<table>
<thead>
<tr>
<th>Title</th>
<th>Development of New Insertion Reactions Triggered by Nickel-Catalyzed Denitrogenation of 1,2,3-Triazo Compounds</th>
</tr>
</thead>
<tbody>
<tr>
<td>Author(s)</td>
<td>Yamauchi, Motoshi</td>
</tr>
<tr>
<td>Citation</td>
<td>Kyoto University (京都大学)</td>
</tr>
<tr>
<td>Issue Date</td>
<td>2010-03-23</td>
</tr>
<tr>
<td>URL</td>
<td><a href="https://doi.org/10.14989/doctor.k15404">https://doi.org/10.14989/doctor.k15404</a></td>
</tr>
<tr>
<td>Right</td>
<td></td>
</tr>
<tr>
<td>Type</td>
<td>Thesis or Dissertation</td>
</tr>
<tr>
<td>Textversion</td>
<td>author</td>
</tr>
</tbody>
</table>
Development of New Insertion Reactions Triggered by Nickel-Catalyzed Denitrogenation of 1,2,3-Triazo Compounds

Motoshi Yamauchi

2010
Preface

The studies presented in this thesis have been conducted under the direction of Professor Masahiro Mrakami at Kyoto University April 2004 to March 2010. The studies are concerned with the development of new insertion reactions triggered by nickel-catalyzed denitrogenation of 1,2,3-triazo compounds, base-promoted 1,2-rearrangement of a sulfonyl group of 1-sulfonyl-1,2,3-triazoles, and rhodium-catalyzed arylative cyclization of 1,6-diynes.

The author would like to express his sincerest gratitude to Professor Masahiro Murakami for his constant guidance, encouragement, and stimulating discussions throughout this study. All the works in this thesis could be achieved with his constant supervisions.

The author is deeply grateful to Lecturer Tomoya Miura for his helpful support, suggestion, encouragement, and teaching chemical techniques. Lecturer Miura kindly took care of the author during the studies. The author wishes to express his thanks to Lecturer Takanori Matsuda and Assistant Professor Naoki Ishida for their helpful discussions and advises.

The author fortunately had the great assistance of Mr. Masao Morimoto. The author acknowledges to him for his patience, earnest, and collaboration.

The author wishes to express his gratitude to Dr. Sho Kadowaki, Dr. Munehiro Hasegawa, Dr. Masahiro Shimada, Mr. Masaomi Makino, Dr. Shinji Ashida, Mr. Ippei Usui, Mr. Taisuke Sasaki, Mr. Motonori Koyabu, Dr. Masanori Shigeno, Mr. Tatsuro Harumashi, Mr. Soichiro Konno, Mr. Hiroki Nakazawa, Mr. Tsuyoshi Goya, Mr. Yusuke Takahashi, Mr. Tomoya Tsuboi, Mr. Yoshiyuki Yamaguchi, Mr. Yoshiteru Ito, Ms. Mizuna Narumi, Mr. Tatsuo Shinmoto, Mr. Tomohiro Tamai, Mr. Keita Ueda, Mr. Tomohiro Igarashi, Mr. Taisaku Moriya, Mr. Osamu Kozawa, Mr. Yasuhiro Shimamoto, Mr. Masao Morimoto, Mr. Wataru Ikemoto, Mr. Akira Kosaka, Mr. Shota Sawano, Mr. Yusuke Mikano, Dr. Markus Hoffman, Dr. Atsushi Seki, Mr. Sung-Yu Ku, Dr. Markus Mosimann, Dr. Karl Deutsche, Dr. Peter Brüchner, Dr. Akiko Okamoto, Dr. Lantao Liu, Mrs. Yuki Hasegawa, Ms. Chiyo Nagae, and all other past members of Murakami Laboratory for their enthusiasm and kind consideration.
The author is deeply grateful to Professor Michinori Suginome, Lecturer Toshimichi Ohmura, Assistant Professor Yuuya Nagata, Dr. Akihiko Yamamoto, Dr. Hiroyoshi Noguchi, Mr. Noriyuki Iwadate, Mr. Takeshi Yamamoto, Mr. Masamichi Shirakura, Mr. Hiroki Taniguchi, Mr. Tetsuya Yamada, and all other members of Suginome’s laboratory for their hospitality and fruitful discussion.

The author thanks Mr. Haruo Fujita and Ms. Keiko Kuwata for the measurement of NMR spectra and Mass spectra.

The author acknowledges a financial support by the Global COE Program “Integrated Materials Science” (No. B-09).

Finally, the author expresses his deep appreciation to his family, especially his parents, Mr. Danjo Yamauchi and Mrs. Emiko Yamauchi for their constant assistant and encouragement.

Motoshi Yamauchi

Department of Synthetic Chemistry and Biological Chemistry
Graduate School of Engineering
Kyoto University
Contents

General Introduction 1

Chapter 1  Nickel-Catalyzed Denitrogenative Alkyne Insertion Reactions of 1,2,3-Benzotriazin-4(3H)-ones 13

Chapter 2  Nickel-Catalyzed Denitrogenative Allene Insertion Reactions of 1,2,3-Benzotriazin-4(3H)-ones 45

Chapter 3  Nickel-Catalyzed Denitrogenative Annulations of 1,2,3-Benzotriazin-4(3H)-ones with 1,3-Dienes and alkenes 65

Chapter 4  Nickel-Catalyzed Denitrogenative Alkyne Insertion Reactions of 1-Sulfonyl-1,2,3-triazoles 83

Chapter 5  Preparation of 2-Sulfonyl-1,2,3-triazoles by Base-promoted 1,2-Rearrangement of A Sulfonyl Group 97

Chapter 6  Rhodium-Catalyzed Arylative Cyclization Reaction of Diynes with Arylboronic Acids 105

List of Publications 125
General Introduction

Nitrogen-containing heterocyclic compounds are one of the basic units often found in the fields of biological, medicinal, and materials chemistries. Therefore, the development of new efficient methods for their synthesis is highly demanded. Transition metal-catalyzed annulations reactions continue to provide many powerful synthetic methodologies for the construction of heterocyclic compounds. Heterometalacyclic complexes often act as key intermediate, which subsequently incorporate unsaturated compounds through insertion and reductive elimination to construct heterocyclic skeletons.

The author focused here on 1,2,3-triazole compounds as precursory platform to generate heterocyclic intermediates through oxidative addition to a nickel catalyst followed by extrusion of molecular nitrogen. Nickel-catalyzed denitrogenative annulations of 1,2,3-triazole compounds with unsaturated organic compounds were developed. The author has also found base-promoted 1,2-rearrangement of a sulfonyl group of 1-sulfonyl-1,2,3-triazoles and rhodium-catalyzed arylative cyclization of 1,6-diynes. Details of such findings are described in this thesis of six chapters. Prior to this detailed discussion, the author wishes to briefly summarize the background literature and outline important findings of my research project.

(1) Metallacycle Intermediate in Transition-Metal-Catalyzed Heterocycle Synthesis

Heterocyclic skeletons are synthesized by transition-metal-catalyzed bond formations from the corresponding acyclic precursors; (1) C–C bond formation, for example, ring-closing metathesis, Heck, Suzuki, Stille, and Tsuji-Trost reactions, (2) C–N bond formation, for example, the coupling reaction with a heteroatom using aryl and vinyl halides, the amino-Heck reaction, and intramolecular Wacker type oxidation. On the other hand, heterocycle synthesis via metallacycle intermediate are powerful synthetic methodologies because two bond formations take place simultaneously in the cyclization reaction followed by insertion of unsaturated compounds. Various heterocyclic compounds can be synthesized by the combination of metallacycle intermediate and different unsaturated compounds. Some examples are illustrated in Scheme 1. The reaction of two alkynes with transition-metal proceed through formation of the metallacycle intermediate followed by insertion of a carbon-heteroatom multiple bond, such as heterocumulenes (a), nitriles (b), and carbonyls (c). The reaction of an alkyne with a carbon-heteroatom multiple bond proceeds through
formation of the heteroatom-containing metallacycle followed by alkyne insertion (d). Shi and co-worker reported that a palladium-catalyzed reaction of diaziridine with 1,3-dienes proceeded through formation of a four-membered palladacycle via oxidative addition to the N–N bond of diaziridine (e). Metallacycle intermediates are utilized for the synthesis of heterocyclic compounds.

Scheme 1

(2) Transition-metal catalyzed reaction with release of molecular nitrogen

Transition-metal-induced extrusion of molecular nitrogen of diazocarbonyl compounds leads to highly reactive metallocarbenoid species (Scheme 2). The versatile reactivity of the carbene species are recognized by numerous synthetic application, C–H activation and cyclopropanation.

Scheme 2
In an important recent literature contribution, a rhodium-catalyzed extrusion reaction of a molecular nitrogen from pyridotriazoles was utilized for construction of a new heterocyclic system by Gevorgyan and co-workers (Scheme 3). A pyridotriazole undergoes closed/open form equilibrium to produce small amounts of diazo compound which, upon reaction with rhodium(II), generates the rhodium-carbenoid species. Terminal alkynes and nitriles react with the rhodium-carbenoid species to afford indolizines and imidazopyridines, respectively. This reaction is the first report of transition-metal catalyzed annulations of 1,2,3-triazol moiety with release of molecular nitrogen.

In line with these background, the author focused his attention to the activation of 1,2,3-triazol compounds and envisaged that metallacycle intermediates could be provided by transition-metal-induced extrusion of molecular nitrogen of 1,2,3-triazol compounds (Scheme 4). Oxidative addition of a N–N bond to nickel(0), which then prompts extrusion of molecular nitrogen to give metallacycle intermediates. Subsequent insertion of unsaturated compounds followed by reductive elimination would afford various heterocyclic compounds.

Scheme 3

Scheme 4
Chapter 1. Nickel-Catalyzed Denitrogenative Alkyne Insertion Reactions of 1,2,3-Benzotriazin-4(3H)-ones

In chapter 1, the author describes nickel-catalyzed denitrogenative alkyne insertion reactions of 1,2,3-benzotriazin-4(3H)-ones which can be readily prepared from anthranilic acid derivatives.\(^1\) 1,2,3-Benzotriazin-4(3H)-ones reacted with alkynes in the presence of a nickel(0)/phosphine catalyst to give a wide range of substituted 1(2H)-isoquinolones in high yield (eq 1). The reaction proceeded through denitrogenative activation of the triazinone moiety to give a five membered-nickelacycle. Subsequent insertion of alkynes afforded 1(2H)-isoquinolones.

\[
\text{Ni(0)} \quad \text{N=N} \\
R^1 \equiv R^2 
\]

Chapter 2. Nickel-Catalyzed Denitrogenative Allene Insertion Reactions of 1,2,3-Benzotriazin-4(3H)-ones

In chapter 2, the author reports nickel-catalyzed denitrogenative allene insertion reactions of 1,2,3-benzotriazin-4(3H)-ones, which furnish a variety of substituted 4-methylene-3,4-dihydroisoquinolin-1(2H)-ones in a regioselective manner (eq 2). A highly asymmetric version of the reaction would also be described.

\[
\text{Ni(0)} \quad \text{N=N} \\
\text{i-Pr-Foxap} \\
R \equiv R 
\]

up to 97% ee
Chapter 3. Nickel-Catalyzed Denitrogenative Annulations of 1,2,3-Benzotriazin-4(3H)-ones with 1,3-Dienes and Alkenes.

In chapter 3, the author then shows some examples describing nickel-catalyzed denitrogenative annulations of 1,2,3-benzotriazin-4(3H)-ones with unsaturated carbon-carbon bond (eq 3). The nickel-catalyzed reaction of 1,2,3-benzotriazin-4(3H)-ones with 1,3-dienes and alkene afforded 3,4-dihydroisoquinolin-1(2H)-ones in high yields.

\[
\text{Ni}(0) + \text{R}^1\text{R}^2\text{N} = \text{R}
\]

Chapter 4. Nickel-Catalyzed Denitrogenative Alkyne Insertion Reactions of 1-Sulfonyl-1,2,3-triazoles

In chapter 4, a nickel-catalyzed denitrogenative alkyne insertion of 1-sulfonyl-1,2,3-triazoles which can be readily prepared by a copper catalyzed azide/alkyne cycloaddition is described (eq 4). The diazo compound generated by tautomerization of 1-Sulfonyl-1,2,3-triazoles adds to nickel(0) with release of molecular nitrogen to give a nickel-carbenoid, which then cyclizes to form a four-membered-ring nickelacycle. Subsequent insertion of an alkyne and reductive elimination affords a sulfonylpyrrole.

\[
\text{Ni}(0) + \text{R}^2\equiv\text{R}^3
\]
Chapter 5. Preparation of 2-Sulfonyl-1,2,3-triazoles by Base-promoted 1,2-Rearrangement of a Sulfonyl Group

Substituted 1,2,3-triazoles constitute an important class of heterocyclic compounds of a variety of utilities, the area of which covers from pharmaceutical chemistry to materials science. The synthesis of C,N-disubstituted 1,2,3-triazoles often suffers from a regiochemical issue. Thus, it has been the subject of particular interest in current heterocyclic chemistry to prepare them in a desired regiochemical form. The 1,3-dipolar cycloaddition reaction of alkyl (or aryl) azide with terminal alkynes is one of the most reliable procedures for the synthesis of 1,4- and 1,5-disubstituted 1,2,3-triazoles. However, methods for the synthesis of 2,4-disubstituted 1,2,3-triazoles remain relatively undeveloped. During the study on the nickel-catalyzed denitrogenative alkene insertion reaction of 4-sulfonyl-1,2,3-triazoles, the author found that the sulfonyl group underwent rearrangement from N1 position to N2 position to give 4-substituted 2-sulfonyl-1,2,3-triazoles.

Chapter 5 describes a 1,2-rearrangement of a sulfonyl group of 1-Sulfonyl-1,2,3-triazoles promoted by a catalytic amount of DMAP in acetonitrile to give an equilibrium mixture of 1-sulfonyl- and 2-sulfonyl derivatives (eq 5). Subsequent acidic treatment of the mixture caused selective hydrolysis of the 1-sulfonyl derivative, which led to the isolation of the 2-sulfonyl-1,2,3-triazoles in good total yield in pure form (eq 6).

Chapter 6. Rhodium-Catalyzed Arylative Cyclization Reaction of Diynes with Arylboronic Acids

The rhodium(I)-catalyzed carbon–carbon bond-forming reactions using organoboron reagents have been the subject of intensive studies in recent years. An organo-rhodium(I) intermediate generated through transmetalation can undergo carborhodation onto a variety of unsaturated functionalities. It has been demonstrated by the author's group and others.
that multiple carborhodation steps can operate sequentially on acceptor compounds possessing two or more unsaturated functionalities to construct cyclic compounds. The author then studied the use of diynes\textsuperscript{31} as an acceptor compounds being inspired by the synthetic potential of the resulting 1,2-dialkyldenedecycloalkanes.

In chapter 6, the author reports the rhodium-catalyzed cyclization reaction of diynes with arylboronic acids, leading to the formation of 1,2-dialkyldenedecycloalkanes (eq 7). The reaction is initiated by 1,2-addition of arylrhodium species across the carbon-carbon triple bond, following intramolecular addition to another triple bond to give dienylrhodium intermediate. Subsequent hydrolysis gives products, regenerating rhodium active species.

\[
\begin{align*}
\text{R}^1 & \quad \text{R}^2 \\
\text{X} & \quad \text{X}
\end{align*}
\begin{align*}
\text{ArB(OH)}_2 & \quad \text{Rh(I)} \\
\end{align*}
\quad \text{Ar} \\
\quad \text{H} \\
\quad \text{R}^1 \\
\quad \text{R}^2
\]
General Introduction

References and Notes


(17) Recently, denitrogenative annihilations of 1-sulfonyl-1,2,3-triazoles and benzotriazole were reported. See: (a) Horneff, T.; Chuprakov, S.; Chernyak, N.; Gevorgyan, V.; Fokin, V. V. J. Am. Chem. Soc. 2008, 130, 14972. (b) Nakamura, I.; Nemoto, T.; Shiraiwa, N.; Terada, M. Org. Lett. 2009, 11, 1055.


(20) Yoo, E. J.; Ahlquist, M.; Kim, S. H.; Bae, I.; Fokin, V. V.; Sharpless, K. B.; Chang, S. Angew. Chem., Int. Ed., 2007, 46,1730.


General Introduction


Chapter 1

Nickel-Catalyzed Denitrogenative Alkyne Insertion Reactions of 1,2,3-Benzotriazin-4(3H)-ones

Abstract
1,2,3-Benzotriazin-4(3H)-ones reacted with internal and terminal alkynes in the presence of a nickel(0)/phosphine catalyst to give a wide range of substituted 1(2H)-isoquinolones in high yield. The reaction proceeded through denitrogenative activation of the triazinone moiety and the following insertion of alkynes.
Introduction

The 1(2H)-isoquinolone ring system is one of the basic units often found in the structures of plant alkaloids and pharmacologically valuable compounds. Therefore, the development of efficient methods for their synthesis is of great importance. Whereas transition-metal-based catalysis has often been utilized for the synthesis of various heterocyclic compounds, only limited examples applicable to the synthesis of 1(2H)-isoquinolones have appeared. On the other hand, a rhodium-catalyzed extrusion reaction of a molecular dinitrogen from pyridotriazoles was utilized for construction of a new heterocyclic system by Gevorgyan and co-workers. We report herein a nickel-catalyzed denitrogenative alkyne insertion reaction of 1,2,3-benzotriazin-4(3H)-ones, which presents a new synthetic approach to substituted 1(2H)-isoquinolones.

Results and Discussions

1,2,3-Benzotriazin-4(3H)-ones can be readily prepared from anthranilic acid derivatives. Initially, the possibility to activate the triazinone moiety was examined using nickel(0)/phosphine complexes; 3-phenyl-1,2,3-benzotriazin-4(3H)-one (1a, 1.0 equiv) was treated with dec-5-yne (2a, 1.1 equiv) in the presence of a nickel(0) catalyst generated in situ from Ni(cod)2 (5 mol %, cod ) cycloocta-1,5-diene) and PPh3 (20 mol %) at room temperature in THF. The substrate 1a was consumed in 10 h, and subsequent chromatographic isolation on silica gel afforded 3,4-dibutyl-2-phenyl-1(2H)-isoquinolone (3aa) in 91% yield (Scheme 1). Substitution of PMe3 (10 mol %) for PPh3 resulted in a faster reaction, which was completed in 3 h affording 3aa in 93% isolated yield. A catalyst prepared in situ from bench-stable Ni(acac)2, [HPMe3]BF4, and AlEt3 participated in this reaction. We assume that the reaction is initiated by insertion of nickel(0) into the N–N linkage of 1a, which prompts extrusion of a molecular dinitrogen giving azanickelacycle A. Subsequent insertion of the alkyne into the nickel-carbon bond leads to the seven-membered-ring nickelacycle B. Finally, reductive elimination affords 3aa, regenerating the nickel(0) catalyst.

The effect of the substituent on the benzotriazinone was examined (Table 1). Whereas both a sterically and electronically diverse array of the N-aryl substituents underwent the denitrogenative insertion reaction in a similar way at room temperature (entries 1-6), the reaction of benzyl- and methyl-substituted benzotriazinones 1h and 1i required heating at higher temperatures (entries 7 and 8). On the other hand, simple unprotected benzotriazinone
1j failed to react with 2a even at 100 °C (entry 9). Methoxy ether and ester functionalities were tolerated on the aryl group of 1 (entries 10 and 11). Thiophene ring-fused triazinone 1m also participated in this reaction (entry 12).

### Scheme 1

![Scheme 1](image)

### Table 1. Ni(0)-Catalyzed Alkyne Insertion: Scope of Substituent on the Benzotriazinone

<table>
<thead>
<tr>
<th>entry</th>
<th>R¹</th>
<th>R²</th>
<th>R³</th>
<th>3</th>
<th>T (°C)</th>
<th>yield (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>1b</td>
<td>4-MeC₆H₄</td>
<td>H</td>
<td>H</td>
<td>3ba</td>
<td>rt</td>
</tr>
<tr>
<td>2</td>
<td>1c</td>
<td>4-MeOC₆H₄</td>
<td>H</td>
<td>H</td>
<td>3ca</td>
<td>rt</td>
</tr>
<tr>
<td>3</td>
<td>1d</td>
<td>4-CF₃C₆H₄</td>
<td>H</td>
<td>H</td>
<td>3da</td>
<td>rt</td>
</tr>
<tr>
<td>4</td>
<td>1e</td>
<td>4-ClC₆H₄</td>
<td>H</td>
<td>H</td>
<td>3ea</td>
<td>rt</td>
</tr>
<tr>
<td>5</td>
<td>1f</td>
<td>2MeOC₆H₄</td>
<td>H</td>
<td>H</td>
<td>3fa</td>
<td>rt</td>
</tr>
<tr>
<td>6</td>
<td>1g</td>
<td>2,4,6-Me₃C₆H₂</td>
<td>H</td>
<td>H</td>
<td>3ga</td>
<td>rt</td>
</tr>
<tr>
<td>7</td>
<td>1h</td>
<td>Bn</td>
<td>H</td>
<td>H</td>
<td>3ha</td>
<td>60</td>
</tr>
<tr>
<td>8</td>
<td>1i</td>
<td>Me</td>
<td>H</td>
<td>H</td>
<td>3ia</td>
<td>80</td>
</tr>
<tr>
<td>9</td>
<td>1j</td>
<td>H</td>
<td>H</td>
<td>H</td>
<td>3ia</td>
<td>100</td>
</tr>
<tr>
<td>10</td>
<td>1k</td>
<td>Ph</td>
<td></td>
<td></td>
<td></td>
<td>60</td>
</tr>
<tr>
<td>11</td>
<td>1l</td>
<td>Ph</td>
<td></td>
<td></td>
<td></td>
<td>60</td>
</tr>
<tr>
<td>12</td>
<td>1m</td>
<td><img src="image" alt="" /></td>
<td></td>
<td></td>
<td></td>
<td>60</td>
</tr>
</tbody>
</table>

*Conditions: 1 (0.2 mmol), 2 (0.22 mmol), Ni(cod)$_2$ (10 μmol, 5 mol %), and PPh$_3$ (40 μmol, 20 mol %) in THF (1 mL) for 12 h unless otherwise noted. Isolated yield. PMe$_3$ (20 μmol, 10 mol %). PMe$_3$ (20 μmol, 10 mol %) in toluene (1 mL).
Various internal alkynes 2 were subjected to the denitrogenative insertion reaction with benzotriazinones 1a and 1b (Table 2). Symmetrical internal alkynes such as diphenylethynone (2b), 1,4-dibenzyloxybut-2-ynone (2c) and gaseous acetylene (2d) reacted with 1a to give 3ab, 3ac and 3ad in 98, 94 and 97% yields, respectively (entries 1-3). With unsymmetrical internal alkynes, the regioselectivity of the insertion reaction was examined wherein 3-tolyl-benzotriazinone (1b) was used in order to assign the regiochemistry of the products by NOE experiments.\(^9\) 1-Phenylprop-1-ynone (2h) reacted smoothly with 1b to provide 3bh in 99% yield in a fairly regioselective fashion (86:14, entry 7). In the major product, the phenyl group is bound to C(3) next to nitrogen.\(^{13}\) The regioselectivity was enhanced by the presence of electron-donating groups at the para position of the aryl group (entries 8 and 9). In the case of alkynoate 2k, the regiochemistry of the major isomer was consistent with the electronic demand expected in the carbometalation step (i.e., A \(\rightarrow\) B), although an excess amount of 2k and the use of PPh\(_3\) were required to get a high yield (entry 7).\(^{14}\) The high regioselectivity observed with boryl-substituted alkynes\(^{15}\) can also be understood on similar electronic grounds, which assume stabilization of a partial negative charge on the carbon R to boron by the electron-accepting character of boron (entries 11 and 12).\(^{16}\)
Table 2. Ni(0)-Catalyzed Insertion of Internal Alkyne 2

<table>
<thead>
<tr>
<th>entry</th>
<th>1</th>
<th>2 (R¹, R²)</th>
<th>3</th>
<th>yield (%)&lt;sup&gt;b&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>1a</td>
<td>2b (Ph, Ph)</td>
<td>3ab</td>
<td>98</td>
</tr>
<tr>
<td>2</td>
<td>1a</td>
<td>2c (CH₂OBn, CH₂OBn)</td>
<td>3ac</td>
<td>94</td>
</tr>
<tr>
<td>3</td>
<td>1a</td>
<td>2d (H, H) (1 atm)</td>
<td>3ad</td>
<td>97&lt;sup&gt;c&lt;/sup&gt;</td>
</tr>
<tr>
<td>4</td>
<td>1b</td>
<td>2e (i-Pr, Me)</td>
<td>3be</td>
<td>97 (58:42)</td>
</tr>
<tr>
<td>5</td>
<td>1b</td>
<td>2f (i-Bu, Me)</td>
<td>3bf</td>
<td>86 (92:8)&lt;sup&gt;d&lt;/sup&gt;</td>
</tr>
<tr>
<td>6</td>
<td>1b</td>
<td>2g (Me₂Si, Me)</td>
<td>3bg</td>
<td>98 (90:10)&lt;sup&gt;d&lt;/sup&gt;</td>
</tr>
<tr>
<td>7</td>
<td>1b</td>
<td>2h (Me, Ph)</td>
<td>3bh</td>
<td>99 (86:14)</td>
</tr>
<tr>
<td>8</td>
<td>1b</td>
<td>2i (Me, 4-FC₃C₆H₄)</td>
<td>3bi</td>
<td>99 (73:27)</td>
</tr>
<tr>
<td>9</td>
<td>1b</td>
<td>2j (Me, 4-MeOC₃H₄)</td>
<td>3bj</td>
<td>99 (89:11)</td>
</tr>
<tr>
<td>10</td>
<td>1b</td>
<td>2k (Pr, CO₂Et)</td>
<td>3bk</td>
<td>99 (92:8)&lt;sup&gt;e&lt;/sup&gt;</td>
</tr>
<tr>
<td>11</td>
<td>1b</td>
<td>2l (Bu, Bpin)</td>
<td>3bl</td>
<td>93 (98:2)&lt;sup&gt;f&lt;/sup&gt;</td>
</tr>
<tr>
<td>12</td>
<td>1b</td>
<td>2m (Me₃Si, Bpin)</td>
<td>3bm</td>
<td>94 (99:1)&lt;sup&gt;f&lt;/sup&gt;</td>
</tr>
</tbody>
</table>

<sup>a</sup> Conditions: 1 (0.2 mmol), 2 (0.22 mmol), Ni(cod)<sub>2</sub> (10 μmol, 5 mol %), PMe₃ (20 μmol, 10 mol %) in THF (1 mL) at rt for 12 h under N₂ unless otherwise noted.<br><sup>b</sup> Combined yield of isomers unless otherwise noted. Numbers in parentheses describe the regioselectivity. <sup>c</sup> 60 °C. <sup>d</sup> DPPF (20 μmol, 10 mol %). <sup>e</sup> 2 (0.4 mmol) and PPh₃ (40 mmol %, 20 mol %) at 60 °C. <sup>f</sup> Isolated yield of the major regioisomer. DPPF = 1,1'-Bis(diphenylphosphino)ferrocene.

We then examined the reaction of terminal alkynes with 1b (Table 3). Although oct-1-yne (2n) is capable of undergoing a self-oligomerization reaction, it instead reacted via the insertion reaction giving 3bn in 98% yield with the Ni(0)/PMe₃ catalyst (entry 1). However, the regioselectivity was modest (73:27). Several phosphine ligands of nickel(0) were tested to improve the selectivity in this case. To the author’s delight, the bidentate phosphine ligand, 1,1'-bis(diphenylphosphino) ferrocene (DPPF), afforded very high regioselectivity (98:2, entry 2).<sup>17,18</sup> This catalyst system proved to be general, catalyzing the insertion reaction of other terminal alkynes 2o-2r with similarly high regioselectivity giving the corresponding products 3bo-3br in yields ranging from 92% to 99% (entries 3-6).
Table 3. Ni(0)-Catalyzed Insertion of Terminal Alkyne 2

<table>
<thead>
<tr>
<th>entry</th>
<th>2 (R¹)</th>
<th>3</th>
<th>yield (%)&lt;sup&gt;b&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>2n (n-Hex)</td>
<td>3bn</td>
<td>98 (73:27)&lt;sup&gt;c&lt;/sup&gt;</td>
</tr>
<tr>
<td>2</td>
<td>2n (n-Hex)</td>
<td>3bn</td>
<td>99 (98:2)</td>
</tr>
<tr>
<td>3</td>
<td>2o (c-Pent)</td>
<td>3bo</td>
<td>98 (99:1)</td>
</tr>
<tr>
<td>4</td>
<td>2p (t-Bu)</td>
<td>3bp</td>
<td>99 (&gt;99:1)&lt;sup&gt;c&lt;/sup&gt;</td>
</tr>
<tr>
<td>5</td>
<td>2q (TMS)</td>
<td>3bq</td>
<td>94 (99:1)&lt;sup&gt;d&lt;/sup&gt;&lt;sup&gt;e&lt;/sup&gt;</td>
</tr>
<tr>
<td>6</td>
<td>2r (n-Bu&lt;sub&gt;3&lt;/sub&gt;Sn)</td>
<td>3br</td>
<td>92 (99:1)&lt;sup&gt;d&lt;/sup&gt;&lt;sup&gt;f&lt;/sup&gt;</td>
</tr>
</tbody>
</table>

<sup>a</sup>Conditions: 1 (0.2 mmol), 2 (0.22 mmol), Ni(cod)<sub>2</sub> (10 µmol, 5 mol %), DPPF (20 µmol, 10 mol %) in THF (1 mL) at rt for 3–12 h under N<sub>2</sub> unless otherwise noted. <sup>b</sup>Combined yield of regioisomers unless otherwise noted. Numbers in parentheses describe the regioselectivity. <sup>c</sup>PMe<sub>3</sub> (20 µmol, 10 mol %). <sup>d</sup>Isolated yield of the major regio isomer. <sup>e</sup>60 °C. <sup>f</sup>Ni(cod)<sub>2</sub> (20 µmol, 10 mol %), DPPF (40 µmol, 20 mol %) at 60 °C.

In the case of phenylethyne (2s), however, different regioisomers were preferentially obtained depending on the ligand employed, although the selectivity was modest (eq 1).

However, employing the densely functionalized products 3bm and 3br, it was possible to prepare both isomers, 3bs and 3bs', with high regioselectivity (Scheme 2). Starting with compound 3bm, the silyl group was selectively removed by treatment with trifluoroacetic acid (TFA) at room temperature, giving 3-boryl-1(2H)-isoquinolone 4bm in 87% yield. A subsequent palladium-catalyzed cross-coupling reaction of 4bm with iodobenzene (5) afforded 3-phenyl-1(2H)-isoquinolone 3bs' (92% yield). On the other hand, an analogous cross-coupling reaction performed directly on the stannyl-substituted 3br with 5 furnished the
other regioisomer, 4-phenyl-1(2H)-isoquinolone 3bs in 95% yield. Thus, 4bm and 3br provide synthetic platforms for the preparation of a wide variety of 3- and 4-substituted 1(2H)-isoquinolone.

**Scheme 2**

Next, the author examined isolation and characterization of the postulated azanickelacycle intermediate. 1,2,3-benzotriazin-4(3H)-one (1b) was treated with equimolar amounts of Ni(cod)$_2$ and 1,2-bis(diphenylphosphino)-benzene (Dppbenz) in THF at room temperature for 3 h. Recrystallization of the reaction mixture from CH$_2$Cl$_2$/hexane afforded the azanickelacycle 6 as dark brown crystals in 79% yield (eq 2).

The five-membered cyclic structure of 6 was unambiguously determined by single crystal X-ray analysis (Figure 1). The nickel(II) complex 6 has a square planar geometry and the nitrogen atom of the amidate moiety is bound to the nickel center in an η$^1$-fashion.
Presumably, oxidative insertion of nickel(0) into the N–N(tolyl) bond of 1b and subsequent retro-insertion of dinitrogen furnished 6.

![Figure 1. X-ray crystal structure of 6](image)

Next, the reactivity of the azanickelacycle 6 was examined. When dec-5-yne (2a, 3 equiv) was reacted with 6 in toluene at 110 °C, an 1(2H)-isoquinolone 3ba was obtained in 99% yield (eq 3).

![Chemical Reaction Equation](image)

Conclusions

In conclusion, we have demonstrated a facile approach for the preparation of substituted 1(2H)-isoquinolones. A wide variety of alkyne substrates including borylalkynes were regioselectively incorporated into 1,2,3-benzotriazin-4(3H)-ones with loss of a dinitrogen molecule.
Experimental Section

General Methods. All reactions were carried out under a nitrogen atmosphere unless otherwise noted. Infrared spectra were recorded on a Shimadzu FTIR-8100 spectrometer. $^1$H and $^{13}$C NMR spectra were recorded on a Varian Gemini 2000 ($^1$H at 300 MHz and $^{13}$C at 75 MHz) spectrometer using CHCl$_3$ ($^1$H, $\delta$ = 7.26) and CDCl$_3$ ($^{13}$C, $\delta$ = 77.0) as an internal standard unless otherwise noted. In the case of the azanickelacycle 2, NMR spectra were recorded on a JEOL JNM-EC600 ($^1$H at 600 MHz, $^{13}$C at 150 MHz and $^{31}$P at 244 MHz) spectrometer using CDCl$_3$ ($^1$H, $\delta$ = 5.32), CD$_2$Cl$_2$ ($^{13}$C, $\delta$ = 53.8) as an internal standard and P(OMe)$_3$ ($^{31}$P, $\delta$ = 140.0) as an external standard. High-resolution mass spectra were recorded on a JEOL JMS-SX102A (EI) or a JEOL JMS-HX110A (FAB) spectrometer. All reactions were carried out under a nitrogen atmosphere unless otherwise noted. Column chromatography was performed with silica gel 60 N (Kanto). Preparative thin-layer chromatography was performed with silica gel 60 PF254 (Merck).

Materials. THF and toluene were dried and deoxygenized using an alumina/catalyst column system (Glass Contour Co.). Anhydrous CH$_2$Cl$_2$ (Kanto), DMF (Wako), and CH$_3$CN (Kanto) were purchased from the commercial sources. Triphenylphosphine (nacalai), trimethylphosphine (Aldrich), methyl anthranilate (TCI), aniline (Wako), 1,2,3-benzotriazin-4(3H)-one (1j) (TCI), 2-isobutyrylcyclohexanone (Aldrich), 1,2-bis(diphenylphosphino)benzene (Wako), 1,1’-bis(diphenylphosphino)ferrocene (Kanto), tri-t-butylphosphine (Wako), diphenylethyne (2b) (Aldrich), ethynyltributylstannane (2r) (Aldrich), trifluoroacetic acid (Aldrich), phenyl iodide (nacalai), and copper iodide (nacalai) were used as received from the commercial sources. Ni(cod)$_2$ (Kanto) was obtained from the commercial sources and purified by recrystallization from toluene before use. Pd(dba)$_2$ and Pd(PPh$_3$)$_4$ were prepared according to the literature procedures. Benzotriazinones 1a-1g and 1k-1m were prepared according to the literature procedure $^7$ 1,4-Bis(benzyloxy)but-2-yne (2e) $^{21}$ 1-(4-trifluoromethylphenyl)-1-propyne (2i) $^{22}$ 1-(4-methoxyphenyl)-1-propyne (2j) $^{22}$ and alkynylboranes (2l, 2m) $^{25}$ were prepared according to the literature procedures. All other alkynes were purchased from the commercial sources and purified by bulb-to-bulb distillation prior to use.

General Procedure for the Synthesis of N-Aryl-1,2,3-benzotriazin-4(3H)-ones from Methyl Anthranilate.

To a solution of methyl anthranilate (1.59 g, 12.9 mmol) in 2N HCl (21 mL) was slowly added NaNO$_2$ (1.03 g, 14.9 mmol) in water (6 mL) at 0 °C. The mixture was stirred for 30 min. Then, NaOAc · 3H$_2$O (6.80 g, 50.0 mmol) in water (10 mL) and aniline (1.8 mL, 19.8 mmol) was slowly added at 0 °C. The reaction mixture was stirred at 0 °C for 11 h. The precipitate was collected by filtration, washed with cold water (30 mL), and recrystallized from ethanol to give the triazene as a yellow solid. The resulting triazene was boiled in ethanol (35 mL) for 4 h. The reaction mixture was cooled to –30 °C. The precipitate was collected by filtration and washed with cold ethanol (30 mL) to give 1a (1.80 g, 8.06 mmol, 62% yield) as a white solid: 1b (78%), 1c (35%), 1d (81%), 1e (43%), 1f (32%), 1g (19%), 1k (29%), 1l (36%). In the case of 1m, the triazene was boiled in ethanol/DIPEA = 5/1. 1m (30%).
General Procedure for the Synthesis of N-Aryl-1,2,3-benzotriazin-4(3H)-ones from NH-1,2,3-benzotriazin-4(3H)-one.

In an N₂-filled glove-box, to an oven-dried 4 mL-vial equipped with a stir bar was added NH-1,2,3-benzotriazin-4(3H)-one (29.7 mg, 0.20 mmol), K₂CO₃ (55.3 mg, 0.40 mmol), p-iodotoluene (65.4 mg, 0.30 mmol), CuI (3.8 mg, 20 μmol), 2-isobutyrylcyclohexanone (6.7 μL, 40 μmol), and DMSO (1 mL) at room temperature. The vial capped with a Teflon film was taken outside the glove-box and heated at 80 °C for 24 h, and then the reaction mixture was cooled to room temperature. The resulting mixture was diluted with ethyl acetate (30 mL), washed with water (3 x 20 mL) and brine, and dried over MgSO₄. The solvent was removed under reduced pressure and the residue was purified by preparative thin-layer chromatography (chloroform/ethyl acetate 40:1) to give the product 1b as a white solid (45.1 mg, 0.19 mmol, 95% yield).

3-Phenyl-1,2,3-benzotriazin-4(3H)-one (1a)

IR (KBr): 1682, 1495, 1460, 1337, 1314, 1088, 1036 cm⁻¹; ¹H NMR: δ = 7.44–7.60 (m 3H), 7.62–7.70 (m, 2H), 7.78–7.88 (m, 1H), 7.93–8.02 (m, 1H) 8.17–8.24 (m, 1H), 8.39–8.46 (m, 1H); ¹³C NMR: δ = 120.2, 125.5, 125.9, 128.4, 128.8, 128.9, 132.6, 135.0, 138.7, 143.5, 155.1; HRMS (EI⁺): Calcd for C₁₅H₁₈N₂O, M⁺ 223.0746. Found m/z 223.0749.

3-(4-Methylphenyl)-1,2,3-benzotriazin-4(3H)-one (1b)

IR (KBr): 1682, 1495, 1460, 1337, 1314, 1088, 1036 cm⁻¹; ¹H NMR: δ = 2.44 (s, 3H), 7.35 (d, J = 8.7 Hz, 2H), 7.53 (d, J = 8.4 Hz, 2H), 7.78–7.87 (m, 1H), 7.92–8.01 (m, 1H), 8.17–8.24 (m, 1H), 8.42 (dd, J = 8.1, 1.5 Hz, 1H); ¹³C NMR: δ = 21.2, 120.3, 125.5, 125.7, 128.3, 129.5, 132.5, 134.9, 136.2, 138.9, 143.6, 155.1; HRMS (EI⁺): Calcd for C₁₅H₁₉N₂O, M⁺ 237.0902. Found m/z 237.0900.

3-(4-Methoxyphenyl)-1,2,3-benzotriazin-4(3H)-one (1c)

IR (KBr): 2951, 1655, 1611, 1593, 1510, 1250, 1022 cm⁻¹; ¹H NMR: δ = 3.86 (s, 3H), 7.00–7.09 (m 2H), 7.51–7.60 (m, 2H), 7.78–7.86 (m, 1H), 7.92–8.00 (m, 1H), 8.19 (d, J = 8.1, 1H), 8.41 (dd, J = 8.1, 1.4 Hz, 1H); ¹³C NMR: δ = 55.5, 114.2, 120.2, 125.4, 127.2, 128.3, 131.6, 132.5, 134.9, 143.6, 155.2, 159.7; HRMS (EI⁺): Calcd for C₁₅H₁₆N₂O₂, M⁺ 253.0851. Found m/z 253.0854.
3-(4-Trifluorophenyl)-1,2,3-benzotriazine-4(3H)-one (1d)

IR (KBr): 2961, 1651, 1588, 1329, 1169, 1121, 1071 cm\(^{-1}\); \(^1\)H NMR: \(\delta = 7.79–7.93 (m, 5H)\), 7.99–8.07 (m, 1H), 8.22–8.28 (m, 1H), 8.46 (dd, \(J = 7.8, 1.5\) Hz, 1H); \(^13\)C NMR: \(\delta = 120.2, 123.7 (q, \(J = 270.5\) Hz), 125.7, 126.2, 128.7, 130.8 (q, \(J = 32.9\) Hz), 131.1, 135.4, 141.6, 143.4, 155.1; HRMS (EI\(^{+}\)): Calcd for C\(_{14}\)H\(_8\)F\(_3\)N\(_3\)O, M\(^+\) 291.0619.  Found m/z 291.0618.

3-(4-Chlorophenyl)-1,2,3-benzotriazine-4(3H)-one (1e)

IR (KBr): 1696, 1491, 1320, 1082, 1042 cm\(^{-1}\); \(^1\)H NMR: \(\delta = 7.51 (dt, \(J = 8.7, 2.5\) Hz, 2H), 7.62 (dt, \(J = 8.7, 2.4\) Hz, 2H), 7.84 (td, \(J = 7.7, 1.1\) Hz, 1H), 7.99 (td, \(J = 7.8, 1.6\) Hz, 1H) 8.20 (dd, \(J = 7.8, 0.6\) Hz, 1H), 8.41 (dd, \(J = 8.1, 0.9\) Hz, 1H); \(^13\)C NMR: \(\delta = 120.1, 125.6, 127.1, 128.5, 129.1, 132.9, 134.7, 135.2, 137.1, 143.4, 155.0\); HRMS (EI\(^{+}\)): Calcd for C\(_{13}\)H\(_8\)ClN\(_3\)O, M\(^+\) 257.0356.  Found m/z 257.0346.

3-(2-Methoxyphenyl)-1,2,3-benzotriazine-4(3H)-one (1f)

IR (KBr): 2957, 1655, 1612, 1593, 1501 cm\(^{-1}\); \(^1\)H NMR: \(\delta = 3.80 (s, 3H), 7.06–7.18 (m, 2H), 7.40–7.54 (m, 2H), 7.86 (td, \(J = 7.5\) Hz, 1H), 7.97 (td, \(J = 7.7, 0.9\) Hz, 1H) 8.21 (d, \(J = 8.1\) Hz, 1H), 8.42 (dt, \(J = 8.1, 0.6\) Hz, 1H); \(^13\)C NMR: \(\delta = 55.9, 112.1, 120.3, 120.8, 125.4, 127.6, 128.3, 131.1, 132.4, 134.8, 143.8, 154.7, 155.0\); HRMS (EI\(^{+}\)): Calcd for C\(_{14}\)H\(_{11}\)N\(_3\)O\(_2\), M\(^+\) 253.0851.  Found m/z 253.0856.

3-(2,4,6-Trimethylphenyl)-1,2,3-benzotriazine-4(3H)-one (1g)

IR (KBr): 2957, 1655, 1612, 1593, 1501 cm\(^{-1}\); \(^1\)H NMR: \(\delta = 2.09 (s, 6H), 2.37 (s, 3H), 7.06–7.18 (m, 2H), 7.40–7.54 (m, 2H), 7.82 (t, \(J = 7.5\) Hz, 1H), 7.97 (td, \(J = 7.7, 0.9\) Hz, 1H) 8.21 (d, \(J = 8.1\) Hz, 1H), 8.42 (dt, \(J = 8.1, 0.6\) Hz, 1H); \(^13\)C NMR: \(\delta = 17.7, 21.1, 120.2, 125.5, 128.4, 129.3, 132.5, 134.3, 135.0, 135.2, 139.6, 144.0, 155.0\); HRMS (EI\(^{+}\)): Calcd for C\(_{16}\)H\(_{15}\)N\(_3\)O, M\(^+\) 265.1215.  Found m/z 265.1221.

6,7-Dimethoxy-1,2,3-benzotriazine-4(3H)-one (1k)

IR (KBr): 1684, 1605, 1512, 1291, 1092 cm\(^{-1}\); \(^1\)H NMR: \(\delta = 4.04 (s, 3H), 4.06 (s, 3H), 7.42–7.58 (m, 4H), 7.60–7.70 (m, 3H); \(^13\)C NMR: \(\delta = 56.6, 56.7, 104.0, 108.1, 114.9, 126.0, 128.7, 129.8, 138.9, 140.1, 153.4, 154.9, 155.0\); HRMS (EI\(^{+}\)): Calcd for C\(_{16}\)H\(_{15}\)N\(_3\)O\(_3\), M\(^+\) 283.0957.  Found m/z 283.0954.
7-Methoxycarbonyl-3-phenyl-1,2,3-benzotriazine-4(3H)-one (1I)

IR (KBr): 1719, 1700, 1495, 1441, 1341, 1308, 1198, 1082, 1046 cm\(^{-1}\); \(^1\)H NMR: \(\delta = 4.04\) (s, 3H), 7.46–7.70 (m, 5H), 8.40–8.54 (m, 2H), 8.84–8.88 (m, 1H); \(^1^3\)C NMR: \(\delta = 53.0, 123.1, 125.9, 126.1, 129.06, 129.11, 130.1, 132.6, 136.3, 138.4, 143.4, 154.5, 165.0\); HRMS (EI\(^+\)): Calcd for C\(_{15}\)H\(_{11}\)N\(_3\)O\(_3\), M\(^+\) 281.0800. Found m/z 281.0796.

3-Phenylthieno[3,2-\(d\)]-1,2,3-triazin-4(3H)-one (1M)

IR (KBr): 1679, 1497, 1458, 1302 cm\(^{-1}\); \(^1\)H NMR: \(\delta = 7.43–7.71\) (m, 5H), 7.75 (d, \(J = 5.1\) Hz, 1H), 7.95 (d, \(J = 5.7\) Hz, 1H); \(^1^3\)C NMR: \(\delta = 125.0, 126.2, 127.4, 129.0, 129.2, 135.5, 138.2, 152.9, 153.4\); HRMS (EI\(^+\)): Calcd for C\(_{11}\)H\(_7\)N\(_3\)OS, M\(^+\) 229.0310. Found m/z 229.0304.

3-Benzyl-1,2,3-benzotriazine-4(3H)-one (1H)

To an oven-dried flask was added 1,2,3-benzotriazine-4(3H)-one (1.03 g, 7.0 mmol), K\(_2\)CO\(_3\) (969 mg, 7.0 mmol), and DMF (20 mL) at room temperature. To the reaction mixture was added BnBr (0.9 mL, 7.6 mmol) at 0 °C and the mixture was stirred at room temperature for 31 h under a nitrogen atmosphere, and then quenched with addition of water (20 mL). The resulting aqueous solution was extracted with AcOEt (3 x 20 mL). The combined extracts were washed with brine (3 x 20 mL), brine and dried over MgSO\(_4\). The solvent was removed under reduced pressure and the residue was purified by flash chromatography (chloroform) and recrystallization (chloroform/hexane) to give the product \(1h\) (1.19 g, 5.0 mmol, 71% yield) as a white solid. IR (KBr): 1674, 1455, 1279, 1046 cm\(^{-1}\); \(^1\)H NMR: \(\delta = 5.62\) (s, 2H), 7.24–7.38 (m, 3H), 7.49–7.56 (m, 2H), 7.72–7.79 (m, 1H), 7.86–7.94 (m, 1H), 8.10–8.16 (m, 1H), 8.29–8.35 (m, 1H); \(^1^3\)C NMR: \(\delta = 53.3, 120.0, 125.0, 128.1, 128.2, 128.6, 128.8, 132.2, 134.7, 135.7, 144.2, 155.2\); HRMS (FAB\(^+\)): Calcd for C\(_{14}\)H\(_{12}\)N\(_3\)O, M\(^+\)H\(^+\) 238.0980. Found m/z 238.0980.

3-Methyl-1,2,3-benzotriazine-4(3H)-one (1I)

To an oven-dried flask was added 1,2,3-benzotriazine-4(3H)-one (1.00 g, 6.8 mmol), K\(_2\)CO\(_3\) (1.41 g, 10 mmol), and CH\(_3\)CN (10 mL) at room temperature. To the reaction mixture was added MeI (0.7 mL, 11 mmol) at 0 °C and the mixture was stirred at room temperature for 18 h under a nitrogen atmosphere, and then quenched with addition of water. The resulting aqueous solution was extracted with chloroform (3 x 20 mL). The combined extracts were washed with brine and dried over MgSO\(_4\). The solvent was removed under reduced pressure and the residue was purified by flash chromatography (chloroform) and recrystallization (chloroform/hexane) to give the product \(1i\) (646 mg, 4.0 mmol, 59% yield) as a white solid. IR (KBr): 1680, 1458, 1335, 1302, 1235, 1107 cm\(^{-1}\); \(^1\)H NMR: \(\delta = 4.03\) (s, 3H), 7.73–7.80 (m, 1H), 7.87–7.95 (m, 1H), 8.08–8.14 (m, 1H), 8.28–8.34 (m, 1H); HRMS (FAB\(^+\)): Calcd for C\(_{13}\)H\(_{12}\)N\(_3\)O, M\(^+\)H\(^+\) 238.0980. Found m/z 238.0980.
General Procedure for the Nickel-Catalyzed Denitrogenative Alkyne Insertion of Benzotriazinones. In an N\textsubscript{2}-filled glove-box, 1a (44.8 g, 0.20 mmol) was charged into an oven-dried 4 mL-vial equipped with a stir bar. A solution of Ni(cod)_2 (2.8 mg, 10 \( \mu \)mol) and PPh\textsubscript{3} (10.4 mg, 40 \( \mu \)mol) in THF (1 mL) and dec-5-yne (40 \( \mu \)L, 0.22 mmol) were added, the vial capped with a Teflon film and the reaction mixture left to stir at room temperature for 10 hours. After this time, the reaction mixture was removed from the glove-box, diluted with ethyl acetate (2 mL) and stirred for 30 min in open air. The resulting mixture was passed through a pad of Florisil\textsuperscript{®} with ethyl acetate and concentrated under reduced pressure. The residue was purified by preparative thin-layer chromatography (hexane/ethyl acetate 5:1) to give the product 3aa (60.6 mg, 91% yield) as a white solid.

General Procedure for the Nickel-Catalyzed Denitrogenative Alkyne Insertion of Benzotriazinones Using the Catalyst Prepared from Bench-Stable Ni(acac)_2.

To an oven-dried flask was added 1b (92.0 mg, 0.387 mmol), Ni(acac)_2 (2.2 mg, 8 \( \mu \)mol), [HPMe\textsubscript{3}]BF\textsubscript{4}, (2.6 mg, 16 \( \mu \)mol), and THF (2 mL). To the suspension was added a 1.0 M solution of AlEt\textsubscript{3} in hexane (80 \( \mu \)L, 80 \( \mu \)mol) dropwise and dec-5-yne (2a, 80 \( \mu \)L, 0.8 mmol). After heated at 60 °C for 24 h under Ar atmosphere, the reaction mixture was cooled to room temperature and stirred over 30 min in open air. The resulting mixture was passed through a pad of Florisil\textsuperscript{®} with ethyl acetate and the solvent was concentrated under reduced pressure. The residue was purified by preparative thin-layer chromatography (hexane/ethyl acetate 5:1) to give the products 3ba (127 mg, 0.365 mmol, 94% yield).

3,4-Dibutyl-2-phenyl-1(2H)-isoquinolone (3aa)

IR (KBr): 2959, 1649, 1590, 1483, 1331 cm\textsuperscript{-1}; \textsuperscript{1}H NMR: \( \delta = 0.68 \) (t, \( J = 7.4 \) Hz, 3H), 1.01 (t, \( J = 7.1 \) Hz, 3H), 1.08 (sextet, \( J = 7.3 \) Hz, 2H), 1.31–1.69 (m, 6H), 2.31–2.42 (m, 2H), 2.68–2.80 (m, 2H), 7.24–7.30 (m, 2H), 7.39–7.56 (m, 4H), 7.64–7.73 (m, 2H), 8.42–8.48 (m, 1H); \textsuperscript{13}C NMR: \( \delta = 13.2, 14.0, 22.6, 23.1, 27.3, 29.7, 31.2, 32.5, 113.6, 122.6, 125.3, 125.7, 128.3, 128.4, 128.9, 129.2, 132.3, 137.0, 139.5, 140.1, 162.9; \) HRMS (EI\textsuperscript{+}): Calcd for C\textsubscript{25}H\textsubscript{27}NO, M\textsuperscript{+} 333.2093. Found m/z 333.2093.

3,4-Dibutyl-2-(4-methylphenyl)-1(2H)-isoquinolone (3ba)

\( \textsuperscript{13}C \) NMR: \( \delta = 37.3, 119.5, 124.8, 128.1, 132.2, 134.6, 144.4, 155.7; \) HRMS (EI\textsuperscript{+}): Calcd for C\textsubscript{24}H\textsubscript{29}N\textsubscript{2}O, M\textsuperscript{+} 161.0589. Found m/z 161.0589.
Chapter 1

IR (KBr): 2955, 1649, 1607, 1590, 1510, 1333 cm\(^{-1}\); \(^1\)H NMR: \(\delta = 0.72\) (t, \(J = 7.7\) Hz, 3H), 1.02 (t, \(J = 7.2\) Hz, 3H), 1.12 (sextet, \(J = 7.3\) Hz, 2H), 1.31–1.70 (m, 6H), 2.35–2.45 (m, 2H), 2.69–2.79 (m, 2H), 7.21 (dt, \(J = 8.4, 2.5\) Hz, 2H), 7.39–7.54 (m, 3H), 7.64–7.74 (m, 2H), 8.43 (d, \(J = 8.1\) Hz, 1H); \(^1\)C NMR: \(\delta = 13.3, 13.9, 22.6, 23.1, 27.2, 29.7, 31.3, 32.5, 113.9, 122.7, 125.1, 125.8, 128.4, 129.4, 130.4, 132.5, 134.2, 137.0, 138.0, 139.6, 162.9; HRMS (EI\(^{+}\)): Calcd for C\(_{22}\)H\(_{24}\)ClNO, M\(^+\) 367.1703. Found m/z 367.1701.

3,4-Dibutyl-2-(4-methoxyphenyl)-1(2\(H\))-isoquinolone (3ca)

IR (KBr): 2955, 1649, 1607, 1590, 1510, 1333 cm\(^{-1}\); \(^1\)H NMR: \(\delta = 0.73\) (t, \(J = 7.4\) Hz, 3H), 1.01 (t, \(J = 7.1\) Hz, 3H), 1.12 (sextet, \(J = 7.3\) Hz, 2H), 1.32–1.70 (m, 6H), 2.35–2.45 (m, 2H), 2.69–2.79 (m, 2H), 7.02 (d, \(J = 8.7\) Hz, 2H), 7.17 (d, \(J = 9.0\) Hz, 2H), 7.38–7.48 (m, 1H), 7.64–7.72 (m, 2H), 8.45 (d, \(J = 7.8\) Hz, 1H); \(^1\)C NMR: \(\delta = 13.3, 14.0, 22.7, 23.1, 27.3, 29.8, 31.3, 32.5, 55.4, 113.5, 114.4, 122.6, 125.2, 125.6, 128.5, 129.8, 132.1, 132.2, 137.0, 140.5, 159.1, 163.2; HRMS (EI\(^{+}\)): Calcd for C\(_{22}\)H\(_{24}\)O\(_{2}\), M\(^+\) 363.2196. Found m/z 363.2196.

3,4-Dibutyl-2-(4-trifluoromethylphenyl)-1(2\(H\))-isoquinolone (3da)

IR (KBr): 2955, 1687, 1111, 1086, 1038 cm\(^{-1}\); \(^1\)H NMR: \(\delta = 0.70\) (t, \(J = 7.4\) Hz, 3H), 1.03 (t, \(J = 7.1\) Hz, 3H), 1.12 (sextet, \(J = 7.3\) Hz, 2H), 1.31–1.45 (m, 2H), 1.47–1.72 (m, 4H), 2.31–2.43 (m, 2H), 2.71–2.82 (m, 2H), 7.39–7.51 (m, 3H), 7.67–7.76 (m, 2H), 7.80 (d, \(J = 8.4\) Hz, 2H), 8.44 (d, \(J = 7.5\) Hz, 1H); \(^1\)C NMR: \(\delta = 13.1, 13.9, 22.4, 23.0, 27.2, 29.6, 31.1, 32.4, 114.2, 122.8, 123.7 (q, \(J = 270.5\) Hz), 125.0, 125.9, 126.3 (q, \(J = 3.5\) Hz), 128.3, 129.7, 130.5 (q, \(J = 32.7\) Hz), 132.6, 137.0, 139.1, 142.8, 162.7; HRMS (EI\(^{+}\)): Calcd for C\(_{22}\)H\(_{24}\)F\(_3\)NO, M\(^+\) 401.1966. Found m/z 401.1969.

3,4-Dibutyl-2-(4-chlorophenyl)-1(2\(H\))-isoquinolone (3ea)

IR (KBr): 2957, 1653, 1611, 1582, 1491, 1329, 1086, 1017 cm\(^{-1}\); \(^1\)H NMR: \(\delta = 0.74\) (t, \(J = 7.2\) Hz, 3H), 1.02 (t, \(J = 7.2\) Hz, 3H), 1.13 (sext, \(J = 7.3\) Hz, 2H), 1.30–1.44 (m, 2H), 1.45–1.70 (m, 4H), 2.31–2.43 (m, 2H), 2.68–2.79 (m, 2H), 7.21 (dt, \(J = 8.4, 2.5\) Hz, 2H), 7.39–7.54 (m, 3H), 7.64–7.74 (m, 2H), 8.43 (d, \(J = 8.1\) Hz, 1H); \(^1\)C NMR: \(\delta = 13.3, 13.9, 22.6, 23.1, 27.2, 29.7, 31.3, 32.5, 113.9, 122.7, 125.1, 125.8, 128.4, 129.4, 130.4, 132.5, 134.2, 137.0, 138.0, 139.6, 162.9; HRMS (EI\(^{+}\)): Calcd for C\(_{22}\)H\(_{24}\)ClNO, M\(^+\) 367.1703. Found m/z 367.1701.
3,4-Dibutyl-2-(2-methoxyphenyl)-1(2H)-isoquinolone (3fa)

IR (KBr): 1694, 1603, 1501, 1466, 1281, 1250, 1080, 1049, 1020 cm\(^{-1}\); \(^1\)H NMR: \(\delta = 0.69\) (t, \(J = 7.5\) Hz, 3H), 1.02 (t, \(J = 7.4\) Hz, 3H), 1.09 (sext, \(J = 7.3\) Hz, 2H), 1.29–1.42 (m, 2H), 1.45–1.72 (m, 4H), 2.16–2.29 (m, 1H), 2.41–2.55 (m, 1H), 2.67–2.85 (m, 2H), 3.76 (s, 3H), 7.02–7.12 (m, 2H), 7.21 (dd, \(J = 7.5, 1.5\) Hz, 1H), 7.38–7.48 (m, 2H), 7.63–7.73 (m, 2H), 8.47 (dt, \(J = 8.1, 0.8\) Hz, 1H); \(^{13}\)C NMR: \(\delta = 13.3, 14.0, 22.6, 23.1, 27.3, 29.7, 30.8, 32.5, 55.5, 111.8, 113.3, 120.7, 122.6, 125.3, 128.0, 128.5, 129.8, 130.2, 132.1, 137.2, 140.6, 155.1, 162.5; HRMS (EI\(^+\)): Calcd for C\(_{24}\)H\(_{30}\)NO\(_2\), M\(^+\) 363.2198. Found m/z 363.2201.

3,4-Dibutyl-2-(2,4,6-trimethylphenyl)-1(2H)-isoquinolone (3ga)

IR (KBr): 2961, 1655, 1613, 1594, 1487, 1327 cm\(^{-1}\); \(^1\)H NMR: \(\delta = 0.72\) (t, \(J = 7.1\) Hz, 3H), 1.02 (t, \(J = 7.4\) Hz, 3H), 1.17 (sext, \(J = 7.1\) Hz, 2H), 1.24–1.37 (m, 2H), 1.45–1.71 (m, 4H), 2.01 (s, 6H), 2.25–2.37 (m, 5H), 2.72–2.82 (m, 2H), 6.99 (s, 2H), 7.44 (ddd, \(J = 8.0, 6.1, 2.0\) Hz, 1H), 7.66–7.76 (m, 2H), 8.49 (d, \(J = 7.8\) Hz, 1H); \(^{13}\)C NMR: \(\delta = 13.3, 14.0, 18.0, 21.1, 22.7, 23.1, 27.3, 29.5, 30.8, 32.6, 114.3, 122.6, 125.39, 125.45, 128.6, 129.2, 132.2, 135.1, 135.2, 137.1, 137.8, 140.0, 161.6; HRMS (EI\(^+\)): Calcd for C\(_{25}\)H\(_{33}\)NO, M\(^+\) 375.2562. Found m/z 375.2558.

3,4-Dibutyl-2-benzyl-1(2H)-isoquinolone (3ha)

IR (KBr): 2955, 1644, 1590, 1495, 1464, 1458, 1381, 1343 cm\(^{-1}\); \(^1\)H NMR: \(\delta = 0.96\) (t, \(J = 7.2\) Hz, 3H), 1.00 (t, \(J = 7.1\) Hz, 3H), 1.36–1.66 (m, 8H), 2.57–2.78 (m, 4H), 5.50 (br s, 2H), 7.08–7.18 (m, 2H), 7.18–7.34 (m, 3H), 7.40–7.51 (m, 1H), 7.63–7.73 (m, 2H), 8.50–8.57 (m, 1H); \(^{13}\)C NMR: \(\delta = 13.7, 13.9, 22.9, 23.1, 27.3, 29.4, 32.0, 32.5, 47.1, 114.4, 122.6, 124.9, 125.6, 126.0, 126.9, 128.6, 132.2, 136.7, 137.7, 139.9, 162.8; HRMS (EI\(^+\)): Calcd for C\(_{23}\)H\(_{29}\)NO, M\(^+\) 347.2249. Found m/z 347.2249.

3,4-Dibutyl-2-methyl-1(2H)-isoquinolone (3ia)

IR (neat): 2957, 1649, 1611, 1593, 1557, 1487, 1466, 1337, 1034 cm\(^{-1}\); \(^1\)H NMR: \(\delta = 0.99\) (t, \(J = 7.2\) Hz, 3H), 1.00 (t, \(J = 7.1\) Hz, 3H), 1.41–1.62 (m, 8H), 2.66–2.77 (m, 4H), 3.65 (s, 3H), 7.35–7.45 (m, 1H), 7.57–7.65 (m, 2H), 8.43–8.48 (m, 1H); \(^{13}\)C NMR: \(\delta = 13.7, 13.9, 22.9, 23.0, 27.3, 29.4, 31.2, 32.5, 113.8, 122.5, 124.7, 125.4, 128.2, 131.8, 136.4, 139.8, 162.8; HRMS (EI\(^+\)): Calcd for C\(_{18}\)H\(_{25}\)NO, M\(^+\) 271.1936. Found m/z 271.1926.
3,4-Dibutyl-6,7-dimethoxy-2-phenyl-1(2H)-isoquinolone (3ka)

IR (KBr): 2955, 1655, 1603, 1509, 1464, 1397, 1267, 1215, 1165 cm\(^{-1}\); \(^1\)H NMR: \(\delta = 0.67\) (t, \(J = 7.3\) Hz, 3H), 0.98–1.15 (m, 5H), 1.30–1.43 (m, 2H), 1.45–1.71 (m, 4H), 2.29–2.40 (m, 2H), 2.66–2.76 (m, 2H), 3.96 (s, 3H), 4.02 (s, 3H), 7.04 (s, 1H), 7.25 (d, \(J = 7.2\) Hz, 2H), 7.40–7.55 (m, 3H), 7.83 (s, 1H); \(^{13}\)C NMR: \(\delta = 13.2, 13.9, 22.5, 23.0, 27.4, 29.6, 31.3, 32.3, 55.8, 55.9, 103.3, 108.3, 113.1, 119.1, 128.1, 128.9, 129.0, 132.5, 138.7, 139.7, 148.3, 153.3, 162.2; HRMS (EI\(^+\)): Calcd for C\(_{25}\)H\(_{29}\)NO\(_3\), M\(^+\) 393.2304. Found m/z 393.2305.

3,4-Dibutyl-6-methoxycarbonyl-2-phenyl-1(2H)-isoquinolone (3la)

IR (neat): 2957, 1728, 1661, 1590, 1559, 1491, 1437, 1335, 1260, 1109 cm\(^{-1}\); \(^1\)H NMR: \(\delta = 0.68\) (t, \(J = 7.4\) Hz, 3H), 0.98–1.16 (m, 5H), 1.32–1.45 (m, 2H), 1.46–1.70 (m, 4H), 2.33–2.43 (m, 2H), 2.74–2.83 (m, 2H), 3.99 (s, 3H), 7.23–7.29 (m, 2H), 7.42–7.56 (m, 3H), 8.02 (dd, \(J = 8.3, 1.4\) Hz, 1H), 8.39–8.44 (m, 1H), 8.48 (d, \(J = 8.4\) Hz, 1H); \(^{13}\)C NMR: \(\delta = 13.2, 13.9, 22.5, 23.0, 27.1, 29.8, 31.2, 32.5, 52.4, 113.8, 124.9, 125.6, 128.0, 128.5, 128.8, 129.3, 133.2, 136.9, 139.2, 141.1, 162.4, 166.7; HRMS (EI\(^+\)): Calcd for C\(_{25}\)H\(_{29}\)NO\(_3\), M\(^+\) 391.2148. Found m/z 391.2148.

4,5-Dibutyl-6-phenylthieno[2,3-c]pyridin-7(6H)-one (3ma)

IR (KBr): 2955, 1647, 1570, 1524 cm\(^{-1}\); \(^1\)H NMR: \(\delta = 0.67\) (t, \(J = 7.4\) Hz, 3H), 0.99 (t, \(J = 7.4\) Hz, 3H), 1.08 (sext, \(J = 7.3\) Hz, 2H), 1.28–1.40 (m, 2H), 1.48 (sext, \(J = 7.2\) Hz, 2H), 1.55–1.68 (m, 2H), 2.31–2.40 (m, 2H), 2.64–2.75 (m, 2H), 7.23–7.30 (m, 3H), 7.40–7.55 (m, 3H), 7.69 (d, \(J = 5.1\) Hz, 1H); \(^{13}\)C NMR: \(\delta = 13.2, 13.9, 22.5, 22.9, 29.1, 29.3, 31.4, 32.9, 113.9, 122.9, 128.3, 128.4, 128.9, 129.1, 133.1, 139.1, 141.4, 146.4, 159.0; HRMS (EI\(^+\)): Calcd for C\(_{25}\)H\(_{29}\)NOS, M\(^+\) 339.1657. Found m/z 339.1654.

2,3,4-Triphenyl-1(2H)-isoquinolone (3ab)

2,3,4-Triphenyl-1(2H)-isoquinolone is a known compound.\(^24\) Only NMR data are shown here. \(^1\)H NMR: \(\delta = 6.83–6.99\) (m, 5H), 7.19–7.32 (m, 11H), 7.50–7.64 (m, 2H), 8.56–8.63 (m, 1H); \(^{13}\)C NMR: \(\delta = 118.7, 125.4, 125.5, 126.8, 127.0, 127.1, 127.4, 127.9, 128.1, 128.5, 129.4, 130.9, 131.5, 132.4, 134.6, 136.2, 137.5, 139.3, 140.9, 162.5.
Chapter 1

3,4-Bis(benzyloxymethyl)-2-phenyl-1(2H)-isoquinolone (3ac)

IR (KBr): 1667, 1619, 1592, 1487, 1453, 1364, 1323, 1073 cm\(^{-1}\); \(^1\)H NMR: \(\delta = 4.04\) (s, 2H), 4.09 (s, 2H), 4.63 (s, 2H), 4.72 (s, 2H), 7.14–7.22 (m, 2H), 7.27–7.44 (m, 10H), 7.45–7.58 (m, 4H), 7.69–7.78 (m, 1H), 7.87 (d, \(J = 8.1\) Hz, 1H), 8.49 (dd, \(J = 8.4, 1.1\) Hz, 1H); \(^1^3^C\) NMR: \(\delta = 64.5, 65.0, 72.6, 72.9, 113.4, 123.6, 126.1, 127.2, 127.8, 127.9, 128.15, 128.3, 128.4, 128.5, 129.00, 129.03, 132.7, 136.3, 137.0, 137.7, 138.3, 138.6, 162.7; HRMS (FAB\(^+\)): Calcd for C\(_{31}\)H\(_{28}\)NO\(_3\), M+H\(^+\) 462.2069. Found m/z 462.2066.

2-Phenyl-1(2H)-isoquinolone (3ad)

IR (KBr): 1661, 1624, 1588, 1293 cm\(^{-1}\); \(^1\)H NMR: \(\delta = 6.56\) (d, \(J = 7.5\) Hz, 1H), 7.18 (d, \(J = 7.8\) Hz, 1H), 7.36–7.59 (m, 7H), 7.63–7.71 (m, 1H), 8.45–8.51 (m, 1H); \(^1^3^C\) NMR: \(\delta = 106.1, 125.8, 126.4, 126.7, 127.0, 127.9, 128.1, 129.1, 132.0, 132.4, 136.9, 141.2, 161.8; HRMS (EI\(^+\)): Calcd for C\(_{15}\)H\(_{11}\)NO, M+ 221.0841. Found m/z 221.0844.

3-Methyl-4-isopropyl-2-phenyl-1(2H)-isoquinolone (3be)

IR (KBr): 2932, 1651, 1592, 1483, 1333, 1181 cm\(^{-1}\); \(^1\)H NMR: \(\delta = 1.49\) (d, \(J = 7.2\) Hz, 6H), 2.07 (s, 3H), 2.43 (s, 3H), 3.57 (sept, \(J = 7.2\) Hz, 1H), 7.08–7.15 (m, 2H), 7.28–7.34 (m, 2H), 7.35–7.42 (m, 1H), 7.62–7.70 (m, 1H), 7.95 (d, \(J = 8.4\) Hz, 1H) 8.48–8.54 (m, 1H); \(^1^3^C\) NMR: \(\delta = 18.8, 21.1, 21.6, 28.0, 118.8, 123.6, 125.3, 125.7, 128.1, 128.7, 130.1, 131.6, 135.3, 136.4, 137.4, 137.9, 162.7; HRMS (EI\(^+\)): Calcd for C\(_{20}\)H\(_{21}\)NO, M+ 291.1623. Found m/z 291.1625.

3-Methyl-4-tert-butyl-2-(4-methylphenyl)-1(2H)-isoquinolone (3bf)

IR (KBr): 1655, 1510, 1478 cm\(^{-1}\); \(^1\)H NMR: \(\delta = 1.63\) (s, 9H), 2.12 (s, 3H), 2.43 (s, 3H), 7.08–7.14 (m, 2H), 7.28–7.34 (m, 2H), 7.35–7.42 (m, 1H), 7.55–7.62 (m, 1H), 8.05 (d, \(J = 8.7\) Hz, 1H), 8.40–8.45 (m, 1H); \(^1^3^C\) NMR: \(\delta = 21.2, 23.2, 33.4, 36.3, 123.2, 124.8, 125.7, 125.8, 128.1, 128.3, 130.1, 130.2, 135.9, 137.2, 137.5, 138.0, 162.6; HRMS (EI\(^+\)): Calcd for C\(_{23}\)H\(_{32}\)NO, M+ 305.1780. Found m/z 305.1776.
Chapter 1

3-Methyl-4-trimethylsilyl-2-(4-methylphenyl)-1(2H)-isoquinolone (3bg)

IR (KBr): 1651, 1510, 1474, 1300, 1252 cm$^{-1}$; $^1$H NMR: $\delta = 0.48$ (s, 9H), 2.11 (s, 3H), 2.43 (s, 3H), 7.10 (d, $J = 7.8$ Hz, 2H), 7.13 (d, $J = 7.8$ Hz, 2H), 7.41 (t, $J = 7.5$ Hz, 1H), 7.61 (td, $J = 8.4, 1.4$ Hz, 1H), 7.84 (d, $J = 8.4$ Hz, 1H), 8.43 (dd, $J = 8.1, 1.8$ Hz, 1H); $^{13}$C NMR: $\delta = 14.8, 21.0, 23.4, 110.1, 125.2, 125.4, 126.5, 128.1, 128.4, 130.4, 131.4, 137.1, 138.1, 140.2, 145.2, 163.4; HRMS (EI$^+$): Calcd for C$_{20}$H$_{23}$NOSi, M$^+$ 321.1549. Found m/z 321.1548.

4-Methyl-3-phenyl-2-(4-methylphenyl)-1(2H)-isoquinolone (3bh)

IR (KBr): 1661, 1592, 1510, 1483, 1327 cm$^{-1}$; $^1$H NMR: $\delta = 2.11$ (s, 3H), 2.23 (s, 3H), 6.93 (d, $J = 8.4$ Hz, 2H), 7.01 (d, $J = 8.7$ Hz, 2H), 7.05–7.24 (m, 5H), 7.50–7.62 (m, 1H), 7.72–7.80 (m, 2H), 8.58 (d, $J = 7.8$ Hz, 1H); $^{13}$C NMR: $\delta = 14.8, 21.0, 110.1, 123.2, 125.6, 126.5, 127.67, 127.63, 128.4, 129.0, 129.1, 130.3, 132.4, 135.3, 136.90, 136.93, 137.4, 140.2, 162.4; HRMS (EI$^+$): Calcd for C$_{23}$H$_{19}$NO, M$^+$ 325.1467. Found m/z 325.1465.

4-Methyl-3-(4-trifluoromethylphenyl)-2-(4-methylphenyl)-1(2H)-isoquinolone (3bi)

IR (KBr): 1657, 1611, 1510, 1485, 1323, 1125, 1067 cm$^{-1}$; $^1$H NMR: $\delta = 2.08$ (s, 3H), 2.24 (s, 3H), 6.91 (d, $J = 8.1$ Hz, 2H), 7.01 (d, $J = 8.4$ Hz, 2H), 7.23 (d, $J = 8.4$ Hz, 2H), 7.47 (d, $J = 8.1$ Hz, 2H), 7.52–7.63 (m, 1H), 7.74–7.81 (m, 2H), 8.56 (d, $J = 8.1$ Hz, 1H); $^{13}$C NMR: $\delta = 14.8, 21.0, 110.5, 123.3, 123.7 (q, J = 270.3 Hz), 124.7 (q, $J = 3.5$ Hz), 125.8, 127.0, 128.5, 128.9, 129.4, 129.7 (q, $J = 32.3$ Hz), 130.9, 132.6, 136.5, 137.2, 137.5, 138.6, 139.1, 162.4; HRMS (EI$^+$): Calcd for C$_{24}$H$_{18}$F$_3$NO, M$^+$ 393.1340. Found m/z 393.1344.

4-Methyl-3-(4-methoxyphenyl)-2-(4-methylphenyl)-1(2H)-isoquinolone (3bj)

IR (KBr): 1655, 1613, 1510, 1483, 1327, 1244, 1032 cm$^{-1}$; $^1$H NMR: $\delta = 2.10$ (s, 3H), 2.24 (s, 3H), 3.74 (s, 3H), 6.71 (d, $J = 8.4$ Hz, 2H), 6.91 (d, $J = 8.1$ Hz, 2H), 6.94–7.05 (m, 4H), 7.48–7.59 (m, 1H), 7.70–7.78 (m, 2H), 8.52–8.58 (m, 1H); $^{13}$C NMR: $\delta = 14.9, 21.1, 55.0, 110.5, 113.1, 123.2, 125.7, 126.4, 127.7, 128.4, 128.9, 129.2, 131.6, 132.4, 136.9, 137.1, 137.5, 140.1, 158.6, 162.6; HRMS (EI$^+$): Calcd for C$_{24}$H$_{21}$NO$_2$, M$^+$ 355.1572. Found m/z 355.1566.
3-Ethoxycarbonyl-4-propyl-2-(4-methylphenyl)-1(2H)-isoquinolone (3bk)

IR (KBr): 2940, 1734, 1663, 1599, 1509, 1325, 1206, 1134, 1007 cm⁻¹; ¹H NMR: δ = 0.97 (t, J = 7.2 Hz, 3H), 1.02 (t, J = 7.5 Hz, 3H), 1.71 (sextet, J = 7.6 Hz, 2H), 2.38 (s, 3H), 2.62–2.73 (m, 2H), 3.93 (q, J = 7.1 Hz, 2H), 7.20–7.28 (m, 4H), 7.48–7.60 (m, 1H), 7.68–7.78 (m, 2H), 8.51 (d, J = 7.8 Hz, 1H); ¹³C NMR: δ = 13.4, 14.1, 21.1, 23.4, 30.0, 61.6, 114.9, 123.7, 126.5, 127.5, 128.2, 128.6, 129.4, 132.5, 133.5, 135.8, 138.4, 161.3, 163.3; HRMS (EI⁺): Calcd for C₃₂H₂₃NO₃, M⁺ 479.1678. Found m/z 479.1682.

4-Butyl-3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-2-(4-methylphenyl)-1(2H)-isoquinolone (3bl)

IR (KBr): 2953, 1653, 1510, 1455, 1375, 1331, 1213, 1144 cm⁻¹; ¹H NMR: δ = 0.97 (t, J = 7.4 Hz, 3H), 1.01 (s, 12H), 1.46 (sextet, J = 7.4 Hz, 2H), 1.59–1.72 (m, 2H), 2.39 (s, 3H), 2.68–2.77 (m, 2H), 7.26 (s, 4H), 7.46–7.54 (m, 1H), 7.65–7.73 (m, 2H), 8.45–8.51 (m, 1H); ¹³C NMR: δ = 14.0, 21.1, 23.1, 24.5, 29.9, 33.3, 84.4, 121.6, 123.0, 126.6, 126.8, 128.4, 128.7, 129.5, 132.0, 136.3, 138.3, 138.7, 162.2 (The boron-bound carbon was not detected due to the quadrupolar relaxation); HRMS (EI⁺): Calcd for C₃₂H₂₃NO₃B, M⁺ 417.2475. Found m/z 417.2476.

3-(4,4,5,5-Tetramethyl-1,3,2-dioxaborolan-2-yl)-4-trimethylsilyl-2-(4-methylphenyl)-1(2H)-isoquinolone (3bm)

IR (KBr): 1653, 1343, 1252, 1138 cm⁻¹; ¹H NMR: δ = 0.48 (s, 9H), 1.02 (s, 12H), 2.41 (s, 3H), 7.21–7.31 (m, 4H), 7.43–7.50 (m, 1H), 7.60–7.67 (m, 1H), 7.89 (d, J = 8.1 Hz, 1H), 8.46 (dd, J = 7.7, 1.4 Hz, 1H); ¹³C NMR: δ = 23.3, 21.2, 26.0, 84.8, 117.8, 126.3, 126.5, 127.1, 128.1, 129.6, 129.8, 131.2, 138.0, 138.7, 139.8, 162.8 (The boron-bound carbon was not detected due to the quadrupolar relaxation); HRMS (EI⁺): Calcd for C₃₅H₳₁NO₃B, M⁺ 533.2243. Found m/z 533.2245.

4-Hexyl-2-(4-methylphenyl)-1(2H)-isoquinolone (3bn)

IR (neat): 2929, 1661, 1634, 1605, 1512, 1487, 1460, 1329, 1294, 1210, 1028 cm⁻¹; ¹H NMR: δ = 0.85–0.95 (m, 3H), 1.25–1.49 (m, 6H), 1.67 (quint, J = 7.6 Hz, 2H), 2.42 (s, 3H), 2.64–2.73 (m, 2H), 7.00 (s, 1H), 7.27–7.36 (m, 4H), 7.47–7.58 (m, 1H), 7.66–7.76 (m, 2H), 8.51–8.57 (m, 1H); ¹³C NMR: δ = 14.1, 21.1, 22.6, 29.2, 29.38, 29.44, 31.6, 116.3, 122.8, 126.5, 126.6, 128.7, 129.68, 129.74, 132.2, 136.8, 137.7, 138.9, 161.7; HRMS (EI⁺): Calcd for C₂₅H₂₅NO, M⁺ 319.1936. Found m/z 319.1930.
Chapter 1

4-Cyclopentyl-2-(4-methylphenyl)-1(2H)-isoquinolone (3bo)

IR (KBr): 2951, 1655, 1628, 1605, 1483, 1294 cm\(^{-1}\); \(^1\)H NMR: \(\delta = 1.52–1.88\) (m, 6H), 2.06–2.20 (m, 2H), 2.43 (s, 3H), 3.32 (quint, \(J = 8.1\) Hz, 1H), 7.04 (s, 1H), 7.27–7.37 (m, 4H), 7.48–7.56 (m, 1H), 7.67–7.75 (m, 1H), 7.81 (d, \(J = 7.8\) Hz, 1H), 8.52–8.59 (m, 1H); \(^{13}\)C NMR: \(\delta = 21.1, 24.8, 32.2, 38.9, 119.4, 123.1, 126.4, 126.5, 126.6, 128.6, 129.7, 132.0, 137.1, 137.7, 139.1, 161.5\); HRMS (EI\(^+\)): Calcd for C\(_{21}\)H\(_{21}\)NO, M\(^+\) 303.1623. Found m/z 303.1623.

4-tert-Butyl-2-(4-methylphenyl)-1(2H)-isoquinolone (3bp)

IR (KBr): 2963, 1655, 1619, 1512, 1480, 1341, 1312 cm\(^{-1}\); \(^1\)H NMR: \(\delta = 1.51\) (s, 9H), 2.43 (s, 3H), 7.08 (s, 1H), 7.27–7.38 (m, 4H), 7.47–7.55 (m, 1H), 7.65–7.72 (m, 1H), 8.12 (d, \(J = 8.4\) Hz, 1H), 8.62 (dd, \(J = 7.8, 1.8\) Hz, 1H); \(^{13}\)C NMR: \(\delta = 21.1, 30.9, 33.8, 123.7, 125.7, 126.1, 126.5, 127.3, 128.8, 129.3, 129.8, 131.2, 136.1, 137.8, 139.2, 161.4\); HRMS (EI\(^+\)): Calcd for C\(_{20}\)H\(_{21}\)NO, M\(^+\) 291.1623. Found m/z 291.1625.

4-Trimethylsilyl-2-(4-methylphenyl)-1(2H)-isoquinolone (3bq)

IR (KBr): 1655, 1605, 1592, 1510, 1478, 1321, 1296, 1250 cm\(^{-1}\); \(^1\)H NMR: \(\delta = 0.40\) (s, 9H), 2.43 (s, 3H), 7.16 (s, 1H), 7.33 (s, 4H), 7.48–7.55 (m, 1H), 7.65–7.72 (m, 1H), 8.53–8.58 (m, 1H); \(^{13}\)C NMR: \(\delta = 0.3, 21.1, 112.6, 126.5, 126.6, 128.7, 129.8, 132.0, 137.7, 137.9, 138.9, 139.6, 162.2\); HRMS (EI\(^+\)): Calcd for C\(_{19}\)H\(_{21}\)NOSi, M\(^+\) 307.1392. Found m/z 307.1395.

4-Tributyltin-2-(4-methylphenyl)-1(2H)-isoquinolone (3br)

IR (neat): 2926, 1661, 1605, 1510, 1476, 1318, 1293, cm\(^{-1}\); \(^1\)H NMR: \(\delta = 0.89\) (t, \(J = 7.2\) Hz, 9H), 1.02–1.27 (m, 6H), 1.35 (sextet, \(J = 7.3\) Hz, 6H), 1.42–1.71 (m, 6H), 2.44 (s, 3H), 7.02 (s, 1H), 7.28–7.39 (m, 4H), 7.43–7.55 (m, 2H), 7.63–7.72 (m, 1H), 8.51–8.58 (m, 1H); \(^{13}\)C NMR: \(\delta = 10.1, 13.6, 21.1, 27.2, 29.0, 114.6, 126.5, 126.6, 127.1, 128.1, 128.6, 129.8, 132.2, 137.4, 137.7, 139.0, 141.8, 162.2\); HRMS (EI\(^+\)): Calcd for C\(_{28}\)H\(_{36}\)NOSn, M\(^+\) 525.2054. Found m/z 525.2053.
4-Phenyl-2-(4-methylphenyl)-1(2H)-isoquinolone (3bs)

IR (neat): 3060, 1667, 1628, 1601, 1329, 1271, 1030 cm\(^{-1}\); \(^1\)H NMR: \(\delta = 2.42\) (s, 3H), 7.18 (s, 1H), 7.30 (d, \(J = 8.7\) Hz, 2H), 7.37 (d, \(J = 8.1\) Hz, 2H), 7.40–7.69 (m, 8H), 8.56–8.61 (m, 1H); \(^1^3\)C NMR: \(\delta = 21.2, 119.5, 124.7, 126.3, 126.5, 127.1, 127.7, 128.6, 129.8, 129.9, 131.3, 132.3, 136.2, 136.4, 138.0, 138.7, 161.6\); HRMS (EI\(^{+}\)): Calcd for C\(_{22}\)H\(_{17}\)NO, M\(^+\) 311.1310. Found m/z 311.1310.

3-Phenyl-2-(4-methylphenyl)-1(2H)-isoquinolone (3bs’)

IR (KBr): 1649, 1622, 1512, 1482, 1383, 1277 cm\(^{-1}\); \(^1\)H NMR: \(\delta = 2.28\) (s, 3H), 6.59 (s, 1H), 7.01 (d, \(J = 8.4\) Hz, 2H), 7.07 (d, \(J = 8.7\) Hz, 2H), 7.15–7.23 (m, 5H), 7.47–7.54 (m, 1H), 7.55 (d, \(J = 7.8\) Hz, 1H), 7.64–7.72 (m, 1H), 8.45–8.50 (m, 1H); \(^1^3\)C NMR: \(\delta = 21.1, 107.7, 125.3, 125.9, 126.7, 127.7, 127.8, 128.3, 128.9, 129.17, 129.20, 132.6, 136.2, 136.3, 136.7, 137.3, 143.6, 163.1\); HRMS (EI\(^{+}\)): Calcd for C\(_{22}\)H\(_{17}\)NO, M\(^+\) 311.1310. Found m/z 311.1310.

**Procedure for the De-Silylation of 3bm.**

To a solution of 3bm (81.1 mg, 0.187 mmol) in CH\(_2\)Cl\(_2\) (3.7 mL) was added TFA (21 \(\mu\)L, 0.283 mmol). The mixture was stirred at room temperature for 4 hours, and then concentrated under reduced pressure. The residue was purified by preparative thin-layer chromatography (chloroform/ethyl acetate 10:1) to give the product 4bm (58.5 mg, 0.162 mmol, 87% yield) as a white solid.

3-(4,4,5,5-Tetramethyl-1,3,2-dioxaborolan-2-yl)-2-(4-methylphenyl)-1(2H)-isoquinolone (4bm)

IR (KBr): 2979, 1653, 1510, 1451, 1395, 1347, 1262, 1213, 1142 cm\(^{-1}\); \(^1\)H NMR: \(\delta = 1.07\) (s, 12H), 2.40 (s, 3H), 6.96 (s, 1H), 7.17–7.25 (m, 4H), 7.49–7.59 (m, 2H), 7.62–7.70 (m, 1H), 8.44 (d, \(J = 7.8\) Hz, 1H); \(^1^3\)C NMR: \(\delta = 21.1, 24.2, 84.3, 115.0, 126.2, 127.2, 127.75, 127.82, 128.0, 129.3, 132.2, 136.2, 137.6, 139.2, 162.6\) (The boron-bound carbon was not detected due to the quadrupolar relaxation); HRMS (EI\(^{+}\)): Calcd for C\(_{22}\)H\(_{24}\)BNO\(_3\), M\(^+\) 361.1849. Found m/z 361.1847.
Procedure for the Cross-Coupling Reaction of 4bm with Phenyl iodide.\textsuperscript{15c}

\begin{figure}
\centering
\includegraphics[width=0.5\textwidth]{reaction_diagram1}
\caption{Reaction scheme for the cross-coupling of 4bm with phenyl iodide.}
\end{figure}

To an oven-dried flask was added 4bm (46.7 mg, 0.129 mmol), a solution of Pd(dbac)\(_2\) (7.4 mg, 12.9 μmol) and P(t-Bu)\(_3\) (6.3 μL, 26 μmol) in THF (2.6 mL), phenyl iodide (16 μL, 0.144 mmol), and KOH aqueous solution (0.26 mL, 1.5 M solution, 0.39 mol) at room temperature. The reaction mixture was stirred at room temperature for 12 hours under an argon atmosphere, and then quenched with ammonium chloride, and extracted with ethyl acetate (5 x 10 mL). The combined extracts were washed with brine and dried over MgSO\(_4\). The solvent was removed under reduced pressure and the residue was purified by preparative thin-layer chromatography (chloroform/ethyl acetate 20:1) to give the product 3bs\(^*\) (37.1 mg, 0.119 mmol, 92% yield).

Procedure for the Cross-Coupling Reaction of 3br with Phenyl iodide.\textsuperscript{25}

\begin{figure}
\centering
\includegraphics[width=0.5\textwidth]{reaction_diagram2}
\caption{Reaction scheme for the cross-coupling of 3br with phenyl iodide.}
\end{figure}

To an oven-dried flask was added Pd(PPh\(_3\))\(_4\) (12.8 mg, 11.1 μmol), copper iodide (21.3 mg, 11.2 μmol), a solution of 3br (57.6 mg, 0.11 mmol) in DMF (2.2 mL), and phenyl iodide (25 μL, 0.224 mmol) at room temperature. The reaction mixture was stirred at 60 °C for 3 hours under an argon atmosphere, and then quenched with water, and extracted with ethyl acetate (5 x 10 mL). The combined extracts were washed with water (3 x 20 mL), brine and dried over MgSO\(_4\). The solvent was removed under reduced pressure and the residue was purified by preparative thin-layer chromatography (chloroform/ethyl acetate 20:1) to give the product 3bs (32.4 mg, 0.104 mmol, 95% yield).

Procedure for the Isolation of Azanickelacycle 6 (eq 2).

\begin{figure}
\centering
\includegraphics[width=0.5\textwidth]{reaction_diagram3}
\caption{Reaction scheme for the isolation of azanickelacycle 6.}
\end{figure}

In an N\(_2\)-filled glove-box, 1b (23.9 g, 0.10 mmol) and THF (2 mL) were charged into an oven-dried 4 mL-vial equipped with a stir bar. Then, a solution of Ni(cod)\(_2\) (27.3 mg, 0.10 mmol) and Dppbenz (45.1 mg, 0.10 mmol) in THF (2 mL) was added. After stirred at room temperature for 3 h, the resulting mixture was concentrated under reduced pressure. The residue was purified by recrystallization from CH\(_2\)Cl\(_2\)/hexane to give the azanickelacycle 6 as dark brown crystals (57.1 mg, 79 μmol, 79% yield). 6: IR (KBr): 1619, 1505, 1435, 1345, 1094 cm\(^{-1}\); \(^1\)H NMR (CD\(_2\)Cl\(_2\)): δ = 2.08 (s, 3H), 6.33–6.37 (m 2H), 6.58–6.65 (m, 3H), 6.82–6.86 (m 1H), 6.88–6.92 (m 1H), 7.01–7.05 (m 1H), 7.19–7.27 (m, 5H), 7.32–7.50 (m 15H), 7.82–7.88 (m 4H); \(^{13}\)C NMR (CD\(_2\)Cl\(_2\)): δ = 21.0, 124.7, 126.2
(dd, J = 3.8, 1.3 Hz), 128.4, 128.66 (d, J = 2.6 Hz), 128.67 (d, J = 10.1 Hz), 128.8, 129.2 (d, J = 10.4 Hz), 129.8 (dd, J = 37.6, 1.0 Hz), 130.4 (d, J = 2.6 Hz), 130.6 (dd, J = 46.1, 2.4 Hz), 131.4 (d, J = 2.6 Hz), 131.8 (dd, J = 5.6, 1.9 Hz), 132.1 (dd, J = 4.9, 2.0 Hz), 132.6, 132.9 (dd, J = 13.9, 1.3 Hz), 133.1 (dd, J = 13.1, 1.0 Hz), 133.9 (d, J = 12.0 Hz), 134.3 (d, J = 11.6 Hz), 138.0 (dd, J = 14.3, 2.6 Hz), 143.5 (dd, J = 44.9, 32.8 Hz), 143.9 (dd, J = 49.3, 40.7 Hz), 146.3 (d, J = 2.0 Hz), 149.9 (dd, J = 4.7, 1.6 Hz), 150.2 (dd, J = 74.9, 31.1 Hz), 180.9 (d, J = 6.5 Hz); \(^{31}\)P NMR (CD\(_2\)Cl\(_2\)): \(\delta = 39.9, 53.6;\) HRMS (FAB\(^{+}\)): Calcd for C\(_{44}\)H\(_{36}\)NNiO\(_2\), M+H\(^{+}\) 714.1626. Found m/z 714.1652.

**Stoichiometric Reaction of Azanickelacycle 6 with Dec-5-yne (2a) (eq 3).**

In an N\(_2\)-filled glove-box, azanickelacycle 6 (35.2 g, 49.3 \(\mu\)mol) was charged into an oven-dried 4 mL-vial equipped with a stir bar. Then, toluene (2 mL) and dec-5-yne (2a, 27 \(\mu\)L, 0.15 mmol) were added. The vial was capped with a Teflon film and the reaction mixture was taken outside the glove-box. After heated at 110 °C for 12 h, the reaction mixture was cooled to room temperature and stirred over 30 min in open air. The resulting mixture was passed through a pad of Florisil\(^{\circledR}\) with ethyl acetate and the solvent was concentrated under reduced pressure. The residue was purified by preparative thin-layer chromatography (hexane/ethyl acetate 5:1) to give products 3ba (17 mg, 49.2 \(\mu\)mol, 99% yield).

**Determination of Stereochemistries.**

Stereochemistries of the products were determined by single crystal X-ray analysis and nOe experiments are shown below with curved arrows that indicate the observed nOe.

**[Compound 3be, 3bf and 3bg]**

The following results suggested that the substituent group was bound to the C(4).

**[Compound 3bh, 3bi, and 3bj]**

The following results suggested that the aryl group was bound to the C(3).
[Compound 3bk]
The following results of 3bk and 3bk' (minor product) suggested that the ethoxycarbonyl group was bound to the C(3) in the major product.

[Compound 3bl and 3bm]
The following results suggested that the boryl group was bound to the C(3).

[Compound 3bn, 3bo, 3bp, 3bq, and 3br]
The following results suggested that the substituent group was bound to the C(4).

[Compound 3bs, 3bs’]
The following results suggested that the phenyl group was bound to the C(4) of 3bs and the C(3) of 3bs’.
Detail of the Single-Crystal X-ray Analysis
A single-crystal of 2 suitable for X-ray analysis was obtained from the reaction mixture (CH$_2$Cl$_2$/hexane). The single crystal was mounted on a glass fiber. All measurements were made on a Rigaku-RAXIS imaging plate area detector. Details of crystal and data collection parameters are shown in Table S1–S4.

Table S1. Crystal and Experimental Data

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Formula</td>
<td>C$<em>{44}$H$</em>{35}$NiOP$_2$</td>
</tr>
<tr>
<td>Fw</td>
<td>714.38</td>
</tr>
<tr>
<td>Crystal system</td>
<td>monoclinic</td>
</tr>
<tr>
<td>space group</td>
<td>p$_{21}$/n</td>
</tr>
<tr>
<td>a [Å]</td>
<td>12.3776(3)</td>
</tr>
<tr>
<td>b [Å]</td>
<td>14.4722(4)</td>
</tr>
<tr>
<td>c [Å]</td>
<td>19.9190(6)</td>
</tr>
<tr>
<td>α, deg</td>
<td>90.00</td>
</tr>
<tr>
<td>β, deg</td>
<td>92.9745(10)</td>
</tr>
<tr>
<td>γ, deg</td>
<td>90.00</td>
</tr>
<tr>
<td>V, [Å$^3$]</td>
<td>3563.30(17)</td>
</tr>
<tr>
<td>Z</td>
<td>4</td>
</tr>
<tr>
<td>dcalc, g/cm$^3$</td>
<td>1.332</td>
</tr>
<tr>
<td>m(Mo Ka), mm$^{-1}$</td>
<td>0.670</td>
</tr>
<tr>
<td>data/restraints/params</td>
<td>8134/0/443</td>
</tr>
<tr>
<td>R1</td>
<td>0.0295</td>
</tr>
<tr>
<td>wR2</td>
<td>0.0814</td>
</tr>
</tbody>
</table>

Table S2. Atomic Coordinates and Equivalent Isotropic Thermal Parameters

<table>
<thead>
<tr>
<th>atom</th>
<th>X</th>
<th>Y</th>
<th>Z</th>
<th>Ueq</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ni1</td>
<td>0.853839(14)</td>
<td>0.254820(12)</td>
<td>0.576260(8)</td>
<td>0.02926(6)</td>
</tr>
<tr>
<td>P2</td>
<td>0.74868(3)</td>
<td>0.28958(3)</td>
<td>0.660585(17)</td>
<td>0.02872(8)</td>
</tr>
<tr>
<td>P3</td>
<td>0.99004(3)</td>
<td>0.26819(3)</td>
<td>0.647075(18)</td>
<td>0.03008(8)</td>
</tr>
<tr>
<td>C4</td>
<td>0.94663(11)</td>
<td>0.30438(10)</td>
<td>0.72947(7)</td>
<td>0.0327(3)</td>
</tr>
<tr>
<td>C5</td>
<td>0.94626(13)</td>
<td>0.24761(10)</td>
<td>0.49955(7)</td>
<td>0.0345(3)</td>
</tr>
<tr>
<td>C6</td>
<td>0.83557(11)</td>
<td>0.30953(10)</td>
<td>0.73622(7)</td>
<td>0.0319(3)</td>
</tr>
<tr>
<td>C7</td>
<td>0.64734(11)</td>
<td>0.21163(10)</td>
<td>0.69199(7)</td>
<td>0.0319(3)</td>
</tr>
<tr>
<td>C8</td>
<td>0.68214(12)</td>
<td>0.40122(10)</td>
<td>0.64627(7)</td>
<td>0.0348(3)</td>
</tr>
<tr>
<td>N1</td>
<td>0.73917(10)</td>
<td>0.23601(9)</td>
<td>0.51009(6)</td>
<td>0.0361(3)</td>
</tr>
<tr>
<td>C10</td>
<td>0.105827(12)</td>
<td>0.157581(11)</td>
<td>0.66209(8)</td>
<td>0.0367(3)</td>
</tr>
<tr>
<td>C11</td>
<td>0.63122(12)</td>
<td>0.20756(11)</td>
<td>0.52169(7)</td>
<td>0.0349(3)</td>
</tr>
<tr>
<td>C54</td>
<td>0.76513(14)</td>
<td>0.23979(12)</td>
<td>0.44507(8)</td>
<td>0.0427(4)</td>
</tr>
<tr>
<td>C13</td>
<td>1.09116(13)</td>
<td>0.35577(11)</td>
<td>0.62961(7)</td>
<td>0.0373(3)</td>
</tr>
<tr>
<td>C14</td>
<td>0.79607(13)</td>
<td>0.32621(12)</td>
<td>0.79868(7)</td>
<td>0.0420(4)</td>
</tr>
<tr>
<td>H9</td>
<td>0.7219</td>
<td>0.3353</td>
<td>0.8038</td>
<td>0.050</td>
</tr>
<tr>
<td>C15</td>
<td>0.53654(12)</td>
<td>0.22642(12)</td>
<td>0.68445(7)</td>
<td>0.0369(3)</td>
</tr>
<tr>
<td>H10</td>
<td>0.5101</td>
<td>0.2797</td>
<td>0.6632</td>
<td>0.044</td>
</tr>
<tr>
<td>C16</td>
<td>0.88355(13)</td>
<td>0.24896(10)</td>
<td>0.43937(7)</td>
<td>0.0345(3)</td>
</tr>
<tr>
<td>C17</td>
<td>0.97736(14)</td>
<td>0.34775(12)</td>
<td>0.84569(8)</td>
<td>0.0449(4)</td>
</tr>
<tr>
<td>H11</td>
<td>1.0247</td>
<td>0.3606</td>
<td>0.8823</td>
<td>0.054</td>
</tr>
<tr>
<td>C18</td>
<td>0.51021(14)</td>
<td>0.08678(12)</td>
<td>0.55358(8)</td>
<td>0.0441(4)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>---</td>
<td>---</td>
<td>---</td>
<td>---</td>
<td>---</td>
</tr>
<tr>
<td>H1</td>
<td>0.5004</td>
<td>0.0269</td>
<td>0.5690</td>
<td>0.053</td>
</tr>
<tr>
<td>C19</td>
<td>1.01757(13)</td>
<td>0.32516(12)</td>
<td>0.78446(8)</td>
<td>0.0414(3)</td>
</tr>
<tr>
<td>H12</td>
<td>0.3797</td>
<td>0.2710</td>
<td>0.5105</td>
<td>0.055</td>
</tr>
<tr>
<td>C21</td>
<td>1.10354(16)</td>
<td>0.25195(14)</td>
<td>0.43097(9)</td>
<td>0.0541(5)</td>
</tr>
<tr>
<td>H4</td>
<td>0.6725</td>
<td>0.0794</td>
<td>0.5531</td>
<td>0.048</td>
</tr>
<tr>
<td>C23</td>
<td>0.86737(14)</td>
<td>0.35135(13)</td>
<td>0.85266(7)</td>
<td>0.0455(4)</td>
</tr>
<tr>
<td>H13</td>
<td>0.8408</td>
<td>0.3665</td>
<td>0.8941</td>
<td>0.055</td>
</tr>
<tr>
<td>O1</td>
<td>0.70150(11)</td>
<td>0.23331(14)</td>
<td>0.39561(6)</td>
<td>0.0783(5)</td>
</tr>
<tr>
<td>C25</td>
<td>1.13651(13)</td>
<td>0.14165(13)</td>
<td>0.71378(9)</td>
<td>0.0462(4)</td>
</tr>
<tr>
<td>H15</td>
<td>0.7583</td>
<td>0.1196</td>
<td>0.7287</td>
<td>0.055</td>
</tr>
<tr>
<td>C28</td>
<td>1.03888(16)</td>
<td>0.25715(13)</td>
<td>0.37284(9)</td>
<td>0.0491(4)</td>
</tr>
<tr>
<td>H5</td>
<td>1.0695</td>
<td>0.2623</td>
<td>0.3314</td>
<td>0.059</td>
</tr>
<tr>
<td>C29</td>
<td>0.92793(15)</td>
<td>0.25464(12)</td>
<td>0.37682(8)</td>
<td>0.0439(4)</td>
</tr>
<tr>
<td>H6</td>
<td>0.8831</td>
<td>0.2567</td>
<td>0.3379</td>
<td>0.053</td>
</tr>
<tr>
<td>C30</td>
<td>0.54262(13)</td>
<td>0.26491(12)</td>
<td>0.50965(8)</td>
<td>0.0421(4)</td>
</tr>
<tr>
<td>H7</td>
<td>0.5526</td>
<td>0.3254</td>
<td>0.4954</td>
<td>0.051</td>
</tr>
<tr>
<td>C31</td>
<td>1.05157(18)</td>
<td>0.43766(13)</td>
<td>0.60208(10)</td>
<td>0.0565(5)</td>
</tr>
<tr>
<td>H16</td>
<td>0.9774</td>
<td>0.4454</td>
<td>0.5943</td>
<td>0.068</td>
</tr>
<tr>
<td>C32</td>
<td>0.46511(13)</td>
<td>0.16191(13)</td>
<td>0.70853(8)</td>
<td>0.0463(4)</td>
</tr>
<tr>
<td>H17</td>
<td>0.3910</td>
<td>0.1723</td>
<td>0.7034</td>
<td>0.056</td>
</tr>
<tr>
<td>C34</td>
<td>1.02693(16)</td>
<td>0.08434(13)</td>
<td>0.62040(10)</td>
<td>0.0522(4)</td>
</tr>
<tr>
<td>H18</td>
<td>0.9742</td>
<td>0.0936</td>
<td>0.5861</td>
<td>0.063</td>
</tr>
<tr>
<td>C35</td>
<td>0.57212(17)</td>
<td>0.52878(14)</td>
<td>0.67984(11)</td>
<td>0.0601(5)</td>
</tr>
<tr>
<td>H19</td>
<td>0.5269</td>
<td>0.5550</td>
<td>0.7105</td>
<td>0.072</td>
</tr>
<tr>
<td>C36</td>
<td>1.05812(14)</td>
<td>0.24690(14)</td>
<td>0.49360(9)</td>
<td>0.0491(4)</td>
</tr>
<tr>
<td>H8</td>
<td>1.1034</td>
<td>0.2430</td>
<td>0.5322</td>
<td>0.059</td>
</tr>
<tr>
<td>C37</td>
<td>1.20196(14)</td>
<td>0.34561(14)</td>
<td>0.64072(10)</td>
<td>0.0516(4)</td>
</tr>
<tr>
<td>H20</td>
<td>1.2300</td>
<td>0.2910</td>
<td>0.6591</td>
<td>0.062</td>
</tr>
<tr>
<td>C38</td>
<td>0.70608(17)</td>
<td>0.45048(13)</td>
<td>0.58929(9)</td>
<td>0.0525(4)</td>
</tr>
<tr>
<td>H21</td>
<td>0.7508</td>
<td>0.4245</td>
<td>0.5583</td>
<td>0.063</td>
</tr>
<tr>
<td>C39</td>
<td>0.61428(14)</td>
<td>0.44147(13)</td>
<td>0.69161(9)</td>
<td>0.0476(4)</td>
</tr>
<tr>
<td>H22</td>
<td>0.5972</td>
<td>0.4094</td>
<td>0.7301</td>
<td>0.057</td>
</tr>
<tr>
<td>C40</td>
<td>0.50268(16)</td>
<td>0.08301(13)</td>
<td>0.73978(9)</td>
<td>0.0539(4)</td>
</tr>
<tr>
<td>H23</td>
<td>0.4543</td>
<td>0.0403</td>
<td>0.7560</td>
<td>0.065</td>
</tr>
<tr>
<td>C41</td>
<td>1.18279(15)</td>
<td>0.05441(15)</td>
<td>0.72160(11)</td>
<td>0.0615(5)</td>
</tr>
<tr>
<td>H24</td>
<td>1.2356</td>
<td>0.0443</td>
<td>0.7557</td>
<td>0.074</td>
</tr>
<tr>
<td>C42</td>
<td>0.61214(17)</td>
<td>0.06738(13)</td>
<td>0.74709(10)</td>
<td>0.0570(5)</td>
</tr>
<tr>
<td>H25</td>
<td>0.6378</td>
<td>0.0137</td>
<td>0.7681</td>
<td>0.068</td>
</tr>
<tr>
<td>C43</td>
<td>0.30834(18)</td>
<td>0.10619(18)</td>
<td>0.55043(10)</td>
<td>0.0639(6)</td>
</tr>
<tr>
<td>H33</td>
<td>0.3132</td>
<td>0.0463</td>
<td>0.5712</td>
<td>0.096</td>
</tr>
<tr>
<td>H34</td>
<td>0.2693</td>
<td>0.1014</td>
<td>0.5077</td>
<td>0.096</td>
</tr>
<tr>
<td>H35</td>
<td>0.2711</td>
<td>0.1478</td>
<td>0.5788</td>
<td>0.096</td>
</tr>
<tr>
<td>C44</td>
<td>0.6639(2)</td>
<td>0.53830(15)</td>
<td>0.57814(12)</td>
<td>0.0778(7)</td>
</tr>
<tr>
<td>H26</td>
<td>0.6812</td>
<td>0.5711</td>
<td>0.5400</td>
<td>0.093</td>
</tr>
<tr>
<td>C45</td>
<td>1.1214(2)</td>
<td>0.50814(15)</td>
<td>0.58603(12)</td>
<td>0.0751(7)</td>
</tr>
</tbody>
</table>
Table S3. Anisotropic Thermal Parameters

<table>
<thead>
<tr>
<th>atom</th>
<th>U11</th>
<th>U22</th>
<th>U33</th>
<th>U23</th>
<th>U13</th>
<th>U12</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ni1</td>
<td>0.02773(10)</td>
<td>0.03812(11)</td>
<td>0.02199(9)</td>
<td>-0.00200(7)</td>
<td>0.00178(7)</td>
<td>0.00342(7)</td>
</tr>
<tr>
<td>P2</td>
<td>0.02699(17)</td>
<td>0.03694(19)</td>
<td>0.02228(16)</td>
<td>-0.00127(13)</td>
<td>0.00183(12)</td>
<td>0.00242(14)</td>
</tr>
<tr>
<td>P3</td>
<td>0.02727(17)</td>
<td>0.03643(19)</td>
<td>0.02662(17)</td>
<td>0.00054(14)</td>
<td>0.00208(13)</td>
<td>0.00292(14)</td>
</tr>
<tr>
<td>C4</td>
<td>0.0335(7)</td>
<td>0.0388(8)</td>
<td>0.0256(6)</td>
<td>-0.0006(6)</td>
<td>0.0005(5)</td>
<td>0.0016(6)</td>
</tr>
<tr>
<td>C53</td>
<td>0.0372(8)</td>
<td>0.0390(8)</td>
<td>0.0277(7)</td>
<td>-0.0032(6)</td>
<td>0.0059(6)</td>
<td>0.0042(6)</td>
</tr>
<tr>
<td>C6</td>
<td>0.0384(7)</td>
<td>0.0391(7)</td>
<td>0.0233(6)</td>
<td>0.0060(5)</td>
<td>0.0095(5)</td>
<td>0.0025(6)</td>
</tr>
<tr>
<td>C7</td>
<td>0.0337(7)</td>
<td>0.0373(7)</td>
<td>0.0254(6)</td>
<td>-0.0034(5)</td>
<td>0.0042(5)</td>
<td>-0.0008(6)</td>
</tr>
<tr>
<td>C8</td>
<td>0.0352(7)</td>
<td>0.0362(7)</td>
<td>0.0325(7)</td>
<td>-0.0024(6)</td>
<td>-0.0017(6)</td>
<td>0.0030(6)</td>
</tr>
<tr>
<td>N1</td>
<td>0.0308(6)</td>
<td>0.0518(8)</td>
<td>0.0257(6)</td>
<td>-0.0032(5)</td>
<td>0.0006(5)</td>
<td>-0.0025(5)</td>
</tr>
<tr>
<td>C10</td>
<td>0.0316(7)</td>
<td>0.0383(8)</td>
<td>0.0410(8)</td>
<td>0.0086(6)</td>
<td>0.0086(6)</td>
<td>0.0035(6)</td>
</tr>
<tr>
<td>C11</td>
<td>0.0332(7)</td>
<td>0.0483(9)</td>
<td>0.0230(6)</td>
<td>-0.0057(6)</td>
<td>-0.0010(5)</td>
<td>-0.0012(6)</td>
</tr>
<tr>
<td>C54</td>
<td>0.0423(9)</td>
<td>0.0580(10)</td>
<td>0.0275(7)</td>
<td>-0.0018(7)</td>
<td>0.0002(6)</td>
<td>-0.0071(7)</td>
</tr>
<tr>
<td>C13</td>
<td>0.0422(8)</td>
<td>0.0382(8)</td>
<td>0.0318(7)</td>
<td>-0.0010(6)</td>
<td>0.0067(6)</td>
<td>-0.0027(6)</td>
</tr>
<tr>
<td>C14</td>
<td>0.0392(8)</td>
<td>0.0599(10)</td>
<td>0.0272(7)</td>
<td>-0.0023(7)</td>
<td>0.0050(6)</td>
<td>-0.0003(7)</td>
</tr>
<tr>
<td>C15</td>
<td>0.0339(7)</td>
<td>0.0498(9)</td>
<td>0.0268(7)</td>
<td>-0.0003(6)</td>
<td>0.0005(6)</td>
<td>-0.0011(6)</td>
</tr>
<tr>
<td>C16</td>
<td>0.0406(8)</td>
<td>0.0350(7)</td>
<td>0.0282(7)</td>
<td>-0.0011(5)</td>
<td>0.0052(6)</td>
<td>-0.0013(6)</td>
</tr>
<tr>
<td>C17</td>
<td>0.0500(9)</td>
<td>0.0542(10)</td>
<td>0.0293(7)</td>
<td>-0.0032(7)</td>
<td>-0.0092(6)</td>
<td>0.0015(8)</td>
</tr>
<tr>
<td>C18</td>
<td>0.0500(9)</td>
<td>0.0436(9)</td>
<td>0.0391(8)</td>
<td>-0.0072(7)</td>
<td>0.0059(7)</td>
<td>-0.0064(7)</td>
</tr>
<tr>
<td>C19</td>
<td>0.0344(7)</td>
<td>0.0543(10)</td>
<td>0.0349(8)</td>
<td>-0.0030(7)</td>
<td>-0.0053(6)</td>
<td>0.0033(7)</td>
</tr>
<tr>
<td>C20</td>
<td>0.0351(8)</td>
<td>0.0660(11)</td>
<td>0.0356(8)</td>
<td>0.0101(7)</td>
<td>-0.0021(6)</td>
<td>0.0087(7)</td>
</tr>
<tr>
<td>C21</td>
<td>0.0413(9)</td>
<td>0.0797(14)</td>
<td>0.0425(9)</td>
<td>-0.0045(8)</td>
<td>0.0150(7)</td>
<td>0.0051(9)</td>
</tr>
<tr>
<td>C22</td>
<td>0.0380(8)</td>
<td>0.0433(8)</td>
<td>0.0385(8)</td>
<td>-0.0062(6)</td>
<td>0.0007(6)</td>
<td>0.0042(7)</td>
</tr>
<tr>
<td>C23</td>
<td>0.0529(9)</td>
<td>0.0600(10)</td>
<td>0.0236(7)</td>
<td>-0.0034(7)</td>
<td>0.0014(6)</td>
<td>0.0012(8)</td>
</tr>
<tr>
<td>O1</td>
<td>0.0482(8)</td>
<td>0.1584(17)</td>
<td>0.0278(6)</td>
<td>-0.0014(8)</td>
<td>-0.0043(5)</td>
<td>-0.0243(9)</td>
</tr>
<tr>
<td>C25</td>
<td>0.0369(8)</td>
<td>0.0528(10)</td>
<td>0.0492(9)</td>
<td>0.0144(8)</td>
<td>0.0032(7)</td>
<td>0.0032(7)</td>
</tr>
<tr>
<td>C26</td>
<td>0.0370(8)</td>
<td>0.0653(11)</td>
<td>0.0292(7)</td>
<td>-0.0096(7)</td>
<td>0.0032(6)</td>
<td>-0.0051(7)</td>
</tr>
<tr>
<td>C27</td>
<td>0.0435(9)</td>
<td>0.0421(9)</td>
<td>0.0530(10)</td>
<td>0.0041(7)</td>
<td>0.0067(7)</td>
<td>0.0065(7)</td>
</tr>
<tr>
<td>C28</td>
<td>0.0541(10)</td>
<td>0.0597(11)</td>
<td>0.0350(8)</td>
<td>0.0031(7)</td>
<td>0.0180(8)</td>
<td>0.0034(8)</td>
</tr>
<tr>
<td>C29</td>
<td>0.0525(10)</td>
<td>0.0522(10)</td>
<td>0.0272(7)</td>
<td>0.0024(6)</td>
<td>0.0054(7)</td>
<td>-0.0001(7)</td>
</tr>
<tr>
<td>C30</td>
<td>0.0411(8)</td>
<td>0.0504(9)</td>
<td>0.0347(8)</td>
<td>0.0051(7)</td>
<td>-0.0014(6)</td>
<td>0.0027(7)</td>
</tr>
<tr>
<td>C31</td>
<td>0.0682(12)</td>
<td>0.0419(9)</td>
<td>0.0600(11)</td>
<td>0.0060(8)</td>
<td>0.0080(9)</td>
<td>0.0034(9)</td>
</tr>
<tr>
<td>C32</td>
<td>0.0380(8)</td>
<td>0.0647(11)</td>
<td>0.0366(8)</td>
<td>-0.0051(7)</td>
<td>0.0056(6)</td>
<td>-0.0097(8)</td>
</tr>
<tr>
<td>C34</td>
<td>0.0555(10)</td>
<td>0.0424(9)</td>
<td>0.0583(11)</td>
<td>0.0004(8)</td>
<td>0.0008(8)</td>
<td>0.0051(8)</td>
</tr>
<tr>
<td>C35</td>
<td>0.0596(11)</td>
<td>0.0543(11)</td>
<td>0.0661(12)</td>
<td>-0.0160(10)</td>
<td>0.0014(9)</td>
<td>0.0204(9)</td>
</tr>
<tr>
<td>C36</td>
<td>0.0379(9)</td>
<td>0.0766(13)</td>
<td>0.0331(8)</td>
<td>-0.0075(8)</td>
<td>0.0054(7)</td>
<td>0.0078(6)</td>
</tr>
<tr>
<td>C37</td>
<td>0.0428(9)</td>
<td>0.0542(10)</td>
<td>0.0578(11)</td>
<td>0.0054(8)</td>
<td>0.0038(8)</td>
<td>-0.0085(8)</td>
</tr>
</tbody>
</table>
Table S4. Interatomic Distances (Å) and Angles (deg)

| Ni1-N1 | 1.9057(12) | Ni1-C53 | 1.9584(15) |
| Ni1-P3 | 2.1500(4)  | Ni1-P2  | 2.2350(4)  |
| P2-C7  | 1.8218(15) | P2-C6   | 1.8280(14) |
| P2-C8  | 1.8291(15) | P3-C10  | 1.8273(15) |
| P3-C13 | 1.8274(16) | P3-C4   | 1.8298(14) |
| C4-C6  | 1.390(2)   | C4-C19  | 1.400(2)   |
| C53-C16| 1.394(2)   | C53-C36 | 1.396(2)   |
| C6-C14 | 1.4006(19) | C7-C15  | 1.388(2)   |
| C7-C27 | 1.393(2)   | C8-C38  | 1.385(2)   |
| C8-C39 | 1.393(2)   | N1-C54  | 1.352(2)   |
| N1-C11 | 1.4284(19) | C10-C34 | 1.389(2)   |
| C10-C25| 1.396(2)   | C11-C30 | 1.386(2)   |
| C11-C22| 1.386(2)   | C54-O1  | 1.233(2)   |
| C54-C16| 1.482(2)   | C13-C31 | 1.385(2)   |
| C13-C37| 1.386(2)   | C14-C23 | 1.382(2)   |
| C15-C32| 1.388(2)   | C16-C29 | 1.390(2)   |
| C17-C23| 1.377(2)   | C17-C19 | 1.380(2)   |
| C18-C26| 1.382(2)   | C18-C22 | 1.383(2)   |
| C20-C26| 1.384(3)   | C20-C30 | 1.395(2)   |
| C21-C28| 1.375(3)   | C21-C36 | 1.397(2)   |
| C25-C41| 1.392(3)   | C26-C43 | 1.513(2)   |
| C27-C42| 1.381(3)   | C28-C29 | 1.380(3)   |
| C31-C45| 1.385(3)   | C32-C40 | 1.370(3)   |
| C34-C52| 1.389(3)   | C35-C49 | 1.371(3)   |
| C35-C39| 1.382(3)   | C37-C51 | 1.391(3)   |
| C38-C44| 1.388(3)   | C40-C42 | 1.374(3)   |
| C41-C48| 1.373(3)   | C44-C49 | 1.379(3)   |
| C45-C46| 1.377(4)   | C46-C51 | 1.363(4)   |
| C48-C52| 1.369(3)   |

| N1-Ni1-C53 | 84.09(6) | N1-Ni1-P3 | 175.66(4) |
| C53-Ni-P3  | 92.68(5) | N1-Ni1-P2  | 96.32(4)  |
| C53-Ni-P2  | 170.00(5) | P3-Ni1-P2  | 87.368(14) |
| C7-P2-C6   | 101.59(6) | C7-P2-C8   | 106.74(7) |
| C6-P2-C8   | 103.29(7) | C7-P2-Ni1  | 123.84(5) |
| C6-P2-Ni1  | 108.32(5) | C8-P2-Ni1  | 110.90(5) |
Chapter 1

C10-P3-C13 108.87(7)  C10-P3-C4 104.99(7)
C13-P3-C4 102.01(7)  C10-P3-Ni1 111.63(5)
C13-P3-Ni1 117.32(5)  C4-P3-Ni1 110.95(5)
C6-C4-C19 119.73(13)  C6-C4-P3 116.10(10)
C19-C4-P3 124.17(11)  C16-C53-C36 115.94(14)
C16-C53-Ni1 110.39(11)  C36-C53-Ni1 133.54(12)
C4-C6-C14 119.42(13)  C4-C6-P2 117.02(10)
C14-C6-P2 123.51(11)  C15-C7-C27 118.57(14)
C15-C7-P2 124.14(12)  C27-C7-P2 117.26(12)
C38-C8-C39 118.55(15)  C38-C8-P2 117.94(12)
C39-C8-P2 123.38(12)  C54-N1-C11 115.95(12)
C54-N1-Ni1 116.83(11)  C11-N1-Ni1 126.78(9)
C34-C10-C25 118.46(15)  C34-C10-P3 117.27(12)
C25-C10-P3 124.23(13)  C30-C11-C22 118.55(15)
C30-C11-N1 122.53(15)  C22-C11-N1 118.90(14)
O1-C54-Ni1 126.08(16)  O1-C54-C16 122.62(15)
N1-C54-C16 112.24(13)  N1-C13-C37 118.76(16)
C31-C13-P3 115.92(13)  C37-C13-P3 125.31(13)
C23-C14-C6 119.97(15)  C32-C15-C7 120.14(15)
C29-C16-C53 122.91(15)  C29-C16-C54 120.83(14)
C53-C16-C54 116.21(13)  C23-C17-C19 120.12(14)
C26-C18-C22 121.21(16)  C17-C19-C4 120.12(15)
C26-C20-C30 121.42(16)  C28-C21-C36 120.75(17)
C18-C22-C11 120.86(15)  C17-C23-C14 120.60(14)
C41-C25-C10 119.88(18)  C18-C26-C20 117.90(15)
C18-C26-C43 120.32(18)  C20-C26-C43 121.77(17)
C42-C27-C7 120.49(16)  C21-C28-C29 119.18(15)
C28-C29-C16 119.59(16)  C11-C30-C20 120.03(16)
C13-C31-C45 120.6(2)  C40-C32-C15 120.68(16)
C10-C34-C52 120.89(19)  C49-C35-C39 120.53(18)
C53-C36-C21 121.51(16)  C13-C37-C51 120.10(19)
C8-C38-C44 120.52(18)  C35-C39-C8 120.49(18)
C32-C40-C42 119.67(17)  C48-C41-C25 120.74(19)
C40-C42-C27 120.45(18)  C49-C44-C38 120.2(2)
C46-C45-C31 120.0(2)  C51-C46-C45 119.9(2)
C52-C48-C41 119.9(2)  C35-C49-C44 119.66(19)
C46-C51-C37 120.6(2)  C48-C52-C34 120.1(2)

Symmetry Operations:
(1) x, y, z
(2) -x+1/2, y+1/2, -z+1/2
(3) -x, -y, -z
(4) x-1/2, -y-1/2, z-1/2
Chapter 1

References and Notes


(3) For a review, see: Glushkov, V. A.; Shklyaev, Y. V. Chem. Heterocycl. Comp. 2001, 37, 663.


(7) (a) Clark, A. S.; Deans, B.; Stevens, M. F. G.; Tisdale, M. J.; Wheelhouse, R. T.; Denny, B. J.; Hartley, J. A. J. Med. Chem. 1995, 38, 1493. (b) We developed a facile route to 1 from NH-1,2,3-benzotriazin-4(3H)-one which was commercially available. For details of the Ullmann-type coupling reaction with aryl halides, see the Experimental Section.


(9) See the Experimental Section for details.

For a preceding example of alkyne insertion into a related seven-membered ring nickelacycle intermediate, see: Korivi, R. P.; Cheng, C.-H. *Org. Lett.* **2005**, 7, 5179. The authors assumed that a carbon–carbon triple bond can insert into both carbon–nickel and nitrogen–nickel linkages depending on alkynes. The regiochemistry observed in the present reaction using ethyl hex-2-ynoate (2k) suggests that a carbon–nickel linkage react with 2k. In the reaction of other alkynes such as terminal alkynes, however, insertion into a nitrogen–nickel linkage cannot be ruled out.

The benzotriazinone 1j was recovered.

Although a similar regiochemical preference was explained by assuming stabilization of a partial negative charge on the carbon α to nickel in reference 9b, the effect of the aryl substituent observed with the present reaction is inconsistent with this explanation. Further studies including a theoretical one are necessary for elucidation of the mechanistic and regiochemical issue.

The major undesired process under the standard conditions using PMe₃ was self-oligomerization of 2k.


Representative results (regioisomers ratio) with other phosphine ligands: PMe₂Ph (75:25), PMePh₂ (87:13), P(n-Bu)₃ (85:15), DPPPen (92:8), DPEphos (88:12), XANTPHOS (93:7).

The reaction of 1-phenylprop-1-yn using dpff in place of PMe₃ as the ligand required heating at 80 °C in toluene, giving inferior regioselectivity of 65:35.


Chapter 2

Nickel-Catalyzed Denitrogenative Allene Insertion Reactions of 1,2,3-Benzotriazin-4(3H)-ones with Allenes

Abstract

A denitrogenative anulation reaction of 1,2,3-benzotriazin-4(3H)-ones with allenes catalyzed by a nickel/phosphine complex, to produce a variety of substituted 3,4-dihydroquinolin-1(2H)-ones in a regioselective manner, is described. A highly enantioselective version, as well as structural evidence for the mechanistic course of this reaction, is also presented.
Introduction

Transition metal-catalyzed annihilation reactions continue to provide many powerful synthetic methodologies for the construction of heterocyclic compounds. Heterometalacyclic complexes often act as key intermediates, which subsequently incorporate unsaturated compounds through insertion and reductive elimination to construct heterocyclic skeletons. It has been reported that heterocyclic compounds such as triazoles, phthalimides, and isatoic anhydrides can be exploited as the precursory platform to generate heterometalacyclic intermediates through oxidative addition to a low-valent transition metal and subsequent extrusion of gaseous molecules like dinitrogen, carbon monoxide, and carbon dioxide. In chapter 1, the author developed a nickel-catalyzed denitrogenative annulation of 1,2,3-benzotriazin-4(3H)-ones with alkynes. A five-membered azanickelacycle was postulated as the intermediate. In chapter 2, the author reports on stoichiometric reactions of azanickelacycle intermediate with allenes, which is successfully extended to a catalytic asymmetric denitrogenative annulation of 1,2,3-benzotriazin-4(3H)-ones.

Results and Discussions

First, the author examined a stoichiometric allene insertion of azanickelacycle, which was prepared from N-Tolyl-1,2,3-benzotriazin-4(3H)-one (1a), Ni(cod)$_2$, and 1,2-bis(diphenylphosphino)-benzene (eq 1). The five-membered cyclic structure of 2 was unambiguously determined by single crystal X-ray analysis. Presumably, oxidative insertion of nickel(0) into the N–N(tolyl) bond of 1a and subsequent retro-insertion of dinitrogen furnished 2.

![Chemical Structure of 1a and 2](image)

When nona-1,2-diene (3a, 3 equiv) was reacted with 2 in THF at 60 °C, an isomeric mixture of 3,4-dihyroisoquinolin-1(2H)-ones 4aa and 5aa was obtained in a ratio of 54:46 (93% total yield, eq 2). The allene functionality was successfully incorporated into the precursory skeleton.
The possibility of developing a catalytic reaction incorporating allenes was then pursued. When a mixture of 1a and 3a (1.5 equiv) in THF was heated at 60 °C for 3 h in the presence of a nickel catalyst (5 mol %) prepared from Ni(cod)$_2$ and PMe$_3$ (Ni:P = 1:4), the products 4aa and 5aa were obtained (94%, 4aa:5aa = 94:6, Scheme 1). Other ligands such as PCy$_3$, Pr-Bu$_3$, PPh$_3$, and Dppbenz gave inferior results.

**Scheme 1**

A possible mechanism is shown in Scheme 1. The reaction is initiated by oxidative addition to a nickel(0) into N–N linkage and subsequent extrusion of a molecular dinitrogen, giving azanickelacycle A. The following insertion of nona-1,2-diene (3a) leads to the π-allyl nickel intermediate B or B'. Finally, reductive elimination affords the products 4aa and 5aa. The product 4aa resulted in preference to 5aa due to the electronic reason.

Under the conditions using PMe$_3$ as the ligand, a wide variety of aryl substituents on the nitrogen atom afforded the corresponding 3,4-dihyroisoquinolin-1(2H)-ones 4ba–4ea in yields ranging from 76% to 94% with high regioselectivities, suggesting less steric and
electronic impact of the aryl group (R$_1$) (Table 1, entries 1–4). The 4-methoxyphenyl group of 4ca was readily removed on treatment with CAN.$^7$ Benzotriazinones 1f and 1g having electron-donating and -withdrawing ring substituents also participated in the reaction (entries 5 and 6).

Table 1. Ni(0)-Catalyzed Annulation of N-Aryl-1,2,3-benzotriazin-4(3H)-ones 1 with Nona-1,2-diene (3a)$^a$

| entry | 1 | R$_1$ | R$_2$ | R$_3$ | 4 | 5 | yield (%)$^b$
|-------|---|-----|-----|-----|---|---|----------------
| 1     | 1b | Ph  | H   | H   | 4ba | 5ba | 90 (91:9)$^c$
| 2     | 1c | 4-MeOC$_6$H$_4$ | H | H | 4ca | 5ca | 76 (94:6)$^d$
| 3     | 1d | 4-CIC$_6$H$_4$ | H | H | 4da | 5da | 82 (93:7)$^{c,h}$
| 4     | 1e | 2-MeOC$_6$H$_4$ | H | H | 4ea | 5ea | 94 (95:5)$^{j,i}$
| 5     | 1f | Ph  | MeO | MeO | 4fa | 5fa | 79 (95:5)$^{j,h,i}$
| 6     | 1g | Ph  | H   | CO$_2$Me | 4ga | 5ga | 88 (85:15)$^g$

$^a$ Conditions: 1 (0.2 mmol), 2a (0.3 mmol), Ni(cod)$_2$ (5 mol %), PMe$_3$ (20 mol %) in THF (2 mL) at 60 °C for 3–16 h. $^b$ Combined yield of isomers. Numbers in parentheses describe the ratio of 4:5. $^c$ Z:E = 78:22. $^d$ Z:E = 83:17. $^e$ Z:E = 86:14. $^f$ Z:E = >95:5. $^g$ Z:E = 80:20. $^h$ Dioxane (2 mL) at 80 °C. $^i$ Ni(cod)$_2$ (10 mol %), PMe$_3$ (40 mol %).

Terminal allenes having a variety of R substituents were subjected to the annulation reaction of 1a. The regioselectivity was significantly affected by the sterics of the R substituent (Table 2). As with simple nona-1,2-diene (3a), functionalized allenes 3b–3e having one primary substituent exhibited good regio-selectivity to give the corresponding 3,4-dihydropseudoquinolin-1(2H)-ones 4ab–4ae in good yields (entries 1–4). On the other hand, cyclohexylpropa-1,2-diene (3f) afforded a mixture of regioisomers 4af and 5af in a 55:45 ratio (entry 5).$^h$ The allene 3g bearing a tert-butyl group gave the insertion products in favor of 5ag (4ag:5ag = 18:82, entry 6) and complete regioselectivity for 5 was observed with trialkylsilyl-substituted allene 3h (entry 7). Whereas reductive elimination at the more substituted carbon is preferred by electronic reasons, the steric bulk of tert-butyl and trialkylsilyl groups favors reductive elimination at the less substituted carbon.
Table 2. Ni(0)-Catalyzed Annulation of N-Toryl-1,2,3-benzotriazin-4(3H)-one (1a) with Allenes 3a

<table>
<thead>
<tr>
<th>entry</th>
<th>3</th>
<th>R</th>
<th>4</th>
<th>5</th>
<th>yield (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>3b</td>
<td>(CH$_2$)$_2$OBn</td>
<td>4ab</td>
<td>5ab</td>
<td>91 (94:6)$^{ae}$</td>
</tr>
<tr>
<td>2</td>
<td>3c</td>
<td>(CH$_2$)$_2$OSi-Bu$_2$Me$_2$</td>
<td>4ac</td>
<td>5ac</td>
<td>81 (93:7)$^c$</td>
</tr>
<tr>
<td>3</td>
<td>3d</td>
<td>(CH$_2$)$_2$OH</td>
<td>4ad</td>
<td>5ad</td>
<td>76 (91:9)$^d$</td>
</tr>
<tr>
<td>4</td>
<td>3e</td>
<td>(CH$_2$)$_2$CN</td>
<td>4ae</td>
<td>5ae</td>
<td>95 (92:8)$^c$</td>
</tr>
<tr>
<td>5</td>
<td>3f</td>
<td>c-Hex</td>
<td>4af</td>
<td>5af</td>
<td>89 (55:45)$^{ef}$</td>
</tr>
<tr>
<td>6</td>
<td>3g</td>
<td>t-Bu</td>
<td>4ag</td>
<td>5ag</td>
<td>99 (18:82)$^f$</td>
</tr>
<tr>
<td>7</td>
<td>3h</td>
<td>Si-BuMe$_2$</td>
<td>4ah</td>
<td>5ah</td>
<td>82 (0:100)$^c$</td>
</tr>
</tbody>
</table>

$^a$ The reaction conditions are the same as those in Table 1. $^b$ Total yield of isomers. Numbers in parentheses describe the ratio of 4:5. $^c$ Z:E = >95:5. $^d$ Z:E = 67:23. $^e$ Dioxane (2 mL) at 80 °C. $^f$ Ni(cod)$_2$ (10 mol %), PMe$_3$ (40 mol %).

The use of 1,3-disubstituted allenes was also examined. To our surprise, the product outcome varied with the ligand employed (eq 3). Thus, whereas the use of PMe$_3$ furnished the imino ester 6ai in 75% yield, bidentate phosphine ligand (R,R)-Me-DuPhos afforded 4ai as a sole product in 99% yield at 100 °C.$^{10,11}$

Next, the catalytic reaction was extended to an asymmetric version, and various chiral ligands were examined using 1a and 3a (Table 3). Whereas bidentate phosphine ligands such as (R,R)-Me-DuPhos and (S,S,R,R)-TangPhos exhibited reasonable enantioselectivities, the regioselectivities were poor (entries 1 and 2). Regio- and enantioselectivities both became
acceptable when the phosphino-oxazoline ligand \((S,S)-i\text{-Pr-FOXAP}\) was employed (entry 3). Lowering the reaction temperature to 60 °C led to the best result (94%, 90% ee, \(4\text{aa}:5\text{aa} = 98:2\), entry 4). The asymmetric process worked well with a sterically and electronically diverse array of the \(N\)-aryl substituents (entries 5–11). The reaction tolerated the presence of a variety of functional groups (entries 12–19).

**Table 3.** Ni(0)-Catalyzed Enantioselective Annulation of \(N\)-Aryl-1,2,3-benzotriazin-4(3\(H\))-one (1\(a\)) with Allenes 3\(^a\)

<table>
<thead>
<tr>
<th>entry</th>
<th>1</th>
<th>3</th>
<th>chiral ligand</th>
<th>(T (°C))</th>
<th>4</th>
<th>yield (%)(^b)</th>
<th>ee (%)(^c)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>1(a)</td>
<td>3(a)</td>
<td>Me-DuPhos</td>
<td>80</td>
<td>4(aa)</td>
<td>95 (83:17)</td>
<td>78</td>
</tr>
<tr>
<td>2</td>
<td>1(a)</td>
<td>3(a)</td>
<td>TangPhos</td>
<td>80</td>
<td>4(aa)</td>
<td>96 (66:34)</td>
<td>91</td>
</tr>
<tr>
<td>3</td>
<td>1(a)</td>
<td>3(a)</td>
<td>(i)-Pr-FOXAP</td>
<td>80</td>
<td>4(aa)</td>
<td>99 (97:3)</td>
<td>87</td>
</tr>
<tr>
<td>4</td>
<td>1(a)</td>
<td>3(a)</td>
<td>(i)-Pr-FOXAP</td>
<td>60</td>
<td>4(aa)</td>
<td>94 (98:2)</td>
<td>90</td>
</tr>
<tr>
<td>5</td>
<td>1(b)</td>
<td>3(a)</td>
<td>(i)-Pr-FOXAP</td>
<td>60</td>
<td>4(ba)</td>
<td>99 (97:3)</td>
<td>91</td>
</tr>
<tr>
<td>6</td>
<td>1(c)</td>
<td>3(a)</td>
<td>(i)-Pr-FOXAP</td>
<td>60</td>
<td>4(ca)</td>
<td>99 (96:4)</td>
<td>92</td>
</tr>
<tr>
<td>7</td>
<td>1(d)</td>
<td>3(a)</td>
<td>(i)-Pr-FOXAP</td>
<td>60</td>
<td>4(da)</td>
<td>94 (95:5)</td>
<td>93</td>
</tr>
<tr>
<td>8</td>
<td>1(e)</td>
<td>3(a)</td>
<td>(i)-Pr-FOXAP</td>
<td>60</td>
<td>4(ea)</td>
<td>98 (98:2)</td>
<td>91(^d)</td>
</tr>
<tr>
<td>9</td>
<td>1(f)</td>
<td>3(a)</td>
<td>(i)-Pr-FOXAP</td>
<td>60</td>
<td>4(fa)</td>
<td>99 (94:6)</td>
<td>92(^d)</td>
</tr>
<tr>
<td>10</td>
<td>1(g)</td>
<td>3(a)</td>
<td>(i)-Pr-FOXAP</td>
<td>60</td>
<td>4(ga)</td>
<td>95 (95:5)</td>
<td>97</td>
</tr>
<tr>
<td>11</td>
<td>1(h) ((R(_1), R(_2), R(_3) = 4-CF(_3)C(_6)H(_4), H, H))</td>
<td>3(a)</td>
<td>(i)-Pr-FOXAP</td>
<td>60</td>
<td>4(ha)</td>
<td>92 (93:7)</td>
<td>93</td>
</tr>
<tr>
<td>12</td>
<td>1(i) ((R(_1), R(_2), R(_3) = CONPh(_2), H, H))</td>
<td>3(a)</td>
<td>(i)-Pr-FOXAP</td>
<td>40</td>
<td>4(ia)</td>
<td>81 (99:1)</td>
<td>95(^e)</td>
</tr>
<tr>
<td>13</td>
<td>1(a)</td>
<td>3(a)</td>
<td>(i)-Pr-FOXAP</td>
<td>60</td>
<td>4(ja)</td>
<td>95 (98:2)</td>
<td>96</td>
</tr>
<tr>
<td>14</td>
<td>1(a)</td>
<td>3(b)</td>
<td>(i)-Pr-FOXAP</td>
<td>60</td>
<td>4(ab)</td>
<td>98 (94:6)</td>
<td>91</td>
</tr>
<tr>
<td>15</td>
<td>1(a)</td>
<td>3(c)</td>
<td>(i)-Pr-FOXAP</td>
<td>60</td>
<td>4(ac)</td>
<td>92 (95:5)</td>
<td>91</td>
</tr>
<tr>
<td>16</td>
<td>1(a)</td>
<td>3(d)</td>
<td>(i)-Pr-FOXAP</td>
<td>60</td>
<td>4(ad)</td>
<td>91 (92:8)</td>
<td>97</td>
</tr>
<tr>
<td>17</td>
<td>1(a)</td>
<td>3(e)</td>
<td>(i)-Pr-FOXAP</td>
<td>60</td>
<td>4(ae)</td>
<td>99 (94:6)</td>
<td>93(^d)</td>
</tr>
<tr>
<td>18</td>
<td>1(a)</td>
<td>3(f)</td>
<td>(i)-Pr-FOXAP</td>
<td>60</td>
<td>4(af)</td>
<td>76 (73:27)</td>
<td>96</td>
</tr>
<tr>
<td>19</td>
<td>1(a)</td>
<td>3(j) ((R = (\text{CH}_2)_2N(\text{Phth})))</td>
<td>(i)-Pr-FOXAP</td>
<td>60</td>
<td>4(aj)</td>
<td>99 (96:4)</td>
<td>97</td>
</tr>
</tbody>
</table>

\(^a\) Conditions: 1 (0.2 mmol), 3 (0.3 mmol), Ni(cod)_2 (10 mol %), chiral ligand (20 mol %) in THF (2 mL) for 12 h. \(^b\) Total yield of isomers. Numbers in parentheses describe the ratio of 4:5. \(^c\) Determined by HPLC analysis using chiral column. \(^d\) CH\(_3\)CN was used. \(^e\) Ni(cod)_2 (20 mol %).
Conclusions

In summary, a denitrogenative annulation reaction of 1,2,3-benzotriazin-4(3H)-ones with allenes provides a unique method for the regio- and enantioselective synthesis of substituted 3,4-dihydroisoquinolin-1(2H)-ones, which are found in a wide variety of plant alkaloids and bioactive compounds.\textsuperscript{13}
Experimental Section

**General Methods.** All reactions were carried out under a nitrogen atmosphere unless otherwise noted. Infrared spectra were recorded on a Shimadzu FTIR-8100 spectrometer. $^1$H and $^{13}$C NMR spectra were recorded on a Varian Gemini 2000 ($^1$H at 300 MHz and $^{13}$C at 75 MHz) spectrometer using CDCl$_3$ ($^1$H, $\delta = 7.26$) and CDC$_3$ ($^{13}$C, $\delta = 77.0$) as an internal standard unless otherwise noted. High-resolution mass spectra were recorded on a JEOL JMS-SX102A (EI) or a JEOL JMS-HX110A (FAB) spectrometer. HPLC analysis was performed by 4.6 x 250 mm column. Flash column chromatography was performed with silica gel 60 N (Kanto). Preparative thin-layer chromatography was performed on silica gel plates with PF$_{254}$ indicator (Merck).

**Materials.** THF, 1,4-dioxane, and toluene were distilled from sodium/benzophenone ketyl. Anhydrous DMSO (Wako) was purchased from the commercial sources. Anhydrous CH$_3$CN (Wako) was purchased from the commercial sources and degassed by ultrasound before use. Ni(cod)$_2$ (Kanto) was obtained from the commercial sources and purified by recrystallization from toluene before use. NH$_2$-1,2,3-Benzotriazine-4(3H)-one (TCI), 2-isobutyrylcyclohexanone (Aldrich), trimethylphosphine (Strem), (-)-1,2-bis[(2R,5R)-2,5-dimethylphospholano]benzene ((R,R)-Me-DuPhos, Strem), (1S,1'S,2R,2'R)-1',1''-di-tert-butyl-(2,2'')-diphenolphosphate ((S,S)-TangPhos, Strem), (S,S)-[2-(4'-isopropylxazolin-2'-yl)ferroceny]-diphenylphosphine ((S,S)-i-Pr-FOXAP, Wako), and 1,2-bis(diphenylphosphinopheno)benzene (Wako) were used as received from the commercial sources. N-Aryl-1,2,3-benzotriazin-4(3H)-ones 1a–1h and 1j were prepared according to the literature procedure. N-(N'N'-Diphenylearbamoyl)-1,2,3-benzotriazin-4(3H)-one (II) was prepared according to the literature procedure. Nona-1,2,diene (3a), 1-benzyloxy-penta-3,4-diene (3b), 1-(tert-butyl-dimethylsiloxy)-penta-3,4-diene (3c), 1-hydroxy-penta-3,4-diene (3d), 1-cyanohexan-5,6-diene (3e), cyclohexylpropa-1,2-diene (3f), tert-butylpropa-1,2-diene (3g), tert-butyldimethylsilylpropa-1,2-diene (3h), and cyclonona-1,2-diene (3i) were prepared according to the literature procedures.

**General Procedure for the Synthesis of N-Aryl-1,2,3-benzotriazin-4(3H)-ones from Methyl Anthranilate.**

![Chemical Reaction](image)

To a solution of methyl anthranilate (3.07 g, 20.3 mmol) in 2M HCl (32 mL) was slowly added a solution of NaNO$_2$ (1.62 g, 23.5 mmol) in water (11 mL) at 0 °C. The reaction mixture was stirred at 0 °C for 30 min. A solution of NaOAc (6.33 g, 77.2 mmol) in water (25 mL) was slowly added at 0 °C, and then p-toluidine (3.26 g, 30.4 mmol) was added in one step. The resulting mixture was stirred at 0 °C for 3 h. The precipitate was collected by filtration, washed with cold water (50 mL), and purified by recrystallization from ethanol to give the triazene as a yellow solid. Then, the triazene was boiled in ethanol (220 mL) for 3 h (monitored by TLC). The reaction mixture was cooled to −30 °C. The precipitate was collected by filtration and washed with cold ethanol (50 mL) to give 1a as a white solid (3.74 g, 15.8 mmol, 78 % yield (two steps)).
General Procedure for the Synthesis of N-Aryl-1,2,3-benzotriazin-4(3H)-ones from NH-1,2,3-benzotriazin-4(3H)-one.\textsuperscript{21}

In an N\textsubscript{2}-filled glove-box, to an oven-dried 4 mL-vial equipped with a stir bar was added NH-1,2,3-benzotriazine-4(3H)-one (29.7 mg, 0.20 mmol), K\textsubscript{2}CO\textsubscript{3} (55.3 mg, 0.40 mmol), p-iodotoluene (65.4 mg, 0.30 mmol), Cul (3.8 mg, 20 µmol), 2-isobutyrylcyclohexanone (6.7 µL, 40 µmol), and DMSO (1 mL) at room temperature. The vial capped with a Teflon film was taken outside the glove-box, to an oven-dried 4 mL-vial equipped with a stir bar was added 1H NMR: δ = 0.80 (t, J = 6.9 Hz, 3H), 0.99–1.28 (m, 8H), 1.48–1.62 (m, 1H), 1.70–1.84 (m, 1H), 2.39 (s, 3H), 4.31 (dd, J = 10.2, 3.9 Hz, 1H), 5.23 (s, 1H), 5.63 (s, 1H), 7.20–7.30 (m, 4H), 7.42–7.60 (m, 3H), 8.16–8.20 (m, 1H); \textsuperscript{13}C NMR: δ = 13.9, 21.1, 22.4, 25.7, 28.7, 31.5, 33.8, 67.1, 112.8, 123.9, 127.3, 127.8, 128.5, 128.7, 129.7, 132.2, 135.1, 136.7, 139.1, 140.3, 162.6; HRMS (EI\textsuperscript{+}): Calcd for C\textsubscript{23}H\textsubscript{25}NO, M\textsuperscript{+} 333.2093. Found m/z 333.2094.
General Procedure for Nickel-Catalyzed Denitrogenative Annulation of 1,2,3-Benzotriazin-4(3H)-ones with Allenes Using PMe$_3$ as the Ligand (Scheme 1, Table 1, and Table 2). To an oven-dried flask was added 1a (47.3 mg, 0.20 mmol), a solution of Ni(cod)$_2$ (2.8 mg, 10 µmol) and PMe$_3$ (4.1 µL, 40 µmol) in THF (2 mL), and nona-1,2-diene (3a, 37.3 mg, 0.30 mmol). After heated at 60 °C for 3 h, the reaction mixture was cooled to room temperature and stirred over 30 min in open air. The resulting mixture was passed through a pad of Florisil with ethyl acetate and the solvent was concentrated under reduced pressure. The residue was purified by preparative thin-layer chromatography (hexane/ethyl acetate 5:1) to give the products 4aa and 5aa (62.7 mg, 0.19 mmol, 94% total yield, 4aa:5aa = 94:6).

3-Hexyl-4-methylene-2-phenyl-3,4-dihydroisoquinolin-1(2H)-one (4ba)

IR (neat): 2930, 1657, 1464, 1404 cm$^{-1}$; $^1$H NMR: $\delta = 0.81$ (t, $J = 6.6$ Hz, 3H), 0.98–1.28 (m, 8H), 1.50–1.66 (m, 1H), 1.72–1.86 (m, 1H), 4.37 (dd, $J = 10.2$, 3.9 Hz, 1H), 5.24 (s, 1H), 5.64 (s, 1H), 7.28–7.61 (m, 8H), 8.17–8.23 (m, 1H); $^{13}$C NMR: $\delta = 13.9$, 22.4, 25.6, 28.6, 31.5, 33.8, 67.0, 112.9, 123.9, 126.9, 127.5, 127.7, 128.5, 128.7, 129.0, 132.2, 135.0, 140.1, 141.6, 162.5; HRMS (EI$^+$): Calcd for C$_{22}$H$_{25}$NO, M$^+$ 319.1936. Found m/z 319.1937.

3-Hexyl-2-(4-methoxyphenyl)-4-methylene-3,4-dihydroisoquinolin-1(2H)-one (4ca)

IR (neat): 2928, 1655, 1510, 1464, 1248 cm$^{-1}$; $^1$H NMR: $\delta = 0.80$ (t, $J = 6.6$ Hz, 3H), 1.00–1.27 (m, 8H), 1.48–1.62 (m, 1H), 1.70–1.83 (m, 1H), 3.83 (s, 3H), 4.28 (dd, $J = 9.6$, 3.9 Hz, 1H), 5.22 (s, 1H), 5.62 (s, 1H), 6.93–7.00 (m, 2H), 7.26–7.33 (m, 2H), 7.42–7.59 (m, 3H), 8.15–8.19 (m, 1H); $^{13}$C NMR: $\delta = 14.0$, 22.5, 25.7, 28.7, 31.6, 33.7, 55.5, 67.3, 112.9, 114.4, 123.9, 127.8, 128.5, 128.7, 128.8, 132.2, 134.5, 135.1, 140.3, 158.3, 162.8; HRMS (EI$^+$): Calcd for C$_{23}$H$_{27}$NO$_2$, M$^+$ 349.2042. Found m/z 349.2046.

2-(4-Chlorophenyl)-3-hexyl-4-methylene-3,4-dihydroisoquinolin-1(2H)-one (4da)

IR (neat): 2930, 1655, 1493, 1464, 1399, 1283 cm$^{-1}$; $^1$H NMR: $\delta = 0.81$ (t, $J = 6.3$ Hz, 3H), 1.00–1.27 (m, 8H), 1.48–1.63 (m, 1H), 1.67–1.80 (m, 1H), 4.32 (dd, $J = 10.2$, 4.2 Hz, 1H), 5.25 (s, 1H), 5.64 (s, 1H), 7.31–7.61 (m, 7H), 8.14–8.20 (m, 1H); $^{13}$C NMR: $\delta = 14.0$, 22.4, 25.7, 28.6, 31.5, 33.8, 67.0, 113.2, 124.0, 127.5, 128.5, 128.8, 129.0, 129.2, 132.4, 132.5, 135.0, 139.9, 140.1, 162.6; HRMS (EI$^+$): Calcd for C$_{22}$H$_{23}$ClNO, M$^+$ 353.1546. Found m/z 353.1547.
3-Hexyl-2-(2-methoxyphenyl)-4-methylene-3,4-dihydroisoquinolin-1(2H)-one (4ea)

IR (neat): 2930, 1657, 1501, 1466, 1267 cm\(^{-1}\); \(^1\)H NMR: \(\delta = 0.81\) (t, \(J = 6.6\) Hz, 3H), 0.98–1.32 (m, 8H), 1.50–1.65 (m, 1H), 1.66–1.80 (m, 1H), 3.82 (s, 3H), 4.23 (dd, \(J = 9.6, 3.9\) Hz, 1H), 5.21 (s, 1H), 5.62 (s, 1H), 7.00–7.07 (m, 2H), 7.29–7.61 (m, 5H), 8.15–8.21 (m, 1H); \(^{13}\)C NMR (150 MHz): \(\delta = 13.9, 22.4, 25.6, 28.8, 31.6, 33.9, 55.8, 65.6, 112.6, 112.7, 120.8, 123.8, 128.2, 128.52, 128.53, 128.8, 130.1, 132.1, 135.6, 140.8, 155.1, 162.5; HRMS (EI\(^+\)): Calcd for C\(_{23}\)H\(_{27}\)NO\(_2\), M\(^+\) 349.2042. Found m/z 349.2040.

3-Hexyl-6,7-dimethoxy-4-methylene-2-phenyl-3,4-dihydroisoquinolin-1(2H)-one (4fa)

IR (neat): 2930, 1651, 1599, 1507, 1266 cm\(^{-1}\); \(^1\)H NMR: \(\delta = 0.80\) (t, \(J = 6.6\) Hz, 3H), 0.99–1.30 (m, 8H), 1.52–1.67 (m, 1H), 1.68–1.81 (m, 1H), 3.96 (s, 3H), 3.99 (s, 3H), 4.33 (dd, \(J = 9.6, 4.2\) Hz, 1H), 5.15 (s, 1H), 5.53 (s, 1H), 6.99 (s, 1H), 7.26–7.47 (m, 5H), 7.66 (s, 1H); \(^{13}\)C NMR: \(\delta = 14.0, 22.5, 25.7, 28.7, 31.6, 33.9, 56.0, 56.1, 67.1, 105.7, 110.3, 111.2, 120.9, 126.8, 127.6, 128.9, 129.0, 140.2, 141.7, 149.6, 152.4, 162.5; HRMS (EI\(^+\)): Calcd for C\(_{25}\)H\(_{29}\)NO\(_2\), M\(^+\) 379.2147. Found m/z 379.2148.

3-Hexyl-6-methoxycarbonyl-4-methylene-2-phenyl-3,4-dihydroisoquinolin-1(2H)-one (4fa)

IR (neat): 2923, 1727, 1659, 1441, 1267, 1252 cm\(^{-1}\); \(^1\)H NMR: \(\delta = 0.79\) (t, \(J = 6.9\) Hz, 3H), 0.99–1.25 (m, 8H), 1.44–1.60 (m, 1H), 1.72–1.85 (m, 1H), 3.97 (s, 3H), 4.38 (dd, \(J = 10.2, 3.9\) Hz, 1H), 5.32 (s, 1H), 5.75 (s, 1H), 7.30–7.51 (m, 5H), 8.06–8.13 (m, 1H), 8.22–8.29 (m, 2H); \(^{13}\)C NMR: \(\delta = 14.0, 22.5, 25.7, 28.7, 31.6, 33.9, 52.5, 67.1, 114.3, 125.6, 127.2, 127.5, 128.9, 129.2, 129.4, 131.3, 133.4, 135.3, 139.3, 141.4, 161.8, 166.3; HRMS (EI\(^+\)): Calcd for C\(_{25}\)H\(_{27}\)NO\(_2\), M\(^+\) 377.1991. Found m/z 377.1994.

3-(2-Benzzyloxyethyl)-4-methylene-2-(4-methylphenyl)-3,4-dihydroisoquinolin-1(2H)-one (4ab)

IR (neat): 1659, 1651, 1603, 1512, 1464, 1429, 1404 cm\(^{-1}\); \(^1\)H NMR: \(\delta = 1.74–1.87\) (m, 1H), 2.18–2.30 (m, 1H), 2.40 (s, 3H), 3.40 (dd, \(J = 7.2, 4.5\) Hz, 2H), 4.28 (d, \(J = 11.4\) Hz, 1H), 4.33 (d, \(J = 12\) Hz, 1H), 4.70 (dd, \(J = 9.6, 4.2\) Hz, 1H), 5.25 (s, 1H), 5.64 (s, 1H), 7.18–7.37 (m, 9H), 7.43–7.60 (m, 3H), 8.19–8.24 (m, 1H); \(^{13}\)C NMR: \(\delta = 21.0, 33.7, 63.6, 65.9, 72.8, 113.1, 123.9, 127.0, 127.5, 127.6, 127.8, 128.2, 128.6, 128.7, 129.6, 132.2, 134.8, 136.6, 137.9, 138.9, 139.6, 162.6; HRMS (EI\(^+\)): Calcd for C\(_{36}\)H\(_{32}\)NO\(_2\), M\(^+\) 383.1885. Found m/z 383.1881.

55
3-(2-tert-Butyldimethylsilyloxyethyl)-4-methylene-2-(4-methylphenyl)-3,4-dihydroisoquinolin-1(2H)-one (4ac)

IR (neat): 2928, 1659, 1514, 1464, 1256 cm\(^{-1}\); \(^{1}H\) NMR: \(\delta = -0.10\) (s, 3H), –0.03 (s, 3H), 0.81 (s, 9H), 1.63–1.75 (m, 1H), 2.03–2.16 (m, 1H), 2.37 (s, 3H), 3.45–3.56 (m, 2H), 4.70 (dd, \(J = 10.2, 3.6\) Hz, 1H), 5.30 (s, 1H), 5.66 (s, 1H), 7.20–7.36 (m, 4H), 7.42–7.60 (m, 3H), 8.17–8.22 (m, 1H); \(^{13}C\) NMR (100 MHz): \(\delta = -5.63, -5.60, 18.0, 21.0, 25.7, 36.3, 58.6, 63.2, 113.1, 124.0, 126.6, 128.0, 128.6, 128.7, 129.6, 132.2, 134.9, 136.4, 139.0, 139.7, 162.7; \)HRMS (EI\(^{+}\)): Calcd for C\(_{25}\)H\(_{33}\)NO\(_2\)Si, M\(^{+}\) 407.2281. Found m/z 407.2281.

3-(2-Hydroxyethyl)-4-methylene-2-(4-methylphenyl)-3,4-dihydroisoquinolin-1(2H)-one (4ad)

IR (KBr): 3450, 2874, 1655, 1638, 1601, 1512, 1466, 1279 cm\(^{-1}\); \(^{1}H\) NMR: \(\delta = 1.31–1.39\) (br s, 1H), 1.69–1.82 (m, 1H), 2.02–2.16 (m, 1H), 2.37 (s, 3H), 3.43–3.62 (m, 2H), 4.64 (dd, \(J = 10.2, 4.2\) Hz, 1H), 5.33 (s, 1H), 5.67 (s, 1H), 7.19–7.31 (m, 4H), 7.42–7.49 (m, 1H), 7.50–7.59 (m, 2H), 8.14–8.19 (m, 1H); \(^{13}C\) NMR: \(\delta = 21.0, 36.0, 58.4, 63.5, 113.4, 123.9, 127.1, 127.6, 128.5, 128.8, 129.7, 132.3, 134.8, 136.7, 138.7, 139.5, 162.8; \)HRMS (EI\(^{+}\)): Calcd for C\(_{19}\)H\(_{19}\)NO, M\(^{+}\) 293.1416. Found m/z 293.1419.

3-(3-Cyanopropyl)-4-methylene-2-(4-methylphenyl)-3,4-dihydroisoquinolin-1(2H)-one (4ae)

IR (neat): 2921, 2245, 1651, 1512 cm\(^{-1}\); \(^{1}H\) NMR: \(\delta = 1.36–1.97\) (m, 4H), 2.19 (t, \(J = 6.9\) Hz, 2H), 2.38 (s, 3H), 4.39 (dd, \(J = 9.0, 3.9\) Hz, 1H), 5.26 (s, 1H), 5.67 (s, 1H), 7.21–7.28 (m, 4H), 7.43–7.59 (m, 3H), 8.14–8.20 (m, 1H); \(^{13}C\) NMR: \(\delta = 16.8, 21.1, 21.9, 33.1, 66.2, 113.5, 118.9, 123.8, 127.3, 127.6, 128.7, 129.1, 129.9, 132.5, 134.5, 137.2, 138.7, 139.7, 162.4; \)HRMS (EI\(^{+}\)): Calcd for C\(_{20}\)H\(_{20}\)N\(_2\)O, M\(^{+}\) 316.1576. Found m/z 316.1581.

3-Cyclohexyl-4-methylene-2-(4-methylphenyl)-3,4-dihydroisoquinolin-1(2H)-one (3af)

IR (KBr): 2923, 1647, 1638, 1512, 1466, 1304 cm\(^{-1}\); \(^{1}H\) NMR: \(\delta = 0.43–0.59\) (m, 1H), 0.86–1.18 (m, 4H), 1.46–1.74 (m, 6H), 2.39 (s, 3H), 4.30 (d, \(J = 5.4\) Hz, 1H), 5.18 (s, 1H), 5.67 (s, 1H), 7.21–7.30 (m, 4H), 7.39–7.46 (m, 1H), 7.47–7.57 (m, 2H), 8.13–8.18 (m, 1H); \(^{13}C\) NMR (150 MHz): \(\delta = 21.1, 26.00, 26.03, 26.2, 28.3, 29.8, 41.8, 71.7, 114.1, 123.1, 127.6, 128.2, 128.4, 128.6, 129.7, 132.2, 136.5, 136.7, 138.7, 139.7, 163.1; \)HRMS (EI\(^{+}\)): Calcd for C\(_{25}\)H\(_{25}\)NO, M\(^{+}\) 331.1936. Found m/z 331.1937.
(Z)-4-Cyclohexylmethylen-2-(4-methylphenyl)-3,4-dihydroisoquinolin-1(2H)-one (Z)-5af

\[
\begin{align*}
&\text{IR (KBr): } 2924, 1655, 1509, 1298 \text{ cm}^{-1}; \quad ^1\text{H NMR: } \delta = 1.12–1.34 \text{ (m, 6H), } 1.60–1.80 \text{ (m, 4H), } \\
&2.22–2.38 \text{ (m, 1H), } 2.39 \text{ (s, 3H)}, 4.60 \text{ (d, } J = 1.8 \text{ Hz, 2H)}, 5.98 \text{ (dt, } J = 11.4, 1.8 \text{ Hz, 1H)}, 7.23–7.32 \text{ (m, 4H), } 7.34–7.58 \text{ (m, 3H), } 8.16–8.21 \text{ (m, 1H)}; \quad ^{13}\text{C NMR: } \delta = 21.1, 25.7, 25.8, 33.0, 37.2, 50.6, 122.6, \\
&125.6, 126.1, 127.7, 127.8, 128.7, 129.7, 132.1, 134.6, 136.5, 137.5, 140.3, 163.6; \quad \text{HRMS (EI)}: \text{ Calcd for } \text{C}_{23}\text{H}_{25}\text{NO, M}^+ 331.1936. \text{ Found m/z 331.1946.}
\end{align*}
\]

(Z)-4-tert-Butylmethylene-2-(4-methylphenyl)-3,4-dihydroisoquinolin-1(2H)-one (Z)-5ag

\[
\begin{align*}
&\text{IR (KBr): } 2957, 1659, 1509, 1293 \text{ cm}^{-1}; \quad ^1\text{H NMR: } \delta = 1.22 \text{ (s, 9H), } 2.38 \text{ (s, 3H), } 4.68–4.72 \text{ (m, 2H), } \\
&6.12–6.15 \text{ (m, 1H), } 7.20–7.30 \text{ (m, 4H), } 7.34–7.43 \text{ (m, 1H), } 7.45–7.52 \text{ (m, 2H), } 8.13–8.19 \text{ (m, 1H)}; \quad ^{13}\text{C NMR: } \delta = 21.1, 31.3, 32.9, 50.8, 123.1, 125.7, 127.7, 127.8, 128.1, 128.5, 129.8, 132.1, 136.5, 139.0, \\
&140.1, 140.3, 163.7; \quad \text{HRMS (EI)}: \text{ Calcd for } \text{C}_{21}\text{H}_{23}\text{NO, M}^+ 305.1780. \text{ Found m/z 305.1785.}
\end{align*}
\]

(Z)-4-tert-Butyldimethylsilylmethylene-2-(4-methylphenyl)-3,4-dihydroisoquinolin-1(2H)-one (Z)-5ag

\[
\begin{align*}
&\text{IR (KBr): } 1655, 1514, 1466, 1298 \text{ cm}^{-1}; \quad ^1\text{H NMR (C}_6\text{D}_6): \delta = 0.02 \text{ (s, 6H), } 0.84 \text{ (s, 9H), } 2.07 \text{ (s, 3H), } \\
&4.41 \text{ (s, 2H), } 6.15 \text{ (s, 1H), } 6.94–7.40 \text{ (m, 7H), } 8.55–8.62 \text{ (m, 1H)}; \quad ^{13}\text{C NMR (C}_6\text{D}_6): \delta = -4.1, 17.4, \\
&21.0, 26.5, 54.9, 123.6, 125.5, 125.6, 129.1, 129.2, 129.3, 129.7, 132.0, 135.7, 138.6, 141.0, 146.4, \\
&162.8; \quad \text{HRMS (EI)}: \text{ Calcd for } \text{C}_{23}\text{H}_{29}\text{NOSi, M}^+ 363.2018. \text{ Found m/z 363.2020.}
\end{align*}
\]

(Z)-6-(4-Methylphenyl)-6,6a,7,8,9,10,11,12-octahydro-cyclonona[c]isoquinolin-5(5H)-one (4ai)

\[
\begin{align*}
&\text{IR (KBr): } 2917, 1651, 1642, 1426, 1273 \text{ cm}^{-1}; \quad ^1\text{H NMR: } \delta = 1.19–1.98 \text{ (m, 10H), } 2.14–2.29 \text{ (m, 1H), } \\
&2.39 \text{ (s, 3H), } 2.44–2.58 \text{ (m, 1H), } 4.98 \text{ (dd, } J = 11.1, 4.5 \text{ Hz, 1H), } 6.38 \text{ (dd, } J = 9.6, 8.4 \text{ Hz, 1H), } \\
&7.22–7.32 \text{ (m, 4H), } 7.36–7.62 \text{ (m, 3H), } 8.14–8.20 \text{ (m, 1H)}; \quad ^{13}\text{C NMR: } \delta = 21.1, 22.7, 25.7, 26.3, 27.57, \\
&27.63, 33.0, 60.8, 123.2, 127.1, 127.6, 127.8, 128.5, 128.6, 129.8, 132.1, 135.9, 136.7, 139.7, 162.8; \quad \text{HRMS (EI)}: \text{ Calcd for } \text{C}_{23}\text{H}_{25}\text{NO, M}^+ 331.1936. \text{ Found m/z 331.1940.}
\end{align*}
\]
**N-((Z)-7,8,9,10,11,12-Hexahydrocyclonona[c]isochromen-5(6aH)-ylidene)-4-methylaniline (6ai)**

The imino ester 6ai was obtained as a single stereoisomer, whereas the stereochemistry was not determined. IR (KBr): 2924, 1646, 1634, 1599, 1505 cm\(^{-1}\); \(^1\)H NMR: \(\delta = 1.20-1.99\) (m, 10H), 2.12–2.29 (m, 1H), 2.39 (s, 3H), 2.42–2.54 (m, 1H), 5.54 (dd, \(J = 11.1, 5.4\) Hz, 1H), 6.45 (t, \(J = 9.0\) Hz, 1H), 7.04–7.23 (m, 4H), 7.36–7.64 (m, 3H), 8.33–8.39 (m, 1H); \(^13\)C NMR: \(\delta = 20.9, 22.8, 25.7, 26.6, 27.3, 27.5, 33.1, 75.7, 122.3, 123.1, 126.0, 127.7, 127.9, 128.0, 131.0, 131.3, 132.4, 133.5, 144.9, 151.3; HRMS (EI\(^{}\)): Calcd for C\(_{23}\)H\(_{25}\)NO, M\(^{+}\) 331.1936. Found m/z 331.1937.

**Hydrolysis of the Imino Ester 6ai.**

To confirm the structure, we attempted hydrolysis of the imino ester 6ai with an acid catalyst. To a flask was added 6ai (50.8 mg, 0.151 mmol) and AcOH/\(\text{H}_2\text{O}\) (3.0/0.3 mL). The reaction mixture was stirred at 60 °C. After 10 h, the reaction mixture was cooled to room temperature and concentrated under reduced pressure. The residue was purified by preparative thin-layer chromatography (hexane/ethyl acetate 10:1) to give the lactam 7 (33.8 mg, 0.139 mmol, 92% yield).

**General Procedure for Nickel-Catalyzed Denitrogenative Annulation of 1,2,3-Benzotriazin-4(3H)-ones with Allenes Using (S,S)-i-Pr-FOXAP as the Ligand (Table 3).** In an N\(_2\)-filled glove-box, 1a (47.6 mg, 0.20 mmol) was charged into an oven-dried 4 mL-vial equipped with a stir bar. Then, a solution of Ni(cod)\(_2\) (5.6 mg, 20 \(\mu\)mol) and (S,S)-i-Pr-FOXAP (19.1 mg, 40 \(\mu\)mol) in THF (2 mL) and nona-1,2-diene (3a, 37.2 mg, 0.30 mmol) was added. The vial was capped with a Teflon film and the reaction mixture was taken outside the glove-box. After heated at 60 °C for 12 h, the reaction mixture was cooled to room temperature and stirred over 30 min in open air. The resulting mixture was passed through a pad of Florisil\(^{}\) with ethyl acetate and the solvent was
concentrated under reduced pressure. The residue was purified by preparative thin-layer chromatography (hexane/ethyl acetate 5:1) to give products **4aa** and **5aa** (62.9 mg, 0.19 mmol, 94% total yield, **4aa**: **5aa** = 98:2).

**4aa**: \([\alpha]_D^{26.4} = +65.3 \, (c = 1.05, \text{ CHCl}_3, 89\% \, \text{ee})\); HPLC (Daicel Chiralcel OJ-H, hexane/i-PrOH = 85/15, flow rate = 0.6 mL/min, \(\lambda = 254 \, \text{nm})\): \(t_1 = 12.4 \, \text{min}, \, t_2 = 14.7 \, \text{min}\).

**4ba**: \([\alpha]_D^{26.5} = +127.0 \, (c = 1.68, \text{ CHCl}_3, 93\% \, \text{ee})\); HPLC (Daicel Chiralcel OJ-H, hexane/i-PrOH = 85/15, flow rate = 0.6 mL/min, \(\lambda = 254 \, \text{nm})\): \(t_1 = 17.0 \, \text{min}, \, t_2 = 20.5 \, \text{min}\).

**4ca**: \([\alpha]_D^{26.5} = +105.6 \, (c = 1.01, \text{ CHCl}_3, 92\% \, \text{ee})\); HPLC (Daicel Chiralcel OJ-H, hexane/i-PrOH = 85/15, flow rate = 0.6 mL/min, \(\lambda = 254 \, \text{nm})\): \(t_1 = 15.3 \, \text{min}, \, t_2 = 24.2 \, \text{min}\).

**4da**: \([\alpha]_D^{24.8} = +127.0 \, (c = 0.98, \text{ CHCl}_3, 93\% \, \text{ee})\); HPLC (Daicel Chiralcel OJ-H, hexane/i-PrOH = 85/15, flow rate = 0.6 mL/min, \(\lambda = 254 \, \text{nm})\): \(t_1 = 12.6 \, \text{min}, \, t_2 = 15.5 \, \text{min}\).

**4ea**: \([\alpha]_D^{23.9} = +55.6 \, (c = 1.67, \text{ CHCl}_3, 91\% \, \text{ee})\); HPLC (Daicel Chiralcel OJ-H, hexane/i-PrOH = 85/15, flow rate = 0.6 mL/min, \(\lambda = 254 \, \text{nm})\): \(t_1 = 15.3 \, \text{min}, \, t_2 = 24.2 \, \text{min}\).

**4fa**: \([\alpha]_D^{23.5} = +81.1 \, (c = 0.99, \text{ CHCl}_3, 92\% \, \text{ee})\); HPLC (Daicel Chiralpak IA, hexane/DCM = 50/50, flow rate = 0.6 mL/min, \(\lambda = 254 \, \text{nm})\): \(t_1 = 10.6 \, \text{min}, \, t_2 = 13.8 \, \text{min}\).

**4ga**: \([\alpha]_D^{26.6} = +94.8 \, (c = 1.00, \text{ CHCl}_3, 96\% \, \text{ee})\); HPLC (Daicel Chiralcel OJ-H, hexane/i-PrOH = 85/15, flow rate = 0.6 mL/min, \(\lambda = 254 \, \text{nm})\): \(t_1 = 25.5 \, \text{min}, \, t_2 = 35.7 \, \text{min}\).

3-Hexyl-4-methylene-2-(4-trifluoromethylphenyl)-3,4-dihydroisoquinolin-1(2H)-one (4ca)

\[
\begin{align*}
\text{[\alpha]}_D^{23.1} &= +108.2 \, (c = 1.84, \text{ CHCl}_3, 93\% \, \text{ee})\); \text{HPLC (Daicel Chiralcel OJ-H, hexane/i-PrOH = 85/15,} \\
&\quad \text{flow rate = 0.6 mL/min, } \lambda = 254 \, \text{nm}: t_1 = 10.6 \, \text{min}, \, t_2 = 12.4 \, \text{min}. \text{IR (neat): } 2932, 1659, 1402, 1325, \\
&\quad 1167, 1127 \, \text{cm}^{-1}; ^1\text{H NMR: } \delta = 0.81 \, (t, \, J = 6.3 \, \text{Hz, } 3\, \text{H}), \, 1.00–1.30 \, (m, \, 8\, \text{H}), \, 1.52–1.68 \, (m, \, 1\, \text{H}), \, 1.69–1.83 \, (m, \, 1\, \text{H}), \\
&\quad 4.42 \, (dd, \, J = 10.2, 4.5 \, \text{Hz, } 1\, \text{H}), \, 5.28 \, (s, \, 1\, \text{H}), \, 5.67 \, (s, \, 1\, \text{H}), \, 7.43–7.74 \, (m, \, 7\, \text{H}), \\
&\quad 8.17–8.23 \, (m, \, 1\, \text{H}); ^13\text{C NMR: } \delta = 13.9, 22.4, 25.7, 28.6, 31.5, 34.0, 66.8, 113.3, 123.8 \, (q, \, J = 270.9 \, \text{Hz}), \\
&\quad 124.0, 126.1 \, (q, \, J = 3.5 \, \text{Hz}), \, 127.3, 127.4, 128.5 \, (q, \, J = 32.3 \, \text{Hz}), \, 128.6, 128.8, 132.6, 135.0, \\
&\quad 139.7, 144.8, 162.6 ; \text{HRMS (EI\textsuperscript{+}): Calcd for } C_{23}H_{24}F_3NO, M^+ 387.1810. \text{Found m/z 387.1806.}
\end{align*}
\]

3-Hexyl-4-methylene-2-diphenylcarbamoyl-3,4-dihydroisoquinolin-1(2H)-one (4ai)

\[
\begin{align*}
\text{[\alpha]}_D^{22.6} &= -317.7 \, (c = 1.51, \text{ CHCl}_3, 95\% \, \text{ee})\); \text{HPLC (Daicel Chiralcel OD-H, hexane/i-PrOH = 85/15,} \\
&\quad \text{flow rate = 0.6 mL/min, } \lambda = 254 \, \text{nm}: t_1 = 14.8 \, \text{min}, \, t_2 = 29.7 \, \text{min}. \text{IR (neat): } 2928, 1674, 1601, 1498, \\
&\quad 1339, 1264, 1163 \, \text{cm}^{-1}; ^1\text{H NMR: } \delta = 0.82 \, (t, \, J = 6.8 \, \text{Hz, } 3\, \text{H}), \, 1.10–1.34 \, (m, \, 8\, \text{H}), \, 1.44–1.60 \, (m, \, 1\, \text{H}), \\
&\quad 2.18–2.32 \, (m, \, 1\, \text{H}), \, 4.50 \, (dd, \, J = 10.8, 3.9 \, \text{Hz, } 1\, \text{H}), \, 5.26 \, (s, \, 1\, \text{H}), \, 5.59 \, (s, \, 1\, \text{H}), \, 6.79–7.63 \, (m, \, 13\, \text{H}), \\
&\quad 7.84 \, (d, \, J = 7.8 \, \text{Hz, } 1\, \text{H}); ^13\text{C NMR: } \delta = 14.0, 22.5, 26.1, 28.6, 31.6, 34.6, 63.8, 113.0, 124.2, 126.3,
\end{align*}
\]
Chapter 2

126.5, 126.7, 128.3, 128.5, 128.7, 133.1, 135.2, 139.2, 142.9, 156.7, 161.9; HRMS (EI): Calcd for C_{20}H_{30}N_{2}O_{2}, M^{+} 438.2307. Found m/z 438.2304.

5-Hexyl-4-methylene-6-phenyl-4,5-dihydrothieno[2,3-c]pyridin-7(6H)-one (4ja)

![Chemical Structure]

[\alpha_{D}]^{24.5} = +35.5 (c = 1.17, CHCl_{3}, 96% ee); HPLC (Daicel Chiracel OJ-H, hexane/i-PrOH = 85/15, flow rate = 0.6 mL/min, \lambda = 254 nm): \tau_1 = 15.4 min, \tau_2 = 19.3 min. IR (neat): 2920, 1659, 1456 cm\(^{-1}\); \(\text{H NMR (CD}_{3}\text{OD)}:\) \delta = 0.78 (t, \(J = 6.9\) Hz, 3H), 0.83–1.65 (m, 10H), 4.29 (t, \(J = 6.6\) Hz, 1H), 4.78 (s, 1H), 5.16 (s, 1H), 6.71–6.77 (m, 2H), 6.96–7.03 (m, 1H), 7.08–7.18 (m, 2H), 7.33–7.38 (m, 2H); \(^{13}\text{C NMR}:\) \delta = 14.2, 22.9, 25.5, 29.0, 31.9, 35.2, 68.3, 111.3, 123.3, 126.7, 128.2, 129.0, 132.0, 134.1, 138.1, 141.5, 141.8, 158.8; HRMS (EI): Calcd for C_{20}H_{22}NOS, M^{+} 325.1500. Found m/z 325.1496.

4ab: [\alpha_{D}]^{26.7} = +93.1 (c = 1.02, CHCl_{3}, 92% ee); HPLC (Daicel Chiracel OJ-H, hexane/i-PrOH = 50/50, flow rate = 0.6 mL/min, \lambda = 254 nm): \tau_1 = 27.1 min, \tau_2 = 48.5 min.

4ac: [\alpha_{D}]^{26.6} = +46.8 (c = 1.05, CHCl_{3}, 90% ee); HPLC (Daicel Chiracel OD-H, hexane/i-PrOH = 90/10, flow rate = 0.6 mL/min, \lambda = 254 nm): \tau_1 = 19.1 min, \tau_2 = 27.6 min.

4ad: [\alpha_{D}]^{25.9} = +143.5 (c = 1.01, CHCl_{3}, 97% ee); HPLC (Daicel Chiracel OJ-H, hexane/i-PrOH = 85/15, flow rate = 0.6 mL/min, \lambda = 254 nm): \tau_1 = 55.5 min, \tau_2 = 59.1 min.

4ae: [\alpha_{D}]^{26.2} = +104.6 (c = 1.02, CHCl_{3}, 93% ee); HPLC (Daicel Chiralpak IA, DCM 100%, flow rate = 0.6 mL/min, \lambda = 254 nm): \tau_1 = 10.0 min, \tau_2 = 16.2 min.

4af: [\alpha_{D}]^{26.3} = +78.8 (c = 1.04, CHCl_{3}, 96% ee); HPLC (Daicel Chiralpak AD-H, hexane/i-PrOH = 85/15, flow rate = 0.6 mL/min, \lambda = 254 nm): \tau_1 = 22.4 min, \tau_2 = 35.4 min.

3-(2-Phthalimidoethyl)-4-methylene-2-(4-methylphenyl)-3,4-dihydroisoquinolin-1(2H)-one (4aj)

![Chemical Structure]

[\alpha_{D}]^{26.1} = +71.0 (c = 0.98, CHCl_{3}, 97% ee); HPLC (Daicel Chiralpak IA, DCM 100%, flow rate = 0.6 mL/min, \lambda = 254 nm): \tau_1 = 9.39 min, \tau_2 = 10.5 min. IR (neat): 3000, 2874, 1771, 1713, 1651, 1399 cm\(^{-1}\); \(\text{H NMR}:\) \delta = 1.92–2.06 (m, 1H), 2.13–2.25 (m, 1H), 2.27 (s, 3H), 3.55 (t, \(J = 7.2\) Hz, 2H), 4.46 (dd, \(J = 9.3, 3.3\) Hz, 1H), 5.49 (s, 1H), 5.70 (s, 1H), 7.08–7.25 (m, 4H), 7.42–7.78 (m, 7H), 8.14–8.20 (m, 1H); \(^{13}\text{C NMR}:\) \delta = 21.0, 32.7, 34.6, 64.5, 113.8, 123.0, 124.0, 127.1, 127.6, 128.6, 128.9, 129.7, 131.7, 132.4, 133.8, 134.6, 136.8, 138.4, 139.5, 162.4, 167.9; HRMS (EI): Calcd for C_{27}H_{32}N_{2}O_{3}, M^{+} 422.1630. Found m/z 422.1617.
Oxidative Removal of 4-Methoxyphenyl Group Using Cerium Ammonium Nitrate (CAN).\textsuperscript{23}

\[ \text{4ca, 88\% ee} \quad \xrightarrow{4 \text{ equiv CAN}} \quad \text{8, 63\%, 88\% ee} \]

(4ca:5ca = 95:5)

To a solution of 4ca (69 mg, 0.197 mmol, 4ca:5ca = 95:5, 88\% ee) in CH\textsubscript{3}CN (12 mL) was slowly added CAN (434 mg, 0.792 mmol) in water (12 mL) at –5 °C. After stirred for 30 min (monitored by TLC), the reaction mixture was quenched by addition of aqueous NaHCO\textsubscript{3} (20 mL) and extracted with AcOEt (4 x 20 mL). The organic layer was washed with aqueous Na\textsubscript{2}SO\textsubscript{3} (20 mL), brine and dried over Na\textsubscript{2}SO\textsubscript{4}. The solvent was passed through a pad of Florisil\textsuperscript{®} and concentrated under reduced pressure. The residue was purified by preparative thin-layer chromatography (hexane/ethyl acetate 2:1) to give the amide 8 (30.4 mg, 0.125 mmol, 63\% yield, 88\% ee).

3-Hexyl-4-methylene-3,4-dihydroisoquinolin-1(2H)-one (8)

\[ \text{[\(\alpha\)l\textsubscript{D}]\textsuperscript{22.5} = +230.1 (c = 1.32, CHCl\textsubscript{3}, 88\% ee); HPLC (Daicel Chiralcel OD-H, hexane/i-PrOH = 85/15, flow rate = 0.6 mL/min, \(\lambda\) = 254 nm): \(t\textsubscript{1} = 13.3\) min, \(t\textsubscript{2} = 18.8\) min. IR (neat): 3198, 2930, 1669, 1603, 1474, 1404 cm\textsuperscript{-1}; \textsuperscript{1}H NMR: \(\delta = 0.84\) (t, \(J = 6.5\) Hz, 3H), 1.12–1.40 (m, 8H), 1.47–1.73 (m, 2H), 4.07–4.17 (m, 1H), 5.18 (s, 1H), 5.59 (s, 1H), 6.78–6.94 (m, 1H), 7.38–7.46 (m, 1H), 7.47–7.60 (m, 2H), 8.06–8.14 (m, 1H); \textsuperscript{13}C NMR: \(\delta = 14.0, 22.5, 25.5, 28.9, 31.7, 37.6, 57.6, 112.8, 124.1, 127.1, 127.9, 128.6, 132.5, 135.7, 140.6, 164.7; HRMS (El\textsuperscript{+}): Calcd for C\textsubscript{16}H\textsubscript{21}NO, M\textsuperscript{+} 243.1623. Found m/z 243.1620.} \]
**Determination of Stereochemistries.**

Stereochemistries of the products were determined by nOe experiments are shown below with curved arrows that indicate the observed nOe.

**[Compound 4aa and 4ad]**
The following results suggested that the substituent group was bound to the C(3).

![Compound 4aa and 4ad](image)

**[Compound 5aa]**
The following results suggested that the major isomer of 5aa was Z-isomer.

![Compound 5aa](image)

**[Compound 5af, 5ag and 5ah]**
The following results suggested that the major isomer was Z-isomer.

![Compound 5af, 5ag and 5ah](image)
References and Notes


(6) See chapter 1.

(7) See the Experimental Section.


(10) The enantiomeric excess of 4ai was low (19% ee).

(11) Treatment of 6ai with Ni(cod)$_2$ (10 mol %) and (R,R)-Me-DuPhos (20 mol %) in toluene at 100 °C caused isomerization to 4ai (97% yield) indicating that 4ai is the thermodynamically more stable isomer.

(12) (S,S)-i-Pr-FOXAP = (S,S)-[2-(4′-Isoproxyloxazolin-2′-yl)ferrocenyl]-diphenylphosphine, see: Miyake, Y.; Nishibayashi, Y.; Uemura, S. Synlett, 2008, 1747.


(15) Fernandez-Forner, D.; Eritja, R.; Bardella, F.; Ruizperez, C.; Solans, X.; Giralt, E; Pedroso, E. 

(16) Brandsma, L. *Synthesis of Acetylenes, Allenes and Cumulenes: Methods and Techniques*; 


Chapter 3

Nickel-Catalyzed Denitrogenative Annulations of 1,2,3-Benzotriazin-4(3H)-ones with 1,3-Dienes and Alkenes

Abstract

A denitrogenative annulation reaction of 1,2,3-benzotriazin-4(3H)-ones with dienes and alkenes catalyzed by a nickel/phosphine complex, which produces a variety of substituted 3,4-dihydroquinolin-1(2H)-ones in a regioselective manner, is described.
Introduction

Transition metal-catalyzed annulation reactions continue to provide many powerful synthetic methodologies for the construction of heterocyclic compounds. Heterometalacyclic complexes often act as key intermediates, which subsequently incorporate unsaturated compounds through insertion and reductive elimination to construct heterocyclic skeletons. In chapter 1, the author reported that 1,2,3-benzotriazin-4(3H)-ones can be exploited as the precursory platform to generate heterometalacyclic intermediates through oxidative addition to a nickel/phosphine complex into the N–N linkage and subsequent extrusion of a molecular dinitrogen. Subsequent insertion of unsaturated carbon–carbon bond such as alkynes and allenes to give 1(2H)-isoquinolones. In chapter 2, nickel-catalyzed denitrogenative allene insertion reactions of 1,2,3-benzotriazin-4(3H)-ones to give 3,4-dihydroisoquinolin-1(2H)-ones were also described. In this chapter, the author examined that analogous nickel-catalyzed denitrogenative insertion reactions of 1,2,3-benzotriazin-4(3H)-ones with different carbon units such as 1,3-dienes and alkenes.

Results and Discussions

Initially, a denitrogenative insertion reaction of 1,2,3-benzotriazin-4(3H)-ones with 1,3-dienes was examined. 3-Tolyl-1,2,3-benzotriazin-4(3H)-one (1a) was heated with 2,3-dimethylbuta-1,3-diene (2a) in the presence of a nickel(0) catalyst generated in situ from Ni(cod)$_2$ (10 mol %, cod = cycloocta-1,5-diene) and an additional ligand (Table 1). Under the condition using PMe$_3$ as the ligand, a mixture of the desired product 3aa (38%) and linear product 4aa (62%) was obtained (entry 1). The formation of the linear product 4aa is explained by assuming that intermediate B undergoes β-hydride elimination followed by reductive elimination. Several phosphine ligands were tested to improve the selectivity in favor for 4aa (entries 2-8). To the author’s delight, the use of the bidentate phosphine ligand, 1,1’-bis(diphenylphosphino)ferrocene (DPPF) afforded the product 3aa (94%) selectively with a trace amount of 4aa (entry 6).

Under the condition using DPPF, the reaction of various benzotriazinones 1 with 1,3-diene 2a were examined (Table 1). A variety of aryl substituents on the nitrogen atom afforded the corresponding products 3ba-3da in yields ranging from 85% to 88% (entries 2-4). Benzotriazinone 1e and 1f having electron-donating and -withdrawing substituents on the
benzene moiety reacted with 2a to give 3ea and 3fa in yields 86% and 74%, respectively (entries 5 and 6).

**Table 1. Ligand Screening**

<table>
<thead>
<tr>
<th>entry</th>
<th>ligand (mol%)</th>
<th>yield (%) of 3aa&lt;sup&gt;b&lt;/sup&gt;</th>
<th>yield (%) of 4aa&lt;sup&gt;b&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>PMe₃ (20)</td>
<td>37</td>
<td>63</td>
</tr>
<tr>
<td>2</td>
<td>PMe₂Ph (20)</td>
<td>56</td>
<td>44</td>
</tr>
<tr>
<td>3</td>
<td>PMePh₂ (20)</td>
<td>8</td>
<td>-</td>
</tr>
<tr>
<td>4</td>
<td>PPh₃ (20)</td>
<td>2</td>
<td>-</td>
</tr>
<tr>
<td>5</td>
<td>P(n-Bu)₃ (20)</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>6</td>
<td>DPPF (10)</td>
<td>95 (94)</td>
<td>5</td>
</tr>
<tr>
<td>7</td>
<td>DPEphos (10)</td>
<td>24</td>
<td>4</td>
</tr>
<tr>
<td>8</td>
<td>DPPB (10)</td>
<td>62</td>
<td>7</td>
</tr>
</tbody>
</table>

<sup>a</sup> Conditions: 1 (0.1 mmol), 2a (0.2 mmol), Ni(cod)<sub>2</sub> (10 µmol, 10 mol %), and ligand in THF (1 mL) at 60 °C for 15-18 h unless otherwise noted. <sup>b</sup> Determined by <sup>1</sup>H NMR using CDCl₃/CDCl₂ as an internal standard. Isolated yield in parentheses.

**Table 2. Ni(0)-Catalyzed denitrogenative annulation of 1 with 1,3-diene 2a<sup>a</sup>**

<table>
<thead>
<tr>
<th>entry</th>
<th>1</th>
<th>R&lt;sup&gt;1&lt;/sup&gt;</th>
<th>R&lt;sup&gt;2&lt;/sup&gt;</th>
<th>R&lt;sup&gt;3&lt;/sup&gt;</th>
<th>yield (%)&lt;sup&gt;b&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>1a</td>
<td>4-MeC₆H₄</td>
<td>H</td>
<td>H</td>
<td>3aa</td>
</tr>
<tr>
<td>2</td>
<td>1b</td>
<td>Ph</td>
<td>H</td>
<td>H</td>
<td>3ba</td>
</tr>
<tr>
<td>3</td>
<td>1c</td>
<td>4-MeOC₆H₄</td>
<td>H</td>
<td>H</td>
<td>3ca</td>
</tr>
<tr>
<td>4</td>
<td>1d</td>
<td>4-ClC₆H₄</td>
<td>H</td>
<td>H</td>
<td>3da</td>
</tr>
<tr>
<td>5</td>
<td>1e</td>
<td>Ph</td>
<td>MeO</td>
<td>MeO</td>
<td>3ea</td>
</tr>
<tr>
<td>6</td>
<td>1f</td>
<td>Ph</td>
<td>H</td>
<td>CO₂Me</td>
<td>3fa</td>
</tr>
</tbody>
</table>

<sup>a</sup> Conditions: 1 (0.2 mmol), 2a (0.4 mmol), Ni(cod)<sub>2</sub> (20 µmol, 10 mol %), and DPPF (20 µmol, 10 mol %) in THF (1 mL) at 60 °C for 12 h unless otherwise noted. <sup>b</sup> Isolated yield. <sup>c</sup> Toluene (1 mL) at 80°C.
Various diene 2 were subjected to the denitrogenative insertion reaction with benzotriazinone 1a (Table 3). Symmetrical dienes such as 1,2-dimethylene cyclohexane (2b) and gaseous buta-1,3-diene (2c) reacted with 1a to give 3ab and 3ac in 92% and 81% yields, respectively (entry 1 and 2). 2-Methylbuta-1,3-diene (2d) reacted with 1a to provide 3ad and 5ad in fairly regioselective fashion (86:14, entry 3). The major product was obtained by the insertion of 2d at the more substituted double bond. Myrcene (2e) showed reactivity similar to 2d (entry 4). When 1-penta-1,3-diene (2f) was employed, the major regioisomer 3af was generated as a mixture of two diastereomers (cis/trans = 12:88, entry 5). This result indicates that isomerization of the π-allyl nickel intermediate B occurred.

Table 3. Ni(0)-Catalyzed denitrogenative annulation of 1a with 1,3-dienes 2<sup>a</sup>

<table>
<thead>
<tr>
<th>entry</th>
<th>2</th>
<th>3</th>
<th>5</th>
<th>yield (%)&lt;sup&gt;b&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>2b</td>
<td></td>
<td>3ab</td>
<td>92&lt;sup&gt;c&lt;/sup&gt;</td>
</tr>
<tr>
<td>2</td>
<td>2c</td>
<td></td>
<td>3ac</td>
<td>81</td>
</tr>
<tr>
<td>3</td>
<td>2d</td>
<td></td>
<td>3ad</td>
<td>66 (86:14)&lt;sup&gt;d&lt;/sup&gt;</td>
</tr>
<tr>
<td>4</td>
<td>2e</td>
<td></td>
<td>3ae</td>
<td>53 (83:17)&lt;sup&gt;d&lt;/sup&gt;</td>
</tr>
<tr>
<td>5</td>
<td>2f</td>
<td></td>
<td>3af&lt;sup&gt;e&lt;/sup&gt;</td>
<td>85 (90:10)&lt;sup&gt;f,g&lt;/sup&gt;</td>
</tr>
</tbody>
</table>

<sup>a</sup> Conditions: 1 (0.2 mmol), 2 (0.4 mmol), Ni(cod)<sub>2</sub> (20 μmol, 10 mol %), DPPF (20 μmol, 10 mol %) in THF (2 mL) at 60 °C for 6–12 h unless otherwise noted. <sup>b</sup> Isolated yield of 3 unless otherwise noted. Numbers in parentheses describe the ratio of 3:5. <sup>c</sup> Toluene at 80 °C. <sup>d</sup> The ratio was determined by crude 1H NMR. <sup>e</sup> cis/trans = 12:88. <sup>f</sup> Combined yield of isomers. <sup>g</sup> Ni(cod)<sub>2</sub> (40 μmol, 20 mol %) and DPPF (40 μmol, 20 mol %).
Next, the author examined denitrogenative annulation reactions of 1,2,3-benzotriazinon-4(3H)-ones with alkenes. 3-Toly1-1,2,3-benzotriazin-4(3H)-one (1a) was heated with methyl acrylate (6a) in the presence of a nickel(0) catalyst generated in situ from Ni(cod)$_2$ (10 mol %) and an additional ligand (Table 4). All phosphine ligands except tri-$t$-butylphosphine showed excellent reactivity. Especially, the best yield of 7aa was obtained when the reaction was carried out using tri-$n$-butylphosphine (99% yield, entry 3).

**Table 4. Ligand screening**

<table>
<thead>
<tr>
<th>entry</th>
<th>ligand (mol%)</th>
<th>yield (%)$^b$</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>PMe$_3$ (40)</td>
<td>90$^c$</td>
</tr>
<tr>
<td>2</td>
<td>PPh$_3$ (40)</td>
<td>96</td>
</tr>
<tr>
<td>3</td>
<td>P($t$-Bu)$_3$ (40)</td>
<td>99$^c$</td>
</tr>
<tr>
<td>4</td>
<td>PCy$_3$ (40)</td>
<td>96</td>
</tr>
<tr>
<td>5</td>
<td>P($t$-Bu)$_3$ (40)</td>
<td>trace</td>
</tr>
<tr>
<td>6</td>
<td>DPPF (20)</td>
<td>88</td>
</tr>
</tbody>
</table>

$^a$ Conditions: 1 (0.1 mmol), 6a (0.15 mmol), Ni(cod)$_2$ (10 µmol, 10 mol %), and ligand in toluene (1 mL) at 110 °C for 13-14 h unless otherwise noted. $^b$ NMR yield determined by $^1$H NMR using CHCl$_2$CHCl$_2$ as internal standard. $^c$ Isolated yield.

A possible mechanism for the formation of 7aa from 1a is shown in Scheme 1. The reaction is initiated by oxidative addition of the N–N linkage to a nickel(0). Subsequent extrusion of a molecule dinitrogen gives azanickelacycle A, which reacts with methyl acrylate. The regioselective insertion of 6a into carbon–nickel bond due to the electronic demand leads to the seven-membered-ring azanickelacycle C. Finally, reductive elimination affords the product 7aa and the nickel(0) catalyst is regenerated.

Various benzotriazinone 1 were examined to the denitrogenative insertion with 6a (Table 5). A wide variety of aryl substituents on the nitrogen atom afforded the corresponding 3,4-dihydroisoquinolin-1(2H)-ones 7ba-7da, 7ga, and 7ha in yields ranging from 77% to 99% (entries 1-5). Benzotriazinone 1e and 1f having electron-donating and -withdrawing substituents reacted with 6a to give 7ea and 7fa in yields 99% and 97%, respectively (entry 6
and 7). Benzyl- and methyl-substituted benzotriazinones 1i and 1j also participated in the reaction (entries 8 and 9).

**Scheme 1**

![Scheme 1 diagram](image)

**Table 5. Ni(0)-Catalyzed denitrogenative annihilations of 1 with alkenes 6a**

<table>
<thead>
<tr>
<th>entry</th>
<th>1</th>
<th>R²</th>
<th>R¹</th>
<th>6a</th>
<th>10 mol% Ni(cod)₂</th>
<th>20 mol% P(n-Bu)₃</th>
<th>110 °C, 12 h</th>
<th>7</th>
<th>yield (%)⁶</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>1b</td>
<td>Ph</td>
<td>H</td>
<td>H</td>
<td>7ba</td>
<td>99</td>
<td></td>
<td></td>
<td>99</td>
</tr>
<tr>
<td>2</td>
<td>1c</td>
<td>4-MeOC₆H₄</td>
<td>H</td>
<td>H</td>
<td>7ca</td>
<td>96</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>1d</td>
<td>4-CF₃C₆H₄</td>
<td>H</td>
<td>H</td>
<td>7da</td>
<td>98</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>1g</td>
<td>4-ClC₆H₄</td>
<td>H</td>
<td>H</td>
<td>7ga</td>
<td>81</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>5</td>
<td>1h</td>
<td>2MeOC₆H₄</td>
<td>H</td>
<td>H</td>
<td>7ha</td>
<td>77</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>6</td>
<td>1e</td>
<td>Ph</td>
<td>MeO</td>
<td>MeO</td>
<td>7ea</td>
<td>99</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>7</td>
<td>1f</td>
<td>Ph</td>
<td>H</td>
<td>CO₂Me</td>
<td>7fa</td>
<td>97</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>8</td>
<td>1i</td>
<td>Bn</td>
<td>H</td>
<td>H</td>
<td>7ia</td>
<td>98</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>9</td>
<td>1j</td>
<td>Me</td>
<td>H</td>
<td>H</td>
<td>7ia</td>
<td>96</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

⁶ Conditions: 1 (0.2 mmol), 6 (0.3 mmol), Ni(cod)₂ (20 μmol, 10 mol %), and P(n-Bu)₃ (40 μmol, 20 mol %) in toluene (2 mL) at 110 °C for 12 h unless otherwise noted.

Various functionalized alkenes were subjected to the denitrogenative insertion reaction with benzotriazinones 1a (Table 6). The functionalized alkenes 6b-6e reacted with 1b to afford the products 7ab-7ae in yields ranging 73% to 92% (entries 1-4). Amido, pyridyl, and
cyano group were tolerated in the reaction. $\alpha,\beta$- Unsaturated ketone 6f was less reactive than $\alpha,\beta$-unsaturated ester 6a even heating at 160 °C (entry 5). $p$-Trifluoromethyl- and $p$-methoxy-substituted styrene were not suitable coupling partners (entries 6 and 7).

Table 6. Ni(0)-Catalyzed denitrogenative annihilation of 1 with alkenes 6a

<table>
<thead>
<tr>
<th>entry</th>
<th>6 (equiv)</th>
<th>R</th>
<th>7</th>
<th>yield (%)$^b$</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>6b (3.0)</td>
<td>CONMe$_2$</td>
<td>7ab</td>
<td>83</td>
</tr>
<tr>
<td>2</td>
<td>6c (3.0)</td>
<td>2-pyridyl</td>
<td>7ac</td>
<td>83$^c$</td>
</tr>
<tr>
<td>3</td>
<td>6d (1.5)</td>
<td>4-pyridyl</td>
<td>7ad</td>
<td>73$^d$</td>
</tr>
<tr>
<td>4</td>
<td>6e (1.5)</td>
<td>CN</td>
<td>7ae</td>
<td>92</td>
</tr>
<tr>
<td>5</td>
<td>6f (1.5)</td>
<td>COEt</td>
<td>7af</td>
<td>39$^e$</td>
</tr>
<tr>
<td>6</td>
<td>6g (1.5)</td>
<td>4-CF$_3$C$_6$H$_4$</td>
<td>7ag</td>
<td>11$^f$</td>
</tr>
<tr>
<td>7</td>
<td>6h (1.5)</td>
<td>4-MeOC$_6$H$_4$</td>
<td>7ah</td>
<td>0$^e$</td>
</tr>
</tbody>
</table>

$^a$ Conditions: 1 (0.2 mmol), 6 (0.3-0.6 mmol), Ni(cod)$_2$ (20 μmol, 10 mol %), and P(n-Bu)$_3$ (40 μmol, 20 mol %) in toluene (2 mL) at 110 °C for 12 h unless otherwise noted. $^b$ Isolated yield. $^c$ PMe$_3$ (80 mmol, 40 mol %). $^d$ Toluene (4 mL). $^e$ Mesitylene (2 mL) at 160 °C.

Conclusions

In summary, 1,3-dienes and alkenes also participate in the denitrogenative annihilation reaction of 1,2,3-benzotriazin-4(3H)-ones to provide the corresponding substituted 3,4-dihydroisoquinolin-1(2H)-ones.
Experimental Section

General Methods. All reactions were carried out under a nitrogen atmosphere unless otherwise noted. Infrared spectra were recorded on a Shimadzu FTIR-8100 spectrometer. $^1$H and $^{13}$C NMR spectra were recorded on a Varian Gemini 2000 ($^1$H at 300 MHz and $^{13}$C at 75 MHz) spectrometer using CHCl$_3$ ($^1$H, $\delta$ = 7.26) and CDCl$_3$ ($^{13}$C, $\delta$ = 77.0) as an internal standard unless otherwise noted. High-resolution mass spectra were recorded on a JEOL JMS-SX102A (EI) or a JEOL JMS-HX110A (FAB) spectrometer. HPLC analysis was performed by 4.6 x 250 mm column. Flash column chromatography was performed with silica gel 60 N (Kanto). Preparative thin-layer chromatography was performed on silica gel plates with PF$_{254}$ indicator (Merck).

Materials. THF and toluene were distilled from sodium/benzophenone ketyl. Ni(cod)$_2$ (Kanto) was obtained from the commercial sources and purified by recrystallization from toluene before use. 1,1'-Bis(diphenylphosphino)ferrocene (TCI), tri- n-butylphosphine (TCI) were used as received from the commercial sources. 1,2,3-benzotriazine-4(3H)-ones 1a–1j were prepared according to the literature procedure. $^4$ 1,2-Dimethylenecyclohexane (3b) was prepared according to the literature procedures.$^8$ All other 1,3-dienes and alkenes were used as received from the commercial sources.

Spectroscopic data of 1a–1j have been reported.$^4$

**General Procedure for Nickel-Catalyzed Denitrogenative Annulation of 1,2,3-Benzotriazin-4(3H)-ones with 1,3-Dienes (Table 2 and 3).** To an oven-dried flask was added 1a (44.6 mg, 0.2 mmol), a solution of Ni(cod)$_2$ (5.6 mg, 20 µmol) and DPPF (11.0 mg, 20 µmol) in THF (1 mL), and 2,3-dimethylbuta-1,3-diene (2a, 45 µl, 0.4 mmol). After heated at 60 °C for 12 h, the reaction mixture was cooled to room temperature and stirred over 30 min in open air. The resulting mixture was passed through a pad of Florisil$^6$ with ethyl acetate and the solvent was concentrated under reduced pressure. The residue was purified by preparative thin-layer chromatography (hexane/ethyl acetate 5:1 to 3:1) to give the product 3aa (48.2 mg, 0.174 mmol, 87% yield).

**3-Methyl-2-(4-methylphenyl)-3-(prop-1-en-2-yl)-3,4-dihydroisoquinolin-1(2H)-one (3aa)**

IR (KBr): 2980, 1644, 1512, 1374 cm$^{-1}$; $^1$H NMR: $\delta$ = 1.31 (s, 3H), 1.71 (s, 3H), 2.37 (s, 3H), 3.18 (d, $J$ = 15.9 Hz, 1H), 3.28 (d, $J$ = 15.6 Hz, 1H), 4.93 (s, 1H), 5.05 (s, 1H), 7.12 (d, $J$ = 7.5 Hz, 1H), 7.16–7.20 (m, 4H), 7.29–7.37 (m, 1H), 7.39–7.46 (m, 1H), 8.05–8.10 (m, 1H); $^{13}$C NMR: $\delta$ = 19.8, 21.1, 26.5, 41.2, 64.6, 114.8, 126.7, 126.9, 128.2, 128.8, 129.2, 129.6, 131.8, 136.1, 136.8, 137.1, 146.0, 165.5; HRMS (EI$^+$): Calcd for C$_{20}$H$_{21}$NO, M$^+$ 291.1623. Found m/z 291.1626.
3-Methyl-2-phenyl-3-(prop-1-en-2-yl)-3,4-dihydroisoquinolin-1(2H)-one (3ba)

IR (KBr): 1644, 1605, 1491, 1460, 1372 cm\(^{-1}\); \(^1\)H NMR: \(\delta = 1.31\) (s, 3H), 1.72 (s, 3H), 3.19 (d, \(J = 15.9\) Hz, 1H), 3.29 (d, \(J = 15.9\) Hz, 1H), 4.95 (s, 1H), 5.06 (s, 1H), 7.14 (d, \(J = 7.2\) Hz, 1H), 7.26–7.48 (m, 7H), 8.08 (d, \(J = 7.5\) Hz, 1H); \(^{13}\)C NMR: \(\delta = 19.7, 26.5, 41.2, 64.7, 114.8, 126.7, 127.0, 127.1, 128.2, 128.5, 129.0, 129.5, 131.9, 136.1, 139.8, 145.9, 165.4; HRMS (EI\(^+\)): Calcd for C\(_{19}\)H\(_{19}\)NO, M\(^+\) 277.1467. Found m/z 277.1478.

2-(4-Methoxyphenyl)-3-methyl-3-(prop-1-en-2-yl)-3,4-dihydroisoquinolin-1(2H)-one (3ca)

IR (KBr): 1644, 1603, 1510, 1460, 1445, 1377, 1248, 1034 cm\(^{-1}\); \(^1\)H NMR: \(\delta = 1.30\) (s, 3H), 1.71 (s, 3H), 3.17 (d, \(J = 15.9\) Hz, 1H), 3.27 (d, \(J = 15.9\) Hz, 1H), 3.81 (s, 3H), 4.92 (s, 1H), 5.03 (s, 1H), 6.86–6.93 (m, 2H), 7.12 (d, \(J = 7.5\) Hz, 1H), 7.16–7.24 (m, 2H), 7.32 (t, \(J = 7.4\) Hz, 1H), 7.38–7.46 (m, 1H), 8.03–8.10 (m, 1H); \(^{13}\)C NMR: \(\delta = 19.8, 26.6, 41.1, 55.3, 64.7, 113.8, 114.7, 126.7, 126.9, 128.2, 129.6, 130.0, 131.8, 132.5, 134.1, 146.0, 158.3, 165.7; HRMS (EI\(^+\)): Calcd for C\(_{20}\)H\(_{21}\)NO\(_2\), M\(^+\) 307.1572. Found m/z 307.1580.

3-Methyl-3-(prop-1-en-2-yl)-2-(4-trifluoromethylphenyl)-3,4-dihydroisoquinolin-1(2H)-one (3da)

IR (KBr): 1642, 1323, 1165, 1123 cm\(^{-1}\); \(^1\)H NMR: \(\delta = 1.33\) (s, 3H), 1.73 (s, 3H), 3.21 (d, \(J = 15.9\) Hz, 1H), 3.30 (d, \(J = 15.9\) Hz, 1H), 4.97 (s, 1H), 5.03 (s, 1H), 7.15 (d, \(J = 7.2\) Hz, 1H), 7.35 (t, \(J = 7.5\) Hz, 1H), 7.41–7.50 (m, 5H), 7.64 (d, \(J = 9.0\) Hz, 2H), 8.04–8.09 (m, 1H); \(^{13}\)C NMR: \(\delta = 19.7, 26.6, 41.2, 64.9, 115.1, 123.9 (q, \(J = 270.3\) Hz), 125.6 (q, \(J = 3.9\) Hz), 126.9, 127.2, 128.3, 129.0, 129.1 (q, \(J = 32.7\) Hz), 129.4, 132.2, 136.0, 143.2, 145.8, 165.4; HRMS (EI\(^+\)): Calcd for C\(_{20}\)H\(_{18}\)F\(_3\)NO, M\(^+\) 345.1340. Found m/z 345.1343.

6,7-Dimethoxy-3-methyl-2-phenyl-3-(prop-1-en-2-yl)-3,4-dihydroisoquinolin-1(2H)-one (3ea)

IR (KBr): 1644, 1603, 1512, 1360, 1273 cm\(^{-1}\); \(^1\)H NMR: \(\delta = 1.30\) (s, 3H), 1.73 (s, 3H), 3.09 (d, \(J = 15.6\) Hz, 1H), 3.22 (d, \(J = 15.9\) Hz, 1H), 3.90 (s, 3H), 3.92 (s, 3H), 4.96 (s, 1H), 5.06 (s,
1H), 6.59 (s, 1H), 7.23–7.41 (m, 5H), 7.59 (s, 1H); $^{13}$C NMR: $\delta =$ 19.9, 26.6, 40.8, 55.96, 55.99, 64.7, 109.2, 110.7, 114.7, 122.0, 127.1, 128.5, 129.1, 129.7, 140.0, 146.2, 147.8, 152.1, 165.4; HRMS (EI$^+$): Calcd for C$_{21}$H$_{23}$NO$_3$, M$^+$ 337.1678. Found m/z 337.1682.

6-Methoxycarbonyl-3-methyl-2-phenyl-3-(prop-1-en-2-yl)-3,4-dihydroisoquinolin-1(2H)-one (3fa)

IR (KBr): 1713, 1646, 1445, 1368, 1279, 1210 cm$^{-1}$; $^1$H NMR: $\delta =$ 1.31 (s, 3H), 1.71 (s, 3H), 3.24 (d, $J = 15.9$ Hz, 1H), 3.31 (d, $J = 15.9$ Hz, 1H), 3.93 (s, 3H), 4.94 (s, 1H), 5.04 (s, 1H), 7.27–7.43 (m, 5H), 7.81–7.84 (m, 1H), 7.96–8.01 (m, 1H), 8.13 (d, $J = 8.1$ Hz, 1H); $^{13}$C NMR: $\delta =$ 19.7, 26.4, 41.0, 52.3, 64.9, 115.1, 127.4, 128.06, 128.14, 128.4, 128.7, 128.9, 132.9, 133.4, 136.1, 139.5, 145.7, 164.7, 166.4; HRMS (EI$^+$): Calcd for C$_{21}$H$_{21}$NO$_3$, M$^+$ 335.1521. Found m/z 335.1516.

2-Methylene-2'-(4-methylphenyl)-2',4'-dihydro-1'H-spiro[cyclohexane-1,3'-isoquinolin]-1'-one (3ab)

IR (KBr): 2934, 1655, 1605, 1512, 1462, 1374, 1345 cm$^{-1}$; $^1$H NMR: $\delta =$ 1.14–1.32 (m, 1H), 1.40–1.54 (m, 1H), 1.58–1.86 (m, 4H), 2.11–2.32 (m, 2H), 2.38 (s, 3H), 3.14 (d, $J = 15.6$ Hz, 1H), 3.55 (d, $J = 15.6$ Hz, 1H), 4.91 (s, 1H), 5.00 (s, 1H), 7.14 (d, $J = 7.2$ Hz, 1H), 7.16–7.24 (m, 4H), 7.29–7.36 (m, 1H), 7.39–7.46 (m, 1H), 8.04–8.10 (m, 1H); $^{13}$C NMR: $\delta =$ 21.1, 22.6, 27.0, 33.1, 38.9, 39.0, 65.4, 112.3, 126.9, 127.0, 128.1, 129.4, 130.0, 131.7, 135.5, 136.7, 137.1, 147.3, 166.1; HRMS (EI$^+$): Calcd for C$_{22}$H$_{23}$NO, M$^+$ 317.1780. Found m/z 317.1776.

2-(4-Methylphenyl)-3-vinyl-3,4-dihydroisoquinolin-1(2H)-one (3ac)

IR (KBr): 1659, 1514, 1460, 1404 cm$^{-1}$; $^1$H NMR: $\delta =$ 2.36 (s, 3H), 2.95 (dd, $J = 15.9$, 3.0 Hz, 1H), 3.62 (dd, $J = 15.9$, 5.7 Hz, 1H), 4.48–4.56 (m, 1H), 5.10 (d, $J = 10.5$ Hz, 1H), 5.15 (d, $J = 17.1$ Hz, 1H), 5.86 (dd, $J = 17.0$, 10.3, 6.5 Hz, 1H), 7.16–7.22 (m, 3H), 7.23–7.30 (m, 2H), 7.32–7.40 (m, 1H), 7.42–7.49 (m, 1H), 8.10–8.16 (m, 1H); $^{13}$C NMR: $\delta =$ 21.0, 34.3, 62.2, 117.3, 126.3, 127.1, 127.4, 128.4, 129.5, 129.6, 132.0, 135.9, 136.3, 136.5, 139.7, 163.8; HRMS (EI$^+$): Calcd for C$_{18}$H$_{17}$NO, M$^+$ 263.1310. Found m/z 263.1316.

3-Methyl-2-(4-methylphenyl)-3-vinyl-3,4-dihydroisoquinolin-1(2H)-one (3ad)
IR (KBr): 2982, 1510, 1460, 1385 cm\(^{-1}\); \(^1\)H NMR: \(\delta = 1.31\) (s, 3H), 2.37 (s, 3H), 3.09 (d, \(J = 15.6\) Hz, 1H), 3.29 (d, \(J = 15.9\) Hz, 1H), 5.05 (d, \(J = 10.5\) Hz, 1H), 5.11 (d, \(J = 17.4\) Hz, 1H), 5.95 (dd, \(J = 17.4, 10.8\) Hz, 1H), 7.06–7.13 (m, 2H), 7.16–7.23 (m, 3H), 7.31–7.39 (m, 1H), 7.42–7.50 (m, 1H), 8.08–8.13 (m, 1H); \(^13\)C NMR: \(\delta = 21.1, 25.7, 42.5, 61.3, 114.6, 127.0, 127.1, 128.5, 129.1, 129.5, 132.0, 136.1, 136.8, 137.2, 141.3, 165.1\); HRMS (EI\(^^+\)): Calcd for C\(_{19}\)H\(_{19}\)NO, M\(^+\) 277.1467. Found m/z 277.1464.

3-(4-Methylpent-3-enyl)-2-(4-methylphenyl)-3-vinyl-3,4-dihydroisoquinolin-1(2H)-one (3ae)

IR (neat): 2923, 1512, 1462, 1375 cm\(^{-1}\); \(^1\)H NMR: \(\delta = 1.46\) (s, 3H), 1.61 (s, 3H), 1.52–1.99 (m, 4H), 2.38 (s, 3H), 3.20 (d, \(J = 15.9\) Hz, 1H), 3.31 (d, \(J = 15.6\) Hz, 1H), 4.84–4.92 (m, 1H), 5.12 (d, \(J = 11.1\) Hz, 1H), 5.13 (d, \(J = 17.4\) Hz, 1H), 5.75 (dd, \(J = 17.6, 10.7\) Hz, 1H), 7.08–7.15 (m, 2H), 7.17–7.24 (m, 3H), 7.31–7.39 (m, 1H), 7.42–7.50 (m, 1H), 8.07–8.12 (m, 1H); \(^13\)C NMR: \(\delta = 17.5, 21.1, 23.0, 25.6, 37.3, 37.8, 63.8, 115.5, 123.2, 126.9, 127.1, 128.4, 129.3, 129.4, 132.0, 136.1, 136.4, 137.1, 139.7, 165.3\); HRMS (EI\(^^+\)): Calcd for C\(_{24}\)H\(_{27}\)NO, M\(^+\) 345.2093. Found m/z 345.2096.

trans-4-Methyl-2-(4-methylphenyl)-3-vinyl-3,4-dihydroisoquinolin-1(2H)-one (3af)

IR (KBr): 2973, 1514, 1462, 1404, 1262 cm\(^{-1}\); \(^1\)H NMR: \(\delta = 1.37\) (d, \(J = 6.9\) Hz, 3H), 2.36 (s, 3H), 3.63–3.75 (m, 1H), 4.21 (dd, \(J = 8.1, 5.4\) Hz, 1H), 5.10 (dt, \(J = 17.1, 1.1\) Hz, 1H), 5.14 (d, \(J = 10.5\) Hz, 1H), 5.68 (dd, \(J = 17.0, 10.2, 8.1\) Hz, 1H), 7.16–7.28 (m, 5H), 7.33–7.41 (m, 1H), 7.47–7.55 (m, 1H), 8.11–8.16 (m, 1H); \(^13\)C NMR: \(\delta = 14.4, 21.0, 36.0, 68.6, 119.5, 124.6, 126.6, 126.8, 128.3, 129.5, 132.1, 133.0, 136.4, 139.5, 140.4, 163.8\); HRMS (EI\(^^+\)): Calcd for C\(_{19}\)H\(_{19}\)NO, M\(^+\) 277.1467. Found m/z 277.1470.

General Procedure for Nickel-Catalyzed Denitrogenative Annulation of 1,2,3-Benzotriazin-4(3H)-ones with Alkene (Table 5 and 6). To an oven-dried flask was added 1a (47.5 mg, 0.2 mmol), a solution of Ni(cod)\(_2\) (5.6 mg, 20 \(\mu\)mol) and P(n-Bu\(_3\)) (10 \(\mu\)L, 40 \(\mu\)mol) in toluene (2 mL), and methyl acrylate (6a, 28 \(\mu\)L, 0.3 mmol). After heated at 60 °C for 12 h, the reaction mixture was cooled to room temperature and stirred over 30 min in open air. The resulting mixture was passed through a pad of Florisil\(^\text{®}\) with ethyl acetate and the solvent was concentrated under reduced pressure. The residue was purified by preparative thin-layer chromatography (hexane/ethyl acetate 3:1) to give the product 7aa (57.8 mg, 0.196 mmol, 98% yield).
3-Methoxycarbonyl-2-(4-methylphenyl)-3,4-dihydroisoquinolin-1(2H)-one (7aa)

IR (KBr): 1740, 1698, 1514, 1383, 1150 cm\(^{-1}\); \(^1\)H NMR: \(\delta = 2.36\) (s, 3H), 2.48 (dd, \(J = 15.9, 8.4\) Hz, 1H), 2.93 (dd, \(J = 16.2, 3.9\) Hz, 1H), 3.62 (s, 3H), 5.53 (dd, \(J = 8.7, 4.2\) Hz, 1H), 7.21–7.29 (m, 2H), 7.39–7.45 (m, 2H), 7.47–7.61 (m, 3H), 7.89–7.95 (m, 1H); \(^1^3\)C NMR: \(\delta = 21.0, 37.6, 51.9, 57.6, 122.5, 124.0, 124.1, 128.8, 129.8, 131.9, 132.1, 133.7, 135.8, 144.1, 166.7, 170.8\); HRMS (EI\(^+\)): Calcd for C\(_{18}\)H\(_{17}\)NO\(_3\), M\(^+\) 295.1208. Found m/z 295.1204.

3-Methoxycarbonyl-2-phenyl-3,4-dihydroisoquinolin-1(2H)-one (7ba)

IR (KBr): 1742, 1684, 1499, 1395 cm\(^{-1}\); \(^1\)H NMR: \(\delta = 2.50\) (dd, \(J = 16.2, 8.7\) Hz, 1H), 2.95 (dd, \(J = 16.2, 7.2\) Hz, 1H), 3.63 (s, 3H), 5.59 (dd, \(J = 8.6, 4.1\) Hz, 1H), 7.21–7.29 (m, 1H), 7.41–7.63 (m, 7H), 7.90–7.95 (m, 1H); \(^1^3\)C NMR: \(\delta = 37.6, 51.9, 57.4, 122.5, 123.8, 124.2, 125.9, 128.8, 129.2, 131.8, 132.3, 136.3, 144.1, 166.7, 170.8\); HRMS (EI\(^+\)): Calcd for C\(_{17}\)H\(_{15}\)NO\(_3\), M\(^+\) 281.1052. Found m/z 281.1051.

3-Methoxycarbonyl-2-(4-methoxyphenyl)-3,4-dihydroisoquinolin-1(2H)-one (7ca)

IR (KBr): 1736, 1698, 1514, 1387, 1248 cm\(^{-1}\); \(^1\)H NMR: \(\delta = 2.50\) (dd, \(J = 16.2, 8.7\) Hz, 1H), 2.89 (dd, \(J = 16.1, 4.4\) Hz, 1H), 3.61 (s, 3H), 3.82 (s, 3H), 5.49 (dd, \(J = 8.6, 4.7\) Hz, 1H), 6.94–7.01 (m, 2H), 7.38–7.46 (m, 2H), 7.47–7.62 (m, 3H), 7.89–7.94 (m, 1H); \(^1^3\)C NMR: \(\delta = 37.6, 51.9, 55.5, 58.1, 114.5, 122.4, 124.1, 126.0, 128.8, 129.0, 131.8, 132.0, 144.1, 157.8, 166.8, 170.7\); HRMS (EI\(^+\)): Calcd for C\(_{18}\)H\(_{17}\)NO\(_4\), M\(^+\) 311.1158. Found m/z 311.1154.

3-Methoxycarbonyl-2-(4-trifluoromethylphenyl)-3,4-dihydroisoquinolin-1(2H)-one (7da)

IR (KBr): 1742, 1686, 1613, 1397, 1339, 1161, 1115, 1067 cm\(^{-1}\); \(^1\)H NMR: \(\delta = 2.53\) (dd, \(J = 16.2, 8.4\) Hz, 1H), 2.97 (dd, \(J = 16.2, 4.2\) Hz, 1H), 3.65 (s, 3H), 5.65 (dd, \(J = 8.6, 3.8\) Hz, 1H), 7.50–7.57 (m, 2H), 7.58–7.66 (m, 1H), 7.67–7.73 (m, 1H), 7.74–7.80 (m, 1H), 7.90–7.95 (m, 1H); \(^1^3\)C NMR: \(\delta = 37.3, 52.1, 57.0, 122.5, 122.6, 123.9\) (q, \(J = 269.8\) Hz), 124.4, 126.3 (q, \(J = 3.8\) Hz), 127.1 (q, \(J = 32.3\) Hz), 129.1, 131.2, 132.8, 139.7, 143.9, 166.8, 170.5; HRMS (EI\(^+\)): Calcd for C\(_{18}\)H\(_{14}\)F\(_3\)NO\(_3\), M\(^+\) 349.0926. Found m/z 349.0916.
2-(4-Chlorophenyl)-3-methoxycarbonyl-3,4-dihydroisoquinolin-1(2H)-one (7ga)

IR (KBr): 1742, 1684, 1497, 1391 cm\(^{-1}\); \(^1\)H NMR: \(\delta = 2.51\) (dd, \(J = 16.1, 8.6\) Hz, 1H), 2.92 (dd, \(J = 15.8, 4.1\) Hz, 1H), 3.64 (s, 3H), 5.56 (dd, \(J = 8.6, 4.1\) Hz, 1H), 7.38–7.46 (m, 2H), 7.48–7.64 (m, 5H), 7.89–7.94 (m, 1H); \(^{13}\)C NMR: \(\delta = 37.4, 52.0, 57.3, 122.5, 124.2, 124.7, 129.0, 129.3, 131.2, 131.5, 132.5, 135.0, 143.9, 166.7, 170.6\); HRMS (EI\(^+\)): Calcd for C\(_{17}\)H\(_{14}\)ClNO\(_3\), M\(^+\) 315.0662. Found m/z 315.0667.

3-Methoxycarbonyl-2-(2-methoxyphenyl)-3,4-dihydroisoquinolin-1(2H)-one (7ha)

IR (KBr): 1736, 1702, 1505, 1387, 1266, 1152 cm\(^{-1}\); \(^1\)H NMR: \(\delta = 2.58\) (dd, \(J = 16.2, 7.2\) Hz, 1H), 2.74 (dd, \(J = 16.2, 6.0\) Hz, 1H), 3.51 (s, 3H), 3.81 (s, 3H), 5.56 (dd, \(J = 6.9, 6.3\) Hz, 1H), 6.98–7.07 (m, 2H), 7.31–7.38 (m, 2H), 7.47–7.54 (m, 2H), 7.91–7.96 (m, 1H); \(^{13}\)C NMR: \(\delta = 37.9, 51.7, 55.6, 58.2, 112.0, 120.8, 122.4, 124.1, 124.4, 128.4, 129.4, 130.4, 131.9, 145.1, 155.6, 167.5, 170.8\); HRMS (EI\(^+\)): Calcd for C\(_{18}\)H\(_{17}\)NO\(_4\), M\(^+\) 311.1158. Found m/z 311.1155.

6,7-Dimethoxy-3-methoxycarbonyl-2-phenyl-3,4-dihydroisoquinolin-1(2H)-one (7ea)

IR (KBr): 1734, 1692, 1497, 1385, 1256 cm\(^{-1}\); \(^1\)H NMR: \(\delta = 2.44\) (dd, \(J = 16.2, 9.0\) Hz, 1H), 2.93 (dd, \(J = 16.2, 6.0\) Hz, 1H), 3.63 (s, 3H), 3.93 (s, 3H), 3.94 (s, 3H), 5.47 (dd, \(J = 8.7, 3.9\) Hz, 1H), 6.99 (s, 1H), 7.17–7.25 (m, 1H), 7.35 (s, 1H), 7.38–7.46 (m, 2H), 7.50–7.56 (m, 2H); \(^{13}\)C NMR: \(\delta = 37.7, 51.9, 56.2, 56.9, 104.7, 105.5, 123.5, 124.0, 125.5, 129.1, 136.5, 137.9, 150.2, 153.0, 166.8, 171.1\); HRMS (EI\(^+\)): Calcd for C\(_{19}\)H\(_{19}\)NO\(_5\), M\(^+\) 341.1263. Found m/z 341.1260.

3,6-Dimethoxycarbonyl-2-phenyl-3,4-dihydroisoquinolin-1(2H)-one (7fa)

IR (KBr): 1745, 1717, 1690, 1383, 1294, 1217 cm\(^{-1}\); \(^1\)H NMR: \(\delta = 2.57\) (dd, \(J = 16.2, 8.4\) Hz, 1H), 2.96 (dd, \(J = 16.3, 4.1\) Hz, 1H), 3.63 (s, 3H), 3.97 (s, 3H), 5.63 (dd, \(J = 8.4, 4.2\) Hz, 1H), 7.24–7.32 (m, 1H), 7.42–7.50 (m, 2H), 7.53–7.59 (m, 2H), 7.96–8.02 (m, 1H), 8.17–8.24 (m, 1H); \(^{13}\)C NMR: \(\delta = 37.2, 52.0, 52.5, 57.6, 123.9, 124.2, 126.3, 129.3, 130.3, 133.6, 135.7, 136.0, 144.0, 165.7, 166.1, 170.3\); HRMS (EI\(^+\)): Calcd for C\(_{19}\)H\(_{17}\)NO\(_5\), M\(^+\) 339.1107. Found m/z 339.1105.
2-Benzyl-3-methoxycarbonyl-3,4-dihydroisoquinolin-1(2H)-one (7ia)

IR (KBr): 1732, 1678, 1435, 1408, 1242 cm⁻¹; ¹H NMR: δ = 2.61 (dd, J = 16.1, 7.4 Hz, 1H), 2.86 (dd, J = 16.2, 5.7 Hz, 1H), 3.63 (s, 3H), 4.40 (d, J = 15.0 Hz, 1H), 4.83 (dd, J = 6.8, 5.3 Hz, 1H), 5.20 (d, J = 15.6 Hz, 1H), 7.20–7.35 (m, 5H), 7.36–7.41 (m, 1H), 7.44–7.57 (m, 2H), 7.87–7.92 (m, 2H); ¹³C NMR: δ = 37.3, 44.2, 51.9, 56.0, 122.3, 123.8, 127.5, 127.8, 128.5, 128.7, 131.6, 131.8, 136.9, 144.7, 168.3, 170.5; HRMS (EI⁺): Calcd for C₁₈H₁₇NO₃, M⁺ 295.1208. Found m/z 295.1212.

3-Methoxycarbonyl-2-methyl-3,4-dihydroisoquinolin-1(2H)-one (7ja)

IR (KBr): 1736, 1698, 1437, 1397 cm⁻¹; ¹H NMR: δ = 2.65 (dd, J = 16.1, 6.8 Hz, 1H), 2.87 (dd, J = 16.1, 5.6 Hz, 1H), 3.09 (s, 3H), 3.72 (s, 3H), 4.85 (t, J = 6.3 Hz, 1H), 7.38–7.54 (m, 3H), 7.78–7.83 (m, 1H); ¹³C NMR: δ = 27.4, 37.4, 52.1, 58.3, 122.1, 123.5, 128.5, 131.5, 131.9, 144.3, 168.0, 170.8; HRMS (EI⁺): Calcd for C₁₂H₁₃NO₃, M⁺ 219.0895. Found m/z 219.0894.

3-Dimethylcarbamoyl-2-phenyl-3,4-dihydroisoquinolin-1(2H)-one (7ab)

IR (KBr): 1688, 1651, 1512, 1383, 1146 cm⁻¹; ¹H NMR: δ = 2.35 (s, 3H), 2.39 (dd, J = 15.9, 9.6 Hz, 1H), 2.77 (s, 3H), 2.88 (dd, J = 16.2, 3.3 Hz, 1H), 2.95 (s, 3H), 5.81 (dd, J = 9.9, 3.6 Hz, 1H), 7.20–7.28 (m, 2H), 7.45–7.59 (m, 4H), 7.60–7.66 (m, 1H), 7.87–7.93 (m, 1H); ¹³C NMR: δ = 21.0, 35.5, 36.8, 37.1, 58.0, 123.2, 123.3, 123.9, 128.5, 129.7, 131.8, 132.1, 134.0, 135.2, 145.4, 166.8, 169.6; HRMS (EI⁺): Calcd for C₁₉H₂₀N₂O₂, M⁺ 308.1525. Found m/z 308.1522.

2-Phenyl-3-(pyridin-2-yl)-3,4-dihydroisoquinolin-1(2H)-one (7ac)

IR (KBr): 1682, 1514, 1389 cm⁻¹; ¹H NMR: δ = 2.34 (s, 3H), 2.86 (dd, J = 13.8, 8.7 Hz, 1H), 3.49 (dd, J = 13.8, 4.5 Hz, 1H), 5.81 (dd, J = 8.7, 4.5 Hz, 1H), 6.86 (d, J = 8.1 Hz, 2H), 7.10–7.17 (m, 1H), 7.22 (d, J = 8.1 Hz, 2H), 7.36–7.58 (m, 5H), 7.83–7.91 (m, 1H), 8.52–8.59 (m, 1H); ¹³C NMR: δ = 20.9, 41.1, 60.4, 121.7, 122.7, 123.4, 123.9, 124.4, 128.3, 129.6, 131.4, 132.0, 134.3, 135.1, 136.2, 144.6, 149.3, 156.8, 166.8; HRMS (EI⁺): Calcd for C₂₁H₁₈N₂O, M⁺ 314.1419. Found m/z 314.1416.
2-Phenyl-3-(pyridin-4-yl)-3,4-dihydroisoquinolin-1(2H)-one (7ad)

IR (KBr): 1698, 1597, 1512, 1383 cm\(^{-1}\); \(^1\)H NMR: \(\delta = 2.37\) (s, 3H), 3.02 (dd, \(J = 13.8, 6.9\) Hz, 1H), 3.27 (dd, \(J = 14.0, 3.8\) Hz, 1H), 5.46 (dd, \(J = 6.9, 3.6\) Hz, 1H), 6.65–6.72 (m, 2H), 7.19–7.30 (m, 3H), 7.40–7.55 (m, 4H), 7.79 (d, \(J = 7.2\) Hz, 1H), 8.27–8.34 (m, 2H); \(^1^3\)C NMR: \(\delta = 21.0, 37.0, 60.2, 122.4, 123.1, 124.2, 124.8, 128.7, 129.8, 131.7, 132.3, 134.1, 135.1, 143.0, 144.1, 149.2, 166.6; HRMS (EI\(^{+}\)): Calcd for C\(_{21}\)H\(_{18}\)N\(_2\)O, M\(^+\) 314.1419. Found m/z 314.1416.

3-Cyano-2-phenyl-3,4-dihydroisoquinolin-1(2H)-one (7ae)

IR (KBr): 1684, 1387, 1217 cm\(^{-1}\); \(^1\)H NMR: \(\delta = 2.37\) (s, 3H), 2.67 (dd, \(J = 16.7, 2.7\) Hz, 1H), 2.99 (dd, \(J = 16.8, 2.7\) Hz, 1H), 5.28 (dd, \(J = 7.4, 3.5\) Hz, 1H), 7.26 (d, \(J = 8.4\) Hz, 2H), 7.37 (d, \(J = 8.1\) Hz, 2H), 7.55–7.72 (m, 3H), 7.92–7.98 (m, 1H); \(^1^3\)C NMR: \(\delta = 21.0, 21.8, 56.7, 115.3, 122.3, 124.1, 124.5, 129.6, 130.1, 132.0, 132.5, 132.8, 136.6, 141.7, 166.5; HRMS (EI\(^{+}\)): Calcd for C\(_{17}\)H\(_{14}\)N\(_2\)O, M\(^+\) 262.1106. Found m/z 262.1100.

2-Phenyl-3-propionyl-3,4-dihydroisoquinolin-1(2H)-one (7af)

IR (KBr): 1698, 1375 cm\(^{-1}\); \(^1\)H NMR: \(\delta = 1.00\) (t, \(J = 7.4\) Hz, 3H), 2.31 (q, \(J = 7.4\) Hz, 2H), 2.35 (s, 3H), 2.58 (dd, \(J = 17.7, 6.0\) Hz, 1H), 2.98 (dd, \(J = 17.7, 3.6\) Hz, 1H), 5.69 (dd, \(J = 9.2, 3.5\) Hz, 1H), 7.20–7.28 (m, 2H), 7.39–7.58 (m, 5H), 7.87–7.93 (m, 1H); \(^1^3\)C NMR: \(\delta = 7.5, 20.9, 36.8, 45.3, 56.8, 122.7, 123.5, 124.0, 128.6, 129.8, 131.8, 132.1, 133.8, 135.5, 145.0, 166.7, 208.9; HRMS (EI\(^{+}\)): Calcd for C\(_{19}\)H\(_{19}\)N\(_2\)O, M\(^+\) 293.1412. Found m/z 293.1412.

2-Phenyl-3-(4-trifluoromethylphenyl)-3,4-dihydroisoquinolin-1(2H)-one (7ag)

IR (KBr): 1676, 1516, 1391, 1325, 1154, 1113, 1067 cm\(^{-1}\); \(^1\)H NMR: \(\delta = 2.40\) (s, 3H), 3.07 (dd, \(J = 14.0, 7.1\) Hz, 1H), 3.36 (dd, \(J = 13.8, 3.6\) Hz, 1H), 5.47 (dd, \(J = 4.7, 3.8\) Hz, 1H), 6.90 (d, \(J = 7.8\) Hz, 2H), 7.18–7.23 (m, 1H), 7.25–7.32 (m, 2H), 7.37 (d, \(J = 8.1\) Hz, 2H), 7.43–7.57 (m, 4H), 7.80–7.85 (m, 1H); \(^1^3\)C NMR: \(\delta = 21.0, 37.7, 60.8, 122.6, 123.2, 124.0\) (q, \(J = 270.3\) Hz), 124.2, 124.9 (q, \(J = 3.8\) Hz), 128.7, 129.1 (q, \(J = 32.3\) Hz), 129.8, 129.9, 131.6,
132.4, 134.2, 135.3, 139.1, 143.3, 166.8; HRMS (EI^-): Calcd for C_{19}H_{19}N_2O, M^- 293.1416. Found m/z 293.1412.

**Determination of Stereochemistries.**
Stereochemistries of the products were determined by nOe experiments are shown below with curved arrows that indicate the observed nOe.

**[Compound 3aa and 3ad]**
The following results suggested that the substituent group was bound to the C(3).

**[Compound 3ad and 3ae]**
The following results suggested that the substituent group was bound to the C(3).

**[Compound trans-3af and cis-3af]**
The following results suggested that the vinyl group was bound to the C(3). Stereochemistries of two diastereomers were determined by coupling constants.

**[Compound 4aa]**
The following results suggested that the methoxycarbonyl group was bound to the C(3).
References and Notes


(4) For synthetic methods of 1,2,3-benzotriazin-4(3H)-ones, see Experimental Section of chapter 1.


Chapter 4

Nickel-Catalyzed Denitrogenative Alkene Insertion Reactions of 1-Sulfonyl-1,2,3-triazoles

Abstract

1-Sulfonyl-1,2,3-triazoles reacted with alkynes in the presence of a nickel(0)/phosphine catalyst to give substituted pyrroles, with the extrusion of molecular nitrogen; the triazole moiety isomerised to an a-imino diazo species, and the denitrogenative addition to nickel(0) was followed by the insertion of alkynes and reductive elimination.
Chapter 4

Introduction

The development of efficient methods for the synthesis of heterocyclic compounds is highly valuable, particularly in the field of medicinal chemistry because most biologically active compounds contain heterocyclic cores.\(^1\) Recently, transition metal-catalysed denitrogenative reactions of triazole derivatives forming new heterocyclic systems have been reported, in which diazo compounds were generated \textit{in situ} by the ring-chain tautomerisation and subsequently converted to a reactive metal-carbenoid species. 7-Halo-substituted pyridotriazoles\(^2\) and 1-sulfonyl-1,2,3-triazoles\(^3\) reacted with alkynes and nitriles in the presence of a rhodium catalyst forming indolizines, imidazopyridines and imidazoles, respectively. Benzotriazoles were also utilised in the palladium-catalysed reaction with alkynes to provide indoles.\(^4\) On the other hand, the author found that a nickel-catalysed denitrogenative alkyne insertion reaction of 1,2,3-benzotriazin-4(3\(\text{H}\))-ones gave a wide range of substituted 1(2\(\text{H}\))-isoquinolines in high yields.\(^5\) It was then envisaged that an analogous denitrogenative reaction of 1-sulfonyl-1,2,3-triazoles with alkynes would be feasible, if the dizaa tautomers could add to nickel(0) with extrusion of molecular nitrogen providing a reactive Ni-carbenoid species.\(^6\) In chapter 4, the author reports a nickel-catalysed denitrogenative alkyne insertion reaction of 1-sulfonyl-1,2,3-triazoles, which presents a new approach to substituted pyrroles.\(^7\)

Results and Discussions

The starting materials, 4-substituted 1-(N-tosyl)-1,2,3-triazoles, could be readily prepared by the copper-catalysed azide/alkyne cycloaddition.\(^8\) When 4-phenyl-1-(N-tosyl)-1,2,3-triazole (1a) was treated with dec-5-yne (2a, 2 equiv), 10 mol% of Ni(cod)\(_2\) and 20 mol% of PMe\(_3\) in toluene at 100 °C for 12 h, only a trace of the desired pyrrole 3aa was obtained (Table 1, entry 1). However, the use of sterically-hindered phosphine ligands increased the yield up to 51% (entries 2–4). Next, the effect of Lewis-acid (LA) catalysts as additives was examined (entries 5–8).\(^9\) It was found that the reaction in the presence of AlPh\(_3\) (5 mol%) gave 3aa in 73% isolated yield.
Table 1. Optimisation study of the formation of pyrrole 3aa.  

<table>
<thead>
<tr>
<th>Entry</th>
<th>Ligand</th>
<th>Lewis acid</th>
<th>Yield (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>PMe₃</td>
<td>-</td>
<td>2</td>
</tr>
<tr>
<td>2</td>
<td>PCy₃</td>
<td>-</td>
<td>8</td>
</tr>
<tr>
<td>3</td>
<td>P(t-Bu)₃</td>
<td>-</td>
<td>13</td>
</tr>
<tr>
<td>4</td>
<td>P(n-Bu)Ad₂</td>
<td>-</td>
<td>51</td>
</tr>
<tr>
<td>5</td>
<td>P(n-Bu)Ad₂</td>
<td>BPh₃</td>
<td>49</td>
</tr>
<tr>
<td>6</td>
<td>P(n-Bu)Ad₂</td>
<td>ZnPh₂</td>
<td>62</td>
</tr>
<tr>
<td>7</td>
<td>P(n-Bu)Ad₂</td>
<td>AlMe₃</td>
<td>38</td>
</tr>
<tr>
<td>8</td>
<td>P(n-Bu)Ad₂</td>
<td>AlPh₃</td>
<td>81 (73)</td>
</tr>
</tbody>
</table>

a Conditions: 1a (0.1 mmol), 2a (0.2 mmol), Ni(cod)₂ (10 mol %), Ligand (20 mol %), Lewis acid (5 mol %) in toluene (1 mL) for 12 h. b Determined by ¹H NMR using CHCl₃CHCl₃ as an internal standard. Isolated yield in parenthesis.

A possible reaction pathway for the production of 3aa from 1a and 2a is depicted in Scheme 1. Initially, a ring-chain tautomerisation of 1-sulfonyl-1,2,3-triazole 1a occurs to generate α-imino diazo compound 1a', although the equilibrium lies far to the left. Diazoo compound 1a' adds to nickel(0) with release of molecular nitrogen to give Ni-carbenoid A, which then cyclises to form azanickelacycle A'. Subsequent insertion of alkyne 2a into the Ni–C bond leads to the six-membered-ring nickelacycle B. Finally, reductive elimination affords 3aa, regenerating the nickel(0) catalyst. Possible effects of the LA catalysts may be 1) promoting the formation of α-imino diazo species 1a', and/or 2) acceleration of reductive elimination, although we have no experimental result to support either of these postulates.
Scheme 1. Proposed reaction pathway.

Under optimised reaction conditions, a variety of N-sulfonyltriazoles 1b–1j reacted with 2a to furnish substituted pyroles 3ba–3ja in yields ranging from 46% to 65% (Table 2, entries 1–9). However, the reaction of alkyl-substituted triazole 1k proceeded sluggishly to form the desired product 3ka in only 5% yield (entry 10).

Table 2. The Nickel(0)-catalyzed alkyne insertion reactions of 1 with 2a

<table>
<thead>
<tr>
<th>entry</th>
<th>1</th>
<th>R&lt;sup&gt;1&lt;/sup&gt;</th>
<th>R&lt;sup&gt;2&lt;/sup&gt;</th>
<th>3</th>
<th>yield (%)&lt;sup&gt;b&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>1b</td>
<td>Ph</td>
<td>Ph</td>
<td>3ba</td>
<td>65</td>
</tr>
<tr>
<td>2</td>
<td>1c</td>
<td>4-F-C&lt;sub&gt;6&lt;/sub&gt;H&lt;sub&gt;4&lt;/sub&gt;</td>
<td>Ph</td>
<td>3ca</td>
<td>46</td>
</tr>
<tr>
<td>3</td>
<td>1d</td>
<td>4-MeO-C&lt;sub&gt;6&lt;/sub&gt;H&lt;sub&gt;4&lt;/sub&gt;</td>
<td>Ph</td>
<td>3da</td>
<td>56&lt;sup&gt;c&lt;/sup&gt;</td>
</tr>
<tr>
<td>4</td>
<td>1e</td>
<td>2-naphthyl</td>
<td>Ph</td>
<td>3ea</td>
<td>58&lt;sup&gt;c&lt;/sup&gt;</td>
</tr>
<tr>
<td>5</td>
<td>1f</td>
<td>Tol</td>
<td>Tol</td>
<td>3fa</td>
<td>64</td>
</tr>
<tr>
<td>6</td>
<td>1g</td>
<td>Tol</td>
<td>4-CF&lt;sub&gt;3&lt;/sub&gt;-C&lt;sub&gt;6&lt;/sub&gt;H&lt;sub&gt;4&lt;/sub&gt;</td>
<td>3ga</td>
<td>64&lt;sup&gt;d&lt;/sup&gt;</td>
</tr>
<tr>
<td>7</td>
<td>1h</td>
<td>Tol</td>
<td>4-MeO-C&lt;sub&gt;6&lt;/sub&gt;H&lt;sub&gt;4&lt;/sub&gt;</td>
<td>3ha</td>
<td>59&lt;sup&gt;c&lt;/sup&gt;</td>
</tr>
<tr>
<td>8</td>
<td>1i</td>
<td>Tol</td>
<td>4-Ph-C&lt;sub&gt;6&lt;/sub&gt;H&lt;sub&gt;4&lt;/sub&gt;</td>
<td>3ia</td>
<td>54</td>
</tr>
<tr>
<td>9</td>
<td>1j</td>
<td>Tol</td>
<td>2-naphthyl</td>
<td>3ja</td>
<td>58</td>
</tr>
<tr>
<td>10</td>
<td>1k</td>
<td>Tol</td>
<td>2-hex</td>
<td>3ka</td>
<td>5</td>
</tr>
</tbody>
</table>

<sup>a</sup> Conditions: 1 (0.2 mmol), 2a (0.4 mmol), Ni(cod)<sub>2</sub> (10 mol %), P(n-Bu)<sub>2</sub>Ad (20 mol %), AlPh<sub>3</sub> (5 mol %) in toluene (2 mL) for 12 h. <sup>b</sup> Isolated yield. <sup>c</sup> Ni(cod)<sub>2</sub> (15 mol %) and P(n-Bu)<sub>2</sub>Ad (30 mol %) were used. <sup>d</sup> 110 °C.
Various alkyne reactions (2) were subjected to the denitrogenative insertion reaction with 1a (Table 3). Symmetrical alkyne such as 4-octyne (2b) and diphenylethyne (2c) reacted to give 3ba and 3ca in 65 and 38% yields, respectively (entries 1 and 2). The reaction of unsymmetrical alkyne gave a mixture of regioisomers (entries 3–5). Terminal alkyne such as 1-octyne and phenylethyne failed to participate in the reaction, presumably due to a rapid self-oligomerisation reaction.

<table>
<thead>
<tr>
<th>entry</th>
<th>2</th>
<th>R¹</th>
<th>R²</th>
<th>3</th>
<th>yield (%)&lt;sup&gt;b&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>2b</td>
<td>n-Pr</td>
<td>n-Pr</td>
<td>3ab</td>
<td>68</td>
</tr>
<tr>
<td>2</td>
<td>2c</td>
<td>Ph</td>
<td>Ph</td>
<td>3ac</td>
<td>31</td>
</tr>
<tr>
<td>3</td>
<td>2d</td>
<td>Me</td>
<td>i-Pr</td>
<td>3ad</td>
<td>68 (50:50)</td>
</tr>
<tr>
<td>4</td>
<td>2e</td>
<td>Me</td>
<td>SiMe₃</td>
<td>3ae</td>
<td>48 (58:42)&lt;sup&gt;c&lt;/sup&gt;</td>
</tr>
<tr>
<td>5</td>
<td>2f</td>
<td>Bpin</td>
<td>n-Bu</td>
<td>3af</td>
<td>37 (57:43)&lt;sup&gt;c&lt;/sup&gt;</td>
</tr>
</tbody>
</table>

<sup>a</sup> Conditions: 1a (0.2 mmol), 2 (0.2 mmol), Ni(cod)<sub>2</sub> (10 mol %), P(n-Bu)<sub>2</sub>Ad (20 mol %), AlPh₃ (5 mol %) in toluene (2 mL) for 12 h. <sup>b</sup> Isolated yield. Ratio of regioisomers in parenthesis. <sup>c</sup> Ni(cod)<sub>2</sub> (15 mol%) and P(n-Bu)Ad₂ (30 mol%) were used.

**Conclusions**

In summary, the author has demonstrated that the nickel-catalysed denitrogenative alkyne insertion reaction of 1-sulfonyltriazoles provides a new synthetic route to substituted pyrroles from readily available starting materials. In this reaction, the triazole moiety is effectively activated by a combined use of nickel and a LA catalyst.
Experimental Section

General. Infrared spectra were recorded on a Shimadzu FTIR-8100 spectrometer. $^1$H and $^{13}$CNMR spectra were recorded on a Varian Gemini 2000 ($^1$H at 300 MHz and $^{13}$C at 75 MHz) spectrometer using CHCl$_3$ ($^1$H, $\delta$ = 7.26) and CDCl$_3$ ($^{13}$C, $\delta$ = 77.0) as an internal standard. Highresolution mass spectra were recorded on a JEOL JMS-SX102A (EI) or a JEOL JMS-HX110A (FAB) spectrometer. All reactions were carried out under a nitrogen atmosphere unless otherwise noted. Column chromatography was performed with silica gel 60 N (Kanto). Preparative thinlayer chromatography was performed with silica gel 60 PF 254 (Merck).

Materials. Toluene was distilled from sodium/benzophenone ketyl. Trimethylphosphine (Aldrich), tricyclohexylphosphine (Strem), triDdtbutylphosphine (Wako), nDdbutylDdiD1Dadamantylphosphine (Strem), triphenylborane (Aldrich), diphenylzinc (Aldrich), trimethylaluminium toluene solution (Kanto) and diphenylethyne (2b) (Aldrich) were used as received from the commercial sources. Ni(cod)$_2$ (Kanto) was obtained from the commercial sources and purified by recrystallisation from toluene before use. Triphenylaluminium was prepared according to the literature procedure.1 $N$-Sulfonyl-1,2,3-triazoles (1a–1k) were prepared according to the literature procedure.8 1a, 1f and 1g have been already reported.8 Alkynylboranes (2f) was prepared according to the literature procedure.3 All other alkynes were purchased from the commercial sources and purified by bulb-to-bulb distillation prior to use.

4-Phenyl-1-phenylsulfonyl-$^1$H-1,2,3-triazole (1b)

IR (KBr): 3129, 1451, 1393, 1181 cm$^{-1}$; $^1$H NMR: $\delta$ = 7.33–7.48 (m, 3H), 7.56–7.66 (m, 2H), 7.69–7.77 (m, 1H), 7.80–7.86 (m, 2H), 8.12–8.19 (m, 2H), 8.33 (s, 1H); $^{13}$C NMR: $\delta$ = 119.0, 126.0, 128.4, 128.6, 128.9, 129.0, 129.7, 135.6, 136.0, 147.3; HRMS (EI$^+$): Calcd for C$_{14}$H$_{11}$N$_3$O$_2$S, M$^+$ 285.0572. Found m/z 285.0567.

1-(4-Fluorophenylsulfonyl)-4-phenyl-1H-1,2,3-triazole (1c)

IR (KBr): 3144, 1586, 1493, 1395, 1244, 1188 cm$^{-1}$; $^1$H NMR: $\delta$ = 7.23–7.33 (m, 2H), 7.34–7.48 (m, 3H), 7.79–7.86 (m, 2H), 8.15–8.24 (m, 2H), 8.32 (s, 1H); $^{13}$C NMR: $\delta$ = 117.3 (d, $J$ = 23.0 Hz), 118.9, 126.0, 128.6, 129.0, 129.2, 131.8 (d, $J$ = 10.4 Hz), 132.0 (d, $J$ = 2.3 Hz), 147.5, 166.8 (d, $J$ = 258.2 Hz); HRMS (EI$^+$): Calcd for C$_{14}$H$_{10}$FN$_3$O$_2$S, M$^+$ 303.0478. Found m/z 303.0474.
1-(4-Methoxyphenylsulfonyl)-4-phenyl-1H-1,2,3-triazole (1d)

IR (KBr): 3092, 1592, 1397, 1271, 1202, 1167, 1090 cm\(^{-1}\); \(^1\)H NMR: \(\delta = 3.87\) (s, 3H), 6.99–7.06 (m, 2H), 7.32–7.46 (m, 3H), 7.79–7.85 (m, 2H), 8.03–8.11 (m, 2H), 8.31 (s, 1H); \(^1\)C NMR: \(\delta = 55.9, 115.0, 118.8, 126.0, 126.9, 128.9, 129.0, 131.1, 147.2, 165.3\); HRMS (EI\(^{+}\)): Calcd for C\(_{13}\)H\(_{13}\)N\(_3\)O\(_3\)S, M\(^+\) 315.0678. Found m/z 315.0678.

1-(Naphthalen-2-ylsulfonyl)-4-phenyl-1H-1,2,3-triazole (1h)

IR (KBr): 3125, 1395, 1179, 995 cm\(^{-1}\); \(^1\)H NMR: \(\delta = 7.31–7.47\) (m, 3H), 7.61–7.75 (m, 2H), 7.78–8.06 (m, 2H), 7.94–8.08 (m, 2H), 8.38 (s, 1H), 8.74–8.80 (m, 1H); \(^1\)C NMR: \(\delta = 119.0, 122.1, 126.0, 128.0, 128.2, 128.7, 128.9, 129.0, 129.7, 130.2, 130.4, 131.2, 131.8, 132.7, 135.9, 147.4\); HRMS (EI\(^{+}\)): Calcd for C\(_{18}\)H\(_{17}\)N\(_3\)O\(_2\)S, M\(^+\) 335.0728. Found m/z 335.0731.

4-(4-Methoxyphenyl)-1-tosyl-1H-1,2,3-triazole (1h)

IR (KBr): 3115, 1497, 1393, 1256, 1179 cm\(^{-1}\); \(^1\)H NMR: \(\delta = 2.40\) (s, 3H), 3.81 (s, 3H), 6.90–6.97 (m, 2H), 7.34 (d, \(J = 8.1\) Hz, 2H), 7.70–7.78 (m, 2H), 7.99 (d, \(J = 8.4\) Hz, 2H), 8.23 (s, 1H); \(^1\)C NMR: \(\delta = 21.7, 55.2, 114.3, 117.9, 121.3, 127.3, 128.5, 130.3, 133.0, 147.1, 147.2, 160.1\); HRMS (EI\(^{+}\)): Calcd for C\(_{16}\)H\(_{15}\)N\(_3\)O\(_2\)S, M\(^+\) 329.0834. Found m/z 329.0833.

4-(Biphenyl-4-yl)-1-tosyl-1H-1,2,3-triazole (1i)

IR (KBr): 3139, 1593, 1483, 1389, 1177 cm\(^{-1}\); \(^1\)H NMR: \(\delta = 2.43\) (s, 3H), 7.33–7.41 (m, 3H), 7.42–7.50 (m, 2H), 7.59–7.70 (m, 4H), 7.88–7.95 (m, 2H), 8.01–8.07 (m, 2H), 8.38 (s, 1H); \(^1\)C NMR: \(\delta = 21.7, 118.9, 126.4, 126.8, 127.5, 127.6, 127.7, 128.5, 128.8, 130.4, 132.9, 140.1, 141.6, 147.0, 147.3\); HRMS (EI\(^{+}\)): Calcd for C\(_{21}\)H\(_{17}\)N\(_3\)O\(_2\)S, M\(^+\) 375.1041. Found m/z 375.1045.
4-(Naphthalen-2-yl)-1-tosyl-1H-1,2,3-triazole (1j)

IR (KBr): 3141, 1389, 1325, 1198, 1175 cm\(^{-1}\); \(^1\)H NMR: \(\delta = 2.43\) (s, 3H), 7.34–7.41 (m, 2H), 7.45–7.55 (m, 2H), 7.79–7.92 (m, 4H), 8.01–8.08 (m, 2H), 8.34–8.38 (m, 1H), 8.43 (s, 1H); \(^{13}\)C NMR: \(\delta = 21.8, 119.1, 123.5, 125.2, 126.1, 126.6, 127.7, 128.2, 128.6, 130.4, 133.0, 133.3, 133.4, 147.3, 147.4\); HRMS (EI\(^+\)): Calcd for C\(_{19}\)H\(_{15}\)N\(_3\)O\(_2\)S, M\(^+\) 349.0885. Found m/z 349.0889.

4-Hexyl-1-tosyl-1H-1,2,3-triazole (1k)

IR (neat): 2930, 1595, 1395, 1194 cm\(^{-1}\); \(^1\)H NMR: \(\delta = 0.87\) (t, \(J = 6.8\) Hz, 3H), 1.21–1.40 (m, 6H), 1.64 (quint, \(J = 7.5\) Hz, 2H), 2.44 (s, 3H), 2.64–2.75 (m, 2H), 7.34–7.40 (m, 2H), 7.82–7.84 (m, 1H), 7.94–8.01 (m, 2H); 13C NMR: \(\delta = 14.0, 21.8, 22.5, 25.4, 28.7, 28.8, 31.4, 120.2, 128.5, 130.3, 133.3, 147.0, 148.3\); HRMS (EI\(^+\)): Calcd for C\(_{15}\)H\(_{21}\)N\(_3\)O\(_2\)S, M\(^+\) 307.1354. Found m/z 307.1344.

**General Procedure for the Nickel-Catalyzed Reaction of 1-Sulfonyl-1,2,3-triazoles with Alkynes.**

In a glove-box, 1 (0.20 mmol) and AlPh\(_3\) (2.6 mg, 10 \(\mu\)mol) were charged into an oven-dried 4 mL vial equipped with a stir bar. A solution of Ni(cod)\(_2\) (5.5 mg, 20 \(\mu\)mol) and P(n-Bu)\(_2\)Ad\(_3\) (14.3 mg, 40 \(\mu\)mol) in toluene (2 mL) and 2 (0.40 mmol) were added, and then the vial capped with a Teflon film was removed from the glove-box. The reaction mixture was heated at 100 °C for 12 h. After this time, the reaction mixture was cooled to room temperature and stirred in open air for 30 min. The resulting mixture was passed through a pad of Florisil and eluted with ethyl acetate. The filtrate was concentrated under reduced pressure. The residue was purified by preparative thin layer chromatography (hexane/dichloromethane) to give the product 3.

**2,3-Dibutyl-4-phenyl-1-tosyl-1H-pyrrole (3a)**

IR (neat): 2957, 1597, 1368, 1175, 1094 cm\(^{-1}\); \(^1\)H NMR: \(\delta = 0.77\) (t, \(J = 7.1\) Hz, 3H), 0.91 (t, \(J = 7.2\) Hz, 3H), 1.10–1.53 (m, 8H), 2.35–2.46 (m, 2H), 2.41 (s, 3H), 2.60–2.70 (m, 2H), 7.24–7.42 (m, 8H), 7.61–7.67 (m, 2H); \(^{13}\)C NMR: \(\delta = 13.7, 13.8, 21.6, 22.6, 22.8, 24.3, 25.3, 32.6, 33.1, 119.3, 125.2, 126.5, 126.7, 128.0, 128.3, 129.8, 132.3, 134.9, 136.8, 144.4\); HRMS (EI\(^+\)): Calcd for C\(_{25}\)H\(_{31}\)NO\(_2\)S, M\(^+\) 409.2075. Found m/z 409.2073.

**2,3-Dibutyl-4-phenyl-1-phenylsulfonyl-1H-pyrrole (3b)**

IR (neat): 2957, 1368, 1175, 1094 cm\(^{-1}\); \(^1\)H NMR: \(\delta = 0.78\) (t, \(J = 7.1\) Hz, 3H), 0.91 (t, \(J = 7.2\) Hz, 3H), 1.10–1.54 (m, 8H), 2.36–2.48 (m, 2H), 2.62–2.72 (m, 2H), 7.26–7.42 (m, 6H), 7.45–7.53 (m, 2H), 7.45–7.53 (m, 2H), 7.45–7.53 (m, 2H).
7.55–7.63 (m, 1H), 7.73–7.80 (m, 2H); $^{13}$C NMR: \( \delta = 13.7, 13.8, 22.6, 22.8, 24.3, 25.3, 32.6, 33.1, 119.4, 125.5, 126.4, 126.8, 128.1, 128.4, 128.6, 129.2, 132.4, 133.4, 134.8, 139.8; \) HRMS (EI$^+$): Calcd for C$_{24}$H$_{25}$NO$_2$S, M$^+$ 395.1919. Found m/z 395.1920.

**2,3-Dibutyl-1-(4-fluorophenylsulfonyl)-4-phenyl-1H-pyrrole (3ca)**

![Diagram of 2,3-Dibutyl-1-(4-fluorophenylsulfonyl)-4-phenyl-1H-pyrrole (3ca)](image)

IR (neat): 2957, 1593, 1495, 1372, 1183, 1092 cm$^{-1}$; $^1$H NMR: \( \delta = 0.78 \) (t, \( J = 7.1 \) Hz, 3H), 0.92 (t, \( J = 7.2 \) Hz, 3H), 1.10–1.56 (m, 8H), 2.35–2.47 (m, 2H), 2.59–2.71 (m, 2H), 7.12–7.22 (m, 2H), 7.25–7.43 (m, 6H), 7.74–7.83 (m, 2H); $^{13}$C NMR: \( \delta = 13.7, 13.8, 22.6, 22.8, 24.3, 25.4, 32.6, 33.2, 116.6 \) (d, \( J = 21.9 \) Hz), 119.3, 125.8, 126.9, 128.1, 128.4, 129.0, 129.3 (d, \( J = 10.4 \) Hz), 132.4, 134.6, 135.8 (d, \( J = 3.5 \) Hz), 165.4 (d, \( J = 254.7 \) Hz); HRMS (EI$^+$): Calcd for C$_{24}$H$_{25}$FNO$_2$S, M$^+$ 413.1825. Found m/z 413.1824.

**2,3-Dibutyl-1-(4-methoxyphenylsulfonyl)-4-phenyl-1H-pyrrole (3da)**

![Diagram of 2,3-Dibutyl-1-(4-methoxyphenylsulfonyl)-4-phenyl-1H-pyrrole (3da)](image)

IR (neat): 2957, 1595, 1499, 1366, 1264, 1167, 1094 cm$^{-1}$; $^1$H NMR: \( \delta = 0.78 \) (t, \( J = 7.1 \) Hz, 3H), 0.91 (t, \( J = 7.1 \) Hz, 3H), 1.11–1.53 (m, 8H), 2.36–2.45 (m, 2H), 2.60–2.70 (m, 2H), 3.85 (s, 3H), 6.90–6.97 (m, 2H), 7.25–7.41 (m, 6H), 7.67–7.74 (m, 2H); $^{13}$C NMR: \( \delta = 13.75, 13.83, 22.6, 22.9, 24.3, 25.3, 32.6, 33.1, 55.7, 114.4, 119.2, 125.2, 126.7, 128.1, 128.3, 128.8, 131.3, 132.2, 134.9, 163.4; \) HRMS (EI$^+$): Calcd for C$_{25}$H$_{31}$NO$_2$S, M$^+$ 425.2025. Found m/z 425.2026.

**2,3-Dibutyl-1-(naphthalen-2-ylsulfonyl)-4-phenyl-1H-pyrrole (3ea)**

![Diagram of 2,3-Dibutyl-1-(naphthalen-2-ylsulfonyl)-4-phenyl-1H-pyrrole (3ea)](image)

IR (neat): 2957, 1366, 1177, 1076 cm$^{-1}$; $^1$H NMR: \( \delta = 0.78 \) (t, \( J = 6.9 \) Hz, 3H), 0.89 (t, \( J = 7.2 \) Hz, 3H), 1.12–1.57 (m, 8H), 2.38–2.49 (m, 2H), 2.68–2.79 (m, 2H), 7.28–7.45 (m, 6H), 7.58–7.74 (m, 3H), 7.85–8.01 (m, 3H), 8.42 (d, \( J = 2.1 \) Hz, 1H); $^{13}$C NMR: \( \delta = 13.7, 13.8, 22.5, 22.8, 24.2, 25.3, 32.5, 33.1, 119.4, 121.4, 125.4, 126.7, 127.7, 127.9, 128.0, 128.1, 128.3, 128.5, 129.2, 129.3, 129.6, 131.9, 132.4, 134.8, 135.0, 136.5; \) HRMS (EI$^+$): Calcd for C$_{28}$H$_{31}$NO$_2$S, M$^+$ 445.2075. Found m/z 445.2076.
2,3-Dibutyl-1-tosyl-4-(4-trimethylphenyl)-1H-pyrrole (3fa)

IR (neat): 2957, 1368, 1175, 1094 cm⁻¹; ¹H NMR: δ = 0.78 (t, J = 7.2 Hz, 3H), 0.90 (t, J = 7.2 Hz, 3H), 1.09–1.52 (m, 8H), 2.32–2.45 (m, 2H), 2.37 (s, 3H), 2.40 (s, 3H), 2.60–2.69 (m, 2H), 7.14–7.20 (m, 2H), 7.22–7.30 (m, 5H), 7.60–7.66 (m, 2H); ¹³C NMR: δ = 13.75, 13.81, 21.1, 21.57, 22.60, 22.8, 24.3, 25.3, 32.6, 33.1, 119.1, 125.3, 126.5, 127.9, 128.3, 129.1, 129.8, 131.9, 132.3, 136.3, 136.9, 144.3; HRMS (EI⁺): Calcd for C₂₆H₃₃NO₃S, M⁺ 423.2232. Found m/z 423.2235.

2,3-Dibutyl-1-tosyl-4-(4-trifluoromethylphenyl)-1H-pyrrole (3ga)

IR (neat): 2959, 1619, 1370, 1325, 1175, 1127, 1073 cm⁻¹; ¹H NMR: δ = 0.79 (t, J = 7.1 Hz, 3H), 0.91 (t, J = 7.2 Hz, 3H), 1.10–1.52 (m, 8H), 2.36–2.48 (m, 2H), 2.42 (s, 3H), 2.61–2.71 (m, 2H), 7.27–7.33 (m, 2H), 7.34 (s, 1H), 7.45–7.52 (m, 2H), 7.60–7.70 (m, 4H); ¹³C NMR: δ = 13.7, 13.8, 21.6, 22.6, 22.8, 24.3, 25.2, 32.7, 33.1, 119.8, 124.3 (q, J = 270.1 Hz), 124.8, 125.3 (q, J = 3.5 Hz), 126.6, 126.9, 128.2, 128.8 (q, J = 31.7 Hz), 129.9, 132.7, 136.6, 138.7, 144.7; HRMS (EI⁺): Calcd for C₂₆H₃₀F₃NO₃S, M⁺ 477.1949. Found m/z 477.1946.

2,3-Dibutyl-4-(4-methoxyphenyl)-1-tosyl-1H-pyrrole (3ha)

IR (neat): 2957, 1539, 1368, 1246, 1173, 1094 cm⁻¹; ¹H NMR: δ = 0.78 (t, J = 7.1 Hz, 3H), 0.90 (t, J = 7.1 Hz, 3H), 1.10–1.52 (m, 8H), 2.32–2.43 (m, 2H), 2.40 (s, 3H), 2.59–2.68 (m, 2H), 3.83 (s, 3H), 6.87–6.95 (m, 2H), 7.22 (s, 1H), 7.23–7.31 (m, 4H), 7.60–7.67 (m, 2H); ¹³C NMR: δ = 13.77, 13.81, 21.6, 22.6, 22.8, 24.3, 25.3, 32.6, 33.1, 55.3, 113.8, 118.9, 125.4, 126.5, 127.3, 128.0, 129.2, 129.8, 132.2, 136.9, 144.3, 158.5; HRMS (EI⁺): Calcd for C₂₆H₃₃NO₃S, M⁺ 439.2181. Found m/z 439.2179.

4-(Biphenyl-4-yl)-2,3-dibutyl-1-tosyl-1H-pyrrole (3ia)

IR (neat): 2957, 1368, 1175, 1094 cm⁻¹; ¹H NMR: δ = 0.82 (t, J = 7.2 Hz, 3H), 0.94 (t, J = 7.2 Hz, 3H), 1.16–1.56 (m, 8H), 2.42 (s, 3H), 2.43–2.52 (m, 2H), 2.64–2.74 (m, 2H), 7.27–7.32 (m, 2H), 7.33–7.40 (m, 2H), 7.43–7.51 (m, 4H), 7.60–7.71 (m, 6H); ¹³C NMR: δ = 13.77, 13.83, 21.6, 22.6, 22.8, 24.4, 25.3, 32.7, 33.1, 119.3, 125.2, 126.6, 126.9, 127.0, 127.2, 127.9, 128.3, 128.7, 129.8, 132.5, 133.9, 136.8, 139.5, 140.7, 144.5; HRMS (EI⁺): Calcd for C₃₁H₅₃NO₃S, M⁺ 485.2389. Found m/z 485.2390.
2,3-Dibutyl-4-(naphthalen-2-yl)-1-tosyl-1H-pyrrole (3ja)

IR (neat): 2957, 1368, 1173, 1094 cm⁻¹; ¹H NMR: δ = 0.78 (t, J = 7.2 Hz, 3H), 0.93 (t, J = 7.2 Hz, 3H), 1.12–1.56 (m, 8H), 2.42 (s, 3H), 2.46–2.56 (m, 2H), 2.65–2.75 (m, 2H), 7.26–7.33 (m, 2H), 7.41 (s, 2H), 7.43–7.56 (m, 3H), 7.65–7.72 (m, 2H), 7.80–7.89 (m, 4H); ¹³C NMR: δ = 13.7, 13.8, 21.6, 22.6, 22.9, 24.4, 25.3, 32.6, 33.1, 119.6, 125.3, 125.6, 126.1, 126.3, 126.60, 126.63, 127.6, 127.8, 127.9, 128.2, 129.8, 132.3, 132.4, 132.5, 133.5, 136.8, 144.5; HRMS (EI⁺): Caled for C₂₀H₃₃NO₅S, M⁺ 459.2232. Found m/z 459.2233.

2,3-Dibutyl-4-hexyl-1-tosyl-1H-pyrrole (3ka)

IR (neat): 2930, 1466, 1368, 1175, 1094, 1065 cm⁻¹; ¹H NMR: δ = 0.78–0.98 (m, 9H), 1.18–1.62 (m, 16H), 2.16–2.35 (m, 4H), 2.38 (s, 3H), 2.51–2.61 (m, 2H), 6.93–6.97 (m, 1H), 7.20–7.27 (m, 2H), 7.52–7.58 (m, 2H); ¹³C NMR: δ = 13.8, 13.9, 14.1, 21.5, 22.65, 22.73, 22.8, 24.2, 25.3, 29.1, 29.2, 31.7, 32.8, 33.2, 118.4, 126.3, 126.5, 127.7, 129.6, 131.8, 137.2, 144.0; HRMS (EI⁺): Caled for C₂₀H₃₅NO₅S, M⁺ 417.2702. Found m/z 417.2702.

4-Phenyl-2,3-dipropyl-1-tosyl-1H-pyrrole (3ab)

IR (neat): 2961, 1368, 1175, 1092 cm⁻¹; ¹H NMR: δ = 0.77 (t, J = 7.4 Hz, 3H), 0.95 (t, J = 7.2 Hz, 3H), 1.21–1.36 (m, 2H), 1.46–1.62 (m, 2H), 2.35–2.46 (m, 2H), 2.41 (s, 3H), 2.59–2.69 (m, 2H), 7.25–7.42 (m, 8H), 7.62–7.68 (m, 2H); ¹³C NMR: δ = 14.0, 14.2, 21.6, 23.6, 24.3, 26.7, 27.5, 119.4, 125.2, 126.5, 126.7, 128.0, 128.3, 129.8, 132.3, 134.9, 136.8, 144.4; HRMS (EI⁺): Caled for C₂₀H₂₇NO₅S, M⁺ 381.1762. Found m/z 381.1758.

2,3,4-Triphenyl-1-tosyl-1H-pyrrole (3ac)

IR (KBr): 1368, 1171, 1103 cm⁻¹; ¹H NMR: δ = 2.38 (s, 3H), 6.83–6.91 (m, 2H), 6.98–7.08 (m, 5H), 7.10–7.34 (m, 12H), 7.65 (s, 1H); ¹³C NMR: δ = 21.6, 119.9, 126.3, 126.6, 126.9, 127.1, 127.5, 127.6, 127.7, 128.2, 128.4, 129.4, 130.2, 130.4, 132.1, 132.6, 133.3, 133.7, 135.7, 144.7; HRMS (EI⁺): Caled for C₂₀H₂₉NO₅S, M⁺ 449.1449. Found m/z 449.1447.
3-Isopropyl-2-methyl-4-phenyl-1-tosyl-1H-pyrrole and
2-Isopropyl-3-methyl-4-phenyl-1-tosyl-1H-pyrrole (3ad mixture)

IR (neat): 2965, 1364, 1173, 1094 cm\(^{-1}\); \(^1\)H NMR: \(\delta = 1.125\) (d, \(J = 7.2\) Hz, 3H), 1.132 (d, \(J = 6.9\) Hz, 3H), 2.10 (s, 1.5H), 2.36 (s, 1.5H), 2.42 (s, 1.5H), 2.43 (s, 1.5H), 2.92 (sept, \(J = 7.2\) Hz, 0.5H), 3.61 (sept, \(J = 7.1\) Hz, 0.5H), 7.23 (s, 0.5H), 7.27–7.44 (m, 7.5H), 7.64–7.74 (m, 2H); \(^{13}\)C NMR: \(\delta = 11.5, 12.0, 21.0, 21.6, 22.4, 25.1, 25.5, 118.2, 118.7, 119.1, 125.8, 126.6, 126.7, 126.8, 126.9, 128.0, 128.2, 128.3, 128.5, 128.8, 129.4, 129.86, 129.89, 130.2, 134.4, 135.2, 136.0, 136.5, 136.9, 144.5; HRMS (EI\(^+\)): Calcd for C\(_{22}\)H\(_{22}\)NO\(_2\), M\(^+\) 353.1449. Found m/z 353.1447.

2-Methyl-4-phenyl-1-tosyl-3-(trimethylsilyl)-1H-pyrrole (3ae (major))

IR (KBr): 2953, 1360, 1173, 1101 cm\(^{-1}\); \(^1\)H NMR: \(\delta = 0.00\) (s, 9H), 2.41 (s, 3H), 2.44 (s, 3H), 7.23–7.37 (m, 8H), 7.71–7.78 (m, 2H); \(^{13}\)C NMR: \(\delta = 1.2, 14.3, 21.7, 120.1, 126.9, 127.1, 127.7, 129.6, 130.0, 133.0, 136.1, 136.4, 136.8, 144.8; HRMS (EI\(^+\)): Calcd for C\(_{22}\)H\(_{22}\)NO\(_2\)Si, M\(^+\) 383.1375. Found m/z 383.1374.

3-Methyl-4-phenyl-1-tosyl-2-(trimethylsilyl)-1H-pyrrole (3ae (minor))

IR (KBr): 2953, 1356, 1169, 1100 cm\(^{-1}\); \(^1\)H NMR: \(\delta = 0.37\) (s, 9H), 2.17 (s, 3H), 2.40 (s, 3H), 7.22–7.42 (m, 7H), 7.42 (s, 1H), 7.49–7.55 (m, 2H); \(^{13}\)C NMR: \(\delta = 2.4, 13.2, 21.6, 125.4, 126.0, 126.9, 128.3, 128.9, 129.6, 131.4, 131.7, 134.0, 134.6, 137.6, 144.1; HRMS (EI\(^+\)): Calcd for C\(_{21}\)H\(_{23}\)NO\(_2\)Si, M\(^+\) 383.1375. Found m/z 383.1371.

3-Methyl-4-phenyl-2-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1-tosyl-1H-pyrrole (3af (major))

IR (neat): 2930, 1374, 1173, 1111 cm\(^{-1}\); \(^1\)H NMR: \(\delta = 0.78\) (t, \(J = 7.4\) Hz, 3H), 1.13–1.39 (m, 4H), 1.39 (s, 12H), 2.40 (s, 3H), 2.53–2.63 (m, 2H), 7.23–7.39 (m, 8H), 7.88–7.94 (m, 2H); \(^{13}\)C NMR: \(\delta = 13.7, 21.6, 22.7, 24.9, 25.6, 33.7, 84.1, 122.6, 126.7, 127.6, 128.3, 129.4, 130.0, 134.4, 136.4, 137.9, 144.3 (The boron-bound carbon was not detected due to the quadrupolar relaxation); HRMS (EI\(^+\)): Calcd for C\(_{21}\)H\(_{23}\)BNO\(_2\), M\(^+\) 479.2302. Found m/z 479.2303.
4-Methyl-4-phenyl-3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1-tosyl-1H-pyrrole (3af (minor))

IR (neat): 2977, 1372, 1306, 1175, 1117 cm⁻¹; ¹H NMR: δ = 0.90 (t, J = 7.2 Hz, 3H), 1.25 (s, 12H), 1.29–1.54 (m, 4H), 2.40 (s, 3H), 2.84–2.94 (m, 2H), 7.21–7.35 (m, 5H), 7.36 (s, 1H), 7.40–7.46 (m, 2H), 7.66–7.72 (m, 2H); ¹³C NMR: δ = 13.8, 21.6, 22.9, 24.7, 27.3, 34.4, 83.2, 119.7, 126.6, 126.9, 127.7, 128.4, 129.9, 131.9, 134.9, 136.5, 144.8, 145.3 (The boron-bound carbon was not detected due to the quadrupolar relaxation); HRMS (EI⁺): Calcd for C₂₇H₃₅BNO₅S, M⁺ 479.2302. Found m/z 479.2303.

Determination of Regiochemistries.
Regiochemistries of the products were determined by nOe experiments. Curved arrows shown below indicate the observed nOe.

[Compound 3ae]
The following results of 3ae (major product) and 3ae (minor product) suggested that the methyl group was bound to C(2) in the major product.

![Diagram of 3ae (major) and 3ae (minor)]

[Compound 3af]
The following results of 3af (major product) and 3af (minor product) suggested that the boryl group was bound to C(2) in the major product.

![Diagram of 3af (major) and 3af (minor)]
References and Notes


(8) Yoo, E. J.; Ahlquist, M.; Kim, S. H.; Bae, I.; Fokin, V. V.; Sharpless, K. B.; Chang, S. Angew. Chem., Int. Ed., 2007, 46, 1730.


Chapter 5

Preparation of 2-Sulfonyl-1,2,3-Triazoles by Base-promoted 1,2-Rearrangement of A Sulfonyl Group

Abstract

1,2-Rearrangement of a sulfonyl group occurs on treatment of 1-sulfonyl-1,2,3-triazoles with a catalytic amount of 4-dimethylaminopyridine (DMAP) in acetonitrile to give an equilibrium mixture of 1-sulfonyl- and 2-sulfonyl derivatives, with considerable predominance of the latter. Subsequent acidic treatment of the mixture caused selective hydrolysis of the 1-sulfonyl derivative, which led to the isolation of the 2-sulfonyl-1,2,3-triazole in good total yield in a pure form.
Introduction

1,2,3-Triazoles are five-membered ring heterocycles containing three nitrogen atoms of mixed hybridized forms in array, and substituted 1,2,3-triazoles constitute an important class of heterocyclic compounds of a variety of utilities, the area of which covers from pharmaceutical chemistry to materials science.\(^1\) The synthesis of \(C,N\)-disubstituted 1,2,3-triazoles often suffers from a regiochemical issue. Thus, it has been the subject of particular interest in current heterocyclic chemistry to prepare them in a desired regiochemical form.\(^2\) The 1,3-dipolar cycloaddition reaction of alkyl (or aryl) azide with terminal alkynes is one of the most reliable procedures for the synthesis of \(C,N\)-disubstituted 1,2,3-triazoles. Either 1,4- or 1,5-disubstituted 1,2,3-triazoles could be regioselectively prepared by the use of copper\(^3\) or ruthenium\(^4\) catalysts, respectively (Figure 1).

\[
\begin{align*}
\text{1,4-disubstituted} & \quad \text{1,5-disubstituted} & \quad \text{2,4-disubstituted} \\
\text{Figure 1. Spacial display of substituent in } C,N\text{-disubstituted 1,2,3-triazoles.}
\end{align*}
\]

However, methods for the synthesis of 2,4-disubstituted 1,2,3-triazoles remain relatively undeveloped.\(^5\)\(^6\) A substitution reaction of 4-substituted 1,2,3-triazoles with electrophiles often produces a mixture of regioisomers, \(i.e.,\) 1,4-disubstituted and 2,4-disubstituted 1,2,3-triazoles.\(^7\) Higher electron density is allocated on the N1 nitrogen atom, which reacts better with an electrophile giving 1,4-disubstituted 1,2,3-triazoles under conditions of kinetic control.\(^8\) On the other hand, 2,4-disubstituted 1,2,3-triazoles experience less steric hindrance than 1,4-disubstituted 1,2,3-triazoles, and therefore, the thermodynamically more stable 2,4-disubstituted 1,2,3-triazoles predominate under conditions of equilibrium control.\(^9\) The thermodynamic preference for 2,4-disubstituted 1,2,3-triazoles was exploited by Fokin and co-workers in the regioselective synthesis of 4-substituted 2-hydroxymethyl-1,2,3-triazoles by a copper-catalyzed cycloaddition reaction of a terminal alkyne with sodium azide in the presence of formaldehyde.\(^10\) During the study on the nickel-catalyzed denitrogenative reaction of 4-substituted 1-sulfonyl-1,2,3-triazoles,\(^11\) the author found that the sulfonyl group underwent rearrangement from the N1 position to the N2 position to give 4-substituted 2-sulfonyl-1,2,3-triazoles,\(^12\) which is the subject of the present communication.
Results and Discussions

4-Phenyl-1-tosyl-1,2,3-triazole (1a) could be readily prepared according to the literature procedure of the copper-catalyzed azide/alkyne cycloaddition.\textsuperscript{13} The 1,2,3-triazole 1a thus obtained was treated with a catalytic amount of 4-dimethylaminopyridine (DMAP, 10 mol%) in MeCN at room temperature for 12 h. An extractive work-up afforded a regioisomeric mixture of 4-phenyl-2-tosyl-1,2,3-triazole (2a) and 1a (2a:1a = 88:12), suggesting that the sulfonyl group migrated from the N1 position to the N2 position (Table 1, entry 1).\textsuperscript{14}

Table 1. Synthesis of 2-sulfonyl-1,2,3-triazoles.\textsuperscript{a}

<table>
<thead>
<tr>
<th>entry</th>
<th>1</th>
<th>R\textsuperscript{1}</th>
<th>R\textsuperscript{2}</th>
<th>N2:N1\textsuperscript{b}</th>
<th>2</th>
<th>yield\textsuperscript{c}</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>1a</td>
<td>4-MeC\textsubscript{6}H\textsubscript{4}</td>
<td>Ph</td>
<td>88:12</td>
<td>2a</td>
<td>82%</td>
</tr>
<tr>
<td>2</td>
<td>1b</td>
<td>4-FC\textsubscript{6}H\textsubscript{4}</td>
<td>Ph</td>
<td>91:9</td>
<td>2b</td>
<td>86%</td>
</tr>
<tr>
<td>3</td>
<td>1c</td>
<td>4-MeOC\textsubscript{6}H\textsubscript{4}</td>
<td>Ph</td>
<td>87:13</td>
<td>2c</td>
<td>73%\textsuperscript{d}</td>
</tr>
<tr>
<td>4</td>
<td>1d</td>
<td>2-Naphthyl</td>
<td>Ph</td>
<td>88:12</td>
<td>2d</td>
<td>80%</td>
</tr>
<tr>
<td>5</td>
<td>1e</td>
<td>n-Bu</td>
<td>Ph</td>
<td>86:14</td>
<td>2e</td>
<td>72%</td>
</tr>
<tr>
<td>6</td>
<td>1f</td>
<td>4-MeC\textsubscript{6}H\textsubscript{4}</td>
<td>4-CF\textsubscript{3}C\textsubscript{6}H\textsubscript{4}</td>
<td>85:15</td>
<td>2f</td>
<td>75%</td>
</tr>
<tr>
<td>7</td>
<td>1g</td>
<td>4-MeC\textsubscript{6}H\textsubscript{4}</td>
<td>4-MeOC\textsubscript{6}H\textsubscript{4}</td>
<td>92:8</td>
<td>2g</td>
<td>86%</td>
</tr>
<tr>
<td>8</td>
<td>1h</td>
<td>4-MeC\textsubscript{6}H\textsubscript{4}</td>
<td>2-Naphthyl</td>
<td>92:8</td>
<td>2h</td>
<td>78%</td>
</tr>
<tr>
<td>9</td>
<td>1l</td>
<td>4-MeC\textsubscript{6}H\textsubscript{4}</td>
<td>1-Cyclohexenyl</td>
<td>89:11</td>
<td>2i</td>
<td>76%\textsuperscript{d}</td>
</tr>
<tr>
<td>10</td>
<td>1j</td>
<td>4-MeC\textsubscript{6}H\textsubscript{4}</td>
<td>n-Hex</td>
<td>90:10</td>
<td>2j</td>
<td>78%\textsuperscript{e}</td>
</tr>
</tbody>
</table>

\textsuperscript{a} Reaction conducted on a 0.5 mmol scale. \textsuperscript{b} Determined by \textsuperscript{1}H NMR analysis. \textsuperscript{c} Isolated yield. \textsuperscript{d} 20 mol % of DMAP was used. \textsuperscript{e} The reaction was carried out with 50 mol % of DMAP at 60 °C, and then the isomeric mixture was heated at 70 °C.

Unfortunately, the regioisomeric mixture failed to be separated with flash column chromatography on silica gel. However, when the isomeric mixture was heated at 60 °C in AcOH/H\textsubscript{2}O (10/1), the N1 sulfonyl group of 1a was selectively hydrolyzed in preference to
the N2 sulfonyle group of 2a. Subsequent chromatographic isolation readily afforded analytically pure 2a in 82% overall yield. The structure of 2a was unambiguously confirmed by X-ray crystallographic analysis.

In order to gain a mechanistic insight, the isolated 2a was subjected to the identical reaction conditions for the rearrangement [DMAP (10 mol%), acetonitrile, room temperature, 12 h] (eq 1). A regioisomeric mixture of 2a and 1a was again formed with the former predominating by 90:10. This result indicated that the sulfonyle group rearrangement was reversible under the reaction conditions and that 2a was the thermodynamically more stable isomer. The author presumes that an N-sulfonyle(p-dimethylaminopyridinium) ion intermediate is involved in the rearrangement process as the intermediate. A computational study at the B3LYP/6-31G* level also suggested that 2a was more stable than 1a by 0.39 kcal/mol.

We examined the rearrangement reaction of 4-phenyl-1,2,3-triazoles 1b–1e having various sulfonyle groups (R1) at the N1 position. Substituted benzenesulfonyle groups as well as a naphthalenesulfonyle group rearranged from the N1 position to the N2 position (Table 1, entries 2–4). Even a butanesulfonyle group successfully participated in the reaction (Table 1, entry 5). Variation of the substituent (R2) at the C4 position was also examined. Aryl- and alkenyl-substituted substrates 1f–1i worked well to afford the corresponding products 2f–2i in yields ranging from 75% to 86% (Table 1, entries 6–9). The reaction of alkyl-substituted triazole 1j required more forcing conditions to afford the product 2j in 78% yield (Table 1, entry 10).

Conclusions

In summary, the author has found a new base-promoted pathway starting from readily accessible 4-substituted 1-sulfonyle-1,2,3-triazoles leading to 4-substituted 2-sulfonyle-1,2,3-triazoles.
Experimental Section

General. Infrared spectra were recorded on a Shimadzu FTIR-8100 spectrometer. $^1$H and $^{13}$C NMR spectra were recorded on a Varian Gemini 2000 ($^1$H at 300 MHz and $^{13}$C at 75 MHz) spectrometer using CDCl$_3$ ($^{13}$C, δ = 77.0) as an internal standard. High-resolution mass spectra were recorded on a JEOL JMS-SX102A (EI) or a JEOL JMS-HX110A (FAB) spectrometer. All reactions were carried out under a nitrogen atmosphere unless otherwise noted. Column chromatography was performed with Wakogel® C-200 (Wako). Preparative thin-layer chromatography was performed with silica gel 60 PF254 (Merck).

Materials. CH$_3$CN was distilled from CaH$_2$. DMAP (nacalai) and AcOH (nacalai) were used as received from the commercial sources. 1-Sulfonyl-1,2,3-triazoles (1a-1j) were prepared according to the literature procedure. 1a, 1e, 1f and 1i have been already reported.$^{13}$ Supplementary Informations of 1b, 1c, 1d, 1g, 1h, and 1j have been reported.$^{11}$

General Procedure for Base-Promoted 1,2-Rearrangement of a Sulfonyl Group. To an oven-dried, Ar-purged flask was added 1a (151 mg, 0.5 mmol), DMAP (6.5 mg, 0.05 mmol), and MeCN (5 mL). The reaction mixture was stirred at room temperature for 12 h, and then concentrated under reduced pressure. The residue was diluted with EtOAc (30 mL). The organic solution was washed with 1 M HCl (10 mL) and brine (10 mL), dried over Na$_2$SO$_4$, and evaporated. The residue was again dissolved in AcOH (5 mL) and brine (10 mL), dried over Na$_2$SO$_4$, and evaporated. The crude product was purified by flash column chromatography (hexane/EtOAc = 5/1) to yield 2a as a white solid (124 mg, 0.41 mmol, 82%).

4-Phenyl-2-tosyl-2H-1,2,3-triazole (2a)

IR (KBr): 1391, 1196, 1163, 1086 cm$^{-1}$; $^1$H NMR: δ = 2.41 (s, 3H), 7.34 (d, $J$ = 8.7 Hz, 2H), 7.39–7.48 (m, 3H), 7.79–7.86 (m, 2H), 7.97–8.03 (m, 2H), 8.08 (s, 1H); $^{13}$C NMR: δ = 21.7, 126.6, 128.2, 128.6, 128.9, 129.9, 130.1, 132.9, 135.6, 146.6, 151.4; HRMS (FAB$^+$): Calcd for C$_{15}$H$_{13}$N$_3$O$_2$S, M+H$^+$ 300.0807. Found m/z 300.0801.

2-(4-Fluorophenylsulfonyl)-4-phenyl-2H-1,2,3-triazole (2b)

IR (KBr): 3065, 1586, 1493, 1402, 1231, 1194, 1084 cm$^{-1}$; $^1$H NMR: δ = 7.18–7.28 (m, 2H), 7.38–7.49 (m, 3H), 7.78–7.86 (m, 2H), 8.10 (s, 1H), 8.12–8.20 (m, 2H); $^{13}$C NMR: δ = 117.0 (d, $J$ = 21.9 Hz), 126.6, 128.0, 129.0, 130.1, 131.7 (d, $J$ = 10.4 Hz), 131.9 (d, $J$ = 3.5 Hz), 136.0, 151.8, 166.5 (d, $J$ = 258.2 Hz); HRMS (EI$^+$): Calcd for C$_{14}$H$_{10}$FN$_3$O$_2$S, M$^+$ 303.0478. Found m/z 303.0482.

2-(4-Methoxyphenylsulfonyl)-4-phenyl-2H-1,2,3-triazole (2c)

IR (KBr): 1593, 1497, 1399, 1271, 1200, 1159, 1090 cm$^{-1}$; $^1$H NMR: δ = 3.83 (s, 3H), 6.94–7.01 (m, 2H), 7.34–7.46 (m, 3H), 7.76–7.84 (m, 2H), 8.01–8.08 (m, 2H), 8.06 (s, 1H); $^{13}$C NMR: δ = 55.8,
Chapter 5

114.7, 126.5, 126.8, 128.2, 128.9, 129.8, 131.0, 135.4, 151.2, 164.8; HRMS (EI\(^{+}\)): Caled for C\(_{16}\)H\(_{13}\)N\(_{3}\)S\(_{2}\), M\(^{+}\) 315.0678. Found m/z 315.0680.

2-(Naphthalen-2-ylsulfonyl)-4-phenyl-2H-1,2,3-triazole (2d)

IR (KBr): 1401, 1186, 1167 cm\(^{-1}\); \(^{1}\)H NMR: \(\delta = 7.36–7.48\) (m, 3H), 7.59–7.73 (m, 2H), 7.78–7.85 (m, 2H), 7.89 (d, \(J = 8.1\) Hz, 1H), 7.94–8.07 (m, 3H), 8.08 (s, 1H), 8.73–8.77 (m, 1H); \(^{13}\)C NMR: \(\delta = 122.3, 126.6, 127.88, 127.94, 128.9, 129.6, 129.8, 129.9, 130.1, 130.9, 131.0, 131.7, 132.5, 135.6, 135.9, 151.5; HRMS (EI\(^{+}\)): Caled for C\(_{16}\)H\(_{13}\)N\(_{3}\)S\(_{2}\), M\(^{+}\) 315.0728. Found m/z 315.0725.

2-Butylsulfonyl-4-phenyl-2H-1,2,3-triazole (2e)

IR (neat): 2965, 1387, 1184 cm\(^{-1}\); \(^{1}\)H NMR: \(\delta = 0.89\) (t, \(J = 7.2\) Hz, 3H), 1.41 (sext, \(J = 7.4\) Hz, 2H), 1.68–1.82 (m, 2H), 3.50–3.60 (m, 2H), 7.40–7.52 (m, 3H), 7.84–7.92 (m, 2H), 8.18 (s, 1H); \(^{13}\)C NMR: \(\delta = 13.3, 21.1, 24.6, 54.3, 126.6, 128.0, 129.0, 130.0, 135.3, 151.3; HRMS (EI\(^{+}\)): Caled for C\(_{16}\)H\(_{13}\)N\(_{3}\)S\(_{2}\), M\(^{+}\) 265.0885. Found m/z 265.0885.

2-Tosyl-(4-(4-trifluoromethylphenyl)-2H-1,2,3-triazole (2f)

IR (KBr): 1401, 1321, 1196, 1161, 1132 cm\(^{-1}\); \(^{1}\)H NMR: \(\delta = 2.43\) (s, 3H), 7.33–7.40 (m, 2H), 7.70 (d, \(J = 8.4\) Hz, 2H), 7.92–7.98 (m, 2H), 7.99–8.05 (m, 2H), 8.12 (s, 1H); \(^{13}\)C NMR: \(\delta = 21.7, 123.7\) (q, \(J = 270.5\) Hz), 125.8 (q, \(J = 3.8\) Hz), 126.9, 128.7, 130.2, 131.5 (q, \(J = 32.7\) Hz), 131.7, 132.5, 135.6; HRMS (EI\(^{+}\)): Caled for C\(_{16}\)H\(_{13}\)F\(_{3}\)N\(_{3}\)O\(_{2}\), M\(^{+}\) 367.0602. Found m/z 367.0603.

4-(4-Methoxyphenyl)-2-tosyl-2H-1,2,3-triazole (2g)

IR (KBr): 1610, 1495, 1393, 1254, 1196, 1161 cm\(^{-1}\); \(^{1}\)H NMR: \(\delta = 2.41\) (s, 3H), 3.84 (s, 3H), 6.91–6.99 (m, 2H), 7.33 (d, \(J = 8.1\) Hz, 2H), 7.72–7.80 (m, 2H), 7.99 (d, \(J = 8.4\) Hz, 2H), 8.01 (s, 1H); \(^{13}\)C NMR: \(\delta = 21.7, 55.3, 114.3, 120.6, 128.1, 128.5, 130.1, 132.9, 135.5, 146.5, 151.4, 160.9; HRMS (EI\(^{+}\)): Caled for C\(_{16}\)H\(_{15}\)N\(_{3}\)O\(_{3}\), M\(^{+}\) 329.0834. Found m/z 329.0834.

4-(Naphthalen-2-yl)-2-tosyl-2H-1,2,3-triazole (2h)

IR (KBr): 1389, 1194, 1161 cm\(^{-1}\); \(^{1}\)H NMR: \(\delta = 2.41\) (s, 3H), 7.35 (d, \(J = 8.4\) Hz, 2H), 7.48–7.56 (m, 2H), 7.80–7.98 (m, 4H), 8.04 (d, \(J = 8.4\) Hz, 2H), 8.21 (s, 1H), 8.30 (s, 1H); \(^{13}\)C NMR: \(\delta = 21.7,
123.7, 125.5, 126.2, 126.7, 127.0, 127.7, 128.3, 128.6, 128.8, 130.1, 132.9, 133.0, 133.8, 135.9, 146.6, 151.5; HRMS (EI\(^+\)): Calcd for C\(_{19}\)H\(_{15}\)N\(_3\)O\(_2\)S, M\(^+\) 349.0885. Found m/z 349.0884.

4-Cyclohexenyl-2-tosyl-2H-1,2,3-triazole (2i)

IR (KBr): 2926, 1395, 1198, 1167 cm\(^{-1}\); \(^1\)H NMR: \(\delta = 1.58–1.78\) (m, 4H), 2.14–2.24 (m, 2H), 2.38–2.47 (m, 2H), 2.41 (s, 3H), 6.41–6.48 (m, 1H), 7.32 (d, \(J = 8.1\) Hz, 2H), 7.81 (s, 1H), 7.90–7.97 (m, 2H); \(^1^3\)C NMR: \(\delta = 21.76, 21.82, 22.0, 25.5, 25.6, 127.2, 128.5, 130.0, 130.6, 133.1, 135.2, 146.2, 153.4\); HRMS (EI\(^+\)): Calcd for C\(_{15}\)H\(_{17}\)N\(_3\)O\(_2\)S, M\(^+\) 303.1041. Found m/z 303.1044.

4-Hexyl-2-tosyl-2H-1,2,3-triazole (2j)

IR (KBr): 2932, 1393, 1198, 1165 cm\(^{-1}\); \(^1\)H NMR: \(\delta = 0.84\) (t, \(J = 6.6\) Hz, 3H), 1.16–1.34 (m, 6H), 1.54–1.69 (m, 2H), 2.41 (s, 3H), 2.68 (t, \(J = 7.8\) Hz, 2H), 7.32 (d, \(J = 8.4\) Hz, 2H), 7.61 (s, 1H), 7.94 (d, \(J = 8.7\) Hz, 2H); \(^1^3\)C NMR: \(\delta = 14.0, 21.7, 22.4, 25.5, 28.4, 28.6, 31.3, 128.4, 130.0, 133.0, 138.0, 146.3, 153.4\); HRMS (EI\(^+\)): Calcd for C\(_{15}\)H\(_{21}\)N\(_3\)O\(_2\)S, M\(^+\) 307.1354. Found m/z 307.1356.

References and Notes


(8) The reaction of 4-phenyl-1,2,3-triazole with TsCl in the presence of NEt$_3$ in CH$_2$Cl$_2$ afforded a mixture of 1-tosyl and 2-tosyl triazoles (80%, 1-tosyl:2-tosyl = 82:18). See also: Horneff, T.; Chuprakov, S.; Chernyak, N.; Gevorgyan, V.; Fokin, V. V. J. Am. Chem. Soc., 2008, 130, 14972.


(14) Other amines such as NEt$_3$, NHEt$_2$, and NEt(i-Pr)$_2$ were also effective for the rearrangement of sulfonyl group.

Chapter 6

Rhodium-Catalyzed Arylative Cyclization Reaction of Diynes with Arylboronic Acids

Abstract

Diynes having malonate-based tethers react with arylboronic acids in the presence of a rhodium(I) catalyst to give 1,2-dialkylidene cycloalkanes. The regioselectivity of the initial carborhodation depends on the sterics and the directing nature of the alkyne substituents.
Introduction

The rhodium(I)-catalyzed carbon–carbon bond-forming reactions using organoboron reagents have been the subject of intensive studies in recent years. An organo-rhodium(I) intermediate generated through transmetalation can undergo carborhodation onto a variety of unsaturated functionalities.\(^1\) It has been demonstrated by the author’s group\(^2\) and others\(^3\) that multiple carborhodation steps can operate sequentially on acceptor compounds possessing two or more unsaturated functionalities to construct cyclic compounds. The author then studied the use of diynes\(^4\) as an acceptor compounds being inspired by the synthetic potential of the resulting 1,2-dialkylidenecycloalkanes. In chapter 6 the author reports the rhodium-catalyzed cyclization reaction of diynes with arylboronic acids, leading to the formation of 1,2-dialkylidenecycloalkanes.

Results and Discussions

1,6-Diyne \(1a\) was treated with phenylboronic acid (\(2a\), 2.0 equiv) in the presence of \([\text{Rh(OH)(cod)}]_2\) (5 mol % Rh, cod = cycloocta-1,5-diene) in dioxane-H\(_2\)O (20:1) at room temperature for 12 h. Chromatographic isolation afforded 1,2-dialkylidenecyclopentane \(3aa\) in 80% yield (Scheme 1). The stereochemistries of the exocyclic double bonds were assigned by a difference NOE study. It is assumed that the reaction is initiated by \(cis\) 1,2-addition of a phenylrhodium(I) species, generated from \(2a\) and rhodium(I) via transmetalation,\(^5\) across the carbon–carbon triple bond in a regioselective manner.\(^6\) The resulting alkenylrhodium(I) intermediate \(A\) then undergoes intramolecular carborhodation onto the other alkyne moiety in a 5-\(exo\)-dig mode to form the dienyllrhodium(I) intermediate \(B\). Finally, protonolysis with H\(_2\)O or \(2a\) yields \(3aa\) with regeneration of hydroxorhodium(I) or rhodium(I) boronate, which engages in the next catalytic cycle.\(^7\) The high regioselectivity of the initial 1,2-addition is to be ascribed not only to the directing effect of the other alkynyl group but also to the difference in steric's between two substituents flanking the carbon–carbon triple bond. The reaction of \(1a\) and phenylboroxine\(^8\) in the presence of dioxane-D\(_2\)O gave \(3aa-d_1\) in 80% yield with incorporation of deuterium at the vinylic position (>86% D), which is consistent with the proposed mechanism.

The results of the reaction of \(1a\) with various arylboronic acids \(2\) are listed in Table 1. The catalytic process worked well with a sterically and electronically diverse array of
arylboronic acids 2b–2j including 3-pyridylboronic acid to give the corresponding products 3ab–3aj in yields ranging from 67% to 90%.

**Scheme 1**

![Scheme 1](image)

**Table 1. Rh(I)-Catalyzed Arylative Cyclization of 1a with Various Arylboronic Acids 2**

<table>
<thead>
<tr>
<th>entry</th>
<th>2</th>
<th>Ar</th>
<th>3</th>
<th>yield (%)&lt;sup&gt;b&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>2b</td>
<td>4-Me-C₆H₄</td>
<td>3ab</td>
<td>76</td>
</tr>
<tr>
<td>2</td>
<td>2c</td>
<td>3-Me-C₆H₄</td>
<td>3ac</td>
<td>77</td>
</tr>
<tr>
<td>3</td>
<td>2d</td>
<td>2-Me-C₆H₄</td>
<td>3ad</td>
<td>84</td>
</tr>
<tr>
<td>4</td>
<td>2e</td>
<td>3-MeO-C₆H₄</td>
<td>3ae</td>
<td>83</td>
</tr>
<tr>
<td>5</td>
<td>2f</td>
<td>2-MeO-C₆H₄</td>
<td>3af</td>
<td>90</td>
</tr>
<tr>
<td>6</td>
<td>2g</td>
<td>4-CF₃-C₆H₄</td>
<td>3ag</td>
<td>84</td>
</tr>
<tr>
<td>7</td>
<td>2h</td>
<td>4-MeO₂C-C₆H₄</td>
<td>3ah</td>
<td>77</td>
</tr>
<tr>
<td>8</td>
<td>2i</td>
<td>3-Br-C₆H₄</td>
<td>3ai</td>
<td>79</td>
</tr>
<tr>
<td>9</td>
<td>2j</td>
<td>3-pyridyl</td>
<td>3aj</td>
<td>67&lt;sup&gt;c&lt;/sup&gt;</td>
</tr>
</tbody>
</table>

<sup>a</sup> Reaction conditions: 1a (0.2 mmol), 2 (0.4 mmol), [Rh(OH)(cod)]₂ (5.0 μmol, 2.5 mol %) in dioxane (2 mL) and H₂O (0.1 mL) at room temperature for 12 h under Ar unless otherwise noted. <sup>b</sup> Isolated yields. <sup>c</sup> 2 (0.6 mmol), [Rh(OH)(cod)]₂ (10 μmol, 5 mol %) at 100 °C.
Next, the use of other symmetrical dyne 1 in the reaction with 2a was examined (Table 2). Primary and secondary alkyl groups were suitable as the substituent at the alkyne termini (entries 1 and 2). The substrates 1e and 1f having sulfonamide and trimethylene tethers, respectively, gave complex mixtures, and the desired products 3ea and 3fa were obtained in low yields (entries 4 and 5). 1,7-Diyne 1g having a malonate-based tether longer by one carbon also underwent the cyclization reaction to give the cyclohexane derivative 3ga in 78% yield (entry 6). It is assumed that facile cyclization occurring with diynes having malonate-based tethers benefits from the Thorpe-Ingold effect.

**Table 2.** Rh(I)-Catalyzed Arylative Cyclization of Various Symmetrical Diynes 1 with 2a

<table>
<thead>
<tr>
<th>entry</th>
<th>1</th>
<th>3</th>
<th>yield (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td></td>
<td></td>
<td>89</td>
</tr>
<tr>
<td>2</td>
<td></td>
<td></td>
<td>90</td>
</tr>
<tr>
<td>3</td>
<td></td>
<td></td>
<td>80</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>entry</th>
<th>1</th>
<th>3</th>
<th>yield (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>4</td>
<td></td>
<td></td>
<td>20</td>
</tr>
<tr>
<td>5</td>
<td></td>
<td></td>
<td>18</td>
</tr>
<tr>
<td>6</td>
<td></td>
<td></td>
<td>78</td>
</tr>
</tbody>
</table>

a Reaction conditions: 1 (0.2 mmol), 2a (0.4 mmol), [Rh(OH)(cod)]2 (5.0 μmol) in dioxane (2 mL) and H2O (0.1 mL) at room temperature for 12 h under Ar unless otherwise noted. b Isolated yields. c [Rh(OH)(cod)]2 (10 μmol). d [Rh(OH)(cod)]2 (10 μmol) at 100 °C. e 2a (0.6 mmol), [Rh(OH)(cod)]2 (10 μmol).

The author also examined the regioselectivity of the arylative cyclization reaction of unsymmetrical 1,6-diyne 4, which possessed a methyl substituent at one alkyne terminus.
With Me/Et-disubstituted substrate 4a, the reaction occurred at room temperature and an almost 1:1 mixture of two regioisomers was formed (entry 1). The regioselectivity improved as the difference in stericity between the two terminal substituents increased, and excellent regioselectivity was observed with the Me/SiMe$_3$-disubstituted substrate 4c (entry 3). Initial carborhodation occurred preferentially or selectively at the sterically more accessible methyl side. Interestingly, opposite regioselectivities were observed with the ROCH$_2$/Me-disubstituted substrates 4d–f (entries 4–6). Coordination of the oxygen atom at the propargylic position directed initial carborhodation to occur at the proximal carbon–carbon triple bond. The minor dienylrhodium(I) intermediates underwent protonolysis rather than β-oxygen elimination, unlike the case with the rhodium-catalyzed cyclization reaction of 1,6-enynes having an oxygen atom at the allylic position. Formation of a cumulated double bond might be disfavored.

Table 3. Rh(I)-Catalyzed Arylative Cyclization of Various Unsymmetrical Diynes 4 with 2a

<table>
<thead>
<tr>
<th>entry</th>
<th>4</th>
<th>R</th>
<th>5</th>
<th>6</th>
<th>yield (%)$^b$</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>4a</td>
<td>Et</td>
<td>5a</td>
<td>6a</td>
<td>85 (57:43)</td>
</tr>
<tr>
<td>2</td>
<td>4b</td>
<td>i-Pr</td>
<td>5b</td>
<td>6b</td>
<td>86 (73:27)</td>
</tr>
<tr>
<td>3</td>
<td>4c</td>
<td>SiMe$_3$</td>
<td>5c</td>
<td>6c</td>
<td>77 (&gt;95:5)</td>
</tr>
<tr>
<td>4</td>
<td>4d</td>
<td>CH$_2$OMe</td>
<td>5d</td>
<td>6d</td>
<td>70 (20:80)</td>
</tr>
<tr>
<td>5</td>
<td>4e</td>
<td>CH$_2$OAc</td>
<td>5e</td>
<td>6e</td>
<td>77 (11:89)</td>
</tr>
<tr>
<td>6</td>
<td>4f</td>
<td>CH$_2$OH</td>
<td>5f</td>
<td>6f</td>
<td>72 (9:91)</td>
</tr>
</tbody>
</table>

$^a$ Reaction conditions: 4 (0.2 mmol), 2a (0.4 mmol), [Rh(OH)(cod)]$_2$ (10 μmol) in dioxane (2 mL) and H$_2$O (0.1 mL) at room temperature for 12 h under Ar. $^b$ Total yield of isomers. Numbers in parentheses describe the ratio of 5:6.

The author then examined the possibility of a cascade-type cyclization process with arylboronate 8 possessing an electron-deficient olefin, developed by Lautens$^{12}$ (Scheme 2). The reaction of unsymmetrical 1,6-diyne 7 with 8 (2.0 equiv) afforded a mixture of 9 (20%)
and 10 (48%). Cyclization through conjugate addition to the electron-deficient olefin took place at two stages of the sequence of carborhodation. The alkenylrhodium(I) intermediate formed by initial carborhodation cyclized in a 5-exo-trig mode giving bicyclic compound 9, and the dienylrhodium(I) intermediate formed by the second carborhodation cyclized in a 7-exo-trig mode giving tricyclic compound 10.

**Scheme 2**

The phenylated 1,2-dialkylidene cyclopentanes are active as the diene for a [4+2]-cycloaddition reaction with dienophiles like dimethyl acetylenedicarboxylate and 4-phenyl-1,2,4-triazoline-3,5-dione (Scheme 3).
Conclusions

In summary, the author has developed a new cyclization reaction of diynes with arylboronic acids in the presence of a rhodium(I) catalyst, allowing the stereoselective formation of arylated 1,2-dialkylidenecycloalkanes.
Experimental Section

**General Methods.** Infrared spectra were recorded on a Shimadzu FTIR-8100 spectrometer. $^1$H and $^{13}$C NMR spectra were recorded on a Varian Gemini 2000 ($^1$H at 300 MHz and $^{13}$C at 75 MHz) spectrometer using CHCl$_3$ ($^1$H, $\delta = 7.26$) and CDCl$_3$ ($^{13}$C, $\delta = 77.0$) as an internal standard. High-resolution mass spectra were recorded on a JEOL JMS-SX102A (EI) or a JEOL JMS-HX110A (FAB) spectrometer. All reactions were carried out under an argon atmosphere unless otherwise noted. Thin-layer chromatography was performed with Merck silica gel 60 PF254. Preparative thin-layer chromatography was performed with silica gel 60 PF254 (Merck).

**Materials.** Dioxane, $p$-xylene, toluene were distilled from sodium/benzophenone ketyl. H$_2$O was degassed by ultrasound before use. [RhOH(cod)$_2$]$_2$ was prepared according to the literature procedure. $^{13}$Dimethyl Acetylenedicarboxylate, 4-Phenyl-1,2,4-triazoline-3,5-dione, and all arylboronic acids were used as received from the commercial sources. Diynes 1a-1e, 1f, 1g, 4a-4h were prepared according to the literature procedure.

**Dimethyl 2,2-bis(but-2-ynyl)malonate (1a)**

IR (KBr): 2951, 2361, 1744, 1439, 1294, 1219, 1055 cm$^{-1}$; $^1$H NMR: $\delta = 1.74$ (t, $J = 2.6$ Hz, 6H), 2.88 (q, $J = 2.5$ Hz, 4H), 3.73 (s, 6H); $^{13}$C NMR: $\delta = 3.5$, 22.9, 52.9, 57.0, 73.0, 79.0, 169.7; HRMS (EI$^+$), M+H$^+$ 237.1127. Found m/z 237.1126.

**Dimethyl 2,2-bis(pent-2-ynyl)malonate (1b)**

IR (neat): 2979, 2238, 1744, 1437, 1218, 1055 cm$^{-1}$; $^1$H NMR: $\delta = 1.08$ (t, $J = 7.5$ Hz, 6H), 2.11 (qt, $J = 7.4$, 2.4 Hz, 4H), 2.91 (t, $J = 2.3$ Hz, 4H), 3.74 (s, 6H); $^{13}$C NMR: $\delta = 12.3$, 14.1, 22.8, 52.7, 57.2, 73.3, 85.0, 169.5; HRMS (EI$^+$), M+H$^+$ 264.1362. Found m/z 264.1359.

**Dimethyl 2,2-bis(4-methylpent-2-ynyl)malonate (1c)**

IR (neat): 2971, 2255, 1744, 1437, 1294, 1211 cm$^{-1}$; $^1$H NMR: $\delta = 1.09$ (d, $J = 6.9$ Hz, 12H), 2.46 (septt, $J = 6.9$, 2.1 Hz, 2H), 2.87 (d, $J = 2.4$ Hz, 4H), 3.72 (s, 6H); $^{13}$C NMR: $\delta = 20.4$, 22.9, 23.2, 52.7, 57.5, 73.4, 89.3, 169.6; HRMS (EI$^+$), M+H$^+$ 292.1675. Found m/z 292.1676.

**5,5-Bis(benzoxyomethyl)- nona-2,7-diyne (1d)**

IR (neat): 2919, 2859, 1455, 1366, 1098 cm$^{-1}$; $^1$H NMR: $\delta = 1.82$ (t, $J = 2.7$ Hz, 6H), 2.42 (q, $J = 2.8$ Hz, 4H), 3.54 (s, 4H), 4.59 (s, 4H), 7.26-7.47 (m, 10H); $^{13}$C NMR: $\delta = 3.53$, 22.3, 42.3, 71.3, 73.1, 75.4, 77.4, 127.15, 127.23, 128.1, 138.7; HRMS (EI$^+$), M+H$^+$ 360.2089. Found m/z 360.2085.
$N,N$-Di(but-2-ynyl)-4-methylbenzenesulphonamide (1e)

IR (KBr): 2923, 2217, 1597, 1348, 1161 cm$^{-1}$; $^1$H NMR: $\delta = 1.64$ (t, $J = 2.4$ Hz, 6H), 2.41(s, 3H), 4.06 (q, $J = 2.1$ Hz, 4H), 7.28 (d, $J = 8.7$ Hz, 2H), 7.71 (d, $J = 8.4$ Hz, 2H); $^{13}$C NMR: $\delta = 3.45, 21.5, 36.6, 71.6, 81.6, 128.0, 129.2, 135.4, 143.4$; HRMS (CI$^-$): Calcd for $C_{13}H_{12}NO_2S$, $M^+$ 275.0980.  Found m/z 275.0977.

Nona-2,7-diyn (1f)

IR (KBr): 2921, 2232, 1435 cm$^{-1}$; $^1$H NMR: $\delta = 1.58$ (quint, $J = 7.0$ Hz, 2H), 1.72 (t, $J = 2.6$ Hz, 6H), 2.10-2.24 (m, 4H); $^{13}$C NMR: $\delta = 3.3, 17.8, 28.4, 75.8, 78.2$; HRMS (EI$^+$): Calcd for $C_{22}H_{30}O_8$, $M^+$ 422.1941.  Found m/z 422.1926.

1,2-Bis(but-2-ynyl)-1,1,2,2-tetraethoxycarbonylethane (1g)

IR (neat): 2984, 2240, 1732, 1368, 1206, 1096, 1040 cm$^{-1}$; $^1$H NMR: $\delta = 1.19$ (t, $J = 7.1$ Hz, 12H), 1.64 (t, $J = 2.6$ Hz, 6H), 2.97 (q, $J = 2.4$ Hz, 4H), 4.04-4.24 (m, 8H); $^{13}$C NMR: $\delta = 3.4, 13.6, 22.4, 61.4, 61.5, 74.3, 77.7, 168.4$; HRMS (CI$^+$): Calcd for $C_{22}H_{30}O_8$, $M^+$ 422.1941.  Found m/z 422.1926.

Dimethyl 2-(but-2-ynyl)-2-(pent-2ynyl)-malonate (4a)

IR (neat): 2955, 2238, 1740, 1435, 1293, 1213, 1055 cm$^{-1}$; $^1$H NMR: $\delta = 1.08$ (t, $J = 7.5$ Hz, 3H), 1.75 (t, $J = 2.7$ Hz, 3H), 2.12 (qt, $J = 7.5, 2.4$ Hz, 2H), 2.86-2.94 (m, 4H), 3.74 (s, 6H); $^{13}$C NMR: $\delta = 3.5, 12.3, 14.1, 22.9, 52.8, 57.1, 73.0, 73.3, 78.9, 85.0, 169.5$; HRMS (EI$^+$): Calcd for $C_{14}H_{16}O_4$, $M^+$ 250.1205.  Found m/z 250.1204.

Dimethyl 2-(but-2-ynyl)-2-(4-methylpent-2ynyl)-malonate (4b)

IR (neat): 2971, 2240, 1744, 1437, 1294, 1213, 1059 cm$^{-1}$; $^1$H NMR: $\delta = 1.10$ (d, $J = 7.2$ Hz, 6H), 1.75 (t, $J = 2.3$ Hz, 3H), 2.47 (septt, $J = 6.9, 2.2$ Hz, 1H), 2.83-2.94 (m, 4H), 3.74 (s, 6H); $^{13}$C NMR: $\delta = 3.4, 20.4, 22.8, 23.1, 52.7, 57.2, 73.1, 73.3, 78.8, 89.3, 169.5$; HRMS (EI$^+$): Calcd for $C_{15}H_{20}O_4$, $M^+$ 264.1362.  Found m/z 264.1360.

Dimethyl 2-(but-2-ynyl)-2-(3-trimethylsilyl-prop-2ynyl)-malonate (4c)

IR (neat): 2957, 2180, 1744, 1437, 1293, 1211, 1030 cm$^{-1}$; $^1$H NMR: $\delta = 0.12$ (s, 9H) 1.75 (t, $J = 2.7$ Hz, 3H), 2.90 (q, $J = 2.5$ Hz, 2H), 2.97 (s, 2H), 3.74 (s, 6H); $^{13}$C NMR: $\delta = -0.0, 3.6, 23.0, 24.0, 52.9, 57.1, 73.0, 79.1, 88.2, 101.0, 169.3$; HRMS (CI$^+$): Calcd for $C_{13}H_{22}O_3Si$, $M^+$ 294.1287.  Found m/z 294.1281.
Chapter 6

Dimethyl 2-(but-2-ynyl)-2-(4-methoxy-but-2-ynyl)malonate (4d)

IR (neat): 2956, 2238, 1740, 1437, 1294, 1213, 1096, 1055 cm$^{-1}$; $^1$H NMR: $\delta$ = 1.74 (t, $J$ = 2.6 Hz, 3H), 2.90 (q, $J$ = 2.4 Hz, 2H), 3.01 (t, $J$ = 2.3 Hz, 2H), 3.32 (s, 3H), 3.74 (s, 6H), 4.04 (t, $J$ = 2.0 Hz, 2H); $^{13}$C NMR: $\delta$ = 3.5, 23.0, 23.1, 53.0, 56.8, 57.3, 59.9, 72.8, 79.0, 79.2, 81.0, 169.4; HRMS (CI$^+$): Calcd for C$_{14}$H$_{18}$O$_5$, M$^+$ 266.1154.  Found m/z 266.1154.

Dimethyl 2-(but-2-ynyl)-2-(4-acetoxy-but-2-ynyl)malonate (4e)

IR (neat): 2957, 2242, 1740, 1437, 1294, 1217, 1055, 1028 cm$^{-1}$; $^1$H NMR: $\delta$ = 1.75 (d, $J$ = 2.6 Hz, 3H), 2.08 (s, 3H), 2.89 (q, $J$ = 2.6 Hz, 2H), 3.01 (t, $J$ = 2.3 Hz, 2H), 3.75 (s, 6H), 4.62 (t, $J$ = 2.3 Hz, 2H); $^{13}$C NMR: $\delta$ = 3.2, 20.5, 22.7, 22.8, 52.1, 52.8, 56.5, 72.6, 7 7.1, 79.1, 81.2, 169.0, 169.8; HRMS (EI$^+$): Calcd for C$_{15}$H$_{18}$O$_6$, M$^+$ 294.1103.  Found m/z 294.1097.

Dimethyl 2-(but-2-ynyl)-2-(4-hydroxy-but-2-ynyl)malonate (4f)

IR (neat): 3436, 2957, 2236, 1740, 1437, 1294, 1215, 1055, 1028 cm$^{-1}$; $^1$H NMR: $\delta$ = 1.54 (t, $J$ = 5.9 Hz, 1H), 1.75 (t, $J$ = 2.7 Hz, 3H), 2.90 (q, $J$= 2.5 Hz, 2H), 3.01 (t, $J$ = 2.3 Hz, 2H), 3.71 (s, 6H), 4.21 (dt, $J$ = 6.3, 2.2 Hz, 2H); $^{13}$C NMR: $\delta$ = 3.5, 22.9, 23.0, 51.1, 53.0, 56.8, 72.8, 79.3, 80.2, 81.7, 169.5; HRMS (CI$^+$): Calcd for C$_{13}$H$_{16}$O$_5$, M$^+$ 252.0998.  Found m/z 252.0997.

General Procedure for the Cyclization Reaction of 1a with 2. To an oven-dried, Ar-purged flask was added [Rh(OH)(cod)$_2$] (2.3 mg, 0.5 µmol, 5 mol% Rh), 1a (47.3 mg, 0.2 mmol), and 2 (0.4 mmol) in THF (2.0 mL)/H$_2$O (0.1 mL). The reaction mixture was stirred at room temperature for 12 h, and quenched with addition of water (5 mL). The aqueous layer was extracted with ethyl acetate (5 x 6 mL). The combined extracts were washed with brine and dried over MgSO$_4$. The solvent was removed under reduced pressure and the residue was purified by preparative thin-layer chromatography (hexane:ethyl acetate) to give 3.

(3E,4Z)-1,1-Dimethoxycarbonyl-3-ethylidene-4-(1-phenylethylidene)cyclopentane (3aa)

The 3E,4Z configuration of the double bonds were confirmed on the basis of the observed NOE. IR (KBr): 2951, 1736, 1437, 1289, 1258, 1202, 1159 cm$^{-1}$; $^1$H NMR: $\delta$ =1.41 (d, $J$ = 3.6 Hz, 3H) 2.00 (s, 3H), 2.95 (s, 2H), 3.10 (s, 2H), 3.76 (s, 6H), 4.76 (qt, $J$ = 7.1, 2.4 Hz, 1H), 7.10–7.16 (m, 2H), 7.16–7.24 (m, 1H), 7.25–7.34 (m, 2H); $^{13}$C NMR: $\delta$ = 15.2, 23.4, 38.1, 39.9, 52.8, 56.9, 121.1, 126.3, 127.9, 128.5, 130.2, 132.0, 136.0, 144.4, 172.1; HRMS (CI$^+$): Calcd for C$_{19}$H$_{22}$O$_4$, M$^+$ 314.1518.  Found m/z 314.1517.
(3E,4Z)-1,1-Dimethoxycarbonyl-3-ethylidene-4-(1-(4-methylphenyl)ethylidene)-cyclopentane
(3ab)

IR (neat): 2953, 1738, 1435, 1256, 1204, 1165, 1061 cm\(^{-1}\); \(^1\)H NMR: \(\delta = 1.43 \ (d, J = 6.9 \ Hz, 3H), 1.98 \ (s, 3H), 2.33 \ (s, 3H), 2.96 \ (s, 2H), 3.10 \ (s, 2H), 3.76 \ (s, 6H), 4.84 \ (q, J = 7.0 \ Hz, 1H), 7.04 \ (d, J = 7.8 \ Hz, 2H), 7.10 \ (d, J = 8.1 \ Hz, 2H); \(^{13}\)C NMR: \(\delta = 15.1, 21.2, 24.1, 38.1, 40.0, 52.8, 56.9, 120.9, 127.7, 129.2, 130.2, 131.8, 135.8, 136.1, 141.4, 172.2; HRMS (CI\(^+\)): C\(_{20}\)H\(_{24}\)O\(_4\), M\(^+\) 328.1675. Found m/z 328.1672.

(3E,4Z)-1,1-Dimethoxycarbonyl-3-ethylidene-4-(1-(3-methylphenyl)ethylidene)-cyclopentane
(3ac)

IR (neat): 2953, 1738, 1435, 1260, 1204, 1165, 1061 cm\(^{-1}\); \(^1\)H NMR: \(\delta = 1.42 \ (d, J = 6.9 \ Hz, 3H), 1.99 \ (s, 3H), 2.32 \ (s, 3H), 2.96 \ (s, 2H), 3.10 \ (s, 2H), 3.76 \ (s, 6H), 4.79 \ (qt, J = 7.0, 2.4 \ Hz, 1H), 6.90–6.97 \ (m, 2H), 7.00–7.06 \ (m, 1H), 7.21 \ (t, J = 7.5 \ Hz, 1H); \(^{13}\)C NMR: \(\delta = 15.2, 21.4, 24.0, 38.1, 39.9, 52.8, 56.9, 120.9, 124.8, 127.0, 128.4, 130.4, 131.7, 136.0, 138.0, 144.4, 172.2; HRMS (EI\(^+\)): Calcd for C\(_{20}\)H\(_{24}\)O\(_4\), M\(^+\) 328.1671. Found m/z 328.1671.

(3E,4Z)-1,1-Dimethoxycarbonyl-3-ethylidene-4-(1-(2-methylphenyl)ethylidene)-cyclopentane
(3ad)

IR (neat): 2953, 1738, 1435, 1260, 1206, 1165, 1061 cm\(^{-1}\); \(^1\)H NMR: \(\delta = 1.40 \ (d, J = 7.2 \ Hz, 3H), 1.95 \ (s, 3H), 2.10 \ (d, J = 16.5 \ Hz, 1H), 3.00 \ (d, J = 16.2 \ Hz, 1H), 3.08 \ (d, J = 15.3 \ Hz, 1H), 3.19 \ (d, J = 15.9 \ Hz, 1H), 3.75 \ (s, 3H), 3.76 \ (s, 3H), 4.55 \ (qt, J = 7.2, 2.3 \ Hz, 1H), 6.93–7.00 \ (m, 1H), 7.09–7.20 \ (m, 3H); \(^{13}\)C NMR: \(\delta = 15.4, 18.9, 23.3, 38.3, 39.8, 52.8, 56.9, 119.7, 126.2, 126.5, 127.5, 129.3, 130.1, 131.8, 134.5, 136.4, 143.6, 172.098, 172.144; HRMS (CI\(^+\)): Calcd for C\(_{20}\)H\(_{24}\)O\(_4\), M\(^+\) 328.1675. Found m/z 328.1675.

(3E,4Z)-1,1-Dimethoxycarbonyl-3-ethylidene-4-(1-(3-methoxyphenyl)ethylidene)-cyclopentane
(3ae)

IR (neat): 2953, 1738, 1576, 1483, 1435, 1291, 1262, 1233, 1209, 1167 cm\(^{-1}\); \(^1\)H NMR: \(\delta = 1.42 \ (d, J = 6.9 \ Hz, 3H), 1.98 \ (s, 3H), 2.95 \ (s, 2H), 3.10 \ (s, 2H), 3.75 \ (s, 6H), 3.77 \ (s, 3H), 4.84 \ (qt, J = 7.0, 2.3 \ Hz, 1H), 6.64–6.80 \ (m, 3H), 7.21 \ (t, J = 7.8 \ Hz, 1H); \(^{13}\)C NMR: \(\delta = 15.2, 23.9, 38.1, 39.9, 52.8, 55.1, 56.9,
111.8, 113.2, 120.2, 121.2, 129.5, 129.9, 132.0, 135.8, 145.9, 159.7, 172.1; HRMS (Cl+): Calcd for C20H24O5, M+ 344.1624. Found m/z 344.1623.

\((3E,4Z)\)-1,1-Dimethoxycarbonyl-3-ethylidene-4-(1-((2-methoxyphenyl)ethylidene)-cyclopentane (3af)

\[
\text{IR (neat): 2953, 1736, 1489, 1435, 1253, 1204, 1163, 1061 cm}^{-1}; \quad \text{^1H NMR: } \delta = 1.41 (d, J = 7.2 \text{ Hz}, 3H), 1.96 (s, 3H), 2.92 (d, J = 17.4 Hz, 1H), 2.98 (d, J = 16.2 Hz, 1H), 3.08 (d, J = 15.9 Hz, 1H), 3.18 (d, J = 15.9 Hz, 1H), 3.75 (s, 3H), 3.76 (s, 3H), 3.77 (s, 3H); HRMS (Cl+): Calcd for C20H24O5, M+ 344.1624. Found m/z 344.1623.
\]

\((3E,4Z)\)-1,1-Dimethoxycarbonyl-3-ethylidene-4-(1-((4-trifluoromethylphenyl)ethylidene)-cyclopentane (3ag)

\[
\text{IR (neat): 2955, 1740, 1615, 1437, 1325, 1260, 1165, 1125, 1067 cm}^{-1}; \quad \text{^1H NMR: } \delta = 1.42 (d, J = 6.9 \text{ Hz}, 3H), 1.99 (s, 3H), 2.95 (s, 2H), 3.10 (s, 2H), 3.76 (s, 6H); HRMS (Cl+): Calcd for C20H21O4F3, M+ 382.1392. Found m/z 382.1397.
\]

\((3E,4Z)\)-1,1-Dimethoxycarbonyl-3-ethylidene-4-(1-((4-methoxycarbonylphenyl)ethylidene)-cyclopentane (3ah)

\[
\text{IR (neat): 2953, 1738, 1605, 1435, 1283, 1204, 1177, 1113, 1061 cm}^{-1}; \quad \text{^1H NMR: } \delta = 1.38 (d, J = 6.9 \text{ Hz}, 3H), 1.98 (s, 3H), 2.94 (s, 2H), 3.09 (s, 2H), 3.75 (s, 6H); HRMS (Cl+): Calcd for C21H24O6, M+ 372.1573. Found m/z 372.1568.
\]

\((3E,4Z)\)-1,1-Dimethoxycarbonyl-3-ethylidene-4-(1-((3-bromophenyl)ethylidene)-cyclopentane (3ai)

\[
\text{IR (neat): 2953, 1738, 1605, 1435, 1283, 1204, 1177, 1113, 1061 cm}^{-1}; \quad \text{HRMS (Cl+): Calcd for C21H24O6, M+ 372.1573. Found m/z 372.1568.}
\]
(3E,4Z)-1,1-Dimethoxycarbonyl-3-ethylidene-4-(1-(3-pyridyl)ethylidene)-cyclopentane (3aj)

IR (neat): 2953, 1738, 1590, 1557, 1435, 1260, 1204, 1165, 1061 cm⁻¹; ¹H NMR: δ = 1.43 (d, J = 6.9 Hz, 3H), 1.97 (s, 3H), 2.95 (s, 2H), 3.08 (s, 2H), 3.26 (s, 6H), 4.81 (qt, J = 4.8, 2.4 Hz, 1H), 7.03–7.09 (m, 1H), 7.16 (t, J = 7.8 Hz, 1H), 7.27–7.37 (m, 2H); ¹³C NMR: δ = 15.3, 23.7, 38.0, 39.8, 52.8, 56.8, 121.9, 122.4, 126.7, 128.5, 129.4, 130.1, 130.9, 133.0, 135.8, 146.5, 172.0; HRMS (CI⁺): Calcd for C₁₈H₂₁BrO₄, M⁺ 392.0623. Found m/z 392.0618.

(3Z,4E)-1,1-Dimethoxycarbonyl-3-(1-phenylpropyldiene)-4-propyldenedecyclopentane (3ba)

IR (neat): 2963, 1738, 1435, 1260, 1204, 1069 cm⁻¹; ¹H NMR: δ = 0.63 (t, J = 7.5 Hz, 3H), 0.89 (t, J = 7.5 Hz, 3H), 1.75 (quint, J = 7.5 Hz, 2H), 2.32 (q, J = 7.5, 2H), 2.91 (s, 2H), 3.09 (s, 2H), 3.73 (s, 6H), 4.56 (tt, J = 7.2, 2.4 Hz, 1H), 7.02–7.11 (m, 2H), 7.15–7.22 (m, 1H), 7.25–7.32 (m, 2H); ¹³C NMR: δ = 11.8, 13.4, 22.9, 30.4, 37.7, 39.1, 52.7, 57.1, 126.2, 128.3, 128.5, 129.1, 131.6, 134.3, 136.8, 142.8, 172.0; HRMS (EI⁺): Calcd for C₁₈H₂₁NO₄, M⁺ 315.1471. Found m/z 315.1474.

(3Z,4E)-1,1-Dimethoxycarbonyl-3-(2-methyl-1-phenylpropyldiene)-4-(2-methylpropylidene)cyclopentane (3ca)

IR (neat): 2957, 1732, 1435, 1256, 1204, 1171, 1075 cm⁻¹; ¹H NMR: δ = 0.58 (d, J = 6.6 Hz, 6H), 0.93 (d, J = 6.9 Hz, 6H), 2.13 (dsept, J = 9.3, 6.6 Hz, 1H), 2.88 (sept, J = 7.0 Hz, 1H), 2.90 (d, J = 2.1 Hz, 2H), 3.14 (s, 2H), 3.74 (s, 6H), 4.1 (dt, J = 9.3, 2.2 Hz, 1H), 6.93–7.00 (m, 2H), 7.17–7.33 (m, 3H); ¹³C NMR: δ = 20.8, 22.2, 28.9, 32.8, 37.8, 38.7, 52.7, 57.1, 126.1, 127.9, 129.5, 131.2, 132.6, 135.2, 140.1, 140.6, 172.1; HRMS (EI⁺): Calcd for C₂₂H₂₆O₅, M⁺ 370.2144. Found m/z 370.2145.

(3E,4Z)-1,1-Bis (benzoxyethylidene)-3-ethylidene-4-(1-phenylethylidene)cyclopentane 3da

IR (neat): 2853, 1740, 1597, 1455, 1362, 1102, 1028 cm⁻¹; ¹H NMR: δ = 1.42 (d, J = 6.9 Hz, 3H), 2.02 (s, 3H), 2.35 (s, 2H), 2.50 (s, 2H), 3.50 (s, 4H), 4.60 (s, 4H), 4.78 (qt, J = 7.0, 2.5 Hz, 1H), 7.10–7.20...
(3Z,4E)-3-Ethylidene-4-(1-phenylethylidene)-1-tosylpyrrolidine (3ea)

IR (neat): 2957, 1738, 1435, 1258, 1204, 1165, 1067 cm\(^{-1}\); \(^1\)H NMR: \(\delta = 1.22-1.32\) (m, 15H), 2.02 (s, 3H), 3.05 (s, 2H), 3.11 (s, 2H), 4.14–4.28 (m, 8H), 4.89 (q, J = 7.0 Hz, 1H), 7.06–7.14 (m, 3H), 7.14–7.25 (m, 2H); \(^1^3\)C NMR: \(\delta = 13.3, 13.8, 13.9, 20.7, 32.5, 34.1, 59.7, 60.1, 61.6, 125.6, 127.4, 127.6, 128.3, 132.4, 132.5, 132.7, 145.3, 169.7; HRMS (EI\(^+\)): Calcd for C\(_{38}\)H\(_{36}\)O\(_6\), M\(^+\) 500.2410. Found m/z 498.2405.

(3Z,4E)-1,1-Dimethoxycarbonyl-3-(1-phenylethylidene)-4-propyldenedicyclopentane (5a) and (3Z,4E)-1,1-Dimethoxycarbonyl-3-(1-phenylpropylidene)-4-ethyldenedicyclopentane (6a)

IR (neat): 2957, 1738, 1435, 1258, 1204, 1165, 1067 cm\(^{-1}\); \(^1\)H NMR: \(\delta = 0.67\) (t, J = 7.5 Hz, 1.71H), 0.91 (t, J = 7.5 Hz, 1.29H), 1.39 (d, J = 6.9 Hz, 1.29H), 1.80 (quint, J = 7.4 Hz, 1.14H), 2.01 (s, 1.71H), 3.34 (q, J = 7.5 Hz, 0.86H), 2.95 (s, 2H), 3.03–3.17 (m, 2H), 3.755 (s, 3.42H), 3.764 (s, 2H), 3.766 (s, 1H), 3.768 (s, 1H), 3.769 (s, 1H), 4.70 (dt, 1H); \(^1^3\)C NMR: \(\delta = 13.3, 13.8, 13.9, 20.7, 32.5, 34.1, 59.7, 60.1, 61.6, 125.6, 127.4, 127.6, 128.3, 132.4, 132.5, 132.7, 145.3, 169.7; HRMS (EI\(^+\)): Calcd for C\(_{38}\)H\(_{36}\)O\(_6\), M\(^+\) 500.2410. Found m/z 500.2405.
(3Z,4E)-1,1-Dimethoxycarbonyl-3-(1-phenylethylidene)-4-(2-methylpropylidene)cyclopentane (5b) and
(3Z,4E)-1,1-Dimethoxycarbonyl-3-(2-methyl-1-phenylpropylidene)-4-ethylidenecyclopentane (6b)

IR (neat): 2955, 1738, 1435, 1256, 1204, 1173, 1067 cm⁻¹; ¹H NMR: δ = 0.65 (d, J = 6.6 Hz, 4.38 H), 0.91 (d, J = 6.6 Hz, 1.62H), 1.35 (dt, J = 6.9, 1.5 Hz, 0.81H), 2.00 (s, 2.19H), 2.21 (dsept, J = 9.3, 6.5 Hz, 0.73H), 2.83-2.97 (m, 2.27H), 3.09 (d, J = 1.2 Hz, 1.46H), 3.17 (s, 0.54H), 4.37–4.51 (m, 1H), 6.94–7.36 (m, 5H); ¹³C NMR: δ = 15.4, 20.9, 22.2, 23.5, 29.0, 32.9, 37.8, 38.2, 39.2, 39.5, 52.8, 56.9, 57.2, 121.3, 126.3, 128.1, 128.3, 129.4, 130.4, 130.9, 132.4, 132.5, 134.9, 136.4, 140.0, 140.4, 144.3, 172.1; HRMS (EI⁺): Calcd for C₂₃H₂₆O₄, M⁺ 328.1675. Found m/z 328.1671.

(3Z,4E)-1,1-Dimethoxycarbonyl-3-(1-phenylethylidene)-4-(trimethylsilylmethylene)cyclopentane (5c)

IR (KBr): 2955, 2361, 1734, 1595, 1431, 1296, 1260, 1069 cm⁻¹; ¹H NMR: δ = -0.1 (s, 9H), 2.02 (s, 3H), 3.00 (d, J = 1.8 Hz, 2H), 3.11 (d, J = 1.2 Hz, 2H), 3.76 (s, 6H), 4.80 (s, 1H), 7.06–7.32 (m, 5H); ¹³C NMR: δ = -0.6, 24.1, 39.0, 42.0, 52.8, 57.1, 125.7, 126.4, 127.8, 128.4, 133.2, 133.5, 143.8, 150.5, 172.0; HRMS (EI⁺): Calcd for C₂₃H₂₆O₄Si, M⁺ 372.1757. Found m/z 372.1764.

(3Z,4E)-1,1-Dimethoxycarbonyl-3-(1-phenylethylidene)-4-(2-methoxyethylidene)cyclopentane (5d) and
(3Z,4E)-1,1-Dimethoxycarbonyl-3-(2-methoxy-1-phenylethylidene)-4-ethylidenecyclopentane (6d)

IR (neat): 2953, 1738, 1435, 1258, 1204, 1167, 1096 cm⁻¹; ¹H NMR(C₆D₆): δ = 1.27 (d, J = 7.2 Hz, 2.4H), 1.87 (s, 0.6H), 2.93 (s, 0.6H), 3.08 (s, 2.4H), 3.11 (s, 1.6H), 3.16 (s, 0.4H), 3.25 (s, 0.4H), 3.34 (s, 6H), 3.42 (s, 1.6H), 3.67 (d, J = 6.6 Hz, 0.4H), 4.07 (s, 1.6H), 5.13–5.25 (m, 1H), 6.98–7.23 (m, 4H), 7.25–7.34 (m, 1H); ¹³C NMR: δ = 15.3, 24.2, 37.5, 38.2, 39.4, 39.5, 52.9, 56.9, 57.0, 57.4, 57.5, 69.9, 75.1, 122.5, 123.9, 126.7, 127.6, 128.4, 128.5, 128.7, 130.7, 131.6, 133.0, 135.8, 137.2, 138.4,
141.4, 143.9, 171.9; HRMS (EI\(^+\)): Calcd for C\(_{20}\)H\(_{24}\)O\(_{3}\), M\(^+\) 344.1624. Found m/z 344.1623. (5d), 344.1623. (6d)

\((3Z,4E)-1,1\)-Dimethoxycarbonyl-3-(1-phenylethylidene)-4-(2-acetoxyethylidene)cyclopentane (5e) and \((3Z,4E)-1,1\)-Dimethoxycarbonyl-3-(2-acetoxy-1-phenylethylidene)-4-ethylidenedecyclopentane (6e)

IR (neat): 2955, 1748, 1734, 1435, 1377, 1293, 1167, 1065, 1022 cm\(^{-1}\); \(^1\)H NMR: \(\delta = 1.43\) (d, \(J = 7.2\) Hz, 2.67H), 1.93 (s, 0.33H), 1.96 (s, 2.67H), 2.03 (s, 0.33H), 2.95 (s, 1.78H), 3.04 (s, 0.22H), 3.12 (s, 0.22H), 3.23 (s, 1.78H), 3.77 (s, 6H), 4.34 (d, \(J = 7.2\) Hz, 0.22H), 4.74 (t, \(J = 7.1\) Hz, 0.11H), 4.80 (s, 1.78H), 4.92 (qt, \(J = 7.1, 2.5\) Hz, 0.89H), 7.09–7.37 (m, 5H); \(^{13}\)C NMR: \(\delta = 15.4, 20.88, 20.93, 24.2, 37.6, 38.1, 39.4, 52.9, 56.9, 62.2, 67.1, 119.4, 124.6, 126.7, 127.0, 127.6, 128.4, 128.58, 128.61, 131.5, 134.0, 135.7, 138.1, 140.2, 140.5, 143.6, 170.8, 171.8; HRMS (EI\(^+\)): Calcd for C\(_{21}\)H\(_{26}\)O\(_{6}\), M\(^+\) 372.1573. Found m/z 372.1570.

\((3Z,4E)-1,1\)-Dimethoxycarbonyl-3-(1-phenylethylidene)-4-(2-hydroxyethylidene)cyclopentane (5f) and \((3Z,4E)-1,1\)-Dimethoxycarbonyl-3-(2-hydroxy-1-phenylethylidene)-4-ethylidenedecyclopentane (6f)

IR (neat): 3487, 2955, 1732, 1435, 1260, 1206, 1167, 1063 cm\(^{-1}\); \(^1\)H NMR: \(\delta = 1.41\) (d, \(J = 6.9\) Hz, 2.73H), 1.74–1.91 (m, 1H), 2.01 (s, 0.27H), 2.95 (s, 2H), 3.12 (s, 0.18H), 3.16 (s, 1.82H), 3.75 (s, 6H), 3.89 (d, \(J = 7.2\) Hz, 0.18H), 4.33 (s, 1.82H), 4.83–4.96 (m, 1H), 7.09–7.37 (m, 5H); \(^{13}\)C NMR: \(\delta = 15.3, 24.1, 37.6, 38.1, 39.2, 39.3, 52.9, 56.9, 60.4, 65.7, 123.7, 124.5, 126.7, 127.0, 127.6, 128.68, 128.72, 131.5, 133.1, 135.5, 135.6, 138.3, 140.5, 143.8, 171.9; HRMS (CI\(^-\)): Calcd for C\(_{19}\)H\(_{24}\)O\(_{6}\), M\(^-\) 330.1467. Found m/z 330.1465.

4,4-Bis(benzoxyethyl)-1-trimethylsilylocta-1,6-diyne (7)

IR (neat): 2861, 2174, 1455, 1366, 1250, 1096 cm\(^{-1}\); \(^1\)H NMR: \(\delta = 0.14\) (s, 9H), 1.76 (t, \(J = 2.7\) Hz, 3H), 2.36 (q, \(J = 2.4\) Hz, 2H), 2.45 (s, 2H), 3.49 (s, 4H), 4.53 (s, 4H), 7.23–7.41 (m, 10H); \(^{13}\)C NMR: \(\delta = 0.3, 3.6, 22.4, 23.5, 42.3, 71.4, 73.3, 75.3, 77.6, 86.7, 104.0, 127.3, 128.2, 138.7 (1 carbon missing); HRMS (CI\(^+\)): Calcd for C\(_{27}\)H\(_{34}\)O\(_{2}\)Si, M\(^+\) 418.2328. Found m/z 418.2330.
Chapter 6

2-(2,2-Bis(benzyloxy)methyl)-5-trimethylsilylpent-4-ynyl)-1-(2-Oxypropyl)-3-methyl-1H-indene (9)

IR (neat): 2861, 2174, 1717, 1455, 1362, 1250, 1098 cm⁻¹; ¹H NMR: δ = 0.14 (s, 9H), 1.88 (s, 3H), 2.09 (d, J = 1.7 Hz, 3H), 2.18 (dd, J = 17.3, 10.5 Hz, 1H), 2.35 (d, J = 14.1 Hz, 1H), 2.37 (d, J = 16.5 Hz, 1H), 2.44 (d, J = 16.7 Hz, 1H), 2.79 (d, J = 14.1 Hz, 1H), 3.07 (dd, J = 17.3, 2.8 Hz, 1H), 3.30 (d, J = 8.9 Hz, 1H), 3.43 (d, J = 8.9 Hz, 1H), 3.50 (d, J = 8.9 Hz, 1H), 3.93 (d, J = 10.5 Hz, 1H), 7.08–7.12 (m, 1H), 7.21–7.40 (m, 13H); ¹³C NMR: δ = 0.1, 11.0, 24.6, 27.7, 30.3, 44.1, 45.1, 46.8, 71.8, 72.4, 73.21, 73.25, 87.0, 104.5, 118.5, 123.2, 124.5, 126.6, 127.28, 127.32, 127.33, 127.34, 128.23, 128.25, 136.8, 138.6, 138.7, 140.6, 145.5, 147.3, 207.9; HRMS (CI⁺): Calcd for C₃₇H₄₄O₃Si, M⁺ 564.3060. Found m/z 564.3058.

2,2-Bis(benzyloxy)methyl)-4-methyl-9-(2-oxopropyl)-10-trimethylsilyl-1,2,3,9-tetrahydro-benzof[fl]azulene (10)

IR (neat): 2855, 1715, 1455, 1362, 1246, 1102 cm⁻¹; ¹H NMR (600 Hz): δ = 0.23 (s, 9H), 1.85 (s, 3H), 2.276 (d, J = 14.3 Hz, 1H), 2.279 (s, 3H), 2.49 (d, J = 7.2 Hz, 2H), 2.52 (d, J = 17.2 Hz, 1H), 2.58 (d, J = 14.1 Hz, 1H), 2.59 (d, J = 17.9 Hz, 1H), 3.32 (d, J = 8.8 Hz, 2H), 3.42 (d, J = 8.8 Hz, 1H), 3.46 (d, J = 8.9 Hz, 1H), 3.57 (d, J = 8.8 Hz, 1H), 4.20 (t, J = 7.1 Hz, 1H), 4.47 (d, J = 12.2 Hz, 1H), 4.54 (d, J = 12.4 Hz, 1H), 4.56 (d, J = 12.0 Hz, 1H), 4.57 (d, J = 12.4 Hz, 1H), 7.14–7.17 (m, 1H), 7.22–7.37 (m, 12H), 7.46–7.49 (m, 1H); ¹³C NMR: δ = 0.1, 20.6, 30.5, 38.7, 39.9, 42.7, 43.4, 44.6, 72.4, 73.2, 73.3, 74.2, 125.7, 126.0, 127.39, 127.43, 127.44, 127.5, 128.1, 128.26, 128.27, 128.7, 132.7, 137.5, 138.0, 138.4, 138.6, 138.7, 138.8, 139.7, 140.8, 208.2; HRMS (EI⁺): Calcd for C₃₇H₄₄O₃Si, M⁺ 564.3060. Found m/z 564.3077.

General Procedure for the [4+2] Cyclization Reaction of 3aa with Dienophiles. To an oven-dried, Ar-purged flask was added 3aa (31.6 mg, 0.100 mmol), Dimethyl Acetylenedicarboxylate (37 µL, 0.3 mmol), and p-Xylene (2.0 mL). After heated at 130 °C for 27 h, the reaction mixture was cooled to room temperature and concentrated under reduced pressure. The residue was purified by preparative thin-layer chromatography (hexane/ethyl acetate 3:1) to give product 11 (38.5 ± 0.084 mmol, 84% yield).

trans-4,7-Dimethyl-4-phenyl-2,2,5,6-tetramethoxycarbonyl-2,3,4,7-tetrahydro-1H-indene (11)

IR (neat): 2953, 1728, 1435, 1260, 1028 cm⁻¹; ¹H NMR: δ = 1.18 (d, J = 6.9 Hz, 3H), 1.82 (s, 3H), 2.38 (dd, J = 16.5, 0.6 Hz, 1H), 2.94 (dd, J = 16.2, 1.5 Hz, 1H), 3.01 (d, J = 16.5 Hz, 1H), 3.12 (d, J = 16.2 Hz, 1H), 3.29 (s, 3H), 3.45 (q, J = 6.8 Hz, 1H), 3.62 (s, 3H), 3.71 (s, 3H), 3.74 (s, 3H), 7.09–7.34
(m, 5H); $^{13}$C NMR: $\delta = 18.8, 24.2, 32.5, 39.6, 41.2, 44.9, 51.6, 52.2, 52.7, 52.8, 58.1, 126.8, 127.4, 128.0, 132.8, 134.3, 135.8, 141.7, 143.5, 167.7, 168.1, 171.9, 172.1; HRMS (CI+): Calcd for C$_{25}$H$_{28}$O$_8$, M$^+$ 456.1784. Found m/z 456.1786.

**trans-5,9-Dimethyl-7,7-dimethoxycarbonyl-2,5-diphenyl-6,7,8,9-tetrahydrocyclopenta[d][1,2,4]triazolo[1,2-a]pyridazine-1,3(2H,5H)-dione (12)**

**IR (KBr): 2980, 1769, 1736, 1505, 1414, 1260, 1204, 1173, 1073 cm$^{-1}$;** $^1$H NMR: $\delta = 1.42$ (d, $J = 6.3$ Hz, 3H), 2.20 (s, 3H), 2.60 (dd, $J = 16.5, 2.1$ Hz, 1H), 3.14 (dd, $J = 16.8, 1.5$ Hz, 1H), 3.20 (s, 2H), 3.67 (s, 3H), 3.77 (s, 3H), 4.76 (q, $J = 6.3$ Hz, 1H), 7.21–7.47 (m, 10H); $^{13}$C NMR: $\delta = 15.7, 22.3, 38.9, 40.6, 50.3, 53.0, 53.1, 58.2, 63.9, 125.3, 126.6, 127.8, 128.3, 128.4, 128.8, 130.9, 131.7, 135.2, 137.0, 150.8, 152.3, 171.4; HRMS (CI+): Calcd for C$_{27}$H$_{27}$N$_3$O$_6$, M$^+$ 489.1900. Found m/z 489.1892.
References and Notes


(8) Phenylboroxine was used instead of phenylboronic acid to avoid proton scrambling.

(10) A reaction using unsymmetrical 1,6-diyn disubstituted with methyl and phenyl groups (4, R = Ph) proceeded at 100 °C to afford a complex mixture of products, although the reason is unclear.


List of Publication

Chapter 1
Synthesis of 1(2H)-Isoquinolones by the Nickel-Catalyzed Denitrogenative Alkyne Insertion of 1,2,3-Benzotriazin-4(3H)-ones
Tomoya Miura, Motoshi Yamauchi, and Masahiro Murakami

Chapter 2
Enantioselective Synthesis of 3,4-Dihydroisoquinolin-1(2H)-ones by Nickel-Catalyzed Denitrogenative Annulation of 1,2,3-Benzotriazin-4(3H)-ones with Allenes
Motoshi Yamauchi, Masao Morimoto, Tomoya Miura, and Masahiro Murakami

Chapter 3
Nickel-Catalyzed Denitrogenative Annulation Reactions of 1,2,3-Benzotriazin-4(3H)-ones with 1,3-Dienes and Alkenes
Motoshi Yamauchi, Masao Morimoto, Tomoya Miura, and Masahiro Murakami
in preparation.

Chapter 4
Nickel-Catalysed Denitrogenative Alkyne Insertion Reaction of N-Sulfonyl-1,2,3-triazoles
Tomoya Miura, Motoshi Yamauchi, and Masahiro Murakami

Chapter 5
Preparation of 2-Sulfonyl-1,2,3-triazoles by Base-promoted 1,2-Rearrangement of a Sulfonyl Group
Motoshi Yamauchi, Tomoya Miura, and Masahiro Murakami
Heterocycles, 2010, 80, 177-181.

Chapter 6
Rhodium-Catalyzed Arylative Cyclization Reaction of Diynes with Arylboronic Acids
Tomoya Miura, Motoshi Yamauchi, and Masahiro Murakami
Synlett 2007, 13, 2029-2032.