PPh\textsubscript{3})\textsubscript{4} results in the formation of the ionic Pt(II) complexes containing a $\sigma-$vinyl ligand, three phosphine ligands and a noncoordinating triflate anion.\textsuperscript{30} A similar Pd(II) complex $[\text{ArPdL}_n]^+\{\text{OTf}\}^-$ has been proposed to result from the oxidative addition of ArOTf to Pd(0) in the presence of PPh\textsubscript{3}.\textsuperscript{31} In a reaction analogous to the reaction of $[\text{RPL}_3]^+\{\text{OTf}\}^-$ with R\textsubscript{4}NX,\textsuperscript{30} the ArNi(II)OMs complex may react quickly with Et\textsubscript{4}NI to form ArNi(II)(I)(PPh\textsubscript{3})\textsubscript{2}. The Ni(II) species then undergoes a one electron reduction to ArNi(I)L\textsubscript{3} (L = PPh\textsubscript{3} or THF). ArX oxidatively adds to this species to give a diaryl Ni(III) complex which undergoes rapid reductive elimination, resulting in the formation of the biaryl product and the generation of Ni(I)XL\textsubscript{3}. There are two productive reaction pathways available to this Ni species. Ni(I)XL\textsubscript{3} can be reduced by Zn to regenerate Ni(0)L\textsubscript{3}, which can then repeat the catalytic cycle. Alternatively, ArX can undergo direct oxidative addition to Ni(I)XL\textsubscript{3} followed by reduction by Zn to form the ArNi(I)L\textsubscript{3} species once again.

Although, Scheme I shows the most probably sequence of steps, the rate determining step is ambiguous. The rate of oxidative addition of aryl halides to Ni(0) species is considered to be a fast reaction in other coupling reactions.\textsuperscript{2f} The rate
determining step in the homocoupling reaction of aryl chlorides under similar reaction conditions in the presence of excess Zn, is the reduction of the aryl-Ni(II) species to the aryl Ni(I) species. However, at high conversions of ArX, the rate determining step becomes oxidative addition of ArX to the Ni(I) species. Thus, the rate constants for these reactions are within an order of magnitude of each other. When the reduction occurs by electrochemical means, rather than via Zn, the rate determining step at low concentrations of ArBr is oxidative addition of ArBr to the ArNi(I) species and at higher concentrations of ArBr is the reductive elimination of biaryl from the Ni species.

The highest yields in the coupling reaction of aryl mesylates were obtained with electron withdrawing groups in the para position. The reaction was inhibited by electron-donating groups as well as by sterically hindering ortho groups. However these effects alone can not be used to determine the rate determining step. Electron-withdrawing groups can increase the rate of oxidative addition of aryl halides to Ni(0). The rate of oxidative addition is also influenced by the nature of the leaving group. The electronic properties of the aryl group has also been shown to influence the reactivity of [ArPdL₉]⁺[OTf]⁻. Thus, it is possible that the electronic properties of the aryl group could affect the rate of electron-transfer in the reduction of the aryl-Ni(II) species to an aryl-Ni(I) species. Furthermore, the rate of reductive elimination is increased by positive charge. Thus, the electron-donating groups could slow the reductive elimination step.

The presence of sterically hindering ortho groups can also influence the rate of several steps. For example, the oxidative-addition of ArX to ArNi(I) would be expected to proceed more slowly with ortho substituents on the aryl groups. In addition, the rate of electron transfer to ArNi(II) could also be affected by an ortho substituent, especially if a bridging I⁻ ion is involved.
Another possibility is that the mechanism is similar to the one proposed by Tsou
and Kochi, a double-chain mechanism involving the reaction of Ar-Ni$^{III}$X$_2$ and
ArNi$^{II}$X to form Ar$_2$Ni$^{III}$X in the key step (Scheme II).\textsuperscript{28} Evidence for this mechanism
was obtained using non-polar solvents such as benzene, toluene and hexane. The
bimolecular step involves Ni species expected to be present in trace quantities when
excess Zn is present. Thus this mechanism is expected to be favored when large
amounts of Ni catalyst and small amounts of Zn are present. This mechanism may
have some contribution at high conversions when all aryl sulfonate has been consumed
but before all of the aryl nickel species have reacted to give the coupled product.

2.4.-CONCLUSIONS

The experiments reported here demonstrate that most aryl sulfonates including
aryl mesylate undergo Ni(0) catalyzed homocoupling reactions in THF, dioxane, and
DMAc, generating functional symmetrical biaryls in high yields. The application of this
very convenient synthetic method to the preparation of well known 2,2'-, 3,3'- and
4,4'-biphenyls and biaryls from readily available phenols and of novel biaryls has been
demonstrated. The most reactive leaving group, which is comparable in reactivity with
triflate, is the $p$-fluorobenzene sulfonate group. However, excellent to good yields
were obtained with the inexpensive mesylate group. The highest yields were obtained
when the aryl group had electron-withdrawing substituents in para position. Yields
were reduced slightly when an $o$-substituent was present and the extent of side
reactions increased in this case. The identified side reactions were reduction and
transarylation of the aryl mesylate. When the $o$-substituent contains an ester or
carbonyl group attached to the aryl mesylate the steric effect is partially released.
Because substituted phenols, hydroquinones and bisphenols are readily accessible, the
mesylate leaving group provides an extremely convenient access to already known and
to new functionalized symmetrical biaryls.
REFERENCES


3.1.-INTRODUCTION

Functionalized symmetrically disubstituted dihydroxybiphenyls such as 2,2'-disubstituted-4,4'-dihydroxybiphenyls are an important class of compounds with various applications in materials and polymer chemistry.\(^1\) A general procedure that can be readily applied to the synthesis of a variety of 2,2'-disubstituted-4,4'-dihydroxybiphenyls has not been developed. In fact, the synthesis of only three of these compounds (i.e., 2,2'-bis(trifluoromethyl)-4,4'-dihydroxybiphenyl,\(^1\)\(^a\) 2,2'-dimethyl-4,4'-dihydroxybiphenyl\(^1\)\(^b-e\) and 2,2'-difluoro-4,4'-dihydroxybiphenyl\(^1\)\(^f-g\) has been reported.

2,2'-Bis(trifluoromethyl)-4,4'-dihydroxybiphenyl\(^1\)\(^a\) and 2,2'-dimethyl-4,4'-dihydroxybiphenyl\(^1\)\(^b-c\) were synthesized from the corresponding benzidines (2,2'-bis(trifluoromethyl)benzidine and 2,2'-dimethylbenzidine respectively) by diazotization followed by the reaction of the resulting diazonium salt with water. The application of this method to the preparation of other 2,2'-disubstituted-4,4'-dihydroxybiphenyls is limited by the lack of simple synthetic procedures for other 2,2'-disubstituted benzidines.

2,2'-Dimethyl-4,4'-dihydroxybiphenyl was alternatively synthesized via oxidative coupling of \(m\)-cresol.\(^1\)\(^d\) However, this method produces a mixture of two isomers, i.e., 2,2'-dihydroxy-6,6'-dimethylbiphenyl and 2,2'-dihydroxy-4,4'-dimethylbiphenyl. Similarly, this oxidative coupling of 2-\(t\)-butyl-5-methylphenol, followed by transalkylation with benzene in the presence of \(\text{AlCl}_3\) gave a mixture of 3 isomeric dimethylbiphenyldiols including 2,2'-dimethyl-4,4'-dihydroxybiphenyl, which was separated by preparative gas chromatography.\(^1\)\(^e\) These oxidative coupling
methods proceed with a lack of regioselectivity. Therefore, yields are reduced and tedious purification procedures are required.

2,2'-Difluoro-4,4'-dihydroxybiphenyl was synthesized from 3-nitro-4-aminoanisole in 15% overall yield by a five step reaction procedure, which involves preparation of 3-nitro-4-iodo-anisole by reaction of KI with the diazonium salt of 3-nitro-4-amino-anisole, Ullmann coupling of the resulting aryl iodide to give 4,4'-dimethoxy-2,2'-dinitrobiphenyl, reduction of nitro groups to amino groups, substitution of amino groups by fluorine atoms via the Schiemann-Balz reaction, and demethylation with BBr₃.

Symmetrical biaryls were traditionally obtained by the Ullmann reaction, and more recently by Ni(0) catalyzed homocoupling of aryl halides, aryl triflates, and other aryl sulfonates including mesylates. Since a large number of substituted phenols, hydroquinones and bisphenols are readily available, aryl sulfonates are particularly important substrates for the synthesis of symmetrical biaryls. The regiospecificity and high-yield of the homocoupling of aryl sulfonates allow it to be used in the key reaction step of a general procedure for the synthesis of novel 2,2'-disubstituted-4,4'-dihydroxybiphenyls. This chapter will describe the use of the Ni(0) catalyzed homocoupling reaction of aryl mesylates derived from 4-protected-2-substituted hydroquinones as the key reaction step in a novel method for the synthesis of previously unreported 2,2'-dibenzoyl-4,4'-dihydroxybiphenyl 6a, 2,2'-di(p-fluorobenzoyl)-4,4'-dihydroxybiphenyl 6b and 2,2'-di(p-t-butybenzoyl)-4,4'-dihydroxybiphenyl 6c. This method is general for the preparation of 2,2'-dianoyl-4,4'-dihydroxybiphenyls.

3.2.-EXPERIMENTAL
3.2.1.-Materials

1,4-Dimethoxybenzene (99%), benzoyl chloride (99%), 4-fluorobenzoyl chloride (98%), 4-t-butylbenzoyl chloride (98%), methanesulfonyl chloride (98%), tetraethylammonium iodide (98%) and boron tribromide (1.0 M solution in dichloromethane) were purchased from Aldrich and used without further purification except when reported. Pyridine was dried over CaH₂ and distilled. THF was distilled from sodium-benzophenone ketyl. Zinc dust (325 mesh) was stirred in acetic acid, washed with water and dried in vacuo at 120°C. NiCl₂(PPh₃)₂ was prepared according to a literature procedure.⁸

3.2.2.-Techniques

Unless otherwise noted, all compounds synthesized in the present chapter were purified until their 200 MHz ¹H-NMR spectra corresponded to the expected structure and the purity was established by comparison with published mp or found to be higher than 99.5% by GC or HPLC.

3.2.3.-Synthesis of 2,2′-Diaryl-4,4′-Dihydroxybiphenyls

Scheme I. outlines the general methods used in the synthesis of 2,2′-diaryl-4,4′-dihydroxybiphenyls.

2.5-Dimethoxybenzophenone (2a): A 500 mL three-neck flask equipped with a mechanical stirrer, addition funnel, and nitrogen inlet was charged with 1 (20.0 g, 0.145 mol) and CH₂Cl₂ (150 mL). The solution was cooled to 0°C, and AlCl₃ (23.0 g, 0.174 mol) was added in several portions. After stirring the solution for 10 min, benzoyl chloride (22.2 g, 0.158 mol) was added dropwise over 10 min. The solution was stirred at 0°C for 4 h, and poured into 100 mL of ice-water containing 10 mL conc.
Scheme I. Synthesis of 2,2'-Diaryl-4,4'-dihydroxybiphenyls

\[ \text{Scheme Diagram Here} \]
HCl. The organic phase was separated and washed with 10% NaOH and H₂O repeatedly. The solution was dried (MgSO₄) and the solvent evaporated in vacuo. Recrystallization (Hexane/ethyl acetate 1:1) afforded 30.0 g (85 %) colorless crystals: mp 51°C (benzene) (lit. 6 51.2°C).

4'-Fluoro-2,5-dimethoxybenzophenone (2b) was synthesized by the same procedure as that used for 2a except that 4-fluorobenzoyl chloride was used instead of benzoyl chloride. (90 %): white crystals; mp 52°C (benzene); ¹H NMR δ 7.84 (dd, J= 8.4, 5.5 Hz, 2H, m to fluorine), 7.13-6.90 (m, 5H, aromatic protons), 3.77 (s, 3H, -OCH₃, o to carbonyl), 3.65 (s, 3H, -OCH₃, m to carbonyl); ¹³C¹H NMR δ 194.47 (-C(=O)-), 165.64 (d, ¹JCF= 254.70 Hz, ipso to fluorine), 153.48 (ipso to oxygen and o to carbonyl), 151.21 (ipso to oxygen and m to carbonyl), 134.00 (ipso to carbonyl and o to oxygen), 132.36 (d, ³JCF= 9.2 Hz, m to fluorine), 129.07 (p to fluorine), 117.34 (o to carbonyl and oxygen), 115.28 (d, ²JCF= 22.1 Hz, o to fluorine), 114.35 (o to oxygen and p to carbonyl), 112.95 (o to oxygen and m to carbonyl), 56.14 (-OCH₃, o to carbonyl), 55.73 (-OCH₃, m to carbonyl); EIMS m/e (%) 260 (M⁺, 100), 165 (39), 123 (81), 95 (66); HRMS calcd for C₁₅H₁₃FO₃ 260.0849, found 260.0848.

4'-t-Butyl-2,5-dimethoxybenzophenone (2c) was synthesized by the same procedure as that used for 2a except that 4-t-butylbenzoyl chloride was used instead of benzoyl chloride. (84%): white crystals; mp 39-40 °C (benzene); ¹H NMR δ 7.79 (d, J= 8.4 Hz, 2H, m to t-butyl), 7.45 (d, J= 8.4 Hz, 2H, o to t-butyl), 6.97-6.94 (m, 2H, m and p to carbonyl), 6.90 (d, J= 4.6 Hz, 1H, o to carbonyl and oxygen), 3.77 (s, 3H, -OCH₃, o to carbonyl), 3.68 (s, 3H, -OCH₃, m to carbonyl), 1.34 (s, 9H, -C(CH₃)₃); ¹³C¹H NMR δ 195.63 (-C(=O)-), 156.79 (ipso to oxygen and o to carbonyl), 153.35 (ipso to oxygen and m to carbonyl), 151.21 (ipso to carbonyl and o to oxygen),
134.75 (ipso to carbonyl and p to t-butyl), 129.88 (m to t-butyl), 125.20 (o to t-butyl), 116.78 (o to oxygen and carbonyl), 114.24 (o to oxygen and p to carbonyl), 113.01 (o to oxygen and m to carbonyl), 56.35 (-OCH₃, o to carbonyl), 55.76 (-OCH₃, m to carbonyl), 35.09 (-C(CH₃)₃), 31.05 (-C(CH₃)₃); EIMS m/e (%) 298 (M⁺, 100), 283 (34), 241 (20), 165 (64), 161 (31), 57 (33); HRMS calcd for C₁₉H₂₂O₃ 298.1569, found 298.1563.

**Phenols.**

2-Hydroxy-5-methoxybenzophenone (3a). A 250 mL three-neck flask equipped with a reflux condenser, magnetic stirrer, and nitrogen inlet was charged with 2a (10.2 g, 42 mmol) and 50 mL benzene. AlCl₃ (5.6 g, 42 mmol) was added at 25°C in several portions to the stirred solution. Stirring was continued at 80°C for 12 h. The mixture was cooled to 25°C and poured into 100 mL ice-water containing 10 mL conc. HCl. The resulting mixture was partitioned between Et₂O (50mL) and H₂O. The organic phase was washed with H₂O, dried (MgSO₄), and the solvent evaporated in vacuo. Recrystallization (hexane/ethyl acetate 1:1) afforded 8.6 g (90%) yellow plates: mp 83.5°C (CHCl₃/hexanes) (lit.⁵ 84-85.5°C).

4'-Fluoro-2-hydroxy-5-methoxybenzophenone (3b) was synthesized from 2b by the same procedure as that used for 3a. (66%): yellow crystals; mp 93°C (benzene); ¹H NMR δ 11.44 (s, 1H, -OH), 7.78-7.71 (m, 2H, aromatic protons , m to fluorine), 7.24-7.00 (m, 5H, aromatic protons), 3.72 (s, 3H, -OCH₃); ¹³C{¹H} NMR δ 199.45 (-C(═O)-), 164.95 (d, ¹JCF= 254.0 Hz, o to fluorine), 157.32 (m to carbonyl and o to oxygen), 151.43 (o to carbonyl and ipso to oxygen), 134.02 (ipso to carbonyl and o to oxygen), 131.67(d, ³JCF= 8.9 Hz, m to fluorine), 123.97 (o to carbonyl and oxygen),
119.29 (p to carbonyl and o to oxygen), 118.53 (p to fluorine), 116.00 (m to carbonyl and o to oxygen), 115.55 (d, 2J_C=H = 22.1 Hz, m to fluorine), 55.86 (-OCH$_3$); EIMS m/e (%) 246 (M$^+$, 76), 150 (100), 123 (53), 95 (59); HRMS calcd for C$_{14}$H$_{11}$FO$_3$ 246.0692, found 246.0692.

4'-t-Butyl-2-hydroxy-5-methoxybenzophenone (3c) was synthesized from 2c by the same procedure as that used for 3a. (83%): viscous oil; $^1$H NMR δ 11.64 (s, 1H, -OH), 7.67 (d, J = 8.4 Hz, 2H, m to t-butyl), 7.52 (d, J = 8.4 Hz, 2H, o to t-butyl), 7.15-7.13 (m, 2H, o and p to carbonyl), 7.00 (d, J = 8.2 Hz, 1H, o to -OH), 3.72 (s, 3H, -OCH$_3$), 1.38 (s, 9H, -C(CH$_3$)$_3$); $^{13}$C$_{^1}$H NMR δ 200.70 (-C(=O)-), 157.32 (ipso to -OCH$_3$), 155.75 (ipso to -OH), 151.34 (ipso to carbonyl and o to oxygen), 135.02 (p to t-butyl), 129.24 (m to t-butyl), 125.32 (o to t-butyl), 123.54 (o to carbonyl and oxygen), 119.05 (p to carbonyl and o to oxygen), 118.82 (ipso to t-butyl), 116.51 (o to oxygen and m to carbonyl), 55.90 (-OCH$_3$), 35.04 (-C(CH$_3$)$_3$), 31.09 (-C(CH$_3$)$_3$); EIMS m/e (%) 284 (M$^+$, 62), 269 (13), 227 (44), 150 (100); HRMS calcd for C$_{18}$H$_{20}$O$_3$ 284.1412, found 284.1403.

Aryl Mesylates were prepared by the reaction of methanesulfonyl chloride with the corresponding phenols in pyridine$^9$ and purified by column chromatography (silica gel, hexanes/ethyl acetate).

5-Methoxy-2-methylsulfonyloxybenzophenone (4a). (97%): colorless oil; $^1$H NMR δ 7.82 (d, J = 7.4 Hz, 2H, o to carbonyl), 7.62-7.39 (m, 4H, m and p to carbonyl on benzoyl, and o to carbonyl on phenyl), 7.10-6.99 (m, 2H, o and m to -OSO$_2$CH$_3$), 3.82 (s, 3H, -OCH$_3$), 2.93 (s, 3H, -OSO$_2$CH$_3$); $^{13}$C$_{^1}$H NMR δ 194.00 (-C(=O)-), 157.82 (ipso to methoxy), 139.30 (ipso to -OSO$_2$CH$_3$), 136.75 (m to methoxy),
133.62 (o to methoxy and carbonyl), 133.47 (ips to carbonyl on benzoyl), 130.09 (o to carbonyl on benzoyl), 128.49 (m to carbonyl on benzoyl), 124.63 (p to carbonyl on benzoyl), 117.40 (o to methoxy and p to carbonyl), 115.02 (m to methoxy and carbonyl), 55.82 (-OCH₃), 37.58 (-OSO₂CH₃); EIMS m/e (%) 306 (M⁺, 39), 227 (100), 184 (23), 77 (13); HRMS calcd for C₁₅H₁₄O₅S 306.0562, found 306.0562.

4'-Fluoro-5-methoxy-2-methylsulfonyloxybenzophenone (4b). (84%): pale yellow oil:

¹H NMR δ 7.87-7.81 (m, 2H, m to fluorine), 7.42 (d, J = 8.9 Hz, 1H, o to carbonyl and methoxy), 7.20-7.05 (m, 3H, aromatic protons), 6.96 (d, J= 3.0 Hz, 1H, m to methoxy and carbonyl), 3.82 (s, 3H, -OCH₃), 2.97 (s, 3H, -OSO₂CH₃); ¹³C (¹H) NMR δ 192.30 (-C(=O)-), 166.05 (d, J₇CF= 257.20 Hz, ips to fluorine), 157.98 (ips to methoxy), 139.23 (ips to -OSO₂CH₃), 133.46 (ips to carbonyl and m to methoxy), 133.18 (p to fluorine), 132.89 (d, J₇CF= 9.2 Hz, m to fluorine), 124.76 (o to carbonyl and methoxy), 117.47 (p to carbonyl and o to methoxy), 115.80 (d, J₇CF= 22.4 Hz, o to fluorine), 115.05 (m to methoxy and carbonyl), 55.91 (-OCH₃), 37.69 (-OSO₂CH₃); EIMS m/e (%) 324 (M⁺, 32), 245 (100), 202 (22); HRMS calcd for C₁₅H₁₃FO₅S 324.0467, found 324.0468.

4'-t-Butyl-5-methoxy-2-methylsulfonyloxybenzophenone (4c). (81%): white crystals; mp 88-89°C (benzene); ¹H NMR δ 7.77 (d, J= 8.4 Hz, 2H, m to t-butyl), 7.49 (d, J= 8.4 Hz, 2H, o to t-butyl), 7.43 (d, J= 9.0 Hz, 1H, o to -OSO₂CH₃), 7.06 (dd, J= 9.0, 3.0 Hz, 1H, m to -OSO₂CH₃ and o to -OCH₃), 6.97 (d, J= 3.0 Hz, 1H, o to -OCH₃ and carbonyl), 3.82 (s, 3H, -OCH₃), 2.96 (s, 3H, -OSO₂CH₃), 1.35 (s, 9H, -C(CH₃)₃); ¹³C (¹H) NMR δ 193.49 (-C(=O)-), 157.73 (ips to methoxy), 157.64 (ips to -OSO₂CH₃), 139.38 (ips to carbonyl and m to methoxy), 134.02 (p to t-
butyl), 130.16 (m to t-butyl), 125.69 (o to t-butyl), 125.50 (ipso to t-butyl), 124.66 (o to methoxy and carbonyl), 117.06 (o to methoxy and p to carbonyl), 114.85 (o to -OSO$_2$CH$_3$ and m to carbonyl), 55.82 (-OCH$_3$), 37.59 (-OSO$_2$CH$_3$), 35.20 (-C(CH$_3$)$_3$), 31.00 (-C(CH$_3$)$_3$); EIMS m/e (%) 362 (M$^+$, 31), 324 (11), 283 (6), 245 (34), 227 (100), 57 (83); HRMS calcd for C$_{19}$H$_{22}$O$_5$S 362.1188, found 362.1193.

**General Procedure for Homocoupling Reaction of Aryl Mesylates.**

All reactions were carried out under nitrogen using oven-dried (110°C) glassware. In a typical reaction a 125 mL Schlenk tube was charged with NiCl$_2$(PPh$_3$)$_2$ (0.10 mmol), PPh$_3$ (0.40 mmol), Zn powder (1.7 mmol), Et$_4$Ni (1.5 mmol) and a magnetic stirring bar. After sealing the tube with a rubber septum, the content was dried at 25°C under reduced pressure (1 x 10$^{-3}$ mmHg) for 10 hr. Then the tube was filled with N$_2$ followed by three evacuation-filling cycles. Freshly distilled THF (0.50 ml) was added via a syringe through the rubber septum. The mixture was stirred at room temperature for 5 min and during this time the color of the mixture gradually changed from green into deep red brown. Aryl mesylate (1.0 mmol) was dissolved in freshly distilled THF (0.50 ml) and added to the catalyst mixture via a syringe through the rubber septum. The reaction mixture was heated to reflux temperature and stirred at this temperature for 24 h. Then it was cooled to 25°C, filtered, diluted with water, extracted with CHCl$_3$, dried (MgSO$_4$) and the solvent evaporated *in vacuo*. The corresponding biaryl was purified by column chromatography (silica gel, hexanes/ethyl acetate) and then recrystallized from CHCl$_3$/hexanes.

**2,2′-Diaroyl-4,4′-dimethoxybiphenyls.**
2,2'-Dibenzoyl-4,4'-dimethoxybiphenyl (5a). (65%): white crystals: mp 138-140°C (benzene); $^1$H NMR $\delta$ 7.76 (d, $J = 7.0$ Hz, 4H, $o$ to carbonyl on benzoyl), 7.42-7.39 (m, 2H, aromatic protons), 7.32-7.18 (m, 6H, aromatic protons), 6.92-6.87 (m, 4H, aromatic protons), 3.74 (s, 6H, -OCH$_3$); $^{13}$C($^1$H) NMR $\delta$ 197.43 (-C(=O)-), 157.91 ($ipso$ to oxygen), 139.41 ($ipso$ to carbonyl and $m$ to oxygen), 137.10 ($p$ to oxygen), 132.80 ($o$ to oxygen and carbonyl), 131.75 ($ipso$ to carbonyl on benzoyl), 130.28 ($o$ to carbonyl on benzoyl), 128.01 ($m$ to carbonyl on benzoyl), 115.51 ($o$ to oxygen and $p$ to carbonyl), 114.45 ($m$ to oxygen and carbonyl), 55.34 (-OCH$_3$); EIMS m/e (%) 422 (M$^+$, 5), 317 (100), 151 (25), 105 (32); HRMS calcd for C$_{28}$H$_{22}$O$_4$ 422.1518. found 422.1516.

2,2'-Di(p-fluorobenzoyl)-4,4'-dimethoxybiphenyl (5b). (62%): white crystals: mp 144°C (benzene); $^1$H NMR $\delta$ 7.81-7.74 (m, 4H, $o$ to fluorine), 7.17 (d, $J = 8.3$ Hz, 2H, $o$ to oxygen and carbonyl), 7.00-6.84 (m, 8H, aromatic protons), 3.76 (s, 6H, -OCH$_3$); $^{13}$C($^1$H) NMR $\delta$ 195.86 (-C(=O)-), 165.52 (d, $^1$J$_{CF}$= 255.0 Hz, $ipso$ to fluorine), 158.02 ($ipso$ to oxygen), 139.06 ($ipso$ to carbonyl and $m$ to oxygen), 133.41 ($p$ to oxygen), 132.93 (d, $^3$J$_{CF}$= 9.5 Hz, $m$ to fluorine), 132.73 ($p$ to fluorine), 131.56 ($o$ to oxygen and carbonyl), 115.66 ($o$ to oxygen and $p$ to carbonyl), 115.16 (d, $^2$J$_{CF}$= 21.9 Hz, $o$ to fluorine), 114.36 ($m$ to oxygen and carbonyl), 55.35 (-OCH$_3$); EIMS m/e (%) 458 (M$^+$, 9), 335 (100), 123 (15); HRMS calcd for C$_{28}$H$_{20}$F$_2$O$_4$ 458.1329. found 458.1331.

2,2'-Di(p-t-butylbenzoyl)-4,4'-dimethoxybiphenyl (5c). (45%): white crystals: mp 162-164 °C (benzene); $^1$H NMR $\delta$ 7.76 (d, $J = 8.4$ Hz, 4H, $m$ to t-butyl), 7.34 (d, $J = 8.4$ Hz, 4H, $o$ to t-butyl), 7.20 (d, $J = 9.0$ Hz, 2H, $o$ to oxygen and carbonyl), 6.88-
6.85 (m, 4H, aromatic protons), 3.73 (s, 6H, -OCH₃), 1.30 (s, 18H, -C(CH₃)₃);
¹³C{¹H} NMR δ 197.19 (C=O-), 157.95 (ipsos to oxygen), 156.45 (ipsos to
carbonyl and m to oxygen), 139.83 (p to oxygen), 134.73 (p to t-butyl), 132.83 (ipsos
to t-butyl), 131.89 (o to oxygen and carbonyl), 130.47 (m to t-butyl), 125.07 (o to t-
butyl), 115.41 (o to oxygen and p to carbonyl), 114.65 (m to oxygen and carbonyl),
55.42 (OCH₃), 35.12 (C(CH₃)₃), 31.15 (C(CH₃)₃); EIMS m/e (%) 534 (M⁺, 5),
519 (1), 373 (100), 343 (10); HRMS calcd for C₃₆H₃₈O₄ 534.2770, found 534.2774.

2,2'-Diaroyl-4,4'-dihydroxybiphenyls.

2,2'-Di(p-fluorobenzoyl)-4,4'-dihydroxybiphenyl (6b). A 100 mL three-neck flask
-equipped with an addition funnel, nitrogen inlet, and magnetic stirrer was charged with
12 mL of CH₂Cl₂ and 12 mL of 1.0 M BBr₃ solution in CH₂Cl₂. The solution was
cooled to -70°C and a solution of 5b (1.83g, 4 mmol) in 12 mL CH₂Cl₂ was added
dropwise to the stirred solution. The mixture was allowed to warm to 25°C and stirred
for 8h. Water (10 mL) was added dropwise to the reaction mixture over 10 min. The
organic phase was separated, dried (MgSO₄), and concentrated. Purification by
column chromatography (silica gel, hexanes/ethyl acetate 1:1) gave 1.62 g (94 %)
colorless crystals: mp 256-258°C (benzene); ¹H NMR (CDCl₃/DMSO-d₆) δ 8.77 (s,
2H, -OH), 7.77-7.70 (m, 4H, m to fluorine), 7.00-6.76 (m, 10H, aromatic protons);
¹³C{¹H} NMR (DMSO-d₆) δ 195.36 (C=O-), 164.83 (d, ¹JC=CF= 252.2 Hz, ipsos to
fluorine), 155.90 (ipsos to oxygen), 138.89 (ipsos to carbonyl and m to oxygen), 133.46
(p to oxygen), 132.73 (d, ¹JC=CF= 6.6 Hz, m to fluorine), 129.86 (p to fluorine), 117.32
(o to oxygen and carbonyl), 115.53 (o to oxygen and p to carbonyl), 115.22 (d, ²JC=CF=
12.9 Hz, o to fluorine); EIMS m/e (%) 430 (M⁺, 2), 307 (100), 123 (28), 95 (12);
HRMS calcd for C₂₆H₁₆F₂O₄ 430.1016, found 430.1009.
2,2'-Dibenzoyl-4,4'-dihydroxybiphenyl (6a) was prepared from 5a by the same procedure as that used for 6b (83% by $^1$H NMR). Because of the difficulty of separating the product from the reaction mixture, after usual work-up the crude product was further mesylated and purified by column chromatography (vide infra).

2,2'-Di(p-t-buty benzoyl)-4,4'-dihydroxybiphenyl (6c) was prepared from 5c by the same procedure as that used for 6b, (77%): white crystals; mp 236-238°C (benzene); $^1$H NMR (CDCl₃/DMSO-d₆) δ 8.62 (s, 2H, -OH), 7.66 (d, $J$ = 8.5 Hz, 4H, m to t-buty l), 7.25 (d, $J$ = 8.5 Hz, 4H, o to t-buty l), 7.00 (d, $J$ = 9.1 Hz, 2H, o to oxygen and carbonyl), 6.75-6.71 (m, 4H, aromatic protons), 1.23 (s, 18H, -C(CH₃)₃); $^{13}$C($^1$H} NMR (CDCl₃/DMSO-d₆) δ 197.45 (C=O), 156.03 (ipso to oxygen), 155.34 (ipso to carbonyl and m to oxygen), 139.56 (p to oxygen), 134.74 (p to t-buty l), 132.60 (ipso to t-buty l), 130.70 (o to oxygen and carbonyl), 130.27 (m to t-buty l), 124.79 (o to t-buty l), 116.98 (o to oxygen and p to carbonyl), 116.03 (m to oxygen and carbonyl), 34.92 (C(CH₃)₃), 30.99 (C(CH₃)₃); EIMS m/e (%) 506 (M⁺, 1), 505 (2), 491 (2), 373 (1), 345 (100), 161 (19); HRMS calcd for C₃₄H₃₄O₄ 506.2457, found 506.2465.

Bismesylates of 2,2'-diaryl-4,4'-dihydroxybiphenyls were prepared by the reaction of methanesulfonyl chloride with the corresponding bisphenols in pyridine and purified by column chromatography (silica gel, hexanes/ethyl acetate).

2,2'-Dibenzoyl-4,4'-bis(methanesulfonyloxy)biphenyl (7a). (94%): white crystals; mp 138-140°C (benzene); $^1$H NMR δ 7.65 (d, $J$ = 7.2 Hz, 4H, o to carbonyl on benzoyl), 7.46-7.38 (m, 6H, aromatic protons), 7.31-7.23 (m, 6H, aromatic protons), 3.10 (s,
6H, -OSO₂CH₃); ¹³C {¹H} NMR δ 195.23 (-C(=O)-), 147.71 (ipso to oxygen), 139.69 (ipso to carbonyl and m to oxygen), 138.02 (p to oxygen), 136.25 (o to oxygen and carbonyl), 133.35 (ipso to carbonyl on benzoyl), 133.12 (p to carbonyl on benzoyl), 130.22 (o to carbonyl on benzoyl), 128.22 (m to carbonyl on benzoyl), 123.70 (o to oxygen and p to carbonyl), 122.93 (m to oxygen and carbonyl), 37.54 (-OSO₂CH₃); EIMS m/e (%) 550 (M⁺, 0.1), 471 (12), 445 (100), 105 (75), 77 (37); HRMS calcd for C₂₈H₂₂O₈S₂ 550.0756, found 550.0795.

2,2'-Di(p-fluorobenzoyl)-4,4'-bis(methylsulfonyloxy)biphenyl (7b). (90%): white crystals; mp 153-154°C (benzene); ¹H NMR δ 7.68 (dd, J= 8.8, 5.5 Hz, 4H, m to fluorine), 7.39 (s, 4H, m and p to carbonyl), 7.30 (s, 2H, o to oxygen and carbonyl), 6.96 (dd, J= 8.8, 8.6 Hz, 4H, o to fluorine), 3.15 (s, 6H, -OSO₂CH₃); ¹³C {¹H} NMR δ 193.63 (-C(=O)-), 166.53 (d, JCF= 255.0 Hz, ipso to fluorine), 147.66 (ipso to oxygen), 139.30 (ipso to carbonyl and m to oxygen), 137.87 (p to oxygen), 133.16 (p to fluorine), 132.99 (d, JCF= 9.8 Hz, m to fluorine), 132.55 (o to oxygen and carbonyl), 123.89 (o to oxygen and p to carbonyl), 122.86 (m to oxygen and carbonyl), 115.44 (d, JCF= 21.8 Hz, o to fluorine), 37.67 (-OSO₂CH₃); EIMS m/e (%) 586 (M⁺, 0.1), 507 (4), 463 (97), 305 (21), 123 (100), 95 (31); HRMS calcd for C₂₈H₂₀F₂O₈S₂ 586.0567, found 586.0579.

2,2'-Di(p-t-buty]benzoyl)-4,4'-bis(methylsulfonyloxy)biphenyl (7c). (87%): white crystals; mp 101-103°C (benzene); ¹H NMR δ 7.66 (d, J= 8.4 Hz, 4H, m to t-butyl), 7.38-7.31 (m, 10H, aromatic protons), 3.12 (s, 6H, -OSO₂CH₃), 1.29 (s, 18H, -C(CH₃)₃); ¹³C {¹H} NMR δ 194.85 (-C(=O)-), 157.21 (ipso to oxygen), 147.60 (ipso to carbonyl and m to oxygen), 140.02 (p to oxygen), 138.01 (p to t-butyl),
133.65 (ipso to t-butyl), 133.10 (o to oxygen and carbonyl), 130.34 (m to t-butyl), 125.21 (o to t-butyl), 123.40 (o to oxygen and p to carbonyl), 122.91 (m to oxygen and carbonyl), 37.53 (-OSO₂CH₃), 35.09 (-C(CH₃)₃), 30.97 (-C(CH₃)₃); EIMS m/e (%): 647 (M⁺-CH₃, 1), 583 (1), 501 (100), 423 (23), 161 (13); HRMS calcd for C₃₅H₃₅O₈S₂ 647.1773, found 647.1887.

3.3. RESULTS AND DISCUSSION

The previously unreported 6a-c were synthesized starting from 1,4-dimethoxybenzene 1 according to the sequence of reactions outlined in Scheme I. In this synthetic procedure, substituted 1,4-dimethoxybenzenes 2a-c were obtained by aroylation of 1 (vide supra), followed by regioselective demethylation of the 1-position (i.e., methoxy ortho to the substituent) of 2a-c containing an electron withdrawing substituent with AlCl₃. Thus 2,5-dimethoxybenzophenone 2a, 4'-fluoro-2,5-dimethoxybenzophenone 2b and 4'-t-butyl-2,5-dimethoxybenzophenone 2c were prepared in high yields (85%, 90% and 84% respectively) by the Friedel-Crafts reaction of 1 with the corresponding benzoyl chloride derivative in CH₂Cl₂ at 0°C. By slight variations in the procedure employed for the synthesis of the dimethyl ethers 2a-c, the monomethyl ethers 3a-c were prepared by the regioselective demethylation of the 1-position of 2a-c with anhydrous aluminium chloride in benzene at 80°C (yields: 90%, 66% and 83% respectively). It was found that 3a-c could be prepared from 1 and the corresponding benzoyl chloride derivatives in a one-pot synthesis according to a modified literature procedure, although the obtained yields were reduced in comparison to the two step synthesis described in Scheme I. 3a-c were mesylated, and the Ni(0) catalyzed homocoupling reaction of the corresponding mesylates 4a-c in the presence of an ortho benzoyl group derivative produced the biaryls 5a-c in good yields.
(65%, 62% and 45% respectively). In this case, the electron-withdrawing effect of the benzoyl group derivatives is expected to activate the aryl mesylate toward oxidative addition, although the large ortho substituent would be expected to sterically hinder the reaction. Since the ortho substituents slowed the reaction rate thus leading to catalyst decomposition during the reaction time, it was necessary to use excess PPh₃ to stabilize the Ni(0) catalyst against degradation. The cleavage of methoxy groups of the compounds 5a-c by BBr₃ in CH₂Cl₂ generated the corresponding bisphenols 6a-c in good yields. The treatment of 6a-c with mesyl chloride afforded bismesylates 7a-c. They can be purified easier than the corresponding bisphenols 6a-c and were used for analytical characterization. 200 MHz ¹H-NMR spectra of bismesylates 7a-c are presented in Figure 1-3.

3.4.-CONCLUSIONS

Nickel-catalyzed homocoupling of aryl mesylates of 4-protected-2-substituted hydroquinones was utilized in the key step of a reaction scheme which leads to the synthesis of novel and difficult to prepare by alternative methods, 2,2'-diaroyl-4,4'-dihydroxybiphenyls: 2,2'-dibenzoyl-4,4'-dihydroxybiphenyl, 2,2'-di(p-fluorobenzoyl)-4,4'-dihydroxybiphenyl and 2,2'-di(p-t-butylbenzoyl)-4,4'-dihydroxybiphenyl (overall yield: 40%, 29% and 20% respectively). The synthetic procedure reported in this chapter is of important value since it represents an easy and direct access to a wide variety of 2,2'-disubstituted-4,4'-dihydroxybiphenyls, and employs readily available hydroquinone derivatives as starting materials.
Figure 3. 200 MHz $^1$H-NMR Spectrum of 2,2'$\text{-Di}(p$-$t$-butylbenzoyl)$-4,4'$-
$\text{bis(methylsulfonyloxy)biphenyl (2e).}$
Figure 2. 200 MHz $^{1}$H-NMR Spectrum of 2,2'-Di(p-fluorobenzoyl)-4,4'-bis(methylsulfonyloxy)biphenyl (2b).

\[
\begin{align*}
\text{CH}_3\text{O}_2\text{SO} & \quad \text{C} \\
\text{C} & \quad \text{D} \\
\text{E} & \quad \text{F} \\
\end{align*}
\]
Figure 1. 200 MHz $^1$H-NMR Spectrum of 2,2’-Dibenzoyl-4,4’-bis(methylsulfonyloxy)biphenyl (Za).
REFERENCES


Chapter 4
SYNTHESIS OF 2,2'-DIPHENYL-4,4'-DIHYDROXYBIPHENYL

4.1.-INTRODUCTION

Previous chapters from this series have demonstrated that aryl sulfonates including mesylate derived from phenols undergo homocoupling reactions in the presence of zerovalent nickel catalysts generated in situ to produce biaryls in high yield.\(^1,2\) This reaction was utilized as the key step to elaborate a simple and general synthetic method for the preparation of novel 2,2'-diaroyl-4,4'-dihydroxybiphenyls starting from 1,4-dimethoxybenzene.\(^2\) 2,2'-Disubstituted-4,4'-dihydroxybiphenyls are important starting compounds for various areas of materials and polymer chemistry.\(^3\)-\(^5\) However, with the exception of the previously reported 2,2'-diaroyl-4,4'-dihydroxybiphenyls\(^2\) only the following three compounds are known: 2,2'-bis(trifluoromethyl)-4,4'-dihydroxybiphenyl,\(^3\) 2,2'-dimethyl-4,4'-dihydroxybiphenyl\(^4\) and 2,2'-difluoro-4,4'-dihydroxybiphenyl.\(^5\) This chapter describes two convenient synthetic methods for the synthesis of the novel 2,2'-diphenyl-4,4'-dihydroxybiphenyl \(^6\) by using the commercially available phenylhydroquinone and 2-phenylphenol respectively as starting materials.

4.2.-EXPERIMENTAL

4.2.1.-Materials

Phenylhydroquinone (97 %), 2-phenylphenol (99 %), diethyl sulfate (98 %), methanesulfonyl chloride (98 %) and tetraethylammonium iodide (98 %) were purchased from Aldrich and used without further purification except when reported. Pyridine was dried over CaH\(_2\) and distilled. THF and dioxane were distilled from sodium-benzophenone ketyl. Zinc dust (325 mesh) was stirred in acetic acid, washed
with water and dried in vacuo at 120°C. NiCl₂(PPh₃)₂ was prepared according to a literature procedure.¹⁰

4.2.2.-Techniques

All compounds synthesized in the present chapter were purified until their 200 MHz ¹H-NMR spectra corresponded to the expected structure and the purity was established by comparison with published mp or found to be higher than 99.5% by GC or HPLC.

4.2.3.-Synthesis of 2,2'-Diphenyl-4,4'-dihydroxybiphenyl

Scheme I and II outline the two different synthetic methods used in the synthesis of 2,2'-diphenyl-4,4'-dihydroxybiphenyl.

5-Ethoxy-2-hydroxybiphenyl (2a):

Diethyl sulfate (3.5 ml, 27 mmol) was added dropwise to a rapidly stirred solution of 1 (5.0 g, 27 mmol) in 1.8 M aq NaOH (30.0 ml, 54 mmol) at 25°C. This solution was stirred at 100°C for 3h. After cooling to 25°C the reaction mixture was acidified with concentrated HCl and extracted with CHCl₃. The organic layer was dried (MgSO₄) and evaporated to give a dark oil. Chromatography (basic alumina, hexanes/ethyl acetate 1:1) afforded a dark viscous oil (2.81g, 49 %); TLC (hexanes/Et₂O 2:1) Rf=0.34; ¹H NMR (CDCl₃/TMS): δ= 7.49-7.38 (m, 5H, aromatic protons), 6.88-6.80 (m, 3H, aromatic protons), 4.99 (s, 1H, -OH), 4.00 (q, J=6.9Hz, 2H, -OCH₂CH₃), 1.39 (t, J=6.9Hz, 3H, -OCH₂CH₃).

5-Ethoxy-2-(methylsulfonyl)oxybiphenyl (3):
Scheme I. Synthesis of 2,2'-Diphenyl-4,4'-dihydroxybiphenyl from Phenylhydroquinone

1. NaOH, H₂O, 25°C, 20 min
2. Et₃SO₄, 100°C, 3h
3. aq HCl

1 + EtO-PhOH + HO-PhOEt + EtO-PhOEt

2a (49%)

2a → EtO-PhOMs
25°C, 8h

3 (90%)

NiCl₂(PPh₃)₂, Zn, Et₄NI
Dioxane, 100°C, 24h

EtO-PhOEt

4a (24%)

4 → BBr₃, CH₂Cl₂
25°C, 10h

HO-PhOH

5 (91%)
This compound was prepared by the reaction of methanesulfonyl chloride with 2a in pyridine\textsuperscript{11} and purified by column chromatography (silica gel, hexanes/Et\textsubscript{2}O 2:1); yield: 90 %; viscous oil; TLC (hexanes/Et\textsubscript{2}O 2:1) R\textsubscript{f}=0.30; \textsuperscript{1}H NMR (CDCl\textsubscript{3}/TMS): \( \delta = 7.51-7.35 \) (m, 6H, aromatic protons), 6.94 (dd, \( J=8.9, 2.8 \) Hz, 2H, aromatic protons), 4.06 (q, \( J=7.0 \) Hz, 2H, -OCH\textsubscript{2}CH\textsubscript{3}), 2.47 (s, 3H, -OSO\textsubscript{2}CH\textsubscript{3}), 1.43 (t, \( J=7.0 \) Hz, 3H, -OCH\textsubscript{2}CH\textsubscript{3}).

\textit{2,2'-Diphenyl-4,4'-diethoxybiphenyl (4)}:

This compound was synthesized from \( \mathfrak{2} \) by the same procedure as used for \( \mathfrak{5} \) in Scheme II (\textit{vide infra}); yield: 24 %; white crystals; mp 124-126°C (hexanes); TLC (hexanes/Et\textsubscript{2}O 2:1) R\textsubscript{f}=0.40; \textsuperscript{1}H NMR (CDCl\textsubscript{3}/TMS): \( \delta = 7.27 \) (d, \( J=8.4 \) Hz, 2H, \( m \) to oxygen), 7.07-6.95 (m, 6H, aromatic protons), 6.87 (dd, \( J=8.4, 2.6 \) Hz, 2H, \( o \) to oxygen and \( p \) to phenyl), 6.69 (d, \( J=2.6 \) Hz, 2H, \( o \) to oxygen and phenyl), 6.60 (d, \( J=6.7 \) Hz, 4H, aromatic protons), 4.04 (q, \( J=7.1 \) Hz, 4H, -OCH\textsubscript{2}CH\textsubscript{3}), 1.41 (t, \( J=7.1 \) Hz, 6H, -OCH\textsubscript{2}CH\textsubscript{3}).

\textbf{Preparation of 2,2'-Diphenyl-4,4'-dihydroxybiphenyl (5) from (4)}

To a 0.43 M BBr\textsubscript{3} solution in CH\textsubscript{2}Cl\textsubscript{2} (7 ml, 3 mmol) at -30°C was slowly added 4 (564 mg, 1.43 mmol) in CH\textsubscript{2}Cl\textsubscript{2} (4 ml). The reaction mixture was warmed to 25°C, and stirred for 10 h. Then it was washed with H\textsubscript{2}O, concentrated and chromatographed (silica gel, ethyl ether) to give white crystals (439 mg, 91%); mp 185-187°C (benzene); TLC (ethyl ether) R\textsubscript{f}=0.40; \textsuperscript{1}H NMR (CDCl\textsubscript{3}/TMS): \( \delta = 7.23 \) (d, \( J=8.8 \) Hz, 2H, \( m \) to oxygen), 7.09-6.97 (m, 6H, aromatic protons), 6.81 (dd, \( J=8.4, 2.6 \) Hz, 2H, \( o \) to oxygen and \( p \) to phenyl), 6.62-6.58 (m, 6H, aromatic protons), 4.72 (s, 2H, -OH).
2-Acetoxybiphenyl (7):

This compound was prepared from 6 and acetic anhydride6; yield: 100 %; white crystals; mp 61-62°C (EtOH) (lit.6 62.5-63°C).

2-Phenyl-4-acetylphenol (8a):

This compound was prepared according to a modified literature procedure.7 A 500 ml three-neck flask equipped with a mechanical stirrer, nitrogen inlet and outlet was charged with 7 (24 g, 0.113 mol). AlCl₃ (48 g, 0.361 mol) was added at 80°C in several portions to the stirred melt of 7 over 1 h. The mixture was further stirred at 130°C for additional 2 h, cooled to 25°C and poured into water (500 ml) and ice. The precipitate was then filtered, washed with water and dried. Recrystallization (toluene) gave 16.56 g (69 %) of white crystals; mp 172.5°C (toluene) (lit.7 175.5-176.5°C).

2-Phenyl-4-acetoxyphenol (9):

This compound was prepared from 8a by a Bayer-Villiger oxidation reaction using peracetic acid according to literature7; yield: 90 %; white crystals; mp 154°C (benzene) (lit.7 154-155°C).

5-Acetoxy-2-(methylsulfonyloxy)biphenyl (10):

This compound was prepared by the reaction of methanesulfonyl chloride with 9 in pyridine11 and purified by column chromatography (silica gel, hexanes/ethyl acetate); yield: 93 %; white crystals; mp 58-59°C (hexanes); ¹H NMR (CDCl₃/TMS): δ= 7.56-7.44 (m, 6H, aromatic protons), 7.20 (d, J= 6.3 Hz, 1H, o to oxygen and p to phenyl), 7.14 (s, 1H, o to oxygen and phenyl), 2.53 (s, 3H, -OSO₂CH₃), 2.34 (s, 3H, -OC(=O)CH₃); ¹³C{¹H} NMR (CDCl₃/TMS): δ= 169.06 (-C(=O)-), 149.28 (ipso to oxygen and m to phenyl), 143.60 (ipso to oxygen and o to phenyl), 136.05
(ipso to phenyl and o to oxygen), 135.92 (C_1'), 129.32 (C_2'), 128.64 (C_3'), 128.32 (C_4'), 124.86 (o to oxygen and phenyl), 124.09 (o to oxygen and p to phenyl), 121.92 (o to oxygen and m to phenyl), 37.63 (-OSO_2CH_3), 21.03 (-OC(=O)CH_3); EIMS: m/e (%) = 306 (M^+, 14), 264 (23), 185 (100), 43 (42); HRMS calcd for C_{15}H_{14}O_5S 306.0562, found 306.0561.

**Preparation of 2,2'-Diphenyl-4,4'-dihydroxybiphenyl (5) from (10):**

A 125 mL Schlenk tube was charged with NiCl_2(PPh_3)_2 (65 mg, 0.10 mmol), PPh_3 (105 mg, 0.40 mmol), Zn powder (111 mg, 1.7 mmol), Et_4NI (386 mg, 1.5 mmol) and a magnetic stirring bar. After sealing the tube with a rubber septum, the content was dried at 25°C under reduced pressure (1 x 10^{-3} mmHg) for 10 h. Then the tube was filled with N_2 followed by three evacuation-filling cycles. Freshly distilled dioxane (0.50 ml) was added via a syringe through the rubber septum. The mixture was stirred at room temperature for 5 min and during this time the color of the mixture gradually changed from green into deep red brown. 10 (306 mg, 1.0 mmol) was dissolved in freshly distilled dioxane (0.50 ml) and added to the catalyst mixture via a syringe through the rubber septum. The reaction mixture was heated at 100 °C for 24 h, and then filtered. 1M aqueous NaOH (2 ml) was added to the filtrate and the mixture was stirred for 10 h at room temperature. The aqueous solution was then acidified with conc. HCl to pH ≈ 1. The resulting precipitate was collected by filtration, washed with water, and dried. Because of the difficulty of separating the product from the reaction mixture, the crude product was further converted into the corresponding bismesylate 12 and purified by column chromatography (vide infra); crude yield: 23 % by ^1H NMR.

**2,2'-Diphenyl-4,4'-bis(methylsulfonyloxy)biphenyl (12):**


This compound was prepared by the reaction of methanesulfonyl chloride with 5 in pyridine\textsuperscript{11} and purified by column chromatography (silica gel, hexanes/ethyl acetate); yield: 85 \%; white crystals; mp 58-61° C (benzene); \textsuperscript{1}H NMR (CDCl\textsubscript{3}/TMS): \(\delta=7.47\) (d, \(J=8.4\) Hz, 2H, \(m\) to oxygen and phenyl), 7.35-7.30 (m, 4H, aromatic protons), 7.14-6.98 (m, 6H, aromatic protons), 6.54 (d, \(J=7.06\) Hz, 4H, \(\sigma\) protons on phenyl), 3.17 (s, 6H, -OSO\textsubscript{2}CH\textsubscript{3}); \textsuperscript{13}C\{\textsuperscript{1}H\} NMR (CDCl\textsubscript{3}/TMS): \(\delta=148.71\) (ipso to oxygen), 143.04 (p to oxygen), 138.94 (m to oxygen and ipso to phenyl), 137.87 (ipso carbons on phenyl), 133.00 (\(\sigma\) to oxygen and phenyl), 128.95 (\(\sigma\) carbons on phenyl), 127.75 (m carbons on phenyl), 126.89 (p carbons on phenyl), 123.19 (\(\sigma\) to oxygen and \(\rho\) to phenyl), 120.61 (m to oxygen and phenyl), 37.50 (-OSO\textsubscript{2}CH\textsubscript{3}): EIMS: \(m/e\) (\%) = 494 (M\textsuperscript{+}, 100), 416 (7), 336 (79), 319 (25); HRMS calcd for C\textsubscript{26}H\textsubscript{22}O\textsubscript{6}S\textsubscript{2} 494.0858, found 494.0858.

4.3.-RESULTS AND DISCUSSION

Scheme I outlines the preparation of 5 from phenylhydroquinone 1. This general sequence of reactions consists of: i) protection of the 4-hydroxy group of 1 with an ethoxy group using \(\text{Et}_2\text{SO}_4/aq\ \text{NaOH}\), ii) conversion of 5-ethoxy-2-hydroxybiphenyl 2\textsubscript{a} to 5-ethoxy-2-(methylsulfonyloxy)biphenyl 3 using mesyl chloride, iii) Ni(0) catalyzed homocoupling of mesylate 3 to give 2,2'-diphenyl-4,4'-diethoxybiphenyl 4 and iv) cleavage of the ethoxy protecting groups of 4 resulting in the formation of 5.

An overall yield of 10 \% was obtained for the synthesis of 5 from 1 via this simple method. This new strategy appears to be quite general when the substituted hydroquinone necessary as starting material for the synthesis of various 2,2'-disubstituted-4,4'-dihydroxybiphenyl is available. However, the success of this synthetic procedure is highly dependent on: (a) the regioselective protection of the
hydroxy group from the 4-position of the substituted hydroquinone and (b) the steric and electronic effects of the substituent on the Ni(0) catalyzed homocoupling step (vide infra).

The regioselective monoprotection of the hydroxy group in high yield was one of the most difficult steps in the synthetic procedure from Scheme I. The use of classic protection methods for phenols, such as alkylation, was expected to result in the formation of a mixture of products including two isomeric monoprotected substituted hydroquinones. For example, the protection of the 4-hydroxy group of 1 was accomplished by the slow addition of stoichiometric amounts of diethyl sulfate to an aqueous solution of 1 and sodium hydroxide. A mixture of 3 products (i.e., 5-ethoxy-2-hydroxybiphenyl 2a, 2-ethoxy-5-hydroxybiphenyl 2b and 2,5-diethoxybiphenyl 2c) was obtained. Separation of 2a was accomplished (49% yield) by repeated purifications by column chromatography. The purification of the viscous oil 2a was tedious on a preparative scale. Therefore, a method to efficiently protect the 4-hydroxy group with higher yield and selectivity was required to enhance the synthetic utility of this procedure.

The alternative synthetic route outlined in Scheme II was developed. This method started from the commercially available 2-phenylphenol 6. The quantitative conversion of 6 to 2-acetoxybiphenyl 7 was accomplished by treatment with acetic anhydride. The Fries rearrangement of 7 was performed by heating a mixture of 7 and AlCl3 to 130°C for 3h. The two isomers 2-phenyl-4-acetylphenol 8a (69% yield) and 2-phenyl-6-acetylphenol 8b (28% yield) resulted from this reaction. The desired product 8a was isolated by fractional recrystallization. The use of a one pot reported procedure involving the conversion of 6 to 7 by treatment with acetyl chloride and a catalytic amounts of AlCl3 in nitrobenzene followed by addition of AlCl3 at 40-45°C produced only small amounts of 8a after 24h. Oxidation of 8a by a Bayer-Villiger
reaction gave 2-phenyl-4-acetoxyphenol \( 9 \) in 90 \% yield. In contrast to \( 2a, 9 \) and its precursor \( 8a \) were obtained more selectively. In addition, these compounds are crystalline solids, and could be purified by recrystallization. Treatment of \( 9 \) with mesyl chloride in pyridine afforded the corresponding 5-acetoxy-2-(methylsulfonyloxy)biphenyl 10.

The key step of these two reaction schemes was the homocoupling reaction of the mesylate 10 mediated by a nickel catalyst generated from NiCl\(_2\)(PPh\(_3\))\(_2\) (0.10 equiv) in the presence of PPh\(_3\) (0.4 equiv), excess Zn (1.7 equiv), and Et\(_4\)NI (1.5 equiv). Low conversions were obtained when the Ni(0) catalyzed homocoupling was performed in THF at 67°C (<5 \% yield). An appreciable amount of unreacted starting material was recovered in this case and concomitant decomposition of the catalyst was observed suggesting that the rate of oxidative addition of the mesylate 10 to Ni(0) or Ni(I) species was very slow. One rationalization is that the oxidative addition of 10 to Ni(0) or Ni(I) was inhibited by steric hindrance due to the \( \sigma \)-phenyl group as well as the lack of activation of the leaving group. Ni(0) catalyzed aryl-aryl coupling reactions have been reported to be impeded by substituents in the ortho position.\(^8\) When the reaction was performed in dioxane at a higher temperature (100°C), a modest yield (23 \%) of the desired coupled product 5 was obtained. In addition to the dimer 5, the reduction product 11 (10 \%) was also detected. This is due to the fact that bulky ortho substituted aryl mesylates couple poorly due to steric hindrance, and side reactions compete with the homocoupling reaction. The rate of this reaction increased with an increase in temperature. However, the selectivity to the homocoupled product decreased. Trace amounts of transarylation byproducts were also obtained by the coupling of 10 with a phenyl group from PPh\(_3\). Phenyl group transfer from PPh\(_3\) is a common side reaction in Pd and Ni catalyzed reactions in the presence of PPh\(_3\).\(^9\) Although 5 was prepared by the sequence of reactions outlined in Scheme II, its
separation from the reaction mixture was difficult on a preparative scale. Therefore, after usual work-up the crude product was further mesylated and purified by column chromatography (See Experimental Section, *vide supra*). The bismesylate 12 can be purified easier than the corresponding bisphenol 5 and was used for analytical characterization. 200 MHz $^1$H-NMR spectrum of bismesylate 12 is presented in Figure 1.

4.4.-CONCLUSIONS

Nickel-catalyzed homocoupling of aryl mesylates of 4-protected-2-phenylhydroquinone was utilized in the key step of two reaction schemes which lead to the synthesis of novel and difficult to prepare by alternative methods, 2,2'-diphenyl-4,4'-dihydroxybiphenyl. One of these reaction routes is general for the preparation of other 2,2'-disubstituted-4,4'-dihydroxybiphenyl when the starting substituted hydroquinone is readily available.
Figure 1. 200 MHz $^1$H-NMR Spectrum of 2,2'-Diphenyl-4,4'-bis(methylsulfonyloxy) biphenyl(12).
REFERENCES


PART II. ARYL MESYLATES IN NICKEL-CATALYZED CROSS-COUPLING REACTIONS
5.1-INTRODUCTION

The palladium-catalyzed cross-coupling reaction of organoboron compounds (arylboronic acid and its esters) with aromatic organic electrophiles (i.e., aryl halides\textsuperscript{1a-f} and triflates\textsuperscript{1g-i,k}) in the presence of a base is known as the “Suzuki reaction”. It represents an important method for the formation of aromatic carbon-carbon bond.\textsuperscript{1,2} Several factors such as, high yields obtained with many substrates, wide range of functional groups including ester, ketone and aldehyde tolerated on either coupling partner, and the regiospecificity, stereospecificity and lack of sensitivity towards steric hindrance\textsuperscript{1a-b,j} make this reaction particularly attractive and versatile.

The use of organoboron compounds, especially arylboronic acids, as coupling partner has several attractive features: they are readily synthetically accessible and generally stable in air and high temperature under usual reaction conditions, in most cases they can be purified by recrystallization from water, ethanol, or sublimation, the separation of excess arylboronic acid from the reaction products is relatively facile, and they are much less toxic than some other alternative organometallic reagents.\textsuperscript{2a}

The most reactive and therefore often used aryl halides in Suzuki reaction are aryl bromides and iodides.\textsuperscript{1a-f} Aryl chlorides do not participate in this cross-coupling except when used in conjunction with electron deficient heteroaryl chlorides.\textsuperscript{2d,3} The use of aryl triflates (aryl trifluoromethanesulfonates), which are easily obtained from phenols, has been only recently demonstrated in the Suzuki reaction.\textsuperscript{1g-i,k}

Since a base is essential for the cross-coupling reaction of arylboronic acids with triflates (which are base-sensitive and thermally labile), mild reaction conditions
have been developed for this cross-coupling reaction. These include the selection of more effective catalysts such as PdCl₂(dpff),¹hg,k the utilization of relatively weak non-aqueous basic conditions such as powdered K₃PO₄ suspended in polar solvents (THF, dioxane) to prevent the saponification of base-sensitive triflates,¹hi-k and the addition of alkali metal halide to promote the cross-coupling and/or to prevent the premature catalyst decomposition.¹g,k One of the challenges in the Suzuki-type cross-coupling is to extend this reaction to electron-rich aryl triflates, less reactive aryl sulfonates and aryl chlorides, which show poor reactivity towards oxidative addition in the catalytic cycle. A recent approach to solve this problem involves the activation of the aryl triflate to oxidative addition by the complexation of an electron-withdrawing Cr(CO)₃ to the arene moiety.⁴

Up to date, alternative sulfonate leaving groups besides triflate have not been reported to be active in Suzuki-type reactions.²a-c,e Aryl mesylates, benzenesulfonates and tosylates which are much less expensive than triflates have poor reactivity towards palladium catalysts.

In chapter 2, we have demonstrated that unreactive aryl sulfonates including mesylate are converted in high yields to biaryls by homocoupling in the presence of zero valent nickel catalysts generated in situ.⁵ In this reaction, aryl mesylates undergo oxidative addition to Ni(0) complexes. Since the Suzuki-type cross-coupling reaction also involves oxidative addition (followed by transmetallation and reductive elimination) in the reaction cycle, we decided to use a nickel catalyst for the unprecedented cross-coupling reaction of aryl mesylates with arylboronic acids. In this chapter, the expansion of the utility of mesylate leaving group to the novel nickel-catalyzed Suzuki-type cross-coupling reaction will be demonstrated.

5.2.-EXPERIMENTAL
5.2.1.-Materials

Triphenylphosphine (99%), 1,1'-bis(diphenylphosphino)ferrocene (97%), 1,2-bis(diphenylphosphino)ethane (97%) and 1,3-bis(diphenylphosphino)propane (97%) from Aldrich were used as received. All other reagents, including phenols, were purchased from commercial sources (Aldrich or Lancaster) and used without further purification except when reported. Pyridine was dried over CaH\textsubscript{2} and distilled. THF, dioxane and toluene were distilled from sodium-benzophenone ketyl. Zinc dust (325 mesh) was stirred in acetic acid, washed with water and dried in vacuo at 120°C. Unless otherwise noted, all compounds synthesized in the present paper were purified until their 200 MHz \textsuperscript{1}H-NMR spectra corresponded to the expected structure and the purity was established by comparison with published mp or found to be higher than 99.5% by GC or HPLC.

**Palladium Catalysts**

Pd(OAc)$_2$ [palladium(II) acetate], PdCl$_2$(PPh$_3$)$_2$ [dichlorobis(triphenylphosphine)palladium(II)] and Pd$_2$(dba)$_3$ [tris(dibenzylideneacetone)dipalladium] from Aldrich were used as received. Pd(PPh$_3$)$_4$ [tetrakis(triphenylphosphine)palladium(0)]$^{19}$ and PdCl$_2$(dpff) [dichloro[1,1'-bis(diphenylphosphino)ferrocene]palladium(II)]$^{68}$ were prepared according to literature procedures.

**Nickel Catalysts**

NiCl$_2$(PPh$_3$)$_2$ [dichlorobis(triphenylphosphine)nickel(II)]$^{20}$, NiCl$_2$(dpff) [dichloro[1,1'-bis(diphenylphosphino)ferrocene]nickel(II)]$^{21}$, NiCl$_2$(dppe) [dichloro[1,2-bis(diphenylphosphino)ethane]nickel(II)]$^{22}$ and NiCl$_2$(dppe)
[dichloro[1,3-bis(diphenylphosphino)propane]nickel(II)]\textsuperscript{23} were prepared according to literature procedures.

5.2.2.-Techniques

GC analyses were performed on a Hewlett Packard 5890 gas chromatograph using a flame ionization detector and a 3\% SP-2250 column. The yields were determined by quantitative GC using diphenyl ether as an internal standard, and in some cases by \textsuperscript{1}H-NMR spectroscopy.

5.2.3.-Synthesis of Aryl Sulfonates

The preparations of methyl 4-(trifluoromethyl)sulfonyloxy)benzoate, methyl 4-(((4-fluorophenyl)sulfonyl)oxy)benzoate, 4-acetylphenyl p-fluorobenzenesulfonate, methyl 4-(((4-phenylsulfonyl)oxy)benzoate, methyl 4-(((4-methylphenyl)sulfonyl)oxy)benzoate, methyl 4-methylsulfonyloxybenzoate, phenyl methanesulfonate, 4-acetylphenyl methanesulfonate, 4-tolyl methanesulfonate, and 4-methoxyphenyl methanesulfonate from the corresponding phenols are presented in chapter 2.

5.2.4.-Synthesis of Arylboronic Acids

Phenylboronic acid and 4-methoxyphenylboronic acid were prepared according to the literature procedures.\textsuperscript{24}

\textbf{Phenylboronic acid:} white crystals; mp 218°C (EtOH) (lit.\textsuperscript{24} 217-220°C).
\textbf{4-Methoxyphenylboronic acid:} white crystals; mp 206°C (EtOH) (lit.\textsuperscript{24} 207°C).

5.2.5.-General Procedure for Palladium-Catalyzed Cross-Coupling
A 25 ml three-neck flask equipped with a reflux condenser, nitrogen inlet and rubber septum was charged with aryl sulphonate (0.5 mmol), LiCl (1.5 mmol), aq 2M-Na$_2$CO$_3$ (0.65 ml) and toluene (4 ml). The flask was flushed with nitrogen and the palladium catalyst (0.025 mmol) was added. Arylboronic acid (0.55 mmol) in ethanol (1 ml) was added via a syringe through the rubber septum. Then the mixture was stirred at 90°C under N$_2$ for 12h. The actual yields based on percent conversion of the starting aryl sulphonate were determined by GC measurements using diphenyl ether as an internal standard. The GC yields are summarized in Table I.

5.2.6.-General Procedure for Ni(0)-Catalyzed Cross-Coupling

All reactions were carried out under nitrogen using oven-dried (110°C) glassware. In a typical reaction a 125 mL Schlenk tube was charged with aryl sulphonate (0.5 mmol), arylboronic acid (0.55 mmol), NiCl$_2$(dppe) (0.05 mmol), Zn powder (0.86 mmol), K$_3$PO$_4$ (1.5 mmol) and a magnetic stirring bar. After sealing the tube with a rubber septum, the content was dried at 25°C under reduced pressure (1 $\times$ 10$^{-3}$ mmHg) for 3h. Then the tube was filled with N$_2$ followed by three evacuation-filling cycles. Freshly distilled THF (1.0 ml) was added via a syringe through the rubber septum. The reaction mixture was heated to the reflux temperature and stirred at this temperature for 24 h. Then it was cooled to 25°C, filtered, diluted with water, extracted with CHCl$_3$, dried (MgSO$_4$) and the solvent evaporated in vacuo. The corresponding biaryl was purified by column chromatography (silica gel, hexanes/ethyl acetate) and recrystallized from CHCl$_3$/hexanes. The actual yields based on percent conversion of the starting aryl sulphonate were determined by GC measurements using diphenyl ether as an internal standard. The GC yields are summarized in Table II and III.
Biaryls

4-Carbomethoxybiphenyl: white crystals; mp 116-117°C (benzene) (lit.\textsuperscript{25} 117.5°C).

4-Acetylbutphenyl: white needles; mp 119-120°C (ethanol) (lit.\textsuperscript{26} 121°C).

4-Methylbiphenyl: white crystals; mp 47-48°C (hexanes) (lit.\textsuperscript{27} 47.5°C).

4-Methoxybiphenyl: white crystals; mp 87-88°C (benzene) (lit.\textsuperscript{27} 89-90°C).

5.3.-RESULTS AND DISCUSSION

5.3.1.-Palladium-Catalyzed Cross-Coupling

An initial series of experiments was performed in order to determine the feasibility of using alternative sulfonate leaving groups besides triflate in the Pd(0) catalyzed cross-coupling reaction of aryl sulfonates with phenylboronic acid (Table I). The cross-coupling reaction of various aryl sulfonates and phenylboronic acid was mediated in toluene by the Pd(0) catalyst [Pd(PPh\textsubscript{3})\textsubscript{4}] in the presence of LiCl and 2M Na\textsubscript{2}CO\textsubscript{3}. These reaction conditions are typical for the Suzuki reaction\textsuperscript{1a-e} and were slightly modified by comparison to those used for the cross-coupling of aryl bromide with phenylboronic acid.\textsuperscript{1a} Under these conditions with various p-carbomethoxyphenyl sulfonates only the triflate leaving group gave high yield (>99%) (Table I, entry 1). p-Fluorobenzene sulfonate and methane sulfonate did not undergo the cross-coupling reaction (Table I, entry 2&3). The unreacted starting substrates were isolated from these experiments.

Few other Pd catalysts were investigated (Table I, entries 4-7). PdCl\textsubscript{2}(PPh\textsubscript{3})\textsubscript{2} and Pd(OAc)\textsubscript{2} gave no cross-coupled product (Table I, entries 4-6). PdCl\textsubscript{2}(dppf), an effective catalyst for Suzuki coupling\textsuperscript{1h,k} and other cross-coupling reactions\textsuperscript{6} was found to catalyze the reaction, although the yield was relatively low (25%) (Table I, entry 7). The low yield could be due to the early catalyst decomposition which was observed with PdCl\textsubscript{2}(dppf). Therefore, 1 equiv of PPh\textsubscript{3} relative to PdCl\textsubscript{2}(dppf) was
Table I. Pd(0)-Catalyzed Cross-Coupling of Various Aryl Sulfonates with Phenylboronic Acid\(^a\)

![Chemical Reaction Diagram]

<table>
<thead>
<tr>
<th>Entry</th>
<th>R</th>
<th>X</th>
<th>Catalyst</th>
<th>Yield(^b(%))</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>CH(_3)O(_2)C</td>
<td>CF(_3)SO(_2)O</td>
<td>Pd(PPh(_3))(_4)</td>
<td>&gt;99</td>
</tr>
<tr>
<td>2</td>
<td>CH(_3)O(_2)C</td>
<td>(p)-FPhSO(_2)O</td>
<td>Pd(PPh(_3))(_4)</td>
<td>0</td>
</tr>
<tr>
<td>3</td>
<td>CH(_3)O(_2)C</td>
<td>CH(_3)SO(_2)O</td>
<td>Pd(PPh(_3))(_4)</td>
<td>0</td>
</tr>
<tr>
<td>4</td>
<td>CH(_3)O(_2)C</td>
<td>CH(_3)SO(_2)O</td>
<td>PdCl(_2)(PPh(_3))(_2)</td>
<td>0</td>
</tr>
<tr>
<td>5</td>
<td>CH(_3)O(_2)C</td>
<td>CH(_3)SO(_2)O</td>
<td>Pd(OAc(_2))(_2) + 2 eq PPh(_3)(^c)</td>
<td>0</td>
</tr>
<tr>
<td>6</td>
<td>CH(_3)O(_2)C</td>
<td>CH(_3)SO(_2)O</td>
<td>Pd(OAc(_2))(_2)+1.1 eq dppp(^c)</td>
<td>Traces</td>
</tr>
<tr>
<td>7</td>
<td>CH(_3)O(_2)C</td>
<td>CH(_3)SO(_2)O</td>
<td>PdCl(_2)(dppf)</td>
<td>25(^d)</td>
</tr>
<tr>
<td>8</td>
<td>CH(_3)O(_2)C</td>
<td>CH(_3)SO(_2)O</td>
<td>PdCl(_2)(dppf)</td>
<td>5(^{de})</td>
</tr>
<tr>
<td>9</td>
<td>CH(_3)O(_2)C</td>
<td>CH(_3)SO(_2)O</td>
<td>PdCl(_2)(dppf)+1 eq PPh(_3)(^c)</td>
<td>Traces</td>
</tr>
<tr>
<td>10</td>
<td>CH(_3)O(_2)C</td>
<td>(p)-FPhSO(_2)O</td>
<td>PdCl(_2)(dppf)</td>
<td>21(^d)</td>
</tr>
<tr>
<td>11</td>
<td>CH(_3)O(_2)C</td>
<td>CH(_3)SO(_2)O</td>
<td>PdCl(_2)(dppf)</td>
<td>0(^d)</td>
</tr>
<tr>
<td>12</td>
<td>CH(_3)O(_2)C</td>
<td>CH(_3)SO(_2)O</td>
<td>Pd(OAc(_2))(_2)+1.1 eq dppp(^c)</td>
<td>17(^f)</td>
</tr>
</tbody>
</table>

\(^a\) Reactions were run with 5 mol\% Pd catalyst, 3 equiv of LiCl, and 2.6 equiv of aq Na\(_2\)CO\(_3\) in a mixture of Tol+EtOH at 90°C under N\(_2\) for 12h, unless otherwise noted.

\(^b\) Actual yields determined by GC measurements were based on percent conversion of the starting substrate.

\(^c\) equiv relative to Pd catalyst.

\(^d\) Catalyst decomposed in the early stage of the reaction.

\(^e\) Reaction run in the absence of LiCl.

\(^f\) Trace amounts of acetophenone was detected by GC.
added to the reaction in order to prevent the premature catalyst decomposition. Although this resulted in a substantial enhancement of the stability of the catalyst, the additional PPh$_3$ totally suppressed the cross-coupling reaction (Table I, entry 9). It is likely that the electronic and steric features of dppf ligand play important roles in this cross-coupling reaction. However, the stabilization of the catalyst via the addition of dppf did not improve the yield. LiCl, which was reported to be necessary in the reaction of triflates with boronic acids$^{18}$, was found to be essential for the Pd catalyzed reaction. In the absence of LiCl, much faster catalyst decomposition occurred, resulting in a very low reaction yield (Table I, entry 8).

The effect of various Pd catalysts, when the substrates were $p$-acetyl substituted aryl sulfonates was studied (Table I, entries 10-12). The $p$-fluorobenzene sulfonyl leaving group gave 21% yield, when using PdCl$_2$(dppf) (Table I, entry 10). In contrast, methane sulfonate was quite inert under the same conditions (Table I, entry 11). However, when the catalyst was changed to Pd(OAc)$_2$ with dppp present as a ligand a 17% yield of cross-coupled product was obtained (Table I, entry 12). No further improvement in yield was obtained by employing various reaction conditions.

Phosphine-free ligandless Pd catalysts such as Pd$_2$(dba)$_3$ are known to be the most efficient catalysts for the Stille cross-coupling reaction.$^{7a}$ After our work was completed, it has been reported that Pd$_2$(dba)$_3$·C$_6$H$_6$ under suitable reaction conditions is also the most efficient catalyst for the Suzuki coupling.$^{1f}$ However, the use of the ligandless catalyst [Pd$_2$(dba)$_3$] under conventional conditions did not result in cross-coupled product formation. The utilization of bulky monodentate ligands$^{7b-d}$[P(Cy)$_3$, AsPh$_3$ and P(o-tolyl)$_3$] and bidentate ligands (dppe and dppp)$^{7e}$, which have been reported to accelerate the oxidative addition in other Pd catalyzed cross-coupling reactions, did not produce any cross-coupled product. The use of anhydrous basic conditions (K$_3$PO$_4$ in dioxane)$^{1h,j-k}$ also resulted in failure.
The mechanistic sequence of reactions for the transition metal catalyzed cross-coupling reactions generally involves the sequence: oxidative addition, transmetallation, and reductive elimination.\(^8\) The reductive elimination step is expected to be identical regardless of whether an aryl triflate or aryl mesylate is involved in the reaction. In the reaction of aryl halides with aryl boron acids, a ligand exchange reaction between the halide and an OH\(^{-}\) ion was proposed to take place prior to the transmetallation step.\(^2a,9\)

If a similar ligand exchange reaction takes place between the sulfonate group and an OH\(^{-}\) ion, the transmetallation step would be identical for both aryl triflates and aryl mesylates. Therefore, the transmetallation and reductive elimination steps are not expected to account for the difference in reactivity. If a ligand exchange reaction takes place in the case of aryl sulfonates between the sulfonate group and an OH\(^{-}\) ion prior to transmetallation, the physical properties of the sulfonate are expected to influence the rate of this reaction. However, if the oxidative addition product of aryl mesylate to Pd(0) has ionic character,\(^10\) i.e., [ArPd(PPh\(_3\))\(_2\)]\(^{+}\)[OMs]\(^{-}\), the difference between triflate and mesylate groups may not have a significant impact on the reaction rate of this step. In addition, the difference in leaving group ability (between triflate and mesylate) is expected to influence the rate of oxidative addition.\(^11\) Therefore, it is possible that the low yields obtained in the preceding reaction are the result of a slow rate of oxidative addition of aryl mesylates to the \textit{in situ} generated Pd(0) species. In order to accelerate the rate of oxidative addition by making the Pd catalyst more nucleophilic, various kinds of palladium catalysts were employed. Among them, PdCl\(_2\)(dppf) was found to be the most reactive catalyst, although the obtained yield was not satisfactory enough to be useful for organic reactions. These results indicate that the low yields obtained in Pd(0) catalyzed cross-coupling reactions of aryl mesylates with phenylboronic acid may be due to an inherent low reactivity of aryl mesylates towards Pd(0) species in the oxidative addition step.
5.3.2.-Nickel-Catalyzed Cross-Coupling

Although aryl mesylates and arenesulfonates have a low reactivity towards Pd(0) species, they undergo oxidative addition to Ni(0) complexes.\(^5\) Ni(0) is a stronger nucleophile than Pd(0). The Ni(II) species resulting from the oxidative addition can undergo a further high yield reaction in the presence of Zn with additional aryl mesylate to give symmetrical homocoupled biaryls (eq 1).

\[
\begin{align*}
\text{CH}_{3}\text{-C-} & \text{-} \text{O-} \text{OMs} & \xrightarrow{\text{NiCl}_2(\text{PPh}_3)_2, \text{Zn}, \text{Et}_4\text{N}, \text{THF}} & \text{CH}_{3}\text{-C-} & \text{-} \text{O-} \text{OMs} & \text{NiCl}_2(\text{PPh}_3)_2, \text{Zn} \\
& & & \text{Et}_4\text{N}, \text{THF} & & 67^\circ\text{C}, 10\text{h} & \rightarrow & \text{CH}_{3}\text{-C-} & \text{-} \text{O-} \text{OMs} & \xrightarrow{\text{NiCl}_2(\text{PPh}_3)_2, \text{Zn}, \text{Et}_4\text{N}, \text{THF}} & \text{CH}_{3}\text{-C-} & \text{-} \text{O-} \text{OMs} & \text{NiCl}_2(\text{PPh}_3)_2, \text{Zn} \\
& & & & & & & \rightarrow & \text{CH}_{3}\text{-C-} & \text{-} \text{O-} \text{OMs} & \text{NiCl}_2(\text{PPh}_3)_2, \text{Zn} \\
& & & & & & & & & 67^\circ\text{C}, 10\text{h} & \rightarrow & \text{CH}_{3}\text{-C-} & \text{-} \text{O-} \text{OMs} & \text{NiCl}_2(\text{PPh}_3)_2, \text{Zn} \\
& & & & & & & & & & & \rightarrow & 73\% & \text{NiCl}_2(\text{PPh}_3)_2, \text{Zn} \\
\end{align*}
\]

This indicates that Ni(0) is sufficiently nucleophilic to undergo oxidative addition reactions with aryl mesylates. In addition, the resulting Ni(II) species can participate in further productive reactions with organic nucleophiles. Therefore, the utility of Ni(0) catalysts in the cross-coupling reaction of aryl mesylates with phenylboronic acid was investigated.

It was found that a Ni(0) species incorporating the 1,1′-bis(diphenylphosphino)ferrocene (dpff) ligand is an effective catalyst for the cross-coupling reaction (Table II). Thus moderate yields with high selectivity, were obtained using 10 mol % NiCl\(_2\)(dpff) in the presence of 1.7 equivalents Zn and 3.0 equivalents K\(_3\)PO\(_4\) in THF at 67°C (eq 2).

\[
\begin{align*}
\text{CH}_{3}\text{-C-} & \text{-} \text{O-} \text{OMs} & \xrightarrow{\text{NiCl}_2(\text{dpff}), \text{Zn}, \text{K}_3\text{PO}_4, \text{THF}} & \text{CH}_{3}\text{-C-} & \text{-} \text{O-} \text{OMs} & \text{NiCl}_2(\text{dpff}), \text{Zn} \\
& & & \text{K}_3\text{PO}_4, \text{THF} & & 67^\circ\text{C}, 24\text{h} & \rightarrow & \text{CH}_{3}\text{-C-} & \text{-} \text{O-} \text{OMs} & \text{NiCl}_2(\text{dpff}), \text{Zn} \\
& & & & & & & \rightarrow & \text{CH}_{3}\text{-C-} & \text{-} \text{O-} \text{OMs} & \text{NiCl}_2(\text{dpff}), \text{Zn} \\
& & & & & & & & & 67^\circ\text{C}, 24\text{h} & \rightarrow & \text{CH}_{3}\text{-C-} & \text{-} \text{O-} \text{OMs} & \text{NiCl}_2(\text{dpff}), \text{Zn} \\
& & & & & & & & & & & \rightarrow & 51\% & \text{NiCl}_2(\text{dpff}), \text{Zn} \\
\end{align*}
\]
Table II. Ni(0)-Catalyzed Cross-Coupling of Various Aryl Sulfonates with Phenylboronic Acid<sup>a</sup>

\[
\begin{align*}
R\text{-}[\text{ArX}] + [\text{ArB(OH)}_2] & \xrightarrow{\text{NiCl}_2(\text{dppf})} \xrightarrow{\text{Zn}, \text{K}_3\text{PO}_4} \xrightarrow{\text{THF}, 67^\circ \text{C}} \text{[Ar-Ar']} \\
\end{align*}
\]

<table>
<thead>
<tr>
<th>Entry</th>
<th>R</th>
<th>X</th>
<th>GC Yield (%)</th>
<th>Ar-Ar'</th>
<th>Ar-H</th>
<th>Ar-Ar</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>CH₃O₂C</td>
<td>CF₃SO₂O</td>
<td>80</td>
<td>19</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>CH₃O₂C</td>
<td>p-FPhSO₂O</td>
<td>42</td>
<td>Traces</td>
<td>0&lt;sup&gt;b&lt;/sup&gt;</td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>CH₃O₂C</td>
<td>p-CH₃PhSO₂O</td>
<td>40</td>
<td>Traces</td>
<td>Traces&lt;sup&gt;b&lt;/sup&gt;</td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>CH₃O₂C</td>
<td>PhSO₂O</td>
<td>37</td>
<td>0</td>
<td>0&lt;sup&gt;b&lt;/sup&gt;</td>
<td></td>
</tr>
<tr>
<td>5</td>
<td>CH₃O₂C</td>
<td>CH₃SO₂O</td>
<td>48</td>
<td>Traces</td>
<td>0&lt;sup&gt;b&lt;/sup&gt;</td>
<td></td>
</tr>
<tr>
<td>6</td>
<td>CH₃CO</td>
<td>CH₃SO₂O</td>
<td>51</td>
<td>Traces</td>
<td>Traces&lt;sup&gt;b&lt;/sup&gt;</td>
<td></td>
</tr>
<tr>
<td>7</td>
<td>CH₃</td>
<td>CH₃SO₂O</td>
<td>33&lt;sup&gt;b&lt;/sup&gt;</td>
<td>-</td>
<td>-</td>
<td></td>
</tr>
<tr>
<td>8</td>
<td>CH₃O</td>
<td>CH₃SO₂O</td>
<td>39&lt;sup&gt;b&lt;/sup&gt;</td>
<td>-</td>
<td>-</td>
<td></td>
</tr>
</tbody>
</table>

<sup>a</sup> Reactions were run with 10 mol% NiCl₂(dppf), 1.7 equiv of Zn, and 3 equiv of K₃PO₄ in THF at 67°C under N₂ for 24h. <sup>b</sup>The remaining material isolated was unreacted starting substrate.
Significantly, only trace amounts (<1%) of homocoupled product was detected. Thus slight changes in the reaction conditions (most significantly: the substitution of dppf for PPh₃, the addition of phenylboronic acid and K₃PO₄) virtually closed the reaction pathway which leads to the homocoupled product. This result is very important because this is the first example in which a Ni catalyst is used in a Suzuki reaction. The substitution of Ni catalysts for Pd catalysts represents significant cost savings. In addition, the substitution of the mesylate leaving group for triflate is an improvement on the basis of both ease of synthesis and cost.

The dppf ligand has been shown to be an excellent ligand in other cross-coupling reactions.⁶ The high selectivity and moderate reactivity are due to the electronic and steric features of the dppf ligand. Dppf ligand is known to increase the nucleophilicity of the transition metal (Ni or Pd), and also facilitate the reductive elimination of diorganometal complex (R-M-R'), leading to carbon-carbon bond formation.⁶c The effect of dppf ligand in Pd(0) catalyzed cross-coupling of aryl mesylates with phenylboronic acid was also observed, although the yield was relatively low (vide supra). NiCl₂(dppf) catalyzed cross-coupling of unactivated electrophiles with Grignard reagents,¹² and with diorganozinc reagents¹³ were reported.

The first report of cross-coupling of aryl halides with phenylboronic acid, the Suzuki reaction, employed benzene or toluene as the solvent, and aqueous Na₂CO₃ solution which was proposed to accelerate the rate of transmetallation step of the catalytic cycle.¹ᵃ⁻ᵉ In contrast to other cross-coupling reactions such as Grignard, organotin, and organozinc reactions, the base is essential in the Suzuki reaction. Although extensive studies have been made on the effect of various kinds of base, aqueous systems containing inorganic bases such as Na₂CO₃ have been proved to be the most effective.²ᵃ However, the aqueous systems can not be employed in Ni(0)
catalyzed coupling reaction, since protic sources such as water deactivate the nickel catalyst and also generate substantial amounts of reduction side product.\textsuperscript{14}

Recently, it was reported that a non-aqueous system consisting of powdered K\textsubscript{3}PO\textsubscript{4} suspended in dioxane is sufficient to accelerate the coupling reaction of aryl triflate with organoboron compounds.\textsuperscript{1h,j-k} THF has been found to be an efficient solvent in reference to the rate and selectivity of the Ni(0) catalyzed homocoupling reaction.\textsuperscript{5} Therefore, THF was employed as the solvent and K\textsubscript{3}PO\textsubscript{4} as the base for the initial studies of Ni(0) catalyzed cross-coupling of various aryl sulfonates including mesylate with phenylboronic acid. The results are summarized in Table II.

A series of the nickel-catalyzed cross-coupling reactions was carried out with various \textit{p}-carboxmethoxyphenyl sulfonates, in order to evaluate the relative effectiveness of several sulfonate leaving groups (Table II, entries 1-5). Of the sulfonates examined, the triflate group is the most reactive leaving group.\textsuperscript{15} The highest yield (80\%) of the cross-coupled product was obtained with the triflate leaving group (Table II, entry 1). However, substantial amounts of reduction side products were observed (19\%). The use of four other less reactive sulfonate leaving groups, \textit{p}-fluorobenzene sulfonate, \textit{p}-toluene sulfonate, benzene sulfonate, and methane sulfonate, resulted in moderate yields (37-48\%) (Table II, entries 2-5). It is noteworthy that these four sulfonates including mesylate, which are apparently much less reactive than triflate, gave cross-coupled products highly selectively with only trace amounts (<1\%) of side reaction products. Most of the isolated materials were unreacted starting substrates. In comparison with Pd(0) catalyzed Suzuki reaction of aryl mesylate with phenylboronic acid (Table I, entry 7), the Ni(0) mediated cross-coupling reaction gave much higher yields of cross-coupled product (Table II, entry 5).

The effect of various substituents on the cross-coupling reaction, when using mesylate leaving group, was studied (Table II, entry 5-8). Higher yields were obtained
when using electron withdrawing $p$-acetyl and $p$-carbomethoxyphenyl mesylates, which are substantially more reactive than both the electron donating $p$-methyl and $p$-methoxyphenyl mesylates.

In order to further improve the yield of Ni(0) catalyzed cross-coupling of methyl 4-(methylsulfonyloxy)benzoate with phenylboronic acid, various reaction conditions were employed (Table III). The effect of the amount of the base, K$_3$PO$_4$, was studied in both THF and dioxane (Table III, entries 1-2, 11, and 14-15). At 67°C in THF, a doubling of the amount of K$_3$PO$_4$ resulted in a slightly increased yield (cf. Table III, entries 1 & 2). In contrast, at 95°C in dioxane, the effect of the amount of K$_3$PO$_4$ was more pronounced (Table III, entries 11 vs. 14). A substantially increased yield (67%) was obtained with 3.0 equiv of K$_3$PO$_4$ at 95°C, although side reactions such as reduction (4%) and O-S bond cleavage (8%) occurred (Table III, entry 14). However, when the reaction was performed at 70°C in the presence of 3.0 equiv of K$_3$PO$_4$, the yield decreased (48%) (cf. Table III, entries 14 & 15). These results can be rationalized as follows. The reaction step involving base may occur partly through a heterogeneous mechanism because of the low solubility of K$_3$PO$_4$ in THF or dioxane. As a result, relatively large amounts of K$_3$PO$_4$ are necessary to accelerate the transmetalation step of the catalytic cycle. The yield increased as the relative amount of K$_3$PO$_4$ increased (Table III, entry 1 vs. 2 & 11 vs. 14). Therefore, an additive effect of K$_3$PO$_4$ was evident for this coupling reaction. However, this additive effect was less significant, when using THF at low temperature (67°C) (Table III, entry 1 vs. 2). In contrast, when using dioxane at an elevated temperature (95°C), the K$_3$PO$_4$ additive effect became dramatic due to the enhanced solubility of K$_3$PO$_4$, with a significant increase in yield (Table III, entries 11 vs. 14). When the reaction temperature was lowered to 70°C, the yield also decreased. This could be due to the decreased solubility of K$_3$PO$_4$ and/or decreased reactivity of mesylate (Table III, entries 14 vs. 15).
Table III. Effect of Various Reaction Conditions on the NiCl₂(dppf)-Catalyzed Cross-Coupling of Methyl 4-(methylsulfonyloxy)benzoate [Ar-OSO₂CH₃] with Phenylboronic Acid [Ar′B(OH)₂]⁺

<table>
<thead>
<tr>
<th>Entry</th>
<th>Solvent</th>
<th>Temp (°C)</th>
<th>Base (equiv)</th>
<th>Halide (equiv)</th>
<th>GC Yield (%)</th>
<th>Ar-Ar'</th>
<th>Ar-H</th>
<th>Ar-Ar</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>THF</td>
<td>67</td>
<td>K₃PO₄(1.5)</td>
<td>none</td>
<td>41</td>
<td>Traces</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>2</td>
<td>THF</td>
<td>67</td>
<td>K₃PO₄(3.0)</td>
<td>none</td>
<td>48</td>
<td>Traces</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>3ᵇ</td>
<td>THF</td>
<td>67</td>
<td>K₃PO₄(3.0)</td>
<td>none</td>
<td>37</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>4ᶜ</td>
<td>THF</td>
<td>67</td>
<td>K₃PO₄(3.0)</td>
<td>none</td>
<td>16</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>5ᵈ</td>
<td>THF</td>
<td>67</td>
<td>K₃PO₄(3.0)</td>
<td>none</td>
<td>36</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>6</td>
<td>THF</td>
<td>67</td>
<td>K₃PO₄(3.0)</td>
<td>Et₄NI(1.0)</td>
<td>46</td>
<td>Traces</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>7</td>
<td>THF</td>
<td>67</td>
<td>K₃PO₄(3.0)</td>
<td>KBr(2.0)</td>
<td>46</td>
<td>&lt;1</td>
<td>Traces</td>
<td>0</td>
</tr>
<tr>
<td>8</td>
<td>THF</td>
<td>67</td>
<td>Na₂CO₃(2.0)</td>
<td>none</td>
<td>30</td>
<td>13</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>9ᵉ</td>
<td>THF</td>
<td>67</td>
<td>K₃PO₄(3.0)</td>
<td>none</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>10ᶠ</td>
<td>THF</td>
<td>67</td>
<td>K₃PO₄(3.0)</td>
<td>none</td>
<td>54</td>
<td>4</td>
<td>3</td>
<td></td>
</tr>
<tr>
<td>11</td>
<td>dioxane</td>
<td>95</td>
<td>K₃PO₄(1.5)</td>
<td>none</td>
<td>36</td>
<td>2</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>12</td>
<td>dioxane</td>
<td>95</td>
<td>K₃PO₄(1.5)</td>
<td>LiCl(3.0)</td>
<td>27</td>
<td>3</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>13&lt;sup&gt;g&lt;/sup&gt;</td>
<td>dioxane</td>
<td>95</td>
<td>K₃PO₄(1.5)</td>
<td>none</td>
<td>18</td>
<td>5</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>14&lt;sup&gt;h&lt;/sup&gt;</td>
<td>dioxane</td>
<td>95</td>
<td>K₃PO₄(3.0)</td>
<td>none</td>
<td>67</td>
<td>4</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>15</td>
<td>dioxane</td>
<td>70</td>
<td>K₃PO₄(3.0)</td>
<td>none</td>
<td>48</td>
<td>&lt;1</td>
<td>Traces</td>
<td></td>
</tr>
</tbody>
</table>

<sup>a</sup> Reactions were run with 10 mol% NiCl₂(dppe), 1.7 equiv of Zn, and a base as indicated in THF or dioxane under N₂ for 24h, unless otherwise noted. <sup>b</sup> NiCl₂(PPh₃)₂ was used instead of NiCl₂(dppe). <sup>c</sup> NiCl₂(dppe) was used instead of NiCl₂(dppe). <sup>d</sup> NiCl₂(dppe) was used instead of NiCl₂(dppe). <sup>e</sup> Reaction run in the absence of Zn. <sup>f</sup> Reaction run with 30 mol% NiCl₂(dppe). <sup>g</sup> Reaction run with 3 equiv of Zn. <sup>h</sup> Also produced methyl 4-hydroxybenzoate (8%).
The addition of Et₄NI as a halide source, which was reported to enhance the reaction rate of nickel catalyzed homocoupling of aryl mesylates,⁵ resulted in no change in yield (Table III, entry 6). The use of other halide sources (KBr and LiCl) was not effective (Table III, entries 7&12). The use of Na₂CO₃ instead of K₃PO₄ resulted in a decrease in yield, probably due to the lower solubility of Na₂CO₃ (Table III, entry 8).

In the absence of Zn, no cross-coupled product was obtained (Table III, entry 9). In the Ni(0) catalyzed homocoupling reaction, a reducing agent such as Zn is essential for the in situ generation of the reactive Ni(0) species from Ni(II). In contrast, in the Pd(0) catalyzed reaction, added base and/or solvent are sufficient to reduce the Pd(II) in situ to generate a Pd(0) species. No zinc additive effect was observed for the Ni(0) catalyzed cross-coupling reaction. Increased amounts of Zn actually resulted in a lower yield (Table III, entry 11 vs. 13).

In addition to NiCl₂(dppe), other nickel catalysts such as NiCl₂(PPh₃)₂, NiCl₂(dppe) and NiCl₂(dppp) were employed in the cross-coupling reaction (Table III, entries 2-5). The highest yields were obtained with NiCl₂(dppe). This is due to the unique electronic and steric features of the dppe ligand (vide supra) (Table III, entry 2). The nickel catalyst containing the monodentate PPh₃ ligand was less effective (Table III, entry 3). NiCl₂(dppe) and NiCl₂(dppp) appeared to generate a too stable Ni(0) bidentate ligand complex, resulting in low yields (Table III, entries 4-5). The superiority of bulky dppe ligand over other ligands may be due to an enhanced rate of oxidative addition step by ready formation of a more coordinatively unsaturated nickel species and/or by electron-rich ferrocene moieties. When the amount of NiCl₂(dppe) catalyst was increased, a slight increase in yield was obtained (Table III, entry 10). No significant additive effect on the amount of Ni(0) catalyst was observed.

In regard to the solvent, the coupling proceeded very selectively in THF, resulting exclusively in cross-coupled product in moderate yield (48%) with trace
amounts of side reaction products (Table III, entry 2). When the reaction was carried out in dioxane at a higher temperature (95°C), a good yield (67%) of the desired cross-coupled product was obtained (Table III, entry 14). In addition to the cross-coupled biaryl product, reduction product (4%) and O-S bond cleavage product (8%) were also detected. The latter is probably due to the increased solubility of K$_3$PO$_4$ in dioxane at an elevated temperature (vide supra). The reactivity of the catalyst increased with an increase in temperature. However, the selectivity to the cross-coupled product decreased.

In summary, the highest yield (67%) in the cross-coupling reaction of methyl 4-(methylsulfonyloxy)benzoate with phenylboronic acid was obtained using 0.10 equivalents NiCl$_2$(dpdf), 3 equivalents K$_3$PO$_4$ and 1.7 equivalents Zn in dioxane at 95°C. The same reaction conditions with a slight increase in temperature to 100°C were utilized in the cross-coupling reaction of phenyl mesylate with 4-methoxyphenylboronic acid to give 81% yield of 4-methoxybiphenyl (eq 3).

\[ \text{OMs} + \text{B(OH)}_2 \xrightarrow{\text{NiCl}_2(\text{dpf}), \text{Zn}} \xrightarrow{\text{K}_3\text{PO}_4, \text{dioxane} \text{100°C, 24h}} \text{CH}_3\text{O} \text{CH}_3 \]

There were only trace amounts (<1%) of reduction side product and 18% of the unreacted mesylate. The reaction time is not optimized.

In chapter 2, it was demonstrated that activated aryl mesylates undergo oxidative addition to Ni(0) complexes, resulting in almost quantitative consumption of the starting substrates even though side reactions such as reduction and transarlylation occurred. From the control experiments, all the side reactions were found to occur after the oxidative addition step of the Ni(0) catalyzed homocoupling cycle.
On the other hand, in the present study of Ni(0) catalyzed cross-coupling reactions of aryl sulfonates (except aryl triflates) with arylboronic acids, incomplete reactions were often detected, and most of the materials isolated were unreacted starting substrates. This suggests that oxidative addition of aryl sulfonates including mesylate to Ni(0) complexes under cross-coupling conditions is relatively slow compared to the one under homocoupling conditions. In no case have we observed early formation of black colloidal nickel under Ni(0) catalyzed cross-coupling conditions.

The reason for this incomplete reaction is not clear at present. One possible explanation is that the nickel catalyst forms some type of complex with the polar boronic acid moiety that inhibits the oxidative addition of the aryl mesylate, thus preventing the cross-coupling reaction. This poisoning of the nickel catalyst by boronic acid would be expected to result in incomplete reaction and recovery of starting substrates without the formation of significant amounts of side reaction product. Another possibility is the poisoning of the Ni(0) catalyst by the oxidative addition of a carbon-boron bond of arylboronic acid to Ni(0) catalyst. Oxidative addition of arylboronic acid to naked Pd(0) to give \([\text{ArPd(OH)}_2]\) was recently reported in the Heck-type reaction.\(^{16}\) This poisoning of the Ni(0) catalyst by boronic acid would be expected to have a more significant effect on reaction yields with less reactive substrates (Compare Table II, entries 1 & 5). Complete consumption of aryl triflate occurs with 80% yield cross-coupled product and 20% yield side reaction products (Table II, entry 1), while with the less reactive aryl mesylate incomplete reaction is obtained (48% yield cross-coupled product and only trace amounts of side reaction product) (Table II, entry 5).

5.3.3.-Reaction Mechanism
The general mechanism of a transition-metal (Ni or Pd) catalyzed cross-coupling reaction between organoelectrophiles and organometallic reagents involves sequential oxidative addition, transmetallation and reductive elimination.\(^8\)

The transmetallation step has been considered as the rate-determining step among these three steps in the Pd catalyzed Suzuki reaction of aryl halides with arylboronic acids.\(^2a-c\) This is due to the low nucleophilic nature of arylboronic acid. Recent studies using electrospray ionization mass spectrometry (ESI-MS) to detect transient catalytic intermediates in Pd(0) catalyzed cross-coupling of arylboronic acids with bromopyridines also confirmed the presence of oxidative addition and transmetallation steps in the catalytic cycle.\(^17\)

Since a base is essential to increase the rate of the transmetallation step,\(^1\) the base is expected to enhance the nucleophilic (or anionic) nature of arylboronic acid by the formation of an arylboronate,\(^2a-c\) and/or to undergo a ligand exchange reaction with halide prior to the transmetallation step,\(^9\) resulting in an [ArPdL\(_2\)OH] species (when the base is the hydroxide ion). However, this species was not observed as a catalytic intermediate by ESI-MS studies (\textit{vide supra}).\(^17\)

Although the detailed mechanism is not clear at present, the mechanism for nickel-catalyzed cross-coupling of aryl mesylates with arylboronic acids may be similar to that for palladium-catalyzed cross-coupling of aryl halides with arylboronic acids, suggested by Suzuki.\(^2a,9\) The most plausible mechanism is outlined in Scheme I.

The first step of the mechanism involves the reduction of Ni(II) to Ni(0) by Zn. This is followed by the oxidative addition of ArX (X= mesylate or other sulfonate leaving groups) to the Ni(0) species. This Ni(II) species may have an ionic structure, i.e., [ArNiL\(_2\)]\(^+\)[OMs]\(^-\). A similar Pd(II) complex [ArPdL\(_4\)]\(^+\)[OTf]\(^-\) has been proposed to result from the oxidative addition of ArOTf to Pd(0) in the presence of PPh\(_3\).\(^10b\)
Scheme I. Plausible Mechanism of Ni(0)-Catalyzed Cross-coupling of Aryl Mesylate with Arylboronic Acid
If the mesylate anion, like triflate anion,\textsuperscript{18} is weakly coordinating, the phosphate anion may exchange with the mesylate ion in the oxidative addition product to generate a more reactive intermediate oxo-nickel complex. This nickel complex then undergoes the subsequent transmetallation reaction, resulting in diaryl nickel(II) species. This step is followed by reductive elimination to generate the cross-coupled product and regenerate the catalyst.

5.4.-CONCLUSIONS

Aryl arenesulfonates and aryl mesylate participate in Ni(0) catalyzed Suzuki-type cross-coupling reactions with arylboronic acids in THF or dioxane, forming functional unsymmetrical biaryls in good yields (up to 81\%). This reaction is significant for several reasons. First, the substitution of Ni catalysts for Pd catalysts represents significant cost savings. Second, functional aryl mesylates are readily obtainable from substituted phenols, hydroquinones and bisphenols, and are much less expensive than the corresponding triflates. Third, aryl mesylates are less susceptible to hydrolysis, when compared to aryl triflates on treatment with a base which is essential in Suzuki cross-coupling. The reaction conditions need to be refined in order to improve the reaction yield. Thus, the results reported in this chapter demonstrate the potential applicability of arenesulfonates and mesylate leaving groups in metal catalyzed cross-coupling reactions.
REFERENCES


6.1.-INTRODUCTION

The classic methods for the introduction of the nitrile group into an aromatic ring are the Sandmeyer reaction\textsuperscript{1a-c} and the cyanation of aromatic halides with CuCN.\textsuperscript{1d-e} More recently general methods for the cyanation of aryl halides involving Pd(0)-\textsuperscript{2} or Ni(0)-catalysts\textsuperscript{3} have been developed. Pd-catalysts have been utilized for the cyanation of aryl iodides and bromides,\textsuperscript{2a-e} and activated aryl chlorides.\textsuperscript{2f} Ni-catalysts have been utilized for the cyanation of aryl iodides, aryl bromides, unactivated aryl chlorides,\textsuperscript{3a-c} and heteroaryl bromides and chlorides.\textsuperscript{3d} Tetracyanocobaltate has also been used for the cyanation reaction of several aryl halides.\textsuperscript{4} In addition, aryl triflates have been cyanated in reactions utilizing Pd.\textsuperscript{2a,5a} or Ni-catalysts.\textsuperscript{5} The participation of aryl triflates in the metal catalyzed cyanation reaction is of particular importance since it provides the shortest synthetic route for the conversion of an aromatic hydroxy group to a cyano group. Aryl triflates are readily prepared from phenols\textsuperscript{6} and they undergo facile oxidative addition to transition metals.\textsuperscript{7}

Recently we reported that aryl mesylates, which are much less expensive than the corresponding triflates, undergo Ni(0) catalyzed homocoupling in THF, dioxane and dipolar aprotic solvents resulting in the formation of functional symmetrical biaryls in high yields.\textsuperscript{8} In addition, a novel Suzuki-type Ni(0) catalyzed cross-coupling reaction of aryl arenesulfonates and aryl mesylates with arylboronic acids was developed.\textsuperscript{9} In this chapter, we will demonstrate that aryl mesylates undergo a Ni(0) catalyzed cross-coupling reaction with the cyanide anion resulting in good to high yields of aryl nitriles. Because a variety of substituted phenols are readily available and inexpensive, the use of the mesylate leaving group in Ni(0) catalyzed cyanation reaction
provides a very convenient and general method for the preparation of aryl nitriles starting from phenols.

6.2.-EXPERIMENTAL

6.2.1.-Materials

Tetraethylammonium iodide, potassium cyanide, zinc cyanide, triphenylphosphine and 1,1'-bis(diphenylphosphino)ferrocene (dpff) were purchased from Aldrich and used without further purification except when reported. KCN was dried at 110°C under reduced pressure (1 x 10^{-3} \text{ mmHg}) for 24 h prior to use. THF was freshly distilled from sodium-benzophenone ketyl. CH_{3}CN and DMF were freshly distilled from CaH_{2}. Zinc dust was stirred in acetic acid, washed with water and dried \textit{in vacuo} at 120°C. NiCl_{2}(PPh_{3})_{2}^{11} and NiCl_{2}(dpff)^{12} were prepared according to published procedures.

6.2.2.-Techniques

The actual yields were determined by GC using phenyl ether as an internal standard. All Ni(0) mediated cyanation reactions were carried out under argon in oven-dried (110°C) glassware using standard Schlenk line techniques.\textsuperscript{13}

6.2.3.-Synthesis of Aryl Mesylates

The preparations of phenyl mesylate, 4-acetylphenyl mesylate, methyl 4-(methylsulfonyloxy)benzoate, methyl 2-(methylsulfonyloxy)benzoate, 4-cyanophenyl mesylate, 4-methylphenyl mesylate and 4-methoxyphenyl mesylate were reported previously.\textsuperscript{8}

6.2.4.-General Procedure for Nickel-Catalyzed Cyanation

---
In a typical reaction, a 125 ml Schlenk tube was charged with aryl mesylate (1.0 mmol), NiCl₂(PPh₃)₂ (0.1 mmol), PPh₃ (0.2 mmol), Zn powder (1.0 mmol), KCN (1.5 mmol) and a magnetic stirring bar. After sealing the tube with a rubber septum, the content was dried at 25°C under reduced pressure (1 x 10⁻³ mmHg) for 1 h. Then it was placed under an Ar atmosphere and freshly distilled DMF (0.60 ml) was added via a syringe through the rubber septum. The mixture was stirred at room temperature for 5 min and during this time the color of the mixture gradually changed from green into deep red brown. The reaction mixture was stirred at 80°C for 12 h. After cooling to 25 °C, CHCl₃ (20 ml) and 10 % aq HCl (20 ml) were added. After stirring for 20 min the CHCl₃ layer was separated, washed with H₂O, dried (MgSO₄) and the solvent evaporated in vacuo. The corresponding aryl nitrile was purified by column chromatography (silica gel, hexanes/ethyl acetate). The actual yields based on percent conversion of the starting aryl mesylate were determined by GC measurements using diphenyl ether as an internal standard. The GC yields are summarized in Tables I and II.

**Aryl nitriles**

**Benzonitrile** was identified by comparison with an authentic sample using GC.

**p-Acetylbenzonitrile**: white crystals; mp 56-58°C (hexanes) (lit.²a 56.5-57°C); ¹H NMR (CDCl₃) δ 8.05 (d, J = 8.0 Hz, 2H, m to -CN), 7.78 (d, J = 8.0 Hz, 2H, o to -CN), 2.65 (s, 3H, -C(=O)-CH₃).

**Methyl p-cyanobenzoate**: white crystals; mp 67-68°C (hexanes) (lit.²a 67-68°C); ¹H NMR (CDCl₃) δ 8.14 (d, J = 8.4 Hz, 2H, m to -CN), 7.75 (d, J = 8.4 Hz, 2H, o to -CN), 3.96 (s, 3H, -CO₂CH₃).
**Methyl o-cyanobenzoate:** white crystals; mp 48-49°C (hexanes) (lit.\(^2\)a 48.5-49°C);\(^1\)H NMR (CDCl\(_3\)) \(\delta\) 8.10-8.18 (m, 1H, \(\sigma\) to -CO\(_2\)CH\(_3\)), 7.65-7.80 (m, 3H, aromatic protons), 4.00 (s, 3H, -CO\(_2\)CH\(_3\)).

**1,4-Dicyanobenzene:** white crystals; mp 224°C (hexanes) (lit.\(^2\)a 221-222°C); \(^1\)H NMR (CDCl\(_3\)) \(\delta\) 7.80 (s, 4H, \(\sigma\) to -CN).

**p-Cyanotoluene:** white crystals; mp 27°C (hexanes) (lit.\(^2\)a 25.5-27.5°C); \(^1\)H NMR (CDCl\(_3\)) \(\delta\) 7.73 (d, \(J = 7.7\) Hz, 2H, \(\sigma\) to -CN), 7.26 (d, \(J = 7.8\) Hz, 2H, \(\sigma\) to -CH\(_3\)), 2.41 (s, 3H, -CH\(_3\)).

**p-Methoxybenzonitrile:** white crystals; mp 57-58°C (benzene) (lit.\(^2\)a 56-56.5°C); \(^1\)H NMR (CDCl\(_3\)) \(\delta\) 7.67 (d, \(J = 8.9\) Hz, 2H, \(\sigma\) to -CN), 7.10 (d, \(J = 8.9\) Hz, 2H, \(\sigma\) to -OCH\(_3\)), 3.91 (s, 3H, -OCH\(_3\)).

### 6.3. RESULTS AND DISCUSSION

The general procedure used for the preparation of aryl nitriles utilized the Ni(0) catalyzed cross-coupling reaction of aryl mesylates derived from the corresponding phenols with KCN (eq 1).

\[
\begin{align*}
\text{R} \text{-CH} & \quad \text{MsCl} \quad \text{py} \quad \text{R} \text{-OMs} \quad \text{KCN} \quad \text{Ni(0)} \\
\text{R} = \text{H, CH}_3\text{CO, CH}_3\text{O}_2\text{C, CN, CH}_3 &
\end{align*}
\] (1)
The method used to generate the Ni(0) catalyst in situ was first employed for the cyanation of aryl halides. The Ni(0) catalyst was prepared in situ from NiCl₂(PPh₃)₂ or NiCl₂(dppf) with added phosphine ligand (i.e., PPh₃ or dppf) usually present. Excess Zn powder was used as a reducing agent. In some reactions, Et₄NI was added as an iodide ion source. However, it is not required when a sufficient quantity of added phosphine ligand is present (vide infra). The iodide ion has been reported to facilitate the electron transfer between Ni and Zn in the reduction step. Cyanide ions poison the nickel catalyst when their concentration is too high. One approach to maintaining a low concentration of cyanide ion is to use a cyanide ion source which has low solubility in the reaction solvent. Thus, KCN is frequently used in CH₃CN or DMF for Ni(0) and Pd(0) catalyzed cyanation experiments. A series of cyanation experiments was performed with phenyl mesylate using KCN as cyanide ion source in THF, CH₃CN or DMF at 60°C (Table 1).

When the Ni(0) catalyst was generated from NiCl₂(PPh₃)₂ in THF with no added PPh₃, the cross-coupled product (benzonitrile) was obtained in 21% yield (Table I, entry 1). A side reaction product (biphenyl) was formed in 11% yield. There are several reactions which could generate biphenyl. Perhaps, the most likely one, is the homocoupling reaction of phenyl mesylate to give biphenyl. This reaction has been shown to proceed in 91% yield in THF (eq 2).

\[ \text{OMs} \xrightleftharpoons{\text{NiCl}_2(\text{PPh}_3)_2, \text{Zn}} \xrightarrow{\text{Et}_4\text{NI, THF, 67°C, 10 h}} \text{biphenyl} \quad 91\% \]  

(2)

Another possible source of biphenyl is the coupling of phenyl mesylate with a phenyl group from PPh₃ (eq 3).
Table I. Nickel (0) Catalyzed Cyanation of Phenyl Mesylate.\textsuperscript{d}

\[
\text{Ph-OMs} + \text{KCN} \xrightarrow{\text{Ni(0)}-\text{KOMs}} \text{Ph-CN} + \text{Ph-Ph}
\]

<table>
<thead>
<tr>
<th>Entry</th>
<th>Nickel catalyst</th>
<th>PPh\textsubscript{3} (equiv\textsuperscript{b})</th>
<th>Zn (equiv\textsuperscript{b})</th>
<th>Et\textsubscript{4}NI (equiv\textsuperscript{b})</th>
<th>KCN (equiv\textsuperscript{b})</th>
<th>Solvent</th>
<th>Reaction time (h)</th>
<th>GC yield\textsuperscript{c} (%)</th>
<th>Ph-CN</th>
<th>Ph-Ph</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>NiCl\textsubscript{2}(PPh\textsubscript{3})\textsubscript{2} (0.10)</td>
<td>-</td>
<td>1.7</td>
<td>1.5</td>
<td>1.1</td>
<td>THF</td>
<td>12</td>
<td>21</td>
<td>11</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>NiCl\textsubscript{2}(PPh\textsubscript{3})\textsubscript{2} (0.10)</td>
<td>-</td>
<td>1.7</td>
<td>1.5</td>
<td>1.1</td>
<td>CH\textsubscript{3}CN</td>
<td>12</td>
<td>21</td>
<td>0.09</td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>NiCl\textsubscript{2}(PPh\textsubscript{3})\textsubscript{2} (0.10)</td>
<td>0.2</td>
<td>1.7</td>
<td>1.5</td>
<td>1.1</td>
<td>THF</td>
<td>12</td>
<td>25</td>
<td>1.1</td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>NiCl\textsubscript{2}(PPh\textsubscript{3})\textsubscript{2} (0.10)</td>
<td>0.2</td>
<td>1.7</td>
<td>1.5</td>
<td>1.1</td>
<td>CH\textsubscript{3}CN</td>
<td>12</td>
<td>17</td>
<td>0.01</td>
<td></td>
</tr>
<tr>
<td>5</td>
<td>NiCl\textsubscript{2}(PPh\textsubscript{3})\textsubscript{2} (0.10)</td>
<td>0.8</td>
<td>0.6</td>
<td>-</td>
<td>1.1</td>
<td>CH\textsubscript{3}CN</td>
<td>24</td>
<td>28</td>
<td>0.09</td>
<td></td>
</tr>
<tr>
<td>6</td>
<td>NiCl\textsubscript{2}(dpff) (0.10)</td>
<td>0.1\textsuperscript{d}</td>
<td>0.3</td>
<td>0.3</td>
<td>1.5</td>
<td>CH\textsubscript{3}CN</td>
<td>12</td>
<td>34</td>
<td>5.6</td>
<td></td>
</tr>
<tr>
<td>7</td>
<td>NiCl\textsubscript{2}(dpff) (0.10)</td>
<td>0.4\textsuperscript{d}</td>
<td>0.6</td>
<td>-</td>
<td>1.2</td>
<td>CH\textsubscript{3}CN</td>
<td>12</td>
<td>27</td>
<td>14.2</td>
<td></td>
</tr>
<tr>
<td>8</td>
<td>NiCl\textsubscript{2}(dpff) (0.10)</td>
<td>0.4\textsuperscript{d}</td>
<td>0.6</td>
<td>-</td>
<td>1.5</td>
<td>CH\textsubscript{3}CN</td>
<td>12</td>
<td>32</td>
<td>4.7</td>
<td></td>
</tr>
<tr>
<td>9</td>
<td>NiCl\textsubscript{2}(PPh\textsubscript{3})\textsubscript{2} (0.30)</td>
<td>0.6</td>
<td>0.6</td>
<td>0.6</td>
<td>1.5</td>
<td>CH\textsubscript{3}CN</td>
<td>12</td>
<td>55</td>
<td>0.05</td>
<td></td>
</tr>
<tr>
<td>10</td>
<td>NiCl\textsubscript{2}(PPh\textsubscript{3})\textsubscript{2} (0.30)</td>
<td>0.6</td>
<td>1.0</td>
<td>-</td>
<td>1.2</td>
<td>CH\textsubscript{3}CN</td>
<td>12</td>
<td>42</td>
<td>4.9</td>
<td></td>
</tr>
<tr>
<td>11</td>
<td>NiCl\textsubscript{2}(PPh\textsubscript{3})\textsubscript{2} (0.10)</td>
<td>0.2</td>
<td>1.0</td>
<td>-</td>
<td>1.5</td>
<td>DMF</td>
<td>12</td>
<td>60</td>
<td>-</td>
<td></td>
</tr>
<tr>
<td></td>
<td>NiCl₂(PPh₃)₂ (0.10)</td>
<td>0.2</td>
<td>1.0</td>
<td>-</td>
<td>1.5</td>
<td>DMF</td>
<td>12</td>
<td>80</td>
<td>0.1</td>
<td></td>
</tr>
<tr>
<td>----</td>
<td>------------------</td>
<td>-----</td>
<td>-----</td>
<td>---</td>
<td>-----</td>
<td>-----</td>
<td>----</td>
<td>----</td>
<td>-----</td>
<td></td>
</tr>
<tr>
<td>12&lt;sup&gt;e&lt;/sup&gt;</td>
<td>NiCl₂(PPh₃)₂ (0.10)</td>
<td>0.2</td>
<td>1.0</td>
<td>-</td>
<td>1.0&lt;sup&gt;f&lt;/sup&gt;</td>
<td>DMF</td>
<td>12</td>
<td>3</td>
<td>0.4</td>
<td></td>
</tr>
<tr>
<td>14&lt;sup&gt;g,h&lt;/sup&gt;</td>
<td>NiCl₂(PPh₃)₂ (0.10)</td>
<td>0.2</td>
<td>1.0</td>
<td>-</td>
<td>1.0&lt;sup&gt;f&lt;/sup&gt;</td>
<td>DMF</td>
<td>12</td>
<td>46</td>
<td>11</td>
<td></td>
</tr>
</tbody>
</table>

<sup>a</sup> All reactions were performed at 60°C unless otherwise noted.  
<sup>b</sup> Equiv relative to phenyl mesylate.  
<sup>c</sup> Yields relative to phenyl mesylate were determined by GC using diphenyl ether as an internal standard.  
<sup>d</sup> Dppf was used as added ligand instead of PPh₃.  
<sup>e</sup> The reaction was carried out at 80°C.  
<sup>f</sup> Zn(CN)₂ was used instead of KCN.  
<sup>g</sup> The reaction was carried out at 100°C.  
<sup>h</sup> 1.0 equiv NaBr was added.
When the reaction was performed in a dipolar aprotic solvent such as CH$_3$CN under identical conditions as entry 1 in Table I, the same amount of benzonitrile was formed (21 %) and a greatly reduced amount of biphenyl (0.09 %) was obtained (Table I, entry 2). The addition of 0.2 equiv of PPh$_3$ to the reaction mixture in THF resulted in a slightly increased benzonitrile yield (25 %) and in a greatly reduced amount of biphenyl (1.1 %, Table I, entry 3). When the same reaction conditions were utilized using CH$_3$CN as solvent, the yield was slightly reduced (17 %), but the amount of biphenyl formed (0.01 %) was greatly reduced (Table I, entry 4). The detection of biphenyl in the reaction mixture was not surprising given that THF had previously been shown to be an excellent solvent for the homocoupling reaction.$^8$ Therefore, in order to reduce the amount of homocoupled side product, dipolar aprotic solvents such as CH$_3$CN or DMF were utilized as solvent for most of the cyanation reactions of the present study (vide infra).

A virtually identical yield to that obtained using Et$_4$NI, could be obtained in its absence in CH$_3$CN by increasing the amount of PPh$_3$ to 0.8 equiv with a concurrent decrease in the amount of Zn (cf. Table I, entries 3 & 5). In addition, the formation of biphenyl was greatly reduced in the latter case (1.1 % vs 0.09 %). These results indicate that an identical yield of cyanation product could be obtained in the absence of Et$_4$NI by increasing the amount of PPh$_3$ appropriately. The same trend was also observed previously for the Ni(0) catalyzed homocoupling reaction of aryl mesylates.$^8$
When the Ni(0) catalyst was generated from NiCl$_2$(dpff) in the presence of added dpff, improved yields were obtained (27 %–34 %, Table I, entries 6–8). An almost identical yield was obtained in the absence of Et$_4$N when extra dpff was added (Table I, entries 6 & 8). However, when the cyanation reaction was mediated in the presence of dpff, more biphenyl side product was obtained (up to 14.2 %, Table I, entry 7). Thus, the NiCl$_2$(dpff) catalytic system was more efficient producing a slightly higher yield (34 %, Table I, entry 6), although more biphenyl (5.6 %) was obtained. In contrast, a 28 % yield was obtained with the NiCl$_2$(PPh$_3$)$_2$ catalytic system with only 0.09 % biphenyl formation (Table I, entry 5). An increased conversion to benzonitrile (55 %) was obtained using 0.30 equiv NiCl$_2$(PPh$_3$)$_2$ with only trace amounts of biphenyl (0.05 %) detected (Table I, entry 9). The yield was slightly reduced when the reaction was performed in the absence of Et$_4$N (Table I, entry 10).

The highest yields were obtained when DMF was used as the reaction solvent. When the cyanation was performed using 0.1 equiv NiCl$_2$(PPh$_3$)$_2$ in DMF at 60°C, an increased amount of benzonitrile was obtained, significantly without the formation of the homocoupled side product (60 %, Table I, entry 11). When the same reaction conditions were utilized at a higher temperature of 80°C, a higher yield of benzonitrile with a trace amount of homocoupled side product was obtained (80 %, Table I, entry 12). Previous Ni-catalyzed cyanation procedures have often involved tedious procedures such as the pretreatment of Ni(II) with Zn followed by successive addition of substrate and cyanide, or the slow addition of cyanide into the mixture of catalyst and substrate. These procedures have been employed in order to efficiently generate the active Ni(0) catalysts and to prevent it from being poisoned by the cyanide ion.$^{4b,c}$ However, these precautions were unnecessary in the present cyanation reaction. Therefore, this method is an experimentally convenient procedure.
Recently the Pd(PPh$_3$)$_4$ catalyzed high yield reaction of aryl bromides with Zn(CN)$_2$, which is less soluble than KCN in DMF, was reported.$^{2e}$ However, a very low yield (3%, Table I, entry 13) was obtained using Zn(CN)$_2$ as the cyanide source. Interestingly, the addition of 1 equiv NaBr as a halide source with a concurrent increase in temperature to 100°C promoted the cyanation resulting in a much higher yield of 46 %, although a significant amount of biphenyl (11 %) was obtained (Table I, entry 14).

The highest yield in the cyanation reaction of phenyl mesylate was obtained in the reaction with KCN (1.5 equiv.) in DMF at 80 °C in the presence of NiCl$_2$(PPh$_3$)$_2$ (0.10 equiv.), PPh$_3$ (0.20 equiv.) and Zn (1.0 equiv.) (eq. 4)

\[
\text{Ph-OH} \xrightarrow{\text{MsCl, py}} \text{Ph-OMs} \xrightarrow{\text{KCN (1.5 equiv.), } \text{NiCl}_2\text{(PPh}_3\text{)$_2$ (0.10 equiv.), } \text{PPh}_3\text{(0.20 equiv.), Zn (1.0 equiv.), DMF \atop 80 °C, 12 h}} \text{CN} \]

Using these reaction conditions, the influence of the electronic effects of para-substituents on the cyanation reaction was investigated. The results are presented in Table II. Increased yields, relative to phenyl mesylate, were obtained when the para substituent was an electron-withdrawing group (i.e., acetyl, carbomethoxy or cyano, entries 1-2 & 4 in Table II). When the para-substituent was the electron-donating p-methyl group a reduced yield was obtained (Table II, entry 5). However, slightly increased yield (relative to phenyl mesylate) was obtained when the substituent was methoxy group (82%, entry 6 in Table II).

The position of the substituent also affected the cyanation yield (Table II, entry 2 versus entry 3). The ortho-substituted substrate reacted much more sluggishly than the para-substituted substrate.
Table II. Nickel (0) Catalyzed Cyanation of Various Aryl Mesylates.\(^a\)

\[
\begin{align*}
\text{R-Ph-OMs + KCN} & \xrightarrow{\text{Ni(0) -KOMs}} \text{R-Ph-CN + R-Ph-Ph-R + R-Ph-H} \\
\end{align*}
\]

<table>
<thead>
<tr>
<th>Entry</th>
<th>R</th>
<th>GC yield(^b) (%)</th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>R-Ph-CN</td>
<td>R-Ph-Ph-R</td>
<td>R-Ph-H</td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>(p)-CH(_3)CO</td>
<td>93</td>
<td>-</td>
<td>7</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>(p)-CH(_3)O(_2)C</td>
<td>84</td>
<td>1</td>
<td>15</td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>(o)-CH(_3)O(_2)C</td>
<td>59</td>
<td>-</td>
<td>4(^c)</td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>(p)-CN</td>
<td>81</td>
<td>-</td>
<td>19</td>
<td></td>
</tr>
<tr>
<td>5</td>
<td>(p)-CH(_3)</td>
<td>77</td>
<td>-</td>
<td>23</td>
<td></td>
</tr>
<tr>
<td>6</td>
<td>(p)-CH(_3)O</td>
<td>82</td>
<td>-</td>
<td>18</td>
<td></td>
</tr>
</tbody>
</table>

\(^a\) All reactions were performed in DMF at 80°C for 12 h. Molar ratio of ArOMs/NiCl\(_2\)(PPh\(_3\))\(_2\)/PPh\(_3\)/Zn/KCN was 1.0/0.10/0.20/1.0/1.5. \(^b\) Yields relative to aryl mesylate were determined by GC using diphenyl ether as an internal standard. \(^c\) The remaining material isolated was unreacted starting material (37%).
Of the mesylates examined the highest yield was achieved with 4-acetylphenyl mesylate (93%, entry 1 in Table II). The reduction product (i.e., acetophenone) was also formed in 7% yield.

The general trend in reference to the electronic properties of the aryl substituents is that electron-withdrawing groups activate the aryl mesylate toward the nickel(0) catalyzed cyanation reaction and electron-donating groups deactivate it. In addition, side reactions become more important in cases involving the less reactive aryl mesylate. This is reflected in the increased yield of reduction side product (23%) obtained for p-methylphenyl mesylate (Table II, entry 5). In all cases except for entry 3, complete consumption of the starting substrates was observed even though side reactions such as reduction occurred. This side reaction occurs after the oxidative addition step of the Ni(0) catalytic cycle (vide infra). Therefore, this indicates that premature catalyst inactivation by cyanide ions does not occur to an appreciable extent in DMF using the reported reaction conditions. Otherwise an incomplete reaction with the recovery of unreacted starting substrates would be expected.

The major side reaction product formed in THF and CH$_3$CN was the homocoupled biaryl (vide supra). However, when the reaction was performed in DMF at 80°C, a substantial amount of reduction side product was formed. In this case, the homocoupled side reaction product was formed in zero to one percent yield (Table II, entries 1-6). These results can be rationalized as follows. When THF or CH$_3$CN was used homocoupling can compete with the desired cyanation, because of the relatively low concentration of cyanide. In contrast, when DMF was used the initial oxidative addition product was less stable and could easily be reduced by adventitious proton sources. In DMF the product distribution of the cyanation is influenced by the uniform mixing of the reactants. In some reactions DMF which condensed on the sides of the reaction tube did not efficiently return to the reaction solution. In these cases the
reaction solution became very viscous and a significant amount of biaryl homocoupled side product was obtained. This can be rationalized by a decreased amount of KCN in the solution due to inefficient mixing.

Mechanistic considerations have been discussed for the Ni(0) catalyzed homocoupling\(^{10}\) and for the cyanation of aromatic halides.\(^{4c}\) It is reasonable to expect a similar mechanism for the Ni(0) catalyzed cyanation of aryl mesylate (Scheme I). The success of the cyanation reaction is dependent of the CN\(^-\) ion being present in the proper concentration. If its concentration is too high, the reaction of NiCl\(_2\)(PPh\(_3\))\(_2\) with CN\(^-\) would become important. The resulting product 5 can not be reduced by Zn to 2.\(^{4c}\) In addition, CN\(^-\) can react with 2 to give 6.\(^{4c}\) The aryl mesylate is not expected to oxidatively add to 6. A high concentration of CN\(^-\) is known to poison the nickel catalyst and the use of CH\(_3\)CN or DMF as solvent decreases its concentration in solution.\(^{4c}\) If its concentration is too low, homocoupling may be favored as 3 may be reduced by Zn to give 7 before 3 can react with CN\(^-\) to produce 4.

6.4.-CONCLUSIONS

Various aryl mesylates undergo Ni(0) catalyzed cyanation reaction in dipolar aprotic solvents (CH\(_3\)CN and DMF) or less polar THF to produce aryl nitriles in high yields. Of the three solvents employed, DMF was found to be most efficient with KCN as the source of cyanide. Homocoupled biaryl and reduction side reaction products were identified. The amount of the homocoupled side product could be reduced by performing the reaction in dipolar aprotic solvents (vs. THF), using PPh\(_3\) (vs. dppf), and adding extra ligand (in addition to NiCl\(_2\)L\(_2\)). The reaction yield is sensitive to the concentration of CN\(^-\) and therefore it can be further optimized. Because substituted phenols are readily available, the mesylate leaving group in this cross-coupling reaction provides a very convenient access to various aryl nitriles.
Scheme I. Plausible Mechanism of Ni(I)-Catalyzed Cyanation of Aryl Mesylate.
REFERENCES


Chapter 7

NICKEL CATALYZED CROSS-COUPLING REACTIONS OF ARYL MESYLATES
WITH VARIOUS ORGANOMETALLICS (ORGANOTIN, M- MAGNESIUM AND
-ZINC COMPOUNDS) AND SODIUM BENZENETHIOLATE

7.1.-INTRODUCTION

The transition metal (palladium or nickel) catalyzed cross-coupling reaction of
an organic electrophile with an organometallic reagent is a versatile method for carbon-
carbon bond formation.\textsuperscript{1} Aromatic electrophiles such as aryl halides (mostly aryl
bromides and iodides) and aryl triflates couple efficiently with various organometallic
reagents such as organotin, -zinc, -boron and -magnesium compounds. The
participation of aryl triflates in these cross-coupling reactions is especially important
since this provides an efficient two-step method for the conversion of the phenolic
carbon-oxygen bond to a carbon-carbon bond.

The typical method for the formation of aromatic carbon-heteroatom bonds is
via nucleophilic displacement of a halogen. Since aryl halides usually exhibit low
reactivity toward nucleophiles, this process requires very severe conditions involving
very basic reagents or high temperatures. The introduction of certain electron-
withdrawing groups ortho or para to the halogen group allows the nucleophilic
substitution reaction to proceed readily. Recently transition metal catalysts have been
utilized to mediate the nucleophilic displacement reaction of aryl halides with hetero-
nucleophiles such as thiolate, amine and phosphorous. These reactions usually proceed
regiospecifically under mild conditions (See: General Introduction in Chapter 1).

In regard to sulfur containing nucleophiles, Ni(0) catalyzed thiation of aryl
halides (mostly bromides and iodides) with thiol,\textsuperscript{2} thiourea,\textsuperscript{3} and thiolate anion\textsuperscript{4} have
been described. Pd(0) catalyzed thiation of aryl halides with thioamide\textsuperscript{5} and thiolate
anion\(^6\) was also reported. Recently, it has been described that chloroanilines (and their derivatives) reacted efficiently with arene thiolate anions to give the corresponding aryl sulfides in NMP at high temperature (up to 190°C) in the absence of transition metal catalysis.\(^7\)

Ni(0) catalyzed nucleophilic displacement of aryl halides with phosphorus compounds was reported.\(^8\) Aryl triflate was also reported to undergo Pd(0) catalyzed nucleophilic substitution reaction with phosphorus nucleophile\(^9\), thereby providing a method for the conversion of phenolic oxygen into a phosphorus atom. However, a synthetic procedure for the conversion of a phenolic oxygen to a sulfur atom has not been reported.

In previous chapters, aryl mesylates were reported to participate in both nickel catalyzed homo-coupling reactions as well as cross-coupling reactions with arylboronic acids or the cyanide anion. These homo- and cross-coupling reactions were best catalyzed by nickel-phosphine complexes, since they readily undergo oxidative addition to aryl mesylates. Palladium catalysts were found to show poor reactivity toward the mesylate resulting in low yield. The synthetic utility of the mesylate leaving group was extended by an investigation of the reactivity of aryl mesylates in nickel catalyzed cross-coupling reactions of aryl mesylates with various organometallic carbanion synthons (i.e., organotin-, zinc and -magnesium compounds) and a heteroatom-nucleophile (phenylthiolate anion).

7.2.-EXPERIMENTAL
7.2.1.-Materials

Triphenylphosphine (99%), 1,1'-bis(diphenylphosphino)ferrocene (97%), and 1,3-bis(diphenylphosphino)propane (97%) from Aldrich were used as received. All other reagents, including phenols, were purchased from commercial sources (Aldrich
or Lancaster) and used without further purification except when reported. Pyridine was
dried over CaH₂ and distilled. DMF was dried with CaH₂, filtered, and distilled under
reduced pressure. THF was distilled from sodium-benzophenone ketyl. Zinc dust
(325 mesh) was stirred in acetic acid, washed with water and dried in vacuo at 120°C.
Unless otherwise noted, all compounds synthesized in the present paper were purified
until their 200 MHz ¹H-NMR spectra corresponded to the expected structure and the
purity was established by comparison with published mp or found to be higher than
99.5% by GC or HPLC.

PdCl₂(dpff),¹⁰ NiCl₂(PPh₃)₂,¹¹ NiCl₂(dpff)¹² and tri-n-butylphenyl-
stannane¹³ were prepared according to literature procedures.

**Grignard Reagents**

Methyl magnesium iodide (3.0 M solution in Et₂O) was obtained from Aldrich.
Other Grignard reagents were prepared by the reaction of magnesium turnings with the
corresponding halides in THF.

**Zinc Reagents**

Zinc reagents were prepared in situ by mixing anhydrous zinc chloride (1.1
equiv) with the corresponding Grignard reagents (1.0 equiv) in THF at 0°C-25°C for
0.5 h. After the reaction was complete, the mixture was transferred via cannula
through a small pad of Celite in sintered glass funnel directly into a Schlenk tube
containing a mixture of aryl mesylate, NiCl₂(dpff) and Zn (vide infra).

7.2.2.-Synthesis of Aryl Sulfonates
The synthesis of 4-acetylphenyl para-fluorobenzenesulfonate, 4-acetylphenyl methanesulfonate, methyl 4-(methylsulfonyloxy)benzoate, phenyl methanesulfonate, 4-cyanophenyl methanesulfonate, 4-tolyl methanesulfonate and 4-methoxyphenyl methanesulfonate was presented in Chapter 2.

2-Tolylmethane sulfonate was prepared by the reaction of methanesulfonyl chloride with o-cresol in pyridine.\(^{14}\) (85%): colorless oil, purified by column chromatography (SiO\(_2\), hexanes/Et\(_2\)O = 10/1) and vacuum distilled: bp 105-107°C / 0.005 mmHg; \(^1\)H NMR \(\delta\) 7.27-7.18 (m, 4H, aromatic protons), 3.12 (s, 3H, -OSO\(_2\)CH\(_3\)), 2.33 (s, 3H, -CH\(_3\)).

7.2.3.-General Procedure for Pd(0)-Catalyzed Cross-Coupling of Aryl Sulfonates with Tri-\(n\)-butylphenylstannane.

A 25 ml three-neck flask equipped with a reflux condenser, nitrogen inlet and rubber septum was charged with aryl sulfonate (0.5 mmol), LiCl (1.5 mmol), and DMF (2 ml). The flask was flushed with nitrogen and the palladium catalyst (0.025 mmol) was added. After 10 min of stirring, tri-\(n\)-butylphenylstannane was added. The mixture was stirred at 110°C under N\(_2\) for 24 h. The actual yields based on percent conversion of the starting aryl sulfonate were determined by GC measurements using diphenyl ether as an internal standard. The GC yields are summarized in Table I.

7.2.4.-General Procedure for Ni(0)-Catalyzed Cross-Coupling of Aryl Sulfonates with Tri-\(n\)-butylphenylstannane.

All reactions were carried out under nitrogen using oven-dried (110°C) glassware. In a typical reaction a 125 mL Schlenk tube was charged with aryl sulfonate (0.5 mmol), tri-\(n\)-butylphenylstannane (0.55 mmol), NiCl\(_2\)(PPh\(_3\))\(_2\) (0.05 mmol), Zn powder (0.86 mmol), Et\(_4\)NI (0.75 mmol) and a magnetic stirring bar. After sealing the
tube with a rubber septum, the contents were placed under N₂ by three evacuation-filling cycles. Freshly distilled THF (1.0 ml) was added via a syringe through the rubber septum. The reaction mixture was heated to the reflux temperature and stirred at this temperature for 24 h. Then it was cooled to 25°C, filtered, diluted with water, extracted with CHCl₃, and dried (MgSO₄). The yields based on percent conversion of the starting aryl sulfonate were determined by GC measurements using diphenyl ether as an internal standard. The GC yields are summarized in Table I.

**Biaryls**

4-Carbomethoxybiphenyl: white crystals: mp 116-117°C (benzene) (lit.¹⁵ 117.5°C).

4-Acetyl biphenyl: white needles: mp 119-120°C (ethanol) (lit.¹⁶ 121°C).

7.2.5.-General Procedure for Ni(0)-Catalyzed Cross-Coupling of Aryl Mesylates with Grignard- and Zinc Reagents.

In a typical reaction a 125 mL Schlenk tube was charged with aryl mesylate (0.5 mmol), NiCl₂(dpfp) (0.05 mmol), Zn powder (0.5 mmol) and a magnetic stirring bar. After sealing the tube with a rubber septum, the contents were dried at 25°C under reduced pressure (1 × 10⁻³ mmHg) for 3h. The tube was filled with N₂ followed by three evacuation-filling cycles. Freshly distilled THF (0.5 ml) was added via syringe through the rubber septum. The mixture was stirred at room temperature for 10 min. During this time the color of the mixture gradually became deep red-brown. Grignard reagent (0.5-1.0 mmol in THF) was added to the reaction mixture via syringe through the rubber septum. The mixture was stirred at room temperature for 10h, filtered, diluted with water, extracted with CHCl₃, dried (MgSO₄) and the solvent removed in vacuo. The corresponding cross-coupled product was purified by column chromatography (SiO₂, hexanes/ethyl acetate). The yields based on percent conversion
of the starting aryl mesylate were determined by GC measurements using diphenyl ether as an internal standard. The GC yields are summarized in Table II.

**Cross-Coupled Products**

Butylbenzene, o-xylene, p-xylene, and 4-methylanisole were identified by coinjection with authentic samples (Aldrich) using GC. 4-Methylbiphenyl: white crystals; mp 47-48°C (hexanes) (lit.\(^\text{17}\) 47.5°C). 4-Methoxybiphenyl: white crystals; mp 87-88°C (benzene) (lit.\(^\text{17}\) 89-90°C).

7.2.6.- General Procedure for Ni(0)-Catalyzed Cross-Coupling of Aryl Mesylates with Sodium Benzenethiolate.

**Diphenyl sulfide.**\(^\text{23}\) All reactions were carried out under argon using oven-dried (110°C) glassware. In a typical reaction a 125 mL Schlenk tube was charged with phenyl mesylate (1.0 mmol), sodium benzenethiolate (1.2 mmol), NiCl\(_2\)(PPh\(_3\))\(_2\) (0.10 mmol), Zn powder (1.0 mmol) and a magnetic stirring bar. The tube was sealed with a rubber septum and placed under an Ar atmosphere. DMF (1.0 ml) was added via a syringe through the rubber septum. The solution immediately turned red. The reaction mixture was stirred at 80°C for 3h. After the reaction mixture cooled to room temperature, diphenyl ether and CH\(_2\)Cl\(_2\) (3 mL) were added. The mixture was washed with 10% HCl(aq) (3 x 3 mL), H\(_2\)O (2 x 3 mL), filtered, and dried (MgSO\(_4\)). The yield was then determined by GC. Diphenyl sulfide was identified by its \(^1\)H NMR spectra and by its GC retention time when coinjected with an authentic sample. Isolated yields were determined by a modified procedure in which Ph\(_2\)O was not added and the CH\(_2\)Cl\(_2\) was evaporated in vacuo. The corresponding diaryl sulfide was obtained after column chromatography (silica gel, n-hexane/ethyl acetate).
4-(Phenylthio)acetophenone\textsuperscript{24} (32\%): \( ^1\text{H} \) NMR \( \delta \) 7.82 (d, \( J = 8.5 \) Hz, 2H, o to -C(=O)CH\textsubscript{3}), 7.49 (m, 2H, o to sulfur on phenyl), 7.39 (m, 3H, m and p to sulfur on phenyl), 7.21 (d, \( J = 8.5 \) Hz, 2H, m to -C(=O)CH\textsubscript{3}), 2.55 (s, 3H, -C(=O)CH\textsubscript{3}).

**Methyl 4-(phenylthio)benzoate.** (16\%): \( ^1\text{H} \) NMR \( \delta \) 7.82 (d, \( J = 8.4 \) Hz, 2H, o to -CO\textsubscript{2}CH\textsubscript{3}), 7.40 (m, 2H, o to sulfur on phenyl), 7.31 (m, 3H, m and p to sulfur on phenyl), 7.13 (d, \( J = 8.4 \) Hz, 2H, m to -CO\textsubscript{2}CH\textsubscript{3}), 3.82 (s, 3H, -CO\textsubscript{2}CH\textsubscript{3}).

4-(Phenylthio)benzonitrile\textsuperscript{23} (10\%): \( ^1\text{H} \) NMR \( \delta \) 7.68-7.25 (m, 7H, aromatic protons), 7.08 (d, \( J = 8.4 \) Hz, 2H, m to -CN).

7.3.-RESULTS AND DISCUSSION

7.3.1.-Pd(0)- and Ni(0)-Catalyzed Cross-Coupling Reactions of Aryl Sulfonates with Tri-\( n \)-butylphenylstannane

**Palladium(0)-Catalyzed Cross-Coupling**

Table I summarizes a few results on the Pd(0)- and Ni(0)- catalyzed cross-coupling of various aryl sulfonates including mesylate with tri-\( n \)-butylphenylstannane. A series of palladium catalyzed reactions with electron-withdrawing \( p \)-acetyl and \( p \)-methoxycarbony substituted sulfonates was performed to examine the applicability of the well known "Stille coupling" methodology (i.e., palladium catalyzed reaction of aryl triflate with organostannane) to the use of less reactive aryl mesylate as substrate. Previously, the cross-coupling of 4-acetylphenyl \( p \)-fluorobenzenesulfonate with tri-\( n \)-butylphenylstannane, catalyzed by Pd(OAc)\textsubscript{2} in the presence of dppp ligand in DMF, was reported to give a 85\% yield of 4-acetylbenzophenyl.\textsuperscript{18} Under the same conditions,
Table I. Pd(0)- and Ni(0)-Catalyzed Cross-Coupling Reactions of Various Aryl Sulfonates with Tri-\textit{n}-butylphenylstannane\textsuperscript{a}

\[
\begin{array}{c c c c}
\text{entry} & \text{R} & \text{X} & \text{catalyst} & \text{yield}\textsuperscript{b}(\%)
\end{array}
\]

\[
\begin{array}{c c c c}
1 & \text{CH}_3\text{CO} & p-\text{FPhSO}_2\text{O} & \text{Pd(OAc)}_2+1.1\text{ equiv of dpppc}\textsuperscript{c} & 55 \\
2 & \text{CH}_3\text{CO} & p-\text{FPhSO}_2\text{O} & \text{Pd(OAc)}_2+1.1\text{ equiv of PPh}_3\textsuperscript{c} & 24 \\
3 & \text{CH}_3\text{CO} & \text{CH}_3\text{SO}_2\text{O} & \text{Pd(OAc)}_2+1.1\text{ equiv of dpppc}\textsuperscript{c} & 0 \\
4 & \text{CH}_3\text{CO} & \text{CH}_3\text{SO}_2\text{O} & \text{PdCl}_2(\text{dppf})+2.0\text{ equiv of dppfc}\textsuperscript{c} & 13 \\
5 & \text{CH}_3\text{O}_2\text{C} & \text{CH}_3\text{SO}_2\text{O} & \text{NiCl}_2(\text{PPh}_3)_2 & 24\textsuperscript{d} \\
6 & \text{CH}_3\text{O}_2\text{C} & \text{CH}_3\text{SO}_2\text{O} & \text{NiCl}_2(\text{dppf}) & 23\textsuperscript{e}
\end{array}
\]

\textsuperscript{a} Pd(0)-catalyzed reactions were run with 5 mol \% Pd catalyst, 3 equiv of LiCl and 1.2 equiv of PhSn(\textit{n}-Bu)\textsubscript{3} in DMF at 110°C under N\textsubscript{2} for 24h. Ni(0)-catalyzed reactions were run with 10 mol \% Ni catalyst, 1.7 equiv of Zn, 1.5 equiv of Et\textsubscript{4}NI and 1.1 equiv of PhSn(\textit{n}-Bu)\textsubscript{3} in THF at 67°C under N\textsubscript{2} for 24h. \textsuperscript{b} Actual yields determined by GC measurements were based on percent conversion of the starting substrate. \textsuperscript{c} Equivalents relative to Pd catalyst. \textsuperscript{d} Also produced 4,4'-dicarbomethoxybiphenyl (64\%). \textsuperscript{e} Also produced 4,4'-dicarbomethoxybiphenyl (45%).
however, much lower yield was obtained from p-fluorobenzene sulfonate (55%, entry 1 in Table I), and only unreacted starting substrate was isolated from the same reaction with mesylate (entry 3 in Table I). In contrast, PdCl₂(dppf) was found to catalyze the reaction, although the yield was low (13%, entry 4 in Table I). No further improvement in yield was obtained by employing various conditions. It is likely that the low yields obtained in Pd(0)-catalyzed Stille reaction of aryl mesylates are due to an inherent low reactivity of aryl mesylates toward palladium catalysts.

Nickel(0)-Catalyzed Cross-Coupling

Since aryl mesylates have a high reactivity toward Ni(0) species,¹⁹ cross-coupling of p-methoxycarbonylphenyl mesylate with tri-n-butylphenylstannane in the presence of a nickel catalyst (NiCl₂(PPh₃)₂ or NiCl₂(dppf)) was attempted (entry 5&6 in Table I). In both cases, relatively low yields (23-24%) of cross-coupled product, as well as fairly large amount of homo-coupled side product (45-64%), were obtained (eq 1).

\[
\text{CH}_3\text{O}_2\text{C-} \begin{array}{c} \text{OMs} \\
\end{array} + \begin{array}{c} \text{(n-Bu)}_3\text{Sn} \\
\end{array} \xrightarrow{\text{NiCl}_2(\text{PPh}_3)_2} \begin{array}{c} \text{Zn, Et}_3\text{Ni,THF} \\
\end{array}
\]

\[
\begin{array}{c} \text{CH}_3\text{O}_2\text{C-} \begin{array}{c} \text{OMs} \\
\end{array} + \begin{array}{c} \text{CH}_3\text{O}_2\text{C-} \begin{array}{c} \text{OMs} \\
\end{array} + \text{CO}_2\text{CH}_3 + \text{Starting Substrate} \\
\end{array} \\
\end{array}
\]

This large amount of side product may be rationalized by the poor reactivity of organostannane toward the ArNi(II)L₃ species (L=PPh₃ or THF) resulting from the oxidative addition of aryl mesylate to Ni(0) (i.e., sluggish transmetallation step of the reaction cycle), which retard the reaction leading to the cross-coupled product. On the other hand, the Ni(II) species can be further reduced by zinc to give Ni(I) species.
Another mesylate can oxidatively add to this species to give a diaryl Ni(III) complex which undergoes rapid reductive elimination, resulting in the formation of the homocoupled product. In general, the transmetalation has been considered as the rate determining step in the catalytic cycle of Pd(0) catalyzed Stille reaction.\textsuperscript{20} Efforts to enhance the reactivity of the tin compound toward transmetalation resulted only in low yields.

\subsection*{7.3.2.-Ni(0)-Catalyzed Cross-Couplings of Aryl Mesylates with Organomagnesium and -Zinc Compounds.}

The utility of organomagnesium and -zinc compounds as coupling partners with aryl mesylates in nickel(0)-catalyzed reactions was investigated. These compounds are more reactive than organostannanes toward organic electrophiles due to the partial covalent bond character of the C-Sn bond. Therefore, the slow transmetalation step (\textit{vide supra}) was avoided. Zinc reagents were prepared \textit{in situ} by transmetalation of the corresponding Grignard reagents with zinc chloride. For our feasibility study, we selected aryl mesylates containing no sensitive functional groups toward Grignard- or zinc reagents. Table II lists the range of the substrates and organometallics studied.

All experiments were performed by using a catalytic system consisting of 0.1 equiv of NiCl\textsubscript{2}(dpff) and 1.0 equiv of Zn. When the nickel catalyst was changed to NiCl\textsubscript{2}(PPh\textsubscript{3})\textsubscript{2} even in the presence of excess of PPh\textsubscript{3}, early catalyst decomposition was observed. Zn was not essential for the reduction of Ni(II) to Ni(0) in the presence of Grignard- & zinc reagents. However, the amount of homocoupled side products derived from the Grignard- & zinc reagents increased in the absence of Zn (\textit{vide infra}). These side products are often difficult to separate from the desired cross-coupled products. In all cases, complete consumption of the starting mesylates was observed, and the cross-coupled products were obtained in moderate yields (Table II). However,
Table II. Ni(0)-Catalyzed Cross-Coupling Reaction of Aryl Mesylates with Organomagnesium and -Zinc Compounds.\(^a\)

<table>
<thead>
<tr>
<th>entry</th>
<th>ArOSO(_2)CH(_3)</th>
<th>R-M-X</th>
<th>product</th>
<th>yield(^b)(%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>PhOSO(_2)CH(_3)</td>
<td>(p)-CH(_3)PhMgBr</td>
<td>(p)-CH(_3)PhPh</td>
<td>46</td>
</tr>
<tr>
<td>2</td>
<td>PhOSO(_2)CH(_3)</td>
<td>(p)-CH(_3)OPhMgBr</td>
<td>(p)-CH(_3)OPhPh</td>
<td>53</td>
</tr>
<tr>
<td>3</td>
<td>PhOSO(_2)CH(_3)</td>
<td>(p)-CH(_3)OPhZnCl</td>
<td>(p)-CH(_3)OPhPh</td>
<td>31</td>
</tr>
<tr>
<td>4</td>
<td>PhOSO(_2)CH(_3)</td>
<td>n-BuMgBr</td>
<td>n-BuPh</td>
<td>31</td>
</tr>
<tr>
<td>5</td>
<td>(p)-CH(_3)PhOSO(_2)CH(_3)</td>
<td>CH(_3)MgI</td>
<td>(p)-CH(_3)PhCH(_3)</td>
<td>83</td>
</tr>
<tr>
<td>6</td>
<td>(p)-CH(_3)PhOSO(_2)CH(_3)</td>
<td>CH(_3)ZnCl</td>
<td>(p)-CH(_3)PhCH(_3)</td>
<td>73</td>
</tr>
<tr>
<td>7</td>
<td>(o)-CH(_3)PhOSO(_2)CH(_3)</td>
<td>CH(_3)MgI</td>
<td>(o)-CH(_3)PhCH(_3)</td>
<td>66</td>
</tr>
<tr>
<td>8</td>
<td>(p)-CH(_3)OPhOSO(_2)CH(_3)</td>
<td>CH(_3)MgI</td>
<td>(p)-CH(_3)OPhCH(_3)</td>
<td>54</td>
</tr>
<tr>
<td>9</td>
<td>(p)-CH(_3)OPhOSO(_2)CH(_3)</td>
<td>PhMgBr</td>
<td>(p)-CH(_3)OPhPh</td>
<td>60</td>
</tr>
</tbody>
</table>

\(^a\) Reactions were run with 10 mol % NiCl\(_2\)(dpff), 1.0 equiv of Zn and 1.0-2.0 equiv of R-M-X in THF at RT under N\(_2\) for 10h. \(^b\) Actual yields determined by GC measurement were based on percent conversion of the starting substrate.
variable amounts of the two homo-coupled side products, derived from aryl mesylate and Grignard reagent (or zinc reagent) were also produced (eq 2).

\[
\begin{align*}
\text{Ph-OMs} + \text{CH}_3\text{O-Ph-MgBr} \rightarrow & \quad \text{Ni(0)} \\
\text{ca. 2 equiv} & \\
\text{Ph-CH}_3 + \text{Ph} + \text{Ph} + \text{Ph-OH} & \\
(53\%) & \quad (24\%) & \quad (2\%) & \quad (21\%)
\end{align*}
\]

\[
\begin{align*}
+ \text{CH}_3\text{O-Ph-CH}_3 + \text{Ph-OCH}_3 & \\
(25\%) & \quad (13\%)
\end{align*}
\]

Based on Grignard reagent initially added. \hfill (2)

Homo-coupling of Grignard reagent can be rationalized by the nucleophilic attack of Grignard reagent on the Ni(0) to give aryl Ni(0) species, substitution with another Grignard reagent, and reductive coupling to give the homo-coupled product. Reduction of the aryl mesylate and Grignard reagent also occurred during the cross-coupling process. In addition, the highly reactive Grignard reagent also effected the cleavage of the sulfur-oxygen bond in aryl mesylate.

It is note-worthy that the coupling reaction with Grignard reagents, more reactive than the corresponding zinc reagents, gave higher yield of product (entry 2 vs entry 3 and entry 5 vs entry 6 in Table II). When a substituent group was introduced at the ortho-position of the mesylate, Grignard coupling was inhibited. Thus, the ortho-substituted substrate reacted more sluggishly than the para-substituted substrate (entry 5 vs entry 7 in Table II).
7.3.3.-Cross-Coupling of Aryl Mesylates with Sodium Benzenethiolate.

The reaction of phenyl mesylate with sodium benzenethiolate in the presence of a Ni(0) catalyst generated from NiCl2(dppf) gave high yields of diphenyl sulfide (eq 3).

\[
\text{Ph-OMs} + \text{Ph-SNa} \xrightarrow{10 \% \text{NiCl}_2(\text{dppf}), 20\% \text{dppf}} \text{1.0 equiv Zn, DMF, 80°C, 4 h} \rightarrow \text{Ph-SPh}
\]

94%

(3)

The reaction products are summarized in Table III. The side products are benzene and biphenyl. The highest yield of cross-coupled product (94%) was obtained when 20% dppf was added to the reaction solution containing NiCl2(dppf) (Table III, entry 5). Lower yields of cross-coupled product were obtained when lower amounts of dppf were added. One function of the dppf is to stabilize the catalyst against premature decomposition. Catalyst decomposition occurred within 2.5 hours at 60°C when no dppf was added (Table III, entry 1). Diphenyl sulfide was formed in 74.5% yield. Substantial amounts of side products (10.4% benzene and 3.7% biphenyl) and unreacted phenyl mesylate (11.6%) were also detected. An improved yield of diphenyl sulfide (77%) and complete consumption of phenyl mesylate were obtained by increasing the reaction temperature to 80°C and adding 5% dppf to the reaction solution (Table III, entry 2). An increased amount of benzene (21%) was also obtained and a reduced amount of biphenyl (2%) were obtained. The yield of diphenyl sulfide improved to 83% by adding 10% dppf (Table III, entry 3). The amount of the side product formation (16% benzene, 1% biphenyl) was reduced. The addition of 20%
Table III. Ni(0)-Catalyzed Cross-Coupling of Phenyl Mesylate with Sodium Benzenethiolate.\(^d\)

\[
\text{Ph-OMs} + \text{Ph-SNa} \overset{\text{NiCl}_2(\text{dpff}), L}{\longrightarrow} \text{Ph-SPh}
\]

<table>
<thead>
<tr>
<th>entry</th>
<th>added ligand</th>
<th>amount of ligand (mol%)</th>
<th>temp (°C)</th>
<th>time (h)</th>
<th>yield(^b) (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>PhSPh</td>
</tr>
<tr>
<td>1</td>
<td>-</td>
<td>0</td>
<td>60</td>
<td>2.5(^d)</td>
<td>74.5</td>
</tr>
<tr>
<td>2</td>
<td>dpff</td>
<td>5</td>
<td>80</td>
<td>12</td>
<td>77</td>
</tr>
<tr>
<td>3</td>
<td>dpff</td>
<td>10</td>
<td>80</td>
<td>12</td>
<td>83</td>
</tr>
<tr>
<td>4</td>
<td>dpff</td>
<td>20</td>
<td>80</td>
<td>6</td>
<td>87</td>
</tr>
<tr>
<td>5</td>
<td>dpff</td>
<td>20</td>
<td>80</td>
<td>4</td>
<td>94</td>
</tr>
<tr>
<td>6</td>
<td>dpff</td>
<td>20</td>
<td>80</td>
<td>21.5</td>
<td>88</td>
</tr>
<tr>
<td>7</td>
<td>PPh(_3)</td>
<td>20</td>
<td>80</td>
<td>12</td>
<td>83</td>
</tr>
<tr>
<td>8(^c)</td>
<td>PPh(_3)</td>
<td>20</td>
<td>80</td>
<td>2.5(^d)</td>
<td>34</td>
</tr>
</tbody>
</table>

\(^{a}\)Reactions were run with 1.0 mmol PhOMs, 1.2 mmol PhSNa, 0.10 mmol NiCl\(_2\)(dpff) and 1.0 mmol Zn in 1.0 mL DMF under an inert atmosphere. \(^{b}\)Yield determined by GC using Ph\(_2\)O as an internal standard. \(^{c}\)NiCl\(_2\)(PPh\(_3\))\(_2\) substituted for NiCl\(_2\)(dpff). \(^{d}\)Rapid catalyst decomposition.
dppf resulted in a further improvement in the yield of diphenyl sulfide (87%) with a further reduction in the amount of side product formation (15% benzene, 2% biphenyl, entry 4 in Table III). A higher yield of diphenyl sulfide (94%) and lower yields of side product formation (3.9% benzene, 0.2% biphenyl) were obtained by quenching the reaction after 4 hours (Table III, entry 5). A small amount of phenyl mesylate (1.9%) remained unreacted. A lowering of the reaction temperature to 60°C resulted in 88% yield of Ph₂S after 21.5 h and in greatly reduced side reaction product formation (1.5% benzene and 0.09% biphenyl, entry 6 in Table III). However, 9.6% unreacted phenyl mesylate remained. The addition of 20% PPh₃ resulted in the formation of 83% diphenyl sulfide, 15% benzene, and 2% biphenyl (Table III, entry 7). The generation of the Ni(0) catalyst from NiCl₂(PPh₃)₂ in the presence of an additional 20% PPh₃ resulted in premature catalyst decomposition and only 34% conversion to Ph₂S (Table III, entry 8).

The Ni(0) catalyzed cross-coupling reaction of para-substituted aryl mesylates with sodium benzenethiolate resulted in the low yield formation of unsymmetrical diaryl sulfides (Table IV). The aryl mesylate which gave the highest yield of cross-coupled product was 4-acetylphenyl methansulfonate (32% isolated). Lower yields were obtained with methyl 4-methylsulfonyloxybenzoate (29%) and 4-cyanophenyl methansulfonate (20%). The major side reaction products were Ph₂S and the reduced aryl mesylate, i.e., ArH.

Diphenyl sulfide was formed in trace amounts (0.7%) when sodium benzenethiolate was reacted with the nickel catalyst in the absence of aryl mesylate (eq 4). This low yield indicates that the reaction of PhSNa with the Ni catalyst was not the source of the Ph₂S side product.
Table IV. Ni(0)-Catalyzed Cross-Coupling of Substituted Aryl Mesylates with Sodium Benzenethiolate.$^d$

\[
\text{Ar-OMs} + \text{PhSNa} \xrightarrow{10\% \text{ NiCl}_2(\text{dppt}), 20\% \text{ dpf}} 1.0 \text{ equiv. Zn, DMF} \rightarrow \text{Ar-S-Ph}
\]

<table>
<thead>
<tr>
<th>entry</th>
<th>ArOMs</th>
<th>time (h)</th>
<th>yield$^b$ (%)</th>
<th>ArSPh</th>
<th>PhSPh</th>
<th>ArH</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td><img src="image" alt="ArOMs" /></td>
<td>4.0</td>
<td>94</td>
<td>3.9</td>
<td></td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>CH$_3$O-C-<img src="image" alt="ArOMs" /></td>
<td>1.8</td>
<td>29 (16)</td>
<td>30</td>
<td>11</td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>CH$_3$-C-<img src="image" alt="ArOMs" /></td>
<td>3.0</td>
<td>(32)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>N=O-<img src="image" alt="ArOMs" /></td>
<td>1.8</td>
<td>20 (10)</td>
<td>36</td>
<td>18</td>
<td></td>
</tr>
</tbody>
</table>

$^d$Reactions were run with 1.0 mmol ArOMs, 1.2 mmol PhSNa, 0.10 mmol NiCl$_2$(dpf) and 1.0 mmol Zn in 1.0 mL DMF under an inert atmosphere at 80°C. $^b$Yield determined by GC using Ph$_2$O as an internal standard, isolated yield in parenthesis.
A possible sequence of reactions leading to the formation of Ph$_2$S is shown in Figure 1. This sequence is analogous to one suggested in the reaction of aryl halides with aromatic thiols.$^2$ This sequence begins with the oxidative addition of aryl mesylate to a Ni(0) species to form ArNi(OMs)L$_2$. A ligand exchange reaction gives ArNi(SPh)L$_2$. Reductive elimination of ArSPh from this species gives the cross-coupled product and regenerates a Ni(0) species. ArSPh can participate in reactions which lead to side product formation. This is because ArSPh can oxidatively add to Ni(0). This can occur by cleavage of the aryl-sulfur bond or the phenyl-sulfur bond. Cleavage of the aryl-sulfur bond regenerates ArNi(SPh)L$_2$. Reductive elimination from this species results in no change in the product distribution. However, cleavage of the phenyl-sulfur bond gives PhNi(SAr)L$_2$. The ArS$^-$ group can exchange with a PhS$^-$ group to give PhNi(SPh)L$_2$. Reductive elimination gives Ph$_2$S and the Ni(0) species.

7.3.4.-Attempt on Ni(0)-Catalyzed Heck-Type Olefination of Aryl Mesylate.

Various efforts to develop Heck-type olefination of aryl mesylate based on the use of Ni(0)-phosphine complexes did not produce coupled product. In all experiments, only unreacted starting substrates were recovered. It is likely that vinyl compounds coordinate to the Ni(0) species so strongly that the catalyst becomes inactive toward oxidative addition of the aryl mesylates.
Figure 1. Possible Mechanism of Diaryl Sulfide Formation.
REFERENCES


PART III. SYNTHESIS OF FUNCTIONAL POLYARYLENES FROM
SUBSTITUTED HYDROQUINONES AND BISPHEROLS VIA
NICKEL CATALYZED HOMO-COUPLING OF THEIR
BISMESYLATES
Chapter 8
SYNTHESIS OF FUNCTIONAL REGIOREGULAR AND REGIOIRRREGULAR
SUBSTITUTED POLY(\(p\)-PHENYLENE)S FROM HYDROQUINONES VIA
NICKEL(0) CATALYZED COUPLING OF THEIR BISMESYLATES

8.1. - INTRODUCTION

Poly(\(p\)-phenylene) (PPP) is the simplest aromatic polymer containing only carbon and hydrogen and, therefore, is the aromatic homologue of polyethylene (PE). PE was and is used as a model for fundamental investigations on the crystallization and morphology of flexible chain polymers.\(^1\) Its present status was facilitated by the availability of synthetic methods for the preparation of linear and cyclic oligomers of polyethylene with well-defined size and uniform molecular weight distribution,\(^{1c,2}\) and also by their solubility.

PPP is the simplest rigid rod-like polymer, and convenient methods for its synthesis would generate a model for rigid rod-like polymers. Unfortunately, only oligo(\(p\)-phenylene)s with seven and less than seven phenylenic units are soluble, the larger only in low concentration and at elevated temperatures.\(^3\)

Several synthetic strategies were elaborated for the preparation of PPPs. Oxidative polymerization of benzene is the simplest direct method but the resulting polymers do not contain only para-structural units and their molecular weight is low since it is determined by the limited solubility of the polymer.\(^4\) Indirect methods for the synthesis of soluble precursors of PPP followed by their chemical transformation into PPP were most successfully used to prepare the unsubstituted and insoluble PPP. Anionic polymerization of 1,3-cyclohexadiene followed by bromination and dehydrogenation\(^{5a}\) and radical polymerization of bis(octyl) or bis(methoxycarbonyl)
derivatives of cis-5,6-dihydroxy-1,3-cyclohexadiene followed by thermally induced acid elimination\textsuperscript{5b,d} yield mixtures of para and other phenylene structural units, and respectively, provide cleavage during pyrolysis. The most successful indirect method reported for the synthesis of PPP is based on the polymerization of cis-5,6-bis(trimethylsiloxy)-1,3-cyclohexadiene followed by a three step aromatization reaction to yield PPP with number average degrees of polymerization of up to 150.\textsuperscript{5e-g} The utility of the insoluble PPP for physical investigations is however, very limited.

Soluble PPPs are obtained by increasing their configurational entropy.\textsuperscript{6} This can be accomplished by attaching functional side groups to the backbone of PPP\textsuperscript{4b,7} by increasing the number of constitutional isomers in the main chain,\textsuperscript{8} by increasing the configurational entropy of the main chain through a proper combination of kinked phenylene units which generate a linear extended chain conformation,\textsuperscript{10} and by combinations of all these techniques. Thus, soluble high molecular weight phenylated poly(p-phenylene)s were synthesized by Diels-Alder reaction of bis(tetracyclone)s with p- or m- diethynylbenzene\textsuperscript{8a,c} and of the bibenzynes with bis(tetracyclone)s.\textsuperscript{8d} Additional classes of soluble poly(p-phenylene)s were obtained by the polymerization of 2,5-dibromo-1,4-di-\textit{n}-alkylbenzenes\textsuperscript{10a} and 2,5-dibromobiphenyl\textsuperscript{10b} using the Yamamoto reaction, Pd(0)-catalyzed polymerization of 4-bromo-2,5-di-\textit{n}-hexylbenzeneboronic acid,\textsuperscript{10c,d} anionic polymerization of 2-phenyl-1,3-cyclohexadiene followed by aromatization\textsuperscript{6} and spontaneous polymerization of 1-bromo-4-lithiobenzene in hexamethylphosphoramide.\textsuperscript{10e}

Highly branched and dendrimeric polyphenylenes were synthesized by cocyclotrimerization of \textit{p}-diethynylbenzene with phenylacetylene,\textsuperscript{11} by Pd(0)-catalyzed coupling of (3,5-dibromophenyl)boronic acid\textsuperscript{12a} and by a stepwise variant of it\textsuperscript{12b} The first examples of macrocyclic oligo(p-phenylene) with degrees of oligomerization of up
to 10 were synthesized by an indirect method.\textsuperscript{12c} Both branched and macrocyclic polyphenylenes are soluble.

Soluble polyarylenes containing binaphthylene structural units were synthesized by the cation-radical polymerization of bis(1-naphthyl)biphenyl\textsuperscript{13a} and by Ni(0) catalyzed polymerization of 2,5-bis-(4-chloro-1-naphthyl)biphenyl.\textsuperscript{13b} The bulky and twisted binaphthylene structural unit is responsible for the solubility of the resulting polymers.

Recently we have reported a novel synthetic method for the preparation of functional poly(p-phenylene)s and polyarylenes starting from readily available hydroquinones and bisphenols via Ni(0) catalyzed homocoupling of their corresponding triflates\textsuperscript{14} and by the homocoupling of substituted dihalophenylene.\textsuperscript{14b} This method provides an easy access to a large variety of functional groups substituted and soluble PPPs.\textsuperscript{14b} Some of these polymers can also be transformed into the unsubstituted and insoluble PPP via subsequent chemical modifications.\textsuperscript{15} One of the main limitations of this novel synthetic method is the high price of triflic anhydride. In chapter 2, we have demonstrated that under suitable conditions a large variety of aryl sulfonates including aryl mesylate undergo Ni(0) catalyzed homocoupling reactions.\textsuperscript{16} The goal of this chapter is to report a novel method for the synthesis of functional polyphenylenes via the Ni(0) catalyzed homocoupling of functional bis[methylsulfonyloxy] derivatives (i.e., bismesylates) of substituted hydroquinones and 2,2'-disubstituted-4,4'-dihydroxybiphenyls. This novel synthetic procedure represents one of the most convenient and versatile method for the synthesis of soluble, well-defined and functional PPPs with high molecular weight and opens novel synthetic capabilities in this field.

8.2.-EXPERIMENTAL
8.2.1.-Materials

All reagents were purchased from commercial sources (Aldrich or Lancaster) and used without further purification except when reported. Pyridine was dried over CaH₂ and distilled. THF was distilled over sodium / benzophenone. Zinc dust was stirred in acetic acid, washed with water and dried in vacuo at 120°C. NiCl₂(PPh₃)₂ was prepared according to a literature procedure.²³

2,5-Dihydroxybenzoic acid, 3,5-dihydroxybenzoic acid, phenylhydroquinone, methylhydroquinone, tert-butylhydroquinone, 1,4-dimethoxybenzene, 1,4-dichlorobenzoic acid (all from Aldrich), 2,5-dimethoxybenzonitrile, 1,4-dibromobenzoic acid (Lancaster), and diethyl 2,5-dihydroxyterephthalate (Riedel-Dehaen Co.), were used as received.

2,2′-Dibenzoyl-4,4′-bis(methylsulfonyloxy)biphenyl,¹⁶ 2,2′-bis(p-fluorobenzoyl)-4,4′-bis(methylsulfonyloxy)biphenyl,¹⁶ 2,2′-bis(p-tert-butylbenzoyl)-4,4′-bis(methylsulfonyloxy)biphenyl,¹⁶ and 2,5-dihydroxybenzophenone²⁵ were synthesized by published procedures. (2-Ethylhexyl) 2,5-dibromobenzoate and (2-ethylhexyl) 2,5-dichlorobenzoate were prepared by the acid catalyzed esterification of 2,5-dibromobenzoic acid and 2,5-dichlorobenzoic acid with 2-ethyl-1-hexanol.²⁴ Unless otherwise noted, all compounds synthesized in the present chapter were purified until their 200 MHz ¹H-NMR spectra corresponded to the expected structure and the purity was established by comparison with published mp or found to be higher than 99.5% by GC or HPLC.

8.2.2.-Synthesis of Monomers

All dihydroxybenzoates were prepared by the acid catalyzed esterification of dihydroxybenzoic acid with the corresponding alcohols.²⁴
Methyl 2,5-dihydroxybenzoate. (78%): white crystals (hexanes/EtOAc); mp 84-85°C; 
$^1$H NMR δ 7.28 (d, $J = 2.0$ Hz, 1H, $\sigma$ to -CO$_2$CH$_3$), 7.01 (d, $J = 8.2$ Hz, 1H, $p$ to -CO$_2$CH$_3$), 6.87 (d, $J = 8.0$ Hz, 1H, $m$ to -CO$_2$CH$_3$), 3.87 (s, 3H, -CO$_2$CH$_3$).

Methyl 3,5-dihydroxybenzoate. (94%): white crystals (hexanes/EtOAc); mp 163-165°C; 
$^1$H NMR δ 8.60 (br s, 2H, -OH), 6.63 (d, $J = 2.2$ Hz, 2H, $\sigma$ to -CO$_2$CH$_3$), 6.20 (d, $J = 2.2$ Hz, 1H, $p$ to -CO$_2$CH$_3$), 3.50 (s, 3H, -CO$_2$CH$_3$).

(2-Ethylhexyl) 2,5-dihydroxybenzoate. (88%): colorless oil; $^1$H NMR δ 10.53 (s, 1H, -OH), 7.30 (d, $J = 2.9$ Hz, 1H, $\sigma$ to -CO$_2$-), 7.01 (dd, $J = 8.9, 3.0$ Hz, 1H, $p$ to -CO$_2$-), 6.89 (d, $J = 8.9$ Hz, 1H, $m$ to -CO$_2$-), 5.86 (s, 1H, -OH), 4.24 (d, $J = 5.7$ Hz, 2H, -CO$_2$CH$_2$CH$_2$-), 1.73-1.67 (m, 1H, -CO$_2$CH$_2$CH(CH$_2$CH$_3$)(CH$_2$)$_3$CH$_3$), 1.46-1.24 (m, 8H, -CO$_2$CH$_2$CH(CH$_2$CH$_3$)(CH$_2$)$_3$CH$_3$), 0.96-0.84 (m, 6H, -CO$_2$CH$_2$CH(CH$_2$CH$_3$)(CH$_2$)$_3$CH$_3$).

Isopropyl 2,5-dihydroxybenzoate. (77%): colorless oil; $^1$H NMR δ 7.91 (d, $J = 3.0$ Hz, 1H, $\sigma$ to -CO$_2$-), 7.62 (d, $J = 10.0$, Hz, 1H, $p$ to -CO$_2$-), 7.60 (d, $J = 9.0$ Hz, 1H, $m$ to -CO$_2$-), 5.85 (septet, $J = 7.0$ Hz, 1H, -CO$_2$CH(CH$_3$)$_2$), 5.70 (br s, 2H, -OH), 1.95 (d, $J = 7.0$ Hz, 6H, -CO$_2$CH(CH$_3$)$_2$).

2,5-Dihydroxybenzonitrile was prepared from 2,5-dimethoxybenzonitrile.$^{26}$ (88%): 
white crystals (EtOH); mp 150°C; $^1$H NMR δ 9.75 (br s, 2H, -OH), 6.93-6.80 (m, 3H, aromatic protons).

(2-Ethylhexyl) 2,5-dibromobenzoate. (82%): colorless oil; bp 110-113°C/0.1 mmHg; 
$^1$H NMR δ 7.90 (d, $J = 2.3$ Hz, 1H, $\sigma$ to -CO$_2$-), 7.50 (d, $J = 8.5$ Hz, 1H, $m$ to
-CO₂⁻), 7.46 (dd, J = 8.5, 2.1 Hz, 1H, p to -CO₂⁻), 4.28 (d, J = 5.7 Hz, 2H, -CO₂CH₂H₂CH⁻), 1.78-1.66 (m, 1H, -CO₂CH₂CH((CH₂CH₃)(CH₂)₃CH₃), 1.42-1.34 (m, 8H, -CO₂CH₂CH₂CH(CH₂CH₃)(CH₂)₃CH₃), 0.98-0.90 (m, 6H, -CO₂CH₂CH(CH₂CH₃)(CH₂)₃CH₃).

(2-Ethylhexyl) 2,5-dichlorobenzoate, (82%): colorless oil; bp 111-114°C/0.06 mmHg; ¹H NMR δ 7.80 (d, J = 1.5 Hz, 1H, o to -CO₂⁻), 7.39 (s, 2H, m and p to -CO₂⁻), 4.28 (d, J = 5.6 Hz, 2H, -CO₂CH₂H₂CH⁻), 1.77-1.63 (m, 1H, -CO₂CH₂CH₂CH(CH₂CH₂CH₃)(CH₂)₃CH₃), 1.52-1.25 (m, 8H, -CO₂CH₂CH₂CH(CH₂CH₂CH₃)(CH₂)₃CH₃), 0.98-0.89 (m, 6H, -CO₂CH₂CH(CH₂CH₃)(CH₂)₃CH₃).

4-Chloro-3-methylphenyl acetate.

4-Chloro-3-methyl phenol (43g, 0.30 mol), acetic anhydride (34 mL, 0.36 mol) and a few drops of H₂SO₄ were stirred at 60°C for 2h, cooled to 22°C, and poured into H₂O (200mL). The resulting mixture was stirred (1h) and extracted with Et₂O (200 mL). The organic phase was dried (MgSO₄), concentrated and chromatographed (SiO₂, Hexanes/Et₂O 10/1) to give a colorless liquid (51g, 92%): bp 65-68°C / 0.15 mm Hg; ¹H NMR δ 7.32 (d, J = 8.5 Hz, 1H, o to chlorine), 6.96 (d, J = 2.5 Hz, 1H, o to -CH₃), 6.87 (dd, J = 8.5, 2.5 Hz, 1H, p to -CH₃), 2.35 (s, 3H, -OC(=O)CH₃), 2.27 (s, 3H, -CH₃).

2,2'-Dimethyl-4,4'-dihydroxybiphenyl.

4-Chloro-3-methylphenyl acetate (43g, 0.23 mmol) was homocoupled by an analogous procedure to other aryl chlorides.17e After completion of the reaction, the reaction mixture was filtered, and poured into a solution of NaOH (50 g / 500 ml H₂O).
The mixture was stirred overnight at 22°C, washed with Et₂O (300 ml), acidified with conc. of HCl to pH ~ 1. The resulting precipitate was collected by filtration, washed with water, dried, and recrystallized (Hexanes/CHCl₃ 10/1) to give brownish crystals (16 g, 63%): mp 154-155°C (lit. 27 156°C); ¹H NMR δ 6.92 (d, J = 8.1 Hz, 2H, m to hydroxy and methyl), 6.66 (s, 2H, -OH), 6.77-6.70 (m, 4H, aromatic protons, o and p to methyl), 1.98 (s, 6H, -CH₃).

Substituted 2,5-dimethoxybenzophenones were obtained by the Friedel-Crafts acylation of 1,4-dimethoxybenzene with the appropriate acid chloride.

**2,5-Dimethoxy-4'-fluorobenzophenone.**

**A**lCl₃ (21g, 0.158 mol) was slowly added to a solution of 1,4-dimethoxybenzene (20g, 0.145 mol) in CH₂Cl₂ (140 mL) at 0°C. 4-Fluorobenzoyl chloride (25.3 g, 0.160 mole) (prepared from 4-fluorobenzoic acid and thionyl chloride) was added dropwise. The reaction mixture was stirred at 0°C for 8h, then poured into ice water (100 mL) containing conc. HCl (10 mL). The organic phase was separated, washed (10% NaOH), dried (MgSO₄) and evaporated. Recrystallization (95% EtOH) gave 34 g (90%): mp 51-52°C; ¹H NMR δ 7.88-7.81 (m, 2H, aromatic protons m to fluorine), 7.13-6.90 (m, 5H, 2 aromatic protons o to fluorine, and 3 aromatic protons o, m, and p to carbonyl), 3.77 (s, 3H, -OCH₃ o to carbonyl), 3.65 (s, 3H, -OCH₃ m to carbonyl).

**2,5-Dimethoxy-4'-chlorobenzophenone** was prepared using 4-chlorobenzoyl chloride (85%): white crystals (benzene); mp 72-73°C; ¹H NMR δ 7.60 (d, J = 8.6 Hz, 2H, m to chlorine), 7.40 (d, J = 8.6Hz, 2H, o to chlorine), 7.02-6.90 (m, 3H, o, m, and p to carbonyl), 3.80 (s, 3H, -OCH₃ o to carbonyl), 3.67 (s, 3H, -OCH₃ m to carbonyl).
2,5-Dimethoxy-4'-tert-butylbenzophenone, (84%): white crystals (benzene); mp 50°C; \( ^1H \text{NMR} \delta 7.78 (d, J = 8.4 \text{ Hz}, 2H, m \text{ to t-butyl}), 7.45 (d, J = 8.4 \text{ Hz}, 2H, o \text{ to t-butyl}), 6.98-6.89 (m, 3H, o, m, and p \text{ to carbonyl}), 3.78 (s, 3H, -OCH\text{H}_3 o \text{ to carbonyl}), 3.69 (s, 3H, -OCH\text{H}_3 m \text{ to carbonyl}), 1.34 (s, 9H, -C(CH\text{H}_3)_3). \)

**Substituted 2,5-dihydroxybenzophenones** were synthesized by the BBr\text{3} induced cleavage of the CH\text{3}-O bonds of the corresponding substituted 2,5-dimethoxybenzophenones.\textsuperscript{28}

**2,5-Dihydroxy-4'-fluorobenzophenone.**

2,5-Dimethoxy-4'-fluorobenzophenone (20 g, 0.077 mole, in 150 mL CH\text{2}Cl\text{2}) was added dropwise to a solution of 1.0 M BBr\text{3} in CH\text{2}Cl\text{2} (195 mL, 0.195 mol) and CH\text{2}Cl\text{2} (150 mL) at -30°C, over 30 min. The reaction mixture was allowed to warm to 22°C, and stirred for 5 h and slowly poured into a mixture of ice water (500 mL) and Et\text{2}O (300 mL). The organic phase was separated, washed (H\text{2}O and dried (MgSO\text{4}). Evaporation and recrystallization (hexane/EtOAc) gave 12.0 g (80%) yellow crystals: mp 140-141°C; \( ^1H \text{NMR} \delta 11.31 (br s, 2H, -OH), 7.74-7.68 (m, 2H, aromatic protons m to fluorine), 7.19-7.00 (m, 5H, 2 aromatic protons o to fluorine, and 3 aromatic protons o, m, and p to p-fluorobenzoyl).

**2,5-Dihydroxy-4'-tert-butylbenzophenone, (86%):** yellow crystals (hexanes/EtOAc); mp 115-116°C; \( ^1H \text{NMR} \delta 11.63 (br s, 2H, -OH), 7.62 (d, J = 8.4 \text{ Hz}, 2H, m \text{ to t-butyl}), 7.50 (d, J = 8.4 \text{ Hz}, 2H, o \text{ to t-butyl}), 7.09-6.97 (m, 3H, aromatic protons o, m, and p to p-t-butylbenzoyl), 1.36 (s, 9H, -C(CH\text{H}_3)_3). \)
**Aryl bismesylates**: Aryl bismesylates were synthesized by the reaction of methanesulfonyl chloride with the corresponding phenol in pyridine.  

**4'-Fluoro-2,5-bis(methylsulfonyloxy)benzophenone.**

Methanesulfonyl chloride (16.3 g, 0.142 mole) was added dropwise to a solution of 4'-fluoro-2,5-dihydroxybenzophenone (11 g, 0.047 mole) in pyridine (80 mL) at 0°C. The mixture was warmed to 22°C and stirred for 12 h. The reaction mixture was poured into water (800 mL) and the resulting precipitate was collected, washed (H₂O) and recrystallized twice (CHCl₃/EtOAc) to yield white crystals (12.9 g, 71%): mp 141-142°C; ¹H NMR δ 7.73-7.66 (m, 2H, m to fluorine), 7.40 (br s, 2H, o and p to p-fluorobenzoyl), 7.28 (br s, 1H, m to p-fluorobenzoyl), 7.08-6.99 (m, 2H, o to fluorine), 3.10 (s, 3H, -OSO₂CH₃ o to carbonyl), 2.93 (s, 3H, -OSO₂CH₃ m to carbonyl).

**Methyl 2,5-bis(methylsulfonyloxy)benzoate.** (81%): white crystals (benzene); mp 70-71°C; ¹H NMR δ 7.90 (s, 1H, o to -CO₂CH₃), 7.52 (s, 2H, m and p to -CO₂CH₃), 3.95 (s, 3H, -CO₂CH₃), 3.31 (s, 3H, -OSO₂CH₃ o to -CO₂CH₃), 3.22 (s, 3H, -OSO₂CH₃ m to -CO₂CH₃).

**Methyl 3,5-bis(methylsulfonyloxy)benzoate.** (84%): white crystals (benzene); mp 96-97°C; ¹H NMR δ 7.92 (d, J = 2.3 Hz, 2H, o to -CO₂CH₃), 7.47 (d, J = 2.3 Hz, 1H, p to -CO₂CH₃), 3.95 (s, 3H, -CO₂CH₃), 3.23 (s, 6H, -OSO₂CH₃).

**2-Ethylhexyl 2,5-bis(methylsulfonyloxy)benzoate.** (73%): viscous oil; ¹H NMR δ 7.85 (br s, 1H, o to -CO₂-), 7.52 (br s, 2H, m and p to -CO₂-), 4.25 (d, J = 5.6 Hz, 2H, CO₂CH₂CH(CH₂CH₃)CH₂-), 3.31 (s, 3H, -OSO₂CH₃ o to -CO₂-), 3.21 (s, 3H, -OSO₂CH₃ m to -CO₂-), 1.73 (m, 1H, -CO₂CH₂CH(CH₂CH₃)CH₂-), 1.51-1.25 (m,
$8H$, -CO$_2$CH$_2$CH(CH$_2$CH$_3$)CH(CH$_2$CH$_3$), 0.93-0.83 (m, 6H, 
-CO$_2$CH$_2$CH(CH$_2$CH$_3$)(CH$_2$)$_3$CH$_3$).

**Isopropyl 2,5-bis(methylsulfonyloxy)benzoate. (78%)**: white crystals (benzene); mp 69-70°C; $^1$H NMR δ 7.84 (br s, 1H, o to -CO$_2$-), 7.50 (br s, 2H, m and p to -CO$_2$-), 5.26 (septet, $J = 6.5$ Hz, 1H, -CO$_2$CH(CH$_3$)$_2$), 3.30 (s, 3H, -OSO$_2$CH$_3$ o to -CO$_2$-), 3.22 (s, 3H, -OSO$_2$CH$_3$ m to -CO$_2$-), 1.39 (d, $J = 6.5$ Hz, 6H, -CO$_2$CH(CH$_3$)$_2$).

**2,5-Bis(methylsulfonyloxy)benzonitrile. (67%)**: white crystals (CHCl$_3$/EtOAc); mp 111-112°C; $^1$H NMR δ 7.41 (d, $J = 2.3$ Hz, 1H, o to -CN), 7.30-7.27 (m, 2H, m and p to -CN), 3.07 (s, 3H, -OSO$_2$CH$_3$ o to -CN), 2.96 (s, 3H, -OSO$_2$CH$_3$ m to -CN).

**2,5-Bis(methylsulfonyloxy)benzophenone. (80%)**: white crystals (CHCl$_3$/EtOAc); mp 118-119°C; $^1$H NMR δ 7.85-7.78 (m, 2H, o to carbonyl on phenyl), 7.70-7.41 (m, 6H, aromatic protons), 3.21 (s, 3H, -OSO$_2$CH$_3$ o to benzoyl), 3.01 (s, 3H, -OSO$_2$CH$_3$ m to benzoyl).

**4'-Chloro-2,5-bis(methylsulfonyloxy)benzophenone. (89%)**: white crystals (CHCl$_3$/EtOAc); mp 153-154°C; $^1$H NMR δ 7.76 (d, $J = 8.8$ Hz, 2H, m to chlorine), 7.57-7.42 (m, 5H, aromatic protons), 3.22 (s, 3H, -OSO$_2$CH$_3$ o to p-chlorobenzoyl), 3.06 (s, 3H, -OSO$_2$CH$_3$ m to p-chlorobenzoyl).

**4'-tert-Butyl-2,5-bis(methylsulfonyloxy)benzophenone. (86%)**: white crystals (hexanes/EtOAc); mp 142-143°C; $^1$H NMR δ 7.74 (d, $J = 8.4$ Hz, 2H, m to t-butyl),
7.56-7.48 (m, 5H, aromatic protons), 3.20 (s, 3H, -OSO₂CH₃ o to p-t-butylbenzoyl),
3.02 (s, 3H, -OSO₂CH₃ m to p-t-butylbenzoyl), 1.34 (s, 9H, -C(CH₃)₃).

**Diethyl 2,5-bis(methylsulfonyloxy)terephthalate (81%):** white crystals (CHCl₃/EtOAc);
mp 134-135°C: ¹H NMR δ 7.98 (s, 2H, aromatic protons), 4.42 (q, J= 7.1 Hz, 4H,
-CO₂CH₂CH₃), 3.33 (s, 6H, -OSO₂CH₃), 1.42 (t, J = 7.1 Hz, 6H, -CO₂CH₂CH₃).

**2-tert-Butyl-1,4-bis(methylsulfonyloxy)benzene (76%):** white crystals (CHCl₃); mp
106-107°C : ¹H NMR δ 7.60 (d, J = 9.1 Hz, 1H, m to t-butyl), 7.34 (d, J = 3.0 Hz.
1H, o to t-butyl), 7.18 (dd, J = 9.1, 3.0 Hz, 1H, p to t-butyl), 3.29 (s, 3H,
-OSO₂CH₃ m to t-butyl), 3.16 (s, 3H, -OSO₂CH₃ o to t-butyl), 1.40 (s, 9H, -C(CH₃)₃).

**1,4-Bis(methylsulfonyloxy)benzene (90%):** white crystals; mp 167-168°C : ¹H NMR
δ 7.36 (s, 4H, o to oxygen), 3.19 (s, 6H, -OSO₂CH₃).

**2-Methyl-1,4-bis(methylsulfonyloxy)benzene (92%):** white crystals (CHCl₃/EtOAc);
mp 87-88°C : ¹H NMR δ 7.35 (d, J = 8.7 Hz, 1H, m to methyl), 7.24-7.13 (m, 2H, o
and p to methyl), 3.23 (s, 3H, -OSO₂CH₃ m to methyl), 3.16 (s, 3H, -OSO₂CH₃ o to
methyl), 2.34 (s, 3H, -CH₃).

**2,5-Bis(methylsulfonyloxy)biphenyl (84%):** white crystals (CHCl₃); mp 118-119°C :
¹H NMR δ 7.52 (m, 8H, aromatic protons), 3.20 (s, 3H, -OSO₂CH₃ m to phenyl),
2.56 (s, 3H, -OSO₂CH₃ o to phenyl).
2,2'-Dimethyl-4,4'-bis(methylsulfonyloxy)biphenyl (97%): pale yellowish oil; \(^{1}H\) NMR \(\delta\) 7.22-7.10 (m, 6H, aromatic protons), 3.21 (s, 6H, -OSO\(_2\)CH\(_3\)), 2.07 (s, 6H, -CH\(_3\)).

Aryl bistriflates and aryl bis(p-fluorobenzenesulfonate)s.

Aryl bistriflates\(^{30}\) were synthesized by the reaction of triflic anhydride with the appropriate phenol in pyridine, and aryl bis(p-fluorobenzenesulfonate)s were synthesized by the reaction of the p-fluorobenzenesulfonyl chloride with the corresponding phenol in pyridine.

(2-Ethylhexyl) 2,5-bis(4-fluorophenylsulfonyloxy)benzoate (69%): pale yellowish oil; \(^{1}H\) NMR \(\delta\) 7.95-7.84 (m, 4H, m to fluorine), 7.43 (d, \(J = 2.7\) Hz, 1H, \(\alpha\) to -CO\(_2\>-\)), 7.29-7.12 (m, 6H, 4 aromatic protons \(\alpha\) to fluorine on p-fluorophenyl, and 2 aromatic protons \(m\) and \(p\) to -CO\(_2\>-\)), 4.12 (d, \(J = 6.5\) Hz, 2H, -CO\(_2\)CH\(_2\)CH(CH\(_2\)CH\(_3\))CH\(_2\>-\)), 1.77-1.61 (m, 1H, -CO\(_2\)CH\(_2\)CH\(_2\)CH(CH\(_2\)CH\(_3\))CH\(_2\>-\)), 1.43-1.29 (m, 8H, -CO\(_2\)CH\(_2\)CH(CH\(_2\)CH\(_3\))CH\(_2\)CH\(_3\)), 0.94-0.86 (m, 6H, -CO\(_2\)CH\(_2\)CH(CH\(_2\)CH\(_3\))CH\(_2\)CH\(_3\)).

(2-Ethylhexyl) 2,5-bis(trifluoromethylsulfonyloxy)benzoate (78%): colorless oil; bp 117-120°C/0.1 mmHg; \(^{1}H\) NMR \(\delta\) 7.95 (d, \(J = 3.1\) Hz, 1H, \(\alpha\) to -CO\(_2\>-\)), 7.54 (dd, \(J = 9.0, 3.1\) Hz, 1H, \(p\) to -CO\(_2\>-\)), 7.45 (d, \(J = 9.0\) Hz, 1H, \(m\) to -CO\(_2\>-\)), 4.31 (d, \(J = 5.1\) Hz, 2H, -CO\(_2\)CH\(_2\)CH\(_2\)CH(CH\(_2\)CH\(_3\))CH\(_2\>-\)), 1.85-1.67 (m, 1H, -CO\(_2\)CH\(_2\)CH\(_2\)CH(CH\(_2\)CH\(_3\))CH\(_2\)CH\(_3\)), 1.41-1.33 (m, 8H, -CO\(_2\)CH\(_2\)CH\(_2\)CH(CH\(_2\)CH\(_3\))CH\(_2\)CH\(_3\)), 0.99-0.90 (m, 6H, -CO\(_2\)CH\(_2\)CH(CH\(_2\)CH\(_3\))CH\(_2\)CH\(_3\)).
8.2.3.-Polymerizations

Method A

In a typical polymerization (Table I, Entry 1), a 125 mL Schlenk tube was charged with NiCl$_2$(PPh$_3$)$_2$ (115 mg, 0.175 mmol), Zn (800 mg, 12.3 mmol), Et$_4$NI (675 mg, 2.63 mmol), and a magnetic stirring bar. The tube was sealed with a rubber septum and the contents were dried at 22°C under vacuum (1x10$^{-6}$ mmHg) for 24 h. After placing the contents under an Ar atmosphere, dry THF (1.0 mL) was added via a syringe through the rubber septum. The mixture was stirred at 22°C for 5 min (the color of the mixture gradually changed to deep red brown). Methyl 2,5-bis(methylsulfonyloxy)benzoate (568 mg, 1.75 mmol) in THF (0.5 mL) was added and the mixture was heated at 67°C for 10 h. After cooling to 22°C, the reaction mixture was poured into 100 mL of methanol acidified with 25 mL conc. HCl. The resulting precipitate was collected by filtration and dissolved in 2 mL of CHCl$_3$. The solution was filtered and poured into 100 mL of methanol. The precipitate was collected by filtration and dried in vacuo (75 mg, 75%). The polymer was purified by reprecipitation into MeOH from CHCl$_3$ solution before being analyzed by GPC. (Mn = 3950 g/mol, Mw/Mn = 2.24, DP = 29).

Method B

In a typical polymerization (Table V, Entry 5), a 125 mL Schlenk tube was charged with NiCl$_2$(PPh$_3$)$_2$ (115 mg, 0.175 mmol), Zn (800 mg, 12.25 mmol), Et$_4$NI (675 mg, 2.625 mmol), PPh$_3$ (275 mg, 1.048 mmol), 2,5-bis(methylsulfonyloxy)biphenyl (599 mg, 1.75 mmol) and a magnetic stirring bar. The tube was sealed with a rubber septum and the contents were dried at 22°C under
vacuum \((1 \times 10^{-6} \text{ mmHg})\) for 2 h. After the reactants were placed under an Ar atmosphere, 1.5 mL of dry THF was added via a syringe through the rubber septum. The mixture was stirred at 22°C for 20 min (the color of the mixture gradually changed to deep red brown) and heated at 67°C for 24 h. After cooling to 22°C, the reaction mixture was poured into 100 mL of methanol acidified with 25 mL conc. HCl. The resulting precipitate was collected by filtration and dissolved in 2 mL of CHCl₃. The solution was filtered and poured into 100 mL of methanol. The resulting precipitate was collected by filtration and vacuum dried (218 mg, 82%). The polymer was purified by reprecipitation into methanol from CHCl₃ solution before being analyzed by GPC (Mn = 1310 g/mol, Mw/Mn = 1.3, DP = 9).

8.3.-RESULTS AND DISCUSSION

The general procedure for the preparation of functional poly(\(p\)-phenylene)s utilized the Ni(0) catalyzed homocoupling reaction of aryl bismesylates derived from substituted hydroquinones (eq 1).

\[
\begin{align*}
\text{HO-} & \quad \text{CH₃SO₂Cl} \quad \text{Ni(0)} \\
\text{R} & \quad \text{py} \quad \text{R} \\
\text{OH} & \quad \text{MsO} \quad \text{Mn} \\
\text{R} & \quad \text{OMs} \quad \text{n}
\end{align*}
\]

Two general methods for the \textit{in situ} preparation of Ni(0) catalysts were used. Two methods have been used to generate effective catalytic systems in Ni(0) mediated coupling reactions of aryl halides and aryl triflates.\(^{17}\) The first method (Method A) involved generating the Ni(0) catalyst from NiCl₂(PPh₃)₂, Zn and Et₄NI usually in THF.\(^{17a}\) Et₄NI is believed to function as a bridging agent between Ni and Zn, thus facilitating electron transfer in the reduction of Ni(II) to Ni(0) and Ni(III) to Ni(I).\(^{17a,b}\)
The second method (Method B) involved generating the Ni(0) catalyst from NiCl₂, Zn, PPh₃ and/or 2,2'-dipyridyl in DMAc. This method has been used in dipolar aprotic solvents such as DMF and DMAc. The Ni(0) catalysts prepared by either method had a deep red-brown color. The color could be used to indicate Ni(0) catalyst formation as well as catalyst decomposition.

The initial polymerization reactions utilized methyl 2,5-bis(methylsulfonyloxy)benzoate as the monomer (eq 2).

\[ \text{Meso} \quad \text{OCH}_3 \quad \text{Ni}(0) \quad \text{OCH}_3 \quad \text{OCH}_3 \quad \text{OCH}_3 \quad \text{n} \]

This monomer was chosen for the initial polymerization reactions because electron-withdrawing substituent groups (including p-alkoxycarbonyl) have been demonstrated to activate aryl halides, triflates, and mesylates in Ni(0) mediated homocoupling reactions. The results obtained for the polymerization of methyl 2,5-bis(methylsulfonyloxy)benzoate are summarized in Table I. In THF, optimum results (75 % yield, Mₙ= 3950) were obtained using 10% nickel catalyst (Table I, entry 1). Reaction yields dropped dramatically when lesser amounts of catalyst were used (Table I, entries 2-5). The addition of PPh₃ to Ni(0) catalysts is known to stabilize the Ni(0) catalyst, resulting in less premature catalyst decomposition, as well as reducing side products formed by phenyl group transfer from PPh₃. The addition of 20 mol %
Table I. Ni(0) Catalyzed Polymerization of Methyl 2,5-bis(methylsulfonyloxy)benzoate

![Chemical structure image]

<table>
<thead>
<tr>
<th>Entry</th>
<th>Reaction Conditions</th>
<th>Polymer</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Ni(0) Method$^a$ Solvent Temp Time Yield Mn Mw/Mn DP T$_g$</td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>10 A THF 67 10 75 3950 2.24 29</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>7 A THF 67 10 50 2379 1.60 18</td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>5 A THF 67 10 33 2109 1.34 16</td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>3 A THF 67 1 5 2116 1.34 16</td>
<td></td>
</tr>
<tr>
<td>5</td>
<td>1.5 A THF 67 0.1 oligomers</td>
<td></td>
</tr>
<tr>
<td>6$^c$</td>
<td>10 A THF 67 24 71 3006 1.91 22</td>
<td></td>
</tr>
<tr>
<td>7</td>
<td>10 A Dioxane 80 10 85 4260 2.00 32</td>
<td></td>
</tr>
<tr>
<td>8</td>
<td>10 A Dioxane 80 24 80 4544 1.94 34 101</td>
<td></td>
</tr>
<tr>
<td>$g^d$</td>
<td>10</td>
<td>A</td>
</tr>
<tr>
<td>---</td>
<td>---</td>
<td>---</td>
</tr>
<tr>
<td>10</td>
<td>15</td>
<td>A</td>
</tr>
<tr>
<td>11</td>
<td>10</td>
<td>A</td>
</tr>
<tr>
<td>12</td>
<td>10</td>
<td>B</td>
</tr>
<tr>
<td>$13^e$</td>
<td>10</td>
<td>B</td>
</tr>
<tr>
<td>$14^f$</td>
<td>10</td>
<td>B</td>
</tr>
<tr>
<td>$15^g$</td>
<td>10</td>
<td>B</td>
</tr>
<tr>
<td>$16^h$</td>
<td>10</td>
<td>B</td>
</tr>
</tbody>
</table>

Oligomers

$^a$ Method A: NiCl$_2$(PPh$_3$)$_2$/Et$_4$NI/Zn. Method B: NiCl$_2$(PPh$_3$)$_2$/Zn/PPh$_3$/DMAc. $^b$ The catalyst decomposed immediately. $^c$ Additional PPh$_3$ (20 mol%). $^d$ Additional PPh$_3$ (10 mol%). $^e$ NiCl$_2$/PPh$_3$/bpy/Zn. $^f$ AsPh$_3$, $^g$ P(o-toly)$_3$, and $^h$ PCy$_3$ were used respectively instead of PPh$_3$. 
PPh$_3$ resulted in an increased reaction time (10h to 24h) and a slight decrease in molecular weight (cf. Table I, entries 1 & 6). Slightly increased yields and molecular weight were obtained in dioxane at higher temperatures (cf. Table I, entries 1 & 7) which enhance the solubility. The addition of PPh$_3$ to the reaction solution did not result in improved molecular weight (cf. Table I, entries 8 & 9). Also, molecular weight was not increased by an increase to 15% Ni catalyst (cf. Table I, entries 8 & 10). Decreased yields and molecular weights were obtained when the polymerization was performed in DMAc using method A (cf. Table I, entries 1,8, & 11). There was no significant change in molecular weight when method B was used (Table I, entry 12). Phenyl group transfer is often a side reaction in Ni(0) catalyzed reactions.$^{19}$ The occurrence of this side reaction in the polymerization reaction would result in a reduction of molecular weight. 2,2'-Dipyridyl has been effective in some Ni(0) catalyzed reactions in suppressing a phenyl group transfer.$^{17e}$ The addition of 2,2'-dipyridyl resulted in a decreased yield and molecular weight (Table I, entries 12 & 13). The substitution of the PPh$_3$ ligand with AsPh$_3$, P(p-tolyl)$_3$, or P(cy)$_3$ resulted in rapid catalyst decomposition and the concomitant formation of oligomers (Table I, entries 14-16). The highest molecular weight obtained with methyl 2,5-bis(methanesulfonyloxy)benzoate was 4544 (Table I, entry 8). The glass transition temperature of the polymer from entry 8 is 101°C.

A larger and branched substituent, 2-ethylhexyloxycarbonyl, was used in an effort to increase the molecular weight (eq 3).

![Chemical Structure](image)

$$\text{(3)}$$
Through increased configurational entropy, this group was expected to make the resulting polymer more soluble, consequently increasing the number of repeat units allowed in the polymer chain before precipitation occurred. Even though the resulting polymer was very soluble, there was no improvement in molecular weight (Table II). This result is consistent with a retardation of the coupling reaction due to the large size of this group. Although the use of this group did not result in the desired increase in molecular weight, some noteworthy observations can be made from the results obtained with this series of reactions.

Relatively large amounts of Zn were necessary for the polymerization of sterically hindered monomers. Increases in both molecular weight and yield occurred as the relative amount of Zn increased (Table II, entries 1-3). Thus, an additive effect was evidenced in regard to the amount of Zn required for polymerizations. This has precedent, as a Zn additive effect has, to a certain limit, been reported in Ni(0) mediated reactions.17e,20 The highest molecular weight polymers obtained from the sterically hindered monomer 3 were obtained with 7 equivalents of Zn relative to monomer. In contrast, only 1.7 equivalents of Zn (relative to the aryl mesylate) was necessary to obtain high conversions to symmetrical biaryls in the Ni(0) mediated homocoupling reaction of aryl mesylates.16 Thus, a larger amount of Zn was required for polymerizations. Finally, the Ni(0) coupling reaction employed is truly heterogeneous as Zn is not soluble in THF.

Increasing the amount of PPh₃ decreases the reaction rate by forming a more stable (and hence less reactive) Ni species.18 Although a longer reaction time was required, a higher molecular weight was obtained with an increased amount of PPh₃ (Table II, entries 4-7). A change in solvent to dioxane allowed an increase in reaction temperature. This was expected to increase the reactivity of the Ni catalyst toward the aryl bismesylates. However, the increase in temperature resulted in a lower molecular
Table II. Ni(O) Catalyzed Polymerization of (2-Ethylhexyl)-2,5-bis(methylsulfonyloxy) Benzoate

![Chemical structure of 3 and 4](image)

<table>
<thead>
<tr>
<th>Entry</th>
<th>Additional PPh₃ (equiv)b</th>
<th>Zn (equiv)b</th>
<th>Solvent</th>
<th>Temp (°C)</th>
<th>Time (h)</th>
<th>Yield (%)</th>
<th>Mn (g/mol)</th>
<th>Mw/Mn</th>
<th>DP</th>
<th>Tg (°C)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>none</td>
<td>1.7</td>
<td>THF</td>
<td>67</td>
<td>10</td>
<td>16</td>
<td>1852</td>
<td>1.24</td>
<td>8</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>none</td>
<td>5</td>
<td>THF</td>
<td>67</td>
<td>10</td>
<td>45</td>
<td>1870</td>
<td>1.28</td>
<td>8</td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>none</td>
<td>7</td>
<td>THF</td>
<td>67</td>
<td>10</td>
<td>66</td>
<td>2443</td>
<td>1.63</td>
<td>11</td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>0.1</td>
<td>7</td>
<td>THF</td>
<td>67</td>
<td>24</td>
<td>89</td>
<td>1670</td>
<td>1.52</td>
<td>7</td>
<td></td>
</tr>
<tr>
<td>5</td>
<td>0.2</td>
<td>7</td>
<td>THF</td>
<td>67</td>
<td>24</td>
<td>90</td>
<td>2351</td>
<td>1.82</td>
<td>10</td>
<td></td>
</tr>
<tr>
<td>6</td>
<td>0.4</td>
<td>7</td>
<td>THF</td>
<td>67</td>
<td>24</td>
<td>97</td>
<td>4960</td>
<td>2.47</td>
<td>21</td>
<td></td>
</tr>
<tr>
<td>7</td>
<td>0.6</td>
<td>7</td>
<td>THF</td>
<td>67</td>
<td>24</td>
<td>2.60</td>
<td>31</td>
<td>-3&lt;sup&gt;d&lt;/sup&gt;</td>
<td></td>
<td></td>
</tr>
<tr>
<td>----</td>
<td>-----</td>
<td>---</td>
<td>-----</td>
<td>-----</td>
<td>-----</td>
<td>------</td>
<td>-----</td>
<td>---------------</td>
<td></td>
<td></td>
</tr>
<tr>
<td>8</td>
<td>none&lt;sup&gt;c&lt;/sup&gt;</td>
<td>7</td>
<td>THF</td>
<td>67</td>
<td>24</td>
<td>1.72</td>
<td>10</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>9</td>
<td>none</td>
<td>7</td>
<td>Dioxane</td>
<td>80</td>
<td>10</td>
<td>1.35</td>
<td>9</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<sup>a</sup> NiCl<sub>2</sub>(PPh<sub>3</sub>)<sub>2</sub>/Et<sub>4</sub>Ni/Zn.  
<sup>b</sup> Equiv relative to monomer  
<sup>c</sup> 0.1 Equiv of 2,2’-dipyridyl was added.  
<sup>d</sup> T<sub>n-1</sub>=59°C (1st heating scan).
weight and yield (Table II, entry 9). Contributing factors, to this, may be faster catalyst decomposition as well as the increased proportion of side reactions that often accompany a temperature increase.\textsuperscript{21} As with 3, the addition of 2,2'-dipyridyl did not result in an increase in molecular weight (Table II, entries 3 & 8).

On the first heating scan of the DSC measurement of the polymer from entry 7 in Table II, a glass transition and an endothermic peak were observed at -3°C and 59°C, respectively. The endothermic peak was related to the liquid crystalline to isotropic transition. From the study of optical microscopy, a typical texture of a nematic phase was obtained. The peak, however, was not observed on the subsequent cooling and second heating scans.

Attachment of the bulky and noncrystallizable substituent (2-ethylhexyloxycarbonyl) to the backbone of the polyarylene resulted in highly enhanced solubility of the polymer. However, the molecular weight of the polymer may be limited by the increased number of side reactions associated with sterically hindered substrates. To investigate this, four other aryl monomers with the 2-ethylhexyloxycarbonyl substituent but different leaving groups (Br, Cl, OSO\textsubscript{2}C\textsubscript{6}H\textsubscript{4}-p-F, OSO\textsubscript{2}CF\textsubscript{3}) were polymerized. The results of polymerization of five monomers under the identical conditions are summarized in Table III. In THF, the molecular weight and polymer yield increase in the order of OSO\textsubscript{2}CH\textsubscript{3} < Br < OSO\textsubscript{2}C\textsubscript{6}H\textsubscript{4}-p-F < OSO\textsubscript{2}CF\textsubscript{3} < Cl (Table III, entries 1-5). Using dioxane as solvent at an elevated reaction temperature, the less reactive bismesylate and bis-p-fluorobenzenesulfonate gave slight changes in molecular weight. In comparison, the more reactive dichloro and bistriflate were sensitive to the increase in temperature, resulting in a significant decrease in molecular weight (Table III, entries 8 & 9). This is consistent with the more reactive groups becoming much less selective under more vigorous reaction conditions. However this lessening of selectivity was less pronounced with less
Table III. Ni(O) Catalyzed Polymerization of 2-Ethylhexyloxycarbonyl Substituted Benzene Derivatives Containing Bromine, Chlorine, Trifluoromethanesulfonate, 4-Fluoro-benzenesulfonate, and Methanesulfonate Leaving Groups.

![Chemical structure](image)

<table>
<thead>
<tr>
<th>Entry</th>
<th>X</th>
<th>Solvent</th>
<th>Temp (°C)</th>
<th>Yield (%)</th>
<th>Mn (g/mol)</th>
<th>Mw/Mn</th>
<th>DP</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>OSO₂CH₃</td>
<td>THF</td>
<td>67</td>
<td>66</td>
<td>2443</td>
<td>1.63</td>
<td>11</td>
</tr>
<tr>
<td>2</td>
<td>OSO₂PhF</td>
<td>THF</td>
<td>67</td>
<td>80</td>
<td>6467</td>
<td>1.70</td>
<td>28</td>
</tr>
<tr>
<td>3</td>
<td>OSO₂CF₃</td>
<td>THF</td>
<td>67</td>
<td>81</td>
<td>8471</td>
<td>2.60</td>
<td>36</td>
</tr>
<tr>
<td>4</td>
<td>Cl</td>
<td>THF</td>
<td>67</td>
<td>87</td>
<td>12905</td>
<td>2.88</td>
<td>56</td>
</tr>
<tr>
<td>5</td>
<td>Br</td>
<td>THF</td>
<td>67</td>
<td>81</td>
<td>2729</td>
<td>1.55</td>
<td>12</td>
</tr>
<tr>
<td>6</td>
<td>OSO₂CH₃</td>
<td>Dioxane</td>
<td>80</td>
<td>48</td>
<td>2064</td>
<td>1.35</td>
<td>9</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>---</td>
<td>------</td>
<td>-----</td>
<td>---</td>
<td>-----</td>
<td>---</td>
<td>---</td>
<td></td>
</tr>
<tr>
<td>7</td>
<td>OSO₂PhF</td>
<td>Dioxane</td>
<td>80</td>
<td>94</td>
<td>6805</td>
<td>2.60</td>
<td>29</td>
</tr>
<tr>
<td>8</td>
<td>OSO₂CF₃</td>
<td>Dioxane</td>
<td>80</td>
<td>83</td>
<td>4223</td>
<td>1.97</td>
<td>18</td>
</tr>
<tr>
<td>9</td>
<td>Cl</td>
<td>Dioxane</td>
<td>80</td>
<td>82</td>
<td>5068</td>
<td>2.89</td>
<td>22</td>
</tr>
<tr>
<td>10</td>
<td>Br</td>
<td>Dioxane</td>
<td>80</td>
<td>84</td>
<td>1924</td>
<td>1.82</td>
<td>8</td>
</tr>
</tbody>
</table>

*a* Polymerization Method A: NiCl₂(PPh₃)₂/Et₄NI/Zn
reactive bismesylate and bis-\textit{p}-fluorobenzene sulfonate. Side reactions compete more effectively with homocoupling as steric hindrance increases. The dichloride, which is usually the least reactive leaving group (ArCl<ArBr<ArI) among aryl halides in most other Ni(0) homocoupling reactions produce higher molecular weight polymers than bistriflate (Table III, entries 3 & 4). However, at higher reaction temperature, the selectivity is less than \textit{p}-fluorobenzene sulfonate (Table III, entries 7 & 9). The dibromo monomers which contain a usually more reactive leaving group than the chloro group gave poor results in both THF and dioxane (Table III, entries 5 & 10). This was again consistent with the more reactive substrates possessing less selectivity when a large sterically hindering group was present ortho to the carbon which could participate in the coupling reaction. To summarize the results of Table III, four monomers (i.e., Br, Cl, \textit{OSO}_2C_6H_4-p-F, \textit{OSO}_2CF_3), which are expected to be more reactive than bismesylate monomers, did not give the high molecular weight polymers. This indicated that high molecular weights would not be obtained through the homopolymerization of a 1,4-bismesylate monomer containing the sterically bulky (2-ethylhexyl)oxycarbonyl group, under the reaction conditions employed.

The copolymerization of two monomers was the next method investigated in the effort to obtain soluble high molecular weight polymers by increasing the configurational entropy of the main chain. Methyl 2,5-bis(methylsulfonyloxy)benzoate had limited solubility which resulted in premature precipitation of the polymer from the reaction solution. This gave low molecular weight polymer (Table I). In order to increase the solubility of the polymer, it was copolymerized with (2-ethylhexyl) 2,5-bis(methylsulfonyloxy)benzoate in different molar ratios under the same reaction conditions (Table IV, entries 1-4). Highest molecular weight and yield were obtained with 25 mol % of (2-ethylhexyl) 2,5-bis(methylsulfonyloxy)benzoate (Table IV, entry 3). A slightly decreased molecular weight was observed when 50 mol % of this
Table IV. Ni(0) Catalyzed Copolymerization of Methyl 2,5-Bis(methylsulfonyloxy) benzoate With Various Comonomers. 

<table>
<thead>
<tr>
<th>Entry</th>
<th>Ar</th>
<th>Mol%</th>
<th>Yield (%)</th>
<th>Mn</th>
<th>Mw/Mn</th>
<th>n+m</th>
<th>Tg. °C</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td><img src="image1" alt="Structure" /></td>
<td>5</td>
<td>82</td>
<td>4390</td>
<td>1.6</td>
<td>32</td>
<td>98</td>
</tr>
<tr>
<td>2</td>
<td><img src="image2" alt="Structure" /></td>
<td>10</td>
<td>89</td>
<td>7760</td>
<td>3.1</td>
<td>54</td>
<td>80</td>
</tr>
<tr>
<td>3</td>
<td><img src="image3" alt="Structure" /></td>
<td>25</td>
<td>90</td>
<td>8860</td>
<td>2.3</td>
<td>56</td>
<td>54</td>
</tr>
<tr>
<td>4</td>
<td><img src="image4" alt="Structure" /></td>
<td>50</td>
<td>99</td>
<td>9400</td>
<td>2.2</td>
<td>51</td>
<td>30</td>
</tr>
<tr>
<td>5</td>
<td><img src="image5" alt="Structure" /></td>
<td>10</td>
<td>82</td>
<td>4880</td>
<td>1.7</td>
<td>36</td>
<td>106</td>
</tr>
<tr>
<td>6</td>
<td><img src="image6" alt="Structure" /></td>
<td>50</td>
<td>88</td>
<td>7250</td>
<td>2.3</td>
<td>49</td>
<td>90</td>
</tr>
</tbody>
</table>
$a$ Polymerization Method A: NiCl$_2$(PPh$_3$)$_2$/Et$_4$N/I/Zn.
comonomer was used, probably due to the increased steric hindrance during polymerization. All the polymers from these copolymerizations are soluble. When using isopropyl 2,5-bis(methylsulfonyloxy)benzoate as comonomer, a large mol % was required to increase the solubility and molecular weight (Table IV, entries 5 & 6) since it has a smaller branched substituent group than (2-ethylhexyl) 2,5-bis(methylsulfonyloxy) benzoate. However, when methyl 3,5-bis(methylsulfonyloxy)benzoate was the comonomer, 10 mol% of comonomer ratio was enough to give soluble and relative high molecular weight polymers (Table IV, entries 7 & 8). This is because kinked phenylenic units are generated in the main chain from this unit.

A wide variety of aryl bismesylates were polymerized (Table V). Insoluble products were obtained in the homopolymerization of 1,4-bis(methylsulfonyloxy)benzene and 2-cyano-1,4-bis(methylsulfonyloxy)benzene (Table V, entries 1 & 2). The attachment of a methyl substituent to 1,4-bis(methylsulfonyloxy)benzene resulted in a large increase in solubility (Mn=2150, entry 3 in Table V). In comparison with unsubstituted PPP, the attachment of tert-butyl or phenyl substituents also resulted in improved solubility (Table V, entries 4 & 5). However, in regard to increasing the molecular weight of the resulting polymers they were not as effective as the methyl group. Substituents ortho to the mesylate group are known to retard the reaction.16 The larger size of these groups inhibited the coupling reaction. Thus, the steric bulk of the tert-butyl group is sufficient enough to hinder the coupling reaction.

The attachment of an alkoxy carbonyl substituent to 1,4-bis(methylsulfonyloxy)benzene results in much higher molecular weights (up to Mn = 7230, Table II entry 7). This group has several positive effects on the polymerization reaction. For example, the polymer is more soluble than unsubstituted poly(p-phenylene), so higher molecular weights are attainable. In addition, the alkoxy carbonyl
Table V. Ni(0) Catalyzed Homocoupling Polymerization of Various Aryl Bismesylates

MsO-Ar-OMs $\xrightarrow{\text{Ni (0)}} \{\text{Ar} \}_n$

<table>
<thead>
<tr>
<th>Entry</th>
<th>Ar</th>
<th>Yield (%)</th>
<th>Mn</th>
<th>Mw/Mn</th>
<th>DP</th>
<th>Tg, °C</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td><img src="image1" alt="Image" /></td>
<td>50</td>
<td>insoluble</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2</td>
<td><img src="image2" alt="Image" /></td>
<td>68</td>
<td>insoluble</td>
<td>163</td>
<td></td>
<td></td>
</tr>
<tr>
<td>3</td>
<td><img src="image3" alt="Image" /></td>
<td>87</td>
<td>2150</td>
<td>1.4</td>
<td>24</td>
<td>62</td>
</tr>
<tr>
<td>4</td>
<td><img src="image4" alt="Image" /></td>
<td>85</td>
<td>690</td>
<td>1.1</td>
<td>6</td>
<td>54</td>
</tr>
<tr>
<td>5</td>
<td><img src="image5" alt="Image" /></td>
<td>82</td>
<td>1410</td>
<td>1.4</td>
<td>9</td>
<td>126</td>
</tr>
<tr>
<td>6</td>
<td><img src="image6" alt="Image" /></td>
<td>85</td>
<td>1150</td>
<td>1.2</td>
<td>9</td>
<td>136</td>
</tr>
<tr>
<td>7</td>
<td><img src="image7" alt="Image" /></td>
<td>88</td>
<td>4920</td>
<td>2.0</td>
<td>30</td>
<td>85</td>
</tr>
<tr>
<td>8</td>
<td><img src="image8" alt="Image" /></td>
<td>95</td>
<td>7370</td>
<td>3.3</td>
<td>41</td>
<td>162</td>
</tr>
<tr>
<td>9</td>
<td><img src="image9" alt="Image" /></td>
<td>68</td>
<td>20030</td>
<td>2.2</td>
<td>101</td>
<td>168</td>
</tr>
</tbody>
</table>
10

11

12

---

Polymerization using Method B: NiCl₂(PPh₃)₂/PPPh₃/Et₄N/Zn/THF.
group activates the aryl mesylate toward reaction with the Ni(0) catalyst. An important factor in this increased reactivity is its electron-withdrawing ability via resonance. When the group was in a position where it cannot interact through resonance with the carbon undergoing substitution, there was no improvement of molecular weight (cf. Table V, entries 5 & 6).

The benzoyl group is also an activating group through electron-withdrawing by resonance. The benzoyl group gave molecular weight 7370 which corresponds to a DP 41 (Table V, entry 8). The group can be made even more electron-withdrawing by the substitution with a p-fluoro group. The highest molecular weight obtained in the homocoupling reaction was realized with this monomer. \( \text{Mn}=20030, \text{DP}=101 \) (Table V, entry 9). In addition, the p-fluoro group makes the polymer more soluble. The p-chlorobenzoyl substituted monomer gave an insoluble gel (Table V, entry 10). Apparently through participation of the chloro group in the polymerization reaction to give a highly crosslinked polymer.

An increase in molecular weight and solubility of poly(p-phenylene) polymers were realized by two general strategies. In the first, high molecular weight poly(p-phenylene)s were obtained by the homopolymerization of monomers containing strongly activating groups that were bulky enough to solubilize the corresponding polymers, but not so bulky that they inhibited the coupling reaction in a deleterious manner. In an example, an aryl mesylate monomer containing the p-fluorobenzoyl group was polymerized to give high-molecular weight substituted poly(p-phenylene) \( \text{Mn}=20030, \text{Table V}, \text{entry 9} \). The alternative strategy which resulted in high molecular weight substituted poly(p-phenylene)s was the copolymerization of appropriately selected monomers (Table IV, entries 3 & 6).

Another factor which may affect the molecular weight is the effect of the substituent on the reactivity of the adjacent (i.e., ortho) mesylate. Yields in the
homocoupling reaction of aryl mesylates are decreased to varying extents by the presence of an ortho substituent group. In these cases, side reactions such as reduction and transarylation become more important. In the Ni(0) catalyzed polymerization reaction of aryl bismesylates, these side reactions would terminate polymer chain growth by end-capping the polymer. Furthermore, results from the polymerization of 3 indicate that the polymerization reaction is inhibited by bulky substituent groups ortho to the mesylate group. Additional evidence of the inhibitory effect of a substituent ortho to the mesylate can be found in the reaction of (2-ethylhexyl) 2,5-bis(methylsulfonyloxy)benzoate. The $^{1}$H NMR spectra (Figure 1) of the oligomer resulting from (2-ethylhexyl) 2,5-bis(methylsulfonyloxy)benzoate shows an important result. The 5-mesylate substituent was consumed to a greater degree than the 2-mesylate substituent. This implies that the 2-mesylate group was less reactive due to steric hindrance. If it was assumed that no side reactions occurred, the molecular weight can be calculated from the integration of the $^{1}$H NMR spectrum of the oligomer. However its molecular weight is much higher than the one obtained from GPC using a polystyrene standard. This implies that the other side reactions also consume the mesylate group. Since the oligomer shows a complicated $^{1}$H NMR spectrum probably due to the presence of various constitutional isomeric structural units, the chain ends (except mesylate end) were not fully characterized. In conclusion, the mesylate group ortho to a substituent group is less reactive towards the coupling reaction and is more susceptible to participation in side reactions.

It is helpful to consider the first reaction that takes place in the polymerization sequence (Scheme I). The polymerization begins with the dimerization of 2-substituted 1,4-bis(methylsulfonyloxy)benzene, 5, resulting in the formation of a disubstituted 4,4'-bis(methylsulfonyloxy)biphenyl. There are three isomeric products expected: 6, 7, and 8. Reaction of 5 at the 4-position would be favored. Thus the relative amount
Figure 1. $^1$H-NMR Spectra of (a) (2-ethylhexyl) 2,5-bis(methysulfonyloxy)benzoate and (b) the resulting oligomer.
Scheme I. Generation of Constitutional Isomeric Structural Units during the Polymerization of Bismesylates

\[ \text{MSO-OMs} \rightarrow \text{R-OMs} \rightarrow \text{R-OMs} \rightarrow \text{R-OMs} \]

Steps:
- \( a \)
- \( b \)
- \( c \)
of the dimers formed would be expected to follow the order $6 > 7 > 8$. There are sterically hindered reactive positions on both ends of 6. The reactivity of the dimeric molecule 6 is expected to be much lower than that of 7 and 8 and therefore, the polymerization reaction would be significantly retarded. Side reactions such as reduction and transarylation would become much more competitive with the polymerization reaction. As a result a low molecular weight polymer would be formed. The solubility of polymer 9 is most probably determined by the large number of constitutional isomeric structural units present in its chain. This increases its configurational entropy and decreases its crystallization ability. New bismesylates containing dimeric structures 8 with no steric hindrance were made from the corresponding 2,2'-disubstituted-4,4'-dihydroxybiphenyls: 2,2'-dibenzoyl-4,4'-bis-(methylsulfonyloxy)biphenyl, 2,2'-di(p-fluorobenzoyl)-4,4'-bis(methylsulfonyloxy)-biphenyl, 2,2'-di(p-t-butylbenzoyl)-4,4'-bis(methylsulfonyloxy)biphenyl and 2,2'-dimethyl-4,4'-bis(methylsulfonyloxy)biphenyl. Homopolymerization of all these bismesylates gave insoluble polymers except for entry 7 (Table VI, entries 1, 4, & 9). Their insolubility is probably due to the regioregular structure of the resulting polymer. However, copolymerization of these bismesylates with the corresponding monomer (1:1 mol ratio) resulted in highly soluble polymers with sizeable increases in molecular weight over that obtained in homopolymerization of monomers (Table VI, entries 2, 5, & 10). The highest molecular weight, was obtained with p-fluorobenzoyl substituent (Table VI, entry 5). In this case the number of phenylene repeating units was 176. This copolymerization strategy which employed 2,2'-disubstituted-4,4'-bismesylbiphenyls which have no steric hindrance on the reacting site, and monomers also increase the molecular weight significantly even for the monomer with non activating substituent such as methyl (Table VI, entry 10). In this case, $^1$H-NMR analysis of the homo- and copolymers clearly shows the difference in regiochemistry of
Table VI. Nickel(0) Catalyzed Copolymerization of 2,2'-Disubstituted-4,4'-bis(methylsulfonyloxy)biphenyl with 2-Substituted 1,4-Bis(methylsulfonyloxy)benzene.$^a$

![Chemical structure](image)

<table>
<thead>
<tr>
<th>Entry</th>
<th>R-</th>
<th>mol%</th>
<th>Yield (%)</th>
<th>Mn</th>
<th>Mw/Mn</th>
<th>(2m+n)</th>
<th>$T_g,^{\circ}C$</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>C$_6$H$_5$CO-</td>
<td>100</td>
<td>92</td>
<td>insoluble</td>
<td>-</td>
<td></td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>C$_6$H$_5$CO-</td>
<td>50</td>
<td>94</td>
<td>11090</td>
<td>2.0</td>
<td>62</td>
<td>170</td>
</tr>
<tr>
<td>3</td>
<td>C$_6$H$_5$CO-</td>
<td>0</td>
<td>95</td>
<td>7370</td>
<td>3.3</td>
<td>41</td>
<td>162</td>
</tr>
<tr>
<td>4</td>
<td>$p$-FC$_6$H$_4$CO-</td>
<td>100</td>
<td>95</td>
<td>insoluble</td>
<td>-</td>
<td></td>
<td></td>
</tr>
<tr>
<td>5</td>
<td>$p$-FC$_6$H$_4$CO-</td>
<td>50</td>
<td>79</td>
<td>34790</td>
<td>1.9</td>
<td>176</td>
<td>191</td>
</tr>
<tr>
<td>6</td>
<td>$p$-FC$_6$H$_4$CO-</td>
<td>0</td>
<td>68</td>
<td>20030</td>
<td>2.2</td>
<td>101</td>
<td>168</td>
</tr>
<tr>
<td>7</td>
<td>$p$-t-C$_6$H$_4$CO-</td>
<td>100</td>
<td>68</td>
<td>11120</td>
<td>3.7</td>
<td>47</td>
<td>197</td>
</tr>
<tr>
<td>8</td>
<td>$p$-t-C$_6$H$_4$CO-</td>
<td>0</td>
<td>82</td>
<td>7170</td>
<td>2.9</td>
<td>30</td>
<td>184</td>
</tr>
<tr>
<td>9</td>
<td>CH$_3$-</td>
<td>100</td>
<td>66</td>
<td>insoluble</td>
<td>-</td>
<td></td>
<td></td>
</tr>
<tr>
<td>10</td>
<td>CH$_3$-</td>
<td>50</td>
<td>76</td>
<td>3580</td>
<td>1.5</td>
<td>40</td>
<td>75</td>
</tr>
<tr>
<td>11</td>
<td>CH$_3$-</td>
<td>0</td>
<td>87</td>
<td>2150</td>
<td>1.4</td>
<td>24</td>
<td>62</td>
</tr>
</tbody>
</table>

$^a$ Polymerization Method B: NiCl$_2$(PPh$_3$)$_2$/PPh$_3$/Et$_4$Ni/Zn/THF.
the polymer backbone (Figure 2). Typically, $^1$H-NMR spectrum of regioirregular PPP consists of two methyl resonances at 2.44 and 2.16 ppm. As the regioregularity of the polymer chain increases (i.e., going from (a) to (c) in Figure 2), the intensity of the methyl resonance peak at 2.16 ppm also increases, and this peak corresponds to the methyl group at 2,2'-position in biphenyl unit of the polymer with a completely regioregular structure in the polymer chain.

Several different reaction mechanisms have been suggested for Ni(0) catalyzed homo-coupling reactions of aryl halides. The primary mechanistic pathway followed is highly dependent on the reaction conditions. Under the conditions utilized for the coupling of aryl mesylates, the most plausible mechanism is shown in Scheme II.17e,20

The first step of the mechanism involves the reduction of Ni(II) to Ni(0) by Zn. This is followed by the oxidative addition of ArX (X= mesylate or other sulfonate leaving group) to the Ni(0) species. The resulting Ni(II) species then undergoes an one electron reduction to form ArNi(I)L₃. ArX oxidatively adds to this species to give a diaryl Ni(III) complex which undergoes rapid reductive elimination, resulting in the formation of the biaryl product and the generation of Ni(I)XL₃. There are two productive reaction pathways available to this Ni species. Ni(I)XL₃ can be reduced by Zn to regenerate Ni(0)L₃, which can then repeat the catalytic cycle. Alternatively, ArX can undergo direct oxidative addition to Ni(I)XL₃ followed by reduction by Zn to form the ArNi(I)L₃ species once again.

The oxidative addition of aryl triflate or aryl halide to Ni(0) and Ni(I) species and the reductive elimination of aryl groups from the bisaryl-Ni(III) complex are considered to be fast reactions. The rate determining step in homocoupling reaction of aryl halides under similar reaction conditions is the reduction of the unreactive aryl-
Figure 2. $^1$H-NMR Spectra of (a) Regioirregular PPP and (b), (c) Regioregular PPPs
Scheme II. Plausible Mechanism of Ni(0) Catalyzed Homo-Coupling of Aryl Mesylate in the Presence of Excess Zn.

$X$ = Mesylate or other leaving groups
$L$ = PPh$_3$ or THF
Ni(II) species to the reactive aryl-Ni(I) species. The mechanism outlined in Scheme II is favored by excess amounts of Zn as well as the presence of iodide ion which enhances the reaction rate by bridging between Ni and Zn species in the single electron transfer reduction process. At high conversion of ArX the rate determining step becomes addition of ArX to the Ni(I) species.

The mechanism shown in Scheme II can not be operative at high conversions when 10% Ni(0) catalyst is used. As the polymerization approaches completion all of the aryl mesylate is consumed, but there is still aryl nickel species present that have not reacted to give the coupled product. At this point, one possibility is that the polymerization reaction is completed following a mechanism similar to the one proposed by Tsou and Kochi, a double-chain mechanism involving the reaction of Ar-Ni\(\text{III}\)X\(_2\) and ArNi\(\text{II}\)X to form Ar\(_2\)Ni\(\text{III}\)X in the key step.\(^{22}\) However, the bimolecular step involves Ni species expected to be present in trace quantities when excess Zn is present. Thus this mechanism is not expected to be favored when large amounts of Zn are present. Another possibility is that the final coupled product is formed as the result of a metathesis reaction proposed by Colon et al.\(^{17e}\)

THF was the best solvent in reference to the rate and selectivity of the homocoupling reaction. Typical dipolar aprotic solvents for Ni(0) homocoupling such as DMF and DMAc, which can increase the nucleophilicity of Ni(0) and also act as donor ligands gave poor results under our reaction conditions. When these solvents were utilized, deposition of a significant amount of nickel-black occurred within minutes of reaction initiation. Early catalyst decomposition was avoided by increasing the amount of PPh\(_3\) present. However, this resulted in a substantial retardation of the reaction rate. Consequently, longer reaction times were required when additional PPh\(_3\) was added. However, when using THF, no additional PPh\(_3\) was required, except with sterically hindered substrates. It is likely that in situ generated Ni(0)(PPh\(_3\))\(_2\) complexes were
unstable in the more polar and strongly dissociating solvents such as DMF, producing Ni colloidal metal relatively fast before the completion of the reaction. In THF (less polar and slightly dissociating) the complexes are substantially less prone to decomposition. The effectiveness of NiCl₂(PPh₃)₂ catalyst without additional PPh₃ in less polar solvents such as THF especially in the presence of iodide source for Ni homocoupling also has been reported. Although it has been reported that Ni(0) PPh₃ complexes exist in solution entirely as the tris complex (i.e., Ni(0)(PPh₃)₃ due to the bulky PPh₃, our catalyst system generates Ni(0)(PPh₃)₂ in the absence of added PPh₃. This highly coordinatively unsaturated reactive Ni complex might be stabilized by partial iodide coordination at the reaction temperature (67°C). It is well known that side reactions occur during the slow reaction and decrease the yield. Furthermore, at extended reaction times, deactivation of the catalyst would limit the yield. Therefore, the NiCl₂(PPh₃)₂, Zn, Et₄NI, THF system was employed in order to avoid the side reaction and shorten the reaction time by in-situ generating the reactive Ni(0)(PPh₃)₂ species which would realize selective homocoupling almost free from side reactions. The selection of reaction temperature is another important factor in Ni catalyzed homocoupling reactions. At higher temperatures side reactions occur to a greater extent. Thus, it is advantageous to perform the reaction at as low of a temperature as possible. Consequently, the temperature was kept at 67°C in most reactions.

8.4.-CONCLUSIONS

Functional regioregular and regiorregular substituted poly(p-phenylene)s have been synthesized by the Ni(0) catalyzed homocoupling of functional bimesylates of substituted hydroquinones and 2,2'-disubstituted-4,4'-dihydroxybiphenyls. This novel synthetic approach provides a convenient and versatile method for the synthesis of soluble, well-defined and functional PPPs with high molecular weight. These
functional PPPs are suitable starting materials for the synthesis of segmented copolymers and other polymers with more complex architectures.
REFERENCES


SYNTHESIS OF AROMATIC BIPHENYLENE POLYMERS BY NICKEL(0)
CATALYZED HOMO-COUPLING OF ARYLENE BISMESEYLATES DERIVED
FROM BISPHENOLS

9.1.-INTRODUCTION

The results described in previous chapter have demonstrated that soluble poly(p-phenylene)s are obtained under mild conditions by nickel(0) catalyzed homo-coupling of the bismesylates of substituted hydroquinones and of 2,2'-disubstituted-4,4'-dihydroxybiphenyls. The synthetic utility of this procedure can be further extended to the use of other various bisphenols which are commercially available and easy to prepare.

This chapter describes a simple and general procedure for the preparation of aromatic biphenylene polymers containing alternating biphenylene and spacer (e.g., -O-, -SO2-, -C(CH3)2-, etc) units by nickel (0) catalyzed homo-coupling of the bismesylates derived from various bisphenols. Also, we will describe a random copolymerization experiment of two different bismesylates, and the influence of the regioirregular structure of the resulting copolymer on the molecular weight and solubility will be discussed.

9.2.-EXPERIMENTAL

9.2.1.-Techniques

Unless otherwise noted, all compounds synthesized in the present chapter were purified until their 200 MHz 1H-NMR spectra corresponded to the expected structure and the purity was established by comparison with published mp or found to be higher than 99.5% by GC or HPLC.
9.2.2.-Materials

All reagents including bisphenols were purchased from commercial sources (Aldrich or Lancaster) and used without further purification except when reported. Pyridine was dried over CaH₂ and distilled. THF was distilled over sodium / benzophenone. Zinc dust was stirred in acetic acid, washed with water and dried in vacuo at 120°C. NiCl₂(PPh₃)₂ was prepared according to a literature procedure.¹ (2-Ethylhexyl) 2,5-dihydroxybenzoate was prepared by the acid catalyzed esterification of 2,5-dihydroxybenzoic acid with 2-ethyl-1-hexanol.²

9.2.3.-Synthesis of Monomers

Aryl bismesylates were prepared from the reaction of bisphenols and methanesulfonyl chloride.³

4.4'-Bis(methylsulfonyloxy)benzophenone.

Methanesulfonyl chloride (9.6 g, 0.084 mmol) was added slowly to a stirred solution of 4,4'-dihydroxybenzophenone (6 g, 0.028 mole), dimethylaminopyridine (trace) and pyridine (50 mL) at 0°C. The mixture was warmed to 22 °C and stirred for 12 h. The reaction mixture was poured into 10% aqueous HCl (500 mL). The resulting precipitate was collected, washed (H₂O), dried, and twice recrystallized (benzene) yielding white crystals (6.2 g, 70%): mp 130-131°C; ¹H NMR δ 7.88 (d, J = 8.3 Hz, 4H, o to carbonyl), 7.43 (d, J = 8.3 Hz, 4H, m to carbonyl), 3.24 (s, 6H, -OSO₂CH₃).
2,2'-Bis(4-methylsulfonyloxyphenyl)propane. (83%): white crystals; mp 97-98°C (benzene); \(^1\)H NMR \(\delta\) 7.26 (d, \(J = 8.6\) Hz, 4H, \(m\) to oxygen), 7.20 (d, \(J = 8.6\) Hz, 4H, \(o\) to oxygen), 3.14 (s, 6H, -OSO\(_2\)CH\(_3\)), 1.68 (s, 6H, -C(CH\(_3\))\(_2\)).

2-(3-methylsulfonyloxyphenyl)-2-(4'-methylsulfonyloxyphenyl)propane. (63%): colorless oil; \(^1\)H NMR \(\delta\) 7.46-7.19 (m, 8H, aromatic protons), 3.14 (s, 3H, -OSO\(_2\)CH\(_3\) \(m\) to -C(CH\(_3\))\(_2\)), 3.10 (s, 3H, -OSO\(_2\)CH\(_3\) \(p\) to -C(CH\(_3\))\(_2\)), 1.69 (s, 6H, -C(CH\(_3\))\(_2\)).

4,4'-Bis(methylsulfonyloxy)phenyl ether. (89%): white crystals; mp 140-141°C (chloroform); \(^1\)H NMR \(\delta\) 7.28 (d, \(J = 8.9\) Hz, 4H, \(o\) to -OSO\(_2\)CH\(_3\)), 7.05 (d, \(J = 8.9\) Hz, 4H, \(m\) to -OSO\(_2\)CH\(_3\)), 3.17 (s, 6H, -OSO\(_2\)CH\(_3\)).

4,4'-Bis(methylsulfonyloxy)phenyl sulfone. (80%): white crystals; mp 150-151°C (benzene); \(^1\)H NMR \(\delta\) 8.02 (d, \(J = 8.4\) Hz, 4H, \(o\) to -SO\(_2\)), 7.45 (d, \(J = 8.4\) Hz, 4H, \(m\) to -SO\(_2\)), 3.22 (s, 6H, -OSO\(_2\)CH\(_3\)).

1,1'-Bis(4-methylsulfonyloxyphenyl)cyclohexane. (61%): white crystals; mp 116-117°C (benzene); \(^1\)H NMR \(\delta\) 7.31 (d, \(J = 8.5\) Hz, 4H, \(m\) to oxygen), 7.19 (d, \(J = 8.5\) Hz, 4H, \(o\) to oxygen), 2.89 (s, 6H, -OSO\(_2\)CH\(_3\)), 2.25 (br s, 4H, aliphatic protons), 1.51 (br s, 6H, aliphatic protons).

3,3'-Bis((4-methylsulfonyloxy)phenyl)-1-[3H]isobenzofuranone. (70%): white crystals; mp 166-167°C (benzene); \(^1\)H NMR \(\delta\) 7.98 (d, \(J = 7.5\) Hz, 1H, \(o\) to carbonyl), 7.76 (m, 1H, \(p\) to carbonyl), 7.65-7.55 (m, 2H, \(m\) to carbonyl), 7.41 (d, \(J\))
= 8.5 Hz, 4H, m to -OSO₂CH₃), 7.28 (d, J = 8.5 Hz, 4H, o to -OSO₂CH₃), 3.16 (s, 6H, -OSO₂CH₃).

(2-Ethylhexyl) 2,5-bis(methylsulfonyloxy)benzoate. (73%): viscous oil; ¹H NMR δ 7.85 (br s, 1H, o to -CO₂-), 7.52 (br s, 2H, m and p to -CO₂-), 4.25 (d, J = 5.6 Hz, 2H, CO₂CH₂CH(CH₂CH₃)CH₂-), 3.31 (s, 3H, -OSO₂CH₃ o to -CO₂-), 3.21 (s, 3H, -OSO₂CH₃ m to -CO₂-), 1.73 (m, 1H, -CO₂CH₂CH(CH₂CH₃)CH₂-), 1.51-1.25 (m, 8H, -CO₂C₆H₄CH₃) (C₆H₂)₃CH₃), 0.93-0.83 (m, 6H, -CO₂CH₂CH(CH₂CH₃)(CH₂)₃CH₃).

9.2.4.-Polymerization

In a typical polymerization, a 125 mL Schlenk tube was charged with NiCl₂(PPh₃)₂ (115 mg, 0.175 mmol), Zn (800 mg, 12.25 mmol), Et₄N (675 mg, 2.625 mmol), PPh₃ (275 mg, 1.048 mmol), 3,3'-Bis((4-methylsulfonyloxy)phenyl)-1-[3H]isobenzofuranone (778 mg, 1.75 mmol), and a magnetic stirring bar. The tube was sealed with a rubber septum and the contents were dried at 22°C under vacuum (1x10⁻⁶ mmHg) for 3h. The reactants were placed under an Ar atmosphere and 1.5 mL of dry THF was added via a syringe through the rubber septum. The mixture was stirred at 22°C for 5 min (the color of the mixture gradually changed to deep red brown) and heated at 67°C for 24 h. After cooling to 22°C, the reaction mixture was poured into 100 mL of methanol acidified with 25 mL conc. HCl. The resulting precipitate was collected by filtration and dissolved in 2 mL of CHCl₃. The solution was filtered and poured into 100 mL of methanol. The resulting precipitate was collected by filtration and vacuum dried (350 mg, 70%). The polymer was further purified by reprecipitation into methanol from CHCl₃ solution before being analyzed by GPC (Mn = 3440g/mol, Mw/Mn = 1.5, DP = 12).
9.3.-RESULTS AND DISCUSSION

The general procedure for the preparation of aromatic biphenylene polymers utilized the Ni(0) catalyzed homocoupling reaction of aryl bismesylates derived from bisphenols (eq 1).

\[
\begin{align*}
\text{HO} & \quad \xrightarrow{\text{MsCl}} \quad \text{MsO} \\
\text{X} & \quad \text{X} \\
\text{OH} & \quad \text{OMs} \\
\end{align*}
\]

(1)

Ni(0) catalyst was prepared in situ from NiCl\(_2\)(PPh\(_3\))\(_2\), Zn, PPh\(_3\) and Et\(_4\)NI usually in THF.\(^4\) The advantage of using THF, instead of dipolar aprotic solvents such as DMAC was described previously.\(^5\) Et\(_4\)NI is believed to function as a bridging agent between Ni and Zn, thus facilitating electron transfer in the reduction of Ni(II) to Ni(0) and Ni(III) to Ni(I).\(^{4a,b}\)

The results obtained for the polymerization of various aryl bismesylates are summarized in Table I. Relatively low yield and low molecular weight were obtained from 2,2-bis(4-methylsulfonyloxyphenyl)propane in the absence of additional PPh\(_3\) (Table I, entry 1). However, the resulting polymer is soluble in common solvents such as CHCl\(_3\). It was found that the addition of extra PPh\(_3\) to the catalyst significantly enhances the yield and molecular weight for less reactive and/or sterically hindered aryl bismesylates (See Chapter 8). Addition of 0.6 equiv of PPh\(_3\) to the reaction increased the yield dramatically. However, this increase was accompanied by the formation of an insoluble polymer, probably due to the increased degree of crystallizability (Table I, entry 2).
Table I. Ni (0) Catalyzed Polymerization of Aryl Bismesylates Derived from Various Bisphenols<sup>a</sup>

<table>
<thead>
<tr>
<th>Entry</th>
<th>Ar</th>
<th>Yield(%)</th>
<th>Mn</th>
<th>Mw/Mn</th>
<th>DP</th>
<th>T&lt;sub&gt;g&lt;/sub&gt; °C</th>
<th>T&lt;sub&gt;m&lt;/sub&gt; °C</th>
</tr>
</thead>
<tbody>
<tr>
<td>1&lt;sup&gt;b&lt;/sup&gt;</td>
<td></td>
<td>54</td>
<td>1393</td>
<td>1.4</td>
<td>7</td>
<td></td>
<td></td>
</tr>
<tr>
<td>2</td>
<td></td>
<td>90</td>
<td>insoluble</td>
<td></td>
<td>128</td>
<td></td>
<td></td>
</tr>
<tr>
<td>3</td>
<td></td>
<td>94</td>
<td>2490</td>
<td>2.0</td>
<td>13</td>
<td>92</td>
<td></td>
</tr>
<tr>
<td>4</td>
<td></td>
<td>98</td>
<td>insoluble</td>
<td></td>
<td></td>
<td>250</td>
<td></td>
</tr>
<tr>
<td>5</td>
<td></td>
<td>100</td>
<td>insoluble</td>
<td></td>
<td></td>
<td>340</td>
<td></td>
</tr>
<tr>
<td>6</td>
<td></td>
<td>90</td>
<td>insoluble</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>7</td>
<td></td>
<td>99</td>
<td>insoluble</td>
<td></td>
<td></td>
<td>187</td>
<td></td>
</tr>
</tbody>
</table>
Polymerization of monomer (1.75 mmol) was carried out with NiCl$_2$(PPh$_3$)$_2$ (0.175 mmol), Zn (12.25 mmol), Et$_4$NI (2.63 mmol), and PPh$_3$ (1.05 mmol) in THF (1.5 mL) at 67°C for 24h. The polymerization was carried out in the absence of additional PPh$_3$. 
Increasing the configurational entropy of the main chain through a proper combination of kinked phenyleneic units has been used in other cases to obtain soluble polyphenyleneis.\(^6\) Polymerization of \(2-(3\text{-methylsulfonyloxyphenyl)-2-(4'}\text{-methylsulfonyloxyphenyl})\) propane resulted in the formation of a soluble polymer with number average degree of polymerization of 13, which indicates approximately 26 phenylene units in the main chain (Table I, entry 3). Although this polymer is very soluble, further increases in molecular weight were not obtained. This indicates that the difficulty in obtaining a higher molecular weight was due to an inherent lack of reactivity of the monomer under the reaction conditions used. This is consistent with the deactivating influence of \(p\)-alkyl substituents, through an electron-donating effect, in the \(\text{Ni(0)}\) catalyzed homocoupling reaction of aryl mesylates.\(^5\) In addition, in the case where the alkyl substituent is meta to the mesylate group the large size of the group may also impede the reaction. Polymerization of aryl bismesylates containing ether, carbonyl, and sulfonyl moieties gave insoluble polymers due to the regioregular structure of the resulting polymer (Table I, entry 4, 5, and 6). These three intractable polymers have also been prepared by the \(\text{Ni(0)}\) catalyzed homocoupling of aryl dihalides.\(^7\)

The effect of the introduction of a bulky spacer group between the two aryl groups of the bismesylate was investigated (Table I, entries 7 & 8). When this group was symmetrical, an insoluble polymer was obtained (Table I, entry 7). This insoluble polymer has a regioregular structure. From the results obtained with symmetrical spacer groups (Table I, entries 2, & 4-7), it can be deduced that in regard to poly(\(p\)-arylene)s, the homopolymerization of symmetrical bismesylates of this type results in the formation of insoluble polymers with a high degree of rigidity and crystallinity.

The introduction of an unsymmetrical bulky spacer group between the two aryl groups of the bismesylate resulted in an increase in the solubility of the resulting
polymer. Phenolphthalein (3,3-bis(4-hydroxyphenyl)-1[3H]-isobenzofuranone) is a widely used indicator containing bulky benzofuranone group. Bismesylate derivative of phenolphthalein was found to undergo Ni(0) catalyzed polymerization, resulting in quite soluble polymer with number average degree of polymerization of 12, which means approximately 24 phenylene units in the main chain and 36 phenylene units if the benzofuranone groups are included (Table I, entry 8).

In chapter 8, we demonstrated that copolymerization of two different aryl bismesylates gave highly soluble poly(p-phenylene)s due to the significant increase in configurational entropy of the main chain. Copolymerization of 4,4’-bis(methylsulfonyloxy)phenyl ether with 2,2-bis(4-methylsulfonyloxy)propane in 1:1 mol ratio gave highly soluble polymer of Mn of 2820 which has approximately 32 phenylene units in the main chain (Table II, entry 1). It is notable that although homopolymerization of each monomer gave insoluble polymer, respectively (Table I, entry 2 and 4), random copolymerization of these monomers which have similar reactivity towards Ni(0) catalyst, reduces the intermolecular chain packing forces which results in the enhanced solubility. The enhanced solubility and higher molecular weight polymers were obtained even from the highly crystallizable carbonyl, sulfonyl and ether containing symmetrical aryl bismesylates by copolymerization with (2-ethylhexyl) 2,5-bis(methylsulfonyloxy)benzoate (Table II, entries 2-4). This monomer has been shown to give soluble polymers in copolymerization reactions (See chapter 8). The highest molecular weight was obtained with strongly electron withdrawing sulfonyl containing aryl bismesylate (Table II, entry 3).

The copolymer structure of the resulting polymer is intriguing (Fig 1). The sulfonyl containing monomer shows higher reactivity and has no steric hindrance on either end. The (2-ethylhexyl) 2,5-bis(methylsulfonyloxy) benzoate has diminished reactivity due to severe steric hindrance. However, the copolymerization of these two
Table II. Ni(0) Catalyzed Copolymerization of Various Aryl Bismesylates.\(^a\)

\[
\text{MsO–Ar–OMs} + \text{MsO–Ar′–OMs} \xrightarrow{\text{Ni(0)}} (\text{Ar})_n (\text{Ar′})_m
\]

<table>
<thead>
<tr>
<th>Entry</th>
<th>Ar</th>
<th>Ar′</th>
<th>Yield (%)</th>
<th>Mn</th>
<th>Mw/Mn</th>
<th>n+m</th>
<th>T:(°\text{C} )</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>![Ar structure]</td>
<td>![Ar′ structure]</td>
<td>97</td>
<td>2820</td>
<td>1.8</td>
<td>16</td>
<td>135</td>
</tr>
<tr>
<td>2</td>
<td>![Ar structure]</td>
<td>![Ar′ structure]</td>
<td>94</td>
<td>3690</td>
<td>2.0</td>
<td>18</td>
<td>41</td>
</tr>
<tr>
<td>3</td>
<td>![Ar structure]</td>
<td>![Ar′ structure]</td>
<td>95</td>
<td>4150</td>
<td>1.8</td>
<td>19</td>
<td>64</td>
</tr>
<tr>
<td>4</td>
<td>![Ar structure]</td>
<td>![Ar′ structure]</td>
<td>89</td>
<td>3780</td>
<td>2.7</td>
<td>19</td>
<td></td>
</tr>
</tbody>
</table>

\(^a\) Copolymerization of MsO-Ar-OMs (0.875 mmol) with MsO-Ar′-OMs (0.875 mmol) was carried out with NiCl\(_2\)(PPh\(_3\))\(_2\) (0.175 mmol), Zn (12.25 mmol), Et\(_4\)NI (2.63 mmol), and PPh\(_3\) (1.05 mmol) in THF (1.5 mL) at 67°C for 24h.
Figure 1. Various Kinds of Constitutional Isomers Generated from Copolymerization of 4,4'-Bis(methylsulfonyloxy)phenylsulfone with (2-Ethylhexyl)2,5-bis(methylsulfonyloxy)benzoate
monomers would generate numerous polyphenylene based constitutional isomers in the main chain. In addition to the bulkiness of the noncrystallizable 2-ethylhexyl group, these various kinds of constitutional isomers may be responsible for the high solubility of this copolymer.
REFERENCES


CHAPTER 1


44. (a) M. Portnoy, Y. Ben-David and D. Milstein, Organometallics, 12, 4734 (1993); (b) Y. Ben-David, M. Portnoy, M. Gozin and D. Milstein, Organometallics, 11, 1995 (1992).


51. V. V. Grushin and H. Alper, Organometallics, 12, 3846 (1993).


CHAPTER 2


52. H. Kondo and T. Ikeda, *Ber.*, 73, 867 (1940).
CHAPTER 3


CHAPTER 4


**CHAPTER 5**


CHAPTER 6


CHAPTER 7


CHAPTER 8


**CHAPTER 9**


