

**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 Murakami 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 arylation 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 Br  chner, 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(3 <i>H</i>)-ones	13
Chapter 2	Nickel-Catalyzed Denitrogenative Allene Insertion Reactions of 1,2,3-Benzotriazin-4(3 <i>H</i>)-ones	45
Chapter 3	Nickel-Catalyzed Denitrogenative Annulations of 1,2,3-Benzotriazin-4(3 <i>H</i>)-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.¹ Heterometalacyclic complexes often act as key intermediate, which subsequently incorporate unsaturated compounds through insertion and reductive elimination to construct heterocyclic skeletons.

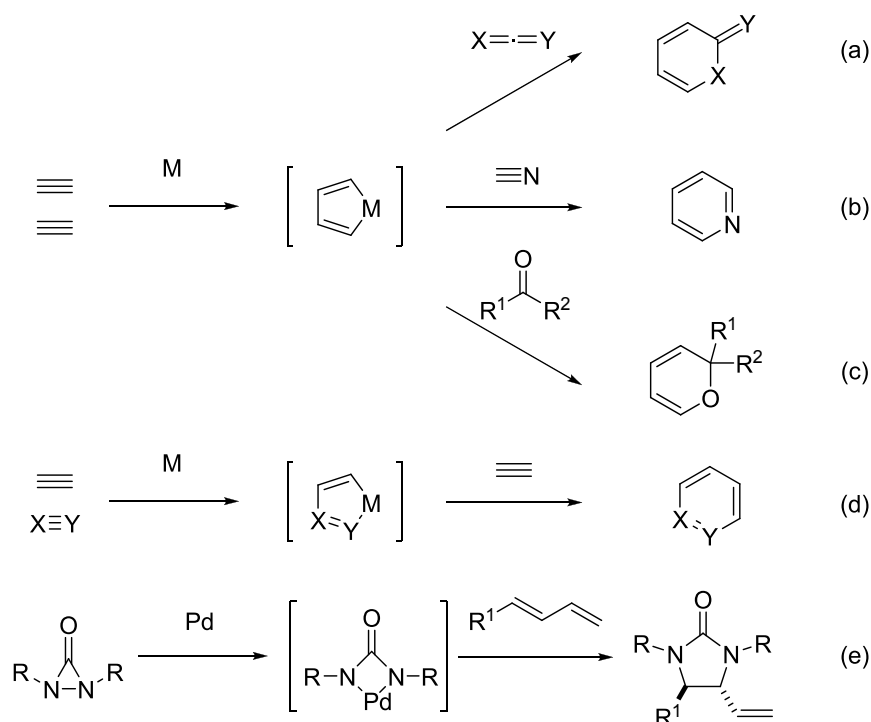
The author focused here on 1,2,3-triazo compounds as precursory platform to generate heterocyclic intermediates through oxidative addition to a nickel catalyst followed by extrusion of molecular nitrogen. Nickel-catalyzed denitrogenative annulations of 1,2,3-triazo compounds with unsaturated organic 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 arylation 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 Synthesis¹

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,² Heck,³ Suzuki,⁴ Stille,⁵ and Tsuji-Trost⁶ reactions, (2) C–N bond formation, for example, the coupling reaction with a heteroatom using aryl and vinyl halides,⁷ the amino-Heck reaction,⁸ and intramolecular Wacker type oxidation.⁹ 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),¹⁰ nitriles (b),¹¹ and carbonyls (c).¹² The reaction of an alkyne with a carbon-heteroatom multiple bond proceeds through

formation of the heteroatom-containing metallacycle followed by alkyne insertion (d).¹³ 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).¹⁴ Metallacycle intermediates are utilized for the synthesis of heterocyclic compounds.

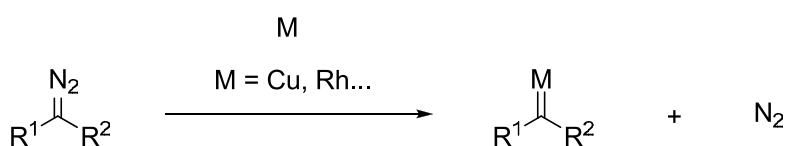
Scheme 1



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

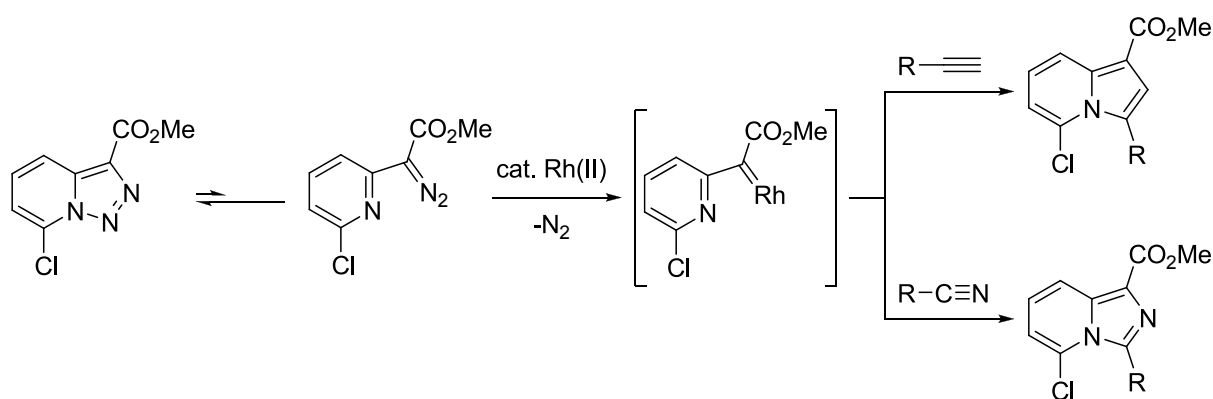
Transition-metal-induced extrusion of molecular nitrogen of diazocarbonyl compounds leads to highly reactive metallocarbenoid species (Scheme 2). The versatile reactivity of the carbene species are recognized by numerous synthetic application,¹⁵ C–H activation and cyclopropanation.

Scheme 2



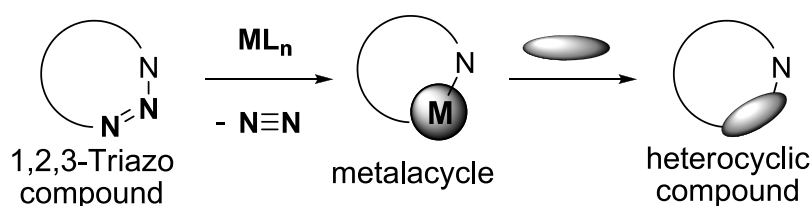
In an important recent literature contribution, a rhodium-catalyzed extrusion reaction of a molecular nitrogen from pyridotriazoles was utilized for construction of a new heterocyclic system by Gevorgyan and co-workers (Scheme 3).¹⁶ A pyridotriazole undergoes closed/open form equilibrium to produce small 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-triazo moiety with release of molecular nitrogen.

Scheme 3



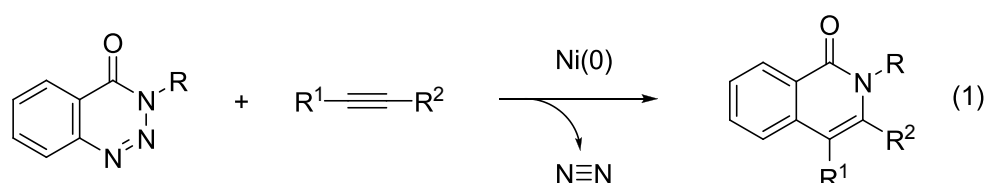
In line with these background, the author focused his attention to the activation of 1,2,3-triazo compounds and envisaged that metallacycle intermediates could be provided by transition-metal-induced extrusion of molecular nitrogen of 1,2,3-triazo compounds (Scheme 4). Oxidative addition of a N–N bond to nickel(0), which then prompts extrusion of molecular nitrogen¹⁷ to give metallacycle intermediates. Subsequent insertion of unsaturated compounds followed by reductive elimination would afford various heterocyclic compounds.¹⁸

Scheme 4



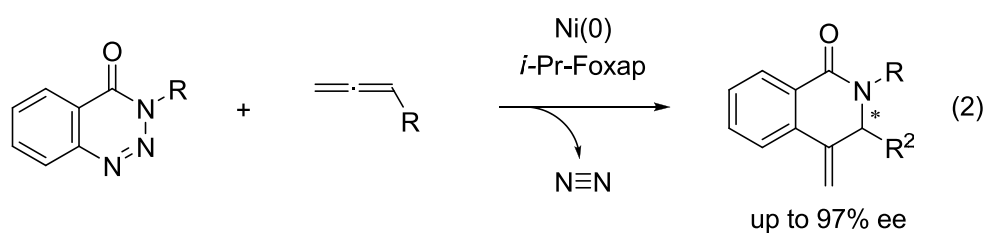
Chapter 1. Nickel-Catalyzed Denitrogenative Alkyne Insertion Reactions of 1,2,3-Benzotriazin-4(3*H*)-ones

In chapter 1, the author describes nickel-catalyzed denitrogenative alkyne insertion reactions of 1,2,3-benzotriazin-4(3*H*)-ones which can be readily prepared from anthranilic acid derivatives.¹⁹ 1,2,3-Benzotriazin-4(3*H*)-ones reacted with alkynes in the presence of a nickel(0)/phosphine catalyst to give a wide range of substituted 1(2*H*)-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(2*H*)-isoquinolones.



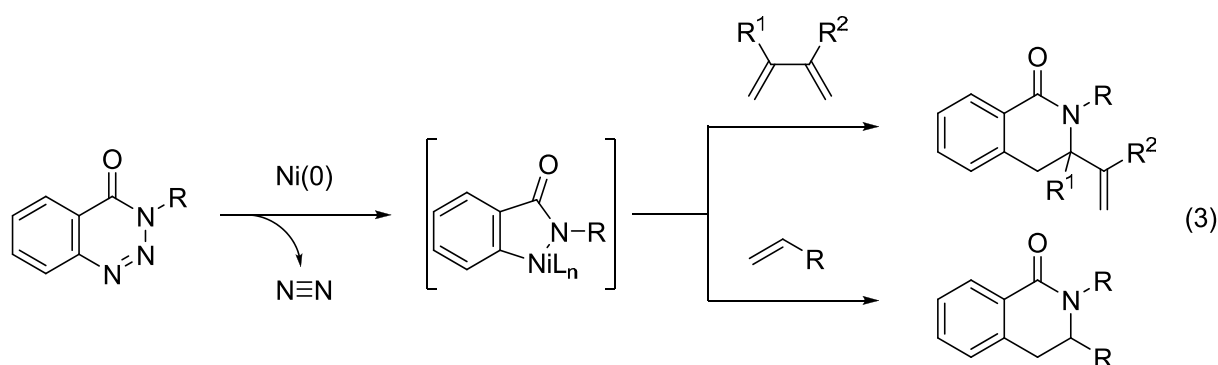
Chapter 2. Nickel-Catalyzed Denitrogenative Allene Insertion Reactions of 1,2,3-Benzotriazin-4(3*H*)-ones

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



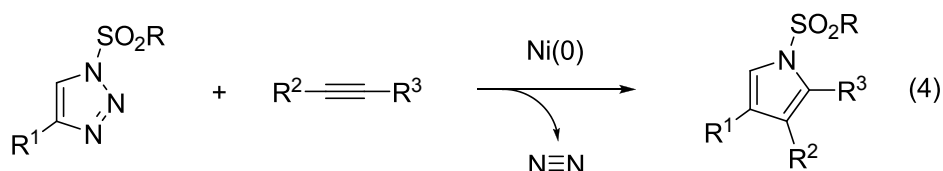
Chapter 3. Nickel-Catalyzed Denitrogenative Annulations of 1,2,3-Benzotriazin-4(3*H*)-ones with 1,3-Dienes and Alkenes.

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



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

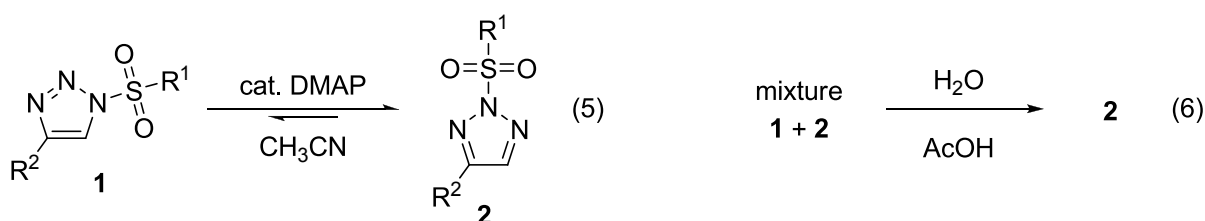
In chapter 4, a nickel-catalyzed denitrogenative alkyne insertion of 1-sulfonyl-1,2,3-triazoles which can be readily prepared by a copper catalyzed azide/alkyne cycloaddition²⁰ is described (eq 4). The diazo compound generated by tautomerization of 1-Sulfonyl-1,2,3-triazoles adds to nickel(0) with release 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.



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.²¹ 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.²² 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 1,4-²³ and 1,5-disubstituted²⁴ 1,2,3-triazoles. However, methods for the synthesis of 2,4-disubstituted 1,2,3-triazoles remain relatively undeveloped.^{25, 26} During the study on the nickel-catalyzed denitrogenative alkene insertion reaction of 4-sulfonyl-1,2,3-triazoles,²⁷ 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).

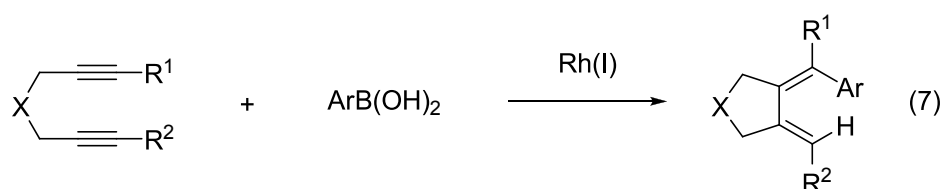


Chapter 6. Rhodium-Catalyzed Arylative Cyclization Reaction of Diynes with Arylboronic Acids

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.²⁸ It has been demonstrated by the author's group²⁹ and others³⁰

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 diynes³¹ 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 (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 dienyrrhodium intermediate. Subsequent hydrolysis gives products, regenerating rhodium active species.



References and Notes

- (1) For reviews, see: (a) Nakamura, I.; Yamamoto, Y. *Chem. Rev.* **2004**, *104*, 2127. (b) Zeni, G.; Larock, R. C. *Chem. Rev.* **2004**, *104*, 2285. (c) D'Souza, D. M.; Müller, T. J. J. *Chem. Soc. Rev.* **2007**, *36*, 1095.
- (2) For reviews, see: (a) *Alkene Metathesis in Organic Synthesis*; Fürstner, A., Ed.; Springer-Verlag: Berlin, 1998. (b) Grubbs, R. H.; Chang, S. *Tetrahedron* **1998**, *54*, 4413. (c) Armstrong, S. K. *J. Chem. Soc., Perkin Trans. I.* **1998**, 371. (d) Schuster, M.; Blechert, S. In *Transition Metals for Organic Synthesis*; Beller, M., Bolm, C., Ed.; WILEY-VCH: Weinheim, 1998; p 275. (e) Phillips, A. J.; Abell, A. D. *Aldrichimica Acta* **1999**, *32*, 75. (f) Fürstner, A. *Angew. Chem., Int. Ed.* **2000**, *39*, 3012. (g) Tsuji, J. *Transition Metal Reagents and Catalysts*; John Wiley & Sons Ltd.: New York, 2000; p 305. (h) Dörwald, F. Z. *Transition-Metal-Catalyzed Heterocyclic Synthesis Chemical Reviews*, 2004, Vol. 104, No. 5 **2191** *Metal Carbenes in Organic Synthesis*; Verlag GmbH: Weinheim, 1999; p 134. (i) Hoveyda, A. H.; Schrock, R. R. *Chem. Eur. J.* **2001**, *7*, 945. (j) Sémeril, D.; Bruneau, C.; Dixneuf, P. H. *Adv. Synth. Catal.* **2002**, *344*, 585.
- (3) For a review, see: (a) Bräse, S.; de Meijere, A. In *Metal-catalyzed Cross-coupling Reactions*; Diederich, F., Stang, P. J., Eds.; Wiley-VCH: Weinheim, p 99. (b) Beller, M.; Riermeier, T. H.; Stark, G. In *Transition Metals for Organic Synthesis*; Beller, M., Bolm, C., Eds.; WILEY-VCH: Weinheim, 1998; p 209. (c) Dyker, G. In *Handbook of Organopalladium Chemistry for Organic Synthesis*; Negishi, E., Ed.; John Wiley & Sons: New York, 2000; IV.2.2.2, p 1255.
- (4) For a review, see: (a) Miyaura, N.; Suzuki, A. *Chem. Rev.* **1995**, *95*, 2457. (b) Chemler, S. R.; Trauner, D.; Danishefsky, S. J. *Angew. Chem., Int. Ed.* **2001**, *40*, 4544. (c) Suzuki, A. In *Handbook of Organopalladium Chemistry for Organic Synthesis*; Negishi, E., Ed.; John Wiley & Sons: New York, 2000; III.2.2, p 249.
- (5) For a review, see: (a) Duncanson, M. A. J.; Pattenden, G. *J. Chem. Soc., Perkin Trans. I* **1999**, 1235. (b) Pattenden, G.; Sinclair, D. J. *J. Organomet. Chem.* **2002**, *653*, 261. (c) Kosugi, M.; Fugami, K. In *Handbook of Organopalladium Chemistry for Organic Synthesis*; Negishi, E., Ed.; John Wiley & Sons: New York, 2000; III.2.3, p 263.
- (6) For a review, see: (a) Trost, B. M. *Angew. Chem., Int. Ed. Engl.* **1989**, *28*, 1173. (b) Courillon, C.; Thorimbert, S.; Malacri'a, M. In *Handbook of Organopalladium Chemistry for Organic Synthesis*; Negishi, E., Ed.; John Wiley & Sons: New York, 2000; V.2.1.5, p 1795.

- (7) For a review, see: (a) Wolfe, J. P.; Rennels, R. A.; Buchwald, S. L. *Tetrahedron* **1996**, *52*, 7525. (b) Yang, B. H.; Buchwald, S. L. *J. Organomet. Chem.* **1999**, *576*, 125. (c) Hartwig, J. F. In *Handbook of Organopalladium Chemistry for Organic Synthesis*; Negishi, E., Ed.; John Wiley & Sons: New York, 2000; III.3.2, p 1051
- (8) (a) Tsutsui, H.; Narasaka, K. *Chem. Lett.* **1999**, 45. (b) Koganemaru, Y.; Kitamura, M.; Narasaka, K. *Chem. Lett.* **2002**, 784. (c) Kitamura, M.; Zaman, S.; Narasaka, K. *Synlett.* **2001**, 974. (d) Tsutsui, H.; Narasaka, K. *Chem. Lett.* **2001**, 526. (e) Kitamura, M.; Chiba, S.; Saku, O.; Narasaka, K. *Chem. Lett.* **2002**, 606.
- (9) For a review, see: (a) Hosokawa, T.; Murahashi, S.-I. In *Handbook of Organopalladium Chemistry for Organic Synthesis*; Negishi, E., Ed.; John Wiley & Sons: New York, 2000; V. 3.2.1, p 2169. (b) Hosokawa, T. In *Handbook of Organopalladium Chemistry for Organic Synthesis*; Negishi, E., Ed.; John Wiley & Sons: New York, 2000; V. 3.3.1, p 2211. (c) Gabriele, B.; Salerno, G. In *Handbook of Organopalladium Chemistry for Organic Synthesis*; Negishi, E., Ed.; John Wiley & Sons: New York, 2000; VI.4.4.2, p 2623. (d) Schmalz, H. G.; Geis, O. In *Handbook of Organopalladium Chemistry for Organic Synthesis*; Negishi, E., Ed.; John Wiley & Sons: New York, 2000; VI.2.1.3, p 2377. (e) Feringa, B. L. In *Transition Metals for Organic Synthesis*; Beller, M., Bolm, C., Eds.; WILEY-VCH Verlag GmbH: Weinheim, 1998; Vol. 2, p 307. For a recent report, see: (f) Fix, S. R.; Brice, J. L.; Stahl, S. S. *Angew. Chem., Int. Ed.* **2002**, *41*, 164. (g) Uozumi, Y.; Kyota, H.; Kato, K.; Ogasawara, M.; Hayashi, T. *J. Org. Chem.* **1999**, *64*, 1620. (h) Arai, M. A.; Kuraishi, M.; Arai, T.; Sasai, H. *J. Am. Chem. Soc.* **2001**, *123*, 2907. (i) Macsári, I.; Szabó, K. J. *Chem. Eur. J.* **2001**, *7*, 4097.
- (10) (a) Yamamoto, Y.; Takagishi, H.; Itoh, K. *Org. Lett.* **2001**, *3*, 2117. (b) Louie, J.; Gibby, J. E.; Farnworth, M. V.; Tekavec, T. N. *J. Am. Chem. Soc.* **2002**, *124*, 15188. (c) Yamamoto, Y.; Takagishi, H.; Itoh, K. *J. Am. Chem. Soc.* **2002**, *124*, 28. (d) Duong, H. A.; Cross, M. J.; Louie, J. J. *J. Am. Chem. Soc.* **2004**, *126*, 11438.
- (11) (a) Chelucci, G. *Tetrahedron: Asymmetry* **1995**, *6*, 811. (b) Fatland, A. W.; Eaton, B. E. *Org. Lett.* **2000**, *2*, 3131. (c) Moretto, A. F.; Zhang, H.-C.; Maryanoff, B. E. *J. Am. Chem. Soc.* **2001**, *123*, 3157. (d) Yamamoto, Y.; Ogawa, R.; Itoh, K. *J. Am. Chem. Soc.* **2001**, *123*, 6189. (e) Yamamoto, Y.; Okuda, S.; Itoh, K. *Chem. Commun.* **2001**, 1102. (f) McCormick, M. M.; Duong, H. A.; Zuo, G.; Louie, J. J. *J. Am. Chem. Soc.* **2005**, *127*, 5030.
- (12) (a) Yamamoto, Y.; Takagishi, H.; Itoh, K. *J. Am. Chem. Soc.* **2002**, *124*, 6844. (b) Tekavec, T. N.; Louie, J. *Org. Lett.* **2005**, *7*, 4037.

- (13) For a recent report, see: (a) Varela, J. A.; Castedo, L.; Saá, C. *J. Org. Chem.* **1997**, *62*, 4189. (b) Varela, J. A.; Castedo, L.; Saá, C. *J. Am. Chem. Soc.* **1998**, *120*, 12147. (c) Varela, J. A.; Castedo, L.; Saá, C. *Org. Lett.* **1999**, *1*, 2141. (d) Varela, J. A.; Castedo, L.; Maestro, M.; Mahía, J.; Saá, C. *Chem. Eur. J.* **2001**, *7*, 5203. (e) Duong, H. A.; Louie, J. *Tetrahedron* **2006**, *62*, 7552. (f) Ogoshi, S.; Ikeda, H.; Kurosawa, H. *Angew. Chem. Int. Ed.* **2007**, *46*, 4930.
- (14) (a) Du, H.; Zhao, B.; Shi, Y. *J. Am. Chem. Soc.* **2007**, *129*, 762. (b) Du, H.; Yuan, W.; Zhao, B.; Shi, Y. *J. Am. Chem. Soc.* **2007**, *129*, 7496. (c) Du, H.; Yuan, W.; Zhao, B.; Shi, Y. *J. Am. Chem. Soc.* **2007**, *129*, 11688. (d) Du, H.; Zhao, B.; Shi, Y. *J. Am. Chem. Soc.* **2008**, *130*, 8590.
- (15) For recent reviews, see: (a) Davies, H. M. L.; Manning, J. R. *Nature* **2008**, *451*, 417. (b) Doyle, M. P. In *Modern Rhodium-Catalyzed Organic Reactions*; Evans, P. A., Ed.; Wiley: New York, 2005; pp 341-355. (c) Davies, H. M. L.; Beckwith, R. E. J. *Chem. Rev.* **2003**, *103*, 2861. (d) Lebel, H.; Marcoux, J.-F.; Molinaro, C.; Charette, A. B. *Chem. Rev.* **2003**, *103*, 977.
- (16) (a) Chuprakov, S.; Hwang, F. W.; Gevorgyan, V. *Angew. Chem. Int. Ed.* **2007**, *46*, 4757. (b) Chuprakov, S.; Gevorgyan, *Org. Lett.* **2007**, *9*, 4463.
- (17) Recently, denitrogenative annulations 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.
- (18) Recently, Matsubara and co-workers reported nickel-catalyzed decarbonylative and decarboxylate annulations. See: (a) Kajita, Y.; Matsubara, S.; Kurahashi, T. *J. Am. Chem. Soc.* **2008**, *130*, 6058. (b) Kajita, Y.; Kurahashi, T.; Matsubara, S. *J. Am. Chem. Soc.* **2008**, *130*, 17226. (c) Yoshino, Y.; Kurahashi, T.; Matsubara, S. *J. Am. Chem. Soc.* **2009**, *131*, 7494.
- (19) 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.
- (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.
- (21) Reviews: (a) Lutz, J.-F. *Angew. Chem. Int. Ed.*, **2007**, *46*, 1018. (b) Moses, J. E.; Moorhouse, A. D. *Chem. Soc. Rev.*, **2007**, *36*, 1249. (c) Fournier, D.; Hoogenboom, R.; Schubert, U. S. *Chem. Soc. Rev.*, **2007**, *36*, 1369. (d) Angell Y. L.; Burgess, K. *Chem. Soc. Rev.*, **2007**, *36*, 1674.
- (22) Reviews: (a) Krivopalov, V. P.; Shkurko, O. P. *Russ. Chem. Rev.*, **2005**, *74*, 339. (b) Wu, P.; Fokin, V. V. *Aldrichim. Acta*, **2007**, *40*, 7.

- (23) (a) Rostovtsev, V.V.; Green, L.G.; Fokin, V.V.; Sharpless, K. B. *Angew. Chem. Int. Ed.*, **2002**, *41*, 2596. (b) Tornøe, C. W.; Christensen, C.; Meldal, M. *J. Org. Chem.*, **2002**, *67*, 3057.
- (24) Zhang, L.; Chen, X.; Xue, P.; Sun, H. H. Y.; Williams, I. D.; Sharpless, K. B.; Fokin, V. V.; Jia, G. *J. Am. Chem. Soc.*, **2005**, *127*, 15998.
- (25) For reports on the synthesis of 2-sulfonyl-1,2,3-triazoles, see: (a) Abdel-Halim, A. M.; Abdel-Rahman, R. M.; Mohamed, E. A. *Acta Pharm. Jugosl.*, **1985**, *35*, 89. (b) Potapova, I. A.; Purygin, P. P.; Lipatov, I. S.; Belousova, Z. P.; Yakimova, N. A.; Tezikov, Y. V.; Selezneva, E. S. *Pharm. Chem. J.*, **2001**, *35*, 588. (c) Meshcheryakov, V. I.; Shainyan, B. A.; Tolstikova, L. L.; Albanov, A. I. *Russ. J. Org. Chem.*, **2003**, *39*, 1517.
- (26) For reports on the pharmaceutical activity of 2,4-disubstituted triazoles, see: (a) Balle, T.; Perregaard, J.; Ramirez, M. T.; Larsen, A. K.; Søby, K. K.; Liljefors, T.; Andersen, K. *J. Med. Chem.*, **2003**, *46*, 265. (b) Roppe, J.; Smith, N. D.; Huang, D.; Tehrani, L.; Wang, B.; Anderson, J.; Brodtkin, J.; Chung, J.; Jiang, X.; King, C.; Munoz, B.; Varney, M. A.; Prasit, P.; Cosford, N. D. P. *J. Med. Chem.*, **2004**, *47*, 4645.
- (27) Miura, T.; Yamauchi, M.; Murakami, M. *Chem. Commun.*, **2009**, 1470.
- (28) For reviews, see: (a) Fagnou, K.; Lautens, M. *Chem. Rev.* **2003**, *103*, 169. (b) Hayashi, T.; Yamasaki, K. *Chem. Rev.* **2003**, *103*, 2829.
- (29) Miura, T.; Murakami, M. *Chem. Commun.* **2007**, 217.
- (30) For selected papers, see: (a) Cauble, D. F.; Gipson, J. D.; Krische, M. J. *J. Am. Chem. Soc.* **2003**, *125*, 1110. (b) Shintani, R.; Okamoto, K.; Otomaru, Y.; Ueyama, K.; Hayashi, T. *J. Am. Chem. Soc.* **2005**, *127*, 54. (c) Shintani, R.; Tsurusaki, A.; Okamoto, K.; Hayashi, T. *Angew. Chem. Int. Ed.* **2005**, *44*, 3909. (d) Tseng, N.-W.; Mancuso, J.; Lautens, M. *J. Am. Chem. Soc.* **2006**, *128*, 5338. (e) Harada, Y.; Nakanishi, J.; Fujihara, H.; Tobisu, M.; Fukumoto, Y.; Chatani, N. *J. Am. Chem. Soc.* **2007**, *129*, 5766; and references therein.
- (31) (a) For a review on transition-metal catalyzed carbocyclizations of diynes, see: Ojima, I.; Tzamarioudaki, M.; Li, Z.; Donovan, R. J. *Chem. Rev.* **1996**, *96*, 635. (b) Hydrostannanes: Lautens, M.; Smith, N. D.; Ostrovsky, D. *J. Org. Chem.* **1997**, *62*, 8970. (c) Stannylsilanes: Gréau, S.; Radetich, B.; Rajanbabu, T. V. *J. Am. Chem. Soc.* **2000**, *122*, 8579. (d) Borylsilanes: Onozawa, S.; Hatanaka, Y.; Tanaka, M. *Chem. Commun.* **1997**, 1229. (e) Borylstannanes: Onozawa, S.; Hatanaka, Y.; Choi, N.; Tanaka, M. *Organometallics* **1997**, *16*, 5389. (f) Hydrogen: Jang, H.-Y.; Krische, M. J. *J. Am. Chem. Soc.* **2004**, *126*, 7875. (g) Hydrogen equivalent: Trost, B. M.; Lee, D. C. *J. Am. Chem. Soc.* **1988**, *110*, 7255. (h) Hydrosilylation:

- Ojima, I.; Zhu, J.; Vidal, E. S.; Kass, D. F. *J. Am. Chem. Soc.* **1998**, *120*, 6690. (i)
Hydrosilylation: Madine, J. W.; Wang, X.; Widenhoefer, R. A. *Org. Lett.* **2001**, *3*, 385. (j)
Hydration: Trost, B. M.; Rudd, M. T. *J. Am. Chem. Soc.* **2003**, *125*, 11516. (k)
Hydrocarboxylation: Kim, H.; Goble, S. D.; Lee, C. J. *J. Am. Chem. Soc.* **2007**, *129*, 1030

Chapter 1

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

Abstract

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

Introduction

The 1(2*H*)-isoquinolone ring system is one of the basic units often found in the structures of plant alkaloids¹ and pharmacologically valuable compounds.² Therefore, the development of efficient methods for their synthesis is of great importance.³ Whereas transition-metal-based catalysis has often been utilized for the synthesis of various heterocyclic compounds,⁴ only limited examples applicable to the synthesis of 1(2*H*)-isoquinolones have appeared.⁵ 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.⁶ We report herein a nickel-catalyzed denitrogenative alkyne insertion reaction of 1,2,3-benzotriazin-4(3*H*)-ones, which presents a new synthetic approach to substituted 1(2*H*)-isoquinolones.

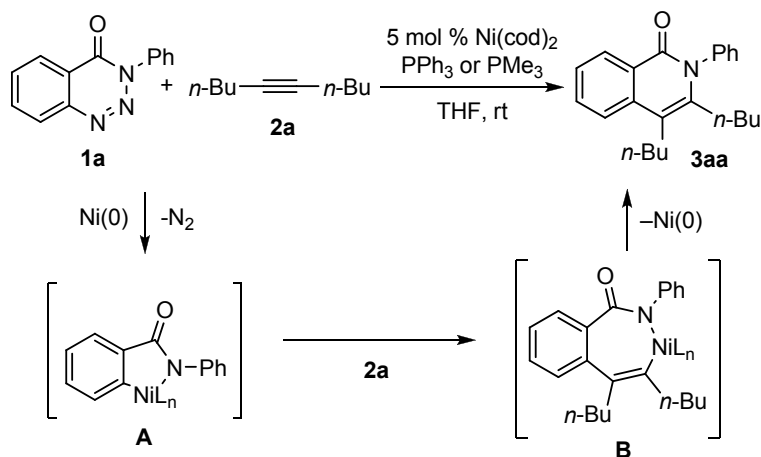
Results and Discussions

1,2,3-Benzotriazin-4(3*H*)-ones can be readily prepared from anthranilic acid derivatives.⁷ Initially, the possibility to activate the triazinone moiety was examined using nickel(0)/phosphine complexes;⁸ 3-phenyl-1,2,3-benzotriazin-4(3*H*)-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(2*H*)-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.⁹ 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**.^{5f,10} Subsequent insertion of the alkyne into the nickel-carbon bond leads to the seven-membered-ring nickelacycle **B**.¹¹ 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).¹² 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

Table 1. Ni(0)-Catalyzed Alkyne Insertion: Scope of Substituent on the benzotriazinone^a

entry	1	R ¹	R ²	R ³	3	T (°C)	yield (%) ^b
1	1b	4-MeC ₆ H ₄	H	H	3ba	rt	98
2	1c	4-MeOC ₆ H ₄	H	H	3ca	rt	95
3	1d	4-CF ₃ C ₆ H ₄	H	H	3da	rt	99
4	1e	4-ClC ₆ H ₄	H	H	3ea	rt	98 ^c
5	1f	2MeOC ₆ H ₄	H	H	3fa	rt	96 ^c
6	1g	2,4,6-Me ₃ C ₆ H ₂	H	H	3ga	rt	96 ^c
7	1h	Bn	H	H	3ha	60	96 ^c
8	1i	Me	H	H	3ia	80	95 ^d
9	1j	H	H	H	3ia	100	0 ^d
10	1k	Ph	MeO	MeO	3ka	60	99
11	1l	Ph	H	CO ₂ Me	3la	rt	97
12	1m				3ma	60	96 ^c

^a Conditions: **1** (0.2 mmol), **2** (0.22 mmol), $\text{Ni}(\text{cod})_2$ (10 μmol , 5 mol %), and PPh_3 (40 μmol , 20 mol %) in THF (1 mL) for 12 h unless otherwise noted. ^b Isolated yield. ^c PMe_3 (20 μmol , 10 mol %). ^d PMe_3 (20 μmol , 10 mol %) in toluene (1 mL).

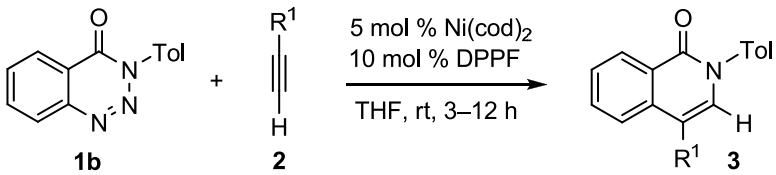
Various internal alkynes **2** were subjected to the denitrogenative insertion reaction with benzotriazinones **1a** and **1b** (Table 2). Symmetrical internal alkynes such as diphenylethyne (**2b**), 1,4-dibenzyloxybut-2-yne (**2c**) and gaseous acetylene (**2d**) reacted with **1a** to give **3ab**, **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-yne (**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 PPh₃ were required to get a high yield (entry 7).¹⁴ The high regioselectivity observed with boryl-substituted alkynes¹⁵ 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**^a

entry	1	2 (R ¹ , R ²)	3	yield (%) ^b
1	1a	2b (Ph, Ph)	3ab	98
2	1a	2c (CH ₂ OBn, CH ₂ OBn)	3ac	94
3	1a	2d (H, H) (1 atm)	3ad	97 ^c
4	1b	2e (<i>i</i> -Pr, Me)	3be	97 (58:42)
5	1b	2f (<i>t</i> -Bu, Me)	3bf	86 (92:8) ^d
6	1b	2g (Me ₃ Si, Me)	3bg	98 (90:10) ^d
7	1b	2h (Me, Ph)	3bh	99 (86:14)
8	1b	2i (Me, 4-CF ₃ C ₆ H ₄)	3bi	99 (73:27)
9	1b	2j (Me, 4-MeOC ₆ H ₄)	3bj	99 (89:11)
10	1b	2k (Pr, CO ₂ Et)	3bk	99 (92:8) ^e
11	1b	2l (Bu, Bpin)	3bl	93 (98:2) ^{c,f}
12	1b	2m (Me ₃ Si, Bpin)	3bm	94 (99:1) ^c

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

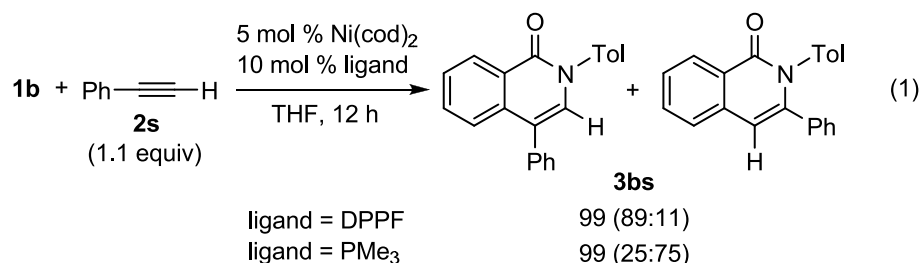
We then examined the reaction of terminal alkynes with **1b** (Table 3). Although oct-1-yne (**2n**) is capable of undergoing a self-oligomerization reaction, it instead reacted via the insertion reaction giving **3bn** in 98% yield with the Ni(0)/PMe₃ catalyst (entry 1). However, the regioselectivity 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).^{17,18} 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**^a


entry	2 (R ¹)	3	yield (%) ^b
1	2n (<i>n</i> -Hex)	3bn	98 (73:27) ^c
2	2n (<i>n</i> -Hex)	3bn	99 (98:2)
3	2o (<i>c</i> -Pent)	3bo	98 (99:1)
4	2p (<i>t</i> -Bu)	3bp	99 (>99:1) ^e
5	2q (TMS)	3bq	94 (99:1) ^{d,e}
6	2r (<i>n</i> -Bu ₃ Sn)	3br	92 (99:1) ^{d,f}

^a Conditions: **1** (0.2 mmol), **2** (0.22 mmol), Ni(cod)₂ (10 μmol, 5 mol %), DPPF (20 μmol, 10 mol %) in THF (1 mL) at rt for 3–12 h under N₂ unless otherwise noted. ^b Combined yield of regioisomers unless otherwise noted. Numbers in parentheses describe the regioselectivity. ^c PMe₃ (20 μmol, 10 mol %). ^d Isolated yield of the major regio isomer. ^e 60 °C. ^f Ni(cod)₂ (20 μmol, 10 mol %), DPPF (40 μmol, 20 mol %) at 60 °C.

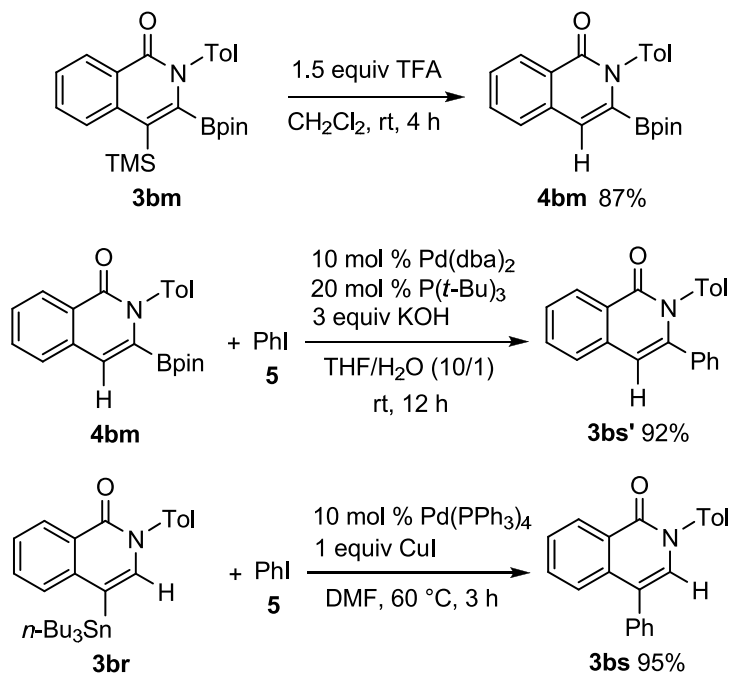
In the case of phenylethyne (**2s**), however, different regioisomers were preferentially obtained depending on the ligand employed, although the selectivity was modest (eq 1).



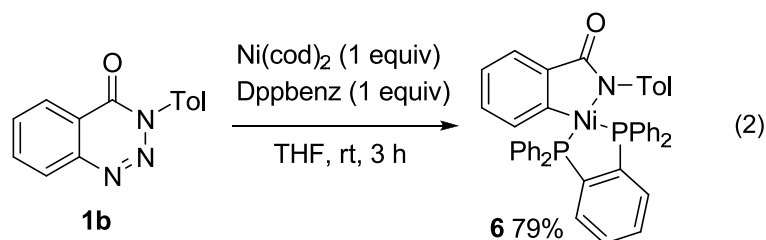
However, employing the densely functionalized products **3bm** and **3br**, it was possible to prepare both isomers, **3bs** and **3bs'**, with high regioselectivity (Scheme 2). Starting with compound **3bm**, the silyl group was selectively removed by treatment with trifluoroacetic acid (TFA) at room temperature, giving 3-boryl-1(2*H*)-isoquinolone **4bm** in 87% yield. A subsequent palladium-catalyzed cross-coupling reaction of **4bm** with iodobenzene (**5**) afforded 3-phenyl-1(2*H*)-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(2*H*)-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(2*H*)-isoquinolone.

Scheme 2



Next, the author examined isolation and characterization of the postulated azanickelacycle intermediate. 1,2,3-benzotriazin-4(3*H*)-one (**1b**) was treated with equimolar amounts of $\text{Ni}(\text{cod})_2$ and 1,2-bis(diphenylphosphino)-benzene (Dppbenz) in THF at room temperature for 3 h. Recrystallization of the reaction mixture from CH_2Cl_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**.

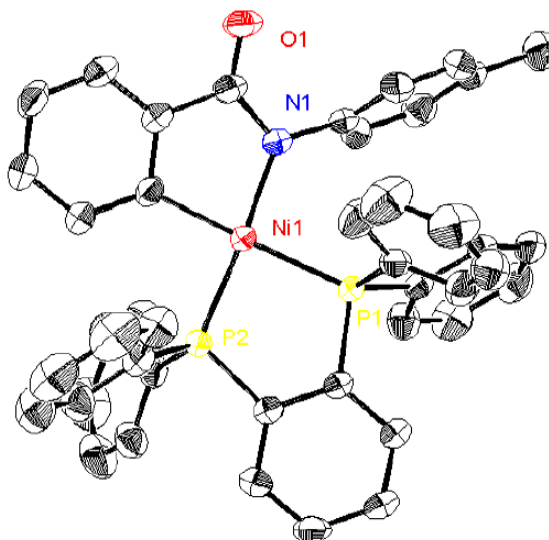
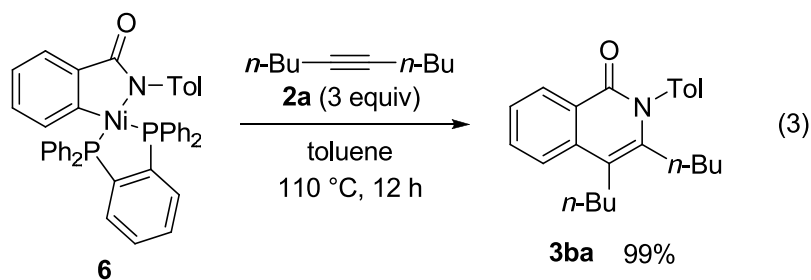


Figure 1. X-ray crystal structure of **6**

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(2*H*)-isoquinolone **3ba** was obtained in 99% yield (eq 3).



Conclusions

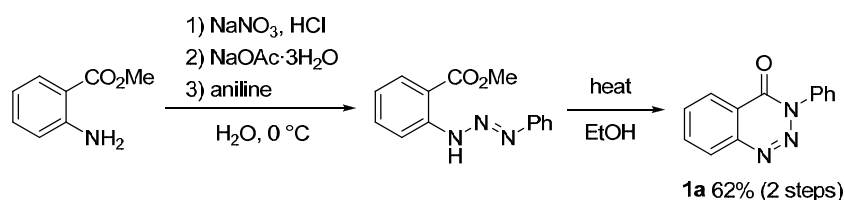
In conclusion, we have demonstrated a facile approach for the preparation of substituted 1(2*H*)-isoquinolones. A wide variety of alkyne substrates including borylalkynes were regioselectively incorporated into 1,2,3-benzotriazin-4(3*H*)-ones with loss of a dinitrogen molecule.

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. ^1H and ^{13}C NMR spectra were recorded on a Varian Gemini 2000 (^1H at 300 MHz and ^{13}C at 75 MHz) spectrometer using CHCl_3 (^1H , $\delta = 7.26$) 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-ECA600 (^1H at 600 MHz, ^{13}C at 150 MHz and ^{31}P at 244 MHz) spectrometer using CDHCl_2 (^1H , $\delta = 5.32$), CD_2Cl_2 (^{13}C , $\delta = 53.8$) as an internal standard and $\text{P}(\text{OMe})_3$ (^{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).

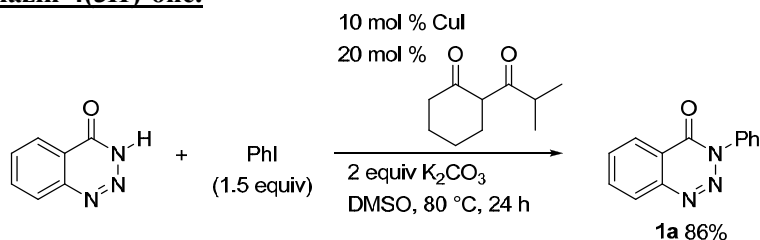
Materials. THF and toluene were dried and deoxygenized using an alumina/catalyst column system (Glass Contour Co.). Anhydrous CH_2Cl_2 (Kanto), DMF (Wako), and CH_3CN (Kanto) were purchased from the commercial sources. Triphenylphosphine (nacalai), trimethylphosphine (Aldrich), methyl anthranilate (TCI), aniline (Wako), 1,2,3-benzotriazin-4(3*H*)-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. $\text{Ni}(\text{cod})_2$ (Kanto) was obtained from the commercial sources and purified by recrystallization from toluene before use. $\text{Pd}(\text{dba})_2$ ¹⁹ and $\text{Pd}(\text{PPh}_3)_4$ ²⁰ 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 (**2c**),²¹ 1-(4-trifluoromethylphenyl)-1-propyne (**2i**),²² 1-(4-methoxyphenyl)-1-propyne (**2j**),²² and alkynylboranes (**2l**, **2m**)^{15c} 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(3*H*)-ones from Methyl Anthranilate.⁷



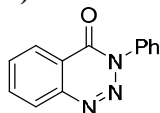
To a solution of methyl anthranilate (1.59 g, 12.9 mmol) in 2N HCl (21 mL) was slowly added NaNO_2 (1.03 g, 14.9 mmol) in water (6 mL) at 0 °C. The mixture was stirred for 30 min. Then, $\text{NaOAc} \cdot 3\text{H}_2\text{O}$ (6.80 g, 50.0 mmol) in water (10 mL) and aniline (1.8 mL, 19.8 mmol) was slowly 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*-Arvl-1,2,3-benzotriazin-4(3*H*)-ones from *NH*-1,2,3-benzotriazin-4(3*H*)-one.²³



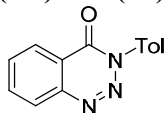
In an N₂-filled glove-box, to an oven-dried 4 mL-vial equipped with a stir bar was added *NH*-1,2,3-benzotriazin-4(3*H*)-one (29.7 mg, 0.20 mmol), K₂CO₃ (55.3 mg, 0.40 mmol), *p*-iodotoluene (65.4 mg, 0.30 mmol), CuI (3.8 mg, 20 μmol), 2-isobutyrylcyclohexanone (6.7 μL, 40 μmol), and DMSO (1 mL) at room 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(3*H*)-one (1a)



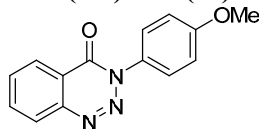
IR (KBr): 1682, 1495, 1460, 1337, 1314, 1088, 1036 cm⁻¹; ¹H NMR: δ = 7.44–7.60 (m, 3H), 7.62–7.70 (m, 2H), 7.78–7.88 (m, 1H), 7.93–8.02 (m, 1H), 8.17–8.24 (m, 1H), 8.39–8.46 (m, 1H); ¹³C NMR: δ = 120.2, 125.5, 125.9, 128.4, 128.8, 128.9, 132.6, 135.0, 138.7, 143.5, 155.1; HRMS (EI⁺): Calcd for C₁₃H₉N₃O, M⁺ 223.0746. Found m/z 223.0749.

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

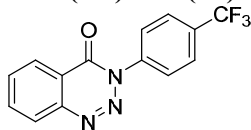


IR (KBr): 1686, 1510, 1462, 1337, 1312, 1090, 1032 cm⁻¹; ¹H NMR: δ = 2.44 (s, 3H), 7.35 (d, *J* = 8.7 Hz, 2H), 7.53 (d, *J* = 8.4 Hz, 2H), 7.78–7.87 (m, 1H), 7.92–8.01 (m, 1H), 8.17–8.24 (m, 1H), 8.42 (dd, *J* = 8.1, 1.5 Hz, 1H); ¹³C NMR: δ = 21.2, 120.3, 125.5, 125.7, 128.3, 129.5, 132.5, 134.9, 136.2, 138.9, 143.6, 155.1; HRMS (EI⁺): Calcd for C₁₄H₁₁N₃O, M⁺ 237.0902. Found m/z 237.0900.

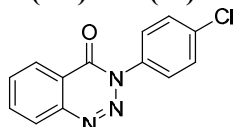
3-(4-Methoxyphenyl)-1,2,3-benzotriazin-4(3*H*)-one (1c)



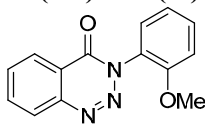
IR (KBr): 2951, 1655, 1611, 1593, 1510, 1250, 1022 cm⁻¹; ¹H NMR: δ = 3.86 (s, 3H), 7.00–7.09 (m, 2H), 7.51–7.60 (m, 2H), 7.78–7.86 (m, 1H), 7.92–8.00 (m, 1H), 8.19 (d, *J* = 8.1, 1H), 8.41 (dd, *J* = 8.1, 1.4 Hz, 1H); ¹³C NMR: δ = 55.5, 114.2, 120.2, 125.4, 127.2, 128.3, 131.6, 132.5, 134.9, 143.6, 155.2, 159.7; HRMS (EI⁺): Calcd for C₁₄H₁₁N₃O₂, M⁺ 253.0851. Found m/z 253.0854.

3-(4-Trifluorophenyl)-1,2,3-benzotriazine-4(3H)-one (1d)

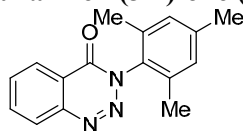
IR (KBr): 2961, 1651, 1588, 1329, 1169, 1121, 1071 cm^{-1} ; ^1H NMR: δ = 7.79–7.93 (m 5H), 7.99–8.07 (m, 1H), 8.22–8.28 (m, 1H), 8.46 (dd, J = 7.8, 1.5 Hz, 1H); ^{13}C NMR: δ = 120.2, 123.7 (q, J = 270.5 Hz), 125.7, 126.2, 128.7, 130.8 (q, J = 32.9 Hz), 133.1, 135.4, 141.6, 143.4, 155.1; HRMS (EI^+): Calcd for $\text{C}_{14}\text{H}_8\text{F}_3\text{N}_3\text{O}$, M^+ 291.0619. Found m/z 291.0618.

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

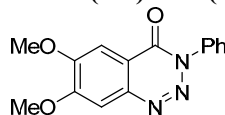
R (KBr): 1696, 1491, 1320, 1082, 1042 cm^{-1} ; ^1H NMR: δ = 7.51 (dt, J = 8.7, 2.5 Hz, 2H), 7.62 (dt, J = 8.7, 2.4 Hz, 2H), 7.84 (td, J = 7.7, 1.1 Hz, 1H), 7.99 (td, J = 7.8, 1.6 Hz, 1H), 8.20 (dd, J = 7.8, 0.6 Hz, 1H), 8.41 (dd, J = 8.1, 0.9 Hz, 1H); ^{13}C NMR: δ = 120.1, 125.6, 127.1, 128.5, 129.1,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

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

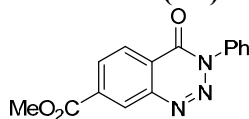
IR (KBr): 2957, 1655, 1612, 1593, 1501 cm^{-1} ; ^1H NMR: δ = 3.80 (s, 3H), 7.06–7.18 (m 2H), 7.40–7.54 (m, 2H), 7.82 (t, J = 7.5 Hz, 1H), 7.97 (td, J = 7.7, 0.9 Hz, 1H), 8.21 (d, J = 8.1 Hz, 1H), 8.42 (dt, J = 8.1, 0.6 Hz, 1H); ^{13}C NMR: δ = 55.9, 112.1, 120.3, 120.8, 125.4, 127.6, 128.3, 128.7, 131.1, 132.4, 134.8, 143.8, 154.7, 155.0; HRMS (EI^+): Calcd for $\text{C}_{14}\text{H}_{11}\text{N}_3\text{O}_2$, M^+ 253.0851. Found m/z 253.0856.

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

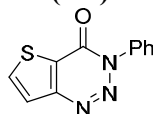
IR (KBr): 1690, 1460, 1333, 1296, 1082 cm^{-1} ; ^1H NMR: δ = 2.09 (s, 6H), 2.37 (s, 3H), 7.06 (s, 2H), 7.86 (td, J = 7.4, 1.1 Hz, 1H), 8.02 (td, J = 7.8, 1.4 Hz, 1H), 8.26 (dt, J = 8.4, 0.7 Hz, 1H), 8.46 (dt, J = 7.8, 0.8 Hz, 1H); ^{13}C NMR: δ = 17.7, 21.1, 120.2, 125.5, 128.4, 129.3, 132.5, 134.3, 135.0, 135.2, 139.6, 144.0, 155.0; HRMS (EI^+): Calcd for $\text{C}_{16}\text{H}_{15}\text{N}_3\text{O}$, M^+ 265.1215. Found m/z 265.1221.

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

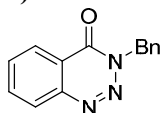
IR (KBr): 1684, 1605, 1512, 1291, 1092 cm^{-1} ; ^1H NMR: δ = 4.04 (s, 3H), 4.06 (s, 3H), 7.42–7.58 (m, 4H), 7.60–7.70 (m, 3H); ^{13}C NMR: δ = 56.6, 56.7, 104.0, 108.1, 114.9, 126.0, 128.7, 128.9, 138.9, 140.1, 153.4, 154.9, 155.0; HRMS (EI^+): Calcd for $\text{C}_{15}\text{H}_{13}\text{N}_3\text{O}_3$, M^+ 283.0957. Found m/z 283.0954.

7-Methoxycarbonyl-3-phenyl-1,2,3-benzotriazine-4(3H)-one (1l)

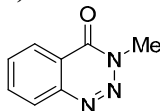
IR (KBr): 1719, 1700, 1495, 1441, 1341, 1308, 1198 1082, 1046 cm^{-1} ; ^1H NMR: δ = 4.04 (s, 3H), 7.46–7.70 (m, 5H), 8.40–8.54 (m, 2H), 8.84–8.88 (m, 1H); ^{13}C NMR: δ = 53.0, 123.1, 125.9, 126.1, 129.06, 129.11, 130.1, 132.6, 136.3, 138.4, 143.4, 154.5, 165.0; HRMS (EI^+): Calcd for $\text{C}_{15}\text{H}_{11}\text{N}_3\text{O}_3$, 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} ; ^1H NMR: δ = 7.43–7.71 (m, 5H), 7.75 (d, J = 5.1 Hz, 1H), 7.95 (d, J = 5.7 Hz, 1H); ^{13}C NMR: δ = 125.0, 126.2, 127.4, 129.0, 129.2, 135.5, 138.2, 152.9, 153.4; HRMS (EI^+): Calcd for $\text{C}_{11}\text{H}_7\text{N}_3\text{OS}$, 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-benzotriazin-4(3H)-one (1.03 g, 7.0 mmol), K_2CO_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 $^\circ\text{C}$ 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 water (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} ; ^1H NMR: δ = 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); ^{13}C NMR: δ = 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 $\text{C}_{14}\text{H}_{12}\text{N}_3\text{O}$, $\text{M}+\text{H}^+$ 238.0980. Found m/z 238.0980.

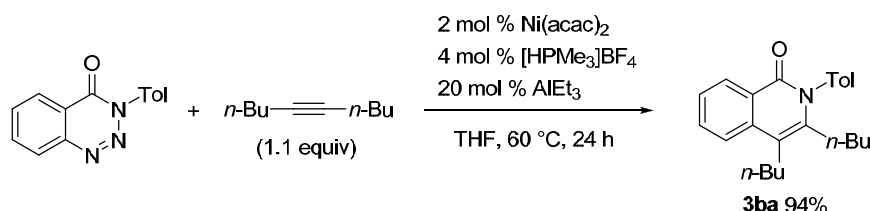
3-Methyl-1,2,3-benzotriazine-4(3H)-one (1i)

To an oven-dried flask was added 1,2,3-benzotriazin-4(3H)-one (1.00 g, 6.8 mmol), K_2CO_3 (1.41 g, 10 mmol), and CH_3CN (10 mL) at room temperature. To the reaction mixture was added MeI (0.7 mL, 11 mmol) at 0 $^\circ\text{C}$ 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} ; ^1H NMR: δ = 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);

^{13}C NMR: δ = 37.3, 119.5, 124.8, 128.1, 132.2, 134.6, 144.4, 155.7; HRMS (EI^+): Calcd for $\text{C}_8\text{H}_7\text{N}_3\text{O}$, M^+ 161.0589. Found m/z 161.0589.

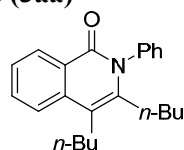
General Procedure for the Nickel-Catalyzed Denitrogenative Alkyne Insertion of Benzotriazinones. In an N_2 -filled glove-box, **1a** (44.8 g, 0.20 mmol) was charged into an oven-dried 4 mL-vial equipped with a stir bar. A solution of $\text{Ni}(\text{cod})_2$ (2.8 mg, 10 μmol) and PPh_3 (10.4 mg, 40 μmol) in THF (1 mL) and dec-5-yne (40 μL , 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[®] 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 $\text{Ni}(\text{acac})_2$.



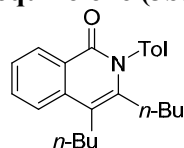
To an oven-dried flask was added **1b** (92.0 mg, 0.387 mmol), $\text{Ni}(\text{acac})_2$ (2.2 mg, 8 μmol), $[\text{HPMe}_3]\text{BF}_4$ (2.6 mg, 16 μmol), and THF (2 mL). To the suspension was added a 1.0 M solution of AlEt_3 in hexane (80 μL , 80 μmol) dropwise and dec-5-yne (**2a**, 80 μL , 0.8 mmol). After heated at 60 $^\circ\text{C}$ 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[®] 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**)



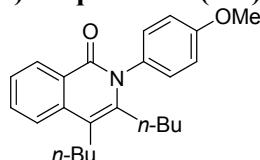
IR (KBr): 2959, 1649, 1590, 1483, 1331 cm^{-1} ; ^1H NMR: δ = 0.68 (t, J = 7.4 Hz, 3H), 1.01 (t, J = 7.1 Hz, 3H), 1.08 (sextet, J = 7.3 Hz, 2H), 1.31–1.69 (m, 6H), 2.31–2.42 (m, 2H), 2.68–2.80 (m, 2H), 7.24–7.30 (m, 2H), 7.39–7.56 (m, 4H), 7.64–7.73 (m, 2H), 8.42–8.48 (m, 1H); ^{13}C NMR: δ = 13.2, 14.0, 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^+): Calcd for $\text{C}_{23}\text{H}_{27}\text{NO}$, M^+ 333.2093. Found m/z 333.2093.

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



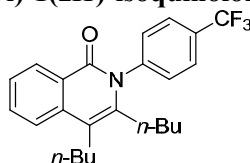
IR (KBr): 2955, 1649, 1607, 1590, 1510, 1333 cm^{-1} ; ^1H NMR: δ = 0.72 (t, J = 7.7 Hz, 3H), 1.02 (t, J = 7.2 Hz, 3H), 1.12 (sextet, J = 7.3 Hz, 2H), 1.33–1.71 (m, 6H), 2.34–2.46 (m, 2H), 2.44 (s, 3H), 2.70–2.80 (m, 2H), 7.14 (d, J = 8.3 Hz, 2H), 7.31 (d, J = 7.8 Hz, 2H), 7.38–7.49 (m, 1H), 7.64–7.73 (m, 2H), 8.43–8.49 (m, 1H); ^{13}C NMR: δ = 13.3, 14.0, 21.2, 22.6, 23.1, 27.3, 29.8, 31.3, 32.5, 113.5, 122.6, 125.3, 125.6, 128.46, 128.54, 129.8, 132.2, 136.8, 137.0, 138.0, 140.3, 163.0; HRMS (EI^+): Calcd for $\text{C}_{24}\text{H}_{29}\text{NO}$, M^+ 347.2249. Found m/z 347.2250.

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



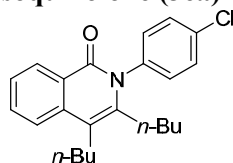
IR (KBr): 1692, 1613, 1514, 1462, 1306, 1258, 1177, 1088, 1042 cm^{-1} ; ^1H NMR: δ = 0.73 (t, J = 7.4 Hz, 3H), 1.01 (t, J = 7.1 Hz, 3H), 1.12 (sextet, J = 7.3 Hz, 2H), 1.32–1.70 (m, 6H), 2.35–2.45 (m, 2H), 2.69–2.79 (m, 2H), 3.86 (s, 3H), 7.02 (d, J = 8.7 Hz, 2H), 7.17 (d, J = 9.0 Hz, 2H), 7.38–7.48 (m, 1H), 7.64–7.72 (m, 2H), 8.45 (d, J = 7.8 Hz, 1H); ^{13}C NMR: δ = 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 $\text{C}_{24}\text{H}_{29}\text{NO}_2$, M^+ 363.2198. Found m/z 363.2196.

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

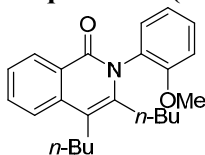


IR (KBr): 1698, 1387, 1111, 1086, 1038 cm^{-1} ; ^1H NMR: δ = 0.70 (t, J = 7.4 Hz, 3H), 1.03 (t, J = 7.1 Hz, 3H), 1.12 (sextet, J = 7.3 Hz, 2H), 1.31–1.45 (m, 2H), 1.47–1.72 (m, 4H), 2.31–2.43 (m, 2H), 2.71–2.82 (m, 2H), 7.39–7.51 (m, 3H), 7.67–7.76 (m, 2H), 7.80 (d, J = 8.4 Hz, 2H), 8.44 (d, J = 7.5 Hz, 1H); ^{13}C NMR: δ = 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 $\text{C}_{24}\text{H}_{26}\text{F}_3\text{NO}$, M^+ 401.1966. Found m/z 401.1969.

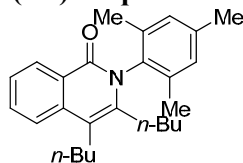
3,4-Dibutyl-2-(4-chlorophenyl)-1(2*H*)-isoquinolone (3ea)



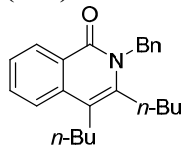
IR (KBr): 2957, 1653, 1611, 1582, 1491, 1329, 1086, 1017 cm^{-1} ; ^1H NMR: δ = 0.74 (t, J = 7.2 Hz, 3H), 1.02 (t, J = 7.2 Hz, 3H), 1.13 (sext, J = 7.3 Hz, 2H), 1.30–1.44 (m, 2H), 1.45–1.70 (m, 4H), 2.31–2.43 (m, 2H), 2.68–2.79 (m, 2H), 7.21 (dt, J = 8.4, 2.5 Hz, 2H), 7.39–7.54 (m, 3H), 7.64–7.74 (m, 2H), 8.43 (d, J = 8.1 Hz, 1H); ^{13}C NMR: δ = 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 $\text{C}_{23}\text{H}_{26}\text{ClNO}$, M^+ 367.1703. Found m/z 367.1701.

3,4-Dibutyl-2-(2-methoxyphenyl)-1(2*H*)-isoquinolone (3fa)

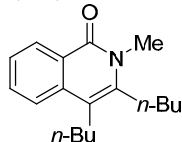
IR (KBr): 1694, 1603, 1501, 1466, 1281, 1250, 1080, 1049, 1020 cm^{-1} ; ^1H NMR: δ = 0.69 (t, J = 7.5 Hz, 3H), 1.02 (t, J = 7.4 Hz, 3H), 1.09 (sext, J = 7.3 Hz, 2H), 1.29–1.42 (m, 2H), 1.45–1.72 (m, 4H), 2.16–2.29 (m, 1H), 2.41–2.55 (m, 1H), 2.67–2.85 (m, 2H), 3.76 (s, 3H), 7.02–7.12 (m, 2H), 7.21 (dd, 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: δ = 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 $\text{C}_{24}\text{H}_{29}\text{NO}_2$, M^+ 363.2198. Found m/z 363.2201.

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

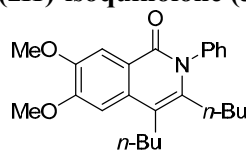
IR (KBr): 2961, 1655, 1613, 1594, 1487, 1327 cm^{-1} ; ^1H NMR: δ = 0.72 (t, J = 7.1 Hz, 3H), 1.02 (t, J = 7.4 Hz, 3H), 1.17 (sext, J = 7.1 Hz, 2H), 1.24–1.37 (m, 2H), 1.45–1.71 (m, 4H), 2.01 (s, 6H), 2.25–2.37 (m, 5H), 2.72–2.82 (m, 2H), 6.99 (s, 2H), 7.44 (ddd, J = 8.0, 6.1, 2.0 Hz, 1H), 7.66–7.76 (m, 2H), 8.49 (d, J = 7.8 Hz, 1H); ^{13}C NMR: δ = 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 $\text{C}_{26}\text{H}_{33}\text{NO}$, M^+ 375.2562. Found m/z 375.2558.

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

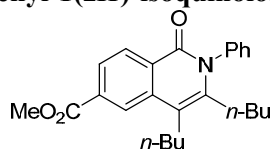
IR (KBr): 2955, 1644, 1590, 1495, 1464, 1458, 1381, 1343 cm^{-1} ; ^1H NMR: δ = 0.96 (t, J = 7.2 Hz, 3H), 1.00 (t, J = 7.1 Hz, 3H), 1.36–1.66 (m, 8H), 2.57–2.78 (m, 4H), 5.50 (br s, 2H), 7.08–7.18 (m, 2H), 7.18–7.34 (m, 3H), 7.40–7.51 (m, 1H), 7.63–7.73 (m, 2H), 8.50–8.57 (m, 1H); ^{13}C NMR: δ = 13.7, 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 $\text{C}_{24}\text{H}_{29}\text{NO}$, M^+ 347.2249. Found m/z 347.2249.

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

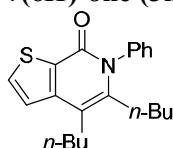
IR (neat): 2957, 1649, 1611, 1593, 1557, 1487, 1466, 1337, 1034 cm^{-1} ; ^1H NMR: δ = 0.99 (t, J = 7.2 Hz, 3H), 1.00 (t, J = 7.1 Hz, 3H), 1.41–1.62 (m, 8H), 2.66–2.77 (m, 4H), 3.65 (s, 3H), 7.35–7.45 (m, 1H), 7.57–7.65 (m, 2H), 8.43–8.48 (m, 1H); ^{13}C NMR: δ = 13.7, 13.9, 22.9, 23.0, 27.3, 29.4, 31.2,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

3,4-Dibutyl-6,7-dimethoxy-2-phenyl-1(2*H*)-isoquinolone (3ka)

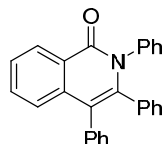
IR (KBr): 2955, 1655, 1603, 1509, 1464, 1397, 1267, 1215, 1165 cm^{-1} ; ^1H NMR: δ = 0.67 (t, J = 7.3 Hz, 3H), 0.98–1.15 (m, 5H), 1.30–1.43 (m, 2H), 1.45–1.71 (m, 4H), 2.29–2.40 (m, 2H), 2.66–2.76 (m, 2H), 3.96 (s, 3H), 4.02 (s, 3H), 7.04 (s, 1H), 7.25 (d, J = 7.2 Hz, 2H), 7.40–7.55 (m, 3H), 7.83 (s, 1H); ^{13}C NMR: δ = 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 $\text{C}_{25}\text{H}_{31}\text{NO}_3$, M^+ 393.2304. Found m/z 393.2305.

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

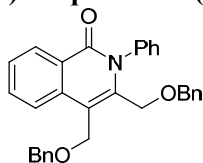
IR (neat): 2957, 1728, 1661, 1590, 1559, 1491, 1437, 1335, 1260, 1109 cm^{-1} ; ^1H NMR: δ = 0.68 (t, J = 7.4 Hz, 3H), 0.98–1.16 (m, 5H), 1.32–1.45 (m, 2H), 1.46–1.70 (m, 4H), 2.33–2.43 (m, 2H), 2.74–2.83 (m, 2H), 3.99 (s, 3H), 7.23–7.29 (m, 2H), 7.42–7.56 (m, 3H), 8.02 (dd, J = 8.3, 1.4 Hz, 1H), 8.39–8.44 (m, 1H), 8.48 (d, J = 8.4 Hz, 1H); ^{13}C NMR: δ = 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 $\text{C}_{25}\text{H}_{29}\text{NO}_3$, M^+ 391.2147. Found m/z 391.2148.

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

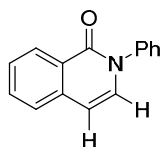
IR (KBr): 2955, 1647, 1570, 1524 cm^{-1} ; ^1H NMR: δ = 0.67 (t, J = 7.4 Hz, 3H), 0.99 (t, J = 7.4 Hz, 3H), 1.08 (sext, J = 7.3 Hz, 2H), 1.28–1.40 (m, 2H), 1.48 (sext, J = 7.2 Hz, 2H), 1.55–1.68 (m, 2H), 2.31–2.40 (m, 2H), 2.64–2.75 (m, 2H), 7.23–7.30 (m, 3H), 7.40–7.55 (m, 3H), 7.69 (d, J = 5.1 Hz, 1H); ^{13}C NMR: δ = 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 $\text{C}_{21}\text{H}_{25}\text{NOS}$, M^+ 339.1657. Found m/z 339.1654.

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

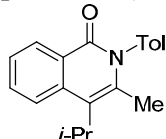
2,3,4-Triphenyl-1(2*H*)-isoquinolone is a known compound.²⁴ Only NMR data are shown here. ^1H NMR: δ = 6.83–6.99 (m, 5H), 7.19–7.32 (m, 11H), 7.50–7.64 (m, 2H), 8.56–8.63 (m, 1H); ^{13}C NMR: δ = 118.7, 125.4, 125.5, 126.8, 127.0, 127.1, 127.4, 127.9, 128.1, 128.5, 129.4, 130.9, 131.5, 132.4, 134.6,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

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

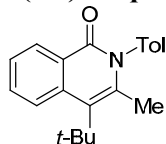
IR (KBr): 1667, 1619, 1592, 1487, 1453, 1364, 1323, 1073 cm^{-1} ; ^1H NMR: δ = 4.04 (s, 2H), 4.09 (s, 2H), 4.63 (s, 2H), 4.72 (s, 2H), 7.14–7.22 (m, 2H), 7.27–7.44 (m, 10H), 7.45–7.58 (m, 4H), 7.69–7.78 (m, 1H), 7.87 (d, J = 8.1 Hz, 1H), 8.49 (dd, J = 8.4, 1.1 Hz, 1H); ^{13}C NMR: δ = 64.5, 65.0, 72.6, 72.9, 113.4, 123.6, 126.1, 127.2, 127.8, 127.9, 128.15, 128.18, 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 $\text{C}_{31}\text{H}_{28}\text{NO}_3$, $\text{M}+\text{H}^+$ 462.2069. Found m/z 462.2066.

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

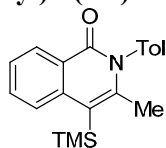
IR (KBr): 1661, 1624, 1588, 1293 cm^{-1} ; ^1H NMR: δ = 6.56 (d, J = 7.5 Hz, 1H), 7.18 (d, J = 7.8 Hz, 1H), 7.36–7.59 (m, 7H), 7.63–7.71 (m, 1H), 8.45–8.51 (m, 1H); ^{13}C NMR: δ = 106.1, 125.8, 126.4, 126.7, 127.0, 127.9, 128.1, 129.1, 132.0, 132.4, 136.9, 141.2, 161.8; HRMS (EI $^+$): Calcd for $\text{C}_{15}\text{H}_{11}\text{NO}$, M^+ 221.0841. Found m/z 221.0844.

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

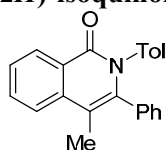
IR (KBr): 2932, 1651, 1592, 1512, 1483, 1333, 1181 cm^{-1} ; ^1H NMR: δ = 1.49 (d, J = 7.2 Hz, 6H), 2.07 (s, 3H), 2.43 (s, 3H), 3.57 (sept, J = 7.2 Hz, 1H), 7.08–7.15 (m, 2H), 7.28–7.35 (m, 2H), 7.39–7.47 (m, 1H), 7.62–7.70 (m, 1H), 7.95 (d, J = 8.4 Hz, 1H), 8.48–8.54 (m, 1H); ^{13}C NMR: δ = 18.8, 21.1, 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 $\text{C}_{20}\text{H}_{21}\text{NO}$, M^+ 291.1623. Found m/z 291.1625.

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

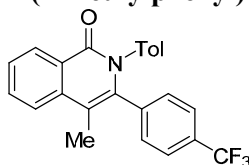
IR (KBr): 1655, 1510, 1478 cm^{-1} ; ^1H NMR: δ = 1.63 (s, 9H), 2.12 (s, 3H), 2.43 (s, 3H), 7.08–7.14 (m, 2H), 7.28–7.34 (m, 2H), 7.35–7.42 (m, 1H), 7.55–7.62 (m, 1H), 8.05 (d, J = 8.7 Hz, 1H), 8.40–8.45 (m, 1H); ^{13}C NMR: δ = 21.2, 23.2, 33.4, 36.3, 123.2, 124.8, 125.7, 125.8, 128.1, 128.3, 130.1, 130.2, 135.9, 137.2, 137.5, 138.0, 162.6; HRMS (EI $^+$): Calcd for $\text{C}_{21}\text{H}_{23}\text{NO}$, M^+ 305.1780. Found m/z 305.1776.

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

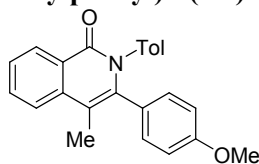
IR (KBr): 1651, 1510, 1474, 1300, 1252 cm^{-1} ; ^1H NMR: δ = 0.48 (s, 9H), 2.11 (s, 3H), 2.43 (s, 3H), 7.10 (d, J = 7.8 Hz, 2H), 7.13 (d, J = 7.8 Hz, 2H), 7.41 (t, J = 7.5 Hz, 1H), 7.61 (td, J = 8.4, 1.4 Hz, 1H), 7.84 (d, J = 8.4 Hz, 1H), 8.43 (dd, J = 8.1, 1.8 Hz, 1H); ^{13}C NMR: δ = 3.7, 21.2, 23.4, 110.1, 125.2, 125.4, 126.5, 128.1, 128.4, 130.2, 131.4, 137.1, 138.1, 140.2, 145.2, 163.4; HRMS (EI^+): Calcd for $\text{C}_{20}\text{H}_{23}\text{NOSi}$, M^+ 321.1549. Found m/z 321.1548.

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

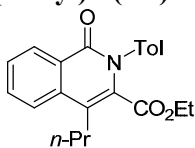
IR (KBr): 1661, 1592, 1510, 1483, 1327 cm^{-1} ; ^1H NMR: δ = 2.11 (s, 3H), 2.23 (s, 3H), 6.93 (d, J = 8.4 Hz, 2H), 7.01 (d, J = 8.7 Hz, 2H), 7.05–7.24 (m, 5H), 7.50–7.62 (m, 1H), 7.72–7.80 (m, 2H), 8.58 (d, J = 7.8 Hz, 1H); ^{13}C NMR: δ = 14.8, 21.0, 110.1, 123.2, 125.6, 126.5, 127.57, 127.63, 128.4, 129.0, 129.1, 130.3, 132.4, 135.3, 136.90, 136.93, 137.4, 140.2, 162.4; HRMS (EI^+): Calcd for $\text{C}_{23}\text{H}_{19}\text{NO}$, M^+ 325.1467. Found m/z 325.1465.

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

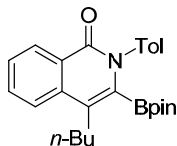
IR (KBr): 1657, 1611, 1510, 1485, 1323, 1125, 1067 cm^{-1} ; ^1H NMR: δ = 2.08 (s, 3H), 2.24 (s, 3H), 6.91 (d, J = 8.1 Hz, 2H), 7.01 (d, J = 8.4 Hz, 2H), 7.23 (d, J = 8.4 Hz, 2H), 7.47 (d, J = 8.1 Hz, 2H), 7.52–7.63 (m, 1H), 7.74–7.81 (m, 2H), 8.56 (d, J = 8.1 Hz, 1H); ^{13}C NMR: δ = 14.8, 21.0, 110.5, 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 $\text{C}_{24}\text{H}_{18}\text{F}_3\text{NO}$, M^+ 393.1340. Found m/z 393.1344.

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

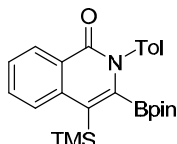
IR (KBr): 1655, 1613, 1510, 1483, 1327, 1244, 1032 cm^{-1} ; ^1H NMR: δ = 2.10 (s, 3H), 2.24 (s, 3H), 3.74 (s, 3H), 6.71 (d, J = 8.4 Hz, 2H), 6.91 (d, J = 8.1 Hz, 2H), 6.94–7.05 (m, 4H), 7.48–7.59 (m, 1H), 7.70–7.78 (m, 2H), 8.52–8.58 (m, 1H); ^{13}C NMR: δ = 14.9, 21.1, 55.0, 110.5, 113.1, 123.2, 125.7, 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 $\text{C}_{24}\text{H}_{21}\text{NO}_2$, M^+ 355.1572. Found m/z 355.1566.

3-Ethoxycarbonyl-4-propyl-2-(4-methylphenyl)-1(2H)-isoquinolone (3bk)

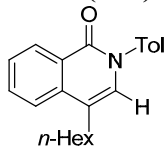
IR (KBr): 2940, 1734, 1663, 1599, 1509, 1325, 1206, 1134, 1007 cm^{-1} ; ^1H NMR: δ = 0.97 (t, J = 7.2 Hz, 3H), 1.02 (t, J = 7.5 Hz, 3H), 1.71 (sextet, J = 7.6 Hz, 2H), 2.38 (s, 3H), 2.62–2.73 (m, 2H), 3.93 (q, J = 7.1 Hz, 2H), 7.20–7.28 (m, 4H), 7.48–7.60 (m, 1H), 7.68–7.78 (m, 2H), 8.51 (d, J = 7.8 Hz, 1H); ^{13}C 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, 135.9, 138.4, 161.3, 163.3; HRMS (EI^+): Calcd for $\text{C}_{22}\text{H}_{23}\text{NO}_3$, M^+ 349.1678. Found m/z 349.1682.

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

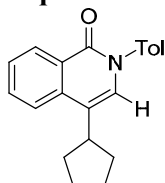
IR (KBr): 2953, 1653, 1510, 1455, 1375, 1331, 1213, 1144 cm^{-1} ; ^1H NMR: δ = 0.97 (t, J = 7.4 Hz, 3H), 1.01 (s, 12H), 1.46 (sextet, J = 7.4 Hz, 2H), 1.59–1.72 (m, 2H), 2.39 (s, 3H), 2.68–2.77 (m, 2H), 7.26 (s, 4H), 7.46–7.54 (m, 1H), 7.65–7.73 (m, 2H), 8.45–8.51 (m, 1H); ^{13}C NMR: δ = 14.0, 21.1, 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, 136.4, 138.3, 138.7, 162.2 (The boron-bound carbon was not detected due to the quadrupolar relaxation); HRMS (EI^+): Calcd for $\text{C}_{26}\text{H}_{32}\text{BNO}_3$, 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)

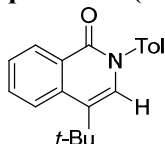
IR (KBr): 1653, 1343, 1252, 1138 cm^{-1} ; ^1H NMR: δ = 0.48 (s, 9H), 1.02 (s, 12H), 2.41 (s, 3H), 7.21–7.31 (m, 4H), 7.43–7.50 (m, 1H), 7.60–7.67 (m, 1H), 7.89 (d, J = 8.1 Hz, 1H), 8.46 (dd, J = 7.7, 1.4 Hz, 1H); ^{13}C NMR: δ = 2.3, 21.2, 26.0, 84.8, 117.8, 126.3, 126.5, 127.1, 128.1, 129.6, 129.8, 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 $\text{C}_{25}\text{H}_{32}\text{BNO}_3\text{Si}$, M^+ 433.2245. Found m/z 433.2243.

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

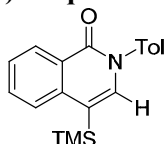
IR (neat): 2929, 1661, 1634, 1605, 1512, 1487, 1460, 1329, 1294, 1210, 1028 cm^{-1} ; ^1H NMR: δ = 0.85–0.95 (m, 3H), 1.25–1.49 (m, 6H), 1.67 (quint, J = 7.6 Hz, 2H), 2.42 (s, 3H), 2.64–2.73 (m, 2H), 7.00 (s, 1H), 7.27–7.36 (m, 4H), 7.47–7.58 (m, 1H), 7.66–7.76 (m, 2H), 8.51–8.57 (m, 1H); ^{13}C NMR: 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 $\text{C}_{22}\text{H}_{25}\text{NO}$, M^+ 319.1936. Found m/z 319.1930.

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

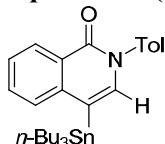
IR (KBr): 2951, 1655, 1628, 1605, 1510, 1483, 1294 cm^{-1} ; ^1H NMR: δ = 1.52–1.88 (m, 6H), 2.06–2.20 (m, 2H), 2.43 (s, 3H), 3.32 (quint, J = 8.1 Hz, 1H), 7.04 (s, 1H), 7.27–7.37 (m, 4H), 7.48–7.56 (m, 1H), 7.67–7.75 (m, 1H), 7.81 (d, J = 7.8 Hz, 1H), 8.52–8.59 (m, 1H); ^{13}C NMR: δ = 21.1, 24.8, 32.2, 38.9, 119.4, 123.1, 126.4, 126.5, 127.6, 128.6, 129.7, 132.0, 137.1, 137.7, 139.1, 161.5; HRMS (EI^+): Calcd for $\text{C}_{21}\text{H}_{21}\text{NO}$, M^+ 303.1623. Found m/z 303.1623.

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

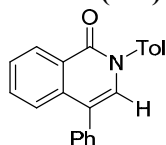
IR (KBr): 2963, 1655, 1619, 1512, 1480, 1341, 1312 cm^{-1} ; ^1H NMR: δ = 1.51 (s, 9H), 2.43 (s, 3H), 7.08 (s, 1H), 7.27–7.38 (m, 4H), 7.47–7.55 (m, 1H), 7.65–7.74 (m, 1H), 8.12 (d, J = 8.4 Hz, 1H), 8.62 (dd, J = 7.8, 1.8 Hz, 1H); ^{13}C NMR: δ = 21.1, 30.9, 33.8, 123.7, 125.7, 126.1, 126.5, 127.3, 128.8, 129.3, 129.8, 131.2, 136.1, 137.8, 139.2, 161.4; HRMS (EI^+): Calcd for $\text{C}_{20}\text{H}_{21}\text{NO}$, M^+ 291.1623. Found m/z 291.1625.

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

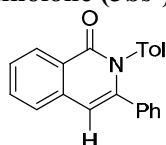
IR (KBr): 1655, 1605, 1592, 1510, 1478, 1321, 1296, 1250 cm^{-1} ; ^1H NMR: δ = 0.40 (s, 9H), 2.43 (s, 3H), 7.16 (s, 1H), 7.33 (s, 4H), 7.48–7.55 (m, 1H), 7.65–7.72 (m, 1H), 7.73–7.78 (m, 1H), 8.53–8.58 (m, 1H); ^{13}C NMR: δ = -0.3, 21.1, 112.6, 126.5, 126.6, 128.7, 129.8, 132.0, 137.7, 137.9, 138.9, 139.6, 162.2; HRMS (EI^+): Calcd for $\text{C}_{19}\text{H}_{21}\text{NOSi}$, M^+ 307.1392. Found m/z 307.1395.

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

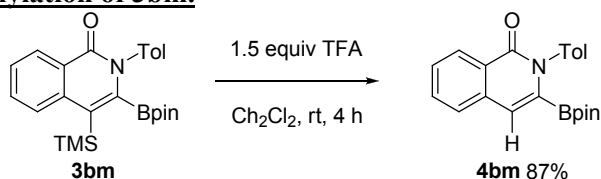
IR (neat): 2926, 1661, 1605, 1510, 1476, 1318, 1293, cm^{-1} ; ^1H NMR: δ = 0.89 (t, J = 7.2 Hz, 9H), 1.02–1.27 (m, 6H), 1.35 (sextet, J = 7.3 Hz, 6H), 1.42–1.71 (m, 6H), 2.44 (s, 3H), 7.02 (s, 1H), 7.28–7.39 (m, 4H), 7.43–7.55 (m, 2H), 7.63–7.72 (m, 1H), 8.51–8.58 (m, 1H); ^{13}C NMR: δ = 10.1, 13.6, 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 $\text{C}_{28}\text{H}_{39}\text{NOSn}$, M^+ 525.2054. Found m/z 525.2053.

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

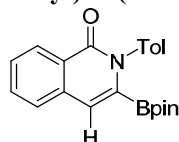
IR (neat): 3060, 1667, 1628, 1601, 1512, 1497, 1445, 1329, 1271, 1030 cm^{-1} ; ^1H NMR: δ = 2.42 (s, 3H), 7.18 (s, 1H), 7.30 (d, J = 8.7 Hz, 2H), 7.37 (d, J = 8.1 Hz, 2H), 7.40–7.69 (m, 8H), 8.56–8.61 (m, 1H); ^{13}C NMR: δ = 21.2, 119.5, 124.7, 126.3, 126.5, 127.1, 127.7, 128.6, 129.8, 129.9, 131.3, 132.3, 136.2, 136.4, 138.0, 138.7, 161.6; HRMS (EI^+): Calcd for $\text{C}_{22}\text{H}_{17}\text{NO}$, M^+ 311.1310. Found m/z 311.1310.

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

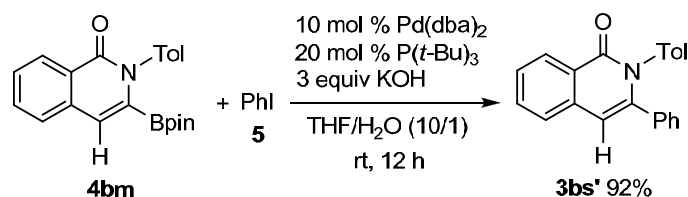
IR (KBr): 1649, 1622, 1512, 1482, 1383, 1277 cm^{-1} ; ^1H NMR: δ = 2.28 (s, 3H), 6.59 (s, 1H), 7.01 (d, J = 8.4 Hz, 2H), 7.07 (d, J = 8.7 Hz, 2H), 7.15–7.23 (m, 5H), 7.47–7.54 (m, 1H), 7.55 (d, J = 7.8 Hz, 1H), 7.64–7.72 (m, 1H), 8.45–8.50 (m, 1H); ^{13}C NMR: δ = 21.1, 107.7, 125.3, 125.9, 126.7, 127.7, 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 $\text{C}_{22}\text{H}_{17}\text{NO}$, M^+ 311.1310. Found m/z 311.1310.

Procedure for the De-Silylation of 3bm.

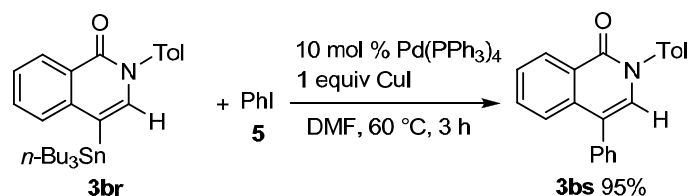
To a solution of **3bm** (81.1 mg, 0.187 mmol) in CH_2Cl_2 (3.7 mL) was added TFA (21 μL , 0.283 mmol). The mixture was stirred at room temperature for 4 hours, and then concentrated under reduced pressure. The residue was purified by preparative thin-layer chromatography (chloroform/ethyl acetate 10:1) 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)

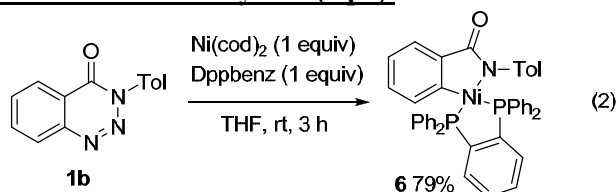
IR (KBr): 2979, 1653, 1510, 1451, 1395, 1347, 1262, 1213, 1142 cm^{-1} ; ^1H NMR: δ = 1.07 (s, 12H), 2.40 (s, 3H), 6.96 (s, 1H), 7.17–7.25 (m, 4H), 7.49–7.59 (m, 2H), 7.62–7.70 (m, 1H), 8.44 (d, J = 7.8 Hz, 1H); ^{13}C NMR: δ = 21.1, 24.2, 84.3, 115.0, 126.2, 127.2, 127.75, 127.82, 128.0, 129.3, 132.2, 136.2, 137.6, 139.2, 162.6 (The boron-bound carbon was not detected due to the quadrupolar relaxation); HRMS (EI^+): Calcd for $\text{C}_{22}\text{H}_{24}\text{BNO}_3$, M^+ 361.1849. Found m/z 361.1847.

Procedure for the Cross-Coupling Reaction of 4bm with Phenyl iodide.^{15c}

To an oven-dried flask was added **4bm** (46.7 mg, 0.129 mmol), a solution of Pd(dba)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 MgSO₄. 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.²⁵

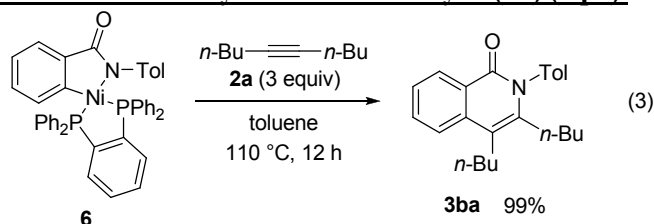
To an oven-dried flask was added Pd(PPh₃)₄ (12.8 mg, 11.1 μmol), copper iodide (21.3 mg, 11.2 μmol), a solution of **3br** (57.6 mg, 0.11 mmol) in DMF (2.2 mL), and phenyl iodide (25 μL, 0.224 mmol) at room temperature. The reaction mixture was stirred at 60 °C for 3 hours under an argon atmosphere, 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 MgSO₄. 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).

In an N₂-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 CH₂Cl₂/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; ¹H NMR (CD₂Cl₂): 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); ¹³C NMR (CD₂Cl₂): 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_2Cl_2): $\delta = 39.9, 53.6$; HRMS (FAB^+): Calcd for $\text{C}_{44}\text{H}_{36}\text{NNiOP}_2$, $\text{M}+\text{H}^+$ 714.1626. Found m/z 714.1652.

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



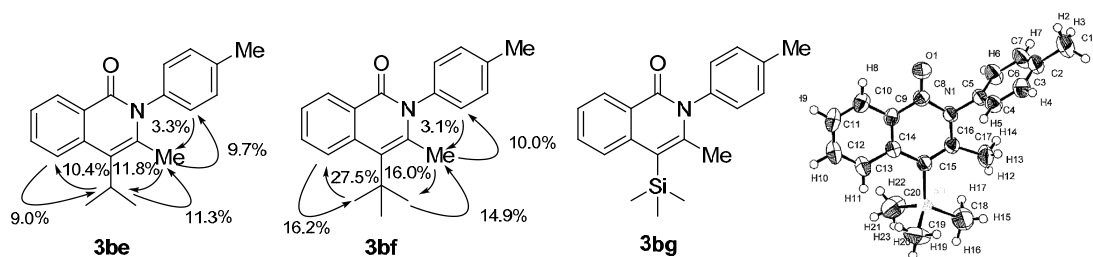
In an N_2 -filled glove-box, azanickelacycle **6** (35.2 g, 49.3 μmol) was charged into an oven-dried 4 mL-vial equipped with a stir bar. Then, toluene (2 mL) and dec-5-yne (**2a**, 27 μL , 0.15 mmol) were added. The vial was capped with a Teflon film and the reaction mixture was taken outside the glove-box. After heated at 110 $^\circ\text{C}$ 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 **3ba** (17 mg, 49.2 μmol , 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.

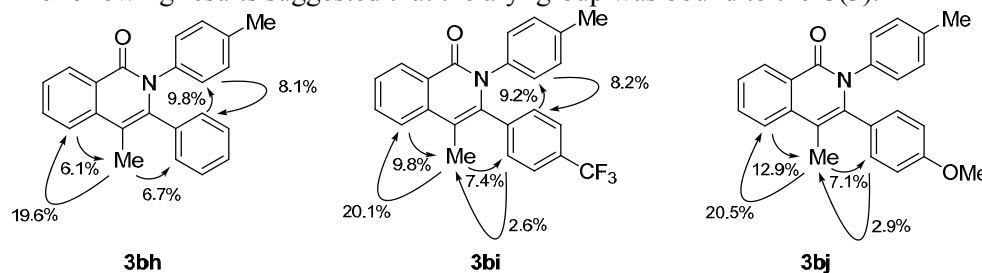
[Compound 3be, 3bf and 3bg]

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



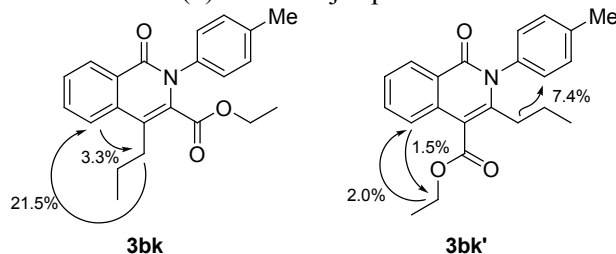
[Compound 3bh, 3bi, and 3bj]

The following results suggested that the aryl group was bound to the C(3).

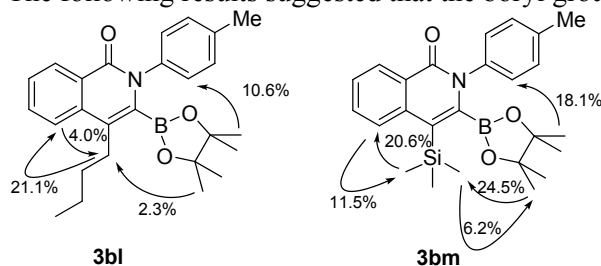


[Compound 3bk]

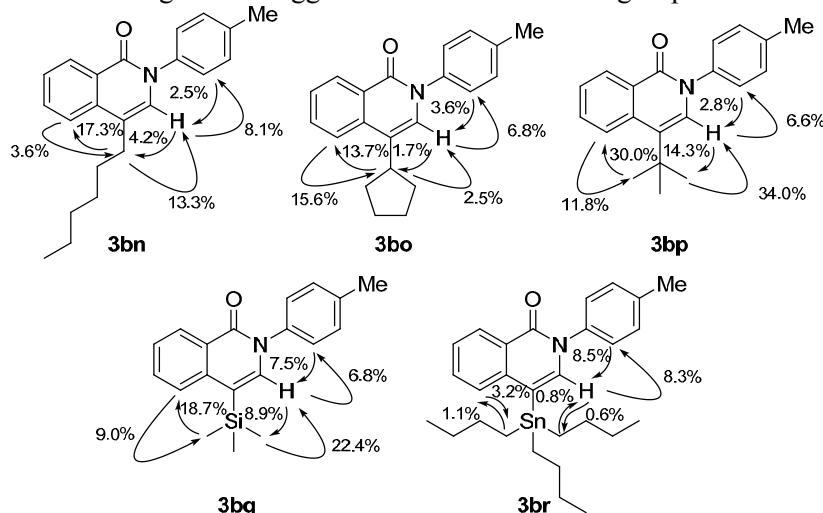
The following results of **3bk** and **3bk'** (minor product) suggested that the ethoxycarbonyl group was bound to the C(3) in the major product.

**[Compound 3bl and 3bm]**

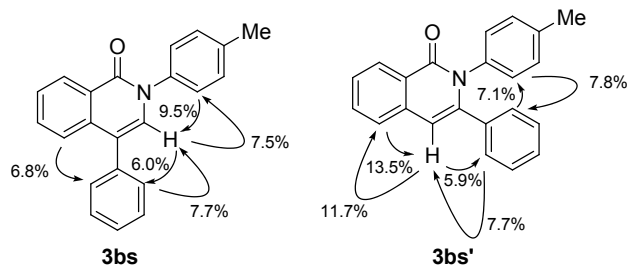
The following results suggested that the boryl group was bound to the C(3).

**[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 (CH₂Cl₂/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

Formula	C ₄₄ H ₃₅ NNiOP ₂
Fw	714.38
Crystal system	monoclinic
space group	p_21/n
<i>a</i> [Å]	12.3776(3)
<i>b</i> [Å]	14.4722(4)
<i>c</i> [Å]	19.9190(6)
α , deg	90.00
β , deg	92.9745(10)
γ , deg	90.00
<i>V</i> , [Å ³]	3563.30(17)
<i>Z</i>	4
<i>d</i> _{calc} , g/cm ³	1.332
<i>m</i> (Mo K α), mm ⁻¹	0.670
data/restraints/params	8134/0/443
R1	0.0295
wR2	0.0814

Table S2. Atomic Coordinates and Equivalent Isotropic Thermal Parameters

atom	X	Y	Z	U _{eq}
Ni1	0.853839(14)	0.254820(12)	0.576260(8)	0.02926(6)
P2	0.74868(3)	0.28958(3)	0.660585(17)	0.02872(8)
P3	0.99004(3)	0.26819(3)	0.647075(18)	0.03008(8)
C4	0.94663(11)	0.30438(10)	0.72947(7)	0.0327(3)
C53	0.94626(13)	0.24761(10)	0.49955(7)	0.0345(3)
C6	0.83557(11)	0.30953(10)	0.73622(7)	0.0319(3)
C7	0.64734(11)	0.21163(10)	0.69199(7)	0.0319(3)
C8	0.68214(12)	0.40122(10)	0.64627(7)	0.0348(3)
N1	0.73917(10)	0.23601(9)	0.51009(6)	0.0361(3)
C10	1.05827(12)	0.15758(11)	0.66209(8)	0.0367(3)
C11	0.63122(12)	0.20756(11)	0.52169(7)	0.0349(3)
C54	0.76513(14)	0.23979(12)	0.44507(8)	0.0427(4)
C13	1.09116(13)	0.35577(11)	0.62961(7)	0.0373(3)
C14	0.79607(13)	0.33261(12)	0.79868(7)	0.0420(4)
H9	0.7219	0.3353	0.8038	0.050
C15	0.53654(12)	0.22642(12)	0.68445(7)	0.0369(3)
H10	0.5101	0.2797	0.6632	0.044
C16	0.88355(13)	0.24896(10)	0.43937(7)	0.0345(3)
C17	0.97736(14)	0.34775(12)	0.84569(8)	0.0449(4)
H11	1.0247	0.3606	0.8823	0.054
C18	0.51021(14)	0.08678(12)	0.55358(8)	0.0441(4)

H1	0.5004	0.0269	0.5690	0.053
C19	1.01757(13)	0.32516(12)	0.78446(8)	0.0414(3)
H12	1.0919	0.3237	0.7797	0.050
C20	0.43853(14)	0.23200(13)	0.51895(8)	0.0457(4)
H2	0.3797	0.2710	0.5105	0.055
C21	1.10354(16)	0.25195(14)	0.43097(9)	0.0541(5)
H3	1.1784	0.2518	0.4285	0.065
C22	0.61377(13)	0.11843(11)	0.54419(8)	0.0400(3)
H4	0.6725	0.0794	0.5531	0.048
C23	0.86737(14)	0.35135(13)	0.85266(7)	0.0455(4)
H13	0.8408	0.3665	0.8941	0.055
O1	0.70150(11)	0.23331(14)	0.39561(6)	0.0783(5)
C25	1.13651(13)	0.14165(13)	0.71378(9)	0.0462(4)
H14	1.1577	0.1892	0.7430	0.055
C26	0.42097(13)	0.14255(13)	0.54044(7)	0.0438(4)
C27	0.68439(14)	0.13084(12)	0.72352(9)	0.0461(4)
H15	0.7583	0.1196	0.7287	0.055
C28	1.03888(16)	0.25715(13)	0.37284(9)	0.0491(4)
H5	1.0695	0.2623	0.3314	0.059
C29	0.92793(15)	0.25464(12)	0.37682(8)	0.0439(4)
H6	0.8831	0.2567	0.3379	0.053
C30	0.54262(13)	0.26491(12)	0.50965(8)	0.0421(4)
H7	0.5526	0.3254	0.4954	0.051
C31	1.05157(18)	0.43766(13)	0.60208(10)	0.0565(5)
H16	0.9774	0.4454	0.5943	0.068
C32	0.46511(13)	0.16191(13)	0.70853(8)	0.0463(4)
H17	0.3910	0.1723	0.7034	0.056
C34	1.02693(16)	0.08434(13)	0.62040(10)	0.0522(4)
H18	0.9742	0.0936	0.5861	0.063
C35	0.57212(17)	0.52878(14)	0.67984(11)	0.0601(5)
H19	0.5269	0.5550	0.7105	0.072
C36	1.05812(14)	0.24690(14)	0.49360(9)	0.0491(4)
H8	1.1034	0.2430	0.5322	0.059
C37	1.20196(14)	0.34561(14)	0.64072(10)	0.0516(4)
H20	1.2300	0.2910	0.6591	0.062
C38	0.70608(17)	0.45048(13)	0.58929(9)	0.0525(4)
H21	0.7508	0.4245	0.5583	0.063
C39	0.61428(14)	0.44147(13)	0.69161(9)	0.0476(4)
H22	0.5972	0.4094	0.7301	0.057
C40	0.50268(16)	0.08301(13)	0.73978(9)	0.0539(4)
H23	0.4543	0.0403	0.7560	0.065
C41	1.18279(15)	0.05441(15)	0.72160(11)	0.0615(5)
H24	1.2356	0.0443	0.7557	0.074
C42	0.61214(17)	0.06738(13)	0.74709(10)	0.0570(5)
H25	0.6378	0.0137	0.7681	0.068
C43	0.30834(15)	0.10619(18)	0.55043(10)	0.0639(6)
H33	0.3132	0.0463	0.5712	0.096
H34	0.2693	0.1014	0.5077	0.096
H35	0.2711	0.1478	0.5788	0.096
C44	0.6639(2)	0.53830(15)	0.57814(12)	0.0778(7)
H26	0.6812	0.5711	0.5400	0.093
C45	1.1214(2)	0.50814(15)	0.58603(12)	0.0751(7)

H27	1.0940	0.5628	0.5674	0.090
C46	1.2313(2)	0.49726(16)	0.59761(12)	0.0755(7)
H28	1.2781	0.5447	0.5871	0.091
C48	1.1514(2)	-0.01687(15)	0.67944(14)	0.0733(6)
H29	1.1832	-0.0748	0.6849	0.088
C49	0.5964(2)	0.57704(15)	0.62334(12)	0.0733(6)
H30	0.5674	0.6356	0.6155	0.088
C51	1.27129(18)	0.41691(17)	0.62447(12)	0.0698(6)
H31	1.3456	0.4097	0.6320	0.084
C52	1.0733(2)	-0.00253(14)	0.62932(13)	0.0715(6)
H32	1.0512	-0.0510	0.6012	0.086

Table S3. Anisotropic Thermal Parameters

atom	U11	U22	U33	U23	U13	U12
Ni1	0.02773(10)	0.03812(11)	0.02199(9)	-0.00200(7)	0.00178(7)	0.00342(7)
P2	0.02699(17)	0.03694(19)	0.02228(16)	-0.00127(13)	0.00183(12)	0.00242(14)
P3	0.02727(17)	0.03643(19)	0.02662(17)	0.00054(14)	0.00208(13)	0.00292(14)
C4	0.0335(7)	0.0388(8)	0.0256(6)	-0.0006(6)	0.0005(5)	0.0016(6)
C53	0.0372(8)	0.0390(8)	0.0277(7)	-0.0032(6)	0.0059(6)	0.0042(6)
C6	0.0332(7)	0.0392(7)	0.0233(6)	0.0006(5)	0.0009(5)	0.0002(6)
C7	0.0332(7)	0.0373(7)	0.0254(6)	-0.0034(5)	0.0042(5)	-0.0008(6)
C8	0.0352(7)	0.0362(7)	0.0325(7)	-0.0024(6)	-0.0017(6)	0.0030(6)
N1	0.0308(6)	0.0518(8)	0.0257(6)	-0.0032(5)	0.0006(5)	-0.0025(5)
C10	0.0316(7)	0.0383(8)	0.0410(8)	0.0086(6)	0.0086(6)	0.0035(6)
C11	0.0332(7)	0.0483(9)	0.0230(6)	-0.0057(6)	-0.0010(5)	-0.0012(6)
C54	0.0423(9)	0.0580(10)	0.0275(7)	-0.0018(7)	0.0002(6)	-0.0071(7)
C13	0.0422(8)	0.0382(8)	0.0318(7)	-0.0010(6)	0.0067(6)	-0.0027(6)
C14	0.0392(8)	0.0599(10)	0.0272(7)	-0.0023(7)	0.0050(6)	-0.0003(7)
C15	0.0339(7)	0.0498(9)	0.0268(7)	-0.0003(6)	0.0005(6)	-0.0011(6)
C16	0.0406(8)	0.0350(7)	0.0282(7)	-0.0011(5)	0.0052(6)	-0.0013(6)
C17	0.0500(9)	0.0542(10)	0.0293(7)	-0.0032(7)	-0.0092(6)	0.0015(8)
C18	0.0500(9)	0.0436(9)	0.0391(8)	-0.0072(7)	0.0059(7)	-0.0064(7)
C19	0.0344(7)	0.0543(10)	0.0349(8)	-0.0030(7)	-0.0053(6)	0.0033(7)
C20	0.0351(8)	0.0660(11)	0.0356(8)	0.0010(7)	-0.0021(6)	0.0087(7)
C21	0.0413(9)	0.0797(14)	0.0425(9)	-0.0045(8)	0.0150(7)	0.0051(9)
C22	0.0380(8)	0.0433(8)	0.0385(8)	-0.0062(6)	0.0007(6)	0.0042(7)
C23	0.0529(9)	0.0600(10)	0.0236(7)	-0.0034(7)	0.0014(6)	0.0012(8)
O1	0.0482(8)	0.1584(17)	0.0278(6)	-0.0014(8)	-0.0043(5)	-0.0243(9)
C25	0.0369(8)	0.0528(10)	0.0492(9)	0.0144(8)	0.0032(7)	0.0032(7)
C26	0.0370(8)	0.0653(11)	0.0292(7)	-0.0096(7)	0.0032(6)	-0.0051(7)
C27	0.0435(9)	0.0421(9)	0.0530(10)	0.0041(7)	0.0067(7)	0.0065(7)
C28	0.0541(10)	0.0597(11)	0.0350(8)	0.0031(7)	0.0180(8)	0.0034(8)
C29	0.0525(10)	0.0522(10)	0.0272(7)	0.0024(6)	0.0054(7)	-0.0001(7)
C30	0.0411(8)	0.0504(9)	0.0347(8)	0.0051(7)	-0.0014(6)	0.0027(7)
C31	0.0682(12)	0.0419(9)	0.0600(11)	0.0060(8)	0.0080(9)	0.0034(9)
C32	0.0380(8)	0.0647(11)	0.0366(8)	-0.0051(7)	0.0056(6)	-0.0097(8)
C34	0.0555(10)	0.0424(9)	0.0583(11)	0.0004(8)	0.0008(8)	0.0051(8)
C35	0.0596(11)	0.0543(11)	0.0661(12)	-0.0160(10)	0.0014(9)	0.0204(9)
C36	0.0379(9)	0.0766(13)	0.0331(8)	-0.0075(8)	0.0054(7)	0.0078(8)
C37	0.0428(9)	0.0542(10)	0.0578(11)	0.0054(8)	0.0038(8)	-0.0085(8)

C38	0.0713(12)	0.0455(10)	0.0413(9)	0.0056(7)	0.0090(8)	0.0117(9)
C39	0.0494(9)	0.0499(10)	0.0440(9)	-0.0045(7)	0.0070(7)	0.0091(8)
C40	0.0602(11)	0.0529(10)	0.0501(10)	-0.0025(8)	0.0166(8)	-0.0172(9)
C41	0.0456(10)	0.0659(13)	0.0733(13)	0.0340(11)	0.0050(9)	0.0118(9)
C42	0.0706(12)	0.0396(9)	0.0616(11)	0.0091(8)	0.0117(9)	0.0010(9)
C43	0.0429(10)	0.0948(16)	0.0549(11)	-0.0099(11)	0.0107(8)	-0.0155(10)
C44	0.125(2)	0.0507(12)	0.0587(12)	0.0164(10)	0.0117(13)	0.0243(13)
C45	0.114(2)	0.0404(11)	0.0717(14)	0.0078(10)	0.0174(14)	-0.0104(12)
C46	0.1033(19)	0.0603(13)	0.0650(13)	-0.0061(10)	0.0235(13)	-0.0408(13)
C48	0.0735(14)	0.0464(11)	0.1009(18)	0.0231(12)	0.0141(13)	0.0178(10)
C49	0.1006(18)	0.0463(11)	0.0717(14)	-0.0011(10)	-0.0079(12)	0.0282(11)
C51	0.0578(12)	0.0786(15)	0.0739(14)	-0.0042(12)	0.0129(10)	-0.0291(11)
C52	0.0822(15)	0.0400(10)	0.0924(17)	0.0005(10)	0.0035(13)	0.0081(10)

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-Ni1-P3	92.68(5)	N1-Ni1-P2	96.32(4)
C53-Ni1-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-N1	126.08(16)	O1-C54-C16	122.62(15)
N1-C54-C16	111.24(13)	C31-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	119.92(19)	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

References and Notes

- (1) (a) Lewis, J. R. *Nat. Prod. Rep.* **1994**, *11*, 329. (b) González, M. C.; Zafra-Polo, C.; Blázquez, A.; Serrano, A.; Cortes, D. *J. Nat. Prod.* **1997**, *60*, 108. (c) Chen, C.-Y.; Chang, F.-R.; Pan, W.-B.; Wu, Y.-C. *Phytochemistry* **2001**, *56*, 753. (d) Zhang, Z.; Li, S.; Zhang, S.; Liang, C.; Gorenstein, D.; Beasley, R. S. *Planta Med.* **2004**, *70*, 1216.
- (2) (a) Nagarajan, M.; Morrell, A.; Fort, B. C.; Meckley, M. R.; Antony, S.; Kohlhagen, G.; Pommier, Y.; Cushman, M. *J. Med. Chem.* **2004**, *47*, 5651. (b) Ruchelman, A. L.; Houghton, P. J.; Zhou, N.; Liu, A.; Liu, L. F.; LaVoie, E. J. *J. Med. Chem.* **2005**, *48*, 792. (c) Cappelli, A.; Mohr, G. P.; Giuliani, G.; Galeazzi, S.; Anzini, M.; Mennuni, L.; Ferrari, F.; Makovec, F.; Kleinrath, E. M.; Langer, T.; Valoti, M.; Giorgi, G.; Vomero, S. *J. Med. Chem.* **2006**, *49*, 6451.
- (3) For a review, see: Glushkov, V. A.; Shklyayev, Y. V. *Chem. Heterocycl. Comp.* **2001**, *37*, 663.
- (4) For reviews, see: (a) Varela, J. A.; Saá, C. *Chem. Rev.* **2003**, *103*, 3787. (b) Nakamura, I.; Yamamoto, Y. *Chem. Rev.* **2004**, *104*, 2127. (c) Alonso, F.; Beletskaya, I. P.; Yus, M. *Chem. Rev.* **2004**, *104*, 3079. (d) Cacchi, S.; Fabrizi, G. *Chem. Rev.* **2005**, *105*, 2873.
- (5) (a) Hudlicky, T.; Olivo, H. F. *J. Am. Chem. Soc.* **1992**, *114*, 9694. (b) Grigg, R.; Sridharan, V.; Xu, L.-H. *J. Chem. Soc., Chem. Commun.* **1995**, 1903. (c) Mahanty, J. S.; De, M.; Kundu, N. G. *J. Chem. Soc., Perkin Trans. 1* **1997**, 2577. (d) Sashida, H.; Kawamukai, A. *Synthesis* **1999**, 1145. (e) Batchu, V. R.; Barange, D. K.; Kumar, D.; Sreekanth, B. R.; Vyas, K.; Reddy, E. A.; Pal, M. *Chem. Commun.* **2007**, 1966. (f) During the preparation of our manuscript, Matsubara and co-workers reported a nickel-catalyzed decarbonylative alkyne insertion of phthalimides: Kajita, Y.; Matsubara, S.; Kurahashi, T. *J. Am. Chem. Soc.* **2008**, *130*, 6058.
- (6) Chuprakov, S.; Hwang, F. W.; Gevorgyan, V. *Angew. Chem. Int. Ed.* **2007**, *46*, 4757.
- (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.
- (8) For thermolysis of 3-aryl-1,2,3-benzotriazin-4(3H)-ones, see: (a) Hey, D. H.; Rees, C. W.; Todd, A. R. *J. Chem. Soc., C*, **1968**, 1028. (b) Barker, A. J.; Paterson, T. M.; Smalley, R. K.; Suschitzky, H. *J. Chem. Soc., Perkin Trans 1*. **1979**, 2203. (c) Cirrincione, G.; Almerico, A. M.; Dattolo, G.; Aiello, E.; Diana, P.; Mingoa, F. *J. Heterocycl. Chem.* **1992**, *29*, 1309.
- (9) See the Experimental Section for details.
- (10) For precedence of an intermediacy of a similar azanickelacycle, see: (a) Takahashi, T.; Tsai, F.-Y.; Li, Y.; Wang, H.; Kondo, Y.; Yamanaka, M.; Nakajima, K.; Kotora, M. *J. Am. Chem. Soc.* **2002**, *124*, 5059. (b) Duong, H. A.; Louie, J. *J. Organomet. Chem.* **2005**, *690*, 5098. (c) Duong, H. A.; Louie, J. *Tetrahedron* **2006**, *62*, 7552.

- (11) 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.
- (12) The benzotriazinone **1j** was recovered.
- (13) 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.
- (14) The major undesired process under the standard conditions using PMe_3 was self-oligomerization of **2k**.
- (15) For examples of the regioselective formation of α -boryl-substituted metalacycle intermediates, see: (a) Quntar, A. A. A.; Srebnik, M. *Org. Lett.* **2004**, *6*, 4243. (b) Hansen, E. C.; Lee, D. *J. Am. Chem. Soc.* **2005**, *127*, 3252. (c) Nishihara, Y.; Miyasaka, M.; Okamoto, M.; Takahashi, H.; Inoue, E.; Tanemura, K.; Takagi, K. *J. Am. Chem. Soc.* **2007**, *129*, 12634. (d) Geny, A.; Lebœuf, D.; Rouquié, G.; Vollhardt, K. P. C.; Malacria, M.; Gandon, V.; Aubert, C. *Chem. Eur. J.* **2007**, *13*, 5408.
- (16) For a similar stabilization by a silyl substituent, see: Buchwald, S. L.; Nielsen, R. B. *J. Am. Chem. Soc.* **1989**, *111*, 2870.
- (17) Representative results (regioisomers ratio) with other phosphine ligands: PMe_2Ph (75:25), PMePh_2 (87:13), $\text{P}(n\text{-Bu})_3$ (85:15), DPPPEn (92:8), DPEphos (88:12), XANTPHOS (93:7).
- (18) The reaction of 1-phenylprop-1-yne using dppf in place of PMe_3 as the ligand required heating at 80 °C in toluene, giving inferior regioselectivity of 65:35.
- (19) Ukai, T.; Kawazura, H.; Ishii, Y.; Bonnet, J. J.; Ibers, J. A. *J. Organomet. Chem.* **1974**, *65*, 253.
- (20) Coulson, D. R. *Inorg. Synth.* **1972**, *13*, 121.
- (21) Ashfeld, B. L.; Martin, S. F. *Tetrahedron* **2006**, *62*, 10497.
- (22) Weiss, H. M.; Touchette, K. M.; Angell, S.; Khan, J. *Org. Biomol. Chem.* **2003**, *1*, 2152.
- (23) (a) Sugahara, M.; Ukita, T. *Chem. Pharm. Bull.* **1997**, *45*, 719. (b) Shafir, A.; Buchwald, S. L. *J. Am. Chem. Soc.* **2006**, *128*, 8742.
- (24) Cobas, A.; Guitián, E.; Castedo, L. *J. Org. Chem.* **1993**, *58*, 3113.
- (25) Duong, H. A.; Louis, J. *Tetrahedron*, **2006**, *62*, 7552.

Chapter 2

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

Abstract

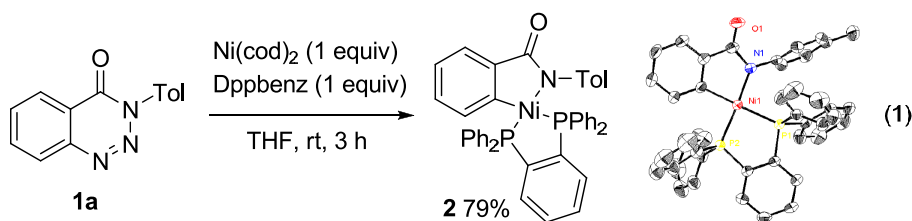
A denitrogenative annulation reaction of 1,2,3-benzotriazin-4(3*H*)-ones with allenes catalyzed by a nickel/phosphine complex, to produce a variety of substituted 3,4-dihydroquinolin-1(2*H*)-ones in a regioselective manner, is described. A highly enantioselective version, as well as structural evidence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

Introduction

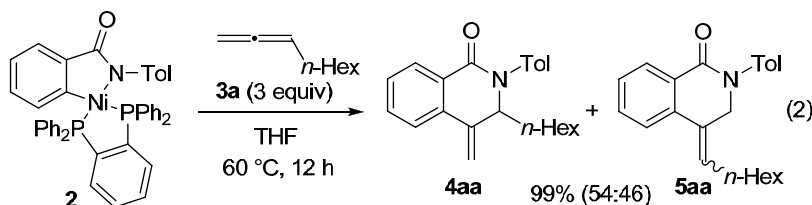
Transition metal-catalyzed annulation reactions continue to provide many powerful synthetic methodologies for the construction of heterocyclic compounds.¹ Heterometalacyclic complexes often act as key intermediates, which subsequently incorporate unsaturated compounds through insertion and reductive elimination to construct heterocyclic skeletons. It has been reported that heterocyclic compounds such as triazoles,² phthalimides,^{3a} and isatoic anhydrides^{3c} 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.⁴ In chapter 1, the author developed a nickel-catalyzed denitrogenative annulation of 1,2,3-benzotriazin-4(3*H*)-ones **1** with alkynes.⁵ 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(3*H*)-ones.

Results and Discussions

First, the author examined a stoichiometric allene insertion of azanickelacycle **2**, which was prepared from *N*-Tolyl-1,2,3-benzotriazin-4(3*H*)-one (**1a**), Ni(cod)₂, and 1,2-bis(diphenylphosphino)-benzene (eq 1).⁶ 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**.

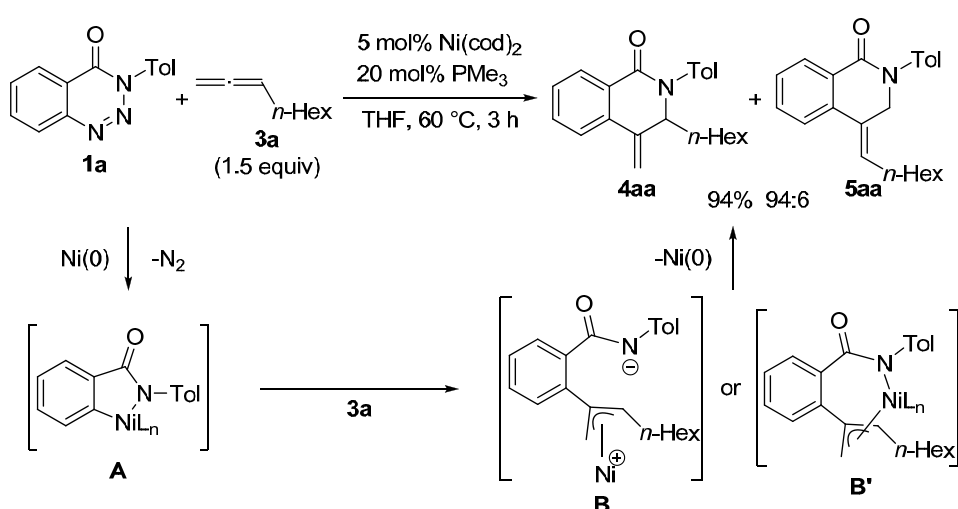


When nona-1,2-diene (**3a**, 3 equiv) was reacted with **2** in THF at 60 °C, an isomeric mixture of 3,4-dihydroisoquinolin-1(2*H*)-ones **4aa** and **5aa** was obtained in a ratio of 54:46 (93% total yield, eq 2). The allene functionality was successfully incorporated into the precursory skeleton.



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 $\text{Ni}(\text{cod})_2$ and PMe_3 ($\text{Ni}:\text{P} = 1:4$), the products **4aa** and **5aa** were obtained (94%, **4aa**:**5aa** = 94:6, Scheme 1). Other ligands such as PCy_3 , Pt-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-dihydroisoquinolin-1(2*H*)-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(3*H*)-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-ClC ₆ H ₄	H	H	4da	5da	82 (93:7) ^{e,h}
4	1e	2-MeOC ₆ H ₄	H	H	4ea	5ea	94 (95:5) ^{f,i}
5	1f	Ph	MeO	MeO	4fa	5fa	79 (95:5) ^{f,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 %), PMe₃ (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 %), PMe₃ (40 mol %).

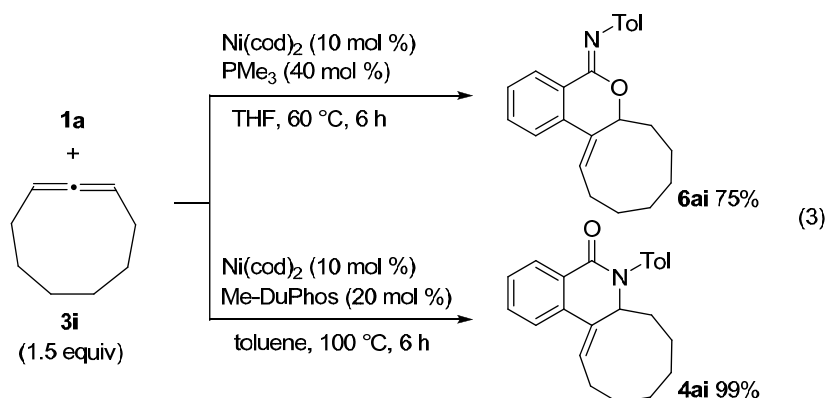
Terminal allenes having a variety of R substituents were subjected to the annulation reaction of **1a**. The regioselectivity was significantly affected by the sterics of the R substituent (Table 2). As with simple nona-1,2-diene (**3a**), functionalized allenes **3b–3e** having one primary substituent exhibited good regio-selectivity to give the corresponding 3,4-dihydroisoquinolin-1(2*H*)-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).⁸ 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(3*H*)-one (**1a**) with Allenes **3**^a

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

^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 %), PMe₃ (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 PMe₃ furnished the imino ester **6ai** in 75% yield,⁹ 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*-Pr-FOXAP was employed (entry 3).¹² Lowering the reaction temperature to 60 °C led to the best result (94%, 90% ee, **4aa**:**5aa** = 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 (**1a**) with Allenes **3**^a

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

^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 CH₃CN was used. ^e Ni(cod)₂ (20 mol %).

Conclusions

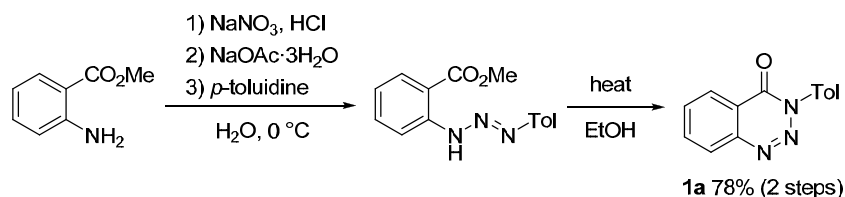
In summary, a denitrogenative annulation reaction of 1,2,3-benzotriazin-4(3*H*)-ones with allenes provides a unique method for the regio- and enantioselective synthesis of substituted 3,4-dihydroisoquinolin-1(2*H*)-ones, which are found in a wide variety of plant alkaloids and bioactive compounds.¹³

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. ^1H and ^{13}C NMR spectra were recorded on a Varian Gemini 2000 (^1H at 300 MHz and ^{13}C at 75 MHz) spectrometer using CHCl_3 (^1H , $\delta = 7.26$) 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).

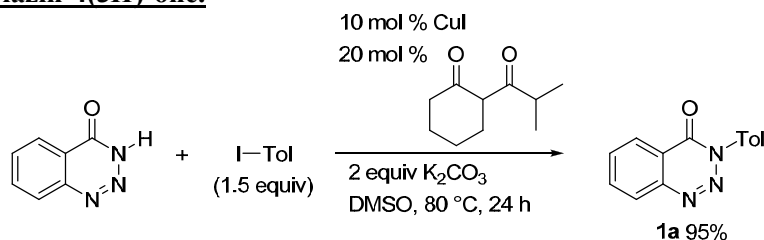
Materials. THF, 1,4-dioxane, and toluene were distilled from sodium/benzophenone ketyl. Anhydrous DMSO (Wako) was purchased from the commercial sources. Anhydrous CH_3CN (Wako) was purchased from the commercial sources and degassed by ultrasound before use. $\text{Ni}(\text{cod})_2$ (Kanto) was obtained from the commercial sources and purified by recrystallization from toluene before use. *NH*-1,2,3-Benzotriazine-4(3*H*)-one (TCI), 2-isobutyrylcyclohexanone (Aldrich), trimethylphosphine (Strem), (–)-1,2-bis[(2*R*,5*R*)-2,5-dimethylphospholano]benzene ((*R,R*)-Me-DuPhos, Strem), (1*S*,1'*S*',2*R*,2'*R*')-1,1'-di-*tert*-butyl-(2,2')-diphospholane ((*S,S,R,R*)-TangPhos, Strem), (*S,S*)-[2-(4'-isopropoxyloxazolin-2'-yl)ferrocenyl]-diphenylphosphine ((*S,S*)-*i*-Pr-FOXAP, Wako), and 1,2-bis(diphenylphosphino)benzene (Wako) were used as received from the commercial sources. *N*-Aryl-1,2,3-benzotriazine-4(3*H*)-ones **1a–1h** and **1j** were prepared according to the literature procedure.¹⁴ *N*-(*N,N*'-Diphenylcarbamoyl)-1,2,3-benzotriazine-4(3*H*)-one (**1i**) was prepared according to the literature procedure.¹⁵ Nona-1,2-diene (**3a**),¹⁶ 1-benzyloxypenta-3,4-diene (**3b**),¹⁷ 1-(*tert*-butyldimethylsiloxy)penta-3,4-diene (**3c**),¹⁷ 1-hydroxypenta-3,4-diene (**3d**),¹⁷ 1-cyanohexan-5,6-diene (**3e**),¹⁷ cyclohexylpropa-1,2-diene (**3f**),¹⁶ *tert*-butylpropa-1,2-diene (**3g**),¹⁸ *tert*-butyldimethylsilylpropa-1,2-diene (**3h**),¹⁹ and cyclonona-1,2-diene (**3i**)²⁰ were prepared according to the literature procedures.

General Procedure for the Synthesis of *N*-Aryl-1,2,3-benzotriazin-4(3*H*)-ones from Methyl Anthranilate.¹⁴



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*-Arvl-1,2,3-benzotriazin-4(3*H*)-ones from *NH*-1,2,3-benzotriazin-4(3*H*)-one.²¹



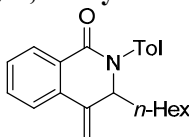
In an N₂-filled glove-box, to an oven-dried 4 mL-vial equipped with a stir bar was added *NH*-1,2,3-benzotriazin-4(3*H*)-one (29.7 mg, 0.20 mmol), K₂CO₃ (55.3 mg, 0.40 mmol), *p*-iodotoluene (65.4 mg, 0.30 mmol), CuI (3.8 mg, 20 μmol), 2-isobutyrylcyclohexanone (6.7 μL, 40 μmol), and DMSO (1 mL) at room 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 **1a** as a white solid (45.1 mg, 0.19 mmol, 95% yield).

Spectroscopic data of **1a-1h**, and **1j** have been reported.²²

Spectroscopic data of **1i** have been reported.¹⁵

Stoichiometric Reaction of Azanickelacycle **2 with Nona-1,2-diene (**3a**) (eq 2).** In an N₂-filled glove-box, azanickelacycle **2** (35.6 g, 50 μmol) was charged into an oven-dried 4 mL-vial equipped with a stir bar. Then, toluene (1 mL) and nona-1,2-diene (**3a**, 20.2 mg, 0.16 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[®] 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** (15.5 mg, 46 μmol, 93% total yield, **4aa:5aa** = 54:46).

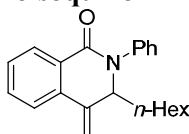
3-Hexyl-4-methylene-2-(4-methylphenyl)-3,4-dihydroisoquinolin-1(2*H*)-one (4aa**)**



IR (neat): 2928, 1655, 1512, 1464, 1429, 1402, 1283 cm⁻¹; 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); ¹³C 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⁺): Calcd for C₂₃H₂₇NO, M⁺ 333.2093. Found *m/z* 333.2094.

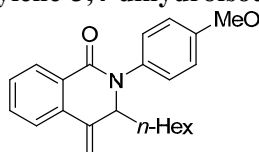
General Procedure for Nickel-Catalyzed Denitrogenative Annulation of 1,2,3-Benzotriazin-4(3H)-ones with Allenes Using PMe_3 as the Ligand (Scheme 1, Table 1, and Table 2). To an oven-dried flask was added **1a** (47.3 mg, 0.20 mmol), a solution of $\text{Ni}(\text{cod})_2$ (2.8 mg, 10 μmol) and PMe_3 (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 $^\circ\text{C}$ 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**)



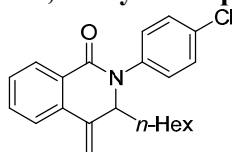
IR (neat): 2930, 1657, 1464, 1404 cm^{-1} ; ^1H NMR: δ = 0.81 (t, J = 6.6 Hz, 3H), 0.98–1.28 (m, 8H), 1.50–1.66 (m, 1H), 1.72–1.86 (m, 1H), 4.37 (dd, J = 10.2, 3.9 Hz, 1H), 5.24 (s, 1H), 5.64 (s, 1H), 7.28–7.61 (m, 8H), 8.17–8.23 (m, 1H); ^{13}C NMR: δ = 13.9, 22.4, 25.6, 28.6, 31.5, 33.8, 67.0, 112.9, 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 $\text{C}_{22}\text{H}_{25}\text{NO}$, M^+ 319.1936. Found m/z 319.1937.

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

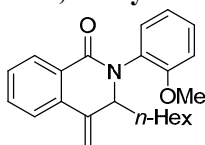


4ca: IR (neat): 2928, 1655, 1510, 1464, 1248 cm^{-1} ; ^1H NMR: δ = 0.80 (t, J = 6.6 Hz, 3H), 1.00–1.26 (m, 8H), 1.48–1.62 (m, 1H), 1.70–1.83 (m, 1H), 3.83 (s, 3H), 4.28 (dd, J = 9.6, 3.9 Hz, 1H), 5.22 (s, 1H), 5.62 (s, 1H), 6.93–7.00 (m, 2H), 7.26–7.33 (m, 2H), 7.42–7.59 (m, 3H), 8.15–8.19 (m, 1H); ^{13}C NMR: δ = 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 $\text{C}_{23}\text{H}_{27}\text{NO}_2$, M^+ 349.2042. Found m/z 349.2046.

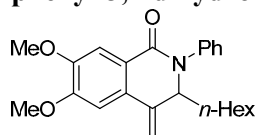
2-(4-Chlorophenyl)-3-hexyl-4-methylene-3,4-dihydroisoquinolin-1(2H)-one (**4da**)



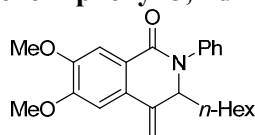
IR (neat): 2930, 1655, 1493, 1464, 1399, 1283 cm^{-1} ; ^1H NMR: δ = 0.81 (t, J = 6.3 Hz, 3H), 1.00–1.27 (m, 8H), 1.48–1.63 (m, 1H), 1.67–1.80 (m, 1H), 4.32 (dd, J = 10.2, 4.2 Hz, 1H), 5.25 (s, 1H), 5.64 (s, 1H), 7.31–7.61 (m, 7H), 8.14–8.20 (m, 1H); ^{13}C NMR: δ = 14.0, 22.4, 25.7, 28.6, 31.5, 33.8, 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 $\text{C}_{22}\text{H}_{24}\text{ClNO}$, M^+ 353.1546. Found m/z 353.1547.

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

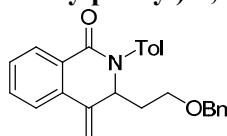
IR (neat): 2930, 1657, 1501, 1466, 1267 cm^{-1} ; ^1H NMR: δ = 0.81 (t, J = 6.6 Hz, 3H), 0.98–1.32 (m, 8H), 1.50–1.65 (m, 1H), 1.66–1.80 (m, 1H), 3.82 (s, 3H), 4.23 (dd, J = 9.6, 3.9 Hz, 1H), 5.21 (s, 1H), 5.62 (s, 1H), 7.00–7.07 (m, 2H), 7.29–7.61 (m, 5H), 8.15–8.21 (m, 1H); ^{13}C NMR (150 MHz): δ = 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 $\text{C}_{23}\text{H}_{27}\text{NO}_2$, M^+ 349.2042. Found m/z 349.2040.

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

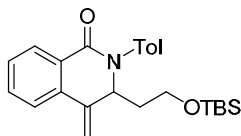
IR (neat): 2930, 1651, 1599, 1507, 1266 cm^{-1} ; ^1H NMR: δ = 0.80 (t, J = 6.6 Hz, 3H), 0.99–1.30 (m, 8H), 1.52–1.67 (m, 1H), 1.68–1.81 (m, 1H), 3.96 (s, 3H), 3.99 (s, 3H), 4.33 (dd, J = 9.6, 4.2 Hz, 1H), 5.15 (s, 1H), 5.53 (s, 1H), 6.99 (s, 1H), 7.26–7.47 (m, 5H), 7.66 (s, 1H); ^{13}C NMR: δ = 14.0, 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 $\text{C}_{24}\text{H}_{29}\text{NO}_3$, M^+ 379.2147. Found m/z 379.2148.

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

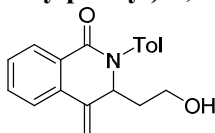
IR (neat): 2923, 1727, 1659, 1441, 1267, 1252 cm^{-1} ; ^1H NMR: δ = 0.79 (t, J = 6.9 Hz, 3H), 0.99–1.25 (m, 8H), 1.44–1.60 (m, 1H), 1.72–1.85 (m, 1H), 3.97 (s, 3H), 4.38 (dd, J = 10.2, 3.9 Hz, 1H), 5.32 (s, 1H), 5.75 (s, 1H), 7.30–7.51 (m, 5H), 8.06–8.13 (m, 1H), 8.22–8.29 (m, 2H); ^{13}C NMR: δ = 14.0, 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 $\text{C}_{24}\text{H}_{27}\text{NO}_3$, M^+ 377.1991. Found m/z 377.1994.

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

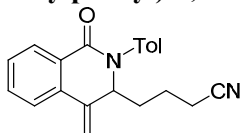
IR (neat): 1659, 1651, 1603, 1512, 1464, 1429, 1404 cm^{-1} ; ^1H NMR: δ = 1.74–1.87 (m, 1H), 2.18–2.30 (m, 1H), 2.40 (s, 3H), 3.40 (dd, J = 7.2, 4.5 Hz, 2H), 4.28 (d, J = 11.4 Hz, 1H), 4.33 (d, J = 12 Hz, 1H), 4.70 (dd, J = 9.6, 4.2 Hz, 1H), 5.25 (s, 1H), 5.64 (s, 1H), 7.18–7.37 (m, 9H), 7.43–7.60 (m, 3H), 8.19–8.24 (m, 1H); ^{13}C NMR: δ = 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 $\text{C}_{26}\text{H}_{25}\text{NO}_2$, M^+ 383.1885. Found m/z 383.1881.

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

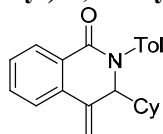
IR (neat): 2928, 1659, 1514, 1464, 1256 cm^{-1} ; ^1H NMR: δ = -0.10 (s, 3H), -0.03 (s, 3H), 0.81 (s, 9H), 1.63–1.75 (m, 1H), 2.03–2.16 (m, 1H), 2.37 (s, 3H), 3.45–3.56 (m, 2H), 4.70 (dd, J = 10.2, 3.6 Hz, 1H), 5.30 (s, 1H), 5.66 (s, 1H), 7.20–7.36 (m, 4H), 7.42–7.60 (m, 3H), 8.17–8.22 (m, 1H); ^{13}C NMR (100 MHz): δ = -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 $\text{C}_{25}\text{H}_{33}\text{NO}_2\text{Si}$, M^+ 407.2281. Found m/z 407.2281.

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

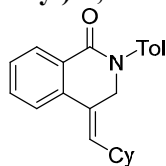
IR (KBr): 3450, 2874, 1655, 1638, 1601, 1512, 1466, 1279 cm^{-1} ; ^1H NMR: δ = 1.31–1.39 (br s, 1H), 1.69–1.82 (m, 1H), 2.02–2.16 (m, 1H), 2.37 (s, 3H), 3.43–3.62 (m, 2H), 4.64 (dd, J = 10.2, 4.2 Hz, 1H), 5.33 (s, 1H), 5.67 (s, 1H), 7.19–7.31 (m, 4H), 7.42–7.49 (m, 1H), 7.50–7.59 (m, 2H), 8.14–8.19 (m, 1H); ^{13}C NMR: δ = 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 $\text{C}_{19}\text{H}_{19}\text{NO}_2$, M^+ 293.1416. Found m/z 293.1419.

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

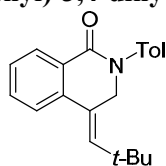
IR (neat): 2921, 2245, 1651, 1512 cm^{-1} ; ^1H NMR: δ = 1.36–1.97 (m, 4H), 2.19 (t, J = 6.9 Hz, 2H), 2.38 (s, 3H), 4.39 (dd, J = 9.0, 3.9 Hz, 1H), 5.26 (s, 1H), 5.67 (s, 1H), 7.21–7.28 (m, 4H), 7.43–7.59 (m, 3H), 8.14–8.20 (m, 1H); ^{13}C NMR: δ = 16.8, 21.1, 21.9, 33.1, 66.2, 113.5, 118.9, 123.8, 127.3, 127.6, 128.7, 129.1, 129.9, 132.5, 134.5, 137.2, 138.7, 139.7, 162.4; HRMS (EI^+): Calcd for $\text{C}_{21}\text{H}_{20}\text{N}_2\text{O}$, M^+ 316.1576. Found m/z 316.1581.

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

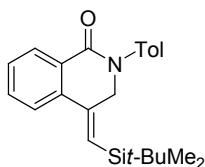
IR (KBr): 2923, 1647, 1638, 1512, 1466, 1304 cm^{-1} ; ^1H NMR: δ = 0.43–0.59 (m, 1H), 0.86–1.18 (m, 4H), 1.46–1.74 (m, 6H), 2.39 (s, 3H), 4.30 (d, J = 5.4 Hz, 1H), 5.18 (s, 1H), 5.67 (s, 1H), 7.21–7.30 (m, 4H), 7.39–7.46 (m, 1H), 7.47–7.57 (m, 2H), 8.13–8.18 (m, 1H); ^{13}C NMR (150 MHz): δ = 21.1, 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 $\text{C}_{23}\text{H}_{25}\text{NO}$, M^+ 331.1936. Found m/z 331.1937.

(Z)-4-Cyclohexylmethylene-2-(4-methylphenyl)-3,4-dihydroisoquinolin-1(2H)-one (Z)-5af

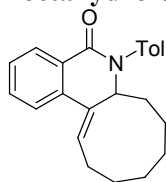
IR (KBr): 2924, 1655, 1509, 1298 cm^{-1} ; ^1H NMR: δ = 1.12–1.34 (m, 6H), 1.60–1.80 (m, 4H), 2.22–2.38 (m, 1H), 2.39 (s, 3H), 4.60 (d, J = 1.8 Hz, 2H), 5.98 (dt, J = 11.4, 1.8 Hz, 1H), 7.23–7.32 (m, 4H), 7.34–7.58 (m, 3H), 8.16–8.21 (m, 1H); ^{13}C NMR: δ = 21.1, 25.7, 25.8, 33.0, 37.2, 50.6, 122.6,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

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

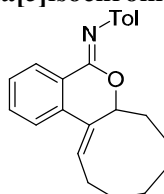
IR (KBr): 2957, 1659, 1509, 1293 cm^{-1} ; ^1H NMR: δ = 1.22 (s, 9H), 2.38 (s, 3H), 4.68–4.72 (m, 2H), 6.12–6.15 (m, 1H), 7.20–7.30 (m, 4H), 7.34–7.43 (m, 1H), 7.45–7.52 (m, 2H), 8.13–8.19 (m, 1H); ^{13}C NMR: δ = 21.1, 31.3, 32.9, 50.8, 123.1, 125.7, 127.7, 127.8, 128.1, 128.5, 129.8, 132.1, 136.5,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

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

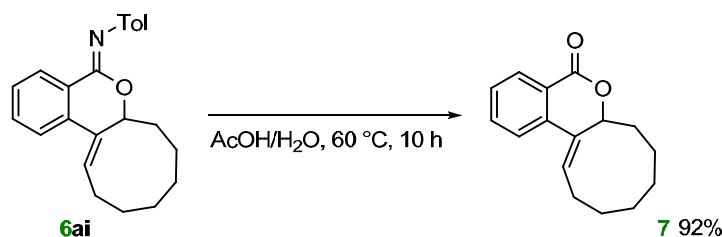
IR (KBr): 1655, 1514, 1466, 1298 cm^{-1} ; ^1H NMR (C_6D_6): δ = 0.02 (s, 6H), 0.84 (s, 9H), 2.07 (s, 3H), 4.41 (s, 2H), 6.15 (s, 1H), 6.94–7.40 (m, 7H), 8.55–8.62 (m, 1H); ^{13}C NMR (C_6D_6): δ = -4.1, 17.4, 21.0, 26.5, 54.9, 123.6, 125.5, 125.6, 129.1, 129.2, 129.3, 129.7, 132.0, 135.7, 138.6, 141.0, 146.4, 162.8; HRMS (EI^+): Calcd for $\text{C}_{23}\text{H}_{29}\text{NOSi}$, M^+ 363.2018. Found m/z 363.2020.

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

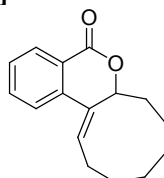
IR (KBr): 2917, 1651, 1642, 1426, 1273 cm^{-1} ; ^1H NMR: δ = 1.19–1.98 (m, 10H), 2.14–2.29 (m, 1H), 2.39 (s, 3H), 2.44–2.58 (m, 1H), 4.98 (dd, J = 11.1, 4.5 Hz, 1H), 6.38 (dd, J = 9.6, 8.4 Hz, 1H), 7.22–7.32 (m, 4H), 7.36–7.62 (m, 3H), 8.14–8.20 (m, 1H); ^{13}C NMR: δ = 21.1, 22.7, 25.7, 26.3, 27.57, 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; HRMS (EI^+): Calcd for $\text{C}_{23}\text{H}_{25}\text{NO}$, M^+ 331.1936. Found m/z 331.1940.

***N*-((*Z*)-7,8,9,10,11,12-Hexahydrocyclonona[*c*]isochromen-5(6*aH*)-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} ; ^1H NMR: δ = 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: δ = 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, 129.0, 131.0, 131.3, 132.4, 133.5, 144.9, 151.3; HRMS (EI^+): Calcd for $\text{C}_{23}\text{H}_{25}\text{NO}$, 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/ H_2O (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).

(*Z*)-7,8,9,10,11,12-Hexahydrocyclonona[*c*]isochromen-5(6*aH*)-one (7**)**

IR (KBr): 2932, 1707, 1460, 1246, 1092 cm^{-1} ; ^1H NMR: δ = 1.16–2.06 (m, 10H), 2.14–2.29 (m, 1H), 2.43–2.57 (m, 1H), 5.66 (dd, J = 10.8, 4.8 Hz, 1H), 6.45 (t, J = 9.0 Hz, 1H), 7.35–7.44 (m, 1H), 7.53–7.64 (m, 2H), 8.08 (d, J = 7.5 Hz, 1H); ^{13}C NMR: δ = 22.7, 25.5, 26.5, 27.2, 27.6, 33.7, 77.8, 123.0, 123.1, 128.0, 129.8, 129.9, 130.1, 133.8, 136.3, 164.0; HRMS (EI^+): Calcd for $\text{C}_{16}\text{H}_{18}\text{O}_2$, M^+ 242.1307. Found m/z 242.1304.

General Procedure for Nickel-Catalyzed Denitrogenative Annulation of 1,2,3-Benzotriazin-4(3*H*)-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 $\text{Ni}(\text{cod})_2$ (5.6 mg, 20 μmol) and (*S,S*)-*i*-Pr-FOXAP (19.1 mg, 40 μmol) 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: $[\alpha]_{\text{D}}^{26.4} = +65.3$ ($c = 1.05$, CHCl_3 , 89% ee); HPLC (Daicel Chiralcel OJ-H, hexane/*i*-PrOH = 85/15, flow rate = 0.6 mL/min, $\lambda = 254$ nm): $t_1 = 12.4$ min, $t_2 = 14.7$ min.

4ba: $[\alpha]_{\text{D}}^{26.5} = +112.7$ ($c = 0.98$, CHCl_3 , 93% ee); HPLC (Daicel Chiralcel OJ-H, hexane/*i*-PrOH = 85/15, flow rate = 0.6 mL/min, $\lambda = 254$ nm): $t_1 = 17.0$ min, $t_2 = 20.5$ min.

4ca: $[\alpha]_{\text{D}}^{26.5} = +105.6$ ($c = 1.01$, CHCl_3 , 92% ee); HPLC (Daicel Chiralcel OJ-H, hexane/*i*-PrOH = 85/15, flow rate = 0.6 mL/min, $\lambda = 254$ nm): $t_1 = 15.3$ min, $t_2 = 24.2$ min.

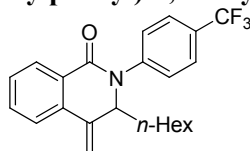
4da: $[\alpha]_{\text{D}}^{24.8} = +127.0$ ($c = 1.68$, CHCl_3 , 93% ee); HPLC (Daicel Chiralcel OJ-H, hexane/*i*-PrOH = 85/15, flow rate = 0.6 mL/min, $\lambda = 254$ nm): $t_1 = 12.6$ min, $t_2 = 15.5$ min.

4ea: $[\alpha]_{\text{D}}^{23.9} = +55.6$ ($c = 1.67$, CHCl_3 , 91% ee); HPLC (Daicel Chiralcel OD-H, hexane/*i*-PrOH = 85/15, flow rate = 0.6 mL/min, $\lambda = 254$ nm): $t_1 = 22.2$ min, $t_2 = 25.8$ min.

4fa: $[\alpha]_{\text{D}}^{23.5} = +81.1$ ($c = 0.99$, CHCl_3 , 92% ee); HPLC (Daicel Chiralpak IA, hexane/DCM = 50/50, flow rate = 0.6 mL/min, $\lambda = 254$ nm): $t_1 = 10.6$ min, $t_2 = 13.8$ min.

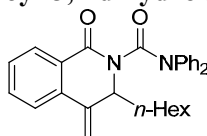
4ga: $[\alpha]_{\text{D}}^{26.6} = +94.8$ ($c = 1.00$, CHCl_3 , 96% ee); HPLC (Daicel Chiralcel OJ-H, hexane/*i*-PrOH = 85/15, flow rate = 0.6 mL/min, $\lambda = 254$ nm): $t_1 = 25.5$ min, $t_2 = 35.7$ min.

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



$[\alpha]_{\text{D}}^{23.1} = +108.2$ ($c = 1.84$, CHCl_3 , 93% ee); HPLC (Daicel Chiralcel OJ-H, hexane/*i*-PrOH = 85/15, flow rate = 0.6 mL/min, $\lambda = 254$ nm): $t_1 = 10.6$ min, $t_2 = 12.4$ min. IR (neat): 2932, 1659, 1402, 1325, 1167, 1127 cm^{-1} ; ^1H NMR: $\delta = 0.81$ (t, $J = 6.3$ Hz, 3H), 1.00–1.30 (m, 8H), 1.52–1.68 (m, 1H), 1.69–1.83 (m, 1H), 4.42 (dd, $J = 10.2, 4.5$ Hz, 1H), 5.28 (s, 1H), 5.67 (s, 1H), 7.43–7.74 (m, 7H), 8.17–8.23 (m, 1H); ^{13}C NMR: $\delta = 13.9, 22.4, 25.7, 28.6, 31.5, 34.0, 66.8, 113.3, 123.8$ (q, $J = 270.9$ Hz), 124.0, 126.1 (q, $J = 3.5$ Hz), 127.3, 127.4, 128.5 (q, $J = 32.3$ Hz), 128.6, 128.8, 132.6, 135.0, 139.7, 144.8, 162.6; HRMS (EI^+): Calcd for $\text{C}_{23}\text{H}_{24}\text{F}_3\text{NO}$, M^+ 387.1810. Found m/z 387.1806.

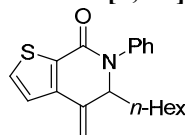
3-Hexyl-4-methylene-2-diphenylcarbamoyl-3,4-dihydroisoquinolin-1(2*H*)-one (**4ai**)



$[\alpha]_{\text{D}}^{22.6} = -317.7$ ($c = 1.51$, CHCl_3 , 95% ee); HPLC (Daicel Chiralcel OD-H, hexane/*i*-PrOH = 85/15, flow rate = 0.6 mL/min, $\lambda = 254$ nm): $t_1 = 14.8$ min, $t_2 = 29.7$ min. IR (neat): 2928, 1674, 1601, 1498, 1339, 1264, 1163 cm^{-1} ; ^1H NMR: $\delta = 0.82$ (t, $J = 6.8$ Hz, 3H), 1.10–1.34 (m, 8H), 1.44–1.60 (m, 1H), 2.18–2.32 (m, 1H), 4.50 (dd, $J = 10.8, 3.9$ Hz, 1H), 5.26 (s, 1H), 5.59 (s, 1H), 6.79–7.63 (m, 13H), 7.84 (d, $J = 7.8$ Hz, 1H); ^{13}C NMR: $\delta = 14.0, 22.5, 26.1, 28.6, 31.6, 34.6, 63.8, 113.0, 124.2, 126.3$,

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 $\text{C}_{29}\text{H}_{30}\text{N}_2\text{O}_2$, M^+ 438.2307. Found m/z 438.2304.

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



$[\alpha]_{\text{D}}^{24.5} = +35.5$ ($c = 1.17$, CHCl_3 , 96% ee); HPLC (Daicel Chiralcel OJ-H, hexane/*i*-PrOH = 85/15, flow rate = 0.6 mL/min, $\lambda = 254$ nm): $t_1 = 15.4$ min, $t_2 = 19.3$ min. IR (neat): 2920, 1659, 1456 cm^{-1} ; ^1H NMR (C_6D_6): $\delta = 0.78$ (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}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 $\text{C}_{20}\text{H}_{23}\text{NOS}$, M^+ 325.1500. Found m/z 325.1496.

4ab: $[\alpha]_{\text{D}}^{26.7} = +93.1$ ($c = 1.02$, CHCl_3 , 92% ee); HPLC (Daicel Chiralcel OJ-H, hexane/*i*-PrOH = 50/50, flow rate = 0.6 mL/min, $\lambda = 254$ nm): $t_1 = 27.1$ min, $t_2 = 48.5$ min.

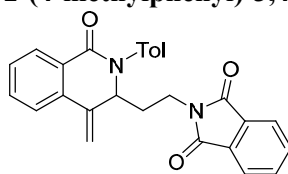
4ac: $[\alpha]_{\text{D}}^{26.6} = +46.8$ ($c = 1.05$, CHCl_3 , 90% ee); HPLC (Daicel Chiralcel OD-H, hexane/*i*-PrOH = 90/10, flow rate = 0.6 mL/min, $\lambda = 254$ nm): $t_1 = 19.1$ min, $t_2 = 27.6$ min.

4ad: $[\alpha]_{\text{D}}^{25.9} = +143.5$ ($c = 1.01$, CHCl_3 , 97% ee); HPLC (Daicel Chiralcel OJ-H, hexane/*i*-PrOH = 85/15, flow rate = 0.6 mL/min, $\lambda = 254$ nm): $t_1 = 55.5$ min, $t_2 = 59.1$ min.

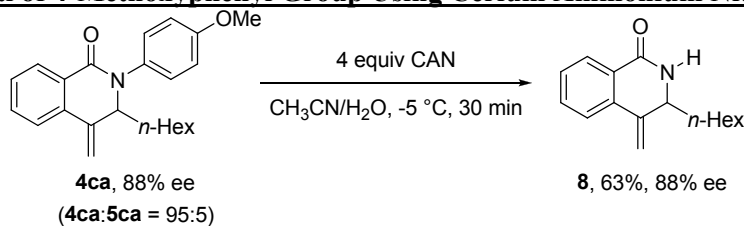
4ae: $[\alpha]_{\text{D}}^{26.2} = +104.6$ ($c = 1.02$, CHCl_3 , 93% ee); HPLC (Daicel Chiralpak IA, DCM 100%, flow rate = 0.6 mL/min, $\lambda = 254$ nm): $t_1 = 10.0$ min, $t_2 = 16.2$ min.

4af: $[\alpha]_{\text{D}}^{26.3} = +78.8$ ($c = 1.04$, CHCl_3 , 96% ee); HPLC (Daicel Chiralpak AD-H, hexane/*i*-PrOH = 85/15, flow rate = 0.6 mL/min, $\lambda = 254$ nm): $t_1 = 22.4$ min, $t_2 = 35.4$ min.

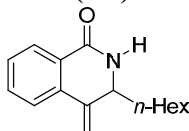
3-(2-Phthalimidoethyl)-4-methylene-2-(4-methylphenyl)-3,4-dihydroisoquinolin-1(2*H*)-one (4aj)



$[\alpha]_{\text{D}}^{26.1} = +71.0$ ($c = 0.98$, CHCl_3 , 97% ee); HPLC (Daicel Chiralcel IA, DCM 100%, flow rate = 0.6 mL/min, $\lambda = 254$ nm): $t_1 = 9.39$ min, $t_2 = 10.5$ min. IR (neat): 3000, 2874, 1771, 1713, 1651, 1399 cm^{-1} ; ^1H 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}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 $\text{C}_{27}\text{H}_{22}\text{N}_2\text{O}_3$, M^+ 422.1630. Found m/z 422.1617.

Oxidative Removal of 4-Methoxyphenyl Group Using Cerium Ammonium Nitrate (CAN).²³

To a solution of **4ca** (69 mg, 0.197 mmol, **4ca:5ca** = 95:5, 88% ee) in CH₃CN (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 NaHCO₃ (20 mL) and extracted with AcOEt (4 x 20 mL). The organic layer was washed with aqueous Na₂SO₃ (20 mL), brine and dried over Na₂SO₄. The solvent was passed through a pad of Florisil[®] 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)

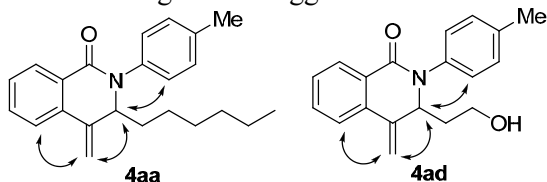
$[\alpha]_D^{22.5} = +230.1$ ($c = 1.32$, CHCl₃, 88% ee); HPLC (Daicel Chiralcel OD-H, hexane/*i*-PrOH = 85/15, flow rate = 0.6 mL/min, $\lambda = 254$ nm): $t_1 = 13.3$ min, $t_2 = 18.8$ min. IR (neat): 3198, 2930, 1669, 1603, 1474, 1404 cm⁻¹; ¹H NMR: $\delta = 0.84$ (t, $J = 6.5$ Hz, 3H), 1.12–1.40 (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); ¹³C 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 (EI⁺): Calcd for C₁₆H₂₁NO, M⁺ 243.1623. Found m/z 243.1620.

Determination of Stereochemistries.

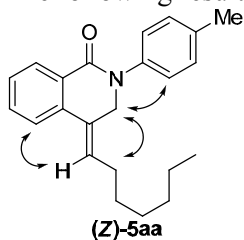
Stereochemistries of the products were determined by nOe experiments are shown below with curved arrows that indicate the observed nOe.

[Compound 4aa and 4ad]

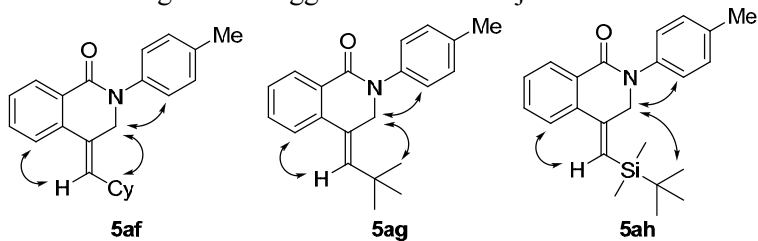
The following results suggested that the substituent group was bound to the C(3).

**[Compound 5aa]**

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

**[Compound 5af, 5ag and 5ah]**

The following results suggested that the major isomer was Z-isomer.



References and Notes

- (1) For reviews, see: (a) Nakamura, I.; Yamamoto, Y. *Chem. Rev.* **2004**, *104*, 2127. (b) Zeni, G.; Larock, R. C. *Chem. Rev.* **2004**, *104*, 2285. (c) D'Souza, D. M.; Müller, T. J. J. *Chem. Soc. Rev.* **2007**, *36*, 1095.
- (2) (a) Chuprakov, S.; Hwang, F. W.; Gevorgyan, V. *Angew. Chem. Int. Ed.* **2007**, *46*, 4757. (b) Chuprakov, S.; Gevorgyan, V. *Org. Lett.* **2007**, *9*, 4463. (c) Horneff, T.; Chuprakov, S.; Chernyak, N.; Gevorgyan, V.; Fokin, V. V. *J. Am. Chem. Soc.* **2008**, *130*, 14972. (d) Miura, T.; Yamauchi, M.; Murakami, M. *Chem. Commun.* **2009**, 1470. (e) Nakamura, I.; Nemoto, T.; Shiraiwa, N.; Terada, M. *Org. Lett.* **2009**, *11*, 1055.
- (3) (a) Kajita, Y.; Matsubara, S.; Kurahashi, T. *J. Am. Chem. Soc.* **2008**, *130*, 6058. (b) Kajita, Y.; Kurahashi, T.; Matsubara, S. *J. Am. Chem. Soc.* **2008**, *130*, 17226. (c) Yoshino, Y.; Kurahashi, T.; Matsubara, S. *J. Am. Chem. Soc.* **2009**, *131*, 7494.
- (4) For related examples, see: (a) O'Brien, E. M.; Bercot, E. A.; Rovis, T. *J. Am. Chem. Soc.* **2003**, *125*, 10498. (b) Wang, C.; Tunge, J. A. *J. Am. Chem. Soc.* **2008**, *130*, 8118.
- (5) Miura, T.; Yamauchi, M.; Murakami, M. *Org. Lett.* **2008**, *10*, 3085.
- (6) See chapter 1.
- (7) See the Experimental Section.
- (8) Lu, G.; Malinakova, H. C. *J. Org. Chem.* **2004**, *69*, 8266.
- (9) (a) Cook, G. R.; Shanker, P. S. Pararajasingham, K. *Angew. Chem. Int. Ed.* **1999**, *38*, 110. (b) Grigg, R.; Kordes, M. *Eur. J. Org. Chem.* **2001**, 707.
- (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'-Isopropylloxazolin-2'-yl)ferrocenyl]-diphenylphosphine, see: Miyake, Y.; Nishibayashi, Y.; Uemura, S. *Synlett*, **2008**, 1747.
- (13) (a) Xiao, X.; Cushman, M. *J. Org. Chem.* **2005**, *70*, 6496. (b) Padwa, A.; Zhang, H. *J. Org. Chem.* **2007**, *72*, 2570. (c) Matveenko, M.; Kokas, O. J.; Banwell, M. G.; Willis, A. C. *Org. Lett.* **2007**, *9*, 3683.
- (14) 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. See also chapter 1.

- (15) Fernandez-Forner, D.; Eritja, R.; Bardella, F.; Ruizperez, C.; Solans, X.; Giralt, E.; Pedroso, E. *Tetrahedron* **1991**, *47*, 8917.
- (16) Brandsma, L. *Synthesis of Acetylenes, Allenes and Cumulenes: Methods and Techniques*; Elsevier: 2004; p 243.
- (17) Trost, B. M.; Pinkerton, A. B.; Seidel, M. *J. Am. Chem. Soc.* **2001**, *123*, 12466.
- (18) Vermeer, P.; Meijer, J.; Brandsma, L. *Recl. Trav. Chim. Pays-bas.* **1975**, *94*, 112.
- (19) Myers, A. G.; Zheng, B.; *Organic Syntheses*; Willey: New York, 2004; Collect. Vol. 10, p 165.
- (20) Skattebol, L.; Salomon, S. *Organic Syntheses*; Willey: New York, 1973; Collect. Vol. 5, p 306.
- (21) (a) Sugahara, M.; Ukita, T. *Chem. Pharm. Bull.* **1997**, *45*, 719. (b) Shafir, A.; Buchwald, S. L. *J. Am. Chem. Soc.* **2006**, *128*, 8742. See also chapter 1.
- (22) Miura, T.; Yamauchi, M.; Murakami, M. *Org. Lett.* **2008**, *10*, 3085. See also Chapter 1.
- (23) Kronenthal, D. R.; Han, C. Y.; Taylor, M. K. *J. Org. Chem.* **1982**, *47*, 2765

Chapter 3

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

Abstract

A denitrogenative annulation reaction of 1,2,3-benzotriazin-4(3*H*)-ones with dienes and alkenes catalyzed by a nickel/phosphine complex, which produces a variety of substituted 3,4-dihydroquinolin-1(2*H*)-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.¹ 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(3*H*)-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(2*H*)-isoquinolones.² In chapter 2, nickel-catalyzed denitrogenative allene insertion reactions of 1,2,3-benzotriazin-4(3*H*)-ones to give 3,4-dihydroisoquinolin-1(2*H*)-ones were also described.³ In this chapter, the author examined that analogous nickel-catalyzed denitrogenative insertion reactions of 1,2,3-benzotriazin-4(3*H*)-ones with different carbon units such as 1,3-dienes and alkenes.

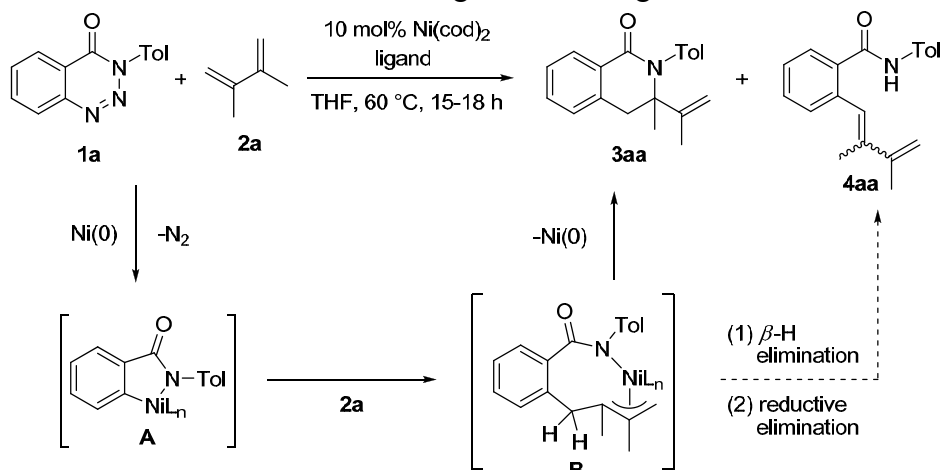
Results and Discussions

Initially, a denitrogenative insertion reaction of 1,2,3-benzotriazin-4(3*H*)-ones with 1,3-dienes was examined. 3-Tolyl-1,2,3-benzotriazin-4(3*H*)-one (**1a**)⁴ 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 PMe₃ 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 elimination⁵ 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^a



entry	ligand (mol%)	yield (%) of 3aa ^b	yield (%) of 4aa ^b
1	PMe ₃ (20)	37	63
2	PMe ₂ Ph (20)	56	44
3	PMePh ₂ (20)	8	-
4	PPh ₃ (20)	2	-
5	P(<i>n</i> -Bu) ₃ (20)	-	-
6	DPPF (10)	95 (94)	5
7	DPEphos (10)	24	4
8	DPPB (10)	62	7

^a Conditions: **1** (0.1 mmol), **2a** (0.2 mmol), Ni(cod)₂ (10 μmol, 10 mol %), and ligand in THF (1 mL) at 60 °C for 15-18 h unless otherwise noted. ^b Determined by ¹H NMR using CHCl₂CHCl₂ as an internal standard. Isolated yield in parentheses.

Table 2. Ni(0)-Catalyzed denitrogenative annulation of **1** with 1,3-diene **2a**^a

entry	1	R ¹	R ²	R ³	3	yield (%) ^b
1	1a	4-MeC ₆ H ₄	H	H	3aa	87
2	1b	Ph	H	H	3ba	87
3	1c	4-MeOC ₆ H ₄	H	H	3ca	85 ^c
4	1d	4-CF ₃ C ₆ H ₄	H	H	3da	88
5	1e	Ph	MeO	MeO	3ea	86 ^c
6	1f	Ph	H	CO ₂ Me	3fa	74

^a Conditions: **1** (0.2 mmol), **2a** (0.4 mmol), Ni(cod)₂ (20 μmol, 10 mol %), and DPPF (20 μmol, 10 mol %) in THF (1 mL) at 60 °C for 12 h unless otherwise noted. ^b Isolated yield. ^c 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-dimethylenecyclohexane (**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.⁶ 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.⁷

Table 3. Ni(0)-Catalyzed denitrogenative annulation of **1a** with 1,3-dienes **2**^a

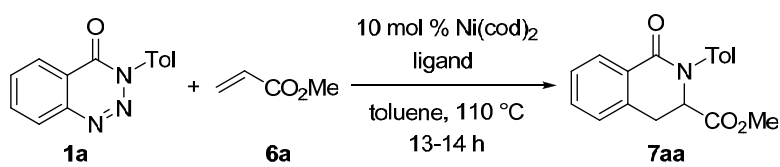
entry	2	3	5	yield (%) ^b
1			—	92 ^c
2			—	81
3				66 (86:14) ^d
4				53 (83:17) ^d
5				85 (90:10) ^{f,g}

^a Conditions: **1** (0.2 mmol), **2** (0.4 mmol), Ni(cod)₂ (20 μ mol, 10 mol %), DPPF (20 μ mol, 10 mol %) in THF (2 mL) at 60 °C for 6–12 h unless otherwise noted. ^b Isolated yield of **3** unless otherwise noted. Numbers in parentheses describe the ratio of **3**:**5**. ^c Toluene at 80 °C.

^d The ratio was determined by crude ¹H NMR. ^e *cis/trans* = 12:88. ^f Combined yield of isomers. ^g Ni(cod)₂ (40 μ mol, 20 mol %) and DPPF (40 μ mol, 20 mol %).

Next, the author examined denitrogenative annulation reactions of 1,2,3-benzotriazinon-4(3*H*)-ones with alkenes. 3-Tolyl-1,2,3-benzotriazin-4(3*H*)-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^a



entry	ligand (mol%)	yield (%) ^b
1	PMe ₃ (40)	90 ^c
2	PPh ₃ (40)	96
3	P(<i>n</i> -Bu) ₃ (40)	99 ^c
4	PCy ₃ (40)	96
5	P(<i>t</i> -Bu) ₃ (40)	trace
6	DPPF (20)	88

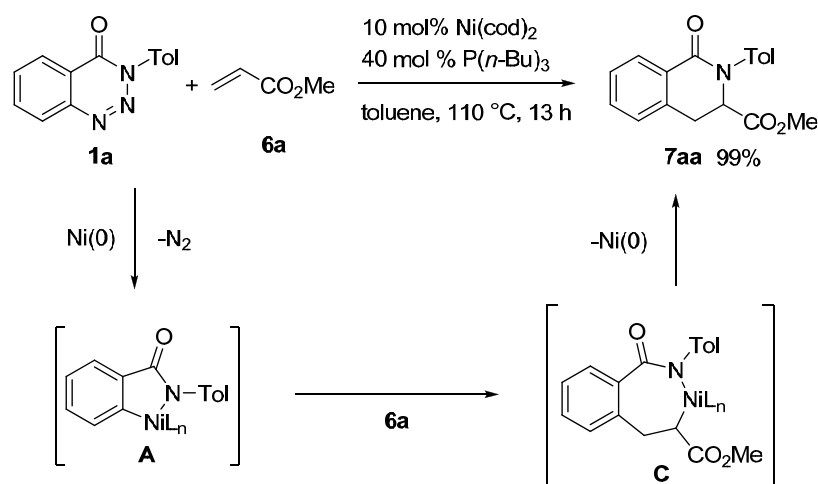
^a Conditions: **1** (0.1 mmol), **6a** (0.15 mmol), Ni(cod)₂ (10 μmol, 10 mol %), and ligand in toluene (1 mL) at 110 °C for 13-14 h unless otherwise noted. ^b NMR yield determined by ¹H NMR using CHCl₂CHCl₂ as internal standard. ^c Isolated yield.

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 molecular 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(2*H*)-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

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

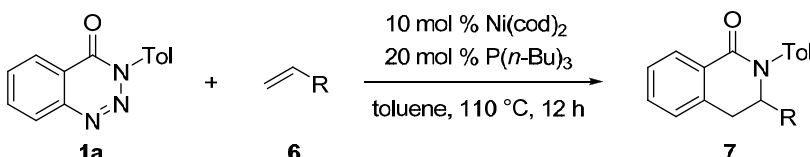
entry	1	R ¹	R ²	R ³	7	yield (%) ^b
1	1b	Ph	H	H	7ba	99
2	1c	4-MeOC ₆ H ₄	H	H	7ca	96
3	1d	4-CF ₃ C ₆ H ₄	H	H	7da	98
4	1g	4-ClC ₆ H ₄	H	H	7ga	81
5	1h	2MeOC ₆ H ₄	H	H	7ha	77
6	1e	Ph	MeO	MeO	7ea	99
7	1f	Ph	H	CO ₂ Me	7fa	97
8	1i	Bn	H	H	7ia	98
9	1j	Me	H	H	7ia	96

^a 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. ^b Isolated yield.

Various functionalized alkene 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. α,β -Unsaturated ketone **6f** was less reactive than α,β -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 annulation of **1** with alkenes **6a**^a

				
entry	6 (equiv)	R	7	yield (%) ^b
1	6b (3.0)	CONMe ₂	7ab	83
2	6c (3.0)	2-pyridyl	7ac	83 ^c
3	6d (1.5)	4-pyridyl	7ad	73 ^d
4	6e (1.5)	CN	7ae	92
5	6f (1.5)	COEt	7af	39 ^{c, e}
6	6g (1.5)	4-CF ₃ C ₆ H ₄	7ag	11 ^e
7	6h (1.5)	4-MeOC ₆ H ₄	7ah	0 ^e

^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 PMe₃ (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 annulation reaction of 1,2,3-benzotriazin-4(3*H*)-ones to provide the corresponding substituted 3,4-dihydroisoquinolin-1(2*H*)-ones.

Experimental Section

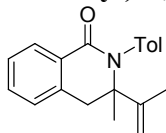
General Methods. All reactions were carried out under a nitrogen atmosphere unless otherwise noted. Infrared spectra were recorded on a Shimadzu FTIR-8100 spectrometer. ^1H and ^{13}C NMR spectra were recorded on a Varian Gemini 2000 (^1H at 300 MHz and ^{13}C at 75 MHz) spectrometer using CHCl_3 (^1H , $\delta = 7.26$) 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. $\text{Ni}(\text{cod})_2$ (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(3*H*)-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.

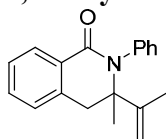
Spectroscopic data of **1a–1j** have been reported.⁴

General Procedure for Nickel-Catalyzed Denitrogenative Annulation of 1,2,3-Benzotriazin-4(3*H*)-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 $\text{Ni}(\text{cod})_2$ (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[®] 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).

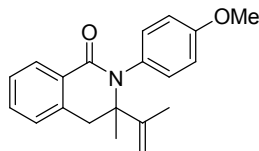
3-Methyl-2-(4-methylphenyl)-3-(prop-1-en-2-yl)-3,4-dihydroisoquinolin-1(2*H*)-one (**3aa**)



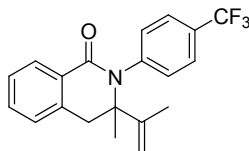
IR (KBr): 2980, 1644, 1512, 1374 cm^{-1} ; ^1H NMR: $\delta = 1.31$ (s, 3H), 1.71 (s, 3H), 2.37 (s, 3H), 3.18 (d, $J = 15.9$ Hz, 1H), 3.28 (d, $J = 15.6$ Hz, 1H), 4.93 (s, 1H), 5.05 (s, 1H), 7.12 (d, $J = 7.5$ Hz, 1H), 7.16–7.20 (m, 4H), 7.29–7.37 (m, 1H), 7.39–7.46 (m, 1H), 8.05–8.10 (m, 1H); ^{13}C 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 $\text{C}_{20}\text{H}_{21}\text{NO}$, 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)

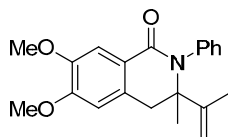
IR (KBr): 1644, 1605, 1582, 1491, 1460, 1372 cm^{-1} ; ^1H NMR: δ = 1.31 (s, 3H), 1.72 (s, 3H), 3.19 (d, J = 15.9 Hz, 1H), 3.29 (d, J = 15.9 Hz, 1H), 4.95 (s, 1H), 5.06 (s, 1H), 7.14 (d, J = 7.2 Hz, 1H), 7.26–7.48 (m, 7H), 8.08 (d, J = 7.5 Hz, 1H); ^{13}C NMR: δ = 19.7, 26.5, 41.2, 64.7, 114.8, 126.7, 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 $\text{C}_{19}\text{H}_{19}\text{NO}$, 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} ; ^1H NMR: δ = 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: δ = 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, 136.1, 146.0, 158.3, 165.7; HRMS (EI^+): Calcd for $\text{C}_{20}\text{H}_{21}\text{NO}_2$, 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)

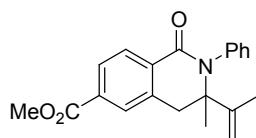
IR (KBr): 1642, 1323, 1165, 1123 cm^{-1} ; ^1H NMR: δ = 1.33 (s, 3H), 1.73 (s, 3H), 3.21 (d, J = 15.9 Hz, 1H), 3.30 (d, J = 15.9 Hz, 1H), 4.97 (s, 1H), 5.03 (s, 1H), 7.15 (d, J = 7.2 Hz, 1H), 7.35 (t, J = 7.5 Hz, 1H), 7.41–7.50 (m, 5H), 7.64 (d, J = 9.0 Hz, 2H), 8.04–8.09 (m, 1H); ^{13}C NMR: δ = 19.7, 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 $\text{C}_{20}\text{H}_{18}\text{F}_3\text{NO}$, 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} ; ^1H NMR: δ = 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,

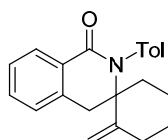
1H), 6.59 (s, 1H), 7.23–7.41 (m, 5H), 7.59 (s, 1H); ^{13}C NMR: δ = 19.9, 26.6, 40.8, 55.96, 55.99, 64.7, 109.2, 110.7, 114.7, 122.0, 127.1, 128.5, 129.1, 129.7, 140.0, 146.2, 147.8, 152.1, 165.4; HRMS (EI^+): Calcd for $\text{C}_{21}\text{H}_{23}\text{NO}_3$, M^+ 337.1678. Found m/z 337.1682.

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



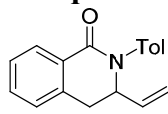
IR (KBr): 1713, 1646, 1445, 1368, 1279, 1210 cm^{-1} ; ^1H NMR: δ = 1.31 (s, 3H), 1.71 (s, 3H), 3.24 (d, J = 15.9 Hz, 1H), 3.31 (d, J = 15.9 Hz, 1H), 3.93 (s, 3H), 4.94 (s, 1H), 5.04 (s, 1H), 7.27–7.43 (m, 5H), 7.81–7.84 (m, 1H), 7.96–8.01 (m, 1H), 8.13 (d, J = 8.1 Hz, 1H); ^{13}C NMR: δ = 19.7, 26.4, 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 $\text{C}_{21}\text{H}_{21}\text{NO}_3$, 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)



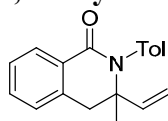
IR (KBr): 2934, 1655, 1605, 1512, 1462, 1374, 1345 cm^{-1} ; ^1H NMR: δ = 1.14–1.32 (m, 1H), 1.40–1.54 (m, 1H), 1.58–1.86 (m, 4H), 2.11–2.32 (m, 2H), 2.38 (s, 3H), 3.14 (d, J = 15.6 Hz, 1H), 3.55 (d, J = 15.6 Hz, 1H), 4.91 (s, 1H), 5.00 (s, 1H), 7.14 (d, J = 7.2 Hz, 1H), 7.16–7.24 (m, 4H), 7.29–7.36 (m, 1H), 7.39–7.46 (m, 1H), 8.04–8.10 (m, 1H); ^{13}C NMR: δ = 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 $\text{C}_{22}\text{H}_{23}\text{NO}$, M^+ 317.1780. Found m/z 317.1776.

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



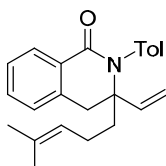
IR (KBr): 1659, 1514, 1460, 1404 cm^{-1} ; ^1H NMR: δ = 2.36 (s, 3H), 2.95 (dd, J = 15.9, 3.0 Hz, 1H), 3.62 (dd, J = 15.9, 5.7 Hz, 1H), 4.48–4.56 (m, 1H), 5.10 (d, J = 10.5 Hz, 1H), 5.15 (d, J = 17.1 Hz, 1H), 5.86 (ddd, J = 17.0, 10.3, 6.5 Hz, 1H), 7.16–7.22 (m, 3H), 7.23–7.30 (m, 2H), 7.32–7.40 (m, 1H), 7.42–7.49 (m, 1H), 8.10–8.16 (m, 1H); ^{13}C NMR: δ = 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 $\text{C}_{18}\text{H}_{17}\text{NO}$, M^+ 263.1310. Found m/z 263.1316.

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



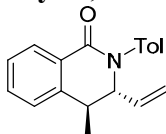
IR (KBr): 2982, 1651, 1510, 1460, 1385 cm^{-1} ; ^1H NMR: δ = 1.31 (s, 3H), 2.37 (s, 3H), 3.09 (d, J = 15.6 Hz, 1H), 3.29 (d, J = 15.9 Hz, 1H), 5.05 (d, J = 10.5 Hz, 1H), 5.11 (d, J = 17.4 Hz, 1H), 5.95 (dd, J = 17.4, 10.8 Hz, 1H), 7.06–7.13 (m, 2H), 7.16–7.23 (m, 3H), 7.31–7.39 (m, 1H), 7.42–7.50 (m, 1H), 8.08–8.13 (m, 1H); ^{13}C NMR: δ = 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 $\text{C}_{19}\text{H}_{19}\text{NO}$, 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)



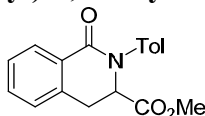
IR (neat): 2923, 1651, 1512, 1462, 1375 cm^{-1} ; ^1H NMR: δ = 1.46 (s, 3H), 1.61 (s, 3H), 1.52–1.99 (m, 4H), 2.38 (s, 3H), 3.20 (d, J = 15.9 Hz, 1H), 3.31 (d, J = 15.6 Hz, 1H), 4.84–4.92 (m, 1H), 5.12 (d, J = 11.1 Hz, 1H), 5.13 (d, J = 17.4 Hz, 1H), 5.75 (dd, J = 17.6, 10.7 Hz, 1H), 7.08–7.15 (m, 2H), 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: δ = 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 $\text{C}_{24}\text{H}_{27}\text{NO}$, M^+ 345.2093. Found m/z 345.2096.

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

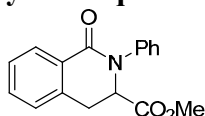


IR (KBr): 2973, 1651, 1514, 1462, 1404, 1262 cm^{-1} ; ^1H NMR: δ = 1.37 (d, J = 6.9 Hz, 3H), 2.36 (s, 3H), 3.63–3.75 (m, 1H), 4.21 (dd, J = 8.1, 5.4 Hz, 1H), 5.10 (dt, J = 17.1, 1.1 Hz, 1H), 5.14 (d, J = 10.5 Hz, 1H), 5.68 (ddd, J = 17.0, 10.2, 8.1 Hz, 1H), 7.16–7.28 (m, 5H), 7.33–7.41 (m, 1H), 7.47–7.55 (m, 1H), 8.11–8.16 (m, 1H); ^{13}C NMR: δ = 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 $\text{C}_{19}\text{H}_{19}\text{NO}$, M^+ 277.1467. Found m/z 277.1470.

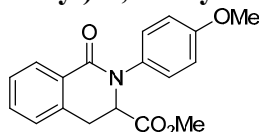
General Procedure for Nickel-Catalyzed Denitrogenative Annulation of 1,2,3-Benzotriazin-4(3H)-ones with Alkene (Table 5 and 6). To an oven-dried flask was added **1a** (47.5 mg, 0.2 mmol), a solution of $\text{Ni}(\text{cod})_2$ (5.6 mg, 20 μmol) and $\text{P}(n\text{-Bu}_3)$ (10 μL , 40 μmol) in toluene (2 mL), and methyl acrylate (**6a**, 28 μL , 0.3 mmol). After heated at 60 $^\circ\text{C}$ 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 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)

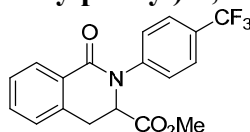
IR (KBr): 1740, 1698, 1514, 1383, 1150 cm^{-1} ; ^1H NMR: δ = 2.36 (s, 3H), 2.48 (dd, J = 15.9, 8.4 Hz, 1H), 2.93 (dd, J = 16.2, 3.9 Hz, 1H), 3.62 (s, 3H), 5.53 (dd, J = 8.7, 4.2 Hz, 1H), 7.21–7.29 (m, 2H), 7.39–7.45 (m, 2H), 7.47–7.61 (m, 3H), 7.89–7.95 (m, 1H); ^{13}C NMR: δ = 21.0, 37.6, 51.9, 57.6, 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 $\text{C}_{18}\text{H}_{17}\text{NO}_3$, M^+ 295.1208. Found m/z 295.1204.

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

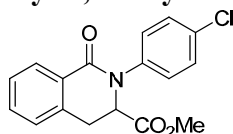
IR (KBr): 1742, 1684, 1499, 1395 cm^{-1} ; ^1H NMR: δ = 2.50 (dd, J = 16.2, 8.7 Hz, 1H), 2.95 (dd, J = 16.2, 7.2 Hz, 1H), 3.63 (s, 3H), 5.59 (dd, J = 8.6, 4.1 Hz, 1H), 7.21–7.29 (m, 1H), 7.41–7.63 (m, 7H), 7.90–7.95 (m, 1H); ^{13}C NMR: δ = 37.6, 51.9, 57.4, 122.5, 123.8, 124.2, 125.9, 128.8, 129.2, 131.8, 132.3, 136.3, 144.1, 166.7, 170.8; HRMS (EI^+): Calcd for $\text{C}_{17}\text{H}_{15}\text{NO}_3$, M^+ 281.1052. Found m/z 281.1051.

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

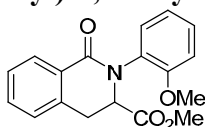
IR (KBr): 1736, 1698, 1514, 1387, 1248 cm^{-1} ; ^1H NMR: δ = 2.50 (dd, J = 16.2, 8.7 Hz, 1H), 2.89 (dd, J = 16.1, 4.4 Hz, 1H), 3.61 (s, 3H), 3.82 (s, 3H), 5.49 (dd, J = 8.6, 4.7 Hz, 1H), 6.94–7.01 (m, 2H), 7.38–7.46 (m, 2H), 7.47–7.62 (m, 3H), 7.89–7.94 (m, 1H); ^{13}C NMR: δ = 37.6, 51.9, 55.5, 58.1, 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 $\text{C}_{18}\text{H}_{17}\text{NO}_4$, M^+ 311.1158. Found m/z 311.1154.

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

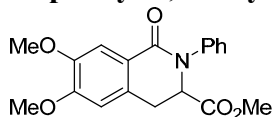
IR (KBr): 1742, 1686, 1613, 1397, 1339, 1161, 1115, 1067 cm^{-1} ; ^1H NMR: δ = 2.53 (dd, J = 16.2, 8.4 Hz, 1H), 2.97 (dd, J = 16.2, 4.2 Hz, 1H), 3.65 (s, 3H), 5.65 (dd, J = 8.6, 3.8 Hz, 1H), 7.50–7.57 (m, 2H), 7.58–7.66 (m, 1H), 7.67–7.73 (m, 1H), 7.74–7.80 (m, 1H), 7.90–7.95 (m, 1H); ^{13}C NMR: δ = 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 $\text{C}_{18}\text{H}_{14}\text{F}_3\text{NO}_3$, M^+ 349.0926. Found m/z 349.0916.

2-(4-Chlorophenyl)-3-methoxycarbonyl-3,4-dihydroisoquinolin-1(2H)-one (7ga)

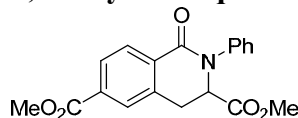
IR (KBr): 1742, 1684, 1497, 1391 cm^{-1} ; ^1H NMR: δ = 2.51 (dd, J = 16.1, 8.6 Hz, 1H), 2.92 (dd, J = 15.8, 4.1 Hz, 1H), 3.64 (s, 3H), 5.56 (dd, J = 8.6, 4.1 Hz, 1H), 7.38–7.46 (m, 2H), 7.48–7.64 (m, 5H), 7.89–7.94 (m, 1H); ^{13}C NMR: δ = 37.4, 52.0, 57.3, 122.5, 124.2, 124.7, 129.0, 129.3, 131.2,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

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

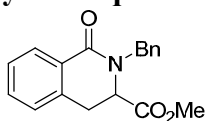
IR (KBr): 1736, 1702, 1505, 1387, 1266, 1152 cm^{-1} ; ^1H NMR: δ = 2.58 (dd, J = 16.2, 7.2 Hz, 1H), 2.74 (dd, J = 16.2, 6.0 Hz, 1H), 3.51 (s, 3H), 3.81 (s, 3H), 5.56 (dd, J = 6.9, 6.3 Hz, 1H), 6.98–7.07 (m, 2H), 7.31–7.38 (m, 2H), 7.47–7.54 (m, 2H), 7.55–7.62 (m, 1H), 7.91–7.96 (m, 1H); ^{13}C NMR: δ = 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 $\text{C}_{18}\text{H}_{17}\text{NO}_4$, M^+ 311.1158. Found m/z 311.1155.

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

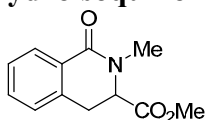
IR (KBr): 1734, 1692, 1497, 1385, 1256 cm^{-1} ; ^1H NMR: δ = 2.44 (dd, J = 16.2, 9.0 Hz, 1H), 2.93 (dd, J = 16.4, 4.1 Hz, 1H), 3.63 (s, 3H), 3.93 (s, 3H), 3.94 (s, 3H), 5.47 (dd, J = 8.7, 3.9 Hz, 1H), 6.99 (s, 1H), 7.17–7.25 (m, 1H), 7.35 (s, 1H), 7.38–7.46 (m, 2H), 7.50–7.56 (m, 2H); ^{13}C NMR: δ = 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 $\text{C}_{19}\text{H}_{19}\text{NO}_5$, M^+ 341.1263. Found m/z 341.1260.

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

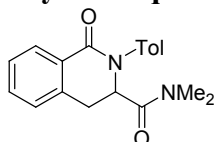
IR (KBr): 1745, 1717, 1690, 1383, 1294, 1217 cm^{-1} ; ^1H NMR: δ = 2.57 (dd, J = 16.2, 8.4 Hz, 1H), 2.96 (dd, J = 16.3, 4.1 Hz, 1H), 3.63 (s, 3H), 3.97 (s, 3H), 5.63 (dd, J = 8.4, 4.2 Hz, 1H), 7.24–7.32 (m, 1H), 7.42–7.50 (m, 2H), 7.53–7.59 (m, 2H), 7.96–8.02 (m, 1H), 8.17–8.24 (m, 1H); ^{13}C NMR: δ = 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 $\text{C}_{19}\text{H}_{17}\text{NO}_5$, M^+ 339.1107. Found m/z 339.1105.

2-Benzyl-3-methoxycarbonyl-3,4-dihydroisoquinolin-1(2H)-one (7ia)

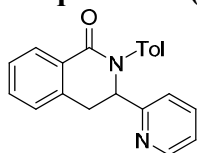
IR (KBr): 1732, 1678, 1435, 1408, 1242 cm^{-1} ; ^1H NMR: δ = 2.61 (dd, J = 16.1, 7.4 Hz, 1H), 2.86 (dd, J = 16.2, 5.7 Hz, 1H), 3.63 (s, 3H), 4.40 (d, J = 15.0 Hz, 1H), 4.83 (dd, J = 6.8, 5.3 Hz, 1H), 5.20 (d, J = 15.6 Hz, 1H), 7.20–7.35 (m, 5H), 7.36–7.41 (m, 1H), 7.44–7.57 (m, 2H), 7.87–7.92 (m, 2H); ^{13}C 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 $\text{C}_{18}\text{H}_{17}\text{NO}_3$, M^+ 295.1208. Found m/z 295.1212.

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

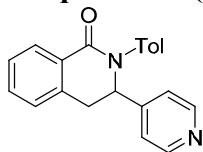
IR (KBr): 1736, 1698, 1437, 1397 cm^{-1} ; ^1H NMR: δ = 2.65 (dd, J = 16.1, 6.8 Hz, 1H), 2.87 (dd, J = 16.1, 5.6 Hz, 1H), 3.09 (s, 3H), 3.72 (s, 3H), 4.85 (t, J = 6.3 Hz, 1H), 7.38–7.54 (m, 3H), 7.78–7.83 (m, 1H); ^{13}C NMR: δ = 27.4, 37.4, 52.1, 58.3, 122.1, 123.5, 128.5, 131.5, 131.9, 144.3, 168.0, 170.8; HRMS (EI^+): Calcd for $\text{C}_{12}\text{H}_{13}\text{NO}_3$, M^+ 219.0895. Found m/z 219.0894.

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

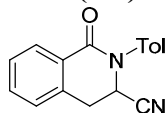
IR (KBr): 1688, 1651, 1512, 1383, 1146 cm^{-1} ; ^1H NMR: δ = 2.35 (s, 3H), 2.39 (dd, J = 15.9, 9.6 Hz, 1H), 2.77 (s, 3H), 2.88 (dd, J = 16.2, 3.3 Hz, 1H), 2.95 (s, 3H), 5.81 (dd, J = 9.9, 3.6 Hz, 1H), 7.20–7.28 (m, 2H), 7.45–7.59 (m, 4H), 7.60–7.66 (m, 1H), 7.87–7.93 (m, 1H); ^{13}C NMR: δ = 21.0, 35.5, 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 $\text{C}_{19}\text{H}_{20}\text{N}_2\text{O}_2$, M^+ 308.1525. Found m/z 308.1522.

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

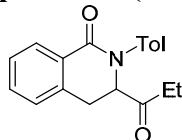
IR (KBr): 1682, 1514, 1389 cm^{-1} ; ^1H NMR: δ = 2.34 (s, 3H), 2.86 (dd, J = 13.8, 8.7 Hz, 1H), 3.49 (dd, J = 13.8, 4.5 Hz, 1H), 5.81 (dd, J = 8.7, 4.5 Hz, 1H), 6.86 (d, J = 8.1 Hz, 2H), 7.10–7.17 (m, 1H), 7.22 (d, J = 8.1 Hz, 2H), 7.36–7.58 (m, 5H), 7.83–7.91 (m, 1H), 8.52–8.59 (m, 1H); ^{13}C NMR: 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 $\text{C}_{21}\text{H}_{18}\text{N}_2\text{O}$, M^+ 314.1419. Found m/z 314.1416.

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

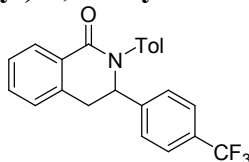
IR (KBr): 1698, 1597, 1512, 1383 cm^{-1} ; ^1H NMR: δ = 2.37 (s, 3H), 3.02 (dd, J = 13.8, 6.9 Hz, 1H), 3.27 (dd, J = 14.0, 3.8 Hz, 1H), 5.46 (dd, J = 6.9, 3.6 Hz, 1H), 6.65–6.72 (m, 2H), 7.19–7.30 (m, 3H), 7.40–7.55 (m, 4H), 7.79 (d, J = 7.2 Hz, 1H), 8.27–8.34 (m, 2H); ^{13}C NMR: δ = 21.0, 37.0, 60.2, 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 $\text{C}_{21}\text{H}_{18}\text{N}_2\text{O}$, M^+ 314.1419. Found m/z 314.1416.

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

IR (KBr): 1684, 1512, 1387, 1217 cm^{-1} ; ^1H NMR: δ = 2.37 (s, 3H), 2.67 (dd, J = 16.7, 6.5 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); ^{13}C NMR: δ = 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 $\text{C}_{17}\text{H}_{14}\text{N}_2\text{O}$, M^+ 262.1106. Found m/z 262.1100.

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

IR (KBr): 1698, 1514, 1375 cm^{-1} ; ^1H NMR: δ = 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); ^{13}C NMR: δ = 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 $\text{C}_{19}\text{H}_{19}\text{N}_2\text{O}$, M^+ 293.1416. 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} ; ^1H NMR: δ = 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); ^{13}C NMR: δ = 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,

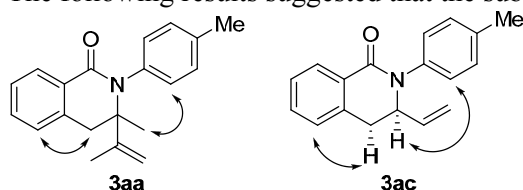
132.4, 134.2, 135.3, 139.1, 143.3, 166.8; HRMS (EI^+): Calcd for $\text{C}_{19}\text{H}_{19}\text{N}_2\text{O}$, M^+ 293.1416. Found m/z 293.1412.

Determination of Stereochemistries.

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

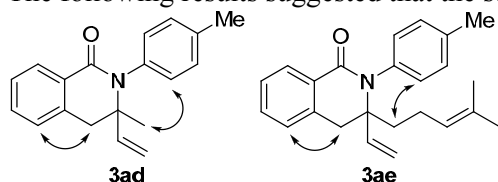
[Compound 3aa and 3ad]

The following results suggested that the substituent group was bound to the C(3).



[Compound 3ad and 3ae]

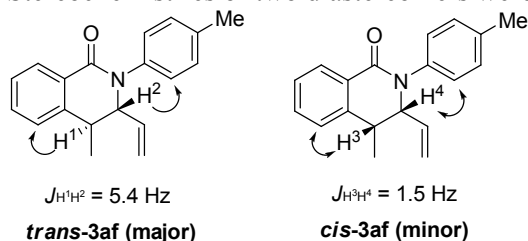
The following results suggested that the substituent group was bound to the C(3).



[Compound *trans*-3af and *cis*-3af]

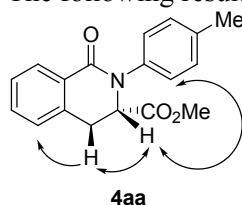
The following results suggested that the vinyl group was bound to the C(3).

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

- (1) For reviews, see: (a) Nakamura, I.; Yamamoto, Y. *Chem. Rev.* **2004**, *104*, 2127. (b) Zeni, G.; Larock, R. C. *Chem. Rev.* **2004**, *104*, 2285. (c) D'Souza, D. M.; Müller, T. J. J. *Chem. Soc. Rev.* **2007**, *36*, 1095.
- (2) Miura, T.; Yamauchi, M.; Murakami, M. *Org. Lett.* **2008**, *10*, 3085. See also chapter 1.
- (3) Yamauchi, M.; Morimoto, M.; Miura, T.; Murakami, M. *J. Am. Chem. Soc.* **2010**, *132*, 54. See also chapter 2.
- (4) For synthetic methods of 1,2,3-benzotriazin-4(3*H*)-ones, see Experimental Section of chapter 1.
- (5) (a) Hoberg, H.; Summermann, K.; Milchereit, A. *Angew. Chem. Int. Ed.* **1985**, *24*, 325. (b) Nakao, Y.; Yaba, A.; Satoh, J.; Ebata, S.; Oda, S.; Hiyama, T. *Chem. Lett.* **2006**, *35*, 790. (c) Schleicher, K. D.; Jamison, T. F. *Org. Lett.* **2007**, *9*, 875. (d) Ogoshi, S.; Nagata, M.; Kurosawa, H. *J. Am. Chem. Soc.* **2006**, *128*, 5350. (e) Hirano, K.; Yorimitsu, H.; Oshima, K. *Org. Lett.* **2006**, *8*, 483. (f) Murakami, M.; Ashida, S.; Matsuda, T. *J. Am. Chem. Soc.* **2005**, *127*, 6932.
- (6) (a) Ogoshi, S.; Tonomori, K.; Oka, M.; Kurosawa, H. *J. Am. Chem. Soc.* **2006**, *128*, 7077. (b) Kimura, M.; Ezoe, A.; Mori, M.; Iwata, K.; Tamaru, Y. *J. Am. Chem. Soc.* **2006**, *128*, 8559.
- (7) (a) Takimoto, M.; Hiraga, Y.; Sato, Y.; Mori, M. *Tetrahedron Lett.* **1998**, 4543. (b) Hirata, Y.; Inui, T.; Nakao, Y.; Hiyama, T. *J. Am. Chem. Soc.* **2009**, *131*, 6624.
- (8) Yurchenko, A.G.; yrij, A.B.; Likhovvorik, I. R.; Melnik, N. N.; Zaharzh, P.; Bzhezovski, V. V.; Kushko, A. O. *Synthesis*, **1990**, 393.

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 α -imino diazo species, and the denitrogenative addition to nickel(0) was followed by the insertion of alkynes and reductive elimination.

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 *in situ* by the ring-chain tautomerisation and subsequently converted to a reactive metal-carbenoid species. 7-Halo-substituted pyridotriazoles² and 1-sulfonyl-1,2,3-triazoles³ 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*H*)-ones gave a wide range of substituted 1(2*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 diazo 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

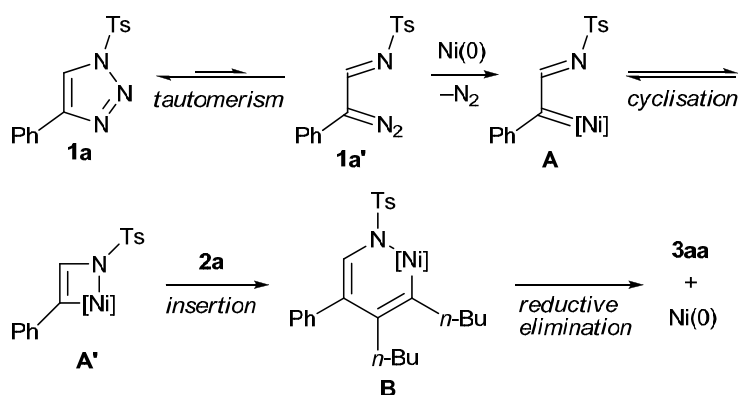
The starting materials, 4-substituted 1-(*N*-tosyl)-1,2,3-triazoles, could be readily prepared by the copper-catalysed azide/alkyne cycloaddition.⁸ When 4-phenyl-1-(*N*-tosyl)-1,2,3-triazole (**1a**) was treated with dec-5-yne (**2a**, 2 equiv), 10 mol% of Ni(cod)₂ and 20 mol% of PMe₃ in toluene at 100 °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 AlPh₃ (5 mol%) gave **3aa** in 73% isolated yield.

Table 1. Optimisation study of the formation of pyrrole **3aa**.^a

Entry	Ligand	Lewis acid	Yield (%) ^b
1	PMe ₃	—	2
2	PCy ₃	—	8
3	P(<i>t</i> -Bu) ₃	—	13
4	P(<i>n</i> -Bu)Ad ₂	—	51
5	P(<i>n</i> -Bu)Ad ₂	BPh ₃	49
6	P(<i>n</i> -Bu)Ad ₂	ZnPh ₂	62
7	P(<i>n</i> -Bu)Ad ₂	AlMe ₃	38
8	P(<i>n</i> -Bu)Ad ₂	AlPh ₃	81 (73)

^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 CHCl₂CHCl₂ 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'**,¹⁰ although the equilibrium lies far to the left. Diazo 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,¹¹ 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 pyrroles **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**^a

entry	1	R ¹	R ²	3	yield (%) ^b
1	1b	Ph	Ph	3ba	65
2	1c	4-F-C ₆ H ₄	Ph	3ca	46
3	1d	4-MeO-C ₆ H ₄	Ph	3da	56 ^c
4	1e	2-naphthyl	Ph	3ea	58 ^c
5	1f	Tol	Tol	3fa	64
6	1g	Tol	4-CF ₃ -C ₆ H ₄	3ga	64 ^d
7	1h	Tol	4-MeO-C ₆ H ₄	3ha	59 ^c
8	1i	Tol	4-Ph-C ₆ H ₄	3ia	54
9	1j	Tol	2-naphthyl	3ja	58
10	1k	Tol	2-hex	3ka	5

^a Conditions: **1** (0.2 mmol), **2a** (0.4 mmol), Ni(cod)₂ (10 mol %), P(*n*-Bu)₂Ad (20 mol %), AlPh₃ (5 mol %) in toluene (2 mL) for 12 h. ^b Isolated yield. ^c Ni(cod)₂ (15 mol %) and P(*n*-Bu)₂Ad₂ (30 mol %) were used. ^d 110 °C.

Various alkynes (**2**) were subjected to the denitrogenative insertion reaction with **1a** (Table 3). Symmetrical alkynes 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 alkynes gave a mixture of regioisomers (entries 3–5). Terminal alkynes such as 1-octyne and phenylethyne failed to participate in the reaction, presumably due to a rapid self-oligomerisation reaction.

Table 3. Denitrogenative alkyne insertion of **1a** with **2**^a

entry	2	R ¹	R ²	3	yield (%) ^b
1	2b	<i>n</i> -Pr	<i>n</i> -Pr	3ab	68
2	2c	Ph	Ph	3ac	31
3	2d	Me	<i>i</i> -Pr	3ad	68 (50:50)
4	2e	Me	SiMe ₃	3ae	48 (58:42) ^c
5	2f	Bpin	<i>n</i> -Bu	3af	37 (57:43) ^c

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

Conclusions

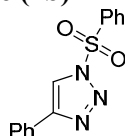
In summary, the author has demonstrated that the nickel-catalysed denitrogenative alkyne insertion reaction of 1-sulfonyltriazoles provides a new synthetic route to substituted pyrroles from readily available starting materials. In this reaction, the triazole moiety is effectively activated by a combined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

Experimental Section

General. Infrared spectra were recorded on a Shimadzu FTIR-8100 spectrometer. ^1H and ^{13}C NMR spectra were recorded on a Varian Gemini 2000 (^1H at 300 MHz and ^{13}C at 75 MHz) spectrometer using CHCl_3 (^1H , $\delta = 7.26$) 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 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 PF254 (Merck).

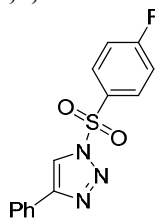
Materials. Toluene was distilled from sodium/benzophenone ketyl. Trimethylphosphine (Aldrich), tricyclohexylphosphine (Strem), tri-*t*-butylphosphine (Wako), *n*-butyl-di-1-adamantylphosphine (Strem), triphenylborane (Aldrich), diphenylzinc (Aldrich), trimethylaluminium toluene solution (Kanto) and diphenylethyne (**2b**) (Aldrich) were used as received from the commercial sources. $\text{Ni}(\text{cod})_2$ (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**)

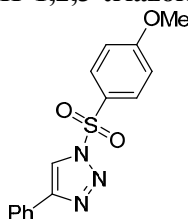


IR (KBr): 3129, 1451, 1393, 1181 cm^{-1} ; ^1H NMR: $\delta = 7.33\text{--}7.48$ (m, 3H), 7.56–7.66 (m, 2H), 7.69–7.77 (m, 1H), 7.80–7.86 (m, 2H), 8.12–8.19 (m, 2H), 8.33 (s, 1H); ^{13}C NMR: $\delta = 119.0$, 126.0, 128.4, 128.6, 128.9, 129.0, 129.7, 135.6, 136.0, 147.3; HRMS (EI^+): Calcd for $\text{C}_{14}\text{H}_{11}\text{N}_3\text{O}_2\text{S}$,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

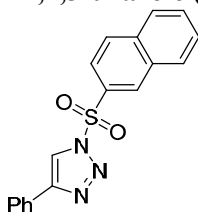
1-(4-Fluorophenylsulfonyl)-4-phenyl-1*H*-1,2,3-triazole (**1c**)



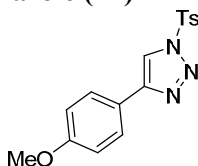
IR (KBr): 3144, 1586, 1493, 1395, 1244, 1188 cm^{-1} ; ^1H NMR: $\delta = 7.23\text{--}7.33$ (m, 2H), 7.34–7.48 (m, 3H), 7.79–7.86 (m, 2H), 8.15–8.24 (m, 2H), 8.32 (s, 1H); ^{13}C NMR: $\delta = 117.3$ (d, $J = 23.0$ Hz), 118.9, 126.0, 128.6, 129.0, 129.2, 131.8 (d, $J = 10.4$ Hz), 132.0 (d, $J = 2.3$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

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

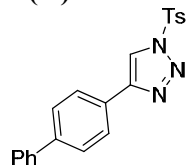
IR (KBr): 3092, 1592, 1397, 1271, 1202, 1167, 1090 cm^{-1} ; ^1H NMR: δ = 3.87 (s, 3H), 6.99–7.06 (m, 2H), 7.32–7.46 (m, 3H), 7.79–7.85 (m, 2H), 8.03–8.11 (m, 2H), 8.31 (s, 1H); ^{13}C NMR: δ = 55.9, 115.0, 118.8, 126.0, 126.9, 128.9, 129.0, 131.1, 147.2, 165.3; HRMS (EI^+): Calcd for $\text{C}_{15}\text{H}_{13}\text{N}_3\text{O}_3\text{S}$, M^+ 315.0678. Found m/z 315.0678.

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

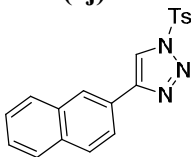
IR (KBr): 3125, 1395, 1179, 995 cm^{-1} ; ^1H NMR: δ = 7.31–7.47 (m, 3H), 7.61–7.75 (m, 2H), 7.78–7.86 (m, 2H), 7.87–7.94 (m, 1H), 7.96–8.08 (m, 3H), 8.38 (s, 1H), 8.74–8.80 (m, 1H); ^{13}C NMR: δ = 119.0, 122.1, 126.0, 128.0, 128.2, 128.7, 128.9, 129.0, 129.7, 130.2, 130.4, 131.2, 131.8, 132.7, 135.9, 147.4; HRMS (EI^+): Calcd for $\text{C}_{18}\text{H}_{13}\text{N}_3\text{O}_2\text{S}$, M^+ 335.0728. Found m/z 335.0731.

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

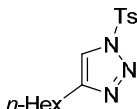
IR (KBr): 3115, 1497, 1393, 1256, 1179 cm^{-1} ; ^1H NMR: δ = 2.40 (s, 3H), 3.81 (s, 3H), 6.90–6.97 (m, 2H), 7.34 (d, J = 8.1 Hz, 2H), 7.70–7.78 (m, 2H), 7.99 (d, J = 8.4 Hz, 2H), 8.23 (s, 1H); ^{13}C NMR: δ = 21.7, 55.2, 114.3, 117.9, 121.3, 127.3, 128.5, 130.3, 133.0, 147.1, 147.2, 160.1; HRMS (EI^+): Calcd for $\text{C}_{16}\text{H}_{15}\text{N}_3\text{O}_3\text{S}$, M^+ 329.0834. Found m/z 329.0833.

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

IR (KBr): 3139, 1593, 1483, 1389, 1177 cm^{-1} ; ^1H NMR: δ = 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); ^{13}C NMR: δ = 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 $\text{C}_{21}\text{H}_{17}\text{N}_3\text{O}_2\text{S}$, M^+ 375.1041. Found m/z 375.1045.

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

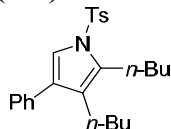
IR (KBr): 3141, 1389, 1325, 1198, 1175 cm^{-1} ; ^1H NMR: δ = 2.43 (s, 3H), 7.34–7.41 (m, 2H), 7.45–7.55 (m, 2H), 7.79–7.92 (m, 4H), 8.01–8.08 (m, 2H), 8.34–8.38 (m, 1H), 8.43 (s, 1H); ^{13}C NMR: δ = 21.8, 119.1, 123.5, 125.2, 126.1, 126.60, 126.63, 127.7, 128.2, 128.6, 128.8, 130.4, 133.0, 133.3, 133.4, 147.3, 147.4; HRMS (EI^+): Calcd for $\text{C}_{19}\text{H}_{15}\text{N}_3\text{O}_2\text{S}$, M^+ 349.0885. Found m/z 349.0889.

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

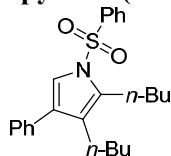
IR (neat): 2930, 1595, 1395, 1194 cm^{-1} ; ^1H NMR: δ = 0.87 (t, J = 6.8 Hz, 3H), 1.21–1.40 (m, 6H), 1.64 (quint, J = 7.5 Hz, 2H), 2.44 (s, 3H), 2.64–2.75 (m, 2H), 7.34–7.40 (m, 2H), 7.82–7.84 (m, 1H), 7.94–8.01 (m, 2H); ^{13}C NMR: δ = 14.0, 21.8, 22.5, 25.4, 28.75, 28.84, 31.4, 120.2, 128.5, 130.3, 133.3, 147.0, 148.3; HRMS (EI^+): Calcd for $\text{C}_{15}\text{H}_{21}\text{N}_3\text{O}_2\text{S}$, 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 μmol) were charged into an oven-dried 4 mL vial equipped with a stir bar. A solution of $\text{Ni}(\text{cod})_2$ (5.5 mg, 20 μmol) and $\text{P}(n\text{-Bu})\text{Ad}_2$ (14.3 mg, 40 μmol) 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 $^\circ\text{C}$ 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 thinlayer chromatography (hexane/dichloromethane) to give the product **3**.

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

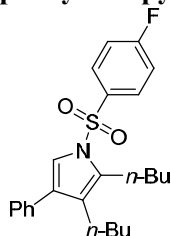
IR (neat): 2957, 1597, 1368, 1175, 1094 cm^{-1} ; ^1H NMR: δ = 0.77 (t, J = 7.1 Hz, 3H), 0.91 (t, J = 7.2 Hz, 3H), 1.10–1.53 (m, 8H), 2.35–2.46 (m, 2H), 2.41 (s, 3H), 2.60–2.70 (m, 2H), 7.24–7.42 (m, 8H), 7.61–7.67 (m, 2H); ^{13}C NMR: δ = 13.7, 13.8, 21.6, 22.6, 22.8, 24.3, 25.3, 32.6, 33.1, 119.3,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

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

IR (neat): 2957, 1368, 1175, 1094 cm^{-1} ; ^1H NMR: δ = 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),

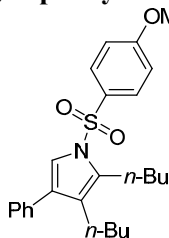
7.55–7.63 (m, 1H), 7.73–7.80 (m, 2H); ^{13}C NMR: δ = 13.7, 13.8, 22.6, 22.8, 24.3, 25.3, 32.6, 33.1, 119.4, 125.5, 126.4, 126.8, 128.1, 128.4, 128.6, 129.2, 132.4, 133.4, 134.8, 139.8; HRMS (EI^+): Calcd for $\text{C}_{24}\text{H}_{29}\text{NO}_2\text{S}$, M^+ 395.1919. Found m/z 395.1920.

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



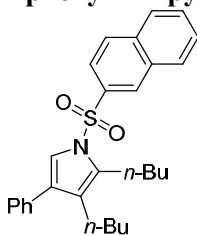
IR (neat): 2957, 1593, 1495, 1372, 1183, 1092 cm^{-1} ; ^1H NMR: δ = 0.78 (t, J = 7.1 Hz, 3H), 0.92 (t, J = 7.2 Hz, 3H), 1.10–1.56 (m, 8H), 2.35–2.47 (m, 2H), 2.59–2.71 (m, 2H), 7.12–7.22 (m, 2H), 7.25–7.43 (m, 6H), 7.74–7.83 (m, 2H); ^{13}C NMR: δ = 13.7, 13.8, 22.6, 22.8, 24.3, 25.4, 32.6, 33.2, 116.6 (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 $\text{C}_{24}\text{H}_{28}\text{FNO}_2\text{S}$, M^+ 413.1825. Found m/z 413.1824.

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

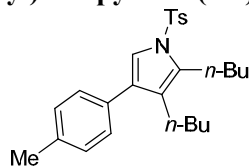


IR (neat): 2957, 1595, 1499, 1366, 1264, 1167, 1094 cm^{-1} ; ^1H NMR: δ = 0.78 (t, J = 7.1 Hz, 3H), 0.91 (t, J = 7.1 Hz, 3H), 1.11–1.53 (m, 8H), 2.36–2.45 (m, 2H), 2.60–2.70 (m, 2H), 3.85 (s, 3H), 6.90–6.97 (m, 2H), 7.25–7.41 (m, 6H), 7.67–7.74 (m, 2H); ^{13}C NMR: δ = 13.75, 13.83, 22.6, 22.9, 24.3, 25.3, 32.6, 33.1, 55.7, 114.4, 119.2, 125.2, 126.7, 128.1, 128.3, 128.4, 128.8, 131.3, 132.2, 134.9, 163.4; HRMS (EI^+): Calcd for $\text{C}_{25}\text{H}_{31}\text{NO}_3\text{S}$, M^+ 425.2025. Found m/z 425.2026.

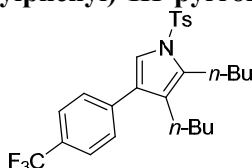
2,3-Dibutyl-1-(naphthalen-2-ylsulfonyl)-4-phenyl-1H-pyrrole (3ea)



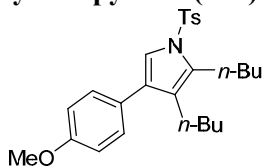
IR (neat): 2957, 1366, 1177, 1076 cm^{-1} ; ^1H NMR: δ = 0.78 (t, J = 6.9 Hz, 3H), 0.89 (t, J = 7.2 Hz, 3H), 1.12–1.57 (m, 8H), 2.38–2.49 (m, 2H), 2.68–2.79 (m, 2H), 7.28–7.45 (m, 6H), 7.58–7.74 (m, 3H), 7.85–8.01 (m, 3H), 8.42 (d, J = 2.1 Hz, 1H); ^{13}C NMR: δ = 13.7, 13.8, 22.5, 22.8, 24.2, 25.3, 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 $\text{C}_{28}\text{H}_{31}\text{NO}_2\text{S}$, M^+ 445.2075. Found m/z 445.2076.

2,3-Dibutyl-1-tosyl-4-(4-trimethylphenyl)-1H-pyrrole (3fa)

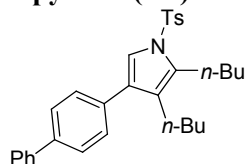
IR (neat): 2957, 1368, 1175, 1094 cm^{-1} ; ^1H NMR: δ = 0.78 (t, J = 7.2 Hz, 3H), 0.90 (t, J = 7.2 Hz, 3H), 1.09–1.52 (m, 8H), 2.32–2.45 (m, 2H), 2.37 (s, 3H), 2.40 (s, 3H), 2.60–2.69 (m, 2H), 7.14–7.20 (m, 2H), 7.22–7.30 (m, 5H), 7.60–7.66 (m, 2H); ^{13}C NMR: δ = 13.75, 13.81, 21.1, 21.57, 22.60, 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 $\text{C}_{26}\text{H}_{33}\text{NO}_2\text{S}$, M^+ 423.2232. Found m/z 423.2235.

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

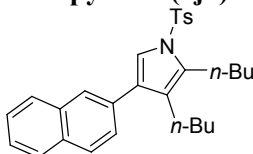
IR (neat): 2959, 1619, 1370, 1325, 1175, 1127, 1073 cm^{-1} ; ^1H NMR: δ = 0.79 (t, J = 7.1 Hz, 3H), 0.91 (t, J = 7.2 Hz, 3H), 1.10–1.52 (m, 8H), 2.36–2.48 (m, 2H), 2.42 (s, 3H), 2.61–2.71 (m, 2H), 7.27–7.33 (m, 2H), 7.34 (s, 1H), 7.45–7.52 (m, 2H), 7.60–7.70 (m, 4H); ^{13}C NMR: δ = 13.7, 13.8, 21.6, 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 $\text{C}_{26}\text{H}_{30}\text{F}_3\text{NO}_2\text{S}$, M^+ 477.1949. Found m/z 477.1946.

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

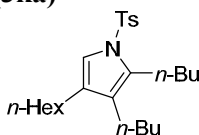
IR (neat): 2957, 1539, 1368, 1246, 1173, 1094 cm^{-1} ; ^1H NMR: δ = 0.78 (t, J = 7.1 Hz, 3H), 0.90 (t, J = 7.1 Hz, 3H), 1.10–1.52 (m, 8H), 2.32–2.43 (m, 2H), 2.40 (s, 3H), 2.59–2.68 (m, 2H), 3.83 (s, 3H), 6.87–6.95 (m, 2H), 7.22 (s, 1H), 7.23–7.31 (m, 4H), 7.60–7.67 (m, 2H); ^{13}C NMR: δ = 13.77, 13.81, 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 $\text{C}_{26}\text{H}_{33}\text{NO}_3\text{S}$, M^+ 439.2181. Found m/z 439.2179.

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

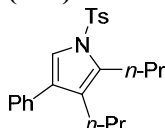
IR (neat): 2957, 1368, 1175, 1094 cm^{-1} ; ^1H NMR: δ = 0.82 (t, J = 7.2 Hz, 3H), 0.94 (t, J = 7.2 Hz, 3H), 1.16–1.56 (m, 8H), 2.42 (s, 3H), 2.43–2.52 (m, 2H), 2.64–2.74 (m, 2H), 7.27–7.32 (m, 2H), 7.33–7.40 (m, 2H), 7.43–7.51 (m, 4H), 7.60–7.71 (m, 6H); ^{13}C NMR: δ = 13.77, 13.83, 21.6, 22.6, 22.8, 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 $\text{C}_{31}\text{H}_{35}\text{NO}_2\text{S}$, M^+ 485.2389. Found m/z 485.2390.

2,3-Dibutyl-4-(naphthalen-2-yl)-1-tosyl-1H-pyrrole (3ja)

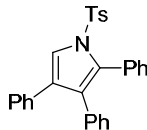
IR (neat): 2957, 1368, 1173, 1094 cm^{-1} ; ^1H NMR: δ = 0.78 (t, J = 7.2 Hz, 3H), 0.93 (t, J = 7.2 Hz, 3H), 1.12–1.56 (m, 8H), 2.42 (s, 3H), 2.46–2.56 (m, 2H), 2.65–2.75 (m, 2H), 7.26–7.33 (m, 2H), 7.41 (s, 1H), 7.43–7.56 (m, 3H), 7.65–7.72 (m, 2H), 7.80–7.89 (m, 4H); ^{13}C NMR: δ = 13.7, 13.8, 21.6, 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^+): Calcd for $\text{C}_{29}\text{H}_{33}\text{NO}_2\text{S}$, 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); ^{13}C 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^+): Calcd for $\text{C}_{25}\text{H}_{39}\text{NO}_2\text{S}$, M^+ 417.2702. Found m/z 417.2702.

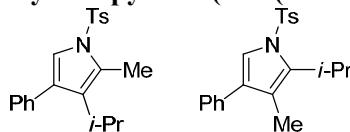
4-Phenyl-2,3-dipropyl-1-tosyl-1H-pyrrole (3ab)

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); ^{13}C 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^+): Calcd for $\text{C}_{23}\text{H}_{27}\text{NO}_2\text{S}$, M^+ 381.1762. Found m/z 381.1758.

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

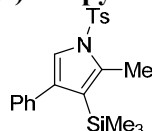
IR (KBr): 1368, 1171, 1103 cm^{-1} ; ^1H NMR: δ = 2.38 (s, 3H), 6.83–6.91 (m, 2H), 6.98–7.08 (m, 5H), 7.10–7.34 (m, 12H), 7.65 (s, 1H); ^{13}C NMR: δ = 21.6, 119.9, 126.3, 126.6, 126.9, 127.1, 127.5, 127.6, 127.7, 128.2, 128.4, 129.4, 130.2, 130.4, 132.1, 132.6, 133.3, 133.7, 135.7, 144.7; HRMS (EI^+): Calcd for $\text{C}_{29}\text{H}_{23}\text{NO}_2\text{S}$, M^+ 449.1449. Found m/z 449.1447.

**3-Isopropyl-2-methyl-4-phenyl-1-tosyl-1*H*-pyrrole and
2-Isopropyl-3-methyl-4-phenyl-1-tosyl-1*H*-pyrrole (3ad (mixture))**



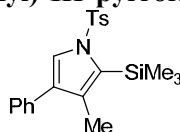
IR (neat): 2965, 1364, 1173, 1094 cm^{-1} ; ^1H NMR: δ = 1.125 (d, J = 7.2 Hz, 3H), 1.132 (d, J = 6.9 Hz, 3H), 2.10 (s, 1.5H), 2.36 (s, 1.5H), 2.42 (s, 1.5H), 2.43 (s, 1.5H), 2.92 (sept, J = 7.2 Hz, 0.5H), 3.61 (sept, J = 7.1 Hz, 0.5H), 7.23 (s, 0.5H), 7.27–7.44 (m, 7.5H), 7.64–7.74 (m, 2H); ^{13}C NMR: δ = 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 $\text{C}_{21}\text{H}_{23}\text{NO}_2\text{S}$, M^+ 353.1449. Found m/z 353.1447.

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



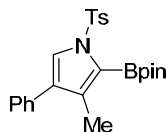
IR (KBr): 2953, 1360, 1173, 1011 cm^{-1} ; ^1H NMR: δ = 0.00 (s, 9H), 2.41 (s, 3H), 2.44 (s, 3H), 7.23–7.37 (m, 8H), 7.71–7.78 (m, 2H); ^{13}C NMR: δ = 1.2, 14.3, 21.7, 120.1, 126.9, 127.1, 127.7, 129.6, 130.0, 133.0, 136.1, 136.4, 136.8, 144.8; HRMS (EI^+): Calcd for $\text{C}_{21}\text{H}_{25}\text{NO}_2\text{SSi}$, M^+ 383.1375. Found m/z 383.1374.

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



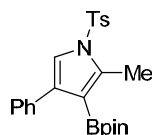
IR (KBr): 2953, 1356, 1169, 1100 cm^{-1} ; ^1H NMR: δ = 0.37 (s, 9H), 2.17 (s, 3H), 2.40 (s, 3H), 7.22–7.42 (m, 7H), 7.42 (s, 1H), 7.49–7.55 (m, 2H); ^{13}C NMR: δ = 2.4, 13.2, 21.6, 125.4, 126.0, 126.9, 128.3, 128.9, 129.6, 131.4, 131.7, 134.0, 134.6, 137.6, 144.1; HRMS (EI^+): Calcd for $\text{C}_{21}\text{H}_{25}\text{NO}_2\text{SSi}$, 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-1*H*-pyrrole (3af (major))



IR (neat): 2930, 1374, 1173, 1111 cm^{-1} ; ^1H NMR: δ = 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: δ = 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 $\text{C}_{27}\text{H}_{34}\text{BNO}_4\text{S}$, 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))



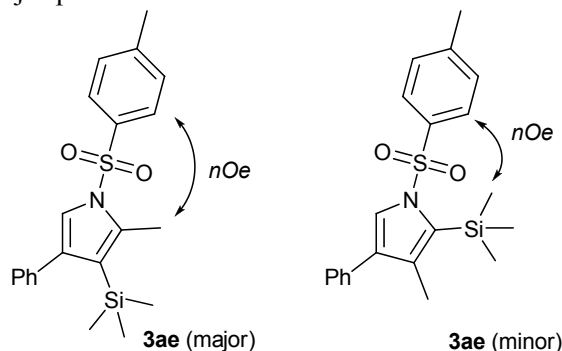
IR (neat): 2977, 1372, 1306, 1175, 1117 cm^{-1} ; ^1H NMR: δ = 0.90 (t, J = 7.2 Hz, 3H), 1.25 (s, 12H), 1.29–1.54 (m, 4H), 2.40 (s, 3H), 2.84–2.94 (m, 2H), 7.21–7.35 (m, 5H), 7.36 (s, 1H), 7.40–7.46 (m, 2H), 7.66–7.72 (m, 2H); ^{13}C NMR: δ = 13.8, 21.6, 22.9, 24.7, 27.3, 34.4, 83.2, 119.7, 126.6, 126.9, 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 $\text{C}_{27}\text{H}_{34}\text{BNO}_4\text{S}$, 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.

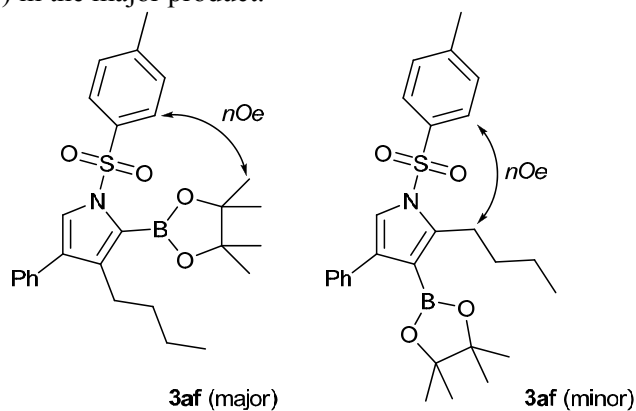
[Compound 3ae]

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.



[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.



References and Notes

- (1) For recent reviews, see: (a) D'Souza D. M.; Müller, T. J. J. *Chem. Soc. Rev.*, **2007**, *36*, 1095. (b) Álvarez-Corral, M.; Muñoz-Dorado, M.; Rodríguez-García, I. *Chem. Rev.*, **2008**, *108*, 3174. (c) Patil, N. T.; Yamamoto, Y. *Chem. Rev.*, **2008**, *108*, 3395.
- (2) (a) Chuprakov, S.; Hwang, F. W.; Gevorgyan, V. *Angew. Chem., Int. Ed.*, **2007**, *46*, 4757. (b) Chuprakov, S.; Gevorgyan, V. *Org. Lett.*, **2007**, *9*, 4463.
- (3) Horneff, T.; Chuprakov, S.; Chernyak, N.; Gevorgyan, V.; Fokin, V. V. *J. Am. Chem. Soc.*, **2008**, *130*, 14972.
- (4) Nakamura, I.; Nemoto, T.; Shiraiwa, N.; Terada, M. *Org. Lett.* **2009**, *11*, 1055.
- (5) Miura, T.; Yamauchi, M.; Murakami, M. *Org. Lett.* **2008**, *10*, 3085. See also Chapter 1.
- (6) For reactions of diazoalkanes with a nickel(0) catalyst, see: (a) Nakamura, A., Yoshida, T.; Cowie, M.; Otsuka, S.; Ibers, J. A. *J. Am. Chem. Soc.*, **1977**, *99*, 2108. (b) Mindiola, D. J., Hillhouse, G. L. *J. Am. Chem. Soc.*, **2002**, *124*, 9976.
- (7) For recent reports on the synthesis of substituted pyrroles, see: (a) Rivero, M. R.; Buchwald, S. L. *Org. Lett.*, **2007**, *9*, 973. (b) Shindo, M.; Yoshimura, Y.; Hayashi, M.; Soejima, H.; Yoshikawa, T.; Matsumoto, K.; Shishido, K. *Org. Lett.*, **2007**, *9*, 1963. (c) Dong, H.; Shen, M.; Redford, J. E.; Stokes, B. J.; Pumphrey, A. L.; Driver, T. G. *Org. Lett.*, **2007**, *9*, 5191. (d) Galliford, C. V.; Scheidt, K. A. *J. Org. Chem.*, **2007**, *72*, 1811. (e) Cadierno, V.; Gimeno, J.; Nebra, N. *Chem.-Eur. J.*, **2007**, *13*, 9973. (f) Chiba, S.; Wang, Y.-F.; Lapointe, G.; Narasaka, K. *Org. Lett.*, **2008**, *10*, 313. (g) Cacchi, S.; Fabrizi, G.; Filisti, E. *Org. Lett.*, **2008**, *10*, 2629. (h) Lu, Y.; Arndtsen, B. A. *Angew. Chem., Int. Ed.*, **2008**, *47*, 5430.
- (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.
- (9) (a) Brunkan, N. M.; Brestensky, D. M.; Jones, W. D. *J. Am. Chem. Soc.*, **2004**, *126*, 3627. (b) Hratchian, H. P.; Chowdhury, S. K.; Gutiérrez-García, V. M.; Amarasinghe, K. K. D.; Heeg, M. J.; Schlegel, H. B.; Montgomery, J. *Organometallics*, **2004**, *23*, 4636. (c) Ogoshi, S.; Ueta, M.; Arai, T.; Kurosawa, H. *J. Am. Chem. Soc.*, **2005**, *127*, 12810. (d) Nakao, Y.; Yada, A.; Ebata, S.; Hiyama, T. *J. Am. Chem. Soc.*, **2007**, *129*, 2428.
- (10) (a) Grünanger, P.; Finzi, P. V. *Tetrahedron. Lett.*, **1963**, *4*, 1839 (b) Harmon, R. E.; Stanley, F.; Gupta, Jr, S. K.; Johnson, J. J. *J. Org. Chem.*, **1970**, *35*, 3444. (c) Himbert, G.; Frank, D.; Regit, M. *Chem. Ber.*, **1976**, *109*, 370.
- (11) Shen, Q.; Hartwig, J. F. *J. Am. Chem. Soc.*, **2007**, *129*, 7734.

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 copper³ or ruthenium⁴ catalysts, respectively (Figure 1).

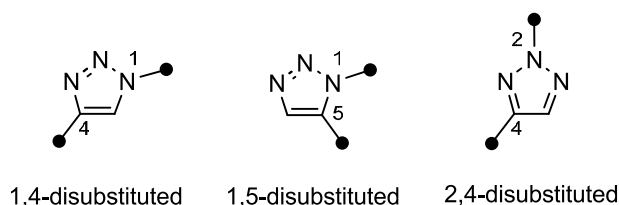


Figure 1. Spacial display of substituent in *C,N*-disubstituted 1,2,3-triazoles.

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.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).¹⁴

Table 1. Synthesis of 2-sulfonyl-1,2,3-triazoles.^a

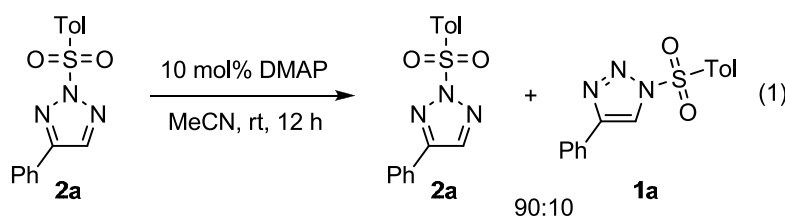
entry	1	R ¹	R ²	N2:N1 ^b	2	yield ^c
1	1a	4-MeC ₆ H ₄	Ph	88:12	2a	82%
2	1b	4-FC ₆ H ₄	Ph	91:9	2b	86%
3	1c	4-MeOC ₆ H ₄	Ph	87:13	2c	73% ^d
4	1d	2-Naphthyl	Ph	88:12	2d	80%
5	1e	<i>n</i> -Bu	Ph	86:14	2e	72%
6	1f	4-MeC ₆ H ₄	4-CF ₃ C ₆ H ₄	85:15	2f	75%
7	1g	4-MeC ₆ H ₄	4-MeOC ₆ H ₄	92:8	2g	86%
8	1h	4-MeC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

^a Reaction conducted on a 0.5 mmol scale. ^b Determined by ¹H NMR analysis. ^c Isolated yield. ^d 20 mol % of DMAP was used. ^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/H₂O (10/1), the N1 sulfonyl group of **1a** was selectively hydrolyzed in preference to

the N2 sulfonyl group of **2a**. Subsequent chromatographic isolation readily afforded analytically pure **2a** in 82% overall yield.¹⁵ 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 sulfonyl group rearrangement was reversible under the reaction conditions and that **2a** was the thermodynamically more stable isomer. The author presumes that an *N*-sulfonyl(*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.¹⁶



We examined the rearrangement reaction of 4-phenyl-1,2,3-triazoles **1b–1e** having various sulfonyl groups (R^1) at the N1 position. Substituted benzenesulfonyl groups as well as a naphthalenesulfonyl group rearranged from the N1 position to the N2 position (Table 1, entries 2–4). Even a butanesulfonyl group successfully participated in the reaction (Table 1, entry 5). Variation of the substituent (R^2) 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-sulfonyl-1,2,3-triazoles leading to 4-substituted 2-sulfonyl-1,2,3-triazoles.

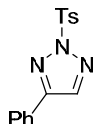
Experimental Section

General. Infrared spectra were recorded on a Shimadzu FTIR-8100 spectrometer. ^1H and ^{13}C NMR spectra were recorded on a Varian Gemini 2000 (^1H at 300 MHz and ^{13}C at 75 MHz) spectrometer using CHCl_3 (^1H , $\delta = 7.26$) 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 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_3CN 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

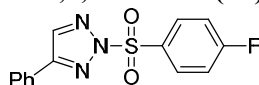
General Procedure for Base-Promoted 1,2-Rearrangement of a Sulfonyl Group. To an oven-dried, Ar-purged flask was added **1a** (151 mg, 0.5 mmol), DMAP (6.5 mg, 0.05 mmol), and MeCN (5 mL). The reaction mixture was stirred at room temperature for 12 h, and then concentrated under reduced pressure. The 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_2SO_4 , and evaporated. The residue was again dissolved in AcOH (5 mL) and H_2O (0.5 mL). The reaction mixture was stirred at 60 °C for 3 h, and then concentrated under reduced pressure. 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**)



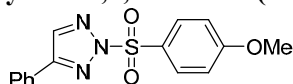
IR (KBr): 1391, 1196, 1163, 1086 cm^{-1} ; ^1H NMR: $\delta = 2.41$ (s, 3H), 7.34 (d, $J = 8.7$ Hz, 2H), 7.39–7.48 (m, 3H), 7.79–7.86 (m, 2H), 7.97–8.03 (m, 2H), 8.08 (s, 1H); ^{13}C NMR: $\delta = 21.7$, 126.6, 128.2, 128.6, 128.9, 129.9, 130.1, 132.9, 135.6, 146.6, 151.4; HRMS (FAB⁺): Calcd for $\text{C}_{15}\text{H}_{13}\text{N}_3\text{O}_2\text{S}$, $\text{M}+\text{H}^+$ 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} ; ^1H NMR: $\delta = 7.18$ –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: $\delta = 117.0$ (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 $\text{C}_{14}\text{H}_{10}\text{FN}_3\text{O}_2\text{S}$, M^+ 303.0478. Found m/z 303.0482.

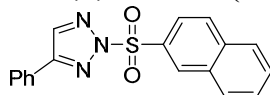
2-(4-Methoxyphenylsulfonyl)-4-phenyl-2H-1,2,3-triazole (**2c**)



IR (KBr): 1593, 1497, 1399, 1271, 1200, 1159, 1090 cm^{-1} ; ^1H NMR: $\delta = 3.83$ (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: $\delta = 55.8$,

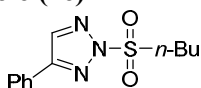
114.7, 126.5, 126.8, 128.2, 128.9, 129.8, 131.0, 135.4, 151.2, 164.8; HRMS (EI^+): Calcd for $\text{C}_{15}\text{H}_{13}\text{N}_3\text{O}_3\text{S}$, M^+ 315.0678. Found m/z 315.0680.

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



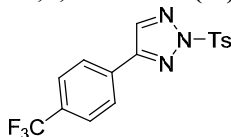
IR (KBr): 1401, 1186, 1167 cm^{-1} ; ^1H NMR: δ = 7.36–7.48 (m, 3H), 7.59–7.73 (m, 2H), 7.78–7.85 (m, 2H), 7.89 (d, J = 8.1 Hz, 1H), 7.94–8.07 (m, 3H), 8.08 (s, 1H), 8.73–8.77 (m, 1H); ^{13}C NMR: δ = 122.3, 126.6, 127.88, 127.94, 128.9, 129.6, 129.8, 129.9, 130.1, 130.9, 131.7, 132.5, 135.6, 135.9, 151.5; HRMS (EI^+): Calcd for $\text{C}_{18}\text{H}_{13}\text{N}_3\text{O}_2\text{S}$, M^+ 335.0728. Found m/z 335.0725.

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



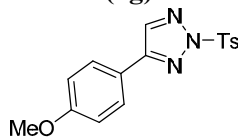
IR (neat): 2965, 1387, 1184 cm^{-1} ; ^1H NMR: δ = 0.89 (t, J = 7.2 Hz, 3H), 1.41 (sext, J = 7.4 Hz, 2H), 1.68–1.82 (m, 2H), 3.50–3.60 (m, 2H), 7.40–7.52 (m, 3H), 7.84–7.92 (m, 2H), 8.18 (s, 1H); ^{13}C NMR: δ = 13.3, 21.1, 24.6, 54.3, 126.6, 128.0, 129.0, 130.0, 135.3, 151.3; HRMS (EI^+): Calcd for $\text{C}_{12}\text{H}_{15}\text{N}_3\text{O}_2\text{S}$, M^+ 265.0885. Found m/z 265.0885.

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



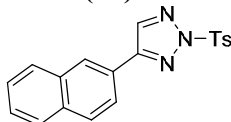
IR (KBr): 1401, 1321, 1196, 1161, 1132 cm^{-1} ; ^1H NMR: δ = 2.43 (s, 3H), 7.33–7.40 (m, 2H), 7.70 (d, J = 8.4 Hz, 2H), 7.92–7.98 (m, 2H), 7.99–8.05 (m, 2H), 8.12 (s, 1H); ^{13}C NMR: δ = 21.7, 123.7 (q, J = 270.5 Hz), 125.8 (q, J = 3.8 Hz), 126.9, 128.7, 130.2, 131.5 (q, J = 32.7 Hz), 131.7, 132.5, 135.6; HRMS (EI^+): Calcd for $\text{C}_{16}\text{H}_{12}\text{F}_3\text{N}_3\text{O}_2\text{S}$, 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} ; ^1H NMR: δ = 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: δ = 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^+): Calcd for $\text{C}_{16}\text{H}_{15}\text{N}_3\text{O}_3\text{S}$, M^+ 329.0834. Found m/z 329.0834.

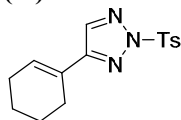
4-(Naphthalen-2-yl)-2-tosyl-2H-1,2,3-triazole (2h)



IR (KBr): 1389, 1194, 1161 cm^{-1} ; ^1H NMR: δ = 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: δ = 21.7,

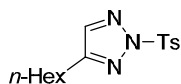
123.7, 125.5, 126.2, 126.7, 127.0, 127.7, 128.3, 128.6, 128.8, 130.1, 132.9, 133.0, 133.8, 135.9, 146.6, 151.5; HRMS (EI⁺): Calcd for C₁₉H₁₅N₃O₂S, M⁺ 349.0885. Found m/z 349.0884.

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



IR (KBr): 2926, 1395, 1198, 1167 cm⁻¹; ¹H NMR: δ = 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); ¹³C NMR: δ = 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 C₁₅H₁₇N₃O₂S, M⁺ 303.1041. Found m/z 303.1044.

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



IR (KBr): 2932, 1393, 1198, 1165 cm⁻¹; ¹H NMR: δ = 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); ¹³C NMR: δ = 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 C₁₅H₂₁N₃O₂S, M⁺ 307.1354. Found m/z 307.1356.

References and Notes

- Reviews: (a) Lutz, J.-F. *Angew. Chem. Int. Ed.*, **2007**, *46*, 1018. (b) Moses, J. E.; Moorhouse, A. D. *Chem. Soc. Rev.*, **2007**, *36*, 1249. (c) Fournier, D.; Hoogenboom, R.; Schubert, U. S. *Chem. Soc. Rev.*, **2007**, *36*, 1369. (d) Angell Y. L.; Burgess, K. *Chem. Soc. Rev.*, **2007**, *36*, 1674.
- Reviews: (a) Krivopalov, V. P.; Shkurko, O. P. *Russ. Chem. Rev.*, **2005**, *74*, 339. (b) Wu, P; Fokin, V. V. *Aldrichim. Acta*, **2007**, *40*, 7.
- (a) Rostovtsev, V.V.; Green, L.G.; Fokin, V.V.; Sharpless, K. B. *Angew. Chem. Int. Ed.*, **2002**, *41*, 2596. (b) Tornøe, C. W.; Christensen, C.; Meldal, M. *J. Org. Chem.*, **2002**, *67*, 3057.

- (4) Zhang, L.; Chen, X.; Xue, P.; Sun, H. H. Y.; Williams, I. D.; Sharpless, K. B.; Fokin, V. V.; Jia, G. *J. Am. Chem. Soc.*, **2005**, *127*, 15998.
- (5) For reports on the synthesis of 2-sulfonyl-1,2,3-triazoles, see: (a) Abdel-Halim, A. M.; Abdel-Rahman, R. M.; Mohamed, E. A. *Acta Pharm. Jugosl.*, **1985**, *35*, 89. (b) Potapova, I. A.; Purygin, P. P.; Lipatov, I. S.; Belousova, Z. P.; Yakimova, N. A.; Tezikov, Y. V.; Selezneva, E. S. *Pharm. Chem. J.*, **2001**, *35*, 588. (c) Meshcheryakov, V. I.; Shainyan, B. A.; Tolstikova, L. L.; Albanov, A. I. *Russ. J. Org. Chem.*, **2003**, *39*, 1517.
- (6) For reports on the pharmaceutical activity of 2,4-disubstituted triazoles, see: (a) Balle, T.; Perregaard, J.; Ramirez, M. T.; Larsen, A. K.; Søby, K. K.; Liljefors, T.; Andersen, K. *J. Med. Chem.*, **2003**, *46*, 265. (b) Roppe, J.; Smith, N. D.; Huang, D.; Tehrani, L.; Wang, B.; Anderson, J.; Brodtkin, J.; Chung, J.; Jiang, X.; King, C.; Munoz, B.; Varney, M. A.; Prasit, P.; Cosford, N. D. P. *J. Med. Chem.*, **2004**, *47*, 4645.
- (7) Liu, Y.; Yan, W.; Chen, Y.; Petersen, J. L.; Shi, X. *Org. Lett.*, **2008**, *10*, 5389 and references therein.
- (8) The reaction of 4-phenyl-1,2,3-triazole with TsCl in the presence of NEt₃ in CH₂Cl₂ 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.
- (9) (a) Birkofer, L.; Wegner, P. *Chem. Ber.*, **1967**, *100*, 3485. (b) Iddon B.; Nicholas, M. *J. Chem. Soc., Perkin Trans. 1*, **1996**, 1341. (c) Kamijo, S.; Jin, T.; Huo, Z.; Yamamoto, Y. *J. Am. Chem. Soc.*, **2003**, *125*, 7786. (d) Kwok, S. W.; Hein, J. E.; Fokin, V. V.; Sharpless, K. B. *Heterocycles*, **2008**, *76*, 1141.
- (10) Kalisiak, J.; Sharpless, K. B.; Fokin, V. V. *Org. Lett.*, **2008**, *10*, 3171.
- (11) Miura, T.; Yamauchi, M.; Murakami, M. *Chem. Commun.*, **2009**, 1470. See also Chapter 4.
- (12) For sulfonyl group rearrangement of other heterocycles, see: (a) Kohori, K.; Kinoshita, H.; Inomata, K.; *Chem. Lett.*, **1995**, 799. (b) Woydziak, Z. R.; Frost, B. J.; Lightner, D. A. *J. Heterocycl. Chem.*, **2005**, *42*, 731. (c) Inomata, K. *Bull. Chem. Soc. Jpn.*, **2008**, *81*, 25.
- (13) 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.
- (14) Other amines such as NEt₃, NHET₂, and NEt(*i*-Pr)₂ were also effective for the rearrangement of sulfonyl group.
- (15) Foces-Foces, C.; Llamas Saiz, A. L.; Elguero, J. *Heterocycl. Commun.*, **1999**, *5*, 137.

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-dialkylidenecycloalkanes. 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 group² and others³ 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 diynes⁴ 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..

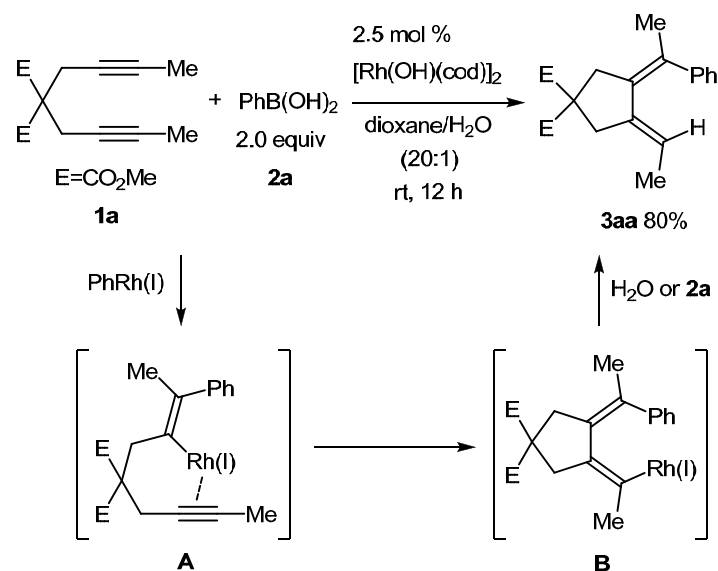
Results and Discussions

1,6-Diyne **1a** was treated with phenylboronic acid (**2a**, 2.0 equiv) in the presence of [Rh(OH)(cod)]₂ (5 mol % Rh, cod = cycloocta-1,5-diene) in dioxane-H₂O (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 dienylnrhodium(I) intermediate **B**. Finally, protonolysis with H₂O or **2a** yields **3aa** with regeneration of hydroxrhodium(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 sterics between two substituents flanking the carbon–carbon triple bond. The reaction of **1a** and phenylboroxine⁸ in the presence of dioxane-D₂O gave **3aa-d₁** 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

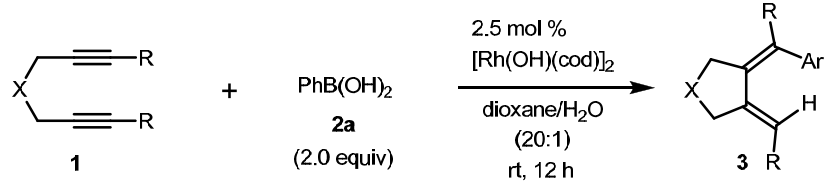
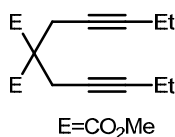
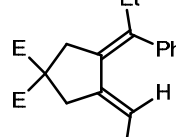
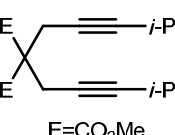
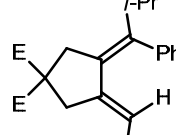
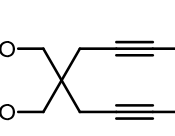
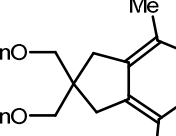
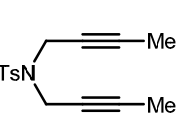
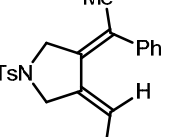
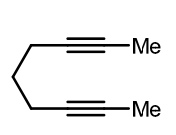
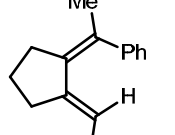
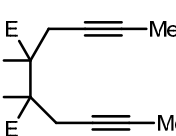
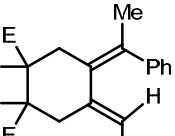
Table 1. Rh(I)-Catalyzed Arylative Cyclization of **1a** with Various Arylboronic Acids **2^a**

entry	2	Ar	3	yield (%) ^b
1	2b	4-Me-C ₆ H ₄	3ab	76
2	2c	3-Me-C ₆ H ₄	3ac	77
3	2d	2-Me-C ₆ H ₄	3ad	84
4	2e	3-MeO-C ₆ H ₄	3ae	83
5	2f	2-MeO-C ₆ H ₄	3af	90
6	2g	4-CF ₃ -C ₆ H ₄	3ag	84
7	2h	4-MeO ₂ C-C ₆ H ₄	3ah	77
8	2i	3-Br-C ₆ H ₄	3ai	79
9	2j	3-pyridyl	3aj	67 ^c

^a 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. ^b Isolated yields. ^c **2** (0.6 mmol), [Rh(OH)(cod)]₂ (10 μmol, 5 mol %) at 100 °C.

Next, the use of other symmetrical diynes **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-Diynes **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**^a

				
entry	1	3	yield (%) ^b	
1	 1b	 3ba	89	
2	 1c	 3ca	90 ^c	
3	 1d	 3da	80	
4	 1e	 3ea	20 ^d	
5	 1f	 3fa	18 ^c	
6	 1g	 3ga	78 ^e	

^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-diynes **4**, which possessed a methyl substituent at one alkyne terminus

(Table 3).⁹ 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 sterics between the two terminal substituents increased, and excellent regioselectivity was observed with the Me/SiMe₃-disubstituted substrate **4c** (entry 3).¹⁰ Initial carborhodation occurred preferentially or selectively at the sterically more accessible methyl side. Interestingly, opposite regioselectivities were observed with the ROCH₂/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 dienylnrhodium(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.¹¹ Formation of a cumulated double bond might be disfavored.

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

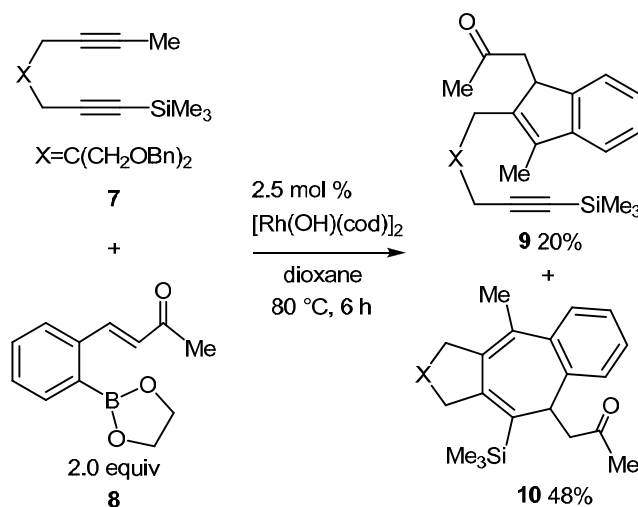
entry	4	R	5	6	yield (%) ^b
1	4a	Et	5a	6a	85 (57:43)
2	4b	<i>i</i> -Pr	5b	6b	86 (73:27)
3	4c	SiMe ₃	5c	6c	77 (>95:5)
4	4d	CH ₂ OMe	5d	6d	70 (20:80)
5	4e	CH ₂ OAc	5e	6e	77 (11:89)
6	4f	CH ₂ OH	5f	6f	72 (9:91)

^a Reaction conditions: **4** (0.2 mmol), **2a** (0.4 mmol), [Rh(OH)(cod)]₂ (10 μ mol) in dioxane (2 mL) and H₂O (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 Lautens¹² (Scheme 2). The reaction of unsymmetrical 1,6-diyne **7** with **8** (2.0 equiv) afforded a mixture of **9** (20%)

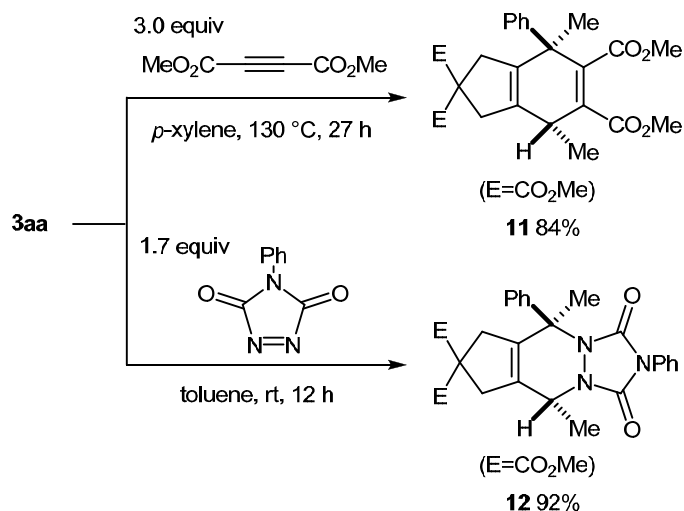
and **10** (48%). Cyclization through conjugate addition to the electron-deficient olefin took place at two stages of the sequence of carborhodation. The alkenylrhodium(I) intermediate formed by initial carborhodation cyclized in a 5-*exo*-trig mode giving bicyclic compound **9**, and the dienylrhodium(I) intermediate formed by the second carborhodation cyclized in a 7-*exo*-trig mode giving tricyclic compound **10**.

Scheme 2



The phenylated 1,2-dialkylidenecyclopentanes 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).

Scheme 3



Conclusions

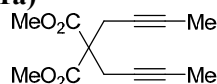
In summary, the author has developed a new cyclization reaction of diynes with arylboronic acids in the presence of a rhodium(I) catalyst, allowing the stereoselective formation of arylated 1,2-dialkylidenecycloalkanes.

Experimental Section

General Methods. Infrared spectra were recorded on a Shimadzu FTIR-8100 spectrometer. ^1H and ^{13}C NMR spectra were recorded on a Varian Gemini 2000 (^1H at 300 MHz and ^{13}C at 75 MHz) spectrometer using CHCl_3 (^1H , $\delta = 7.26$) 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. Column chromatography was performed with Wakogel[®] C-200 (Wako). Preparative thin-layer chromatography was performed with silica gel 60 PF254 (Merck).

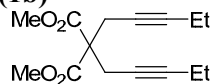
Materials. Dioxane, *p*-xylene, toluene were distilled from sodium/benzophenone ketyl. H_2O was degassed by ultrasound before use. $[\text{RhOH}(\text{cod})]_2$ was prepared according to the literature procedure.¹³ Dimethyl Acetylenedicarboxylate, 4-Phenyl-1,2,4-triazoline-3,5-dione, and all arylboronic acids were used as received from the commercial sources. Diynes **1a-1e**,¹⁴ **1f**,¹⁵ **1g**,¹⁴ **4a-4f**¹⁴ were prepared according to the literature procedure.

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



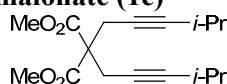
IR (KBr): 2951, 2361, 1744, 1439, 1294, 1219, 1055 cm^{-1} ; ^1H NMR: $\delta = 1.74$ (t, $J = 2.6$ Hz, 6H), 2.88 (q, $J = 2.5$ Hz, 4H), 3.73 (s, 6H); ^{13}C NMR: $\delta = 3.5, 22.9, 52.9, 57.0, 73.0, 79.0, 169.7$; HRMS (CI^+): Calcd for $\text{C}_{13}\text{H}_{17}\text{O}_4$, $\text{M}+\text{H}^+$ 237.1127. Found m/z 237.1126.

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



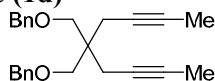
IR (neat): 2979, 2238, 1744, 1437, 1218, 1055 cm^{-1} ; ^1H NMR: $\delta = 1.08$ (t, $J = 7.5$ Hz, 6H), 2.11 (qt, $J = 7.4, 2.4$ Hz, 4H), 2.91 (t, $J = 2.3$ Hz, 4H), 3.74 (s, 6H); ^{13}C NMR: $\delta = 12.3, 14.1, 22.8, 52.7, 57.2, 73.3, 85.0, 169.5$; HRMS (CI^+): Calcd for $\text{C}_{15}\text{H}_{20}\text{O}_4$, M^+ 264.1362. Found m/z 264.1359.

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

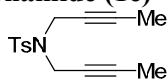


IR (neat): 2971, 2255, 1744, 1437, 1294, 1211 cm^{-1} ; ^1H NMR: $\delta = 1.09$ (d, $J = 6.9$ Hz, 12H), 2.46 (septt, $J = 6.9, 2.1$ Hz, 2H), 2.87 (d, $J = 2.4$ Hz, 4H), 3.72 (s, 6H); ^{13}C NMR: $\delta = 20.4, 22.9, 23.2, 52.7, 57.5, 73.4, 89.3, 169.6$; HRMS (EI^+): Calcd for $\text{C}_{17}\text{H}_{24}\text{O}_4$, M^+ 292.1675. Found m/z 292.1676.

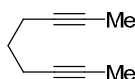
5,5-Bis(benzoxymethyl)- nona-2,7-diyne (**1d**)



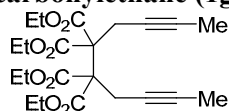
IR (neat): 2919, 2859, 1455, 1366, 1098 cm^{-1} ; ^1H NMR: $\delta = 1.82$ (t, $J = 2.7$ Hz, 6H), 2.42 (q, $J = 2.8$ Hz, 4H), 3.54 (s, 4H), 4.59 (s, 4H), 7.26-7.47 (m, 10H); ^{13}C NMR: $\delta = 3.53, 22.3, 42.3, 71.3, 73.1, 75.4, 77.4, 127.15, 127.23, 128.1, 138.7$; HRMS (EI^+): Calcd for $\text{C}_{25}\text{H}_{28}\text{O}_2$, M^+ 360.2089. Found m/z 360.2085.

***N,N*-Di(but-2-ynyl)-4-methylbenzenesulfonamide (1e)**

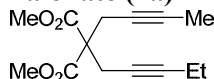
IR (KBr): 2923, 2217, 1597, 1348, 1161 cm^{-1} ; ^1H NMR: δ = 1.64 (t, J = 2.4 Hz, 6H), 2.41 (s, 3H), 4.06 (q, J = 2.1 Hz, 4H), 7.28 (d, J = 8.7 Hz, 2H), 7.71 (d, J = 8.4 Hz, 2H); ^{13}C NMR: δ = 3.45, 21.5, 36.6, 71.6, 81.6, 128.0, 129.2, 135.4, 143.4; HRMS (CI^+): Calcd for $\text{C}_{15}\text{H}_{17}\text{NO}_2\text{S}$, M^+ 275.0980. Found m/z 275.0977.

Nona-2,7-diyne (1f)

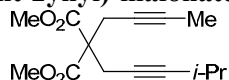
IR (neat): 2921, 2232, 1435 cm^{-1} ; ^1H NMR: δ = 1.58 (quint, J = 7.0 Hz, 2H), 1.72 (t, J = 2.6 Hz, 6H), 2.10–2.24 (m, 4H); ^{13}C NMR: δ = 3.3, 17.8, 28.4, 75.8, 78.2; HRMS (EI^+): Calcd for C_9H_{12} , M^+ 120.0939. Found m/z 120.0935.

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

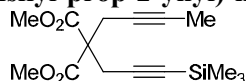
IR (neat): 2984, 2240, 1732, 1368, 1206, 1096, 1040 cm^{-1} ; ^1H NMR: δ = 1.19 (t, J = 7.1 Hz, 12H), 1.64 (t, J = 2.6 Hz, 6H), 2.97 (q, J = 2.4 Hz, 4H), 4.04–4.24 (m, 8H); ^{13}C NMR: δ = 3.4, 13.6, 22.4, 61.4, 61.5, 74.3, 77.7, 168.4; HRMS (CI^+): Calcd for $\text{C}_{22}\text{H}_{30}\text{O}_8$, M^+ 422.1941. Found m/z 422.1926.

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

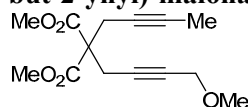
IR (neat): 2955, 2238, 1740, 1435, 1293, 1213, 1055 cm^{-1} ; ^1H NMR: δ = 1.08 (t, J = 7.5 Hz, 3H), 1.75 (t, J = 2.7 Hz, 3H), 2.12 (qt, J = 7.5, 2.4 Hz, 2H), 2.86–2.94 (m, 4H), 3.74 (s, 6H); ^{13}C NMR: δ = 3.5, 12.3, 14.1, 22.9, 52.8, 57.1, 73.0, 73.3, 78.9, 85.0, 169.5; HRMS (CI^+): Calcd for $\text{C}_{14}\text{H}_{18}\text{O}_4$, M^+ 250.1205. Found m/z 250.1204.

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

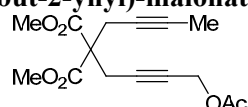
IR (neat): 2971, 2240, 1744, 1437, 1294, 1213, 1059 cm^{-1} ; ^1H NMR: δ = 1.10 (d, J = 7.2 Hz, 6H), 1.75 (t, J = 2.3 Hz, 3H), 2.47 (septt, J = 6.9, 2.2 Hz, 1H), 2.83–2.94 (m, 4H), 3.74 (s, 6H); ^{13}C NMR: δ = 3.4, 20.4, 22.8, 23.1, 52.7, 57.2, 73.1, 73.3, 78.8, 89.3, 169.5; HRMS (EI^+): Calcd for $\text{C}_{15}\text{H}_{20}\text{O}_4$, M^+ 264.1362. Found m/z 264.1360.

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

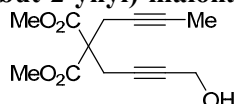
IR (neat): 2957, 2180, 1744, 1437, 1293, 1211, 1030 cm^{-1} ; ^1H NMR: δ = 0.12 (s, 9H), 1.75 (t, J = 2.7 Hz, 3H), 2.90 (q, J = 2.5 Hz, 2H), 2.97 (s, 2H), 3.74 (s, 6H); ^{13}C NMR: δ = -0.0, 3.6, 23.0, 24.0, 52.9, 57.1, 73.0, 79.1, 88.2, 101.0, 169.3; HRMS (CI^+): Calcd for $\text{C}_{15}\text{H}_{22}\text{O}_4\text{Si}$, M^+ 294.1287. Found m/z 294.1281.

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} ; ^1H NMR: δ = 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: δ = 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 $\text{C}_{14}\text{H}_{18}\text{O}_5$, M^+ 266.1154. Found m/z 266.1154.

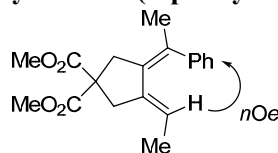
Dimethyl 2-(but-2-ynyl)-2-(4-acetoxy-but-2-ynyl)-malonate (4e)

IR (neat): 2957, 2242, 1740, 1437, 1294, 1217, 1055, 1028 cm^{-1} ; ^1H NMR: δ = 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: δ = 3.2, 20.5, 22.7, 22.8, 52.1, 52.8, 56.5, 72.6, 77.1, 79.1, 81.2, 169.0, 169.8; HRMS (EI^+): Calcd for $\text{C}_{15}\text{H}_{18}\text{O}_6$, M^+ 294.1103. Found m/z 294.1097.

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

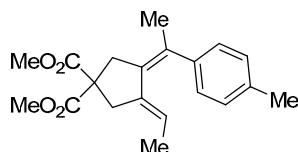
IR (neat): 3436, 2957, 2236, 1740, 1437, 1296, 1215, 1055, 1017 cm^{-1} ; ^1H NMR: δ = 1.54 (t, J = 5.9 Hz, 1H), 1.75 (t, J = 2.7 Hz, 3H), 2.90 (q, J = 2.5 Hz, 2H), 3.01 (t, J = 2.3 Hz, 2H), 3.71 (s, 6H), 4.21 (dt, J = 6.3, 2.2 Hz, 2H); ^{13}C NMR: δ = 3.5, 22.9, 23.0, 51.1, 53.0, 56.8, 72.8, 79.3, 80.2, 81.7, 169.5; HRMS (CI^+): Calcd for $\text{C}_{13}\text{H}_{16}\text{O}_5$, 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 $[\text{Rh}(\text{OH})(\text{cod})]_2$ (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_2O (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**.

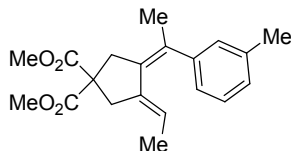
(3E,4Z)-1,1-Dimethoxycarbonyl-3-ethylidene-4-(1-phenylethylidene)cyclopentane (3aa)

The 3E,4Z configuration of the double bonds were confirmed on the basis of the observed NOE.

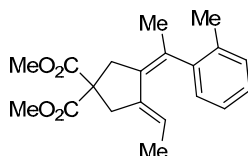
IR (KBr): 2951, 1736, 1437, 1289, 1258, 1202, 1159 cm^{-1} ; ^1H NMR: δ = 1.41 (d, J = 3.6 Hz, 3H), 2.00 (s, 3H), 2.95 (s, 2H), 3.10 (s, 2H), 3.76 (s, 6H), 4.76 (qt, J = 7.1, 2.4 Hz, 1H), 7.10–7.16 (m, 2H), 7.16–7.24 (m, 1H), 7.25–7.34 (m, 2H); ^{13}C NMR: δ = 15.2, 23.4, 38.1, 39.9, 52.8, 56.9, 121.1, 126.3, 127.9, 128.5, 130.2, 132.0, 136.0, 144.4, 172.1; HRMS (CI^+): Calcd for $\text{C}_{19}\text{H}_{22}\text{O}_4$, M^+ 314.1518. Found m/z 314.1517.

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

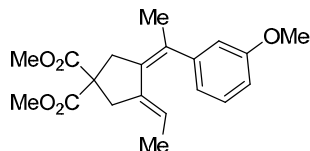
IR (neat): 2953, 1738, 1435, 1256, 1204, 1165, 1061 cm^{-1} ; ^1H NMR: δ = 1.43 (d, J = 6.9 Hz, 3H), 1.98 (s, 3H), 2.33 (s, 3H), 2.96 (s, 2H), 3.10 (s, 2H), 3.76 (s, 6H), 4.84 (q, J = 7.0 Hz, 1H), 7.04 (d, J = 7.8 Hz, 2H), 7.10 (d, J = 8.1 Hz, 2H); ^{13}C NMR: δ = 15.1, 21.2, 24.1, 38.1, 40.0, 52.8,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

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

IR (neat): 2953, 1738, 1435, 1260, 1204, 1165, 1061 cm^{-1} ; ^1H NMR: δ = 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: δ = 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 $\text{C}_{20}\text{H}_{24}\text{O}_4$, M^+ 328.1675. Found m/z 328.1671.

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

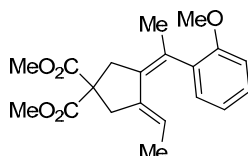
IR (neat): 2953, 1738, 1435, 1256, 1206, 1165, 1061 cm^{-1} ; ^1H NMR: δ = 1.40 (d, J = 7.2 Hz, 3H), 1.95 (s, 3H), 2.10 (s, 3H), 2.93 (d, J = 16.5 Hz, 1H), 3.00 (d, J = 16.2 Hz, 1H), 3.08 (d, J = 15.3 Hz, 1H), 3.19 (d, J = 15.9 Hz, 1H), 3.75 (s, 3H), 3.76 (s, 3H), 4.55 (qt, J = 7.2, 2.3 Hz, 1H), 6.93–7.00 (m, 1H), 7.09–7.20 (m, 3H); ^{13}C NMR: δ = 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 $\text{C}_{20}\text{H}_{24}\text{O}_4$, M^+ 328.1675. Found m/z 328.1677.

(3*E*,4*Z*)-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} ; ^1H NMR: δ = 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: δ = 15.2, 23.9, 38.1, 39.9, 52.8, 55.1, 56.9,

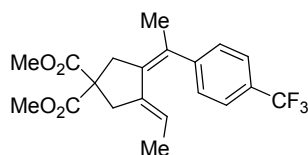
111.8, 113.2, 120.2, 121.2, 129.5, 129.9, 132.0, 135.8, 145.9, 159.7, 172.1; HRMS (CI^+): Calcd for $\text{C}_{20}\text{H}_{24}\text{O}_5$, M^+ 344.1624. Found m/z 344.1623.

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



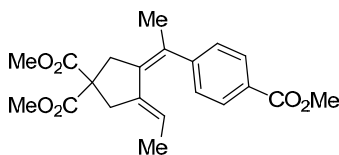
IR (neat): 2953, 1736, 1489, 1435, 1253, 1204, 1163, 1061 cm^{-1} ; ^1H NMR: δ = 1.41 (d, J = 7.2 Hz, 3H), 1.96 (s, 3H), 2.92 (d, J = 17.4 Hz, 1H), 2.98 (d, J = 16.2 Hz, 1H), 3.08 (d, J = 15.9 Hz, 1H), 3.18 (d, J = 15.9 Hz, 1H), 3.75 (s, 3H), 3.76 (s, 3H), 3.77 (s, 3H), 4.74 (qt, J = 7.0, 2.4 Hz, 1H), 6.84–6.93 (m, 2H), 6.97 (dd, J = 7.4, 2.0 Hz, 1H), 7.16–7.25 (m, 1H); ^{13}C NMR: δ = 15.2, 22.6, 38.1, 39.8, 52.7, 55.6, 57.0, 111.3, 120.0, 121.0, 127.5, 127.8, 129.7, 132.6, 133.0, 136.4, 156.3, 172.1, 172.2; HRMS (CI^+): Calcd for $\text{C}_{20}\text{H}_{24}\text{O}_5$, M^+ 344.1624. Found m/z 344.1627.

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



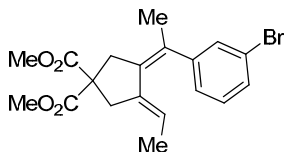
IR (neat): 2955, 1740, 1615, 1437, 1325, 1260, 1165, 1125, 1067 cm^{-1} ; ^1H NMR: δ = 1.42 (d, J = 6.9 Hz, 3H), 1.99 (s, 3H), 2.95 (s, 2H), 3.10 (s, 2H), 3.76 (s, 6H), 4.75 (qt, J = 7.0, 4.5 Hz, 1H), 7.26 (d, J = 7.8 Hz, 2H), 7.54 (d, J = 7.8 Hz, 2H); ^{13}C NMR: δ = 15.2, 23.6, 37.9, 39.8, 52.9, 56.8, 122.1, 124.2 (q, J = 270 Hz), 125.5 (q, J = 3.5 Hz), 128.4 (q, J = 32.3 Hz), 128.5, 128.6, 133.4, 135.9, 148.2, 172.0; HRMS (CI^+): Calcd for $\text{C}_{20}\text{H}_{21}\text{O}_4\text{F}_3$, M^+ 382.1392. Found m/z 382.1397.

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



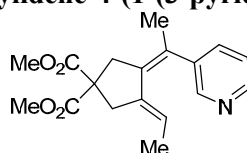
IR (neat): 2953, 1738, 1605, 1435, 1283, 1204, 1177, 1113, 1061 cm^{-1} ; ^1H NMR: δ = 1.38 (d, J = 6.9 Hz, 3H), 1.98 (s, 3H), 2.94 (s, 2H), 3.09 (s, 2H), 3.75 (s, 6H), 3.89 (s, 3H), 4.75 (qt, J = 7.0, 4.7 Hz, 1H), 7.16–7.24 (m, 2H), 7.90–7.99 (m, 2H); ^{13}C NMR: δ = 15.1, 23.5, 37.9, 39.8, 52.0, 52.8, 56.8, 122.0, 128.0, 128.1, 129.0, 129.9, 133.2, 135.8, 149.5, 167.0, 172.0; HRMS (CI^+): Calcd for $\text{C}_{21}\text{H}_{24}\text{O}_6$, M^+ 372.1573. Found m/z 372.1568.

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



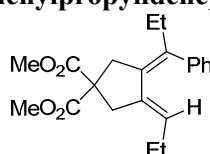
IR (neat): 2953, 1738, 1590, 1557, 1435, 1260, 1204, 1165, 1061 cm^{-1} ; ^1H NMR: δ = 1.43 (d, J = 6.9 Hz, 3H), 1.97 (s, 3H), 2.95 (s, 2H), 3.08 (s, 2H), 3.76 (s, 6H), 4.81 (qt, J = 4.8, 2.4 Hz, 1H), 7.03–7.09 (m, 1H), 7.16 (t, J = 7.8 Hz, 1H), 7.27–7.37 (m, 2H); ^{13}C NMR: δ = 15.3, 23.7, 38.0, 39.8, 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 (Cl^+): Calcd for $\text{C}_{19}\text{H}_{21}\text{BrO}_4$, M^+ 392.0623. Found m/z 392.0618.

(3*E*,4*Z*)-1,1-Dimethoxycarbonyl-3-ethylidene-4-(1-(3-pyridyl)ethylidene)-cyclopentane (3aj)



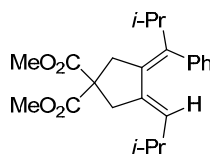
IR (neat): 2953, 1738, 1435, 1260, 1203, 1165, 1063 cm^{-1} ; ^1H NMR: δ = 1.40 (d, J = 7.2 Hz, 3H), 1.98 (s, 3H), 2.93 (s, 2H), 3.09 (s, 2H), 3.74 (s, 6H), 4.74 (qt, J = 7.0, 2.5 Hz, 1H), 7.17–7.24 (m, 1H), 7.45 (dt, J = 7.8, 4.1 Hz, 1H), 8.35–8.39 (m, 1H), 8.43 (dd, J = 4.8, 1.5 Hz, 1H); ^{13}C NMR: δ = 15.2, 23.5, 37.9, 39.8, 52.9, 56.8, 122.3, 123.3, 126.2, 134.5, 135.7, 136.1, 139.9, 147.5, 149.3, 172.0; HRMS (Cl^+): Calcd for $\text{C}_{18}\text{H}_{21}\text{NO}_4$, M^+ 315.1471. Found m/z 315.1474.

(3*Z*,4*E*)-1,1-Dimethoxycarbonyl-3-(1-phenylpropylidene)-4-propylidenecyclopentane (3ba)



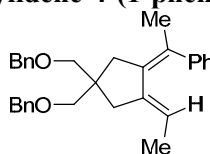
IR (neat): 2963, 1738, 1435, 1260, 1204, 1069 cm^{-1} ; ^1H NMR: δ = 0.63 (t, J = 7.5 Hz, 3H), 0.89 (t, J = 7.5 Hz, 3H), 1.75 (quint, J = 7.5 Hz, 2H), 2.32 (q, J = 7.5, 2H), 2.91 (s, 2H), 3.09 (s, 2H), 3.73 (s, 6H), 4.56 (tt, J = 7.2, 2.4 Hz, 1H), 7.02–7.11 (m, 2H), 7.15–7.22 (m, 1H), 7.25–7.32 (m, 2H); ^{13}C 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 $\text{C}_{21}\text{H}_{26}\text{O}_4$, M^+ 342.1831. Found m/z 342.1827.

(3*Z*,4*E*)-1,1-Dimethoxycarbonyl-3-(2-methyl-1-phenylpropylidene)-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); ^{13}C 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 $\text{C}_{23}\text{H}_{30}\text{O}_4$, M^+ 370.2144. Found m/z 370.2145.

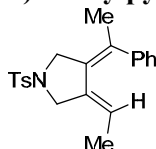
(3*E*,4*Z*)-1,1-Bis (benzoxymethyl)- 3-ethylidene-4-(1-phenylethylidene)cyclopentane 3da



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

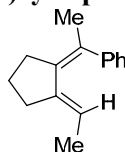
(m, 1H), 7.20–7.46 (m, 14H); ^{13}C NMR: δ = 15.3, 24.1, 36.7, 38.6, 44.2, 73.2, 73.3, 120.5, 126.0, 127.3, 127.4, 128.0, 128.2, 128.4, 129.5, 134.4, 138.4, 138.8, 145.2; HRMS (EI^+): Calcd for $\text{C}_{31}\text{H}_{34}\text{O}_2$, M^+ 438.2559. Found m/z 438.2554.

(3Z,4E)-3-Ethylidene-4-(1-phenylethylidene)-1-tosylpyrrolidine (3ea)



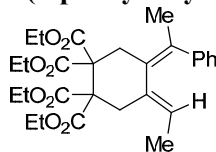
IR (neat): 2919, 1736, 1597, 1441, 1345, 1165, 1100, 1053 cm^{-1} ; ^1H NMR: δ = 1.35 (d, J = 7.2 Hz, 3H), 1.92 (s, 3H), 2.45 (s, 3H), 3.93 (q, J = 1.3 Hz, 2H), 4.06 (d, J = 1.2 Hz, 2H), 4.71 (qt, J = 6.9, 2.5 Hz, 1H), 6.97–7.07 (m, 2H), 7.17–7.43 (m, 5H), 7.70–7.84 (m, 2H); ^{13}C NMR: δ = 15.2, 21.6, 24.0, 51.5, 52.8, 120.8, 126.8, 127.3, 127.8, 128.4, 128.8, 129.7, 130.9, 132.8, 132.9, 143.1, 143.6; HRMS (EI^+): Calcd for $\text{C}_{21}\text{H}_{23}\text{NO}_2\text{S}$, M^+ 353.1449. Found m/z 353.1448.

(1E,2Z)-1-Ethylidene-2-(1-phenylethylidene)cyclopentane (3fa)



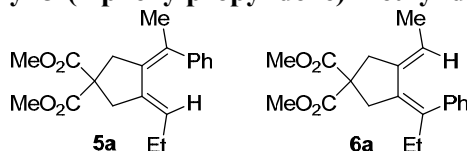
IR (neat): 2953, 1597, 1489, 1441, 1026 cm^{-1} ; ^1H NMR: δ = 1.41 (d, J = 6.6 Hz, 3H), 1.72 (quint, J = 7.5 Hz, 2H), 2.01 (s, 3H), 2.34 (t, J = 7.4 Hz, 2H), 2.49 (t, J = 7.2 Hz, 2H), 4.74 (qt, J = 7.0, 2.4 Hz, 1H), 7.11–7.24 (m, 3H), 7.27–7.37 (m, 2H); ^{13}C NMR: δ = 15.4, 23.2, 24.3, 30.9, 32.9, 119.3, 126.0, 128.0, 128.5, 128.6, 136.0, 140.3, 145.4; HRMS (EI^+): Calcd for $\text{C}_{15}\text{H}_{18}$, M^+ 198.1409. Found m/z 198.1412.

(4Z,5E)-1,1,2,2-Tetramethoxycarbonyl-4-(1-phenylethylidene)-5-ethylidenecyclohexane (3ga)



IR (KBr): 2988, 1755, 1736, 1720, 1264, 1198, 1048 cm^{-1} ; ^1H NMR: δ = 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, 7.0 Hz, 1H), 7.06–7.14 (m, 3H), 7.14–7.25 (m, 2H); ^{13}C NMR: δ = 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 $\text{C}_{28}\text{H}_{36}\text{O}_8$, M^+ 500.2410. Found m/z 500.2405.

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

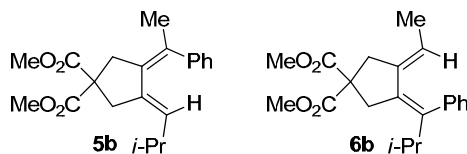


A mixture of regioisomer (5a/6a = 57/43)

IR (neat): 2957, 1738, 1435, 1258, 1204, 1165, 1067 cm^{-1} ; ^1H NMR: δ = 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,

2.58H), 4.63–4.76 (m, 1H), 7.04–7.36 (m, 5H); ^{13}C NMR: δ = 11.8, 13.5, 15.2, 22.9, 23.8, 30.5, 37.87, 37.93, 39.3, 39.7, 52.8, 56.96, 57.02, 121.3, 126.3, 127.9, 128.38, 128.43, 128.9, 130.4, 131.4, 132.2, 134.3, 136.0, 136.6, 142.8, 144.3, 172.05, 172.11; HRMS (EI^+): Calcd for $\text{C}_{20}\text{H}_{24}\text{O}_4$, M^+ 328.1675. Found m/z 328.1671.

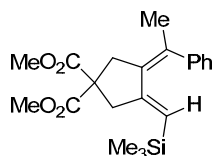
(3Z,4E)-1,1-Dimethoxycarbonyl-3-(1-phenylethylidene)-4-(2-methylpropylidene)cyclopentane (5b) and (3Z,4E)-1,1-Dimethoxycarbonyl-3-(2-methyl-1-phenylpropylidene)-4-ethylidenecyclopentane (6b)



A mixture of regioisomer (**5b/6b** = 73/27)

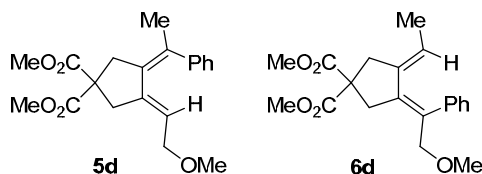
IR (neat): 2955, 1738, 1435, 1256, 1204, 1173, 1067 cm^{-1} ; ^1H NMR: δ = 0.65 (d, J = 6.6 Hz, 4.38 H), 0.91 (d, J = 6.6 Hz, 1.62H), 1.35 (dt, J = 6.9, 1.5 Hz, 0.81H), 2.00 (s, 2.19H), 2.21 (dsept, J = 9.3, 6.5 Hz, 0.73H), 2.83–2.97 (m, 2.27H), 3.09 (d, J = 1.2 Hz, 1.46H), 3.17 (s, 0.54H), 4.37–4.51 (m, 1H), 6.94–7.36 (m, 5H); ^{13}C 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 $\text{C}_{21}\text{H}_{26}\text{O}_4$, M^+ 342.1831. Found m/z 342.1827. (**5b**), 342.1848. (**6d**)

(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); ^{13}C 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 (CI^+): Calcd for $\text{C}_{21}\text{H}_{28}\text{O}_4\text{Si}$, 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)

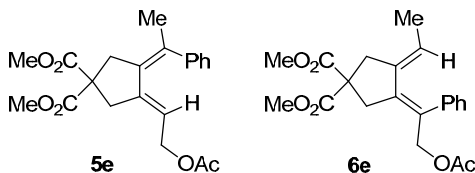


A mixture of regioisomer (**5d/6d** = 20/80)

IR (neat): 2953, 1738, 1435, 1258, 1204, 1167, 1096 cm^{-1} ; ^1H NMR(C_6D_6): 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); ^{13}C 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 $\text{C}_{20}\text{H}_{24}\text{O}_5$, 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-ethylidenecyclopentane (6e)

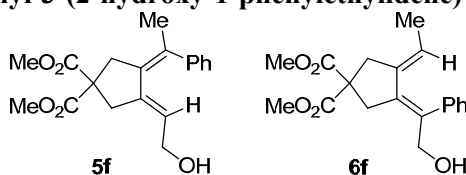


A mixture of regioisomer (5e/6e = 11/89)

IR (neat): 2955, 1748, 1734, 1435, 1377, 1293, 1167, 1065, 1022 cm^{-1} ; ^1H NMR: δ = 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: δ = 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 $\text{C}_{21}\text{H}_{24}\text{O}_6$, M^+ 372.1573. Found m/z 372.1570.

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

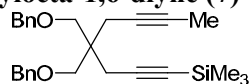
(3Z,4E)-1,1-Dimethoxycarbonyl-3-(2-hydroxy-1-phenylethylidene)-4-ethylidenecyclopentane (6f)



A mixture of regioisomer (5f/6f = 9/91)

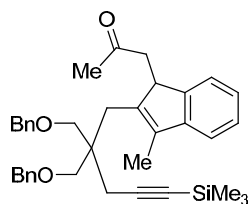
IR (neat): 3487, 2955, 1732, 1435, 1260, 1206, 1167, 1063 cm^{-1} ; ^1H NMR: δ = 1.41 (d, J = 6.9 Hz, 2.73H), 1.74–1.91 (m, 1H), 2.01 (s, 0.27H), 2.95 (s, 2H), 3.12 (s, 0.18H), 3.16 (s, 1.82H), 3.75 (s, 6H), 3.89 (d, J = 7.2 Hz, 0.18H), 4.33 (s, 1.82H), 4.83–4.96 (m, 1H), 7.09–7.37 (m, 5H); ^{13}C NMR: δ = 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 $\text{C}_{19}\text{H}_{22}\text{O}_5$, M^+ 330.1467. Found m/z 330.1465.

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



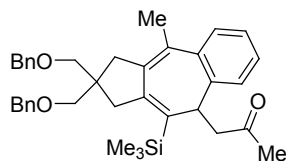
IR (neat): 2861, 2174, 1455, 1366, 1250, 1096 cm^{-1} ; ^1H NMR: δ = 0.14 (s, 9H), 1.76 (t, J = 2.7 Hz, 3H), 2.36 (q, J = 2.4 Hz, 2H), 2.45 (s, 2H), 3.49 (s, 4H), 4.53 (s, 4H), 7.23–7.41 (m, 10H); ^{13}C NMR: δ = 0.3, 3.6, 22.4, 23.5, 42.3, 71.4, 73.3, 75.3, 77.6, 86.7, 104.0, 127.3, 128.2, 138.7 (1 carbon missing); HRMS (CI^+): Calcd for $\text{C}_{27}\text{H}_{34}\text{O}_2\text{Si}$, M^+ 418.2328. Found m/z 418.2330.

2-(2,2-Bis(benzyloxymethyl)-5-trimethylsilylpent-4-ynyl)-1-(2-Oxypropyl)-3-methyl-1*H*-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), 3.45 (d, J = 8.9 Hz, 1H), 3.50 (d, J = 8.9 Hz, 1H), 3.93 (d, J = 10.5 Hz, 1H), 4.45 (d, J = 12.0 Hz, 1H), 4.480 (d, J = 12.2 Hz, 1H), 4.485 (d, J = 12.0 Hz, 1H), 4.52 (d, J = 11.9 Hz, 1H), 7.08–7.12 (m, 1H), 7.21–7.40 (m, 13H); ^{13}C 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 $\text{C}_{37}\text{H}_{44}\text{O}_3\text{Si}$, M^+ 564.3060. Found m/z 564.3058.

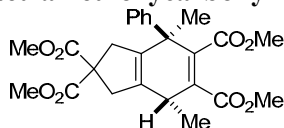
2,2-Bis(benzyloxymethyl)-4-methyl-9-(2-oxopropyl)-10-trimethylsilanyl-1,2,3,9-tetrahydro-benzof[*h*]azulene (10)



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); ^{13}C 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, 138.8, 139.7, 148.0, 208.2; HRMS (EI^+): Calcd for $\text{C}_{37}\text{H}_{44}\text{O}_3\text{Si}$, 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 $^\circ\text{C}$ 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).

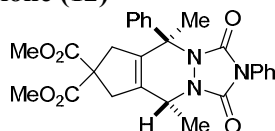
***trans*-4,7-Dimethyl-4-phenyl-2,2,5,6-tetramethoxycarbonyl-2,3,4,7-tetrahydro-1*H*-indene (11)**



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: δ = 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 $\text{C}_{25}\text{H}_{28}\text{O}_8$, 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(2*H*,5*H*)-dione (12)**



IR (KBr): 2980, 1769, 1736, 1713, 1505, 1414, 1260, 1204, 1173, 1073 cm^{-1} ; ^1H NMR: δ = 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: δ = 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 $\text{C}_{27}\text{H}_{27}\text{N}_3\text{O}_6$, M^+ 489.1900. Found m/z 489.1892.

References and Notes

- (1) For reviews, see: (a) Fagnou, K.; Lautens, M. *Chem. Rev.* **2003**, *103*, 169. (b) Hayashi, T.; Yamasaki, K. *Chem. Rev.* **2003**, *103*, 2829.
- (2) Miura, T.; Murakami, M. *Chem. Commun.* **2007**, 217.
- (3) For selected papers, see: (a) Cauble, D. F.; Gipson, J. D.; Krische, M. J. *J. Am. Chem. Soc.* **2003**, *125*, 1110. (b) Shintani, R.; Okamoto, K.; Otomaru, Y.; Ueyama, K.; Hayashi, T. *J. Am. Chem. Soc.* **2005**, *127*, 54. (c) Shintani, R.; Tsurusaki, A.; Okamoto, K.; Hayashi, T. *Angew. Chem. Int. Ed.* **2005**, *44*, 3909. (d) Tseng, N.-W.; Mancuso, J.; Lautens, M. *J. Am. Chem. Soc.* **2006**, *128*, 5338. (e) Harada, Y.; Nakanishi, J.; Fujihara, H.; Tobisu, M.; Fukumoto, Y.; Chatani, N. *J. Am. Chem. Soc.* **2007**, *129*, 5766; and references therein.
- (4) (a) For a review on transition-metal catalyzed carbocyclizations of diynes, see: Ojima, I.; Tzamarioudaki, M.; Li, Z.; Donovan, R. J. *Chem. Rev.* **1996**, *96*, 635. (b) Hydrostannanes: Lautens, M.; Smith, N. D.; Ostrovsky, D. *J. Org. Chem.* **1997**, *62*, 8970. (c) Stannylsilanes: Gréau, S.; Radetich, B.; Rajanbabu, T. V. *J. Am. Chem. Soc.* **2000**, *122*, 8579. (d) Borylsilanes: Onozawa, S.; Hatanaka, Y.; Tanaka, M. *Chem. Commun.* **1997**, 1229. (e) Borylstannanes: Onozawa, S.; Hatanaka, Y.; Choi, N.; Tanaka, M. *Organometallics* **1997**, *16*, 5389. (f) Hydrogen: Jang, H.-Y.; Krische, M. J. *J. Am. Chem. Soc.* **2004**, *126*, 7875. (g) Hydrogen equivalent: Trost, B. M.; Lee, D. C. *J. Am. Chem. Soc.* **1988**, *110*, 7255. (h) Hydrosilylation: Ojima, I.; Zhu, J.; Vidal, E. S.; Kass, D. F. *J. Am. Chem. Soc.* **1998**, *120*, 6690. (i) Hydrosilylation: Madine, J. W.; Wang, X.; Widenhoefer, R. A. *Org. Lett.* **2001**, *3*, 385. (j) Hydration: Trost, B. M.; Rudd, M. T. *J. Am. Chem. Soc.* **2003**, *125*, 11516. (k) Hydrocarboxylation: Kim, H.; Goble, S. D.; Lee, C. J. *J. Am. Chem. Soc.* **2007**, *129*, 1030.
- (5) Hayashi, T.; Takahashi, M.; Takaya, Y.; Ogasawara, M. *J. Am. Chem. Soc.* **2002**, *124*, 5052.
- (6) (a) Hayashi, T.; Inoue, K.; Taniguchi, N.; Ogasawara, M. *J. Am. Chem. Soc.* **2001**, *123*, 9918. (b) Murakami, M.; Igawa, H. *Helv. Chim. Acta.* **2002**, *85*, 4182. (c) Lautens, M.; Yoshida, M. *Org. Lett.* **2002**, *4*, 123. (d) Genin, E.; Michelet, V.; Genêt, J.-P. *Tetrahedron Lett.* **2004**, *45*, 4157.
- (7) Zhao, P.; Incarvito, C. D.; Hartwig, J. F. *J. Am. Chem. Soc.* **2007**, *129*, 1876.
- (8) Phenylboroxine was used instead of phenylboronic acid to avoid proton scrambling.
- (9) For regioselectivities of transition metal-catalyzed reactions of unsymmetrical 1,6-diynes, see: (a) Tekavec, T. N.; Arif, A. M.; Louie, J. *Tetrahedron* **2004**, *60*, 7431. (b) Murakami, M.; Ashida, S.; Matsuda, T. *J. Am. Chem. Soc.* **2006**, *128*, 2166. (c) Tanaka, K.; Hara, H.; Nishida, G.; Hirano, M. *Org. Lett.* **2007**, *9*, 1907.

- (10) A reaction using unsymmetrical 1,6-diyne 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.
- (11) (a) Miura, T.; Shimada, M.; Murakami, M. *J. Am. Chem. Soc.* **2005**, *127*, 1094. (b) Miura, T.; Shimada, M.; Murakami, M. *Chem. Asian J.* **2006**, *1*, 868.
- (12) (a) Lautens, M.; Mancuso, J. *J. Org. Chem.* **2004**, *69*, 3478. (b) Lautens, M.; Marquardt, T. *J. Org. Chem.* **2004**, *69*, 4607.
- (13) Uson, R.; Oro, L. A.; Cabeza, J. A. *Inorg. Synth.* **1985**, *23*, 129.
- (14) Liu, C.; Widenhoefer, R. A. *Organometallics* **2002**, *21*, 5666.
- (15) Han, Y.; Harlan, C. J.; Stoessel, P.; Frost, B. J.; Norton, J. R.; Miller, S.; Bridgewater, B.; Xu, Q. *Inorg. Chem.* **2001**, *40*, 2942.

List of Publication

Chapter 1

Synthesis of 1(2*H*)-Isoquinolones by the Nickel-Catalyzed Denitrogenative Alkyne Insertion of 1,2,3-Benzotriazin-4(3*H*)-ones

Tomoya Miura, Motoshi Yamauchi, and Masahiro Murakami

Org. Lett. **2008**, *10*, 3085-3088.

Chapter 2

Enantioselective Synthesis of 3,4-Dihydroisoquinolin-1(2*H*)-ones by Nickel-Catalyzed Denitrogenative Annulation of 1,2,3-Benzotriazin-4(3*H*)-ones with Allenes

Motoshi Yamauchi, Masao Morimoto, Tomoya Miura, and Masahiro Murakami

J. Am. Chem. Soc. **2010**, *132*, 54-55.

Chapter 3

Nickel-Catalyzed Denitrogenative Annulation Reactions of 1,2,3-Benzotriazin-4(3*H*)-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

Chem. Commun. **2009**, 1470-1471.

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.