Transition Metal-Catalyzed Tandem Electrocyclization
Migration Reaction Using Styryl Azides

By

Chen Kong
B.S., Shandong University, 2010

THESIS

Submitted as partial fulfillment of the requirements for the degree of Doctor of Philosophy in Chemistry in the Graduate College of the University of Illinois at Chicago, 2015

Chicago, Illinois

Defense Committee
Tom Driver, Chair and Advisor
Laura Anderson, Department of Chemistry
Justin Mohr, Department of Chemistry
Donald Wink, Department of Chemistry
Terry Moore, Department of Medicinal Chemistry and Pharmacognosy
ACKNOWLEDGMENTS

My greatest gratitude is extended to my advisor Prof. Tom Driver, who has been always helpful and inspiring on my way to become a chemist. His dedication to chemistry and his attitude for science are precious treasure I have learnt. I am so grateful to have him leading me to the path I am going through. His trust and encouragement supported me to finish my graduate study. He is a great person and fantastic mentor.

I would also like to thank my committee member for their guidance and constructive comments on my thesis. Professor Laura Anderson provides me a lot of valuable suggestions for my research and has been very supportive. Professor Justin Mohr is a great lecturer and taught me a lot in class. Professor Donald Wink helped me with my first crystal structure, which I am still excited for. Professor Terry Moore offers chemicals for our collaboration research and provides insightful advice on our project.

I also want to acknowledge my current and former labmates for their companion and help: Dr. Huijun Dong, Dr. Ke Sun, Dr. Sheng Liu, Dr. Ashley Pumphrey, Dr. Crystalann Jones, Dr. Quyen Nguyen, Dr. Duosheng Wang, Fei, Naijing, Navendu, Wrickban and Russell. This work would not have been done without them.

I would like to thank the whole UIC chemistry department. Thank them for their efforts to keep things running so we can enjoy our teaching and research.

Special thanks to my family for their unconditional love and support. My mom has always been my role model, who gives me strength and confidence. My dad flew to Chicago immediately when I broke my ankle last winter and took care of me for two months after the surgery. My aunt, who started her academic career at Michigan, helped me a lot, materially and spiritually.

I am very fortunate to have so many friends in my life. Yi was my roommate and is my best friend in Chicago. Her companion and sense of humor enriched my life and make it easier to live and study abroad. My friends from college and my home are always caring and responsive. I feel lucky to have them all.
CONTRIBUTION OF AUTHORS

Chapter 1 is a literature review that introduces the context of the research and remaining challenges of the discussed field. The structure of the chapter followed the recent published review of my colleague Navendu Jana (Org. Biomol. Chem., 2015, DOI: 10.1039/C5OB01334H). Chapter 2 represents a paraphrased published manuscript (Kong, C.; Jana, N.; Driver, T. G.; Org. Lett. 2013, 15, 824.) for which I am the primary author and major contributor of the work. Navendu Jana assisted me in developing the experiment scope of Table 2.4 and he conducted the work in Scheme 2.5, 2.6 and 2.7. Chapter 3 represents a paraphrased published manuscript (Kong, C.; Driver, T. G. Org. Lett. 2015, 17, 802.) for which I am the first author and completed all the work supervised by my advisor Tom Driver. Chapter 4 represents a paraphrased published manuscript (Kong, C.; Su, N.; Zhou, F.; Jana, N.; Driver, T. G. Tetrahedron Lett. 2015, 56, 3262.) for which I am the first author. Naijing Su, Fei Zhou helped me develop part of Table 4.1, 4.2 and Navendu Jana completed Scheme 4.4. Chapter 5 describes my unpublished work about mechanism study, which is nearly completion. The work will be published soon and I will be the first author.
# TABLE OF CONTENTS

## CHAPTER 1 Introduction
- Background ......................................................................................... 1
- C–C Bond Formation through Tandem Electrocyclization-[1,2] Migration Reaction .......................................................... 2
- C–C Bond Formation through Tandem [1,2] Migration-Electrocyclization Reaction ......................................................... 4
- C–N Bond Formation through Tandem Electrocyclization-[1,2] Migration Reaction ............................................................. 17
- Summary and Outlook ........................................................................ 29
- References .......................................................................................... 42

## CHAPTER 2 Rh$_2$(II)-Catalyzed Selective Aminomethylene Migration from Styryl Azides
- Experimental ...................................................................................... 46
- References .......................................................................................... 58

## CHAPTER 3 Rh$_2$(II)-Catalyzed Ester Migration to Afford 3H-Indoles from Trisubstituted Styryl Azides
- Experimental ...................................................................................... 122
- References .......................................................................................... 132

## CHAPTER 4 Rh$_2$(II)-Catalyzed Ester Migration to Afford 1,2,3-Trisubstituted Indoles from Congested Styryl Azides
- Experimental ...................................................................................... 177
- References .......................................................................................... 185

## CHAPTER 5 Catalyst and Substrate Manipulation to Control Chemoselectivity of Electrocyclization and Sp$^3$ C–H Bond Amination from Styryl Azides
- Experimental ...................................................................................... 210
- Reference ............................................................................................ 224

## VITA
- ............................................................................................................. 247
LIST OF TABLES

Table 1.1. Nazarov cyclization of divinyl ketone.
Table 1.2. Effect of catalyst identity and quantity on Nazarov cyclization outcome.
Table 1.3. Ligand control of chemoselectivity of Nazarov cyclization.
Table 1.4. Scope of 1,2-aryl shift in electrocyclization of o-(ethynyl)styrenes.
Table 1.5. Rautenstrauch rearrangement for functionalized substrates.
Table 1.6. Photolysis of thiophene azides to produce thienopyrrols.
Table 2.1. Survey of the effect of the N-substituent identity on reaction outcome.
Table 2.2. Survey of reaction conditions for 2,3-indole formation.
Table 2.3. Scope of Rh$_2$(II)-Catalyzed Aminomethylene 1,2-Shift.
Table 2.4. Scope of Rh$_2$(II)-Catalyzed Selective Methylene Shift.
Table 3.1. Optimization for reaction to form 3H-indoles.
Table 3.2. Scope of electronic nature of aryl azides.
Table 3.3. Scope of varying identity of o-substituent of aryl azides.
Table 3.4. Synthesis of 3,3-diaryl oxindoles.
Table 4.1. Effect of changing the electronic nature of styryl azides.
Table 4.2. Effect of changing electronic nature for pinene-derived azide.
Table 5.1. Scope of Rh$_2$(II)-catalyzed sp$^3$ C–H bond amination.
Table 5.2. Condition screening for styryl azide 5.21c.
Table 5.3. Effect of R$^1$ substituents on reaction outcome.
Table 5.4. Effect of R$^2$ substituents on reaction outcome.
Table 5.5. Rhodium carboxylate screening for styryl azide 5.24.
Table 5.6. Catalyst screening for styryl azide 5.24.
LIST OF FIGURES

Figure 5.1. Correlation of $\log(\frac{k_{\text{electro.}}}{k_{\text{sp3}}})$ of Rh$_2$(II) catalyzed C–H amination of 5.21 with $\sigma_p$ values in the Hammett equation.

Figure 5.2. Correlation of $\log(\frac{k_{\text{electro.}}}{k_{\text{sp3}}})$ of Rh$_2$(II) catalyzed C–H amination of 5.21’ with $\sigma_p$ values in the Hammett equation.
LIST OF SCHEMES

Scheme 1.1. The Nazarov Reaction.
Scheme 1.2. “Interrupted” Nazarov Reaction.
Scheme 1.3. Methyl shift in Nazarov cyclization.
Scheme 1.4. FeCl₃ promoted reaction of vinyl dieny ketones.
Scheme 1.5. FeCl₃ promoted electrocyclization-[1,2]-migration reaction.
Scheme 1.6. FeCl₃ promoted electrocyclization-[1,2]-migration reaction.
Scheme 1.7. Scope of Cu(II)-promoted Nazarov cyclization-migration.
Scheme 1.8. Mechanism proposed for spirocycle formation.
Scheme 1.9. Scope for cyclization-migration of dienone variants.
Scheme 1.10. Cu(II)-promoted formation of alkylidene cyclopentenone.
Scheme 1.11. Proposed mechanism for Nazarov reaction followed by oxidation.
Scheme 1.12. Scope of 1,2-halide shift in electrocyclization of o-(ethynyl)styrenes.
Scheme 1.13. Proposed Mechanism for 1,2-shift in electrocyclization of o-(ethynyl)styrenes.
Scheme 1.15. Proposed mechanism for Rautenstrauch rearrangement.
Scheme 1.16. [1,2]-sulfide shift from propargyl dithioacetals.
Scheme 1.17. Control of regioselectivity of indene formation.
Scheme 1.18. Pd-catalyzed cyclization of propargylic esters.
Scheme 1.19. Tungsten-catalyzed [1,2]-iodine-shift electrocyclization.
Scheme 1.20. Enantioselective Rautenstrauch rearrangements.
Scheme 1.21. Proposed mechanism for enantioenriched cyclopentenone formation.
Scheme 1.22. Enantioselective Au-catalyzed Rautenstrauch rearrangement.
Scheme 1.23. Proposed catalytic cycle involving enantioselective electrocyclization.
Scheme 1.24. Scope of Rh(I)-catalyzed Rautenstrauch rearrangement.
Scheme 1.25. Proposed mechanism for seven-membered ring formation.
Scheme 1.26. Phosphite-mediated reductive cyclization–[1,2]-phenyl migration to form 2,3-disubstituted indoles.
Scheme 1.27. Proposed cyclization migration mechanism.
Scheme 1.28. Proposed tandem electrocyclization [1,2]-shift mechanism.
Scheme 1.29. Rh(II)-catalyzed N-heterocycle formation from aryl azides.
Scheme 1.30. Rh(II)-catalyzed phenyl migration from gem-diphenyl styryl azide.
Scheme 1.31. Rh\(_{2}\)(II)-Catalyzed formation of 2-alkyl-3-aryl indoles from \(\beta,\beta\)disubstituted styryl azides.
Scheme 1.32. Mechanism for Rh\(_{2}\)(II)-catalyzed formation of 2-alkyl-3-aryl indoles.
Scheme 1.33. Scope of Rh\(_{2}\)(II)-catalyzed NO\(_2\) migration reactions.
Scheme 1.34. Preference for electron-withdrawing group to migrate over hydrogen.
Scheme 1.35. Competition experiments to compare migration preferences.
Scheme 1.36. Cul-mediated photolysis of substituted 3-(2-azidobenzylidene)-lactams.
Scheme 1.37. Effect of \(\alpha\)-substituent on Rh\(_{2}\)(II)-catalyzed acyl migration.
Scheme 1.38. Pd(II)-catalyzed transformation of nitrostyrrenes into 3H-indoles.
Scheme 1.39. Potential catalytic cycle for Pd(II)-catalyzed formation of 3H-indoles from nitrostyrene.
Scheme 2.1. Rh\(_{2}\)(II)-catalyzed selective aryl group migration.
Scheme 2.2. Hypothesis for \(\beta\)-methylene selective migration.
Scheme 2.3. Retrosynthesis of styryl azides.
Scheme 2.4. Proposed catalytic cycle.
Scheme 2.5. Reactivity of enantiomerically enriched styryl azide.
Scheme 2.6. Reaction of styryl azide 2.33.
Scheme 2.7. Crossover experiment.
Scheme 2.8. Route to synthesize styryl azide 2.21.
Scheme 2.9. Route to synthesize styryl azide 2.23.
Scheme 3.1. Transition metal catalyzed migrating group1,2-shift.
Scheme 3.2. Synthesis of trisubstituted styryl azides 3.11.
Scheme 3.3. Possible mechanism for Rh\(_{2}\)(II)-catalyzed 3H-indole formation.
Scheme 3.4. Double crossover reaction.
Scheme 3.5. Proposed ring contraction with EDG as \(\beta\)-substituent.
Scheme 3.6. Route to synthesize trisubstituted styryl Azides.
Scheme 4.1. Regioselectivity dependence of β-migrating group identity.

Scheme 4.2. Transition state of iminium ion.

Scheme 4.3. Effect of increasing the steric environment.

Scheme 4.4. Effect of changing the identity of bridge.

Scheme 4.5. Proposed catalytic cycle.

Scheme 4.6. Mechanistic experiments.

Scheme 5.1. Rh$_2$(II)-catalyzed migration reaction to form trisubstituted indoles.

Scheme 5.2. Rh$_2$(II)-catalyzed sp$^3$ C-H bond amination.

Scheme 5.3. Rh$_2$(II)-catalyzed electrocyclization.

Scheme 5.4. Competition of electrocyclization and sp$^3$ C–H bond amination.
**LIST OF ABBREVIATIONS**

<table>
<thead>
<tr>
<th>Abbreviation</th>
<th>Meaning</th>
</tr>
</thead>
<tbody>
<tr>
<td>Å</td>
<td>Angstrom</td>
</tr>
<tr>
<td>Ac</td>
<td>acetyl</td>
</tr>
<tr>
<td>alloc</td>
<td>allyloxy carbonyl</td>
</tr>
<tr>
<td>Ar</td>
<td>aryl</td>
</tr>
<tr>
<td>ATR</td>
<td>attenuated total reflection</td>
</tr>
<tr>
<td>bp</td>
<td>boiling point</td>
</tr>
<tr>
<td>Bn</td>
<td>benzyl</td>
</tr>
<tr>
<td>Boc</td>
<td>tert-butoxyl carbonyl</td>
</tr>
<tr>
<td>box</td>
<td>bisoxazoline</td>
</tr>
<tr>
<td>bpin</td>
<td>boron pinacolato</td>
</tr>
<tr>
<td>br</td>
<td>broad</td>
</tr>
<tr>
<td>Bu</td>
<td>butyl</td>
</tr>
<tr>
<td>Bz</td>
<td>benzoyl</td>
</tr>
<tr>
<td>cap</td>
<td>caprolactam</td>
</tr>
<tr>
<td>cod</td>
<td>cyclooctadiene</td>
</tr>
<tr>
<td>d</td>
<td>doublet</td>
</tr>
<tr>
<td>DBU</td>
<td>1,8-diazabicyclo[5.4.0]undec-7-ene</td>
</tr>
<tr>
<td>DCE</td>
<td>1,2-dichloroethane</td>
</tr>
<tr>
<td>DCM</td>
<td>dichloromethane</td>
</tr>
<tr>
<td>DFT</td>
<td>density functional theory</td>
</tr>
<tr>
<td>DME</td>
<td>1,2-dimethoxyethane</td>
</tr>
<tr>
<td>DMF</td>
<td>N,N-dimethylformamide</td>
</tr>
<tr>
<td>DMSO</td>
<td>dimethyl sulfoxide</td>
</tr>
<tr>
<td>DOSP</td>
<td>N-(para-dodecylphenylsulfonoyl)prolinato</td>
</tr>
<tr>
<td>dppf</td>
<td>diphenylphosphino</td>
</tr>
<tr>
<td>EDG</td>
<td>electron-donating group</td>
</tr>
<tr>
<td>EI</td>
<td>electron impact</td>
</tr>
<tr>
<td>Abbreviation</td>
<td>Full Form</td>
</tr>
<tr>
<td>--------------</td>
<td>-----------</td>
</tr>
<tr>
<td>Equiv</td>
<td>Molar equivalent</td>
</tr>
<tr>
<td>ESI</td>
<td>electrospray ionization</td>
</tr>
<tr>
<td>esp</td>
<td>(\alpha,\alpha,\alpha',\alpha'-\text{tetramethyl-1,3-benzenedipropionate})</td>
</tr>
<tr>
<td>Et</td>
<td>ethyl</td>
</tr>
<tr>
<td>EWG</td>
<td>electron-withdrawing group</td>
</tr>
<tr>
<td>FG</td>
<td>functional group</td>
</tr>
<tr>
<td>FT</td>
<td>Fourier transform</td>
</tr>
<tr>
<td>GC</td>
<td>gas chromatography</td>
</tr>
<tr>
<td>h</td>
<td>hour</td>
</tr>
<tr>
<td>Hex</td>
<td>hexyl</td>
</tr>
<tr>
<td>HRMS</td>
<td>high-resolution mass spectrometry</td>
</tr>
<tr>
<td>HWE</td>
<td>Horner–Wadsworth–Emmons</td>
</tr>
<tr>
<td>Hz</td>
<td>hertz</td>
</tr>
<tr>
<td>i-</td>
<td>iso</td>
</tr>
<tr>
<td>IR</td>
<td>infrared</td>
</tr>
<tr>
<td>J</td>
<td>coupling constant</td>
</tr>
<tr>
<td>L.A.</td>
<td>Lewis acid</td>
</tr>
<tr>
<td>LDA</td>
<td>lithium diisopropylamide</td>
</tr>
<tr>
<td>m</td>
<td>multiplet</td>
</tr>
<tr>
<td>M</td>
<td>metal</td>
</tr>
<tr>
<td>Me</td>
<td>methyl</td>
</tr>
<tr>
<td>MG</td>
<td>migrating group</td>
</tr>
<tr>
<td>MPLC</td>
<td>Medium pressure liquid chromatography</td>
</tr>
<tr>
<td>mmol</td>
<td>millinole</td>
</tr>
<tr>
<td>MS</td>
<td>molecular sieves</td>
</tr>
<tr>
<td>M/z</td>
<td>mass-to-charge</td>
</tr>
<tr>
<td>NMR</td>
<td>nuclear magnetic resonance</td>
</tr>
</tbody>
</table>
LIST OF ABBREVIATIONS (continued)

OEP  octaethylporphyrinato
Ph   phenyl
Phen phenanthroline
Piv  pivaloyl
PMP  para-methoxyphenyl
PNP  para-nitrophenyl
Pr   propyl
PTAD (1-adamantyl)-(N-phthalimido)acetato
Py   pyridine
q    quartet
R    carbon-centered functional group
Rf   retention factor
rt   room temperature
s    singlet
t    triplet
t-   tertiary
TBS  tert-butyldimethylsilyl
td   triplet of doublets
TEMPO (2,2,6,6-tetramethylpiperidin-1-yl)oxidanyl
TFA  trifluoroacetic acid
THF  tetrahydrofuran
TLC  thin-layer chromatography
TMP  trimethoxyphenyl
Tol  tolyl
Tp   trispyrazolyl
TPP  tetraphenylporphyrin
Ts   tosyl(para-toluenesulfonyl)
### LIST OF ABBREVIATIONS (continued)

<table>
<thead>
<tr>
<th>Abbreviation</th>
<th>Definition</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tf</td>
<td>triflyl(trifluoromethanesulfonate)</td>
</tr>
<tr>
<td>tt</td>
<td>triplet of triplet</td>
</tr>
<tr>
<td>UV</td>
<td>ultraviolate</td>
</tr>
<tr>
<td>wt</td>
<td>weight</td>
</tr>
<tr>
<td>μm</td>
<td>micrometer</td>
</tr>
</tbody>
</table>
SUMMARY

This thesis describes transition metal-catalyzed tandem electrocyclization reaction employing styryl azides as the nitrogen source to form highly functionalized N-heterocycles.

Chapter one briefly highlights methods that construct new C–C bond or C–N bond via domino electrocyclization migration reaction. Nazarov reaction, Rantenstrauch rearrangement and transition metal catalyzed electrocyclization migration using styryl azide as nitrogen sources are discussed.

In Chapter two, I show that dirhodium(II) carboxylate complex can trigger a preferential aminomethylene [1,2]-shift when exposed to β,β-dimethylene-substituted styryl azides, completing the migratorial aptitude scale. In Chapter three and four, I describe my effort to explore the migration selectivity of ester and how steric environment influence the reaction outcome. I also extend the method to oxindole synthesis.

Chapter five describes a way to manipulate the selectivity of sp³ C–H bond amination and electrocyclization by controlling reaction conditions and functionality on substrates. Using certain catalyst can achieve selective transformation.
CHAPTER 1

Introduction
**Background**

Extensive research has been conducted to streamline the synthesis of functionalized carbocycles and heterocycles due to their important structural role in biologically active natural products or molecules with electronic activity. Among numerous methodologies developed, electrocyclization reactions proved to be advantageous to construct new C–C bond and C–N bond in a facile construction of complexity.

Nazarov reaction, in particular, showed its efficiency and selectivity in the synthesis of substituted cyclopentenones, thus attracting much attention. Originally discovered by Nazarov in 1941\(^2\), classical Nazarov reaction is promoted by a stoichiometric Lewis acid or protic acid from divinyl ketone (Scheme 1.1).\(^3\) Coordination of divinyl ketone \(1.1\) and Lewis acid generates pentadienyl cation \(1.3\), which undergoes \(4\pi\)-conrotatory electrocyclization followed by \(\beta\)-hydrogen elimination. Subsequent tautomerization of enolate \(1.5\) then generates cyclopentenone \(1.2\).\(^4\) The importance of Nazarov reactions rises from the ubiquity of cyclopentenones as common motifs in natural products and their usefulness as synthetic intermediates in total synthesis.\(^5,6\)

![Scheme 1.1. The Nazarov Reaction.](image-url)
Since Nazarov reaction provides a facile method to construct complex highly substituted five-member ring, modifications to the reaction continue to be a popular research interest. Modifications to reaction condition focused on developing catalytic or milder promoter, while substrates variants can either generate pentadienyl cation in an unorthodox fashion or have oxyallyl cation intercepted. Among all these area, interception of oxyallyl cation by a suitable reagent or rearrangement before elimination produced more variety to this transformation. West and co-workers reported a series of successful “interrupted” Nazarov cyclization reaction by trapping oxyallyl cation with various partners. A cascade reaction with successive trapping of oxyallyl cation occurred when divinyl ketone 1.7 was promoted by TiCl₄. Pentacyclic product 1.8 was generated in one step with complete diastereoselectivity.

![Scheme 1.2. “Interrupted” Nazarov Reaction.](image)

In this Chapter, I will focus on “interrupted” Nazarov cyclization reaction followed by [1,2]-migration. I will discuss C–C bond and C–N bond formation through the tandem electrocyclization migration reaction, which provide efficient methods to construct densely functionalized carbocycles and heterocycles.
C–C Bond Formation through Tandem Electrocyclization-[1,2] Migration

Reaction

The early observation of [1,2]-migration in Nazarov electrocyclization was reported in the photolysis of divinyl ketones.\textsuperscript{12} An example of acid promoted tandem electrocyclization migration reaction was reported by Ohloff and co-workers in 1971 (Scheme 1.3).\textsuperscript{13} Thermolysis of damascenone 1.11 produced a 3:2 mixture of fused carbocycles 1.12 and 1.13. While 1.12 was formed by electrocyclization of isomer of oxyallyl 1.14, 1.13 was generated from more stable allylic cation 1.16.

![Scheme 1.3. Methyl shift in Nazarov cyclization.](image)

Denmark and Hite first reported a systematic study of Nazarov pinacol rearrangement from vinyl dienyl ketones.\textsuperscript{14} Exposure of 1.17 to stoichiometric amount of ferric chloride generated an unexpected product 1.18. The authors proposed a mechanism via electrocyclization [1,2]-migration based on the reactivity trends (Scheme 1.4). Electrocyclic closure seemed to favor the linearly conjugated dienyl ketone instead of the cross-conjugated divinyl ketone. Electrocyclization of FeCl\textsubscript{3}-coordinated pentadienyl cation 1.20 produces cyclopentenyl cation 1.21, resulting in a facile 1,2-vinyl migration.
This reaction showed great generality to vinyl dienyl ketones (Scheme 1.5). The vinyl migrating group is essential for the transformation: phenyl, tert-butyl and methyl dienyl ketones showed no reactivity to the reaction conditions. While SiMe$_3$, Me and Ph group on $\beta$ position converted to 1.23 smoothly (cf. 1.23a, 1.23d, and 1.23e), methyl group on migrating center or without led to significantly reduced yields (cf. 1.23b and 1.23c). Submission of $(E,E)$-1.22f to reaction conditions produced a mixture of 1.23f and its protodesilylated congener in overall 78% yield. Both products were formed as single diastereoisomers.
Migration of substituents on dienyl ketone was also observed.\textsuperscript{15} Chiu and Li investigated the outcome of Nazarov reaction when changing different acid promoter identities.\textsuperscript{16} Treatment of dienone 1.24 with 1:1 mixture of sulfuric acid and methanol resulted in a clean Nazarov cyclization product, hydroazulenone 1.25 in 91\% yield (entry 1), while a spirocyclic product 1.26 was obtained when only sulfuric acid or triflic acid were employed (entries 2 and 3). Boron Lewis acid BF\textsubscript{3}\textperiodcentered{}Et\textsubscript{2}O promoted the conversion of dienone to 1.25 as the sole product and employment of BCl\textsubscript{3} led to the formation of 1.26 exclusively. Another rearrangement product 1.30 was observed when cyclohexadienone 1.27 was treated with several acids (eq. 1.1). The overall reactivity trend suggests that Brønsted- and Lewis acids in non-coordinating solvent favored ring contraction to spirocycle 1.26 formation and in the presence of Lewis basic solvents, elimination was induced first, leading to 1.25.

**Table 1.1.** Nazarov cyclization of divinyl ketone.

<table>
<thead>
<tr>
<th>entry</th>
<th>acid</th>
<th>solvent</th>
<th>1.25:1.26</th>
<th>%, yield</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>H\textsubscript{2}SO\textsubscript{4}</td>
<td>MeOH</td>
<td>&gt;95:5</td>
<td>91</td>
</tr>
<tr>
<td>2</td>
<td>H\textsubscript{2}SO\textsubscript{4}</td>
<td>–</td>
<td>17:83</td>
<td>90</td>
</tr>
<tr>
<td>3</td>
<td>CF\textsubscript{3}SO\textsubscript{3}H</td>
<td>CH\textsubscript{2}Cl\textsubscript{2}</td>
<td>7:93</td>
<td>96</td>
</tr>
<tr>
<td>4</td>
<td>BF\textsubscript{3}\textperiodcentered{}Et\textsubscript{2}O</td>
<td>CH\textsubscript{2}Cl\textsubscript{2}</td>
<td>&gt;95:5</td>
<td>98</td>
</tr>
<tr>
<td>5</td>
<td>BCl\textsubscript{3}</td>
<td>CH\textsubscript{2}Cl\textsubscript{2}</td>
<td>5:95</td>
<td>92</td>
</tr>
</tbody>
</table>

\textsuperscript{1}
The authors proposed the mechanism pathways accounting for the formation of all three products (Scheme 1.6). Oxyallyl cation 1.31 was generated by conrotatory electrocyclicization of protonated divinyl ketone 1.27. In the presence of Lewis basic solvent (methanol or ether), elimination occurs, leading to usual Nazarov product 1.28 after tautomerization (Path a). In the absence of these proton acceptors, [1,2]-migration predominates. Ring contraction is favored when ring strain is released by rearrangement (path b) or alternatively, acyclic alkyl group migrates via successive [1,2]-shift when ring strain accumulates after contraction (path c).

Scheme 1.6. FeCl₃ promoted electrocyclization-[1,2]-migration reaction.

Recently, more attention has been focused on transition metal-mediated Nazarov electrocyclization migration reaction. The Frontier group reported a Cu-promoted Nazarov cyclization migration reaction that produced spirocycles. They found that the outcome of the reaction could be controlled by the identity and quantity of metal complexes (Table 1.2). While lower loading of Cu(OTf)₂ promoted dienone to produce Nazarov cyclization product 1.37, stoichiometric amount of copper bisoxazoline complex 1.39 and Cu(SbF₆)₂ led to formation of spirocycle 1.38.
Table 1.2. Effect of catalyst identity and quantity on Nazarov cyclization outcome.

<table>
<thead>
<tr>
<th>entry</th>
<th>MX</th>
<th>10 mol%</th>
<th>50 mol%</th>
<th>100 mol%</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Cu(OTf)$_2$</td>
<td>&lt;5:95</td>
<td>8:92</td>
<td>13:87</td>
</tr>
<tr>
<td>2</td>
<td>1.39</td>
<td>20:80</td>
<td>67:33</td>
<td>&gt;95:5</td>
</tr>
<tr>
<td>3</td>
<td>AgSbF$_6$</td>
<td>9:91</td>
<td>50:50</td>
<td>70:30</td>
</tr>
<tr>
<td>4</td>
<td>Cu(SbF$_6$)$_2$</td>
<td>20:80</td>
<td>69:31</td>
<td>&gt;95:5</td>
</tr>
</tbody>
</table>

The scope of Nazarov cyclization-migration reaction was then investigated using 1.0 equivalent of copper bioxazoline complex (Scheme 1.7). Alkylidene β-ketoester of dienone 1.40 can be selectively converted to spirocycle 1.41 or 1.42, depending on the identity of R substituent. While 2,4,6-trimethoxyphenyl and alkyl substituent generated spirocycle 1.41, 4-methoxyphenyl and styryl substituent migrated to adjacent allylic position. An extra double bond in cyclohexenyl group enabled diastereoselective migration, producing spirocycle 1.41b.

The authors proposed a mechanism for this Nazarov cyclization-migration reaction accounting for the several products (Scheme 1.8). Oxyallyl cation 1.44 is generated from 4π–conrotatory electrocyclization. Elimination produces usual Nazarov product 1.45 (path a). Ring contraction leads to spirocycles 1.46 (path b). Depending on the identity of the substituent, a [1,2]-migration of either hydrogen or R group leads to spirocycle 1.48 (path b2) or 1.47 (path b1). Together with the migration ability shown in reaction scope, the authors suggest that the migration selectivity is governed by both steric- and electronic considerations. Dienone with steric congested trimethoxyphenyl group favors hydride shift, whereas the smaller p-methoxyphenyl migrates. In contrast, the isopropyl group is less favored to migrate due to the more stabilized tertiary carbocation. The mechanism also explains
stereochemistry in the spirocycles. Suprafacial shift of migrating group (R or H) results in single diastereoisomers.

Scheme 1.7. Scope of Cu(II)-promoted Nazarov cyclization-migration.

Scheme 1.8. Mechanism proposed for spirocycle formation.
The outcome manipulated by catalyst loading can also be explained by the mechanism. When low loading of Cu(II) complex is used, free carbonyl group can act as Lewis base, thus accelerating elimination process. The employment of non-coordinating counterion SbF$_6^-$ allows $[1,2]$-migration to compete with elimination.

The authors then investigated more 1,4-diene-3-ones bearing different substituents to compare migratory aptitudes (Scheme 1.9). With non-migrating substituents on C5 (TMP and $i$Pr), one of the substituents on C1 migrated to C2, generating enone 1.50a-d. The reaction results suggest a higher migratory aptitude for aryl group than alkyl group, while siloxymethyl and branched alkyl group migrate in preference to methyl group. The migrating group on C5 was also examined. The less steric demanding structure and more electron-donating group are prone to migrate to C1 (2-thienyl, cinnamyl, aryl, 2-furyl). DFT computations support the possible E/Z isomerization of the enone, explaining the compromised stereoselectivity in 1.51 formation.

Scheme 1.9. Scope for cyclization-migration of dienone variants.
Knowing that non-coordinating counterion can interfere with the electrocyclization migration sequence, Frontier and co-workers examined how additives can influence the minimum loading of metal complex (eq. 1.2). The authors anticipated that exchangeable additives could selectively induce rearrangement by coordinating the carbonyl lone pair electrons. Among several additives tested, NaBAr\(^+\) proved to be most effective as additive for Cu(II) catalyzed cyclization-migration, which the authors attributed to its non-coordinating nature of counterion and its solubility in dichloromethane.

In addition to the substrates bearing an electron-donating group on C5, Frontier and co-workers examined substrates bearing electron-withdrawing groups on C5 for Nazarov cyclization as well (Scheme 1.10).\(^{21}\) Treatment of dienone 1.52 with stoichiometric amount of Cu(II) complex in open vessel resulted in the formation of an unexpected product 4-alkylidene cyclopentenone 1.53, consistent with DFT calculations. In comparison with the previous Nazarov cyclization-migration study, the formation of cyclopentenone requires higher temperature, while lower temperature resulted in C1-C2 bond isomerization; the second [1,2]-shift is suppressed by an oxidative process. The scope of the reaction was proved to be broad with arenes bearing different electron-withdrawing groups (a-d). Dienone 1.52a-d were converted to 1.53a-d exclusively in good yields. Surprisingly, even the substrate 1.52e transformed to 1.53e without the second [1,2]-phenyl shift. In contrast with the reaction at room temperature, the suprafacial [1,2]-phenyl shift is not favored, apparently hindered by the steric interactions with the phenyl group on C2.
Scheme 1.10. Cu(II)-promoted formation of alkylidene cyclopentenone.

Further investigation revealed that this oxidation-involved transformation was not limited to substrates bearing electron-withdrawing group on C5. Exposure of dienone 1.52 with 2-methoxyphenyl on C5 with t-BuBox-Cu(SBF₆)₂ in reflux dichloroethane generated 4-methyldiene cyclopentenone 1.53 (eq. 1.3). However, reaction in reflux dichloromethane produced 1.53 without oxidation process or [1,2]-phenyl migration (eq. 1.4).

The authors proposed a mechanism based on several mechanistic experiments they conducted to account for the oxidation process (Scheme 1.11). Dienone 1.52 undergoes Nazarov electrocyclization followed by [1,2]-shift, generating oxyallyl cation 1.54. Then β-hydride elimination produces diene 1.55, which is oxidized by copper(II) via cation radical. Hydroperoxide 1.56 is then reduced to alcohol 1.57.
through a Fenton-type fragmentation. Acid-promoted dehydration produces alkylidene 1.53.

Scheme 1.11. Proposed mechanism for Nazarov reaction followed by oxidation.
Besides migratory aptitude and steric bulk of the competing migrating groups, Frontier and coworkers reported another factor—copper(II) ligand—could affect chemoselectivity of Nazarov cyclization reaction.\textsuperscript{23} Acyclic dienone 1.63 was tested with Cu(II)-complex and common ligands (Table 1.3). When (MeCN)\textsubscript{5}Cu(SbF\textsubscript{6})\textsubscript{2} was used to promote electrocyclization of 1.63, the usual cycloadduct 1.64 was formed without any observed [1,2]-migration. When bulkier Cu(II)-bisoxazoline complex was applied, the elimination process was completely suppressed. While L1 and L2 produced a mixture of cyclopentenone 1.65 and 1.66, L3 afforded 1.65 selectively with an enantiomeric excess of 23%. Although the chirality of bisoxazoline ligand had little impact on torquoselectivity of the transformation, steric profile of the ligand was shown influence the feasibility of the second rearrangement.

**Table 1.3. Ligand control of chemoselectivity of Nazarov cyclization.**

<table>
<thead>
<tr>
<th>entry</th>
<th>L</th>
<th>h, time</th>
<th>1.64:1.65:1.66</th>
<th>%, yield</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>(MeCN)\textsubscript{5}</td>
<td>0.2</td>
<td>1:0:0</td>
<td>92</td>
</tr>
<tr>
<td>2</td>
<td>L1</td>
<td>0.4</td>
<td>0:1.2:1</td>
<td>80</td>
</tr>
<tr>
<td>3</td>
<td>L2</td>
<td>0.4</td>
<td>0:1.5:1</td>
<td>79</td>
</tr>
<tr>
<td>4</td>
<td>L3</td>
<td>0.4</td>
<td>0:&gt;20:1</td>
<td>83 (ee 23%)</td>
</tr>
</tbody>
</table>

In comparison with 4\pi-electron cyclization reaction, research on 6\pi-electron electrocyclization is much more rare. On the basis of investigation of ruthenium- or tungsten- catalyzed aromatization of dienyl alkynes, Liu and coworkers reported a
novel skeletal rearrangement in electrocyclization catalyzed by ruthenium complex.\textsuperscript{24} The authors first tested various 2-ethynylstyrenes-\textsubscript{d\textsubscript{1}} with catalytic amount of TpRu(PPh\textsubscript{3})(CH\textsubscript{3}CN)\textsubscript{2}PF\textsubscript{6} (Scheme 1.12). Deuterated samples were used to confirm the 1,2-shift using NMR spectrum. The deuterium species of \textbf{1.67} bearing a range of substituents were converted to napthalene \textbf{1.68a} – \textbf{1.68d} with a 1,2-iodo shift, while 1,2-bromo shift yielded \textbf{1.68e} less efficiently. Next, the authors examined dienynes \textbf{1.67f} and \textbf{1.68g} to determine if an aryl bridging group was required, and found that both were transformed to arenes \textbf{1.68f} and \textbf{1.68g} smoothly. For 1-ethyl-2-iodovinyl species, however, a 1:1 mixture of napthalene \textbf{1.68h} and \textbf{1.68h}‘ resulted from 1,2-iodo shift and nonmigration pathways, respectively.

\begin{center}
\begin{tikzpicture}
  \node at (0,0) (a) {1.67};
  \node at (2,0) (b) {1.68};
  \node at (0,-1) (c) {1.68a \ 82\%};
  \node at (2,-1) (d) {1.68b \ 65\%};
  \node at (4,-1) (e) {1.68c \ 82\%};
  \node at (0,-2) (f) {1.68d \ 78\%};
  \node at (2,-2) (g) {1.68e \ 40\%};
  \node at (4,-2) (h) {1.68f \ 60\%};
  \node at (0,-3) (i) {1.68g \ 90\%};
  \node at (2,-3) (j) {1.68h \ 35\%};
  \node at (4,-3) (k) {1.68h' \ 38\%};
  \draw (a) -- (b);
  \node at (1,-1.5) {TpRu(PPh\textsubscript{3})(MeCN)\textsubscript{2}PF\textsubscript{6} (10 mol \%)};
  \node at (1,-0.5) {Toluene, 110 °C};
\end{tikzpicture}
\end{center}

\textbf{Scheme 1.12.} Scope of 1,2-halide shift in electrocyclization of \(\alpha\)-(ethynyl)styrenes.
In addition to halides, aryl group on 2'-vinyl position showed its ability to migrate with different selectivity (Table 1.4). The scope study suggests that electron-efficient environment—mainly on migration group—is more suitable for [1,2]-aryl shift to 1'-vinyl carbon. Methoxy group either on styrenes (entries 3 – 5) or on 2'-vinyl aryl group (entries 2, 3 and 6) promoted the yields of migration product 1.71.

**Table 1.4. Scope of 1,2-aryl shift in electrocyclization of o-(ethynyl)styrenes.**

<table>
<thead>
<tr>
<th>entry</th>
<th>R&lt;sup&gt;1&lt;/sup&gt;</th>
<th>R&lt;sup&gt;2&lt;/sup&gt;</th>
<th>Ar</th>
<th>%, 1.70 yield</th>
<th>%, 1.71 yield</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>H</td>
<td>H</td>
<td>Tol</td>
<td>35</td>
<td>35</td>
</tr>
<tr>
<td>2</td>
<td>H</td>
<td>H</td>
<td>p-OMeC&lt;sub&gt;6&lt;/sub&gt;H&lt;sub&gt;4&lt;/sub&gt;</td>
<td>15</td>
<td>60</td>
</tr>
<tr>
<td>3</td>
<td>H</td>
<td>OMe</td>
<td>p-OMeC&lt;sub&gt;6&lt;/sub&gt;H&lt;sub&gt;4&lt;/sub&gt;</td>
<td>6</td>
<td>64</td>
</tr>
<tr>
<td>4</td>
<td>O–CH&lt;sub&gt;2&lt;/sub&gt;–O</td>
<td>Ph</td>
<td>56</td>
<td>18</td>
<td></td>
</tr>
<tr>
<td>6</td>
<td>O–CH&lt;sub&gt;2&lt;/sub&gt;–O</td>
<td>p-OMeC&lt;sub&gt;6&lt;/sub&gt;H&lt;sub&gt;4&lt;/sub&gt;</td>
<td>trace</td>
<td>73</td>
<td></td>
</tr>
</tbody>
</table>

A plausible mechanism was proposed to rationalize the selectivity of this electrocyclization-migration domino reaction (Scheme1.13). After the coordination of o-(ethynyl)styrenes with ruthenium complex, ruthenium vinylidene 1.73 is in the equilibrium with the ruthenium alkyne complex 1.72. Substrates with an iodo group undergo 6-endo-dig electrocyclization (path a) followed by [1,2]-iodo-shift to terminal alkyne carbon. The resulting ruthenium η2-naphthalene 1.75 ultimately produces product 1.76 and regenerates the ruthenium catalyst. For substrates with aryl group, 5-endo-dig electrocyclization (path b) generates indenyl cation 1.77, which induces a [1,2]-Ar shift followed by a subsequent [1,2]-H shift. Dissociation of the ruthenium complex produces the desired product 1.80.
Scheme 1.13. Proposed Mechanism for 1,2-shift in electrocyclization of o-(ethynyl)styrenes.

C–C Bond Formation through Tandem [1,2] Migration-Electrocyclization Reaction

Reversing the order of the migration and electrocyclization steps has proven to be another powerful tool to assemble cyclopentenones. In 1984, Rautenstrauch first reported a Pd-catalyzed rearrangement of 1-ethynyl-2-propenyl acetates to access 2-cyclopentenone (Scheme 1.14). Exposure of 1.81 to catalytic amount of PdCl₂(MeCN)₂ and one equivalent of acetic acid in heated acetonitrile afforded 1.82 and acetic anhydride. The reaction tolerated alkyl substituents for R1 and R2, but substituents on either ethynyl or vinyl group suppressed the reaction.

Based on the observed reactivity, the authors proposed the mechanism outlined in Scheme 1.15. Coordination of enyne 1.81 with the palladium catalyst forms chelate 1.83, which induces a [1,2]-acetoxy shift to produce acetoxonium 1.84. Ring opening produces butadienylcarbene 1.85, which undergoes a 6π-electron electrocyclization to produce diene 1.86. Hydrolysis then generates the product cyclopentadienone 1.82.

Scheme 1.15. Proposed mechanism for Rautenstrauch rearrangement.

In support of their proposed mechanism, the authors reported several trapping experiments (eq. 1.5). Most importantly, the existence of cyclopentadiene intermediate 1.86 was probed by attempting to intercept it with a dienophile. The authors reported that the addition of N-phenyl phthalimide to the reaction mixture produced the Diels-Alder adduct 1.87.
In 2007, Frontier group reported an improved protocol of Rautenstrauch rearrangement. Substituents on terminal alkynyl and vinyl group were introduced, which enabled access to more highly functionalized products (Table 1.5). Exposure of propargyl acetate 1.88 with PdCl$_2$ in acetonitrile upon acid work up resulted in cyclized product 1.89 or 1.90. The substrates bearing different vinyl and acetylenic substituents were tested. While terminal alkynes were converted to cyclopentenones 1.90a, 1.90b, and 1.90d (entries 1, 2 and 4), substituted alkynes 1.88 resulted in enol acetates 1.89c, 1.90e, and 1.90f (entries 3, 5 and 6). The authors also reported that longer alkyl group (eg. butyl group) or benzyloxy derivatives on terminal alkyne position inactivated the migration-cyclization reaction.

Table 1.5. Rautenstrauch rearrangement for functionalized substrates.

<table>
<thead>
<tr>
<th>entry</th>
<th>#</th>
<th>acetate</th>
<th>product</th>
<th>%, yield</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>a</td>
<td><img src="AcO" alt="AcO" /> <img src="R1" alt="R1" /> <img src="R2" alt="R2" /> <img src="R3" alt="R3" /> <img src="R4" alt="R4" /> <img src="H" alt="H" /></td>
<td><img src="AcO" alt="AcO" /> <img src="R1" alt="R1" /> <img src="R2" alt="R2" /> <img src="R3" alt="R3" /> <img src="R4" alt="R4" /> <img src="OAc" alt="OAc" /> <img src="Ph" alt="Ph" /></td>
<td><img src="AcO" alt="AcO" /> <img src="R1" alt="R1" /> <img src="R2" alt="R2" /> <img src="R3" alt="R3" /> <img src="R4" alt="R4" /> <img src="OAc" alt="OAc" /> <img src="Ph" alt="Ph" /></td>
</tr>
<tr>
<td></td>
<td></td>
<td><img src="AcO" alt="AcO" /> <img src="R1" alt="R1" /> <img src="R2" alt="R2" /> <img src="R3" alt="R3" /> <img src="R4" alt="R4" /> <img src="CO$_2$Et" alt="CO$_2$Et" /> <img src="Ph" alt="Ph" /></td>
<td><img src="AcO" alt="AcO" /> <img src="R1" alt="R1" /> <img src="R2" alt="R2" /> <img src="R3" alt="R3" /> <img src="R4" alt="R4" /> <img src="OAc" alt="OAc" /> <img src="CO$_2$Et" alt="CO$_2$Et" /> <img src="Ph" alt="Ph" /></td>
<td><img src="AcO" alt="AcO" /> <img src="R1" alt="R1" /> <img src="R2" alt="R2" /> <img src="R3" alt="R3" /> <img src="R4" alt="R4" /> <img src="OAc" alt="OAc" /> <img src="CO$_2$Et" alt="CO$_2$Et" /> <img src="Ph" alt="Ph" /></td>
</tr>
<tr>
<td>2</td>
<td>b</td>
<td><img src="AcO" alt="AcO" /> <img src="R1" alt="R1" /> <img src="R2" alt="R2" /> <img src="R3" alt="R3" /> <img src="R4" alt="R4" /> <img src="CO$_2$Et" alt="CO$_2$Et" /> <img src="Ph" alt="Ph" /></td>
<td><img src="AcO" alt="AcO" /> <img src="R1" alt="R1" /> <img src="R2" alt="R2" /> <img src="R3" alt="R3" /> <img src="R4" alt="R4" /> <img src="OAc" alt="OAc" /> <img src="Ph" alt="Ph" /></td>
<td><img src="AcO" alt="AcO" /> <img src="R1" alt="R1" /> <img src="R2" alt="R2" /> <img src="R3" alt="R3" /> <img src="R4" alt="R4" /> <img src="OAc" alt="OAc" /> <img src="Ph" alt="Ph" /></td>
</tr>
<tr>
<td>3</td>
<td>c</td>
<td><img src="AcO" alt="AcO" /> <img src="R1" alt="R1" /> <img src="R2" alt="R2" /> <img src="R3" alt="R3" /> <img src="R4" alt="R4" /> <img src="Ph" alt="Ph" /></td>
<td><img src="AcO" alt="AcO" /> <img src="R1" alt="R1" /> <img src="R2" alt="R2" /> <img src="R3" alt="R3" /> <img src="R4" alt="R4" /> <img src="OAc" alt="OAc" /> <img src="Ph" alt="Ph" /></td>
<td><img src="AcO" alt="AcO" /> <img src="R1" alt="R1" /> <img src="R2" alt="R2" /> <img src="R3" alt="R3" /> <img src="R4" alt="R4" /> <img src="OAc" alt="OAc" /> <img src="Ph" alt="Ph" /></td>
</tr>
<tr>
<td>4</td>
<td>d</td>
<td><img src="AcO" alt="AcO" /> <img src="R1" alt="R1" /> <img src="R2" alt="R2" /> <img src="R3" alt="R3" /> <img src="R4" alt="R4" /> <img src="Ph" alt="Ph" /></td>
<td><img src="AcO" alt="AcO" /> <img src="R1" alt="R1" /> <img src="R2" alt="R2" /> <img src="R3" alt="R3" /> <img src="R4" alt="R4" /> <img src="OAc" alt="OAc" /> <img src="Ph" alt="Ph" /></td>
<td><img src="AcO" alt="AcO" /> <img src="R1" alt="R1" /> <img src="R2" alt="R2" /> <img src="R3" alt="R3" /> <img src="R4" alt="R4" /> <img src="OAc" alt="OAc" /> <img src="Ph" alt="Ph" /></td>
</tr>
<tr>
<td>1</td>
<td></td>
<td><img src="AcO" alt="AcO" /> <img src="R1" alt="R1" /> <img src="R2" alt="R2" /> <img src="R3" alt="R3" /> <img src="R4" alt="R4" /> <img src="OAc" alt="OAc" /> <img src="Ph" alt="Ph" /></td>
<td><img src="AcO" alt="AcO" /> <img src="R1" alt="R1" /> <img src="R2" alt="R2" /> <img src="R3" alt="R3" /> <img src="R4" alt="R4" /> <img src="OAc" alt="OAc" /> <img src="Ph" alt="Ph" /></td>
<td><img src="AcO" alt="AcO" /> <img src="R1" alt="R1" /> <img src="R2" alt="R2" /> <img src="R3" alt="R3" /> <img src="R4" alt="R4" /> <img src="OAc" alt="OAc" /> <img src="Ph" alt="Ph" /></td>
</tr>
<tr>
<td>2</td>
<td></td>
<td><img src="AcO" alt="AcO" /> <img src="R1" alt="R1" /> <img src="R2" alt="R2" /> <img src="R3" alt="R3" /> <img src="R4" alt="R4" /> <img src="CO$_2$Et" alt="CO$_2$Et" /> <img src="Ph" alt="Ph" /></td>
<td><img src="AcO" alt="AcO" /> <img src="R1" alt="R1" /> <img src="R2" alt="R2" /> <img src="R3" alt="R3" /> <img src="R4" alt="R4" /> <img src="OAc" alt="OAc" /> <img src="CO$_2$Et" alt="CO$_2$Et" /> <img src="Ph" alt="Ph" /></td>
<td><img src="AcO" alt="AcO" /> <img src="R1" alt="R1" /> <img src="R2" alt="R2" /> <img src="R3" alt="R3" /> <img src="R4" alt="R4" /> <img src="OAc" alt="OAc" /> <img src="CO$_2$Et" alt="CO$_2$Et" /> <img src="Ph" alt="Ph" /></td>
</tr>
<tr>
<td>3</td>
<td></td>
<td><img src="AcO" alt="AcO" /> <img src="R1" alt="R1" /> <img src="R2" alt="R2" /> <img src="R3" alt="R3" /> <img src="R4" alt="R4" /> <img src="Ph" alt="Ph" /></td>
<td><img src="AcO" alt="AcO" /> <img src="R1" alt="R1" /> <img src="R2" alt="R2" /> <img src="R3" alt="R3" /> <img src="R4" alt="R4" /> <img src="OAc" alt="OAc" /> <img src="Ph" alt="Ph" /></td>
<td><img src="AcO" alt="AcO" /> <img src="R1" alt="R1" /> <img src="R2" alt="R2" /> <img src="R3" alt="R3" /> <img src="R4" alt="R4" /> <img src="OAc" alt="OAc" /> <img src="Ph" alt="Ph" /></td>
</tr>
<tr>
<td>4</td>
<td></td>
<td><img src="AcO" alt="AcO" /> <img src="R1" alt="R1" /> <img src="R2" alt="R2" /> <img src="R3" alt="R3" /> <img src="R4" alt="R4" /> <img src="Ph" alt="Ph" /></td>
<td><img src="AcO" alt="AcO" /> <img src="R1" alt="R1" /> <img src="R2" alt="R2" /> <img src="R3" alt="R3" /> <img src="R4" alt="R4" /> <img src="OAc" alt="OAc" /> <img src="Ph" alt="Ph" /></td>
<td><img src="AcO" alt="AcO" /> <img src="R1" alt="R1" /> <img src="R2" alt="R2" /> <img src="R3" alt="R3" /> <img src="R4" alt="R4" /> <img src="OAc" alt="OAc" /> <img src="Ph" alt="Ph" /></td>
</tr>
</tbody>
</table>

PdCl$_2$ (5-20 mol %) MeCN, 60 °C then, MeOH/p-TsOH
Rautenstrauch rearrangement is not limited to 1-ethynyl-2-propenyl acetate systems. Extending the vinyl moiety to aryl substituents enabled facile synthesis of functionalized indenes. For example, Ohe and co-workers reported a Pt-catalyzed [1,2]-acetoxy shift-electrocyclization reaction, converting terminal propargyl esters to indenes.27 Sec-propargyl ester 1.91 with more electron-rich substituents yielded indene 1.92 more efficiently (eq. 1.6). tert-Parpargyl ester 1.93, however, led to a mixture of indene product 1.94 and 1.95, attributing to non-selective proton shift (eq. 1.7).

Wang and coworkers reported a similar reactivity for sulfur migration using gold catalyst.28 Submission of propargyl sulfide 1.96 to gold(I)- or gold(III) complex resulted in a mixture of indenes (eq. 1.8). Replacing aryl sulfide with a dithioacetal improved selectivity attributing to the rigidity of the substrates. Both phenyl- and alkyl- alkyne underwent sulfide shift, affording ring expansion product 1.100.
Changing the aryl group moiety to furan, however, attenuated the reaction conversion with starting material recovered.

\[
\begin{align*}
\text{Me} & \text{SPh} & \text{AuCl}_3 & \text{(5 mol %)} & \text{PhMe, 80 °C} & \rightarrow & \text{Me} & \text{SPh} & + & \text{Me} & \text{SPh} \\
1.96 & & & & & & 1.97 & & & 1.98 & & (8)
\end{align*}
\]

**Scheme 1.16.** [1,2]-sulfide shift from propargyl dithioacetals.

In 2012, Clark and co-workers reported that the regioselectivity of the acetoxy-migration electrocyclization could be manipulated by changing the reaction conditions (Scheme 1.17). While PtCl₄ induced exclusive less substituted indene 1.103 formation, treatment of propargyl carbonate 1.101 with Ptl₂ and 20% DBU generated only 1.102. The authors proposed that the DBU base was responsible for isomerizing the tri-substituted enol acetate in the thermodynamic tetrasubstituted isomer 1.102.
Scheme 1.17. Control of regioselectivity of indene formation.

Scheme 1.18. Pd-catalyzed cyclization of propargylic esters.

Sarpong and coworkers reported another regioselective and efficient transformation from propargylic ester to indenes using PtCl₂(PPh₃)₂ as precatalyst and iodosobenzene as the additive. The authors proposed that cyclization occurred via Pt–carbenoid intermediate and reported that the reaction tolerates several substituents on propargylic position including both aromatic (a-d) and heteroaromatic (e-f) substituents to yielding indenes in good yield. Electron-deficient alkyne is required for this transformation, however, since alkyl, phenyl and silyl substitution on...
the terminal alkyne did not produce the desired indene product. The aryl group was found not to be necessary: the non-aromatic acyclic propargylic ester transformed to cyclopentadiene 1.92g smoothly. In contrast, cyclic propargylic ester led to formation of 1.92h via an allylic C–H insertion.

In addition to [1,2]-carbonate and [1,2]-sulfide shift, tandem [1,2]-halide migration electrocyclization domino reactions are also possible (Scheme 1.19). Iwasawa and co-workers reported a tungsten-catalyzed 6π-electrocyclization of α-(iodoethynyl)styrenes to produce naphthalenes 1.107. In all cases, treatment of 1-iodo-alkyne with W(CO)$_5$(thf) at room temperature provided iodo-substituted arenes, which is readily for further functionalization of the iodine group. The mechanism of this transformation is believed to begin with a W(CO)$_5$ π-complex which isomerizes to idodinated vinylidene intermediate 1.108 via a [1,2]-iodine shift. Then 6π-electrocyclization occurs, affording tungsten carbene 1.109. The following 1,2-hydrogen migration forms iodo-substituted naphthalene 1.107 with regeneration of tungsten complex.

![Scheme 1.19. Tungsten-catalyzed [1,2]-iodine-shift electrocyclization.](image)

In 2005, Toste group filled in the blank of a stereoselective version of Rautenstrauch rearrangement. They reported a Au(I)-catalyzed enantioselective
cyclopentenone formation from enantioenriched propargyl pivaloates with excellent chirality transfer. Ph₃PAuSbF₆ with non-coordinating counterion is crucial for retaining chirality, since replacing SbF₆⁻ with triflate led to significant diminishment of enantiomer excess. Both acyclic and cyclic ethynyl propenyl pivaloates were converted smoothly (Scheme 1.20). Enlarging ring size had little impact to either the yield or chirality transfer.

The proposed mechanism accounting for stereochemistry in this transformation is depicted in Scheme 1.21. Coordination of the alkyne to gold(I) complex forms vinyl gold species 1.113. The formation of gold carbene is not an option since stepwise [1,2]-pivaloate shift could destroy the chiral elements. So a helix transition state 1.114 was proposed for this 4π-electron-5-atom electrocyclization. The chirality is remained since the C–O bond cleavage is only slightly before the C-C bond formation.³³ Cyclopentenone 1.112 is generated from pentadienyl cation 1.115 upon release of gold complex and hydrolysis.

\[
\text{Scheme 1.20. Enantioselective Rautenstrauch rearrangements.}
\]
Recently, Toste and coworkers reported the first enantioselective catalyzed Rautenstrauch rearrangement. The previous method transfers chirality via a cyclic transition state with helical chirality. To achieve enantioselective transformation with ligand control, propargyl ketal is used instead of acetoxy group for fully planar, achiral intermediate. Treatment of propargyl ketal 1.116 with optimal chiral gold catalyst produced the corresponding dearomatized indole 1.118 with excellent enantioselectivity (Scheme 1.22). Their transformation appears broad: a range of substituents on the indole moiety is tolerated to afford heterocycles 1.118b – 1.118f. Substrates bearing both electron-donating and withdrawing groups form cyclopenta[b]indoles smoothly, albeit diminished enantioselectivity with C4 substituents resulting from steric interactions with the R2-substituent. Similarly, bulkier R2 groups led to diminished enantioselectivity as well (entry g). Changing the identity of methyl ester to an allyl ester generated corresponding indole 1.118h exclusively. Propargyl ketal with benzoyl group on alkyne terminus, however, was converted to 1.118i in lower yield and slightly diminished enantioselectivity. Pyrrole-based substrate, however, was transformed to 1.118j with a moderate yield and excellent enantioselectivity.
Scheme 1.22. Enantioselective Au-catalyzed Rautenstrauch rearrangement.

The authors proposed a catalytic cycle to account for the enantioselectivity of this transformation (Scheme 1.23). Gold-complexed propargyl acetal 1.119 initiates the anti-attack of the proximal ethoxy ether, generating oxonium species 1.120. Ring-opening of this oxonium ion produces oxocarbenium 1.121. Extrusion of acetaldehyde leads to formation of pentadienyl cation 1.122. Delocalization of the positive charge in 1.122 can be considered gold carbenoid 1.123. The enantioselective imino-Nazarov electrocyclization of 1.123 is then controlled by the chiral gold complex to afford 1.124. Decomplexation and hydrolysis furnishes the dearomatized indole 1.118a.
Scheme 1.23. Proposed catalytic cycle involving enantioselective electrocyclization.

Besides five- and six- membered rings, Rautenstrauch rearrangement can be used to synthesize fused seven-membered rings as well. Tang and co-workers reported a Rh(I)-complex catalyzed Rautenstrauch rearrangement intercepted by a tethered alkyne (Scheme 1.24). Treatment of 1,6- enyne 1.125 with Rh(I)-catalyst afforded bicyclic compounds 1.126. This transformation tolerates a range of substitution patterns: substrates with an oxygen, nitrogen or gem-diester linker converted to bicyclic products 1.126a – 1.126c smoothly. In contrast, substrates bearing an all methylene tether (e.g. 1.125d) required a phosphine ligand to improve yield. The addition of the electron-poor phosphite ligand also promoted transformation of internal alkyne 1.125e and substrates with substituted tether (e.g.
1.125f and 1.125h). However, the reaction proceeded smoothly for substituents adjacent to alkyne (e.g. 1.125g).

The authors proposed a mechanism for the transformation of the linear enediynes to cycloheptatrienes with three well-differentiated double bonds (Scheme 1.25). Rhodium(I) complex first coordinates with the triple bond. This coordination promotes [1,2]-pivaloate migration to form vinyl metal species 1.128. Then cyclization of 1.128 or 6\pi-electrocyclization of metal carbene 1.129 provides metallacyclohexadiene 1.130, followed by alkyne insertion. Reductive elimination of the metallacyclooctatriene 1.131 furnishes the product containing a fused five-seven-membered ring.

**Scheme 1.24.** Scope of Rh(I)-catalyzed Rautenstrauch rearrangement.
C–N Bond Formation through Tandem Electrocyclization-[1,2] Migration Reaction

In comparison with Nazarov-migration reaction, studies for C–N bond formation via electrocyclization are rare. Early in 1967, Sundberg and co-workers found that deoxygenation of β,β-disubstituted o-nitrostyrenes by triethyl phosphite produced rearranged indole as a product. They reported that exposure of β-phenyl-β-methyl-ortho-nitrostyrene to reaction conditions triggered selective [1,2]-phenyl migration affording 2-methyl-3-phenyl indole (Scheme 1.26). The migration selectivity is not dependent on the configuration of nitrostyrene: Z- and E- isomer of 1.132 showed nearly equal efficiency and reactivity in the formation of indole products 1.133, 1.134 and 1.135.
Scheme 1.26. Phosphite-mediated reductive cyclization–[1,2]-phenyl migration to form 2,3-disubstituted indoles.

Sundberg and co-workers proposed a mechanism by cyclization involved with electrophilic attack followed by [1,2]-shift of β-susbtituent to C3 (Scheme 1.27). The nitrogen attack could be initiated by nitrene 1.139 or nitroso 1.138 species formed from phosphite-mediated deoxygenation of nitroarenes. Cadagon also reported a cyclization migration mechanism for heterocycles synthesis from rearrangement induced by nitrenes or their precursors via phosphite reduction of nitroarenes or photolysis and thermolysis of aryl azides.  

Scheme 1.27. Proposed cyclization migration mechanism.
In 1981, Rees, Moody and co-workers reported a tandem electrocyclization migration reactions observed in thermolysis of azides 1.142 (Table 1.6). Irradiation of \( \beta,\beta\)-disubstituted 3-azido-2-alkenylthiophenes 1.142a produced thienopyrroles 1.143a via new C–N bond construction followed by sigmatropic shift of ethyl carboxylate. When \( \beta\)-substituents with different identities were introduced, acyl and sulfur groups were found to migrate in preference of the ethyl carboxylate group (entries 2 – 4). In contrast to the migration activity of sulfide and sulfoxide (entries 5 and 6), sulfone was not found to migrate with only C–H bond amination product observed (entry 7). The authors summarized a migration aptitude as: RSO > RS ~ H > RSO\(_2\) > RCO > EtO\(_2\)C. Aryl azide analogs were also studied and proved to afford more selective migration indole product 1.146 (eq. 1.9).

### Table 1.6. Photolysis of thiophene azides to produce thienopyrrols.

<table>
<thead>
<tr>
<th>entry</th>
<th>X</th>
<th>Y</th>
<th>%, yield</th>
<th>1.143:1.144</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>a</td>
<td>CO(_2)Et</td>
<td>CO(_2)Et</td>
<td>76</td>
</tr>
<tr>
<td>2</td>
<td>b</td>
<td>COMe</td>
<td>CO(_2)Et</td>
<td>90</td>
</tr>
<tr>
<td>3</td>
<td>c</td>
<td>SPh</td>
<td>CO(_2)Et</td>
<td>55</td>
</tr>
<tr>
<td>4</td>
<td>d</td>
<td>SMe</td>
<td>CO(_2)Et</td>
<td>40</td>
</tr>
<tr>
<td>5</td>
<td>e</td>
<td>SOMe</td>
<td>SMe</td>
<td>55</td>
</tr>
<tr>
<td>6</td>
<td>f</td>
<td>H</td>
<td>SMe</td>
<td>49</td>
</tr>
<tr>
<td>7</td>
<td>g</td>
<td>H</td>
<td>SO(_2)Me</td>
<td>86</td>
</tr>
</tbody>
</table>

The authors proposed a tandem electrocyclization migration mechanism for this transformation (Scheme 1.28). Photolysis of azide 1.147 induces the formation of
nitrene 1.150, which conducts a $4\pi$-electron-5-atom electrocyclization to produce thiophene-fused 2$H$-pyrrole 1.151. A [1,2]-shift of migrating group occurs and aromatization of 1.152 to 1.149 can be achieved by either a direct photochemically allowed [1,3]-H shift or two successive ‘dark’ [1,5]-H shifts. When $R = H$, C–H bond amination can occur to afford thiophene-fused pyrrole 1.148. The R-group was also reported to migrate to nitrogen when all positions are blocked.42

Scheme 1.28. Proposed tandem electrocyclization [1,2]-shift mechanism.

In 2007, the Driver group reported that Rh$_2$(II) carboxylates complex can catalyze the formation of $N$-heterocycles from vinyl- or aryl azides.43 Mechanistic studies suggest that C–H bond amination occurs in a step-wise fashion with C–N bond construction proceeding C–H bond cleavage (Scheme 1.29).44 After aryl azide 1.154 coordinates with rhodium complex, extrusion of N$_2$ produces rhodium nitrene 1.157. Increasing electron density on the biaryl system by using electron-rich R group can accelerate the formation of rhodium nitrenoid. The planar nature of 1.157 enables a $4\pi$-electron-5-atom electrocyclization to construct the C–N bond. For indole formation, resonance structure 1.158 can visualize the contiguous, planar array of $\pi$-orbitals. Dissociation with rhodium catalyst followed by a [1,5]-hydride shift provides carbazole 1.155. In support of this step-wise electrocyclization mechanism, a gem-diphenyl-substituted aryl azide was tested (Scheme 1.30).45 Exposure of
1.161 to rhodium carboxylate complex resulted in the formation of 2,3-diphenyl indole 1.162. The associated 2,3-phenyl shift implicates the intermediacy of cation 1.163 to suggest that C–N bond forms prior to N–H bond.

Scheme 1.29. Rh(II)-catalyzed N-heterocycle formation from aryl azides.

Scheme 1.30. Rh(II)-catalyzed phenyl migration from gem-diphenyl styryl azide.
The Driver group then investigated the selective migratory behavior for different \( \beta \)-substituents. A series of \( \beta,\beta \)-disubstituted styryl azides 1.164 was exposed to optimal conditions to examine the migration selectivity between alkyl- and aryl- group (Scheme 1.31).\(^{46} \) In all cases, [1,2]-aryl shift occurred exclusively to afford 2-alkyl-3-phenyl indoles 1.165 irrespective of the electronic nature of the migrating group or stereochemistry of styryl azides. The reaction reactivity is not dependent on the ring size. High yields and selectivity can be achieved by incorporating oxygen in the tether or using independent \( \beta \)-substituents (entries d and e).

\[
\begin{align*}
\text{Scheme 1.31.} \quad \text{Rh}_2(\text{II})\text{-Catalyzed formation of 2-alkyl-3-aryl indoles from } \beta,\beta\text{-disubstituted styryl azides.}
\end{align*}
\]

The selectivity of the phenyl migration was explained in the proposed mechanism (Scheme 1.32). Coordination of the rhodium complex to the styryl azide promotes extrusion of \( \text{N}_2 \), forming rhodium nitrene 1.168, which undergoes
electrocyclization to produce 1.169. The preference of aryl migration is rationalized by the more stable transition state phenonium ion 1.170 and tertiary iminium ion 1.171. Tautomerization of 1.171 produces indole 1.172 and recovers rhodium catalyst. The equal reactivity of Z- and E-isomer of 1.166 can be explained by perpendicular structure of benzylic carbocation 1.169.

Scheme 1.32. Mechanism for Rh$_2$(II)-catalyzed formation of 2-alkyl-3-aryl indoles.

More migrating groups were tested to establish a migratory aptitude scale. In 2011, the Driver group reported the tandem electrocyclization [1,2]-nitro shift reaction of aryl azides (Scheme 1.33). In contrast to the thermolysis results reported by Gribble and Pelkey, exposure of β-nitro-substituted 1.173 to dirhodium tetradentate complexes provided [1,2]-nitro shift indole product 1.175 exclusively (eq. 1.10). The scope of the reaction is not limited to the electronic nature of the styryl azide moiety. However, introducing ortho-substituent to the azides resulted in competitive 2-
nitroindole formation. Styryl azide bearing a strong electron-withdrawing group at ortho position afforded 2-nitroindole as the only product.

Scheme 1.3. Scope of Rh$_2$(II)-catalyzed NO$_2$ migration reactions.

In addition to nitro group, styryl azides bearing other electron-withdrawing groups at the β-position were investigated (Scheme 1.34). While benzoyl and acyl groups migrated to provide only 3-substituted indole 1.180a and 1.180b, isopropyl ester 1.179d only formed 2-carboxylate indole 1.181d. A mixture of indoles resulted from Weinreb amide 1.179c with 2-substituted indole as the major product. As expected, sulfone migrated dominantly at a ratio of 9:1 when styryl azide 1.179e was subjected to reaction conditions. Together with the results from Scheme 1.32, EWG migration was suppressed by the additional ortho substituent. These migration results suggest that the more strongly electron-deficient groups are more prone to migrate.
To compare migration ability between different identities of substituents, a series of β,β-disubstituted styryl azides were tested (Scheme 1.35). No aryl- or alkyl group migration was observed for substrates 1.182a and 1.182b with the presence of β-hydrogen. When azide 1.182c was exposed to reaction conditions, aryl group selectively migrated in preference to alkyl groups. Not surprisingly, the more electron-withdrawing sulfone and amide migrated compared to aryl group. The reaction of 1.182f afforded only nitro migration product without observed benzoyl migration.
Scheme 1.35. Competition experiments to compare migration preferences.

Other than dirhodium carboxylate, CuI was also reported to promote tandem electrocyclization-[1,2]-amide migration reactions. In 2010, Zhang and coworkers reported that photolysis of 3-(2-azidobenzylidene)-lactams mediated by stoichiometric amount of CuI triggered cyclization-ring expansion (Scheme 1.36). Photochemical reactions with reduced amount of CuI or thermolysis of styryl azides 1.184 led to reduced yield of indole formation. The substrates bearing both electron-donating and electron-attracting groups were converted to indole smoothly with the addition of CuI. More fused indoles 1.185a-c can be produced via cyclization-ring expansion reaction from corresponding styryl azides. Consistent with the results from Driver’s work, 2,3-disubstituted indoles resulted from exclusive amide group migration from β,β-disubstituted styryl azides.
Scheme 1.36. Cul-mediated photolysis of substituted 3-(2-azidobenzylidene)-lactams.

Driver lab then investigated on trisubstituted styryl azides (Scheme 1.37) for potential tandem electrocyclization migration reaction.\(^{50}\) Styryl azide 1.186 was tested with the expectation of acyl group migration. Previous study showed that β-acyl group migrated to C3 position as a facile process. However, exposure of styryl azide 1.186 to optimal conditions resulted in acyl group migrated to nitrogen with additional α-substituent. A range of substituents on aryl azide moiety is tolerated for this transformation. An additional ortho substituent on aryl azide 1.186i did not alter the reaction result albeit leading to a slightly reduced yield. Electronic nature of α-aryl group exerted little impact in the reaction (entries a-e). Styryl azides bearing alkyl group on α-position also converted to 1,2,3-trisubstituted indoles smoothly (entries g and h).
Scheme 1.37. Effect of $\alpha$-substituent on Rh$_2$(II)-catalyzed acyl migration.

Recently, Driver and coworkers reported a tandem electrocyclization migration achieved via Mo(CO)$_6$ and Pd(II)-catalyzed reduction of ortho-substituted nitrostyrenes (Scheme 1.38). Conversion of nitroarenes to indoles or carbazoles via C–H bond amination was used to be achieved using superstoichiometric quantity of a reductant such phosphite, zinc dust, Grignard reagent or high pressure of carbon monoxide. Driver group found out that Mo(CO)$_6$ can act as CO substitute. The easily accessed $\beta$-phenyl trisubstituted nitrostyrenes 1.188 could be transformed to spirocycles 1.189 upon exposure to (phen)Pd(OAc)$_2$ and Mo(CO)$_6$. The transformation tolerates a range of electron-releasing and electron-withdrawing groups on nitroarenes. Electron-donating group on $\beta$-phenyl substituent performs more efficiently (entries b and c). Nitrostyrene 1.188d with $\beta$-methyl group can also be converted to spirocycle 1.189d using higher loading of Pd catalyst. Switching $\beta$-substituent to carboxylate group, however, changed the product identity to 3$H$-indoles 1.190. Carboxylate migration is not dependent on the ring size and
heteroatom in the tether (entry f). When allylic or homoallylic substituents were introduced, the reaction became diastereoselective (entries g and h).

Scheme 1.38. Pd(II)-catalyzed transformation of nitrostyrenes into 3H-indoles.

The authors proposed a catalytic cycle for this transformation to account for 3H-indole formation (Scheme 1.39). Mo(CO)₆ serving as CO source for Pd-catalyzed N–O bond reduction, could also coordinate with nitrosoarene 1.191, facilitating the following cyclization. The resulting benzylic cation in 1.192 triggers a ring contraction to produce spirocycle N-oxide 1.193. Another reduction of the N–O bond produces 3H-indole 1.189a and regenerates palladium catalyst.
Scheme 1.39. Potential catalytic cycle for Pd(II)-catalyzed formation of 3H-indoles from nitrostyrene.

Summary and Outlook

A variety of electrocyclization [1,2]-migration reactions have been described. Nazarov reaction and Rautenstrauch rearrangement are applied to assemble functionalized carbocycles. Systematic study has been done by Frontier and Toste group to gain access to non-racemic cycloalkanes. Driver group established a series of transition metal catalyzed electrocyclization migration reaction using styryl azides. Remaining challenges include the expansion of substrate scope, construction of quaternary center and stereoselective C–N bond, mechanism involved in the selective migration and chemoselectivity in competitive pathways. My efforts to further explore the system to address these challenges follows in the next chapters.
References


CHAPTER 2

Rh₂(II)-Catalyzed Selective Aminomethylene Migration from Styryl Azides
As mentioned in Chapter 1, Driver laboratories have investigated transition metal catalyzed C–H bond amination to afford N-heterocycles using aryl azides.\textsuperscript{1,2} We exploited the 4\pi-electron-5-atom electrocyclization mechanism to induce 1,2-shift of \(\beta\)-substituents and established a migratory aptitude scale to be alkyl < aryl < amide < H < sulfonyl < ketone < nitro.\textsuperscript{3} Our data suggested that more electron-withdrawing group prefer to migrate. Sulfonyl group, ketone and nitro group can even migrate with the presence of \(\beta\)-H. The potential for selectivity in the 1,2-migration was demonstrated early on with \(\beta,\beta\)-disubstituted styryl azides. When styryl azide 2.1 was exposed to reaction conditions, aryl group migration could be selectively triggered to afford 2-alkyl-3-aryl indole 2.4 as the only product (Scheme 2.1).\textsuperscript{4,5}

![Scheme 2.1](image)

**Scheme 2.1.** Rh\textsubscript{2}(II)-catalyzed selective aryl group migration.

The migration process is selective for distinct \(\beta\)-substituents. We wondered if our migration process could distinguish between two \(\beta\)-methylene units when one was substituted with an aminomethylene group. The use of heteroatoms as stereochemical controlling elements is well established in many transformations.\textsuperscript{6} However, their use to control the selectivity of 1,2-shifts is surprisingly rare.\textsuperscript{7} To our best knowledge, use of amines to control the selectivity of 1,2-shifts was not reported prior to our study. If the process is selective, we can transform \(\beta,\beta\)-disubstituted styryl azide 2.5 to tetrahydrocarboline derivatives 2.7 or 2.8 with either methylene group migration.\textsuperscript{8} Carbolines are instrumental scaffolds in natural products and have shown potential in pharmaceuticals.\textsuperscript{9} While \(\beta\)-carbolines, structurally related to tryptophan and serotonin, have attracted more attention, chemical studies of \(\gamma\)-carbolines are limited, despite of their various biological
activities in antibiotic\textsuperscript{10}, antipsychotic\textsuperscript{11} and antitumor\textsuperscript{12} fields. Recently, tetrahydro-γ-carbolines\textsuperscript{13} was found to be a potent MCH-1 antagonist in treatment of obesity\textsuperscript{14}. In this chapter, reactions I performed using Rh\textsubscript{2}(II) carboxylate to catalyze tandem electrocyclization migration to afford tetrahydrocarbolines are presented (Scheme 2.2).

\begin{center}
\includegraphics[width=0.7\textwidth]{Scheme_2.2.png}

\textbf{Scheme 2.2.} Hypothesis for \(\beta\)-methylene selective migration.
\end{center}

The styryl azides 2.9 for our study were synthesized from nitroarene 2.10 (Scheme 2.3). While double bond for styrene was constructed by Horner-Wadsworth-Emmons reaction of benzyl phosphonate 2.12 and piperidine 2.13, azido group was obtained from nitro through reduction and azidation of aniline. Functional group on N can be installed after removing the Boc group.

\begin{center}
\includegraphics[width=0.7\textwidth]{Scheme_2.3.png}

\textbf{Scheme 2.3.} Retrosynthesis of styryl azides.
\end{center}

DuBois’s tetradoentate Rh\textsubscript{2}(esp)\textsubscript{2}\textsuperscript{15} was first used to examine the effect of the distal substitution on the selectivity of methylene migration due to its success in our previous work.\textsuperscript{16} We anticipated that the identity of γ-aminosubstituents could influence the alkyl 1,2-shift by varying its electronic nature. The reaction for amine
with sulfonyl group turned out to be the most efficient and selective transformation. Other common protecting groups led to lower conversion. When nitrogen was substituted with a Boc or Bz group, selectivity of the methylene migration was significantly attenuated, providing a 2:1 mixture of indoles 2.15 and 2.16 (entries 2 and 3). Selectivity was restored when Bn group was used, albeit significantly diminished yield (entry 4). The low conversion could be caused by complexation of the benzyl nitrogen atom with the Lewis acidic catalyst. Based on this result, we decided to further investigate the reaction scope of aminomethylene migration using substrate bearing a phenylsulfonyl N-substituent. Both E and Z isomer of 2.14 were used for this transformation. The outcome of the reaction indicates nearly equal reactivity for the isomers, providing essential evidence for mechanism involving a perpendicular intermediate.

**Table 2.1.** Survey of the effect of the N-substituent identity on reaction outcome.

<table>
<thead>
<tr>
<th>entry</th>
<th>R</th>
<th>%, yield&lt;sup&gt;a&lt;/sup&gt;</th>
<th>2.15:2.16</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>SO(_2)Ph</td>
<td>87</td>
<td>100:0&lt;sup&gt;c&lt;/sup&gt;</td>
</tr>
<tr>
<td>2</td>
<td>Boc</td>
<td>46</td>
<td>60:40&lt;sup&gt;c&lt;/sup&gt;</td>
</tr>
<tr>
<td>3</td>
<td>Bz</td>
<td>42</td>
<td>66:34&lt;sup&gt;b&lt;/sup&gt;</td>
</tr>
<tr>
<td>4</td>
<td>Bn</td>
<td>18</td>
<td>100:0</td>
</tr>
</tbody>
</table>

<sup>a</sup> as determined using \(^1\)H NMR spectroscopy using CH\(_2\)Br\(_2\) as the internal standard. <sup>b</sup> DMSO-\(d_6\) was used as the NMR solvent. <sup>c</sup> acetone-\(d_6\) was used as the NMR solvent.

Although our previous studies had established Rh\(_2\)(esp)\(_2\) as a competent catalyst, we still screened different transition metal complexes as potential catalysts (Table 2.2). While no reaction was observed in the absence of catalyst (entry 1), exposure of 2.17 to rhodium carboxylate complexes did trigger the desired aminomethylene migration. Both yield and migration selectivity depended on the identity of the catalyst. The best results were obtained with Rh\(_2\)(esp)\(_2\) or
Rh₂(O₂CC₇H₁₅)₄ to afford indole 2.18 as the only product (entries 2 and 3).¹⁷ Rh₂(II) catalyst with fluorinated ligands and [(cod)Ir(OMe)]₂ afforded a mixture of migration indole products with much lower yield (entries 4, 5, 7). No reaction was observed with Rh₂(OAc)₄ (entry 6). Other metal catalysts (Fe, Au, Cu, Zn, Pd, Ru) were also tested and proved to be unsuitable for this transformation (entries 8–15).¹⁸ Our screen identified Rh₂.esp₂ as the optimal catalyst. Next, we examined different solvents. The reaction outcome did not improve when solvent was changed from toluene to chlorinated or ethereal solvents with Rh₂.esp₂ catalyst used. The stereochemistry of the starting material did not impact the conversion and selectivity due to a proposed benzyl carbocation intermediate. Both E and Z isomer of 2.17 transformed to 2.18 smoothly.

Table 2.2. Survey of reaction conditions for 2,3-indole formation.

<table>
<thead>
<tr>
<th>entry</th>
<th>catalyst</th>
<th>%, yield</th>
<th>2.18 : 2.19</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>none</td>
<td>n.r.</td>
<td>n.a.</td>
</tr>
<tr>
<td>2</td>
<td>Rh₂.esp₂</td>
<td>87</td>
<td>100:0</td>
</tr>
<tr>
<td>3</td>
<td>Rh₂(O₂CC₇H₁₅)₄</td>
<td>85</td>
<td>100:0</td>
</tr>
<tr>
<td>4</td>
<td>Rh₂(O₂CC₃F₇)₄</td>
<td>32</td>
<td>86:14</td>
</tr>
<tr>
<td>5</td>
<td>Rh₂(O₂CCF₃)₄</td>
<td>36</td>
<td>80:20</td>
</tr>
<tr>
<td>6</td>
<td>Rh₂(O₂CCH₃)₄</td>
<td>n.r.</td>
<td>n.a.</td>
</tr>
<tr>
<td>7</td>
<td>[(cod)Ir(OMe)]₂</td>
<td>13</td>
<td>91:9</td>
</tr>
<tr>
<td>8</td>
<td>FeBr₂</td>
<td>trace</td>
<td>n.a.</td>
</tr>
<tr>
<td>9</td>
<td>FeBr₃</td>
<td>0</td>
<td>n.a.</td>
</tr>
<tr>
<td>10</td>
<td>AuCl</td>
<td>n.r.</td>
<td>n.a.</td>
</tr>
<tr>
<td>11</td>
<td>Cu(OTf)₂</td>
<td>trace</td>
<td>n.a.</td>
</tr>
<tr>
<td>12</td>
<td>CuCl</td>
<td>n.r.</td>
<td>n.a.</td>
</tr>
<tr>
<td>13</td>
<td>ZnI₂</td>
<td>n.r.</td>
<td>n.a.</td>
</tr>
<tr>
<td>14</td>
<td>Pd(PPh₃)₂Cl₂</td>
<td>n.r.</td>
<td>n.a.</td>
</tr>
<tr>
<td>15</td>
<td>Ru(TPP)CO</td>
<td>0</td>
<td>n.a.</td>
</tr>
</tbody>
</table>

² as determined using ¹H NMR spectroscopy using CH₂Br₂ as the internal standard.
With the optimal conditions, a series of styryl azides 2.20 were examined to determine the scope and limitation of the aminomethylene 1,2-shift reaction (Table 2.3). The scope of our migration reaction was found to be quite broad for substrate modification converting styryl azide 2.20 to indole 2.21 as the only product (entries 1–3). The size of ring expansion did not influence the reaction efficiency. Both azetidine 2.20a and pyrrolidine 2.20b were converted to only one indole product. The migration reaction was also tolerant to modification of the electronic nature of the aryl azides. Substrates with more electron-withdrawing group can be converted in slightly higher yields (entries 4–10). The ortho-\(R^3\)-substituent exerted a larger effect on the efficiency of the migration reaction (entries 11 and 12). Comparing styryl azide 2.20k and 2.20l indicates that an \(o\)-methoxy group had a more deleterious effect than an \(o\)-methyl group, which was attributed to steric interaction with rhodium nitrene formation. Importantly, our reaction provides access to 8-substituted indoloazepines 2.21g-2.21j, which cannot be synthesized regioselectively using Fischer-indole reaction.\(^{19}\)

**Table 2.3.** Scope of Rh\(_2\)(II)-Catalyzed Aminomethylene 1,2-Shift.

<table>
<thead>
<tr>
<th>entry</th>
<th>Styryl azide 2.20</th>
<th>Indole 2.21</th>
<th>Yield, %(^{a})</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td><img src="2.20" alt="image" /></td>
<td><img src="2.21" alt="image" /></td>
<td>82</td>
</tr>
<tr>
<td>2</td>
<td><img src="2.20" alt="image" /></td>
<td><img src="2.21" alt="image" /></td>
<td>78</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>---</td>
<td>---</td>
<td>---</td>
<td>---</td>
</tr>
<tr>
<td>3</td>
<td>c</td>
<td><img src="image" alt="Chemical Structure" /></td>
<td><img src="image" alt="Chemical Structure" /></td>
</tr>
<tr>
<td>4</td>
<td>d</td>
<td><img src="image" alt="Chemical Structure" /></td>
<td><img src="image" alt="Chemical Structure" /></td>
</tr>
<tr>
<td>5</td>
<td>e</td>
<td><img src="image" alt="Chemical Structure" /></td>
<td><img src="image" alt="Chemical Structure" /></td>
</tr>
<tr>
<td>6</td>
<td>f</td>
<td><img src="image" alt="Chemical Structure" /></td>
<td><img src="image" alt="Chemical Structure" /></td>
</tr>
<tr>
<td>7</td>
<td>g</td>
<td><img src="image" alt="Chemical Structure" /></td>
<td><img src="image" alt="Chemical Structure" /></td>
</tr>
<tr>
<td>8</td>
<td>h</td>
<td><img src="image" alt="Chemical Structure" /></td>
<td><img src="image" alt="Chemical Structure" /></td>
</tr>
<tr>
<td>9</td>
<td>i</td>
<td><img src="image" alt="Chemical Structure" /></td>
<td><img src="image" alt="Chemical Structure" /></td>
</tr>
<tr>
<td>10</td>
<td>j</td>
<td><img src="image" alt="Chemical Structure" /></td>
<td><img src="image" alt="Chemical Structure" /></td>
</tr>
<tr>
<td>11</td>
<td>k</td>
<td><img src="image" alt="Chemical Structure" /></td>
<td><img src="image" alt="Chemical Structure" /></td>
</tr>
</tbody>
</table>
Then the effect of changing the identity of $\beta$-substituents was investigated (Table 2.4). First, acyclic aminomethylene groups were found to migrate as well (entries 1–6). In contrast to our previous results, only the $E$-isomer of the proline-derived styryl azides 2.22 was smoothly converted to 2,3-disubstituted indoles 2.23. The lack of reactivity of $Z$-isomer was attributed to destabilizing steric interactions with rhodium catalyst and bigger proline substituent. The reaction was tolerant to the modification on the electronic nature of the aryl azide with slightly higher yield with electron deficient substrates (entries 2–4). Enlarging the ring size of the migrating group from proline to piperidine did not prevent the migration (entry 5). Piperidine 2.22e was transformed to corresponding product smoothly in a slightly lower yield.

Our previous results indicated that no alkyl group migration was observed when a $\beta$-aryl group was present. To test the migratorial aptitude between an aminomethylene and aryl group, we synthesized aryl azide 2.22f with $\beta$-aminoalkyl and $\beta$-phenyl group (entry 6). When 2.22f was exposed in reaction condition, aminoalkyl migration product was observed as the major product with 15% formation of 2-phenylindole. The phenomenon can also be extended to selective ethereal methylene migration (entry 7). Styryl azide 2.22g was found to produce indole 2.23g as the major product with < 5% of the other regioisomer observed. As we observed before, both $E$- and $Z$-isomers can be converted to the indole product due to a reduced steric interaction.
Table 2.4. Scope of Rh$_2$(II)-Catalyzed Selective Methylene Shift.

![Chemical structures](image)

<table>
<thead>
<tr>
<th>entry</th>
<th>Styryl azide 2.22</th>
<th>Indole 2.23</th>
<th>Yield, %$^a$</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td><img src="image" alt="Styryl azide 2.22" /></td>
<td><img src="image" alt="Indole 2.23" /></td>
<td>83</td>
</tr>
<tr>
<td>2</td>
<td><img src="image" alt="Styryl azide 2.22" /></td>
<td><img src="image" alt="Indole 2.23" /></td>
<td>69</td>
</tr>
<tr>
<td>3</td>
<td><img src="image" alt="Styryl azide 2.22" /></td>
<td><img src="image" alt="Indole 2.23" /></td>
<td>81</td>
</tr>
<tr>
<td>4</td>
<td><img src="image" alt="Styryl azide 2.22" /></td>
<td><img src="image" alt="Indole 2.23" /></td>
<td>75</td>
</tr>
<tr>
<td>5</td>
<td><img src="image" alt="Styryl azide 2.22" /></td>
<td><img src="image" alt="Indole 2.23" /></td>
<td>58</td>
</tr>
<tr>
<td>6</td>
<td><img src="image" alt="Styryl azide 2.22" /></td>
<td><img src="image" alt="Indole 2.23" /></td>
<td>56$^b$</td>
</tr>
<tr>
<td>7</td>
<td><img src="image" alt="Styryl azide 2.22" /></td>
<td><img src="image" alt="Indole 2.23" /></td>
<td>75$^c,d$</td>
</tr>
</tbody>
</table>

$^a$Isolated yield of 2.23 after silica gel chromatography; only product obtained. $^b$2-Phenylindole (15%) also isolated. $^c$Indole formed as a 95:5 mixture of regioisomers. $^d$Reaction performed in toluene using a 78:22 E/Z mixture of isomers of 2.22g. Entry a-d,f are done by Navendu Jana.
The reactivity trends of our azide substrates suggested a potential catalytic cycle for the Rh$_2$(II)-catalyzed aminomethylene migration reaction (Scheme 2.4). Coordination of Rh$_2$(esp)$_2$ to styryl azide 2.17 on the $\alpha$- or $\gamma$- nitrogen is followed by N$_2$ extrusion, resulting in the formation of rhodium nitrene 2.25. A 4$\pi$-electron-5-atom electrocyclization of 2.25 forms benzyl cation 2.26. Carbon-nitrogen bond formation via this cation explains the nearly equal reactivity of the $E$- and $Z$-isomer of the styryl azide 2.17. Formation of 2.26 triggers migration of the aminomethylene in an either concerted$^{22}$ or stepwise pathway via iminium ion 2.28. Tautomerization of 2.29 produces indole 2.18 and regenerates the catalyst.

Scheme 2.4. Proposed catalytic cycle.
Further insight into the mechanism of tandem electrocyclization migration reaction was obtained by examining the reactivity of enantiomerically enriched styryl azide 2.30 (Scheme 2.5). We anticipated that if the indole product remained enantiomerically enriched, the migration should be concerted. In contrast, racemates should be obtained if the migration is stepwise with the formation of iminium ion species. The observation of racemic product 2.31, however, indicates a stepwise mechanism with the intermediate ion pair 2.32.

Scheme 2.5. Reactivity of enantiomerically enriched styryl azide.

Further support of the stepwise mechanism is the observation of the isolated 2-phenylindole and dihydropyrrole as byproducts when styryl azide 2.33 was exposed to reaction conditions (Scheme 2.6). This result suggests that the presence of a β-phenyl substituent stabilizes the cation catalytic intermediate to allow deprotonation of the iminium ion intermediate and diffusion of 2.36 to occur. These byproducts were only observed for substrate 2.33, probably because alkyl substitution does not stabilize the cation intermediate enough to allow for a bimolecular process to occur.

Scheme 2.6. Reaction of styryl azide 2.33.
Next, we conducted a double crossover reaction of 2.37 and 2.38 to determine if the iminium ion escaped the solvent shell. If diffusion occurs faster than 1,2-shift, more than 2 indole products should be observed. On the other hand, only 2 corresponding indoles should be formed from 2 azides. Submission of a 1:1 mixture of 2.37 and 2.38 only produced 2.39 and 2.40, revealing that 1,2-aminomethylene shift occurs stepwise without diffusion of the iminium ion intermediate.

Scheme 2.7. Crossover experiment.

In conclusion, we have discovered that dirhodium(II) carboxylate complex can trigger a preferential aminomethylene 1,2-shift when exposed to β,β-dimethylene-substituted styryl azide. Mechanism study suggests a tandem electrocyclization migration reaction with migration occurring stepwise before diffusion of the iminium ion. Together with our previous studies, our migratorial aptitude scale can be updated to alkyl < aryl < aminomethylene < amide < H < sulfone < ketone < nitro.
Experimental

This part was taken from supporting information of my published paper: Kong, C.; Jana, N.; Driver, T. G. Org. Lett. 2013, 15, 824.

A. General. $^1$H NMR and $^{13}$C NMR spectra were recorded at ambient temperature using 500 MHz or 300 MHz spectrometers. The data are reported as follows: chemical shift in ppm from internal tetramethylsilane on the d scale, multiplicity (br = broad, s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet), coupling constants (Hz) and integration. High-resolution mass spectra were obtained by peak matching. Melting points are reported uncorrected. Analytical thin layer chromatography was performed on 0.25 mm silica gel plates with UV254 fluorescent indicator. Liquid chromatography was performed using forced flow (flash chromatography) of the indicated solvent system on 60Å (40 – 60 μm) mesh silica gel (SiO$_2$). Medium pressure liquid chromatography (MPLC) was performed using pumps to force flow the indicated solvent system down columns that had been packed with 60Å (40 – 60 μm) mesh silica gel (SiO$_2$). All reactions were carried out under an atmosphere of nitrogen in glassware that was oven-dried. Unless otherwise noted, all reagents were commercially obtained and, where appropriate, purified prior to use. Acetonitrile, methanol, toluene, THF, Et$_2$O, and CH$_2$Cl$_2$ were dried by filtration through alumina according to the procedure of Grubbs. Metal salts were stored in a nitrogen atmosphere dry box.

B. Route to synthesize styryl azide.

Substituted styryl azide 2.21 was synthesized via the following route. The synthesis starts from 2-nitrobenzyl bromide followed by substitution to form benzyl phosphonate which reacts with N-boc-3-piperidone in Horner-Wadsworth-Emmons reaction. Then the nitro group is reduced to aniline by Iron. Azidation of aniline forms the initial styryl azide substrate. Replacement of the boc group to SO$_2$Ph furnishes our final substrates which are ready for the following decomposition.
Scheme 2.8. Route to synthesize styryl azide 2.21.

The pyrrolidine substrates 2.23 were synthesized following the routes outlined below. Styrene is formed through Suzuki coupling from vinyl triflate and arylboronic acid pinacol ester.

Scheme 2.9. Route to synthesize styryl azide 2.23.
C. Preparation of \(\beta,\beta\)-disubstituted nitrostyrenes.

To a solution of diisopropylamine (1.21 equiv) in THF at \(-78 \, ^\circC\) was added a 2.5 M solution of \(n\)-butyl lithium in hexane (1.1 equiv). The mixture was stirred at room temperature for 40 min and then cooled to \(-78 \, ^\circC\). Once cool, a solution of the substituted diethyl 2-nitrobenzylphosphonate 2.42 (1 equiv) in THF was added dropwise. The reaction mixture was allowed to warm to room temperature. After 30 min, the mixture was cooled to \(-78 \, ^\circC\) and a solution of \(N\)-Boc-3-piperidone 2.43 (1 equiv) in THF was added dropwise. The reaction mixture was allowed to slowly warm to room temperature. After 16h, visualization of the reaction progress using thin layer chromatography revealed that the reaction was complete. The reaction mixture was then concentrated in \textit{vacuo}. Purification of the resulting residue by MPLC (2:100 – 20:80 EtOAc:hexanes) afforded the product 2.44.

\[
\begin{align*}
\text{2.42} & \quad \text{+} \quad \text{2.43} & \quad \text{\textit{LDA, THF}} & \quad \text{\textit{\(-78 \, ^\circC \rightarrow r.t.\)}} \quad \text{2.44} \\
\end{align*}
\]

1-Boc-3-(2-nitrobenzylidene)piperidine 2.44c. The general procedure was followed by using 4.00 g of 2.42 (14.6 mmol), 2.92 g of \(N\)-Boc-3-piperidone (14.6 mmol), 150 mL of THF and 7.3 mL of a 2.5 M solution of LDA. Purification by MPLC (2:100 – 20:80 EtOAc:hexanes) afforded the product, a yellow oil, as a 81:19 mixture of isomers (2.98 g, 64%). Spectral data for the major product: \(^1\text{H NMR}\) (500MHz, CDCl\(_3\)) \(\delta\) 7.79 (d, \(J = 8.1\) Hz, 1H), 7.40 (t, \(J = 4.5\) Hz, 1H), 7.24 (t, \(J = 7.7\) Hz, 1H), 7.12 (d, \(J = 7.6\) Hz, 1H), 6.46 (s, 1H), 3.87 (s, 2H), 3.33 (t, \(J = 5.1\) Hz, 2H), 2.09 (s, 2H), 1.41 (s, 2H), 1.32 (s, 9H); \(^{13}\text{C NMR}\) (125 MHz, CDCl\(_3\)) \(\delta\) 154.5 (C), 148.4 (C), 138.2 (C), 132.6 (CH), 132.0 (C), 131.9 (CH), 127.8 (CH), 124.3 (CH), 120.7 (CH), 79.4 (C), 34.4 (CH\(_2\)), 28.3 (CH\(_3\)), 27.6 (CH\(_2\)), 26.8 (CH\(_2\)), 26.2 (CH\(_2\)). ATR-FTIR (thin
film): 2973, 2928, 2852, 1685, 1521, 1161 cm\(^{-1}\); HRMS (EI) \(m/z\) calculated for C\(_{17}\)H\(_{21}\)N\(_2\)O\(_4\) (M–H\(^+\)): 317.15014, found: 317.15068.

1-Boc-3-(2-nitrobenzylidene)azetidine 2.44a. The general procedure was followed by using 1.60 g of 2.42 (5.8 mmol), 0.96 g of N-boc-3-azetidinone (5.8 mmol), 40 mL of THF and 3.0 mL of a 2.5 M solution of LDA. Purification by MPLC (2:100 – 20:80 EtOAc:hexanes) afforded the product as a yellow solid (1.19 g, 76 %): \(^1\)H NMR (500MHz, CDCl\(_3\)) \(\delta\) 7.87 (d, \(J = 8.2\) Hz, 1H), 7.52 (t, \(J = 7.6\) Hz, 1H), 7.33 (t, \(J = 7.8\) Hz, 1H), 7.22 (d, \(J = 7.8\) Hz, 1H), 6.70 (s, 1H), 4.68 (s, 2H), 4.61 (s, 2H), 1.41 (s, 9H); \(^{13}\)C NMR (125 MHz, CDCl\(_3\)) \(\delta\) 156.2 (C), 147.7 (C), 135.7 (C), 133.0 (CH), 130.5 (C), 128.6 (CH), 127.9 (CH), 124.9 (CH), 117.6 (CH), 80.0 (C), 58.5 (CH\(_2\)), 28.3 (CH\(_3\)). ATR-FTIR (thin film): 2977, 2960, 1702, 1514, 1347, 1117 cm\(^{-1}\); HRMS (EI) \(m/z\) calculated for C\(_{15}\)H\(_{18}\)N\(_2\)O\(_4\) (M): 290.12666, found: 290.12641.

1-Boc-3-(2-nitrobenzylidene)pyrrolidine 2.44b. The general procedure was followed by using 2.70 g of 2.42 (9.9 mmol), 1.89 g of N-Boc-3-pyrrolidinone (9.9 mmol), 80 mL of THF and 5.1 mL of a 2.5 M solution of LDA. Purification by MPLC (2:100 – 20:80 EtOAc:hexanes) afforded the product, a yellow oil, as a 55:45 mixture of isomers (0.84 g, 28%). Spectral data for the mixture: \(^1\)H NMR (500MHz, CDCl\(_3\)) \(\delta\) 7.90 (d, \(J = 8.1\) Hz, 1H), 7.52 (t, \(J = 7.5\) Hz, 1H), 7.34 (t, \(J = 7.2\) Hz, 1.5H), 7.26 (d, \(J = 7.6\) Hz, 0.6H), 6.68 (s, 1H), 4.11 (s, 1H), 4.01 (s, 0.7H), 3.95 (s, 0.4H), 3.43 (s, 2H), 2.73 (s, 1H), 2.59 (t, \(J = 7.1\) Hz, 1H), 1.42 (s, 4H), 1.39 (s, 5H); \(^{13}\)C NMR (125 MHz, CDCl\(_3\)) \(\delta\) 154.3 (C), 148.1 (C), 141.9 (C), 132.9 (CH), 131.9 (C), 130.9 (CH), 127.8 (CH), 124.6 (CH), 118.1 (CH), 79.6 (C), 51.7 (CH\(_2\)), 48.2 (CH\(_2\)), 45.5 (CH\(_2\)), 44.6 (CH\(_2\)), 33.6 (CH\(_2\)), 28.5 (CH\(_3\)). Selected data for minor product: \(^{13}\)C NMR (125
MHz, CDCl$_3$) $\delta$ 147.9 (C), 142.8 (C), 132.7 (CH), 132.2 (C), 130.6 (CH), 127.8 (CH), 124.5 (CH), 117.6 (CH), 51.4 (CH$_2$), 45.9 (CH$_2$), 44.3 (CH$_2$), 33.0 (CH$_2$), 28.4 (CH$_3$).  

ATR-FTIR (thin film): 2976, 1685, 1522, 1402, 1157 cm$^{-1}$; HRMS (EI) $m/z$ calculated for C$_{16}$H$_{19}$N$_2$O$_4$ (M–H)$^+$: 303.13449, found: 303.13511.

**1-Boc-3-(5-methoxy-2-nitrobenzylidene)piperidine 2.44d.** The general procedure was followed by using 1.2 mL of diisopropylamine (8 mmol), 2.9 mL of a 2.5 M solution of $n$-BuLi in hexane (7.3 mmol), 2.0 g of 2.42d (6.6 mmol), 1.40 g of N-Boc-3-piperidone (7.3 mmol) and 80 mL of THF. Purification by MPLC (2:100 – 20:80 EtOAc:hexanes) afforded the product as a yellow solid (1.8 g, 80%): $^1$H NMR (500 MHz, CDCl$_3$) $\delta$ 8.07 (d, $J$ = 9.1 Hz, 1H), 6.84 (dd, $J$ = 9.1, 2.6 Hz, 1H), 6.67 (d, $J$ = 2.6 Hz, 1H), 6.65 (s, 1H), 4.02 (s, 2H), 3.85 (s, 3H), 3.47 (t, $J$ = 5.1 Hz, 2H), 2.25 (s, 2H), 1.58 (s, 2H), 1.46 (s, 9H); $^{13}$C NMR (125 MHz, CDCl$_3$) $\delta$ 162.8 (C), 154.8 (C), 141.5 (C), 137.4 (C), 135.2 (C), 127.3 (CH), 121.9 (CH), 116.9 (CH), 112.6 (CH), 79.7 (C), 55.9 (CH$_3$), 28.5 (CH$_3$), 27.8 (CH$_2$), 26.2 (CH$_2$) only visible signals. ATR-FTIR (thin film): 2977, 2851, 1680, 1508, 1152 cm$^{-1}$; HRMS (EI) $m/z$ calculated for C$_{18}$H$_{25}$N$_2$O$_5$ (M+H)$^+$: 349.17635, found: 349.17726.

**1-Boc-3-(5-methyl-2-nitrobenzylidene)piperidine 2.44e.** The general procedure was followed by using 2.5 mL of diisopropylamine (17.9 mmol), 8.2 mL of a 2.5 M solution of $n$-BuLi in hexane (16.4 mmol), 4.26 g of 2.42e (14.8 mmol), 2.96 g of N-Boc-3-piperidone (14.8 mmol) and 150 mL of THF. Purification by MPLC (2:100 – 20:80 EtOAc:hexanes) afforded the product as a yellow oil (3.31 g, 67%): $^1$H NMR (500 MHz, CDCl$_3$) $\delta$ 7.84 (d, $J$ = 8.3 Hz, 1H), 7.13 (d, $J$ = 8.3 Hz, 1H), 6.99 (s, 1H), 6.56 (s, 1H), 3.97 (s, 2H), 3.43 (t, $J$ = 5.4 Hz, 2H), 2.35 (s, 3H), 2.19 (s, 2H), 1.53
(quintet, \( J = 5.6 \text{ Hz}, 2\text{H} \)); \(^{13}\text{C} \) NMR (125 MHz, CDCl\(_3\)) \( \delta \) 154.7 (C), 146.2 (C), 143.8 (C), 137.6 (C), 132.4 (CH), 128.4 (CH), 124.7 (CH), 121.3 (CH), 79.6 (C), 28.4 (CH\(_3\)), 27.7 (CH\(_2\)), 26.2 (CH\(_2\)), 21.4 (CH\(_3\)) only visible signals. ATR-FTIR (thin film): 2978, 2858, 1686, 1519, 1326 cm\(^{-1}\); HRMS (EI) \( m/z \) calculated for C\(_{18}\)H\(_{23}\)N\(_2\)O\(_4\) (M–H\(^+\)): 331.16579, found: 331.16484.

1-Boc-3-(5-chloro-2-nitrobenzylidene)piperidine 2.44f. The general procedure was followed by using 3.52 g of 2.42f (11.4 mmol), 2.50 g of \( N \)-Boc-3-piperidone (12.5 mmol), 50 mL of THF and 6.5 mL of a 2.5 M solution of LDA in THF. Purification by MPLC (2:100 – 20:80 EtOAc:hexanes) afforded the product as a yellow solid as a mixture of \( Z \)- and \( E \)-isomers (2.65 g, 66%). \(^1\text{H} \) NMR (500 MHz, CDCl\(_3\)) \( \delta \) 7.97 (d, \( J = 8.5 \text{ Hz}, 1\text{H} \)), 7.38 (dd, \( J = 9.0 \text{ Hz}, 2.0 \text{ Hz}, 1\text{H} \)), 7.25 (d, \( J = 4.5 \text{ Hz}, 1\text{H} \)), 6.59 (s, 1H), 4.03 (s, 2H), 3.49 (t, \( J = 4.0 \text{ Hz}, 2\text{H} \)), 2.26 (m, 2H), 1.61 – 1.60 (m, 2H), 1.48 (s, 9H); \(^{13}\text{C} \) NMR (125 MHz, CDCl\(_3\)) \( \delta \) 154.7 (C), 146.7 (C), 139.3 (C), 139.0 (C), 134.2 (C), 131.8 (CH), 127.9 (CH), 126.1 (CH), 119.9 (CH), 79.8 (C), 52.4 (CH\(_2\)), 44.2 (CH\(_2\)), 28.4 (CH\(_3\)), 27.8 (CH\(_2\)), 26.1 (CH\(_2\)). ATR-FTIR (thin film): 2971, 2921, 1678, 1523, 1336, 1157, 1112 cm\(^{-1}\); HRMS (EI) \( m/z \) calculated for C\(_{17}\)H\(_{20}\)O\(_4\)N\(_2\)Cl (M–H\(^+\)): 351.11116, found: 351.11095.

1-Boc-3-(4-methoxy-2-nitrobenzylidene)piperidine 2.44g. The general procedure was followed by using 2.0 mL of diisopropylamine (14 mmol), 6.3 mL of a 2.5 M solution of \( n \)-BuLi in hexane (12.7 mmol), 3.49 g of 2.42g (11.5 mmol), 2.30 g of \( N \)-Boc-3-piperidone (11.5 mmol) and 110 mL of THF. Purification by MPLC (2:100 – 20:80 EtOAc:hexanes) afforded the product, a yellow oil, as an 82:18 mixture of \( E/Z \) isomers (2.11 g, 63%). Spectral data for the major isomer: \(^1\text{H} \) NMR (500 MHz,
CDCl\(_3\) δ 7.51 (d, \(J = 2.1\) Hz, 1H), 7.16 (s, 1H), 7.11 (d, \(J = 2.6\) Hz, 1H), 6.56 (s, 1H), 4.01 (s, 2H), 3.92 (s, 3H), 3.48 (t, \(J = 5.2\) Hz, 2H), 2.23 (s, 2H), 1.58 (d, \(J = 5.7\) Hz, 2H), 1.48 (s, 9H); \(^{13}\)C NMR (125 MHz, CDCl\(_3\)) δ 158.8 (C), 154.8 (C), 149.0 (C), 137.5 (C), 132.9 (CH), 124.6 (C), 120.7 (CH), 119.5 (CH), 109.0 (CH), 79.7 (C), 55.9 (CH\(_3\)), 28.5 (CH\(_3\)), 27.8 (CH\(_2\)), 26.2 (CH\(_2\)) only visible signals. ATR-FTIR (thin film): 2972, 1686, 1526, 1246, 1162 cm\(^{-1}\); HRMS (EI) \(m/z\) calculated for C\(_{18}\)H\(_{25}\)N\(_2\)O\(_5\) (M+H)\(^+\): 349.17635, found: 349.17539.

1-Boc-3-(4-methyl-2-nitrobenzylidene)piperidine 2.44h. The general procedure was followed by using 1.35 g of 2.42h (4.7 mmol), 1.02 g of N-boc-3-piperidone (5.17 mmol), 20 mL of THF and 2.5 mL of a 2.5 M solution of LDA in THF. Purification by MPLC (2:100 – 20:80 EtOAc:hexanes) afforded the product as a yellow solid as a mixture of Z- and E-isomers (1.03 g, 66%). The major E-isomer was separated. Spectral data for the E-isomer: \(^1\)H NMR (500 MHz, CDCl\(_3\)) δ 7.8 (s, 1H), 7.35 (d, \(J = 7.5\) Hz, 1H), 7.14 (d, \(J = 8\) Hz, 1H), 6.59 (s, 1H), 4.02 (s, 2H), 3.48 (t, \(J = 5.0\) Hz, 2H), 2.42 (s, 3H), 2.23 (m, 2H), 1.59 – 1.57 (m, 2H), 1.48 (s, 9H); \(^{13}\)C NMR (125 MHz, CDCl\(_3\)) δ 154.8 (C), 148.4 (C), 138.3 (C), 137.8 (C), 133.5 (CH), 131.8 (CH), 129.4 (C), 124.8 (CH), 120.8 (CH), 79.7 (C), 52.6 (CH\(_2\)), 44.3 (CH\(_2\)), 28.5 (CH\(_3\)), 27.8 (CH\(_2\)), 26.2 (CH\(_2\)), 20.9 (CH\(_3\)). ATR-FTIR (thin film): 2975, 2931, 2853, 1689, 1526, 1410, 1343, 1238, 1159 cm\(^{-1}\).

3-(4-Chloro-2-nitrobenzylidene)-1-(phenylsulfonyl)piperidine 2.44i. The general procedure was followed by using 1.7 mL of diisopropylamine (12.1 mmol), 5.5 mL of a 2.5 M solution of \(n\)-BuLi in hexane (11 mmol), 3.01 g of 2.42i (9.8 mmol), 2.4 g of \(N\)-phenylsulfonyl-3-piperidone (10 mmol) and 80 mL THF. Purification by MPLC
(2:100 – 20:80 EtOAc:hexanes) afforded the product as a yellow solid (1.98 g, 51%): 

$^1$H NMR (500 MHz, CDCl$_3$) $\delta$ 8.06 (d, $J = 2.1$ Hz, 1H), 7.68 (d, $J = 7.5$ Hz, 2H), 7.64 (dd, $J = 8.3$, 2.1 Hz, 1H), 7.59 (t, $J = 7.4$ Hz, 1H), 7.50 (t, $J = 7.7$ Hz, 2H), 7.44 (d, $J = 8.3$ Hz, 1H), 6.61 (s, 1H), 3.52 (s, 2H), 3.17 (t, $J = 5.5$ Hz, 2H), 2.30 (d, $J = 6.0$ Hz, 2H), 1.85 (quintet, $J = 5.7$ Hz, 2H); 

$^{13}$C NMR (125 MHz, CDCl$_3$) $\delta$ 148.2 (C), 136.6 (C), 136.0 (C), 134.1 (C), 133.9 (CH), 133.6 (CH), 132.9 (CH), 130.1 (C), 129.1 (CH), 127.6 (CH), 124.9 (CH), 121.6 (CH), 47.8 (CH$_2$), 46.8 (CH$_2$), 33.9 (CH$_2$), 26.3 (CH$_2$). 

ATR-FTIR (thin film): 2952, 1518, 1340, 1162 cm$^{-1}$; 

HRMS (EI) $m/z$ calculated for C$_{18}$H$_{16}$N$_2$O$_4$ScI (M–H)$^+$: 391.05193, found: 391.05278.

1-Boc-3-(2-nitro-4-(trifluoromethyl)benzyldene)piperidine 2.44j. The general procedure was followed by using 1.4 mL of diisopropylamine (9.8 mmol), 3.6 mL of a 2.5 M solution of $n$-BuLi in hexane (8.9 mmol), 2.75 g of 2.42j (8.1 mmol), 1.65 g of N-sulfonyl-3-piperidone (8.1 mmol) and 100 mL of THF. Purification by MPLC (2:100 – 20:80 EtOAc:hexanes) afforded the product, a yellow solid, as a 79:21 mixture of isomers (1.86 g, 63%). Spectral data for the major isomer: 

$^1$H NMR (500 MHz, CDCl$_3$) $\delta$ 8.24 (s, 1H), 7.79 (d, $J = 8.1$ Hz, 1H), 7.43 (d, $J = 8.1$ Hz, 1H), 6.63 (s, 1H), 4.04 (s, 2H), 3.49 (t, $J = 5.1$ Hz, 2H), 2.24 (s, 2H), 1.60 (s, 2H), 1.47 (s, 9H); 

$^{13}$C NMR (125 MHz, CDCl$_3$) $\delta$ 154.7 (C), 148.4 (C), 140.3 (C), 135.9 (C), 133.0 (CH), 130.4 (q, $J_{CF} = 32.4$ Hz, C), 129.1 (CH), 122.8 (q, $J_{CF} = 273$ Hz, CF$_3$), 121.9 (CH), 119.7 (CH), 79.9 (C), 34.6 (CH$_2$), 28.4 (CH$_3$), 27.9 (CH$_2$), 26.9 (CH$_2$), 26.2 (CH$_2$). 

ATR-FTIR (thin film): 2945, 1572, 1340, 1162 cm$^{-1}$; 

HRMS (EI) $m/z$ calculated for C$_{18}$H$_{21}$N$_2$O$_4$F$_3$ (M)$^+$: 386.14535, found: 386.14606.
1-Boc-3-(3-methyl-2-nitrobenzylidene)piperidine 2.44k. The general procedure was followed by using 3.00 g of 2.42k (10.4 mmol), 2.15 g of N-Boc-3-piperidone (10.8 mmol), 100 mL of THF and 6.3 mL of a 2.5 M solution of LDA in THF. Purification by MPLC (2:100 – 20:80 EtOAc:hexanes) afforded the product, a yellow oil, as a 66:34 ratio of E/Z isomers (2.8 g, 81%). Spectral data for the major product: $^1$H NMR (500 MHz, CDCl$_3$) $\delta$ 7.27 (t, $J$ = 7.1 Hz, 1H), 7.14 (d, $J$ = 7.6 Hz, 1H), 7.03 (d, $J$ = 7.7 Hz, 1H), 6.23 (s, 1H), 3.91 (s, 2H), 3.42 (t, $J$ = 5.2 Hz, 2H), 2.26 (s, 3H), 2.23 (s, 2H), 1.53 (quintet, 2H), 1.43 (s, 9H); $^{13}$C NMR (125 MHz, CDCl$_3$) $\delta$ 154.7 (C), 150.6 (C), 151.1 (C), 140.8 (C), 129.9 (CH), 129.7 (CH), 129.5 (C), 128.5 (CH), 128.2 (CH), 118.2 (C), 79.7 (C), 28.4 (CH$_3$), 27.8 (CH$_2$), 26.2 (CH$_2$), 17.3 (CH$_3$) only visible signals. ATR-FTIR (thin film): 2974, 1686, 1526, 1363, 1162 cm$^{-1}$; HRMS (El) m/z calculated for C$_{18}$H$_{23}$N$_2$O$_4$ (M–H)$^+$: 331.16579, found: 331.1666.

1-Boc-3-(3-methoxy-2-nitrobenzylidene)piperidine 2.44l. The general procedure was followed by using 3.35 g of 2.42l (11.5 mmol), 2.27 g of N-boc-3-piperidone (11.4 mmol), 100 mL of THF and 7 mL of a 2.5 M solution of LDA in THF. Purification by MPLC (2:100 – 20:80 EtOAc:hexanes) afforded the product, a yellow oil, as a 66:34 mixture of E/Z isomers (3.35 g, 87%). Spectral data for the major isomer: $^1$H NMR (500 MHz, CDCl$_3$) $\delta$ 7.26 (t, $J$ = 8.1 Hz, 1H), 6.86 (d, $J$ = 8.4 Hz, 1H), 6.71 (d, $J$ = 7.7 Hz, 1H), 6.14 (s, 1H), 3.85 (s, 2H), 3.76 (s, 3H), 3.37 (t, $J$ = 5.2 Hz, 2H), 2.20 (s, 2H), 1.48 (quintet, 2H), 1.37 (s, 9H); $^{13}$C NMR (125 MHz, CDCl$_3$) $\delta$ 154.6 (C), 150.6 (C), 141.1 (C), 130.5 (CH), 122.2 (C), 121.9 (CH), 117.4 (CH), 111.1 (CH), 79.6 (C), 56.3 (CH$_3$), 28.3 (CH$_3$), 27.9 (CH$_2$), 26.2 (CH$_2$) only visible signals. ATR-
FTIR (thin film): 2978, 1686, 1533, 1363, 1159 cm\(^{-1}\); HRMS (El) \(m/z\) calculated for \(\text{C}_{18}\text{H}_{23}\text{N}_{2}\text{O}_{5}\) (M–H\(^+\)): 347.16154, found: 347.16070.

**3-(2-nitrobenzylidene)tetrahydro-2H-pyran 2.49.** The general procedure was followed by using 2.73 g of 2.42 (10.0 mmol), 1.00 g of 3-oxacyclohexanone (10.0 mmol), 100 mL THF and 5.0 mL of 2.5 M solution of LDA in THF. Purification by MPLC (2:100 – 20:80 EtOAc:hexanes) afforded the product, a yellow oil, as a 78:22 mixture of isomers (1.19 g, 54\%). Spectral data for the major isomer: \(^1\)H NMR (500MHz, CDCl\(_3\)) \(\delta\) 8.00 (d, \(J = 8.2\) Hz, 1H), 7.60 (t, \(J = 7.6\) Hz, 1H), 7.44 (t, \(J = 7.5\) Hz, 1H), 7.34 (d, \(J = 7.4\) Hz, 1H), 6.63 (s, 1H), 4.20 (s, 2H), 3.80 (t, \(J = 5.2\) Hz, 2H), 2.36 (t, \(J = 6.3\) Hz, 2H), 1.71 (quintet, \(J = 5.7\) Hz, 2H); \(^{13}\)C NMR (125 MHz, CDCl\(_3\)) \(\delta\) 148.5 (C), 139.4 (C), 132.7 (CH), 132.0 (CH), 127.9 (CH), 124.5 (CH), 120.3 (CH), 73.9 (CH\(_2\)), 68.3 (CH\(_2\)), 27.6 (CH\(_2\)), 26.8 (CH\(_2\)) only visible signals. Diagnostic spectral data for the minor isomer: \(^{13}\)C NMR (125 MHz, CDCl\(_3\)) \(\delta\) 148.4 (2C), 132.8 (CH), 127.9 (CH), 124.6 (CH), 120.6 (C), 67.5 (CH\(_2\)), 33.4 (CH\(_2\)), 28.4 (CH\(_2\)) only visible signals; ATR-FTIR (thin film): 2946, 2835, 1521, 1340, 1082 cm\(^{-1}\); HRMS (El) \(m/z\) calculated for \(\text{C}_{12}\text{H}_{12}\text{NO}_3\) (M–H\(^+\)): 218.08172, found: 218.08141.

**D. Preparation of aniline from nitrobenzylidine.**

To a 0.1 M solution of nitrobenzylidene in a 1:1 mixture of EtOH and acetic acid was added iron powder (8 equiv). The resulting mixture was heated to reflux. After 2h, the reaction mixture was cooled to room temperature and filtered over a bed of silica gel. The residue was eluted with ethyl acetate. The filtrate was concentrated
in vacuo, diluted with a saturated aqueous solution of Na₂CO₃ and extracted with 5 × 15 mL of ethyl acetate. The combined organic phases were dried over Na₂SO₄, filtered and concentrated in vacuo. Purification of the resulting residue by MPLC (10:90 – 50:50 EtOAc:hexanes) afforded the product.

1-Boc-(2-aminobenzylidene)piperidine 2.45c. The general procedure was followed by using 1.75 g of 2.44c (5.50 mmol), 2.45 g of iron powder (43.8 mmol) and 100 mL of the 1:1 mixture of ethanol and acetic acid. Purification by MPLC (10:90 – 50:50 EtOAc:hexanes) afforded the product, a yellow solid, as a 70:30 mixture of isomers (1.26 g, 80%). Spectral data for the major isomer: ¹H NMR (500 MHz, CDCl₃) δ 7.07 (t, J = 7.5 Hz, 1H), 6.97 (d, J = 7.5 Hz, 1H), 6.71 (dd, J = 18.7, 7.6 Hz, 2H), 6.22 (s, 1H), 4.03 (s, 2H), 3.67 (s, 2H), 3.49 (t, J = 5.0 Hz, 2H), 2.34 (t, J = 6.1 Hz, 2H), 1.58 (s, 2H), 1.48 (s, 9H); ¹³C NMR (125 MHz, CDCl₃) δ 154.9 (C), 144.4 (C), 129.9 (CH), 128.1 (CH), 122.5 (C), 120.8 (CH), 118.0 (CH), 115.1 (CH), 99.6 (C), 44.6 (CH₂), 34.4 (CH₂), 28.5 (CH₃), 27.8 (CH₂), 26.4 (CH₂) only visible signals. ATR-FTIR (thin film): 3465, 3348, 2938, 1673, 1410, 1158 cm⁻¹; HRMS (EI) m/z calculated for C₁₇H₂₄N₂O₂ (M)⁺: 288.18378, found: 288.18465.

2-((1-(Phenylsulfonyl)azetidin-3-ylidene)methyl)aniline 2.45a. The general procedure was followed by using 1.29 g of nitrobenzylidineazetidine (3.90 mmol), 1.74 g of iron powder (31.1 mmol) and 50 mL of the 1:1 mixture of ethanol and acetic acid. Purification by MPLC (10:90 – 50:50 EtOAc:hexanes) afforded the product as a yellow solid (0.220 g, 19%): ¹H NMR (500 MHz, CDCl₃) δ 7.94 (d, J = 7.5 Hz, 2H), 7.69 (t, J = 7.4 Hz, 1H), 7.62 (t, J = 7.6 Hz, 2H), 7.08 (t, J = 7.5 Hz, 1H), 6.82 (d, J = 7.4 Hz, 1H), 6.73 (t, J = 7.5 Hz, 1H), 6.70 (d, J = 8.0 Hz, 1H), 6.25 (s, 1H), 4.64 (s,
2H), 4.60 (s, 2H), 3.70 (br s, 2H); $^{13}$C NMR (125 MHz, CDCl$_3$) $\delta$ 143.8 (C), 134.9 (C), 133.5 (CH), 129.4 (CH), 128.8 (CH), 128.4 (CH), 127.8 (C), 127.4 (CH), 120.8 (C), 118.9 (CH), 118.8 (CH), 116.4 (CH), 60.1 (CH$_2$). ATR-FTIR (thin film): 3466, 3377, 3068, 2928, 1623, 1158 cm$^{-1}$; HRMS (EI) m/z calculated for C$_{16}$H$_{16}$N$_2$O$_2$S (M)$^+$: 300.09325, found: 300.09007.

2-((1-(Phenylsulfonyl)pyrrolidin-3-ylidene)methyl)aniline 2.45b. The general procedure was followed by using 0.830 mg of nitrobenzylidene.pyrrolidine (2.40 mmol), 1.08 g of iron powder (19.3 mmol) and 40 mL of the 1:1 mixture of ethanol and acetic acid. Purification by MPLC (10:90 – 50:50 EtOAc:hexanes) afforded the product as a yellow oil (0.545 g, 72%). $^1$H NMR (500 MHz, CDCl$_3$) $\delta$ 7.86 (d, $J$ = 7.4 Hz, 2H), 7.62 (t, $J$ = 7.4 Hz, 1H), 7.56 (t, $J$ = 7.5 Hz, 2H), 7.03 (t, $J$ = 7.6 Hz, 1H), 6.95 (d, $J$ = 7.5 Hz, 1H), 6.69 (t, $J$ = 7.4 Hz, 1H), 6.66 (d, $J$ = 8.0 Hz, 1H), 6.25 (s, 1H), 3.99 (s, 2H), 3.49 (br s, 2H), 3.33 (t, $J$ = 7.1 Hz, 2H), 2.57 (t, $J$ = 6.8 Hz, 2H); $^{13}$C NMR (125 MHz, CDCl$_3$) $\delta$ 144.0 (C), 138.5 (C), 135.8 (C), 133.0 (CH), 129.2 (CH), 128.9 (CH), 128.4 (CH), 127.9 (CH), 122.4 (C), 118.4 (CH), 118.2 (CH), 115.6 (CH), 53.1 (CH$_2$), 48.3 (CH$_2$), 29.5 (CH$_2$). ATR-FTIR (thin film): 3463, 3376, 2958, 1619, 1445, 1334, 1154 cm$^{-1}$; HRMS (EI) m/z calculated for C$_{17}$H$_{18}$N$_2$O$_2$S (M)$^+$: 314.10890, found: 314.10987.

4-Methoxy-2-((1-(phenylsulfonyl)piperidin-3-ylidene)methyl)aniline 2.45d. The general procedure was followed by using 1.66 g of nitrobenzylidene.piperidine (4.3 mmol), 1.70 g of iron powder (30.4 mmol) and 60 mL of the 1:1 mixture of ethanol and acetic acid. Purification by MPLC (10:90 – 50:50 EtOAc:hexanes) afforded the product as a yellow solid (1.47 g, 96%): $^1$H NMR (500 MHz, CDCl$_3$) $\delta$ 7.80 (d, $J$ = 7.3 Hz, 2H), 6.90 (d, $J$ = 7.8 Hz, 1H), 6.75 (d, $J$ = 7.8 Hz, 1H), 6.50 (d, $J$ = 7.8 Hz, 1H), 6.25 (s, 1H), 3.80 (s, 2H), 3.30 (br s, 2H), 2.80 (t, $J$ = 6.8 Hz, 2H); $^{13}$C NMR (125 MHz, CDCl$_3$) $\delta$ 144.0 (C), 138.5 (C), 135.8 (C), 133.0 (CH), 129.2 (CH), 128.9 (CH), 128.4 (CH), 127.9 (CH), 122.4 (C), 118.4 (CH), 118.2 (CH), 115.6 (CH), 53.1 (CH$_2$), 48.3 (CH$_2$), 29.5 (CH$_2$). ATR-FTIR (thin film): 3463, 3376, 2958, 1619, 1445, 1334, 1154 cm$^{-1}$; HRMS (EI) m/z calculated for C$_{17}$H$_{18}$N$_2$O$_2$S (M)$^+$: 314.10890, found: 314.10987.
Hz, 2H), 7.60 (t, J = 7.2 Hz, 1H), 7.54 (t, J = 7.4 Hz, 2H), 6.66–6.60 (m, 2H), 6.45 (d, J = 2.3 Hz, 1H), 6.26 (s, 1H), 3.68 (s, 5H), 3.44 (s, 2H), 3.15 (t, J = 5.2 Hz, 2H), 2.18 (t, J = 5.7 Hz, 2H), 1.62 (s, 2H); ^{13}C NMR (125 MHz, CDCl$_3$) δ 152.1 (C), 138.2 (C), 136.4 (C), 135.9 (C), 132.9 (CH), 129.1 (CH), 127.8 (CH), 123.1 (C), 122.7 (CH), 116.4 (CH), 115.2 (CH), 114.0 (CH), 55.8 (CH$_3$), 53.8 (CH$_2$), 46.9 (CH$_2$), 27.1 (CH$_2$), 25.3 (CH$_2$). ATR-FTIR (thin film): 3438, 3352, 2985, 1578, 1496, 1279, 1167 cm$^{-1}$; HRMS (EI) m/z calculated for C$_{19}$H$_{22}$N$_2$O$_2$S (M)$^+$: 358.13512, found: 358.13422.

2.45e

4-Methyl-2-((1-(phenylsulfonyl)piperidin-3-ylidene)methyl)aniline 2.45e. The general procedure was followed by using 2.60 g of nitrobenzylidene piperidine (7.8 mmol), 3.50 g of iron powder (62.5 mmol) and 120 mL of the 1:1 mixture of ethanol and acetic acid. Purification by extraction afforded the product as a yellow oil (2.30 g, 97%). This product was converted to the azide without purification by MPLC. $^1$H NMR (500 MHz, CDCl$_3$) δ 6.86 (d, J = 7.8 Hz, 1H), 6.78 (s, 1H), 6.61 (d, J = 8.0 Hz, 1H), 6.20 (s, 1H), 5.52 (br s, 2H), 4.01 (s, 2H), 3.48 (t, J = 5.3 Hz, 2H), 2.33 (t, J = 5.9 Hz, 2H), 2.21 (s, 3H), 1.57 (s, 2H), 1.47 (s, 9H); $^{13}$C NMR (125 MHz, CDCl$_3$) δ 175.8 (C), 155.0 (C), 141.6 (C), 130.2 (CH), 128.6 (CH), 127.3 (C), 122.7 (C), 121.0 (CH), 115.5 (CH), 79.7 (C), 53.5 (CH$_2$), 34.3 (CH$_2$), 28.5 (CH$_3$), 27.8 (CH$_2$), 23.3 (CH$_2$), 20.5 (CH$_3$); ATR-FTIR (thin film): 3470, 3365, 2930, 1680, 1496, 1279, 1167 cm$^{-1}$; HRMS (EI) m/z calculated for C$_{18}$H$_{22}$N$_2$O$_2$S (M)$^+$: 302.19943, found: 302.20010.

2.45f

4-Chloro-2-((1-(phenylsulfonyl)piperidin-3-ylidene)methyl)aniline 2.45f. The general procedure was followed by using 1.60 g of nitrobenzylidene piperidine (4.0 mmol), 1.79 g of iron powder (32 mmol) in 40 mL of a 1:1 mixture of glacial acetic acid and ethanol. Purification by MPLC (0:100 – 20:80 EtOAc:hexanes) afforded the
product, a yellow solid, as a 50:50 mixture of E- and Z- isomers (0.72 g, 49%).
Spectral data for one isomer: $^1$H NMR (500 MHz, CDCl$_3$) $\delta$ 7.80 (d, $J$ = 7.5 Hz, 2H), 7.63 – 7.43 (m, 3H), 7.02 (dd, $J$ = 8.5, 2.0 Hz, 1H), 6.91 (d, $J$ = 1.5 Hz, 1H), 6.63 (d, $J$ = 7.5 Hz, 1H), 6.18 (s, 1H), 3.68 (s, 2H), 3.55(s, 2H), 3.16 (t, $J$ = 5.5 Hz, 2H), 2.25 (t, $J$ = 5.5 Hz, 2H), 1.81 – 1.77 (m, 2H); $^{13}$C NMR (125 MHz, CDCl$_3$) $\delta$ 143.1 (C), 136.6 (C), 136.4 (C), 132.9 (CH), 129.3 (CH), 129.1 (CH), 128.3 (CH), 127.8 (CH), 123.2 (C), 122.6 (C), 121.6 (CH), 116.7 (CH), 53.7 (CH$_2$), 47.8 (CH$_2$), 27.1 (CH$_2$), 25.3 (CH$_2$). ATR-FTIR (thin film): 3476, 3374, 2940, 2835, 1570, 1159 cm$^{-1}$; HRMS (EI) m/z calculated for C$_{18}$H$_{19}$O$_2$N$_2$SCl (M)$^+$: 362.08558, found: 362.08544.

2.45g 3-Methoxy-6-((1-(phenylsulfonyl)piperidin-3-ylidene)methyl)aniline 2.45g. The general procedure was followed by using 1.56 g of nitrobenzylideneepiperidine (4.0 mmol), 1.80 g of iron powder (32.1 mmol) and 60 mL of the 1:1 mixture of ethanol and acetic acid. Purification by MPLC (10:90 – 50:50 EtOAc:hexanes) afforded the product, a yellow oil, as a 84:16 mixture of isomers (1.40 g, 98%). Spectral data for the major product: $^1$H NMR (500 MHz, CDCl$_3$) $\delta$ 7.80 (d, $J$ = 7.5 Hz, 2H), 7.60 (t, $J$ = 7.4 Hz, 1H), 7.53 (t, $J$ = 7.5 Hz, 2H), 6.76 (d, $J$ = 8.2 Hz, 1H), 6.27–6.23 (m, 2H), 6.21 (s, 1H), 3.72 (s, 5H), 3.67 (s, 2H), 3.15 (t, $J$ = 5.4 Hz, 2H), 2.18 (t, $J$ = 6.1 Hz, 2H), 1.61 (quintet, $J$ = 5.8 Hz, 2H); $^{13}$C NMR (125 MHz, CDCl$_3$) $\delta$ 160.0 (C), 145.8 (C), 136.4 (C), 134.9 (C), 132.9 (CH), 130.7 (CH), 129.1 (CH), 127.8 (CH), 122.4 (CH), 114.8 (C), 103.7 (CH), 100.5 (CH), 55.2 (CH$_3$), 53.9 (CH$_2$), 47.0 (CH$_2$), 27.0 (CH$_2$), 25.4 (CH$_2$). ATR-FTIR (thin film): 3476, 3374, 2940, 2835, 1570, 1159 cm$^{-1}$; HRMS (EI) m/z calculated for C$_{19}$H$_{22}$N$_2$O$_3$S (M)$^+$: 358.13512, found: 358.13438.
3-Methyl-2-((1-(phenylsulfonyl)piperidin-3-ylidene)methyl)aniline 2.45h. The general procedure was followed by using 0.77 g of nitrobenzyldenepiperidine (2.1 mmol), 0.94 g of iron powder (16.8 mmol) in 40 mL of a 1:1 mixture of glacial acetic acid and ethanol. Purification by MPLC (0:100 − 20:80 EtOAc:hexanes) afforded the product, a yellow solid, as a mixture of E- and Z- isomers (0.36 g, 56%). The major (E) isomer was separated. Spectral data for major E- isomer: $^1$H NMR (500 MHz, CDCl$_3$) δ 7.82 (dd, $J$ = 8.0 Hz, 1.0 Hz, 2H), 7.61 − 7.54 (m, 3H), 6.77 (d, $J$ = 8.0 Hz, 1H), 6.52 (d, $J$ = 6.5 Hz, 2H), 6.26 (s, 1H), 3.70 (s, 2H), 3.64 (s, 2H), 3.17 (t, $J$ = 5.5 Hz, 2H), 2.24 (s, 3H), 2.20 (t, $J$ = 6.0 Hz, 2H), 1.62 (t, $J$ = 5.5 Hz, 2H); $^{13}$C NMR (125 MHz, CDCl$_3$) δ 141.4 (C), 138.3 (C), 136.4 (C), 135.2 (C), 132.9 (CH), 129.7 (CH), 129.1 (CH), 127.8 (CH), 122.7 (CH), 119.1 (C), 118.8 (CH), 115.9 (CH), 53.9 (CH$_2$), 46.9 (CH$_2$), 27.1 (CH$_2$), 25.4 (CH$_2$), 21.3 (CH$_3$). ATR-FTIR (thin film): 3470, 3375, 2948, 2924, 1617, 1441, 1340, 1159 cm$^{-1}$; HRMS (EI) m/z calculated for C$_{19}$H$_{22}$N$_2$O$_2$S (M)$^+$: 342.14020, found: 342.13961.

3-chloro-6-((1-(phenylsulfonyl)piperidin-3-ylidene)methyl)aniline 2.45i. The general procedure was followed by using 0.552 g of nitrobenzyldenepiperidine (1.4 mmol), 0.629 g of iron powder (11.2 mmol) and 30 mL of the 1:1 mixture of ethanol and acetic acid. Purification by MPLC (10:90 − 50:50 EtOAc:hexanes) afforded the product as a yellow solid with 80% purity (0.426 g, 84%). This material was converted to the aryl azide without further purification. $^1$H NMR (500 MHz, CDCl$_3$) δ 7.79 (d, $J$ = 7.5 Hz, 2H), 7.59 (d, $J$ = 7.5 Hz, 1H), 7.53 (t, $J$ = 7.5 Hz, 2H), 6.74 (d, $J$ = 8.1 Hz, 1H), 6.64 (s, 1H), 6.60 (d, $J$ = 8.0 Hz, 1H), 6.17 (s, 1H), 3.80 (br s, 2H), 3.66 (s, 2H), 3.14 (t, $J$ = 5.3 Hz, 2H), 2.12 (t, $J$ = 6.0 Hz, 2H), 1.60 (quintet, $J$ = 5.6 Hz,
2H). ATR-FTIR (thin film): 3471, 3378, 2944, 1565, 1163 cm⁻¹; HRMS (EI) m/z calculated for C₁₈H₁₉ClN₂O₂S (M)⁺: 362.08558, found: 362.08516.

5-Trifluoromethyl-2-((1-(phenylsulfonyl)piperidin-3-ylidene)methyl)aniline

2.45j. The general procedure was followed by using 1.79 g of nitrobenzylidenepiperidine (4.2 mmol), 1.90 g of iron powder (34.0 mmol) and 60 mL of the 1:1 mixture of ethanol and acetic acid. Purification by extraction afforded the product as a brown oil (1.50 g, 90%). This material was converted to the aryl azide without further purification. ¹H NMR (500 MHz, CDCl₃) δ 7.70 (d, J = 7.4 Hz, 2H), 7.58 (t, J = 7.4 Hz, 1H), 7.50 (t, J = 7.7 Hz, 2H), 7.06 (d, J = 7.9 Hz, 1H), 6.98 (d, J = 7.9 Hz, 1H), 6.93 (s, 1H), 6.18 (s, 1H), 3.56 (s, 2H), 3.19 (t, J = 5.4 Hz, 2H), 2.29 (t, J = 6.0 Hz, 2H), 1.84 (quintet, J = 5.7 Hz, 2H). ATR-FTIR (thin film): 3476, 3381, 2941, 2846, 1623, 1329, 1161 cm⁻¹; HRMS (EI) m/z calculated for C₁₉H₁₉F₃N₂O₂S (M)⁺: 396.11194, found: 396.11275.

2-Methyl-6-((1-(phenylsulfonyl)piperidin-3-ylidene)methyl)aniline 2.45k. The general procedure was followed by using 2.11 g of nitrobenzylidenepiperidine (5.7 mmol), 2.50 g of iron powder (44.6 mmol) and 100 mL of the 1:1 mixture of ethanol and acetic acid. Purification by extraction afforded the product as a yellow solid (1.90 g, 98%). This material was converted to the aryl azide without further purification. ¹H NMR (500 MHz, CDCl₃) δ 7.81 (d, J = 7.5 Hz, 2H), 7.67 (d, J = 7.6 Hz, 1H), 7.55 (t, J = 7.3 Hz, 2H), 6.96 (d, J = 7.3 Hz, 1H), 6.75 (d, J = 7.5 Hz, 1H), 6.61 (t, J = 7.5 Hz, 1H), 6.30 (s, 1H), 3.70 (s, 2H), 3.67 (br s, 2H), 3.16 (t, J = 5.0 Hz, 2H), 2.18 (t, J = 6.3 Hz, 2H), 2.15 (s, 3H), 1.62 (quintet, J = 5.5 Hz, 2H). ATR-FTIR
(thin film): 3433, 3362, 2940, 1573, 1441, 1159 cm$^{-1}$; HRMS (El) m/z calculated for C$_{19}$H$_{22}$N$_2$O$_3$S (M)$^+$: 342.14020, found: 342.13987.

2.45I

2-Methoxy-6-((1-phenylsulfonyl)piperidin-3-ylidene)methyl)aniline 2.45I. The general procedure was followed by using 2.30 g of nitrobenzylidenepiperidine (5.9 mmol), 2.65 g of iron powder (47.3 mmol) and 100 mL of the 1:1 mixture of ethanol and acetic acid. Purification by extraction afforded the product as a yellow solid (2.05 g, 97%). This material was converted to the aryl azide without further purification. $^1$H NMR (500 MHz, CDCl$_3$) δ 7.81 (d, J = 7.5 Hz, 2H), 7.60 (t, J = 7.1 Hz, 1H), 7.54 (t, J = 7.4 Hz, 2H), 6.69 (d, J = 7.8 Hz, 1H), 6.63 (t, J = 7.8 Hz, 1H), 6.53 (d, J = 7.6 Hz, 1H), 6.28 (s, 1H), 3.82 (br s, 2H), 3.80 (s, 3H), 3.70 (s, 2H), 3.15 (t, J = 5.3 Hz, 2H), 2.17 (t, J = 6.1 Hz, 2H), 1.60 (quintet, J = 5.6 Hz, 2H). ATR-FTIR (thin film): 3474, 3379, 2944, 2832, 1567, 1349, 1164 cm$^{-1}$; HRMS (El) m/z calculated for C$_{19}$H$_{22}$N$_2$O$_3$S (M)$^+$: 358.13512, found: 358.13461.

2.50

2-((2H-pyran-3(4H,5H,6H)-ylidene)methyl)aniline 2.50. The general procedure was followed by using 1.09 g of 2.49 (5.00 mmol), 2.23 g of iron powder (40.0 mmol) and 100 mL of the 1:1 mixture of ethanol and acetic acid. Purification by MPLC (10:90 – 50:50 EtOAc:hexanes) afforded the product, a yellow oil, as a 78:22 mixture of isomers (0.930 g, 99%). Spectral data for the major isomer: $^1$H NMR (500MHz, CDCl$_3$) δ 7.09 (t, J = 7.6 Hz, 1H), 7.00 (t, J = 7.5 Hz, 1H), 6.74 (t, J = 7.5 Hz, 1H), 6.70 (d, J = 8.1 Hz, 1H), 6.19 (s, 1H), 4.20 (s, 2H), 3.81 (t, J = 5.2 Hz, 2H), 3.74 (br s, 2H), 2.44 (t, J = 5.9 Hz, 2H), 1.69 (quintet, J = 5.7 Hz, 2H); $^{13}$C NMR (125 MHz, CDCl$_3$ δ 144.5 (C), 139.2 (C), 129.9 (CH), 128.2 (CH), 122.2 (C), 120.3 (CH), 118.0
(CH), 115.2 (CH), 74.2 (CH₂), 68.6 (CH₂), 27.8 (CH₂), 27.0 (CH₂). Diagnostic data for the minor isomer: $^{13}$C NMR (125 MHz, CDCl₃ $\delta$ 144.2 (C), 139.1 (C), 130.2 (CH), 122.2 (C), 120.6 (CH), 118.1 (CH), 68.3 (CH₂), 68.0 (CH₂), 33.2 (CH₂), 28.7 (CH₂). ATR-FTIR (thin film): 3456, 3358, 2951, 2832, 1615, 1492, 1078 cm⁻¹; HRMS (EI) $m/z$ calculated for C₁₂H₁₅NO (M)$^+$: 189.11537, found: 189.11456.

E. Preparation of styryl azide from aniline.

Following the procedure of Zhang and Moses, the azides were prepared. Yields were not optimized.

\begin{center}
\begin{tikzpicture}
\node[draw,shape=circle,inner sep=1.5pt] (a) at (0,0) {2.45};
\node[draw,shape=circle,inner sep=1.5pt] (b) at (1,0) {2.46};
\node[above] at (0.5,0.5) {F.G.};
\node[above] at (1.5,0.5) {F.G.};
\draw[->] (a) -- (b) node[midway,above] {t-BuONO \ Me₃SiN₃ MeCN};
\end{tikzpicture}
\end{center}

To a cooled solution of aniline in MeCN (0.1 M) was added dropwise t-BuNO₂ (4 equiv) and Me₃SiN₃ (3 equiv). The resulting solution was warmed to room temperature. After 1h, visualization of the reaction progress using TLC indicated the consumption of the starting material. De–ionized water was added to the reaction mixture. The mixture then was extracted with $2 \times 30$ mL of CH₂Cl₂. The combined organic phases were washed with 20 mL of brine. The resulting organic phase was dried over Na₂SO₄, filtered, and the filtrate was concentrated in vacuo. Purification of the residue by MPLC (2:98 – 10:90 EtOAc: hexanes) afforded azide.

\begin{center}
\begin{tikzpicture}
\node[draw,shape=circle,inner sep=1.5pt] (a) at (0,0) {2.46c};
\node[above] at (0.5,0.5) {Boc};
\node[above] at (0.5,0.8) {H};
\end{tikzpicture}
\end{center}

1-Boc-3-(2-azidobenzylidene)piperidine 2.46c. The general procedure was followed by using 0.894 g of 2.45c (3.1 mmol), 1.50 mL of t-BuNO₂ (12.4 mmol), 1.31 mL of Me₃SiN₃ (9.3 mmol) and 20 mL of MeCN. Purification by MPLC (2:98 – 10:90 EtOAc: hexanes) afforded the product, a yellow oil, as a 76:24 mixture of isomers (0.894 g, 91%). Spectral data for the major isomer: $^1$H NMR (500 MHz, CDCl₃) $\delta$ 7.27 (t, $J = 7.7$ Hz, 1H), 7.15 (dd, $J = 12.3$, 7.6 Hz, 2H), 7.10 (q, $J = 6.8$ Hz,
1H), 6.35 (s, 1H), 4.04 (s, 2H), 3.51 (t, J = 5.4 Hz, 2H), 2.38 (t, J = 6.0 Hz, 2H), 1.63 (s, 2H), 1.51 (s, 9H); 13C NMR (125 MHz, CDCl\textsubscript{3}) δ 154.8 (C), 138.2 (C), 137.7 (C), 130.7 (CH), 128.8 (C), 128.2 (CH), 124.4 (CH), 120.4 (CH), 118.4 (CH), 79.5 (C), 34.7 (CH\textsubscript{2}), 31.6 (CH\textsubscript{2}), 28.5 (CH\textsubscript{3}), 27.7 (CH\textsubscript{2}), 26.2 (CH\textsubscript{2}). ATR-FTIR (thin film): 2975, 2852, 2115, 2083, 1688, 1163 cm\textsuperscript{-1}; HRMS (EI) m/z calculated for C\textsubscript{17}H\textsubscript{22}N\textsubscript{2}O\textsubscript{2} (M–N\textsubscript{2})\textsuperscript{+} : 286.16813, found: 286.16872.

![2.46a](image)

3-(2-Azidobenzylidene)-1-(phenylsulfonyl)azetidine 2.46a. The general procedure was followed by using 0.200 g of 2.45a (0.67 mmol), 0.32 mL of t-BuNO\textsubscript{2} (2.7 mmol), 0.28 mL of Me\textsubscript{3}SiN\textsubscript{3} (2.0 mmol) and 10 mL of MeCN. Purification by MPLC (2:98 – 10:90 EtOAc: hexanes) afforded the product as a white solid (0.0924 mg, 43%): 1H NMR (500 MHz, CDCl\textsubscript{3}) δ 7.90 (d, J = 7.2 Hz, 2H), 7.65 (t, J = 7.4 Hz, 1H), 7.59 (t, J = 7.5 Hz, 2H), 7.26 (t, J = 7.7 Hz, 1H), 7.11 (d, J = 8.0 Hz, 1H), 7.06 (t, J = 7.5 Hz, 1H), 6.89 (d, J = 7.7 Hz, 1H), 6.42 (s, 1H), 4.68 (s, 2H), 4.57 (s, 2H); 13C NMR (125 MHz, CDCl\textsubscript{3}) δ 137.2 (C), 135.0 (C), 133.4 (CH), 129.3 (CH), 128.8 (CH), 128.7 (C), 128.4 (CH), 127.4 (C), 126.8 (C), 124.8 (CH), 118.6 (CH), 118.0 (CH), 60.3 (CH\textsubscript{2}), 60.1 (CH\textsubscript{2}). ATR-FTIR (thin film): 3008, 2813, 2121, 1485, 1343, 1152 cm\textsuperscript{-1}; HRMS (EI) m/z calculated for C\textsubscript{16}H\textsubscript{14}N\textsubscript{4}O\textsubscript{2}S (M)\textsuperscript{+}: 326.08374, found: 326.08331.

![2.46b](image)

3-(2-Azidobenzylidene)-1-(phenylsulfonyl)pyrrolidine 2.46b. The general procedure was followed by using 0.537 g of 2.45b (1.7 mmol), 0.81 mL of t-BuNO\textsubscript{2} (6.8 mmol), 0.72 mL of Me\textsubscript{3}SiN\textsubscript{3} (5.1 mmol) and 15 mL of MeCN. Purification by MPLC (2:98 – 10:90 EtOAc: hexanes) afforded the product, a yellow oil, as a 56:44 mixture of isomers (0.421 g, 72%). Spectral data for the mixture: 1H NMR (500 MHz,
CDCl$_3$ $\delta$ 7.85 (d, $J = 7.5$ Hz, 1H), 7.81 (d, $J = 7.6$ Hz, 1H), 7.62 – 7.49 (m, 3H), 7.26 (dt, $J = 15.9$, 7.6 Hz, 1H), 7.17–7.09 (m, 2H), 7.07 (t, $J = 6.3$ Hz, 1H), 6.43 (s, 1H), 3.99 (s, 2H), 3.34 (t, $J = 7.1$ Hz, 1H), 3.32 (t, $J = 7.1$ Hz, 1H), 2.68 (t, $J = 6.7$ Hz, 1H), 2.63 (t, $J = 6.3$ Hz, 1H); $^{13}$C NMR (125 MHz, CDCl$_3$) $\delta$ 138.6 (C), 138.4 (C), 137.6 (C), 137.5 (C), 136.0 (C), 135.7 (C), 133.0 (CH), 132.9 (CH), 129.2 (CH), 129.1 (CH), 128.9 (CH), 128.6 (CH), 128.4 (CH), 128.4 (C), 128.2 (C), 128.1 (C), 127.9 (CH), 127.7 (CH), 124.8 (CH), 124.6 (CH), 118.4 (CH), 118.3 (CH), 117.6 (CH), 53.4 (CH$_2$), 50.3 (CH$_2$), 48.4 (CH$_2$), 46.9 (CH$_2$), 33.5 (CH$_2$), 29.8 (CH$_2$) only visible signals. ATR-FTIR (thin film): 3061, 2954, 2857, 2118, 2086, 1286, 1155 cm$^{-1}$; HRMS (El) $m/z$ calculated for C$_{17}$H$_{16}$N$_2$O$_2$S (M–N$_2$)$^+$: 312.09325, found: 312.09302.

3-(2-Azido-5-methoxybenzylidene)-1-(phenylsulfonyl)piperidine 2.46d. The general procedure was followed by using 0.255 g of 2.45d (0.71 mmol), 0.34 mL of t-BuNO$_2$ (2.8 mmol), 0.30 mL of Me$_3$SiN$_3$ (2.1 mmol) and 10 mL of MeCN. Purification by MPLC (2:98 – 10:90 EtOAc: hexanes) afforded the product as a yellow solid (196 mg, 71%). $^1$H NMR (500 MHz, CDCl$_3$) $\delta$ 7.70 (d, $J = 7.7$ Hz, 2H), 7.59 (t, $J = 7.4$ Hz, 1H), 7.50 (t, $J = 7.7$ Hz, 2H), 7.07 (d, $J = 8.7$ Hz, 1H), 6.89 (dd, $J = 8.7$, 2.9 Hz, 1H), 6.86 (d, $J = 2.8$ Hz, 1H), 6.30 (s, 1H), 3.89 (s, 3H), 3.68 (s, 2H), 3.16 (t, $J = 5.5$ Hz, 2H), 2.26 (t, $J = 5.9$ Hz, 2H), 1.81 (quintet, $J = 5.8$ Hz, 2H); $^{13}$C NMR (125 MHz, CDCl$_3$) $\delta$ 156.7 (C), 136.0 (C), 135.1 (C), 132.8 (CH), 130.5 (C), 129.1 (CH), 128.8 (C), 127.7 (CH), 122.2 (CH), 119.4 (CH), 115.4 (CH), 115.1 (CH), 55.8 (CH$_3$), 47.8 (CH$_2$), 47.0 (CH$_2$), 34.0 (CH$_2$), 26.2 (CH$_2$). ATR-FTIR (thin film): 2941, 2836, 2115, 1571, 1486, 1158 cm$^{-1}$; HRMS (El) $m/z$ calculated for C$_{19}$H$_{20}$N$_2$O$_3$S (M–N$_2$)$^+$: 356.11947, found: 356.11969.
3-(2-Azido-5-methoxybenzylidene)-1-Boc-piperidine 2.46e. To a solution of aniline 2.45e (2.50 g, 8.3 mmol) in 100 mL of CH₂Cl₂ was added consecutively 5.8 mL of Et₃N (41.5 mmol) and a solution of CuSO₄ (0.150 g, 0.6 mmol CuSO₄ in 2 mL of H₂O). Freshly prepared TfN₃ (25.0 mmol in 40 mL of CH₂Cl₂) was then added and the solution was brought to homogeneity by adding MeOH (ca. 5 mL). The resulting solution was stirred at room temperature and the progress of the reaction was monitored by TLC. After TLC analysis revealed completion of the reaction, the reaction mixture was poured into a saturated aqueous solution of NaHCO₃ (30 mL) and extracted with 3 x 30 mL of CH₂Cl₂. The combined organic phases were washed with 30 mL of brine, dried over anhydrous Na₂SO₄, filtered and concentrated in vacuo. Purification of the residue by MPLC (2:98 – 10:90 EtOAc:hexanes) afforded the product as a yellow oil (2.0 g, 73%). ¹H NMR (500 MHz, CDCl₃) δ 7.09 (d, J = 6.8 Hz, 1H), 7.03 (d, J = 8.0 Hz, 1H), 6.95 (s 1H), 6.29 (s, 1H), 4.01 (s, 2H), 3.49 (t, J = 5.5 Hz, 2H), 2.37 (t, J = 5.8 Hz, 2H), 2.31 (s, 3H), 1.61 (s, 2H), 1.48 (s, 9H); ¹³C NMR (125 MHz, CDCl₃) δ 155.0 (C), 135.4 (C), 134.0 (C), 131.2 (CH), 128.9 (CH), 128.4 (C), 120.5 (CH), 118.2 (CH), 80.0 (C), 28.5 (CH₃), 27.7 (CH₂), 26.0 (CH₂), 20.9 (CH₃) only visible signals. ATR-FTIR (thin film): 2924, 2846, 2122, 2089, 1332, 1166 cm⁻¹; HRMS (EI) m/z calculated for C₁₈H₂₅N₄O₂ (M+H)⁺: 329.19775, found: 329.19761.

3-(2-Azido-5-chloro-benzylidene)-1-benzenesulfonyl-piperidine 2.46f. The general procedure was followed by using 0.20 g of aniline s.45f (0.55 mmol), 0.10 mL of t-BuNO₂ (0.83 mmol), 0.11 mL of azidotrimethyilsilane (0.83 mmol) in 2 mL of acetonitrile. Purification by MPLC (2:100 – 20:80 EtOAc:hexanes) afforded the product, a yellow solid, as a 76:24 mixture of E- and Z-isomers (0.20 g, 95%).
Spectral data for the major Z-isomer: \(^1\)H NMR (500 MHz, CDCl\(_3\)) \(\delta\) 7.82 (d, \(J = 7.0\) Hz, 2H), 7.63 – 7.50 (m, 4H), 7.07 (m, 1H), 7.01 (d, \(J = 1.0\) Hz, 1H), 6.32 (s, 1H), 3.71 (s, 2H), 3.19 (t, \(J = 5.5\) Hz, 2H), 2.19 (t, \(J = 5.5\) Hz, 2H), 1.70 – 1.60 (m, 2H); \(^{13}\)C NMR (125 MHz, CDCl\(_3\)) \(\delta\) 137.0 (C), 136.5 (C), 136.3 (C), 132.8 (CH), 130.3 (CH), 130.2 (C), 130.0 (C), 129.1 (CH), 128.4 (CH), 127.8 (CH), 121.2 (CH), 119.6 (CH), 53.8 (CH\(_2\)), 46.7 (CH\(_2\)), 27.0 (CH\(_2\)), 25.0 (CH\(_2\)); Selected spectral data for minor E-isomer: \(^1\)H NMR (500 MHz, CDCl\(_3\)) \(\delta\) 6.22 (s, 1H), 3.65 (s, 2H), 2.27 (t, 2H), 1.79 (m, 2H); \(^{13}\)C NMR (125 MHz, CDCl\(_3\)) \(\delta\) 132.8 (CH), 129.0 (CH), 127.6 (CH), 47.5 (CH\(_2\)), 33.2 (CH\(_2\)), 26.0 (CH\(_2\)). ATR-FTIR (thin film): 3067, 2944, 2120, 2089, 1475, 1347, 1295, 1163 cm\(^{-1}\). HRMS (El) \(m/z\) calculated for C\(_{18}\)H\(_{17}\)ClN\(_4\)O\(_2\)S (M\(^+\)): 388.07607, found: 388.07671.

3-(2-azido-4-methoxybenzylidene)-1-(phenylsulfonyl)piperidine 2.46g. The general procedure was followed by using 0.460 g of 2.45g (1.28 mmol), 0.61 mL of t-BuNO\(_2\) (5.1 mmol), 0.54 mL of Me\(_3\)SiN\(_3\) (3.8 mmol) and 15 mL of MeCN. Purification by MPLC (2:98 – 10:90 EtOAc: hexanes) afforded the product, a yellow solid, as an 88:12 mixture of isomers (148 mg, 30%). Spectral data for the major product: \(^1\)H NMR (500 MHz, CDCl\(_3\)) \(\delta\) 7.81 (d, \(J = 7.8\) Hz, 2H), 7.60 (t, \(J = 7.4\) Hz, 1H), 7.53 (t, \(J = 7.7\) Hz, 2H), 6.96 (d, \(J = 8.4\) Hz, 1H), 6.65 (d, \(J = 2.0\) Hz, 1H), 6.62 (dd, \(J = 8.5, 1.8\) Hz, 1H), 6.32 (s, 1H), 3.80 (s, 3H), 3.69 (s, 2H), 3.17 (t, \(J = 5.3\) Hz, 2H), 2.19 (t, \(J = 6.1\) Hz, 2H), 1.62 (quintet, \(J = 5.6\) Hz, 2H); \(^{13}\)C NMR (125 MHz, CDCl\(_3\)) \(\delta\) 159.8 (C), 139.3 (C), 136.5 (C), 134.1 (C), 132.8 (CH), 131.4 (CH), 129.1 (CH), 127.8 (CH), 121.9 (CH), 120.9 (C), 110.1 (CH), 104.2 (CH), 55.5 (CH\(_3\)), 54.0 (CH\(_2\)), 46.8 (CH\(_2\)), 26.9 (CH\(_2\)), 25.1 (CH\(_2\)). ATR-FTIR (thin film): 2950, 2837, 2106, 1603, 1500, 1348, 1147 cm\(^{-1}\); HRMS (El) \(m/z\) calculated for C\(_{19}\)H\(_{20}\)N\(_4\)O\(_3\)S (M\(^+\)): 384.12561, found: 384.12483.
3-(2-Azido-4-methyl-benzylidene)-1-phenylsulfonyl-piperidine 2.46h. To a solution of aniline 2.45h (0.35 g, 1.02 mmol) in 2 mL of CH$_2$Cl$_2$ was added consecutively 0.6 mL of Et$_3$N (4.0 mmol) and a solution of CuSO$_4$ (0.025 g, 0.10 mmol CuSO$_4$ in 0.5 mL of H$_2$O). Freshly prepared TfN$_3$ (5.1 mmol in 2 mL of CH$_2$Cl$_2$) was then added and the solution was brought to homogeneity by adding MeOH (ca. 1 mL). The resulting solution was stirred at room temperature and the progress of the reaction was monitored by TLC. After TLC analysis revealed completion of the reaction, the reaction mixture was poured into a saturated aqueous solution of NaHCO$_3$ (30 mL) and extracted with 3 × 30 mL of CH$_2$Cl$_2$. The combined organic phases were washed with 30 mL of brine, dried over anhydrous Na$_2$SO$_4$, filtered and concentrated in vacuo. Purification of the residue by MPLC (2:98 – 10:90 EtOAc: hexanes) afforded the product, a light yellow oil, as a 90:10 mixture of isomers (0.18 g, 48%). Spectral data for major E-isomer: $^1$H NMR (500 MHz, CDCl$_3$) δ 7.82 (d, $J = 8.0$ Hz, 2H), 7.60 – 7.52 (m, 3H), 6.94 – 6.87 (m, 3H), 6.36 (s, 1H), 3.71 (s, 2H), 3.17 (t, $J = 5.0$ Hz, 2H), 2.35 (s, 3H), 2.19 (t, $J = 6.0$ Hz, 2H), 1.71 – 1.52 (m, 2H); $^{13}$C NMR (125 MHz, CDCl$_3$) δ 138.7 (C), 138.0 (C), 136.6 (C), 134.6 (C), 132.7 (CH), 130.4 (CH), 129.0 (CH), 127.8 (CH), 125.3 (C), 125.2 (CH), 122.2 (CH), 118.9 (CH), 54.0 (CH$_2$), 46.7 (CH$_2$), 26.9 (CH$_2$), 25.1 (CH$_2$), 21.2 (CH$_3$). Selected spectral data for minor Z-isomer: $^1$H NMR (500 MHz, CDCl$_3$) δ 7.70 (d, $J = 8.0$ Hz, 2H), 6.27 (s, 1H), 3.68 (s, 2H), 2.37 (s, 3H); $^{13}$C NMR (125 MHz, CDCl$_3$) δ 47.6 (CH$_2$), 26.1 (CH$_2$). ATR-FTIR (thin film): 2951, 2920, 2853, 2102, 1445, 1347, 1333, 1163 cm$^{-1}$; HRMS (El) $m/z$ calculated for C$_{19}$H$_{20}$O$_2$N$_4$S (M)$^+$: 368.13069, found: 368.13083.

3-(2-Azido-4-chlorobenzylidene)-1-(phenylsulfonyl)piperidine 2.46i. The general procedure was followed by using 0.425 g of 2.45i (1.7 mmol), 0.56 mL of t-BuNO$_2$
(4.7 mmol), 0.50 mL of Me$_3$SiN$_3$ (3.5 mmol) and 20 mL of MeCN. Purification by MPLC (2:98 – 10:90 EtOAc: hexanes) afforded the product, an orange solid, as an 80:20 mixture of isomers (0.330 g, 72%). Spectral data for the major product: $^1$H NMR (500 MHz, CDCl$_3$) δ 7.81 (d, $J = 7.6$ Hz, 2H), 7.61 (t, $J = 7.4$ Hz, 1H), 7.54 (t, $J = 7.6$ Hz, 2H), 7.11 (d, $J = 1.7$ Hz, 1H), 7.04 (dd, $J = 8.2$, 1.7 Hz, 1H), 6.98 (d, $J = 8.2$ Hz, 1H), 6.31 (s, 1H), 3.70 (s, 2H), 3.17 (t, $J = 5.4$ Hz, 2H), 2.17 (t, $J = 6.1$ Hz, 2H), 1.63 (quintet, $J = 5.8$ Hz, 2H); $^{13}$C NMR (125 MHz, CDCl$_3$) δ 139.6 (C), 136.4 (C), 135.8 (C), 133.9 (C), 132.8 (CH), 131.5 (CH), 129.1 (CH), 127.8 (CH), 126.7 (C), 124.6 (CH), 121.3 (CH), 118.6 (CH), 53.9 (CH$_2$), 46.7 (CH$_2$), 27.0 (CH$_2$), 25.1 (CH$_2$).

Selected spectral data for the minor product: $^1$H NMR (500 MHz, CDCl$_3$) δ 7.69 (d, $J = 7.8$ Hz, 0.54H), 6.23 (s, 0.26H), 3.62 (s, 0.54H), 2.26 (t, $J = 6.0$ Hz, 0.53H), 1.80 (quintet, $J = 5.8$ Hz, 2H); $^{13}$C NMR (125 MHz, CDCl$_3$) δ 136.3 (C), 135.8 (C), 134.1 (C), 131.9 (CH), 129.1 (CH), 127.7 (CH), 126.4 (C), 125.1 (CH), 121.0 (CH), 118.5 (CH), 47.6 (CH$_2$), 33.9 (CH$_2$), 31.6 (CH$_2$), 26.2 (CH$_2$). ATR-FTIR (thin film): 2931, 2840, 2106, 1154 cm$^{-1}$; HRMS (El) m/z calculated for C$_{18}$H$_{17}$N$_4$O$_2$SCl (M)$^+$: 388.07607, found: 388.07702.

3-(2-Azido-4-(trifluoromethyl)benzylidene)-1-(phenylsulfonyl)piperidine  2.46j.

The general procedure was followed by using 0.800 g of 2.45j (2.0 mmol), 0.96 mL of t-BuNO$_2$ (8.0 mmol), 0.85 mL of Me$_3$SiN$_3$ (6.0 mmol) and 20 mL of MeCN. Purification by MPLC (2:98 – 10:90 EtOAc: hexanes) afforded the product, a yellow solid, as a 73:27 mixture of isomers (0.642 g, 80%). Spectral data for the major product: $^1$H NMR (500 MHz, CDCl$_3$) δ 7.78 (d, $J = 7.6$ Hz, 2H), 7.57 (q, $J = 7.0$ Hz, 1H), 7.51 (t, $J = 7.6$ Hz, 2H), 7.30 (s, 1H), 7.28 (d, $J = 8.7$ Hz, 1H), 7.15 (d, $J = 7.9$ Hz, 1H), 6.34 (s, 1H), 3.69 (s, 2H), 3.15 (t, $J = 5.0$ Hz, 2H), 2.16 (t, $J = 5.9$ Hz, 2H), 1.60 (s, 2H); $^{13}$C NMR (125 MHz, CDCl$_3$) δ 139.2 (C), 137.0 (C), 136.4 (C), 132.9 (CH), 131.5 (C), 131.1 (CH), 130.6 (q, $J_{CF} = 32.8$ Hz, C), 129.1 (CH), 127.8 (CH),
123.5 (q, $J_{CF} = 273$ Hz, C), 121.2 (CH), 121.1 (CH), 115.3 (q, CH), 53.8 (CH$_2$), 46.7 (CH$_2$), 27.0 (CH$_2$), 25.1 (CH$_2$). Selected spectral data for the minor product: $^1$H NMR (500 MHz, CDCl$_3$) $\delta$ 7.66 (d, $J = 7.7$ Hz, 0.67H), 7.46 (t, $J = 7.7$ Hz, 0.70H), 7.36 (s, 0.64H), 6.27 (s, 0.36H), 3.61 (s, 0.64H), 2.25 (t, $J = 5.9$ Hz, 0.62H), 1.78 (s, 0.65H); $^{13}$C NMR (125 MHz, CDCl$_3$) $\delta$ 139.0 (C), 136.1 (C), 131.8 (CH), 129.1 (C), 127.7 (CH), 121.5 (C), 120.8 (C), 47.6 (CH$_2$), 46.7 (CH$_2$), 34.0 (CH$_2$), 26.2 (CH$_2$). ATR-FTIR (thin film): 3067, 2946, 2842, 2106, 1325, 1119 cm$^{-1}$; $^{19}$F NMR (282 MHz, CDCl$_3$) $\delta$ –61.9, –63.1; HRMS (EI) m/z calculated for C$_{19}$H$_{17}$N$_2$O$_2$SF$_3$ (M–N$_2$)$^+$: 394.09629, found: 394.09662.

![Image of molecular structure](image)

2.46k

3-(2-Azido-3-methylbenzylidene)-1-(phenylsulfonyl)piperidine 2.46k. The general procedure was followed by using 0.873 g of 2.45k (2.55 mmol), 1.20 mL of t-BuNO$_2$ (10.2 mmol), 1.10 mL of Me$_3$SiN$_3$ (7.6 mmol) and 25 mL of MeCN. Purification by MPLC (2:98 – 10:90 EtOAc: hexanes) afforded the product, a yellow solid, as a 72:28 mixture of isomers (500 mg, 53%). Spectral data for the major product: $^1$H NMR (500 MHz, CDCl$_3$) $\delta$ 7.82 (d, $J = 7.5$ Hz, 2H), 7.61 (t, $J = 7.4$ Hz, 1H), 7.55 (t, $J = 7.5$ Hz, 2H), 7.08 – 7.09 (m, 1H), 7.02 (t, $J = 7.5$ Hz, 1H), 6.87 (d, $J = 7.4$ Hz, 1H), 6.49 (s, 1H), 3.74 (s, 2H), 3.18 (q, $J = 6.3$ Hz, 2H), 2.3 (s, 3H), 2.26 (t, $J = 5.9$ Hz, 2H), 1.65 (quintet, $J = 5.7$ Hz, 2H); $^{13}$C NMR (125 MHz, CDCl$_3$) $\delta$ 136.5 (C), 136.3 (C), 136.1 (C), 132.8 (CH), 132.0 (C), 130.9 (C), 130.1 (CH), 129.1 (CH), 128.4 (CH), 127.8 (CH), 125.3 (CH), 122.5 (CH), 53.6 (CH$_2$), 46.7 (CH$_2$), 27.0 (CH$_2$), 25.1 (CH$_2$), 18.2 (CH$_3$). Selected spectral data for the minor product: $^1$H NMR (500 MHz, CDCl$_3$) $\delta$ 7.69 (d, $J = 7.5$ Hz, 0.81H), 7.48 (t, $J = 7.7$ Hz, 0.82H), 6.41 (s, 0.40H), 3.67 (s, 0.81H), 2.33 (s, 1.26H), 1.81 (quintet, $J = 5.7$ Hz, 0.82H); $^{13}$C NMR (125 MHz, CDCl$_3$) $\delta$ 136.1 (C), 135.8 (C), 132.7 (CH), 131.8 (C), 130.6 (C), 130.3 (CH), 129.0 (CH), 128.7 (CH), 127.7 (CH), 125.6 (CH), 122.2 (CH), 47.5 (CH$_2$), 46.7 (CH$_2$), 33.8 (CH$_2$), 26.1 (CH$_2$). ATR-FTIR (thin film): 2916, 2843, 2100, 1306, 1161.
cm⁻¹; HRMS (El) m/z calculated for C₁₉H₂₁N₄O₂S (M+H)⁺: 369.13852, found: 369.13826.

3-(2-Azido-3-methoxybenzylidene)-1-(phenylsulfonyl)piperidine 2.46l. The general procedure was followed by using 0.935 mg of 2.45l (2.61 mmol), 1.24 mL of t-BuNO₂ (10.4 mmol), 1.10 mL of Me₃SiN₃ (7.8 mmol) and 25 mL of MeCN. Purification by MPLC (2:98 – 10:90 EtOAc: hexanes) afforded the product, a white solid, as a 68:32 mixture of isomers (0.560 g, 56%). Spectral data for the major product: ¹H NMR (500 MHz, CDCl₃) δ 7.79 (d, J = 7.4 Hz, 2H), 7.57 (q, J = 6.6 Hz, 1H), 7.52 (t, J = 7.6 Hz, 2H), 6.98 (t, J = 8.0 Hz, 1H), 6.80 (d, J = 8.4 Hz, 1H), 6.62 (d, J = 7.7 Hz, 1H), 6.39 (s, 1H), 3.84 (s, 3H), 3.69 (s, 2H), 3.15 (t, J = 5.2 Hz, 2H), 2.17 (t, J = 6.0 Hz, 2H), 1.58 (quintet, J = 5.5 Hz, 2H). Selected spectral data for the minor isomer: ¹H NMR (500 MHz, CDCl₃) δ 7.67 (d, J = 7.5 Hz, 1H), 7.47 (t, J = 7.7 Hz, 1H), 7.06 (t, J = 8.0 Hz, 0.5H), 6.77 (d, J = 8.2 Hz, 1H), 6.30 (s, 0.5H), 3.86 (s, 1.5H), 3.68 (s, 1H), 2.23 (t, J = 5.9 Hz, 1H), 1.73 (quintet, J = 5.4 Hz, 1H). Spectral data for the mixture: ¹³C NMR (125 MHz, CDCl₃) δ 153.9 (C), 153.9 (C), 136.5 (C), 134.9 (C), 134.7 (C), 132.8 (CH), 132.8 (CH), 129.8 (C), 129.5 (C), 129.1 (CH), 129.1 (CH), 127.8 (CH), 127.6 (CH), 126.4 (C), 126.2 (C), 125.2 (CH), 124.8 (CH), 122.9 (CH), 122.7 (CH), 122.6 (CH), 122.4 (CH), 110.9 (CH), 110.7 (CH), 56.0 (CH₃), 54.0 (CH₂), 47.7 (CH₂), 46.8 (CH₂), 33.9 (CH₃), 27.0 (CH₂), 26.1 (CH₂), 25.1 (CH₂) only signals visible. ATR-FTIR (thin film): 2944, 2833, 2103, 1575, 1307, 1161 cm⁻¹; HRMS (EI) m/z calculated for C₁₉H₂₁N₄O₃S (M+H)⁺: 385.13344, found: 385.13263.
3-(2-Azidobenzylidene)tetrahydro-2H-pyran 2.51. The general procedure was followed by using 0.823 g of 2.50 (4.4 mmol), 2.07 mL of t-BuNO (17.4 mmol), 1.83 mL of Me₃SiN₃ (13.1 mmol) and 50 mL of MeCN. Purification by MPLC (2.98 – 10.90 EtOAc: hexanes) afforded the product, a yellow oil, as a 78:22 mixture of isomers (0.636 g, 68%). Spectral data for the major isomer: 

\[ \text{^1H NMR (500 MHz, CDCl}_3\text{)} \delta 7.29 (t, J = 7.5 Hz, 1H), 7.17 (dd, J = 12.1, 7.9 Hz, 2H), 7.10 (t, J = 7.6 Hz, 1H), 6.30 (s, 1H), 4.19 (s, 2H), 3.80 (t, J = 5.2 Hz, 2H), 2.45 (t, J = 6.3 Hz, 2H), 1.71 (quintet, J = 5.7 Hz, 2H); \]

\[ \text{^13C NMR (125 MHz, CDCl}_3\text{)} \delta 138.8 (C), 138.3 (C), 130.7 (CH), 128.6 (C), 128.3 (CH), 124.3 (CH), 119.9 (CH), 118.4 (CH), 74.2 (CH₂), 68.4 (CH₂), 27.6 (CH₂), 26.9 (CH₂). \]

Selected data for the minor isomer: 

\[ \text{^1H NMR (500 MHz, CDCl}_3\text{)} \delta 6.28 (s, 0.27H), 4.20 (s, 0.57H), 3.77 (t, J = 5.2 Hz, 0.57H), 2.49 (t, J = 6.2 Hz, 0.58H), 1.83 (quintet, J = 5.6 Hz, 0.58H); \]

\[ \text{^13C NMR (125 MHz, CDCl}_3\text{)} \delta 138.1 (C), 131.0 (CH), 128.5 (C), 128.3 (CH), 124.4 (CH), 120.2 (CH), 118.3 (CH), 68.3 (CH₂), 67.7 (CH₂), 33.4 (CH₂), 28.4 (CH₂); \]

ATR-FTIR (thin film): 2952, 2834, 2115, 2083, 1483, 1283, 1084 cm⁻¹; HRMS (EI) m/z calculated for C₁₂H₁₃N₃O (M⁺): 215.10587, found: 215.10550.

(S)-2-[2-(2-Azido-phenyl)-1-methyl-vinyl]-pyrrolidine-1-carboxylic acid tert-butyl ester 2.60. The general procedure was followed using 0.250 g of aniline (0.83 mmol), 0.39 mL of t-BuNO₂ (3.31 mmol) and 0.33 mL of Me₃SiN₃ (2.48 mmol) in 5 mL of MeCN. Purification by MPLC (0.100 – 10.90 EtOAc:hexanes) afforded the
product, a yellow oil, as a 68:32 mixture of rotamers (0.247 g, 91%). $[\alpha]_D^{20} = –40.0 (c 0.125, CH$_2$Cl$_2$); $^1$H NMR (500 MHz, CDCl$_3$) $\delta$ 7.24 – 7.18 (m, 2H), 7.13 – 7.09 (m, 2H), 6.22 (s, 1H), 4.37 (br s, 0.32 H), 4.27 (br s, 0.68 H), 3.46 – 3.55 (m, 2H), 2.10 (br s, 1H), 1.97 – 1.91 (m, 1H), 1.85 – 1.72 (m, 2H), 1.69 (s, 3H), 1.48 (s, 3H), 1.43 (s, 6H); $^{13}$C NMR (125 MHz, CDCl$_3$) $\delta$ 154.7 (C), 140.9 (C), 138.0 (C), 130.5 (CH), 129.9 (C), 127.7 (CH), 124.2 (CH), 119.0 (CH), 118.3 (CH), 79.2 (C), 63.8 (CH), 49.9 (CH$_2$), 31.9 (CH$_2$), 28.4 (CH$_3$), 23.2 (CH$_2$), 14.8 (CH$_3$); ATR-FTIR (thin film): 2977, 2120, 2086, 1693, 1484, 1386, 1291, 1164 cm$^{-1}$. HRMS (El) $m/z$ calculated for C$_{18}$H$_{24}$N$_4$O$_2$ (M)$^+$: 328.18992, found: 328.18896.

(E)-2-[2-(2-Azido-5-methyl-phenyl)-1-methyl-vinyl]-pyrrolidine-1-carboxylic acid tert-butyl ester 2.59b. The general procedure was followed using 0.230 g of aniline (0.73 mmol), 0.35 mL of t-BuNO$_2$ (2.92 mmol) and 0.29 mL of Me$_3$SiN$_3$ (2.19 mmol) in 4 mL of MeCN. Purification by MPLC (2:100 – 10:90 EtOAc:hexanes) afforded the product, a light yellow oil, as a 65:35 mixture of rotamers (0.219 g, 88%). Spectral data for the mixture: $^1$H NMR (500 MHz, CDCl$_3$) $\delta$ 6.97 – 7.01 (m, 3H), 6.17 (s, 1H), 4.35 (br s, 0.35H), 4.25 (br s, 0.65H), 3.52 – 3.44 (m, 2H), 2.29 (s, 3H), 1.90 – 1.72 (m, 4H), 1.68 (s, 3H), 1.46 (s, 3H), 1.42 (s, 6H); Data for major rotamer: $^{13}$C NMR (125 MHz, CDCl$_3$) $\delta$ 154.6 (C), 140.6 (C), 135.2 (C), 133.8 (C), 131.1 (CH), 129.7 (C), 128.3 (CH), 119.0 (CH), 118.2 (CH), 79.1 (C), 63.8 (CH), 46.9 (CH$_2$), 31.8 (CH$_2$), 28.4 (CH$_3$), 23.1 (CH$_2$), 20.9 (CH$_3$), 14.9 (CH$_3$); diagnostic data for the minor rotamer: $^{13}$C NMR (125 MHz, CDCl$_3$) $\delta$ 63.1 (CH), 30.9 (CH$_2$), 15.6 (CH$_3$); data for mixtures: ATR-FTIR (thin film): 2971, 2931, 2870, 2120, 2086, 1689, 1485, 1387, 1363, 1292 cm$^{-1}$. HRMS (El) $m/z$ calculated for C$_{19}$H$_{26}$N$_4$O$_2$ (M)$^+$: 342.20557, found: 342.20653.
(E)-2-[2-(2-Azido-5-fluoro-phenyl)-1-methyl-vinyl]pyrrolidine-1-carboxylic acid tert-butyl ester 2.59c. The general procedure was followed using 0.114 g of aniline (0.35 mmol), 0.17 mL of t-BuNO₂ (1.42 mmol) and 0.14 mL of Me₃SiN₃ (1.05 mmol) in 2 mL of MeCN. Purification by MPLC (0:100 – 10:90 EtOAc:hexanes) afforded the product, a light yellow oil, as a 65:35 mixture of rotamers (0.219 g, 88%). Spectral data for the mixture: ¹H NMR (500 MHz, CDCl₃) δ 7.03 (br s, 1H), 6.93 – 6.88 (m, 2H), 6.17 (s, 1H), 4.35 (br s, 0.35H), 4.25 (m, 0.65H), 3.53 – 3.44 (m, 2H), 2.11 – 2.08 (m, 1H), 1.93 – 1.88 (m, 1H), 1.84 – 1.74 (m, 2H), 1.70 (s, 3H), 1.47 (s, 3H), 1.41 (s, 6H); spectral data for major rotamer: ¹³C NMR (125 MHz, CDCl₃) δ 159.3 (d, JCF = 242.2 Hz, C), 154.6 (CH), 142.2 (C), 133.8 (C), 131.6 (C), 119.5 (CH), 118.1 (CH), 117.0 (d, JCF = 22.5 Hz, CH), 114.4 (d, J = 24.4 Hz, CH), 79.2 (C), 63.7 (CH), 46.9 (CH₂), 31.8 (CH₂), 28.4 (CH₃), 23.1 (CH₂), 14.9 (CH₃); diagnostic data for the minor rotamer: ¹³C NMR (125 MHz, CDCl₃) δ 63.3 (CH), 23.4 (CH₂); ATR-FTIR (thin film): 2978, 2877, 2113, 1682, 1397, 1327, 1275, 1166 cm⁻¹. HRMS (EI) m/z calculated for C₁₈H₂₃FN₄O₂ (M⁺): 346.18050, found: 346.18117.

(E)-2-[2-(2-Azido-4-trifluoromethyl-phenyl)-1-methyl-vinyl]-pyrrolidine-1-carboxylic acid tert-butyl ester 2.59d. The general procedure was followed using 0.250 g of aniline (0.67 mmol), 0.24 mL of t-BuNO₂ (2.02 mmol) and 0.35 mL of Me₃SiN₃ (2.69 mmol) in 4 mL of MeCN. Purification by MPLC (0:100 – 10:90 EtOAc:hexanes) afforded the product, a yellow oil, as a 58:42 mixture of rotamers (0.248 g, 93%). Spectral data for the mixture: ¹H NMR (500 MHz, CDCl₃) δ 7.32 – 7.30 (m, 3H), 6.21 (s, 1H), 4.37 (br s, 0.42H), 4.27 (br s, 0.58H), 3.54 – 3.46 (m, 2H), 2.20 – 1.91 (m, 2H), 1.84 – 1.74 (m, 2H), 1.70 (s, 3H), 1.47 (s, 4H), 1.41 (s, 5H);
data for major rotamer: $^{13}$C NMR (125 MHz, CDCl$_3$) $\delta$ 154.6 (C), 143.1 (C), 138.8 (C), 133.5 (C), 130.9 (CH), 130.0 (q, $J_{CF}$ = 31.2 Hz, C), 123.7 (q, $J_{CF}$ = 270.1 Hz, CF$_3$), 120.9 (CH), 117.9 (CH), 115.2 (C), 79.3 (CH), 63.8 (CH), 46.9 (CH$_2$), 31.8 (CH$_2$), 28.4 (CH$_3$), 23.1 (CH$_2$), 15.0 (CH$_3$); diagnostic data for minor rotamer: $^{13}$C NMR (125 MHz, CDCl$_3$) $\delta$ 142.0 (C), 117.4 (CH), 63.2 (CH), 30.7 (CH$_2$), 15.6 (CH$_3$); data for the mixture: ATR-FTIR (thin film): 2977, 2111, 1686, 1399, 1329, 1169, 1129 cm$^{-1}$. HRMS (EI) $m/z$ calculated for C$_{19}$H$_{23}$F$_3$N$_4$O$_2$ (M)$^+$: 396.17731, found: 396.17637.

(E)-1-Boc-2-(1-(2-azidophenyl)prop-1-en-2-yl)piperidine E-2.59e. The general procedure was followed using 0.230 g of E-aniline (0.73 mmol), 0.35 mL of t-BuNO$_2$ (2.9 mmol) and 0.30 mL of Me$_3$SiN$_3$ (2.2 mmol) in 10 mL of MeCN. Purification by MPLC (0:100 – 10:90 EtOAc:hexanes) afforded the product as a yellow oil (0.212 g, 85%). $^1$H NMR (500 MHz, CDCl$_3$) $\delta$ 7.25 (t, $J$ = 7.7 Hz, 1H), 7.19 (d, $J$ = 7.5 Hz, 1H), 7.13 (d, $J$ = 7.9 Hz, 1H), 7.09 (t, $J$ = 7.5 Hz, 1H), 6.23 (s, 1H), 4.78 (s, 1H), 4.02 (d, $J$ = 12.1 Hz, 1H), 2.86 (td, $J$ = 12.9, 2.8 Hz, 1H), 2.11 (d, $J$ = 13.6 Hz, 1H), 1.68 (s, 3H), 1.72 – 1.51 (m, 5H), 1.49 (s, 9H); $^{13}$C NMR (125 MHz, CDCl$_3$) $\delta$ 155.5 (C), 138.1 (C), 137.6 (C), 130.8 (CH), 130.1 (C), 127.8 (CH), 124.2 (CH), 121.2 (CH), 118.2 (CH), 79.4 (C), 56.0 (CH), 40.3 (CH$_2$), 28.5 (CH$_3$), 26.6 (CH$_2$), 25.5 (CH$_2$), 19.6 (CH$_2$), 16.1 (CH$_3$).

(Z)-1-Boc-2-(1-(2-azidophenyl)prop-1-en-2-yl)piperidine Z-2.59e. The general procedure was followed using 0.258 g of Z-aniline (0.82 mmol), 0.39 mL of t-BuNO$_2$ (3.3 mmol) and 0.34 mL of Me$_3$SiN$_3$ (2.4 mmol) in 10 mL of MeCN. Purification by
MPLC (0:100 – 10:90 EtOAc:hexanes) afforded the product as a yellow oil (157 g, 56%). $^1$H NMR (500 MHz, CDCl$_3$) $\delta$ 7.25 (t, $J$ = 7.7 Hz, 1H), 7.19 (d, $J$ = 7.4 Hz, 1H), 7.13 (d, $J$ = 7.8 Hz, 1H), 7.09 (t, $J$ = 7.5 Hz, 1H), 6.22 (s, 1H), 4.77 (s, 1H), 4.02 (d, $J$ = 13.1 Hz, 1H), 2.86 (td, $J$ = 12.9, 2.7 Hz, 1H), 2.10 (d, $J$ = 13.8 Hz, 1H), 1.67 (s, 3H), 1.73 – 1.53 (m, 5H), 1.48 (s, 9H); $^{13}$C NMR (125 MHz, CDCl$_3$) $\delta$ 155.5 (C), 138.1 (C), 137.6 (C), 130.7 (CH), 130.1 (C), 127.8 (CH), 124.2 (CH), 121.3 (CH), 118.2 (CH), 79.4 (C), 56.0 (CH), 40.3 (CH$_2$), 28.5 (CH$_3$), 26.6 (CH$_2$), 25.5 (CH$_2$), 19.6 (CH$_2$), 16.1 (CH$_3$). ATR-FTIR (thin film): 2838, 2116, 2089, 1682, 1414, 1157 cm$^{-1}$. HRMS (El) $m/z$ calculated for C$_{19}$H$_{26}$N$_4$O$_2$ (M)$^+$: 342.20557, found: 342.20637.

(E)-2-[2-(2-Azido-phenyl)-1-phenyl-vinyl]-pyrrolidine-1-carboxylic acid tert-butyl ester 2.59f. The general procedure was followed using 0.06 g of aniline (0.16 mmol) in 2 mL of MeCN, 0.06 mL of t-BuNO$_2$ (0.49 mmol), 0.08 mL of Me$_3$SiN$_3$ (0.64 mmol). Purification by MPLC (0:100 – 10:90 EtOAc:hexanes) afforded the product, a yellow solid, as a 70:30 mixture of rotamers (0.06 g, 87%). mp 136 – 138 °C. Data for mixtures: $^1$H NMR (500 MHz, CDCl$_3$) $\delta$ 7.25 – 7.23 (m, 3H), 7.16 – 7.05 (m, 4H), 6.71 – 6.65 (m, 2H), 6.42 (s, 1H), 4.78 (br s, 0.30 H), 4.65 (br s, 0.70 H), 3.60 – 3.45 (m, 2H), 1.97 – 1.66 (m, 4H), 1.48 (s, 9H); data for major rotamer: $^{13}$C NMR (125 MHz, CDCl$_3$) $\delta$ 154.6 (C), 144.9 (C), 139.1 (C), 138.0 (C), 130.5 (CH), 129.2 (C), 129.1 (CH), 128.5 (CH), 127.6 (CH), 127.2 (CH), 124.0 (CH), 120.3 (CH), 118.0 (CH), 79.4 (C), 63.7 (CH), 46.9 (CH$_2$), 31.2 (CH$_2$), 28.6 (CH$_2$), 22.4 (CH$_3$); diagnostic data for minor rotamer: $^{13}$C NMR (125 MHz, CDCl$_3$) $\delta$ 30.4 (CH$_2$). Data for mixtures: ATR-FTIR (thin film): 2971, 2920, 2123, 2093, 1682, 1475, 1394, 1166, 1115, 909 cm$^{-1}$. HRMS (El) $m/z$ calculated for C$_{23}$H$_{26}$N$_4$O$_2$ (M)$^+$: 390.20557, found: 390.20644.
F. Substitution of the Boc-Group with a Phenylsulfonyl group.

To a cooled solution (0 °C) of N-Boc protected styryl azide (1 equiv) in anhydrous CH₂Cl₂ was added dropwise trifluoroacetic acid (4 equiv). After 2 h, analysis of the reaction progress using TLC indicated that the deprotection was complete. The reaction mixture was concentrated in vacuo. The resulting residue was dissolved in anhydrous CH₂Cl₂ and cooled to 0 °C. To the resulting solution was added Et₃N (8 equiv). After 10 min, benzenesulfonyl chloride (2 equiv) was added and the solution was allowed to warm at room temperature. After 2 h, the solution was concentrated in vacuo, and the resulting residue was purified by MPLC (5:100 – 10:100 EtOAc:hexane) to afford the product.

3-(2-Azidobenzylidene)-1-(phenylsulfonyl)piperidine 2.62c. The general procedure was followed by using 0.199 g of azide 2.46c (0.63 mmol), 5 mL of trifluoroacetic acid, 0.44 mL of triethylamine (3.2 mmol), 0.24 mL of benzensulfonyl chloride (1.9 mmol) and 10 mL of CH₂Cl₂. Purification by MPLC (2:98 – 20:80 EtOAc:hexanes) afforded the product, a white solid, as a 77:23 mixture of isomers (0.138 g, 62%). Spectral data for the major isomer: ¹H NMR (500 MHz, CDCl₃) δ 7.82 (d, J = 7.5 Hz, 2H), 7.60 (q, J = 6.9 Hz, 1H), 7.54 (t, J = 7.6 Hz, 2H), 7.33 – 7.24 (m, 1H), 7.14 (t, J = 8.3 Hz, 1H), 7.06 (t, J = 6.8 Hz, 2H), 6.39 (s, 1H), 3.72 (s, 2H), 3.17 (t, J = 5.4 Hz, 2H), 2.20 (t, J = 6.1 Hz, 2H), 1.63 (quintet, J = 5.8 Hz, 2H); ¹³C NMR (125 MHz, CDCl₃) δ 138.3 (C), 136.5 (C), 135.1 (C), 132.8 (CH), 130.6 (CH), 129.1 (CH), 128.5 (CH), 128.2 (C), 127.8 (CH), 124.4 (CH), 122.3 (CH), 118.4 (CH), 54.0 (CH₂), 46.8 (CH₂), 27.0 (CH₂), 25.1 (CH₂). Selected data for the minor isomer:
$^1$H NMR (500 MHz, CDCl$_3$) $\delta$ 7.69 (d, $J$ = 7.5 Hz, 0.6H), 7.49 (t, $J$ = 7.7 Hz, 0.6H), 6.30 (s, 0.3H), 3.68 (s, 0.6H), 2.26 (t, $J$ = 6.0 Hz, 0.6H), 1.78 (quintet, $J$ = 5.8 Hz, 0.6H); $^{13}$C NMR (125 MHz, CDCl$_3$) $\delta$ 135.0 (C), 132.8 (CH), 131.0 (CH), 129.0 (CH), 127.7 (CH), 124.9 (CH), 122.0 (CH), 118.3 (CH), 47.6 (CH$_2$), 33.9 (CH$_2$), 26.2 (CH$_2$). ATR-FTIR (thin film): 2921, 2849, 2122, 2087, 1482, 1304, 1158 cm$^{-1}$; HRMS (EI) $m/z$ calculated for C$_{18}$H$_{19}$N$_4$O$_2$S (M+H)$^+$: 355.12287, found: 355.12369.

![2.62a](image)

3-(2-Nitrobenzylidene)-1-(phenylsulfonyl)azetidine 2.62a. The general procedure was followed by using 1.17 g of 2.44a (4.03 mmol), 15 mL of trifluoroacetic acid, 5.6 mL of triethylamine (40 mmol), 1.54 mL of benzensulfonyl chloride (12.0 mmol) and 60 mL of CH$_2$Cl$_2$. Purification by MPLC (2:98 – 20:80 EtOAc:hexanes) afforded the product as a yellow solid (1.29 g, 97%): $^1$H NMR (500 MHz, CDCl$_3$) $\delta$ 7.92 (d, $J$ = 8.6 Hz, 1H), 7.90 (d, $J$ = 7.5 Hz, 2H), 7.67 (t, $J$ = 7.4 Hz, 1H), 7.60 (t, $J$ = 7.7 Hz, 2H), 7.54 (t, $J$ = 7.7 Hz, 1H), 7.38 (t, $J$ = 7.7 Hz, 1H), 7.12 (d, $J$ = 7.7 Hz, 1H), 6.71 (s, 1H), 4.64 (s, 2H), 4.60 (s, 2H); $^{13}$C NMR (125 MHz, CDCl$_3$) $\delta$ 147.6 (C), 135.1 (C), 133.6 (CH), 133.1 (CH), 132.1 (C), 130.0 (C), 129.4 (CH), 128.6 (CH), 128.32 (CH), 128.30 (CH), 125.1 (CH), 119.0 (CH), 60.4 (CH$_2$), 59.4 (CH$_2$). ATR-FTIR (thin film): 3083, 2948, 1566, 1516, 1333, 1150 cm$^{-1}$; HRMS (ESI) $m/z$ calculated for C$_{16}$H$_{15}$N$_2$O$_4$S (M+H)$^+$: 331.0753, found: 331.0757.

![2.62b](image)

3-(2-Nitrobenzylidene)-1-(phenylsulfonyl)pyrrolidine 2.62b. The general procedure was followed by using 0.762 g of 2.44b (2.5 mmol), 15 mL of trifluoroacetic acid, 3.6 mL of triethylamine (26 mmol), 1.0 mL of benzensulfonyl chloride (7.8 mmol) and 40 mL of CH$_2$Cl$_2$. Purification by MPLC (2:98 – 20:80 EtOAc:hexanes) afforded the product, a yellow oil, as a 55:45 mixture of isomers.
(0.842 g, 98%). Spectral data for the major product: $^1$H NMR (500 MHz, CDCl$_3$) $\delta$ 7.92 (d, $J$ = 8.2 Hz, 0.5H), 7.90 (d, $J$ = 8.2 Hz, 0.5H), 7.81 (d, $J$ = 7.5 Hz, 1H), 7.74 (d, $J$ = 7.6 Hz, 1H), 7.61-7.47 (m, 4H), 7.39 (t, $J$ = 7.8 Hz, 0.6H), 7.35 (t, $J$ = 7.8 Hz, 0.5H), 7.27 (d, $J$ = 7.8 Hz, 0.5H), 7.22 (d, $J$ = 7.7 Hz, 0.5H), 6.64 (s, 1H), 3.99 (s, 1H), 3.88 (s, 1H), 3.32 (t, $J$ = 7.1 Hz, 1H), 3.30 (t, $J$ = 7.1 Hz, 1H), 2.66 (t, $J$ = 6.9 Hz, 1H), 2.52 (t, $J$ = 6.4 Hz, 1H); $^{13}$C NMR (125 MHz, CDCl$_3$) $\delta$ 147.8 (C), 147.7 (C), 140.5 (C), 140.3 (C), 135.8 (C), 135.5 (C), 133.3 (CH), 133.1 (CH), 133.0 (CH), 131.8 (C), 131.7 (C), 130.6 (CH), 130.4 (CH), 129.2 (CH), 128.2 (CH), 128.1 (CH), 127.8 (CH), 127.6 (CH), 124.7 (CH), 124.6 (CH), 119.2 (CH), 118.5 (CH), 53.2 (CH$_2$), 50.0 (CH$_2$), 48.2 (CH$_2$), 47.0 (CH$_2$), 33.0 (CH$_2$), 29.5 (CH$_2$). ATR-FTIR (thin film): 3065, 2858, 1519, 1338, 1156 cm$^{-1}$; HRMS (EI) m/z calculated for C$_{17}$H$_{17}$N$_2$O$_4$S (M+H)$^+$: 345.09091, found: 345.09133.

2.62d

3-(5-Methoxy-2-nitrobenzylidene)-1-(phenylsulfonyl)piperidine 2.62d. The general procedure was followed by using 1.49 g of 2.44d (4.3 mmol), 10 mL of trifluoroacetic acid, 6.0 mL of triethylamine (43 mmol), 1.7 mL of benzenesulfonyl chloride (12.8 mmol) and 40 mL of CH$_2$Cl$_2$. Purification by MPLC (2:98 – 20:80 EtOAc:hexanes) afforded the product as a yellow solid (1.55 g, 94%): $^1$H NMR (500 MHz, CDCl$_3$) $\delta$ 8.01 (d, $J$ = 9.1 Hz, 1H), 7.74 (d, $J$ = 7.4 Hz, 2H), 7.54 (t, $J$ = 7.2 Hz, 1H), 7.49 (t, $J$ = 7.5 Hz, 2H), 6.81 (dd, $J$ = 9.1, 2.5 Hz, 1H), 6.67 (s, 1H), 6.52 (s, 1H), 3.79 (s, 3H), 3.69 (s, 2H), 3.12 (t, $J$ = 5.2 Hz, 2H), 2.04 (t, $J$ = 5.7 Hz, 2H), 1.53 (s, 2H); $^{13}$C NMR (125 MHz, CDCl$_3$) $\delta$ 162.9 (C), 141.1 (C), 136.5 (C), 134.8 (C), 134.6 (C), 132.9 (CH), 129.2 (CH), 127.7 (CH), 127.4 (CH), 123.6 (CH), 116.8 (CH), 112.9 (CH), 56.0 (CH$_3$), 53.7 (CH$_2$), 46.6 (CH$_2$), 27.0 (CH$_2$), 25.0 (CH$_2$). ATR-FTIR (thin film): 2941, 2836, 1582, 1504, 1321, 1167 cm$^{-1}$; HRMS (EI) m/z calculated for C$_{19}$H$_{21}$N$_2$O$_5$S (M+H)$^+$: 389.11712, found: 389.11746.
3-(5-Methyl-2-azidobenzylidene)-1-(phenylsulfonyl)piperidine 2.62e. The general procedure was followed by using 1.02 g of 2.46e (3.1 mmol), 10 mL of trifluoroacetic acid, 2.1 mL of triethylamine (31 mmol), 1.2 mL of benzenesulfonyl chloride (9.2 mmol) and 40 mL of CH$_2$Cl$_2$. Purification by MPLC (2:98 – 20:80 EtOAc:hexanes) afforded the product, a white solid, as a 68:32 mixture of isomers (0.66 g, 59%). Major product: $^1$H NMR (500 MHz, CDCl$_3$) δ 7.81 (d, $J = 7.5$ Hz, 2H), 7.59 (q, $J = 7.3$ Hz, 1H), 7.53 (t, $J = 7.6$ Hz, 2H), 7.08 (d, $J = 7.2$ Hz, 1H), 7.02 (t, $J = 8.9$ Hz, 1H), 6.85 (s, 1H), 6.35 (s, 1H), 3.70 (s, 2H), 3.17 (t, $J = 8.9$ Hz, 2H), 2.28 (s, 3H), 2.19 (t, $J = 6.0$ Hz, 2H), 1.62 (quintet, $J = 5.7$ Hz, 2H); $^{13}$C NMR (125 MHz, CDCl$_3$) δ 136.5 (C), 135.4 (C), 135.0 (C), 134.1 (C), 132.8 (CH), 131.1 (CH), 129.2 (CH), 129.1 (CH), 128.0 (C), 127.8 (CH), 122.3 (CH), 118.3 (CH), 54.0 (CH$_2$), 46.8 (CH$_2$), 27.0 (CH$_2$), 25.1 (CH$_2$), 20.9 (CH$_3$). Selected data for minor product: $^{13}$C NMR (125 MHz, CDCl$_3$) δ 136.3 (C), 135.4 (C), 135.0 (C), 134.1 (C), 132.8 (CH), 131.1 (CH), 129.3 (CH), 129.0 (CH), 128.0 (C), 127.7 (C), 127.0 (CH), 122.0 (CH), 118.1 (CH), 46.9 (CH$_2$), 42.1 (CH$_2$), 34.0 (CH$_2$), 26.3 (CH$_2$), 20.8 (CH$_3$). ATR-FTIR (thin film): 3059, 2923, 2122, 2089, 1165 cm$^{-1}$; HRMS (El) m/z calculated for C$_{19}$H$_{20}$N$_2$O$_2$S (M–N$_2$)$^+$: 340.12455, found: 340.12511.

3-(5-Chloro-2-nitrobenzylidene)-1-(phenylsulfonyl)piperidine 2.62f. The general procedure was followed by using 2.65 g of 2.44f (7.5 mmol), 2.31 mL of trifluoroacetic acid (30.1 mmol) in 35 mL of dichloromethane. Purification by extraction followed by evaporation gives crude amine. To this crude product was added 1.25 mL of benzenesulfonyl chloride (9.7 mmol) and 4.2 mL of Et$_3$N (30 mmol). Purification by MPLC (2:100 – 20:80 EtOAc:hexanes) afforded the product, a yellow solid, as a 75:25 mixture of Z- and E- isomers (1.70 g, 58% over 2 steps).
Spectral data for major *E*- isomer: $^1$H NMR (500 MHz, CDCl$_3$) $\delta$ 7.94 (d, $J$ = 8.5 Hz, 1H), 2.28 (d, $J$ = 7.5 Hz, 2H), 7.58 – 7.34 (m, 4H), 7.08 (d, $J$ = 2.0 Hz, 1H), 6.62 (s, 1H), 3.72 (s, 2H), 3.16 (t, $J$ = 5.5 Hz, 2H), 2.06 (t, $J$ = 6.0 Hz, 2H), 1.63 – 1.53 (m, 2H); $^{13}$C NMR (125 MHz, CDCl$_3$) $\delta$ 146.5 (C), 139.9 (C), 139.2 (C), 136.8 (C), 133.6 (C), 132.9 (CH), 131.7 (CH), 129.2 (CH), 128.3 (CH), 127.8 (CH), 126.2 (CH), 121.6 (CH), 53.5 (CH$_2$), 46.5 (CH$_2$), 27.1 (CH$_2$), 25.0 (CH$_2$); Selected spectral data for minor *Z*- isomer: $^1$H NMR (500 MHz, CDCl$_3$) $\delta$ 7.99 (d, $J$ = 8.5 Hz, 1H), 6.57 (s, 1H), 3.53 (s, 2H), 2.26 (t, $J$ = 5.5 Hz, 2H), 1.86 – 1.73 (m, 2H); $^{13}$C NMR (125 MHz, CDCl$_3$) $\delta$ 146.2 (C), 139.9 (C), 136.1 (C), 133.4 (C), 132.3 (CH), 47.6 (CH$_2$), 46.7 (CH$_2$), 33.8 (CH$_2$), 26.2 (CH$_2$); ATR-FTIR (thin film): 2975, 2931, 2857, 1686, 1519, 1340, 1234, 1163 cm$^{-1}$; HRMS (EI) $m/z$ calculated for C$_{18}$H$_{16}$O$_4$N$_2$S (M–H)$^+$: 391.05193, found: 391.05181.

3-(4-Methoxy-2-nitrobenzylidene)-1-(phenylsulfonyl)piperidine  2.62g. The general procedure was followed by using 1.74 g of 2.44g (5.0 mmol), 10 mL of trifluoroacetic acid, 7.0 mL of triethylamine (50 mmol), 1.9 mL of benzenesulfonyl chloride (15.0 mmol) and 40 mL of CH$_2$Cl$_2$. Purification by MPLC (2:98 – 20:80 EtOAc:hexanes) afforded the product as a yellow solid (1.90 g, 98%): $^1$H NMR (500 MHz, CDCl$_3$) $\delta$ 7.68 (d, $J$ = 7.7 Hz, 2H), 7.58 (s, 2H), 7.50 (t, $J$ = 7.6 Hz, 2H), 7.37 (d, $J$ = 8.5 Hz, 1H), 7.21 (dd, $J$ = 8.5, 2.5 Hz, 1H), 6.59 (s, 1H), 3.90 (s, 3H), 3.56 (s, 2H), 3.16 (t, $J$ = 5.3 Hz, 2H), 2.28 (t, $J$ = 5.8 Hz, 2H), 1.82 (quintet, $J$ = 5.3 Hz, 2H); $^{13}$C NMR (125 MHz, CDCl$_3$) $\delta$ 159.2 (C), 148.5 (C), 136.1 (C), 134.8 (C), 133.6 (CH), 132.8 (CH), 129.1 (CH), 127.6 (CH), 123.9 (C), 122.5 (CH), 119.8 (CH), 109.6 (CH), 55.9 (CH$_3$), 47.9 (CH$_2$), 46.9 (CH$_2$), 33.8 (CH$_2$), 26.3 (CH$_2$). ATR-FTIR (thin film): 2945, 2840, 1522, 1344, 1161 cm$^{-1}$; HRMS (EI) $m/z$ calculated for C$_{19}$H$_{21}$N$_2$O$_5$S (M+H)$^+$: 389.11712, found: 389.11709.
3-(4-Methyl-2-nitrobenzylidene)-1-(phenylsulfonyl)piperidine 2.62h. The general procedure was followed by using 1.0 g of 2.44h (3.0 mmol), 0.92 mL of trifluoroacetic acid (12.0 mmol) in 15 mL of dichloromethane. Purification by extraction followed by evaporation gives crude amine. To this crude product was added 0.5 mL of benzenesulfonyl chloride (3.9 mmol) and 1.7 mL of Et$_3$N (12 mmol). Purification by MPLC (2:100 – 20:80 EtOAc:hexanes) afforded 81:19 mixture of Z- and E- isomers as a yellow solid (0.82 g, 73% over 2 steps). Spectral data for the major (E) isomer: $^1$H NMR (500 MHz, CDCl$_3$) δ 7.81 – 7.75 (m, 3H), 7.58 (m, 1H), 7.52 (m, 2H), 7.33 (d, $J$ = 7.5 Hz, 1H), 7.03 (d, $J$ = 7.5 Hz, 1H), 6.65 (s, 1H), 3.72 (s, 2H), 3.16 (t, $J$ = 5.5 Hz, 2H), 2.39 (s, 3H), 2.05 (t, $J$ = 6.0 Hz, 2H), 1.57 (m, 2H); $^{13}$C NMR (125 MHz, CDCl$_3$) δ 148.2 (C), 138.7 (C), 136.6 (C), 135.3 (C), 133.7 (CH), 132.8 (CH), 131.7 (CH), 129.1 (CH), 128.8 (C), 127.7 (CH), 124.8 (CH), 122.6 (CH), 53.7 (CH$_2$), 46.6 (CH$_2$), 26.9 (CH$_2$), 25.1 (CH$_2$), 20.9 (CH$_3$). Selected spectral data for the minor (E) isomer: $^1$H NMR (500 MHz, CDCl$_3$) δ 6.59 (s, 1H), 3.54 (s, 2H), 2.26 (t, $J$ = 6.0 Hz, 2H); $^{13}$C NMR (125 MHz, CDCl$_3$) δ 138.8 (C), 135.2 (C), 134.3 (CH), 132.4 (CH), 129.0 (CH), 128.7 (C), 127.6 (CH), 124.9 (CH), 47.8 (CH$_2$), 46.8 (CH$_2$), 37.8 (CH$_2$), 26.2 (CH$_2$) ATR-FTIR (thin film): 3067, 2948, 2927, 1526, 1343, 1166 cm$^{-1}$; HRMS (EI) $m/z$ calculated for C$_{19}$H$_{19}$O$_4$N$_2$S (M–H)$^+$: 371.10656, found: 371.10595.

3-(4-Trifluoromethyl-2-nitrobenzylidene)-1-(phenylsulfonyl)piperidine 2.62j. The general procedure was followed by using 1.86 g of 2.44j (4.8 mmol), 10 mL of trifluoroacetic acid, 6.7 mL of triethylamine (48 mmol), 1.9 mL of benzenesulfonyl chloride (14.4 mmol) and 40 mL of CH$_2$Cl$_2$. Purification by MPLC (2:98 – 20:80 EtOAc:hexanes) afforded the product, a yellow liquid, as a 80:20 mixture of isomers.
(1.95 g, 95%). Spectral data for the major product: $^1$H NMR (500MHz, CDCl$_3$) $\delta$ 8.25 (s, 1H), 7.80 (d, $J = 7.8$ Hz, 3H), 7.60 (d, $J = 7.4$ Hz, 1H), 7.54 (t, $J = 7.6$ Hz, 2H), 7.35 (d, $J = 8.0$ Hz, 1H), 6.71 (s, 1H), 3.75 (s, 2H), 3.18 (t, $J = 5.4$ Hz, 2H), 2.08 (t, $J = 5.9$ Hz, 2H), 1.62 (quintet, $J = 5.1$ Hz, 2H); $^{13}$C NMR (125 MHz, CDCl$_3$) $\delta$ 148.2 (C), 137.7 (C), 136.5 (C), 135.4 (C), 133.0 (CH), 133.0 (CH), 130.7 (q, $J_C$= 34.3 Hz, C), 129.3 (CH), 129.2 (CH), 127.7 (CH), 122.8 (q, $J_C$= 272 Hz, C), 122.0 (m, CH), 121.4 (CH), 53.6 (CH$_2$), 46.5 (CH$_2$), 27.1 (CH$_2$), 25.1 (CH$_2$). Diagnostic data for the minor product: $^{13}$C NMR (125 MHz, CDCl$_3$) $\delta$ 137.8 (C), 135.9 (C), 135.2 (C), 133.8 (CH), 133.0 (CH), 129.1 (CH), 127.6 (CH), 121.3 (CH); ATR-FTIR (thin film): 2944, 1571, 1321, 1080 cm$^{-1}$; HRMS (El) $m/z$ calculated for C$_{19}$H$_{18}$N$_2$O$_4$SF$_3$ (M+H)$^+$: 425.07829, found: 425.07926.

![2.62k](image)

**3-(3-Methyl-2-nitrobenzylidene)-1-(phenylsulfonyl)piperidine** 2.62k. The general procedure was followed by using 2.80 g of **2.44k** (8.4 mmol), 20 mL of trifluoroacetic acid, 11.7 mL of triethylamine (84 mmol), 3.3 mL of benzenesulfonyl chloride (25.3 mmol) and 80 mL of CH$_2$Cl$_2$. Purification by MPLC (2:98 – 20:80 EtOAc:hexanes) afforded the product as a yellow solid (3.05 g, 97%): $^1$H NMR (500 MHz, CDCl$_3$) $\delta$ 7.76 (d, $J = 7.5$ Hz, 2H), 7.59 (t, $J = 7.4$ Hz, 1H), 7.53 (t, $J = 7.5$ Hz, 2H), 7.29 (t, $J = 7.7$ Hz, 1H), 7.18 (d, $J = 7.6$ Hz, 1H), 6.97 (d, $J = 7.6$ Hz, 1H), 6.33 (s, 1H), 3.63 (s, 2H), 3.13 (t, $J = 5.4$ Hz, 2H), 2.27 (s, 3H), 2.08 (t, $J = 6.1$ Hz, 2H), 1.58 (quintet, $J = 5.8$ Hz, 2H); $^{13}$C NMR (125 MHz, CDCl$_3$) $\delta$ 150.9 (C), 138.4 (C), 136.4 (C), 132.9 (CH), 130.3 (CH), 129.9 (CH), 129.7 (C), 129.2 (CH), 128.9 (C), 128.2 (CH), 127.7 (CH), 120.0 (CH), 53.4 (CH$_2$), 46.5 (CH$_2$), 27.1 (CH$_2$), 25.1 (CH$_2$), 17.4 (CH$_3$). ATR-FTIR (thin film): 2966, 1521, 1347, 1160 cm$^{-1}$; HRMS (El) $m/z$ calculated for C$_{19}$H$_{21}$N$_2$O$_4$S (M+H)$^+$: 373.12221, found: 373.12124.
3-(3-Methoxy-2-nitrobenzylidene)-1-(phenylsulfonyl)piperidine 2.62l. The general procedure was followed by using 2.97 g of 2.44l (8.5 mmol), 20 mL of trifluoroacetic acid, 11.9 mL of triethylamine (85 mmol), 3.3 mL of benzensulfonyl chloride (25.5 mmol) and 80 mL of CH$_2$Cl$_2$. Purification by MPLC (2:98 – 20:80 EtOAc:hexanes) afforded the product, a yellow solid, as a 74:26 mixture of isomers (3.3 g, 99%). Spectral data for the major product: $^1$H NMR (500 MHz, CDCl$_3$) $\delta$ 7.77 (d, $J = 7.7$ Hz, 2H), 7.59 (q, $J = 6.6$ Hz, 1H), 7.54 (t, $J = 7.6$ Hz, 2H), 7.34 (t, $J = 8.1$ Hz, 1H), 6.94 (d, $J = 8.4$ Hz, 1H), 6.72 (d, $J = 7.6$ Hz, 1H), 6.31 (s, 1H), 3.86 (s, 3H), 3.63 (s, 2H), 3.14 (t, $J = 5.3$ Hz, 2H), 2.10 (t, $J = 5.9$ Hz, 2H), 1.60 (s, 2H); $^{13}$C NMR (125 MHz, CDCl$_3$) $\delta$ 150.8 (C), 141.0 (C), 139.0 (C), 136.3 (C), 132.9 (CH), 130.7 (CH), 130.2 (C), 129.2 (CH), 127.7 (CH), 121.8 (CH), 119.3 (CH), 111.4 (CH), 56.4 (CH$_3$), 53.4 (CH$_2$), 46.5 (CH$_2$), 27.2 (CH$_2$), 25.1 (CH$_2$). Diagnostic data for the minor product: $^{13}$C NMR (125 MHz, CDCl$_3$) $\delta$ 141.0(C), 136.0(C), 131.1(CH), 129.7(C), 129.1(CH), 127.7 (CH), 122.3(CH), 118.9(CH), 111.6(CH), 47.6(CH$_2$), 46.6(CH$_2$), 33.7(CH$_2$), 26.0(CH$_2$). ATR-FTIR (thin film): 2943, 1574, 1369, 1160 cm$^{-1}$; HRMS (El) m/z calculated for C$_{19}$H$_{21}$N$_2$O$_5$S (M+H)$^+$: 389.11712, found: 389.11775.

(S)-2-[2-(2-Azido-phenyl)-1-methyl-vinyl]-1-benzenesulfonyl-pyrrolidine 2.63. The general procedure was followed by using 0.119 g of azide 2.60 (0.51 mmol), 0.16 mL of TFA in 2 mL of dichloromethane. Sulfonyl protection was accomplished.
using 0.57 mL of Et₃N (4.08 mmol) followed by the addition of 0.12 mL of benzenesulfonyl chloride (1.02 mmol). The reaction mixture was purified by MPLC (5:100 – 10:100 EtOAc:hexane) to afford the product as a yellow solid (0.112 g, 84% over 2 steps). [α]D²⁰: −19.6 (c 0.125, CH₂Cl₂); mp 103 – 105 °C. 

1H NMR (500 MHz, CDCl₃) δ 7.89 (d, J = 7.5 Hz, 2H), 7.57 (t, J = 7.5 Hz, 1H), 7.51 (t, J = 7.5 Hz, 2H), 7.27 – 7.21 (m, 2H), 7.13 – 7.07 (m, 2H), 6.45 (s, 1H), 4.15 (t, J = 6.5 Hz, 1H), 3.55 – 3.51 (m, 1H), 3.43 – 3.41 (m, 1H), 3.43 – 3.41 (m, 1H); 13C NMR (125 MHz, CDCl₃) δ 139.3 (C), 139.0 (C), 137.9 (C), 132.6 (CH), 130.7 (CH), 129.4 (C), 128.9 (CH), 127.9 (CH), 127.6 (CH), 124.3 (C), 121.7 (C), 118.2 (CH), 66.7 (CH), 49.6 (CH₂), 31.8 (CH₂), 24.1 (CH₂), 14.3 (CH₃). ATR-FTIR (thin film): 2972, 2878, 2113, 2094, 1482, 1443, 1346, 1291, 1160, 1092 cm⁻¹.

HRMS (EI) m/z calculated for C₁₉H₂₀O₂N₂S (M–N₂)⁺: 340.12455, found: 340.12401.

(E)-2-[2-(2-Azido-5-methyl-phenyl)-1-methyl-vinyl]-1-benzenesulfonyl-pyrroldidine 2.58b. The general procedure was followed by using 0.056 g of azide 2.59b (0.16 mmol), 0.06 mL of TFA in 1 mL of dichloromethane. Sulfonyl protection was accomplished using 0.23 mL of Et₃N (1.63 mmol) followed by the addition of 0.04 mL of benzenesulfonyl chloride (0.32 mmol). The reaction mixture was purified by MPLC (5:100 – 10:100 EtOAc:hexane) to afford the product as a yellow solid (0.049 g, 79% over 2 steps). mp 107 – 109 °C. ¹H NMR (500 MHz, CDCl₃) δ 7.89 (d, J = 7.0 Hz, 2H), 7.58 (t, J = 7.5 Hz, 1H), 7.52 (d, J = 7.5 Hz, 2H), 7.07 – 7.01 (m, 3H), 6.40 (s, 1H), 4.14 (t, J = 6.0 Hz, 1H), 3.56 – 3.52 (m, 1H), 3.44 – 3.40 (m, 1H), 2.31 (s, 3H), 1.92 – 1.81 (m, 3H), 1.71 (s, 3H), 1.66 – 1.60 (m, 1H); ¹³C NMR (125 MHz, CDCl₃) δ 139.1 (C), 138.1 (C), 135.2 (C), 133.9 (C), 132.5 (CH), 131.3 (CH), 129.2 (C), 128.9 (CH), 128.6 (CH), 127.6 (CH), 121.8 (CH), 118.1 (CH), 66.7 (CH), 49.6 (CH₂), 31.8 (CH₂), 24.1 (CH₂), 20.9 (CH₃), 14.3 (CH₃). ATR-FTIR (thin film):
2978, 2931, 2120, 1448, 1333, 1295, 1159, 1092, 1007 cm\(^{-1}\). HRMS (El) \(m/z\) calculated for \(C_{20}H_{22}O_{2}N_{4}S\) \((M)^{+}\): 382.14634, found: 382.14712.

\[
\begin{align*}
&(E)-2-[2-(2-Azido-5-fluoro-phenyl)-1-methyl-vinyl]-1-benzenesulfonyl-pyrrolidine 2.58c. \text{ The general procedure was followed by using 0.100 g of azide 2.59c (0.29 mmol), 0.09 mL of TFA (1.15 mmol) in 1 mL of dichloromethane. Sulfonyl protection was accomplished using 0.32 mL of Et}_3\text{N (2.32 mmol) followed by the addition of 0.07 mL of benzenesulfonyl chloride (0.58 mmol). The reaction mixture was purified by MPLC (5:100 – 10:100 EtOAc:hexane) to afford the product as a yellow solid (0.084 g, 76% over 2 steps). mp 90 – 92 °C.} \\
&{^1}\text{H NMR (500 MHz, CDCl}_3\delta 7.87 \,(d, \, J = 7.5 \text{ Hz, 2H}), \, 7.58 \,(t, \, J = 7.5 \text{ Hz, 3H}), \, 7.51 \,(t, \, J = 7.5 \text{ Hz, 1H}), \, 7.07 - 7.04 \,(m, \, 1H), \, 6.97 - 6.92 \,(m, \, 2H), \, 6.41 \,(s, \, 1H), \, 4.13 \,(t, \, J = 7.5 \text{ Hz, 1H}), \, 3.55 - 3.51 \,(m, \, 1H), \, 3.42 - 3.38 \,(m, \, 1H), \, 1.89 - 1.78 \,(m, \, 3H), \, 1.73 \,(s, \, 3H), \, 1.64 - 1.60 \,(m, \, 1H). {^{13}}\text{C NMR (125 MHz, CDCl}_3\delta 159.3 \,(d, \, J_{CF} = 242 \text{ Hz, C}), \, 140.6 \,(C), \, 137.9 \,(C), \, 133.8 \,(C), \, 132.6 \,(CH), \, 131.1 \,(C), \, 129.0 \,(CH), \, 127.6 \,(CH), \, 120.8 \,(CH), \, 119.4 \,(CH), \, 117.3 \,(d, \, J_{CF} = 29.7 \text{ Hz, CH}), \, 114.6 \,(d, \, J_{CF} = 23.4 \text{ Hz, CH}), \, 66.5 \,(CH), \, 49.6 \,(CH_2), \, 31.8 \,(CH_2), \, 24.1 \,(CH_2), \, 14.5 \,(CH}_3). {^{19}}\text{F NMR (282 MHz, CDCl}_3\delta -118.6.} \\
&\text{ATR-FTIR (thin film): 3036, 2977, 2888, 2125, 2101, 1484, 1345, 1272 cm}^{-1}. \text{ HRMS (El) }m/z\text{ calculated for }C_{19}H_{19}O_2N_4SF \,(M)^{+}: 386.12127, \text{ found: 386.12138.}
\end{align*}
\]

\[
\begin{align*}
&(E)-2-[2-(2-Azido-4-trifluoromethyl-phenyl)-1-methyl-vinyl]-1-benzenesulfonyl-pyrrolidine 2.58d. \text{ The general procedure was followed by using 0.025 g of azide 2.59d (0.064 mmol), 0.02 mL of TFA (0.26 mmol) in 1 mL of dichloromethane. Sulfonyl protection was accomplished using 0.09 mL of Et}_3\text{N (0.64 mmol) followed by}
\end{align*}
\]
the addition of 0.016 mL of benzenesulfonyl chloride (0.128 mmol). The reaction mixture was purified by MPLC (5:100 – 10:100 EtOAc:hexane) to afford the product as a yellow solid (0.021 g, 77% over 2 steps). mp 146 – 148 °C. \(^1\)H NMR (500 MHz, CDCl\(_3\)) \(\delta\) 7.88 (d, \(J = 7.5\) Hz, 2H), 7.59 (t, \(J = 7.5\) Hz, 1H), 7.52 (t, \(J = 7.5\) Hz, 2H), 7.34 (br s, 3H), 6.5 (s, 1H), 4.15 (t, \(J = 6.0\) Hz, 1H), 3.57 – 3.53 (m, 1H), 3.42 – 3.37 (m, 1H), 1.92 – 1.78 (m, 3H), 1.74 (s, 3H), 1.65 – 1.60 (m, 1H); \(^{13}\)C NMR (125 MHz, CDCl\(_3\)) \(\delta\) 141.5 (C), 138.8 (C), 137.8 (C), 133.1 (C), 132.7 (CH), 131.2 (CH), 130.1 (q, \(J_{CF} = 32.5\) Hz, C), 129.0 (CH), 127.6 (CH), 123.7 (q, \(J_{CF} = 270\) Hz, CF\(_3\)), 121.0 (CH), 120.6 (CH), 115.1 (CH), 66.5 (CH), 49.6 (CH\(_2\)), 31.8 (CH\(_2\)), 24.1 (CH\(_2\)), 14.6 (CH\(_3\)); \(^{19}\)F NMR (282 MHz, CDCl\(_3\)) \(\delta\) –63.01. ATR-FTIR (thin film): 3063, 2982, 2859, 2109, 1418, 1329, 1275, 1010, 867 cm\(^{-1}\). HRMS (EI) m/z calculated for C\(_{20}\)H\(_{19}\)F\(_3\)N\(_4\)O\(_2\)S (M – N\(_2\))^+: 408.11194, found: 408.11231.

(E)-2-(1-(2-azidophenyl)prop-1-en-2-yl)-1-(phenylsulfonyl)piperidine  E-2.58e.

The general procedure was followed by using 0.212 mg of azide E-2.59e (0.62 mmol), 5 mL of TFA in 20 mL of anhydrous dichloromethane. Sulphonyl protection was accomplished using 0.86 mL of Et\(_3\)N (6.2 mmol) followed by the addition of 0.24 mL of benzenesulfonyl chloride (1.86 mmol). The reaction mixture was purified by MPLC (3:100 – 5:100 EtOAc:hexane) afforded product as yellow solid (0.115 g, 49%). \(^1\)H NMR (500 MHz, CDCl\(_3\)) \(\delta\) 7.91 (d, \(J = 7.1\) Hz, 2H), 7.56 (t, \(J = 7.3\) Hz, 1H), 7.51 (t, \(J = 7.4\) Hz, 2H), 7.27 (t, \(J = 7.7\) Hz, 1H), 7.17 (d, \(J = 6.9\) Hz, 1H), 7.13 (d, \(J = 8.0\) Hz, 1H), 7.10 (t, \(J = 7.5\) Hz, 1H), 6.35 (s, 1H), 4.58 (s, 1H), 3.73 (d, \(J = 14.0\) Hz, 1H), 3.20 (td, \(J = 13.2, 2.4\) Hz, 1H), 2.03 (d, \(J = 9.2\) Hz, 1H), 1.82 – 1.75 (m, 1H), 1.71 (s, 3H), 1.60 – 1.48 (m, 4H); \(^{13}\)C NMR (125 MHz, CDCl\(_3\)) \(\delta\) 141.3 (C), 138.1 (C), 136.7 (C), 132.2 (CH), 130.7 (CH), 129.7 (C), 129.0 (CH), 128.0 (CH), 127.2 (CH), 121.0 (CH), 115.1 (CH), 66.5 (CH), 49.6 (CH\(_2\)), 31.8 (CH\(_2\)), 24.1 (CH\(_2\)), 14.6 (CH\(_3\)).
124.3 (CH), 122.9 (CH), 118.2 (CH), 58.6 (CH), 42.6 (CH₂), 26.6 (CH₂), 24.5 (CH₂), 19.6 (CH₂), 16.3 (CH₃).

**(Z)-2-(1-(2-azidophenyl)prop-1-en-2-yl)-1-(phenylsulfonyl)piperidine  Z-2.58e.**
The general procedure was followed by using 0.150 g of azide **Z-2.59e** (0.44 mmol), 5 mL of TFA in 20 mL of anhydrous dichloromethane. Sulphonyl protection was accomplished using 0.60 mL of Et₃N (4.4 mmol) followed by the addition of 0.17 mL of benzenesulfonyl chloride (1.32 mmol). The reaction mixture was purified by MPLC (3:100 – 5:100 EtOAc:hexane) to afford the product as a yellow solid (0.053 g, 32%).

**1H NMR (500 MHz, CDCl₃)** δ 7.91 (d, J = 7.5 Hz, 2H), 7.56 (t, J = 7.3 Hz, 1H), 7.51 (t, J = 7.5 Hz, 2H), 7.27 (t, J = 7.7 Hz, 1H), 7.17 (d, J = 7.6 Hz, 1H), 7.13 (d, J = 7.9 Hz, 1H), 7.10 (t, J = 7.5 Hz, 1H), 6.35 (s, 1H), 4.58 (s, 1H), 3.73 (d, J = 14.0 Hz, 1H), 3.20 (td, J = 13.1, 2.3 Hz, 1H), 2.03 (d, J = 8.5 Hz, 1H), 1.71 (s, 3H), 1.60 – 1.48 (m, 5H); **13C NMR (125 MHz, CDCl₃)** δ 141.3 (C), 138.1 (C), 136.7 (C), 132.2 (CH), 130.7 (CH), 129.7 (C), 129.0 (CH), 128.0 (CH), 127.2 (CH), 124.3 (CH), 122.9 (CH), 118.2 (CH), 58.6 (CH), 42.6 (CH₂), 26.6 (CH₂), 24.5 (CH₂), 19.6 (CH₂), 16.3 (CH₃).

**ATR-FTIR (thin film):** 3060, 2940, 2120, 2086, 1445, 1285, 1150 cm⁻¹. **HRMS (ESI) m/z calculated for C₂₀H₂₃N₄O₂S (M+H)⁺:** 383.1542, found: 383.1546.

**(E)-2-[2-(2-Azido-phenyl)-1-phenyl-vinyl]-1-benzenesulfonyl-pyrroldine  2.58f.**
The general procedure was followed by using 0.025 g of azide **2.59f** (0.064 mmol), 0.02 mL of TFA (0.26 mmol) in 1 mL of dichloromethane. Sulfonyl protection was accomplished using 0.09 mL of Et₃N (0.64 mmol) followed by the addition of 0.016 mL of benzenesulfonyl chloride (0.128 mmol). The reaction mixture was purified by
MPLC (5:100 – 10:100 EtOAc:hexane) to afford the product as a yellow solid (0.023 g, 83% over 2 steps). \(^1\)H NMR (500 MHz, CDCl\(_3\)) \(\delta\) 7.25 – 7.23 (m, 3H), 7.16 – 7.05 (m, 4H), 6.71 – 6.65 (m, 2H), 6.42 (s, 1H), 4.78 (br s, 0.30 H), 4.65 (br s, 0.70 H), 3.60 – 3.45 (m, 2H), 1.97 – 1.66 (m, 4H), 1.48 (s, 9H); \(^{13}\)C NMR (125 MHz, CDCl\(_3\)) \(\delta\) 143.6 (C), 138.5 (C), 138.3 (C), 138.0 (C), 132.6 (CH), 130.7 (CH), 129.4 (CH), 129.0 (CH), 128.7 (C), 128.6 (CH), 127.8 (CH), 127.5 (CH), 127.4 (CH), 124.0 (C), 122.8 (CH), 117.8 (CH), 66.1 (CH), 49.3 (CH\(_2\)), 31.5 (CH\(_2\)), 23.7 (CH\(_2\)); ATR-FTIR (thin film): 2927, 2857, 2120, 2089, 1482, 1441, 1343, 1289, 1157, 1095 cm\(^{-1}\). HRMS (EI) \(m/z\) calculated for C\(_{24}\)H\(_{22}\)N\(_4\)O\(_2\)S (M\(^+\)): 430.14634, found: 430.14677.

2-[2-(2-Azido-5-methyl-phenyl)-1-methyl-vinyl]-1-(toluene-4-sulfonyl)-pyrrolidine 2.38. The general procedure was followed by using 0.145 g of azide (0.42 mmol), 0.16 mL of TFA (2.11 mmol) in 2 mL of dichloromethane. Sulfonyl protection was accomplished using 0.59 mL of Et\(_3\)N (4.20 mmol) followed by the addition of 0.16 g of tosyl chloride (0.84 mmol). The reaction mixture was purified by MPLC (5:100 – 10:100 EtOAc:hexane) to afford product as a yellow solid (0.126 g, 75%). \(^1\)H NMR (500 MHz, CDCl\(_3\)) \(\delta\) 7.77 (d, \(J = 8.0\) Hz, 2H), 7.31 (d, \(J = 8.0\) Hz, 2H), 7.07 – 7.00 (m, 3H), 6.40 (s, 1H), 4.10 (t, \(J = 5.5\) Hz, 1H), 3.51 – 3.54 (m, 1H), 3.38 – 3.40 (m, 1H), 2.42 (s, 3H), 2.31 (s, 3H), 1.92 – 1.80 (m, 3H), 1.73 (s, 3H), 1.65 – 1.60 (m, 1H); \(^{13}\)C NMR (125 MHz, CDCl\(_3\)) \(\delta\) 143.3 (C), 139.3 (C), 135.2 (C), 135.0 (C), 132.9 (C), 131.3 (CH), 129.6 (CH), 129.3 (C), 128.6 (CH), 127.7 (C), 121.7 (CH), 118.1 (CH), 66.6 (CH), 49.6 (CH\(_2\)), 31.8 (CH\(_2\)), 24.1 (CH\(_2\)), 21.5 (CH\(_3\)), 20.9 (CH\(_3\)), 14.3 (CH\(_3\)). ATR-FTIR (thin film): 3375, 2920, 2849, 1686, 1539, 1329, 1157, 1088 cm\(^{-1}\). HRMS (EI) \(m/z\) calculated for C\(_{21}\)H\(_{24}\)N\(_4\)O\(_2\)S (M\(^+\)): 396.16199, found: 396.16259.
G. Rh$_2$(II)-Catalyzed Synthesis of 2,3-Disubstituted Indoles from Styryl Azides.

Optimization

To a mixture of styryl azide and metal catalyst (5 mol%) was added toluene (0.1M). The resulting mixture was heated for 16 h. The mixture was cooled to room temperature, diluted with CH$_2$Cl$_2$ and concentrated in vacuo. Dibromomethane (0.7 µL, 0.1 mmol) was added, and the mixture was analyzed using $^1$H NMR spectroscopy to determine the outcome of the reaction.

Table 2.2. Survey of reaction conditions for 2,3-indole formation.

<table>
<thead>
<tr>
<th>entry</th>
<th>catalyst</th>
<th>%, yield$^a$</th>
<th>2.18 : 2.19</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>none</td>
<td>n.r.</td>
<td>n.a.</td>
</tr>
<tr>
<td>2</td>
<td>Rh$_2$(esp)$_2$</td>
<td>87</td>
<td>100:0</td>
</tr>
<tr>
<td>3</td>
<td>Rh$_2$(O$_2$CC$<em>7$H$</em>{15}$)$_4$</td>
<td>85</td>
<td>100:0</td>
</tr>
<tr>
<td>4</td>
<td>Rh$_2$(O$_2$CC$_3$F$_7$)$_4$</td>
<td>32</td>
<td>86:14</td>
</tr>
<tr>
<td>5</td>
<td>Rh$_2$(O$_2$CCF$_3$)$_4$</td>
<td>36</td>
<td>80:20</td>
</tr>
<tr>
<td>6</td>
<td>Rh$_2$(OCCH)$_4$</td>
<td>n.r.</td>
<td>n.a.</td>
</tr>
<tr>
<td>7</td>
<td>[(cod)Ir(OMe)]$_2$</td>
<td>13</td>
<td>91:9</td>
</tr>
<tr>
<td>8</td>
<td>FeBr$_2$</td>
<td>trace</td>
<td>n.a.</td>
</tr>
<tr>
<td>9</td>
<td>FeBr$_3$</td>
<td>0</td>
<td>n.a.</td>
</tr>
<tr>
<td>10</td>
<td>AuCl</td>
<td>n.r.</td>
<td>n.a.</td>
</tr>
<tr>
<td>11</td>
<td>Cu(OTf)$_2$</td>
<td>trace</td>
<td>n.a.</td>
</tr>
<tr>
<td>12</td>
<td>CuCl</td>
<td>n.r.</td>
<td>n.a.</td>
</tr>
<tr>
<td>13</td>
<td>ZnI$_2$</td>
<td>n.r.</td>
<td>n.a.</td>
</tr>
<tr>
<td>14</td>
<td>Pd(PPh$_3$)$_2$Cl$_2$</td>
<td>n.r.</td>
<td>n.a.</td>
</tr>
<tr>
<td>15</td>
<td>Ru(TPP)CO</td>
<td>0</td>
<td>n.a.</td>
</tr>
</tbody>
</table>

$^a$ as determined using $^1$H NMR spectroscopy using CH$_2$Br$_2$ as the internal standard.
To a mixture of styryl azide and Rh$_2$(esp)$_2$ (5 mol%) was added toluene (0.1M). The resulting mixture was heated at 80 °C. After 16 h, the mixture was cooled to room temperature, diluted with CH$_2$Cl$_2$ and concentrated in vacuo. Dibromomethane (7 µL, 0.1 mmol) was added, and the mixture was analyzed using $^1$H NMR spectroscopy to determine the outcome of the reaction. Purification of the residue by MPLC (3:97 – 0:100 EtOAc: hexanes) afforded the product.

Table 2.1 Survey of the effect of the N-substituent identity on reaction outcome.

<table>
<thead>
<tr>
<th>entry</th>
<th>R</th>
<th>%, yield $^a$</th>
<th>2.15:2.16</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>SO$_2$Ph</td>
<td>87</td>
<td>100:0$^c$</td>
</tr>
<tr>
<td>2</td>
<td>Boc</td>
<td>46</td>
<td>60:40$^c$</td>
</tr>
<tr>
<td>3</td>
<td>Bz</td>
<td>42</td>
<td>66:34$^b$</td>
</tr>
<tr>
<td>4</td>
<td>Bn</td>
<td>18</td>
<td>100:0</td>
</tr>
</tbody>
</table>

$^a$ as determined using $^1$H NMR spectroscopy using CH$_2$Br$_2$ as the internal standard.

$^b$ DMSO-$d_6$ was used as the NMR solvent.

$^c$ acetone-$d_6$ was used as the NMR solvent.

2-(Phenylsulfonyl)-1,2,3,4,5,6-hexahydroazepino[4,3-b]indole 2.21c. The general procedure was followed by using 0.0404 g of 2.62c (0.11 mmol), 0.0043 g of Rh$_2$(esp)$_2$ and 1.1 mL of toluene. Purification by MPLC (3:97 – 20:80 EtOAc: hexanes) afforded the product as a white solid (31 mg, 84%): $^1$H NMR (500MHz, C$_3$D$_6$O) $\delta$ 9.95 (s, 1H), 7.74 (d, $J = 7.4$ Hz, 2H), 7.56 (t, $J = 7.4$ Hz, 1H), 7.51 (dd, $J = 5.7$, 3.1 Hz, 1H), 7.43 (t, $J = 7.8$ Hz, 2H), 7.26 – 7.28 (m, 1H), 7.03 (dd, $J = 6.0$, 3.1 Hz, 2H), 4.62 (s, 2H), 3.62 (t, $J = 5.5$ Hz, 2H), 2.87 (t, $J = 5.9$ Hz, 2H), 1.94 – 1.89 (m, 2H); $^{13}$C NMR (125 MHz, C$_3$D$_6$O) $\delta$ 140.1 (C), 137.5 (C), 134.8 (C), 132.2 (CH),
128.8 (CH), 127.7 (C), 127.1 (CH), 120.5 (CH), 119.0 (CH), 116.9 (CH), 110.6 (CH), 109.0 (C), 51.0 (CH₂), 44.0 (CH₂), 26.7 (CH₂), 26.5 (CH₂). ATR-FTIR (thin film): 3405, 3057, 2909, 1321, 1158 cm⁻¹; HRMS (EI) m/z calculated for C₁₈H₁₈N₂O₂S (M)⁺: 326.10890, found: 326.10983.

2-Boc-1,2,3,4,5,6-hexahydroazepino[4,3-b]indole 2.64. The general procedure was followed by using 0.097 g of azide (0.31 mmol), 0.0117 g of Rh₂(esp)₂ and 3.1 mL of toluene. Dibromomethane (7 µL, 0.1 mmol) was added, and the mixture was analyzed using ¹H NMR spectroscopy to determine the outcome of the reaction. Purification by MPLC (3:97 – 20:80 EtOAc:hexanes) afforded the product, a yellow oil as a 60:40 mixture of product 2.64a and 2.64b each as mixture of rotamers (0.0406 g, 46%): ¹H NMR (500 MHz, acetone-d₆) δ 9.95 (s, 0.56H), 9.91 (s, 0.29H), 7.47 (d, J = 8.1 Hz, 1H), 7.26 (s, 1H), 7.00 (d, J = 1.7 Hz, 1H), 6.99 (d, J = 3.3 Hz, 1H), 4.82 (s, 0.3H), 4.65 (s, 0.7H), 4.59 (s, 1H), 3.70 (s, 2H), 2.99 (t, J = 6.0 Hz, 2H), 1.94 (s, 0.8H), 1.88 (s, 1.2H), 1.40 (s, 4H), 1.30 (s, 5H). ¹³C NMR (125 MHz, acetone-d₆) δ 154.7 (C), 138.1 (C), 137.5 (C), 137.0 (CH), 136.7 (C), 134.7 (C), 129.1 (C), 127.7 (CH), 126.4 (CH), 124.1 (CH), 120.3 (CH), 120.2 (CH), 118.7 (CH), 118.2 (CH), 117.9 (CH), 117.3 (CH), 117.0 (CH), 112.6 (CH), 111.6 (C), 110.6 (CH), 110.5 (CH), 78.3 (C), 49.5 (CH₂), 49.2 (CH₂), 46.7 (CH₂), 45.4, 42.6 (CH₂), 42.2 (CH₂), 27.8 (CH₃), 27.2 (CH₃), 27.0 (CH₂), 26.4 (CH₂) only visible peaks.
2-Benzoyl-1,2,3,4,5,6-hexahydroazepino[4,3-b]indole 2.65. The general procedure was followed by using 0.0845 mg of azide (0.28 mmol), 0.0101 g of Rh₂(esp)₂ and 3.5 mL of toluene. Dibromomethane (7 µL, 0.1 mmol) was added, and the mixture was analyzed using ¹H NMR spectroscopy to determine the outcome of the reaction. Purification by MPLC (3:97 – 20:80 EtOAc: hexanes) afforded the product, a white solid as a 66:34 mixture of products (0.034 g, 44%). Spectral data for major product: ¹H NMR (500MHz, DMSO-d₆) δ 10.98 (s, 1H), 7.44 (d, J = 7.3 Hz, 1H), 7.42 (s, 2H), 7.30 (t, J = 7.8 Hz, 2H), 7.26 (d, J = 7.7 Hz, 1H), 7.18 (d, J = 7.3 Hz, 2H), 6.97 (t, J = 7.3 Hz, 1H), 4.54 (s, 2H), 3.92 (s, 2H), 3.00 (t, J = 5.4 Hz, 2H), 1.99 (s, 2H); ¹³C NMR (125 MHz, DMSO-d₆) δ 170.0 (C), 138.4 (C), 137.0 (C), 134.7 (C), 129.8 (CH), 128.6 (CH), 127.1 (CH), 126.6 (C), 120.6(CH), 119.0 (CH), 116.9 (CH), 111.3 (CH), 109.5 (C), 48.3 (CH₂), 45.9 (CH₂), 27.2 (CH₂), 26.6 (CH₂). Selected data for minor product 11c: ¹H NMR (500MHz, DMSO-d₆) δ 6.84 (t, J = 7.3 Hz, 1H), 6.75 (d, J = 7.9 Hz, 1H), 4.84 (s, 1H), 3.65 (s, 1H), 2.92 (s, 1H), 1.81 (s, 1H); ¹³C NMR (125 MHz, DMSO-d₆) δ 138.0 (C), 137.5 (C), 129.5 (CH), 128.9 (CH), 126.8 (CH), 117.6 (CH), 110.0 (C), 55.4 (CH₂), 52.3 (CH₂), 28.0 (CH₂), 26.7 (CH₂). ATR-FTIR (thin film): 3260, 3056, 2917, 1608, 1445, 1258 cm⁻¹; HRMS (EI) m/z calculated for C₁₉H₁₈N₂O (M)⁺: 290.14192, found: 290.14096.

2-Benzyl-1,2,3,4,5,6-hexahydroazepino[4,3-b]indole 2.66. The general procedure was followed by using 0.0825 g of azide (0.27 mmol), 0.0090 g of Rh₂(esp)₂ and 3.0 mL of toluene. Dibromomethane (7 µL, 0.1 mmol) was added, and the mixture was
analyzed using $^1$H NMR spectroscopy to determine the outcome of the reaction (18% yield). Purification by MPLC (3:97 – 0:100 EtOAc: hexanes) afforded the product, a brown oil with 90% purity. Diagnostic peaks in the spectral data: $^1$H NMR (500 MHz, CDCl$_3$) δ 8.14 (br s, 1H), 7.42 (d, $J$ = 7.2 Hz, 1H), 7.31 (m, 5H), 7.24 (d, $J$ = 7.8 Hz, 1H), 7.10 (t, $J$ = 7.4 Hz, 1H), 7.05 (t, $J$ = 7.4 Hz, 1H), 4.02 (s, 2H), 3.74 (s, 2H), 3.24 (t, $J$ = 5.0 Hz, 2H), 2.94 (t, $J$ = 5.7 Hz, 2H), 1.92 (s, 2H). HRMS (EI) m/z calculated for C$_{19}$H$_{20}$N$_2$ (M)$^+$: 276.16265, found: 276.16220.

**General Procedure**

To a mixture of styryl azide and Rh$_2$(esp)$_2$ (5 mol%) was added toluene (0.1M). The resulting mixture was heated at 80 °C. After 16 h, the mixture was cooled to room temperature, diluted with CH$_2$Cl$_2$ and concentrated *in vacuo*. Purification of the residue by MPLC (3:97 – 20:80 EtOAc: hexanes) afforded the product.

**2.21a**

2-(Phenylsulfonyl)-1,2,3,4-tetrahydropyrrolo[3,4-b]indole 2.21a. The general procedure was followed by using 0.0600 g of 2.46a (0.18 mmol), 0.0070 g of Rh$_2$(esp)$_2$ and 1.9 mL of toluene. Purification by MPLC (3:97 – 20:80 EtOAc: hexanes) afforded the product as a white solid (0.045 g, 82%): $^1$H NMR (500 MHz, CDCl$_3$) δ 7.99 (br s, 1H), 7.90 (d, $J$ = 7.5 Hz, 2H), 7.57 (t, $J$ = 7.3 Hz, 1H), 7.51 (t, $J$ = 7.4 Hz, 2H), 7.39 (d, $J$ = 7.8 Hz, 1H), 7.33 (d, $J$ = 8.2 Hz, 1H), 7.17 (t, $J$ = 7.5 Hz, 1H), 7.11 (t, $J$ = 7.5 Hz, 1H), 4.67 (s, 4H); $^{13}$C NMR (125 MHz, CDCl$_3$) δ 140.6 (C), 137.4 (C), 135.2 (C), 132.8 (CH), 129.3 (CH), 127.4 (CH), 122.5 (C), 122.2 (CH),
120.6 (CH), 118.7 (CH), 113.9 (C), 111.9 (CH), 49.5 (CH₂), 48.5 (CH₂). ATR-FTIR (thin film): 3369, 3063, 2857, 1448, 1322, 1153 cm⁻¹; HRMS (EI) m/z calculated for C₁₆H₁₄N₂O₂S (M)⁺: 298.07760, found: 298.07810.

2.21b

2-(Phenylsulfonyl)-2,3,4,5-tetrahydro-1H-pyrido[4,3-b]indole 2.21b. The general procedure was followed by using 0.0765 g of 2.46b (0.23 mmol), 0.0085 g of Rh₂(esp)₂ and 2.3 mL of toluene. Purification by MPLC (3:97 – 20:80 EtOAc: hexanes) afforded the product as a white solid (0.055 g, 78%): ¹H NMR (500 MHz, CDCl₃) δ 7.88 (d, J = 7.6 Hz, 2H), 7.82 (s, 1H), 7.58 (t, J = 7.4 Hz, 1H), 7.52 (t, J = 7.7 Hz, 2H), 7.39 (d, J = 7.7 Hz, 1H), 7.28 (d, J = 8.1 Hz, 1H), 7.15 (t, J = 7.6 Hz, 1H), 7.09 (t, J = 7.9 Hz, 1H), 4.42 (s, 2H), 3.56 (t, J = 5.7 Hz, 2H), 2.88 (t, J = 5.6 Hz, 2H); ¹³C NMR (125 MHz, CDCl₃) δ 137.3 (C), 135.9 (C), 132.8 (CH), 130.8 (C), 129.1 (CH), 127.5 (CH), 125.4 (C), 122.0 (CH), 119.8 (CH), 117.5 (CH), 110.8 (CH), 106.2 (C), 43.5 (CH₂), 43.1 (CH₂), 23.7 (CH₂). ATR-FTIR (thin film): 3436, 3052, 1314, 1155 cm⁻¹; HRMS (EI) m/z calculated for C₁₇H₁₆N₂O₂S (M)⁺: 312.09325, found: 312.09273.

2.21d

9-Methoxy-2-(phenylsulfonyl)-1,2,3,4,5,6-hexahydroazepino[4,3-b]indole 2.21d. The optimal procedure was followed by using 0.0580 g of 2.46d (0.150 mmol), 0.0057 g of Rh₂(esp)₂ and 1.5 mL of toluene. Purification by MPLC (3:97 – 20:80
EtOAc: hexanes) afforded the product as a white solid (0.038 g, 70%): $^1$H NMR (500MHz, acetone-$d_6$) δ 9.77 (s, 1H), 7.74 (d, $J = 8.4$ Hz, 2H), 7.55 (t, $J = 7.4$ Hz, 1H), 7.43 (t, $J = 7.7$ Hz, 2H), 7.15 (d, $J = 8.7$ Hz, 1H), 7.02 (d, $J = 2.0$ Hz, 1H), 6.69 (dd, $J = 8.7$, 2.3 Hz, 1H), 4.59 (s, 2H), 3.81 (s, 3H), 3.60 (t, $J = 5.5$ Hz, 2H), 2.83 (t, $J = 5.8$ Hz, 2H), 1.91 – 1.87 (m, 2H); $^{13}$C NMR (125 MHz, acetone-$d_6$) δ 154.2 (C), 140.2 (C), 138.2 (C), 132.1 (CH), 129.9 (C), 128.8 (CH), 128.1 (C), 127.1 (CH), 111.3 (CH), 110.4 (CH), 108.8 (C), 99.3 (CH), 55.1 (CH$_3$), 51.0 (CH$_2$), 44.1 (CH$_2$), 26.7 (CH$_2$), 26.6 (CH$_2$). ATR-FTIR (thin film): 3380, 2931, 2832, 1445, 1321, 1148 cm$^{-1}$; HRMS (EI) $m/z$ calculated for C$_{19}$H$_{20}$N$_2$O$_3$S (M)$^+$: 356.11947, found: 356.11857.

9-Methyl-2-(phenylsulfonyl)-1,2,3,4,5,6-hexahydroazepino[4,3-b]indole  2.21e. The general procedure was followed by using 0.0835 g of 2.62e (0.22 mmol), 0.0085 g of Rh$_2$(esp)$_2$ and 2.3 mL of toluene. Purification by MPLC (3:97 – 20:80 EtOAc: hexanes) afforded the product as a white solid (0.061 g, 81%): $^1$H NMR (500MHz, acetone-$d_6$) δ 9.80 (s, 1H), 7.74 (d, $J = 7.2$ Hz, 2H), 7.55 (t, $J = 7.5$ Hz, 1H), 7.44 (t, $J = 7.8$ Hz, 2H), 7.29 (s, 1H), 7.15 (d, $J = 8.2$ Hz, 1H), 6.87 (d, $J = 8.2$ Hz, 1H), 4.59 (s, 2H), 3.59 (t, $J = 5.5$ Hz, 2H), 2.83 (t, $J = 5.9$ Hz, 2H), 2.41 (s, 3H), 1.87-1.92 (m, 2H); $^{13}$C NMR (125 MHz, acetone-$d_6$) δ 140.1 (C), 137.6 (C), 133.2 (C), 132.2 (CH), 128.8 (CH), 127.9 (C), 127.8 (C), 127.1 (CH), 122.1 (CH), 116.7 (CH), 110.4 (CH), 108.4 (C), 51.0 (CH$_2$), 44.0 (CH$_2$), 26.7 (CH$_2$), 26.6 (CH$_2$), 20.8 (CH$_3$). ATR-FTIR (thin film): 3382, 2931, 2855, 1445, 1321, 1148 cm$^{-1}$; HRMS (EI) $m/z$ calculated for C$_{19}$H$_{20}$N$_2$O$_2$S (M)$^+$: 340.12455, found: 340.12414.
9-Chloro-2-(phenylsulfonyl)-1,2,3,4,5,6-hexahydroazepino[4,3-b]indole  2.21f.
The optimal procedure was followed by using 0.025 g of azide 2.46f (0.06 mmol), 0.0025 g of Rh$_2$(esp)$_2$ (0.003 mmol) and 1.5 mL of toluene at 80 °C. Purification by MPLC (2:100 – 20:80 EtOAc:hexanes) afforded the product as a white solid (0.018 g, 77%). mp 214 – 216 °C; $^1$H NMR (500 MHz, acetone-$d_6$) δ 10.14 (s, 1H), 7.77 – 7.75 (m, 2H), 7.53 – 7.57 (m, 2H), 7.47 – 7.44 (m, 2H), 7.28 (m, 1H), 7.01 (dd, $J = 8.5$ Hz, 2.0 Hz, 1H), 4.59 (s, 2H), 3.61 (t, $J = 5.5$ Hz, 2H), 2.89 – 2.87 (m, 2H), 1.95 – 1.91 (m, 2H); $^{13}$C NMR (125 MHz, acetone-$d_6$) δ 140.0 (C), 139.7 (C), 133.2 (C), 132.2 (CH), 128.9 (CH), 128.7 (C), 127.1 (CH), 124.4 (C), 120.4 (CH), 116.4 (CH), 111.9 (CH), 109.2 (C), 50.9 (CH$_2$), 43.7 (CH$_2$), 26.6 (CH$_2$), 26.5 (CH$_2$). IR: 3389, 3067, 1573, 1472, 1445, 1316, 1153 cm$^{-1}$. HRMS (EI) m/z calculated for C$_{18}$H$_{17}$O$_2$N$_2$S$\text{Cl}$ (M$^+$): 360.06993, found: 360.06933.

8-Methoxy-2-(phenylsulfonyl)-1,2,3,4,5,6-hexahydroazepino[4,3-b]indole  2.21g.
The optimal procedure was followed by using 0.0360 g of 2.46g (0.09 mmol), 0.0036 g of Rh$_2$(esp)$_2$ and 1.0 mL of toluene. Purification by MPLC (3:97 – 20:80 EtOAc: hexanes) afforded the product as a white solid (0.019 g, 58%): $^1$H NMR (500MHz, acetone-$d_6$) δ 9.75 (s, 1H), 7.74 (d, $J = 8.0$ Hz, 2H), 7.56 (t, $J = 7.4$ Hz, 1H), 7.45 (t, $J = 7.8$ Hz, 2H), 7.37 (d, $J = 8.6$ Hz, 1H), 6.82 (d, $J = 2.0$ Hz, 1H), 6.71 (dd, $J = 8.6$, 2.2 Hz, 1H), 4.58 (s, 2H), 3.77 (s, 3H), 3.59 (t, $J = 5.5$ Hz, 2H), 2.82 (t, $J = 6.0$ Hz, 2H), 1.90 (quintet, $J = 5.7$ Hz, 2H); $^{13}$C NMR (125 MHz, acetone-$d_6$) δ 155.8 (C),
140.2 (C), 135.9 (C), 135.5 (C), 132.1 (CH), 128.8 (CH), 127.1 (CH), 122.1 (C), 117.5 (CH), 108.8 (CH), 94.3 (CH), 54.9 (CH₃), 50.9 (CH₂), 44.0 (CH₂), 26.7 (CH₂), 26.5 (CH₂) only visible signals. ATR-FTIR (thin film): 3393, 2925, 2842, 1328, 1154 cm⁻¹; HRMS (EI) m/z calculated for C₁₉H₂₀N₂O₃S (M)⁺: 356.11947, found: 356.12041.

2.21h

8-Methyl-2-(phenylsulfonyl)-1,2,3,4,5,6-hexahydroazepino[4,3-b]indole  2.21h.

The optimal procedure was followed by using 0.035 g of azide 2.46h (0.09 mmol), 0.0036 g of Rh₂(esp)₂ (0.005 mmol) and 1.5 mL of toluene at 80 °C. Purification by MPLC (2:100 – 20:80 EtOAc:hexanes) afforded the product as a white solid (0.021 g, 67%). mp 200 – 202 °C; ¹H NMR (500 MHz, acetone-d₆) δ 9.77 (s, 1H), 7.73 (d, J = 7.5 Hz, 2H), 7.56 (t, J = 7.5 Hz, 1H), 7.46 – 7.40 (m, 2H), 7.37 (d, J = 7.5 Hz, 1H), 7.06 (s, 1H), 6.87 (d, J = 7.5 Hz, 1H), 4.58 (s, 2H), 3.60 (t, J = 5.0 Hz, 2H), 2.37 (s, 3H), 2.08 – 2.00 (m, 2H), 1.94 – 1.86 (d, 2H); ¹³C NMR (125 MHz, acetone-d₆) δ 140.2 (C), 136.7 (C), 135.4 (C), 134.9 (C), 132.1 (CH), 129.8 (C), 128.8 (CH), 127.0 (CH), 126.0 (C), 125.7 (C) 120.6 (CH), 116.7 (CH), 110.6 (CH), 108.7 (C), 50.9 (CH₂), 44.0 (CH₂), 26.7 (CH₂), 26.5 (CH₂), 20.8 (CH₃). ATR-FTIR (thin film): 3382, 2924, 2849, 1689, 1615, 1448, 1329, 1157 cm⁻¹. HRMS (EI) m/z calculated for C₁₉H₂₀O₂N₂S (M)⁺: 340.12455, found: 340.12412.
8-Chloro-2-(phenylsulfonyl)-1,2,3,4,5,6-hexahydroazepino[4,3-b]indole 2.21i. The optimal procedure was followed by using 0.0669 g of 2.46i (0.17 mmol), 0.0065 g of Rh₂(esp)₂ and 1.7 mL of toluene. Purification by MPLC (3:97 – 20:80 EtOAc: hexanes) afforded the product as a white solid (0.0521 mg, 84%): ¹H NMR (500MHz, acetone-d₆) δ 10.11 (s, 1H), 7.73 (d, J = 7.5 Hz, 2H), 7.56 (t, J = 7.4 Hz, 1H), 7.50 (t, J = 8.4 Hz, 1H), 7.44 (t, J = 7.7 Hz, 2H), 7.30 (d, J = 1.3 Hz, 1H), 7.04 (dd, J = 8.4, 1.4 Hz, 1H), 4.61 (s, 2H), 3.63 (t, J = 5.5 Hz, 2H), 2.87 (t, J = 5.8 Hz, 2H), 1.95 – 1.90 (m, 2H); ¹³C NMR (125 MHz, acetone-d₆) δ 140.1 (C), 138.8 (C), 135.1 (C), 132.2 (CH), 128.9 (CH), 127.0 (CH), 126.4 (C), 125.8 (C), 119.4 (CH), 118.2 (CH), 110.5 (CH), 109.4 (C), 50.9 (CH₂), 43.7 (CH₂), 26.5 (CH₂), 26.5 (CH₂). ATR-FTIR (thin film): 3364, 2919, 2849, 1465, 1322, 1151 cm⁻¹; HRMS (EI) m/z calculated for C₁₈H₁₇ClN₂O₂S (M)⁺: 360.06993, found: 360.06938.

2-(Phenylsulfonyl)-8-(trifluoromethyl)-1,2,3,4,5,6-hexahydroazepino[4,3-b]indole 2.21j. The optimal procedure was followed by using 0.0923 g of 2.46j (0.22 mmol), 0.0083 g of Rh₂(esp)₂ and 2.2 mL of toluene. Purification by MPLC (3:97 – 20:80 EtOAc: hexanes) afforded the product as a white solid (0.070 g, 82%): ¹H NMR (500MHz, acetone-d₆) δ 10.45 (s, 1H), 7.75 (d, J = 7.8 Hz, 2H), 7.70 (d, J = 8.3 Hz, 1H), 7.64 (s, 1H), 7.55 (t, J = 7.4 Hz, 1H), 7.44 (t, J = 7.7 Hz, 2H), 7.34 (d, J = 8.3 Hz, 1H), 4.66 (s, 2H), 3.64 (t, J = 5.2 Hz, 2H), 2.93 (t, J = 5.3 Hz, 2H), 1.94 (s, 2H); ¹³C NMR (125 MHz, acetone-d₆) δ 141.4 (C), 140.1 (C), 133.6 (C), 132.3 (CH),
130.0 (C), 128.9 (CH), 127.0 (CH), 125.8 (q, $J_{CF} = 271$ Hz, C), 121.8 (q, $J_{CF} = 31.5$ Hz, C), 117.6 (CH), 115.5 (q, $J_{CF} = 3.3$ Hz, CH), 109.9 (CH), 108.1 (q, $J_{CF} = 2.5$ Hz, CH), 51.0 (CH$_2$), 43.6 (CH$_2$), 26.6 (CH$_2$), 26.4 (CH$_2$); $^{19}$F NMR (282 MHz, CDCl$_3$) δ – 55.8; ATR-FTIR (thin film): 3393, 2972, 2855, 1316, 1154 cm$^{-1}$; HRMS (El) $m/z$ calculated for C$_{19}$H$_{17}$F$_3$N$_2$O$_2$S ($M^+$): 394.09629, found: 394.09555.

![Chemical Structure](image)

**2.21k**

7-Methyl-2-(phenylsulfonyl)-1,2,3,4,5,6-hexahydroazepino[4,3-b]indole  **2.21k.** The optimal procedure was followed by using 0.0995 mg of **2.46k** (0.27 mmol), 0.0102 g of Rh$_2$(esp)$_2$ and 2.7 mL of toluene. Purification by MPLC (3:97 – 20:80 EtOAc: hexanes) afforded the product as a white solid (0.056 g, 61%): $^1$H NMR (500MHz, acetone-$d_6$) δ 9.84 (s, 1H), 7.74 (d, $J = 8.3$ Hz, 2H), 7.55 (t, $J = 7.4$ Hz, 1H), 7.44 (t, $J = 7.7$ Hz, 2H), 7.34 (d, $J = 7.8$ Hz, 1H), 6.95 (t, $J = 7.5$ Hz, 1H), 7.85 (d, $J = 7.1$ Hz, 1H), 4.60 (s, 2H), 3.60 (t, $J = 5.4$ Hz, 2H), 2.87 (t, $J = 5.8$ Hz, 2H), 2.42 (s, 3H), 1.91 (quintet, $J = 5.3$ Hz, 2H); $^{13}$C NMR (125 MHz, acetone-$d_6$) δ 140.1 (C), 137.3 (C), 134.2 (C), 132.2 (CH), 128.8 (CH), 127.3 (C), 127.1 (CH), 121.2 (CH), 119.9 (C), 119.3 (CH), 114.7 (CH), 109.4 (C), 51.0 (CH$_2$), 44.1 (CH$_2$), 26.7 (CH$_2$), 26.5 (CH$_2$), 16.0 (CH$_3$). ATR-FTIR (thin film): 3377, 2931, 2846, 1442, 1319, 1154 cm$^{-1}$; HRMS (El) $m/z$ calculated for C$_{19}$H$_{20}$N$_2$O$_2$S ($M^+$): 340.12455, found: 340.12394.
7-Methoxy-2-(phenylsulfonyl)-1,2,3,4,5,6-hexahydroazepino[4,3-b]indole  2.21l.
The optimal procedure was followed by using 0.0887 g of 2.46l (0.23 mmol), 0.0088 g of Rh$_2$(esp)$_2$ and 2.3 mL of toluene. Purification by MPLC (3:97 – 20:80 EtOAc: hexanes) afforded the product as a white solid (0.029 g, 35%): $^1$H NMR (500MHz, acetone-d$_6$) δ 9.94 (s, 1H), 7.74 (d, J = 7.3 Hz, 2H), 7.55 (t, J = 7.4 Hz, 1H), 7.43 (t, J = 7.8 Hz, 2H), 7.11 (d, J = 8.0 Hz, 1H), 6.96 (t, J = 7.8 Hz, 1H), 6.6 (d, J = 7.7 Hz, 1H), 4.59 (s, 2H), 3.89 (s, 3H), 3.61 (t, J = 5.5 Hz, 2H), 2.91 (t, J = 5.9 Hz, 2H), 1.92 – 1.87 (m, 2H); $^{13}$C NMR (125 MHz, C$_3$D$_6$O) δ 146.0 (C), 140.2 (C), 137.3 (C), 132.2 (CH), 129.0 (C), 128.8 (CH), 127.1 (CH), 124.7 (C), 119.6 (CH), 110.0 (CH), 109.5 (C), 101.1 (CH), 54.7 (CH$_3$), 51.1 (CH$_2$), 44.2 (CH$_2$), 26.7 (CH$_2$), 26.4 (CH$_2$). ATR-FTIR (thin film): 3364, 2931, 2839, 1581, 1328, 1154 cm$^{-1}$; HRMS (EI) m/z calculated for C$_{19}$H$_{20}$N$_2$O$_3$S (M)$^+$: 356.11947, found: 356.12039.

![diagram](image)

3-(2-Benzencesulfonyl-pyrrolidin-1-yl)-2-methyl-1H-indole  2.23a. The optimal procedure was followed by using 0.028 g of styryl azide 2.63 (0.076 mmol), 0.003 g of Rh$_2$(esp)$_2$ (0.004 mmol) in 1.5 mL of anhydrous benzene. The product was purified by MPLC (5:100 – 20:100 EtOAc:hexane) to afford the product as yellow
solid (0.021 g, 83%). $[\alpha]_D^{20}$: 0 (c 0.125, CH$_2$Cl$_2$); $^1$H NMR (500 MHz, acetone-$d_6$) $\delta$ 7.89 (s, 1H), 7.61 (d, $J = 7.0$ Hz, 2H), 7.45 (t, $J = 7.0$ Hz, 1H), 7.36 (dd, $J = 7.5$ Hz, 7.5 Hz, 3H), 7.20 (d, $J = 8.0$ Hz, 1H), 6.94 (t, $J = 8.0$ Hz, 1H), 6.84 (t, $J = 8.0$ Hz, 1H), 5.00 (t, $J = 8.0$ Hz, 1H), 3.76 – 3.72 (m, 1H), 3.68 – 3.63 (m, 1H), 2.45 (s, 3H), 2.15 – 2.11 (m, 2H), 1.95 – 2.04 (m, 1H), 1.66 – 1.63 (m, 1H); $^{13}$C NMR (125 MHz, acetone-$d_6$) $\delta$ 139.2 (C), 135.8 (C), 132.5 (C), 131.9 (CH), 128.5 (CH), 127.0 (CH), 126.8 (C), 120.1 (CH), 118.4 (CH), 118.3 (CH), 111.3 (C), 110.4 (CH), 57.0 (CH), 49.4 (CH$_2$), 33.9 (CH$_2$), 25.0 (CH$_2$), 11.1 (CH$_3$). ATR-FTIR (thin film): 3338, 2967, 2925, 1698, 1462, 1331, 1250, 1155, 1087 cm$^{-1}$.

HRMS (EI) $m/z$ calculated for C$_{19}$H$_{20}$N$_2$O$_2$S (M)$^+$: 340.12455, found: 340.12403.

![Image](image_url)

$2.23b$

3-(1-Benzencesulfonyl-pyrrolidin-2-yl)-2,5-dimethyl-1H-indole $2.23b$. The optimal procedure was followed by using 0.022 g of styryl azide $2.58b$ (0.057 mmol), 0.0022 g of Rh$_2$(esp)$_2$ (0.003 mmol) in 2 mL of anhydrous benzene. The product was purified by MPLC (5:100 – 20:100 EtOAc:hexane) to afford the product as yellow solid (0.014 g, 69%). $^1$H NMR (500 MHz, acetone-$d_6$) $\delta$ 9.71 (s, 1H), 7.57 (d, $J = 7.5$ Hz, 2H), 7.43 (t, $J = 7.0$ Hz, 1H), 7.33 (t, $J = 7.5$ Hz, 2H), 7.09 – 7.07 (m, 2H), 6.77 (d, $J = 8.5$ Hz, 1H), 4.98 (t, $J = 7.5$ Hz, 1H), 3.76 – 3.73 (m, 1H), 3.68 – 3.63 (m, 1H), 2.43 (s, 3H), 2.29 (s, 3H), 2.15 – 2.08 (m, 2H), 2.00 – 1.96 (m, 1H), 1.68 – 1.62 (m, 1H); $^{13}$C NMR (125 MHz, acetone-$d_6$) $\delta$ 139.2 (C), 134.1 (C), 132.6 (C), 131.8 (CH), 128.3 (CH), 127.1 (C), 127.0 (C), 126.9 (CH), 121.6 (CH), 118.2 (CH), 110.6 (C), 110.0 (CH), 57.0 (CH), 49.3 (CH$_2$), 33.8 (CH$_2$), 25.0 (CH$_2$), 20.8 (CH$_3$), 11.1 (CH$_3$). ATR-FTIR (thin film): 3385, 2924, 2857, 1682, 1621, 1587, 1445, 1333, 1305, 1150, 1088; HRMS (EI) $m/z$ calculated for C$_{20}$H$_{22}$O$_2$N$_2$S (M)$^+$: 354.14020, found: 354.14082.
3-(1-Benzylsulfonyl-pyrrolidin-2-yl)-5-fluoro-2-methyl-1H-indole 2.23c. The optimal procedure was followed by using 0.030 g of styryl azide 2.58c (0.077 mmol), 0.003 g of Rh\textsubscript{2}(esp\textsubscript{2}) (0.004 mmol) in 3mL of anhydrous benzene. The crude was purified by MPLC (5:100 – 20:100 EtOAc:hexane) to afford the product as a white solid (0.022 g, 81%). mp 134 – 136 °C. \textsuperscript{1}H NMR (500 MHz, acetone-\textit{d}\textsubscript{6}) \(\delta\) 9.96 (s, 1H), 7.59 (d, J = 7.0 Hz, 2H), 7.45 (t, J = 7.5 Hz, 1H), 7.35 (t, J = 7.5 Hz, 2H), 7.17 (dd, J = 8.5 Hz, 4.0 Hz, 1H), 7.01 (dd, J = 10.0 Hz, 2.0 Hz, 1H), 6.73 (t, J = 9.5 Hz, 1H), 4.96 (t, J = 7.5 Hz, 1H), 3.75 – 3.66 (m, 2H), 2.45 (s, 3H), 2.14 – 2.09 (m, 2H), 2.05 – 2.00 (m, 1H), 1.68 – 1.65 (m, 1H); \textsuperscript{13}C NMR (125 MHz, acetone-\textit{d}\textsubscript{6}) \(\delta\) 157.2 (d, \(J_{CF} = 228\) Hz, C), 139.2 (C), 134.9 (C), 132.3 (C), 131.9 (CH), 128.4 (CH), 127.2 (C), 126.9 (CH), 111.5 (C), 111.0 (d, \(J_{CF} = 9.1\) Hz, CH), 107.8 (d, \(J_{CF} = 25.7\) Hz, CH), 103.3 (d, \(J_{CF} = 23.9\) Hz, CH), 56.8 (CH), 49.4 (CH\textsubscript{2}), 33.8 (CH\textsubscript{2}), 25.0 (CH\textsubscript{2}), 11.2 (CH\textsubscript{3}). \textsuperscript{19}F NMR (282 MHz, CDCl\textsubscript{3}) \(\delta\) –125.6. ATR-FTIR (thin film): 3369, 2978, 2877, 1580, 1482, 1448, 1326, 1153, 1088 cm\textsuperscript{-1}. HRMS (EI) \textit{m/z} calculated for C\textsubscript{19}H\textsubscript{19}FN\textsubscript{2}O\textsubscript{2}S (M\textsuperscript{+}): 358.11513, found: 358.11438.

3-(1-Benzylsulfonyl-pyrrolidin-2-yl)-2-methyl-trifluoromethyl-1H-indole 2.23d. The optimal procedure was followed by using 0.030 g of styryl azide 2.58d (0.069 mmol), 0.0026 g of Rh\textsubscript{2}(esp\textsubscript{2}) (0.0034 mmol) in 1.5 mL of anhydrous benzene. The product was purified by MPLC (5:100 – 20:100 EtOAc:hexane) to afford the product as a white solid (0.021 g, 75%). mp 156 – 158 °C; \textsuperscript{1}H NMR (500
MHz, acetone-$d_6$) 10.35 (br s, 1H), 7.59 – 7.53 (m, 4H), 7.43 (t, $J$ = 7.5 Hz, 1H), 7.33 (t, $J$ = 7.5 Hz, 2H), 7.12 (d, $J$ = 8.5 Hz, 1H), 5.00 (t, $J$ = 7.5 Hz, 1H), 3.79 – 3.75 (m, 1H), 3.73 – 3.68 (m, 1H), 2.50 (s, 3H), 2.28 – 2.14 (m, 2H), 2.04 – 2.00 (m, 1H), 1.72 – 1.68 (m, 1H); $^{13}$C NMR (125 MHz, acetone-$d_6$) δ 139.1 (C), 136.4 (C), 134.6 (C), 131.9 (CH), 129.3 (C), 128.5 (CH), 126.9 (CH), 124.7 (q, $J$ = 268 Hz, C), 121.5 (q, $J$ = 31.1 Hz, C), 118.9 (CH), 115.0 (CH), 112.0 (C), 107.7 (q, $J$ = 4.3 Hz, CH), 56.7 (CH), 49.4 (CH$_2$), 34.0 (CH$_2$), 25.0 (CH$_2$), 11.2 (CH$_3$); $^{19}$F NMR (282 MHz, CDCl$_3$) δ –55.88. ATR-FTIR (thin film): 3382, 2948, 2873, 1509, 1472, 1441, 1326, 1282, 1213, 1153, 1142, 1088, 1065, 1014, 918 cm$^{-1}$. HRMS (EI) $m/z$ calculated for C$_{20}$H$_{19}$F$_3$N$_2$O$_2$S (M$^+$): 408.11194, found: 408.11224.

2-Methyl-3-(1-(phenylsulfonyl)piperidin-2-yl)-1H-indole 2.23e. The general procedure was followed by using 0.0256 g of styryl azide E-2.58e (0.067 mmol), 0.0025 g of Rh$_2$(esp)$_2$ in 1.3 mL of anhydrous benzene. The product was purified by MPLC (5:100 – 20:100 EtOAc:hexane) to afford yellow solid product (0.014 g, 58%).

$^1$H NMR (500 MHz, CDCl$_3$) δ 7.66 (s, 1H), 7.35 (d, $J$ = 8.0 Hz, 1H), 7.30 (d, $J$ = 8.3 Hz, 2H), 7.12 (t, $J$ = 7.4 Hz, 1H), 7.04 (d, $J$ = 8.1 Hz, 1H), 7.01 (t, $J$ = 7.8 Hz, 2H), 6.95 (t, $J$ = 7.6 Hz, 1H), 6.86 (t, $J$ = 7.1 Hz, 1H), 4.56 (dd, $J$ = 10.0, 3.9 Hz, 1H), 4.02 (td, $J$ = 6.2, 4.4 Hz, 1H), 3.22 (ddd, $J$ = 12.5, 9.3, 3.3 Hz, 1H), 2.40 (s, 3H), 2.33 – 2.25 (m, 1H), 1.84-1.81 (m, 2H), 1.72 (dd, $J$ = 9.2, 5.0 Hz, 2H), 1.50 – 1.44 (m, 1H); $^{13}$C NMR (125 MHz, CDCl$_3$) δ 139.7 (C), 134.8 (C), 133.0 (C), 131.1 (CH), 127.6 (CH), 127.3 (C), 126.7 (CH), 120.7 (CH), 119.8 (CH), 119.1 (CH), 110.9 (C), 110.0 (CH), 55.1 (CH), 46.1 (CH$_2$), 31.7 (CH$_2$), 25.2 (CH$_2$), 23.2 (CH$_2$), 12.7 (CH$_3$). ATR-FTIR (thin film): 3382, 2924, 2873, 1509, 1472, 1441, 1326, 1282, 1213, 1153, 1142, 1088, 1065, 1014, 918 cm$^{-1}$. HRMS (EI) $m/z$ calculated for C$_{20}$H$_{22}$N$_2$O$_2$S (M$^+$): 354.14020, found: 354.13959.
3-(1-Benzene sulfonyl-pyrrolidin-2-yl)-2-phenyl-1H-indole 2.23f. The optimal procedure was followed by using 0.0180 g of styryl azide 2.58f (0.041 mmol), 0.0016 g of Rh$_2$(esp)$_2$ (0.002 mmol) in 1.5 mL of anhydrous benzene. The product was purified by MPLC (5:100 – 20:100 EtOAc:hexane) to afford the product as a white solid (0.0094 g, 56%). mp 158 – 160 °C; $^1$H NMR (500 MHz, acetone-d$_6$) δ 10.28 (s, 1H) 7.65 (d, $J$ = 7.0 Hz, 3H), 7.55 (t, $J$ = 7.5 Hz, 2H), 7.51 – 7.43 (m, 2H), 7.38 – 7.33 (m, 3H), 7.26 (t, $J$ = 8.0 Hz, 2H), 7.09 (t, $J$ = 7.5 Hz, 1H), 6.97 (t, $J$ = 7.5 Hz, 1H), 4.88 (t, $J$ = 7.5 Hz, 1H), 3.76 – 3.71 (m, 2H), 2.31 – 2.25 (m, 2H), 1.53 – 1.50 (m, 2H); $^{13}$C NMR (125 MHz, acetone-d$_6$) δ 137.8 (C), 136.8 (C), 135.9 (C), 133.3 (C), 132.0 (CH), 129.2 (CH), 128.6 (CH), 128.5 (CH), 127.8 (CH), 127.3 (CH), 126.6 (C), 121.5 (CH), 120.0 (CH), 118.9 (CH), 113.0 (C), 111.2 (CH), 57.2 (CH), 50.1 (CH$_2$), 34.8 (CH$_2$), 24.9 (CH$_2$); ATR-FTIR (thin film): 3358, 3053, 2971, 1699, 1452, 1340, 1248, 1163 cm$^{-1}$. HRMS (EI) m/z calculated for C$_{24}$H$_{22}$N$_2$O$_2$S (M)$^+$: 402.14020, found: 402.14081.

3,4,5,6-Tetrahydro-1H-oxepino[4,3-b]indole 2.23g. The general procedure was followed by using 0.1037 g of 2.51 (0.48 mmol), 0.0180 g of Rh$_2$(esp)$_2$ and 4.8 mL of toluene. Purification by MPLC (3:97 – 20:80 EtOAc: hexanes) afforded the product, a white solid, as a 95:5 mixture of isomers (0.068 g, 75%). Spectral data for the major product: $^1$H NMR (500MHz, CDCl$_3$) δ 7.94 (s, 1H), 7.43 (d, $J$ = 7.5 Hz, 1H), 7.26 (d, $J$ = 7.3 Hz, 1H), 7.11 (quintet, $J$ = 7.6 Hz, 2H), 4.90 (s, 2H), 4.08 (t, $J$ = 5.0 Hz, 2H), 2.96 (t, $J$ = 5.9 Hz, 2H), 2.00 (quintet, $J$ = 5.4 Hz, 2H); $^{13}$C NMR (125 MHz, CDCl$_3$) δ
137.2 (C), 134.6 (C), 127.4 (C), 121.1 (CH), 119.5 (CH), 117.5 (CH), 113.0 (C), 110.4 (CH), 74.1 (CH₂), 66.1 (CH₂), 29.2 (CH₂), 27.8 (CH₂). Selected data for minor product: \(^1\)H NMR (500MHz, CDCl₃) δ 3.81 (t, \(J = 5.3\) Hz, 0.13H), 1.83 (quintet, \(J = 5.8\) Hz, 0.15H); ATR-FTIR (thin film): 3293, 2934, 2857, 1461, 1255, 1092 cm\(^{-1}\); HRMS (EI) \(m/z\) calculated for C₁₂H₁₃NO (M)\(^+\): 187.09972, found: 187.09909.

![Structure](image)

2.40

2,5-Dimethyl-3-[1-(toluene-4-sulfonyl)-pyrrolidin-2-yl]-1H-indole 2.40. The optimal procedure was followed by using 0.030 g of styryl azide 2.38 (0.076 mmol), 0.0028 g of Rh₂(esp)₂ (0.0037 mmol) in 1.5 mL of anhydrous benzene. The product was purified by MPLC (5:100 – 20:100 EtOAc:hexane) to afford the product as a white solid (0.0023 g, 78%). \(^1\)H NMR (500 MHz, acetone-\(d_6\)) δ 9.7 (s, 1H), 7.40 (d, \(J = 7.5\) Hz, 2H), 7.09 – 7.03 (m, 4H), 6.77 – 6.76 (s, 1H), 4.95 (t, \(J = 7.5\) Hz, 1H), 3.76 – 3.72 (m, 1H), 3.66 – 3.62 (m, 1H), 2.42 (s, 3H), 2.29 (s, 3H), 2.28 (s, 3H), 2.17 – 2.07 (m, 2H), 1.99 – 1.95 (m, 1H), 1.71 – 1.64 (m, 1H); \(^{13}\)C NMR (125 MHz, acetone-\(d_6\)) δ 142.2 (C), 136.5 (C), 134.1 (C), 132.7 (C), 131.7 (C), 128.8 (CH), 128.3 (C), 126.8 (CH), 121.5 (CH), 118.3 (CH), 110.5 (C), 110.0 (CH), 56.9 (CH), 49.3 (CH₂), 33.8 (CH₂), 29.4 (CH₃), 25.0 (CH₂), 20.4 (CH₃), 11.1 (CH₃). ATR-FTIR (thin film): 3375, 2920, 2849, 1686.1593, 1329, 1157, 1088, 994, 804 cm\(^{-1}\). HRMS (EI) \(m/z\) calculated for C₂₁H₂₄N₂O₂S (M)\(^+\): 368.15585, found: 368.15573.
H. Examination of the stereochemistry of the [1,2] aminomethylene migration.

Under an N₂-atmosphere, a dry vial was charged with 0.028 g of optically active styryl azide 2.30 (0.076 mmol, [a]D²⁰ = −19.6° c 0.125, CH₂Cl₂) and 0.003 g of Rh₂.esp₂ (0.004 mmol) and 1.5 mL of anhydrous benzene. The vial was sealed, and the resulting mixture was heated to 80 °C. After 16 h, the reaction mixture was cooled to room temperature and the volatiles were removed in vacuo. The resulting residue was purified by MPLC (5:100 – 20:100 EtOAc:hexane) to afford 2.31 as yellow solid (0.021 g, 83%). The rotation of the product was measured to be [a]D²⁰ = 0.0° (c 0.125, CH₂Cl₂).

I. Double Crossover Experiment.

Under an N₂ atmosphere, a vial was charged with 0.016 g of 2.37 (0.042 mmol) and 0.017 g of 2.38 (0.042 mmol) and 0.0016 g of Rh₂.esp₂ (0.002 mmol). To the resulting mixture was added 2 mL of anhydrous benzene. The mixture was heated at 80 °C. After 16 h, the reaction mixture was cooled to room temperature. The volatiles were removed in vacuo and the resulting residue was purified by MPLC (10:100 – 25:75 EtOAc:hexane) afforded only indoles 2.39 and 2.40. No cross over product was observed.
References


Structure of the major product was established by X-ray crystallography.


Alternatively, the stepwise 1,2-shift could occur via a diradical pair. Products attributed to radical intermediates have been observed in the related Stevens [1,2]-rearrangement of ammonium ylides. See: (a) Eberlein, T. H.; West, F. G.; Tester, R. W. *J. Org. Chem.* **1992**, *57*, 3479. (b) Ollis, W. D.; Rey, M.; Sutherland, I. O. *J. Chem. Soc., Perkin Trans. 1* **1983**, *1*, 1009.


Liu, Q.; Tor, Y. *Org. Lett.* **2003**, *5*, 2571.
CHAPTER 3

Rh$_2$(II)-Catalyzed Ester Migration to Afford 3$H$-Indoles from Trisubstituted Styryl Azides
Based on the study of tandem electrocyclization migration, we concluded a migratorial aptitude for functional group 1,2-shift to form 1H-indoles from β,β-disubstituted styryl azides. The transformation provides a facile route to synthesize N-heterocycles regioselectively. However, development of general methods for the construction of 3H-indoles—particularly nonoxygenated ones—has lagged despite their biological activity in the anti-proliferation of cancer cells and potential value as synthetic intermediates. The structure motif can be synthesized using an interrupted Fisher-indole reaction, which is neither stereo- nor regioselective. Densely functionalized carbocycles can be formed via cyclization triggered structural rearrangement. A good example is the use of Nazarov reaction. Combining the two facts, we anticipated that highly substituted 3H-indoles could be accessed through transition metal catalyzed β-substituent 1,2-shift from trisubstituted styryl azides (Scheme 3.1).

![Scheme 3.1. Transition metal catalyzed migrating group 1,2-shift.](image)

We chose ester to be the migrating group since the Driver group’s previous studies had found it not to migrate. To determine if our tandem process could yield 3H-indole product, we chose aryl azide to investigate. Unlike styryl azides in chapter 2, styryl azide could be synthesized facilely from 2-azidophenylboronate and vinyl triflate via Suzuki coupling (Scheme 3.2). Aryl boronic acid pinacol esters could be synthesized from 2-bromoaniline and vinyl
triflates 3.10 were converted from β-ketoester. Cross coupling were proved tolerant to a range of substrates. However, aryl azides 3.7 with strong electron withdrawing group produced 3.11 in reduced yield.

Scheme 3.2. Synthesis of trisubstituted styryl azides 3.11.

Optimization of the reaction was conducted using styryl azides 3.11. While only little reaction occurred under 140 °C in the absence of transition metal complexes (entry 1), submission of 3.11 to a series of Fe,14 Co,15 Ru,16 or Ir complexes17 did induce decomposition but only poor yields of N-heterocyclic products were observed (entries 2–5). Unexpectedly 3H-indole 3.12 was formed. Ester migration was not expected since this phenomenon was not predicted by our migratorial aptitude scale.1b The yield of our transformation was improved when 3.11 was exposed to Rh(II) carboxylate complexes: clean conversion was observed with alkyl carboxylate catalysts (entries 7 and 8). DuBois’s tetridentate Rh2(esp)218 was proved to be most efficient catalyst, which we attribute to the thermal robustness of this catalyst.19 Changing the solvent from toluene to chlorinated or ethereal solvents did not improve the conversion yield (entries 8–10). Lower temperature (entries 11 and 12) and lower loading of catalyst (entry 13) all led to incomplete reactions.
Using the optimal conditions, the scope of our transformation was investigated by varying the identity of the styryl azide moiety (Table 3.2). Styryl azides bearing a range of functional groups were efficiently converted to 3H-indoles irrespective of the electronic nature of the R\textsuperscript{1} or R\textsuperscript{2} substituents. Styryl azides with electron-donating or electron-withdrawing groups were transformed into 3H-indoles smoothly. 5-Substituted aryl azides transformed successfully to 8-substituted-3H-indole, which cannot be formed as a single isomer using Fischer-indole or Fischer-indole-type reactions.\textsuperscript{20} 6-Substituted aryl azide was not tested because we were unable to make the 2-azidophenylboronate precursors.
Table 3.2. Scope of electronic nature of aryl azides.

<table>
<thead>
<tr>
<th>Entry</th>
<th>Azide Structure</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>3.12a</td>
<td><img src="3.12a.png" alt="Image" /></td>
<td>80%</td>
</tr>
<tr>
<td>3.12b</td>
<td><img src="3.12b.png" alt="Image" /></td>
<td>77%</td>
</tr>
<tr>
<td>3.12c</td>
<td><img src="3.12c.png" alt="Image" /></td>
<td>62%</td>
</tr>
<tr>
<td>3.12d</td>
<td><img src="3.12d.png" alt="Image" /></td>
<td>86%</td>
</tr>
<tr>
<td>3.12e</td>
<td><img src="3.12e.png" alt="Image" /></td>
<td>71%</td>
</tr>
<tr>
<td>3.12f</td>
<td><img src="3.12f.png" alt="Image" /></td>
<td>74%</td>
</tr>
<tr>
<td>3.12g</td>
<td><img src="3.12g.png" alt="Image" /></td>
<td>70%</td>
</tr>
<tr>
<td>3.12h</td>
<td><img src="3.12h.png" alt="Image" /></td>
<td>77%</td>
</tr>
<tr>
<td>3.12i</td>
<td><img src="3.12i.png" alt="Image" /></td>
<td>68%</td>
</tr>
<tr>
<td>3.12j</td>
<td><img src="3.12j.png" alt="Image" /></td>
<td>65%</td>
</tr>
<tr>
<td>3.12k</td>
<td><img src="3.12k.png" alt="Image" /></td>
<td>72%</td>
</tr>
</tbody>
</table>

Further investigation on the scope was conducted by systematically varying the identity of the ortho-substituent of the aryl azide (Table 3.3). First, the reaction is quite tolerant to ring size change: changing from o-cyclohexenyl group to o-cycloheptenyl or o-cyclooctenyl group did not attenuate the yield of 3H-indole (entries 1 and 2). Further, aryl azides containing O- or N-atoms in the o-heterocycle substituent could be efficiently converted to corresponding indole product (entries 3 and 4). Incorporating the Boc-protected nitrogen provides a novel approach to synthesize β-carboline—a ubiquitous structural motif in bioactive alkaloids. A cycloalkenyl o-susbtituent is not required for the tandem migration transformation. Aryl azide 3.13e can be efficiently converted to 3.14e (entry 5). Next, the identity of the migrating ester was modified. We found that changing the methyl ester to iPr, t-Bu and allyl group did not stop the reaction, but the reaction was slightly less efficient. Unfortunately, the camphor-derived ester 3.13i and menthol ester 3.13j
exhibited poor conversion and only modest diastereoselectivity (entries 9 and 10). The diastereoselectivity of our transformation was further investigated by introducing substitution on the o-cyclohexenyl group. While only modest diastereoselectivity was observed with an allylic methyl substituent (entry 11) and homoallylic phenyl group (entry 12), an 82:18 ratio of diasteromers was observed with a homoallylic tert-butyl group (entry 13). When a bulkier tert-butyl ester replaced the methyl ester, a slightly higher diastereoselectivity 86:14 was achieved albeit with a reduced yield (entry 14).

Table 3.3. Scope of varying identity of o-substituent of aryl azides.

<table>
<thead>
<tr>
<th>entry</th>
<th>aryl azide 3.13</th>
<th>3H-indole 3.14</th>
<th>%, yield</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td><img src="image1" alt="Image" /></td>
<td><img src="image2" alt="Image" /></td>
<td>84</td>
</tr>
<tr>
<td>2</td>
<td><img src="image3" alt="Image" /></td>
<td><img src="image4" alt="Image" /></td>
<td>70</td>
</tr>
<tr>
<td>3</td>
<td><img src="image5" alt="Image" /></td>
<td><img src="image6" alt="Image" /></td>
<td>87</td>
</tr>
<tr>
<td>4</td>
<td><img src="image7" alt="Image" /></td>
<td><img src="image8" alt="Image" /></td>
<td>84</td>
</tr>
<tr>
<td>5</td>
<td><img src="image9" alt="Image" /></td>
<td><img src="image10" alt="Image" /></td>
<td>76</td>
</tr>
<tr>
<td>6</td>
<td><img src="image11" alt="Image" /></td>
<td><img src="image12" alt="Image" /></td>
<td>66 (R = iPr)</td>
</tr>
<tr>
<td>7</td>
<td><img src="image13" alt="Image" /></td>
<td><img src="image14" alt="Image" /></td>
<td>57 (R = t-Bu)</td>
</tr>
<tr>
<td>8</td>
<td><img src="image15" alt="Image" /></td>
<td><img src="image16" alt="Image" /></td>
<td>59 (R = allyl)</td>
</tr>
</tbody>
</table>
According to the reaction behavior along with previous study, a tandem electrocyclization [1,2]-migration mechanism is proposed in Scheme 3.3. Coordination of the aryl azide 3.11a to the rhodium carboxylate complex leads to decomposition of azide. The resulting rhodium nitrene undergoes 4π-electron-5-atom electro-cyclization to construct a new C–N bond in 3.16. This electrocyclization also forms a benzylic carbocation that can undergo either ring contraction to produce spirocycle from TS3.17 or [1,2] ester shift to form 3.18. Since the developing positive charge in the transition state 3.17 is destabilized by ester group, ester migration is favored. Release of the rhodium complex form 3.18 affords 3H-indole 3.12a. Double crossover experiment of 3.11h and 3.13f resulted in only two indole
products, revealing that ester group does not escape the solvent sheath during the shift (Scheme 3.4).

\[ \text{Scheme 3.3. Possible mechanism for Rh}_2(\text{II})\text{-catalyzed 3H-indole formation.} \]

\[ \text{Scheme 3.4. Double crossover reaction.} \]

If the catalytic cycle was operating, we anticipated that the selectivity of migration to form 3H-indole might be controlled by the identity of β-substituent. Consequently, we believed that ring contraction might happen if the ester group was replaced with one that would stabilize the developing positive charge in 3.17. To examine this hypothesis, we anticipated that changing the identity of β-substituent from an electron-withdrawing group to an electron-donating group would invert the migration selectivity (Scheme 3.5).
In line with this assertion, we tested a series of styryl azides bearing β-alkoxy substituents in the hope of potentially accessing oxindoles—pharmacetically important scaffold (Table 3.4). The substrates can be easily synthesized by Suzuki coupling 2-azidophenylboronate 3.7 with vinyl triflate 3.22, which was synthesized following a procedure reported by Wood and co-workers. Submission of 3.23a to the optimal reaction conditions produced desired 3H-indole 3.24a, which was converted to oxindole 3.25a upon acid-mediated hydrolysis in 67% yield (entry 1). The identity of the migrating aryl group could be modified to para-tolyl, leading to oxindole 3.25b in 65% yield (entry 2). Changing the β-alkoxy substituent to para-nitrophenol facilitated the synthesis of 3.22c and 3.23c and improved the yield of 3H-indole 3.25c to 81% as well (entry 3). This 3,3-diaryl oxindole structure is important synthetic intermediate and common motif present in anticancer agents, which inhibit translation initiation.

**Table 3.4.** Synthesis of 3,3-diaryl oxindoles.

<table>
<thead>
<tr>
<th>entry</th>
<th>styryl azide 3.23</th>
<th>oxindole 3.25</th>
<th>%, yield</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>3.24a</td>
<td>3.25a</td>
<td>67</td>
</tr>
</tbody>
</table>
In conclusion, I have developed a novel approach to 3H-indoles or oxindoles from trisubstituted styryl azide through an electrocyclization migration reaction of the rhodium nitrene. Different [1,2]-shift selectivity can be triggered by changing the electronic nature of β substituents. The synthesis is step economic accounting for the facile construction of substrates via cross-coupling of 2-azidophenylboronates and vinyl triflates.

*Isolated yield of 3.25 after silica gel chromatography.*
Experimental

This part was taken from supporting information of my published paper: Kong, C.; Driver, T. G. Org. Lett. 2015, 17, 802.

A. General. $^1$H NMR and $^{13}$C NMR spectra were recorded at ambient temperature using 500 MHz or 300 MHz spectrometers. The data are reported as follows: chemical shift in ppm from internal tetramethylsilane on the d scale, multiplicity (br = broad, s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet), coupling constants (Hz) and integration. High-resolution mass spectra were obtained by peak matching. Melting points are reported uncorrected. Analytical thin layer chromatography was performed on 0.25 mm silica gel plates with UV254 fluorescent indicator. Liquid chromatography was performed using forced flow (flash chromatography) of the indicated solvent system on 60Å (40 – 60 μm) mesh silica gel (SiO$_2$). Medium pressure liquid chromatography (MPLC) was performed using pumps to force flow the indicated solvent system down columns that had been packed with 60Å (40 – 60 μm) mesh silica gel (SiO$_2$). All reactions were carried out under an atmosphere of nitrogen in glassware that was oven-dried. Unless otherwise noted, all reagents were commercially obtained and, where appropriate, purified prior to use. Acetonitrile, methanol, toluene, THF, Et$_2$O, and CH$_2$Cl$_2$ were dried by filtration through alumina according to the procedure of Grubbs. Metal salts were stored in a nitrogen atmosphere dry box.

B. Route to Synthesize Trisubstituted Styryl Azides

We found a facile route to synthesize trisubstituted styryl azides, starting with 2-bromoaniline 3.26. Substitution of bromo to pinacolboronic ester affords 2-boronic acid pinacol ester aniline 3.6 which tranforms to 2-azidophenylboronate 3.7 via azidation. Vinyl triflate 3.10 was produced from β-ketoester 3.8. Styryl azides 3.11 and 3.13 are synthesized via Suzuki cross-coupling reaction of 2-azidophenylboronic acid pinacol ester 3.7 and vinyl triflate 3.10.
Scheme 3.6. Route to synthesize trisubstituted styryl azides.

C. Suzuki Cross-Coupling to Prepare Trisubstituted Styryl Azides

To a mixture of vinyl triflate 3.10 (1 equiv), 2-azidoarylboronic acid pinacol ester 3.7 (1.1 equiv), and Pd(PPh₃)₄ (10 mol %) in dimethoxyethane (0.1 M) was added a saturated solution of NaHCO₃ (2 mL:mmol of boronic ester). The resulting mixture was heated to 100 °C. After 1 h, the mixture was cooled to room temperature and diluted with 5 mL of cold water. The solution was extracted with 2 × 10 mL of ether followed by 10 mL of brine. The resulting organic phase was dried over Na₂SO₄ and was concentrated in vacuo. Purification by MPLC (3:97 to 10:90 EtOAc: hexane) afforded the product 3.11 or 3.13.
Methyl-2-(2-azidophenyl)cyclohex-1-enecarboxylate 3.11a.

The general procedure was followed by using 0.107 g of 2-azidophenyl boronate \textbf{3.7a} (0.44 mmol), 0.114 g of vinyl triflate \textbf{3.10} (0.40 mmol), 0.0462 g of Pd(PPh$_3$)$_4$ (0.04 mmol), 0.8 mL of saturated aq. soln. of NaHCO$_3$ and 4 mL of dimethoxyethane. Purification by MPLC (3:97 to 10:90 EtOAc: hexane) afforded the product as yellow oil (0.07 g, 70%): $^1$H NMR (500 MHz, CDCl$_3$) $\delta$ 7.28 (t, $J$ = 7.7 Hz, 1H), 7.13 (d, $J$ = 8.0 Hz, 1H), 7.09 (t, $J$ = 7.5 Hz, 1H), 6.99 (dd, $J$ = 7.5 Hz, 1.2 Hz, 1H), 3.44 (s, 3H), 2.45 (s, 3H), 2.24 (dt, $J$ = 24.5 Hz, 5.9 Hz, 1H), 1.74 (d, $J$ = 3.7 Hz, 4H); $^{13}$C NMR (125 MHz, CDCl$_3$) $\delta$ 168.4 (C), 145.3 (C), 136.3 (C), 135.8 (C), 128.5 (CH), 128.3 (C), 128.1 (CH), 124.7 (CH), 118.3 (CH), 51.2 (CH$_3$), 32.9 (CH$_2$), 26.1 (CH$_2$), 22.1(CH$_2$), 22.0 (CH$_2$). ATR-FTIR (thin film): 2939, 2127, 1720, 1248 cm$^{-1}$; HRMS (El) m/z calculated for C$_{14}$H$_{18}$NO$_2$ (M+H-N$_2$)$^+$: 230.1181, found: 230.1188.

Methyl-2-(2-azido-5-methylphenyl)cyclohex-1-enecarboxylate 3.11b.

The general procedure was followed by using 0.455 g of 2-azidoarylboronate \textbf{3.7b} (1.76 mmol), 0.461 g of vinyl triflate \textbf{3.10} (1.60 mmol), 0.199 g of Pd(PPh$_3$)$_4$ (0.16 mmol), 3.2 mL of saturated aq. soln. of NaHCO$_3$ and 20 mL of dimethoxyethane. Purification by MPLC (3:97 to 10:90 EtOAc: hexane) afforded the product as yellow oil (0.260 g, 55%): $^1$H NMR (500 MHz, CDCl$_3$) $\delta$ 7.08 (d, $J$ = 8.1 Hz, 1H), 7.01 (d, $J$ = 8.1 Hz, 1H), 6.81 (s, 1H), 3.46 (s, 3H), 2.45 (s, 3H), 2.30 (s, 3H), 2.23 (m, 1H), 1.74 (d, $J$ = 3.7 Hz, 4H); $^{13}$C NMR (125 MHz, CDCl$_3$) $\delta$ 168.4 (C), 145.3 (C), 135.6 (C), 134.3 (C), 133.5 (C), 129.0 (CH), 128.8 (CH), 128.2 (C), 118.2 (CH), 51.2 (CH$_3$), 33.0 (CH$_2$), 26.1 (CH$_2$), 22.2 (CH$_2$), 22.0 (CH$_2$), 20.8 (CH$_3$). ATR-FTIR (thin film):
2937, 2858, 2110, 1707, 1229 cm\(^{-1}\); HRMS (El) \(m/z\) calculated for C\(_{15}\)H\(_{18}\)NO\(_2\) (M+H-N\(_2\))^+: 244.1338, found: 244.1332.

Methyl-2-(2-azido-5-fluorophenyl)cyclohex-1-ene-carboxylate 3.11c. The general procedure was followed by using 0.246 g of 2-azidoarylboronate 3.7c (0.93 mmol), 0.245 g of vinyl triflate 3.10 (0.850 mmol), 0.106 g of Pd(PPh\(_3\))\(_4\) (0.090 mmol), 1.7 mL of saturated aq. soln. of NaHCO\(_3\) and 10 mL of dimethoxyethane. Purification by MPLC (3:97:10:90 EtOAc:hexane) afforded the product as yellow oil (0.185 g, 77%): \(^1\)H NMR (500 MHz, CDCl\(_3\)) \(\delta\) 7.06 (dd, \(J = 8.8\) Hz, 4.7 Hz, 1H), 6.97 (td, \(J = 8.3\) Hz, 2.9 Hz, 1H), 6.72 (dd, \(J = 8.7\) Hz, 2.8 Hz, 1H), 3.48 (s, 3H), 2.44 (s, 2H), 2.37 (s, 1H), 2.24 (dt, \(J = 25.0\) Hz, 6.3 Hz, 1H), 1.73 (d, \(J = 4.1\) Hz, 4H); \(^{13}\)C NMR (125 MHz, CDCl\(_3\)) \(\delta\) 167.9 (C), 159.6 (d \(J_{\text{CF}} = 245.7\) Hz, C), 144.2 (C), 137.6 (d, \(J_{\text{CF}} = 8.8\) Hz, C), 132.1 (C), 128.8 (C), 119.6 (d, \(J_{\text{CF}} = 9.2\) Hz, CH), 115.4 (d, \(J_{\text{CF}} = 23.7\) Hz, CH), 114.7 (d, \(J_{\text{CF}} = 23.9\) Hz, CH), 51.3 (CH\(_3\)), 32.8 (CH\(_2\)), 26.0 (CH\(_2\)), 22.1 (CH\(_2\)), 21.9 (CH\(_2\)); \(^{19}\)F NMR (282 MHz, CDCl\(_3\)) \(\delta\) –118.5. ATR-FTIR (thin film): 2937, 2113, 1720, 1485, 1236 cm\(^{-1}\); HRMS (El) \(m/z\) calculated for C\(_{14}\)H\(_{15}\)NO\(_2\)F (M+H-N\(_2\))^+: 248.1087, found: 248.1084.

Methyl-2-(2-azido-5-chlorophenyl)cyclohex-1-ene-carboxylate 3.11d. The general procedure was followed by using 0.060 g of 2-azidoarylboronate 3.7d (0.22 mmol), 0.055 g of vinyl triflate 3.10 (0.20 mmol), 0.025 g of Pd(PPh\(_3\))\(_4\) (0.020 mmol), 0.4 mL of saturated aq. soln. of NaHCO\(_3\) and 5 mL of dimethoxyethane. Purification by MPLC (3:97 to 10:90 EtOAc: hexane) afforded the product as yellow
solid (0.040 g, 71%): $^1$H NMR (500 MHz, CDCl$_3$) δ 7.23 (dd, $J = 8.5$ Hz, 2.4 Hz, 1H), 7.04 (d, $J = 8.5$ Hz, 1H), 6.98 (d, $J = 2.3$ Hz, 1H), 3.49 (s, 3H), 2.44 (s, 2H), 2.36 (s, 1H), 2.23 (dt, $J = 25.4$ Hz, 6.1 Hz, 1H), 1.73 (s, 4H); $^{13}$C NMR (125 MHz, CDCl$_3$) δ 167.9 (C), 144.1 (C), 137.4 (C), 135.0 (C), 129.9 (C), 128.9 (C), 128.3 (CH), 128.0 (CH), 119.5 (CH), 51.4 (CH$_3$), 32.9 (CH$_2$), 26.0 (CH$_2$), 22.1 (CH$_2$), 21.9 (CH$_2$). ATR-FTIR (thin film): 2939, 2858, 2122, 2095, 1721, 1483, 1220 cm$^{-1}$; HRMS (EI) m/z calculated for C$_{14}$H$_{15}$NO$_2$Cl (M+H-N$_2$)$^+$: 264.0791, found: 264.0792.

![Methyl-2-(2-azido-5-trifluoromethoxyphenyl)cyclohex-1-enecarboxylate 3.11e.](image)

The general procedure was followed by using 0.356 g of 2-azidoarylboronate 3.7e (1.08 mmol), 0.283 g of vinyl triflate 3.10 (0.98 mmol), 0.122 g of Pd(PPh$_3$)$_4$ (0.10 mmol), 2.0 mL of saturated aq. soln. of NaHCO$_3$ and 10 mL of dimethoxyethane. Purification by MPLC (3:97 to 10:90 EtOAc: hexane) afforded the product as yellow oil (0.247 g, 73%): $^1$H NMR (500 MHz, CDCl$_3$) δ 7.13 (m, 2H), 6.87 (s, 1H), 3.45 (s, 3H), 2.44 (s, 3H), 2.24 (dt, $J = 24.7$ Hz, 6.2 Hz, 1H), 1.74 (s, 4H); $^{13}$C NMR (125 MHz, CDCl$_3$) δ 168.0 (C), 145.7 (C), 143.8 (C), 137.4 (C), 135.2 (C), 129.2 (C), 121.4 (CH), 120.7 (CH), 119.3 (CH), 51.3 (CH$_3$), 32.6 (CH$_2$), 26.0 (CH$_2$), 22.0 (CH$_2$), 21.8 (CH$_2$), only visible peaks; $^{19}$F NMR (282 MHz, CDCl$_3$) δ −58.6. ATR-FTIR (thin film): 2939, 2127, 2091, 1720, 1248, 1213 cm$^{-1}$; HRMS (EI) m/z calculated for C$_{15}$H$_{15}$NO$_3$F$_3$ (M+H-N$_2$)$^+$: 314.1004, found: 314.1010.
Methyl-2-(2-azido-4-N-Boc-phenyl)cyclohex-1-enecarboxylate 3.11f.
The general procedure was followed by using 0.150 g of 2-azidoarylboronate 3.7f (0.42 mmol), 0.113 g of vinyl triflate 3.10 (0.38 mmol), 0.047 g of Pd(PPh₃)₄ (0.040 mmol), 0.8 mL of saturated aq. soln. of NaHCO₃ and 5 mL of dimethoxyethane. Purification by MPLC (3:97 to 10:90 EtOAc: hexane) afforded the product as yellow oil (0.133 g, 91%): ¹H NMR (500 MHz, CDCl₃) δ 7.35 (s, 1H), 6.95 (d, J = 9.9 Hz, 1H), 6.87 (d, J = 8.2 Hz, 1H), 6.66 (s, 1H), 3.47 (s, 3H), 2.43 (s, 2H), 2.21 (br s, 2H), 1.72 (s, 4H), 1.51 (s, 9H); ¹³C NMR (125 MHz, CDCl₃) δ 168.7 (C), 152.6 (C), 144.8 (C), 138.5 (C), 137.0 (C), 130.2 (C), 128.9 (CH), 128.6 (C), 114.6 (CH), 108.3 (CH), 83.1 (C), 51.3 (CH₃), 32.9 (CH₂), 28.3 (CH₃), 26.2 (CH₂), 22.2 (CH₂), 22.0 (CH₂). ATR-FTIR (thin film): 3336, 2940, 2109, 1722, 1696, 1234, 1152 cm⁻¹; HRMS (EI) m/z calculated for C₁₉H₂₅N₄O₄ (M+H-N₂)⁺: 373.1876, found: 373.1876.

Methyl-2-(2-azido-4-methoxyphenyl)cyclohex-1-enecarboxylate 3.11g.
The general procedure was followed by using 0.311 g of 2-azidoarylboronate 3.7g (1.13 mmol), 0.308 g of vinyl triflate 3.10 (1.03 mmol), 0.125 g of Pd(PPh₃)₄ (0.100 mmol), 2.0 mL of saturated aq. soln. of NaHCO₃ and 10 mL of dimethoxyethane. Purification by MPLC (3:97 to 10:90 EtOAc: hexane) afforded the product as yellow oil (0.195 g, 60%): ¹H NMR (500 MHz, CDCl₃) δ 6.90 (d, J = 8.1 Hz, 1H), 6.65 (s, 2H), 3.81 (s, 3H), 3.47 (s, 3H), 2.43 (s, 2H), 2.30 (m, 2H), 1.72 (s, 4H); ¹³C NMR (125 MHz, CDCl₃) δ 168.7 (C), 159.5 (C), 144.7 (C), 137.2 (C), 129.3 (CH), 128.6 (C), 128.2 (C), 110.2 (CH), 104.3 (CH), 55.4 (CH₃), 51.2 (CH₃), 33.1 (CH₂), 26.3 (CH₂), 22.3 (CH₂), 22.0 (CH₂). ATR-FTIR (thin film): 2937, 2106, 1710, 1606, 1499,
1219 cm\(^{-1}\); HRMS (El) \(m/z\) calculated for C\(_{15}\)H\(_{18}\)NO\(_3\) (M+H-N\(_2\))^+: 260.1287, found: 260.1277.

![3.11h](image)

**Methyl-2-(2-azido-4-methylphenyl)cyclohex-1-enecarboxylate 3.11h.**

The general procedure was followed by using 0.414 g of 2-azidoarylboronate 3.7h (1.60 mmol), 0.420 g of vinyl triflate 3.10 (1.45 mmol), 0.180 g of Pd(PPh\(_3\))\(_4\) (0.150 mmol), 3.0 mL of saturated aq. soln. of NaHCO\(_3\) and 15 mL of dimethoxyethane. Purification by MPLC (3:97 to 10:90 EtOAc: hexane) afforded the product as yellow oil (0.295 g, 64%): \(^1\)H NMR (500 MHz, CDCl\(_3\)) \(\delta\) 6.94 (s, 1H), 6.89 (m, 2H), 3.47 (s, 3H), 2.45 (s, 2H), 2.36 (s, 4H), 2.25 (dt, \(J = 20.7\) Hz, 6.1 Hz, 1H), 1.74 (s, 4H); \(^{13}\)C NMR (125 MHz, CDCl\(_3\)) \(\delta\) 168.4 (C), 145.3 (C), 138.1 (C), 136.0 (C), 133.0 (C), 128.3 (CH), 128.3 (C), 125.6 (CH), 118.9 (CH), 51.2 (CH\(_3\)), 33.0 (CH\(_2\)), 26.2 (CH\(_2\)), 22.3 (CH\(_2\)), 22.0 (CH\(_2\)), 21.2 (CH\(_3\)). ATR-FTIR (thin film): 2933, 2101, 1719, 1229 cm\(^{-1}\); HRMS (El) \(m/z\) calculated for C\(_{15}\)H\(_{18}\)NO\(_2\) (M+H-N\(_2\))^+: 244.1338, found: 244.1333.

![3.11i](image)

**Methyl-2-(2-azido-4-fluorophenyl)cyclohex-1-enecarboxylate 3.11i.**

The general procedure was followed by using 0.300 g of 2-azidoarylboronate 3.7i (1.14 mmol), 0.300 g of vinyl triflate 3.10 (1.04 mmol), 0.129 g of Pd(PPh\(_3\))\(_4\) (0.10 mmol), 2.0 mL of saturated aq. soln. of NaHCO\(_3\) and 10 mL of dimethoxyethane. Purification by MPLC (3:97 to 10:90 EtOAc: hexane) afforded the product as yellow oil (0.214 g, 71%). \(^1\)H NMR (500 MHz, CDCl\(_3\)) \(\delta\) 6.94 (dd, \(J = 7.4\) Hz, 6.2 Hz, 1H), 6.84 (dd, \(J = 9.3\) Hz, 2.3 Hz, 1H), 6.80 (dt, \(J = 8.3\) Hz, 4.2 Hz, 1H), 3.47 (s, 3H), 2.42 (s, 3H), 2.24
(dt, J = 24.4 Hz, 6.3 Hz, 1H), 1.73 (s, 4H); \(^{13}\text{C}\) NMR (125 MHz, CDCl\(_3\)) \(\delta\) 168.3 (C), 162.3 (d, \(J_{CF} = 247.7\) Hz, C), 144.3 (C), 137.8 (d, \(J_{CF} = 8.9\) Hz, C), 131.7 (d, \(J_{CF} = 3.2\) Hz, C), 129.7 (d, \(J_{CF} = 9.2\) Hz, CH), 129.0 (C), 111.7 (d, \(J_{CF} = 20.4\) Hz, CH), 105.8 (d, \(J_{CF} = 25.6\) Hz, CH), 51.3 (CH\(_3\)), 33.0 (CH\(_2\)), 26.1 (CH\(_2\)), 22.2 (CH\(_2\)), 21.9 (CH\(_2\)); \(^{19}\text{F}\) NMR (282 MHz, CDCl\(_3\)) \(\delta\) –113.5. ATR-FTIR (thin film): 2939, 2106, 1713, 1590, 1495, 1226 cm\(^{-1}\); HRMS (EI) \(m/z\) calculated for C\(_{15}\)H\(_{18}\)NO\(_2\) (M+H-N\(_2\))^+: 248.1087, found: 248.1087.

Methyl-2-(2-azido-4-trifluoromethylphenyl)cyclohex-1-enecarboxylate 3.11j.

The general procedure was followed by using 0.072 g of 2-azidoarylboronate 3.7j (0.23 mmol), 0.062 g of vinyl triflate 3.10 (0.21 mmol), 0.026 g of Pd(PPh\(_3\))\(_4\) (0.020 mmol), 0.4 mL of saturated aq. soln. of NaHCO\(_3\) and 5 mL of dimethoxyethane. Purification by MPLC (3:97 to 10:90 EtOAc: hexane) afforded the product as colorless oil (0.050 g, 74%): \(^1\text{H}\) NMR (500 MHz, CDCl\(_3\)) \(\delta\) 7.34 (m, 2H), 7.10 (d, \(J = 8.3\) Hz, 1H), 3.48 (s, 3H), 2.46 (s, 2H), 2.38 (s, 1H), 2.17 (s, 1H), 1.75 (s, 4H); \(^{13}\text{C}\) NMR (125 MHz, CDCl\(_3\)) \(\delta\) 167.8 (C), 144.5 (C), 139.6 (C), 137.2 (C), 130.4 (d, \(J_{CF} = 33.3\), C), 129.0 (CH), 128.9 (C), 123.6 (q, \(J_{CF} = 272.0\), C), 121.5 (CH), 115.3 (CH), 51.4 (CH\(_3\)), 32.8 (CH\(_2\)), 26.0 (CH\(_2\)), 22.0 (CH\(_2\)), 21.9 (CH\(_2\)); \(^{19}\text{F}\) NMR (282 MHz, CDCl\(_3\)) \(\delta\) –63.0. ATR-FTIR (thin film): 2939, 2110, 1720, 1326 1125 cm\(^{-1}\); HRMS (EI) \(m/z\) calculated for C\(_{15}\)H\(_{18}\)NO\(_2\)F\(_3\) (M+H-N\(_2\))^+: 298.1055, found: 298.1049.
Methyl-2-(2-azido-4-acetlyphenyl)cyclohex-1-enecarboxylate 3.11k.

The general procedure was followed by using 0.110 g of 2-azidoarylboronate 3.7k (0.38 mmol), 0.101 g of vinyl triflate 3.10 (0.35 mmol), 0.036 g of Pd(PPh₃)₄ (0.030 mmol), 0.7 mL of saturated aq. soln. of NaHCO₃ and 5 mL of dimethoxyethane. Purification by MPLC (3:97 to 10:90 EtOAc: hexane) afforded the product as colorless oil (0.081 g, 67%): ¹H NMR (500 MHz, CDCl₃) δ 7.72 (s, 1H), 7.66 (d, J = 7.9 Hz, 1H), 7.07 (d, J = 7.9, 1H), 3.46 (s, 3H), 2.58 (s, 3H), 2.44 (s, 2H), 2.38 (s, 1H), 2.15 (s, 1H), 1.73 (d, J = 8.9 Hz, 4H); ¹³C NMR (125 MHz, CDCl₃) δ 196.7 (C), 167.8 (C), 150.1 (C), 145.1 (C), 137.2 (C), 136.9 (C), 128.6 (CH), 128.5 (C), 125.0 (CH), 117.8 (CH), 51.4 (CH₃), 32.7 (CH₂), 26.6 (CH₃), 25.9 (CH₂), 22.0 (CH₂), 21.9 (CH₂). ATR-FTIR (thin film): 2937, 2103, 1720, 1687, 1241 cm⁻¹; HRMS (EI) m/z calculated for C₁₆H₁₈NO₃ (M+H-N₂)⁺: 272.1287, found: 272.1283.

Methyl-2-(2-azidophenyl)cyclohept-1-enecarboxylate 3.13a. The general procedure was followed by using 0.330 g of 2-azidophenylboronate 3.7 (1.35 mmol), 0.370 g of vinyl triflate 3.10a (1.22 mmol), 0.140 g of Pd(PPh₃)₄ (0.120 mmol), 2.5 mL of saturated aq. soln. of NaHCO₃ and 15 mL of dimethoxyethane. Purification by MPLC (3:97 to 10:90 EtOAc: hexane) afforded the product as yellow oil (0.240 g, 72%): ¹H NMR (500 MHz, CDCl₃) δ 7.28 (t, J = 7.7 Hz, 1H), 7.14 (d, J = 7.9 Hz, 1H), 7.06 (t, J = 7.5 Hz, 1H), 6.97 (dd, J = 7.5 Hz, 1.1 Hz, 1H), 3.38 (s, 3H), 2.61 (t, J = 5.5 Hz, 2H), 2.57 (s, 1H), 2.43 (t, J = 10.9 Hz, 1H), 1.86 (s, 2H), 1.78 (s, 1H), 1.69 (s, 1H), 1.61 (m, 2H); ¹³C NMR (125 MHz, CDCl₃) δ 170.0 (C), 150.1 (C), 137.0 (C), 136.3 (C), 134.9 (C), 128.4 (CH), 128.2 (CH), 124.6 (CH), 118.3 (CH), 51.3 (CH₃),
37.1 (CH\(_2\)), 32.4 (CH\(_2\)), 30.3 (CH\(_2\)), 26.4 (CH\(_2\)), 25.5 (CH\(_2\)). ATR-FTIR (thin film): 2922, 2850, 2121, 2092, 1706, 1485, 1439, 1351 cm\(^{-1}\); HRMS (EI) \(m/z\) calculated for C\(_{15}\)H\(_8\)NO\(_2\) (M+H-N\(_2\))^+: 244.1338, found: 244.1339.

![Image of 3.13b](image)

**Methyl-2-(2-azidophenyl)cyclohept-1-enecarboxylate 3.13b.**

The general procedure was followed by using 0.245 g of 2-azidophenylboronate 3.7 (1.00 mmol), 0.288 g of vinyl triflate 3.10b (0.91 mmol), 0.113 g of Pd(PPh\(_3\))\(_4\) (0.0900 mmol), 2.0 mL of saturated aq. soln. of NaHCO\(_3\) and 10 mL of dimethoxyethane. Purification by MPLC (3:97 to 10:90 EtOAc: hexane) afforded the product as yellow oil (0.222 g, 85\%). \(^1\)H NMR (500 MHz, CDCl\(_3\)) \(\delta\) .29 (t, \(J = 7.7\) Hz, 1H), 7.15 (d, \(J = 7.8\) Hz, 1H), 7.08 (t, \(J = 7.8\) Hz, 1H), 6.98 (d, \(J = 7.6\) Hz, 1H), 3.41 (s, 3H), 2.63 (s, 1H), 2.54 (t, \(J = 6.2\) Hz, 2H), 2.44 (s, 1H), 1.82 (s, 2H), 1.62 (s, 4H), 1.49 (m, 2H); \(^{13}\)C NMR (125 MHz, CDCl\(_3\)) \(\delta\) 169.2 (C), 147.5 (C), 136.5 (C), 135.7 (C), 131.6 (C), 128.9 (CH), 128.2 (CH), 124.4 (CH), 118.3 (CH), 51.1 (CH\(_3\)), 34.1 (CH\(_2\)), 28.6 (CH\(_2\)), 30.3 (CH\(_2\)), 28.0 (CH\(_2\)), 26.9 (CH\(_2\)), 26.3 (CH\(_2\)). ATR-FTIR (thin film): 2923, 2855, 2123, 2091, 1707, 1297 cm\(^{-1}\); HRMS (EI) \(m/z\) calculated for C\(_{16}\)H\(_{20}\)NO\(_2\) (M+H-N\(_2\))^+: 258.1494, found: 258.1503.

![Image of 3.13c](image)

**Methyl-4-(2-azidophenyl)-5,6-dihydro-2H-pyran-3-carboxylate 3.13c.**

The general procedure was followed by using 0.125 g of 2-azidophenylboronate 3.7 (0.51 mmol), 0.134 g of vinyl triflate 3.10c (0.46 mmol), 0.057 g of Pd(PPh\(_3\))\(_4\) (0.050 mmol), 1.0 mL of saturated aq. soln. of NaHCO\(_3\) and 5 mL of dimethoxyethane. Purification by MPLC (3:97 to 10:90 EtOAc: hexane) afforded the product as yellow
oil (0.111 g, 92%): $^1$H NMR (500 MHz, CDCl$_3$) $\delta$ 7.33 (td, $J = 7.7$ Hz, 1.1 Hz, 1H), 7.17 (d, $J = 8.0$ Hz, 1H), 7.13 (t, $J = 7.5$ Hz, 1H), 7.03 (dd, $J = 7.6$ Hz, 1.2 Hz, 1H), 4.47 (t, $J = 2.5$ Hz, 2H), 3.88 (t, $J = 5.3$ Hz, 2H), 3.50 (s, 3H), 2.44 (s, 2H); $^{13}$C NMR (125 MHz, CDCl$_3$) $\delta$ 165.2 (C), 145.0 (C), 136.3 (C), 133.6 (C), 128.7 (CH), 128.3 (CH), 126.8 (C), 124.8 (CH), 118.3 (CH), 65.4 (CH$_2$), 63.8 (CH$_2$), 51.3 (CH$_3$), 32.3 (CH$_2$). ATR-FTIR (thin film): 2957, 2837, 2131, 2097, 1717, 1259, 1229 cm$^{-1}$; HRMS (EI) m/z calculated for C$_{13}$H$_{13}$N$_3$O$_3$Na (M+Na)$^+$: 282.0855, found: 282.0857.

![3.13d](image)

**1-tert-Butyl-3-methyl-4-(2-azidophenyl)-5,6-dihydropyridine-1,3(2H)-dicarboxylate 3.13d.** The general procedure was followed by using 0.147 g of 2-azidophenylboronate 3.7 (0.60 mmol), 0.212 g of vinyl triflate 3.10d (0.54 mmol), 0.067 g of Pd(PPh$_3$)$_4$ (0.05 mmol), 1.1 mL of saturated aq. soln. of NaHCO$_3$ and 6 mL of dimethoxyethane. Purification by MPLC (3:97 to 10:90 EtOAc: hexane) afforded the product as green solid (0.155 g, 79%): $^1$H NMR (500 MHz, CDCl$_3$) $\delta$ 7.31 (td, $J = 7.7$ Hz, 1.1 Hz, 1H), 7.15 (d, $J = 7.9$ Hz, 1H), 7.10 (t, $J = 7.5$ Hz, 1H), 6.98 (dd, $J = 7.6$ Hz, 1.2 Hz, 1H), 4.24 (m, 2H), 3.71 (s, 1H), 3.49 (s, 4H), 2.43 (s, 2H), 1.49 (s, 9H); $^{13}$C NMR (125 MHz, CDCl$_3$) $\delta$ 154.6 (C), 145.5 (C), 136.2 (C), 133.9 (C), 128.7 (CH), 128.3 (CH), 124.7 (CH), 118.3 (CH), 80.1 (C), 51.5 (CH$_3$), 43.7 (CH$_2$), 39.1 (CH$_2$), 32.7 (CH$_2$), 28.5 (CH$_3$); only visible peaks. ATR-FTIR (thin film): 2978, 2127, 2094, 1694, 1417 cm$^{-1}$; HRMS (EI) m/z calculated for C$_{19}$H$_{23}$N$_4$O$_4$ (M+H)$^+$: 359.1719, found: 359.1714.
Methyl-3-(2-azidophenyl)-2-methylbut-2-enoate 3.13e. The general procedure was followed by using 0.216 g of 2-azidophenylboronate 3.7 (0.88 mmol), 0.210 g of vinyl triflate 3.10e (0.80 mmol), 0.100 g of Pd(PPh₃)₄ (0.0800 mmol), 1.6 mL of saturated aq. soln. of NaHCO₃ and 10 mL of dimethoxyethane. Purification by MPLC (3:97 to 10:90 EtOAc: hexane) afforded the product as green oil (0.166 g, 89%): ¹H NMR (500 MHz, CDCl₃) δ 7.28 (t, J = 7.7 Hz, 1H), 7.13 (d, J = 8.0 Hz, 1H), 7.08 (t, J = 7.5 Hz, 1H), 6.98 (d, J = 7.5 Hz, 1.2 Hz, 1H), 3.42 (s, 3H), 2.04 (s, 6H); ¹³C NMR (125 MHz, CDCl₃) δ 169.2 (C), 142.4 (C), 136.4 (C), 136.3 (C), 128.5 (CH), 128.2 (CH), 126.9 (C), 124.7 (CH), 118.3 (CH), 51.3 (CH₃), 21.8 (CH₃), 15.7 (CH₃). ATR-FTIR (thin film): 2949, 2123, 2094, 1710 cm⁻¹; HRMS (EI) m/z calculated for C₁₂H₁₃N₃O₂Na (M+Na)⁺: 254.0905, found: 254.0901.

Isopropyl-2-(2-azidophenyl)cyclohex-1-enecarboxylate 3.13f. The general procedure was followed by using 0.179 g of 2-azidophenylboronate 3.7 (0.73 mmol), 0.210 g of vinyl triflate 3.10f (0.66 mmol), 0.077 mg of Pd(PPh₃)₄ (0.070 mmol), 1.5 mL of saturated aq. soln. of NaHCO₃ and 10 mL of dimethoxyethane. Purification by MPLC (3:97 to 10:90 EtOAc: hexane) afforded the product as yellow oil (0.172 g, 91%): ¹H NMR (500 MHz, CDCl₃) δ 7.27 (t, J = 7.7 Hz, 1H), 7.10 (d, J = 8.0 Hz, 1H), 7.07 (t, J = 7.5 Hz, 1H), 6.98 (d, J = 7.5 Hz, 1H), 4.75 (heptet, J = 6.2 Hz, 1H), 2.44 (s, 3H), 2.17 (s, 1H), 1.73 (s, 4H), 0.94 (s, 3H), 0.78 (s, 3H); ¹³C NMR (125 MHz, CDCl₃) δ 168.0 (C), 143.7 (C), 136.6 (C), 136.2 (C), 129.3 (C), 128.8 (CH), 128.0 (CH), 124.6 (CH), 118.2 (CH), 67.2 (CH), 32.7 (CH₂), 26.1 (CH₂), 22.2 (CH₂), 22.0 (CH₂), 21.3 (CH₃). ATR-FTIR (thin film): 2977, 2933, 2120, 2089, 1698, 1286, 1235 cm⁻¹; HRMS (EI) m/z calculated for C₁₆H₂₀N₃O₂ (M+H)⁺: 286.1556, found: 286.1555.
**tert-Butyl-2-(2-azidophenyl)cyclohex-1-enecarboxylate 3.13g.** The general procedure was followed by using 0.189 g of 2-azidophenylboronate 3.7 (0.77 mmol), 0.232 g of vinyl triflate 3.10g (0.70 mmol), 0.081 mg of Pd(PPh₃)₄ (0.070 mmol), 1.5 mL of saturated aq. soln. of NaHCO₃ and 10 mL of dimethoxyethane. Purification by MPLC (3:97 to 10:90 EtOAc: hexane) afforded the product as yellow oil (0.193 g, 92%): \(^1\)H NMR (500 MHz, CDCl₃) δ 7.27 (td, J = 7.7 Hz, 1.5 Hz, 1H), 7.08 (m, 2H), 6.99 (dd, J = 7.5 Hz, 1.5 Hz, 1H), 2.40 (s, 3H), 2.15 (s, 1H), 1.72 (s, 4H), 1.09 (s, 9H); \(^{13}\)C NMR (125 MHz, CDCl₃) δ 168.0 (C), 142.2 (C), 136.6 (C), 136.4 (C), 130.5 (C), 129.0 (CH), 128.0 (CH), 124.6 (CH), 118.4 (CH), 80.0 (C), 32.5 (CH₂), 27.5 (CH₃), 26.1 (CH₂), 22.3 (CH₂), 22.0 (CH₂). ATR-FTIR (thin film): 2973, 2934, 2121, 2094, 1697, 1292 cm⁻¹; HRMS (El) m/z calculated for C_{17}H_{22}N₃O₂ (M+H)⁺: 300.1712, found: 300.1707.

** Allyl-2-(2-azidophenyl)cyclohex-1-enecarboxylate 3.13h.** The general procedure was followed by using 0.229 g of 2-azidophenylboronate 3.7 (0.93 mmol), 0.267 g of vinyl triflate 3.10h (0.85 mmol), 0.098 g of Pd(PPh₃)₄ (0.090 mmol), 1.7 mL of saturated aq. soln. of NaHCO₃ and 10 mL of dimethoxyethane. Purification by MPLC (3:97 to 10:90 EtOAc: hexane) afforded the product as orange oil (0.146 g, 60%): \(^1\)H NMR (500 MHz, CDCl₃) δ 7.28 (td, J = 7.7 Hz, 1.6 Hz, 1H), 7.11 (d, J=8.0 Hz, 1H), 7.08 (td, J = 7.5 Hz, 1.0 Hz, 1H), 7.00 (dd, J = 7.6 Hz, 1.6 Hz, 1H), 5.55 (ddt, J = 17.1 Hz, 10.5 Hz, 5.8 Hz, 1H), 5.08 (dd, J = 10.3 Hz, 1.4 Hz, 1H), 5.05 (dd, J = 3.2 Hz, 1.6 Hz, 1H), 4.35 (d, J = 5.6 Hz, 2H), 2.48 (s, 3H), 2.20 (s, 1H), 1.75 (d, J = 4.4 Hz, 4H); \(^{13}\)C NMR (125 MHz, CDCl₃) δ 167.7 (C), 145.1 (C), 136.4 (C), 135.9
(C), 132.1 (CH), 128.5 (CH), 128.5 (C), 128.1 (CH), 124.7 (CH), 118.3 (CH), 117.8 (CH₂), 64.8 (CH₂), 33.0 (CH₂), 26.2 (CH₂), 22.2 (CH₂), 22.0 (CH₂). ATR-FTIR (thin film): 2293, 2858, 2125, 2093, 1707, 1290 cm⁻¹; HRMS (EI) m/z calculated for C₁₆H₁₇N₃O₂ (M): 283.1321, found: 283.1330.

\[
\text{(1R,2R,4R)-1,7,7-trimethylbicyclo[2.2.1]heptan-2-yl-2-(2-azidophenyl)cyclohex-1-enecarboxylate 3.13i.} \]
The general procedure was followed by using 0.341 g of vinyl triflate 3.10i (0.83 mmol), 0.224 g of 2-azidophenylboronate 3.7 (0.91 mmol), 96 mg of Pd(PPh₃)₄ (0.08 mmol), 1.7 mL of saturated NaHCO₃ aq. and 10 mL dimethoxyethane. Purification by MPLC (3:97 to 10:90 EtOAc: hexane) afforded the product as colorless oil (0.239 g, 76%) with d.r.: 83:17 (determined by NMR of the purified mixture). ³¹H NMR (500 MHz, CDCl₃) δ 7.28 (t, J = 7.8 Hz, 1H), 7.09 (m, 2H), 7.00 (d, J = 7.3 Hz, 1H), 4.77 (d, J = 10.1 Hz, 0.18H), 4.58 (dd, J = 8.1 Hz, 3.6 Hz, 0.85H), 2.44 (m, 3H), 2.18 (s, 1H), 1.75 (s, 4H), 1.63 (s, 4H), 1.48 (dt, J = 13.5 Hz, 7.1 Hz, 1H), 1.07 (td, J = 11.1 Hz, 3.4 Hz, 1H), 1.00 (d, J = 12.6 Hz, 1H), 0.87 (s, 3H), 0.79 (s, 3H), 0.73 (s, 3H); ¹³C NMR (125 MHz, CDCl₃) δ 167.7 (C), 143.8 (C), 136.3 (C), 135.9 (C), 129.3 (C), 128.7 (CH), 128.1 (CH), 124.8 (CH), 118.6 (CH), 80.6 (CH), 53.5 (CH₂), 48.7 (C), 46.8 (C), 45.0 (CH), 33.8 (CH₂), 27.0 (CH₂), 26.3 (CH₂), 22.2 (CH₂), 22.1 (CH₂), 20.1 (CH₃), 18.8 (CH₃), 11.3 (CH₃), only visible peaks. ATR-FTIR (thin film): 2934, 2877, 2121, 2091, 1717, 1232 cm⁻¹.
(1S,2R,5S)-2-Isopropyl-5-methylcyclohexyl-2-(2-azidophenyl)cyclohex-1-enecarboxylate 3.13j. The general procedure was followed by using 0.170 g of 2-azidophenylboronate 3.7 (0.70 mmol), 0.260 g of vinyl triflate 3.10j (0.63 mmol), 0.073 mg of Pd(PPh3)4 (0.060 mmol), 1.3 mL of saturated aq. soln. of NaHCO3 and 10 mL of dimethoxyethane. Purification by MPLC (3:97 to 10:90 EtOAc: hexane) afforded the product as yellow oil (0.229 g, 95%): 1H NMR (500 MHz, CDCl3) δ 7.28 (t, J = 7.7 Hz, 1H), 7.08 (m, 2H), 6.99 (d, J = 7.1 Hz, 1H), 4.49 (td, J = 10.1 Hz, 3.5 Hz, 1H), 2.42 (m, 3H), 2.19 (m, 1H), 1.74 (s, 6H), 1.56 (dd, J = 20.2 Hz, 9.0 Hz, 3H), 1.33 (m, 1H), 0.93 (m, 3H), 0.80 (s, 6H), 0.62 (s, 3H); 13C NMR (125 MHz, CDCl3) δ 167.8 (C), 136.4 (C), 136.2 (C), 129.2 (C), 128.8 (CH), 128.0 (CH), 124.6 (CH), 118.2 (CH), 73.8 (CH), 46.8 (CH), 40.4 (CH2), 34.2 (CH2), 32.9 (CH2), 31.2 (CH), 26.2 (CH2), 23.0 (CH2), 22.2 (CH2), 22.0 (CH2), 21.0 (CH3), 15.9 (CH3); only visible peaks. ATR-FTIR (thin film): 2931, 2869, 2121, 2090, 1697, 1446, 1230 cm⁻¹; HRMS (EI) m/z calculated for C23H32NO2 (M+H-N2)+: 354.2433, found: 354.2430.

Methyl-2-(2-azidophenyl)-6-methylcyclohex-1-enecarboxylate 3.13k. The general procedure was followed by using 0.205 g of 2-azidophenylboronate 3.7 (0.84 mmol), 0.230 g of vinyl triflate 3.10k (0.76 mmol), 0.087 g of Pd(PPh3)4 (0.080 mmol), 1.5 mL of saturated aq. soln. of NaHCO3 and 10 mL of dimethoxyethane. Purification by MPLC (3:97 to 10:90 EtOAc:hexane) afforded the product as yellow oil (0.145 g, 70%): 1H NMR (500 MHz, CDCl3) δ 7.27 (t, J = 8.3 Hz, 1H), 7.11 (d, J = 7.9 Hz, 2H), 7.00 (m, 1H), 3.39 (s, 3H), 2.88 (s, 1H), 2.28 (m, 2H), 1.81 (s, 2H),
1.69 (s, 1H), 1.57 (s, 1H), 1.10 (d, J = 7.0 Hz, 3H); $^1$H NMR (125 MHz, CDCl$_3$) $\delta$ 168.8 (C), 142.8 (C), 137.0 (C), 134.5 (C), 132.3 (CH), 129.5 (C), 128.2 (CH), 124.6 (CH), 118.5 (CH), 51.1 (CH$_3$), 32.1 (CH$_2$), 30.0 (CH$_3$), 29.8 (CH$_2$), 24.8 (CH), 18.9 (CH$_2$). ATR-FTIR (thin film): 2931, 2869, 2118, 2089, 1718, 1484 cm$^{-1}$; HRMS (EI) $m/z$ calculated for C$_{15}$H$_{17}$N$_3$O$_2$Na (M+Na)$^+$: 294.1218, found: 294.1219.

![Methyl-2-(2-azidophenyl)-5-phenylcyclohex-1-enecarboxylate 3.13l](image1.png)

**Methyl-2-(2-azidophenyl)-5-phenylcyclohex-1-enecarboxylate 3.13l.** The general procedure was followed by using 0.392 g of 3.10l (1.01 mmol), 0.290 g of 3.7 (1.11 mmol), 124 mg of Pd(PPh$_3$)$_4$ (0.10 mmol), 2.0 mL of saturated NaHCO$_3$ aq. and 10 mL dimethoxyethane. Purification by MPLC (3:97 to 10:90 EtOAc: hexane) afforded the product as yellow oil (0.164 g, 46%). $^1$H NMR (500 MHz, CDCl$_3$) $\delta$ 7.36 (m, 5H), 7.27 (t, J = 7.1 Hz, 1H), 7.19 (d, J = 7.7 Hz, 1.0 Hz, 1H), 7.15 (t, J = 7.5 Hz, 1H), 7.07 (dd, J = 7.5 Hz, 1.2 Hz, 1H), 3.49 (s, 3H), 2.98 (s, 1H), 2.90 (d, J = 17.5 Hz, 1H), 2.55 (m, 2H), 2.42 (s, 1H), 2.07 (m, 1H), 1.96 (s, 1H); $^1$C NMR (125 MHz, CDCl$_3$) $\delta$ 168.0(C), 145.9 (C), 136.4 (C), 135.3 (C), 128.6 (CH), 128.5 (CH), 128.3 (CH), 128.0 (C), 127.0 (CH), 126.4 (CH), 124.8 (CH), 118.3 (CH), 51.4 (CH$_3$), 39.7 (CH), 34.1 (CH$_2$), 33.6(CH$_2$), 29.3 (CH$_2$), only visible peaks. ATR-FTIR (thin film): 3022, 2931, 2125, 2092, 1725, 1484, 1228 cm$^{-1}$.

![Methyl-2-(2-azidophenyl)-5-tert-butylcyclohex-1-enecarboxylate 3.13m](image2.png)

**Methyl-2-(2-azidophenyl)-5-tert-butylcyclohex-1-enecarboxylate 3.13m.** The general procedure was followed by using 0.183 g of 2-azidophenylboronate 3.7 (0.74 mmol), 0.233 g of vinyl triflate 3.10m (0.67 mmol), 0.077 g of Pd(PPh$_3$)$_4$ (0.070 mmol), 1.5 mL of saturated NaHCO$_3$ aq. and 10 mL of dimethoxyethane. Purification
by MPLC (3:97 to 10:90 EtOAc:hexane) afforded the product as yellow oil (0.139 g, 69%): \(^1\)H NMR (500 MHz, CDCl\(_3\)) \(\delta\) 7.29 (td, \(J = 7.7\) Hz, 1.2 Hz, 1H), 7.14 (d, \(J = 7.9\) Hz, 1H), 7.09 (t, \(J = 7.5\) Hz, 1H), 6.99 (d, \(J = 7.4\) Hz, 1H), 3.45 (s, 3H), 2.60 (d, \(J = 17.5\) Hz, 1H), 2.46 (s, 1H), 2.28 (s, 1H), 2.13 (m, 1H), 1.91 (m, 1H), 1.42 (s, 1H), 1.35 (s, 1H), 0.95 (s, 9H); \(^{13}\)C NMR (125 MHz, CDCl\(_3\)) \(\delta\) 168.6 (C), 145.1 (C), 136.3 (C), 135.6 (C), 128.6 (C), 128.5 (CH), 128.1 (CH), 124.6 (CH), 118.3 (CH), 51.2 (CH\(_3\)), 43.7 (CH), 34.3 (CH\(_2\)), 32.4 (C), 27.9 (CH\(_2\)), 27.3 (CH\(_3\)), 23.6 (CH\(_2\)). ATR-FTIR (thin film): 2950, 2871, 2125, 2090, 1714, 1486 cm\(^{-1}\); HRMS (EI) m/z calculated for C\(_{18}\)H\(_{23}\)N\(_3\)O\(_2\)Na (M+Na\(^+\)): 336.1688, found: 336.1686.

**tert-Butyl-2-(2-azidophenyl)-5-tert-butylcyclohex-1-enecarboxylate 3.13n.** The general procedure was followed by using 0.425 g of vinyl triflate 3.10n (1.10 mmol), 0.296 g of 2-azidophenylboronate 3.7 (1.21 mmol), 0.0635 g of Pd(PPh\(_3\))\(_4\) (0.050 mmol), 2.2 mL of saturated aq. soln. of NaHCO\(_3\) and 11 mL of dimethoxyethane. Purification by MPLC (3:97 to 10:90 EtOAc:hexane) afforded the product as yellow solid (0.330 g, 85%): \(^1\)H NMR (500 MHz, CDCl\(_3\)) \(\delta\) 7.28 (t, \(J = 7.7\) Hz, 1H), 7.09 (m, 2H), 6.99 (s, 1H), 2.60 (m, 1H), 2.40 (m, 1H), 2.21 (m, 1H), 2.08 (t, \(J = 14.1\) Hz, 1H), 1.87 (m, 1H), 1.33 (m, 2H), 1.08 (s, 9H), 0.93 (s, 9H); \(^{13}\)C NMR (125 MHz, CDCl\(_3\)) \(\delta\) 168.3 (C), 149.2 (C), 136.1 (C), 130.6 (C), 129.0 (CH), 128.0 (CH), 124.9 (C), 124.6 (CH), 118.3 (CH), 80.1 (C), 42.9 (CH), 34.1 (CH\(_2\)), 32.4 (C), 29.1 (CH\(_2\)), 27.5 (CH\(_3\)), 27.3 (CH\(_3\)), 23.7 (CH\(_2\)). ATR-FTIR (thin film): 262, 2123, 2087, 1698, 1365, 1276, 1138 cm\(^{-1}\); HRMS (EI) m/z calculated for C\(_{21}\)H\(_{30}\)NO\(_2\) (M+H-N\(_2\))\(^+\): 328.2277, found: 328.2269.
D. Rh\(_{2}(\text{II})\)-Catalyzed Synthesis of \(3H\)-Indoles from Styryl Azides.

Screening of Conditions for to Identify Optimal Conditions for \(3H\)-Indole Formation.

To a mixture of styryl azide 3.11a and Rh\(_{2}\)(esp)\(_{2}\) (5 mol %) was added toluene (0.1M). The resulting mixture was heated at 140 °C. After 16 h, the mixture was cooled to room temperature, diluted with CH\(_2\)Cl\(_2\) and concentrated \textit{in vacuo}. Dibromomethane (0.7 µL, 0.1 mmol) was added, and the mixture was analyzed using \(^1\)H NMR spectroscopy to determine the outcome of the reaction.

<table>
<thead>
<tr>
<th>entry</th>
<th>catalyst</th>
<th>mol %</th>
<th>solvent</th>
<th>T (°C)</th>
<th>yield, %(^a)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>none</td>
<td>–</td>
<td>PhMe</td>
<td>140</td>
<td>trace(^b)</td>
</tr>
<tr>
<td>2</td>
<td>FeBr(_2)</td>
<td>10</td>
<td>PhMe</td>
<td>140</td>
<td>49</td>
</tr>
<tr>
<td>3</td>
<td>CoTPP</td>
<td>10</td>
<td>PhMe</td>
<td>140</td>
<td>40</td>
</tr>
<tr>
<td>4</td>
<td>RuCl(_3)·nH(_2)O</td>
<td>10</td>
<td>PhMe</td>
<td>140</td>
<td>33</td>
</tr>
<tr>
<td>5</td>
<td>[((cod)Ir(OMe)](_2)</td>
<td>5</td>
<td>PhMe</td>
<td>140</td>
<td>33</td>
</tr>
<tr>
<td>6</td>
<td>Rh(_2)(O(_2)CC(_3)F(_7))(_4)</td>
<td>5</td>
<td>PhMe</td>
<td>140</td>
<td>25</td>
</tr>
<tr>
<td>7</td>
<td>Rh(_2)(O(_2)CC(<em>7)H(</em>{15}))(_4)</td>
<td>5</td>
<td>PhMe</td>
<td>140</td>
<td>64</td>
</tr>
<tr>
<td>8</td>
<td>Rh(_2)(esp)(_2)</td>
<td>5</td>
<td>PhMe</td>
<td>140</td>
<td>78</td>
</tr>
<tr>
<td>9</td>
<td>Rh(_2)(esp)(_2)</td>
<td>5</td>
<td>DME</td>
<td>140</td>
<td>60</td>
</tr>
<tr>
<td>10</td>
<td>Rh(_2)(esp)(_2)</td>
<td>5</td>
<td>DME</td>
<td>140</td>
<td>72</td>
</tr>
<tr>
<td>11</td>
<td>Rh(_2)(esp)(_2)</td>
<td>5</td>
<td>PhMe</td>
<td>120</td>
<td>53</td>
</tr>
<tr>
<td>12</td>
<td>Rh(_2)(esp)(_2)</td>
<td>5</td>
<td>PhMe</td>
<td>120</td>
<td>56</td>
</tr>
<tr>
<td>13</td>
<td>Rh(_2)(esp)(_2)</td>
<td>1</td>
<td>PhMe</td>
<td>120</td>
<td>26</td>
</tr>
</tbody>
</table>

\(^a\) As determined using \(^1\)H NMR spectroscopy using CH\(_2\)Br\(_2\) as an internal standard. pin = pinacolate ester; TPP = tetraphenylporphyrin; cod = 1,4-cyclooctadiene; esp = \(\alpha,\alpha,\alpha',\alpha''\)-tetramethyl-1,3-benzene-dipropionate; DME = dimethoxyethane; DCE = 1,2-dichloroethane. \(^b\) Decomposition of 3.11a observed
Optimized Procedure.

To a mixture of styryl azide 3.11a and Rh₂(esp)₂ (5 mol %) was added toluene (0.1M). The resulting mixture was heated at 140 °C. After 16 h, the mixture was cooled to room temperature, diluted with CH₂Cl₂ and concentrated in vacuo. Purification of the residue by MPLC (3:97 – 30:70 EtOAc:hexanes) using alumina afforded the product.

Methyl-2,3,4,4a-tetrahydro-1H-carbazole-4a-carboxylate 3.12a.

The general procedure was followed by using 0.0293 g of styryl azide 3.11a (0.114 mmol), 0.0043 g of Rh₂(esp)₂ (5 mol %) and 1.1 mL of toluene. Purification by MPLC (3:97 to 30:70 EtOAc:hexanes) afforded the product as yellow oil (0.0210 mg, 80%): ¹H NMR (500 MHz, CDCl₃) 7.59 (d, J = 7.7 Hz, 1H), 7.43 (d, J = 7.4 Hz, 1H), 7.37 (td, J = 7.6 Hz, 1.1 Hz, 1H), 7.19 (t, J = 7.5 Hz, 1H), 3.64 (s, 3H), 3.04 (dq, J = 13.3 Hz, 2.6 Hz, 1H), 2.98 (dt, J= 13.5 Hz, 2.0 Hz, 1H), 2.72 (td, J = 13.2 Hz, 6.0 Hz, 1H), 2.19 (ddt, J = 12.4 Hz, 5.7 Hz, 2.9 Hz, 1H), 1.81 (d, J = 13.5 Hz, 1H), 1.58 (qt, J= 13.5 Hz, 3.2 Hz, 1H), 1.48 (dddt, J = 17.3 Hz, 13.0 Hz, 8.8 Hz, 4.3 Hz, 1H), 1.16 (td, J= 13.3 Hz, 3.5 Hz, 1H); ¹³C NMR (125 MHz, CDCl₃) 183.8 (C), 170.6 (C), 155.4 (C), 139.6 (C), 128.9 (CH), 125.4 (CH), 122.4 (CH), 120.4 (CH), 64.9 (C), 52.8 (CH₃), 37.2 (CH₂), 31.4 (CH₂), 28.4 (CH₂), 22.9 (CH₂). ATR-FTIR (thin film): 2928, 2858, 1731, 1584, 1455, 1211 cm⁻¹; HRMS (El) m/z calculated for C₁₄H₁₆NO₂ (M+H)⁺: 230.1181, found: 230.1186.
Methyl-6-methyl-2,3,4,4a-tetrahydro-1H-carbazole-4a-carboxylate 3.12b. The general procedure was followed by using 0.0284 g of styryl azide 3.11b (0.105 mmol), 0.0040 g of Rh2(esp)2 (5 mol %) and 1.1 mL of toluene. Purification by MPLC (3:97 to 30:70 EtOAc: hexane) afforded the product as white solid (0.0198 g, 77%): 1H NMR (500 MHz, CDCl3) δ 7.46 (d, J = 7.9 Hz, 1H), 7.23 (s, 1H), 7.16 (d, J = 7.8 Hz, 1H), 3.64 (s, 3H), 3.01 (dd, J = 13.3 Hz, 2.4 Hz, 1H), 2.96 (d, J = 13.4 Hz, 1H), 2.68 (td, J = 13.2 Hz, 5.9 Hz, 1H), 2.37 (s, 3H), 2.17 (dt, J = 12.7 Hz, 2.8 Hz, 1H), 1.80 (d, J = 13.6 Hz, 1H), 1.56 (qt, J = 13.5 Hz, 3.1 Hz, 1H), 1.47 (dddt, J = 17.4 Hz, 13.2 Hz, 8.9 Hz, 4.2 Hz, 1H), 1.15 (td, J = 13.3 Hz, 3.5 Hz, 1H); 13C NMR (125 MHz, CDCl3) δ 182.8 (C), 170.8 (C), 153.2 (C), 139.7 (C), 135.3 (C), 129.4 (CH), 123.1 (CH), 120.0 (CH), 64.7 (C), 52.8 (CH3), 37.2 (CH2), 31.4 (CH2), 28.5 (CH2), 23.0 (CH2), 21.4 (CH3). ATR-FTIR (thin film): 2934, 2858, 1731, 1585, 1213 cm⁻¹; HRMS (EI) m/z calculated for C15H18NO2 (M+H)+: 244.1338, found: 244.1326.

Methyl-6-fluoro-2,3,4,4a-tetrahydro-1H-carbazole-4a-carboxylate 3.12c. The general procedure was followed by using 0.0579 g of styryl azide 3.11c (0.210 mmol), 0.0079 g of Rh2(esp)2 (5 mol %) and 2.1 mL of toluene. Purification by MPLC (3:97 to 30:70 EtOAc:hexanes) afforded the product as yellow oil (0.0320 mg, 62%): 1H NMR (500 MHz, CDCl3) δ 7.50 (dd, J = 8.5 Hz, 4.6 Hz, 1H), 7.14 (dd, J = 7.8 Hz, 2.5 Hz, 1H), 7.04 (td, J = 8.8 Hz, 2.5 Hz, 1H), 3.66 (s, 3H), 2.97 (t, J = 15.1 Hz, 2H), 2.71 (td, J = 13.2 Hz, 6.0 Hz, 1H), 2.18 (dq, J = 9.7 Hz, 3.0 Hz, 1H), 1.81 (d, J = 13.6 Hz, 1H), 1.57 (qt, J = 13.5 Hz, 3.1 Hz, 1H), 1.47 (qt, J = 13.1 Hz, 3.9 Hz, 1H), 1.18 (td, J = 13.2 Hz, 2.6 Hz, 1H); 13C NMR (125 MHz, CDCl3) δ 183.7 (C), 170.1 (C), 161.2 (d, JCF = 244.1 Hz, C), 151.4 (C), 141.2 (d, JCF = 8.2 Hz, C), 121.1 (CH), 115.4
(d, $J_{CF} = 24.0$ Hz, CH), 110.3 (d, $J_{CF} = 25.1$ Hz, CH), 65.3 (C), 52.9 (CH$_3$), 37.3 (CH$_2$), 31.3 (CH$_2$), 28.4 (CH$_2$), 22.8 (CH$_2$); $^{19}$F NMR (282 MHz, CDCl$_3$) $\delta$ –117.1. ATR-FTIR (thin film): 2950, 2860, 1732, 1588, 1460, 1215 cm$^{-1}$; HRMS (EI) m/z calculated for C$_{14}$H$_{15}$NO$_2$F (M+H)$^+$: 248.1087, found: 248.1079.

**Methyl-6-chloro-2,3,4,4a-tetrahydro-1H-carbazole-4a-carboxylate** 3.12d. The general procedure was followed by using 0.0148 g of styryl azide 3.11d (0.051 mmol), 0.0019 g of Rh$_2$(esp)$_2$ (5 mol %) and 0.5 mL of toluene. Purification by MPLC (3:97 to 30:70 EtOAc:hexanes) afforded the product as white solid (0.0115 mg, 86%): $^1$H NMR (500 MHz, CDCl$_3$) $\delta$ 7.73 (m, 1H), 7.50 (s, 1H), 7.45 (m, 1H), 3.73 (s, 3H), 3.42 (m, 1H), 3.14 (m, 1H), 2.86 (m, 1H), 2.35 (m, 1H), 1.90 (m, 1H), 1.64 (m, 2H), 1.33 (m, 1H); $^{13}$C NMR (125 MHz, CDCl$_3$) $\delta$ 187.9 (C), 168.1 (C), 139.2 (C), 133.6 (C), 132.0 (C), 130.0 (CH), 123.8 (CH), 120.5 (CH), 64.9 (C), 53.9 (CH$_3$), 38.4 (CH$_2$), 30.8 (CH$_2$), 29.1 (CH$_2$), 22.5 (CH$_2$). ATR-FTIR (thin film): 2950, 2859, 1732, 1446, 1214 cm$^{-1}$; HRMS (EI) m/z calculated for C$_{14}$H$_{15}$NO$_2$Cl (M+H)$^+$: 264.0791, found: 264.0789.

**Methyl-6-trifluoromethoxy-2,3,4,4a-tetrahydro-1H-carbazole-4a-carboxylate** 3.12e. The general procedure was followed by using 0.0677 g of styryl azide 3.11e (0.198 mmol), 0.0075 g of Rh$_2$(esp)$_2$ (5 mol %) and 2.0 mL of toluene. Purification by MPLC (3:97 to 30:70 EtOAc:hexanes) afforded the product as yellow oil (0.0439 g, 71%): $^1$H NMR (500 MHz, CDCl$_3$) $\delta$ 7.57 (d, $J$ = 8.4 Hz, 1H), 7.30 (s, 1H), 7.23 (d, $J$ = 8.3 Hz, 1H), 3.68 (s, 3H), 3.00(t, $J$ = 16.6 Hz, 2H), 2.75 (td, $J$= 13.3 Hz, 6.0 Hz, 1H), 2.21 (dq, $J$ = 9.8 Hz, 3.0 Hz, 1H), 1.83 (d, $J$ = 13.8 Hz, 1H), 1.59 (qt, $J$= 13.5
Hz, 3.1 Hz, 1H), 1.48 (dddt, J = 17.4 Hz, 13.1 Hz, 8.9 Hz, 4.3 Hz, 1H), 1.20 (td, J=13.3 Hz, 3.6 Hz, 1H); 13C NMR (125 MHz, CDCl3) δ 185.1 (C), 169.9 (C), 153.8 (C), 147.0 (C), 141.0 (C), 121.8 (CH), 121.0 (CH), 120.5 (q, JCF = 249.8 Hz, C), 116.1 (CH), 65.4 (C), 53.0 (CH3), 37.4 (CH2), 31.5 (CH2), 28.4 (CH2), 22.8 (CH2); 19F NMR (282 MHz, CDCl3) δ –58.5. ATR-FTIR (thin film): 2923, 2852, 1741, 1587, 1460, 1245, 1212, 1155 cm⁻¹; HRMS (EI) m/z calculated for C15H15NO3F3 (M+H)⁺: 314.1004, found: 314.0991.

**Methyl-7-N-Boc-2,3,4,4a-tetrahydro-1H-carbazole-4a-carboxylate 3.12f.** The general procedure was followed by using 0.0164 g of styryl azide 3.11f (0.044 mmol), 0.0017 g of Rh2(esp)2 (5 mol %) and 0.5 mL of toluene. Purification by MPLC (3:97 to 50:50 EtOAc:hexanes) afforded the product as white solid (0.0112 g, 74%): 1H NMR (500 MHz, CDCl3) δ 7.43 (s, 1H), 7.37 (s, 1H), 7.33 (d, J = 8.0 Hz, 1H), 6.55 (s, 1H), 3.64 (s, 3H), 3.00 (t, J = 17.4 Hz, 1H), 2.69 (td, J = 13.1 Hz, 6.9 Hz, 1H), 2.18 (dt, J = 12.2 Hz, 2.9 Hz, 1H), 1.80 (d, J = 13.1 Hz, 1H), 1.57 (dt, J= 13.4 Hz, 3.0 Hz, 1H), 1.52 (s, 9H), 1.26 (t, J= 7.1 Hz, 1H), 1.15 (td, J= 13.1 Hz, 2.7 Hz, 1H); 13C NMR (125 MHz, CDCl3) δ 170.6 (C), 156.3 (C), 152.7 (C), 139.2 (C), 134.1 (C), 122.5 (CH), 115.8 (CH), 111.3 (C), 80.7 (C), 64.5 (C), 52.8 (CH3), 37.2 (CH2), 31.5 (CH2), 28.4 (CH2), 28.4 (CH3), 22.9 (CH2), only visible peaks. ATR-FTIR (thin film): 2933, 1725, 1587, 1531, 1244, 1155 cm⁻¹; HRMS (EI) m/z calculated for C19H25N2O4 (M+H)⁺: 345.1814, found: 345.1813.

**Methyl-7-methoxy-2,3,4,4a-tetrahydro-1H-carbazole-4a-carboxylate 3.12g.** The general procedure was followed by using 0.0314 g of styryl azide 3.11g (0.109
mmol), 0.0041 g of Rh₂(esp)₂ (5 mol %) and 1.1 of mL toluene. Purification by MPLC (3:97 to 30:70 EtOAc:hexanes) afforded the product as yellow oil (0.0197 g, 70%): ¹H NMR (500 MHz, CDCl₃) δ 7.30 (d, J = 8.2 Hz, 1H), 7.16 (d, J = 2.1 Hz, 1H), 6.73 (dd, J = 8.2 Hz, 2.2 Hz, 1H), 3.83 (s, 3H), 3.64 (s, 3H), 3.01 (dd, J = 13.3 Hz, 2.1 Hz, 1H), 2.96 (d, J= 13.7 Hz, 1H), 2.70 (td, J = 6.2 Hz, 3.1 Hz, 1H), 2.19 (td, J = 6.2 Hz, 3.1 Hz, 1H), 1.79 (d, J = 13.8 Hz, 1H), 1.51 (m, 2H), 1.14 (td, J= 13.3 Hz, 3.4 Hz, 1H); ¹³C NMR (125 MHz, CDCl₃) δ 185.2 (C), 170.8 (C), 160.8 (C), 156.9 (C), 131.6 (C), 122.6 (CH), 111.2 (CH), 106.3 (CH), 64.3 (C), 55.6 (CH₃), 52.7 (CH₃), 37.3 (CH₂), 31.5 (CH₂), 28.4 (CH₂), 22.9 (CH₂). ATR-FTIR (thin film): 2935, 2856, 1731, 1585, 1481, 1217 cm⁻¹; HRMS (El) m/z calculated for C₁₅H₁₈NO₃ (M+H)⁺: 260.1287, found: 260.1279.

Methyl-7-methyl-2,3,4,4a-tetrahydro-1H-carbazole-4a-carboxylate 3.12h. The general procedure was followed by using 0.0284 g of styryl azide 3.11h (0.105 mmol), 0.0040 g of Rh₂(esp)₂ (5 mol %) and 1.1 mL of toluene. Purification by MPLC (3:97 to 30:70 EtOAc:hexanes) afforded the product as white solid (0.0198 g, 77%): ¹H NMR (500 MHz, CDCl₃) δ 7.40 (s, 1H), 7.30 (d, J = 7.6 Hz, 1H), 7.01 (d, J = 7.5 Hz, 1H), 3.63 (s, 3H), 3.02 (dd, J = 13.3 Hz, 2.4 Hz, 1H), 2.97 (dd, J= 13.4 Hz, 1.9 Hz, 1H), 2.69 (td, J = 13.2 Hz, 5.9 Hz, 1H), 2.41 (s, 3H), 2.18 (dq, J = 9.7 Hz, 3.0 Hz, 1H), 1.79 (d, J = 13.8 Hz, 1H), 1.56 (qt, J= 13.5 Hz, 3.1 Hz, 1H), 1.47 (tdd, J = 17.4 Hz, 9.0 Hz, 4.2 Hz, 1H), 1.14 (td, J= 13.3 Hz, 3.5 Hz, 1H); ¹³C NMR (125 MHz, CDCl₃) δ 184.0 (C), 170.8 (C), 155.7 (C), 139.0 (C), 126.7 (C), 126.1 (CH), 121.9 (CH), 121.1 (CH), 64.6 (C), 52.7 (CH₃), 37.2 (CH₂), 31.5 (CH₂), 28.5 (CH₂), 23.0 (CH₂), 21.6 (CH₃). ATR-FTIR (thin film): 2948, 2859, 1731, 1586, 1215 cm⁻¹; HRMS (El) m/z calculated for C₁₅H₁₈NO₂ (M+H)⁺: 244.1338, found: 244.1336.
Methyl-7-fluoro-2,3,4,4a-tetrahydro-1H-carbazole-4a-carboxylate 3.12i. The general procedure was followed by using 0.0541 g of styryl azide 3.11i (0.196 mmol), 0.0074 mg of Rh$_2$(esp)$_2$ (5 mol %) and 2.0 mL of toluene. Purification by MPLC (3:97 to 30:70 EtOAc:hexanes) afforded the product as yellow oil (0.0334 g, 68%): $^1$H NMR (500 MHz, CDCl$_3$) $\delta$ 7.35 (d, $J = 8.2$ Hz, 5.2 Hz, 1H), 7.28 (dd, $J = 8.9$ Hz, 2.3 Hz, 1H), 6.89 (td, $J = 8.7$ Hz, 2.0 Hz, 1H), 3.65 (s, 3H), 3.02 (dq, $J = 13.3$ Hz, 2.6 Hz, 1H), 2.97 (dd, $J = 13.4$ Hz, 2.1 Hz, 1H), 2.71 (td, $J = 13.2$ Hz, 6.0 Hz, 1H), 2.19 (ddt, $J = 12.4$ Hz, 5.7 Hz, 2.9 Hz, 1H), 1.81 (d, $J = 13.4$ Hz, 1H), 1.56 (qt, $J = 13.5$ Hz, 3.1 Hz, 1H), 1.46 (qt, $J = 13.1$ Hz, 3.9 Hz, 1H), 1.14 (td, $J = 13.3$ Hz, 3.5 Hz, 1H); $^{13}$C NMR (125 MHz, CDCl$_3$) $\delta$ 186.2 (C), 170.3 (C), 164.5 (C), 156.9 (d, $J_{CF} = 11.1$ Hz, C), 135.1 (C), 122.9 (d, $J_{CF} = 9.2$ Hz, CH), 112.1 (d, $J_{CF} = 22.3$ Hz, CH), 118.2 (d, $J_{CF} = 24.6$ Hz, CH), 64.5 (C), 52.9 (CH$_3$), 37.3 (CH$_2$), 31.5 (CH$_2$), 28.4 (CH$_2$), 22.8 (CH$_2$); $^{19}$F NMR (282 MHz, CDCl$_3$) $\delta$ -113.3. ATR-FTIR (thin film): 2951, 2860, 1731, 1684, 1583, 1472, 1217 cm$^{-1}$; HRMS (EI) $m/z$ calculated for C$_{14}$H$_{15}$NO$_2$F (M+H)$^+$: 248.1087, found: 248.1088.

Methyl-7-trifluoromethyl-2,3,4,4a-tetrahydro-1H-carbazole-4a-carboxylate 3.12j. The general procedure was followed by using 0.0117 g of styryl azide 3.11j (0.036 mmol), 0.0014 g of Rh$_2$(esp)$_2$ (5 mol %) and 0.7 mL of toluene. Purification by MPLC (3:97 to 30:70 EtOAc:hexanes) afforded the product as white solid (0.0070 g, 65%): $^1$H NMR (500 MHz, CDCl$_3$) $\delta$ 7.82 (s, 1H), 7.54 (d, $J = 7.8$ Hz, 1H), 7.48 (d, $J = 7.8$ Hz, 1H), 3.67 (s, 3H), 3.06 (dq, $J = 13.3$ Hz, 2.6 Hz, 1H), 3.01 (dt, $J = 13.5$ Hz, 2.1 Hz, 1H), 2.75 (td, $J = 13.3$ Hz, 6.1 Hz, 1H), 2.23 (dq, $J = 9.9$ Hz, 3.0 Hz, 1H), 1.84 (d, $J = 13.6$ Hz, 1H), 1.61 (qt, $J = 13.6$ Hz, 3.3 Hz, 1H), 1.49 (dddt, $J = 17.5$ Hz, 13.2 Hz, 1.46 (qt, $J = 13.1$ Hz, 3.9 Hz, 1H), 1.14 (td, $J = 13.3$ Hz, 3.5 Hz, 1H); $^{13}$C NMR (125 MHz, CDCl$_3$) $\delta$ 186.2 (C), 170.3 (C), 164.5 (C), 156.9 (d, $J_{CF} = 11.1$ Hz, C), 135.1 (C), 122.9 (d, $J_{CF} = 9.2$ Hz, CH), 112.1 (d, $J_{CF} = 22.3$ Hz, CH), 118.2 (d, $J_{CF} = 24.6$ Hz, CH), 64.5 (C), 52.9 (CH$_3$), 37.3 (CH$_2$), 31.5 (CH$_2$), 28.4 (CH$_2$), 22.8 (CH$_2$); $^{19}$F NMR (282 MHz, CDCl$_3$) $\delta$ -113.3. ATR-FTIR (thin film): 2951, 2860, 1731, 1684, 1583, 1472, 1217 cm$^{-1}$; HRMS (EI) $m/z$ calculated for C$_{14}$H$_{15}$NO$_2$F (M+H)$^+$: 248.1087, found: 248.1088.
Hz, 8.9 Hz, 4.3 Hz, 1H), 1.17 (td, \( J = 13.4 \) Hz, 3.6 Hz, 1H); \(^{13}\)C NMR (125 MHz, CDCl\(_3\)) \( \delta \) 185.8 (C), 169.8 (C), 155.8 (C), 143.1 (C), 131.6 (C), 123.5 (q, \( J_{CF} = 133.0 \) Hz, C), 122.7 (CH), 122.5 (CH), 117.4 (CH), 65.1 (C), 53.1 (CH\(_3\)), 37.2 (CH\(_2\)), 31.5 (CH\(_2\)), 28.4 (CH\(_2\)), 22.8 (CH\(_2\)); \(^{19}\)F NMR (282 MHz, CDCl\(_3\)) \( \delta \) –65.5.

ATR-FTIR (thin film): 2930, 2860, 1735, 1684, 1585, 1426, 1319, 1121 cm\(^{-1}\); HRMS (EI) \( m/z \) calculated for C\(_{15}\)H\(_{15}\)NO\(_2\)F\(_3\) (M+H\(^+\)): 298.1055, found: 298.1053.

**Methyl-7-acetyl-2,3,4,4a-tetrahydro-1\(H\)-carbazole-4a-carboxylate 3.12k.** The general procedure was followed by using 0.0128 g of styryl azide 3.11k (0.043 mmol), 0.0016 g of Rh\(_2\)(esp)\(_2\) (5 mol %) and 0.5 mL of toluene. Purification by MPLC (3:97 to 30:70 EtOAc:hexanes) afforded the product as yellow oil (0.0084 g, 72\%): \(^1\)H NMR (500 MHz, CDCl\(_3\)) \( \delta \) 8.15 (s, 1H), 7.86 (d, \( J = 7.8 \) Hz, 1H), 7.52 (d, \( J = 7.7 \) Hz, 1H), 3.66 (s, 3H), 3.05 (t, \( J = 15.5 \) Hz, 2H), 2.74 (td, \( J = 13.1 \) Hz, 6.0 Hz, 1H), 2.63 (s, 3H), 2.23 (s, 1H), 1.84 (d, \( J = 13.4 \) Hz, 1H), 1.62 (q, \( J = 13.5 \) Hz, 1H), 1.52 (t, \( J = 13.0 \) Hz, 1H), 1.19 (t, \( J = 12.8 \) Hz, 1H); \(^{13}\)C NMR (125 MHz, CDCl\(_3\)) \( \delta \) 197.6 (C), 185.1 (C), 169.9 (C), 155.9 (C), 144.4 (C), 138.3 (C), 125.9 (CH), 122.4 (CH), 120.3 (CH), 65.1 (C), 53.0 (CH\(_3\)), 37.2 (CH\(_2\)), 31.5 (CH\(_2\)), 28.4 (CH\(_2\)), 26.9 (CH\(_3\)), 22.8 (CH\(_2\)). ATR-FTIR (thin film): 2951, 2858, 1733, 1684, 1585, 1420, 1214 cm\(^{-1}\); HRMS (EI) \( m/z \) calculated for C\(_{16}\)H\(_{18}\)NO\(_3\) (M+H\(^+\)): 272.1287, found: 272.1286.

**Methyl-6,7,8,9,10,10a-hexahydrocyclohepta[b]indole-10a-carboxylate 3.14a.** The general procedure was followed by using 0.0386 g of styryl azide 3.13a (0.142 mmol), 0.0054 g of Rh\(_2\)(esp)\(_2\) (5 mol %) and 1.4 mL of toluene. Purification by
MPLC (3:97 to 30:70 EtOAc:hexanes) afforded the product as yellow oil (0.0289 g, 84%): $^1$H NMR (500 MHz, CDCl$_3$) δ 7.50 (d, $J$ = 7.7 Hz, 1H), 7.37 (d, $J$ = 7.4 Hz, 1H), 7.34 (t, $J$ = 7.7 Hz, 1H), 7.19 (t, $J$ = 7.4 Hz, 1H), 3.65 (s, 3H), 3.00 (t, $J$ = 6.2 Hz, 2H), 2.57 (ddd, $J$ = 14.2 Hz, 6.0 Hz, 1.7 Hz, 1H), 1.75 (m, 4H), 1.56 (t, $J$ = 12.9 Hz, 1H), 1.48 (m, 2H); $^{13}$C NMR (125 MHz, CDCl$_3$) δ 186.0 (C), 170.8 (C), 154.8 (C), 139.6 (C), 128.9 (CH), 125.7 (CH), 122.1 (CH), 119.9 (CH), 68.2 (C), 52.7 (CH$_3$), 34.8 (CH$_2$), 33.6 (CH$_2$), 29.2 (CH$_2$), 26.8 (CH$_2$), 26.2 (CH$_2$). ATR-FTIR (thin film): 2927, 2855, 1729, 1697, 1456, 1215 cm$^{-1}$; HRMS (EI) m/z calculated for C$_{15}$H$_{18}$NO$_2$ (M+H)$^+$: 244.1338, found: 244.1338.

![3.14b](image)

**Methyl-6,7,8,9,10,10a-hexahydrocyclohepta[b]indole-10a-carboxylate** 3.14b.

The general procedure was followed by using 0.0400 g of styryl azide 3.13b (0.140 mmol), 0.0053 g of Rh$_2$(esp)$_2$ (5 mol %) and 1.4 mL of toluene. Purification by MPLC (3:97 to 30:70 EtOAc:hexanes) afforded the product as yellow oil (0.0254 g, 70%): $^1$H NMR (500 MHz, CDCl$_3$) δ 7.56 (d, $J$ = 7.7 Hz, 1H), 7.36 (m, 2H), 7.21 (t, $J$ = 7.4 Hz, 1H), 3.58 (s, 3H), 2.96 (dt, $J$ = 13.7 Hz, 6.0 Hz, 1H), 2.76 (ddd, $J$ = 14.0 Hz, 9.9 Hz, 4.3 Hz, 1H), 2.70 (ddd, $J$ = 14.6 Hz, 11.7 Hz, 2.7 Hz, 1H), 2.41 (ddd, $J$ = 14.7 Hz, 6.2 Hz, 3.0 Hz, 1H), 2.04 (m, 1H), 1.92 (dtt, $J$ = 13.9 Hz, 9.4 Hz, 4.6 Hz, 1H), 1.61 (m, 1H), 1.52 (m, 1H), 1.40 (m, 2H), 1.11 (m, 1H), 0.94 (m, 1H); $^{13}$C NMR (125 MHz, CDCl$_3$) δ 186.9 (C), 171.0 (C), 155.7 (C), 137.9 (C), 128.9 (CH), 125.4 (CH), 122.4 (CH), 120.4 (CH), 64.9 (C), 52.8 (CH$_3$), 37.2 (CH$_2$), 31.4 (CH$_2$), 28.4 (CH$_2$), 22.9 (CH$_2$) only signals visible. ATR-FTIR (thin film): 2928, 2858, 1734, 1569, 1456, 1217 cm$^{-1}$; HRMS (EI) m/z calculated for C$_{16}$H$_{20}$NO$_2$ (M+H)$^+$: 258.1494, found: 258.1502.
Methyl-1,3,4,4a-tetrahydropyranono[3,4-b]indole-4a-carboxylate 3.14c. The general procedure was followed by using 0.0504 g of styryl azide 3.13c (0.194 mmol), 0.0074 g of Rh$_2$(esp)$_2$ (5 mol %) and 2.0 mL of toluene. Purification by MPLC (3:97 to 30:70 EtOAc:hexanes) afforded the product as white solid (0.0285 g, 63%): $^1$H NMR (500 MHz, CDCl$_3$) δ 7.81 (d, $J$ = 6.7 Hz, 1H), 7.50 (d, $J$ = 6.8 Hz, 1H), 7.40 (quintet, $J$ = 7.3 Hz, 1.5 Hz, 2H), 4.36 (d, $J$ = 8.2 Hz, 1H), 4.32 (dt, $J$ = 7.9 Hz, 6.2 Hz, 2H), 3.98 (s, 3H), 3.79 (d, $J$ = 8.2 Hz, 1H), 2.85 (ddd, $J$ = 12.4 Hz, 8.2 Hz, 6.2 Hz, 1H), 2.06 (dt, $J$ = 12.9 Hz, 6.6 Hz, 1H); $^{13}$C NMR (125 MHz, CDCl$_3$) δ 170.2 (C), 162.0 (C), 152.0 (C), 144.6 (C), 129.2 (CH), 128.5 (CH), 123.5 (CH), 121.9 (CH), 73.9 (CH$_2$), 69.1 (CH$_2$), 64.2 (C), 52.8 (CH$_3$), 34.7 (CH$_2$). ATR-FTIR (thin film): 2952, 2924, 2875, 1715, 1438, 1150 cm$^{-1}$; HRMS (EI) $m/z$ calculated for C$_{13}$H$_{14}$NO$_3$ (M+H)$^+$: 232.0974, found: 232.0978.

2-tert-Butyl-4a-methyl-4,4a-dihydro-1H-pyrido[3,4-b]indole-2,4a(3H)-dicarboxylate 3.14d. The general procedure was followed by using 0.0242 g of styryl azide 3.13d (0.068 mmol), 0.0025 g of Rh$_2$(esp)$_2$ (5 mol %) and 0.7 mL of toluene at 120 °C for 24 h. Purification by MPLC (3:97 to 30:70 EtOAc:hexanes) afforded the product—a yellow oil—as a mixture of rotamers (0.0186 g, 83%): $^1$H NMR (500 MHz, CDCl$_3$) δ 7.84 (d, $J$ = 7.3 Hz, 1H), 7.44 (q, $J$ = 6.6 Hz, 1H), 7.37 (m, 2H), 4.14 (d, $J$ = 10.6 Hz, 1H), 3.99 (s, 3H), 3.86 (t, $J$ = 10.9 Hz, 2H), 3.52 (d, $J$ = 10.7 Hz, 0.4H), 3.42 (d, $J$ = 10.5 Hz, 0.6H), 2.95 (q, $J$ = 10.9 Hz, 1H), 1.82 (m, 1H), 1.53 (s, 3.5H), 1.44 (s, 5.5H); $^{13}$C NMR (125 MHz, CDCl$_3$) δ 169.1 (C), 161.8 (C), 154.6 (C), 151.9 (C), 145.3 (C), 129.3 (CH), 128.8 (CH), 123.8 (CH), 121.7 (CH), 80.0 (C), 62.8 (C), 52.9 (CH$_3$), 51.3 (CH$_2$), 45.0 (CH$_2$), 32.2 (CH$_2$), 28.4 (CH$_3$). ATR-FTIR (thin
film): 2976, 1691, 1392, 1148, 1120 cm⁻¹; HRMS (EI) m/z calculated for C₁₉H₂₃N₂O₄ (M+H)⁺: 331.1658, found: 331.1662.

![Image](3.14e)

**Methyl-2,3-dimethyl-3H-indole-3-carboxylate 3.14e.** The general procedure was followed by using 0.0476 g of styryl azide 3.13e (0.206 mmol), 0.0078 g of Rh₂(esp)₂ (5 mol %) and 2.1 mL of toluene. Purification by MPLC (3:97 to 30:70 EtOAc:hexanes) afforded the product as yellow solid (0.0317 g, 76%): ¹H NMR (500 MHz, CDCl₃) δ 7.54 (d, J = 7.5 Hz, 1H), 7.36 (m, 2H), 7.21 (t, J = 7.4 Hz, 1H), 3.62 (s, 3H), 2.36 (s, 3H), 1.58 (s, 3H); ¹³C NMR (125 MHz, CDCl₃) δ 181.3 (C), 171.1 (C), 155.0 (C), 140.3 (C), 128.9 (CH), 125.8 (CH), 122.3 (CH), 120.2 (CH), 69.1 (CH₂), 63.7 (C), 52.9 (CH₃), 19.7 (CH₃), 16.9 (CH₃). ATR-FTIR (thin film): 2952, 1731, 1581, 1454, 1255, 1217 cm⁻¹; HRMS (EI) m/z calculated for C₁₂H₁₄NO₂ (M+H)⁺: 204.1025, found: 204.1021.

![Image](3.14f)

**Isopropyl-2,3,4,4a-tetrahydro-1H-carbazole-4a-carboxylate 3.14f.** The general procedure was followed by using 0.0433 g of styryl azide 3.13f (0.150 mmol), 0.0057 g of Rh₂(esp)₂ (5 mol %) and 1.5 mL of toluene. Purification by MPLC (3:97 to 10:90 EtOAc:hexanes) afforded the product as colorless oil (0.0258 g, 66%): ¹H NMR (500 MHz, CDCl₃) δ 7.58 (d, J = 7.7 Hz, 1H), 7.43 (d, J = 7.4 Hz, 1H), 7.35 (td, J = 7.6 Hz, 0.8 Hz, 1H), 7.18 (t, J = 7.4 Hz, 1H), 4.99 (heptet, J = 6.3 Hz, 1H), 2.30 (t, J = 16.6 Hz, 2H), 2.74 (td, J = 13.2 Hz, 6.0 Hz, 1H), 2.19 (dq, J = 9.6 Hz, 3.0 Hz, 1H), 1.81 (d, J = 18.2 Hz, 1H), 1.52 (m, 2H), 1.21 (d, J = 6.3 Hz, 3H), 1.14 (td, J = 13.3 Hz, 3.5 Hz, 1H), 1.08 (d, J = 6.3 Hz, 3H); ¹³C NMR (125 MHz, CDCl₃) δ 184.5 (C), 169.5 (C), 155.4 (C), 139.7 (C), 128.7 (CH), 125.3 (CH), 122.3 (CH), 120.3 (CH), 69.2 (CH),
65.2 (C), 37.3 (CH$_2$), 31.4 (CH$_2$), 28.5 (CH$_2$), 22.9 (CH$_2$), 21.7 (CH$_3$), 21.4 (CH$_3$). ATR-FTIR (thin film): 2979, 2936, 2860, 1721, 1455, 1248, 1213, 1103 cm$^{-1}$; HRMS (El) m/z calculated for C$_{16}$H$_{20}$NO$_2$ (M+H)$^+$: 258.1494, found: 258.1491.

**3.14g.** tert-Butyl-2,3,4,4a-tetrahydro-$1H$-carbazole-4a-carboxylate. The general procedure was followed by using 0.0527 g of styryl azide 3.13g (0.176 mmol), 0.0067 g of Rh$_2$(esp)$_2$ (5 mol %) and 1.8 mL of toluene. Purification by MPLC (3:97 to 10:90 EtOAc:hexanes) afforded the product as white solid (27.0 mg, 57%). $^1$H NMR (500 MHz, CDCl$_3$) $\delta$ 7.57 (d, $J = 7.7$ Hz, 1H), 7.43 (d, $J = 7.4$ Hz, 1H), 7.35 (td, $J = 7.6$ Hz, 0.9 Hz, 1H), 7.18 (t, $J = 7.4$ Hz, 1H), 2.97 (dt, $J = 13.3$ Hz, 2.5 Hz, 2H), 2.75 (td, $J = 13.2$ Hz, 6.0 Hz, 1H), 2.19 (dq, $J = 9.8$ Hz, 3.0 Hz, 1H), 1.80 (d, $J = 13.8$ Hz, 1H), 1.58 (qt, $J = 13.5$ Hz, 3.2 Hz, 1H), 1.47 (qt, $J = 13.1$ Hz, 4.3 Hz, 1H), 1.36 (s, 9H), 1.11 (td, $J = 13.3$ Hz, 3.5 Hz, 1H); $^{13}$C NMR (125 MHz, CDCl$_3$) $\delta$ 184.2 (C), 169.1 (C), 155.4 (C), 139.9 (C), 128.5 (CH), 125.2 (CH), 122.2 (CH), 120.3 (CH), 82.2 (C), 65.9 (C), 37.4 (CH$_2$), 31.4 (CH$_2$), 28.5 (CH$_2$), 27.8 (CH$_3$), 23.0 (CH$_2$). ATR-FTIR (thin film): 2935, 2859, 1721, 1584, 1613, 1251, 1143 cm$^{-1}$; HRMS (El) m/z calculated for C$_{17}$H$_{22}$NO$_2$ (M+H)$^+$: 272.1651, found: 272.1649.

**3.14h.** Allyl-2,3,4,4a-tetrahydro-$1H$-carbazole-4a-carboxylate. The general procedure was followed by using 0.0361 g of styryl azide 3.13h (0.127 mmol), 0.0048 g of Rh$_2$(esp)$_2$ (5 mol %) and 1.3 mL of toluene. Purification by MPLC (3:97 to 10:90 EtOAc:hexanes) afforded the product as white solid (0.0191 g, 59%): $^1$H NMR (500 MHz, CDCl$_3$) $\delta$ 7.63 (d, $J = 7.7$ Hz, 1H), 7.48 (d, $J = 7.4$ Hz, 1H), 7.41 (td, $J = 7.6$ Hz, 1.1 Hz, 1H), 7.24 (t, $J = 7.5$ Hz, 1H), 5.83 (ddt, $J = 17.1$ Hz, 10.9 Hz, 5.8
Hz, 1H), 5.22 (d, J = 1.3 Hz, 1H), 5.19 (dt, J = 3.1 Hz, 1.5 Hz, 1H), 4.64 (ddt, J = 13.3 Hz, 5.6 Hz, 1.3 Hz, 1H), 4.54 (ddt, J = 13.3 Hz, 5.6 Hz, 1.3 Hz, 1H), 3.09 (dq, J = 13.3 Hz, 2.6 Hz, 1H), 3.03 (dd, J = 13.4 Hz, 2.2 Hz, 1H), 2.78 (td, J = 13.3 Hz, 6.0 Hz, 1H), 2.24 (m, 1H), 1.86 (d, J = 14.0 Hz, 1H), 1.63 (qt, J = 13.5 Hz, 3.1 Hz, 1H), 1.53 (qt, J = 13.0 Hz, 3.8 Hz, 1H), 1.21 (m, 1H); \(^{13}\)C NMR (125 MHz, CDCl\(_3\)) \(\delta\) 183.8 (C), 169.8 (C), 155.8 (C), 139.6 (C), 131.4 (CH), 128.9 (CH), 125.4 (CH), 122.4 (CH), 120.5 (CH), 118.7 (CH\(_2\)), 66.1 (CH\(_2\)), 65.0 (C), 37.3 (CH\(_2\)), 31.5 (CH\(_2\)), 28.5 (CH\(_2\)), 23.0 (CH\(_2\)). ATR-FTIR (thin film): 2939, 2860, 1729, 1585, 1455, 1206 cm\(^{-1}\); HRMS (EI) \(m/z\) calculated for C\(_{16}\)H\(_{18}\)NO\(_2\) (M+H\(^{+}\)): 256.1338, found: 256.1338.

\((1R,2R,4R)-1,7,7\text{-trimethylbicyclo[2.2.1]heptan-2-yl-2,3,4,4a-tetrahydro-1H-carbazole-4a-carboxylate} 3.14i.\) The general procedure was followed by using 65.5 mg of 3.13i (0.172 mmol), 6.5 mg of Rh\(_2\)(esp)\(_2\) (5 mol\%) and 1.7 mL toluene. Purification by MPLC (3:97 to 10:90 EtOAc: hexane) afforded the product as yellow solid (31.2 mg, 51%). d.r. = 56:44. \(^1\)H NMR (500 MHz, CDCl\(_3\)) \(\delta\) 7.56 (t, J = 7.7 Hz, 1H), 7.38 (d, J = 7.4 Hz, 1H), 7.34 (t, J = 6.4 Hz, 1H), 7.18 (dd, J = 7.1 Hz, 2.8 Hz, 1H), 4.67 (dd, J = 7.2 Hz, 3.9 Hz, 0.564H), 4.50 (dd, J = 7.8 Hz, 3.3 Hz, 0.444H), 3.00 (m, 2H), 2.65 (dt, J = 20.1 Hz, 13.5 Hz, 6.3 Hz, 1H), 2.18 (dt, J = 9.9 Hz, 2.8 Hz, 1H), 1.81 (d, J = 13.7 Hz, 1H), 1.68 (m, 2H), 1.62 (m, 2H), 1.56 (m, 1H), 1.49 (td, J = 12.4 Hz, 3.7 Hz, 2H), 1.17 (m, 1H), 1.03 (m, 2H), 0.82 (t, J = 9.3 Hz, 3H), 0.70 (d, J = 3.4 Hz, 3H), 0.48 (s, 1.37H), 0.37 (s, 1.73H); \(^{13}\)C NMR (125 MHz, CDCl\(_3\)) \(\delta\) 183.8 (C), 169.3 (C), 155.8 (C), 140.1 (C), 128.7 (CH), 125.2 (CH), 122.2 (CH), 120.3 (CH), 82.7/81.8 (CH), 65.1 (C), 49.2/48.5 (C), 46.8 (C), 44.9 (CH), 38.6/38.3 (CH\(_2\)), 36.0/35.9 (CH\(_2\)), 33.7/33.5 (CH\(_2\)), 31.4 (CH\(_2\)), 28.3 (CH\(_2\)), 26.9 (CH\(_2\)), 22.9 (CH\(_2\)),
20.0/19.9 (CH₃), 19.5/19.2 (CH₃), 11.7/10.7 (CH₃). ATR-FTIR (thin film): 2950, 2876, 1727, 1586, 1454, 1245, 1208 cm⁻¹.

(1R,2R,5S)-2-isopropyl-5-methylcyclohexyl-2,3,4,4a-tetrahydro-1H-carbazole-4a-carboxylate 3.14j. The general procedure was followed by using 0.0338 g of styryl azide 3.13j (0.089 mmol), 0.0034 g of Rh₂(esp)₂ (5 mol %) and 0.9 mL of toluene. Purification by MPLC (3:97 to 10:90 EtOAc:hexanes) afforded the product—a white solid—as a 66:34 mixture of diastereomers (0.0115 g, 37%): ¹H NMR (500 MHz, CDCl₃) δ 7.58 (t, J = 7.3 Hz, 1H), 7.39 (q, J = 6.7 Hz, 1H), 7.35 (q, J = 7.3 Hz, 1H), 7.18 (q, J = 7.7 Hz, 1H), 4.66 (td, J = 10.9 Hz, 4.4 Hz, 0.37H), 4.58 (td, J = 11.0 Hz, 4.3 Hz, 0.74H), 3.05 (d, J = 11.2 Hz, 1H), 2.98 (d, J = 12.3 Hz, 1H), 2.65 (td, J = 13.2 Hz, 5.9 Hz, 1H), 2.19 (m, 1H), 1.94 (d, J = 10.7 Hz, 1H), 1.82 (d, J = 13.8 Hz, 1H), 1.62 (m, 2H), 1.55 (m, 1H), 1.48 (m, 2H), 1.17 (m, 2H), 1.08 (td, J = 7.0 Hz, 2.7 Hz, 1H), 0.95 (t, J = 11.6 Hz, 2H), 0.88 (d, J = 6.7 Hz, 3H), 0.82 (d, J = 6.6 Hz, 2H), 0.72 (d, J = 7.0 Hz, 1H), 0.57 (d, J = 7.0 Hz, 2H), 0.41 (d, J = 7.0 Hz, 2H); ¹³C NMR (125 MHz, CDCl₃) δ 183.9 (C), 169.5 (C), 155.6 (C), 139.9 (C), 128.7 (CH), 125.1 (CH), 122.1 (CH), 120.3 (CH), 75.6 (CH), 65.2 (C), 46.9/46.5 (CH), 40.7/39.9 (CH₂), 37.0/36.3 (CH₂), 34.1/34.0 (CH₂), 31.5/31.5 (CH₂), 31.4/31.3 (CH), 28.5/28.4 (CH₂), 26.0/25.7 (CH), 23.3 (CH₂), 23.0/22.8 (CH₂), 22.0/21.9 (CH₃), 20.9/20.3 (CH₃), 16.0/15.6 (CH₃). ATR-FTIR (thin film): 2953, 1724, 1586, 1455, 1211 cm⁻¹; HRMS (EI) m/z calculated for C₂₃H₃₂NO₂ (M+H)+: 34.2433, found: 354.2432.
Methyl-1-methyl-2,3,4,4a-tetrahydro-1H-carbazole-4a-carboxylate 3.14k. The general procedure was followed by using 0.0440 g of styryl azide 3.13k (0.162 mmol), 0.0062 g of Rh₂(esp)₂ (5 mol %) and 1.6 mL of toluene. Purification by MPLC (3:97 to 30:70 EtOAc:hexanes) afforded the product—a yellow solid—as a 75:25 mixture of diastereomers (0.0273 g, 69%): ¹H NMR (500 MHz, CDCl₃) for major product δ 7.81 (d, J = 7.5 Hz, 1H), 7.39 – 7.34 (m, 3H), 3.69 (s, 3H), 3.67 (s, 0.65H, minor), 3.96 (s, 3H), 3.08 (tt, J = 12.7 Hz, 6.3 Hz, 1H), 2.75-2.70 (m, 1H), 2.21 – 2.10 (m, 3H), 1.84 – 1.75 (m, 2H), 0.36 (d, d, J = 6.8 Hz, 3H); ¹³C NMR (125 MHz, CDCl₃) δ 173.6 (C), 152.7 (C), 145.2 (C), 130.7 (C), 127.9 (CH), 127.9 (CH), 124.4 (CH), 123.3 (CH), 69.0 (C), 52.5 (CH₃), 42.1 (CH), 34.2 (CH₂), 33.6 (CH₂), 24.2 (CH₂), 14.2 (CH₃). ATR-FTIR (thin film): 2951, 2871, 1733, 1716, 1454, 1436, 1200 cm⁻¹; HRMS (EI) m/z calculated for C₁₅H₁₈NO₂ (M+H)+: 244.1338, found: 244.1333.

Methyl-2-phenyl-2,3,4,4a-tetrahydro-1H-carbazole-4a-carboxylate 3.14l. The general procedure was followed by using 52.8 mg of 3.13l (0.158 mmol), 6.0 mg of Rh₂(esp)₂ (5 mol%) and 1.6 mL toluene. Purification by MPLC (3:97 to 10:90 EtOAc:hexane) afforded the product as white solid (33.0 mg, 68%), d.r. = 66:34. ¹H NMR (500 MHz, CDCl₃) δ major product: 7.63 (d, J = 7.7 Hz, 1H), 7.49 (d, J = 7.4 Hz, 1H), 7.41 (t, J = 7.4 Hz, 1H), 7.35 (d, J = 7.6 Hz, 1H), 7.29 (d, J = 7.1 Hz, 2H), 7.23 (m, 3H), 3.71 (s, 3H), 3.20 (dd, J = 12.9 Hz, 2.5 Hz, 1H), 3.13 (dt, J = 13.5 Hz, 3.0 Hz, 1H), 2.94 (t, J = 12.7 Hz, 1H), 2.86 (tt, J = 12.3 Hz, 3.6 Hz, 1H), 2.04 (t, J = 16.0 Hz, 1H), 1.91 (qd, J = 13.1 Hz, 2.6 Hz, 1H), 1.33 (td, J = 13.5 Hz, 3.6 Hz, 1H); selected peaks for minor product: 7.67 (d, J = 7.8 Hz, 1H), 7.31 (d, J = 7.8 Hz, 2H), 7.12 (t, J = 7.4 Hz, 1H), 3.69 (s, 3H), 3.45 (d, J = 14.5 Hz, 1H), 3.26 (dd, J = 12.9 Hz, 2.5 Hz,
1H), 2.76 (d, J = 12.5 Hz, 1H), 2.17 (m, 1H), 1.25 (td, J = 13.7 Hz, 3.3 Hz, 1H); $^{13}$C NMR (125 MHz, CDCl$_3$) δ major: 183.0 (C), 170.5 (C), 155.5 (C), 144.1 (C), 139.4 (C), 139.1 (C), 129.0 (CH), 128.8 (CH), 128.4 (CH), 126.8 (CH), 125.7 (CH), 122.6 (CH), 120.6 (CH), 64.4 (C), 53.0 (CH$_3$), 47.1 (CH), 39.1 (CH$_2$), 35.9 (CH$_2$), 30.7 (CH$_2$), only visible peaks; minor: 182.8 (C), 170.7 (C), 143.8 (C), 129.0 (CH), 127.8 (CH), 126.9 (CH), 126.1 (CH), 125.5 (CH), 40.4 (CH), 34.1 (CH$_2$), 30.1 (CH$_2$). ATR-FTIR (thin film): 3027, 2951, 1730, 1583, 1453, 1243 cm$^{-1}$.

![Methyl-2-tert-butyl-2,3,4,4a-tetrahydro-1H-carbazole-4a-carboxylate 3.14m](image)

**Methyl-2-tert-butyl-2,3,4,4a-tetrahydro-1H-carbazole-4a-carboxylate 3.14m.**

The general procedure was followed by using 0.0377 g of styryl azide 3.13m (0.120 mmol), 0.0046 g of Rh$_2$(esp)$_2$ (5 mol %) and 1.2 mL of toluene. Purification by MPLC (3:97 to 30:70 EtOAc:hexanes) afforded the product—a yellow oil—as an 82:18 mixture of diastereomers (0.0224 g, 65%): $^1$H NMR (500 MHz, CDCl$_3$) δ 7.61 (d, J = 7.6 Hz, 1H), 7.47 (d, J = 7.4 Hz, 1H), 7.41 (t, J = 7.6 Hz, 1H), 7.23 (t, J = 7.5 Hz, 1H), 3.69 (s, 3H), 3.67 (s, 0.65H, minor), 3.08 (dq, J = 13.1 Hz, 3.1 Hz, 2H), 2.96 (d, J = 7.1 Hz, 0.48H, minor), 2.51 (t, J= 12.5 Hz, 1H), 2.37 (m, 0.24H, minor), 1.90 (m, 1H), 1.41 (ddd, J = 16.9 Hz, 12.8 Hz, 3.8 Hz, 2H), 1.14 (td, J = 13.2 Hz, 3.4 Hz, 1H), 0.99 (s, 9H), 0.95 (s, 2H, minor); $^{13}$C NMR (125 MHz, CDCl$_3$) δ 185.0 (C), 170.6 (C), 155.6 (C), 139.6 (C), 128.9 (CH), 125.4 (CH), 122.5 (CH), 120.4 (CH), 64.6 (C), 52.8 (CH$_3$), 51.8 (CH), 36.0 (CH$_2$), 33.0 (C), 32.9 (CH$_2$), 27.6 (CH$_3$), 24.2 (CH$_2$). Selected minor product: δ 123.1 (CH), 122.3 (CH), 119.0 (CH), 110.2 (CH), 62.2 (C), 53.0 (CH$_3$), 52.3 (CH), 31.7 (CH$_2$), 32.9 (CH$_2$), 28.4 (CH$_3$), 23.4 (CH$_2$). ATR-FTIR (thin film): 2952, 2867, 1731, 1582, 1454, 1217 cm$^{-1}$; HRMS (EI) m/z calculated for C$_{18}$H$_{24}$NO$_2$ (M+H): 286.1807, found: 286.1817.
**t-Butyl 2-t-butyl-2,3,4,4a-tetrahydro-1H-carbazole-4a-carboxylate 3.14n.**

The general procedure was followed by using 0.1033 g of styryl azide 3.13n (0.290 mmol), 0.0110 g of Rh$_2$(esp)$_2$ (5 mol %) and 2.9 mL of toluene. Purification by MPLC (3:97 to 10:90 EtOAc: hexane) afforded the product—a white solid—as an 86:14 mixture of diastereomers (0.285 g, 30%): $^1$H NMR (500 MHz, CDCl$_3$) δ 7.56 (d, J = 7.8 Hz, 1H), 7.45 (d, J = 7.4 Hz, 1H), 7.35 (t, J = 7.5 Hz, 1H), 7.18 (td, J = 7.6 Hz, 0.5 Hz, 1H), 3.02 (d, J = 13.1 Hz, 1H), 2.97 (td, J = 13.3 Hz, 2.8 Hz, 1H), 2.54 (t, J = 12.4 Hz, 1H), 1.85 (d, J = 12.1 Hz, 1H), 1.38 (s, 10H), 1.34 (s, 1H), 1.05 (td, J = 13.1 Hz, 3.2 Hz, 1H), 0.96 (s, 8H), 0.92 (s, 1H); $^{13}$C NMR (125 MHz, CDCl$_3$) δ 185.4 (C), 169.1 (C), 155.5 (C), 139.8 (C), 128.6 (CH), 125.1 (CH), 122.3 (CH), 120.2 (CH), 82.2 (C), 65.5 (C), 51.5 (CH), 36.3 (CH$_2$), 33.0 (C), 32.6 (CH$_2$), 27.9 (CH$_3$), 27.5 (CH$_3$), 24.0 (CH$_2$). ATR-FTIR (thin film): 2963, 2868, 1725, 1582, 1367, 1256, 1151 cm$^{-1}$; HRMS (EI) m/z calculated for C$_{21}$H$_{30}$NO$_2$ (M+H)$^+$: 328.2277, found: 328.2272.

**D. Double Crossover Experiment**

To a mixture of styryl azide 3.11h, 3.13f and Rh$_2$(esp)$_2$ (5 mol %) was added toluene (0.1M). The resulting mixture was heated at 140 °C. After 16 h, the mixture was cooled to room temperature, diluted with CH$_2$Cl$_2$ and concentrated in vacuo. Dibromomethane (0.7 µL, 0.1 mmol) was added, and the mixture was analyzed using $^1$H NMR spectroscopy to determine the outcome of the reaction.
E. General Synthesis of Styryl Azides 3.18.

Styryl azides 3.23 were prepared following the synthetic sequence outlined above. The requisite vinyl alkoxy triflates 3.22 were prepared from the Rh$_2$(II)-catalyzed decomposition of $\alpha$-diazo carboxylates 3.28 in the presence of alcohol followed by trapping with triflic anhydride. Cross-coupling of the resulting vinyl triflates 3.22 with 2-azidophenylboronic acid pinacolate ester 3.7 produced styryl azides 3.23.

F. Preparation for Vinyl Alkoxytriflate.

The vinyl alkoxytriflates were prepared from the $\alpha$-diazo carboxylates following the procedure reported by Wood and Moniz.$^{23}$ The yields were not optimized.

To a stirred solution of azibenzil 3.28 (1.0 equiv) and alcohol (1.2 equiv) in CH$_2$Cl$_2$ (0.1 M) was added Rh$_2$(O$_2$CF$_3$)$_4$ (0.01 equiv) resulting in rapid N$_2$(g) loss and decolorization. The solution was cooled to $-78^\circ$C and treated with triflic anhydride (1.4 equiv) and Et$_3$N (4.0 equiv) in rapid succession. The mixture was allowed to stir for 15 min at $-78^\circ$C before being warmed to room temperature. Once warm, the reaction mixture was diluted with 5 mL of CH$_2$Cl$_2$, and washed with 3 x 10 mL of a sat. aqueous solution of NaHCO$_3$. The combined aqueous phases were back extracted with 2 x 10 mL of CH$_2$Cl$_2$. The combined organic phases were dried
over Na$_2$SO$_4$, filtered and concentrated \textit{in vacuo}. The resulting residue was purified by MPLC (3:97 to 10:90 EtOAc: hexane) affording the vinyl alkoxy triflate.

\begin{center}
\includegraphics[width=0.2\textwidth]{image.png}
\end{center}

2-Methoxy-1,2-diphenylvinyl trifluoromethanesulfonate 3.22a.$^{23}$ The general procedure was followed by using 0.4100 g of azibenzil (1.84 mmol), 0.090 mL of methanol, 0.012 g of Rh$_2$(O$_2$CCF$_3$)$_4$, 0.44 mL of triflate anhydride, 1.03 mL of Et$_3$N and 20 mL of CH$_2$Cl$_2$. Purification by MPLC (2:98 to 5:95 EtOAc: hexane) afforded the product as a colorless oil (0.5693 g, 86%). The spectral data of vinyl triflate 3.22a matched that reported by Wood and Moniz.$^{23}$$^1$H NMR (500 MHz, CDCl$_3$) $\delta$ 7.36 – 7.30 (m, 5H), 7.22 – 7.17 (m, 5H), 3.54 (s, 3H); $^{13}$C NMR (125 MHz, CDCl$_3$) $\delta$ 149.9 (C), 133.7 (C), 131.6 (C), 130.4 (C), 130.1 (CH), 129.8 (CH), 129.2 (CH), 128.7 (CH), 128.7 (CH), 128.3 (CH), 118.5 (q, $J_{CF} =$ 320.1 Hz, C), 57.5 (CH$_3$). The vinyl triflate was used in the subsequent cross-coupling reaction without additional characterization.

\begin{center}
\includegraphics[width=0.2\textwidth]{image2.png}
\end{center}

2-Methoxy-1-phenyl-2-p-tolylvinyl trifluoromethanesulfonate 3.22b. The general procedure was followed by using 0.2189 g of azibenzil (0.926 mmol), 0.045 mL of methanol, 0.006 g of Rh$_2$(O$_2$CCF$_3$)$_4$, 0.22 mL of triflate anhydride, 0.52 mL of Et$_3$N and 10 mL of CH$_2$Cl$_2$. Purification by MPLC (2:98 to 5:95 EtOAc: hexane) afforded the product as a white solid (0.220 g, 64%). $^1$H NMR (500 MHz, CDCl$_3$) $\delta$ 7.21 – 7.18 (m, 7H), 7.13 (d, $J = 8.0$ Hz, 2H), 3.54 (s, 3H), 2.35 (s, 3H); $^{13}$C NMR (125 MHz, CDCl$_3$) $\delta$ 150.0 (C), 140.0 (C), 133.4 (C), 131.8 (C), 130.0 (CH), 129.5 (CH), 129.1 (CH), 128.6 (CH), 128.2 (CH), 127.3 (C), 118.5 (q, $J_{CF} =$ 320.5 Hz, C), 57.4 (CH$_3$),
21.4 (CH₃). The vinyl triflate was used in the subsequent cross-coupling reaction without additional characterization.

![3.22c]

**2-(4-Nitrophenoxy)-1-phenyl-2-p-tolyl/vinyl trifluoromethanesulfonate 3.22c.**

The general procedure was followed by using 0.2662 g of azibenzil (1.13 mmol), 0.1880 g of 4-nitrophenol, 0.0074 g of Rh₂(O₂CCF₃)₄, 0.27 mL of triflate anhydride, 0.63 mL of Et₃N and 12 mL of CH₂Cl₂. Purification by MPLC (2:98 to 5:95 EtOAc: hexane) afforded the product as a white solid (0.250 g, 46%). ^1H NMR (500 MHz, CDCl₃) δ 8.13 (d, J = 9.1 Hz, 2H), 7.41 – 7.33 (m, 5H), 7.17 (d, J = 8.0 Hz, 2H), 7.08 (d, J = 9.1 Hz, 2H), 7.01 (d, J = 7.9 Hz, 2H), 2.26 (s, 3H); ^13C NMR (125 MHz, CDCl₃) δ 160.2 (C), 144.3 (C), 143.2 (C), 140.7 (C), 138.3 (C), 130.7 (C), 130.3 (CH), 129.6 (CH), 129.6 (CH), 129.3 (CH), 128.9 (CH), 126.9 (C), 125.8 (CH), 117.3 (CH), 118.3 (q, J_CF = 320.8 Hz, C), 21.4 (CH₃). The vinyl triflate was used in the subsequent cross-coupling reaction without additional characterization.

**G. General Procedure for Pd-catalyzed Cross-Coupling Reaction.**

To a mixture of vinyl alkoxytriflate 3.22 (1 equiv), 2-azidoarylboronic acid pinacol ester 3.7a (1.1 equiv), and Pd(PPh₃)₄ (10 mol %) in dimethoxyethane (0.1 M) was added a saturated solution of NaHCO₃ (2 mL/mmol of boronic ester). The resulting mixture was heated to 100 °C. After 1 h, the mixture was cooled to room temperature and diluted with 5 mL of cold water. The solution was extracted with 2 x 10 mL of ether followed by 10 mL of brine. The resulting organic phase was dried
over Na₂SO₄ and was concentrated *in vacuo*. Purification by MPLC (3:97 to 10:90 EtOAc: hexane) afforded the styryl azide.

![Styryl Azide](image)

(1-(2-Azidophenyl)-2-methoxyethene-1,2-diyl)dibenzene 3.23a. The general procedure was followed by using 0.203 g of vinyl alkoxytriflate 3.22a (0.566 mmol), 0.153 g of 3.7a, 0.065 g of Pd(PPh₃)₄, 1 mL of NaHCO₃ (sat. aqueous soln) and 12 mL of DME. Purification by MPLC (2:98 to 5:95 EtOAc: hexane) afforded the product—a yellow oil—as a 17:83 mixture of *E,Z*-isomers (0.164 g, 85%). ¹H NMR (500 MHz, CDCl₃) δ 7.40 – 7.36 (m, 3H), 7.31 – 7.26 (m, 5H), 7.21 (td, *J* = 7.4 Hz, 1.1 Hz, 1H), 7.12 – 7.10 (m, 3H), 7.03 – 7.02 (m, 2H), 3.60 (s, 0.5H), 3.48 (s, 2.5H); ¹³C NMR (125 MHz, CDCl₃) major isomer δ 153.9 (C), 140.3 (C), 138.3 (C), 134.3 (C), 133.6 (C), 132.0 (CH), 130.6 (CH), 128.4 (CH), 128.2 (CH), 127.8 (CH), 126.0 (CH), 125.0 (CH), 120.7 (C), 119.0 (CH), 57.5 (CH₃) only visible signals. ATR-FTIR (thin film): 3053, 2934, 2833, 2118, 2085, 1483, 1285 cm⁻¹; HRMS (EI) *m/z* calculated for C₂₁H₁₇NO (M+H-N₂)⁺: 300.1388, found: 300.1386.

![Styryl Azide](image)

1-Azido-2-(2-methoxy-1-phenyl-2-*p*-tolylvinyl)benzene 3.23b. The general procedure was followed by using 0.217 g of vinyl alkoxytriflate 3.22b (0.580 mmol), 0.1570 g of 3.7a, 0.072 g of Pd(PPh₃)₄, 1 mL of NaHCO₃ (sat. aqueous soln) and 12 mL of DME. Purification by MPLC (2:98 to 5:95 EtOAc: hexane) afforded the product—a white solid—as a 17:83 mixture of *E,Z*-isomers (0.160 g, 80%). ¹H NMR (500 MHz, CDCl₃) δ 7.35 – 7.32 (m, 1H), 7.24 – 7.20 (m, 4H), 7.19 – 7.15 (m, 1H), 7.15 – 7.07 (m, 5H), 6.98 (dd, *J* = 7.8 Hz, 1.7 Hz, 2H), 3.56 (s, 0.6H), 3.43 (s, 2.4H),
2.35 (s, 2.5H), 2.08 (s, 0.5H); $^{13}$C NMR (125 MHz, CDCl$_3$) major isomer δ 154.0 (C), 140.4 (C), 138.2 (C), 138.2 (C), 133.7 (C), 131.9 (CH), 131.2 (C), 130.5 (CH), 130.4 (CH), 128.9 (CH), 128.1 (CH), 127.7 (CH), 125.9 (CH), 124.9 (CH), 120.2 (C), 119.0 (CH), 57.4 (CH$_3$), 21.4 (CH$_3$). ATR-FTIR (thin film): 2933, 2833, 2119, 2086, 1264 cm$^{-1}$; HRMS (EI) $m/z$ calculated for C$_{22}$H$_{20}$NO (M+H-N$_2$)$^+$: 314.1545, found: 314.1539.

1-Azido-2-(2-(4-nitrophenoxy)-1-phenyl-2-p-tolylvinyl)benzene 3.23c.

The general procedure was followed by using 0.238 g of vinyl alkoxycarbonyl 3.22c (0.500 mmol), 0.134 g of 3.7a, 0.062 g of Pd(PPh$_3$)$_4$, 1 mL of NaHCO$_3$ (sat. aqueous soln) and 12 mL of DME. Purification by MPLC (2:98 to 5:95 EtOAc: hexane) afforded the product—a white solid—as a 23:77 mixture of E,Z-isomers (0.134 g, 60%). $^1$H NMR (500 MHz, CDCl$_3$) δ 8.04 (d, $J = 9.2$ Hz, 2H), 7.52-7.31 (m, 1H), 7.26 (td, $J = 7.7$ Hz, 1.2 Hz, 1H), 7.20-7.14 (m, 7H), 7.10 (q, $J = 8.5$ Hz, 2H), 7.06-7.02 (m, 1H), 7.00-6.95 (m, 3H), 2.36 (s, 2.4H), 2.05 (s, 0.7H); $^{13}$C NMR (125 MHz, CDCl$_3$) major isomer δ 162.2 (C), 147.9 (C), 142.1 (C), 139.0 (C), 138.1 (C), 134.8 (C), 132.9 (C), 131.7 (C), 130.9 (CH), 130.6 (C), 130.3 (CH), 129.8 (CH), 129.1 (CH), 128.9 (CH), 128.2 (CH), 127.2 (CH), 125.4 (CH), 124.8 (CH), 118.8 (CH), 117.2 (CH), 21.3 (CH$_3$). ATR-FTIR (thin film): 3054, 2122, 2093, 1588, 1237 cm$^{-1}$; HRMS (EI) $m/z$ calculated for C$_{22}$H$_{20}$N$_4$O$_3$Na (M+Na)$^+$: 471.1433, found: 471.1433.

**H. Rh$_2$(II)-Catalyzed Synthesis of Oxindoles from Styryl Azides.**

![H. Rh$_2$(II)-Catalyzed Synthesis of Oxindoles from Styryl Azides.](image-url)
To a mixture of styryl azide 3.23 and Rh$_2$(esp)$_2$ (5 mol %) was added toluene (0.1M). The resulting mixture was heated to 140 °C. After 16 h, the mixture was cooled to room temperature, diluted with CH$_2$Cl$_2$ and concentrated in vacuo. Purification by MPLC (3:97 to 10:90 EtOAc: hexane) afforded corresponding indole product 3.24.

To a solution of indole in 5 mL of DCM was added 2 mL of trfluoroacetic acid. The resulting mixture was then heated to 90 °C overnight. The mixture was cooled and concentrated in vacuo. Purification by MPLC (5:95 to 50:50 EtOAc: hexane) afforded the product 3.25.

2-Methoxy-3,3-diphenyl-3H-indole 3.24a. The general procedure was followed by using 0.0420 g of styryl azide 3.23a (0.128 mmol), 0.0049 g of Rh$_2$(esp)$_2$, and 1.3 mL of toluene. Purification by MPLC (2:98 to 5:95 EtOAc: hexane) afforded the product as a white solid (0.0264 g, 69%). $^1$H NMR (500 MHz, CDCl$_3$) δ 7.45 (d, $J = 7.7$ Hz, 1H), 7.31 – 7.27 (m, 7H), 7.20 (dd, $J = 7.5$ Hz, 2.2 Hz, 5H), 7.10 (td, $J = 7.5$ Hz, 0.9 Hz, 1H), 4.10 (s, 3H); $^{13}$C NMR (125 MHz, CDCl$_3$) δ 181.7 (C), 152.3 (C), 141.1 (C), 141.0 (C), 128.5 (CH), 128.3 (CH), 128.2 (CH), 127.4 (CH), 124.5 (CH), 124.0 (CH), 119.0 (CH), 66.6 (C), 57.0 (CH$_3$). ATR-FTIR (thin film): 3056, 2947, 1577, 1428, 1269 cm$^{-1}$; HRMS (El) $m/z$ calculated for C$_{21}$H$_{18}$NO (M+H)$^+$: 300.1388, found: 300.1374.

2-Methoxy-3-phenyl-3-p-tolyl-3H-indole 3.24b. The general procedure was followed by using 0.0372 g of styryl azide 3.23b (0.109 mmol), 0.0041 g of Rh$_2$(esp)$_2$, and 1.1 mL of toluene. Purification by MPLC (2:98 to 5:95 EtOAc: hexane) afforded the product as a white solid (0.0246 g, 69%). $^1$H NMR (500 MHz, CDCl$_3$) δ 7.45 (d, $J = 7.7$ Hz, 1H), 7.31 – 7.27 (m, 7H), 7.20 (dd, $J = 7.5$ Hz, 2.2 Hz, 5H), 7.10 (td, $J = 7.5$ Hz, 0.9 Hz, 1H), 4.10 (s, 3H); $^{13}$C NMR (125 MHz, CDCl$_3$) δ 181.7 (C), 152.3 (C), 141.1 (C), 141.0 (C), 128.5 (CH), 128.3 (CH), 128.2 (CH), 127.4 (CH), 124.5 (CH), 124.0 (CH), 119.0 (CH), 66.6 (C), 57.0 (CH$_3$). ATR-FTIR (thin film): 3056, 2947, 1577, 1428, 1269 cm$^{-1}$; HRMS (El) $m/z$ calculated for C$_{21}$H$_{18}$NO (M+H)$^+$: 300.1388, found: 300.1374.
hexane) afforded the product as a white solid (0.0225 g, 66%). $^1$H NMR (500 MHz, CDCl$_3$) $\delta$ 7.43 (d, $J = 7.7$ Hz, 1H), 7.29 – 7.26 (m, 4H), 7.20 – 7.17 (m, 3H), 7.10 – 7.06 (m, 5H), 4.09 (s, 3H), 2.32 (s, 3H); $^{13}$C NMR (125 MHz, CDCl$_3$) $\delta$ 181.9 (C), 152.2 (C), 141.3 (C), 141.1 (C), 137.9 (C), 137.1 (C), 129.2 (CH), 128.4 (CH), 128.2 (CH), 128.1 (CH), 127.3 (CH), 124.4 (CH), 124.0 (CH), 119.0 (CH), 66.2 (C), 56.9 (CH$_3$), 21.1 (CH$_3$). ATR-FTIR (thin film): 3055, 2943, 1580, 1458, 1268 cm$^{-1}$; HRMS (EI) $m/z$ calculated for C$_{22}$H$_{20}$NO (M+H)$^+$: 314.1545, found: 314.1530.

![Image](image_url)

**3.24a**

**2-(4-Nitrophenoxy)-3-phenyl-3-$p$-tolyl-3$H$-indole 3.24c.** The general procedure was followed by using 0.0371 g of styryl azide 3.23c (0.083 mmol), 0.0031 g of Rh$_2$(esp)$_2$, and 0.9 mL of toluene. Purification by MPLC (2:98 to 5:95 EtOAc:hexane) afforded the product as a white solid (0.0289 g, 83%). $^1$H NMR (500 MHz, CDCl$_3$) $\delta$ 7.96 (d, $J = 8.2$ Hz, 2H), 7.96 (d, $J = 9.3$ Hz, 2H), 7.73 (d, $J = 7.7$ Hz, 1H), 7.50 (d, $J = 7.5$ Hz, 2H), 7.41 (dt, $J = 7.8$ Hz, 4.3 Hz, 1H), 7.32 (t, $J = 7.4$ Hz, 2H), 7.28 – 7.26 (m, 1H), 7.13-7.11 (m, 4H), 6.77 (d, $J = 9.3$ Hz, 2H), 2.30 (s, 3H); $^{13}$C NMR (125 MHz, CDCl$_3$) $\delta$ 177.6 (C), 160.8 (C), 152.9 (C), 142.6 (C), 142.6 (C), 139.4 (C), 138.5 (C), 130.6 (CH), 129.5 (CH), 129.1 (CH), 128.8 (CH), 128.3 (CH), 128.0 (C), 127.3 (CH), 125.6 (CH), 124.0 (CH), 123.3 (CH), 122.1 (CH), 117.7 (CH), 60.4 (C), 21.7 (CH$_3$). ATR-FTIR (thin film): 3058, 2922, 1590, 1516, 1491, 1341, 1243 cm$^{-1}$; HRMS (EI) $m/z$ calculated for C$_{27}$H$_{21}$N$_2$O$_3$ (M+H)$^+$: 421.1552, found: 421.1550.
3,3-Diphenylindolin-2-one 3.25a. The general procedure was followed by using 0.0126 g of 3.24a, 1mL of trifluoroacetic acid and 2 mL of DCM. Purification by MPLC (10:90 to 50:50 EtOAc: hexane) afforded the product as a white solid (0.0120 g, 97%). The spectral data of 3.25a matched that reported by Lygin and de Meijere: \[^1\text{H NMR (500 MHz, CDCl}_3\text{)} \delta 9.17 (s, 1H), 7.33 – 7.24 (m, 11H), 7.11 (t, J = 7.6 Hz, 1H), 7.02 (d, J = 7.8 Hz, 1H), 6.94 (s, 1H); \[^1\text{C NMR (125 MHz, CDCl}_3\text{)} \delta 181.6 (C), 141.0 (C), 139.6 (C), 133.6 (C), 128.6 (CH), 128.5 (CH), 128.4 (CH), 127.6 (CH), 126.4 (CH), 123.5 (CH), 110.8 (CH), 63.5 (C).\]

3-Phenyl-3-(para-tolyl)-indolin-2-one 3.25b. The general procedure was followed by using 0.0134 g of 3.24b (or 3.24c), 1mL of trifluoroacetic acid and 2 mL of DCM. Purification by MPLC (10:90 to 50:50 EtOAc: hexane) afforded the product as a white solid (0.0125 g, 98%). Oxindole 3.25b was previously reported by Petyunin: \[^1\text{H NMR (500 MHz, CDCl}_3\text{)} \delta 8.63 (s, 1H), 7.30 – 7.27 (m, 5H), 7.21 (d, J = 8.8 Hz, 2H), 7.17 (d, J = 8.3 Hz, 2H), 7.11 (d, J = 8.2 Hz, 2H), 7.05 (t J = 7.9 Hz, 1H), 6.96 (d, J = 7.7 Hz, 1H), 2.32 (s, 3H); \[^1\text{C NMR (125 MHz, CDCl}_3\text{)} \delta 180.0 (C), 141.8 (C), 140.2 (C), 138.7 (C), 137.1 (C), 133.8 (C), 129.2 (CH), 128.5 (CH), 128.4 (CH), 128.3 (CH), 128.2 (CH), 127.3 (CH), 126.3 (CH), 122.8 (CH), 110.3 (CH), 62.7 (C), 21.1 (CH\text{\textsubscript{3}}).\]

ATR-FTIR (thin film): 3242, 2917, 1716, 1678, 1469 cm\(^{-1}\); HRMS (EI) \(m/z\) calculated for C\textsubscript{20}H\textsubscript{16}NO (M+H)\(^+\): 286.1232, found: 286.1234.
References


6. For some recent 3H-indole methods, see: (a) Kimura, M.; Futamata, M.; Mukai, R.; Tamaru, Y. J. Am. Chem. Soc. 2005, 127, 4592. (b) Trost, B. M.; Quancard,


CHAPTER 4

\[ \text{Rh}_2(\text{II})\text{-Catalyzed Ester Migration to Afford 1,2,3-Trisubstituted Indoles from Congested Styryl Azides} \]
In Chapter 2 and 3, I have introduced transition-metal catalyzed tandem electrocyclization aminomethylene or ester migration reaction to form polysubstituted indoles.\(^1\) The 4π-electron-5-atom electrocyclization of metal nitrene constructs new C–N bond and leads to [1,2]-shift of the migrating group to C3 position on the indole.\(^2\) Along with the research conducted by my colleague, we found out that the migration selectivity of β–substituent of styryl azides could be controlled by migrating group identity (Scheme 4.1).\(^3\) We observed that β-acetyl group migrated to N1 to yield 1,2,3-trisubstituted indole 4.2, while β-carboxylate group shifted to C3 instead to afford 3H-indole 4.4. The selectivity of 1,2-shift of carboxylate appeared to be under electronic control with the major product resulting from lower energy transition state TS-4.5. At the conclusion of this, we were wondering if the migration preference could be overcome to turnover the regioselectivity of the carboxylate migration by changing steric environment of the migrating group.

\textbf{Scheme 4.1.} Regioselectivity dependence of β-migrating group identity.

\textbf{Scheme 4.2.} Transition state of iminium ion.
To investigate the steric influence on the migration reaction, a more congested [2,2,1]-bicyclic trisubstituted styryl azide 4.9 was examined.4 Styryl azide 4.9 was readily synthesized by Suzuki cross-coupling of 2-azidophenylboronic acid pinacol ester 4.8a and β-ketoester of norcamphor derived vinyl triflate 4.7a.5 Exposure of 4.9 to the optimal conditions reported in Chapter 3 produced a 29:71 mixture of 3H-indole 4.10 and indole 4.11 (Scheme 4.3). We attributed the formation of indole 4.11 to that increasing the steric impact changes the reaction preference from 3H-indole to indole formation. To determine if the selectivity of the reaction could be improved, we decided to examine a styryl azide that contained a gem-dimethyl group on the bridge carbon. This substrate was readily synthesized by cross-coupling a camphor-derived vinyl triflate 4.7b and boronate 4.8a. In line with our hypothesis, submission of styryl azide 4.12a to Rh$_2$(esp)$_2$ at 120 °C produced only indole 4.14a in 84%.

Scheme 4.3. Effect of increasing the steric environment.

To further study the influence of steric environment and electronics on selectivity, a series of [2,2,1]-bicyclic trisubstituted styryl azides were surveyed. First, changing the electronic nature of the styryl azides was examined (Table 4.1). Irrespective of the electronic nature of the substituents, styryl azides 4.12 bearing a
range of electron-releasing- or electron-withdrawing group were efficiently transformed to only indoles 4.14 in high yield and perfect chemoselectivity. We chose to investigate R² substituted styryl azides because the substitution patterns present in the indoles cannot be accessed as single isomers through Fisher-indole type reactions. Next, changing the identity of the migrating ester group was examined: tert-butyl carboxylate migrated to nitrogen to afford Boc protected indole 4.14i smoothly. Unfortunately, other analogous β-allyl ester or β-benzoyl susbstituted aryl azides 4.12 were not tested due to the failure of either triflate synthesis or coupling reaction. In line with our previous work, substitution of the β-carboxylate group to H afforded only the “formal” C–H functionalization indole product, 4.14j in 96% yield.

**Table 4.1. Effect of changing the electronic nature of styryl azides.**

<table>
<thead>
<tr>
<th>R²</th>
<th>R¹</th>
<th>R³</th>
<th>Yield (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>MeO₂C</td>
<td>MeO₂C</td>
<td>MeO₂C</td>
<td>84%</td>
</tr>
<tr>
<td>4.14a</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>MeO₂C</td>
<td>MeO₂C</td>
<td>MeO₂C</td>
<td>88%</td>
</tr>
<tr>
<td>4.14b</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>MeO₂C</td>
<td>MeO₂C</td>
<td>MeO₂C</td>
<td>93%</td>
</tr>
<tr>
<td>4.14c</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>MeO₂C</td>
<td>MeO₂C</td>
<td>MeO₂C</td>
<td>90%</td>
</tr>
<tr>
<td>4.14d</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>MeO₂C</td>
<td>MeO₂C</td>
<td>MeO₂C</td>
<td>97%</td>
</tr>
<tr>
<td>4.14e</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>MeO₂C</td>
<td>MeO₂C</td>
<td>MeO₂C</td>
<td>89%</td>
</tr>
<tr>
<td>4.14f</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>MeO₂C</td>
<td>MeO₂C</td>
<td>MeO₂C</td>
<td>96%</td>
</tr>
<tr>
<td>4.14g</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>MeO₂C</td>
<td>MeO₂C</td>
<td>MeO₂C</td>
<td>85%</td>
</tr>
<tr>
<td>4.14h</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>MeO₂C</td>
<td>MeO₂C</td>
<td>MeO₂C</td>
<td>96%</td>
</tr>
<tr>
<td>4.14j</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>t-BuO₂C</td>
<td>H</td>
<td></td>
<td>77%</td>
</tr>
<tr>
<td>4.14i</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>t-BuO₂C</td>
<td>t-BuO₂C</td>
<td></td>
<td>96%</td>
</tr>
<tr>
<td>4.14j</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Then we investigated the effect of changing the identity of the bicyclic ortho-substituent on the reaction outcome (Scheme 4.4). The carbon bridge of the norcamphor-derived azide 4.9 was replaced in 4.15 with N-Ts group. Submission of 4.15 to reaction condition, however, produced indole 4.16 with ester migrated to nitrogen along with N-Ts bridge opening and β-H elimination as the only product in 34%. 3H-indole 4.17—resulting from ester migration to C3—was not observed. The steric environment controlled chemoselectivity of this reaction may imply that the migration process occurs before β-H elimination. The chirality of N-Ts in the rigid structure may be fixed with Ts group in the way of migration, showing comparable steric impact with C(Me)₂. β-H elimination is favored accounted for the weaker C–N bond and a more rigid bridgehead.

Further insight into the steric impact was investigated: the gem-dimethyl carbon bridge was moved from the allylic position to the homoallylic position to reduce the steric pressure (Table 4.2). As expected, pinene-derived azide 4.18 was tested and afforded a mixture of the 3H-indole 4.19 and 1,2,3-trisubstituted indole 4.20. Changing the electronic nature of the styryl azide 4.18 only had a small, but measurable effect on the ratio of 3H-indole 4.19 and indole 4.20. In all cases, ester migration to nitrogen resulted in major products 4.19. The ratio of 3H-indole 4.19 to indole 4.20 slightly reduced when R-substituents become more electron-releasing.

A similar catalytic cycle is proposed and depicted below (Scheme 4.5). We believe that the reaction behavior can be well explained. Rhodium N-aryl nitrene 4.21 is produced after coordination of azide 4.12a with metal complex and following
N₂ extrusion.⁷ A 4π-electron-5-atom electrocyclization of rhodium nitrene produced benzylic cation species 4.22,⁸ which triggers [1,2] ester migration to either nitrogen or C3 position. Since C3 migration could develop higher steric interactions between the carbon bridge with gem-dimethyl group and the aryl portion, migration to C3 position is disfavored. In contrast, these destabilizing steric interactions do not develop if the methyl ester migrates to the nitrogen. Instead the steric pressure from the bridgehead is diminished because the N-heterocycle flattens as migration to N1 occurs. Release of the rhodium catalyst produces 1,2,3-trisubstituted indole 4.14a.

Table 4.2. Effect of changing electronic nature for pinene-derived azide.

<table>
<thead>
<tr>
<th>Ratio</th>
<th>Yield</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td>MeO</td>
<td>MeO</td>
</tr>
<tr>
<td>4.19a</td>
<td>4.20a</td>
</tr>
<tr>
<td>12:88</td>
<td>94%</td>
</tr>
<tr>
<td>MeO</td>
<td>MeO</td>
</tr>
<tr>
<td>4.19b</td>
<td>4.20b</td>
</tr>
<tr>
<td>19:81</td>
<td>87%</td>
</tr>
<tr>
<td>MeO</td>
<td>MeO</td>
</tr>
<tr>
<td>4.19c</td>
<td>4.20c</td>
</tr>
<tr>
<td>18:82</td>
<td>93%</td>
</tr>
<tr>
<td>F₃CO</td>
<td>F₃CO</td>
</tr>
<tr>
<td>4.19d</td>
<td>4.20d</td>
</tr>
<tr>
<td>22:78</td>
<td>86%</td>
</tr>
</tbody>
</table>
More control experiments were performed to investigate our reaction outcome and proposed mechanism (Scheme 4.6). First, a double crossover reaction was conducted to test the migration behavior. Submission of 1:1 mixture of camphor derived styryl azides 4.12e and 4.12i to the optimal conditions afforded only indoles 4.14e and 4.14i. This result suggests either a concerted migration process or a stepwise pathway in which migration occurs faster than diffusion of the carboxylate in the solvent. Second, the 3H-indole product 4.19c was resubmitted to reaction condition to test the reversibility of the carboxylate migration. If the migration process is reversible, we anticipated 3H-indole 4.19c could transform to indole 4.20c upon exposure to reaction condition. In contrast to our expectations, 3H-indole 4.19c proved to be inert and remained upon submission to rhodium catalyst. The experiment result indicates that the carboxylate migration is irreversible and products are not convertible; product ratio reflects migration preference and effect of steric impact.
In conclusion, a Rh$_2$(II) catalyzed tandem electrocyclization ester migration reaction to form 1,2,3-trisubstituted indoles is described in this chapter. Migration selectivity can be influenced by the electronic nature of the migration species and steric impact as well. Increasing the steric environment around the ortho-alkenyl substituent by adding extra carbon bridge can overwhelm the inherent electronic preference of the system. Mechanistic study suggests the migration process is either concerted or occurring faster than diffusion of the carboxylate. Indole products are not convertible between each other.
Experimental

This part was taken from supporting information of my published paper: Kong, C.; Su, N.; Zhou, F.; Jana, N.; Driver, T. G. *Tetrahedron Lett.* **2015**, *56*, 3262.

**A. General.**

¹H NMR and ¹³C NMR spectra were recorded at ambient temperature using 500 MHz or 300 MHz spectrometers. The data are reported as follows: chemical shift in ppm from internal tetramethylsilane on the δ scale, multiplicity (br = broad, s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet), coupling constants (Hz) and integration. High resolution mass spectra were obtained by peak matching. Melting points are reported uncorrected. Infrared spectroscopy was obtained using a diamond attenuated total reflectance (ATR) accessory. Analytical thin layer chromatography was performed on 0.25 mm extra hard silica gel plates with UV254 fluorescent indicator. Liquid chromatography was performed using forced flow (flash chromatography) of the indicated solvent system on 60Å (40 – 60 µm) mesh silica gel (SiO₂). Medium pressure liquid chromatography (MPLC) was performed to force flow the indicated solvent system down columns that had been packed with 60Å (40 – 60 µm) mesh silica gel (SiO₂). All reactions were carried out under an atmosphere of nitrogen in glassware, which had been oven-dried. Unless otherwise noted, all reagents were commercially obtained and, where appropriate, purified prior to use. Acetonitrile, Methanol, Toluene, THF, Et₂O, and CH₂Cl₂ were dried by filtration through alumina according to the procedure of Grubbs.⁹ Metal salts were stored in a nitrogen atmosphere dry box.

**B. Preparation of trisubstituted styryl azides.**

![Chemical reaction diagram]

To a mixture of vinyl triflate 4.7 (1 equiv), 2-azidoarylboronic acid pinacol ester 4.8 (1.1 equiv), and Pd(PPh₃)₄ (10 mol %) in dimethoxyethane (0.1 M) was added a
saturated solution of NaHCO$_3$ (2 mL/mmol of boronic ester). The resulting mixture was heated to 100 °C. After 1 h, the mixture was cooled to room temperature and diluted with 5 mL of cold water. The solution was extracted with 2 × 10 mL of ethyl acetate followed by 10 mL of brine. The resulting organic phase was dried over Na$_2$SO$_4$ and was concentrated in vacuo. Purification by MPLC (2:98 to 5:95 EtOAc: hexane) afforded the product.

(1S, 4R)-methyl 3-(2-azidophenyl)bicyclo[2.2.1]hept-2-ene-2-carboxylate 4.9.

The general procedure was followed by using 0.180 g of 2-azidophenyl boronate 4.8a (0.73 mmol), 0.203 g of vinyl triflate 4.7a derived from norcamphor (0.67 mmol), 0.083 g of Pd(PPh$_3$)$_4$ (0.067 mmol), 1.3 mL of saturated aq. soln. of NaHCO$_3$ and 10 mL of dimethoxyethane. Purification by MPLC (2:98 to 5:95 EtOAc: hexane) afforded the product as yellow oil (0.140 g, 77%): $\alpha$$_D$$^{25}$: − 3.2 (c 0.250, CH$_2$Cl$_2$); $^1$H NMR (500 MHz, CDCl$_3$) $\delta$ 7.40 – 7.36 (m, 1H), 7.22 (d, $J$ = 8.1 Hz, 1H), 7.15 (s, 1H), 7.14 (s, 1H), 3.64 (s, 3H), 3.42 (s, 1H), 3.21 (s, 1H), 1.88 (ddt, $J$ = 19.8 Hz, 10.0 Hz, 3.3 Hz, 2H), 1.82-1.79 (m, 1H), 1.46 – 1.41 (m, 1H), 1.39 – 1.34 (m, 1H), 1.31 (d, $J$ = 8.6 Hz, 1H); $^{13}$C NMR (125 MHz, CDCl$_3$) $\delta$ 165.6 (C), 155.3 (C), 137.8 (C), 135.8 (C), 130.0 (CH), 129.3 (CH), 128.3 (C), 124.4 (CH), 118.4 (CH), 51.1 (CH), 50.6 (CH$_3$), 47.3 (CH$_2$), 44.4 (CH), 25.8 (CH$_2$), 24.9 (CH$_2$). ATR-FTIR (thin film): 2949, 2871, 2124, 2092, 1714, 1701 cm$^{-1}$; HRMS (El) $m/z$ calculated for C$_{15}$H$_{15}$N$_3$O$_2$ (M)$^+$: 269.1164, found: 269.1165.
(1S, 4R)-methyl 3-(2-azidophenyl)-4,7,7-trimethylbicyclo[2.2.1]hept-2-ene-2-carboxylate 4.12a. The general procedure was followed by using 0.143 g of 2-azidophenyl boronate 4.8a (0.58 mmol), 0.188 g of vinyl triflate derived from camphor 4.7b (0.53 mmol), 0.066 g of Pd(PPh₃)₄ (0.05 mmol), 1.1 mL of saturated aq. soln. of NaHCO₃ and 10 mL of dimethoxyethane. Purification by MPLC (2:98 to 5:95 EtOAc: hexane) afforded the product as yellow oil, as a mixture of rotamer (0.1348 g, 79%) s: [α]D²⁵: +53.6 (c 0.250, CH₂Cl₂); ¹H NMR (500 MHz, CDCl₃) δ 7.34 (t, J = 7.7 Hz, 1H), 7.20 – 6.88 (m, 3H), 3.56 (s, 3H), 2.86 (s, 1H), 2.02 (ddt, J = 11.9 Hz, 8.1 Hz, 3.9 Hz, 1H), 1.73 (m, 1H), 1.36 – 1.27 (m, 2H), 1.10 – 0.97 (m, 3H), 0.87 (s, 6H); ¹³C NMR (125 MHz, CDCl₃) δ 165.4 (C), 157.9 (C), 135.5 (C), 129.9 (C), 128.7 (CH), 128.0 (C), 124.2 (CH), 118.1 (CH), 116.4 (CH), 59.4 (C), 56.6 (C)), 53.0 (CH), 51.0 (CH₃), 32.3 (CH₂), 25.2 (CH₂), 19.6 (CH₃), 12.2 (CH₃), 11.7 (CH₃). ATR-FTIR (thin film): 2952, 2874, 2120, 2087, 1703 cm⁻¹; HRMS (EI) m/z calculated for C₁₈H₂₁N₃O₂ (M)⁺: 311.1634, found: 311.1639.

(1S, 4R)-methyl 3-(2-azido-5-methylphenyl)-4,7,7-trimethylbicyclo[2.2.1]hept-2-ene-2-carboxylate 4.12b. The general procedure was followed by using 0.142 g of 2-azido-5-methylphenyl boronate 4.8b (0.55 mmol), 0.171 g of vinyl triflate 4.7a (0.50 mmol), 0.057 g of Pd(PPh₃)₄ (0.05 mmol), 1.0 mL of saturated aq. soln. of NaHCO₃ and 5 mL of dimethoxyethane. Purification by MPLC (2:98 to 5:95 EtOAc: hexane) afforded the product as yellow oil, as a mixture of rotamers (0.117 g, 72%): [α]D²⁵: +45.6 (c 0.250, CH₂Cl₂); ¹H NMR (500 MHz, CDCl₃) δ 7.13 – 7.12 (b, 1H),
7.08 – 7.06 (b, 1H), 6.86 (s, 0.5H), 6.67 (s, 0.5H), 3.56 (s, 3H), 2.85 (s, 3H), 2.32 (d, J = 14.5 Hz, 1H), 2.04 – 1.99 (m, 1H), 1.69 – 1.64 (b, 1H), 1.35 – 1.21 (m, 2H), 1.09 (s, 1.5H), 0.96 (s, 1.5H), 0.863 (s, 6H); 165.5 (C), 135.3 (C), 133.0 (C), 130.2 (C), 129.3 (CH), 128.3 (C), 118.1 (CH), 117.9 (CH), 59.6 (C), 56.6 (C), 52.9 (CH), 51.0 (CH₃), 32.3 (CH₂), 25.0 (CH₂), 20.9 (CH₃), 19.4 (CH₃), 11.7 (CH₃), only peaks visible. ATR-FTIR (thin film): 2952, 2115, 1702, 1491, 1294, 1237 cm⁻¹; HRMS (El) m/z calculated for C₁₉H₂₃N₃O₂Na [M + Na]⁺: 348.1688, found 348.1689.

(1S, 4R)-methyl 3-(2-azido-5-fluorophenyl)-4,7,7-trimethylbicyclo[2.2.1]hept-2-ene-2-carboxylate 4.12c. The general procedure was followed by using 0.181 g of 2-azido-5-fluorophenyl boronate 4.8c (0.55 mmol), 0.171 g of vinyl triflate 4.7b (0.50 mmol), 0.057 g of Pd(PPh₃)₄ (0.05 mmol), 1.0 mL of saturated aq. soln. of NaHCO₃ and 5 mL of dimethoxyethane. Purification by MPLC (2:98 to 5:95 EtOAc: hexane) afforded the product as yellow solid, as a mixture of rotamers (0.230 g, 70%): [α]D²⁵: +48.8 (c 0.250, CH₂Cl₂); ¹H NMR (500 MHz, CDCl₃) δ 7.12 (b, 1H), 7.03 (dt, J = 9.0 Hz, 2.0 Hz, 1H), 6.78 (s, 0.5H), 6.61 (s, 0.5H), 3.58 (s, 3H), 2.86 (s, 1H), 2.04 – 2.00 (m, 1H), 1.70 (s, 1H), 1.32 – 1.19 (m, 2H), 1.07 (s, 1.5H), 0.94 (s, 1.5H), 0.86 (s, 6H); ¹³C NMR (125 MHz, CDCl₃) δ 165.2 (C), 160.3 (C), 158.3 (C), 136.1 (C), 130.5 (C), 119.4 (CH), 115.4 (CH), 115.3 (CH), 115.0 (C), 59.6 (C), 56.8 (C), 52.9 (CH), 51.2 (CH₃), 32.3 (CH₂), 25.0 (CH₂), 19.4 (CH₃), 12.1 (CH₃), 11.6 (CH₃); ¹⁹F NMR (282 MHz, CDCl₃) δ -118.7. ATR-FTIR (thin film): 2953, 2117, 1707, 1485, 1296 cm⁻¹; HRMS (El) m/z calculated for C₁₉H₂₀N₃O₂F [M]⁺: 329.1540, found: 329.1546.
(1S, 4R)-methyl 3-(2-azido-5-chlorophenyl)-4,7,7-trimethylbicyclo[2.2.1]hept-2-ene-2-carboxylate 4.12d. The general procedure was followed by using 0.153 g of 2-azido-5-chlorophenyl boronate 4.8d (0.55 mmol), 0.171 g of vinyl triflate 4.7b (0.50 mmol), 0.057 g of Pd(PPh₃)₄ (0.05 mmol), 1.0 mL of saturated aq. soln. of NaHCO₃ and 5 mL of dimethoxyethane. Purification by MPLC (2:98 to 5:95 EtOAc: hexane) afforded the product as yellow solid, as a mixture of rotamers (0.131 g, 76%): [α]D²⁵: +34.4 (c 0.250, CH₂Cl₂); ¹H NMR (500 MHz, CDCl₃) δ 7.29 (dd, J = 8.5 Hz, 2.0 Hz, 1H), 7.10 (b, 1H), 6.94 (s, 0.5H), 6.85 (s, 0.5H), 3.57 (s, 3H), 2.85 (s, 1H), 2.04 – 1.99 (m, 1H), 1.67 (b, 1H), 1.32 (b, 2H), 1.07 (s, 1.5H), 0.94 (s, 1.5H), 0.86 (s, 6H); ¹³C NMR (125 MHz, CDCl₃) δ 164.9 (C), 137.3 (C), 136.3 (C), 130.3 (C), 129.6 (CH), 128.5 (CH), 127.8 (C), 119.4 (CH), 119.3 (C), 65.9 (C), 56.9 (C), 52.9 (CH), 51.1 (CH₃), 32.3 (CH₂), 25.1 (CH₂), 19.5 (CH₃), 12.2 (CH₃), 11.6 (CH₃); ATR-FTIR (thin film): 2952, 2120, 2094, 1706, 1481, 1295, 1238 cm⁻¹; HRMS (EI) m/z calculated for C₁₈H₂₀N₃O₂NaCl [M+Na]⁺: 368.1142, found: 368.1140.

(1S, 4R)-methyl 3-(2-azido-4-methoxyphenyl)-4,7,7-trimethylbicyclo[2.2.1]hept-2-ene-2-carboxylate 4.12e. The general procedure was followed by using 0.151 g of 2-azido-4-methoxyphenyl boronate 4.8e (0.55 mmol), 0.171 g of vinyl triflate 4.7b (0.50 mmol), 0.057 g of Pd(PPh₃)₄ (0.05 mmol), 1.0 mL of saturated aq. soln. of NaHCO₃ and 5 mL of dimethoxyethane. Purification by MPLC (2:98 to 5:95 EtOAc: hexane) afforded the product as yellow solid, as a mixture of rotamers (0.143 g,
84%): \([\alpha]_D^{25} +48.8 (c 0.250, \text{CH}_2\text{Cl}_2)\); \(^1\text{H} \text{NMR (500 MHz, CDCl}_3\) \(\delta 7.00 (s, 0.5\text{H}), 6.71 (b, 2.5\text{H}), 3.83 (s, 3\text{H}), 3.57 (s, 3\text{H}), 2.83 (s, 1\text{H}), 2.03 - 1.97 (m, 1\text{H}), 1.66 (b, 1\text{H}), 1.32 - 1.23 (m, 2\text{H}), 1.06 (s, 1.5\text{H}), 0.93 (s, 1.5\text{H}), 0.85 (s, 6\text{H}); \(^{13}\text{C} \text{NMR (125 MHz, CDCl}_3\) \(\delta 159.9 (\text{C}), 135.4 (\text{C}), 130.9 (\text{C}), 128.9 (\text{C}), 121.0 (\text{C}), 119.9 (\text{C}), 109.9 (\text{CH}), 104.1 (\text{CH}), 59.4 (\text{C}), 56.4 (\text{C}), 55.4 (\text{CH}_3), 52.8 (\text{CH}), 51.0 (\text{CH}_3), 32.3 (\text{CH}_2), 25.5 (\text{CH}_2), 19.5 (\text{CH}_3), 12.2 (\text{CH}_3), 11.8 (\text{CH}_3)\) only visible peaks; ATR-FTIR (thin film): 2952, 2104, 1700, 1600, 1501, 1298, 1228 cm\(^{-1}\); HRMS (EI) \(m/z\) calculated for \(\text{C}_{19}\text{H}_{23}\text{N}_3\text{O}_3\text{Na [M+Na]}^+\): 364.1637, found: 364.1639.

(1S, 4R)-methy1 3-(2-azido-4-methylphenyl)-4,7,7-trimethylbicyclo[2.2.1]hept-2-ene-2-carboxylate 4.12f. The general procedure was followed by using 0.142 g of 2-azido-4-methylphenyl boronate 4.8f (0.55 mmol), 0.071 g of vinyl triflate 4.7b (0.50 mmol), 0.057 g of Pd(PPh\(_3\))\(_4\) (0.05 mmol), 1.0 mL of saturated aq. soln. of NaHCO\(_3\) and 5 mL of dimethoxyethane. Purification by MPLC (2:98 to 5:95 EtOAc: hexane) afforded the product as yellow oil, as a mixture of rotamers (0.105 g, 65%): \([\alpha]_D^{25} +42.4 (c 0.250, \text{CH}_2\text{Cl}_2)\); \(^1\text{H} \text{NMR (500 MHz, CDCl}_3\) \(\delta 6.98 (b, 2.5\text{H}), 6.76 (b, 0.5\text{H}), 3.57 (s, 3\text{H}), 2.84 (s, 1\text{H}), 2.38 (s, 3\text{H}), 2.01 (b, 1\text{H}), 1.68 (b, 1\text{H}), 1.30 (b, 2\text{H}), 1.08 (s, 1.5\text{H}), 0.94 (s, 1.5\text{H}), 0.86 (s, 6\text{H}); \(^{13}\text{C} \text{NMR (125 MHz, CDCl}_3\) \(\delta 162.8 (\text{C}), 138.8 (\text{C}), 135.3 (\text{C}), 129.7 (\text{C}), 127.8 (\text{C}), 125.7 (\text{C}), 125.2 (\text{CH}), 118.8 (\text{CH}), 59.6 (\text{C}), 56.6 (\text{C}), 52.8 (\text{CH}), 51.0 (\text{CH}_3), 31.9 (\text{CH}_2), 25.1 (\text{CH}_2), 21.3 (\text{CH}_3), 19.5 (\text{CH}_3), 11.7 (\text{CH}_3)\) only visible peaks. ATR-FTIR (thin film): 2951, 2102, 1702, 1502, 1433, 1294 cm\(^{-1}\); HRMS (EI) \(m/z\) calculated for \(\text{C}_{19}\text{H}_{23}\text{N}_3\text{O}_3\text{Na [M+Na]}^+\): 348.1688, found 348.1689.
(1S, 4R)-methyl 3-(2-azido-4-(trifluoromethyl)phenyl)-4,7,7-trimethyl-bicyclo[2.2.1]hept-2-ene-2-carboxylate 4.12g. The general procedure was followed by using 0.172 g of 2-azido-4-trifluoromethylphenyl boronate 4.8g (0.55 mmol), 0.171 g of vinyl triflate 4.7b (0.50 mmol), 0.057 g of Pd(PPh3)4 (0.05 mmol), 1.0 mL of saturated aq. soln. of NaHCO3 and 5 mL of dimethoxyethane. Purification by MPLC (2:98 to 5:95 EtOAc: hexane) afforded the product as yellow oil, as a mixture of rotamers (0.091 g, 48%): [α]D25: +42.4 (c 0.250, CH2Cl2); 1H NMR (500 MHz, CDCl3) δ 7.12 (s, 1H), 7.03 (dt, J = 8.5 Hz, 3.0 Hz, 1H), 6.78 (s, 0.5H), 6.61 (s, 0.5H), 3.58 (s, 3H), 2.86 (s, 1H), 2.04 – 2.00 (m, 1H), 1.70 (b, 1H), 1.35 – 1.19 (m, 2H), 1.07 (s, 1.5H), 0.99 (s, 1.5H), 0.86 (s, 6H); 13C NMR (125 MHz, CDCl3) δ 159.6 (C), 136.1 (C), 130.5 (C), 126.9 (C), 119.4 (CH), 116.7 (CH), 115.5 (CH), 115.3 (C), 114.9 (C), 59.7 (C), 56.9 (C), 52.9 (CH), 51.2 (CH3), 32.4 (CH2), 32.0 (CH2), 25.0 (CH2), 19.4 (CH3), 12.1 (CH3), only visible peaks; ATR-FTIR (thin film): 2954, 2118, 1711, 1487, 1267, 1240, 1191, 1097, 808 cm−1; HRMS (E) m/z calculated for C19H21F3NO2 [M – N2 + H]+: 352.1524, found 352.1434.

(1S, 4R)-methyl 3-(4-acetyl-2-azidophenyl)-4,7,7-trimethylbicyclo[2.2.1]hept-2-ene-2-carboxylate 4.12h. The general procedure was followed by using 0.158 g of 2-azido-4-acetylphenyl boronate 4.8h (0.55 mmol), 0.171 g of vinyl triflate 4.7b (0.50 mmol), 0.057 g of Pd(PPh3)4 (0.05 mmol), 1.0 mL of saturated aq. soln. of NaHCO3 and 5 mL of dimethoxyethane. Purification by MPLC (2:98 to 5:95 EtOAc: hexane)
afforded the product as yellow oil, as a mixture of rotamers (0.114 g, 64%): \([\alpha]^25_D\) +31.2 (c 0.250, CH\(_2\)Cl\(_2\)); \(^1\)H NMR (500 MHz, CDCl\(_3\)) \(\delta\) 7.78 (s, 0.9H), 7.69 – 7.66 m, 0.8H), 7.23 (d, \(J = 7.5\) Hz, 0.3H), 7.17 – 7.13 (m, 0.9H), 6.97 (b, 0.4H), 3.73 – 3.71 (m, 0.2H), 3.56 (s, 3H), 2.87 (s, 1H), 2.62 (s, 3H), 2.35 (s, 0.8H), 2.06 – 2.01 (m, 1H), 1.74 (b, 1H), 1.35 – 1.20 (m, 1H), 1.09 (s, 1.5H), 0.97 (s, 1.5H), 0.87 (s, 3H), 0.84 (s, 3H); \(^{13}\)C NMR (125 MHz, CDCl\(_3\)) \(\delta\) 1196.7 (C), 176.3 (C), 137.4 (C), 136.2 (C), 133.9 (C), 129.0 (CH), 128.2 (CH), 124.4 (CH), 60.0 (C), 52.9 (CH), 51.2 (CH\(_3\)), 47.1 (C), 32.4 (CH\(_2\)), 26.6 (CH\(_3\)), 25.1 (CH\(_2\)), 19.6 (CH\(_3\)), 12.1 (CH\(_3\)), only visible peaks; ATR-FTIR (thin film): 2953, 2102, 1705, 1685, 1404, 1291 cm\(^{-1}\); HRMS (EI) \(m/z\) calculated for C\(_{20}\)H\(_{23}\)N\(_3\)O\(_3\)Na [M + Na]\(^+\): 376.1637, found: 376.1640.

(1\(S\),4\(R\))-tert-butyl 3-(2-azidophenyl)-4,7,7-trimethylbicyclo[2.2.1]hept-2-ene-2-carboxylate 4.12i. The general procedure was followed by using 0.115 g of 2-azidophenyl boronate 4.8a (0.47 mmol), 0.165 g of vinyl triflate derived from camphor 4.7i (0.43 mmol), 0.0534 g of Pd(PPh\(_3\))\(_4\) (0.04 mmol), 0.8 mL of saturated aq. soln. of NaHCO\(_3\) and 10 mL of dimethoxyethane. Purification by MPLC (2:98 to 5:95 EtOAc: hexane) afforded the product as yellow oil, as a mixture of rotamers (0.0140 g, 92%): \([\alpha]^25_D\) +44.4 (c 0.250, CH\(_2\)Cl\(_2\)); \(^1\)H NMR (500 MHz, CDCl\(_3\)) \(\delta\) 7.30 (t, \(J = 7.7\) Hz, 1H), 7.14 – 6.86 (m, 3H), 2.80 (m, 1H), 1.99 (ddt, \(J = 11.7\) Hz, 8.1 Hz, 3.8 Hz, 1H), 1.67 (m, 2H), 1.35 (m, 1H), 1.17 (s, 9H), 1.09 (s, 1.35H), 0.95 (s, 1.62H), 0.84 (s, 6H); \(^{13}\)C NMR (125 MHz, CDCl\(_3\)) \(\delta\) 162.0 (C), 156.1 (C), 138.5 (C), 137.5 (C), 129.8 (CH), 128.3 (CH), 124.1 (CH), 117.8 (CH), 103.9 (C), 79.4 (C), 59.3 (C), 56.2 (C), 52.6 (CH), 31.1 (CH\(_2\)), 27.9 (CH\(_3\)), 25.2 (CH\(_2\)), 19.2 (CH\(_3\)), 12.3 (CH\(_3\)), 9.2 (CH\(_3\)), only visible peaks. ATR-FTIR (thin film): 2973, 2872, 2122, 2092, 1697 cm\(^{-1}\); HRMS (ESI) \(m/z\) calculated for C\(_{21}\)H\(_{27}\)N\(_3\)O\(_2\)Na (M+Na\(^+\)): 376.2001, found: 376.1998.
(1R, 4R)-2-(2-azidophenyl)-1,7,7-trimethylbicyclo[2.2.1]hept-2-ene 4.12]. The general procedure was followed by using 0.046 g of the vinyl triflate derived from camphor 4.7j (0.162 mmol), 0.047 g of 2-azidophenylboronic acid pinacolate ester 4.8a (0.194 mmol), 0.0092 g of Pd(PPh₃)₄ (5 mol %), 1.6 mL of 1, 2 DME and 0.32 mL of a saturated aqueous solution of NaHCO₃. Purification by MPLC (3:97 – 20:80 EtOAc:hexane) afforded the product as a colorless liquid (0.030 g, 73%): [α]D²⁵: – 86.4 (c 0.125, CH₂Cl₂). ¹H NMR (500 MHz, CDCl₃) δ 7.27 (m, 1H), 7.15 (d, J = 8.0 Hz, 1H), 7.07 (m, 2H), 5.96 (d, J = 3.5 Hz, 1H), 2.40 (t, J = 3.5 Hz, 1H), 1.93 (m, 1H), 1.62 – 1.54 (m, 2H), 1.13 (m, 1H), 0.98 (s, 3H), 0.94 (s, 3H), 0.83 (s, 3H); ¹³C NMR (125 MHz, CDCl₃) δ 146.6 (C), 137.6 (C), 134.2 (CH), 131.0 (C), 130.2 (CH), 127.8 (CH), 124.3 (CH), 118.3 (CH), 57.7 (C), 56.1 (C), 51.9 (CH), 31.6 (CH₂), 25.3 (CH₂), 20.0 (CH₃), 19.8 (CH₃), 12.1 (CH₃). ATR-FTIR (thin film): 2941, 2871, 2121, 2084, 1483, 1439, 1287 cm⁻¹. HRMS (EI) m/z calculated for C₁₆H₁₉N₃ (M)⁺: 253.1579, found: 253.1582.

(1R, 4S)-methyl 3-(2-azidophenyl)-7-tosyl-7-azabicyclo[2.2.1]hept-2-ene-2-carboxylate 4.15. To a mixture of vinyl bromide 60.0 mg (0.155 mmol), 2-azidophenylboronic acid pinacolate ester 4.8a 0.045 g (0.186 mmol) and Pd(OAc)₂ (10 mol %) in ethanol–benzene (1:3, 4 mL) was added Na₂CO₃ 0.032 g (0.310 mmol). The resulting solution was heated to reflux. After 16 h, the mixture was cooled to room temperature and diluted with 5 mL of cold water. The solution was extracted with 2 × 10 mL of ether followed by 1 × 10 mL of brine. The resulting organic phase was dried over Na₂SO₄, and was concentrated in vacuo. Purification
by MPLC (3:97 – 20:80 EtOAc:hexane) afforded the product as a yellow liquid (0.031 g, 47%): 

\[ ^1H \text{ NMR (500 MHz, CDCl}_3 \] \( \delta \) 7.67 (d, \( J = 8.0 \) Hz, 2H), 7.34 (t, \( J = 8.0 \) Hz, 1H), 7.19 (d, \( J = 8.0 \) Hz, 2H), 7.11 (d, \( J = 8.5 \) Hz, 1H), 7.03 (t, \( J = 8.5 \) Hz, 1H), 6.91 (d, \( J = 8.0 \) Hz, 1H), 5.05 (m, 1H), 4.89 (m, 1H), 3.58 (s, 3H), 3.13 (s, 3H), 2.22 – 2.18 (m, 2H), 1.58 – 1.54 (m, 1H), 1.50 – 1.46 (m, 1H); 

\[ ^{13}C \text{ NMR (125 MHz, CDCl}_3 \] \( \delta \) 163.3 (C), 150.4 (C), 143.6 (C), 137.8 (C), 136.2 (C), 134.0 (C), 131.3 (CH), 130.5 (CH), 129.6 (CH), 128.1 (CH), 124.1 (CH), 124.7 (C), 118.3 (CH), 67.9 (CH), 64.1 (CH), 51.4 (CH), 26.0 (CH), 25.5 (CH), 21.5 (CH). ATR-FTIR (thin film): 2950, 2118, 1701, 1483, 1347, 1157, 1088 cm\(^{-1}\). HRMS (ESI) \( m/z \) calculated for C\(_{21}\)H\(_{20}\)O\(_4\)N\(_4\)SNa (M+Na): 447.1103, found: 447.1102.

(1\( R \), 5\( R \))-methyl 2-(2-azidophenyl)-6,6-dimethylbicyclo[3.1.1]hept-2-ene-3-carboxylate 4.18c. The general procedure was followed by using 0.190 g of 2-azidophenyl boronate 4.8a (0.77 mmol), 0.232 g of vinyl triflate derived from pinene 4.7c (0.71 mmol), 0.088 g of Pd(PPh\(_3\))\(_4\) (0.07 mmol), 1.4 mL of saturated aq. soln. of NaHCO\(_3\) and 10 mL of dimethoxyethane. Purification by MPLC (2:98 to 5:95 EtOAc:hexane) afforded the product as yellow oil (0.1439 g, 69%): \([\alpha]_D^{25} = - 122.8 \) (c 0.250, CH\(_2\)Cl\(_2\)); 

\[ ^1H \text{ NMR (500 MHz, CDCl}_3 \] \( \delta \) 7.30 (t, \( J = 7.7 \) Hz, 1H), 7.16 (d, \( J = 8.0 \) Hz, 1H), 7.10 (t, \( J = 7.5 \) Hz, 1H), 6.97 (s, 1H), 3.53 (s, 3H), 2.70 (s, 2H), 2.51 (dt, \( J = 9.0 \) Hz, 5.6 Hz, 1H), 2.35 (s, 1H), 2.28 (dt, \( J = 5.6 \) Hz, 2.8 Hz, 1H), 1.53 (s, 1H), 1.32 (s, 3H), 1.02 (s, 3H); 

\[ ^{13}C \text{ NMR (125 MHz, CDCl}_3 \] \( \delta \) 167.5 (C), 157.0 (C), 136.5 (C), 128.4 (CH), 128.0 (C), 124.5 (CH), 123.5 (C), 118.2 (CH), 53.5 (C), 51.1 (CH\(_3\)), 50.4 (CH), 39.8 (CH), 32.4 (CH\(_2\)), 30.8 (CH\(_2\)), 25.9 (CH\(_3\)), 21.3 (CH\(_3\)) only visible peaks. ATR-FTIR (thin film): 2946, 2917, 2121, 2098, 1432 cm\(^{-1}\); HRMS (El) \( m/z \) calculated for C\(_{17}\)H\(_{19}\)NO\(_2\) (M-N\(_2\))^+: 269.1416, found: 269.1404.
(1R, 5R)-methyl 2-(2-azido-5-methoxyphenyl)-6,6-dimethylbicyclo[3.1.1]hept-2ene-3-carboxylate 4.18a. The general procedure was followed by using 0.151 g of 2-azidophenyl boronate (0.55 mmol), 0.171 g of vinyl triflate 4.7c (0.50 mmol), 0.057 g of Pd(PPh₃)₄ (0.05 mmol), 1.0 mL of saturated aq. soln. of NaHCO₃ and 5 mL of dimethoxyethane. Purification by MPLC (2:98 to 5:95 EtOAc: hexane) afforded the product as yellow oil (0.144 g, 88%): [α]D²⁵⁺ = −48.8 (c 0.250, CH₂Cl₂); ¹H NMR (500 MHz, CDCl₃) δ 7.06 (d, J = 8.5 Hz, 1H), 6.83 (dd, J = 8.5 Hz, 3.0 Hz, 1H), 6.49 (s, 1H), 3.77 (s, 3H), 3.54 (s, 3H), 2.68 (s, 2H), 2.51 − 2.47 (m, 1H), 2.32 − 2.26 (m, 2H), 1.57 − 1.50 (m, 1H), 1.31 (s, 3H), 1.00 (s, 3H); ¹³C NMR (125 MHz, CDCl₃) δ 156.6 (C), 136.2 (C), 129.0 (C), 123.7 (C), 119.4 (C), 119.2 (CH), 113.7 (CH), 55.6 (CH₃), 51.2 (CH₃), 50.3 (CH), 39.8 (CH), 32.3 (CH₂), 30.7 (CH₂), 25.9 (CH₃), 21.3 (CH₃), only visible peaks; ATR-FTIR (thin film): 2946, 2114, 1720, 1490, 1284, 1243 cm⁻¹; HRMS (ESI) m/z calculated for C₁₈H₂₂NO₃ (M+H-N₂)⁺: 300.1600, found: 300.1599.

(1R, 5R)-methyl 2-(2-azido-5-methylphenyl)-6,6-dimethylbicyclo[3.1.1]hept-2ene-3-carboxylate 4.18b. The general procedure was followed by using 0.079 g of 2-azidophenyl boronate 4.8f (0.31 mmol), 0.091 g of vinyl triflate derived from pinene 4.7c (0.28 mmol), 0.032 g of Pd(PPh₃)₄ (0.03 mmol), 0.5 mL of saturated aq. soln. of NaHCO₃ and 5 mL of dimethoxyethane. Purification by MPLC (2:98 to 5:95 EtOAc: hexane) afforded the product as yellow oil (0.0804 g, 93%): [α]D²⁵⁺ = −90.8 (c 0.25,
CH₂Cl₂); ¹H NMR (500 MHz, CDCl₃) δ 7.09 (dd, J = 8.1 Hz, 1.8 Hz, 1H), 7.04 (t, J = 7.4 Hz, 1H), 6.74 (s, 1H), 3.54 (s, 3H), 2.68 (s, 2H), 2.49 (dt, J = 8.9 Hz, 5.6 Hz, 1H), 2.32 (s, 1H), 2.30 (s, 3H), 2.26 (tt, J = 5.7 Hz, 2.8 Hz, 1H), 1.37 (s, 1H), 1.31 (s, 3H), 1.01 (s, 3H); ¹³C NMR (125 MHz, CDCl₃) δ 167.5 (C), 137.4 (C), 134.2 (CH), 133.7 (C), 129.0 (CH), 128.3 (C), 123.4 (C), 118.1 (CH), 51.1 (CH₃), 50.4 (CH), 39.8 (CH), 32.3 (CH₂), 30.7 (CH₂), 25.9 (CH₃), 24.8 (CH₃), 20.9 (CH₃), only visible peaks. ATR-FTIR (thin film): 2946, 2918, 2110, 2074, 1720, 1704, 1491 cm⁻¹; HRMS (ESI) m/z calculated for C₁₁H₁₁N₂O₂ (M+H-N₂)+: 284.1651, found: 284.1650.

(1⁴R, 5⁴R)-methyl 2-(2-azido-5-trifluoromethoxyphenyl)-6,6-dimethylbicyclo[3.1.1]hept-2-ene-3-carboxylate 4.18d. The general procedure was followed by using 0.105 g of 2-azidophenyl boronate (0.32 mmol), 0.095 g of vinyl triflate derived from pinene 4.7c (0.29 mmol), 0.0333 g of Pd(PPh₃)₄ (0.03 mmol), 0.6 mL of saturated aq. soln. of NaHCO₃ and 6 mL of dimethoxyethane. Purification by MPLC (2:98 to 5:95 EtOAc: hexane) afforded the product as yellow oil (0.0846 g, 77%): [α]D₂⁵: 85.6 (c 0.125, CH₂Cl₂); ¹H NMR (500 MHz, CDCl₃) δ 7.17–7.13 (m, 2H), 6.80 (s, 1H), 3.53 (s, 3H), 2.68 (t, J = 2.7 Hz, 2H), 2.51 (dt, J = 9.1 Hz, 5.6 Hz, 1H), 2.32 (s, 1H), 2.27 (tt, J = 5.7 Hz, 2.8 Hz, 1H), 1.57-1.48 (m, 1H), 1.32 (s, 3H), 0.98 (s, 3H); ¹³C NMR (125 MHz, CDCl₃) δ 167.1 (C), 155.2 (C), 145.6 (C), 135.4 (C), 127.7 (C), 124.5 (C), 121.1 (CH), 120.8 (CH), 119.2 (CH), 53.3 (C), 51.2 (CH₃), 50.1 (CH), 39.7 (CH), 32.3 (CH₂), 30.7 (CH₂), 25.8 (CH₃), 21.2 (CH₃) only visible peaks. ATR-FTIR (thin film): 2927, 2120, 2088, 1718, 1253 cm⁻¹; HRMS (ESI) m/z calculated for C₁₈H₁₉NO₃F₃ (M+H-N₂)+: 354.1317, found: 354.1316.
C. Rh\(_2\)(II)-Catalyzed Synthesis of Indoles from Styryl Azides.

To a mixture of styryl azide and Rh\(_2\)(esp)_2 (5 mol %) was added toluene (0.1M). The resulting mixture was heated at 120 °C. After 16 h, the mixture was cooled to room temperature, diluted with CH\(_2\)Cl\(_2\) and concentrated in vacuo. Purification of the residue by MPLC (3:97 – 30:70 EtOAc:hexanes) using alumina afforded the product.

\[ \text{(1S,4R)-methyl 1,2,3,4-tetrahydro-9H-1,4-methanocarbazole-9-carboxylate 4.11.} \]

The general procedure was followed by using 0.0443 g of styryl azide 4.9 (0.165 mmol), 0.0062 g of Rh\(_2\)(esp)_2 (5 mol %) and 1.7 mL of toluene. Purification by MPLC (3:97 to 5:95 EtOAc:hexanes) afforded the products as a white solids (0.0199 g, 50%): \([\alpha]_D^{25}\) – 0.8 (c 0.250, CH\(_2\)Cl\(_2\)); \(^1\)H NMR (500 MHz, CDCl\(_3\)) \(\delta\) 8.16 (d, \(J = 6.4\) Hz, 1H), 7.45 (dd, \(J = 5.9\) Hz, 2.9 Hz, 1H), 7.24 – 7.20 (m, 2H), 4.03 (s, 3H), 3.82 (s, 1H), 3.55 (s, 1H), 1.92 (d, \(J = 8.7\) Hz, 1H), 1.88 (t, \(J = 7.9\) Hz, 2H), 1.56 (d, \(J = 9.1\) Hz, 1H), 1.02 (q, \(J = 8.1\) Hz, 1H), 0.97 (q, \(J = 8.6\) Hz, 1H); \(^{13}\)C NMR (125 MHz, CDCl\(_3\)) \(\delta\) 152.0 (C), 149.5 (C), 139.8 (C), 129.1 (C), 125.9 (C), 123.1 (CH), 122.9 (CH), 119.1 (CH), 115.9 (CH), 53.5 (CH\(_3\)), 49.5 (CH\(_2\)), 42.9 (CH), 39.1 (CH), 27.0 (CH\(_2\)), 26.8 (CH\(_2\)). ATR-FTIR (thin film): 2953, 2869, 1738, 1442, 1358 cm\(^{-1}\); HRMS (ESI) \(m/z\) calculated for C\(_{15}\)H\(_{16}\)NO\(_2\) (M+H\(^{+}\)): 242.1181, found: 242.1179.
(1S,4R)-methyl 4,10,10-trimethyl-1,2,3,4-tetrahydro-9H-1,4-methanocarbazole-9-carboxylate 4.14a. The general procedure was followed by using 0.0590 g of styryl azide 4.12a (0.189 mmol), 0.0072 g of Rh₂(esp)₂ (5 mol %) and 1.9 mL of toluene. Purification by MPLC (3:97 to 5:95 EtOAc:hexanes) afforded the product as a white solid (0.0450 g, 84%): [α]D²⁵: −10.0 (c 0.250, CH₂Cl₂); ¹H NMR (500 MHz, CDCl₃) δ 8.18 (s, 1H), 7.46 (t, J = 4.5 Hz, 1H), 7.20 (t, J = 4.6 Hz, 2H), 4.01 (s, 3H), 3.30 (s, 1H), 2.09 – 2.04 (m, 1H), 1.80 (td, J = 10.1 Hz, 3.1 Hz, 1H), 1.49 (s, 3H), 1.07 (td, J = 10.3 Hz, 2.7 Hz, 1H), 1.01 (td, J = 10.4 Hz, 3.0 Hz, 1H), 0.95 (s, 3H), 0.92 (s, 3H); ¹³C NMR (125 MHz, CDCl₃) δ 152.0 (C), 146.5 (C), 138.7 (C), 129.5 (C), 126.9 (C), 122.8 (CH), 122.5 (CH), 118.4 (CH), 115.8 (CH), 60.2 (C), 53.5 (CH₃), 52.7 (CH), 52.6 (C), 33.7 (CH₂), 26.4 (CH₂), 20.2 (CH₃), 19.2 (CH₃), 12.6 (CH₃). ATR-FTIR (thin film): 2951, 1737, 1441, 1358 cm⁻¹; HRMS (ESI) m/z calculated for C₁₈H₂₂NO₂ (M+H)⁺: 284.1651, found: 284.1646.

(1S,4R)-methyl 6,10,10-trimethyl-1,2,3,4-tetrahydro-9H-1,4-methanocarbazole-9-carboxylate 4.14b. The general procedure was followed by using 0.0325 g of styryl azide 4.12b (0.010 mmol), 0.0038 g of Rh₂(esp)₂ (5 mol %) and 1.0 mL of toluene. Purification by MPLC (3:97 to 5:95 EtOAc:hexanes) afforded the product as a yellow oil (0.0260 g, 88%): [α]D²⁵: −25.6 (c 0.250, CH₂Cl₂); ¹H NMR (500 MHz, CDCl₃) δ 8.04 – 8.02 (m, 1H), 7.25 (d, J = 0.5 Hz, 1H), 7.23 (d, J = 8.5 Hz, 1H), 4.00 (s, 3H), 3.28 – 3.27 (m, 1H), 2.43 (s, 3H), 2.07 – 2.03 (m, 1H), 1.81 – 1.77 (m, 1H), 1.48 (s, 3H), 1.09 – 0.98 (m, 2H), 0.94 (s, 3H), 0.91 (s, 3H); ¹³C NMR (125 MHz, CDCl₃) δ 152.0 (C), 146.5 (C), 137.6 (C), 132.3 (C), 129.2 (C), 127.0 (C), 123.6 (CH),
118.5 (CH), 115.4 (CH), 60.0 (C), 53.4 (CH₃), 52.7 (CH), 33.3 (CH₂), 26.4 (CH₂), 21.4 (CH₃), 20.1 (CH₃), 19.1 (CH₃), 12.6 (CH₃), only peaks visible. ATR-FTIR (thin film): 2952, 2868, 1734, 1441, 1361, 1317 cm⁻¹; HRMS (EI) m/z calculated for C₁₄H₂₄NO₂ [M + H]⁺: 298.1807, found 298.1806.

(1S,4R)-methyl 6-fluoro-4,10,10-trimethyl-1,2,3,4-tetrahydro-9H-1,4-methano-carbazole-9-carboxylate 4.14c. The general procedure was followed by using 0.0329 g of styryl azide 4.12c (0.100 mmol), 0.0038 g of Rh₂(esp)₂ (5.0 mol %) and 1.0 mL of toluene. Purification by MPLC (5:95 EtOAc:hexanes) afforded the product as yellow solids (0.029 g, 93%): [α]D²⁵: −11.2 (c 0.250, CH₂Cl₂); ¹H NMR (500 MHz, CDCl₃) δ 8.09 (s, 1H), 7.09 (dd, J = 9.02 Hz, 2.20 Hz 1H), 6.90 (td, J = 9.10 Hz, 2.34 Hz, 1H), 4.01 (s, 3H), 3.32 (s, 1H), 2.10 – 2.05 (m, 1H), 1.83 – 1.79 (m, 1H), 1.45 (s, J = 13.2 Hz, 3H), 1.09 – 1.00 (m, 2H), 0.95 (s, 3H), 0.90 (s, 3H); ¹³C NMR (125 MHz, CDCl₃) δ 160.4 (C), 158.5 (C), 151.8 (C), 134.9 (C), 129.1 (J_CF = 3.42 Hz, C ), 127.6 (J_CF = 10.36 Hz, C ), 116.4 (J_CF = 9.28 Hz, CH), 109.6 (J_CF = 25.38 Hz, CH), 104.1 (J_CF = 23.82 Hz, CH), 60.3 (C), 53.6 (CH), 52.80(CH₃), 52.5 (C), 33.71 (CH₂), 26.4 (CH₂), 20.1 (CH₃), 19.1 (CH₃), 12.4 (CH₃), only visible peaks. ¹⁹F NMR (282 MHz, , CDCl₃) δ -121.17. ATR-FTIR (thin film): 2992, 2956, 1739, 1583, 1443, 1213 cm⁻¹; HRMS (EI) m/z calculated for C₁₈H₂₁NO₂F (M+H)⁺: 302.1556, found: 302.1554.

(1S,4R)-methyl 6-chloro-4,10,10-trimethyl-1,2,3,4-tetrahydro-9H-1,4-methano-carbazole-9-carboxylate 4.14d. The general procedure was followed by using 0.0346 g of styryl azide 4.12d (0.100 mmol), 0.0038 g of Rh₂(esp)₂ (5 mol %) and
1.0 mL of toluene. Purification by MPLC (5:95 EtOAc:hexanes) afforded the product as yellow solids (0.028 mg, 88%): $[\alpha]_D^{25}$: $–33.6$ (c 0.250, CH$_2$Cl$_2$); $^1$H NMR (500 MHz, CDCl$_3$) $\delta$ 8.08 (d, $J$ = 7.7 Hz, 1H), 7.40 (d, $J$ = 1.1 Hz, 1H), 7.315(dd, $J$ = 8.7 Hz, 1.4 Hz, 1H), 4.01 (s, 3H), 3.29(s, 1H), 2.08 – 2.05 (m, 1H), 1.83 – 1.79 (m, 1H), 1.46 (s, 3H), 1.08 – 0.99 (m, 2H), 0.95 (s, 3H), 0.89 (s, 3H), $^{13}$C NMR (125 MHz, CDCl$_3$) $\delta$ 151.7 (C), 147.8 (C), 137.0 (C), 128.8 (C), 128.5 (C), 127.9 (C), 122.3 (CH), 118.0 (CH), 116.6 (CH), 60.4 (C), 53.6 (CH), 52.8 (CH$_3$), 52.5 (C), 33.7 (CH$_2$), 26.3 (CH$_2$), 20.1 (CH$_3$), 19.1 (CH$_3$), 12.4 (CH$_3$). ATR-FTIR (thin film): 2954, 1741, 1439, 1361, 1215 cm$^{-1}$; HRMS (EI) m/z calculated for C$_{18}$H$_{21}$NO$_2$Cl (M+H)$^+$: 318.1261, found: 318.1259.

(1$S$,4$R$)-methyl 7-methoxy-4,10,10-trimethyl-1,2,3,4-tetrahydro-9$H$-1,4-methanocarbazole-9-carboxylate 4.14e. The general procedure was followed by using 0.0341 g of styryl azide 4.12e (0.100 mmol), 0.0038 g of Rh$_2$(esp)$_2$ (5 mol %) and 1.0 mL of toluene. Purification by MPLC (5:95 EtOAc:hexanes) afforded the product as yellow solid (0.0306 mg, 97%): $[\alpha]_D^{25}$: + 8.0 (c 0.250, CH$_2$Cl$_2$); $^1$H NMR (500 MHz, CDCl$_3$) $\delta$ 7.83 (s, 1H), 7.33 (d, $J$ = 8.5 Hz, 1H), 6.84 (dd, $J$ = 8.5Hz, 2.1 Hz, 1H), 4.00 (s, 3H), 3.87 (s, 3H), 3.25 – 3.25 (m, 1H), 2.05 – 2.01 (m, 1H), 1.76 (td, $J$ = 9.8 Hz, 2.7 Hz, 1H), 1.45 (s, 3H), 1.04 – 0.97 (m, 2H), 0.93 (s, 6H), $^{13}$C NMR (125 MHz, CDCl$_3$) $\delta$ 156.6 (C), 152.1 (C), 144.9 (C), 139.9 (C), 129.5 (C), 120.8 (C), 118.7 (CH), 111.4 (CH), 101.1 (CH), 59.6 (C), 55.8 (CH$_3$), 53.4 (CH), 52.9 (CH$_3$), 52.7 (C), 33.7 (CH$_2$), 26.5 (CH$_2$), 20.1 (CH$_3$), 19.1 (CH$_3$), 12.6 (CH$_3$). ATR-FTIR (thin film): 2951, 1732, 1440, 1364, 1306, 1071 cm$^{-1}$; HRMS (EI) m/z calculated for C$_{19}$H$_{26}$NO$_3$ (M+H)$^+$: 314.1756, found: 314.1752.
(1S,4R)-methyl 4,7,10,10-tetramethyl-1,2,3,4-tetrahydro-9H-1,4-methanocarbazole-9-carboxylate 4.14f. The general procedure was followed by using 0.0325 g of styryl azide 4.12f (0.100 mmol), 0.0038 g of Rh₂(esp)₂ (5 mol %) and 1.0 mL of toluene. Purification by MPLC (3:97 to 5:95 EtOAc:hexanes) afforded the product as a yellow oil (0.0290 g, 89%): [α]D²⁵ = –0.8 (c 0.250, CH₂Cl₂); ¹H NMR (500 MHz, CDCl₃) δ 8.02 (s, 1H), 7.34 (d, J = 8.0 Hz, 1H), 7.03 (d, J = 8.0 Hz, 1H), 4.01 (s, 3H), 3.26 (s, 1H), 2.47 (s, 3H), 2.05 – 2.02 (m, 1H), 1.80 – 1.76 (m, 1H), 1.47 (s, 3H), 1.07 – 0.96 (m, 2H), 0.94 (s, 3H), 0.92 (s, 3H); ¹³C NMR (125 MHz, CDCl₃) δ 152.1 (C), 145.2 (C), 139.8 (C), 132.4 (C), 129.4 (C), 124.6 (C), 124.0 (CH), 118.0 (CH), 116.2 (CH), 59.8 (C), 53.4(CH), 52.8 (CH₃), 52.6 (C), 33.7 (CH₂), 26.4 (CH₂), 21.9 (CH₃), 20.1 (CH₃), 19.1 (CH₃), 12.6 (CH₃). ATR-FTIR (thin film): 2952, 2869, 1733, 1441, 1364, 1304, 1223 cm⁻¹; HRMS (EI) m/z calculated for C₁₄H₂₄NO₂ [M + H]⁺: 298.1807, found 298.1804.

(1S,4R)-methyl-4,10,10-trimethyl-7-(trifluoromethyl)-1,2,3,4-tetrahydro-9H-1,4-methanocarbazole-9-carboxylate 4.14g. The general procedure was followed by using 0.0380 g of styryl azide 4.12g (0.100 mmol), 0.0023 g of Rh₂(esp)₂ (5 mol %) and 0.6 mL of toluene. Purification by MPLC (3:97 to 5:95 EtOAc:hexanes) afforded the product as a yellow oil (0.0333 g, 96%): [α]D²⁵ = –13.6 (c 0.250, CH₂Cl₂); ¹H NMR (500 MHz, CDCl₃) δ 8.10 (s, 1H), 7.09 (dd, J = 9.0 Hz, 2.5 Hz, 1H), 6.90 (dt, J = 9.0 Hz, 2.5 Hz, 1H), 4.01 (s, 3H), 3.28 (s, 1H), 2.09 – 2.05 (m, 1H), 1.83 – 1.79 (m, 1H), 1.46 (s, 3H), 1.09 – 1.02 (m, 2H), 0.95 (s, 3H), 0.90 (s, 3H); ¹³C NMR (125 MHz, CDCl₃) δ 160.4 (C), 158.5 (C), 151.8 (C), 134.9 (C), 129.1 (C), 127.6 (C), 116.4
(CH), 109.5 (CH), 104.2 (CH), 60.3 (C), 53.5 (CH₃), 52.8 (CH), 52.4 (C), 33.7 (CH₂), 26.4 (CH₂), 20.1 (CH₃), 19.1 (CH₃), 12.4 (CH₃), only visible peaks; \(^{19}\)F NMR (282 MHz, CDCl₃) δ -121.2. ATR-FTIR (thin film): 2954, 1739, 1443, 1365, 1321, 1212 cm\(^{-1}\); HRMS (EI) m/z calculated for C\(_{18}\)H\(_{17}\)F\(_3\)NO [M – OCH\(_3\)]\(^+\): 320.1262, found 320.1657.

(1\(S\),4\(R\))-methyl 7-acetyl-4,10,10-trimethyl-1,2,3,4-tetrahydro-9\(H\)-1,4-methanocarbazole-9-carboxylate 4.14h. The general procedure was followed by using 0.0353 g of styryl azide 4.12h (0.100 mmol), 0.0038 g of Rh\(_2\)(esp)\(_2\) (5 mol %) and 1.0 mL of toluene. Purification by MPLC (5: 95 EtOAc:hexanes) afforded the product as green solids (0.0210 mg, 85%): \([\alpha]_D^{25}\): – 4.0 (c 0.250, CH\(_2\)Cl\(_2\)); \(^1\)H NMR (500 MHz, CDCl₃) δ 8.80 (s, 1H), 7.86 (dd, \(J = 8.3\) Hz, 1.0 Hz, 1H), 7.47 (d, \(J = 8.25\) Hz, 1H), 4.06 (s, 3H), 3.34 (d, \(J = 3.32\) Hz 1H), 2.66 (s, 3H), 2.12 – 2.09 (m, 1H), 1.87 – 1.83 (m, 1H), 1.49 (s, 3H), 1.10 – 1.06 (m, 2H), 0.96 (s, 3H), 0.89 (s, 3H); \(^{13}\)C NMR (125 MHz, CDCl₃) δ 198.0 (C), 151.7 (C), 138.1 (C), 131.7 (C), 129.6 (C), 123.2 (CH), 117.8 (CH), 116.8 (CH), 60.8 (C), 53.8 (CH), 52.9 (CH₃), 52.5 (C), 33.7 (CH₂), 26.7 (CH₃), 26.3 (CH₂), 20.2 (CH₃), 19.1 (CH₃), 12.4 (CH₃), only visible peaks. ATR-FTIR (thin film): 2947, 1741, 1674, 1368, 1313, 1114 cm\(^{-1}\); HRMS (EI) m/z calculated for C\(_{20}\)H\(_{24}\)NO\(_3\) (M+H)\(^+\): 326.1756, found: 326.1756.

(1\(S\),4\(R\))-tert-butyl 4,10,10-trimethyl-1,2,3,4-tetrahydro-9\(H\)-1,4-methanocarbazole-9-carboxylate 4.14i. The general procedure was followed by using 0.0313 g of styryl azide 4.12i (0.086 mmol), 0.0034 g of Rh\(_2\)(esp)\(_2\) (5 mol %) and 0.9 mL of
toluene. Purification by MPLC (3:97 to 5:95 EtOAc:hexanes) afforded the product as a yellow oil (0.0223 g, 77%): [α]$_D^{25}$: + 4.0 (c 0.250, CH$_2$Cl$_2$); $^1$H NMR (500 MHz, CDCl$_3$) δ 8.15 (s, 1H), 7.46 – 7.44 (m, 1H), 7.18 – 7.16 (m, 2H), 3.28 (s, 1H), 2.08 – 2.03 (m, 1H), 1.79 (td, $J$ = 9.9 Hz, 3.0 Hz, 1H), 1.66 (s, 9H), 1.48 (s, 3H), 1.07 (td, $J$ = 10.1 Hz, 3.0 Hz, 1H), 1.02-0.99 (m, 1H), 0.94 (s, 3H), 0.92 (s, 3H); $^{13}$C NMR (125 MHz, CDCl$_3$) δ 150.2 (C), 146.9 (C), 138.7 (C), 128.8 (C), 126.8 (C), 122.4 (CH), 122.1 (CH), 118.2 (CH), 115.8 (CH), 83.0 (C), 60.1 (C), 53.0 (CH), 52.4 (C), 33.8 (CH$_2$), 28.3 (CH$_3$), 26.2 (CH$_2$), 20.2 (CH$_3$), 19.2 (CH$_3$), 12.6 (CH$_3$). ATR-FTIR (thin film): 2954, 2871, 1731, 1362 cm$^{-1}$; HRMS (EI) $m/z$ calculated for C$_{21}$H$_{27}$NO$_2$ (M)$^+$: 325.2042, found: 325.2049.

\[
\begin{align*}
(1S,4R)-4,10,10\text{-trimethyl-2,3,4,9-tetrahydro-1H-1,4-methanocarbazole} & \quad 4.14j
\end{align*}
\]

The general procedure was followed by using 0.021 g of aryl azide 4.12j (0.083 mmol), 0.0031 g of Rh$_2$(esp)$_2$ (5 mol %) and 1.0 mL of toluene. Purification by MPLC (3:97 – 20:80 EtOAc: hexanes) afforded the product as a gray solid (0.018 g, 96%): [α]$_D^{25}$: + 364.8 (c 0.250, CH$_2$Cl$_2$), $^1$H NMR (500 MHz, CDCl$_3$) δ 7.86 (br s, 1H), 7.52 (d, $J$ = 6.5 Hz, 1H), 7.33 (m, 1H), 7.05 (m, 2H), 2.87 (d, $J$ = 3.5 Hz, 1H), 2.02 (m, 1H), 1.84 (m, 1H), 1.51 (s, 3H), 1.13 – 1.08 (m, 1H), 0.96 (s, 3H), 0.93 (m, 1H), 0.88 (s, 3H); $^{13}$C NMR (125 MHz, CDCl$_3$) δ 147.0 (C), 138.6 (C), 124.6 (C), 124.4 (C), 119.4 (CH), 119.3 (CH), 117.9 (CH), 111.5 (CH), 60.9 (C), 52.4 (C), 50.5 (CH), 34.7 (CH$_2$), 26.4 (CH$_2$), 20.4 (CH$_3$), 19.4 (CH$_3$), 12.9 (CH$_3$). ATR-FTIR (thin film): 3402, 3965, 2868, 1445, 1258, 1116, 905 cm$^{-1}$. HRMS (EI) $m/z$ calculated for C$_{16}$H$_{19}$N (M)$^+$: 275.1517, found: 275.1522.
Methyl 1-((4-methylphenyl)sulfonamido)-1,2-dihydro-9H-carbazole-9-carboxylate 4.16. The general procedure was followed by using 0.022 g of aryl azide 4.15 (0.052 mmol), 0.0019 g of Rh$_2$(esp)$_2$ (5 mol %) and 1.0 mL of toluene. Purification by MPLC (3:97 – 20:80 EtOAc: hexanes) afforded the product as a white solid (0.007 g, 34%). $^1$H NMR (500 MHz, CDCl$_3$) δ 8.73 (br s, 1H), 7.76 (d, $J$ = 8.5 Hz, 1H), 7.66 (d, $J$ = 8.0 Hz, 2H), 7.34 – 7.29 (m, 2H), 7.24 (d, $J$ = 8.0 Hz, 2H), 7.08 (t, $J$ = 8.0 Hz, 1H), 6.63 (m, 1H), 5.93 (dd, $J$ = 11.5 Hz, 8.0 Hz, 1H), 5.24 (m, 1H), 3.93 (s, 3H), 3.02 – 2.97 (m, 1H), 2.72 – 2.66 (m, 1H), 2.40 (s, 3H); $^{13}$C NMR (125 MHz, CDCl$_3$) δ 162.1 (C), 143.6 (C), 136.1 (C), 133.5 (C), 130.9 (CH), 129.3 (CH), 128.0 (CH), 125.8 (CH), 125.7 (C), 124.4 (C), 122.5 (C), 122.3 (CH), 120.6 (CH), 111.9 (CH), 109.9 (CH), 55.3 (CH$_3$), 51.9 (CH), 39.1 (CH$_2$), 21.6 (CH$_3$). ATR-FTIR (thin film): 3363, 1704, 1553, 1449, 1350, 1165, 912 cm$^{-1}$. HRMS (ESI) m/z calculated for C$_{21}$H$_{21}$O$_4$N$_2$S (M+H)$^+$: 397.1222, found: 397.1218.

(2R,4R,4aR)-methyl 3,3-dimethyl-1,2,3,4-tetrahydro-4aH-2,4-methanocarbazole-4a-carboxylate 4.19c and (2R,4R)-methyl 3,3-dimethyl-1,2,3,4-tetrahydro-9H-2,4-methanocarbazole-9-carboxylate 4.20c. The general procedure was followed by using 0.0458 g of styryl azide 4.18c (0.154 mmol), 0.0058 g of Rh$_2$(esp)$_2$ (5 mol %) and 1.6 mL of toluene. Purification by MPLC (3:97 to 30:70 EtOAc:hexanes) afforded the products—white solids—as a 21:72 separable mixture of 4.19c and 4.20c in 93% yield. Characterization data for 3H-indole 4.19c: $[^{[\alpha]}]_D^{25}$: + 231.6 (c 0.25, CH$_2$Cl$_2$); $^1$H NMR (500 MHz, CDCl$_3$) δ 7.56 (d, $J$ = 7.7 Hz, 1H), 7.45 (d, $J$ = 7.4 Hz, 1H), 7.37 (td, $J$ = 7.6 Hz, 0.9 Hz, 1H), 7.19 (t, $J$ = 7.5 Hz, 1H), 3.56 (s, 3H), 3.27
(dd, $J = 15.9$ Hz, 3.7 Hz, 2.4 Hz, 1H), 3.20 (d, $J = 15.2$ Hz, 1H), 2.97 (t, $J = 5.9$ Hz, 1H), 2.82 (dtd, $J = 11.4$ Hz, 5.7 Hz, 1.9 Hz, 1H), 2.30 (d, $J = 5.5$ Hz, 1H), 1.32 (d, $J = 11.4$ Hz, 1H), 1.26 (s, 3H), 0.43 (s, 3H); $^{13}$C NMR (125 MHz, CDCl$_3$) $\delta$ 171.2 (C), 156.0 (C), 138.1 (C), 129.1 (CH), 127.9 (C), 125.5 (CH), 123.0 (CH), 120.6 (CH), 71.8 (C), 60.2 (C), 52.7 (CH$_3$), 47.9 (CH), 41.8 (CH), 41.0 (C), 36.5 (CH$_2$), 33.9 (CH$_2$), 28.3 (CH$_3$), 19.2 (CH$_3$). ATR-FTIR (thin film): 2947, 1730, 1579, 1223 cm$^{-1}$; HRMS (ESI) m/z calculated for C$_{17}$H$_{20}$NO$_2$ (M+H)$^+$: 270.1494, found: 270.1494;

Characterization data for indole 4.20c: $[\alpha]_D^{25}$: −12.4 (c 0.25, CH$_2$Cl$_2$); $^1$H NMR (500 MHz, CDCl$_3$) $\delta$ 8.17 (d, $J = 7.6$ Hz, 1H), 7.37 (d, $J = 7.7$ Hz, 1H), 7.25-7.20 (m, 2H), 4.03 (s, 3H), 3.26 (dd, $J = 18.0$ Hz, 2.9 Hz, 1H), 3.13 (dd, $J = 18.0$ Hz, 2.5 Hz, 1H), 2.97 (t, $J = 5.5$ Hz, 1H), 2.71 (dt, $J = 9.1$ Hz, 5.6 Hz, 1H), 2.41 (tt, $J = 5.8$ Hz, 2.9 Hz, 1H), 1.45 (s, 3H), 1.39 (d, $J = 9.1$ Hz, 1H), 0.71 (s, 3H); $^{13}$C NMR (125 MHz, CDCl$_3$) $\delta$ 152.5 (C), 135.7 (C), 132.6 (C), 128.9 (C), 127.4 (C), 123.0 (CH), 122.7 (CH), 117.4 (CH), 115.5 (CH), 53.3 (CH$_3$), 41.6 (CH), 40.9 (C), 38.3 (CH), 33.2 (CH$_2$), 31.4 (CH$_2$), 26.4 (CH$_3$), 21.1 (CH$_3$). ATR-FTIR (thin film): 2926, 2854, 1733, 1441, 1409 1216 cm$^{-1}$; HRMS (ESI) m/z calculated for C$_{17}$H$_{20}$NO$_2$ (M+H)$^+$: 270.1494, found: 270.1491.

(2R,4R,4aR)-methyl 3,3-dimethyl-6-methoxy-1,2,3,4-tetrahydro-4aH-2,4-methanocarbazole-4a-carboxy-late 4.19a and (2R,4R)-methyl 3,3-dimethyl-6-methoxy-1,2,3,4-tetrahydro-9H-2,4-methanocarbazole-9-carboxylate 4.20a. The general procedure was followed by using 0.0200 g of styryl azide 4.18a (0.060 mmol), 0.0023 g of Rh$_2$(esp)$_2$ (5 mol %) and 0.6 mL of toluene. Purification by MPLC (3:97 to 30:70 EtOAc:hexanes) afforded the products—yellow oils—as a 11:83 separable mixture of 4.19a and 4.20a in 94% yield overall. Selected peaks for 3H-indole from crude NMR 4.19a: $^1$H NMR (500 MHz, CDCl$_3$) $\delta$ 3.58 (CH$_3$); Characterization data
for indole 4.20a: \([\alpha]_D^{25} : -6.4 (c 0.125, \text{CH}_2\text{Cl}_2); \)\(^1\text{H NMR} (500 \text{ MHz, CDCl}_3) \delta 8.03 (d, J = 9.5 \text{ Hz, 1H}), 6.84 - 6.83 (m, 2H), 4.01 (s, 3H), 3.85 (s, 3H), 3.25 - 3.08 (m, 2H), 2.92 (t, J = 5.5 \text{ Hz, 1H}), 2.70 (dt, J = 9.0 \text{ Hz, 5.5 Hz, 1H}), 2.40 - 2.38 (m, 1H), 1.45 (s, 3H), 1.38 (d, J = 9.0 \text{ Hz, 1H}), 0.70 (s, 3H); \(^13\text{C NMR} (125 \text{ MHz, CDCl}_3) \delta 163.9 (C), 156.0 (C), 152.3 (C), 133.5 (C), 129.7 (C), 127.3 (C), 116.2 (CH), 111.2 (CH), 100.5 (CH), 55.7 (CH\(_3\)), 53.2 (CH\(_3\)), 41.6 (CH), 40.9 (C), 38.3 (CH), 33.2 (CH\(_2\)), 31.4 (CH\(_2\)), 26.4 (CH\(_3\)), 21.1 (CH\(_3\)). \ ATR-\text{FTIR} (\text{thin film}): 2932, 1729, 1460, 1441, 1369, 1216 \text{ cm}^{-1}; \ HRMS (ESI) m/z calculated for C\(_{18}\)H\(_{22}\)NO\(_3\) (M+H\(^+\)): 300.1600, found: 300.1598.

\[(2R,4R,4aR)-\text{methyl 3,3-dimethyl-7-methyl-1,2,3,4-tetrahydro-4aH-2,4-methano-carbazole-4a-carboxylate 4.19b and (2R,4R)-methyl 3,3-dimethyl-7-methyl-1,2,3,4-tetrahydro-9H-2,4-methanocarbazole-9-carboxylate 4.20b.}\]

The general procedure was followed by using 0.0421 g of styryl azide 4.18b (0.135 mmol), 0.0051 g of Rh\(_2\)(esp\(_2\)) (5 mol %) and 1.4 mL of toluene. Purification by MPLC (3:97 to 30:70 EtOAc:hexanes) afforded the products—yellow oil—as a 16:71 separable mixture of 4.19b and 4.20b in 87% yield overall. Selected peaks for 3\(H\)-indole from crude NMR 4.19b: \(^1\text{H NMR} (500 \text{ MHz, CDCl}_3) \delta 3.58 (\text{CH}_3), 1.36 (\text{CH}_3)\); Characterization data for indole 4.20b: \([\alpha]_D^{25} : -14.4 (c 0.25, \text{CH}_2\text{Cl}_2); \)\(^1\text{H NMR} (500 \text{ MHz, CDCl}_3) \delta 8.03 (d, J = 8.3 \text{ Hz, 1H}), 7.17 (s, 1H), 7.05 (d, J = 7.4 \text{ Hz, 1H}), 4.02 (s, 3H), 3.24 (dd, J = 18.0 \text{ Hz, 3.0 Hz, 1H}), 3.11 (dd, J = 18.0 \text{ Hz, 2.6 Hz, 1H}), 2.94 (t, J = 5.5 \text{ Hz, 1H}), 2.69 (dt, J = 9.1 \text{ Hz, 5.6 Hz, 1H}), 2.43 (s, 3H), 2.39 (tt, J = 5.8 \text{ Hz, 2.9 Hz, 1H}), 1.45 (s, 3H), 1.37 (d, J = 9.1 \text{ Hz, 1H}), 0.70 (s, 3H); \(^13\text{C NMR} (125 \text{ MHz, CDCl}_3) \delta 152.5 (C), 138.5 (C), 133.9 (C), 132.1 (C), 129.1 (C), 127.2 (C), 124.2 (CH), 117.5 (CH), 115.2 (CH), 53.2 (CH\(_3\)), 41.6 (CH), 40.9 (C), 38.3 (CH), 33.2 (CH\(_2\)), 31.4 (CH\(_2\)), 26.4 (CH\(_3\)), 21.4 (CH\(_3\)), 21.1 (CH\(_3\)). \ ATR-\text{FTIR} (\text{thin film}): 2923,
2866, 1731, 1441, 1399, 1216 cm⁻¹; HRMS (ESI) m/z calculated for C₁₈H₂₂NO₂ (M+H-N₂)⁺: 284.1651, found: 284.1653.

(2R,4R,4aR)-methyl 3,3-dimethyl-7-trifluoromethoxy-1,2,3,4-tetrahydro-4aH-2,4-methanocarbazole-4a-carboxylate 4.19d and (2R,4R)-methyl 3,3-dimethyl-7-trifluoromethoxy -1,2,3,4-tetrahydro-9H-2,4-methanocarbazole-9-carboxylate 4.20d. The general procedure was followed by using 0.0023 g of styryl azide 4.18d (0.060 mmol), 0.0023 g of Rh₂(esp)₂ (5 mol %) and 0.6 mL of toluene. Purification by MPLC (3:97 to 30:70 EtOAc:hexanes) afforded the products—yellow oils—as a 19:67 separable mixture of 4.19d and 4.20d in 86% yield overall. Selected peaks for 3H-indole from crude NMR 4.19d: ¹H NMR (500 MHz, CDCl₃) δ 3.60 (CH₃); Characterization data for indole 4.20d: [α]D²⁵: −14.4 (c 0.250, CH₂Cl₂); ¹H NMR (500 MHz, CDCl₃) δ 8.16 (d, J = 9.0 Hz, 1H), 7.19 (s, 1H), 7.08 (d, J = 9.0 Hz, 1H), 4.04 (s, 3H), 3.26 – 3.10 (m, 2H), 2.93 (t, J = 5.5 Hz, 1H), 2.71 (dt, J = 9.0 Hz, 5.5 Hz, 1H), 2.42 – 2.40 (m, 1H), 1.45 (s, 3H), 1.37 (d, J = 9.0 Hz, 1H), 0.70 (s, 3H); ¹³C NMR (125 MHz, CDCl₃) δ 152.1 (C), 145.1 (C), 134.7 (C), 133.8 (C), 129.5 (C), 127.2 (C), 120.7 (C, Jₐₛ = 254 Hz, CF₃), 116.2 (CH), 116.1 (CH), 109.8 (CH), 53.5 (CH₃), 41.4 (CH), 40.9 (C), 38.3 (CH), 33.1 (CH₂), 31.4 (CH₂), 26.3 (CH₃), 21.1 (CH₃). ATR-FTIR (thin film): 2933, 1736, 1457, 1442, 1365, 1248, 1213 cm⁻¹; HRMS (ESI) m/z calculated for C₁₈H₁₉NO₃F₃ (M+H-N₂)⁺: 354.1317, found: 354.1311.
D. Double Crossover Experiment

To a mixture of styryl azides 4.12e, 4.12i and Rh₂(esp)₂ (5 mol %) was added toluene (0.1M). The resulting mixture was heated at 120 °C. After 16 h, the mixture was cooled to room temperature, diluted with CH₂Cl₂ and concentrated in vacuo. Dibromomethane (0.7 µL, 0.1 mmol) was added, and the mixture was analyzed using ¹H NMR spectroscopy to determine the outcome of the reaction.

E. 3H-Indole stability toward Reaction Conditions

To a mixture of 3H-indole 4.19c (0.0095 g, 0.035 mmol) and Rh₂(esp)₂ (5 mol %) was added toluene (0.1M). The resulting mixture was heated at 140 °C. After 16 h, the mixture was cooled to room temperature, diluted with CH₂Cl₂ and concentrated in vacuo. Dibromomethane (0.7 µL, 0.1 mmol) was added, and the mixture was analyzed using ¹H NMR spectroscopy to determine the outcome of the reaction.
References


CHAPTER 5

Catalyst and Substrate Manipulation to Control Chemoselectivity of Electrocyclization and $\text{Sp}^3$ C–H Bond Amination from Styryl Azides
In Chapter 2-4, I have shown transition metal catalyzed tandem electrocyclization migration reaction to furnish polysubstituted indoles from styryl azides (Scheme 5.1). Exposure of azides to transition metals can trigger intramolecular 4π-electron-5-atom electrocyclization of the in-situ generated rhodium N-aryl nitrene to form the new carbon–nitrogen bond. Then one of the β-substituents participates in a [1,2]-shift. Release of the catalyst produces the indole product. Our studies indicated that the identity of migrating group as well as the steric environment controls the selectivity of the migration. In this chapter, my research focuses on exploring other possible mechanism for the transformation of styryl azides.

\[ \text{Scheme 5.1. Rh}_2(\text{II})\text{-catalyzed migration reaction to form trisubstituted indoles.} \]

Wondering how bond strength can influence reaction outcome, similar substrates with weaker α-allylic C–H bond were tested (Scheme 5.2). Despite of the facility for electrocyclization, styryl azides 5.5 and 5.8 upon exposure to reaction condition, were converted to 3-alkylidene indolines 5.6 and 5.9 in excellent yields. The tertiary sp\(^3\) C–H bond was activated without observation of any electrocyclization product 5.7 and 5.10 formation. We attribute the reactivity of the tertiary sp\(^3\) C–H bond to lower bond dissociation energy compared with the propensity of the rhodium N-aryl nitrene to engage with the ortho-alkenyl substituent in an electrocyclization. The distinctive results from substrates with similarity suggest
the existence of competition between sp$^3$ C-H bond amination and tandem electrocyclization migration reaction. In this case, tertiary sp$^3$ C-H bond amination is favored since lower activation energy is needed for the transformation. In line with this assumption, we wondered if secondary sp$^3$ C-H bond could be activated as well.

![Scheme 5.2. Rh$_2$(II)-catalyzed sp$^3$ C-H bond amination.](image-url)

Several substrates were made to test the selectivity between sp$^3$ C-H bond amination and electrocyclization (Table 5.1). First, we modified functionality on the ortho-substituents to lower activation energy by making weaker C-H bond. N-Boc group was incorporated in the ortho-alkenyl substituent on the $\beta$-allylic position to weaken $\alpha$-allylic C-H bond (entry 1). Submission of styryl azide 5.11a to reaction condition produced 3-alkylideneindoline 5.12a as the only product in moderate yield with some decomposition. Second, we made changes to the migrating groups. We anticipated that if the migration process becomes less accessible, secondary sp$^3$ C-H bond might have a chance to be activated. To our delight, when we modified the substrates by placing $\beta$-substituents that rank low in the migration aptitude scale, such as an alkyl-, aryl- or acyl group, which is geometrically constrained so it can not migrate to nitrogen, secondary C-H bond amination occurred (entries 2 and 3).
Styryl azides 5.11b and 5.11c can be efficiently converted to indole products after tautomerization. Changing the β-ester to an amide also forms the sp$^3$ C-H bond amination without any observed electrocyclization product, albeit with lower yield (entry 4).

### Table 5.1. Scope of Rh$_2$(II)-catalyzed sp$^3$ C–H bond amination.

<table>
<thead>
<tr>
<th>entry #</th>
<th>styryl azide 5.11</th>
<th>5.12 or 5.13</th>
<th>%, yield$^a$</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>a</td>
<td></td>
<td>48</td>
</tr>
<tr>
<td>2</td>
<td>b</td>
<td></td>
<td>84</td>
</tr>
<tr>
<td>3</td>
<td>c</td>
<td></td>
<td>85</td>
</tr>
<tr>
<td>4</td>
<td>d</td>
<td></td>
<td>26</td>
</tr>
</tbody>
</table>

$^a$ isolated yield after SiO$_2$ chromatography.

As expected, when the stress of migration was released by substituting β-position with hydrogen, electrocyclization yielded sp$^2$ C-H bond amination product exclusively (Scheme 5.3). Exposure of styryl azide 5.14 with β-H and β-acyl to rhodium carboxylate complex led to formation of tetrahydrocarbazol-1-one 5.15 in
excellent yield. When carbonyl group was removed, electrocyclization was still the only transformation despite of the presence of tertiary C–H bond to produce tetrahydrocarbazole 5.17 in a slightly reduced yield.

![Scheme 5.3. Rh$_2$(II)-catalyzed electrocyclization.](image)

The success of selective electrocyclization and sp$^3$ C–H bond amination suggests an approachable way to predict product by comparing facility of the two pathways. While sp$^3$ C–H bond amination favors weak C–H bond, electrocyclization would occur when migration is more feasible.

To gain insight into the electronic demands of the intermediates and see if catalyst could control the reaction outcome, a scaffold that undergoes both competitive pathways was designed to perform a Hammett analysis. We believed that we could produce a mixture of two products by balancing the sp$^3$ C–H bond strength and feasibility of electrocyclization. To our delight, submission of styryl azide 5.18 to rhodium complex yielded a mixture of electrocyclization migration product– 3H-indole 5.19 and sp$^3$ C–H bond amination product–alkylidene indoline 5.14c at a ratio of 73:27. However, the increasing steric environment and low potency for alkyl migration exerted negative impact on the reaction efficiency. The reaction only yielded products in 33% with lots of decomposition. To achieve a more efficient transformation, we modified the styryl azide by increasing reactivity of both pathways. As expected, styryl azide 5.21c with a weaker benzylic C–H bond and
less steric ortho-alkenyl substituent was converted smoothly in excellent yield. The ratio of electrocyclization product indole 5.22c and sp³ C–H bond amination alkylidene indoline 5.23c increased to 86:14. The selectivity and reactivity of the transformation attribute to the extremely facile electrocyclization with little steric environment and the presence of a reactive benzylic C–H bond.

![Scheme 5.4. Competition of electrocyclization and sp³ C–H bond amination.](image)

Then I decided to investigate the influence of transition metal on reaction outcome (Table 5.2). Styryl azide 5.21c was examined to screen a range of catalysts considering its efficient conversion in the initial trial. Thermolysis for azide 5.21c afforded mainly electrocyclization product 5.22c in 77% yield (entry 1). In comparison, the use of rhodium carboxylate complexes resulted in a higher ratio of sp³ C–H bond amination product at lower temperature in better yield (entry 2). First, we investigated the effect of changing the reaction temperature on the indole: 3H-indole ratio. Lowering the temperature had a small but quantifiable effect of increasing the ratio of indole 5.22c (entries 2-4). As a consequence, 120 °C was used for the catalyst screening. The effect of changing the identity of the carboxylate ligand was examined first. While Rh₂(O₂CC₇H₁₅)₄ converted 5.21c in a similar outcome with Rh₂(esp)₂, rhodium carboxylate with fluorinated ligand Rh₂(O₂CCF₃)₄ or Rh₂(O₂CCF₃)₄ led to less sp³ C–H bond amination and incomplete conversion (entries 5-7). Exposure of 5.21c to N-sulfone containing rhodium carboxylate Rh₂(S-
DOSP)₄ afforded the lowest ratio of electrocyclization versus sp³ C–H bond amination (entry 8). The use of a more rigid rhodium carboxamidate complex, Rh₂(cap)₄, however, produced more electrocyclization product compared to Rh₂(esp)₂ (entry 9). These results may suggest that sp³ C–H bond amination is favored by bulkier and less electron-withdrawing dirhodium complexes. Other transition metals were tested as well. While [Ir(cod)OMe]₂ transformed 5.21c to 5.22c as the only product (entry 10), RuCl₃ decomposed 5.21c without formation of either N-heterocycles (entry 11).

Next, the electronic nature of the substrate was modified to gain further insight into the mechanism for the two competitive transformations.¹⁰ First, substituents on the para-position of azides 5.21 were examined (Table 5.3). We believed that p-substituents R¹ could influence the electronic nature of azides and the formation of rhodium nitrene. The product ratio 5.22c:5.23c is plotted against Hammett αₚ values.

**Table 5.2. Condition screening for styryl azide 5.21c.**

<table>
<thead>
<tr>
<th>entry</th>
<th>MLₙ</th>
<th>°C, T</th>
<th>5.22c:5.23c</th>
<th>%, yield⁸</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>none⁵</td>
<td>220</td>
<td>98:2</td>
<td>77</td>
</tr>
<tr>
<td>2</td>
<td>Rh₂(esp)₂</td>
<td>140</td>
<td>86:14</td>
<td>93</td>
</tr>
<tr>
<td>3</td>
<td>Rh₂(esp)₂</td>
<td>120</td>
<td>87:13</td>
<td>95</td>
</tr>
<tr>
<td>4</td>
<td>Rh₂(esp)₂</td>
<td>100</td>
<td>88:12</td>
<td>88</td>
</tr>
<tr>
<td>5</td>
<td>Rh₂(O₂CCF₃)₄</td>
<td>120</td>
<td>98:2</td>
<td>66</td>
</tr>
<tr>
<td>6</td>
<td>Rh₂(O₂CC₃F₇)₄</td>
<td>120</td>
<td>84:6</td>
<td>50⁶</td>
</tr>
<tr>
<td>7</td>
<td>Rh₂(O₂CC₃H₁₅)₄</td>
<td>120</td>
<td>89:11</td>
<td>93</td>
</tr>
<tr>
<td>8</td>
<td>Rh₂(S-DOSP)₄</td>
<td>120</td>
<td>82:18</td>
<td>79</td>
</tr>
<tr>
<td>9</td>
<td>Rh₂(cap)₄</td>
<td>120</td>
<td>96:4</td>
<td>82</td>
</tr>
<tr>
<td>10</td>
<td>[Ir(cod)OMe]₂</td>
<td>120</td>
<td>100:0</td>
<td>84</td>
</tr>
<tr>
<td>11</td>
<td>RuCl₃</td>
<td>120</td>
<td>–</td>
<td>0</td>
</tr>
</tbody>
</table>

⁸ NMR yield determined by using CH₂Br₂ as internal standard. ⁵ used mesitylene as solvent. ⁶ only 81% conversion of starting material.
shown in Figure 5.1. The V-shaped Hammett plot for R\(^1\) on styryl azides suggests a change in mechanism or rate-determining step for electrocyclization because of the opposite ρ value for the two lines. Styryl azides 5.21 with both electron donating and withdrawing group afforded higher ratio of electrocyclization product 5.22.

**Table 5.3.** Effect of R\(^1\) substituents on reaction outcome.

<table>
<thead>
<tr>
<th>entry</th>
<th>#</th>
<th>R</th>
<th>ρ</th>
<th>5.22: 5.23</th>
<th>%, yield(^a)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>a</td>
<td>OMe</td>
<td>-0.27</td>
<td>92 : 8</td>
<td>78</td>
</tr>
<tr>
<td>2</td>
<td>b</td>
<td>Me</td>
<td>-0.17</td>
<td>88 : 12</td>
<td>79</td>
</tr>
<tr>
<td>3</td>
<td>c</td>
<td>H</td>
<td>0</td>
<td>85 : 15</td>
<td>84</td>
</tr>
<tr>
<td>4</td>
<td>d</td>
<td>F</td>
<td>0.06</td>
<td>83 : 17</td>
<td>92</td>
</tr>
<tr>
<td>5</td>
<td>e</td>
<td>Cl</td>
<td>0.23</td>
<td>87 : 13</td>
<td>76</td>
</tr>
<tr>
<td>6</td>
<td>f</td>
<td>OCF(_3)</td>
<td>0.35</td>
<td>91 : 9</td>
<td>80</td>
</tr>
</tbody>
</table>

\(^a\) NMR yield determined by using CH\(_2\)Br\(_2\) as internal standard.
Figure 5.1. Correlation of $\log(k_{\text{electro.}}/k_{\text{sp3}})$ of Rh$_2$(II) catalyzed C–H amination of 5.21 with $\sigma_p$ values in the Hammett equation.

Second, the electronic nature of the benzylic sp$^3$ C–H bond was examined by changing the identity of aryl group (Table 5.4). We assumed that para-substituents on aryl group could only influence the reactivity of the benzylic C–H bond without changing the electronic nature of the alkene, thus laying little impact on the rate of electrocyclization. Despite of the inconspicuous difference, the ratio 5.23': 5.22' was plotted against Hammett $\sigma_p$ values (Figure 5.2). As before, a V-shaped plot was obtained. Since both electron-releasing and electron-withdrawing group can stabilize radicals, the V-shaped Hammett plot suggests a radical mechanism with H atom abstraction involved.$^{13}$
Table 5.4 Effect of R² substituents on reaction outcome.

Table 5.4 Effect of R² substituents on reaction outcome.

<table>
<thead>
<tr>
<th>entry</th>
<th>#</th>
<th>R</th>
<th>σ_p</th>
<th>5.23': 5.22'</th>
<th>%, yield&lt;sup&gt;a&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>a</td>
<td>OMe</td>
<td>-0.27</td>
<td>20 : 80</td>
<td>83</td>
</tr>
<tr>
<td>2</td>
<td>b</td>
<td>Me</td>
<td>-0.17</td>
<td>16 : 84</td>
<td>94</td>
</tr>
<tr>
<td>3</td>
<td>c</td>
<td>H</td>
<td>0</td>
<td>15 : 85</td>
<td>84</td>
</tr>
<tr>
<td>4</td>
<td>d</td>
<td>Cl</td>
<td>0.23</td>
<td>20 : 80</td>
<td>52&lt;sup&gt;b&lt;/sup&gt;</td>
</tr>
<tr>
<td>5</td>
<td>E</td>
<td>CF₃</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<sup>a</sup> NMR yield determined by using CH₂Br₂ as internal standard. <sup>b</sup> only 81% conversion of starting material.

Figure 5.2. Correlation of log(k<sub>electro</sub>/k<sub>sp3</sub>) of Rh₂(II) catalyzed C–H amination of 5.21' with σ_p values in the Hammett equation.

Failure of catalyst manipulation to inverse reaction preference for styryl azide 5.21c can be rationalized by the accelerated electrocyclization with the presence of the more accessible and less electron-donating environment of the double bond.¹⁴
We believed that reducing the electron density in the alkenyl substituent might slow electrocyclization and accelerate sp\textsuperscript{3} C–H amination. Holding this thought in mind, to further investigate the influence of catalysts on reaction outcome, a styryl azide \textbf{5.24} with one β-H, one acyl group and a tertiary sp\textsuperscript{3} C–H bond was designed and used for condition screening (Table 5.5). Submission of \textbf{5.24} to Rh\textsubscript{2}(esp)\textsubscript{2} produced a mixture of electrocyclization and sp\textsuperscript{3} C–H amination products at a ratio of 62:38 in excellent yield (entry 2), while in the absence of catalyst, \textbf{5.24} afforded 94:6 of \textbf{5.25}: \textbf{5.26} for only 15% yield (entry 1). Both efficiency for the reaction and selectivity for sp\textsuperscript{3} C–H amination were promoted by ligating the free nitrene with rhodium carboxylate. Consistent with the results from catalyst screening for \textbf{5.21c}, other alkyl carboxylate Rh\textsubscript{2}(II)-complexes—Rh\textsubscript{2}(O\textsubscript{2}CC\textsubscript{7}H\textsubscript{15})\textsubscript{4}, Rh\textsubscript{2}(S-DOSP)\textsubscript{4} and Rh\textsubscript{2}(cap)\textsubscript{4}—showed similar reactivity trends for \textbf{5.24} transformation (entries 3-6). In our effort to turn over the selectivity of the two pathways, the use of Rh\textsubscript{2}(S-PTAD)\textsubscript{4} afforded a mixture of products at 20:80 with sp\textsuperscript{3} C–H bond amination product \textbf{5.20} as the major product (entry 7). With this promising result in hand, I screened different solvents and additives to change the polarity of the reaction media (entries 13–15). Unfortunately none of these modifications significantly improved the amount of sp\textsuperscript{3} C–H bond amination. The ratio of indole \textbf{5.25} to 3H-indole \textbf{5.26} increased from 18:82 to 26:74 when lower catalyst loadings were surveyed (entries 8 and 9). Lowering the temperature had an opposite slight effect of attenuating the ratio of \textbf{5.25}:\textbf{5.26} to 17:83 (entries 7–10).

\textbf{Table 5.5.} Rhodium carboxylate screening for styryl azide \textbf{5.24}.

<table>
<thead>
<tr>
<th>entry</th>
<th>ML\textsubscript{n}</th>
<th>Mol%</th>
<th>°C, T</th>
<th>solvent</th>
<th>\textbf{5.25}: \textbf{5.26}</th>
<th>%, yield\textsuperscript{a}</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>none</td>
<td>–</td>
<td>125</td>
<td>Tol</td>
<td>94 : 6</td>
<td>15</td>
</tr>
<tr>
<td>2</td>
<td>Rh\textsubscript{2}(esp)\textsubscript{2}</td>
<td>5</td>
<td>120</td>
<td>Tol</td>
<td>62 : 38</td>
<td>91</td>
</tr>
<tr>
<td>Entry</td>
<td>Catalyst</td>
<td>Loading</td>
<td>Solvent</td>
<td>Yield</td>
<td>Conversion</td>
<td></td>
</tr>
<tr>
<td>-------</td>
<td>----------</td>
<td>---------</td>
<td>---------</td>
<td>-------</td>
<td>------------</td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>Rh₂(esp)₂</td>
<td>5</td>
<td>Tol</td>
<td>63 : 37</td>
<td>90</td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>Rh₂(O₂CC₇H₁₅)₄</td>
<td>5</td>
<td>Tol</td>
<td>68 : 32</td>
<td>78</td>
<td></td>
</tr>
<tr>
<td>5</td>
<td>Rh₂(S-DOSP)₄</td>
<td>5</td>
<td>Tol</td>
<td>44 : 56</td>
<td>64&lt;sup&gt;c&lt;/sup&gt;</td>
<td></td>
</tr>
<tr>
<td>6</td>
<td>Rh₂(cap)₄</td>
<td>5</td>
<td>Tol</td>
<td>91 : 9</td>
<td>73</td>
<td></td>
</tr>
<tr>
<td>7</td>
<td>Rh₂(S-PTAD)₄</td>
<td>5</td>
<td>Tol</td>
<td>20 : 80</td>
<td>84</td>
<td></td>
</tr>
<tr>
<td>8</td>
<td>Rh₂(S-PTAD)₄</td>
<td>5</td>
<td>Tol</td>
<td>18 : 82</td>
<td>85</td>
<td></td>
</tr>
<tr>
<td>9</td>
<td>Rh₂(S-PTAD)₄</td>
<td>2</td>
<td>Tol</td>
<td>26 : 74</td>
<td>57&lt;sup&gt;d&lt;/sup&gt;</td>
<td></td>
</tr>
<tr>
<td>10</td>
<td>Rh₂(S-PTAD)₄</td>
<td>5</td>
<td>Tol</td>
<td>17 : 83</td>
<td>61&lt;sup&gt;e&lt;/sup&gt;</td>
<td></td>
</tr>
<tr>
<td>11</td>
<td>Rh₂(S-PTAD)₄</td>
<td>2</td>
<td>Tol+BzEt₃NCl</td>
<td>26 : 74</td>
<td>74</td>
<td></td>
</tr>
<tr>
<td>12</td>
<td>Rh₂(S-PTAD)₄</td>
<td>2</td>
<td>Tol&lt;sup&gt;b&lt;/sup&gt;+BzEt₃NCl</td>
<td>20 : 80</td>
<td>72.5</td>
<td></td>
</tr>
<tr>
<td>13</td>
<td>Rh₂(S-PTAD)₄</td>
<td>5</td>
<td>Tol&lt;sup&gt;b&lt;/sup&gt;+BzEt₃NCl</td>
<td>17 : 83</td>
<td>81</td>
<td></td>
</tr>
<tr>
<td>14</td>
<td>Rh₂(S-PTAD)₄</td>
<td>5</td>
<td>DCE</td>
<td>19 : 81</td>
<td>86</td>
<td></td>
</tr>
<tr>
<td>15</td>
<td>Rh₂(S-PTAD)₄</td>
<td>5</td>
<td>DMSO-d6</td>
<td>–</td>
<td>0&lt;sup&gt;f&lt;/sup&gt;</td>
<td></td>
</tr>
</tbody>
</table>

<sup>a</sup> NMR yield determined by using CH₂Br₂ as internal standard. <sup>b</sup> 100wt% 4 Å MS was added to the reaction. <sup>c</sup> only 84% conversion of starting material. <sup>d</sup> only 80% conversion of starting material. <sup>e</sup> only 72% conversion of starting material.

Other established atom-transfer catalysts were tested as well (Table 5.6). First, I tested [Ir(cod)OMe]₂, FeBr₂, and FeBr₃ since our previous investigations had established their potency to trigger N-heterocycle formation from aryl azides (entries 1–3). The use of these catalysts, however, afforded the electrocyclization product 5.25 as the only product. Next, I screened cobalt porphyrin complexes because they have a rich history as catalysts for both nitrene- and carbene transfer reactions (entries 4–6). These complexes are typically used in acetonitrile as the reaction media. Using these conditions, neither of the desired products was observed (entry 4). Changing solvent to dichloroethane afforded a mixture of products at a ratio of 22:78 (entry 5). Cobalt with more electron-rich octaethylporphyrin ligand increased the ratio to 11:89 albeit with only 28% conversion of the starting material (entry 6). Next, iron(III) porphyrin complexes were examined. To our delight, FeTPP(Cl) promoted the formation of indoline 5.26 with a higher ratio (entry 9). Lowering the temperature of the reaction revealed that the ratio of indoline 5.26 could be improved slightly (entries 7–10). When AgBF₄ was added to Fe(TPP)Cl, the reaction rate was retarded and a lower ratio for 5.26:5.25 was obtained (entries 11 and 12). The result suggests that a more positive iron center leads to less sp³ C–H bond amination process. So next, I examined the effect of changing the electronic nature...
of the porphyrin ligand on the ratio of $N$-heterocyclic products. Consistent with the result from entry 11, the use of the electron-poor Fe(TPFPP)Cl as catalyst significantly reduced the ratio of indoline from 10:90 to 23:77 (entry 13). Increasing the electron density on the porphyrin by using Fe(TOMePP)Cl improved the ratio to 6:94 (entry 14). Further increasing the electron density by using Fe(OEP)Cl produced sp$^3$ C–H bond amination product 5.26 in 76% yield with only trace of 5.25 formation (entry 15). Together with our results using Rh$_2$(II)-carboxylate complexes, these data reveal that increasing the electron richness of the nitrene-transfer complex promotes sp$^3$ C–H bond amination to enable chemoselectivity between two possible reaction sites.

Table 5.6. Catalyst screening for styryl azide 5.24.

<table>
<thead>
<tr>
<th>entry</th>
<th>ML$_n$</th>
<th>Mol%</th>
<th>°C, T</th>
<th>solvent</th>
<th>5.25 : 5.26</th>
<th>%, yield$^a$</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>[Ir(cod)OMe]$_2$</td>
<td>5</td>
<td>110</td>
<td>Tol</td>
<td>100 : 0</td>
<td>88</td>
</tr>
<tr>
<td>2</td>
<td>FeBr$_2$</td>
<td>20</td>
<td>110</td>
<td>Tol$^b$</td>
<td>100 : 0</td>
<td>84</td>
</tr>
<tr>
<td>3</td>
<td>FeBr$_3$</td>
<td>20</td>
<td>110</td>
<td>Tol$^b$</td>
<td>100 : 0</td>
<td>41</td>
</tr>
<tr>
<td>4</td>
<td>CoTPP</td>
<td>2</td>
<td>90</td>
<td>MeCN$^b$</td>
<td>–</td>
<td>0</td>
</tr>
<tr>
<td>5</td>
<td>CoTPP</td>
<td>2</td>
<td>100</td>
<td>DCE$^b$</td>
<td>22 : 78</td>
<td>68</td>
</tr>
<tr>
<td>6</td>
<td>CoOEP</td>
<td>2</td>
<td>100</td>
<td>DCE$^b$</td>
<td>11 : 89</td>
<td>18$^c$</td>
</tr>
<tr>
<td>7</td>
<td>Fe(TPP)Cl</td>
<td>2</td>
<td>90</td>
<td>DCE$^b$</td>
<td>6 : 94</td>
<td>47</td>
</tr>
<tr>
<td>8</td>
<td>Fe(TPP)Cl</td>
<td>2</td>
<td>100</td>
<td>DCE$^b$</td>
<td>7 : 93</td>
<td>52</td>
</tr>
<tr>
<td>9</td>
<td>Fe(TPP)Cl</td>
<td>2</td>
<td>110</td>
<td>DCE$^b$</td>
<td>10 : 90</td>
<td>48.5</td>
</tr>
<tr>
<td>10</td>
<td>Fe(TPP)Cl</td>
<td>2</td>
<td>125</td>
<td>DCE$^b$</td>
<td>12 : 88</td>
<td>52</td>
</tr>
<tr>
<td>11</td>
<td>Fe(TPP)Cl</td>
<td>2</td>
<td>100</td>
<td>DCE$^b$ +AgBF$_4$</td>
<td>13 : 87</td>
<td>30</td>
</tr>
<tr>
<td>12</td>
<td>none</td>
<td>100</td>
<td>100</td>
<td>DCE$^b$ +AgBF$_4$</td>
<td>–</td>
<td>0</td>
</tr>
<tr>
<td>13</td>
<td>Fe(TPFPP)Cl</td>
<td>2</td>
<td>110</td>
<td>DCE$^b$</td>
<td>23 : 77</td>
<td>72</td>
</tr>
<tr>
<td>14</td>
<td>Fe(TOMePP)Cl</td>
<td>2</td>
<td>100</td>
<td>DCE$^b$</td>
<td>6 : 94</td>
<td>52</td>
</tr>
<tr>
<td>15</td>
<td>Fe(OEP)Cl</td>
<td>2</td>
<td>100</td>
<td>DCE$^b$</td>
<td>2 : 98</td>
<td>77</td>
</tr>
</tbody>
</table>

$^a$ NMR yield determined by using CH$_2$Br$_2$ as internal standard. $^b$ 100wt% 4 Å MS was added to the reaction. $^c$ only 28% conversion of starting material.
In this chapter, I investigated how to control the metal N-aryl nitrene participation in an electrocyclization or a sp$^3$ C–H bond amination. My results reveal that the resistance of sp$^3$ C–H bond amination can be overcome by weakening the sp$^3$ C–H bond or increasing the difficulty of the electrocyclization reaction. For substrates with competitive pathways, reaction outcome can be manipulated by reaction conditions. While [Ir(cod)OMe]$_2$ and FeBr$_2$ can produce only electrocyclization product, Fe(OEP)Cl favors sp$^3$ C–H bond amination. Mechanism study suggests a radical pathway for sp$^3$ C–H bond amination and rate-determining step change when electronic nature is altered in electrocyclization.
Experimental

A. General. ¹H NMR and ¹³C NMR spectra were recorded at ambient temperature using 500 MHz or 300 MHz spectrometers. The data are reported as follows: chemical shift in ppm from internal tetramethylsilane on the d scale, multiplicity (br = broad, s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet), coupling constants (Hz) and integration. High-resolution mass spectra were obtained by peak matching. Melting points are reported uncorrected. Analytical thin layer chromatography was performed on 0.25 mm silica gel plates with UV254 fluorescent indicator. Liquid chromatography was performed using forced flow (flash chromatography) of the indicated solvent system on 60Å (40 – 60 μm) mesh silica gel (SiO₂). Medium pressure liquid chromatography (MPLC) was performed using pumps to force flow the indicated solvent system down columns that had been packed with 60Å (40 – 60 μm) mesh silica gel (SiO₂). All reactions were carried out under an atmosphere of nitrogen in glassware that was oven-dried. Unless otherwise noted, all reagents were commercially obtained and, where appropriate, purified prior to use. Acetonitrile, methanol, toluene, THF, Et₂O, and CH₂Cl₂ were dried by filtration through alumina according to the procedure of Grubbs. Metal salts were stored in a nitrogen atmosphere dry box.

B. Suzuki Cross-Coupling to Prepare Styryl Azides

\[
\begin{align*}
\text{R} & \quad \text{Bpin} \\ 5.27 \\
\text{E} & \quad \text{R} \\ 5.28 \\
\text{Pd(PPh₃)₄, NaHCO₃} & \quad \text{H₂O, DME, 100 °C} \\
\text{H₂O, DME, 100 °C} \\
\text{R} & \quad \text{E} \\ 5.11
\end{align*}
\]

To a mixture of vinyl triflate 5.28 (1 equiv), 2-azidoarylboronic acid pinacol ester 5.27 (1.1 equiv), and Pd(PPh₃)₄ (10 mol %) in dimethoxyethane (0.1 M) was added a saturated solution of NaHCO₃ (2 mL/mmol of boronic ester). The resulting mixture was heated to 100 °C. After 1 h, the mixture was cooled to room temperature and diluted with 5 mL of cold water. The solution was extracted with 2 × 10 mL of ether
followed by 10 mL of brine. The resulting organic phase was dried over Na₂SO₄ and was concentrated in *vacuo*. Purification by MPLC (3:97 to 50:50 EtOAc: hexane) afforded the product 5.11.

![Styryl azide 5.5a](image)

**Styryl azide 5.5a.** The general procedure was followed by using 0.164 g of 2-azidophenyl boronate 5.21 (0.67 mmol), 0.209 g of vinyl triflate 5.22a (0.61 mmol), 0.076 g of Pd(PPh₃)₄ (0.06 mmol), 1.2 mL of saturated aq. soln. of NaHCO₃ and 10 mL of dimethoxyethane. Purification by MPLC (3:97 to 10:90 EtOAc: hexane) afforded the product as yellow oil (0.106 g, 56%): ¹H NMR (500 MHz, CDCl₃) δ 7.27 (t, J = 6.6 Hz, 1H), 7.07 (m, 3H), 3.79 (s, 0.64 H), 3.36 (s, 2.34H), 2.67 (s, 1H), 1.67 (m, 2H), 1.57 (m, 2H), 1.28 (d, J = 6.9 Hz, 1H), 1.21 (d, J = 6.9 Hz, 2H), 1.06 (d, J = 6.9 Hz, 1H), 1.00 (d, J = 6.9 Hz, 1H), 0.86 (d, J = 6.8 Hz, 4H), 0.75 (d, J = 6.8 Hz, 2H); ¹³C NMR (125 MHz, CDCl₃) δ 169.8 (C), 144.3 (C), 136.5 (C), 132.9 (C), 131.0 (CH), 128.2 (CH), 124.7 (C), 123.9 (CH), 118.1 (CH), 51.1 (CH₃), 44.0 (CH), 30.6 (CH), 28.7 (CH₂), 28.3 (CH), 21.2 (CH₃), 20.4 (CH₃), 17.0 (CH₂), 16.6 (CH₃).

![Styryl azide 5.8](image)

**Styryl azide 5.8.** The general procedure was followed by using 0.107 g of 2-azidophenyl boronate 5.28 (0.44 mmol), 0.114 g of vinyl triflate (0.40 mmol), 0.0462 g of Pd(PPh₃)₄ (0.04 mmol), 0.8 mL of saturated aq. soln. of NaHCO₃ and 4 mL of dimethoxyethane. Purification by MPLC (3:97 to 10:90 EtOAc: hexane) afforded the product as colorless oil (0.07 g, 70%) as a 79: 21 mixture of *E* and *Z* isomer. Spectrum for major product: ¹H NMR (500 MHz, CDCl₃) δ 7.34 (td, J = 7.7 Hz, 1.2 Hz, 1H), 7.20 (d, J = 7.9 Hz, 1H), 7.14 (t, J = 7.5 Hz, 1H), 6.96 (dd, J = 7.6 Hz, 1.3
Hz, 1H), 4.34 (hept, J = 6.9 Hz, 1H), 2.38 (q, J = 8.0 Hz, 2H), 2.34 (dt, J = 16.2 Hz, 7.9 Hz, 1H), 2.09 (dd, J = 15.3 Hz, 9.1 Hz, 1H), 1.81 (td, J = 12.4 Hz, 5.2 Hz, 1H), 1.75 (dd, J = 13.9 Hz, 6.1 Hz, 1H), 1.02 (d, J = 6.9 Hz, 3H), 0.85 (d, J = 6.9 Hz, 3H); $^{13}$C NMR (125 MHz, CDCl$_3$) δ 208.0 (C), 154.8 (C), 136.9 (C), 133.0 (C), 131.2 (C), 128.9 (CH), 128.6 (CH), 124.6 (CH), 118.4 (CH), 41.1 (CH$_2$), 30.9 (CH$_2$), 28.5 (CH), 21.8 (CH$_3$), 20.3 (CH$_3$), 19.6 (CH$_2$).

Styryl azide 5.11a. The general procedure was followed by using 0.094 g of 2-azidophenyl boronate 5.28 (0.38 mmol), 0.130 g of vinyl triflate 5.27a (0.34 mmol), 0.040 g of Pd(PPh$_3$)$_4$ (0.03 mmol), 0.6 mL of saturated aq. soln. of NaHCO$_3$ and 5 mL of dimethoxyethane. Purification by MPLC (10:90 to 50:50 EtOAc: hexane) afforded the product as yellow oil (0.079 g, 66%). $^1$H NMR (500 MHz, CDCl$_3$) δ 7.30 (t, J = 7.7 Hz, 1H), 7.17 (d, J = 7.6 Hz, 1H), 7.13 (d, J = 8.0 Hz, 1H), 7.07 (t, J = 7.5 Hz, 1H), 3.97 (t, J = 9.2 Hz, 2H), 3.65 (s, 3H), 2.99 (t, J = 9.2 Hz, 2H), 1.44 (s, 9H); $^{13}$C NMR (125 MHz, CDCl$_3$) δ 171.1 (C), 163.3 (C), 152.2 (C), 137.8 (C), 132.2 (C), 129.9 (CH), 129.2 (CH), 126.2 (C), 124.6 (CH), 118.5 (CH), 81.3 (C), 52.0 (CH$_3$), 47.4 (CH$_2$), 33.4 (CH$_2$), 28.2 (CH$_3$).

Styryl azide 5.11b. The general procedure was followed by using 0.104 g of 2-azidophenyl boronate 5.28 (0.42 mmol), 0.123 g of vinyl triflate 5.27b (0.38 mmol), 0.048 g of Pd(PPh$_3$)$_4$ (0.04 mmol), 0.8 mL of saturated aq. soln. of NaHCO$_3$ and 4 mL of dimethoxyethane. Purification by MPLC (10:90 to 50:50 EtOAc: hexane) afforded the product as yellow oil (0.075 g, 68%). $^1$H NMR (500 MHz, CDCl$_3$) δ 7.18
(t, J = 7.7 Hz, 1H), 7.11 (m, 3H), 7.03 (d, J = 8.0 Hz, 1H), 6.95 (d, J = 7.2 Hz, 2H), 6.91 (d, J = 7.4 Hz, 1H), 6.87 (d, J = 7.5 Hz, 1H), 2.82 (s, 1H), 2.69 (t, J = 6.5 Hz, 3H), 2.24 (s, 2H); 13C NMR (125 MHz, CDCl3) δ 198.1 (C), 156.2 (C), 139.2 (C), 136.7 (C), 135.3 (C), 133.0 (C), 130.1 (CH), 129.4 (CH), 129.0 (CH), 127.4 (CH), 126.9 (CH), 124.6 (CH), 118.3 (CH), 38.4 (CH2), 32.7 (CH2), 22.7 (CH2).

5.11c

Styryl azide 5.11c. The general procedure was followed by using 0.200 g of 2-azidophenyl boronate 5.28 (0.82 mmol), 0.191 g of vinyl triflate 5.27c (0.74 mmol), 0.085 g of Pd(PPh3)4 (0.07 mmol), 1.5 mL of saturated aq. soln. of NaHCO3 and 10 mL of dimethoxyethane. Purification by MPLC (10:90 to 50:50 EtOAc: hexane) afforded the product as yellow oil (0.096 g, 57%): 1H NMR (500 MHz, CDCl3) δ 7.36 (t, J = 7.7 Hz, 1H), 7.20 (d, J = 7.9 Hz, 1H), 7.16 (d, J = 7.5 Hz, 1H), 7.04 (dd, J = 7.6 Hz, 1.2 Hz, 1H), 2.61-2.43 (m, 4H), 2.09 (m, 2H), 1.56 (s, 3H); 13C NMR (125 MHz, CDCl3) δ 199.5 (C), 153.9 (C), 136.4 (C), 133.3 (C), 133.0 (C), 129.1 (CH), 128.5 (CH), 125.0 (CH), 118.7 (CH), 37.9 (CH2), 32.4 (CH2), 22.8 (CH2), 12.7 (CH3).

5.11d

Styryl azide 5.11d. The general procedure was followed by using 0.176 g of 2-azidophenyl boronate 5.28 (0.70 mmol), 0.227 g of vinyl triflate 5.27d (0.65 mmol), 0.075 g of Pd(PPh3)4 (0.07 mmol), 1.3 mL of saturated aq. soln. of NaHCO3 and 10 mL of dimethoxyethane. Purification by MPLC (10:90 to 80:20 EtOAc: hexane) afforded the product as yellow oil (0.200 g, 98%): 1H NMR (500 MHz, CDCl3) δ 7.28
Styryl azide 5.14. The general procedure was followed by using 0.200 g of 2-azidophenyl boronate 5.28 (0.82 mmol), 0.181 g of vinyl triflate 5.27e (0.74 mmol), 0.043 g of Pd(PPh₃)₄ (0.04 mmol), 1.5 mL of saturated aq. soln. of NaHCO₃ and 15 mL of dimethoxyethane. Purification by MPLC (3:97 to 10:90 EtOAc: hexane) afforded the product as orange oil (0.117 g, 74%): ¹H NMR (500 MHz, CDCl₃) δ 7.38 (t, J = 7.7 Hz, 1H), 7.18 (d, J = 4.0 Hz, 2H), 7.14 (d, J = 7.5 Hz, 1H), 6.07 (s, 1H), 2.69 (t, J = 5.9 Hz, 2H), 2.47 (t, J = 6.7 Hz, 2H), 2.11 (quintet, J = 6.4 Hz, 2H); ¹³C NMR (125 MHz, CDCl₃) δ 199.5 (C), 160.4 (C), 137.0 (C), 132.6 (C), 130.1 (CH), 129.1 (C), 129.0 (CH), 125.0 (CH), 118.8 (CH), 37.4 (CH₂), 30.4 (CH₂), 23.2 (CH₂).

Styryl azide 5.16. The general procedure was followed by using 0.245 g of 2-azidophenyl boronate 5.28 (0.10 mmol), 0.222 g of vinyl triflate 5.27f (0.91 mmol), 0.105 g of Pd(PPh₃)₄ (0.09 mmol), 2 mL of saturated aq. soln. of NaHCO₃ and 15 mL of dimethoxyethane. Purification by MPLC (3:97 to 10:90 EtOAc: hexane) afforded the product as colorless oil (0.112 g, 58%): ¹H NMR (500 MHz, CDCl₃) δ 7.28 (t, J = 8.3 Hz, 1H), 7.11 (t, J = 9.6 Hz, 3H), 5.63 (s, 1H), 2.78 (d, J = 6.6 Hz, 1H), 2.18 (t, J = 3.0 Hz, 2H), 1.95 (m, 1H), 1.77 (m, 1H), 1.68 (m, 1H), 1.47 (m, 1H), 0.84 (d, J =
7.1 Hz, 3H); $^{13}$C NMR (125 MHz, CDCl$_3$) $\delta$ 141.5 (C), 137.1 (C), 136.0 (C), 130.8 (CH), 127.8 (CH), 127.6 (CH), 124.6 (CH), 118.4 (CH), 32.2 (CH), 31.4 (CH$_2$), 25.9 (CH$_2$), 20.0 (CH$_3$), 19.9 (CH$_2$).

**Styryl azide 5.18.** The general procedure was followed by using 0.213 g of 2-azidophenyl boronate 5.28 (0.87 mmol), 0.195 g of vinyl triflate 5.27g (0.79 mmol), 0.091 g of Pd(PPh$_3$)$_4$ (0.08 mmol), 1.6 mL of saturated aq. soln. of NaHCO$_3$ and 10 mL of dimethoxyethane. Purification by MPLC (3:97 to 10:90 EtOAc: hexane) afforded the product as colorless oil (0.153 g, 90%): $^1$H NMR (500 MHz, CDCl$_3$) $\delta$ 7.29 (td, $J = 7.7$ Hz, 1.4 Hz, 1H), 7.15 (d, $J = 8.0$ Hz, 1H), 7.11 (t, $J = 7.5$ Hz, 1H), 6.98 (dd, $J = 7.6$ Hz, 1.5 Hz, 1H), 3.08 (heptet, $J = 6.9$ Hz, 1H), 1.87 (s, 3H), 1.40 (s, 3H), 1.01 (d, $J = 7.0$ Hz, 3H), 0.86 (d, $J = 6.9$ Hz, 3H); $^{13}$C NMR (125 MHz, CDCl$_3$) $\delta$ 138.4 (C), 136.1 (C), 133.6 (C), 131.6 (CH), 128.5 (CH), 127.6 (C), 124.2 (CH), 118.4 (CH), 30.5 (CH), 22.3 (CH$_3$), 20.7 (CH$_3$), 19.4 (CH$_3$).

**Styryl azide 5.21c.** The general procedure was followed by using 0.381 g of 2-azidophenyl boronate 5.28 (1.55 mmol), 0.396 g of vinyl triflate 5.27h (1.4 mmol), 0.174 g of Pd(PPh$_3$)$_4$ (0.14 mmol), 3 mL of saturated aq. soln. of NaHCO$_3$ and 15 mL of dimethoxyethane. Purification by MPLC (3:97 to 10:90 EtOAc: hexane) afforded the product as colorless oil (0.244 g, 69%): $^1$H NMR (500 MHz, CDCl$_3$) $\delta$ 7.31 (m, 5H), 7.24 (tt, $J = 6.9$ Hz, 1.9 Hz, 1H), 7.17 (dd, $J = 8.0$ Hz, 0.6 Hz, 1H), 7.03 (m, 2H), 5.30 (s, 1H), 5.16 (s, 1H), 4.09 (q, $J = 7.1$ Hz, 1H), 1.54 (d, $J = 7.1$ Hz, 3H); $^{13}$C NMR (125 MHz, CDCl$_3$) $\delta$ 151.9 (C), 144.4 (C), 137.1 (C), 135.4 (C), 131.0 (CH), 128.4
(CH), 128.3 (CH), 128.0 (CH), 126.3 (CH), 124.5 (CH), 118.3 (CH), 115.0 (CH₂), 45.3 (CH), 20.5 (CH₃).

Styryl azide 5.21b. The general procedure was followed by using 0.058 g of 2-azidophenyl boronate 5.27b (0.22 mmol), 0.068 g of vinyl triflate 5.27h (0.20 mmol), 0.025 g of Pd(PPh₃)₄ (0.02 mmol), 0.4 mL of saturated aq. soln. of NaHCO₃ and 8 mL of dimethoxyethane. Purification by MPLC (3:97 to 10:90 EtOAc: hexane) afforded the product as yellow oil (0.046 g, 72%): ¹H NMR (500 MHz, CDCl₃) δ 7.27 (t, J=7.4 Hz, 2H), 7.23 (d, J = 6.9 Hz, 2H), 7.18 (t, J = 7.1 Hz, 1H), 7.05 (t, J = 7.6 Hz, 1H), 7.00 (d, J = 8.1 Hz, 1H), 6.76 (s, 1H), 5.16 (s, 1H), 5.05 (s, 1H), 3.99 (q, J = 7.1 Hz, 3H); ¹³C NMR (125 MHz, CDCl₃) δ 152.0 (C), 144.4 (C), 134.1 (C), 132.1 (C), 131.5 (CH), 130.0 (C), 129.0 (CH), 128.2 (CH), 127.9 (CH), 126.2 (CH), 118.1 (CH), 114.8 (CH₂), 45.1 (CH), 20.8 (CH₃), 20.4 (CH₃).

Styryl azide 5.21e. The general procedure was followed by using 0.160 g of 2-azidophenyl boronate 5.27e (0.57 mmol), 0.164 g of vinyl triflate 5.27h (0.52 mmol), 0.065 g of Pd(PPh₃)₄ (0.05 mmol), 1.0 mL of saturated aq. soln. of NaHCO₃ and 10 mL of dimethoxyethane. Purification by MPLC (3:97 to 10:90 EtOAc: hexane) afforded the product as yellow oil (0.079 g, 47%): ¹H NMR (500 MHz, CDCl₃) δ 7.28 (t, J=7.5 Hz, 2H), 7.21 (m, 2H), 7.20 (m, 2H), 7.02 (d, J = 8.5 Hz, 1H), 6.94 (d, J = 2.4 Hz, 1H), 5.23 (s, 1H), 5.09 (s, 1H), 3.97 (q, J = 7.0 Hz, 1H), 1.45 (d, J = 7.1 Hz, 3H); ¹³C NMR (125 MHz, CDCl₃) δ 150.7 (C), 143.8 (C), 135.7 (C), 131.3 (C), 130.7
(CH), 129.7 (C), 128.3 (CH), 128.2 (CH), 127.8 (CH), 126.4 (CH), 119.5 (CH), 115.7 (CH₂), 45.0 (CH), 20.3 (CH₃).

**Styryl azide 5.24.** The general procedure was followed by using 0.144 g of 2-azidophenyl boronate 5.28 (0.59 mmol), 0.145 g of vinyl triflate 5.27i (0.53 mmol), 0.067 g of Pd(PPh₃)₄ (0.05 mmol), 1.0 mL of saturated aq. soln. of NaHCO₃ and 10 mL of dimethoxyethane. Purification by MPLC (3:97 to 10:90 EtOAc: hexane) afforded the product as yellow oil (0.097 g, 75%): ¹H NMR (500 MHz, CDCl₃) δ 7.37 (t, J = 7.6 Hz, 1H), 7.17 (d, J = 8.0 Hz, 1H), 7.14 (t, J = 7.6 Hz, 1H), 7.10 (dd, J = 7.6 Hz, 1.4 Hz, 1H), 5.92 (s, 1H), 3.28 (m, 1H), 2.55 (m, 1H), 2.15 (dt, J = 13.2 Hz, 4.6 Hz, 1H), 1.54 (td, J = 13.5 Hz, 11.2 Hz, 1H), 1.16 (d, J = 6.7 Hz, 3H), 0.86 (d, J = 7.1 Hz, 3H); ¹³C NMR (125 MHz, CDCl₃) δ 201.8 (C), 164.1 (C), 136.5 (C), 131.8 (C), 129.5 (CH), 129.4 (CH), 128.9 (CH), 125.0 (CH), 118.2 (CH), 41.5 (CH), 40.7 (CH₂), 34.1 (CH), 19.9 (CH₃), 14.8 (CH₃).

C. Preparation of styryl azides from aniline.

Following the procedure of Zhang and Moses,²¹ the azides were prepared. Yields were not optimized.

To a cooled solution of aniline in MeCN (0.1 M) was added dropwise t-BuONO₂ (4 equiv) and Me₃SiN₃ (3 equiv). The resulting solution was warmed to room temperature. After 1h, visualization of the reaction progress using TLC indicated the consumption of the starting material. De-ionized water was added to the reaction
mixture. The mixture then was extracted with $2 \times 30 \text{ mL}$ of $\text{CH}_2\text{Cl}_2$. The combined organic phases were washed with $20 \text{ mL}$ of brine. The resulting organic phase was dried over $\text{Na}_2\text{SO}_4$, filtered, and the filtrate was concentrated in vacuo. Purification of the residue by MPLC (2:98 – 10:90 EtOAc: hexanes) afforded azide.

Styryl azide 5.21a. The general procedure was followed by using 0.085 g of 5.29a (0.34 mmol), 0.17 mL of $t$-BuNO$_2$ (1.34 mmol), 0.14 mL of Me$_3$SiN$_3$ (1.0 mmol) and 10 mL of MeCN. Purification by MPLC (2:98 – 10:90 EtOAc: hexanes) afforded the product, a colorless oil (0.077 g, 83%): $^1$H NMR (500 MHz, CDCl$_3$) $\delta$ 7.26 (m, 4H), 7.18 (t, $J = 7.1$ Hz, 1H), 7.02 (d, $J = 8.7$ Hz, 1H), 6.79 (dd, $J = 8.7$ Hz, 2.9 Hz, 1H), 6.46 (d, $J = 2.9$ Hz, 1H), 5.22 (s, 1H), 5.09 (s, 1H), 3.98 (q, $J = 7.0$ Hz, 1H), 3.67 (s, 3H), 1.47 (d, $J = 7.1$ Hz, 3H); $^{13}$C NMR (125 MHz, CDCl$_3$) $\delta$ 156.3 (C), 151.6 (C), 144.3 (C), 136.3 (C), 129.4 (C), 128.2 (CH), 127.9 (CH), 126.3 (CH), 119.3 (CH), 116.2 (CH), 114.9 (CH$_2$), 113.8 (CH), 55.5 (CH$_3$), 45.2 (CH), 20.3 (CH$_3$).

Styryl azide 5.21d. The general procedure was followed by using 0.130 g of 5.29d (0.54 mmol), 0.28 mL of $t$-BuNO$_2$ (2.15 mmol), 0.23 mL of Me$_3$SiN$_3$ (1.6 mmol) and 10 mL of MeCN. Purification by MPLC (2:98 – 10:90 EtOAc: hexanes) afforded the product, a colorless oil (0.098 g, 68%): $^1$H NMR (500 MHz, CDCl$_3$) $\delta$ 7.29 (t, $J = 7.5$ Hz, 2H), 7.22 (t, $J = 8.2$ Hz, 3H), 7.05 (dd, $J = 8.8$ Hz, 4.7 Hz, 1H), 6.95 (td, $J = 8.3$ Hz, 2.9 Hz, 1H), 6.69 (dd, $J = 9.0$ Hz, 2.9 Hz, 1H), 5.28 (s, 1H), 5.13 (s, 1H), 4.01 (q, $J = 7.3$ Hz, 1H), 1.49 (d, $J = 7.1$ Hz, 3H); $^{13}$C NMR (125 MHz, CDCl$_3$) $\delta$ 159.2 (C, $J_{C-F} = 245.8$ Hz), 150.8 (C), 143.9 (C), 137.0 (C), 132.9 (C), 128.3 (CH), 127.8 (CH),
126.4 (CH), 119.5 (CH, $J_{C,F} = 8.8$ Hz), 117.7 (CH, $J_{C,F} = 22.1$ Hz), 115.5 (CH$_2$), 115.0 (CH, $J_{C,F} = 22.1$ Hz), 45.0 (CH), 20.4 (CH$_3$).

Styryl azide 5.21f. The general procedure was followed by using 0.160 g of 5.29f (0.52 mmol), 0.27 mL of t-BuNO$_2$ (2.1 mmol), 0.22 mL of Me$_3$SiN$_3$ (1.6 mmol) and 10 mL of MeCN. Purification by MPLC (2:98 – 10:90 EtOAc: hexanes) afforded the product, a colorless oil (0.170 g, 98%): $^1$H NMR (500 MHz, CDCl$_3$) $\delta$ 7.27 (t, $J = 7.6$ Hz, 2H), 7.19 (d, $J = 7.2$ Hz, 3H), 7.10 (s, 2H), 6.79 (s, 1H), 5.30 (s, 1H), 5.12 (s, 1H), 3.97 (q, $J = 7.0$ Hz, 1H), 1.49 (d, $J = 7.1$ Hz, 3H); $^{13}$C NMR (125 MHz, CDCl$_3$) $\delta$ 150.4 (C), 145.4 (C), 143.7 (C), 136.7 (C), 135.8 (C), 128.3 (CH), 127.8 (CH), 126.4 (CH), 123.7 (CH), 120.9 (CH), 120.4 (CF$_3$, $J_{C,F} = 257.1$ Hz), 119.3 (CH), 115.6 (CH$_2$), 45.1 (CH), 20.1 (CH$_3$).

Styryl azide 5.21’a. The general procedure was followed by using 0.270 g of 5.29’a (1.1 mmol), 0.52 mL of t-BuNO$_2$ (4.0 mmol), 0.41 mL of Me$_3$SiN$_3$ (3.0 mmol) and 10 mL of MeCN. Purification by MPLC (2:98 – 10:90 EtOAc: hexanes) afforded the product, a yellow oil (0.224 g, 75%): $^1$H NMR (500 MHz, CDCl$_3$) $\delta$ 7.27 (t, $J = 7.6$ Hz, 1H), 7.18 (d, $J = 8.5$ Hz, 2H), 7.14 (d, $J = 8.0$ Hz, 1H), 7.02 (t, $J = 7.4$ Hz, 1H), 6.98 (d, $J = 7.5$ Hz, 1H), 6.85 (d, $J = 8.6$ Hz, 2H), 5.25 (s, 1H), 5.10 (s, 1H), 4.00 (q, $J = 7.0$ Hz, 1H), 3.80 (s, 3H), 1.48 (d, $J = 7.1$ Hz, 3H); $^{13}$C NMR (125 MHz, CDCl$_3$) $\delta$ 158.0 (C), 152.2 (C), 137.0 (C), 136.4 (C), 135.4 (C), 130.9 (CH), 128.8 (CH), 128.3
Styryl azide 5.21'b. The general procedure was followed by using 0.310 g of 5.29'b (1.3 mmol), 0.66 mL of t-BuNO$_2$ (5.2 mmol), 0.55 mL of Me$_3$SiN$_3$ (3.9 mmol) and 15 mL of MeCN. Purification by MPLC (2:98 – 10:90 EtOAc: hexanes) afforded the product, a colorless oil (0.320 g, 93%): $^1$H NMR (500 MHz, CDCl$_3$) δ 7.30 (t, $J$ = 7.5 Hz, 1H), 7.16 (m, 5H), 7.03 (m, 2H), 5.29 (s, 1H), 5.14 (s, 1H), 4.04 (q, $J$ = 7.0 Hz, 1H), 2.37 (s, 3H), 1.52 (d, $J$ = 7.1 Hz, 3H); $^{13}$C NMR (125 MHz, CDCl$_3$) δ 152.0 (C), 141.3 (C), 137.0 (C), 135.7 (C), 135.5 (C), 131.0 (CH), 129.0 (CH), 128.3 (CH), 127.8 (CH), 124.5 (CH), 118.3 (CH), 114.8 (CH$_2$), 44.9 (CH), 21.1 (CH$_3$), 20.6 (CH$_3$).

Styryl azide 5.21'd. The general procedure was followed by using 0.310 g of 5.29'd (1.2 mmol), 0.61 mL of t-BuNO$_2$ (4.8 mmol), 0.50 mL of Me$_3$SiN$_3$ (3.6 mmol) and 10 mL of MeCN. Purification by MPLC (2:98 – 10:90 EtOAc: hexanes) afforded the product, a colorless oil (0.320 g, 94%): $^1$H NMR (500 MHz, CDCl$_3$) δ 7.28 (t, $J$ = 7.5 Hz, 3H), 7.21 (m, 2H), 7.20 (m, 2H), 7.02 (d, $J$ = 8.5 Hz, 1H), 6.94 (d, $J$ = 2.4 Hz, 1H), 5.23 (s, 1H), 5.09 (s, 1H), 3.97 (q, $J$ = 7.0 Hz, 1H), 1.45 (d, $J$ = 7.1 Hz, 3H); $^{13}$C NMR (125 MHz, CDCl$_3$) δ 151.4 (C), 142.9 (C), 137.0 (C), 135.0 (C), 131.9 (C), 130.9 (CH), 129.3 (CH), 128.5 (CH), 128.4 (CH), 124.6 (CH), 118.3 (CH), 115.2 (CH$_2$), 44.6 (CH), 20.4 (CH$_3$).
D. Rh$_2$(II)-Catalyzed sp$^3$ C–H bond Amination and Electrocyclization.

To a mixture of styryl azide 5.11 and Rh$_2$(esp)$_2$ (5 mol %) was added toluene (0.1M). The resulting mixture was heated at 120 °C. After 16 h, the mixture was cooled to room temperature, diluted with CH$_2$Cl$_2$ and concentrated in vacuo. Purification of the residue by MPLC (3:97 – 30:70 EtOAc:hexanes) using silica gel afforded the product 5.12 or 5.13.

Alkylidene indoline 5.6. The general procedure was followed by using 0.0393 g of styryl azide 5.5 (0.125 mmol), 0.0047 g of Rh$_2$(esp)$_2$ (5 mol %) and 1.3 mL of toluene. Purification by MPLC (3:97 to 10:90 EtOAc:hexanes) afforded the product as a white solid (0.0268 g, 75%): $^1$H NMR (500 MHz, CDCl$_3$) δ 7.63 (d, $J$ =7.8 Hz, 1H), 7.09 (t, $J$ = 7.6 Hz, 1H), 6.66 (t, $J$ = 7.6 Hz, 1H), 6.63 (d, $J$ = 7.9 Hz, 1H), 4.18 (s, 1H), 3.83 (s, 3H), 2.99 (hextet, $J$ = 7.7 Hz, 1H), 2.15 (dt, $J$ = 12.7 Hz, 3.3 Hz, 1H), 2.01 (m, 1H), 1.89 (dt, $J$ = 13.7 Hz, 6.8 Hz, 1H), 1.53 (td, $J$ = 13.8 Hz, 4.3 Hz, 1H), 1.35 (tdd, $J$ = 14.1 Hz, 9.3 Hz, 4.6 Hz, 1H), 1.13 (d, $J$ = 7.0 Hz, 3H), 0.95 (d, $J$ =6.9 Hz, 3H), 0.68 (d, $J$ = 6.8 Hz, 3H); $^{13}$C NMR (125 MHz, CDCl$_3$) δ 170.0 (C), 153.2 (C), 148.1 (C), 130.5 (CH), 126.0 (C), 125.3 (C), 124.2 (CH), 118.5 (CH), 109.2 (CH), 67.1 (C), 51.5 (CH$_3$), 36.2 (CH), 32.5 (CH$_2$), 32.1 (CH), 26.4 (CH$_2$), 22.7 (CH$_3$), 17.4 (CH$_3$), 16.6 (CH$_3$).
Alkylidene indoline 5.9. The general procedure was followed by using 0.0300 g of styryl azide 5.8 (0.120 mmol), 0.0045 g of Rh$_2$(esp)$_2$ (5 mol %) and 1.2 mL of toluene. Purification by MPLC (3:97 to 10:90 EtOAc:hexanes) afforded the product as a yellow solid (0.0222 g, 83%): $^1$H NMR (500 MHz, CDCl$_3$) $\delta$ 7.48 (d, $J$ = 8.0 Hz, 1H), 7.20 (t, $J$ = 7.6 Hz, 1H), 6.71 (t, $J$ = 7.6 Hz, 1H), 6.61 (d, $J$ = 8.0 Hz, 1H), 4.17 (s, 1H), 3.00 (t, $J$ = 7.2 Hz, 2H), 2.36 (t, $J$ = 7.9 Hz, 1H), 2.02 (quintet, $J$ = 7.6 Hz, 1H), 1.70 (s, 6H); $^{13}$C NMR (125 MHz, CDCl$_3$) $\delta$ 206.8 (C), 156.6 (C), 154.7 (C), 132.6 (CH), 127.8 (CH), 126.0 (C), 125.6 (C), 117.9 (CH), 109.7 (CH), 66.5 (C), 40.2 (CH$_2$), 33.1 (CH$_2$), 25.3 (CH$_3$), 20.3 (CH$_2$).

Alkylidene indoline 5.12a. The general procedure was followed by using 0.0507 g of styryl azide 5.11a (0.147 mmol), 0.0056 g of Rh$_2$(esp)$_2$ (5 mol %) and 3.0 mL of toluene. Purification by MPLC (3:97 to 10:90 EtOAc:hexanes) afforded the product as a yellow oil (0.0224 g, 48%): $^1$H NMR (500 MHz, CDCl$_3$) $\delta$ 7.79 (d, $J$ =7.6 Hz, 1H), 7.21 (t, $J$ = 7.7 Hz, 1H), 6.87 (t, $J$ = 7.6 Hz, 1H), 6.79 (d, $J$ = 8.0 Hz, 1H), 5.09 (m, 1H), 4.48 (dd, $J$ = 10.7 Hz, 7.5 Hz, 1H), 4.31 (s, 1H), 3.86 (s, 3H), 3.84 (t, $J$ = 11.5 Hz, 1H), 1.48 (s, 9H); $^{13}$C NMR (125 MHz, CDCl$_3$) $\delta$ 163.9 (C), 161.8 (C), 159.4 (C), 153.5 (C), 144.2 (C), 131.6 (CH), 125.8 (CH), 123.7 (C), 120.5 (CH), 111.7 (CH), 81.1 (C), 66.5 (CH$_3$), 60.6 (CH$_2$), 51.8 (CH), 28.2 (CH$_3$).
Indole 5.13b. The general procedure was followed by using 0.0724 g of styryl azide 5.11b (0.250 mmol), 0.0095 g of Rh$_2$(esp)$_2$ (5 mol %) and 2.5 mL of toluene. Purification by MPLC (3:97 to 60:40 EtOAc:hexanes) afforded the product as a white solid (0.0549 g, 84%): $^1$H NMR (500 MHz, CDCl$_3$) $\delta$ 8.03 (s, 1H), 7.36 (t, $J = 8.2$ Hz, 1H), 7.29 (m, 5H), 7.17 (q, $J = 7.8$ Hz, 1H), 7.00 (dq, $J = 24.0$ Hz, 7.8 Hz, 2H), 4.91 (s, 1H), 3.26 (m, 2H), 2.96 (dq, $J = 14.4$ Hz, 7.6 Hz, 1H), 2.60 (m, 1H); $^{13}$C NMR (125 MHz, CDCl$_3$) $\delta$ 208.9 (C), 138.4 (C), 137.1 (C), 133.0 (C), 128.7 (CH), 128.3 (CH), 127.3 (CH), 126.9 (C), 122.2 (CH), 119.8 (CH), 118.9 (CH), 110.8 (CH), 110.2 (C), 53.7 (CH), 35.5 (CH$_2$), 23.4 (CH$_2$).

Indole 5.13c. The general procedure was followed by using 0.0465 g of styryl azide 5.11c (0.200 mmol), 0.0078 g of Rh$_2$(esp)$_2$ (5 mol %) and 2.0 mL of toluene. Purification by MPLC (3:97 to 60:40 EtOAc:hexanes) afforded the product as a colorless oil (0.0347 g, 85%): $^1$H NMR (500 MHz, CDCl$_3$) $\delta$ 7.98 (s, 1H), 7.55 (d, $J = 7.8$ Hz, 1H), 7.32 (d, $J = 8.0$ Hz, 1H), 7.20 (t, $J = 7.6$ Hz, 1H), 7.14 (t, $J = 7.4$ Hz, 1H), 3.77 (q, $J = 7.1$ Hz, 1H), 3.13 (qt, $J = 17.3$ Hz, 7.3 Hz, 2H), 2.89 (dt, $J = 13.7$ Hz, 6.8 Hz, 1H), 2.75 (dt, $J = 13.9$ Hz, 7.0 Hz, 1H), 1.58 (d, $J = 7.2$ Hz, 3H); $^{13}$C NMR (125 MHz, CDCl$_3$) $\delta$ 212.9 (C), 136.9 (C), 131.3 (C), 126.9 (C), 125.3 (C), 121.9 (CH), 119.7 (CH), 118.6 (CH), 111.0 (CH), 41.7 (CH), 36.9 (CH$_2$), 23.0 (CH$_2$), 18.0 (CH$_3$).
**Indole 5.13d.** The general procedure was followed by using 0.0436 g of styryl azide 5.11d (0.140 mmol), 0.0053 g of Rh\(_2\)(esp\(_2\)) (5 mol %) and 1.5 mL of toluene. Purification by MPLC (3:97 to 90:10 EtOAc:hexanes) afforded the product as a white solid (0.0103 g, 26%): \(^1\)H NMR (500 MHz, CDCl\(_3\)) \(\delta\) 7.90 (s, 1H), 7.27 (d, \(J = 9.2\) Hz, 1H), 7.25 (d, \(J = 8.1\) Hz, 1H), 7.09 (t, \(J = 7.5\) Hz, 1H), 7.04 (t, \(J = 7.4\) Hz, 1H), 4.17 (dd, \(J = 7.8\) Hz, 5.4 Hz, 1H), 3.77 (m, 2H), 3.63 (m, 5H), 3.46 (m, 1H), 2.73 (m, 2H), 2.17 (tq, \(J = 10.4\) Hz, 5.3 Hz, 2H), 1.91 (q, \(J = 10.1\) Hz, 1H), 1.83 (ddd, \(J = 18.6\) Hz, 11.1 Hz, 6.6 Hz, 1H); \(^{13}\)C NMR (125 MHz, CDCl\(_3\)) \(\delta\) 173.4 (C), 135.8 (C), 134.7 (C), 126.6 (C), 121.4 (CH), 119.6 (CH), 117.9(CH), 110.7 (CH), 108.5 (C), 67.2 (CH\(_2\)), 66.7 (CH\(_2\)), 46.4 (CH\(_2\)), 42.6 (CH\(_2\)), 38.0 (CH), 27.5 (CH\(_2\)), 22.9 (CH\(_2\)), 21.7 (CH\(_2\)).

**Indole 5.15.** The general procedure was followed by using 0.0400 g of styryl azide 5.14 (0.188 mmol), 0.0071 g of Rh\(_2\)(esp\(_2\)) (5 mol %) and 1.9 mL of toluene. Purification by MPLC (3:97 to 60:40 EtOAc:hexanes) afforded the product as a white solid (0.0285 g, 82%): \(^1\)H NMR (500 MHz, CDCl\(_3\)) \(\delta\) 9.42 (s, 1H), 7.67 (d, \(J = 8.1\) Hz, 1H), 7.44 (d, \(J = 8.4\) Hz, 1H), 7.38 (t, \(J = 7.6\) Hz, 1H), 7.16 (t, \(J = 7.5\) Hz, 1H), 3.02 (t, \(J = 6.1\) Hz, 2H), 2.71 (t, \(J = 6.5\) Hz, 2H), 2.28 (quintet, \(J = 6.3\) Hz, 2H); \(^{13}\)C NMR (125 MHz, CDCl\(_3\)) \(\delta\) 191.8 (C), 138.1 (C), 131.3 (C), 129.7 (C), 127.1 (CH), 125.9 (C), 121.4 (CH), 120.4 (CH), 112.7 (CH), 38.3 (CH\(_2\)), 25.0 (CH\(_2\)), 21.5 (CH\(_2\)).
**Indole 5.17.** The general procedure was followed by using 0.0329 g of styryl azide 5.16 (0.154 mmol), 0.0058 g of Rh$_2$(esp)$_2$ (5 mol %) and 1.6 mL of toluene. Purification by MPLC (3:97 to 60:40 EtOAc:hexanes) afforded the product as a yellow oil (0.0191 g, 67%): $^1$H NMR (500 MHz, CDCl$_3$) δ 7.63 (s, 1H), 7.60 (d, $J = 7.6$ Hz, 1H), 7.29 (d, $J = 7.9$ Hz, 1H), 7.14 (t, $J = 7.5$ Hz, 1H), 7.10 (t, $J = 7.4$ Hz, 1H), 3.14 (q, $J = 5.9$ Hz, 1H), 2.70 (d, $J = 3.6$ Hz, 2H), 2.01 (dd, $J = 9.4$ Hz, 5.2 Hz, 2H), 1.84 (dt, $J = 16.9$ Hz, 7.7 Hz, 1H), 1.61 (t, $J = 12.2$ Hz, 1H), 1.40 (d, $J = 6.9$ Hz, 3H); $^{13}$C NMR (125 MHz, CDCl$_3$) δ 135.8 (C), 133.9 (C), 128.3 (C), 120.8 (CH), 119.0 (CH), 118.7 (CH), 115.1 (C), 110.5 (CH), 32.2 (CH$_2$), 27.2 (CH), 23.5 (CH$_2$), 21.3 (CH$_3$), 20.5 (CH$_2$).

**3H-Indole 5.19 and alkylidene indoline 5.20.** The general procedure was followed by using 0.0446 g of styryl azide 5.18 (0.207 mmol), 0.0078 g of Rh$_2$(esp)$_2$ (5 mol %) and 2.0 mL of toluene. Purification by MPLC (3:97 to 60:40 EtOAc:hexanes) with alumina afforded a mixture of the products 5.19 as a yellow solid (0.0090 g, 24%) and 5.20 as a colorless oil (0.0033 g, 9%) and 36% recovery of reactant. Characteristic data for 5.19: $^1$H NMR (500 MHz, CDCl$_3$) δ 7.52 (d, $J = 7.6$ Hz, 1H), 7.31 (dt, $J = 7.1$ Hz, 3.5 Hz, 2H), 7.16 (t, $J = 7.4$ Hz, 1H), 2.24 (s, 3H), 2.05 (heptet, $J = 6.8$ Hz, 1H), 1.30 (s, 3H), 1.14 (d, $J = 6.9$ Hz, 3H), 0.41 (d, $J = 6.8$ Hz, 3H); $^{13}$C NMR (125 MHz, CDCl$_3$) δ 187.7 (C), 155.0 (C), 142.2 (C), 127.6 (CH), 124.6 (CH), 123.0 (CH), 119.8 (CH), 61.2 (C), 33.6 (CH), 20.7 (CH$_3$), 17.4 (CH$_3$), 17.3 (CH$_3$), 16.3 (CH$_3$).
Characteristic data for 5.20: $^1$H NMR (500 MHz, CDCl$_3$) $\delta$ 7.41 (d, $J = 7.7$ Hz, 1H), 7.00 (t, $J = 7.7$ Hz, 1H), 6.67 (t, $J = 7.6$ Hz, 1H), 6.56 (d, $J = 7.7$ Hz, 1H), 3.70 (s, 1H), 2.07 (s, 3H), 2.01 (s, 3H), 1.49 (s, 6H).

**Indole 5.22c and alkylidene indoline 5.23c.** The general procedure was followed by using 0.0458 g of styryl azide 5.21c (0.184 mmol), 0.0070 g of Rh$_2$(esp)$_2$ (5 mol%) and 1.8 mL of toluene. Purification by MPLC (3:97 to 60:40 EtOAc:hexanes) with alumina afforded a mixture of the products 5.22c as a yellow solid (0.0332 g, 82%) and 5.23c as a colorless oil (0.0051 g, 13%). Characteristic data for 5.22c: $^1$H NMR (500 MHz, CDCl$_3$) $\delta$ 7.91 (s, 1H), 7.40 (d, $J = 8.0$ Hz, 1H), 7.32 (m, 5H), 7.20 (m, 2H), 7.04 (t, $J = 7.5$ Hz, 1H), 7.01 (d, $J = 1.5$ Hz, 1H), 4.41 (q, $J = 7.1$ Hz, 1H), 1.74 (d, $J = 7.2$ Hz, 3H); $^{13}$C NMR (125 MHz, CDCl$_3$) $\delta$ 146.9 (C), 136.7 (C), 128.4 (CH), 127.5 (CH), 126.9 (C), 126.0 (CH), 122.0 (CH), 121.5 (C), 121.1 (CH), 119.8 (CH), 119.3 (CH), 111.1 (CH), 37.0 (CH), 22.5 (CH$_3$).

Characteristic data for 5.23c: $^1$H NMR (500 MHz, CDCl$_3$) $\delta$ 7.47 (d, $J = 7.3$ Hz, 2H), 7.38 (d, $J = 7.5$ Hz, 1H), 7.32 (t, $J = 7.6$ Hz, 2H), 7.24 (t, $J = 7.4$ Hz, 1H), 7.17 (t, $J = 7.6$ Hz, 1H), 6.78 (t, $J = 7.5$ Hz, 1H), 6.71 (d, $J = 7.9$ Hz, 1H), 5.42 (s, 1H), 4.72 (s, 1H), 4.30 (s, 1H), 1.77 (s, 3H); $^{13}$C NMR (125 MHz, CDCl$_3$) $\delta$ 155.1 (C), 150.9 (C), 146.8 (C), 130.3 (CH), 128.4 (CH), 127.0 (CH), 125.6 (CH), 121.4 (CH), 118.8 (CH), 110.1 (CH), 101.3 (CH$_2$), 67.9 (C), 28.5 (CH$_3$), only visible peaks.
Indole 5.25 and alkylidene indoline 5.26. The general procedure was followed by using 0.0309 g of styryl azide 5.24 (0.128 mmol), 0.0048 g of Rh$_2$(esp)$_2$ (5 mol %) and 1.3 mL of toluene. Purification by MPLC (3:97 to 60:40 EtOAc:hexanes) afforded a mixture of the products 5.25 as a white solid (0.0120 g, 44%) and a mixture of diastereomer 5.26 as a yellow oil (0.0103 g, 38%). Characteristic data for 5.25: $^1$H NMR (500 MHz, CDCl$_3$) $\delta$ 9.30 (s, 1H), 7.87 (d, $J = 8.2$ Hz, 1H), 7.45 (d, $J = 8.3$ Hz, 1H), 7.35 (t, $J = 7.6$ Hz, 1H), 7.13 (t, $J = 7.6$ Hz, 1H), 3.40 (m, 1H), 2.71 (dqd, $J = 13.3$ Hz, 4.4 Hz, 1H), 2.25 (dt, $J = 13.1$ Hz, 4.4 Hz, 1H), 1.76 (q, $J = 12.2$ Hz, 1H), 1.61 (d, $J = 6.8$ Hz, 3H), 1.32 (d, $J = 6.8$ Hz, 3H); $^{13}$C NMR (125 MHz, CDCl$_3$) $\delta$ 194.3 (C), 138.3 (C), 132.4 (C), 130.8 (C), 126.4 (CH), 125.8 (C), 122.7 (CH), 120.2 (CH), 112.8 (CH), 43.4 (CH$_2$), 41.7 (CH), 30.0 (CH), 20.9 (CH$_3$), 15.0 (CH$_3$). ATR-FTIR (thin film): cm$^{-1}$; HRMS (El) $m/z$ calculated for C$_{14}$H$_{15}$NO (M)$^+$; found:

Characteristic data for major diastereomer of 5.26: $^1$H NMR (500 MHz, CDCl$_3$) $\delta$ 7.46 (d, $J = 7.9$ Hz, 1H), 7.30 (t, $J = 7.7$ Hz, 1H), 6.85 (t, $J = 7.5$ Hz, 1H), 6.79 (d, $J = 8.0$ Hz, 1H), 6.13 (s, 1H), 4.24 (s, 1H), 2.50 (dquintet, $J = 12.6$ Hz, 6.3 Hz, 1H), 2.30 (dd, $J = 12.5$ Hz, 5.0 Hz, 1H), 1.94 (t, $J = 12.6$ Hz, 1H), 1.49 (s, 3H), 1.25 (d, $J = 6.8$ Hz, 3H); $^{13}$C NMR (125 MHz, CDCl$_3$) $\delta$ 200.2 (C), 153.7 (C), 148.4 (C), 133.6 (CH), 123.9 (CH), 122.8 (C), 119.9 (CH), 114.0 (CH), 111.9 (CH), 63.5 (C), 44.2 (CH$_2$), 38.4 (CH), 26.6 (CH$_3$), 17.0 (CH$_3$).
E. Condition Screening for Styryl Azides 5.21c.

To a mixture of styryl azide 5.21c and metal catalyst (5 mol%) was added toluene (0.1M). The resulting mixture was heated for 16 h. The mixture was cooled to room temperature, diluted with CH₂Cl₂ and concentrated in vacuo. Dibromomethane (0.7 µL, 0.1 mmol) was added, and the mixture was analyzed using ¹H NMR spectroscopy to determine the outcome of the reaction.

<table>
<thead>
<tr>
<th>entry</th>
<th>MLₙ</th>
<th>°C, T</th>
<th>5.22c:5.23c</th>
<th>%, yieldᵃ</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>noneᵇ</td>
<td>220</td>
<td>98:2</td>
<td>77</td>
</tr>
<tr>
<td>2</td>
<td>Rh₂(esp)₂</td>
<td>140</td>
<td>86:14</td>
<td>93</td>
</tr>
<tr>
<td>3</td>
<td>Rh₂(esp)₂</td>
<td>120</td>
<td>87:13</td>
<td>95</td>
</tr>
<tr>
<td>4</td>
<td>Rh₂(esp)₂</td>
<td>100</td>
<td>88:12</td>
<td>88</td>
</tr>
<tr>
<td>5</td>
<td>Rh₂(O₂CCF₃)₄</td>
<td>120</td>
<td>98:2</td>
<td>66</td>
</tr>
<tr>
<td>6</td>
<td>Rh₂(O₂CC₃F₇)₄</td>
<td>120</td>
<td>84:6</td>
<td>50ᶜ</td>
</tr>
<tr>
<td>7</td>
<td>Rh₂(O₂CC₇H₁₅)₄</td>
<td>120</td>
<td>89:11</td>
<td>93</td>
</tr>
<tr>
<td>8</td>
<td>Rh₂(S-DOSP)₄</td>
<td>120</td>
<td>82:18</td>
<td>79</td>
</tr>
<tr>
<td>9</td>
<td>Rh₂(cap)₄</td>
<td>120</td>
<td>96:4</td>
<td>82</td>
</tr>
<tr>
<td>10</td>
<td>[Ir(cod)OMe]₂</td>
<td>120</td>
<td>100:0</td>
<td>84</td>
</tr>
<tr>
<td>11</td>
<td>RuCl₃</td>
<td>120</td>
<td>–</td>
<td>0</td>
</tr>
</tbody>
</table>

ᵃ NMR yield determined by using CH₃Br₂ as internal standard.ᵇ used mesitylene as solvent.ᶜ only 81% conversion of starting material.

F. Mechanistic Study for Rh₂(II)-Catalyzed Electrocyclization and sp³ C–H Bond Amination.

To a mixture of styryl azide 5.21 or 5.21* and Rh₂(esp)₂ (5 mol%) was added toluene (0.1M). The resulting mixture was heated for 5 h. The mixture was cooled to
room temperature, diluted with CH$_2$Cl$_2$ and concentrated \textit{in vacuo}. Dibromomethane (0.7 µL, 0.1 mmol) was added, and the mixture was analyzed using $^1$H NMR spectroscopy to determine the outcome of the reaction.

<table>
<thead>
<tr>
<th>entry</th>
<th>#</th>
<th>R</th>
<th>$\sigma_p$</th>
<th>5.22: 5.23</th>
<th>%, yield$^a$</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>a</td>
<td>OMe</td>
<td>−0.27</td>
<td>92 : 8</td>
<td>78</td>
</tr>
<tr>
<td>2</td>
<td>b</td>
<td>Me</td>
<td>−0.17</td>
<td>88 : 12</td>
<td>79</td>
</tr>
<tr>
<td>3</td>
<td>c</td>
<td>H</td>
<td>0</td>
<td>85 : 15</td>
<td>84</td>
</tr>
<tr>
<td>4</td>
<td>d</td>
<td>F</td>
<td>0.06</td>
<td>83 : 17</td>
<td>92</td>
</tr>
<tr>
<td>5</td>
<td>e</td>
<td>Cl</td>
<td>0.23</td>
<td>87 : 13</td>
<td>76</td>
</tr>
<tr>
<td>6</td>
<td>f</td>
<td>OCF$_3$</td>
<td>0.35</td>
<td>91 : 9</td>
<td>80</td>
</tr>
</tbody>
</table>

$^a$ NMR yield determined by using CH$_2$Br$_2$ as internal standard.

\textbf{Figure 5.1} Correlation of log($k_{\text{electro}}/k_{\text{sp3}}$) of Rh$_2$(II) catalyzed C–H amination of 5.21 with $\sigma_p$ values in the Hammett equation.
<table>
<thead>
<tr>
<th>entry</th>
<th>#</th>
<th>R</th>
<th>( \sigma_p )</th>
<th>5.23': 5.22'</th>
<th>%, yield&lt;sup&gt;a&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>a</td>
<td>OMe</td>
<td>-0.27</td>
<td>20:80</td>
<td>83</td>
</tr>
<tr>
<td>2</td>
<td>b</td>
<td>Me</td>
<td>-0.17</td>
<td>16:84</td>
<td>94</td>
</tr>
<tr>
<td>3</td>
<td>c</td>
<td>H</td>
<td>0</td>
<td>15:85</td>
<td>84</td>
</tr>
<tr>
<td>4</td>
<td>d</td>
<td>Cl</td>
<td>0.23</td>
<td>20:80</td>
<td>52&lt;sup&gt;b&lt;/sup&gt;</td>
</tr>
</tbody>
</table>

<sup>a</sup> NMR yield determined by using \( \text{CH}_2\text{Br}_2 \) as internal standard. <sup>b</sup> only 81% conversion of starting material.

**Figure 5.2.** Correlation of \( \log(\frac{k_{\text{electro.}}}{k_{\text{sp3}}}) \) of Rh(II) catalyzed C–H amination of 5.21’ with \( \sigma_p \) values in the Hammett equation.

**G. Condition Screening for Styryl Azides 5.24.**

To a mixture of styryl azide 5.24 and metal catalyst was added solvent (0.1M) and 100 wt% 4Å MS. The resulting mixture was heated for 16 h. The mixture was cooled to room temperature, diluted with \( \text{CH}_2\text{Cl}_2 \) and concentrated \textit{in vacuo}. 
Dibromomethane (0.7 µL, 0.1 mmol) was added, and the mixture was analyzed using $^1$H NMR spectroscopy to determine the outcome of the reaction.

<table>
<thead>
<tr>
<th>entry</th>
<th>ML$_n$</th>
<th>Mol%</th>
<th>°C, T</th>
<th>solvent</th>
<th>5.25: 5.26</th>
<th>%, yield$^a$</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>none</td>
<td>–</td>
<td>125</td>
<td>Tol</td>
<td>94 : 6</td>
<td>15</td>
</tr>
<tr>
<td>2</td>
<td>Rh$_2$(esp)$_2$</td>
<td>5</td>
<td>120</td>
<td>Tol</td>
<td>62 : 38</td>
<td>91</td>
</tr>
<tr>
<td>3</td>
<td>Rh$_2$(esp)$_2$</td>
<td>5</td>
<td>110</td>
<td>Tol</td>
<td>63 : 37</td>
<td>90</td>
</tr>
<tr>
<td>4</td>
<td>Rh$_2$(O$_2$CC$<em>7$H$</em>{15}$)$_4$</td>
<td>5</td>
<td>110</td>
<td>Tol</td>
<td>68 : 32</td>
<td>78</td>
</tr>
<tr>
<td>5</td>
<td>Rh$_2$(S-DOSP)$_4$</td>
<td>5</td>
<td>100</td>
<td>Tol</td>
<td>44 : 56</td>
<td>64$^c$</td>
</tr>
<tr>
<td>6</td>
<td>Rh$_2$(cap)$_4$</td>
<td>5</td>
<td>100</td>
<td>Tol</td>
<td>91 : 9</td>
<td>73</td>
</tr>
<tr>
<td>7</td>
<td>Rh$_2$(S-PTAD)$_4$</td>
<td>5</td>
<td>110</td>
<td>Tol</td>
<td>20 : 80</td>
<td>84</td>
</tr>
<tr>
<td>8</td>
<td>Rh$_2$(S-PTAD)$_4$</td>
<td>5</td>
<td>100</td>
<td>Tol</td>
<td>18 : 82</td>
<td>85</td>
</tr>
<tr>
<td>9</td>
<td>Rh$_2$(S-PTAD)$_4$</td>
<td>2</td>
<td>100</td>
<td>Tol</td>
<td>26 : 74</td>
<td>57$^d$</td>
</tr>
<tr>
<td>10</td>
<td>Rh$_2$(S-PTAD)$_4$</td>
<td>5</td>
<td>90</td>
<td>Tol</td>
<td>17 : 83</td>
<td>61$^e$</td>
</tr>
<tr>
<td>11</td>
<td>Rh$_2$(S-PTAD)$_4$</td>
<td>2</td>
<td>110</td>
<td>Tol+BzEt$_3$NCl</td>
<td>26 : 74</td>
<td>74</td>
</tr>
<tr>
<td>12</td>
<td>Rh$_2$(S-PTAD)$_4$</td>
<td>2</td>
<td>110</td>
<td>Tol$^b$+BzEt$_3$NCl</td>
<td>20 : 80</td>
<td>72.5</td>
</tr>
<tr>
<td>13</td>
<td>Rh$_2$(S-PTAD)$_4$</td>
<td>5</td>
<td>100</td>
<td>Tol$^b$+BzEt$_3$NCl</td>
<td>17 : 83</td>
<td>81</td>
</tr>
<tr>
<td>14</td>
<td>Rh$_2$(S-PTAD)$_4$</td>
<td>5</td>
<td>110</td>
<td>DCE</td>
<td>19 : 81</td>
<td>86</td>
</tr>
<tr>
<td>15</td>
<td>Rh$_2$(S-PTAD)$_4$</td>
<td>5</td>
<td>110</td>
<td>DMSO-d6</td>
<td>100 : 0</td>
<td>0$^f$</td>
</tr>
<tr>
<td>16</td>
<td>[Ir(cod)OMe]$_2$</td>
<td>5</td>
<td>110</td>
<td>Tol</td>
<td>100 : 0</td>
<td>88</td>
</tr>
<tr>
<td>17</td>
<td>FeBr$_2$</td>
<td>20</td>
<td>110</td>
<td>Tol$^b$</td>
<td>100 : 0</td>
<td>84</td>
</tr>
<tr>
<td>18</td>
<td>FeBr$_3$</td>
<td>20</td>
<td>110</td>
<td>Tol$^b$</td>
<td>–</td>
<td>41</td>
</tr>
<tr>
<td>19</td>
<td>CoTPP</td>
<td>2</td>
<td>90</td>
<td>MeCN$^b$</td>
<td>22 : 78</td>
<td>0</td>
</tr>
<tr>
<td>20</td>
<td>CoTPP</td>
<td>2</td>
<td>100</td>
<td>DCE$^b$</td>
<td>11 : 89</td>
<td>68</td>
</tr>
<tr>
<td>21</td>
<td>CoOEP</td>
<td>2</td>
<td>100</td>
<td>DCE$^b$</td>
<td>6 : 94</td>
<td>18$^g$</td>
</tr>
<tr>
<td>22</td>
<td>Fe(TPP)Cl</td>
<td>2</td>
<td>90</td>
<td>DCE$^b$</td>
<td>7 : 93</td>
<td>47</td>
</tr>
<tr>
<td>23</td>
<td>Fe(TPP)Cl</td>
<td>2</td>
<td>100</td>
<td>DCE$^b$</td>
<td>10 : 90</td>
<td>52</td>
</tr>
<tr>
<td>24</td>
<td>Fe(TPP)Cl</td>
<td>2</td>
<td>100</td>
<td>DCE$^b$</td>
<td>12 : 88</td>
<td>48.5</td>
</tr>
<tr>
<td>25</td>
<td>Fe(TPP)Cl</td>
<td>2</td>
<td>125</td>
<td>DCE$^b$</td>
<td>13 : 87</td>
<td>52</td>
</tr>
<tr>
<td>26</td>
<td>Fe(TPP)Cl</td>
<td>2</td>
<td>100</td>
<td>DCE$^b$+AgBF$_4$</td>
<td>–</td>
<td>30</td>
</tr>
<tr>
<td>27</td>
<td>none</td>
<td>100</td>
<td>DCE$^b$+AgBF$_4$</td>
<td>–</td>
<td>30</td>
<td></td>
</tr>
<tr>
<td>28</td>
<td>Fe(TPFPPP)Cl</td>
<td>2</td>
<td>110</td>
<td>DCE$^b$</td>
<td>6 : 94</td>
<td>72</td>
</tr>
<tr>
<td>29</td>
<td>Fe(TOMEPP)Cl</td>
<td>2</td>
<td>100</td>
<td>DCE$^b$</td>
<td>2 : 98</td>
<td>52</td>
</tr>
<tr>
<td>30</td>
<td>Fe(OEP)Cl</td>
<td>2</td>
<td>100</td>
<td>DCE$^b$</td>
<td>100 : 0</td>
<td>77</td>
</tr>
</tbody>
</table>

$^a$ NMR yield determined by using CH$_2$Br$_2$ as internal standard. $^b$ 100 wt% 4 Å MS was added to the reaction. $^c$ only 84% conversion of starting material. $^d$ only 80% conversion of starting material. $^e$ only 72% conversion of starting material. $^f$ 34% recovery of starting material. $^g$ only 28% conversion of starting material.
Reference


Chen Kong

chen.kong.88@gmail.com; (309)750-4303

Education

University of Illinois at Chicago 2010–2015
Ph.D., Organic Chemistry
Shandong University, Jinan, China 2006–2010
Bachelor of Science in Chemistry

Selected Research Experience

Graduate Research Assistant with Prof. Tom G. Driver 2010–2015

▷ Transition metal-catalyzed reactions involving azides.
  • Investigated Rh₂(II)-catalyzed electrocyclization reaction with functional group migration to afford highly substituted N-heterocycles from styryl azides.
  • Designed a novel o-azidoarylboronic acid pinacolate ester, enabling a step-economical synthesis for functionalized aryl azides.
  • Gained experience on crystallization for XRD to determine molecule structure.
  ▷ Mechanism study on electrocyclization and sp³ C–H bond amination using styryl azides.
  • Manipulated substrate and catalyst to trigger electrocyclization or sp³ C–H bond amination.
  • Optimized condition to afford sp³ C–H bond amination product in the presence of competitive sp² C–H bond.
   ▷ Design and synthesis of luminogenic lanthanide probe precursor for the quantitative time-gated luminescence detection of sulfide in aqueous.
   • Synthesized the precursor in multiple steps.
   • Advantages of the lanthanide probe: high selectivity and sensitivity, good water solubility and most importantly, long-lived luminescence.

Undergraduate Research Assistant with Prof. Baoxiang Zhao Aug 2009–2010

  • Compared two ways to synthesize carbazolyl chalcone derivatives.
  • Screened three conditions to optimize pyrazoline synthesis using pyridazinyl hydrazine and carbazolyl chalcone.
  • Analyzed ultraviolet and fluorescence properties for pyrazoline derivatives and investigated the influence of substituents, solvents and concentration.

Team Leader: National Undergraduate Innovation Experiment Program Apr 2008–Jun 2009
Key Lab of Colloid and Interface Chemistry, Advisor: Prof. Jingcheng Hao

▷ Project: Phase behaviors of branched cationic/anionic surfactant combination system (TTAB/HDEHPNa) in aqueous solution.
  • Led a team of four and participated in National Undergraduate Innovation Experiment Competition. Won the first level award.
  • Designed a catanionic surfactant system, depicted phase diagram and located birefringent vesicular Lα phase.
  • Obtained characterization data for conductivity, surface tension, salt effect, polarizer, TEM, POM and rheological properties.
Technical Skills

- Advanced experimental skills at synthesis of organic precursors and organometallic compounds, asymmetric catalysis, transition metal catalysis and organocatalysis.
- Experienced at manipulation of organic compounds under strictly anaerobic and anhydrous conditions using Glovebox and Schlenk techniques.
- Adept at the application of modern analytical and purification methods in organic chemistry (NMR, GC-MS, HPLC, IR, UV, X-Ray, Flash Chromatography).

Publications

5. Yao, Y.; Kong, C.; Driver, T. G.; Miller, L.; Lanthanide-based luminescent probe for selective time-gated detection of hydrogen sulfide in water, in writing.
3. Kong, C.; Driver, T. G.; Rh₂(II)-Catalyzed Ester Migration to Afford 3H-Indoles from Trisubstituted Styryl Azides, Org. Lett. 2015, 17, 802.

Presentations


Honors and Awards

- Skyray Instrument Cooperation Scholarship 2010
- First level award in National Undergraduate Innovation Experiment Program 2009
- Awards and Scholarship for excellent student in social practice 2009
- Excellent Leader Scholarship 2008/2009
- Outstanding Student Scholarship 2007/2008/2009

Teaching Experience

Teaching Assistant at University of Illinois at Chicago 2010-2015
CHEM 101 Preparatory Chemistry
CHEM 130 Survey of Organic and Biochemistry
CHEM 232/234 Organic Chemistry I/II
CHEM 233 Organic Chemistry Lab I
Volunteer Teaching at Tongshi Primary School, Shandong, China Jul 2008
Organized a team for volunteer teaching at a rural primary school for summer.