UNIVERSITY OF CALIFORNIA, MERCED

New Reactions of α-Quaternary Homobenzylstyrenes and Homobenzaldehydes

A dissertation submitted in partial satisfaction of the requirements
for the degree Doctor of Philosophy

in

Chemistry

by

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2019

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University of California, Merced

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List of Abbreviations

Å	Angstrom
Ac	acetyl (MeCO)
Ar	aryl
ATR	attenuated total reflection
bp	boiling point
Bn	benzyl
Boc	*tert*-butoxylcarbonyl
br	broad
Bu	butyl (C4H9)
d	doublet
dba	dibenzylideneacetone
DCE	1,2-dichloroethane
DCM	dichloromethane
DFT	density functional theory
DMF	N, N-dimethylformamide
DMSO	dimethyl sulfoxide
dt	doublet of triplets
equiv	molar equivalent
EOM	ethoxymethyl
ESI	electrospray ionization
Et	ethyl
EI	electron impact
FT	Fourier transform
GC	gas chromatography
h	hour
HRMS	high-resolution mass spectrometry
Hz	hertz

i-	iso
IR	infrared
J	coupling constant
m	multiplet
Me	methyl
MPLC	medium-pressure liquid chromatography
mmol	millimole
ms	methanesulfonyl
MS	molecular sieves
m/z	mass-to-charge
n-	normal
NMR	nuclear magnetic resonance
ph	phenyl
ppm	parts per million
Pr	propyl
PSI	pounds per square inch
PTFE	poly(tetralfuoroethylene)
py	pyridine
q	quartet
R	carbon-centered functional group
Rf	retention factor
rt	room temperature
s	singlet
t	triplet
t-	tertiary
td	triplet of doublets
TEMPO	(2,2,6,6-tetramethylpiperidin-1-yl)oxidanyl
THF	tetrahydrofuran
TLC	thin-layer chromatography

Tol	tolyl
Ts	tosyl (*para*-toluenesulfonyl)
Tf	triflyl (trifluoromethanesulfonate)
tt	triplet of triplets
UV	ultraviolet

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Chapter 3 of this dissertation is an adapted reprint of the material as it appears in (Cai, X.; Tohti, A.; Ramirez, C.; Harb, H.; Fettinger, J. C.; Hratchian, H. P.; Stokes, B. J., "Dispersion-Controlled Regioselective Acid-Catalyzed Intramolecular Hydroarylation of *cis*-Methindolylstyrenes to Access Tetrahydrobenzo[cd]indoles" *Org. Lett.* **2019**, *21*, 1574.)

Chapter 4 of this dissertation is currently in preparation intended for future publication (Cai, X.; Stokes, B. J., "Ambient Temperature *tert*-Butoxide-Mediated Decarbonylation of *α*-Quaternary Homobenzaldehydes" **2019**, *in preparation*)

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2015 – 2019	Ph.D., Chemistry (Benjamin J. Stokes – Advisor)
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Associate Scientist
Process R&D

Work with a team of process R&D scientists in conjugation with Analytical Development Department and be responsible for developing safe, efficient and scalable processes for producing starting materials, intermediates and active pharmaceutical ingredients (API's). Assist in tech transferring projects to kilo lab, pilot plant and plant scales and contribute to the safe and cGMP compliant execution of API manufacturing processes. Work with internal Quality Assurance team to ensure that high quality standards are maintained, and appropriate documentation related to process development and scale-up including batch product records (BPR's) are completed in a timely manner and that SOP's are written and followed.

05/2018 – 08/2018 ABBVIE INC. AT NORTH CHICAGO, IL

Summer Intern, Graduate Level
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High-throughput kinetic study of photocatalysis reactions on model substrates using various photocatalysts. Process laboratory scales of photochemical reactions with state-of-the-art equipment. Monitoring reaction rates in correlation to photochemical properties of photosensitizers with UV/Vis Spectrophotometer and Fluorometer. Familiar with ChemELN, electronic data archiving, Excel data processing.

2015 – 2019 UNIVERSITY OF CALIFORNIA AT MERCED

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Synthetic methodology utilizing air-free chemistry (including glove box and Schlenk manifold); NMR acquisition and analysis (1D and 2D); HPLC; GC/MS; X-ray crystal growth; chromatography (including MPLC). Proficient in Microsoft, Chem Office, Varian, MestReNova, SciFinder, EndNote, FTP.

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Natural product total synthesis utilizing environmentally-benign reagents and solvent systems; familiar with retrosynthetic analysis and efficient with multistep synthesis process; utilizing air-free chemistry (including Schlenk manifold); NMR acquisition and analysis (1D and 2D) on Bruker and Varian; recrystallization; distillations; chromatography.

Manuscript in Preparation

4. Cai, X.; Stokes, B. J., "Ambient Temperature *tert*-Butoxide-Mediated Decarbonylation of α-Quaternary Homobenzaldehydes".

Publications

3. Cai, X.; Tuohedi, A.; Ramirez, C.; Harb, H.; Fettinger, J. C.; Hrachian, H. P.; Stokes, B. J., "Dispersion-Controlled Regioselective Acid-Catalyzed Intramolecular Hydroarylation of *cis*-Methindolylstyrenes to Access Tetrahydrobenzo[cd]indoles", *Org. Lett.* **2019**, *21*, 1574.

2. Cai, X.; Keshavarz, A.; Omaque, J. D.; Stokes, B. J., "Brønsted Acid-Catalyzed Intramolecular Hydroarylations of β-Benzylstyrenes Enabled by a Geminal Dialkyl Effect", *Org. Lett.* **2017**, *19*, 2626-2629.

1. Cai, X.; Ng, K.; Panesar, H.; Moon, S.-J.; Paredes, M.; Ishida, K.; Hertweck, C.; Minehan, T.G., "Total Synthesis of the Antitumor Natural Product Polycarcin V and Evaluation of Its DNA Binding Profile", *Org. Lett.* **2014**, *16*, 2962-2965.

Oral and Poster Presentations *(presenter underlined)*

6. "*Gem*-Dimethyl-Induced π–π Interactions Enable Acid-Catalyzed Regioselective Hydroarylation of *cis*-*β*-4'-Methindolylstyrenes, Giving Tetrahydrobenzo[*cd*]indoles" Cai, X. Presented at 33rd Annual Johnson Symposium, Stanford University, Stanford, CA, Oct 2018 (poster).

5. "Kinetic Study of Photoisomerization of *trans*-Alkenes *via* Energy Transfer Pathway" Cai, X. Presented at Department of Process Research and Development, AbbVie, North Chicago, IL, Aug 2018 (oral).

4. "Highly Selective 5,5-Dimethyl-1,3,4,5-tetrahydrobenz[*cd*]indole Synthesis by Acid-Catalyzed Intramolecular Alkene Hydroarylation." Cai, X.; Ramirez, C.; Tuoheti, A.; Harb, H.; Hranchian, H. P.; Stokes, B. J. Presented at the 46th National Organic Symposium, UC Davis, Davis, CA, June 2017 (poster).

3. "Brønsted Acid-Catalyzed Intramolecular Hydroarylations of *β*-Benzylstyrenes Enabled by a Geminal Dialkyl Effect." Cai, X.; Keshavarz, A.; Omaque, J. D.; Stokes, B. J. Presented at the 253rd National Meeting of the American Chemical Society, San Francisco, CA, April 2017 (oral).

2. "Brønsted Acid-Catalyzed Electrophilic Substitution Reactions for the Synthesis of Chiral Carbocycles." Cai, X.; Keshavarz, A.; Omaque, J. D.; Stokes, B. J. Presented at the ISACS19: Challenges in Organic Chemistry by Royal Society of Chemistry, UC Irvine, Irvine, CA, March 2016 (poster).

1. "Direct Study towards the Total Synthesis of Polycarcin V." Cai, X. Presented at the California State University Sigma X Research Symposium, Northridge, CA, April 2013 (oral).

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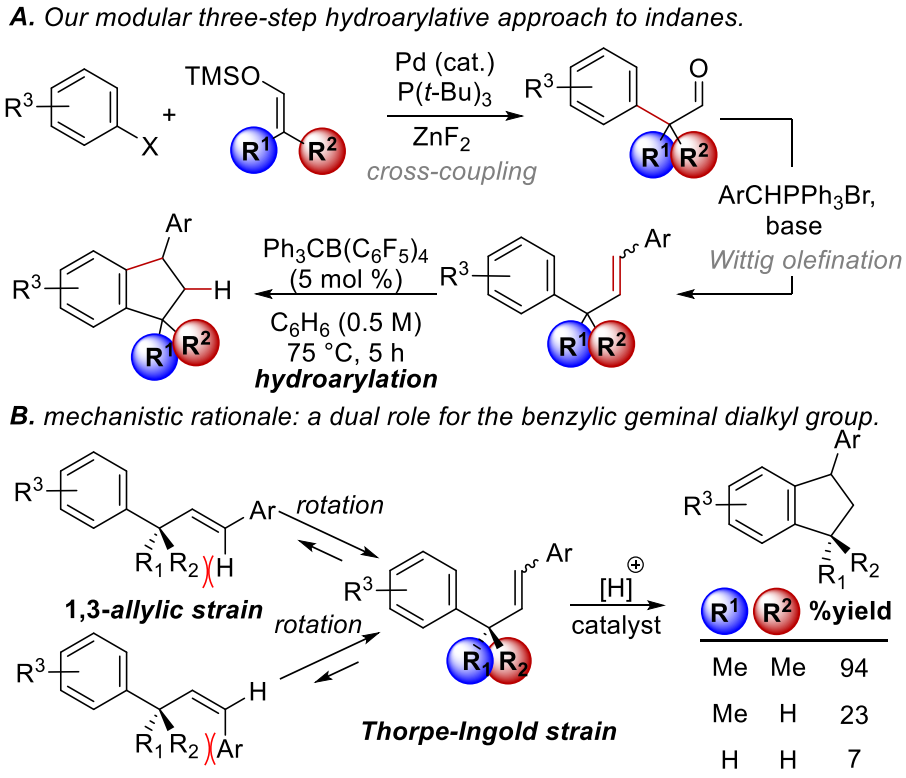
Chapter 1

Introduction

Geminal dialkyl quaternary carbon center is biologically valuable.[1] In addition, organic chemists have long been utilizing its steric biasing feature in methodology development to synthesize bio-active small molecules.[2] In this dissertation, three newly developed synthetic protocols have been described as to contribute in this area.

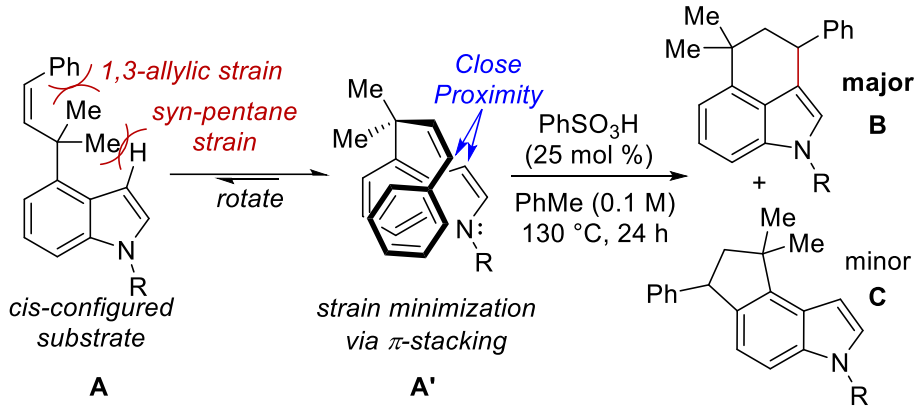
Scheme 1. Catalytic Hydroarylation of Geminal Dialkyl-substituted *β*-benzylstyrenes



My doctoral study was commenced with a rapid construction of a synthetically challenging motif, benzocyclopentane, commonly known as indane. Due to the difficult trajectory of a formal 5-*endo-trig* Friedel-Crafts-type cyclization, method development of indane synthesis is less common compared to tetraline in a modular fashion, in which a favoralble 6-*endo-trig* cyclization is involved.[3-5] In addition to this challenge, direct synthesis of benzylic quaternaty carbon containing indane skelontons is not known. This study opened an access to a facile three-step-assembly towards indane, in which a quaternary benzylic carbon center is already equipped prior to cyclization (Scheme 1A). It is hypothesized that both 1,3-allylic and Thorpe-Ingold strains (Scheme 1B) are necessary to substantially raise the ground state energy of the substrate. Without those strains, high activation energy, which is often associated with compromised temperature and reaction time, is almost always required to pre-organize the structure to a desired orientation to undergo 5-*endo-trig* cyclization. In contrast, steric biasing induced pre-organization allows the transformation to occur with short reaction time, in which side reactions, such as

oligomerization, was significantly diminished. Moreover, cyclization of the pre-organized substrate can be catalyzed under a mild temperature.

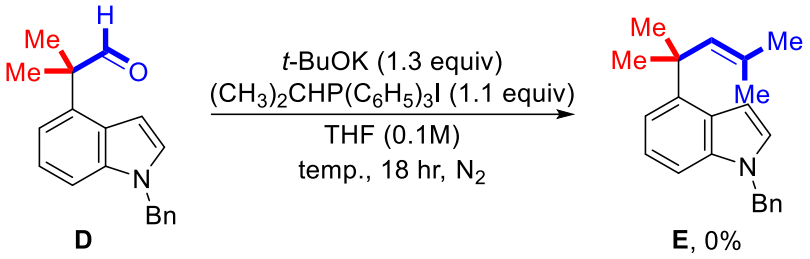
Scheme 2. Catalytic Hydroarylation of *cis*-configured 4'-methindolylstyrenes for the Synthesis of Tetrahydrobenzo[*cd*]indoles



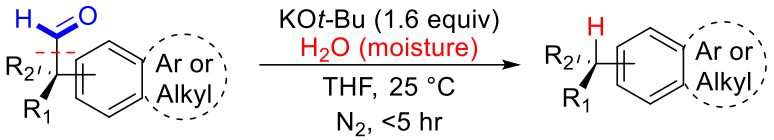
Following the publication of the indane synthesis, I was motivated to develop a protocol that provides more biological related small molecules. With a fond comprehension of steric biasing from the first project, I devised a methindolylstyrenes framework, in which the gem-dimethyl moiety conveyed a syn-pentane strain in addition to 1,3-allylic and Thorp-Ingold strains. It was originally hypothesized that this additional strain could induce a rotary biasing, which could further create an enhanced regio-selectivity between an indane analog and tetrahydrobenzo[*cd*]indole (Scheme 2). Indeed, with those steric features, formation of **B** is significantly preffered over **C**. Intriguingly, good reactivity was only observed when the starting material was in a *cis* form. After careful experimentations along with a series of computational analyses, it was found that a secondary intramolecular non-covalent interaction, namely dispersive π–π stabilization, was earned in the *cis*-configured substrate **A'**. The provocative utility of non-covalent π–π stabilization has rarely been exploited in a seemingly conventional electrophilic aromatic substitution reaction.

Scheme 3. KO*t*-Bu Enables Decarbonylation of Quaternary Center-Containing Aldehydes

A. *Unfruitful Wittig Olefination*



B. *Decarbonylation of quaternary center-containing aldehydes* via *C-C Cleavage*



During the investigation of the necessity of the intramolecular aromatic stabilization, I discovered that the synthesis of alkyl substituted indolic alkene structure (Schem 3A) was extremely difficult to realize in part due to the steric hinderance of the substrate. Unfruitful olefination using isopropyl phosphonium ylide made it abundant clear that the hypothetical indolic alkene product **F** had limited space for the additional gem-dimethyl groups, which were also lacking π–π stacking ability. Although, alkene was not observed, an unexpected decarbonylation *via* C-C cleavage gave rise to a new synthetic method where a formal decarbonylation can be achieved without metal catalysis (Scheme 3B).

The purpose of this dissertation is to introduce and describe the details about the full development of my three novel synthetic methods, which all involve the utility of a benzylic gem-dialkyl substitution. These protocols are synthetically beneficial and the products including all intermeidates that have been synthesized and characterizaed in this dissertation are highly influential with potential medicinal value.

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(2) For a recent review, see: Jung, M. E.; Piizzi, G. *Chem. Rev.* **2005**, *105*, 1735.
(3) For a recent review on Baldwin's rules, see: (a) Alabugin, I. V.; Gilmore, K. *Chem. Commun.* **2013**, 49, 11246. For Baldwin's original reports, see: (b) Baldwin, J. E. *J. Chem. Soc., Chem. Commun*. **1976**, 734. (c) Baldwin, J. E. J. Chem. Soc., *Chem. Commun*. **1976**, 736.
(4) For a recent catalytic enantioselective indane synthesis involving a 5-endo-trig Michael addition, see: Johnston, C. P.; Kothari, A.; Sergeieva, T.; Okovytyy, S. I.; Jackson, K. E.; Paton, R. S.; Smith, M. D. *Nat. Chem.* **2015**, 7, 171.

(5) For examples involving benzylic quaternary center-containing alcohol substrates, see: (a) Blunt, J. W.; Coxon, J. M.; Robinson, W. T.; Schuyt, H. A. *Aust. J. Chem.* **1983**, *36*, 565. (b) Khalaf, A. A.; El-Khawaga, A. M.; Awad, I. M.; Abd El-Aal, H. A. K. *ARKIVOC* **2010**, 314. For other examples of other alcohol substrates, see: (c) Barrow, C. J.; Bright, S. T.; Coxon, J. M.; Steel, P. J. *J. Org. Chem*. **1989**, *54*, 2542. (d) Bright, S. T.; Coxon, J. M.; Steel, P. J. *J. Org. Chem*. **1990**, *55*, 1338. (e) Begouin, J.-M.; Capitta, F.; Wu, X.; Niggemann, M. *Org. Lett.* **2013**, *15*, 1370.

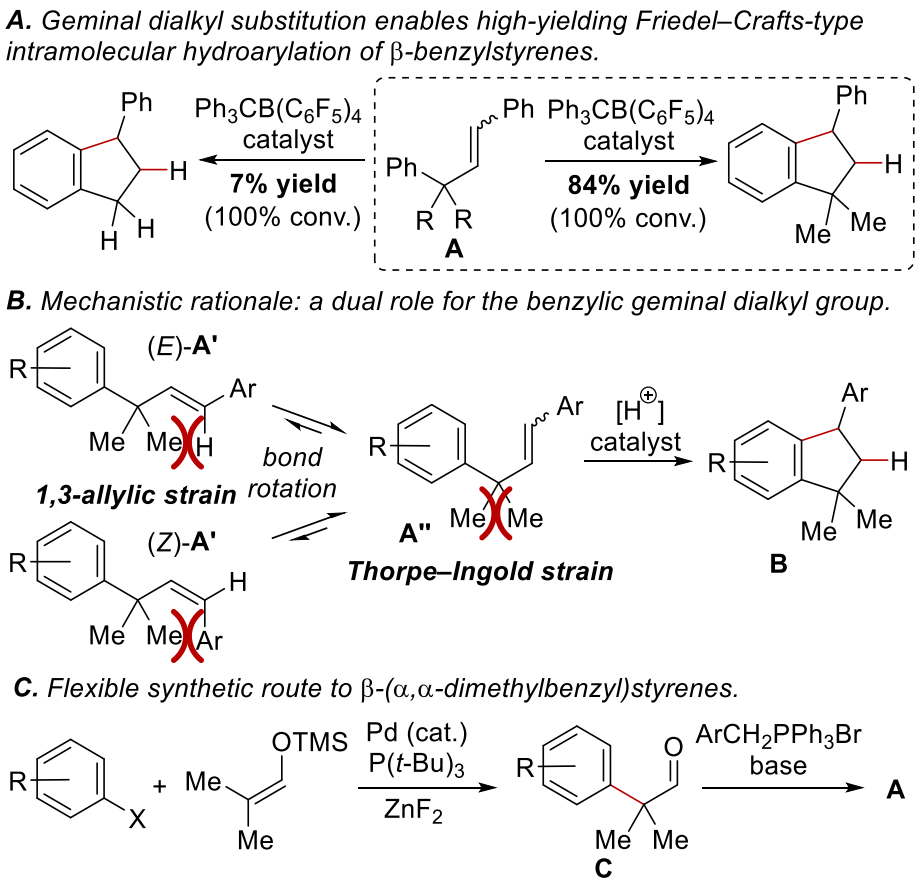
Chapter 2

Gem-Dialkyl Enables Brønsted Acid-Catalyzed Intramolecular Hydroarylation of *β*-Benzylstyrenes to Afford Aryl Indanyl Motifs

Background

The most direct way to construct arene cabocycles[1] is through hydroarylation of alkenes.[2] Catalytic intramolecular Friedel–Crafts-type electrophilic alkene hydroarylation reactions are useful for the synthesis of many types of benzocycloalkanes,[3] but the desired ring closure is required by such methods to outcompete intermolecular side reactions. Thus, there are relatively few strategies for Friedel–Crafts-type benzocyclopentane (indane[4]) synthesis, presumably because of the challenging trajectory of electrophilic aromatic attack required to achieve the formal 5-endo-trig cyclization.[5–7] Prior to my first published protocol during my doctoral study, the most common strategy was the Friedel–Crafts-type cyclization of tertiary alcohols, which presented challenge to prepare in systematic fashion.[4a,7]

Scheme 4. Intramolecular Hydroarylation of *β*-Benzylstyrenes: Challenges and Opportunities



In contrast, a method for indane synthesis using strictly aliphatic substrates had not yet been developed. Herein, our investigation of electrophilic cyclizations of *β*-benzylstyrenes is described in this chapter (A, Scheme 1A). The complication of intermolecular side reactions is made very clear considering that the unsubstituted *β*-

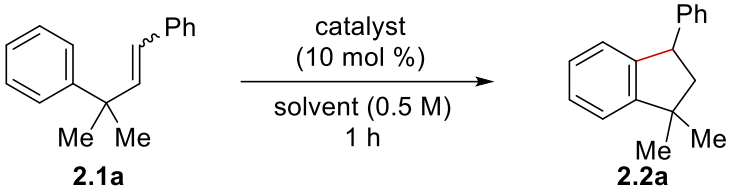
benzylstyrene, A (R = H), affords only in 7% yield of the cyclized product. Fortunately, installation of a geminal dimethyl group (R = Me) enabled cyclization of **A** to outcompete intermolecular polymerization, resulting in excellent yield (inset, Scheme 1A). This disparity suggests that the geminal dialkyl group assists cyclization through steric biasing of the substrate *via* both 1,3-allylic strain (A′) and Thorpe−Ingold strain (A″, Scheme 1B).[8] Based on this exciting discovery, I devised a rapid synthesis of *β*-(*α*,*α*-dimethylbenzyl)styrenes to enable modification of either of the two aromatic rings, as well as the substituents on the benzylic carbon atom (Scheme 1C). This route commenced with a zinc enolate cross-coupling to produce benzylic quaternary center-containing benzaldehydes (C),[9] followed by Wittig olefination. Thus, in just three steps total, I am able to prepare a wide variety of indanes that contain benzylic geminal dimethyl-containing quaternary centers. It is worth mentioning that benzylic geminal dimethyl quaternary centers are medicinally significant because they are metabolically robust compared to benzylic methylenes.[10] In addition, 1-aryl-3,3-dimethylindanes such as **B** have been used in microporous polymers[11a] and as composites in thermoplastics materials.[11b]

Results and Discussion

At the outset of this study, I used *β*-benzylstyrene **2.1a** as a model substrate and evaluated a series of Brønsted and Lewis acids for their propensity to catalyze intramolecular hydroarylation (Table 1). Initially, it was found that 10 mol % of *p*-toluenesulfonic acid monohydrate did not efficiently consume substrate **2.1a** at 80 °C, but full conversion and fair yield could be achieved at 135 °C (entries 1 and 2). In comparison, under otherwise identical conditions, 85% aqueous sulfuric acid converted the substrate much less efficiently (entry 3), while 37% aqueous hydrochloric acid failed to convert the substrate appreciably (entry 4). The evaluation of a stronger Brønsted acid, namely trifluoromethanesulfonic acid, was more fruitful, with the solvents dichloromethane, toluene, and benzene affording increasing yields of indane **2.2a**; the former provides nearly quantitative yield of product (entries 5−7). The transition metal complex $Ph_3PAuOTf$ failed to engage the starting material at all (entry 8), while a modest 58% yield was obtained using $Pd(OAc)_2$ in the presence of trifluoroacetic acid (entry 9). Main group Lewis acids were more suitable, with trimethylsilyltriflate (TMSOTf) delivering **2.2a** in 91% yield at just 40 °C (entry 10). An excellent yield was also achieved using a triphenylmethylium (tritylium) Lewis acid salt, specifically commercially available tritylium tetrakis(pentafluorophenyl) borate (TPFPB), which delivered indane **2.2a** with virtually quantitative yield at temperatures as low as 75 °C (entry 11). Notably, other tritylium salts, including Ph_3CBF_4, Ph_3CSnCl_5, and Ph_3CPF_6, resulted in little or no conversion of **2.1a** at 75 °C, presumably due to their visible insolubility. No product was detected in the presence of triethylamine (entry 12), which suggests that this variant is catalyzed by the *in situ* generated Brønsted acid H−TPFPB.[12] Finally, no conversion was observed when the tritylium salt was used at ambient temperature (entry 13). Although lower reaction temperatures are possible using either trifluoromethanesulfonic acid (entry 7) or trimethylsilyltriflate (entry 10), they are difficult to measure reliably, prone to

decomposition, and volatile, whereas the tritylium TPFPB salt is a solid that can be easily handled.

Table 1. Optimization of the Intramolecular Hydroarylation of *β*-(*α*,*α*-Dimethylbenzyl)styrene[a]

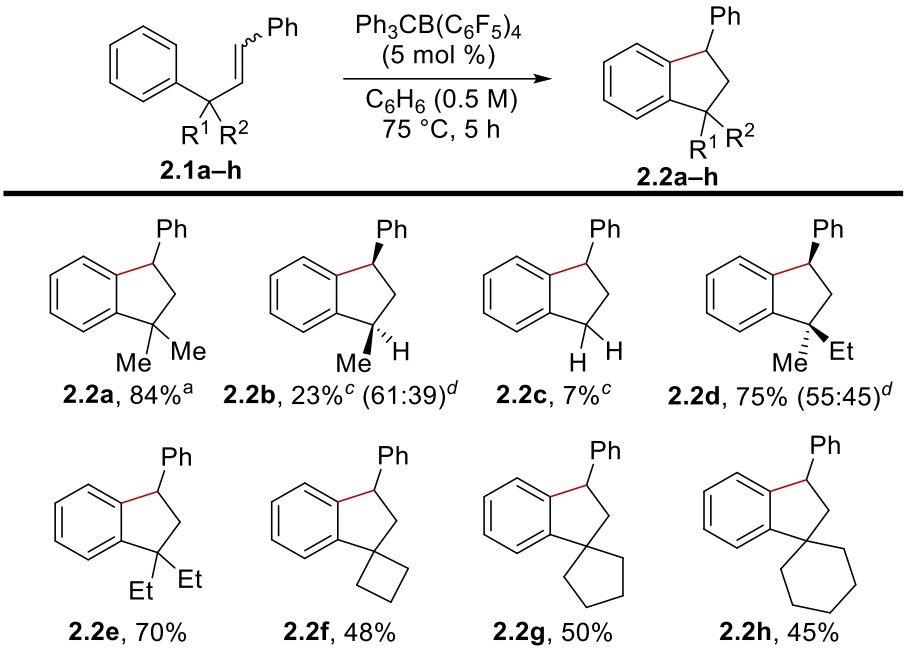


2.1a **2.2a**

entry	catalyst or precatalyst	solvent	temp (°C)	conv (%)[b] of **2.1a**	yield (%)[b] of **2.2a**
1	*p*-TsOH•H_2O	C_6H_6	80	7	6
2	*p*-TsOH•H_2O	C_6H_6	135	100	71
3	H_2SO_4 (85 wt %)	C_6H_6	135	60	50
4	HCl (37 wt %)	C_6H_6	135	<5	0
5	HOTf	CH_2Cl_2	0 - rt	100	60
6	HOTf	PhMe	0 - rt	100	85
7	HOTf	C_6H_6	0 - rt	100	>95
8	$Ph_3PAuOTf$	C_6H_6	135	<5	0
9	$Pd(OAc)_2$	TFA/DCM	100	100	58
10	TMSOTf	C_6H_6	40	100	91
11	$Ph_3CB(C_6F_5)_4$	C_6H_6	75	100	94
12[c]	$Ph_3CB(C_6F_5)_4$	C_6H_6	75	10	0
13	$Ph_3CB(C_6F_5)_4$	C_6H_6	rt	<5	0

[a]Reactions were conducted on 0.1 mmol scale in a sealed vial. [b]Determined by 1H NMR analysis using 1,3,5-trimethoxybenzene as an internal standard. [c]10 mol % of triethylamine was used in this case.

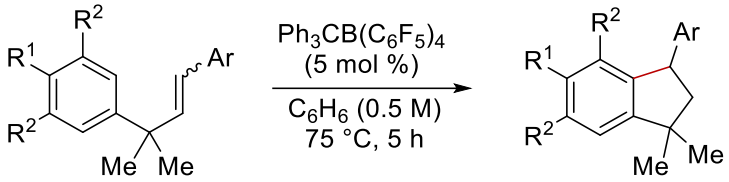
Table 2. Influence of Alkyl Substitution at the Benzylic Position of β-Benzylstyrenes[a]



[a]Reactions were conducted on 0.25 mmol scale unless otherwise noted and monitored by TLC. In each case, the starting material was fully consumed within 5 h. Yields refer to isolated product unless otherwise noted. [b]Reaction was conducted on 1.0 mmol scale. [c]Determined by 1H NMR analysis using 1,3,5-trimethoxybenzene as an internal standard. [d]Ratio of diastereomers as determined by 1H NMR of the crude reaction mixture; the major diastereomer is depicted.

Utilizing the tritylium TPFPB precatalyst, I next systematically probed the impact of geminal dialkyl substitution on empowering the cyclization of *β*-benzylstyrenes (Table 2). Affirmatively, whereas **2.2a** is readily formed in excellent yield on 1.0 mmol scale using 5 mol % of the precatalyst at [**2.1a**] = 0.5 M, diminishing yields resulted as methyl groups were removed from the benzylic position. Specifically, despite complete substrate conversion, monomethyl indane **2.2b** was obtained in just 23% yield, while, as mentioned previously, desmethylated **2.2c** was barely observed. Of note, *cis*-**2.2b** was formed with a slight preference over *trans*-**2.2b**. I then evaluated the scope of benzylic dialkyl substituents on *β*-benzylstyrenes **2.1**. To that end, 1,1-ethylmethyl-3-phenylindane **2.2d** was formed in good yield as a 55:45 mixture of diastereomers. Diethyl indane **2.2e** was also formed in good yield, while cycloalkyl-containing β-benzylstyrenes **2.1f**−**2.1h** afforded diminished yields of the corresponding hydroarylation products **2.2f**−**2.2h**. The attenuated yields of **2.2f**−**2.2h** also support our hypothesis of an enabling steric bias, such as a Thorpe−Ingold effect, whereby angle compression is diminished for cyclic alkanes compared to acyclic ones.[8] In addition, unfruitful cyclization of cyclopropane equipped substrate (not shown) was attempted by Mr. Amir Keshavarz, my peer fellow graduate student.

Table 3. Scope of the Intramolecular Hydroarylation of β-(α,α-Dimethylbenzyl)styrenes[a]



2.3a–o **2.4a–o**

entry	substrate ID	R^1	R^2	Ar	Yield (%) of **2.4**
1	**2.3a**	OMe	H	Ph	29[b,c]
2	**2.3b**	Me	H	Ph	76
3	**2.3c**	Br	H	Ph	62
4	**2.3d**	Cl	H	Ph	65
5	**2.3e**	F	H	Ph	52
6	**2.3f**	CF_3	H	Ph	0
7	**2.3g**	Ph	H	Ph	31[c]
8	**2.3h**	H	OMe	Ph	93[c]
9	**2.3i**	H	Me	Ph	91
10	**2.3j**	H	H	(*p*-OMe)C_6H_4	15[c]
11	**2.3k**	H	H	(*p*-Me)C_6H_4	28
12	**2.3l**	H	H	(*p*-Cl)C_6H_4	46
13	**2.3m**	H	H	(*p*-CF_3)C_6H_4	41[b,d]
14	**2.3n**	H	H	(*m*-Cl)C_6H_4	73[e]
15	**2.3o**	H	H	2-naphthyl	69

[a]Starting material was fully consumed within 5 h. Yields refer to isolated product unless otherwise noted. [b]1H NMR yield determined using 1,3,5-trimethoxybenzene as an internal standard. [c]Reaction employed 10 mol % of trifluoromethanesulfonic acid as catalyst at 0 °C for 1 h. [d]Reaction employed 0.6 equiv of trifluoromethanesulfonic acid for 1 h. [e]Reaction employed 15 mol % of $Ph_3CB(C_6F_5)_4$.

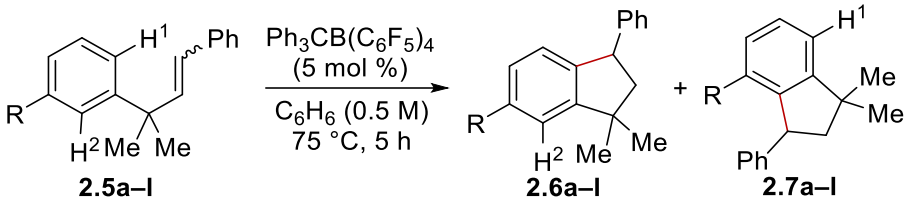
My next aim was to investigate the functional group tolerance of the reaction conditions on hydroarylations of substituted β-(α,α dimethylbenzyl)styrenes (Table 3). In general, the tritylium TPFPB catalyst fully converted substrates containing a wide variety of functional groups, with the exception of Lewis basic alkoxyl or hydroxyl groups. However, in such cases, triflic acid may be used; for example, **2.3a** was converted to indane **2.4a**, albeit in low yield (entry 1). Also in the R^1 position, nonbasic substituents, such as methyl (entry 2) and halogens, including bromine, chlorine, and fluorine (entries 3−5), were effectively hydroarylated in the presence of the trityl TPFPB salt. In contrast, a substrate bearing a trifluoromethyl substituent (**2.3f**) was fully consumed, but a complex mixture of undesired products resulted (entry 6). A phenyl-substituted substrate (**2.3g**) afforded a 31% hydroarylation yield when using triflic acid as the catalyst (entry 7); surprisingly, no cyclization occurred in the presence of the trityl TPFPB precatalyst.

Excellent yields were obtained for meta-dimethoxy- and metadimethyl- substituted substrates (entries 8 and 9), the former also requiring triflic acid as the catalyst. Methoxy, methyl, chloro, and trifluoromethyl-containing substrates afforded only modest yields in the styrene para-position (entries 10−13), whereas a m-chloro substituent delivered indane **2.4n** in fair yield in the presence of 15 mol % of tritylium TPFPB (entry 14). Lastly, we found that substrate **2.3o**, which contains a 2-naphthyl substituent, afforded a 69% yield of hydroarylation product **2.4o** (entry 15).

With the assistance and support from Mr. Amir Keshavarz, together, we then evaluated the outcomes of intramolecular hydroarylations in which two regioisomeric indane products are possible (Table 4). The cyclization of *t*-Bu-substituted substrate **2.5a** formed the least-hindered cyclization product, 6-*tert*-butylindane **2.6a**, exclusively (entry 1). Cyclization also favored the 6-substituted regioisomer in >2:1 ratio for methoxy (entry 2),[13] fluoro (entry 3), and hydroxyl (entry 4) substituted *β*-benzylstyrenes, which is consistent with cyclization at the more nucleophilic position.[14] In contrast to the *t*-Bu-bearing substrate (entry 1), the analogous *i*-Pr-substituted substrate **2.5e** cyclized with only a modest preference for indane **2.6e**. As alkyl substituents became even less bulky (entries 6 and 10), the 4-alkylindanes **2.7f** and **2.7j** were formed preferentially.[15] Other halogenated substrates (**2.5g** and **2.5i**) and a phenyl-substituted substrate (**2.5h**) all favored the formation of the corresponding 4-substituted indane regioisomers **2.7g**−**2.7i** (entries 7−9). Finally, bicyclic arene-containing substrates **2.5k** and **2.5l** (Table 4, bottom) delivered the corresponding sterically congested isomers **2.7k** and **2.7l** in near exclusivity.

Notably, Mr. Keshavarz Synthesized products and their precursors of **2.2f**, **2.6a**, **2.6c**, **2.6e**, **2.6f**−**2.6l**, **2.7a**, **2.7c**, **2.7e** and **2.7f**−**2.7l**. These products are discussed here solely for the completeness of the project development and have been excluded from my experimental section. For a detailed Support Information, please refer to the original publication.[16]

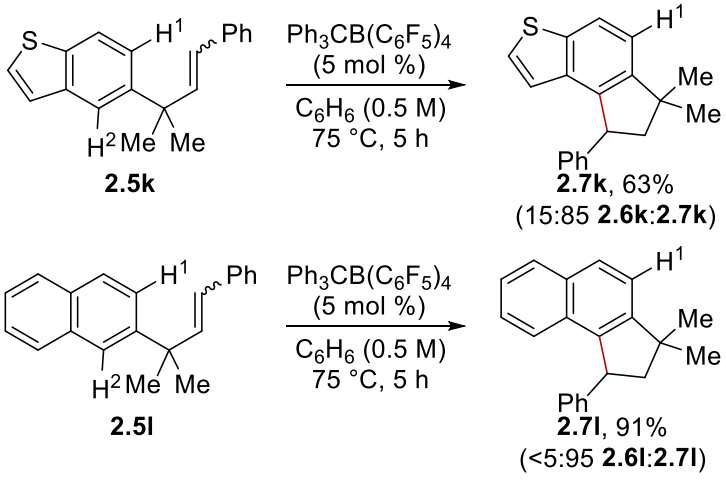
Table 4. Assessing the Regioselectivity of Intramolecular Hydrorylations of *β*-(*α*,*α*-Dimethylbenzyl)styrenes[a]



2.5a–l **2.6a–l** **2.7a–l**

entry	substrate ID	R	Yield (%) of **2.6**+**2.7**	rr[b] (**2.6**:**2.7**)
1	**2.5a**	*t*-Bu	88	>95:5
2[c]	**2.5b**	OMe	91	81:19
3	**2.5c**	F	85	78:22
4[c]	**2.5d**	OH	70	67:33
5	**2.5e**	*i*-Pr	83	60:40
6	**2.5f**	Et	78	50:50
7	**2.5g**	Cl	91	40:60
8	**2.5h**	Ph	98	35:65
9	**2.5i**	Br	96	35:65
10	**2.5j**	Me	70	33:67

[a]Starting material was fully consumed within 5 h. Yields refer to the sum of regioisomers. [b]rr = regioisomeric ratio, which was determined by 1H NMR spectroscopy of the crude mixture. [c]Reaction employed 10 mol % of trifluoromethanesulfonic acid as catalyst for 1 h.



2.5k

2.7k, 63%
(15:85 **2.6k**:**2.7k**)

2.5l

2.7l, 91%
(<5:95 **2.6l**:**2.7l**)

Conclusion

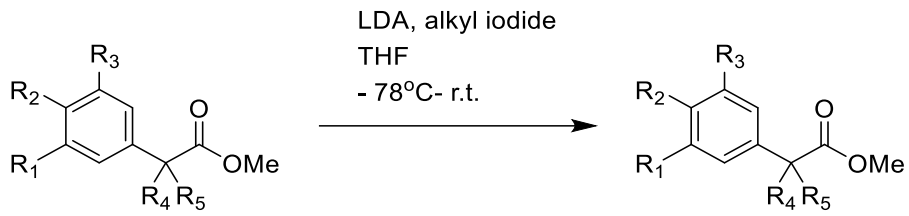
We have demonstrated the feasibility and utility of catalytic intramolecular hydroarylations of *β*-(*α*,*α*-dimethylbenzyl)-styrenes. These reactions are readily accomplished with an easily handled trityl TPFPB precatalyst, or catalytic triflic acid. After I published this initial study, I continued pursuing the development of new methods based on the utility of *α*,*α*-dimethylbenzyl-substituted alkenes, while also working to better understand the mechanism of the reaction, including the relative contributions of steric and electronic effects upon the regioselectivity of the reaction, which led to the discovery of a synthetic method of more bio-related scaffold discussed in chapter 3 of this dissertation.

Experimental

General Considerations

Tritylium salts, including tritylium tetrakis(pentafluorophenyl)borate (TPFPB) were used as purchased from Strem or Sigma-Aldrich and stored in a desiccator when not in use. Silyl enol ethers were used as purchased from Gelest. A Mettler Toledo XS105 balance (repeatable to 0.1 mg) was used to measure mass. Flash column chromatography was performed using 40–63 μm 60 Å silica. Melting points were obtained on an electrothermal melting point apparatus and are uncorrected. NMR spectra were obtained on Agilent spectrometers. ^{1}H NMR spectra were obtained at 400 or 500 MHz and referenced to the residual $CHCl_3$ singlet at 7.26 ppm unless otherwise noted. The abbreviations s, d, t, q, dd, td, qd, and m stand for the resonance multiplicities singlet, doublet, triplet, quartet, doublet of doublet, triplet of doublet, quartet of doublet, and multiplet, respectively. ^{13}C NMR spectra were obtained at 100 or 125 MHz and referenced to the center line of the residual $CDCl_3$ triplet at 77.2 ppm unless otherwise noted. Carbon atom degree of substitution was determined using ^{1}H–^{13}C HSQC. ^{19}F NMR spectra were obtained at 376 MHz subsequent to ^{1}H NMR acquisition and were otherwise unreferenced. FT-IR analysis was performed on a Thermo-Nicolet 380 using a diamond GladiATR from Pike technologies. APCI/ESI HRMS data were obtained on an Agilent LC-TOF (NSF CHE-0541848); EI HRMS data were obtained on a Waters GCT GC/MS (NSF CHE-0742001). Glassware for all reactions was oven-dried at 145 °C and cooled in a desiccator prior to use.

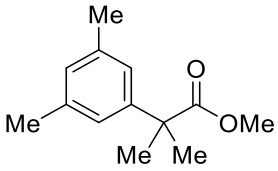
Scheme 5. Alkylation of Benzyl Methyl Esters



1. $R_1 = R_3 = Me$, $R_2 = H$, $R_4 = R_5 = H$
2. $R_1 = R_3 = H$, $R_2 = Me$, $R_4 = R_5 = H$
3. $R_1 = R_2 = R_3 = H$, $R_4 = Me$, $R_5 = H$
4. $R_1 = R_2 = R_3 = R_4 = R_5 = H$
5. $R_1 = R_3 = H$, $R_2 = Ph$, $R_4 = R_5 = H$
6. $R_1 = EOM$, $R_2 = R_3 = H$, $R_4 = R_5 = H$

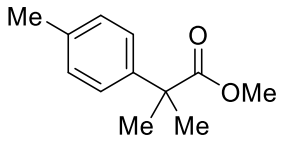
S2.1. $R_1 = R_3 = Me$, $R_2 = H$, $R_4 = R_5 = Me$
S2.2. $R_1 = R_3 = H$, $R_2 = Me$, $R_4 = R_5 = Me$
S2.3. $R_1 = R_2 = R_3 = H$, $R_4 = Me$, $R_5 = Et$
S2.4. $R_1 = R_2 = R_3 = H$, $R_4 = R_5 = Et$
S2.5. $R_1 = R_3 = H$, $R_2 = Ph$, $R_4 = R_5 = Me$
S2.6. $R_1 = EOM$, $R_2 = R_3 = H$, $R_4 = R_5 = Me$

General Procedure I: Alkylation of Benzyl Methyl Ester



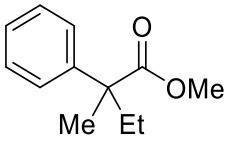
S2.1

Methyl 2-(3,5-dimethylphenyl)-2-methylpropanoate S2.1. In a 250 mL round bottom flask charged with a PTFE-coated magnetic stir bar were added 3.0 g of methyl 2-(3,5-dimethylphenyl)acetate (16.83 mmol, 1.00 equiv) and minimal THF (~10 mL). The reaction solution was cooled to -78 °C and 9.3 mL of lithium diisopropylamine solution (18.6 mmol, 1.1 equiv, 2M in THF/heptane/ethylbenzene) was added through syringe dropwise. The lithium enolate solution was allowed to stir for additional 10 minutes at -78 °C before 2.63 g of methyl iodide (18.53 mmol, 1.1 equiv) was then added to this reaction mixture. The reaction flask was brought to room temperature and allowed to stir for an hour. The reaction was then quenched with saturated $NaHCO_3$ solution (20mL) and the methylated ester was extracted with EtOAc (3 x 20mL), washed with brine, dried over sodium sulfate anhydrous and filtered before it was concentrated under reduced pressure. The above alkylation was repeated on the crude product once and after all starting material was fully converted (monitored by ^1H NMR), the crude ester was purified by flushing through silica gel packed column (100:0 → 90:10 hexane: benzene) to obtain **S2.1** as colorless oil (2.88g, 13.97 mmol, 83% yield). ^1H NMR (400MHz, $CDCl_3$): δ 6.94 (s, 3H), 3.67 (s, 3H), 2.38 (s, 6H), 1.59 (s, 6H).



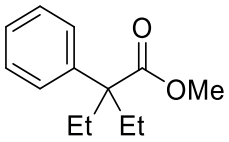
S2.2

methyl 2-methyl-2-(p-tolyl)propanoate S2.2. The general procedure I was followed by using 1.46 g of methyl 2-(p-tolyl)acetate (8.92 mmol) in THF (5 mL), 4.9 mL of LDA (9.81 mmol) and 1.40 g of iodomethane (9.81 mmol). The alkylation was repeated once on the crude product. Purification by flash column chromatography (100:0 → 90:10 hexanes:EtOAc) afforded **S2.2** as a light brown oil (1.10 g, 64% yield). ^{1}H NMR (400 MHz, CDCl3): δ 7.23 (2H, d, *J* = 8.0 Hz), 7.14 (2H, d, *J* = 8.0 Hz), 3.65 (3H, s), 2.33 (3H, s), 1.57 (6H, s). ^{13}C NMR (CDCl3): δ 177.46, 141.73, 136.31, 129.11, 125.49, 52.21, 46.16, 26.59, 20.96. The product matched with literature data that has been reported.[17]



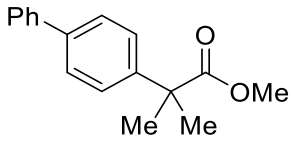
S2.3

Methyl 2-ethyl-2-phenylbutanoate S2.3. The general procedure I was followed by using 1.46 g of methyl 2-phenylpropanoate (8.92 mmol) in THF (5 mL), 4.9 mL of LDA (9.81 mmol) and 1.53 g of iodoethane (9.81 mmol). The alkylation was not repeated on the crude product for this compound. Purification by flash column chromatography (100:0 → 90:10 hexanes:EtOAc) afforded **S2.3** as a light brown oil (1.10 g, 64% yield). ^{1}H NMR (400MHz, $CDCl_3$): δ 7.40-7.32 (m, 4H), 3.65 (s, 3H), 7.28-7.23 (m, 1H), 2.21-2.10 (m, 1H), 2.05-1.96 (m, 1H), 1.58 (s, 3H), 0.88 (t, *J* = 7.4 Hz, 3H).



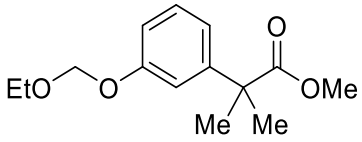
S2.4

Methyl 2-ethyl-2-phenylbutanoate S2.4. The general procedure I was followed by using 1.32 g of methyl 2-phenylacetate (8.92 mmol) in THF (5 mL), 4.9 mL of LDA (9.81 mmol) and 1.53 g of iodoethane (9.81 mmol). The alkylation was repeated once on the crude product. Purification by flash column chromatography (100:0 → 95:5 hexanes:EtOAc) afforded **S2.4** as a light brown oil.



S2.5

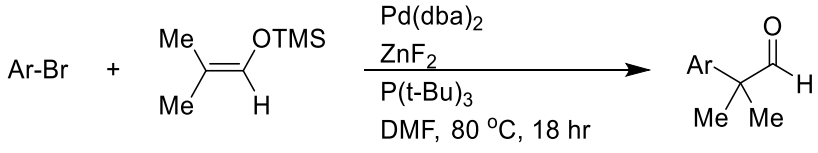
Methyl 2-([1,1'-biphenyl]-4-yl)-2-methylpropanoate S2.5. The general procedure I was followed by using 2.02 g of methyl methyl 2-([1,1'-biphenyl]-4-yl)acetate (8.92 mmol) in THF (5 mL), 4.9 mL of LDA (9.81 mmol) and 1.39 g of iodomethane (9.81 mmol). The alkylation was repeated once on the crude product. Purification by flash column chromatography (100:0 → 85:15 hexanes:EtOAc) afforded **S2.5** as colorless oil.



S2.6

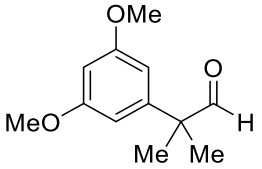
Methyl 2-(3-(ethoxymethoxy)phenyl)-2-methylpropanoate S2.6. The general procedure I was followed by using 2 g of methyl 2-(3-(ethoxymethoxy)phenyl)acetate (8.92 mmol) in THF (5 mL), 4.9 mL of LDA (9.81 mmol) and 1.39 g of iodomethane (9.81 mmol). The alkylation was repeated once on the crude product. Purification by flash column chromatography (100:0 → 75:25 hexanes:EtOAc) afforded **S2.6** as a light brown oil. ^{1}H NMR (400MHz, $CDCl_3$):δ 7.24 (t, *J* = 8.0 Hz, 1H), 7.03-6.99 (m, 1H), 6.99-6.93 (m, 2H), 5.21 (s, 2H), 3.73 (q, *J* = 7.1 Hz, 2H), 3.66 (s, 3H), 1.57 (s, 6H), 1.23 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (100MHz, $CDCl_3$): δ 177.04 (CO), 157.5 (C), 146.3 (C), 129.3 (CH), 119.1 (CH), 114.3 (CH), 114.0 (CH), 93.3 (CH_2), 64.1 (CH_2), 52.2 (CH_3), 46.5 (C), 26.5 (CH_3), 15.1 (CH_3).

Scheme 6. Synthesis of Aryl Geminal Dimethyl Carbonyl Complexes



S2.6

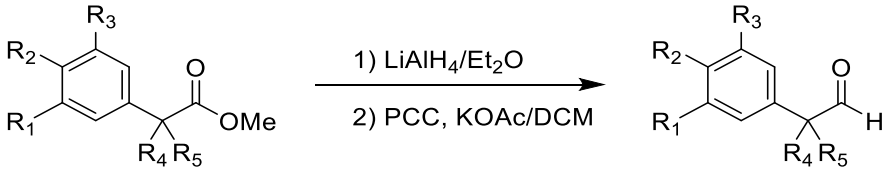
General Procedure II: Synthesis of Aryl Geminal Dimethyl Carbonyl Complexes



S2.6

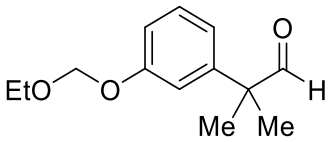
2-(3,5-dimethoxyphenyl)-2-methylpropanal S2.6. The general procedure II was followed using 1.0 g of 1-bromo-3,5-dimethoxybenzene (4.60 mmol), 0.38 g of zinc fluoride (3.68mmol), 0.26 g of bis(dibenzylideneacetone)palladium(0) (0.46 mmol), 0.88mL tri-tert-butylphosphine (0.88 mmol), 1.29 mL trimethyl((2-methylprop-1-en-1-yl)oxy)silane (6.9 mmol) in 46 mL DMF. Purification by silica gel chromatography (100:0→85:15 hexanes: ethyl acetate) afforded **S2.6** (0.72g, 75% yield) as yellow oil. ^{1}H NMR (400MHz, $CDCl_3$):δ 9.44 (s, 1H), 6.39 (s, 2H), 6.37 (s, 1H), 3.76 (s, 6H), 1.41 (s, 6H); ^{13}C NMR (100MHz, $CDCl_3$): δ 201.8 (CO), 161.1 (C), 143.6 (C), 105.1 (CH), 98.6 (CH), 55.3 (CH_3), 50.5 (C), 24.0 (CH_3).

Scheme 7. Preparation of Aryl Geminal Dialkyl Aldehyde Intermediates *via* Sequential Reduction-Oxidation of Ester



S2.7-**S2.12**

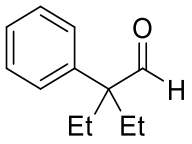
General Procedure III: synthesis of Aryl Geminal Dialkyl Aldehyde Intermediates of Ester



S2.7

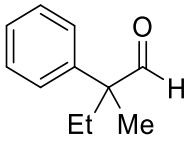
2-(3-(Ethoxymethoxy)phenyl)-2-methylpropanal S2.7. Into a dry 250 mL round bottom flask charged with a PTFE-coated magnetic stir bar were added 1.00 g of methyl 2-(3-(ethoxymethoxy)phenyl)-2-methylpropanoate (3.96 mmol, 1.00 equiv) and 40 mL of diethyl ether. The solution was chilled in an ice bath and purged with argon. To this mixture, 0.356 g of lithium aluminum hydride (8.91 mmol, 2.25 equiv) was added in four approximately equal portions over 10 minutes. The reaction was allowed to warm to room temperature and stir for an additional 30 minutes. After TLC monitoring showed complete

consumption of the methyl ester, the flask was returned to an ice bath and quenched with 10 mL of 1 M aqueous HCl. The primary alcohol product was extracted with diethyl ether (3 x 20 mL). The combined organic layers were dried over anhydrous $MgSO_4$, filtered, and concentrated under reduced pressure. The residue was then dissolved in 20 mL of DCM. To this solution were added 0.939 g of pyridinium chlorochromate (4.36 mmol, 1.10 equiv) and 0.428 g of KOAc (4.36 mmol, 1.10 equiv) at ambient temperature. The oxidation was monitored by TLC and was complete after two hours. The reaction mixture was then diluted with 20 mL of EtOAc and the organic liquid was filtered through a packed celite cake. The combined liquor was dried over anhydrous Na_2SO_4, concentrated *in vacuo* and the crude brown oil was transferred to a packed silica gel column and flushed with a mixture of hexane and EtOAc (100:0→90:10 hexanes:EtOAc). The pure aldehyde product **S2.15(7)** was obtained after evaporation of organic solvents as light-yellow oil (651 mg, 74% yield over 2 steps). ^{1}H NMR (400 MHz, $CDCl_3$): δ 9.49 (s, H). 7.29 (t, *J* = 8.0 Hz, 1H), 6.99 (d, *J* = 8.3 Hz, 1H), 6.96 (s, 1H), 6.90 (d, *J* = 7.8 Hz, 1H), 5.22 (s, 2H), 3.73 (q, *J* = 7.0 Hz, 2H), 1.45 (s, 6H), 1.22 (t, *J* = 7.0 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 201.9 (CO), 157.9 (C), 142.9 (C), 129.8 (CH), 120.1 (CH), 115.2 (CH), 114.5 (CH), 93.2 (CH_2), 64.2 (CH_2), 50.4 (C), 22.4 ($2CH_3$), 15.1 (CH_3).



S2.8

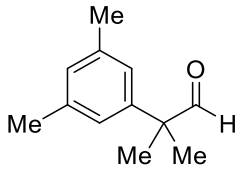
2-ethyl-2-phenylbutanal S2.8. The general procedure III was followed using 1.00 g of methyl 2-ethyl-2-phenylbutanoate (4.85 mmol) and 0.415 g of $LiAlH_4$ (10.9 mmol) in 50 mL of Et_2O. The crude isolate was then oxidized using 1.15 g of PCC (5.33 mmol) and 523.1 mg of KOAc (5.33 mmol) in 25 mL of DCM. Purification by flash column chromatography (100:0 → 90:10 hexanes:EtOAc) afforded **S2.8** as a light yellow oil (598.4 mg, 70% yield over two steps).^{1}H NMR (400 MHz, $CDCl_3$): δ 9.49 (s, 1H), 7.42-7.32 (m, 2H), 7.30-7.20 (m, 3H), 1.98 (q, *J* = 7.5 Hz, 4H), 0.77 (t, *J* = 7.5 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 203.1 (CO), 139.1 (C), 128.7 (CH), 127.7 (2CH), 127.1 (CH), 58.1 (C), 24.0 (CH_2), 8.1 (CH_3).



S2.9

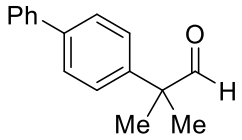
2-methyl-2-phenylbutanal S2.9. The general procedure III was followed using 2 g of methyl 2-methyl-2-phenylbutanoate (9.70 mmol) and 829.35 mg of $LiAlH_4$ (21.83 mmol) in 97 mL of Et_2O. The crude isolate was then oxidized using 2.54 g of PCC (11.63 mmol) and 1.14 g of KOAc (11.63 mmol) in 40 mL of DCM. Purification by flash column

chromatography (100:0 → 85:15 hexanes:EtOAc) afforded **S2.9** as light yellow oil. (1.38 g, 63% yield over two steps). The product matched with literature data that has been reported.[18]



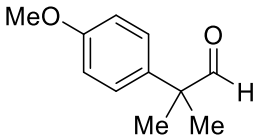
S2.10

2-(3,5-dimethylphenyl)-2-methylpropanal S2.10. The general procedure III was followed using 2.84 g of methyl 2-(3,5-dimethylphenyl)-2-methylpropanoate (13.8 mmol) and 1.2 g of $LiAlH_4$ (31 mmol) in 140 mL of Et_2O. The crude isolate was then oxidized using 3.3 g of PCC (15.2 mmol) and 1.5 g of KOAc (15.2 mmol) in 30 mL of DCM. Purification by flash column chromatography (100:0 → 90:10 hexanes:EtOAc) afforded **S2.10** as a light yellow oil (1.7 g, 69% yield over two steps).^{1}H NMR (400 MHz, $CDCl_3$): δ 9.47 (s, 1H), 6.93 (s, 1H), 6.88 (s, 2H), 2.33 (s, 6H), 1.44 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 202.4 (CO), 141.1 (C), 138.4 (2C), 128.9 (CH), 124.5 (2CH), 50.3(C), 22.4 ($2CH_3$), 21.4 ($2CH_3$).



S2.11

2-([1,1'-biphenyl]-4-yl)-2-methylpropanal S2.11. The general procedure III was followed using 5.00 g of methyl 2-(3,5-dimethylphenyl)-2-methylpropanoate (22.1 mmol) and 1.89 g of $LiAlH_4$ (49.7 mmol) in 220 mL of Et_2O. The crude isolate was then oxidized using 5.8 g of PCC (26.52 mmol) and 2.6 g of KOAc (26.52 mmol) in 89 mL of DCM. Purification by flash column chromatography (100:0 → 80:20 hexanes:EtOAc) afforded **S2.11** as light yellow oil. (3.0 g, 60% yield over two steps). ^{1}H NMR (400 MHz, $CDCl_3$): δ 9.64 (s, 1H), 7.77-7.65 (m, 3H), 7.55 (t, *J* = 7.5 Hz, 1H), 7.48-7.45 (m, 5H), 1.61 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 202.0 (CO), 140.6 (C), 140.3 (C), 140.2 (C), 129.0 (CH), 128.5 (CH), 127.7 (CH), 127.3 (CH), 127.2 (CH), 50.3(C), 22.62 (CH_3).

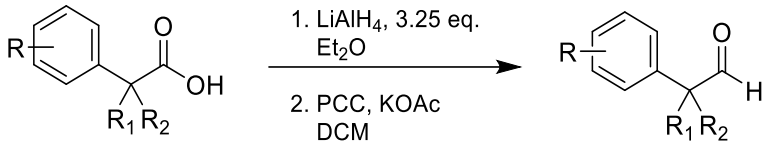


S2.12

2-(4-methoxyphenyl)-2-methylpropanal S2.12. The general procedure III was followed using 2.50 g of methyl 2-(4-methoxyphenyl)-2-methylpropanoate (12.0 mmol) and 1.03 g

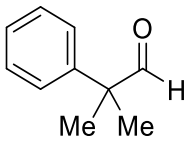
of $LiAlH_4$ (27.0 mmol) in 120 mL of Et_2O. The crude isolate was then oxidized using 2.9 g of PCC (13.2 mmol) and 1.3 g of KOAc (13.2 mmol) in 60 mL of DCM. Purification by flash column chromatography (100:0 → 80:20 hexanes:EtOAc) afforded **S2.12** as light yellow oil. (1.65 g, 77% yield over two steps). ^{1}H NMR (400 MHz, $CDCl_3$): δ 9.44 (s, 1H), 7.19 (d, *J* = 8.4 Hz, 2H), 6.91 (d, *J* = 8.6 Hz, 2H), 3.78 (s, 3H), 1.43 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 202.1 (CO), 158.7 (C), 133.0 (C), 127.8 (CH), 114.2 (CH), 55.2 (CH_3), 49.7 (C), 22.5 (CH_3).

Scheme 8. Preparation of Aryl Geminal Dialkyl Aldehyde Intermediates *via* Sequential Reduction-Oxidation of Carboxylic Acid



S2.13-S2.18

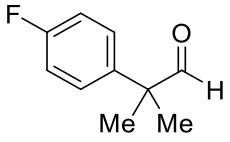
General Procedure IV: Preparation of Aryl Geminal Dialkyl Aldehyde Intermediates *via* Sequential Reduction-Oxidation of Carboxylic Acid



S2.13

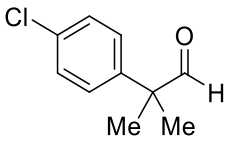
2-methyl-2-phenylpropanal S2.27. To a dry 250 mL round bottom flask charged with a PTFE-coated magnetic stir bar were added 2-methyl-2-phenylpropanoic acid (1.0 g, 6.1 mmol, 1.00 equiv) and diethyl ether (122 mL, 0.05 M). The solution was then cooled to 0 ºC and purged with argon for 5 minutes. To the chilled mixture was added $LiAlH_4$ (753.4 mg, 3.25 equiv) in 4 portions over 10 minutes. The reaction was then warmed to room temperature and stirred for one hour. The reaction was monitored by TLC. Once all carboxylic acid was consumed, the reaction was carefully quenched by addition of 1 M aqueous HCl (~10 mL) at 0 ºC. The primary alcohol intermediate was extracted with diethyl ether three times. The ether solution was dried over anhydrous magnesium sulfate before it was concentrated *in vacuo*. The crude product was then dissolved with DCM (24.5 mL, 0.25 M). The solution was chilled in an ice bath and allowed to purge with argon. To this inert gas-protected mixture, PCC (1.60 g, 1.2 equiv) and KOAc (718 mg, 1.20 equiv) were added. The reaction was allowed to stir at 0 ºC for 2 hours until all primary alcohol had been consumed as determined by TLC. The mixture was then diluted with EtOAc (20 mL) and the organic solution was filtered through a pad of Celite®. The combined liquid was dried over anhydrous sodium sulfate. All organic solvents were removed under

reduced pressure and the residue was purified by flash column chromatography on SiO_2 using hexanes:EtOAc (100:0→92:8) to afford aldehyde **S2.13** (701 mg, 77% yield), which was prone to decomposition over time. The product matched with literature. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 9.50 (s, 1H), 7.40-7.27 (m, 5H), 1.47 (s, 6H); ^{13}C NMR (100 MHz, CDCl3) δ: 202.3, 141.4, 129.0, 127.4, 126.8, 50.6, 22.6.[19]



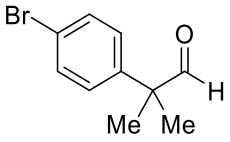
S2.14

2-(4-Fluorophenyl)-2-methylpropanal S2.14. The general procedure IV was followed using 1.10 g of 2-(4-fluorophenyl)-2-methylpropanoic acid (6.1 mmol) and 0.753 g of $LiAlH_4$ (19.8 mmol) in 122 mL of Et_2O. The crude isolate was then oxidized using 1.60 g of PCC (7.32 mmol) and 718 mg of KOAc (7.32 mmol) in 25 mL of DCM. Purification by flash column chromatography (100:0 → 90:10 hexanes:EtOAc) afforded **S2.14** as a light yellow oil. (710 mg, 70% yield over two steps). ^{1}H NMR (400 MHz, $CDCl_3$): δ 9.47 (s, 1H), 7.24 (dd, *J* = 8.3, 5.4 Hz, 2H), 7.06 (t, *J* = 8.5 Hz, 2H), 1.45 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): 201.8 (CO), 161.9 (d, *J* = 246.5 Hz, C), 136.9 (C), 128.4 (d, *J* = 8.1 Hz, CH), 115.7 (d, *J* = 21.3 Hz, CH), 49.9 (C), 22.6 (CH_3); ^{19}F (376 MHz, $CDCl_3$): δ –115.5;



S2.15

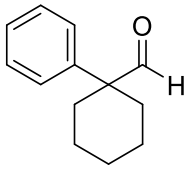
2-(4-chlorophenyl)-2-methylpropanal S2.15. The general procedure IV was followed using 1.21 g of 2-(4-chlorophenyl)-2-methylpropanoic acid (6.1 mmol) and 0.753 g of $LiAlH_4$ (19.8 mmol) in 122 mL of Et_2O. The crude isolate was then oxidized using 1.60 g of PCC (7.32 mmol) and 718 mg of KOAc (7.32 mmol) in 25 mL of DCM. Purification by flash column chromatography (100:0 → 90:10 hexanes:EtOAc) afforded **S2.15** as a light yellow oil (802.2 mg, 72% over two steps). ^{1}H NMR (400 MHz, $CDCl_3$): δ 9.47 (s, 1H), 7.35 (dd, *J* = 8.6 Hz, 2H), 7.20 (d, *J* = 8.6 Hz, 2H), 1.45 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 201.7 (CO), 139.7 (C), 133.3 (C), 128.9 (CH), 128.1 (CH), 50.1 (C), 22.5 (CH_3).



S2.16

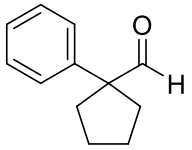
2-(4-bromophenyl)-2-methylpropanal S2.16. The general procedure IV was followed using 1.48 g of 2-(4-bromophenyl)-2-methylpropanoic acid (6.1 mmol) and 0.753 g of

$LiAlH_4$ (19.8 mmol) in 122 mL of Et_2O. The crude isolate was then oxidized using 1.60 g of PCC (7.32 mmol) and 718 mg of KOAc (7.32 mmol) in 25 mL of DCM. Purification by flash column chromatography (100:0 → 90:10 hexanes:EtOAc) afforded **S2.16** as a light yellow oil (1.19 g, 86% over two steps). ^{1}H NMR (400 MHz, $CDCl_3$): δ 9.47 (s, 1H), 7.50 (d, *J* = 8.7 Hz, 2H), 7.20 (d, *J* = 8.7 Hz, 2H), 1.45 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 201.6 (CO), 140.2 (C), 131.9 (CH), 128.5 (CH), 121.4 (C), 50.2 (C), 22.5 (CH_3).



S2.17

1-phenylcyclohexane-1-carbaldehyde S2.17. The general procedure IV was followed using 1.25 g of 1-phenylcyclohexane-1-carboxylic acid (6.1 mmol) and 0.753 g of $LiAlH_4$ (19.8 mmol) in 122 mL of Et_2O. The crude isolate was then oxidized using 1.60 g of PCC (7.32 mmol) and 718 mg of KOAc (7.32 mmol) in 25 mL of DCM. Purification by flash column chromatography (100:0 → 95:5 hexanes:EtOAc) afforded **S2.17** as a light yellow oil (0.90 g, 78% over two steps). ^{1}H NMR (400 MHz, $CDCl_3$): δ 9.38 (s, 1H), 7.41-7.31 (m, 4H), 7.30-7.24 (m, 1H), 2.38-2.26 (m, 2H), 1.91-1.80 (m, 2H), 1.73-1.57 (m, 3H), 1.56-1.43 (m, 2H), 1.37-1.26 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 202.3 (CO), 139.7 (C), 128.9 (CH), 127.2 (CH), 127.1 (CH), 54.4 (C), 31.3 (CH_2), 25.6 (CH_2), 22.8 (CH_2).[19]

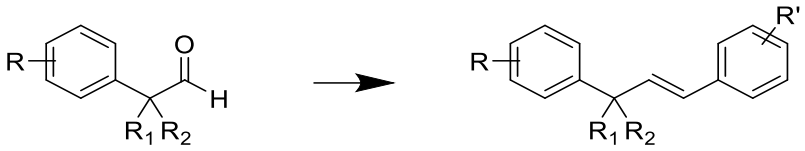


S2.18

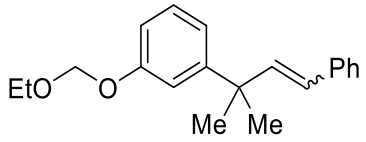
1-phenylcyclopentane-1-carbaldehyde S2.18. The general procedure IV was followed using 1.16 g of 1-phenylcyclopentane-1-carboxylic acid (6.1 mmol) and 0.753 g of $LiAlH_4$ (19.8 mmol) in 122 mL of Et_2O. The crude isolate was then oxidized using 1.60 g of PCC (7.32 mmol) and 718 mg of KOAc (7.32 mmol) in 25 mL of DCM. Purification by flash column chromatography (100:0 → 95:5 hexanes:EtOAc) afforded **S2.18** as a light yellow oil (0.71 g, 67% over two steps). The product matched with literature. ^{1}H NMR (400 MHz, $CDCl_3$): δ: 9.31 (s, 1H), 7.24–7.28 (m, 2H), 7.15–7.19 (m, 3H), 2.41–2.47 (m, 2H), 1.76–1.83 (m, 2H), 1.64–1.68 (m, 2H), 1.54–1.60 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ: 200.6, 140.3, 128.7, 127.6, 127.1, 63.6, 32.3, 24.2.[20]

Scheme 9. Preparation of *β*-Benzylstyrenes

General Procedure V: Synthesis of Diaryl Geminal Dialkyl *β*-Benzylstyrenes *via* Wittig Olefination



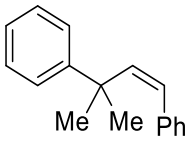
In a dry 25-50 mL round bottom flask charged with Teflon coated magnetic stir bar, benzyl triphenylphosphonium bromide (1.6 eq.) was dissolved in 2mL THF. The reaction flask was then sealed with a rubber septum before t-BuOK (1.6 M in THF solution, 1.6 eq.) was syringed into the mixture at room temperature. The reaction mixture immediately turned red and was continuously being stirred for an additional 20 minutes before it was chilled to 0 ^{o}C. A solution of aryl-dialkyl-aldehydes in minimal amount of THF (0.5 mmol-2.5 mmol, 1.0 eq.) was then added to the ylides drop-wise through syringe. The reaction was then brought to room temperature and allowed to stir for 18 hours. After all the aldehyde was consumed, the reaction was quenched with saturated aqueous NH_4Cl solution. Based on the polarity of the product, the alkene was extracted with a mixture solution of hexane and ethyl acetate three times. The combined organic solution was collected and dried over sodium sulfate anhydrous before it was concentrated under reduced pressure to afford crude alkene product as a mixture of E and Z isomers. Purification by silica gel chromatography using gradient elution afforded analytically pure E and Z alkenes as a mixture. The impurity is not tabulated in the following characterizations, and does not substantially affect the yield.



S2.19

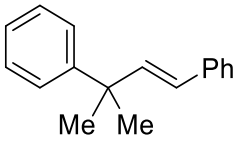
(Z, E)-1-(ethoxymethoxy)-3-(2-methyl-4-phenylbut-3-en-2-yl)benzene S2.19. The general procedure V was followed using 555.8 mg of **S2.7** (2.5 mmol), 1.7 g triphenyl phosphonium bromide (4.0 mmol, 1.6 eq.) and 2.5 mL t-BuOK solution in THF. Purification by flash column chromatography (100:0→85:15 hexanes:EtOAc) afforded inseparable Z/E (68:32) stereoisomers (666.9 mg, 90% yield) as light yellow oil; **Selected spectra for Z isomer:** ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.05 (dd, *J* = 7.2, 1.7 Hz, 2H), 6.61 (d, *J* = 12.6 Hz, 1H), 6.00 (d, *J* = 12.6 Hz, 1H), 5.26 (s, 2H), 3.80 (q, *J* = 7.1 Hz, 2H), 1.47 (s, 6H), 1.32 (td, *J* = 7.0, 2.3 Hz, 3H), **other peaks in aromatic region were obscured by E isomer.** ^{13}C NMR (100 MHz, $CDCl_3$): δ 157.4 (C), 151.7 (C), 141.5 (CH), 138.1 (C), 129.1 (CH), 128.9 (2CH), 128.9 (CH), 127.5 (2CH), 126.3 (CH), 119.7 (CH), 114.9 (CH), 113.1 (CH), 93.4 (CH_2), 64.1 (CH_2), 41.1 (C), 31.2 ($2CH_3$), 15.2 (CH_3); **Selected spectra**

for E isomer: ^{1}H NMR (400 MHz, $CDCl_3$): δ 6.93 (ddd, *J* = 8.1, 2.5, 0.9 Hz, 2H), 6.52 (appr s, 2H), 5.29 (s, 2H), 3.81 (q, *J* = 7.1 Hz, 2H), 1.60 (s, 6H), 1.31 (t, *J* = 7.1 Hz, 3H). **other peaks in aromatic region were obscured by Z isomer.** ^{13}C NMR (100 MHz, $CDCl_3$): δ 157.5 (C), 150.6 (C), 140.0 (CH), 137.8 (C), 129.2 (CH), 128.6 (2CH), 127.1 (CH), 126.3 (2CH), 126.3 (CH), 119.9 (CH), 115.1 (CH), 113.3 (CH), 93.4 (CH_2), 64.2 (CH_2), 40.9 (C), 28.8 ($2CH_3$), 24.1 (CH_3). HRMS (GCMS) m/z calculated for $C_{20}H_{24}O_2[M]^+$: 296.1776, found: 296.1776.



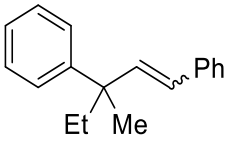
2.1a-Z

(Z)-(3-methylbut-1-ene-1,3-diyl)dibenzene 2.1a-Z. The general procedure V was followed using 370 mg of 2-methyl-2-phenylpropanal (2.5 mmol), 1.7 g of triphenyl phosphonium bromide (4.0 mmol, 1.6 eq.) and 2.5 mL t-BuOK solution in THF. Purification by flash column chromatography (100:0→99:5 hexanes: benzene) afforded Z alkene **2.1a-Z** (125.8 mg, 56.6% yield) as colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.66 (d, *J* = 8.4 Hz, 2H), 7.53 (t, *J* = 7.7 Hz, 2H), 7.44-7.35 (m, 4H), 7.26-7.24 (m, 2H), 6.83 (d, *J* = 12.6 Hz, 1H), 6.24 (d, *J* = 12.6 Hz, 1H), 1.70 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 150.3 (C), 141.8 (CH), 138.1 (C), 129.2 (2CH), 129.1 (CH), 128.4 (2CH), 127.8 (2CH), 126.5 (CH), 126.4 (2CH), 125.9 (CH), 41.3 (C), 31.5 (CH_3); ATR-FTIR (neat): cm^{-1}; HRMS (GCMS) m/z calculated for $C_{17}H_{18}[M]^+$: 222.1403, found 222.1393.



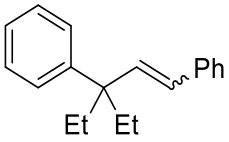
2.1a-E

(E)-(3-methylbut-1-ene-1,3-diyl)dibenzene 2.1a-E. The general procedure V was followed using 370 mg of 2-methyl-2-phenylpropanal (2.5 mmol), 1.7 g of triphenyl phosphonium bromide (4.0 mmol, 1.6 eq.) and 2.5 mL t-BuOK solution in THF. Purification by flash column chromatography (100:0→99:5 hexanes: benzene) afforded Z alkene **2.1a-E** (62.9 mg, 28.3% yield) as colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.60-7.21 (m, 10H), 6.52 (appr t, *J* = 16.8 Hz, 2H), 1.61 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 148.8 (C), 140.2 (CH), 137.7 (C), 128.6 (2CH), 128.3 (CH), 127.1 (2CH), 126.3 (2CH), 126.3 (CH), 126.1 (2CH), 126.0 (CH), 40.1 (C), 28.8 (CH_3); ATR-FTIR (neat): cm^{-1}; HRMS (GCMS) m/z calculated for $C_{17}H_{18}[M]^+$: 222.1403, found 222.1393.



2.1d

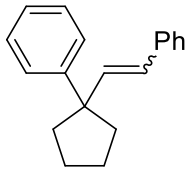
(Z, E)-(3-methylpent-1-ene-1,3-diyl)dibenzene 2.1d. The general procedure V was followed using 405.6 mg of 2-methyl-2-phenylbutanal (2.5 mmol), 1.7 g triphenyl phosphonium bromide (4.0 mmol, 1.6 eq.) and 2.5 mL t-BuOK solution in THF. Purification by flash column chromatography (100:0→90:10 hexanes:benzene) afforded inseparable Z/E (66:34) stereoisomers (496.4 mg, 84% yield) as colorless oil;^{1}H NMR (400 MHz, $CDCl_3$): δ 6.65 (d, *J* = 12.7 Hz, 1H), 6.01 (d, *J* = 12.7 Hz, 1H), 1.83 (q, *J* = 7.4 Hz, 2H), 1.40 (s, 3H), 0.85 (t, *J* = 7.4 Hz, 3H). **Other peaks were obscured by E isomer.** ^{13}C NMR (100 MHz, $CDCl_3$): δ 149.0 (C), 140.6 (CH), 138.3 (C), 129.6 (CH), 128.9 (CH), 128.0 (CH), 127.5 (CH), 126.9 (CH), 126.8 (CH), 125.5 (CH), 44.3 (C), 37.9 (CH_2), 25.3 (CH_3), 9.1 (CH_3); **Selected spectra for E isomer:** ^{1}H NMR (400 MHz, $CDCl_3$): δ 6.53 (d, *J* = 16.3 Hz, 1H), 6.48 (d, *J* = 16.3 Hz, 1H), 2.00 (pd, *J* = 14.2, 7.4 Hz, 2H), 1.55 (s, 3H), 0.92 (t, *J* = 7.4 Hz, 3H). **Other peaks were obscured by Z isomer.** ^{13}C NMR (100 MHz, $CDCl_3$): δ 147.7 (C), 139.2 (CH), 137.9 (C), 128.8 (CH), 128.6 (CH), 127.7 (CH), 127.2 (CH), 126.2 (2CH), 125.9 (CH), 44.3 (C), 34.0 (CH_2), 25.1 (CH_3), 9.2 (CH_3); HRMS (GCMS) m/z calculated for $C_{18}H_{20}[M]^{+}$: 236.1565, found: 236.1570.



2.1e

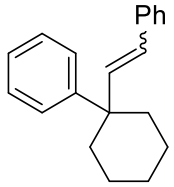
(Z, E)-(3-ethylpent-1-ene-1,3-diyl)dibenzene 2.1e. The general procedure V was followed using 440.7 mg of 2-ethyl-2-phenylbutanal (2.5 mmol), 1.7 g triphenyl phosphonium bromide (4.0 mmol, 1.6 eq.) and 2.5 mL t-BuOK solution in THF. Purification by flash column chromatography (100:0→90:10 hexanes:benzene) afforded inseparable Z/E (54:46) stereoisomers (557.1 mg, 89% yield) as colorless oil; **Selected spectra for Z isomer:** ^{1}H NMR (400 MHz, $CDCl_3$): δ 6.73 (d, *J* = 13.1 Hz, 1H), 5.95 (d, *J* = 12.8 Hz, 1H), 2.07 (m, 2H), 0.94 (t, *J* = 7.4 Hz, 3H). **Other peaks were obscured by E isomer.** ^{13}C NMR (100 MHz, $CDCl_3$): δ 146.3 (C), 138.2 (CH), 138.1 (C), 129.9 (CH), 128.7 (2CH), 128.1 (2CH), 127.8 (2CH), 127.1 (CH), 126.3 (2CH), 125.9 (CH), 47.9 (C), 29.9 (CH_2), 8.8 (CH_3). Other peaks were obscured by E isomer; **Selected spectra for E isomer:** ^{1}H NMR (400 MHz, $CDCl_3$): δ 6.61 (d, *J* = 16.5 Hz, 1H), 6.51 (d, *J* = 16.5 Hz, 1H), 1.95 (ddd, *J* = 14.5, 7.2, 3.0 Hz, 2H), 0.86 (t, *J* = 7.4 Hz, 3H). **Other peaks were obscured by Z isomer.** ^{13}C NMR (100 MHz, $CDCl_3$): δ 148.1 (C), 139.8 (CH), 138.5 (C), 128.7 (2CH), 128.2 (CH), 127.9 (2CH), 127.6 (2CH), 127.5 (2CH), 126.7 (CH), 125.5

(CH), 47.8 (C), 30.7 ($2CH_2$), 8.7 ($2CH_3$); HRMS (GCMS) m/z calculated for $C_{19}H_{22}[M]^+$: 250.1722, found: 250.1726.



2.1g

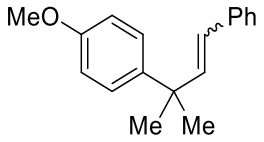
(Z, E)-(2-(1-phenylcyclopentyl)vinyl)benzene 2.1g. The general procedure V was followed using 435.6 mg of 1-phenylcyclohexane-1-carbaldehyde (2.5 mmol), 1.7 g triphenyl phosphonium bromide (4.0 mmol, 1.6 eq.) and 2.5 mL t-BuOK solution in THF. Purification by flash column chromatography (100:0→99:1 hexanes:benzene) afforded inseparable Z/E (59:41) stereoisomers (565.1 mg, 91% yield) as colorless oil; **Selected spectra for Z isomer:** ^{1}H NMR (400 MHz, $CDCl_3$): δ 6.83 (d, *J* = 12.4 Hz, 1H), 6.32 (d, *J* = 12.4 Hz, 1H). **Other peaks were obscured by E isomer.** ^{13}C NMR (100 MHz, $CDCl_3$): δ 149.0 (C), 141.2 (CH), 138.1 (C), 130.0 (CH), 129.2 (CH), 128.4 (CH), 127.8 (CH), 126.9 (CH), 126.7 (CH), 125.8 (CH), 53.2 (C), 41.4 (CH_2), 24.2 (CH_2); **Selected spectra for E isomer:** ^{1}H NMR (400 MHz, $CDCl_3$): δ 6.69 (d, *J* = 16.1 Hz, 1H), 6.59 (d, *J* = 16.1 Hz, 1H). **Other peaks were obscured by Z isomer.** ^{13}C NMR (100 MHz, $CDCl_3$): δ 147.6 (C), 138.8 (CH), 138.0 (C), 128.8 (CH), 128.5 (CH), 127.4 (CH), 127.3 (CH), 127.1 (CH), 126.5 (CH), 126.2 (CH), 54.0 (C), 38.0 (CH_2), 23.6 (CH_2); HRMS (GCMS) m/z calculated for $C_{19}H_{20}[M]^+$: 248.1565, found: 248.1552.



2.1h

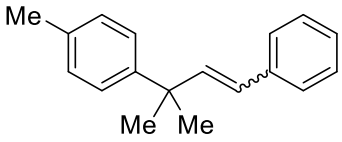
(Z, E)-(2-(1-phenylcyclohexyl)vinyl)benzene 2.1h. The general procedure V was followed using 470.8 mg of 1-phenylcyclohexane-1-carbaldehyde (2.5 mmol), 1.7 g triphenyl phosphonium bromide (4.0 mmol, 1.6 eq.) and 2.5 mL t-BuOK solution in THF. Purification by flash column chromatography (100:0→99:1 hexanes:benzene) afforded inseparable Z/E (59:41) stereoisomers (610.1 mg, 93% yield) as colorless oil; **Selected spectra for Z isomer:** ^{1}H NMR (400 MHz, $CDCl_3$): δ 6.63 (d, *J* = 12.7 Hz, 1H), 5.95 (d, *J* = 12.7 Hz, 1H). **Other peaks were obscured by E isomer.** ^{13}C NMR (100 MHz, $CDCl_3$): δ 150.9 (C), 139.5 (CH), 138.4 (C), 130.1 (CH), 128.6 (CH), 128.2 (CH), 127.5 (CH), 126.4 (CH), 126.3 (CH), 125.5 (CH), 44.3 (C), 38.1 (CH_2), 26.1 (CH_2), 22.9 (CH_2); **Selected spectra for E isomer:** ^{1}H NMR (400 MHz, $CDCl_3$): δ 6.28 (m, 2H). **Other peaks were obscured by Z isomer.** ^{13}C NMR (100 MHz, $CDCl_3$): δ 147.2 (C), 139.6 (CH), 137.9 (C), 128.5 (CH), 128.3 (CH), 126.9 (2CH), 126.8 (CH), 126.1 (CH), 125.7 (CH), 44.4 (C),

36.5 (CH_2), 26.4 (CH_2), 22.7 (CH_2); HRMS (GCMS) m/z calculated for $C_{20}H_{22}[M]^+$: 262.1722, found: 262.1725



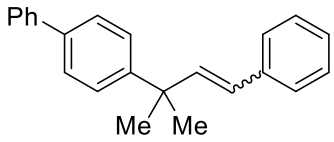
2.3a

1-methoxy-4-(2-methyl-4-phenylbut-3-en-2-yl)benzene 2.3a. The general procedure V was followed using 445.6 mg of **s26** (2.5 mmol), 1.7 g triphenyl phosphonium bromide (4.0 mmol, 1.6 eq.) and 2.5 mL t-BuOK solution in THF. Purification by flash column chromatography (100:0→70:30 hexanes:benzene) afforded inseparable Z/E (71:29) stereoisomers (551 mg, 88.5% yield) as light yellow oil; **Selected spectra for Z isomer:** ^{1}H NMR (400 MHz, $CDCl_3$): δ 6.90-6.86 (m, 2H), 6.60 (d, *J* = 12.7 Hz, 1H), 6.01 (d, *J* = 12.6 Hz, 1H), 3.85 (s, 3H), 1.46 (s, 6H). **Other peaks were obscured by E isomer.** ^{13}C NMR (100 MHz, $CDCl_3$): δ 157.5 (C), 142.3 (C), 141.8 (CH), 138.2 (C), 129.0 (CH), 128.6 (CH), 127.5 (CH), 127.1 (CH), 126.2 (CH), 113.5 (CH), 55.3 (CH_3), 40.5 (C), 31.3 (CH_3). **Selected spectra for E isomer:** ^{1}H NMR (400 MHz, $CDCl_3$): δ 6.97-6.93 (m, 2H), 6.53 (d, *J* = 16.4 Hz, 1H), 6.48 (d, *J* = 16.4 Hz, 1H), 3.87(s, 3H), 1.59 (s, 6H). **Other peaks were obscured by Z isomer**; ^{13}C NMR (100 MHz, $CDCl_3$): δ 157.8 (C), 140.9 (C), 140.5 (CH), 137.8 (C), 128.8 (CH), 128.5 (CH), 127.3 (CH), 127.1 (CH), 126.0 (CH), 113.6 (CH), 55.3 (CH_3), 40.3 (C), 29.0 (CH_3).



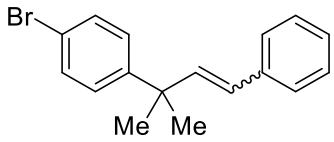
2.3b

(Z, E)-1-methyl-4-(2-methyl-4-phenylbut-3-en-2-yl)benzene 2.3b. The general procedure V was followed using 405.6 mg of 2-methyl-2-(p-tolyl)propanal (2.5 mmol), 1.7 g triphenyl phosphonium bromide (4.0 mmol, 1.6 eq.) and 2.5 mL t-BuOK solution in THF. Purification by flash column chromatography (100:0→90:10 hexanes:benzene) afforded inseparable Z/E (78:22) stereoisomers (520.0 mg, 88% yield) as colorless oil; **Selected spectra for Z isomer:** ^{1}H NMR (400 MHz, $CDCl_3$): δ 6.63 (d, *J* = 12.6 Hz, 1H), 6.04 (d, *J* = 12.6 Hz, 1H), 2.42 (s, 3H), 1.48 (s, 3H). **Other peaks were obscured by E isomer.** ^{13}C NMR (100 MHz, $CDCl_3$): δ 147.3 (C), 141.7 (CH), 138.3 (C), 135.0 (C), 129.0 (CH), 128.9 (CH), 128.6 (CH), 127.5 (CH), 126.3(CH), 126.0 (CH), 40.8 (C), 31.2 (CH_3), 21.0 (CH_3); **Selected spectra for E isomer:** ^{1}H NMR (400 MHz, $CDCl_3$): δ 6.56 (d, *J* = 16.2 Hz, 1H), 6.51 (d, *J* = 16.3 Hz, 1H), 2.44 (s, 3H), 1.62 (s, 3H). **Other peaks were obscured by Z isomer.** ^{13}C NMR (100 MHz, $CDCl_3$): δ). 145.8 (C), 140.4 (CH), 137.9 (C), 135.5 (C), 129.0 (CH), 128.6 (CH), 127.1 (CH), 126.3 (2CH), 126.0 (CH), 40.5 (C), 28.9 (CH_3), 21.0 (CH_3); HRMS (GCMS) m/z calculated for $C_{18}H_{20}[M]^+$: 236.1565, found: 236.1563.



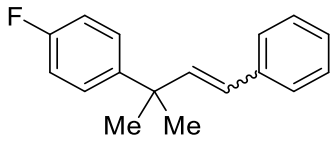
2.3c

(Z, E)-4-(2-methyl-4-phenylbut-3-en-2-yl)-1,1'-biphenyl 2.3c. The general procedure V was followed using 560.75 mg of 2-([1,1'-biphenyl]-4-yl)-2-methylpropanal (2.5 mmol), 1.7 g triphenyl phosphonium bromide (4.0 mmol, 1.5 eq.) and 2.5 mL *t*-BuOK solution in THF. Purification by flash column chromatography (100:0→75:25 hexanes:benzene) afforded inseparable Z/E (60:40) stereoisomers (520.0 mg, 88% yield) as colorless oil; **Selected spectra for Z isomer:** ^{1}H NMR (400 MHz, $CDCl_3$): δ 6.71 (d, *J* = 12.6 Hz, 1H), 6.11 (d, *J* = 12.6 Hz, 1H), 1.59 (s, 3H). **Other peaks were obscured by E isomer.** ^{13}C NMR (100 MHz, $CDCl_3$): δ 149.2 (C), 141.6 (CH), 141.2 (C), 138.5 (C), 138.2 (C), 129.0 (2CH), 128.8 (CH), 127.6 (CH), 127.2 (CH), 127.1 (CH), 126.9 (CH), 126.7 (CH), 126.4 (CH), 41.0 (C), 31.3 (CH_3); **Selected spectra for E isomer:** ^{1}H NMR (400 MHz, $CDCl_3$): δ 6.64 (d, *J* = 16.3 Hz, 1H), 6.60 (d, *J* = 16.5 Hz, 1H), 1.71 (s, 3H). **Other peaks were obscured by Z isomer.** ^{13}C NMR (100 MHz, $CDCl_3$): δ) 148.0 (C), 141.1 (C), 140.1 (CH), 139.0 (C), 137.8 (C), 128.9 (CH), 128.7 (CH), 127.2 (2CH), 127.1 (2CH), 126.9 (CH), 126.4 (CH), 126.3 (CH), 40.8 (C), 28.9 (CH_3); HRMS (GCMS) m/z calculated for $C_{23}H_{22}[M]^+$: 298.1722, found: 298.1711.



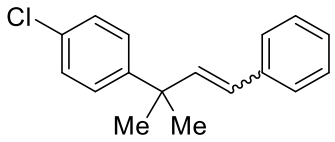
2.3d

(Z, E)-1-bromo-4-(2-methyl-4-phenylbut-3-en-2-yl)benzene 2.3d. The general procedure V was followed using 567.8 mg of 2-(4-bromophenyl)-2-methylpropanal (2.5 mmol), 1.7 g triphenyl phosphonium bromide (4.0 mmol, 1.6 eq.) and 2.5 mL t-BuOK solution in THF. Purification by flash column chromatography (100:0→85:15 hexanes:EtOAc) afforded inseparable Z/E (69:31) stereoisomers (677.8 mg, 90% yield) as colorless oil; **Selected spectra for Z isomer:** ^{1}H NMR (400 MHz, $CDCl_3$): δ 6.98-6.94 (m, 1H)), 6.60 (d, *J* = 12.6 Hz, 1H), 5.99 (d, *J* = 12.6 Hz, 1H), 1.46 (s, 6H). **Other peaks in aromatic region were obscured by E isomer.** ^{13}C NMR (100 MHz, $CDCl_3$): δ 148.9 (C), 141.0 (CH), 137.7 (C), 131.2 (CH), 131.0 (CH), 129.2 (CH), 128.7 (CH), 128.0 (CH), 127.5 (CH), 119.3 (C), 40.7 (C), 31.1 (CH_3); **Selected spectra for E isomer:** ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.09-7.05 (m, 1H), 6.48 (appr s, 2H), 1.58 (s, 6H), **other peaks in aromatic region were obscured by Z isomer.** ^{13}C NMR (100 MHz, $CDCl_3$): δ 147.8 (C), 139.4 (CH), 137.4 (C), 128.6 (2CH), 128.2 (2CH), 127.2 (CH), 126.5 (CH), 126.3 (2CH), 126.2 (CH), 119.8 (C), 40.6 (C), 28.7 (CH_3); HRMS (GCMS) m/z calculated for $C_{17}H_{17}Br[M]^+$: 300.0514, found: 300.0518.



2.3e

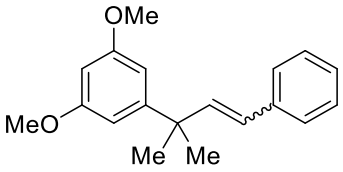
(Z, E)-1-fluoro-4-(2-methyl-4-phenylbut-3-en-2-yl)benzene 2.3e. The general procedure V was followed using 415.5 mg of 2-(4-fluorophenyl)-2-methylpropanal (2.5 mmol), 1.7 g triphenyl phosphonium bromide (4.0 mmol, 1.6 eq.) and 2.5 mL t-BuOK solution in THF. Purification by flash column chromatography (100:0→85:15 hexanes:EtOAc) afforded inseparable Z/E (69:31) stereoisomers (528.7 mg, 88% yield) as colorless oil. **Selected spectra for Z isomer:** ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.48 - 7.25 (m, ?H), 7.19 - 7.15 (m, ?H), 6.99 - 6.93 (m, ?H), 6.60 (d, *J* = 12.6 Hz, 1H), 5.99 (d, *J* = 12.6 Hz, 1H), 1.46 (s, 6H). **Other peaks in aromatic region were obscured by E isomer.** ^{13}C NMR (100 MHz, $CDCl_3$): δ 161.0 (d, *J* = 243.7 Hz, C), 145.6 (d, *J* = 3.2 Hz, C), 141.4 (CH), 137.9 (C), 129.0 (CH), 128.8 (2CH), 128.6 (CH), 127.7 (d, *J* = 7.7 Hz, CH), 127.5 (2CH), 114.7 (d, *J* = 20.7 Hz, CH), 40.6 (C), 31.4 ($2CH_3$). ^{19}F NMR (MHz, $CDCl_3$): δ -118.2; **Selected spectra for E isomer:** ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.48 - 7.25 (m, ?H), 7.19 - 7.15 (m, ?H), 6.99 - 6.93 (m, ?H), 6.48 (appr s, 2H), 1.58 (s, 6H), **other peaks in aromatic region were obscured by Z isomer.** ^{13}C NMR (100 MHz, $CDCl_3$): δ 161.2 (d, *J* = 244.3 Hz, C), 144.4 (d, *J* = 3.1 Hz, C), 139.9 (CH), 137.6 (C), 129.0 (CH), 127.9 (d, *J* = 7.7 Hz, CH), 126.4 (CH), 114.9 (d, *J* = 20.3 Hz, CH), 126.3 (2CH), 40.5 (C), 29.0 (CH_3). ^{19}F NMR (376 MHz, $CDCl_3$): δ -117.6; HRMS (GCMS) m/z calculated for $C_{17}H_{17}F[M]^+$: 240.1314, found: 240.1313.



2.3g

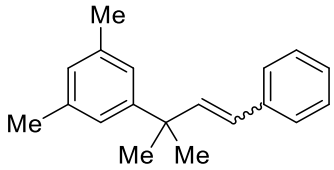
(Z, E)-1-chloro-4-(2-methyl-4-phenylbut-3-en-2-yl)benzene 2.3g. The general procedure V was followed using 456.6 mg of 2-(4-chlorophenyl)-2-methylpropanal (2.5 mmol), 1.7 g triphenyl phosphonium bromide (4.0 mmol, 1.6 eq.) and 2.5 mL t-BuOK solution in THF. Purification by flash column chromatography (100:0→85:15 hexanes:EtOAc) afforded inseparable Z/E (62:38) stereoisomers (552.1 mg, 86% yield) as colorless oil. **Selected spectra for Z isomer:** ^{1}H NMR (400 MHz, $CDCl_3$): δ 6.63 (d, *J* = 12.6 Hz, 1H), 6.00 (d, *J* = 12.6 Hz, 1H), 1.47 (s, 6H). **Other peaks in aromatic region were obscured by E isomer.** ^{13}C NMR (100 MHz, $CDCl_3$): δ 148.5 (C), 141.1 (CH), 137.9 (C), 130.4 (C), 129.3 (CH), 128.8 (CH), 128.2 (CH), 127.9 (CH), 127.7 (CH), 127.6 (CH), 40.7 (C), 31.2 (CH_3). **Selected spectra for E isomer:** ^{1}H NMR (400 MHz, $CDCl_3$): δ 6.52 (d, *J* = 16.5 Hz, 1H), 6.48 (d, *J* = 16.5 Hz, 1H), 1.60 (s, 6H), **other peaks in aromatic region were obscured by Z isomer.** ^{13}C NMR (100 MHz, $CDCl_3$): δ 147.3 (C), 139.6

(CH), 137.5 (C), 131.3 (C), 128.7 (CH), 128.4 (CH), 128.3 (CH), 126.6 (CH), 126.4 (CH), 126.3 (CH), 40.6 (C), 28.8 (CH_3); HRMS (GCMS) m/z calculated for $C_{17}H_{17}Cl[M]^+$: 256.1019, found: 256.1021.



2.3h

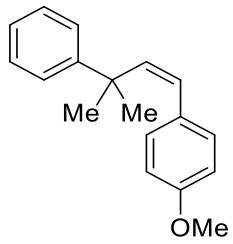
(Z, E)-1,3-dimethoxy-5-(2-methyl-4-phenylbut-3-en-2-yl)benzene 2.3h. The general procedure V was followed using 520.7 mg of 2-(3,5-dimethoxyphenyl)-2-methylpropanal (2.5 mmol), 1.7 g triphenyl phosphonium bromide (4.0 mmol, 1.6 eq.) and 2.5 mL t-BuOK solution in THF. Purification by flash column chromatography (100:0→50:50 hexanes:benzene) afforded inseparable Z/E (60:40) stereoisomers (586.0 mg, 83% yield) as light yellow oil; **Selected spectra for Z isomer:** ^{1}H NMR (400 MHz, $CDCl_3$): δ 6.52 (d, *J* = 12.6 Hz, 1H), 6.52 (d, *J* = 2.3 Hz, 1H), 6.26 (t, *J* = 2.3 Hz, 1H), 5.89 (d, *J* = 12.6 Hz, 1H), 3.79 (s, 6H), 1.50 (s, 6H). **Other peaks in aromatic region were obscured by E isomer.** ^{13}C NMR (100 MHz, $CDCl_3$): δ 160.5 (C), 152.5 (C), 141.2 (CH), 138.0 (C), 128.8 (2CH), 128.5 (CH), 127.4 (CH), 104.8 (CH), 97.2 (CH), 55.2 (CH_3), 41.2 (C), 31.0 (CH_3); **Selected spectra for E isomer:** ^{1}H NMR (400 MHz, $CDCl_3$): δ 6.57 (d, *J* = 2.3 Hz, 1H), 6.34 (t, *J* = 2.3 Hz, 1H), 6.44 (d, *J* = 16.4 Hz, 2H), 6.39 (d, *J* = 16.4 Hz, 1H), 3.76 (s, 6H), 1.37 (s, 6H), **other peaks in aromatic region were obscured by Z isomer.** ^{13}C NMR (100 MHz, $CDCl_3$): δ 160.6 (C), 151.4 (C), 139.8 (CH), 137.7 (C), 127.0 (CH), 126.2 (2CH), 126.1 (CH), 104.9 (CH), 97.3 (CH), 55.3 (CH_3), 41.0 (C), 28.6 (CH_3); HRMS (GCMS) m/z calculated for $C_{19}H_{22}O_2[M]^+$: 282.1620, found: 282.1621.



2.3i

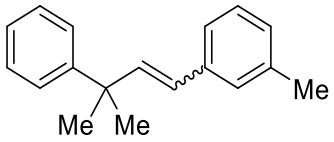
(Z, E)-1,3-dimethyl-5-(2-methyl-4-phenylbut-3-en-2-yl)benzene 2.3i. The general procedure V was followed using 440.8 mg of 2-(3,5-dimethylphenyl)-2-methylpropanal (2.5 mmol), 1.7 g triphenyl phosphonium bromide (4.0 mmol, 1.6 eq.) and 2.5 mL t-BuOK solution in THF. Purification by flash column chromatography (100:0→50:50 hexanes:benzene) afforded inseparable Z/E (74:26) stereoisomers (582.2 mg, 93% yield) as colorless oil; **Selected spectra for Z isomer:** ^{1}H NMR (400 MHz, $CDCl_3$): δ 6.59 (d, *J* = 12.6 Hz, 1H), 5.98 (d, *J* = 12.6 Hz, 1H), 2.35 (s, 6H), 1.43 (s, 6H). **Other peaks in aromatic region were obscured by E isomer.** ^{13}C NMR (100 MHz, $CDCl_3$): δ 150.0 (C), 141.8(CH), 137.6 (C), 137.4 (C), 128.9 (CH), 128.5 (CH), 127.4 (CH), 127.2 (CH), 126.2

(CH), 124.0 (CH), 40.9 (C), 31.1 (CH_3), 21.6 (CH_3); **Selected spectra for E isomer:** ^{1}H NMR (400 MHz, $CDCl_3$): δ 6.5 (appr s, 2H), 2.39 (s, 6H), 1.57 (s, 6H), **other peaks in aromatic region were obscured by Z isomer.** ^{13}C NMR (100 MHz, $CDCl_3$): δ 148.8 (C), 140.4 (CH), 138.3 (C), 137.8 (C), 128.6 (CH), 127.7 (CH), 127.0 (CH), 126.3 (CH), 125.8 (CH), 124.1 (CH), 40.6 (C), 28.8 (CH_3), 21.6 (CH_3); HRMS (GCMS) m/z calculated for $C_{19}H_{22}[M]^+$: 250.1722, found: 250.1711.



2.3j

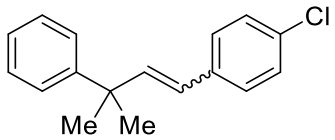
(Z)-1-methoxy-4-(3-methyl-3-phenylbut-1-en-1-yl)benzene 2.3j. The general procedure V was followed using 400 mg of 2-methyl-2-phenylpropanal (2.70 mmol), 1.9 g (4.10 mmol, 1.6 eq.) (4-methoxybenzyl)triphenylphosphonium bromide and 2.7 mL t-BuOK solution in THF. The reaction mixture was allowed to stir under argon. Purification by flash column chromatography (100:0 → 80:20 hexanes: benzene) afforded inseparable Z/E (85:15) (510.70 mg, 75% yield) as light yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.38-7.32 (m, 1H), 7.26 (t, *J* = 7.7 Hz, 2H), 7.2-7.13 (m, 1H), 6.85 (d, *J* = 8.7 Hz, 2H), 6.64 (d, *J* = 8.7 Hz, 2H), 6.46 (d, *J* = 12.5 Hz, 1H), 5.89 (d, *J* = 12.5 Hz, 1H), 3.74 (s, 3H), 1.41 (s, 6H)**.** ^{13}C NMR (100 MHz, $CDCl_3$): δ158.0 (C), 150.2 (C), 140.6 (CH), 130.4 (C), 130.1 (CH), 128.4 (CH), 128.1 (CH), 126.0 (CH), 125.5 (CH), 112.9 (CH), 55.1 (CH_3), 40.8 (C), 31.2 (CH_3); HRMS (GCMS) m/z calculated for $C_{23}H_{22}[M]^+$: 252.1514, found: 252.1513.



2.3k

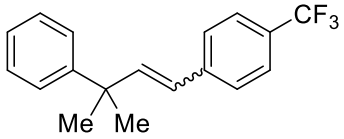
(Z, E) 1-methyl-3-(3-methyl-3-phenylbut-1-en-1-yl)benzene 2.3k. The general procedure V was followed using 400 mg of 2-methyl-2-phenylpropanal (2.70 mmol), 1.93 g (4-methylbenzyl)triphenylphosphonium bromide (4.32 mmol, 1.6 eq.) and 2.7 mL *t*-BuOK solution in THF. Purification by flash column chromatography (100:0→85:15 hexanes:EtOAc) afforded inseparable Z/E (67:33) stereoisomers (568.0 mg, 89% yield) as colorless oil. **Selected spectra for Z isomer:** ^{1}H NMR (400 MHz, $CDCl_3$): 6.92 (d, *J* = 7.8 Hz, 2H), 6.83 (d, *J* = 7.9 Hz, 2H), 6.48 (d, *J* = 12.6 Hz, 1H), 5.90 (d, *J* = 12.6 Hz, 1H), 2.26 (s, 3H), 1.38 (s, 6H). **other peaks were obscured by E isomer.** ^{13}C NMR (100 MHz, $CDCl_3$): δ 150.3 (C), 141.0 (CH), 135.8 (C), 135.1 (C), 128.7 (CH), 40.9 (C), 31.1 (CH_3), 21.1 (CH_3). **Aromatic peaks were obscured. Selected spectra for E isomer:** ^{1}H NMR

(400 MHz, $CDCl_3$): 6.38 (appr s, 2H), 2.33 (s, 3H), 1.51 (s, 6H).**other peaks were obscured by Z isomer.** ^{13}C NMR (100 MHz, $CDCl_3$): δ 148.6 (C), 139.1 (CH), 136.7 (C), 134.9 (C), 125.8 (CH), 40.7 (C), 28.6 (CH_3), 21.1 (CH_3). **Aromatic peaks were obscured.**



2.3l

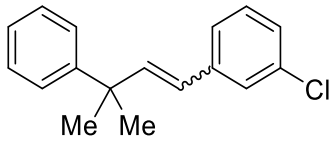
(Z, E) 1-chloro-4-(3-methyl-3-phenylbut-1-en-1-yl)benzene 2.3l. The general procedure V was followed using 247 mg of 2-methyl-2-phenylpropanal (1.67 mmol), 1.06 g (4-chlorobenzyl)triphenylphosphonium chloride (2.505 mmol, 1.5 eq.) and 1.67 mL *t*-BuOK solution in THF. Purification by flash column chromatography (100:0→85:15 hexanes:EtOAc) afforded inseparable Z/E (75:25) stereoisomers (332mg, 77% yield) as colorless oil. **Selected spectra for Z isomer:** ^1H NMR (400 MHz, $CDCl_3$): 7.05 (d, *J* = 8.2 Hz, 1H), 6.82 (d, *J* = 8.2 Hz, 1H), 6.44 (d, *J* = 13.7 Hz, 1H), 5.99 (d, *J* = 13.7 Hz, 1H), 1.42 (s, 6H), **other peaks in the aromatic region were obscured by E isomer.** (100 MHz, $CDCl_3$): δ 149.7 (C), 142.5 (CH), 136.4 (CH), 132.0 (C), 130.1 (CH), 128.2 (CH), 127.5 (CH), 126.1 (CH), 125.7 (CH), 40.9 (C), 31.1 (CH_3). **Selected spectra for E isomer:** 6.43 (d, *J* = 16.1 Hz, 1H), 6.36 (d, *J* = 16.1 Hz, 1H), 1.53 (s, 6H), **other peaks in the aromatic region were obscured by Z isomer.** ^{13}C NMR (100 MHz, $CDCl_3$): δ 148.4 (C), 140.9 (CH), 136.2 (C). 132.6 (C), 128.6 (CH), 128.2 (CH), 127.4 (CH), 126.2 (CH), 126.0 (CH), 125.0 (CH), 40.8 (C), 28.7 (CH_3); HRMS (EI) m/z calculated for $C_{17}H_{17}Cl$ $[M]^+$: 256.1013, found: 256.1012.



2.3m

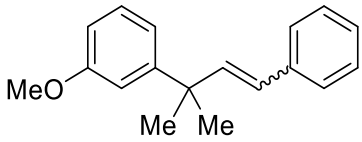
(Z, E)-1-(3-methyl-3-phenylbut-1-en-1-yl)-4-(trifluoromethyl)benzene 2.3m. The general procedure V was followed using 400 mg of 2-methyl-2-phenylpropanal (2.70 mmol), 0.744 g (4.10 mmol, 1.6 eq.) triphenyl(4-(trifluoromethyl)benzyl)phosphonium bromide and 2.7 mL t-BuOK solution in THF. The reaction mixture was allowed to stir overnight under argon. Purification by flash column chromatography (100:0 → 70:30 hexanes: benzene) afforded inseparable Z/E (70:30) (301 mg, 40% yield) as light brown oil. **Selected spectra for Z isomer:** ^1H NMR (400 MHz, $CDCl_3$): δ 6.57 (d, *J* = 12.7 Hz, 1H), 6.13 (d, *J* = 12.6 Hz, 1H), 1.48 (s, 3H). **Other peaks were obscured by E isomer.** ^{13}C NMR (100 MHz, $CDCl_3$): δ 149.3 (C), 143.5 (CH), 141.7 (q, *J* = 1.5 Hz, C), 129.0 (CH), 128.9 (q, *J* = 48.6 Hz, C), 128.2 (CH), 127.4 (CH), 126.2 (CH), 125.8 (CH), 124.3 (q, *J* = 3.8 Hz, CH), 124.3 (q, *J* = 271.8 Hz, CF_3), 41.0 (C), 31.1 (CH_3); **Selected spectra for E isomer:** ^1H NMR (400 MHz, $CDCl_3$): δ 6.62 (d, *J* = 16.2 Hz, 1H), 6.52 (d, *J* = 16.2

Hz, 1H), 1.62 (s, 3H). **Other peaks were obscured by Z isomer.** ^{13}C NMR (100 MHz, $CDCl_3$): δ 148.2 (C), 143.0 (CH), 141.3 (d, *J* = 1.3 Hz, C), 128.4 (CH), 126.4 (CH), 126.2 (2CH), 125.5 (q, *J* = 3.8 Hz, CH), 125.1 (CH), 124.4 (q, *J* = 271.8 Hz, CF_3), 41.0 (C), 28.6 (CH_3); HRMS (GCMS) m/z calculated for $C_{23}H_{22}[M]^+$: 290.1282, found: 290.1287.



2.3n

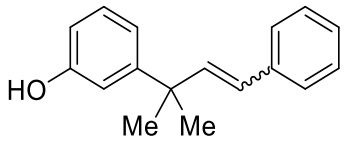
(Z, E)1-chloro-3-(3-methyl-3-phenylbut-1-en-1-yl)benzene 2.3n. The general procedure V was followed using 400 mg of 2-methyl-2-phenylpropanal (2.70 mmol), 1.83 g (3-chlorobenzyl)triphenylphosphonium chloride (4.32 mmol, 1.6 eq.) and 2.7 mL *t*-BuOK solution in THF. Purification by flash column chromatography (100:0→85:15 hexanes:EtOAc) afforded inseparable Z/E (67:33) stereoisomers (554.6 mg, 80% yield) as colorless oil. **Selected spectra for Z isomer:** ^{1}H NMR (400 MHz, $CDCl_3$): 6.42 (d, *J* = 12.6 Hz, 1H), 5.99 (d, *J* = 12.6 Hz, 1H), 1.40 (s, 6H). **other peaks were obscured by E isomer.** ^{13}C NMR (100 MHz, $CDCl_3$): δ 149.4 (C), 143.0 (CH), 139.7 (C), 133.2 (C), 127.2 (CH), 40.9 (C), 31.0 (CH_3). **Aromatic peaks were obscured. Selected spectra for E isomer:** ^{1}H NMR (400 MHz, $CDCl_3$): 6.45 (d, *J* = 16.1 Hz, 1H), 6.35 (d, *J* = 16.1 Hz, 1H), 1.52 (s, 6H). **other peaks were obscured by Z isomer.** ^{13}C NMR (100 MHz, $CDCl_3$): δ 148.2 (C), 141.7 (CH), 139.6 (C), 134.5 (C), 124.9 (CH), 40.9 (C), 28.6 (CH_3). **Aromatic peaks were obscured.**



2.5b

(Z, E)-1-methoxy-3-(2-methyl-4-phenylbut-3-en-2-yl)benzene 2.5b. The general procedure V was followed using 445.6 mg of 2-(3-methoxyphenyl)-2-methylpropanal (2.5 mmol), 1.73 g triphenyl phosphonium bromide (4.0 mmol, 1.6 eq.) and 2.5 mL t-BuOK solution in THF. Purification by flash column chromatography (100:0→70:30 hexanes:benzene) afforded inseparable Z/E (67:34) stereoisomers (600 mg, 95% yield) as light yellow oil; **Selected spectra for Z isomer:** ^{1}H NMR (400 MHz, $CDCl_3$): δ 6.69 (ddd, *J* = 8.2, 2.6, 0.8 Hz, 1H), 6.53 (d, *J* = 12.6 Hz, 1H), 5.93 (d, *J* = 12.6 Hz, 1H), 3.78 (s, 3H), 1.39 (s, 3H). **Other peaks were obscured by E isomer.** ^{13}C NMR (100 MHz, $CDCl_3$): δ 159.4 (C), 151.7 (C), 141.3 (CH), 138.1 (C), 128.8 (2CH), 127.4 (CH), 126.2 (2CH), 118.6 (CH), 112.6 (CH), 110.5 (CH), 55.1 (OCH_3), 41.1 (C), 31.0 (CH_3); **Selected spectra for E isomer:** ^{1}H NMR (400 MHz, $CDCl_3$): δ 6.77 (ddd, *J* = 8.2, 2.5, 0.8 Hz, 1H), 6.43 (appr s, 2H), 3.81 (s, 3H), 1.52 (s, 3H). **Other peaks were obscured by Z isomer**; ^{13}C NMR (100 MHz, $CDCl_3$): δ 159.5 (C), 150.5 (C), 139.9 (CH), 137.7 (C), 129.1 (CH), 129.0 (CH),

128.5 (CH), 127.0 (CH), 126.1 (CH), 118.8 (CH), 112.9 (CH), 110.5 (CH), 55.2 (OCH_3), 40.8 (C), 28.7 (CH_3); HRMS (GCMS) m/z calculated for $C_{18}H_{20}O[M]^+$: 252.1514, found: 252.1504.

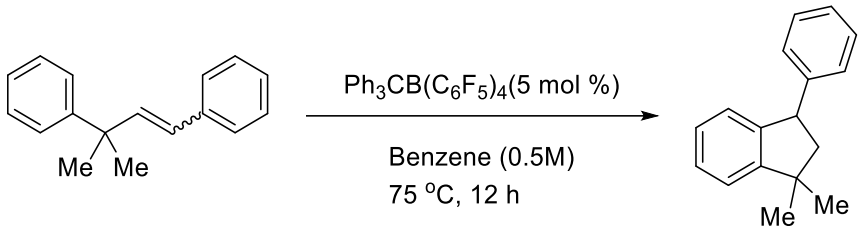


2.5d

(Z, E)-3-(2-methyl-4-phenylbut-3-en-2-yl)phenol 2.5d. In a 100 mL round bottom flask charged with a Teflon coated magnetic stir bar, a mixture of **(Z), (E)-1-(ethoxymethoxy)-3-(2-methyl-4-phenylbut-3-en-2-yl)benzene (S2.19)** (650 mg, 2.2 mmol) was dissolved with 25 mL DCM. To this solution, 1 mL of 10% HCl in methanol solution was added dropwise at 0 ^oC. The reaction was then brought up to room temperature and allowed to stir. The reaction was monitored by TLC. After the complete removal of the protecting group, a new spot appeared on the bottom the TLC plate. The residual solvent was removed under reduced pressure and the crude product was flushed through silica gel packed column chromatography (100:0 → 80:20 hexanes: EtOAc) to provide inseparable mixture of Z/E (67:33) stereoisomers (518 mg, 98% yield) as white cloudy oil.; **Selected spectra for Z isomer:** ^1H NMR (400 MHz, $CDCl_3$): δ 6.84 (m, 1H), 6.62 (ddd, *J* = 8.0, 2.5, 0.8 Hz, 1H), 6.53 (d, *J* = 12.6 Hz, 1H), 5.91 (d, *J* = 12.6 Hz, 1H), 4.90 (s, brd, 1H), 1.37 (s, 6H). **Other peaks in aromatic region were obscured by E isomer.** ^{13}C NMR (100 MHz, $CDCl_3$): δ 155.2 (C), 152.2 (C), 141.2 (CH), 138.0 (C), 129.3 (CH), 128.9 (CH), 128.8 (CH), 127.5 (CH), 126.3 (CH), 118.7 (CH), 113.4 (CH), 112.4 (CH), 40.9 (C), 31.0 (CH_3); **Selected spectra for E isomer:** ^1H NMR (400 MHz, $CDCl_3$): δ 6.88 (m, 1H), 5.69 (ddd, *J* = 8.1, 2.6, 0.8 Hz, 1H), 6.43 (appr s, 2H), 4.98 (s, brd, 1H), 1.51 (s, 6H), **other peaks in aromatic region were obscured by Z isomer.** ^{13}C NMR (100 MHz, $CDCl_3$): δ 155.3 (C), 150.9 (C), 139.8 (CH), 137.6 (C), 129.4 (CH), 128.6 (CH), 127.1 (CH), 126.2 (2CH), 118.7 (CH), 113.5 (CH), 112.8 (CH), 40.8 (C), 28.7 (CH_3); HRMS (GCMS) m/z calculated for $C_{17}H_{18}O[M]^+$: 238.1358, found: 238.1346.

Scheme 10. Synthesis of Diaryl Geminal Dialkyl Indanes *via* $Ph_3CB(C_6F_5)_4$ Catalyzied Hydroarylation

Optimized General Procedure VI: $Ph_3CB(C_6F_5)_4$ Catalyzied Hydroarylation

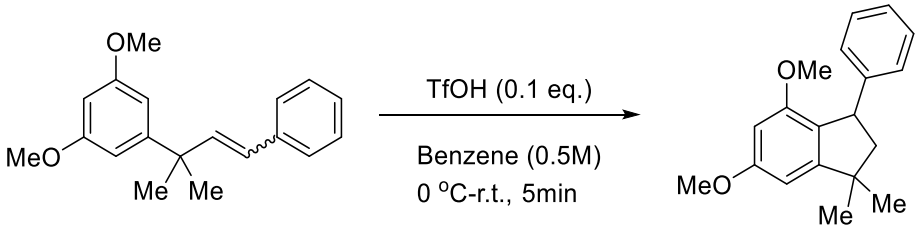


2.1a **2.2a**

In a dry 4 mL glass vial charged with Teflon coated magnetic stir bar, the alkenes **2.1a** (mixture of E, Z isomers, 0.25 mmol, 1.0 eq.) were dissolved with 0.50 mL dry benzene (0.5 M). To the solution, 11.53 mg of Trityl tetrakis(pentafluorophenyl)borate (0.0125 mmol) was added. The vial was then capped with a septum and purged with argon for 1 min. The reaction mixture was then sealed with a Teflon cap and was allowed to stir for 12 h at 75 ^oC. After the E, Z isomeric spots on TLC plate (visualized under UV Lamp, 254 nm) merged to one, the reaction was cooled to room temperature before it was quenched with 1 mL of saturated $NaHCO_3$. The cyclized product was extracted with 1 mL of CH_2Cl_2 twice and the combined organic layers were then washed with brine (2 mL) and dried over anhydrous Na_2SO_4. After filtration, the dry solution was concentrated *in vacuo* to furnish crude product as a light brown oil. Purification by silica gel chromatography using gradient elution afforded analytically pure cyclized product. The impurity is not tabulated in the following characterizations, and does not substantially affect the yield.

Scheme 11. Synthesis of Diaryl Geminal Dialkyl Indanes *via* TfOH Catalyzied Hydroarylation

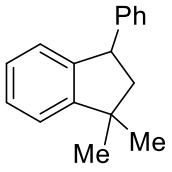
Optimized General Procedure VII: TfOH Catalyzied Hydroarylation



2.3h **2.4h**

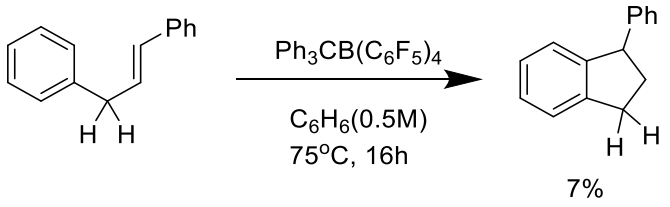
In a dry 4 mL glass vial charged with Teflon coated magnetic stir bar, the alkenes **2.3h** (mixture of E, Z isomers, 0.25 mmol, 1.0 eq.) were dissolved with 0.5 mL dry benzene (0.54 M). The vial was then capped with a septum and purged with argon for 1 min. To the

solution, 2.25 mg of TfOH (0.015 mmol, 0.06 eq.) was added at 0 °C. The septum was quickly switched to a Teflon cap with purging argon. The reaction mixture was allowed to stir at room temperature for an hour. After TLC indicated complete consumption of the E, Z isomers the reaction solution was then quenched by addition of 1 mL of saturated $NaHCO_3$. The indane product was extracted with DCM (1 mL) twice and the combined organic solution was washed with brine (2 mL) and dried over anhydrous sodium sulfate. The solids were filtered through vacuum and the organic solvent was removed under reduced pressure. The crude product was then transferred to a silica gel packed column. The silica cake was flashed with a mixture of hexanes and benzene (100:0 → 70:30, hexane:benzene) to furnish the pure corresponding cyclized product.



2.2a

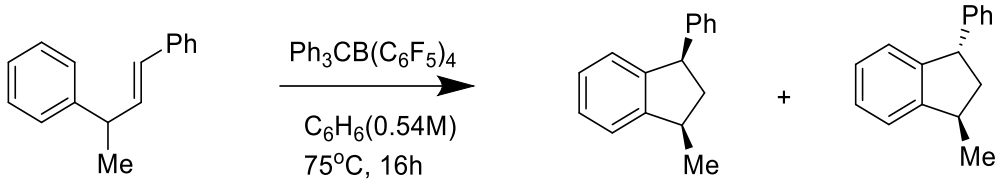
1,1-dimethyl–3–phenyl-2,3-dihydro-1H-indene 2.2a. The general procedure VI was followed using 55.6 mg of alkene **2.1a** (0.25 mmol), 11.53 mg of Trityl tetrakis(pentafluorophenyl)borate (0.0125 mmol) and 0.46 mL of benzene. Purification by flash column chromatography (100% hexanes) afforded indane **2.2a** (47.26 mg, 85%) as colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.36-7.34 (m, 2H), 7.34-7.16 (m, 4H), 7.15-7.14 (m, 2H), 6.91 (dd, *J* = 7.5 Hz, 0.7 Hz, 1H), 4.42 (dd, *J* = 10.1 Hz, 7.7 Hz, 1H), 2.43 (dd, *J* = 12.5 Hz, 7.5 Hz, 1H), 2.01 (dd, *J*= 12.4 Hz, 10.3 Hz, 1H), 1.45 (s, 3H), 1.29 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 152.7 (C), 145.4 (C), 145.1 (C), 128.4 (CH), 128.4 (CH), 126.9 (CH), 126.5 (CH), 126.3 (CH), 125.0 (CH), 121.9 (CH), 52.8 (CH_2), 49.0 (CH), 43.1 (C), 29.1 (CH_3), 28.7 (CH_3); ATR-FTIR (neat): 3061, 2948, 2858, 1599, 1493, 1452, 1152 cm^{-1}; HRMS (ESI/APCI) m/z calculated for $C_{17}H_{17}$ $[M-H]^+$: 221.1325, found 221.1327. [21]



2.1b **2.2b**

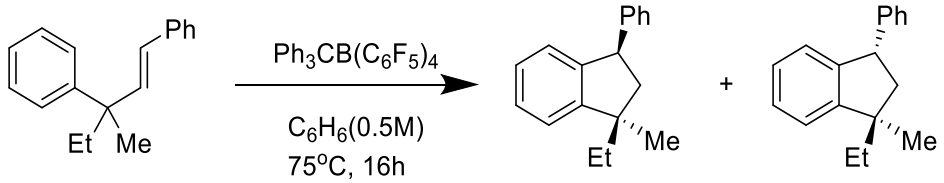
1-phenyl-2,3-dihydro-1H-indene 2.2b. The general procedure VI was followed using 48.5 mg of alkene **2.1b** (0.25 mmol), 11.53 mg of Trityl tetrakis(pentafluorophenyl)borate (0.0125 mmol) and 0.46 mL of benzene. The product was not isolated due to low NMR yield (7%). (^{1} H NMR (500 MHz, $CDCl_3$): δ 7.40-7.37 (m, 3H), 7.32-7.25 (m, 4H), 7.20 (t, *J* = 7.5 Hz, 1H), 7.04 (dd, *J* = 0.5, 7.5 Hz, 1H), 4.42 (t, *J* = 8.5 Hz, 1H), 3.16-3.11 (m,

1H), 3.07-3.00 (m, 1H), 2.70-2.63 (m, 1H), 2.19-2.11 (m, 1H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 147.2, 145.7, 144.6, 128.8, 128.4, 126.9, 126.7, 126.6, 125.2, 124.7, 52.0, 36.9, 32.2.[22]



2.1c **2.2c**

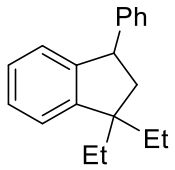
1-methyl-3-phenyl-2,3-dihydro-1H-indene 2.2c. The general procedure VI was followed using 52.0 mg of alkene **2.1c** (0.25 mmol), 11.53 mg of Trityl tetrakis(pentafluorophenyl)borate (0.0125 mmol) and 0.46 mL of benzene. Purification by flash column chromatography (100% hexanes) afforded indane **2.2c** (11.90 mg, 23%, dr 61:39) as colorless oil. Lit data : trans-1-Methyl-3-phenylindane: δ: 7.35-7.10 (m, 8H), 7.01 (m, 1H), 4.43 (m, 1H), 3.38 (m, 1H), 2.35-2.13 (m, 2H), 1.38 (d, *J* = 7.4 Hz, 3H); minor isomer cis-1-Methyl-3-phenylindane δ: 7.35-7.20 (m, 8H), 6.88 (m, 1H), 4.22 (m,1H), 3.20 (m, 1H), 2.71 (m, 1H), 1.63 (m, 1H), 1.29 (d, *J* = 7.7 Hz, 3H).[23]



2.1d **2.2d**

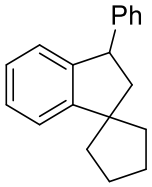
1-ethyl-1-methyl-3-phenyl-2,3-dihydro-1H-indene 2.2d. The general procedure VI was followed using 59.0 mg of alkene **2.1d** (0.25 mmol), 11.53 mg of Trityl tetrakis(pentafluorophenyl)borate (0.0125 mmol) and 0.46 mL of benzene. Purification by flash column chromatography (100% hexanes) afforded inseparable diastereomers **2.2d** (dr: 55:45 44.28 mg, 75%) as colorless oil. **Major(anti)**: ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.36-7.31 (m, 2H), 7.30-7.13 (m, 6H), 6.90 (d, *J* = 7.5 Hz, 1H), 4.39 (dd, *J* = 9.9, 18.0 Hz, 1H), 2.54 (dd, *J* = 7.8, 12.8 Hz, 1H), 1.91 (dd, *J* = 10.1, 12.8 Hz, 1H), 1.61 (qd, *J* = 2.0, 7.5 Hz, 2H), 3.05 (s, 3H), 0.90 (t, *J* = 7.5 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 151.6 (C), 146.1 (C), 145.5 (C), 128.4(2CH), 126.5 (2CH), 126.2 (CH), 125.0 (CH), 122.8 (CH), 50.3 (CH_2), 48.8 (CH), 46.8 (C), 34.1 (CH_2), 26.2 (CH_3), 9.6 (CH_3); **Minor (syn)**: ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.36-7.31 (m, 2H), 7.30-7.13 (m, 6H), 6.90 (d, *J* = 7.5 Hz, 1H), 4.39(dd, *J* = 9.9, 18.0 Hz, 1H), 2.28 (dd, *J* = 7.7, 12.6 Hz, 1H), 2.04 (dd, *J* = 10.3, 12.5 Hz, 1H), 1.78 (m, 1H), 1.83 (m, 1H), 2.94 (s, 3H), 0.93 (t, *J* = 7.5 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 152.0 (C), 145.4 (C), 145.8 (C), 128.4 (2CH), 126.8 (CH), 126.5 (CH), 126.3 (CH), 125.0 (CH), 122.2 (CH), 49.3 (CH_2), 48.9 (CH), 46.9 (C), 33.2 (CH_2), 26.9 (CH_3), 9.2 (CH_3).

ATR-FTIR (neat): 3029, 2958, 2922, 2853, 1477, 1453 cm^{-1}; HRMS (ESI/APCI) m/z calculated for $C_{18}H_{19}[M-H]^+$: 235.1481, found 235.1477.



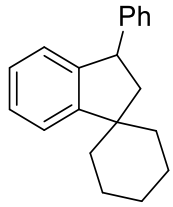
2.2e

1,1-diethyl-3-phenyl-2,3-dihydro-1H-indene 2.2e. The general procedure VI was followed using 62.6 mg of alkene **2.1e** (0.25 mmol), 11.53 mg of Trityl tetrakis(pentafluorophenyl)borate (0.0125 mmol) and 0.46 mL of benzene. Purification by flash column chromatography (100% hexanes) afforded indane **2.2e** (44.45 mg, 71%) as colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.33-7.27 (m, 2H), 7.28-7.17 (m, 4 H), 7.17-7.09 (m, 2 H), 6.88 (d, *J* = 8.0 Hz, 1H), 4.37 (dd, *J* = 9.1 Hz, 9.0 Hz, 1H), 2.36 (dd, *J* = 12.9 Hz, 8.1 Hz, 1H), 2.01 (dd, *J* = 12.9 Hz, 10.0 Hz, 1H), 1.84 (dq, *J* = 14.8 Hz, 7.4 Hz, 1H), 1.74-1.69 (m, 1H), 1.63 (dq, *J* = 7.4 Hz, 1.4 Hz, 2H), 0.87 (t, *J* = 8.5 Hz, 3H), 0.83 (t, *J* = 8.5 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 149.9 (C), 146.7 (C), 146.0 (C), 128.4 (CH), 128.4 (CH), 126.5 (CH), 126.3 (CH), 126.2 (CH), 125.0 (CH), 123.4 (CH), 50.7 (C), 49.3 (CH), 47.2 (CH_2), 32.2 (CH_2), 30.5 (CH_2), 9.0 (CH_3), 8.9 (CH_3); ATR-FTIR (neat): 3033, 2961, 2922, 2854, 1478, 1454 cm^{-1}; HRMS (ESI/APCI) m/z calculated for $C_{19}H_{21}$ $[M-H]^+$: 249.1638, found 249.1633.



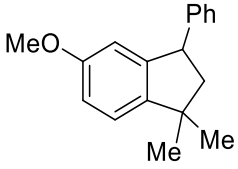
2.2g

3'-phenyl-2',3'-dihydrospiro[cyclopentane-1,1'-indene] 2.2g. The general procedure VI was followed using 62.1 mg of alkene **2.1g** (0.25 mmol), 11.53 mg of Trityl tetrakis(pentafluorophenyl)borate (0.0125 mmol) and 0.46 mL of benzene. Purification by flash column chromatography (100% hexanes) afforded indane **2.2g** (31.1 mg, 50%) as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.40-7.30 (m, 2H), 7.30-7.21 (m, 5H), 7.18-7.11 (m, 1H), 6.92 (d, *J* = 7.4 Hz, 1H), 4.38 (dd, *J* = 9.4 Hz, 8.0 Hz, 1H), 2.52 (dd, *J* = 12.4 Hz, 7.5 Hz, 1H), 2.23-2.04 (m, 2 H), 1.99 (dd, *J* = 12.3 Hz, 10.0 Hz, 1H), 1.95-1.83 (m, 2H), 1.83-1.70 (m, 2H), 1.69-1.52 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 151.8 (C), 146.2 (C), 145.2 (C), 128.4 (CH), 128.4 (CH), 126.9 (CH), 126.4 (CH), 126.3 (CH), 124.8 (CH), 122.0 (CH), 54.4 (C), 51.7 (CH_2), 49.5 (CH), 40.1 (CH_2), 40.0 (CH_2), 25.2 ($2CH_2$); ATR-FTIR (neat): 3025, 2946, 2857, 1600, 1493, 1473 cm^{-1}; HRMS (ESI/APCI) m/z calculated for $C_{19}H_{19}$ $[M-H]^+$: 247.1481, found 247.1485.



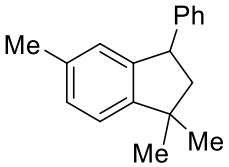
2.2h

3'-phenyl-2',3'-dihydrospiro[cyclohexane-1,1'-indene] 2.2h. The general procedure VI was followed using 65.6 mg of alkene **2.1h** (0.25 mmol), 11.53 mg of Trityl tetrakis(pentafluorophenyl)borate (0.0125 mmol) and 0.46 mL of benzene. Purification by flash column chromatography (100% hexanes) afforded indane **2.2h** (29.6 mg, 45%) as a white crystal. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.36-7.27 (m, 2H), 7.28-7.19 (m, 5H), 7.18-7.09 (m, 1H), 6.90 (dd, *J* = 7.5 Hz, 0.8 Hz, 1H), 4.35 (dd, *J* = 9.0 Hz, 8.9 Hz, 1H), 2.74 (dd, *J* = 12.8 Hz, 7.9 Hz), 1.94-1.88 (m, 1H), 1.83-1.63 (m, 5H), 1.56- 1.26 (m, 5H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 152.9 (C), 145.6 (C), 145.5 (C), 128.4 (CH), 128.4 (CH), 126.8 (CH), 126.7 (CH), 126.2 (CH), 125.0 (CH), 122.3 (CH), 49.0 (CH_2), 47.4 (C), 46.9 (CH), 38.5 (CH_2), 36.7 (CH_2), 26.1 (CH_2), 24.0 (CH_2), 23.1 (CH_2); ATR-FTIR (neat): 3025, 2922, 2851, 1493, 1449 cm^{-1}; HRMS (ESI/APCI) m/z calculated for $C_{20}H_{21}$ $[M-H]^+$: 261.1638, found 261.1645.



2.4a

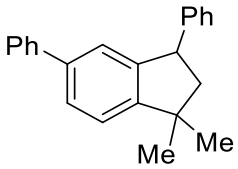
5-methoxy-1,1-dimethyl-3-phenyl-2,3-dihydro-1H-indene 2.4a. The general procedure VII was followed using 63.04 mg of alkene **2.3a** (0.25 mmol), 11.53 mg of Trityl tetrakis(pentafluorophenyl)borate (0.0125 mmol) and 0.46 mL of benzene. NMR yield (28%) was reported using 1,3,5-trimethoxybenzene as an internal standard.



2.4b

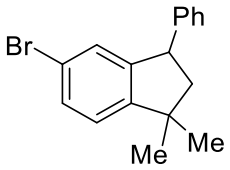
1,1,5-trimethyl-3-phenyl-2,3-dihydro-1H-indene 2.4b. The general procedure VI was followed using 59.1 mg of alkene **2.3b** (0.25 mmol), 11.53 mg of Trityl tetrakis(pentafluorophenyl)borate (0.0125 mmol) and 0.46 mL of benzene. Purification by flash column chromatography (100% hexanes) afforded indane **2.4b** (45.0 mg, 76%) as colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.35-7.32 (m, 2H), 7.27-7.23 (m, 3H), 7.12-

7.04 (m, 2H), 6.70 (s, 1H), 4.37 (dd, *J* = 10.1 Hz, 7.7 Hz, 1H), 2.39 (dd, *J* = 12.4 Hz, 7.5 Hz, 1H), 2.27 (s, 3H), 1.98 (dd, *J*= 12.3 Hz, 10.4 Hz, 1H), 1.41 (s, 3H), 1.26 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 149.9 (C), 145.6 (C), 145.1 (C), 136.2 (C), 128.5 (CH), 128.4 (CH), 127.7 (CH), 126.2 (C), 125.5 (CH), 121.6 (CH), 52.9 (CH_2), 48.9 (CH), 42.7 (C), 29.1 (CH_3), 28.8 (CH_3), 21.2 (CH_3); ATR-FTIR (neat): 3022, 2955, 2946, 2923, 2858, 1491, 1453 cm^{-1}; HRMS (ESI/APCI) m/z calculated for $C_{18}H_{19}$ $[M-H]^+$: 235.1481, found 235.1482.



2.4c

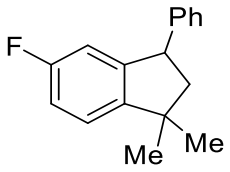
1,1-dimethyl-3,5-diphenyl-2,3-dihydro-1H-indene 2.4c. The general procedure VII was followed using 74.55 mg of alkene **2.3c** (0.25 mmol), 2.25 mg of TfOH (0.015 mmol) and 0.46 mL of benzene. Purification by flash column chromatography (100:0→90:10 hexanes: benzene) afforded indane **2.4c** (23.5mg, 32% yield) as colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.54-7.39 (m, 3H), 7.38-7.26 (m, 8H), 7.14 (s, 2H), 4.49 (dd, *J* = 9.0 Hz, 8.7 Hz, 1H), 2.48 (dd, *J* = 12.4 Hz, 7.5 Hz, 1H), 2.07 (dd, *J* = 11.4 Hz, 11.4 Hz, 1H), 1.49 (s, 3H), 1.34 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 152.1 (C), 146.1 (C), 144.9 (C), 141.5 (C), 139.9 (C), 128.6 (CH), 128.5 (CH), 128.5 (CH), 127.2 (CH), 126.9 (CH), 126.4 (CH), 126.1 (CH), 123.8 (CH), 122.2 (CH), 53.1 (CH_2), 49.1 (CH), 42.9 (C), 29.1 (CH_3), 28.7 (CH_3); ATR-FTIR (neat): 3022, 2947, 2924, 2861, 1477, 1599, 1070 cm^{-1}; HRMS (ESI/APCI) m/z calculated for $C_{23}H_{21}$ $[M-H]^+$: 297.1638, found 297.1643.



2.4d

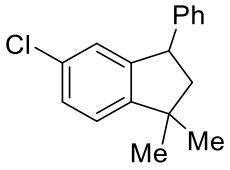
5-bromo-1,1-dimethyl-3-phenyl-2,3-dihydro-1H-indene 2.4d. The general procedure VI was followed using 75.31 mg of alkene **2.3d** (0.25 mmol), 11.53 mg of Trityl tetrakis(pentafluorophenyl)borate (0.0125 mmol) and 0.46 mL of benzene. Purification by flash column chromatography (100% hexanes) afforded indane **2.4d** (46.7 mg, 62%) as a white solide. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.35-7.31 (m, 3H), 7.27-7.19 (m, 3H), 7.07 (d, *J* = 8.1 Hz, 1H), 6.99 (s, 1H), 4.36 (dd, *J* = 9.9 Hz, 8.0 Hz, 1H), 2.38 (dd, *J* = 12.5 Hz, 7.5 Hz, 1H), 1.99 (dd, *J* = 12.3 Hz, 10.7 Hz, 1H), 1.40 (s, 3H), 1.24 (s, 3H) ; ^{13}C NMR (100 MHz, $CDCl_3$): δ 151.7 (C), 147.9 (C), 144.1 (C), 130.0 (CH), 128.6 (CH), 128.3 (CH), 128.0 (CH), 126.6 (CH), 123.6 (CH), 120.3 (C), 52.6 (CH_2), 48.8 (CH), 42.9 (C), 28.9

(CH_3), 28.5 (CH_3); ATR-FTIR (neat): 3091, 3071, 3035, 2925, 1478, 1035 cm^{-1}; HRMS (EI/GCMS) m/z calculated for $C_{17}H_{17}Br$ $[M]^+$: 300.0514, found 300.0518.



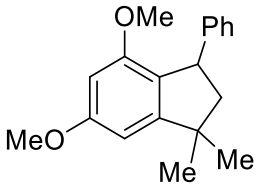
2.4e

5-fluoro-1,1-dimethyl-3-phenyl-2,3-dihydro-1H-indene 2.4e. The general procedure VI was followed using 60.1 mg of alkene **2.3e** (0.25 mmol), 11.53 mg of Trityl tetrakis(pentafluorophenyl)borate (0.0125 mmol) and 0.46 mL of benzene. Purification by flash column chromatography (100% hexanes) afforded indane **2.4e** (31 mg, 51.5%) as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.35-7.31 (m, 2H), 7.27-7.20 (m, 3H), 7.14-7.11 (m, 1H), 6.94-6.86 (m, 1H), 6.55 (d, J = 9.1 Hz), 4.36 (dd, J = 8.8 Hz, 8.8 Hz, 1 H), 2.41 (dd, J = 12.5 Hz, 7.5 Hz, 1H), 2.01 (dd, J = 12.1 Hz, 10.7 Hz, 1H), 1.41 (s, 3H), 1.25 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 162.2 (d, ^1J =242.7, C), 148.2 (d, ^4J = 2.5 Hz, C), 147.6 (d, ^3J = 7.5 Hz, C), 144.3 (C), 128.5 (CH), 128.3 (CH), 126.5 (CH), 122.8 (d, ^3J = 8.7 Hz, CH), 113.8 (d, ^2J = 22.5 Hz, CH), 111.7 (d, ^2J = 22.0 Hz, CH), 52.9 (CH_2), 48.8 (CH), 42.6 (C), 29.1 (CH_3), 28.7 (CH_3); ^{19}F NMR (376 MHz, $CDCl_3$): δ -117.15. ATR-FTIR (neat): 3090, 3035, 2925, 1478, 1034 cm^{-1}; HRMS (EI/GCMS) m/z calculated for $C_{17}H_{17}F$ $[M]^+$: 240.1314, found 240.1317.



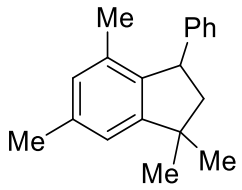
2.4g

5-chloro-1,1-dimethyl-3-phenyl-2,3-dihydro-1H-indene 2.4g. The general procedure VI was followed using 64.2 mg of alkene **2.3g** (0.25 mmol), 11.53 mg of Trityl tetrakis(pentafluorophenyl)borate (0.0125 mmol) and 0.46 mL of benzene. Purification by flash column chromatography (100% hexanes) afforded indane **2.4g** (41.4 mg, 64.5%) as a white solid. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.70-7.19 (m, 6H), 7.12 (d, J = 8.0 Hz, 1H), 6.84 (s, 1H), 4.37 (dd, J = 9.5 Hz, 8.3 Hz, 1H), 2.41 (dd, J = 12.4 Hz, 7.5 Hz, 1H), 2.01 (dd, J = 11.5, 11.4 Hz, 1H), 1.41 (s, 3H), 1.25 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 151.2 (C), 147.5 (C), 144.1 (C), 132.2 (C), 128.6 (CH), 128.3(CH), 127.1 (CH), 126.6 (CH), 125.1 (CH), 123.1 (CH), 52.7 (CH_2), 48.8 (CH), 42.8 (C), 29.0 (CH_3), 28.6 (CH_3); ATR-FTIR (neat): 3026, 2955, 2924, 2863, 2355, 1471 cm^{-1}; HRMS (ESI/APCI) m/z calculated for $C_{17}H_{16}Cl$ $[M-H]^+$: 255.0941, found 255.0945.



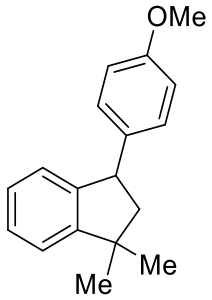
2.4h

4,6-dimethoxy-1,1-dimethyl-3-phenyl-2,3-dihydro-1H-indene 2.4h. The general procedure VII was followed using 70.55 mg of alkene **2.3h** (0.25 mmol), 2.25 mg of TfOH (0.015 mmol) and 0.46 mL of benzene. Purification by flash column chromatography (100:0→90:10 hexanes: benzene) afforded indane **2.4h** (65.6mg, 93% yield) as a light yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.26-7.23 (m, 2H), 7.17-7.10 (m, 3H), 6.39 (d, *J* = 2.0 Hz, 1H), 6.32 (d, *J* = 2.0 Hz, 1H), 4.42 (dd, *J* = 8.6 Hz, 6.2 Hz, 1H), 3.85 (s, 3H), 3.57 (s, 3H), 2.48 (dd, *J* = 12.8 Hz, 8.7 Hz, 1H), 1.92 (dd, *J*= 12.8 Hz, 6.1 Hz, 1H), 1.25 (s, 3H), 1.25 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 161.2 (C), 157.1 (C), 156.0 (C), 146.6 (C), 127.9 (CH), 127.3 (CH), 125.4 (CH), 123.5 (C), 98.5 (CH), 97.0 (CH), 55.5 (CH_3), 55.2 (CH_3), 52.6 (CH_2), 46.2 (CH), 44.2 (C), 29.7 (CH_3), 29.5 (CH_3); ATR-FTIR (neat): 2951, 2918, 2854, 1593, 1454, 1207, 1139, 1050 cm^{-1}; HRMS (ESI/APCI) m/z calculated for $C_{19}H_{23}O_2$ $[MH]^+$: 283.1693, found 283.1692.



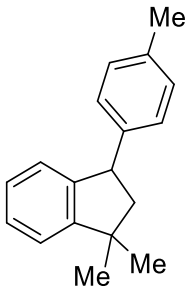
2.4i

1,1,4,6-tetramethyl-3-phenyl-2,3-dihydro-1H-indene 2.4i. The general procedure VI was followed using 62.6 mg of alkene **2.3i** (0.25 mmol), 11.53 mg of Trityl tetrakis(pentafluorophenyl)borate (0.0125 mmol) and 0.46 mL of benzene. Purification by flash column chromatography (100% hexanes) afforded indane **2.4i** (57.0 mg, 91%) as colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.31-7.26 (m, 2H), 7.22-7.19 (m, 1H), 7.16-7.13 (m, 2H), 6.92 (s, 1H), 6.84 (s, 1H), 4.42 (dd, *J* = 7.7 Hz, 7.7 Hz, 1H), 2.52 (dd, *J* = 12.8 Hz, 8.7 Hz, 1H), 2.39 (s, 3H), 1.96 (dd, *J* = 12.8 Hz, 6.8 Hz, 1H), 1.85 (s, 3H), 1.33 (s, 3H), 1.28 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 153.6 (C), 146.6 (C), 139.5 (C), 137.1 (C), 134.8 (C), 129.3 (CH), 128.4 (CH), 127.8 (CH), 125.8 (CH), 120.3 (CH), 52.9 (CH_2), 48.3 (CH), 43.4 (C), 30.2 (CH_3), 29.8 (CH_3), 21.4 (CH_3), 19.4 (CH_3); ATR-FTIR (neat): 2984, 1737, 1373, 1236, 1044 cm^{-1}; HRMS (ESI/APCI) m/z calculated for $C_{19}H_{21}$ $[M-H]^+$: 249.1638, found 249.1636.



2.4j

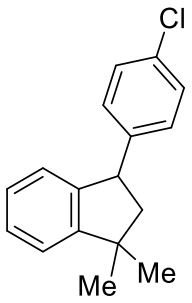
3-(4-methoxyphenyl)-1,1-dimethyl-2,3-dihydro-1H-indene 2.4j. The general procedure VII was followed using 63.1 mg of alkene **2.3j** (0.25 mmol), 2.5 mg of TfOH (0.03 mmol) and 0.46 mL of benzene. Purification by flash column chromatography (100:0→90:10 hexanes: benzene) afforded indane **2.4j** (9.5mg, 15% yield) as colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.25-7.19 (m, 3H), 7.13 (d, *J* = 8 Hz, 2H), 6.87 -6.65 (m, 3H), 4.34 (dd, *J* = 9.9 Hz, 7.8 Hz, 1H), 3.80 (s, 3H), 2.36 (dd, *J* = 12.4 Hz, 7.5 Hz, 1H), 1.93 (dd, *J*= 12.1 Hz, 10.7 Hz, 1H), 1.41 (s, 3H), 1.25 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 158.1 (C), 152.6 (C), 145.7 (C), 137.1 (C), 129.3 (CH), 126.8 (CH), 126.5 (CH), 124.8 (CH), 121.8 (CH), 113.8 (CH), 55.3 (CH_3), 52.8 (CH_2), 48.1 (CH), 43.0 (C), 29.0 (CH_3), 28.6 (CH_3); ATR-FTIR (neat): 2951, 2921, 2856, 2360, 1608, 1511, 1247, 1463 cm^{-1}; HRMS (EI/GCMS) m/z calculated for $C_{18}H_{20}O$ $[M]^+$: 252.1509, found 252.1516.



2.4k

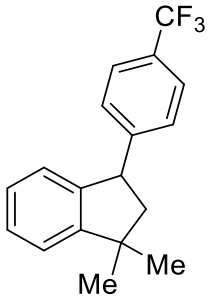
1,1-dimethyl-3-(4-mehtylphenyl)-indane 2.4k. The general procedure VI was followed using 53 mg of alkene **2.3k** (0.22 mmol), 10.0 mg of Trityl tetrakis(pentafluorophenyl)borate (0.011 mmol) and 0.42 mL of benzene. Purification by flash column chromatography (100% hexanes) afforded indane **2.4k** (20 mg, 28% yield) as colorless oil. (Rf= 0.40 hexanes, visualized by 254 nm light). The spectral data matched those reported by Blunt and co-workers.[1] ^{1}H NMR (400 MHz, $CDCl_3$): δ7.27-7.19 (m, 3H), 7.17-7.10 (m, 5H), 6.89 (d, *J* = 7.6 Hz,1H), 4.37 (dd, *J* = 7.9, 10.5 Hz, 1H) 2.40 (dd, *J* = 3.2, 10.5 Hz, 1H), 2.36 (s, 3H), 1.96 (dd, *J* = 10.8, 12.9 Hz, 1H), 1.43 (s, 3H) 1.27 (s, 3H); ^{13}C NMR (100MHz, $CDCl_3$): δ 152.7 (C), 145.6 (C), 142.0 (C), 135.8 (C), 129.2 (CH), 129.1 (CH), 128.3 (2CH), 126.8 (CH), 126.5 (CH), 124.9 (CH), 121.8 (CH), 52.8 (CH_2), 48.6 (CH), 43.1 (C), 29.0 (CH_3), 28.6 (CH_3), 21.0 (CH_3); ATR-FTIR: (thin film): 2956,

2924, 2360, 1738, 1372, 1236, 1044 cm^{-1}:HRMS (EI) m/z calculated for $C_{18}H_{20}$ $[M]^+$: 236.1565, found: 236.1549.



2.4l

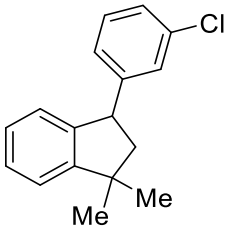
3-(4-Chlorophenyl)-1,1-dimethy-indane 2.4l. The general procedure VI was followed using 62 mg of alkene **2.3l** (0.33 mmol), 15.0 mg of Trityl tetrakis(pentafluorophenyl)borate (0.017 mmol) and 0.61 mL of benzene. Purification by flash column chromatography (100% hexanes) afforded indane **2.4l** (39 mg, 46% yield) as colorless oil. (Rf= 0.44 hexanes, visualized by 254 nm light). The spectral data matched those reported by Blunt and co-workers.[1] ^{1}H NMR (400 MHz, $CDCl_3$): δ7.30-7.19 (m, 5H), 7.17-7.11 (m, 3H), 6.85 (d, *J* = 8.3 Hz,1H), 4.37 (dd, *J* = 8.0, 10.2 Hz, 1H), 2.38 (dd, *J* = 7.4, 12.3 Hz, 1H), 1.92 (dd, *J* = 10.5, 13.1 Hz, 1H), 1.42 (s, 3H) 1.26 (s, 4H); ^{13}C NMR (100MHz, $CDCl_3$): δ 152.7 (C), 144.8 (C), 143.7 (C), 132.0 (C), 129.7 (2CH), 128.6 (2CH), 127.1 (CH), 126.6 (CH), 124.8 (CH), 122.0 (CH), 52.7 (CH_2), 48.3 (CH), 43.1 (C), 29.0 (CH_3), 28.6 (CH); ATR-FTIR: (thin film): 2984, 1737, 1373, 1236, 1044 cm^{-1}:HRMS (EI) m/z calculated for $C_{17}H_{17}Cl[M]^+$: 256.1013, found 256.101.



2.4m

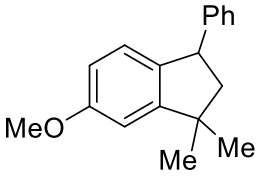
1,1-dimethyl-3-(4-(trifluoromethyl)phenyl)-2,3-dihydro-1H-indene 2.4m. The general procedure VII was followed using 72.53 mg of alkene **2.3m** (0.25 mmol), 22.5 mg of TfOH (0.15 mmol, 0.6 eq.) and 0.46 mL of benzene. Purification by flash column chromatography (100:0→90:10 hexanes: benzene) afforded indane **2.4m** (30.0 mg, 41% yield) as white crystal. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.59 (d, *J* = 8 Hz, 2H), 7.35 (d, *J* = 8 Hz, 2H), 7.28-7.26 (m, 2H), 7.19-7.14 (m, 1H), 6.87 (d, *J* = 8 Hz, 1H), 4.48 (dd, *J* = 10 Hz, 8 Hz, 1H), 2.45 (dd, *J* = 12 Hz, 8Hz, 1H), 1.97 (dd, *J* = 12 Hz, 8Hz, 1H), 1.44 (s, 3H), 1.29 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 152.8 (C), 149.4 (C), 144.4 (C), 128.7 (2CH),

127.3 (CH), 126.7 (CH), 125.4(q, ^{3}J = 3.8 Hz, 2CH), 127.0 (q, ^{2}J = 36.6 Hz, C), 125.0 (q, ^{1}J = 278 Hz, or 124.3 (q, ^{1}J = 270 Hz, CF_3), 124.8 (CH), 122.1 (CH), 52.7 (CH_2), 48.9 (CH), 43.3 (C), 29.1 (CH_3), 28.6 (CH_3); ^{19}F NMR (376 MHz, $CDCl_3$): δ -62.29; ATR-FTIR (neat): 3053, 2987, 1326, 1264 cm^{-1}; HRMS (EI/GCMS) m/z calculated for $C_{18}H_{17}F_3$ $[M]^+$: 290.1277, found 290.1272.

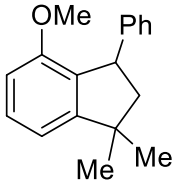


2.4n

3-(3-chlorophenyl)-1,1-dimethyl-2,3-dihydro-1*H*-indene 2.4n. The general procedure VI was followed using 70.4 mg of alkene **2.3n** (0.27 mmol), 25 mg of Trityl tetrakis(pentafluorophenyl)borate (0.027 mmol) and 0.55 mL of benzene. Purification by flash column chromatography (100% hexanes) afforded indane **2.4n** (51.4 mg, 73% yield) as colorless oil.^{1}H NMR (400 MHz, $CDCl_3$): 7.36-7.09 (m, 8H), 6.89 (d, *J* = 7.4 Hz, 1H), 4.38 (dd, *J* = 10.2, 7.9 Hz, 1H), 2.40 (dd, *J* = 13.1, 8.0 Hz, 1H), 1.95 (dd, *J* = 12.2, 10.4 Hz, 1H), 1.43 (s, 3H), 1.27 (s, 3H). ^{13}C NMR (100MHz, $CDCl_3$): δ 152.7 (C), 147.3 (C), 144.5 (C), 134.3 (C), 129.7 (CH), 128.5 (CH), 127.2 (CH), 126.7 (2CH), 126.5 (CH), 124.9 (CH), 122.0 (CH), 52.6 (CH_2), 48.7 (CH), 43.2 (C), 29.0 (CH_3), 28.6 (CH_3).



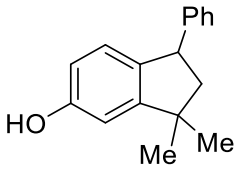
2.6b



2.7b

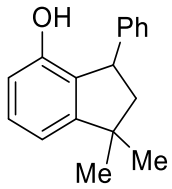
6-methoxy-1,1-dimethyl-3-phenyl-2,3-dihydro-1H-indene 2.6b. The general procedure VII was followed using 63.1 mg of alkene **2.5b** (0.25 mmol), 2.25 mg of TfOH (0.015 mmol) and 0.46 mL of benzene. Purification by flash column chromatography (100:0→95:5 hexanes: benzene) afforded inseparable indanes **2.6b** and **2.7b** as a mixture (**2.6b**: **2.7b** 78:22, 57.4 mg, 91% yield) as a light yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.33-7.21 (m, 5H), 6.79 (dd, *J* = 8.3, 0.5 Hz, 1H), 6.75 (d, *J* = 2.4 Hz, 1H), 6.69 (dd, *J* = 8.3 Hz, 2.5 Hz, 1H), 4.34 (dd, *J* = 9.8 Hz, 7.7 Hz, 1H), 3.82 (s, 3H), 2.40 (dd, *J* = 12.4 Hz, 7.4 Hz, 1H), 1.97 (dd, *J*= 12.4 Hz, 10.1 Hz, 1H), 1.40 (s, 3H), 1.26 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 159.2 (C), 154.4 (C), 145.4 (C), 137.5 (C), 128.4 (CH), 128.3 (CH), 126.2 (CH), 125.6 (CH), 112.1 (CH), 107.5 (CH), 55.4 (CH_3), 53.2 (CH_2), 48.3 (CH), 43.2 (C), 29.0 (CH_3), 28.5 (CH_3); **4-methoxy-1,1-dimethyl-3-phenyl-2,3-dihydro-1H-indene 2.7b.** ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.31-7.10 (m, 6H), 7.00-6.91 (m, 1H), 6.86 (d, *J* = 7.5 Hz,

1H), 4.49 (dd, *J* = 8.7 Hz, 6.3 Hz, 1H), 3.59 (s, 3H), 2.48 (dd, *J* = 12.8 Hz, 8.8 Hz, 1H), 1.94 (dd, *J* = 12.7 Hz, 5.3 Hz, 1H), 1.40 (s, 3H), 1.26 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 156.6 (C), 155.4 (C), 146.3 (C), 131.2 (C), 129.0 (CH), 128.0 (CH), 127.4 (CH), 125.5 (CH), 114.7 (CH), 108.9 (CH), 55.2 (CH_3), 52.3 (CH_2), 46.7 (CH), 44.0 (C), 30.0 (CH_3), 29.7 (CH_3); ATR-FTIR (neat): 3027, 2953, 2859, 1738, 1605, 1479, 1226 cm^{-1}; HRMS (EI/GCMS) m/z calculated for $C_{18}H_{20}O$ $[M]^+$: 252.1509, found 252.1503.



2.6d

3,3-dimethyl-1-phenyl-2,3-dihydro-1H-inden-5-ol 2.6d. The general procedure VII was followed using 60 mg of alkene **2.5d** (0.25 mmol), 2.25 mg of TfOH (0.015 mmol) and 0.46 mL of benzene. Purification by flash column chromatography (100:0→70:30 hexanes: benzene) afforded indane **2.6d** (28 mg, 48% yield, 70% total yield combined with regioisomer.) as colorless oil. ^{1}H NMR (400 MHz, C_6D_6): δ 7.17-7.15 (m, 2H), 7.10-7.04 (m, 3H), 6.67 (dd, *J* = 8.2, 1.1 Hz, 1H), 6.40 (d, *J* = 2.4 Hz, 1H), 6.31 (dd, *J* = 8.1 Hz, 2.4 Hz, 1H), 4.19 (dd, *J* = 9.6 Hz, 7.8 Hz, 1H), 3.96 (br s, 1H), 2.18 (dd, *J* = 12.4 Hz, 7.4 Hz, 1H), 1.88 (dd, *J* = 12.4 Hz, 10.0 Hz, 1H), 1.21 (s, 3H), 1.08 (s, 3H); ^{13}C NMR (100 MHz, C_6D_6): δ 155.6 (C), 154.3 (C), 145.6 (C), 137.0 (C), 128.4 (CH), 128.3 (CH), 126.2 (CH), 125.7 (CH), 113.7 (CH), 108.7 (CH), 53.2 (CH_2), 48.4 (CH), 42.8 (C), 28.6 (CH_3), 28.2 (CH_3); ATR-FTIR (neat): 3090, 3035, 2925, 1478, 1035 cm^{-1}; HRMS (EI/GCMS) m/z calculated for $C_{17}H_{18}O$ $[M]^+$: 238.1352, found 238.1355.



2.7d

1,1-dimethyl-3-phenyl-2,3-dihydro-1H-inden-4-ol 2.7d. The general procedure VII was followed using 60.0 mg of alkene **2.5d** (0.25 mmol), 2.25 mg of TfOH (0.015 mmol) and 0.46 mL of benzene. Purification by flash column chromatography (100:0→90:10 hexanes: benzene) afforded indane **2.7d** (14 mg, 24% yield, 70% total yield combined with regioisomer.) as colorless oil. ^{1}H NMR (400 MHz, C_6D_6): δ 7.08 (t, *J* = 7.8 Hz, 1H), 7.02-7.01 (m, 4H), 6.99-6.94 (m, 1H), 6.70 (app. dd, *J* = 7.8, 4.5 Hz, 2H), 4.23 (br s, 1H), 4.15 (app t, *J* = 8.4 Hz, 1H), 2.14 (dd, *J* = 12.6 Hz, 7.9 Hz, 1H), 1.77 (dd, *J* = 12.6 Hz, 9.0 Hz, 1H), 1.22 (s, 3H), 1.08 (s, 3H); ^{13}C NMR (100 MHz, C_6D_6): δ 154.8 (C), 153.2 (C), 143.5 (C), 129.5 (CH), 129.0 (CH), 128.7 (C), 127.8 (CH), 127.5 (CH), 126.9 (CH), 114.3 (CH), 53.2 (CH_2), 46.7 (CH), 43.5 (C), 29.1 (CH_3), 28.6 (CH_3); ^{13}C NMR (100 MHz, $CDCl_3$): δ

155.1 (C), 152.6 (C), 143.2 (C), 129.4 (CH), 129.3 (CH), 128.7 (C), 127.8 (CH), 127.4 (CH), 114.5 (CH), 114.1 (CH), 53.5 (CH_2), 46.8 (CH), 43.9 (C), 29.3 (CH_3), 28.7 (CH_3); ATR-FTIR (neat): 3090, 3071, 3035, 2925, 1478, 1034 cm^{-1}; HRMS (EI/GCMS) m/z calculated for $C_{17}H_{18}O$ $[M]^+$: 238.1352, found 238.1347.

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Chapter 3

Dispersion-Controlled Regioselective Acid-Catalyzed Intramolecular Hydroindolation of *cis*-Methindolylstyrenes to Access Tetrahydrobenzo[*cd*]indoles

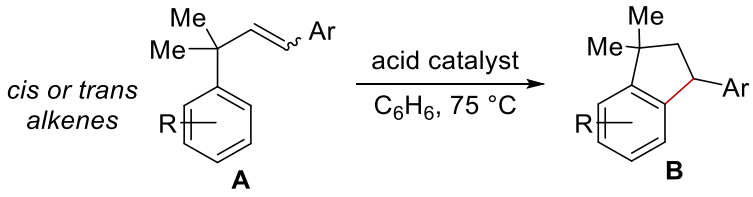
Background

Substrate conformational biasing arising from steric constraints, such as those imposed by geminal dialkyl groups (i.e., the Thorpe–Ingold effect),[1] are often used to circumvent energetic barriers to bond formation in order to prepare new and useful molecules. In the previous chapter of this dissertation, I have demonstrated an intramolecular acid-catalyzed hydroarylation of *β*-(*α'*,*α'*-dialkyl)benzylstyrenes (**A**, Scheme 1A), showing that a *gem*-dialkyl group can be used to synthesize indanes efficiently (**B**).[2,3] I then became interested in applying this design concept to more complex and medicinally relevant substrates, namely 4-bromoindole-derived *β*-(*α*',*α*'-dimethyl)-4'-methindolylstyrenes like **C (**Scheme 1B), which are rapidly prepared by sequential enolate cross-coupling, Wittig, and benzyl protection reactions.[4] Cyclization could occur at either C3 to afford tetrahydrobenzo[*cd*]indole **D**, or at C5 to afford tetrahydrocyclopenta[*e*]indole **E**. During my investigation, it was found that a variety of 3-aryl-5,5-dimethyl-1,3,4,5-tetrahydrobenzo[*cd*]indoles (**D**) are efficiently prepared in good yield by treating the *cis*-configured isomer of **C** with Brønsted acid catalysts (Scheme 1B, top pathway). In contrast, *trans*-configured substrates predominantly oligomerize (Scheme 1B, bottom pathway). The experimental and computational data suggest that angle compression can induce a ground state stabilization of *cis*-substrates through dispersive interactions, presumably between arene π systems,[5] enabling a concerted protonation and electrophilic attack to afford **G**, which rearomatizes to **H** (Scheme 1C).[6] A concerted mechanism avoids generating a long-lived carbocation intermediate that would be more likely to participate in competing intermolecular decomposition pathways—which may explain the disparate cyclizing ability of *trans*-configured starting materials, and non-dispersable *cis*-configured substrates (see below).

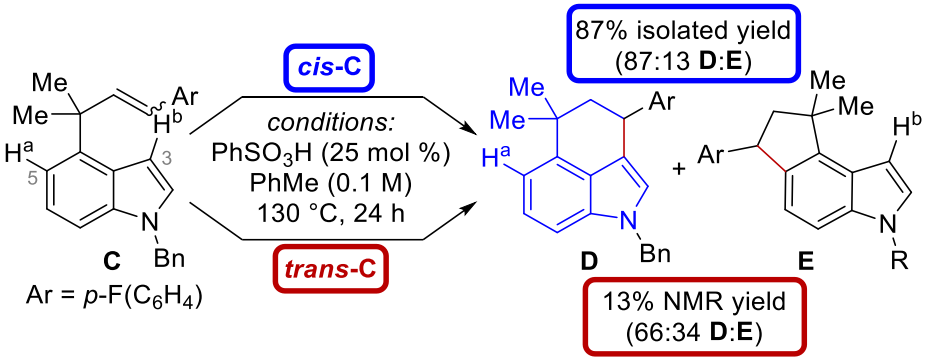
Products like **H** contain quaternary geminal dimethyl and diarylmethine motifs, which are well-represented in natural products and medicines,[7] and contains the 5,5-dimethyl-1,3,4,5-tetrahydrobenzo[*cd*]indole framework (in blue) common to the important ambiguine and hapalindole natural product families, and closely related to lysergic acid.[8] Despite significant synthetic attention devoted to 5,5-dimethyl-1,3,4,5-tetrahydrobenzo[*cd*]indoles, a general method for their synthesis has not been reported prior to this publicarion. Target-oriented cyclization strategies have included stoichiometric Lewis acid-mediated alkene hydroindolations using 7-methoxy substituted 3-alkenylindoles[9] or additions to carbonyls,[10] and intramolecular Heck reactions of 4-bromoindoles.[11]

Scheme 12. Geminal Dimethyl-Enabled Catalytic Intramolecular Alkene Hydroarylation Reactions

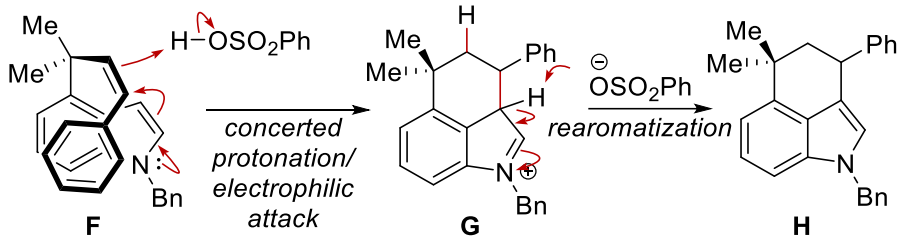
A. Prior work (Chapter 1): *Thorpe–Ingold-assisted catalytic intramolecular hydroarylations of β-benzylstyrenes.*[2]



B. This work: *a catalytic regioselective intramolecular hydroarylation unique to cis-configured β-4'-methindolylstyrenes.*



C. Putative mechanism: *conformational biasing of cis substrates enables concerted protonation and electrophilic attack.*

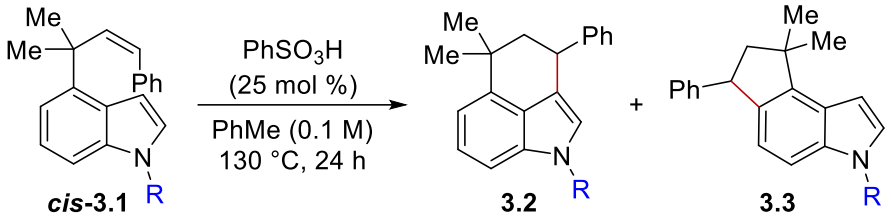


Results and Discussion

The optimization (see experimental section) revealed that *cis*-configured indole analogues could be cyclized with good regioselectivity (85:15) favoring tetrahydrobenzo[*cd*]indole by using arene-containing Brønsted acid catalysts in non-Lewis basic polarizable aprotic solvents.[4] Good yield was obtained after heating for 24 hours at 130 °C in the presence of 25 mol % of anhydrous benzenesulfonic acid in toluene. Under the optimized conditions, I also evaluated various N protecting groups, which revealed their influence on the yield and regioselectivity of the reaction (Table 1). The best result was obtained using *cis*-configured benzyl-protected substrate **3.1a**, which afforded 73% isolated yield of major product **3.2a** on 0.2 mmol scale (entry 1), and similar yield at 1.0 mmol scale (entry 2).

The benzyl group in **3.2a** is readily deprotected in 91% yield.[12] Another readily-deprotected indole, N-ethylsulfonyl analogue **3.1b**, afforded **3.2b** in slightly reduced yield and selectivity (entry 3).[13] Yields and regioselectivities for N-alkylindolyl substrates were similar to those of **3.1a**, and include methyl (**3.1c**) ethyl (**3.1d**) and *iso*-propyl (**3.1e**) groups (entries 4–6). When an electron-withdrawing tosyl protecting group was used, selectivity diminished (**3.1f**, entry 7). Acetyl protection prevented substrate conversion (entry 8). Lastly, free N–H indole **3.1h** simply decomposed (entry 9).

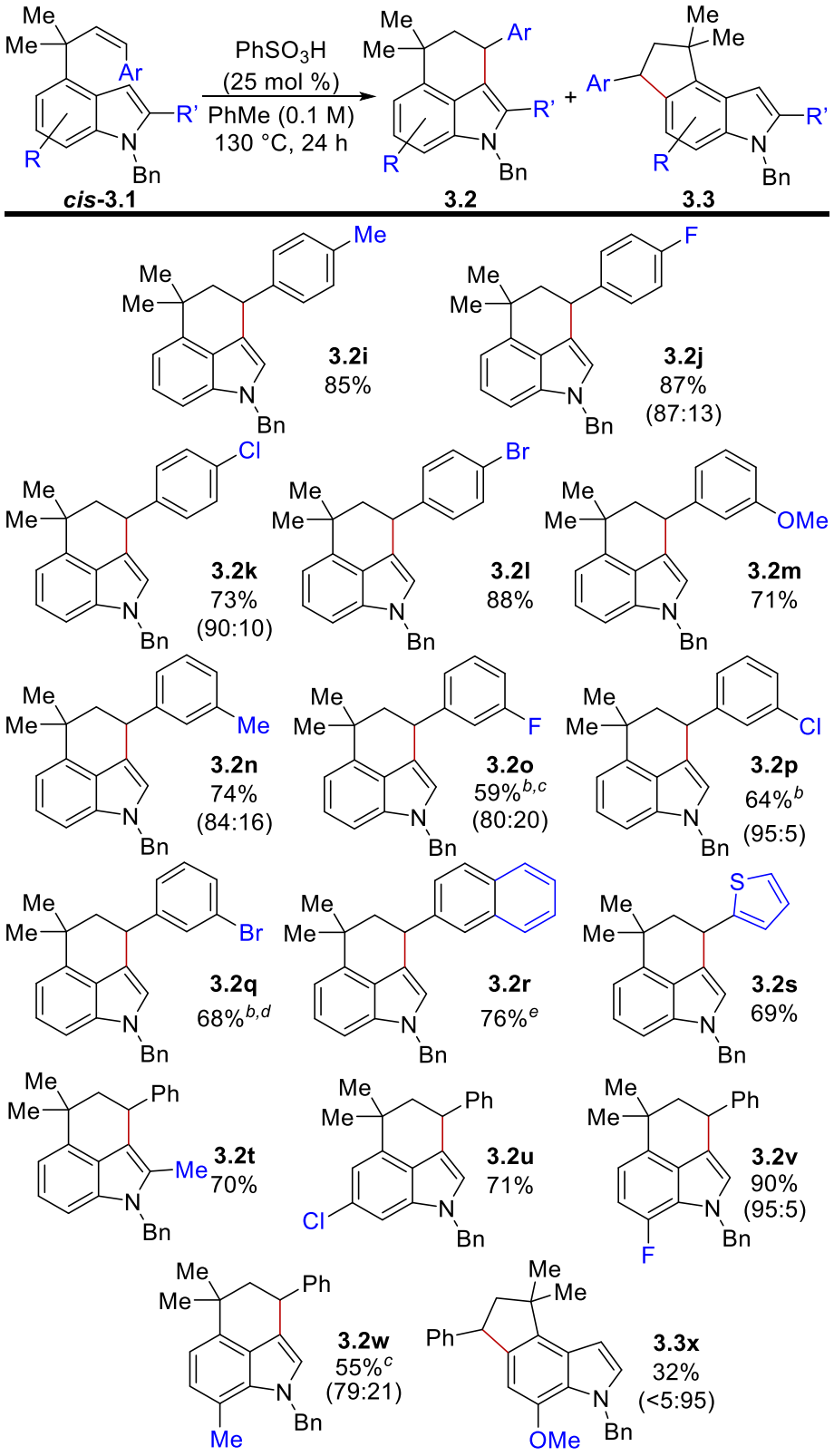
Table 5. Evaluation of Indole N-Protecting Groups[a]



entry	substrate ID	R	conv. (%)	isolated yield (%) of **3.2**	rr (**3.2**:**3.3**)[b]
1	**3.1a**	Bn	100	73	85:15
2[c]	**3.1a**	Bn	100	69	85:15
3	**3.1b**	$C_2H_4SO_2Ph$	100	57	80:20
4	**3.1c**	Me	100	68	83:17
5	**3.1d**	Et	100	72	83:17
6[d]	**3.1e**	*i*-Pr	100	75	83:17
7	**3.1f**	Ts	100	72[e]	60:40
8	**3.1g**	Ac	<5	<5	n.d.
9[f]	**3.1h**	H	100	<5	n.d.

[a]Reactions were conducted on 0.2 mmol scale in a closed vial unless otherwise noted. [b]Regioisomeric ratio determined by ^{1}H NMR analysis of the crude reaction. [c]Reaction was conducted on 1.0 mmol scale. [d]Structure of **3.2e** confirmed by X-ray crystallography. [e]Combined yield of inseparable regioisomers. [f]Structure of **3.1h** confirmed by X-ray crystallography.

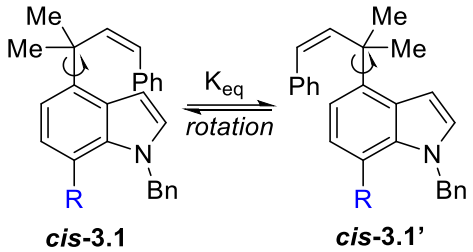
Scheme 13. Scope of the Cyclization[a]



[a]Reactions employed pure *cis*-alkenyl starting materials unless otherwise noted and were conducted on 0.2 mmol scale in a closed vial. The substrates were fully consumed in all cases. Unless otherwise noted, yields refer to the isolated indicated major product, and regioselectivities (**3.2**:**3.3**, indicated in parentheses) were determined by ^{1}H NMR analysis of the crude reaction. [b]80 mol % of $PhSO_3H$ was used. [c]Yield refers to an inseparable mixture of **3.2** and **3.3**. [d]Starting material was a 65:35 mixture of *cis* and *trans* isomers. [e]Starting material was a 78:22 mixture of *cis* and *trans* isomers.

Next, I evaluated the influence of functional groups on the cyclization of N-benzylindolyl substrates (Scheme 2). Owing to the generally good regioselectivity of the reaction (ranging from 80:20 to >95:5), I was typically able to obtain the fused tricyclic isomer in good or excellent yield. *Para*-substituents on the styrene moiety, including Me, F, Cl, and Br (**3.1i**–**3.1l**), afforded fused tricycles in high yield, as did electron-donating groups positioned *meta*, like methoxy (**3.1m**) and methyl (**3.1n**). In contrast, stoichiometric amounts of benzenesulfonic acid are required to obtain acceptable yields when halogens are positioned *meta* to the alkene (**3.1o**–**3.1q**); *meta*-bromo substrate **3.1q** cyclized in 68% yield from an inseparable 65:35 mixture of *cis* and *trans* isomers. Beyond substituted benzenes, it was found that 2-naphthyl analogue **3.1r** gave 76% yield of **3.2r** from a 78:22 mixture of *cis* and *trans* starting stereoisomers, respectively. In the final variation of the alkene aromatic substituent, a 2-thiophene analogue also afforded the fused tricycle **3.2s** in good yield. Shifting the focus to functional group tolerance on the indole ring, a 2-methyl substituent was well-tolerated, as were 6-chloro and 7-fluoro variants (**3.2t**–**3.2v**, respectively). The latter afforded the best yield and regioselectivity that we observed in this study. Surprisingly, adding electron-donating substituents to the 7 position impacted the regioselectivity significantly, with 7-methyl substrate **3.1w** affording a 55% yield of an inseparable regioisomeric mixture of **3.2w** and **3.3w**. Even more intriguingly, formation of the 6-membered ring was completely prohibited by the presence of a 7-methoxy substituent—only **3.3x** was isolated. It should be noted that **3.2w**, **3.3x** were prepared by second year graduate student from Professor Stokes' group Ms. Anargul Tohti. Ms. Tohti also repeated the preparation of **3.2s** with an improved yield. I should also note that undergraute research assistant Mr. Cristian Ramirez assisted with prepratation of muiltipile starting materials (benzylindolyl substrates) and successfully prepared the product **3.2u** and **3.8**.

Table 6. Calculated Enthalpies of Substrate Rotamers[a]



cis-3.1 *cis*-3.1'

substrate	R	ΔΔH (kcal/mol)	K_{eq} (130 °C)
3.1v	F	6.66	2.5×10^{-4}
3.1a	H	5.36	1.2×10^{-3}
3.1w	Me	4.95	2.1×10^{-3}
3.1x	OMe	3.54	1.4×10^{-2}

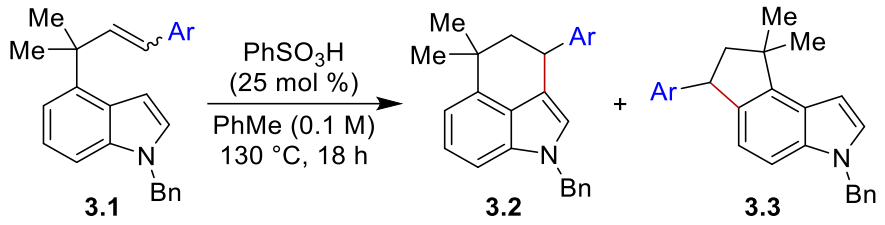
[a]Gas phase calculations of ΔΔH using B3PW91/6-311G(d) with the GD3 empirical dispersion correction.

The disparate regioselectivity outcomes for substrates **3.1v**–**3.1x** imply a high degree of dependence on the electronic nature of the indole ring. It was hypothesized that

this could be due to the Thorpe–Ingold effect inducing overlap between the indole and styrene, which would necessarily deconjugate the styrenyl alkene. As an indirect measure of the distortion of the C=C bond, our collaborators, Professor Hratchian and 4th year graduate student Mr. Hassan Harb, computed the relative gas phase enthalpies (ΔΔH) of the two rotamers (***cis*-3.1** and ***cis*-3.1'**) of 7-substituted indole substrates that would lead to the respective products **3.2** or **3.3** using B3PW91/6-311G(d) with the GD3 empirical dispersion correction (Table 2).[14] (Note: the computed rotamer enthalpies do not differ significantly without GD3 correction.[4]) Fluorinated rotamer ***cis*-3.1v** is 6.66 kcal/mol more stable than rotamer ***cis*-3.1v'** (incidentally corresponding to an equilibrium constant favoring ***cis*-3.1v** by a factor of over 4000 at 130 °C). As R becomes more electron-rich, dispersion is attenuated (ΔΔH diminishes). Greater dispersion appears to facilitate alkene protonation, hypothetically by attenuating the alkene's conjugation to the phenyl ring. It should be noted that all computational calculations were run by Mr. Harb under the guidance of Professor Hratchian, which significantly improved the competency of this publication. All details in regards to the computational study can be found on the original publication.

In contrast to *cis* alkenes (odd-numbered entries, Table 3), *trans* alkenes (even-numbered entries) afford uniformly low yields and reduced regioselectivities, presumably due to the absence of dispersion (see the Supporting Information for *trans* enthalpies). Further, while non-indolic *cis*-*β*-benzylstyrene ***cis*-A** isomerizes to ***trans*-A** in just 1 hour at 80 °C (Scheme 3A), indole analogue ***cis*-1c** is unreactive after 24 hours (Scheme 3B). Combined with the DFT data, these configurational reactivity differences suggest that dispersion-induced deconjugated alkenes undergo concerted hydroindolation, since *cis* alkenes resist isomerization to *trans* alkenes despite the cation-promoting conditions. Incidentally, ***trans*-A** cleanly cyclizes to indane **B** by increasing the reaction temperature to 130 °C (Scheme 3A), perhaps due to sufficiently fast five-membered ring formation.

Table 7. Influence of *cis* and *trans* Alkene Configuration on the Cyclization of Methindolylstyrenes[a]

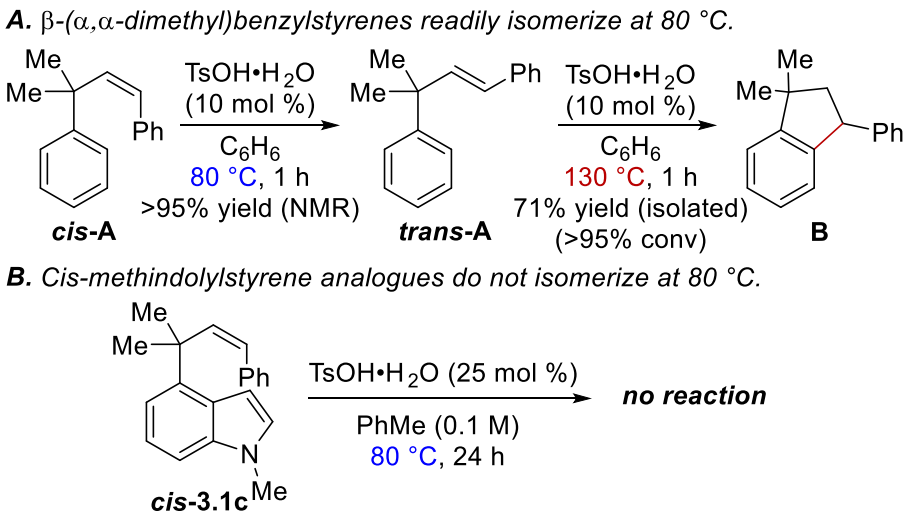


entry	substrate ID	Ar	NMR yield (%, **3.2**+**3.3**)[a]	rr (**3.2**:**3.3**)[b]
1	***cis*-3.1j**	*p*-F(C_6H_4)	99	87:13
2	***trans*-3.1j**		13	66:34
3	***cis*-3.1k**	*p*-Cl(C_6H_4)	81	90:10
4	***trans*-3.1k**		32	60:40
5	***cis*-3.1n**	*m*-Me(C_6H_4)	88	84:16
6	***trans*-3.1n**		37	65:35
7[c]	***cis*-3.1p**	*m*-Cl(C_6H_4)	69	95:5
8[c]	***trans*-3.1p**		10	n.d.

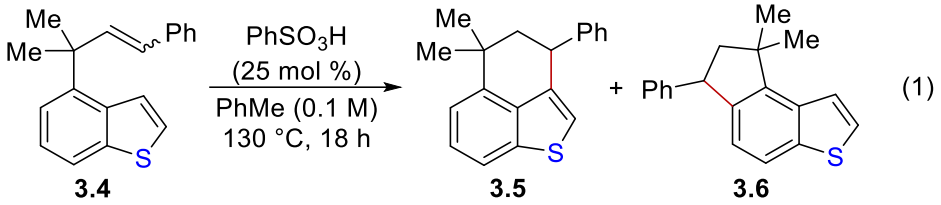
[a]Reactions were conducted on 0.2 mmol scale in a closed vial and substrates were consumed in full in all cases. The major decomposition pathway for *trans* substrates is oligomerization. [b]Yield and regioselectivity were determined by ^{1}H NMR analysis of the crude reaction mixture. [c]80 mol % of catalyst was used.

We also found that benzothiophene analogue ***cis*-3.4** cyclizes with regioselectivity similar to indoles under identical conditions, albeit a bit more sluggishly. In contrast, ***trans*-3.4** cyclized with slightly improved yield and regioselectivity compared to *trans* indoles (eq 1).

Scheme 14. Disparate Behavior of *cis*-*β*-Benzylstyrene and *cis*-*β*-4'-Methindolylstyrene

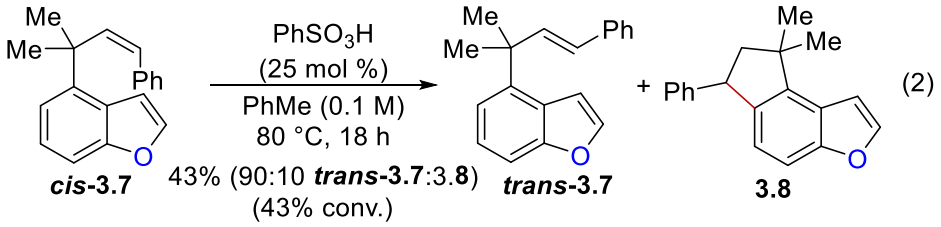


In contrast, we did not observe formation of the corresponding fused tricycle when using benzofuran analogues (eq 2). Rather, ***cis*-3.7** isomerized to ***trans*-3.7** at just 80 °C, with some formation of regioisomer **3.8** observed. This disparate behavior compared to indoles and benzothiophenes is likely due to a combination of diminished nucleophilicity at C3 and diminished dispersion (our DFT calculations show ΔΔH = 3.16 kcal/mol for the two *cis* rotamers of **3.7**).[4]



3.4 **3.5** **3.6**

substrate	conv. (%)	yield (%, **3.5**+**3.6**)	rr (**3.5**:**3.6**)
***cis*-3.4**	81	57	91:09
***trans*-3.4**	100	40	80:20



***cis*-3.7** 43% (90:10 ***trans*-3.7**:3.**8**) (43% conv.) ***trans*-3.7** **3.8**

Conclusion

In this chapter, I have demonstrated a catalytic intramolecular alkene hydroindolation to construct medicinally significant tetrahydrobenzo[*cd*]indoles from *cis*-methindolylstyrenes bearing a benzylic *gem*-dimethyl group, putatively *via* a concerted protonation and C–C bond formation. Empirical trends (substrate isomerizability, regioselectivity outcomes, electronic sensitivity, and temperature profile) and calculated ground state enthalpies suggest that the regioselectivity is dependent on dispersive interactions between the styrene and indole, which are forced into proximity by the *gem* dimethyl.

Experimental

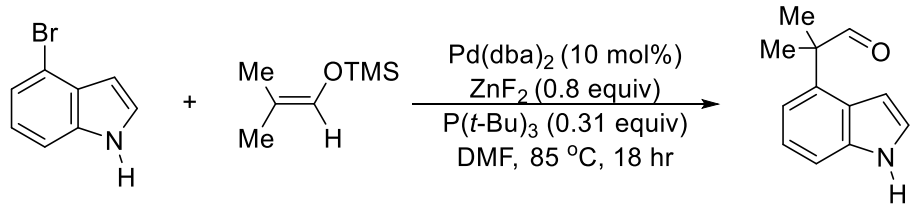
General Considerations

Anhydrous benzenesulfonic acid was used as purchased from Strem or Sigma-Aldrich and stored in a desiccator when not in use. Silyl enol ethers were used as purchased from Gelest.

A Mettler Toledo XS105 balance (repeatable to 0.1 mg) was used to measure mass. Flash column chromatography was performed using 40–63 μm 60 Å silica. TLC plate information; stored in a desiccator when not in use. Melting points were obtained on an electrothermal melting point apparatus and are uncorrected. NMR spectra were obtained on Agilent spectrometers. ^{1}H NMR spectra were obtained at 400 or 500 MHz and referenced to the residual $CHCl_3$ singlet at 7.26 ppm unless otherwise noted. The abbreviations s, d, t, q, dd, td, qd, and m stand for the resonance multiplicities singlet, doublet, triplet, quartet, doublet of doublet, triplet of doublet, quartet of doublet, and multiplet, respectively ('app.' denotes apparent). ^{13}C NMR spectra were obtained at 100 or 125 MHz and referenced to the center line of the $CDCl_3$ triplet at 77.2 ppm unless otherwise noted. Carbon atom degree of substitution was determined using ^{1}H–^{13}C HSQC. ^{19}F NMR spectra were obtained at 376 MHz subsequent to ^{1}H NMR acquisition and were otherwise unreferenced. FT-IR analysis was performed on a Thermo-Nicolet 380 using a diamond GladiATR from Pike technologies. APCI/ESI HRMS data were obtained on an Agilent LC-TOF (NSF CHE-0541848); EI HRMS data were obtained on a Waters GCT GC/MS (NSF CHE-0742001). Glassware for all reactions was oven-dried at 145 °C and cooled in a desiccator prior to use.

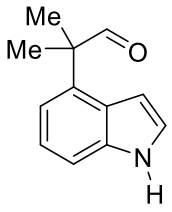
Scheme 15. Preparation of α-Quaternary Aldehydes

A. General Cross-Coupling Procedure



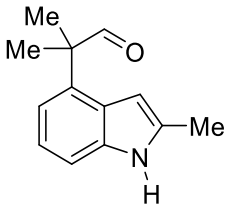
The cross-coupling procedure previously reported by Cai and coworkers was followed.[2] To a dry 50 mL round bottom flask charged with a PTFE-coated magnetic stir bar were added 212.1 mg of zinc fluoride (2.04 mmol, 0.80 equiv) and 146.6 mg of bis(dibenzylideneacetone) palladium (0) (0.26 mmol, 0.10 equiv). The reaction flask was then sealed with a rubber septum, degassed, and back-filled with nitrogen. Then 25.5 mL of DMF (0.1 M) and 535.1 mg of 4-bromoindole (2.55 mmol, 1.00 equiv) were added at room temperature. To this mixture were added 0.8 mL of a 1.0 M solution of tri-*tert*-butylphosphine in toluene (0.80 mmol, 0.31 equiv) and 0.7 mL of trimethyl((2-methylprop-1-en-1-yl)oxy)silane (3.83 mmol, 1.5 equiv) at the same time through syringe. The reaction mixture was heated to 85 °C and was allowed to stir in an N_2 atmosphere overnight. The reaction mixture was cooled to room temperature before filtration through Celite®, and the Celite® cake was washed with 15 mL of ethyl acetate. The filtrate was concentrated under reduced pressure. The crude product was purified by silica gel chromatography.

B. Synthesis and Characterization of Aldehydes



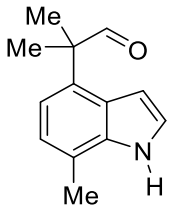
S3.1

2-(1H-Indol-4-yl)-2-methylpropanal S3.1. The general cross-coupling procedure was followed using 535.1 mg of 4-bromo-2-methyl-1H-indole (2.55 mmol), 212.1 mg of zinc fluoride (2.04 mmol), 146.6 mg of bis(dibenzylideneacetone)palladium(0) (0.26 mmol), 0.8 mL of tri-*tert*-butylphosphine solution (0.80 mmol), and 0.7 mL of trimethyl(2-methylprop-1-enyloxy)silane (3.83 mmol) in 25.5 mL of DMF. Purification by flash column chromatography (100:0→80:20 hexanes:benzne) afforded **S3.1** as colorless oil (405.8 mg, 85%), R_f = 0.25 (80:20 hexanes:benzene, visualized by 254 nm UV light and *p*-anisaldehyde stain). ^{1}H NMR (400 MHz, $CDCl_3$): δ 9.62 (s, 1H), 8.38 (s, 1H), 7.38 (d, *J* = 8.1 Hz, 1H), 7.26 (app. t, *J* = 7.8 Hz, 1H), 7.18 (m, 1H), 7.14 (d, *J* = 7.4 Hz, 1H), 6.48–6.46 (m, 1H), 1.61 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 204.2 (C=O), 136.4 (C), 133.5 (C), 126.3 (C), 124.4 (CH), 122.3 (CH), 117.4 (CH), 111.2 (CH), 102.2 (CH), 51.2 (C), 22.1 (CH_3); ATR-FTIR (neat): 3409, 2971, 2933, 2809, 2709, 1717, 1611, 1503 cm^{-1}; HRMS (ESI) m/z calculated for $C_{12}H_{14}NO$ $[M+H]^+$: 188.1070, found 188.1072.



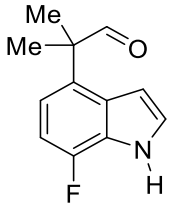
S3.2

2-Methyl-2-(2-methyl-1H-indol-4-yl)propanal S3.2. The general cross-coupling procedure was followed using 500.0 mg of 4-bromo-2-methyl-1H-indole (2.38 mmol), 198.0 mg of zinc fluoride (1.90 mmol), 136.9 mg of bis(dibenzylideneacetone)palladium(0) (0.24 mmol), 0.7 mL of tri-*tert*-butylphosphine solution (0.71 mmol), and 0.7 mL of trimethyl(2-methylprop-1-enyloxy)silane (3.57 mmol) in 23.8 mL of DMF. Purification by flash column chromatography (100:0→80:20 hexanes:benzne) afforded **S3.2** as a light yellow oil (273.0 mg, 57%), R_f = 0.31 (80:20 hexanes:benzene, visualized by 254 nm UV light and *p*-anisaldehyde stain). ^{1}H NMR (400 MHz, $CDCl_3$): δ 9.58 (s, 1 H), 8.06 (s, 1 H), 7.27 (d, *J* = 8.1 Hz, 1H), 7.16 (app. t, *J* = 7.7 Hz, 1H), 7.08 (dd, *J* = 7.4, 1.0 Hz, 1H), 6.16 (s, 1H), 2.41 (s, 3H), 1.57 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 204.2 (C=O), 136.6 (C), 135.4 (C), 132.4 (C), 127.5 (C), 121.3 (CH), 117.2 (CH), 110.3 (CH), 100.1 (CH), 51.1 (C), 22.0 (CH_3), 13.9 (CH_3); HRMS (ESI) m/z calculated for $C_{13}H_{16}NO$ $[M+H]^+$: 202.1226, found 202.1229.



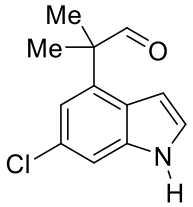
S3.3

2-Methyl-2-(7-methyl-1H-indol-4-yl)propanal S3.3. The general cross-coupling procedure was followed using 500.0 mg of 4-bromo-7-methyl-1H-indole (2.38 mmol), 198.0 mg of zinc fluoride (1.90 mmol), 136.9 mg of bis(dibenzylideneacetone)palladium(0) (0.24 mmol), 0.7 mL of tri-*tert*-butylphosphine solution (0.71 mmol), and 0.7 mL of trimethyl(2-methylprop-1-enyloxy)silane (3.57 mmol) in 23.8 mL of DMF. Purification by flash column chromatography (100:0→90:10 hexanes:benzene) afforded **S3.3** as a colorless oil (349.7 mg, 73%), R_f = 0.30 (80:20 hexanes:benzene, visualized by 254 nm UV light and *p*-anisaldehyde stain). ^{1}H NMR (400 MHz, $CDCl_3$): δ 9.62 (s, 1 H), 8.71 (s, 1 H), 7.19–7.17 (m, 1H), 7.05 (app. s, 2H), 6.50 (dd, *J* = 3.3, 1.9 Hz, 1H), 2.49 (s, 3H), 1.59 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 204.2 (C=O), 135.9 (C), 130.9 (C), 125.7 (C), 124.2 (CH), 122.5 (CH), 120.4 (C), 117.4 (CH), 102.3 (CH), 50.8 (C), 22.0 (CH_3), 16.6 (CH_3); ATR-FTIR (neat): 3472, 2963, 2920, 1711 cm^{-1}; HRMS (ESI) m/z calculated for $C_{13}H_{16}NO$ $[M+H]^+$: 202.1226, found 202.1228.



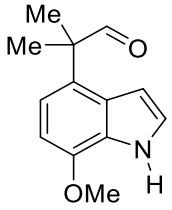
S3.4

2-(7-Fluoro-1H-indol-4-yl)-2-methylpropanal S3.4. The general cross-coupling procedure was followed using 513.2 mg of 4-bromo-7-fluoroindole (2.44 mmol), 203.0 mg of zinc fluoride (1.95 mmol), 140.3 mg of bis(dibenzylideneacetone)palladium(0) (0.24 mmol), 0.7 mL of tri-*tert*-butylphosphine solution (0.73 mmol), and 0.7 mL of trimethyl(2-methylprop-1-enyloxy)silane (3.66 mmol) in 24.0 mL of DMF. Purification by flash column chromatography (100:0→80:20 hexanes:benzene) afforded **S3.4** (345.5 mg, 69% yield) as colorless oil, R_f = 0.35 (80:20 hexanes:benzene, visualized by 254 nm UV light and *p*-anisaldehyde stain). ^{1}H NMR (500 MHz, $CDCl_3$): δ 9.58 (s, 1H), 8.82 (s, br, 1H), 7.23 (t, *J* = 2.8 Hz, 1H), 7.04–7.01 (m, 1H), 6.96–6.93 (m, 1H), 6.50–6.49 (m, 1H), 1.59 (s, 6H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 203.9 (C=O), 149.5 (d, *J* = 244.4 Hz, C-F), 129.7 (d, *J* = 5.3 Hz, C), 129.1 (d, *J* = 3.6 Hz, C), 125.1 (CH), 124.6 (d, *J* = 13.6 Hz, C), 117.6 (d, *J* = 6.5 Hz, CH), 106.6 (d, *J* = 16.0 Hz, CH), 102.9 (d, *J* = 1.9 Hz, CH), 50.2 (C), 21.68 (CH_3); ^{19}F NMR (470 MHz, $CDCl_3$): δ –136.2; ATR-FTIR (neat): 3318, 3090, 3071, 2970, 1728, 1649, 1619, 1525 cm^{-1}; HRMS (ESI) m/z calculated for $C_{12}H_{13}FNO$ $[M+H]^+$: 206.0976, found 206.0977.



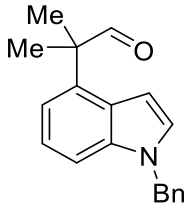
S3.5

2-(6-Chloro-1H-indol-4-yl)-2-methylpropanal S3.5. The general cross-coupling procedure was I followed using 455.0 mg of 4-bromo-6-chloro-1H-indole (2.17 mmol), 180.5 mg of zinc fluoride (1.74 mmol), 124.8 mg of bis(dibenzylideneacetone)palladium(0) (0.22 mmol), 0.7 mL of tri-*tert*-butylphosphine solution (0.65 mmol), and 0.6 mL of trimethyl(2-methylprop-1-enyloxy)silane (3.26 mmol) in 21.7 mL of DMF. Purification by flash column chromatography (100:0→80:20 hexanes:benzene) afforded **S3.5** (279.0 mg, 58% yield) as colorless oil, R_f = 0.30 (80:20 hexanes:benzene, visualized by 254 nm UV light and *p*-anisaldehyde stain). ^{1}H NMR (400 MHz, $CDCl_3$): δ 9.56 (s, 1 H), 8.53 (s, 1 H), 7.36 (dd, *J* = 1.8, 1.0 Hz, 1H), 7.17 (dd, *J* = 3.4, 2.5 Hz, 1H), 7.09 (d, *J* = 1.8 Hz, 1H), 6.39 (ddd, *J* = 3.2, 2.0, 1.0 Hz, 1H), 1.57 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 203.4 (C=O), 136.7 (C), 134.7 (C), 128.1 (C), 125.1 (C), 124.9 (CH), 118.3 (CH), 111.0 (CH), 102.2 (CH), 51.1 (C), 22.0 (CH_3); ATR-FTIR (neat): 3410, 3037, 3003, 1711 cm^{-1}; HRMS (ESI) m/z calculated for $C_{12}H_{13}ClNO$ $[M+H]^+$: 222.0680, found 222.0683.



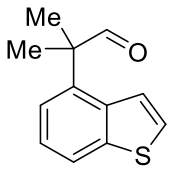
S3.6

2-(7-Methoxy-1H-indol-4-yl)-2-methylpropanal S3.6. The general cross-coupling procedure was followed using 500.0 mg of 4-bromo-7-methoxy-1H-indole (2.30 mmol), 191.3 mg of zinc fluoride (1.84 mmol), 132.2 mg of bis(dibenzylideneacetone)palladium(0) (0.23 mmol), 0.7 mL of tri-*tert*-butylphosphine solution (0.69 mmol), and 0.6 mL of trimethyl(2-methylprop-1-enyloxy)silane (3.45 mmol) in 23.0 mL of DMF. Purification by flash column chromatography (100:0:0→92:3:5 hexanes:benzene:ethyl acetate) afforded **S3.6** (284.8 mg, 57% yield) as a yellow oil, R_f = 0.33 (92:3:5 hexanes:benzene:ethyl acetate, visualized by 254 nm UV light and *p*-anisaldehyde stain). ^{1}H NMR (400 MHz, $CDCl_3$): δ 9.57 (s, 1 H), 8.59 (s, br, 1 H), 7.16 (dd, *J* = 3.2, 2.5 Hz, 1H), 7.03 (d, *J* = 8.0 Hz, 1H), 6.68 (d, *J* = 8.0 Hz, 1H), 6.46 (dd, *J* = 3.2, 2.2 Hz, 1H), 3.98 (s, 3H), 1.58 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 203.8 (C=O), 146.0 (C), 127.3 (C), 126.7 (C), 125.8 (C), 123.7 (CH), 117.6 (CH), 102.5 (CH), 101.5 (CH), 55.3 (OCH_3), 50.4 (C), 22.0 (CH_3); HRMS (ESI) m/z calculated for $C_{13}H_{16}NO_2$ $[M+H]^+$: 218.1176, found 218.1178.



S3.7

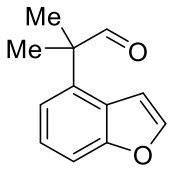
2-(1-Benzyl-1H-indol-4-yl)-2-methylpropanal S3.7. To a solution of aldehyde **S3.1** (1.5 g, 8.0 mmol) in DMF (16.0 mL, 0.5M), 60 wt.% NaH (480.0 mg, 1.5 equiv) was added in an ice bath through four portions. The slurry was allowed to stir at room temperature for 30 minutes before it was cooled to 0 ^{o}C. Benzyl bromide (2.0 g, 1.5 equiv) was diluted with DMF (1.0 mL) before it was added to the deprotonated indole solution through syringe. The reaction mixture was then allowed to stir at room temperature for overnight. After the complete consumption of the starting material indicated by TLC, the reaction was quenched by addition of saturated $NaHCO_3$ solution (~10mL) at 0 ^{o}C. The product was extracted with EtOAc three times and combined organic layers were washed with brine and dried over anhydrous sodium sulfate before it was concentrated under reduced pressure. The crude benzylated aldehyde was flushed through silica gel column with mixture of hexanes and ethyl acetate (hexanes:ethyl acetate , 100:0→90:10) to obtain pure aldehyde **S3.7** (2.0 g, 89% yield) as light yellow oil, R_f = 0.40 (90:10 hexanes:ethyl acetate, visualized by 254 nm UV light and *p*-anisaldehyde stain). ^{1}H NMR (400 MHz, $CDCl_3$): δ 9.64 (s, 1 H), 7.38 – 7.21 (m, 5H), 7.17 – 7.13 (m, 4H), 6.49 (dd, *J* = 3.3, 0.7 Hz, 1H), 5.33 (s, 2H), 1.62 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 203.8 (C=O), 137.3 (C), 136.8 (C), 133.8 (C), 128.9 (CH), 128.4 (CH), 127.8 (CH), 127.1 (C), 127.0 (CH), 122.0 (CH), 117.2 (CH) , 109.7 (CH), 101.3 (CH), 51.1 (C), 50.3 (CH_2), 22.1 (CH_3); ATR-FTIR (neat): 2970, 2931, 1722 cm^{-1}; HRMS (ESI) m/z calculated for $C_{19}H_{20}NO$ $[M+H]^+$: 278.1539, found 278.1539.



S3.8

2-(Benzo[b]thiophen-4-yl)-2-methylpropanal S3.8. The general cross-coupling procedure was followed using 485.5 mg of 4-bromobenzo[b]thiophene (2.30 mmol), 191.3 mg of zinc fluoride (1.84 mmol), 132.3 mg of bis(dibenzylideneacetone)palladium(0) (0.23 mmol), 0.7 mL of tri-*tert*-butylphosphine solution (0.69 mmol), and 0.6 mL of trimethyl(2-methylprop-1-enyloxy)silane (3.45 mmol) in 23.0 mL of DMF. Purification by flash column chromatography (100:0→90:10 hexanes:benzene) afforded **S3.8** (352.4 mg, 75% yield) as a yellow oil, R_f = 0.40 (90:10 hexanes:benzene, visualized by 254 nm UV light and *p*-anisaldehyde stain). ^{1}H NMR (400 MHz, $CDCl_3$): δ 9.58 (s, 1 H), 7.88 (td, *J* = 4.5, 0.9 Hz, 1H), 7.46 (d, *J* = 5.7 Hz, 1H), 7.40(dd, *J* = 4.6, 0.8 Hz, 2H), 7.28 (dd, *J* = 5.7, 1.0 Hz, 1H), 1.59 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 203.5 (C=O), 141.2 (C), 137.6 (C),

136.4 (C), 126.8 (CH), 124.4 (CH), 122.6 (CH), 122.3 (CH), 121.9 (CH), 51.4 (C), 22.4 (CH_3).

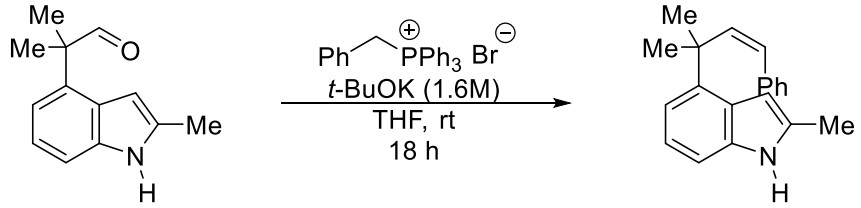


S3.9

2-(Benzofuran-4-yl)-2-methylpropanal S3.9. The general cross-coupling procedure was followed using 394.1 mg of 4-bromobenzofuran (2.00 mmol), 166.4 mg of zinc fluoride (1.6 mmol), 115.0 mg of bis(dibenzylideneacetone)palladium(0) (0.2 mmol), 0.60 mL of tri-*tert*-butylphosphine solution (0.60 mmol), and 0.6 mL of trimethyl(2-methylprop-1-enyloxy)silane (3.0 mmol) in 20.0 mL of DMF. Purification by flash column chromatography (100:0→95:5 hexanes:benzene) afforded **S3.9** (335.0 mg, 89% yield) as a yellow oil, R_f = 0.30 (90:10 hexanes:benzene, visualized by 254 nm UV light and *p*-anisaldehyde stain). ^{1}H NMR (400 MHz, $CDCl_3$): δ 9.54 (s, 1 H), 7.60 (appr s, 1H), 7.49 (d, *J* = 8.3 Hz, 1H), 7.33 (t, *J* = 7.9 Hz, 1H), 7.23 (d, *J* = 7.6 Hz, 1H), 6.71 (appr s, 1H), 1.56 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 202.4 (C=O), 155.3 (C), 144.8 (CH), 134.3 (C), 126.0 (C), 124.5 (CH), 120.1 (CH), 111.1 (CH), 105.9 (CH), 50.8 (C), 22.0 (CH_3); HRMS (ESI) m/z calculated for $C_{12}H_{13}O_2$ $[M+H]^+$: 189.0910, found: 189.0903.

Scheme 16. Preparation of Alkenyl Substrates

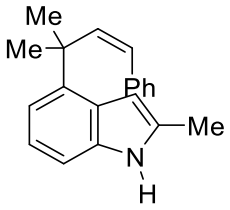
A. General Wittig-Olefination Procedure



In a dry 25 mL round bottom flask charged with PTFE coated magnetic stir bar, benzyl triphenylphosphonium bromide (542.0 mg, 1.25 mmol) was dissolved in 2.0 mL THF. The reaction flask was then sealed with a rubber septum before 0.8 mL *t*-BuOK solution (1.28 mmol, 1.10 equiv) was syringed into the mixture at room temperature. The red reaction mixture was continuously being stirred for an additional 20 minutes before it was chilled to 0 °C. A solution of aryl-dialkyl-aldehyde **S3.2** (201.3 mg, 1.00 mmol,) in minimal amount of THF (~0.5 mL) was then added to the ylides drop-wise through syringe. The reaction was then brought to room temperature and allowed to stir for 18 hours. After the aldehyde was consumed, the reaction was quenched with saturated aqueous NH_4Cl solution. The alkene product was then extracted with ethyl acetate (10 mL x 3). The combined

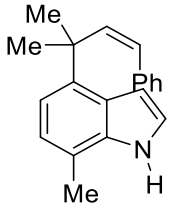
organic solution was collected and dried over sodium sulfate anhydrous before it was concentrated under reduced pressure to afford crude alkene product as a mixture of *E* and *Z* isomers. Purification by silica gel chromatography afforded ananlytically pure *Z* alkenes unless otherwise noted.

B. Synthesis and Characterization of Alkenyl Indole Substrates



S3.10

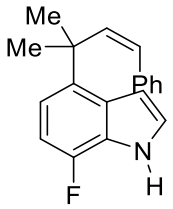
(Z)-2-methyl-4-(2-methyl-4-phenylbut-3-en-2-yl)-1H-indole S3.10. The general Wittig-olefination procedure was followed using 201.3 mg of **S3.2** (1.0 mmol), 542.0 mg of triphenyl phosphonium bromide (1.25 mmol) and 0.8 mL of a 1.6 M solution of *t*-BuOK (1.28 mmol) in THF. Purification by flash column chromatography (100:0→98:2 hexanes: benzene) afforded *Z* stereoisomer **S3.10** (130.0 mg, 48% yield) as light yellow oil, R_f = 0.30 (90:10 hexanes:benzene, visualized by 254 nm UV light and *p*-anisaldehyde stain). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.60 (s, 1H), 7.14–7.05 (m, 6H), 6.98–6.93 (m, 2H), 6.58 (d, *J* = 12.6 Hz, 1H), 6.50 (s, 1H), 6.25 (d, *J* = 12.6 Hz, 1H), 2.45 (s, 3H), 1.65 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 142.2 (CH), 141.4 (C), 138.2 (C), 136.7 (C), 133.5 (C), 128.8 (CH), 128.6 (CH), 127.2 (CH), 126.8 (C), 126.0 (CH), 120.8 (CH), 115.7 (CH), 108.8 (CH), 102.1 (CH), 41.2 (C), 30.1 (CH_3), 13.8 (CH_3); ATR-FTIR (neat): 3060, 2986, 1737 cm^{-1}; HRMS (ESI) m/z calculated for $C_{20}H_{22}N$ $[M+H]^+$: 276.1747, found: 276.1740.



S3.11

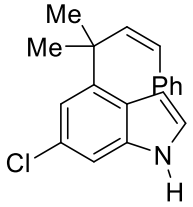
(Z)-7-methyl-4-(2-methyl-4-phenylbut-3-en-2-yl)-1H-indole S3.11. The general Wittig-olefination procedure was followed using 201 mg of **S3** (1.0 mmol), 542.0 mg of triphenyl phosphonium bromide (1.25 mmol) and 0.8 mL of a 1.6 M solution of *t*-BuOK (1.28 mmol) in THF. Purification by flash column chromatography (100:0→98:2 hexanes: benzene) afforded *Z* stereoisomer **S3.11** (151.5 mg, 55% yield) as light yellow oil, R_f = 0.33 (90:10 hexanes:benzene, visualized by 254 nm UV light and *p*-anisaldehyde stain). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.86 (s, 1H), 7.19–7.13 (m, 4H), 7.12 (d, *J* = 7.5 Hz, 1H), 7.07–7.02 (m, 3H), 6.91 (dd, *J* = 3.3, 2.1 Hz, 1H), 6.65 (d, *J* = 12.6 Hz, 1H), 6.32 (d, *J* = 12.6 Hz, 1H), 2.52 (s, 3H), 1.74 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 142.3 (CH), 140.2 (C), 138.2

(C), 135.9 (C), 128.7 (CH), 128.5 (CH), 127.1 (CH), 125.9 (CH), 125.2 (C), 122.5 (CH), 122.3 (CH), 118.3 (C), 116.0 (CH), 104.6 (CH), 41.2 (C), 30.3 (CH_3), 16.5 (CH_3); ATR-FTIR (neat): 3059, 2984, 1729 cm^{-1}; HRMS (ESI) m/z calculated for $C_{20}H_{22}N$ $[M+H]^+$: 276.1747, found: 276.1739.



S3.12

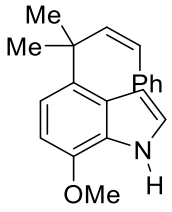
(Z)-7-fluoro-4-(2-methyl-4-phenylbut-3-en-2-yl)-1H-indole S3.12. General procedure II was followed using 205.0 mg of **S4** (1.0 mmol), 542.0 mg of triphenyl phosphonium bromide (1.25 mmol) and 0.8 mL of a 1.6 M solution of *t*-BuOK (1.28 mmol) in THF. Purification by flash column chromatography (100:0→95:5 hexanes: benzene) afforded *Z* stereoisomer **S3.12** (176.0 mg, 63% yield) as a light brown oil. R_f = 0.30 (90:10 hexanes:benzene, visualized by 254 nm UV light and *p*-anisaldehyde stain). ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.16 (s, 1H), 7.15 (dd, *J* = 3.2, 2.4 Hz, 1H), 6.99–6.92 (m, 3H), 6.85 (dd, *J* = 8.2, 4.7 Hz, 1H), 6.78–6.70 (m, 4H), 6.47 (d, *J* = 12.6 Hz, 1H), 6.11 (d, *J* = 12.5 Hz, 1H), 4.0 (s, 3H), 1.57 (s, 6H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 148.6 (d, *J* = 241.6 Hz, C-F), 141.8 (CH), 137.8 (d, *J* = 3.7 Hz, C), 129.3 (d, *J* = 4.8 Hz, C), 128.9 (CH), 128.4 (CH), 126.9 (CH), 126.0 (CH), 124.5 (d, *J* = 13.6 Hz, C), 123.3 (d, *J* = 0.9 Hz, C), 116.1 (d, *J* = 6.1 Hz, CH), 106.1 (CH), 105.9 (CH), 105.3 (d, *J* = 2.2 Hz, CH), 40.9 (C), 30.5 (CH_3); ^{19}F NMR (470 MHz, $CDCl_3$): δ - 139.34; HRMS (ESI) m/z calculated for $C_{19}H_{19}FN$ $[M+H]^+$: 280.1496, found: 280.1488.



S3.13

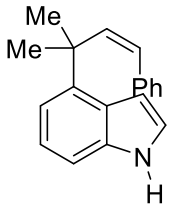
(Z)-6-chloro-4-(2-methyl-4-phenylbut-3-en-2-yl)-1H-indole S3.13. The general Wittig-olefination procedure was followed using 222.0 mg of **S5** (1.0 mmol), 542.0 mg of triphenyl phosphonium bromide (1.25 mmol) and 0.8 mL of a 1.6 M solution of *t*-BuOK (1.28 mmol) in THF. Purification by flash column chromatography (100:0→85:15 hexanes:benzene) afforded *Z* stereoisomer **S3.13** (210.1 mg, 71% yield) as a light yellow oil. R_f = 0.30 (90:10 hexanes:benzene, visualized by 254 nm UV light and *p*-anisaldehyde stain). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.87 (s, 1H), 7.11 (dd, *J* = 1.8, 1.0 Hz, 1H), 7.08 (dd, *J* = 3.3, 2.4 Hz, 1H), 7.05–6.95 (m, 4H), 6.8–6.74 (m, 2H), 6.73–6.68 (m, 1H), 6.51 (d, *J* = 12.6 Hz, 1H), 6.12 (d, *J* = 12.5 Hz, 1H), 1.60 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): ^{13}C NMR (100 MHz, $CDCl_3$): δ 143.3 (C), 141.2 (CH), 137.6 (C), 136.5 (C), 129.2 (CH), 128.3

(CH), 127.7 (C), 126.9 (CH), 126.1 (CH), 124.5 (C), 123.3 (CH), 117.3 (CH), 109.1 (CH), 104.4 (CH), 41.3 (C), 30.3 (CH_3); ATR-FTIR (neat): 3059, 1732, 1374, 1240 cm^{-1}; HRMS (ESI) m/z calculated for $C_{19}H_{19}ClN$ $[M+H]^+$: 296.1201, found: 296.1192.



S3.14

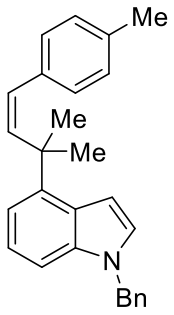
(Z)-1-benzyl-7-methoxy-4-(2-methyl-4-phenylbut-3-en-2-yl)-1H-indole S3.14. The general Wittig-olefination procedure was followed using 217.0 mg of **S6** (1.0 mmol), 542.0 mg of triphenyl phosphonium bromide (1.25 mmol) and 0.8 mL of a 1.6 M (1.28 mmol) solution of *t*-BuOK in THF. Purification by flash column chromatography (100:0→85:15 hexanes:benzene) afforded *Z* stereoisomer **S3.14** (201.1 mg, 69% yield) as a light yellow oil. R_f = 0.30 (90:10 hexanes:benzene, visualized by 254 nm UV light and *p*-anisaldehyde stain). ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.38 (s, 1H), 7.16 (t, *J* = 2.8 Hz, 1H), 7.11–7.07 (m, 3H), 6.97 (d, *J* = 8.1 Hz, 1H), 6.9 –6.92 (m, 2H), 6.79 (dd, *J* = 3.2, 2.2 Hz, 1H), 6.60–6.54 (m, 2H), 6.21 (d, *J* = 12.6 Hz, 1H), 4.0 (s, 3H), 1.64 (s, 6H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 144.9 (C), 142.3 (CH), 138.3 (C), 135.1 (C), 128.7 (CH), 128.6 (C), 128.5 (CH), 127.1 (CH), 127.0 (C), 125.9 (CH), 122.4 (CH), 115.9 (CH), 104.6 (CH), 101.2 (CH), 55.4 (OCH_3), 40.9 (C), 30.3 (CH_3); ATR-FTIR (neat): 2984, 1733, 1242 cm^{-1}; HRMS (ESI) m/z calculated for $C_{20}H_{22}NO$ $[M+H]^+$: 292.1696, found: 292.1685.



3.1h

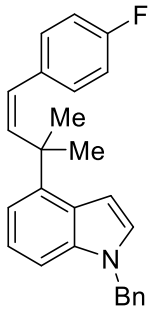
(Z)-4-(2-methyl-4-phenylbut-3-en-2-yl)-1H-indole 3.1h. The general Wittig-olefination procedure was followed using 187.0 mg of **S1** (1.0 mmol), 542.0 mg of triphenyl phosphonium bromide (1.25 mmol) and 0.8 mL of a 1.6 M solution of *t*-BuOK (1.28 mmol) in THF. Purification by flash column chromatography (100:0→90:10 hexanes: benzene) afforded *Z* stereoisomer **3.1h** (190.3 mg, 73% yield) as a white crystal. R_f = 0.32 (90:10 hexanes:benzene, visualized by 254 nm UV light and *p*-anisaldehyde stain). ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.01 (s, 1H), 7.21–7.12 (m, 2H), 7.08 (t, *J* = 7.7 Hz, 1H), 7.02–6.96 (m, 4H), 6.83–6.78 (m, 2H), 6.77–6.73 (m, 1H), 6.48 (d, *J* = 12.5 Hz, 1H), 6.16 (d, *J* = 12.6 Hz, 1H), 1.58 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 142.4 (C), 142.1 (CH), 138.1 (C), 136.5 (C), 128.7 (CH), 128.6 (CH), 127.1 (CH), 126.0 (CH), 125.8 (C), 122.6 (CH), 121.9 (CH), 116.0 (CH), 109.5 (CH), 104.3 (CH), 41.3 (C), 30.3 (CH_3); ATR-FTIR (neat): 3409,

3105, 2962, 1599, 1576 cm^{-1}; HRMS (ESI) m/z calculated for $C_{19}H_{20}N$ $[M+H]^+$: 262.1596, found: 262.1596.



3.1i

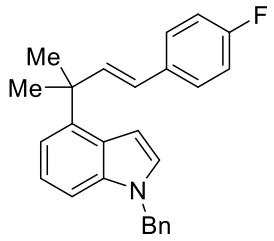
(Z)-1-benzyl-4-(2-methyl-4-(p-tolyl)but-3-en-2-yl)-1H-indole 3.1i. The general Wittig-olefination procedure was followed using 277.0 mg of **S7** (1.0 mmol), 559.2 mg of (4-methylbenzyl)triphenyl phosphonium bromide (1.25 mmol) and 0.8 mL of a 1.6 M solution of *t*-BuOK (1.28 mmol) in THF. Purification by flash column chromatography (100:0→95:5 hexanes: benzene) afforded *Z* stereoisomer **3.1i** (252.2 mg, 69% yield) as a light yellow oil. :15 hexanes:benzene) afforded *Z* stereoisomer **S3.14** (201.1 mg, 69% yield) as a light yellow oil. R_f = 0.50 (90:10 hexanes:benzene, visualized by 254 nm UV light and *p*-anisaldehyde stain). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.33–7.25 (m, 3H), 7.09–6.99 (m, 6H), 6.81–6.68 (m, 5H), 6.44 (d, *J* = 12.6 Hz, 1H), 6.12 (d, *J* = 12.6 Hz, 1H), 5.27 (s, 2H), 2.20 (s, 3H), 1.58 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 142.7 (C), 141.8 (CH), 137.9 (C), 137.0 (C), 135.5 (C), 135.2 (C), 128.8 (CH), 128.6 (2CH), 127.9 (CH), 127.6 (CH), 126.9 (CH), 126.8 (CH), 126.6 (C), 121.6 (CH), 115.8 (CH), 108.0 (CH), 103.4 (CH), 50.2 (CH_2), 41.3 (C), 30.4 (CH_3), 21.3 (CH_3); ATR-FTIR (neat): 2999, 2963, 2924, 2868, 1495 cm^{-1}; HRMS (ESI) m/z calculated for $C_{27}H_{28}N$ $[M+H]^+$: 366.2216, found: 366.2211.



***cis*-3.1j**

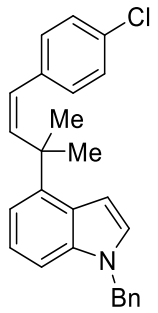
(Z)-1-benzyl-4-(4-(4-fluorophenyl)-2-methylbut-3-en-2-yl)-1H-indole *cis*-3.1j. The general Wittig-olefination procedure was followed using 277.0 mg of **S7** (1.0 mmol), 564.0 mg of (4-fluorobenzyl)triphenyl phosphonium bromide (1.25 mmol) and 0.8 mL of a 1.6 M solution of *t*-BuOK (1.28 mmol) in THF. Purification by flash column chromatography (100:0→95:5 hexanes:ethyl acetate) afforded *Z* stereoisomer ***cis*-3.1j** (214.3 mg, 58% yield) as a light yellow oil. R_f = 0.65 (95:5 hexanes:ethyl acetate visualized by 254 nm UV light and *p*-anisaldehyde stain). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.37–7.23 (m, 3H), 7.09–6.92

(m, 6H), 6.68–6.59 (m, 3H), 6.51 (t, J = 8.8 Hz, 2H), 6.38 (d, J = 12.4 Hz, 1H), 6.13 (d, J = 12.4 Hz, 1H), 5.24 (s, 2H), 1.60 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 161.1 (d, J = 244.3 Hz, C-F), 142.2 (CH), 141.6 (C), 137.8 (C), 136.8 (C), 133.6 (d, J = 3.3 Hz, C), 129.9 (CH), 129.8 (CH), 128.9 (CH), 127.7 (d, J = 1.5 Hz, CH), 126.8 (CH), 126.6 (C), 121.6 (CH), 116.0 (CH), 113.6 (CH), 113.4 (CH), 108.1 (CH), 103.4 (CH), 50.2 (CH_2), 41.1 (C), 30.7 (CH_3); ^{19}F NMR (376 MHz, $CDCl_3$): δ -117.0; ATR-FTIR (neat): 3090, 3071, 3035, 2963, 2925, 1959, 1814, 1602, 1506 cm^{-1}; HRMS (ESI) m/z calculated for $C_{26}H_{25}FN$ $[M+H]^+$: 370.1966, found: 370.1958.



***trans*-3.1j**

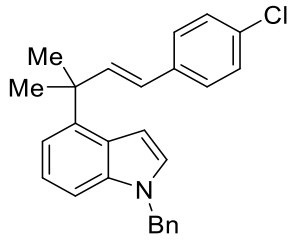
(E)-1-benzyl-4-(4-(4-fluorophenyl)-2-methylbut-3-en-2-yl)-1H-indole *trans*-3.1j. The general Wittig-olefination procedure was followed using 277.0 mg of **S7** (1.0 mmol), 564.0 mg of (4-fluorobenzyl)triphenyl phosphonium bromide (1.25 mmol) and 0.8 mL of a 1.6 M solution of *t*-BuOK (1.28 mmol) in THF. Purification by flash column chromatography (100:0→95:5 hexanes:ethyl acetate) afforded *E* stereoisomer ***trans*-3.1j** (66.5 mg, 18% yield) as colorless oil. R_f = 0.63 (95:5 hexanes:ethyl acetate visualized by 254 nm UV light and *p*-anisaldehyde stain). Selected spectral data for *E* isomer: ^{1}H NMR (400 MHz, $CDCl_3$): 7.36–7.13 (m, 9H), 7.06–6.96 (m, 4H), 6.69 (dd, J = 3.3, 0.9 Hz, 1H), 6.57 (d, J = 16.3 Hz, 1H), 6.47 (d, J = 16.3 Hz, 1H), 5.30 (s, 2H), 1.69 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 162.1 (d, J = 245.5 Hz, C-F), 140.9 (d, J = 2.2 Hz, CH), 137.6 (C), 137.1 (C), 134.4 (d, J = 3.3 Hz, C), 130.0 (d, J = 7.8 Hz, C), 128.9 (CH), 127.7 (CH), 127.2 (CH), 127.1 (CH), 126.8 (C), 125.2 (CH), 121.6 (CH), 116.3 (CH), 115.6 (CH), 115.4 (CH), 108.7 (CH), 103.1 (CH), 50.3 (CH_2), 41.6 (C), 28.7 (CH_3); ATR-FTIR (neat): 3090, 3071, 3035, 2963, 2925, 1959, 1814, 1602, 1506 cm^{-1}; HRMS (ESI) m/z calculated for $C_{26}H_{25}FN$ $[M+H]^+$: 370.1966, found: 370.1958.



***cis*-3.1k**

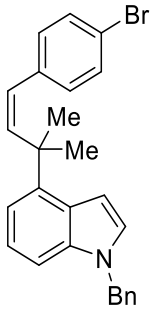
(Z)-1-benzyl-4-(4-(4-chlorophenyl)-2-methylbut-3-en-2-yl)-1H-indole *cis*-3.1k. The general Wittig-olefination procedure was followed using 277.0 mg of **S7** (1.0 mmol), 585.0

mg of (4-chlorobenzyl)triphenyl phosphonium bromide (1.25 mmol) and 0.8 mL of a 1.6 M solution of *t*-BuOK (1.28 mmol) in THF. Purification by flash column chromatography (100:0→85:15 hexanes:ethyl acetate) afforded *Z* stereoisomer ***cis*-3.1k** (270.2 mg, 70% yield) as a light yellow oil. R_f = 0.65 (95:5 hexanes:ethyl acetate visualized by 254 nm UV light and *p*-anisaldehyde stain). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.42–7.27 (m, 3H), 7.12–6.93 (m, 6H), 6.82 (d, *J* = 8.4 Hz, 2H), 6.67 (d, *J* = 3.2 Hz, 1H), 6.61 (d, *J* = 8.3 Hz, 2H), 6.38 (d, *J* = 12.4 Hz, 1H), 6.17 (d, *J* = 12.5 Hz, 1H), 5.26 (s, 2H), 1.62 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 142.7 (CH), 141.5 (C), 137.8 (C), 136.9 (C), 136.1 (C), 131.4 (C), 129.7 (CH), 128.9 (CH), 127.7 (CH), 127.5 (CH), 126.9 (CH), 126.8 (CH), 126.7 (CH), 126.5 (C), 121.6 (CH), 116.1 (CH), 108.1 (CH), 103.4 (CH), 50.1 (CH_2), 41.2 (C), 30.6 (CH_3); ATR-FTIR (neat): 3030, 2963, 2925, 2868, 1695, 1602, 1572, 1516 cm^{-1}; HRMS (ESI) m/z calculated for $C_{26}H_{25}ClN$ $[M+H]^+$: 386.1670, found: 386.1661.



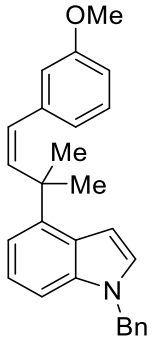
***trans*-3.1k**

(E)-1-benzyl-4-(4-(4-chlorophenyl)-2-methylbut-3-en-2-yl)-1H-indole *trans*-3.1k. The general Wittig-olefination procedure was followed using 277.0 mg of **S7** (1.0 mmol), 585.0 mg of (4-chlorobenzyl)triphenyl phosphonium bromide (1.25 mmol) and 0.8 mL of a 1.6 M solution of *t*-BuOK (1.28 mmol) in THF. Purification by flash column chromatography (100:0→85:15 hexanes:EtOAc) afforded *E* stereoisomer ***trans*-3.1k** (81.1 mg, 21% yield) as a light yellow oil. R_f = 0.64 (95:5 hexanes:ethyl acetate visualized by 254 nm UV light and *p*-anisaldehyde stain). Selected spectral data for *E* isomer: ^{1}H NMR (500 MHz, $CDCl_3$): 7.36–7.24 (m, 8H), 7.22–7.15 (m, 4H), 7.07 (d, *J* = 3.3 Hz, 1H), 6.70 (dd, *J* = 3.3, 0.9 Hz, 1H), 6.66 (d, *J* = 16.2 Hz, 1H), 6.49 (d, *J* = 16.2 Hz, 1H), 5.32 (s, 2H), 1.72 (s, 6H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 141.8 (CH), 141.0 (C), 137.6 (C), 137.1 (C), 136.7 (C), 132.5 (C), 128.9 (CH), 128.7 (CH), 127.8 (CH), 127.5 (CH), 127.3 (CH), 127.1 (CH), 126.9 (C), 125.2 (CH), 121.7 (CH), 116.3 (CH), 108.7 (CH), 103.1 (CH), 50.3 (CH_2), 41.6 (C), 28.6 (CH_3); ATR-FTIR (neat): 3030, 2963, 2925, 2868, 1695, 1602, 1572, 1516 cm^{-1}; HRMS (ESI) m/z calculated for $C_{26}H_{25}ClN$ $[M+H]^+$: 386.1670, found: 386.1661.



3.1l

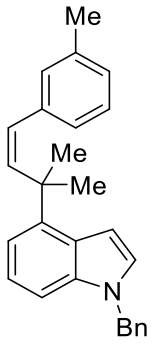
(Z)-1-benzyl-4-(4-(4-bromophenyl)-2-methylbut-3-en-2-yl)-1H-indole 3.1l. The general Wittig-olefination procedure was followed using 277.0 mg of **S7** (1.0 mmol), 640.0 mg of (4-bromobenzyl)triphenyl triphenyl phosphonium bromide (1.25 mmol) and 0.8 mL of a 1.6 M solution of *t*-BuOK (1.28 mmol) in THF. Purification by flash column chromatography (100:0→85:15 hexanes:EtOAc) afforded *Z* stereoisomer **3.1l** (284.0 mg, 66% yield) as light yellow oil. R_f = 0.64 (95:5 hexanes:ethyl acetate visualized by 254 nm UV light and *p*-anisaldehyde stain). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.36–7.24 (m, 3H), 7.07–6.98 (m, 5H), 6.96–6.91 (m, 3H), 6.62 (dd, *J* = 3.2, 0.8 Hz, 1H), 6.53–6.49 (m, 2H), 6.32 (d, *J* = 12.5 Hz, 1H), 6.14 (d, *J* = 12.5 Hz, 1H), 5.23 (s, 2H), 1.58 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 142.8 (CH), 141.5 (C), 137.8 (C), 136.9 (C), 136.6 (C), 130.0 (CH), 129.8 (CH), 128.9 (CH), 127.7 (CH), 127.5 (CH), 126.9 (CH), 126.7 (CH), 126.6 (C), 121.7 (CH), 119.7 (C), 116.1 (CH), 108.2 (CH), 103.4 (CH), 50.2 (CH_2), 41.2 (C), 30.6 (CH_3); ATR-FTIR (neat): 3090, 3035, 2961, 2924, 1481 cm^{-1}; HRMS (ESI) m/z calculated for $C_{26}H_{25}BrN$ $[M+H]^+$: 430.1165, found: 430.1160.



3.1m

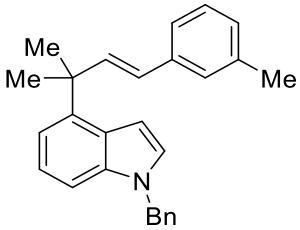
(Z)-1-benzyl-4-(4-(3-methoxyphenyl)-2-methylbut-3-en-2-yl)-1H-indole 3.1m. The general Wittig-olefination procedure was followed using 277.0 mg of **S7** (1.0 mmol), 579.0 mg of (3-methoxybenzyl)triphenyl phosphonium bromide (1.25 mmol) and 0.8 mL of a 1.6 M solution of *t*-BuOK (1.28 mmol) in THF. Purification by flash column chromatography (100:0→80:20 hexanes:EtOAc) afforded *Z* stereoisomer **3.1m** (202.2 mg, 53% yield) as a light yellow oil; R_f = 0.55 (95:5 hexanes:ethyl acetate visualized by 254 nm UV light and *p*-anisaldehyde stain). ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.35–7.25 (m, 4H), 7.13–7.05 (m, 5H), 6.91 (appr t, *J* = 7.9 Hz, 1H), 6.75 (dd, *J* = 3.3, 0.8 Hz, 1H), 6.56 (dd, *J* = 8.2, 2.6 Hz,

1H), 6.49–6.42 (m, 2H), 6.32 (s, 1H), 6.19 (d, J = 12.6 Hz, 1H), 5.29 (s, 2H), 3.46 (s, 3H), 1.61 (s, 6H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 158.6 (C), 142.6 (C), 142.3 (CH), 139.4 (C), 137.8 (C), 137.0 (C), 128.9 (CH), 128.7 (CH), 128.1 (CH), 127.7 (CH), 126.9 (CH), 126.8 (CH), 126.6 (C), 121.7 (CH), 121.4 (CH), 115.9 (CH), 113.4 (CH), 112.6 (CH), 108.1 (CH), 103.4 (CH), 55.0 (OCH_3), 50.2 (CH_2), 41.3 (C), 30.6 (CH_3); HRMS (ESI) m/z calculated for $C_{27}H_{28}NO$ $[M+H]^+$: 382.2165, found: 386.2158.



***cis*-3.1n**

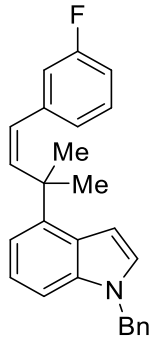
(Z)-1-benzyl-4-(2-methyl-4-(m-toly)but-3-en-2-yl)-1H-indole *cis*-3.1n. The general Wittig-olefination procedure was followed using 277.0 mg of **S7** (1.0 mmol), 559.0 mg of (3-methylbenzyl)triphenyl phosphonium bromide (1.25 mmol) and 0.8 mL of a 1.6 M solution of *t*-BuOK (1.28 mmol) in THF. Purification by flash column chromatography (100:0→95:5 hexanes:EtOAc) afforded *Z* stereoisomer ***cis*-3.1n** (241.2 mg, 66% yield) as a light yellow oil. R_f = 0.60 (95:5 hexanes:ethyl acetate visualized by 254 nm UV light and *p*-anisaldehyde stain). ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.38–7.29 (m, 3H), 7.13–7.05 (m, 6H), 6.93 (appr. t, J = 7.5 Hz, 1H), 6.85 (d, J = 7.6 Hz, 1H), 6.80 (d, J = 3.2 Hz, 1H), 6.69 (d, J = 7.6 Hz, 1H), 6.55 (appr. s, 1H), 6.51 (d, J = 12.6 Hz, 1H), 6.22 (d, J = 12.5 Hz, 1H), 5.31 (s, 2H), 2.12 (s, 3H), 1.66 (s, 6H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 142.7 (C), 142.0 (CH), 137.8 (2C), 136.9 (C), 136.4 (C), 129.5 (CH), 128.9 (CH), 128.8 (CH), 127.6 (CH), 126.9 (2CH), 126.7 (CH, C), 126.6 (CH), 125.7 (CH), 121.6 (CH), 115.8 (CH), 108.0 (CH), 103.5 (CH), 50.1 (CH_2), 41.2 (C), 30.5 (CH_3), 21.3 (CH_3); ATR-FTIR (neat): 3091, 3071, 3035, 1959, 1814, 1478 cm^{-1}; HRMS (ESI) m/z calculated for $C_{27}H_{28}N$ $[M+H]^+$: 366.2216, found: 366.2209.



***trans*-3.1n**

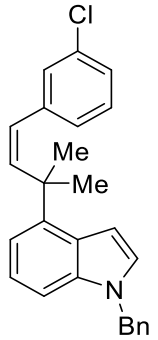
(E)-1-benzyl-4-(2-methyl-4-(m-toly)but-3-en-2-yl)-1H-indole *trans*-3.1n. The general Wittig-olefination procedure was followed using 277.0 mg of **S7** (1.0 mmol), 559.0 mg of (3-methylbenzyl)triphenyl phosphonium bromide (1.25 mmol) and 0.8 mL of a 1.6 M

solution of *t*-BuOK (1.28 mmol) in THF. Purification by flash column chromatography (100:0→90:10 hexanes:EtOAc) afforded *E* stereoisomer ***trans*-3.1n** (85.0 mg, 23% yield) as colorless oil. R_f = 0.58 (95:5 hexanes:ethyl acetate visualized by 254 nm UV light and *p*-anisaldehyde stain). Selected spectral data for *E* isomer: ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.37–7.14 (m, 11H), 7.07 (d, *J* = 3.3 Hz, 2H), 6.75 (d, *J* = 3.2 Hz, 1H), 6.67 (d, *J* = 16.3 Hz, 1H), 6.53 (d, *J* = 16.2 Hz, 1H), 5.33 (s, 2H), 2.37 (3H), 1.73 (s, 6H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 141.3 (C), 140.9 (CH), 138.2 (2C), 137.7 (C), 137.1 (C), 128.9 (CH), 128.6 (CH), 127.8 (CH), 127.7 (CH), 127.2 (CH), 127.1 (CH), 127.0 (CH, C), 126.3 (CH), 123.5 (CH), 121.6 (CH), 116.3 (CH), 108.6 (CH), 103.3 (CH), 50.3 (CH_2), 41.6 (C), 28.7 (CH_3), 21.6 (CH_3); ATR-FTIR (neat): 3091, 3071, 3035, 1959, 1814, 1478 cm^{-1}; HRMS (ESI) m/z calculated for $C_{27}H_{28}N$ $[M+H]^+$: 366.2216, found: 366.2209.



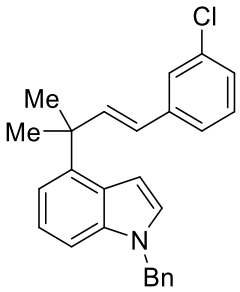
3.1o

(Z)-1-benzyl-4-(4-(3-fluorophenyl)-2-methylbut-3-en-2-yl)-1H-indole 3.1o. The general Wittig-olefination procedure was followed using 277.0 mg of **S7** (1.0 mmol), 564.0 mg of (3-fluorobenzyl)triphenyl phosphonium bromide (1.25 mmol) and 0.8 mL of a 1.6 M solution of *t*-BuOK (1.28 mmol) in THF. Purification by flash column chromatography (100:0→85:15 hexanes:EtOAc) afforded *Z* stereoisomer **3.1o** (243.9 mg, 66% yield) as colorless oil; R_f = 0.65 (95:5 hexanes:ethyl acetate visualized by 254 nm UV light and *p*-anisaldehyde stain). ^{1}H NMR (500 MHz, $CDCl_3$): (chloroform peak is not referenced) δ 7.36–7.26 (m, 3H), 7.09–6.97 (m, 6H), 6.83 (dd, *J* = 14.2, 7.9 Hz, 1H), 6.68 (d, *J* = 3.2 Hz, 1H), 6.62 (td, *J* = 8.5, 2.6 Hz, 1H), 6.51 (d, *J* = 7.5 Hz, 1H), 6.40 (appr t, *J* = 11.2 Hz, 2H), 6.19 (d, *J* = 12.5 Hz, 1H), 5.27 (s, 2H), 1.63 (s, 6H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 161.8 (d, *J* = 243.9 Hz, C-F), 143.0 (CH), 141.5 (C), 140.0 (d, *J* = 7.9 Hz, C), 137.8 (C), 136.9 (C), 128.8 (CH), 128.1 (CH), 128.1 (d, *J* = 8.4 Hz, CH), 127.6 (CH), 127.5 (d, *J* = 2.0 Hz, CH), 126.9 (CH), 126.8 (CH), 126.5 (C), 124.3 (d, *J* = 2.7 Hz, CH), 121.6 (CH), 116.0 (CH), 115.2 (d, *J* = 21.5 Hz, CH), 112.6 (d, *J* = 21.1 Hz, CH), 108.2 (CH), 103.4 (CH), 50.1 (CH_2), 41.2 (C), 30.6 (CH_3); ^{19}F NMR (470 MHz, $CDCl_3$): δ - 115.3; ATR-FTIR (neat): 3090, 3034, 2961, 2924, 2867, 1610, 1580, 1494 cm^{-1}; HRMS (ESI) m/z calculated for $C_{26}H_{25}FN$ $[M+H]^+$: 370.1966, found: 370.1960.



***cis*-3.1p**

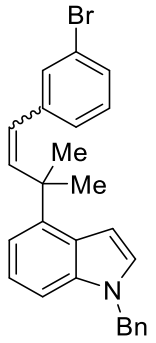
(Z)-1-benzyl-4-(4-(3-chlorophenyl)-2-methylbut-3-en-2-yl)-1H-indole *cis*-3.1p. The general Wittig-olefination procedure was followed using 277.0 mg of **S7** (1.0 mmol), 585.0 mg of (3-chlorobenzyl)triphenyl phosphonium bromide (1.25 mmol) and 0.8 mL of a 1.6 M solution of *t*-BuOK (1.28 mmol) in THF. Purification by flash column chromatography (100:0→85:15 hexanes:EtOAc) afforded *Z* stereoisomer ***cis*-3.1p** (208.4 mg, 54% yield) as a light yellow oil; R_f = 0.65 (95:5 hexanes:ethyl acetate visualized by 254 nm UV light and *p*-anisaldehyde stain). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.37–7.25 (m, 3H), 7.10–7.02 (m, 5H), 6.98 (t, *J* = 4.2 Hz, 1H), 6.89 – 6.86 (m, 1H), 6.76 (t, *J* = 7.8 Hz, 1H), 6.66 (d, *J* = 3.3 Hz, 1H), 6.61 (s, 1H), 6.56 (dd, *J* = 7.5, 1.2 Hz, 1H), 6.37 (d, *J* = 12.4 Hz, 1H), 6.19 (d, *J* = 12.4 Hz, 1H), 5.26 (s, 2H), 1.63 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): ^{13}C NMR (100 MHz, $CDCl_3$): δ 143.1 (CH), 141.3 (C), 139.3 (C), 137.8 (C), 136.9 (C), 132.5 (C), 128.8 (CH), 128.3 (CH), 127.8 (CH), 127.6 (CH), 127.3 (CH), 126.9 (CH), 126.7 (CH), 126.5 (C, CH), 125.8 (CH), 121.7 (CH), 116.1 (CH), 108.2 (CH), 103.4 (CH), 50.1 (CH_2), 41.2 (C), 30.6 (CH_3); ATR-FTIR (neat): 3091, 3071, 3035, 1959, 1814, 1478 cm^{-1}; HRMS (ESI) m/z calculated for $C_{26}H_{25}ClN$ $[M+H]^+$: 386.1670, found: 386.1667.



***trans*-3.1p**

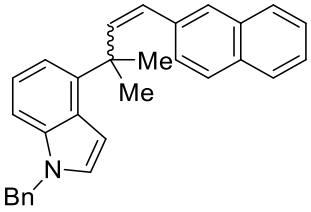
(E)-1-benzyl-4-(4-(3-chlorophenyl)-2-methylbut-3-en-2-yl)-1H-indole *trans*-3.1p. The general Wittig-olefination procedure was followed using 277.0 mg of **S7** (1.0 mmol), 585.0 mg of (3-chlorobenzyl)triphenyl phosphonium bromide (1.25 mmol) and 0.8 mL of a 1.6 M solution of *t*-BuOK (1.28 mmol) in THF. Purification by flash column chromatography (100:0→85:15 hexanes:EtOAc) afforded *E* stereoisomer ***trans*-3.1p** (103.2 mg, 25% yield) as a light yellow oil; R_f = 0.60 (95:5 hexanes:ethyl acetate visualized by 254 nm UV light and *p*-anisaldehyde stain).^{1}H NMR (500 MHz, $CDCl_3$): δ 7.38–7.11 (m, 12H), 7.05 (d, *J* = 3.2 Hz, 1H), 6.66–6.62 (m, 2H), 6.42 (d, *J* = 16.2 Hz, 1H), 5.30 (s, 2H), 1.67 (s, 6H); ^{13}C

NMR (125 MHz, $CDCl_3$): δ 142.6 (CH), 140.8 (C), 140.2 (C), 137.6 (C), 137.1(C), 134.6 (C), 129.8 (CH), 128.9 (CH), 128.5 (C), 127.8 (CH), 127.3 (CH), 127.1 (CH), 126.9 (CH), 126.2 (CH), 125.2 (CH), 124.6 (CH), 121.7 (CH), 116.3 (CH), 108.8 (CH), 103.1 (CH), 50.4 (CH_2), 41.7 (C), 26.8 (CH_3); ATR-FTIR (neat): 3091, 3071, 3035, 1959, 1814, 1478 cm^{-1}; HRMS (ESI) m/z calculated for $C_{26}H_{25}ClN$ $[M+H]^+$: 386.1670, found: 386.1667.



3.1q

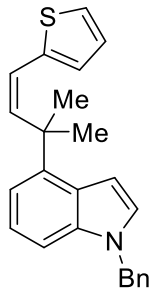
(Z)-1-benzyl-4-(4-(3-bromophenyl)-2-methylbut-3-en-2-yl)-1H-indole 3.1q. The general Wittig-olefination procedure was followed using 277.0 mg of **S7** (1.0 mmol), 640.0 mg of (3-bromobenzyl)triphenyl phosphonium bromide (1.25 mmol) and 0.8 mL of a 1.6 M solution of *t*-BuOK (1.28 mmol) in THF. Purification by flash column chromatography (100:0→95:5 hexanes:benzene) afforded inseparable *Z* and *E* stereoisomers **3.1q** (*Z*:*E* = 65:35, 342.3 mg, 79% yield) as colorless oil; R_f = 0.60 (95:5 hexanes:ethyl acetate visualized by 254 nm UV light and *p*-anisaldehyde stain). Selected spectral data for ***cis*-3.1q**: ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.35–7.24 (m, 3H), 7.08–6.92 (m, 7H), 6.74–6.55 (m, 4H), 6.34 (d, *J* = 12.4 Hz, 1H), 6.16 (d, *J* = 12.4 Hz, 1H), 5.25 (s, 2H), 1.60 (s, 6H); NMR (100 MHz, $CDCl_3$): δ 143.1 (CH), 141.2 (C), 139.6 (C), 137.8 (C), 136.8 (C), 131.2 (CH), 128.9 (CH), 128.7 (CH), 128.1 (CH), 127.6 (CH), 127.3 (CH), 127.0 (CH), 126.9 (CH), 126.7 (CH), 126.5 (C), 121.8 (CH), 120.8 (C), 116.1 (CH), 108.3 (CH), 103.4 (CH), 50.2 (CH_2), 41.2 (C), 30.6 (CH_3); ATR-FTIR (neat): 3062, 3032, 2963, 2923, 2868, 2370, 2363, 1591, 1558, 1515 cm^{-1}; HRMS (ESI) m/z calculated for $C_{26}H_{25}BrN$ $[M+H]^+$: 430.1165, found: 430.1161.



3.1r

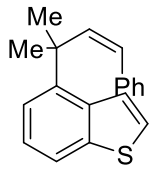
(Z)-1-benzyl-4-(2-methyl-4-(naphthalen-2-yl)but-3-en-2-yl)-1H-indole 3.1r. The general Wittig-olefination procedure was followed using 277.0 mg of **S7** (1.0 mmol), 604.0 mg of triphenyl phosphonium bromide (1.25 mmol) and 0.8 mL of a 1.6 M solution of *t*-BuOK (1.28 mmol) in THF. Purification by flash column chromatography (100:0→93:7 hexanes: benzene) afforded inseparable *Z* and *E* stereoisomers ***cis*-3.1r** and ***trans*-3.1r** (*Z*:*E*

= 78:22, 325.3 mg, 81% yield) as a light yellow oil; R_f = 0.65 (95:5 hexanes:ethyl acetate visualized by 254 nm UV light and *p*-anisaldehyde stain). Selected spectral data for ***cis*-1r** isomer: ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.66–7.63 (m, 1H), 7.43–7.30 (m, 4H), 7.25–7.22 (m, 3H), 7.06 (d, *J* = 3.2, 1H), 7.03–6.97 (m, 6H), 6.94 (dd, *J* = 8.4, 1.7 Hz, 1H), 6.75 (d, *J* = 3.2, 1H), 6.58 (d, *J* = 12.5 Hz, 1H), 6.27 (d, *J* = 12.5 Hz, 1H), 5.22 (s, 2H), 1.60 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 142.8 (C, CH), 137.8 (C), 137.0 (C), 135.4 (C), 132.7 (C), 131.9 (C), 128.8 (2CH), 128.1 (CH), 127.6 (CH), 127.5 (CH), 127.4 (CH), 127.2 (CH), 126.9 (2CH), 126.7 (C), 126.3 (CH), 125.5 (CH), 125.4 (CH), 121.8 (CH), 115.9 (CH), 108.1 (CH), 103.4 (CH), 50.2 (CH_2), 41.2 (C), 30.5 (CH_3); ATR-FTIR (neat): 3059, 3034, 2962, 2921, 2851, 1601, 1574, 1515 cm^{-1}; HRMS (ESI) m/z calculated for $C_{30}H_{28}N$ $[M+H]^+$: 402.2216, found: 402.2208.



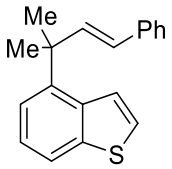
3.1s

(Z)-1-benzyl-4-(2-methyl-4-(thiophen-2-yl)but-3-en-2-yl)-1H-indole 3.1s. The general Wittig-olefination procedure was followed using 139.0 mg of **S7** (0.5 mmol), 276.0 mg of triphenyl(thiophen-2-ylmethyl)phosphonium bromide (0.63 mmol) and 0.4 mL of a 1.6 M solution of *t*-BuOK (1.28 mmol) in THF. Purification by flash column chromatography (100:0→99:1 hexanes:EtOAc) afforded *Z* stereoisomer **3.1s** (128.8 mg, 72% yield) as colorless oil; R_f = 0.70 (95:5 hexanes:ethyl acetate visualized by 254 nm UV light and *p*-anisaldehyde stain). ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.37–7.26 (m, 3H), 7.22–7.15 (m, 3H), 7.10–7.02 (m, 3H), 6.98 (dd, *J* = 5.1, 1.1 Hz, 1H), 6.75 (d, *J* = 3.3 Hz, 1H), 6.67 (dd, *J* = 5.1, 3.6 Hz, 1H), 6.50 (d, *J* = 12.6 Hz, 1H), 6.39 (d, *J* = 3.6 Hz, 1H), 6.19 (d, *J* = 12.6 Hz, 1H), 5.31 (s, 2H), 1.72 (s, 6H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 142.3 (CH), 141.6 (C), 139.7 (C), 137.9 (C), 137.0 (C), 128.8 (CH), 127.6 (2CH), 127.1 (C), 126.8 (2CH), 126.3 (CH), 125.1 (CH), 121.7 (CH), 121.1 (CH), 116.6 (CH), 108.3 (CH), 103.2 (CH), 50.1 (CH_2), 41.0 (C), 30.1 (CH_3); ATR-FTIR (neat): 3062, 3030, 3000, 2963, 2924, 2867, 1603, 1573 cm^{-1}; HRMS (ESI) m/z calculated for $C_{24}H_{24}NS$ $[M+H]^+$: 358.1624, found: 358.1618.



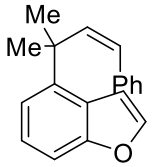
***cis*-3.4**

(Z)-4-(2-methyl-4-phenylbut-3-en-2-yl)benzo[b]thiophene *cis*-3.4. The general Wittig-olefination procedure was followed using 204.3 mg of **S8** (1.0 mmol), 604.0 mg of triphenyl phosphonium bromide (1.25 mmol) and 0.8 mL of a 1.6 M solution of *t*-BuOK (1.28 mmol) in THF. Purification by flash column chromatography (100:0→99:1 hexanes:benzene) afforded *Z* stereoisomer ***cis*-3.4** (153.1 mg, 55% yield) as a light brown oil. R_f = 0.70 (95:5 hexanes:benzene visualized by 254 nm UV light and *p*-anisaldehyde stain). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.64 (dd, *J* = 5.6, 0.8 Hz,), 7.59-7.53 (m, 2H), 7.40–7.30 (m, 2H), 7.20–7.11(m, 2H), 6.91-6.83 (m, 1H), 6.62-6.58 (m, 2H), 6.46 (d, *J* = 12.4 Hz, 1H), 6.12 (d, *J* = 12.4 Hz, 1H), 1.60 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 144.0 (C), 141.4 (CH), 140.6 (C), 137.1 (C), 128.7 (CH), 127.8 (CH), 127.6 (C), 126.6 (CH), 125.8 (CH), 125.1 (CH), 124.1 (CH), 123.8 (CH), 120.6 (CH), 120.5 (CH), 41.2 (C), 30.7 (CH_3); HRMS (ESI) m/z calculated for $C_{19}H_{18}S$ $[M]^+$: 278.1129, found: 278.1118.



***trans*-3.4**

(E)-4-(2-methyl-4-phenylbut-3-en-2-yl)benzo[b]thiophene *trans*-3.4. The general Wittig-olefination procedure was followed using 204.3 mg of **S8** (1.0 mmol), 604.0 mg of triphenyl phosphonium bromide (1.25 mmol) and 0.8 mL of a 1.6 M solution of *t*-BuOK (1.28 mmol) in THF. Purification by flash column chromatography (100:0→99:1 hexanes:benzene) afforded *E* stereoisomer ***trans*-3.4** (43.7 mg, 16 % yield) as colorless oil; R_f = 0.69 (95:5 hexanes:benzene visualized by 254 nm UV light and *p*-anisaldehyde stain). ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.83 (d, *J* = 7.9 Hz, 1H), 7.66–7.64 (m, 1H), 7.43–7.42 (m, 1H), 7.37–7.29 (m, 5H), 7.23–7.12 (m, 1H), 6.92–9.84 (m, 1H), 6.59 (d, *J* = 16.3 Hz, 1H), 6.44 (d, *J* = 16.3 Hz, 1H), 1.68 (s, 6H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 143.5 (C), 140.5 (CH), 137.7 (C), 128.5 (CH), 127.8 (C), 127.0 (2CH), 126.6 (C), 126.1 (CH), 124.9 (CH), 124.8 (CH), 124.0 (CH), 121.1 (CH), 121.0 (CH), 41.7 (C), 29.1 (CH_3); HRMS (ESI) m/z calculated for $C_{19}H_{18}S$ $[M]^+$: 278.1129, found: 278.1118.

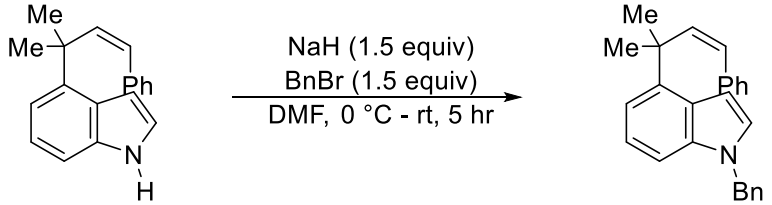


***cis*-3.7**

4-(2-methyl-4-phenylbut-3-en-2-yl)benzofuran *cis*-3.7. The general Wittig-olefination procedure was followed using 188.2 mg of **S9** (1.0 mmol), 604.0 mg of triphenyl phosphonium bromide (1.25 mmol) and 0.8 mL of a 1.6 M solution of *t*-BuOK (1.28 mmol) in THF. Purification by flash column chromatography (100:0→95:5 hexanes: EtOAc) afforded *Z* stereoisomer ***cis*-3.7** (160.1 mg, 61% yield) as a light yellow oil; R_f = 0.60 (95:5 hexanes:benzene visualized by 254 nm UV light and *p*-anisaldehyde stain). ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.54 (d, *J* = 2.2 Hz, 1H), 7.24 (d, *J* = 7.9 Hz, 1H), 7.14–7.08 (m, 2H), 6.96–6.92 (m, 4H), 6.73–6.72 (m, 2H), 6.49 (d, *J* = 12.5 Hz, 1H), 6.08 (d, *J* = 12.5 Hz, 1H), 1.56 (s, 6H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 155.4 (C), 143.4 (CH), 143.0 (C), 141.3 (CH), 137.5 (C), 129.3 (CH), 128.4 (CH), 127.1 (CH), 126.1 (CH), 125.5 (C), 124.0 (CH), 119.0 (CH), 109.5 (CH), 108.0 (CH), 41.1 (C), 30.6 (CH_3); HRMS (LIFDI) m/z calculated for $C_{19}H_{18}O$ $[M]^+$: 262.1358, found: 262.1368.

Scheme 17. Protection of Alkenyl Indole Substrates

A. General Indole Protection Procedure

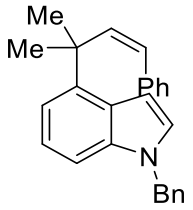


3.1h **3.1a**

To a solution of 523.0 mg of *cis*-alkene **3.1h** (2.00 mmol) in DMF (10.0 mL, 0.2 M), 120 mg of 60 wt.% NaH (3.00 mmol, 3.00 equiv) was added in an ice bath through four portions. The slurry was allowed to stir at room temperature for 30 minutes before it was cooled to 0 °C again and 514 mg of BnBr (1.50 equiv, 3.00 mmol) was diluted with DMF (1.0 mL) prior to being added to the deprotonated indole solution through syringe. The reaction mixture was then allowed to stir at room temperature for 5 hours. After the complete consumption of the starting material indicated by TLC, the reaction was quenched by addition of saturated $NaHCO_3$ solution (~10.0 mL) at 0 °C. The product was extracted with EtOAc (10 mLx3) and combined organic layers were washed with brine and dried over anhydrous sodium sulfate before it was concentrated under reduced pressure. The crude product was then purified through flash column chromatography.

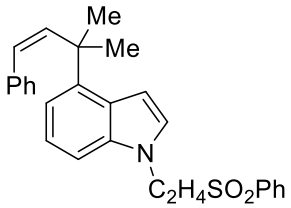
Acyl protection for the synthesis of **3.1g** is described individually below.

B. Synthesis and Characterization of Protected Alkenyl Indoles



3.1a

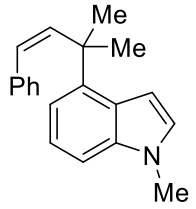
(Z)-1-benzyl-4-(2-methyl-4-phenylbut-3-en-2-yl)-1H-indole 3.1a. The general indole protection procedure was followed using 523.0 mg of **3.1h** (2.0 mmol), 120.0 mg of 60 wt.% NaH (3.0 mmol) and 514.0 mg of benzyl bromide (3.0 mmol in 1.0 mL DMF) in 10.0 mL DMF. Purification by flash column chromatography (100:0→98:2 hexanes: EtOAc) afforded benzylated indole **3.1a** (665.2 mg, 91% yield) as colorless oil. R_f = 0.60 (95:5 hexanes:benzene visualized by 254 nm UV light and *p*-anisaldehyde stain). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.34–7.24 (m, 3H), 7.08–6.90 (m, 9H), 6.77 (dd, *J* = 7.1, 1.2 Hz, 2H), 6.72 (d, *J* = 3.2 Hz, 1H), 6.47 (d, *J* = 12.5 Hz, 1H), 6.15 (d, *J* = 12.5 Hz, 1H), 5.27 (s, 2H), 1.59 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 142.2 (C), 142.0 (CH), 138.0 (C), 137.9 (C), 136.9 (C), 128.8 (CH), 128.7 (CH), 128.6 (CH), 127.6 (CH), 127.0 (CH), 126.9 (CH), 126.7 (CH), 126.6 (C), 125.9 (CH), 121.6 (CH), 115.9 (CH), 108.1 (CH), 103.5 (CH), 50.2 (CH_2), 41.3 (C), 30.5 (CH_3); ATR-FTIR (neat): 3088, 2996, 2963, 2924, 2868, 1601, 1573. 1516, 1494 cm^{-1}; HRMS (ESI) m/z calculated for $C_{26}H_{26}N[M+H]^+$: 356.2060, found: 356.2056.



3.1b

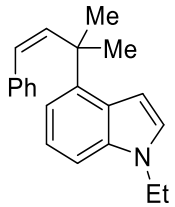
(Z)-4-(2-methyl-4-phenylbut-3-en-2-yl)-1-(2-(phenylsulfonyl)ethyl)-1H-indole 3.1b. The general indole protection procedure was followed using 261.4 mg of **1h** (1.0 mmol), 60.0 mg of 60 wt.% NaH (1.5 mmol) and 307.1 mg of $PhSO_2C_2H_4Cl$ (1.5 mmol in 0.5 mL DMF) in 5.0 mL DMF. Purification by flash column chromatography (100:0:0→60:30:10 hexanes: DCM:EtOAc) afforded protected indole **3.1b** (227.7 mg, 51% yield) as light brown oil. R_f = 0.65 (60:30:10 hexanes: DCM: EtOAc visualized by 254 nm UV light and *p*-anisaldehyde stain). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.91-7.88 (m, 2H), 7.66–7.52 (m, 3H), 7.09–6.89 (m, 7H), 6.74–6.72 (m, 2H), 6.61 (dd, *J* = 3.3, 0.8 Hz, 1H), 6.43 (d, *J* = 12.5 Hz, 1H), 6.08 (d, *J* = 12.6 Hz, 1H), 4.51 (t, *J* = 7.5 Hz, 2H), 3.45 (t, *J* = 7.5 Hz, 2H), 1.55 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 142.5 (CH), 141.7 (C), 141.5 (CH), 138.9

(C), 137.7 (C), 135.8 (C), 134.0 (C), 129.6 (CH), 129.3 (CH), 128.6 (CH), 128.3 (CH), 127.6 (CH), 126.7 (CH), 125.7 (CH), 122.0 (CH), 116.3 (CH), 107.0 (CH), 104.1 (CH), 55.6 (CH_2), 41.2 (CH_2), 39.9 (C), 30.3 (CH_3); HRMS (ESI) m/z calculated for $C_{27}H_{27}NNaO_2S$ $[M+Na]^+$: 452.1660, found 452.1650.



3.1c

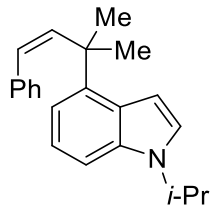
(Z)-1-methyl-4-(2-methyl-4-phenylbut-3-en-2-yl)-1H-indole 3.1c. The general indole protection procedure was followed using 261.4 mg of **3.1h** (1.0 mmol), 60.0 mg of 60 wt.% NaH (1.5 mmol) and 234.0 mg of iodoethane (1.5 mmol in 0.5 mL DMF) in 5.0 mL DMF. Purification by flash column chromatography (100:0→98:2 hexanes: EtOAc) afforded N-Me indole **3.1c** (245.1 mg, 89% yield) as light brown oil. R_f = 0.58 (98:2 hexanes:benzene visualized by 254 nm UV light and *p*-anisaldehyde stain). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.39 (appr. s, 1H), 7.18–7.11 (m, 2H), 7.03–7.00 (m, 4H), 6.86–6.82 (m, 2H), 6.69 (d, J = 3.2 Hz, 1H), 6.49 (d, J = 12.6 Hz, 1H), 6.17 (d, J = 12.6 Hz, 1H), 3.76 (s, 3H), 1.57 (s, 6H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 142.7 (C), 142.2 (CH), 138.2 (C), 137.4 (C), 128.7 (CH), 128.6 (CH), 127.4 (CH), 127.2 (CH), 126.3 (C), 126.0 (CH), 121.5 (CH), 115.5 (CH), 107.7 (CH), 102.6 (CH), 41.4 (CH_3), 33.0 (C), 30.3 (CH_3); ATR-FTIR (neat): 3057, 2926, 1600, 1573, 1516 cm^{-1}; HRMS (ESI) m/z calculated for $C_{20}H_{21}NNa$ $[M+Na]^+$: 298.1572, found: 298.1576.



3.1d

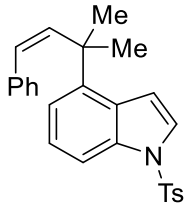
(Z)-1-ethyl-4-(2-methyl-4-phenylbut-3-en-2-yl)-1H-indole 3.1d. The general indole protection procedure was followed using 261.4 mg of **3.1h** (1.0 mmol), 60.0 mg of 60 wt.% NaH (1.5 mmol) and 234.0 mg of iodoethane (1.5 mmol in 0.5 mL DMF) in 5.0 mL DMF. Purification by flash column chromatography (100:0→98:2 hexanes: EtOAc) afforded N-Et indole **3.1d** (275.0 mg, 95% yield) as light brown oil. R_f = 0.63 (98:2 hexanes:benzene visualized by 254 nm UV light and *p*-anisaldehyde stain). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.27–7.09 (m, 7H), 6.96–6.93 (m, 2H), 6.80 (d, *J* = 3.1 Hz, 1H), 6.61 (d, *J* = 12.6 Hz, 1H), 6.28 (d, *J* = 12.5 Hz, 1H), 4.20 (q, *J* = 7.3 Hz, 2H), 1.71 (s, 6H), 1.52 (t, *J* = 7.3 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): ^{13}C NMR (100 MHz, $CDCl_3$): δ 142.4 (C), 142.1 (CH), 138.1 (C), 136.3 (C), 128.6 (2CH), 127.0 (CH), 126.5 (C), 125.9 (CH), 125.5 (CH), 121.3 (CH), 115.5 (CH), 107.7 (CH), 102.7 (CH), 41.3 (C), 41.0 (CH_2), 30.3 (CH_3), 15.6 (CH_3);

ATR-FTIR (neat): 3057, 3034, 2976, 2931, 1600, 1573, 1515 cm^{-1}; HRMS (ESI) m/z calculated for $C_{21}H_{23}NNa$ $[M+Na]^+$: 312.1728, found: 312.1720.



3.1e

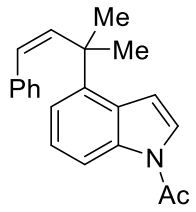
(Z)-1-isopropyl-4-(2-methyl-4-phenylbut-3-en-2-yl)-1H-indole 3.1e. General indole protection procedure was followed using 261.4 mg of **3.1h** (1.0 mmol), 60.0 mg of 60 wt.% NaH (1.5 mmol) and 255.0 mg of isopropyl iodide (1.5 mmol in 0.5 mL DMF) in 5 mL DMF. Purification by flash column chromatography (100:0→98:2 hexanes: EtOAc) afforded N-*i*Pr indole **3.1e** (279.2 mg, 92% yield) as colorless oil. R_f = 0.65 (98:2 hexanes:benzene visualized by 254 nm UV light and *p*-anisaldehyde stain). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.28–7.25 (m, 2H), 7.20 (t, *J* = 7.7 Hz, 1H), 7.13–7.08 (m, 4H), 6.95–6.92 (m, 2H), 6.82 (d, *J* = 3.3 Hz, 1H), 6.60 (d, *J* = 12.5 Hz, 1H), 6.27 (d, *J* = 12.5 Hz, 1H), 4.71 (sept, *J* = 6.7 Hz, 1H), 1.72 (s, 6H), 1.59 (d, *J* = 6.7 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 142.2 (C), 142.1 (CH), 138.1 (C), 136.1 (C), 128.5 (2CH), 126.9 (CH), 126.5 (C), 125.8 (CH), 121.9 (CH), 121.1 (CH), 115.5 (CH), 107.8 (CH), 102.9 (CH), 46.9 (CH), 41.4 (C), 30.3 (CH_3), 22.9 (CH_3); ATR-FTIR (neat): 3056, 3022, 2972, 2929, 2871, 1599, 1573, 1514 cm^{-1}; HRMS (ESI) m/z calculated for $C_{22}H_{25}NNa$ $[M+Na]^+$: 326.1885, found: 326.1886.



3.1f

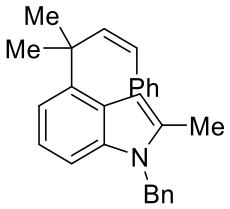
(Z)-4-(2-methyl-4-phenylbut-3-en-2-yl)-1-tosyl-1H-indole 3.1f. General indole protection procedure was followed using 261.4 mg of **3.1h** (1.0 mmol), 60.0 mg of 60 wt.% NaH (1.5 mmol) and 286.0 mg of TsCl (1.5 mmol in 0.5 mL DMF) in 5.0 mL DMF. Purification by flash column chromatography (100:0→95:5 hexanes: EtOAc) afforded N–Ts indole **3.1f** (320.1 mg, 77% yield) as brown oil. R_f = 0.52 (95:5 hexanes:ethyl acetate visualized by 254 nm UV light and *p*-anisaldehyde stain). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.76–7.70 (m, 3H), 7.51 (d, *J* = 3.8 Hz, 1H), 7.24 (d, *J* = 8.0 Hz, 2H), 7.09 (t, *J* = 7.9 Hz, 1H), 7.01 (dd, *J* = 7.6, 1.0 Hz, 1H), 6.86 (dd, *J* = 3.8, 0.9 Hz, 1H), 6.80-6.76 (m, 1H), 6.68 (t, *J* = 7.6 Hz, 2H), 6.50-6.48 (m, 2H), 6.42 (d, *J* = 12.5 Hz, 1H), 6.04 (d, *J* = 12.4 Hz, 1H), 2.36 (s, 3H), 1.51 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 144.8 (C), 142.5 (C), 141.4 (CH), 137.2 (C), 135.7 (C), 135.2 (C), 129.9 (CH), 129.3 (CH), 128.8 (C), 128.0 (CH), 127.0 (CH), 126.7 (CH), 125.9 (CH), 124.6 (CH), 124.3 (CH), 119.6 (CH), 111.5 (CH),

110.3 (CH), 40.9 (C), 30.7 (CH_3), 21.7 (CH_3); HRMS (ESI) m/z calculated for $C_{26}H_{25}NNaO_2S$: 438.1504, found: 438.1521.



3.1g

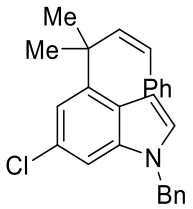
(Z)-1-(4-(2-methyl-4-phenylbut-3-en-2-yl)-1H-indol-1-yl)ethan-1-one 3.1g. To a solution of **3.1h** (261.4 mg, 1 mmol) in acetic anhydride and pyridine (acetic anhydride:pyridine = 50:50, total = 10.0 mL, 0.2M) was added a spatula tip of DMAP. The reaction mixture was allowed to stir vigorously at room temperature until a new spot appeared on TLC and full consumption of starting material was achieved. The reaction was then quenched by slow addition of MeOH (~5.0 mL) in an ice bath and the resulted methyl ester was evaporated under reduced pressure. The residual reaction slurry was then diluted with EtOAc (10.0 mL) and washed with copper sulfate solution (10.0 mL) multiple times until the aqueous layer stopped changing color. The combined organic layers were then washed with brine and dried over anhydrous sodium sulfate before concentrated under reduced pressure. The crude product was then flushed through silica gel packed column (100:0→95:5 hexanes: EtOAc) to obtain pure acylated indole alkene **3.1g** (233.6 mg, 77% yield). ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.32 (d, *J* = 8.3 Hz, 1H), 7.35 (d, *J* = 3.7 Hz, 1H), 7.28–7.25 (m, 1H), 7.21–7.19 (m, 1H), 7.01–6.96 (m, 3H), 6.92–6.91 (m, 1H), 6.77–6.75 (m, 2H), 6.53 (d, *J* = 12.5 Hz, 1H), 6.16 (d, *J* = 12.6 Hz, 1H), 2.61 (s, 3H), 1.62 (s, 6H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 168.6 (C=O), 142.1 (C), 141.6 (CH), 137.3 (C), 136.1 (C), 129.1 (CH), 128.4 (C), 128.3 (CH), 127.0 (CH), 126.1 (CH), 125.0 (CH), 123.7 (CH), 119.9 (CH), 114.7 (CH), 110.4 (CH), 40.9 (C), 30.6 (CH_3), 24.1 (CH_3); HRMS (ESI) m/z calculated for $C_{21}H_{22}NNaO$ $[M+Na]^+$: 326.1521, found: 326.1514.



3.1t

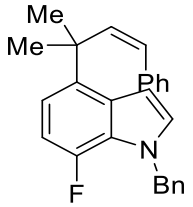
(Z)-1-benzyl-2-methyl-4-(2-methyl-4-phenylbut-3-en-2-yl)-1H-indole 3.1t. The general indole protection procedure was followed using 551.0 mg of **S3.10** (2.0 mmol), 120.0 mg of 60 wt.% NaH (3.0 mmol) and 514.0 mg of benzyl bromide (3.0 mmol in 1.0 mL DMF) in 10.0 mL DMF. Purification by flash column chromatography (100:0→98:2 hexanes: EtOAc) afforded benzylated indole **3.1t** (504.4 mg, 69% yield) as colorless oil. R_f = 0.70 (98:2 hexanes:EtOAc visualized by 254 nm UV light and *p*-anisaldehyde stain). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.30–7.20 (m, 3 H), 7.03–6.90 (m, 8H), 6.85–6.78 (m, 2H),

6.49 (d, *J* = 12.4 Hz, 2H), 6.16 (d, *J* = 12.5 Hz, 1H), 5.26 (s, 2H), 2.37 (s, 3H), 1.58 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 142.2 (CH), 141.2 (C), 138.2 (C), 138.1 (C), 137.8 (C), 135.0 (CH), 128.8 (CH), 128.7 (CH), 128.6 (CH), 127.3 (CH), 127.0 (CH), 126.1 (CH), 126.0 (C), 125.9 (CH), 120.7 (CH), 115.9 (CH), 107.6 (CH), 102.3 (CH), 46.6 (CH_2), 41.2 (C), 30.4 (CH_3), 13.0 (CH_3); ATR-FTIR (neat): 3061, 3030, 2993, 2962, 2925, 2866, 1552, 1494 cm^{-1}; HRMS (ESI) m/z calculated for $C_{27}H_{28}N$ $[M+H]^+$: 366.2216, found: 366.2213.



3.1u

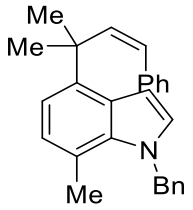
(Z)-1-benzyl-6-chloro-4-(2-methyl-4-phenylbut-3-en-2-yl)-1H-indole 3.1u. The general indole protection procedure was followed using 592.0 mg of **S3.13** (2.0 mmol), 120.0 mg of 60 wt.% NaH (3.0 mmol) and 514.0 mg of benzyl bromide (3.0 mmol in 1.0 mL DMF) in 10.0 mL DMF. Purification by flash column chromatography (100:0→90:10 hexanes:EtOAc) afforded benzylated indole **3.1u** (673.1 mg, 85% yield) as a colorless oil. R_f = 0.70 (90:10 hexanes:EtOAc visualized by 254 nm UV light and *p*-anisaldehyde stain). Selected spectral data for Z isomer: ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.36–7.25 (m, 3H), 7.04–6.86 (m, 8H), 6.70 (d, *J* = 6.8 Hz, 2H), 6.66 (d, *J* = 3.3 Hz, 1H), 6.47 (d, *J* = 12.4 Hz, 1H), 6.08 (d, *J* = 12.4 Hz, 1H), 5.18 (s, 2H), 1.58 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 143.2 (C), 141.2 (CH), 137.5 (C), 137.3 (C), 137.1 (C), 129.1 (CH), 128.9 (CH), 128.3 (CH), 127.8 (CH), 127.6 (C), 127.4 (CH), 126.9 (CH), 126.8 (CH), 126.0 (CH), 125.3 (C), 117.3 (CH), 107.8 (CH), 103.8 (CH), 50.2 (CH_2), 41.2 (C), 30.5 (CH_3); ATR-FTIR (neat): 3059, 2985, 1732, cm^{-1}; HRMS (ESI) m/z calculated for $C_{26}H_{25}ClN$ $[M+H]^+$: 386.1670, found: 386.166.



3.1v

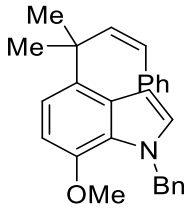
(Z)-1-benzyl-7-fluoro-4-(2-methyl-4-phenylbut-3-en-2-yl)-1H-indole 3.1v. The general indole protection procedure was followed using 559.0 mg of **S3.12** (2.0 mmol), 120.0 mg of 60 wt.% NaH (3.0 mmol) and 514.0 mg of benzyl bromide (3.0 mmol in 1.0 mL DMF) in 10.0 mL DMF. Purification by flash column chromatography (100:0→95:5 hexanes: EtOAc) afforded benzylated indole **3.1v** (541.8 mg, 71% yield) as colorless oil. R_f = 0.68 (95:5 hexanes:EtOAc visualized by 254 nm UV light and *p*-anisaldehyde stain). ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.42–7.31 (m, 3H), 7.14 (appr. d, *J* = 6.9 Hz, 2H), 7.08–6.94 (m, 4H), 6.88 (m, 1H), 6.82–6.71 (m, 4H), 6.54 (d, *J* = 12.5 Hz, 1H), 6.18 (d, *J* = 12.5 Hz, 1H),

5.48 (s, 2H), 1.66 (s, 6H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 149.2 (d, *J* = 241.9 Hz, C-F), 141.7 (CH), 138.6 (C), 137.7 (C), 137.6 (d, *J* = 3.7 Hz, C), 130.5 (d, *J* = 5.1 Hz, C), 128.9 (CH), 128.7 (CH), 128.3 (CH), 128.2 (CH), 127.6 (CH), 126.9 (d, *J* = 1.7 Hz, CH), 125.9 (CH), 124.3 (d, *J* = 9.7 Hz, C), 116.1 (d, *J* = 6.5 Hz, CH), 106.7 (CH), 106.6 (CH), 104.6 (d, *J* = 1.4 Hz, CH), 52.2 (d, *J* = 6.2 Hz, CH_2), 40.8 (C), 30.7 (CH_3); ^{19}F NMR (470 MHz, $CDCl_3$): δ -139.0; ATR-FTIR (neat): 3055, 3027, 2963, 2926, 2870, 1578, 1501 cm^{-1}; HRMS (ESI) m/z calculated for $C_{26}H_{25}FN$ $[M+H]^+$: 370.1966, found: 370.1960.



3.1w

(Z)-1-benzyl-7-methyl-4-(2-methyl-4-phenylbut-3-en-2-yl)-1H-indole 3.1w. The general indole protection procedure was followed using 551.0 mg of **S3.11** (2.0 mmol), 120.0 mg of 60 wt.% NaH (3.0 mmol) and 514.0 mg of benzyl bromide (3.0 mmol in 1.0 mL DMF) in 10.0 mL DMF. Purification by flash column chromatography (100:0→98:2 hexanes: EtOAc) afforded benzylated indole **3.1w** (519.0 mg, 71% yield) as colorless oil. R_f = 0.70 (98:2 hexanes:EtOAc visualized by 254 nm UV light and *p*-anisaldehyde stain). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.40–7.31 (m, 3H), 7.11–7.06 (m, 4H), 7.01–6.95 (m, 5H), 6.86 (m, 2H), 6.59 (d, *J* = 12.5 Hz, 1H), 6.26 (d, *J* = 12.5 Hz, 1H), 5.60 (s, 2H), 2.54 (s, 3H), 1.70 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 142.2 (CH), 140.2 (C), 140.0 (C), 138.1 (C), 135.5 (C), 128.9 (CH), 128.7 (2CH), 128.5 (CH), 127.7 (C), 127.3 (CH), 127.0 (CH), 125.8 (CH), 125.5 (CH), 124.5 (CH), 119.1 (C), 116.1 (CH), 103.7 (CH), 52.2 (CH_2), 41.0 (C), 30.5 (CH_3), 19.5 (CH_3); ATR-FTIR (neat): 2963, 1600, 1576, 1528, 1497 cm^{-1}; HRMS (ESI) m/z calculated for $C_{27}H_{28}N$ $[M+H]^+$: 366.2216, found: 366.2209.

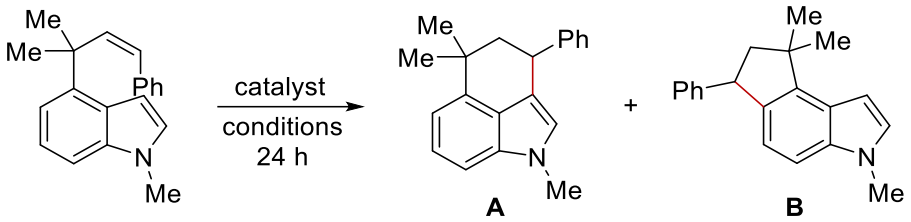


3.1x

(Z)-1-benzyl-7-methoxy-4-(2-methyl-4-phenylbut-3-en-2-yl)-1H-indole 3.1x. The general indole protection procedure was followed using 582.8 mg of **S3.14** (2.0 mmol), 120.0 mg of 60 wt.% NaH (3.0 mmol) and 514.0 mg of benzyl bromide (3.0 mmol in 1.0 mL DMF) in 10.0 mL DMF. Purification by flash column chromatography (100:0→98:2 hexanes: EtOAc) afforded benzylated indole **3.1x** (541.8 mg, 71% yield) as colorless oil. R_f = 0.55 (98:2 hexanes:EtOAc visualized by 254 nm UV light and *p*-anisaldehyde stain). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.40–7.25 (m, 3H), 7.11 (d, *J* = 6.7 Hz, 2H), 7.06–7.0 (m, 4H), 6.92–6.86 (m, 3H), 6.74 (d, *J* = 3.2 Hz, 1H), 6.52 (m, 2H), 6.18 (d, *J* = 12.5, 1H),

5.64 (s, 2H), 3.81 (s, 3H), 1.62 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 146.4 (C), 142.3 (CH), 140.0 (C), 138.2 (C), 134.8 (C), 128.8 (C), 128.6 (CH), 128.5 (2CH), 127.9 (C), 127.8 (CH), 127.1 (CH), 127.0 (CH), 126.8 (CH), 125.8 (CH), 115.9 (CH), 103.8 (CH), 102.4 (CH), 55.5 (OCH_3), 52.5 (CH_2), 40.8 (C), 30.5 (CH_3); ATR-FTIR (neat): 2960, 1577, 1500 cm^{-1}; HRMS (ESI) m/z calculated for $C_{27}H_{28}NO$ $[M+H]^+$: 382.2165, found: 382.2158.

Table 8. Hydroarylation Optimization[a]

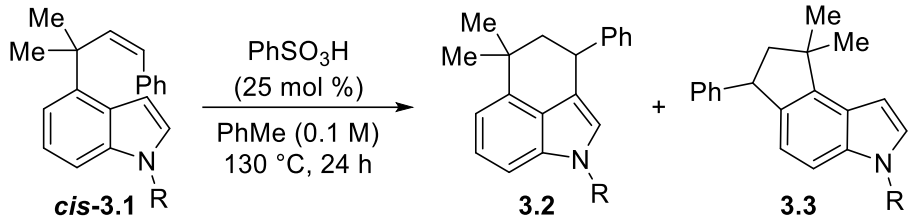


entry	catalyst (mol %)	solvent (M)	temp. (°C)	conv (%)	yield (%, **A** + **B**)	rr (**A** : **B**)
1	$Ph_3CB(C_6F_5)_4$ (5)	C_6H_6 (0.5)	75	<5	<5	n.d.
2	$Ph_3CB(C_6F_5)_4$ (5)	C_6H_6 (0.5)	130	15	<5	n.d.
3	$Ph_3CB(C_6F_5)_4$ (50)	C_6H_6 (0.5)	130	>95	<5	n.d.
4	TfOH (10)	C_6H_6 (0.5)	75	<5	<5	n.d.
5	TfOH (10)	C_6H_6 (0.5)	100	85	52	80:20
6	TfOH (25)	C_6H_6 (0.5)	100	90	47	80:20
7	*p*-TsOH•H_2O (25)	C_6H_6 (0.5)	100	15	<10	n.d.
8	*p*-TsOH•H_2O (25)	C_6H_6 (0.5)	130	75	35	85:15
9	*p*-TsOH•H_2O (25)	PhMe (0.5)	130	78	41	85:15
10	*p*-TsOH•H_2O (25)	PhMe (0.1)	130	67	35	85:15
11	*p*-TsOH (25)	PhMe (0.1)	130	>95	80	83:17
12[b]	$PhSO_3H$ (25)	PhMe (0.1)	130	83	63	85:15
13	$PhSO_3H$ (15)	PhMe (0.1)	130	69	55	81:19
14	$PhSO_3H$ (20)	PhMe (0.1)	130	92	72	83:17
15	$PhSO_3H$ (25)	PhMe (0.1)	130	>95	81	84:16
16[c]	$PhSO_3H$ (10)	PhMe (0.1)	130	75	64	82:18
17	None	PhMe (0.1)	130	<5	<5	n.d.
18	$PhSO_3H$ (25)	PhMe (0.05)	130	35	20	81:19
19	$PhSO_3H$ (50)	$PhCF_3$ (0.1)	130	>95	78	81:19
20	TMSOTf (25)	PhMe (0.1)	130	>95	68	82:18
21	MsOH (25)	PhMe (0.1)	130	100	40	80:20
22	H_2SO_4 (85 wt % aq) (25)	PhMe (0.1)	130	88	72	85:15
23	CSA (25)	PhMe (0.1)	130	<10	<5	n.d.
24	CSA(50)	PhMe (0.1)	130	<10	<5	n.d.

[a]Reactions were conducted on 0.1 mmol scale in a capped vial and assessed by crude 1H NMR analysis, whereby % yield was determined using 1,3,5-trimethoxybenzene as an internal standard. [b]Reaction ran for 12 hours. [c]Reaction ran for 40 hours.

Scheme 18. Synthesis of 1,3,4,5-Tetrahydrobenz[*cd*]indoles and Analogs *via* Hydroarylation

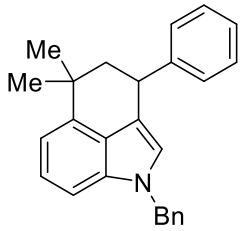
A. General Intramolecular Hydroarylation Procedure



All reactions were conducted with ***cis*-3.1** unless otherwise noticed.

In a dry 4 mL glass vial charged with PTFE coated magnetic stir bar, the *cis*-alkene (0.2 mmol, 1.0 equiv) were dissolved with 2.0 mL of dry toluene (0.1 M). To the solution, 7.9 mg of anhydrous benzenesulfonic acid (0.25 mmol, 25 mol%) was added at room temperature. The vial was then capped with a septum and purged with argon for 1 min. The septum was quickly switched to a PTFE cap with purging argon. The reaction mixture was brought to 130 °C and allowed to stir for 24 hours. TLC indicated complete consumption of the alkene and a new spot stained green with 4-anisaldehyde. The reaction solution was then quenched by addition of 1 mL of saturated $NaHCO_3$ and allowed to stir for 10 minutes. The cyclized product was extracted with DCM (1.0 mL) twice and the combined organic solution was washed with brine (2.0 mL) and dried over anhydrous sodium sulfate. The drying agent was filtered through vacuum and the organic solvent was removed under reduced pressure. The crude product was then transferred to a silica gel packed column. The silica cake was flashed with a mixture of hexanes and benzene to furnish the pure corresponding cyclized product.

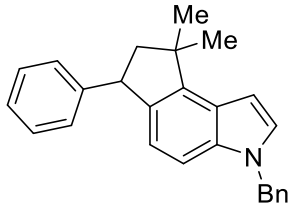
B. Synthesis and Characterization of 1,3,4,5-Tetrahydrobenz[*cd*]indoles and Analogs



3.2a

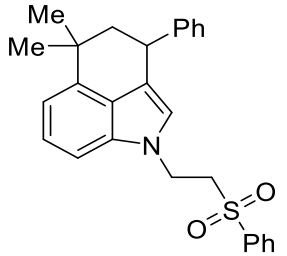
1-benzyl-5,5-dimethyl-3-phenyl-1,3,4,5-tetrahydrobenzo[cd]indole 3.2a. The general cyclization procedure was followed using 351.5 mg of alkene **3.1a** (1.0 mmol), 39.5 mg of anhydrous benzenesulfonic acid (0.25 mmol) and 10.0 mL of dry toluene in a 20.0 mL glass vial. Purification by flash column chromatography (100:0→91:9, hexane:benzene)

afforded major 6-*endo* product **3.2a** (242.5 mg, 69% yield) as a colorless oil. R_f = 0.66 (80:20 hexanes:benzene visualized by 254 nm UV light and *p*-anisaldehyde stain). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.43–7.40 (m, 2H), 7.37–7.23 (m, 6H), 7.22–7.14 (m, 3H), 7.10 (d, *J* = 8.1 Hz, 1H), 7.05 (d, *J* = 7.1 Hz, 1H), 6.59 (d, *J* = 1.6 Hz, 1H), 5.28 (d, *J* = 16.0 Hz, 1H), 5.21 (d, *J* = 15.9 Hz, 1H), 4.31 (ddd, *J* = 12.3, 4.5, 1.6 Hz, 1H), 2.10 (t, *J* = 12.6 Hz, 1H), 1.95 (dd, *J* = 12.9, 4.4 Hz, 1H), 1.50 (s, 3H), 1.38 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 145.9 (C), 140.8 (C), 138.1 (C), 134.9 (C), 128.8 (CH), 128.6 (CH), 128.3 (CH), 127.6 (CH), 127.1 (CH), 126.8 (C), 126.5 (CH), 122.7 (2CH), 117.3 (C), 112.8 (CH), 107.1 (CH), 50.5 (CH_2), 50.2 (CH_2), 38.4 (CH), 35.7 (C), 30.3 (CH_3), 28.2 (CH_3); ATR-FTIR (neat): 3056, 3027, 2957, 2921, 262, 1602, 1495 cm^{-1}; HRMS (ESI) m/z calculated for $C_{26}H_{25}NNa$ $[M+Na]^+$: 374.1885, found: 374.1885.



3.3a

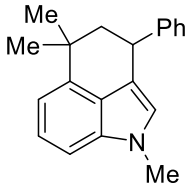
3-benzyl-8,8-dimethyl-6-phenyl-3,6,7,8-tetrahydrocyclopenta[e]indole 3.3a. The general cyclization procedure was followed using 351.5 mg of alkene **3.1a** (1.0 mmol), 39.5 mg of anhydrous benzenesulfonic acid (0.25 mmol) and 10.0 mL of dry toluene in a 20 mL glass vial. Purification by flash column chromatography (100:0→85:15, hexane:benzene) afforded minor 5-*endo* product **3.3a** (45.7 mg, 13% yield) as a colorless oil. R_f = 0.65 (80:20 hexanes:benzene visualized by 254 nm UV light and *p*-anisaldehyde stain). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.37–7.03 (m, 12H), 6.71–6.66 (m, 2H), 5.30 (s, 2H), 4.47 (m, 1H), 2.49 (dd, *J* = 12.5, 7.8 Hz, 1H), 2.06 (dd, *J* = 12.5, 9.6 Hz, 1H), 1.65 (s, 3H), 1.45 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 146.6 (C), 143.7 (C), 137.5 (C), 136.5 (C), 135.8 (C), 128.7 (CH), 128.6 (C), 128.4 (CH), 128.3 (2CH), 128.0 (CH), 127.6 (CH), 126.0 (CH), 118.9 (CH), 108.3 (CH), 99.3 (CH), 53.5 (CH_2), 50.3 (CH_2), 49.4 (CH), 44.4 (C), 29.1 (CH_3), 27.6 (CH_3); ATR-FTIR (neat): 3091, 3071, 3035, 1478 cm^{-1}; HRMS (ESI) m/z calculated for $C_{26}H_{25}NNa$ $[M+Na]^+$: 374.1885, found: 374.1885.



3.2b

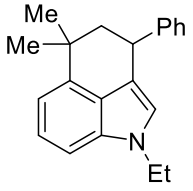
5,5-dimethyl-3-phenyl-1-(2-(phenylsulfonyl)ethyl)-1,3,4,5-tetrahydrobenzo[cd]indole 3.2b. The general cyclization procedure was followed using 85.8 mg of alkene **3.1b** (0.2 mmol), 7.9 mg of anhydrous benzenesulfonic acid (0.25 mmol) and 2.0 mL of dry toluene.

Purification by flash column chromatography (100:0→90:10, hexane:benzene) afforded **3.2b** (48.9 mg, 57% yield) as a colorless oil. R_f = 0.58 (80:20 hexanes:benzene visualized by 254 nm UV light and *p*-anisaldehyde stain). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.81 (dd, *J* = 8.3 Hz, 1.4 Hz, 2H), 7.61 (t, *J* = 7.3 Hz, 1H), 7.48 (t, *J* = 7.7 Hz, 1H), 7.37–7.26 (m, 5H), 7.20 (t, *J* = 7.7 Hz, 1H), 7.01 (t, *J* = 7.0 Hz, 1H), 6.35 (d, *J* = 1.6 Hz, 1H), 4.49 (td, *J* = 7.7 Hz, 2.4 Hz, 2H), 4.15 (dd, *J* = 12.3 Hz, 4.6 Hz, 1H), 3.54 (t, *J* = 7.3 Hz, 2H), 1.99 (appr t, *J* = 12.6 Hz, 1H), 1.89 (dd, *J* = 12.9 Hz, 4.5 Hz, 1H), 1.45 (s, 3H), 1.31 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 145.3 (C), 141.1 (C), 139.0 (C), 134.1 (C, CH), 129.5 (CH), 128.6 (CH), 128.5 (C), 128.2 (CH), 127.9 (CH), 126.8 (C), 126.7 (CH), 123.2 (CH), 121.4 (CH), 118.3 (C), 113.4 (CH), 106.3 (CH), 55.9 (CH_2), 49.7 (CH_2), 40.3 (CH_2), 38.2 (CH), 35.6 (C), 30.1 (CH_3), 28.2 (CH_3); HRMS (ESI/APCI) m/z calculated for $C_{27}H_{27}NNaO_2S$ $[M+Na]^+$: 452.1660, found 452.1649.



3.2c

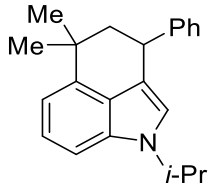
1,5,5-trimethyl-3-phenyl-1,3,4,5-tetrahydrobenzo[cd]indole 3.2c. The general cyclization procedure was followed using 55.1 mg of alkene **3.1c** (0.2 mmol), 7.9 mg of anhydrous benzenesulfonic acid (0.25 mmol) and 2.0 mL of dry toluene. Purification by flash column chromatography (100:0→90:10, hexane:benzene) afforded **3.2c** (37.5 mg, 68% yield) as a colorless oil. R_f = 0.66 (80:20 hexanes:benzene visualized by 254 nm UV light and *p*-anisaldehyde stain). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.42 (d, *J* = 7.1 Hz, 2H), 7.36 (t, *J* = 7.4 Hz, 2H), 7.30–7.22 (m, 2H), 7.15 (d, *J* = 8.0 Hz, 1H), 7.04 (d, *J* = 7.1 Hz, 1H), 6.50 (d, *J* = 1.6 Hz, 1H), 4.30 (ddd, *J* = 12.2 Hz, 4.5 Hz, 1.5 Hz, 1H), 3.74 (s, 3H), 2.08 (appr t, *J* = 12.6 Hz, 1H), 1.95 (dd, *J*= 12.9 Hz, 4.5 Hz, 1H), 1.50 (s, 3H), 1.37 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 145.8 (C), 140.5 (C), 135.0 (C), 128.4 (CH), 128.1 (CH), 126.3 (C, CH), 123.1 (CH), 122.4 (CH), 116.5 (C), 112.4 (CH), 106.4 (CH), 49.9 (CH_2), 38.2 (CH), 35.5 (C), 32.8 (CH_3), 30.0 (CH_3), 28.0 (CH_3); HRMS (ESI/APCI) m/z calculated for $C_{20}H_{22}N$ $[M+H]^+$: 276.1747, found 276.1747.



3.2d

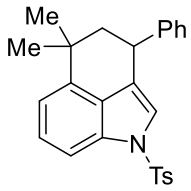
1-ethyl-5,5-dimethyl-3-phenyl-1,3,4,5-tetrahydrobenzo[cd]indole 3.2d. The general cyclization procedure was followed using 57.9 mg of alkene **3.1d** (0.2 mmol), 7.9 mg of anhydrous benzenesulfonic acid (0.25 mmol) and 2.0 mL of dry toluene. Purification by flash column chromatography (100:0→90:10, hexane:benzene) afforded **3.2d** (41.7 mg,

72% yield) as a colorless oil. R_f = 0.68 (80:20 hexanes:benzene visualized by 254 nm UV light and *p*-anisaldehyde stain). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.43–7.34 (m, 3H), 7.29–7.16 (m, 4H), 7.04 (d, *J* = 7.0 Hz, 1H), 6.56 (d, *J* = 1.6 Hz, 1H), 4.29 (ddd, *J* = 12.3, 4.4, 1.6 Hz, 1H), 4.11 (qd, *J* = 7.2, 2.0 Hz, 2H), 2.08 (appr t, *J* = 12.6 Hz, 1H), 1.94 (dd, *J* = 12.9, 4.4 Hz, 1H), 1.5 (s, 3H), 1.44 (t, *J* = 7.3 Hz, 3H), 1.37 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 145.8 (C), 140.6 (C), 134.1 (C), 128.4 (CH), 128.1 (CH), 126.5 (C), 126.3 (CH), 122.2 (CH), 121.3 (CH), 116.5 (C), 112.3 (CH), 106.5 (CH), 50.0 (CH_2), 41.1 (CH_2), 38.2 (CH), 35.5 (C), 30.1 (CH_3), 28.1 (CH_3), 15.8 (CH_3); ATR-FTIR (neat): 3091, 3071, 3036, 1959, 1814, 1478 cm^{-1}; HRMS (ESI/APCI) m/z calculated for $C_{21}H_{23}N$ $[M+Na]^+$: 312.1728, found 312.1713.

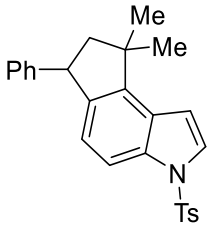


3.2e

1-isopropyl-5,5-dimethyl-3-phenyl-1,3,4,5-tetrahydrobenzo[cd]indole 3.2e. The general cyclization procedure was followed using 60.7 mg of alkene **3.1e** (0.2 mmol), 7.9 mg of anhydrous benzenesulfonic acid (0.25 mmol) and 2.0 mL of dry toluene. Purification by flash column chromatography (100:0→90:10, hexane:benzene) afforded product **3.2e** (45.5 mg, 75% yield) as white solid. R_f = 0.68 (80:20 hexanes:benzene visualized by 254 nm UV light and *p*-anisaldehyde stain). The solid was recrystallized with 1 mL hexane&MeOH mix (hexanes: MeOH = 10:1) to afford colorless needles; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.45–7.36 (m, 4H), 7.31–7.21 (m, 3H), 7.04 (dd, *J* = 6.1, 1.8 Hz, 1H), 6.67 (d, *J* = 1.6 Hz, 1H), 4.62 (sept, *J* = 6.7, 1H), 4.30 (ddd, *J* = 12.3, 4.4, 1.6 Hz, 1H), 2.09 (appr t, *J* = 12.6 Hz, 1H), 1.95 (dd, *J* = 12.9, 4.4 Hz, 1H), 1.50 (d, *J* = 6.6 Hz, 3H), 1.50 (s, 3H), 1.49 (d, *J* = 6.7 Hz, 3H), 1.38 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 146.0 (C), 140.6 (C), 133.8 (C), 128.4 (CH), 128.2 (CH), 126.4 (C), 126.3 (CH), 122.0 (CH), 118.1 (CH), 116.4 (C), 112.3 (CH), 106.9 (CH), 50.1 (CH_2), 47.6 (CH), 38.4 (CH), 35.5 (C), 30.1 (CH_3), 28.1 (CH_3), 23.0 ($2CH_3$); ATR-FTIR (neat): 3056, 3026, 2959, 2925, 2862, 1603, 1444 cm^{-1}; HRMS (ESI) m/z calculated for $C_{22}H_{26}N$ $[M+H]^+$: 304.2060, found: 304.2066; **3.2e** was also characterized by single crystal X-ray diffraction.



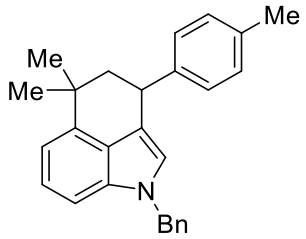
3.2f



3.3f

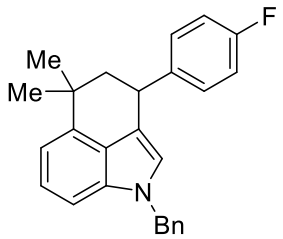
5,5-dimethyl-3-phenyl-1-tosyl-1,3,4,5-tetrahydrobenzo[cd]indole 3.2f & 8,8-dimethyl-6-phenyl-3-tosyl-3,6,7,8-tetrahydrocyclopenta[e]indole 3.3f. The general

cyclization procedure was followed using 83.1 mg of alkene **3.1f** (0.2 mmol), 7.9 mg of anhydrous benzenesulfonic acid (0.25 mmol) and 2.0 mL of dry toluene. Purification by flash column chromatography (100:0→90:10, hexane:benzene) afforded inseparable regioisomers **3.2f** and **3.3f** (**3.2f** : **3.3f** = 60 : 40, 59.8 mg, 72% yield) as a colorless oil. R_f = 0.56 (80:20 hexanes:benzene visualized by 254 nm UV light and *p*-anisaldehyde stain). Selected spectral data for **3.2f**: ^{1}H NMR (400 MHz, $CDCl_3$): δ **other peaks in aromatic region were interfered by regioisomer,** 6.95 (d, *J* = 2.0 Hz, 1H), 4.15 (ddd, *J* = 12.5, 4.8, 2.1 Hz, 1H), 2.36 (s, 3H), 1.98 (appr t, *J* = 12.7 Hz, 1H), 1.90 (dd, *J* = 13.1, 4.8 Hz, 1H), 1.43 (s, 3H), 1.29 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ **other peaks in aromatic region were interfered by regioisomer**, 129.8 (CH), 128.6 (CH), 128.0 (CH), 126.8 (CH), 125.3 (CH), 120.2 (CH), 117.3(CH), 111.0(CH), 48.8(CH_2), 37.8 (CH), 30.0 (CH_3), 28.0 (CH_3), 21.6 (CH_3); Selected spectral data for **3.3f**: ^{1}H NMR (400 MHz, $CDCl_3$): δ **other peaks in aromatic region were interfered by regioisomer**, 7.61 (d, *J* = 3.7 Hz, 1H), 6.44-6.39 (m, 1H), 2.44 (dd, *J* = 12.6, 7.8 Hz, 1H), 2.36 (s, 3H), 2.02 (dd, *J* = 13.7, 8.8 Hz, 1H), 1.56 (s, 3H), 1.35 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ **other peaks in aromatic region were interfered by regioisomer**, 129.9 (CH), 128.4(CH), 128.3(CH), 127.0 (CH), 126.1 (CH), 124.2(CH), 121.5(CH), 111.9(CH), 106.4 (CH), 49.2(CH), 53.2(CH_2), 29.0(CH_3), 27.8(CH_3), 21.6(CH_3); ATR-FTIR (neat): 3091, 3036, 2921, 1959, 114, 1479 cm^{-1}; HRMS (ESI/APCI) m/z calculated for $C_{26}H_{25}NNaO_2S$ $[M+Na]^+$: 438.1504, found 452.1514.



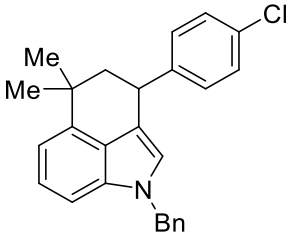
3.2i

1-benzyl-5,5-dimethyl-3-(p-tolyl)-1,3,4,5-tetrahydrobenzo[cd]indole 3.2i. The general cyclization procedure was followed using 73.1 mg of alkene **3.1i** (0.2 mmol), 7.9 mg of anhydrous benzenesulfonic acid (0.25 mmol) and 2.0 mL of dry toluene. Purification by flash column chromatography (100:0→90:10, hexane:benzene) afforded 6-*endo* product **3.2i** (62.1 mg, 85% yield) as a colorless oil. R_f = 0.68 (80:20 hexanes:benzene visualized by 254 nm UV light and *p*-anisaldehyde stain). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.32–7.23 (m, 5H), 7.21–7.13 (m, 5H), 7.09 (d, *J* = 8.1 Hz, 1H), 7.04 (d, *J* = 7.1 Hz, 1H), 6.58 (d, *J* = 1.6 Hz, 1H), 5.27 (d, *J* = 15.9 Hz, 1H), 5.20 (d, *J* = 15.9 Hz, 1H), 4.27 (ddd, *J* = 12.3, 4.5, 1.6 Hz, 1H), 2.36 (s, 3H), 2.07 (appr t, *J* = 12.6 Hz, 1H), 1.92 (dd, *J* = 12.9, 4.5 Hz, 1H), 1.49 (s, 3H), 1.37 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 142.9 (C), 140.8 (C), 138.2 (C), 136.0 (C), 134.9 (C), 129.3 (CH), 128.8 (CH), 128.1 (CH), 127.6 (CH), 127.1 (CH), 126.8 (C), 122.7 (CH), 122.6 (CH), 117.5 (C), 112.8 (CH), 107.0 (CH), 50.5 (CH_2), 50.4 (CH_2), 37.9 (CH), 35.7 (C), 30.3 (CH_3), 28.2 (CH_3), 21.3 (CH_3); ATR-FTIR (neat): 3091, 3071, 3035, 1959, 1814, 1478 cm^{-1}; HRMS (ESI) m/z calculated for $C_{27}H_{28}N$ $[M+H]^+$: 366.2216, found 366.2212.



3.2j

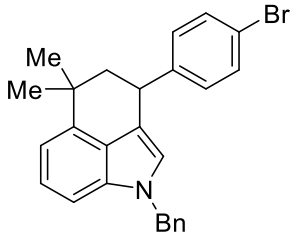
1-benzyl-3-(4-fluorophenyl)-5,5-dimethyl-1,3,4,5-tetrahydrobenzo[cd]indole 3.2j. The general cyclization procedure was followed using 73.1 mg of alkene **3.1j** (0.2 mmol), 7.9 mg of anhydrous benzenesulfonic acid (0.25 mmol) and 2.0 mL of dry toluene. Purification by flash column chromatography (100:0→90:10, hexane:benzene) afforded 6-*endo* product **3.2j** (63.6 mg, 87% yield) as a colorless oil. R_f = 0.66 (80:20 hexanes:benzene visualized by 254 nm UV light and *p*-anisaldehyde stain). ^{1}H NMR (500 MHz, $CDCl_3$):): δ 7.39–7.25 (m, 6H), 7.22–7.14 (m, 3H), 7.11 (d, *J* = 8.1 Hz, 1H), 7.05 (d, *J* = 7.0 Hz, 1H), 7.01 (d, *J* = 8.7 Hz, 1H), 6.56 (d, *J* = 1.6 Hz, 1H), 5.28 (d, *J* = 15.9 Hz, 1H), 5.22 (d, *J* = 16.0 Hz, 1H), 4.29 (ddd, *J* = 12.3, 4.5, 1.6 Hz, 1H), 2.05 (appr t, *J* = 12.6 Hz, 1H), 1.93 (dd, *J* = 12.9, 4.5 Hz, 1H), 1.50 (s, 3H), 1.37 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 161.7 (d, *J* = 243.8 Hz, C-F), 141.5 (d, *J* = 3.0 Hz, C), 140.7 (C), 138.1 (C), 135.0 (C), 129.6 (d, *J* = 7.8 Hz, CH), 128.9 (CH), 127.7 (CH), 127.1 (CH), 126.7 (C), 122.8 (CH), 122.6 (CH), 117.3 (C), 115.3 (d, *J* = 21.0 Hz, CH), 112.9 (CH), 107.1 (CH), 50.5 (CH_2), 50.3 (CH_2), 37.7 (CH), 35.7 (C), 30.3 (CH_3), 28.2 (CH_3); ^{19} F NMR (470 MHz, $CDCl_3$): δ -117.08; ATR-FTIR (neat): 3090, 3035, 2958, 1958, 1816, 1508, 1478 cm^{-1}; HRMS (ESI) m/z calculated for $C_{26}H_{25}FN$ $[M+H]^+$: 370.1966, found 370.1966.



3.2k

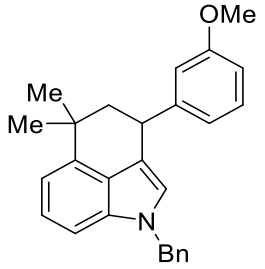
1-benzyl-3-(4-chlorophenyl)-5,5-dimethyl-1,3,4,5-tetrahydrobenzo[cd]indole 3.2k. The general cyclization procedure was followed using 77.2 mg of alkene **3.1k** (0.2 mmol), 7.9 mg of anhydrous benzenesulfonic acid (0.25 mmol) and 2.0 mL of dry toluene. Purification by flash column chromatography (100:0→90:10, hexane:benzene) afforded 6-*endo* product **3.2k** (56.4 mg, 73% yield) as a colorless oil. R_f = 0.67 (80:20 hexanes:benzene visualized by 254 nm UV light and *p*-anisaldehyde stain). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.36–7.25 (m, 7H), 7.21–7.14 (m, 3H), 7.11 (d, *J* = 8.2 Hz, 1H), 7.05 (d, *J* = 7.1 Hz, 1H), 6.55 (d, *J* = 1.6 Hz, 1H), 5.28 (d, *J* = 16.0 Hz, 1H), 5.21 (d, *J* = 15.9 Hz, 1H), 4.28 (ddd, *J* = 12.2, 4.5, 1.6 Hz, 1H), 2.05 (appr t, *J* = 12.6 Hz, 1H), 1.93 (dd, *J* = 12.9, 4.5 Hz, 1H), 1.49 (s, 3H), 1.37 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 144.4 (C), 140.6 (C), 138.0 (C), 134.9 (C), 132.1 (C), 129.6 (CH), 128.9 (CH), 128.7 (CH), 127.7 (CH),

127.1 (CH), 126.6 (C), 122.8 (CH), 122.6 (CH), 116.9 (C), 112.9 (CH), 107.1 (CH), 50.5 (CH_2), 50.1 (CH_2), 37.9 (CH), 35.6 (C), 30.2 (CH_3), 28.2 (CH_3); ATR-FTIR (neat): 3090, 3071, 3035, 1959, 1813, 1478 cm^{-1}; HRMS (ESI) m/z calculated for $C_{26}H_{25}ClN$ $[M+H]^+$: 386.1670, found 386.1651.



3.2l

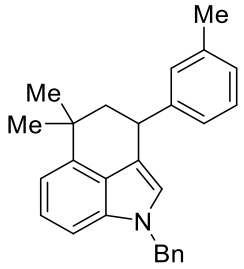
1-benzyl-3-(4-bromophenyl)-5,5-dimethyl-1,3,4,5-tetrahydrobenzo[cd]indole 3.2l. The general cyclization procedure was followed using 86.1 mg of alkene **3.1l** (0.2 mmol), 7.9 mg of anhydrous benzenesulfonic acid (0.25 mmol) and 2.0 mL of dry toluene. Purification by flash column chromatography (100:0→90:10, hexane:benzene) afforded 6-*endo* product **3.2l** (75.7 mg, 88% yield) as a colorless oil. R_f = 0.68 (80:20 hexanes:benzene visualized by 254 nm UV light and *p*-anisaldehyde stain). ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.46 (d, *J* = 8.4 Hz, 2H), 7.33–7.26 (m, 5H), 7.20 (dd, *J* = 8.8, 7.1 Hz, 1H), 7.18–7.15 (m, 2H), 7.12 (d, *J* = 8.1 Hz, 1H), 7.05 (d, *J* = 7.1 Hz, 1H), 6.56 (d, *J* = 1.6 Hz, 1H), 5.28 (d, *J* = 15.9 Hz, 1H), 5.22 (d, *J* = 15.9 Hz, 1H), 4.27 (ddd, *J* = 12.3, 4.4, 1.6 Hz, 1H), 2.07 (appr t, *J* = 12.6 Hz, 1H), 1.93 (dd, *J* = 12.9, 4.5 Hz, 1H), 1.50 (s, 3H), 1.37 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 145.0 (C), 140.6 (C), 138.0 (C), 134.9 (C), 131.7 (CH), 130.1 (CH), 128.9 (CH), 127.7 (CH), 127.1 (CH), 126.6 (C), 122.8 (CH), 122.6 (CH), 120.1 (C), 116.8 (C), 113.0 (CH), 107.1 (CH), 50.5 (CH_2), 50.1 (CH_2), 38.0 (CH), 35.6 (C), 30.2 (CH_3), 28.2 (CH_3); ATR-FTIR (neat): 3033, 2958, 2922, 1605, 1487 cm^{-1}; HRMS (ESI) m/z calculated for $C_{26}H_{25}BrN$ $[M+H]^+$: 430.1165, found 430.1160.



3.2m

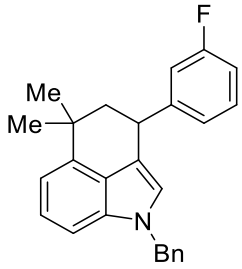
1-benzyl-3-(3-methoxyphenyl)-5,5-dimethyl-1,3,4,5-tetrahydrobenzo[cd]indole 3.2m. The general cyclization procedure was followed using 76.3 mg of alkene **3.1m** (0.2 mmol), 7.9 mg of anhydrous benzenesulfonic acid (0.25 mmol) and 2.0 mL of dry toluene. Purification by flash column chromatography (100:0→90:10, hexane:benzene) afforded 6-*endo* product **3.2m** (54.2 mg, 71% yield) as a colorless oil. R_f = 0.55 (80:20 hexanes:benzene visualized by 254 nm UV light and *p*-anisaldehyde stain). ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.32–7.24 (m, 5H), 7.21–7.09 (m, 4H), 7.08–7.00 (m, 2H), 6.96 (dd, *J* =

2.6, 1.6 Hz, 1H), 6.62 (d, *J* = 1.6 Hz, 1H), 5.28 (d, *J* = 15.9 Hz, 1H), 5.22 (d, *J* = 15.9 Hz, 1H), 4.29 (ddd, *J* = 12.3, 4.4, 1.6 Hz, 1H), 3.77 (s, 3H), 2.08 (appr t, *J* = 12.6 Hz, 1H), 1.96 (dd, *J* = 12.9, 4.5 Hz, 1H), 1.50 (s, 3H), 1.37 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 159.9 (C), 147.6 (C), 140.8 (C), 138.2 (C), 134.9 (C), 129.5 (CH), 128.8 (CH), 127.7 (CH), 127.1 (CH), 122.7 (2CH), 120.8 (CH), 119.5(C), 117.1 (C), 113.6 (CH), 112.8 (CH), 112.2 (CH), 107.1 (CH), 55.3 (OCH_3), 50.5 (CH_2), 50.1 (CH_2), 38.5 (CH), 35.7 (C), 30.3 (CH_3), 28.2 (CH_3); HRMS (ESI) m/z calculated for $C_{27}H_{28}NO$ $[M+H]^+$: 382.2121, found 382.2155.



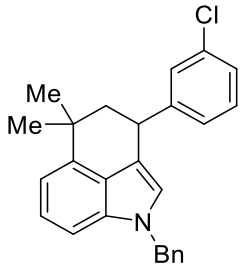
3.2n

1-benzyl-5,5-dimethyl-3-(m-tolyl)-1,3,4,5-tetrahydrobenzo[cd]indole 3.2n. The general cyclization procedure was followed using 73.1 mg of alkene **3.1n** (0.2 mmol), 7.9 mg of anhydrous benzenesulfonic acid (0.25 mmol) and 2.0 mL of dry toluene. Purification by flash column chromatography on ~10% wt. % $AgNO_3$ doped silica gel (100:0:0→90:2:8, hexane:benzene:EtOAc) afforded 6-*endo* product **3.2n** (54.1 mg, 74% yield) as a colorless oil. R_f = 0.60 (80:20 hexanes:benzene visualized by 254 nm UV light and *p*-anisaldehyde stain). ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.34–7.17 (m, 9H), 7.15–7.06 (m, 3H), 6.62 (d, *J* = 1.6 Hz, 1H), 5.30 (d, *J* = 16.0 Hz, 1H), 5.24 (d, *J* = 16.0 Hz, 1H), 4.30 (ddd, *J* = 12.3, 4.5, 1.6 Hz, 1H), 2.38 (s, 3H), 2.11 (appr t, *J* = 12.6 Hz, 1H), 1.97 (dd, *J* = 12.9, 4.4 Hz, 1H), 1.53 (s, 3H), 1.40 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 145.9 (C), 140.8 (C), 138.2 (C), 138.1(C), 134.9 (C), 129.1 (CH), 128.8 (CH), 128.5 (CH), 127.6 (CH), 127.3 (CH), 127.1 (CH), 126.8 (C), 125.3 (CH), 122.7 (CH), 122.6 (CH), 117.4 (C), 112.8 (CH), 107.0 (CH), 50.5 (CH_2), 50.2 (CH_2), 38.3 (CH), 35.6 (C), 30.3 (CH_3), 28.2 (CH_3), 21.7 (CH_3); ATR-FTIR (neat): 3091, 3071, 3035, 1959, 1814, 1478 cm^{-1}; HRMS (ESI) m/z calculated for $C_{27}H_{28}N$ $[M+H]^+$: 366.2216, found 366.2206.



3.2o

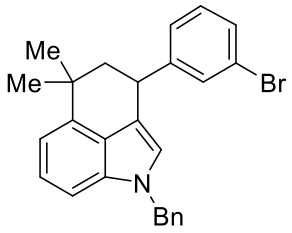
1-benzyl-3-(3-fluorophenyl)-5,5-dimethyl-1,3,4,5-tetrahydrobenzo[cd]indole 3.2o. The general cyclization procedure was followed using 74.0 mg of alkene **3.1o** (0.2 mmol), 25.3 mg of anhydrous benzenesulfonic acid (0.8 mmol) and 2.0 mL of dry toluene. Purification by flash column chromatography on ~10% wt. % $AgNO_3$ doped silica gel (100:0:0→90:2:8, hexane:benzene:EtOAc) afforded inseparable **3.2o** & **3.3o** (43.6 mg, 59% yield) as a colorless oil. R_f = 0.65 (80:10:10 hexanes:benzene:ethyl acetate visualized by 254 nm UV light and *p*-anisaldehyde stain). Selected spectral data for **3.2o**. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.31–7.02 (m, 12H), 6.58 (d, *J* = 1.6 Hz, 1H), 5.28 (d, *J* = 15.9 Hz, 1H), 5.21 (d, *J* = 15.9 Hz, 1H), 4.29 (dd, *J* = 12.1, 4.4 Hz, 1H), 2.05 (appr t, *J* = 12.5 Hz, 1H), 1.94 (dd, *J* = 12.9, 4.6 Hz, 1H), 1.49 (s, 3H), 1.35 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 163.2 (d, *J* = 245.0 Hz, C-F), 148.7 (d, *J* = 6.9 Hz, C), 140.6 (C), 138.1 (C), 135.0 (C), 128.9 (CH), 127.7 (CH), 127.1 (CH), **other peaks in aromatic region were interfered by regioisomer**; ^{19} F NMR (376 MHz, $CDCl_3$): δ -113.64; ATR-FTIR (neat): 2958, 2924, 2862, 1614, 1589, 1495 cm^{-1}; HRMS (ESI) m/z calculated for $C_{26}H_{25}FN$ $[M+H]^+$: 370.1966, found 370.1944.



3.2p

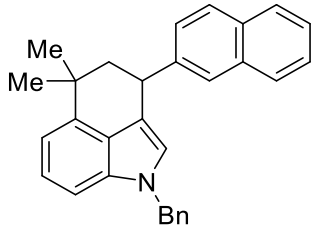
1-benzyl-3-(3-chlorophenyl)-5,5-dimethyl-1,3,4,5-tetrahydrobenzo[cd]indole 3.2p. The general cyclization procedure was followed using 77.2 mg of alkene **3.1p** (0.2 mmol), 25.3 mg of anhydrous benzenesulfonic acid (0.8 mmol) and 2.0 mL of dry toluene. Purification by flash column chromatography on ~10% wt. % $AgNO_3$ doped silica gel (100:0:0→90:2:8, hexane:benzene:EtOAc) afforded 6-*endo* product **3.2p** (49.4 mg, 64% yield) as a colorless oil. R_f = 0.63 (80:10:10 hexanes:benzene:ethyl acetate visualized by 254 nm UV light and *p*-anisaldehyde stain). ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.40 (s, 1H), 7.33–7.14 (m, 9H), 7.11 (d, *J* = 8.1 Hz, 1H), 7.05 (d, *J* = 7.2 Hz, 1H), 6.59 (d, *J* = 1.6 Hz, 1H), 5.29 (d, *J* = 15.9 Hz, 1H), 5.23 (d, *J* = 16.0 Hz, 1H), 4.28 (ddd, *J* = 12.2, 4.5, 1.6 Hz, 1H), 2.06 (appr t, *J* = 12.5 Hz, 1H), 1.94 (dd, *J* = 12.9, 4.5 Hz, 1H), 1.50 (s, 3H), 1.37 (s,

3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 148.1 (C), 140.6 (C), 138.1 (C), 134.9 (C), 134.3 (C), 129.9 (CH), 128.9 (CH), 128.5 (CH), 127.7 (CH), 127.1 (CH), 126.7 (CH), 126.6 (C), 126.5 (CH), 122.8 (CH), 122.7 (CH), 116.6 (C), 113.0 (CH), 107.2 (CH), 50.5 (CH_2), 50.0 (CH_2), 38.3 (CH), 35.7 (C), 30.2 (CH_3), 28.2 (CH_3); ATR-FTIR (neat): 3055, 2957, 2923, 2862, 1595, 1453 cm^{-1}; HRMS (ESI) m/z calculated for $C_{26}H_{25}ClN$ $[M+H]^+$: 386.1670, found 386.1644.



3.2q

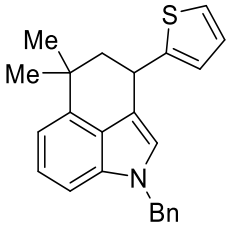
1-benzyl-3-(3-bromophenyl)-5,5-dimethyl-1,3,4,5-tetrahydrobenzo[cd]indole 3.2q. The general cyclization procedure was followed using 86.1 mg of mixture of *cis* and *trans* alkenes ***cis*-3.1q** and ***trans*-3.1q** (0.2 mmol), 25.3 mg of anhydrous benzenesulfonic acid (0.8 mmol) and 2.0 mL of dry toluene. Purification by flash column chromatography on ~10% wt. % $AgNO_3$ doped silica gel (100:0:0→90:2:8, hexane:benzene:EtOAc) afforded 6-*endo* product **3.2q** (57.6 mg, 68% yield) as a colorless oil. R_f = 0.65 (80:10:10 hexanes:benzene:ethyl acetate visualized by 254 nm UV light and *p*-anisaldehyde stain). ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.55 (t, *J* = 1.9 Hz, 1H), 7.33–7.29 (m, 4H), 7.22–7.13 (m, 5H), 7.11 (d, *J* = 8.1 Hz, 1H), 7.04 (d, *J* = 7.1 Hz, 1H), 6.58 (d, *J* = 1.6 Hz, 1H), 5.29 (d, *J* = 15.9 Hz, 1H), 5.23 (d, *J* = 16.0 Hz, 1H), 4.26 (dd, *J* = 12.2, 4.7 Hz, 1H), 2.07-2.01 (m, 1H), 1.93 (dd, *J* = 12.9, 4.5 Hz, 1H), 1.49 (s, 3H), 1.35 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 148.1 (C), 140.6 (C), 138.1 (C), 134.9 (C), 134.3 (C), 129.9 (CH), 128.9 (CH), 128.5 (CH), 127.7 (CH), 127.1 (CH), 126.7 (CH), 126.6 (C), 126.5 (CH), 122.8 (CH), 122.7 (CH), 116.6 (C), 113.0 (CH), 107.2 (CH), 53.0 (CH_2), 52.5 (CH_2), 38.3 (CH), 35.7 (C), 30.2 (CH_3), 28.2 (CH_3); ATR-FTIR (neat): 3091, 3071, 3036, 1959, 1814, 1479 cm^{-1}; HRMS (ESI) m/z calculated for $C_{26}H_{25}BrN$ $[M+H]^+$: 430.1165, found 430.1142.



3.2r

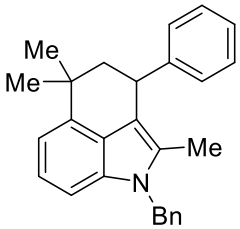
1-benzyl-5,5-dimethyl-3-(naphthalen-2-yl)-1,3,4,5-tetrahydrobenzo[cd]indole 3.2r. The general cyclization procedure was followed using 80.3 mg of mixture *cis* and *trans* alkenes ***cis*-3.1r** and ***trans*-3.1r** (0.2 mmol), 7.9 mg of anhydrous benzenesulfonic acid (0.25 mmol) and 2.0 mL of dry toluene. Purification by flash column chromatography (100:0→90:10, hexane:benzene) afforded 6-*endo* product **3.2r** (61.0 mg, 76% yield) as a

colorless oil. R_f = 0.68 (80:20 hexanes:benzene visualized by 254 nm UV light and *p*-anisaldehyde stain). ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.90 (s, 1H), 7.87–7.80 (m, 3H), 7.53–7.44 (m, 3H), 7.33–7.20 (m, 4H), 7.18–7.12 (m, 3H), 7.08 (d, *J* = 7.1 Hz, 1H), 6.58 (d, *J* = 1.6 Hz, 1H), 5.28 (d, *J* = 15.8 Hz, 1H), 5.21 (d, *J* = 16.0 Hz, 1H), 4.49 (ddd, *J* = 12.3, 4.4, 1.6 Hz, 1H), 2.22 (appr t, *J* = 12.6 Hz, 1H), 2.03 (dd, *J* = 12.9, 4.5 Hz, 1H), 1.53 (s, 3H), 1.43 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 143.4 (C), 140.8 (C), 138.1 (C), 135.0 (C), 133.8 (C), 132.7 (C), 128.8 (CH), 128.2 (CH), 127.8 (2CH), 127.7 (CH), 127.2 (CH), 127.0 (CH), 126.8 (C), 126.6 (CH), 126.0 (CH), 125.5 (CH), 122.8 (CH), 122.7 (CH), 117.3 (C), 112.9 (CH), 107.1 (CH), 50.5 (CH_2), 49.9 (CH_2), 38.5 (CH), 35.7 (C), 30.3 (CH_3), 28.3 (CH_3); ATR-FTIR (neat): 3091, 3071, 3035, 1959, 1814, 1478 cm^{-1}; HRMS (ESI) m/z calculated for $C_{30}H_{28}N$ $[M+H]^+$:402.2216, found 402.2211.



3.2s

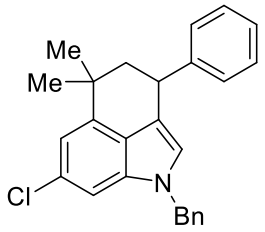
1-benzyl-5,5-dimethyl-3-(thiophen-2-yl)-1,3,4,5-tetrahydrobenzo[cd]indole 3.2s. The general cyclization procedure was followed using 71.6 mg of alkene **3.1s** (0.2 mmol), 7.9 mg of anhydrous benzenesulfonic acid (0.25 mmol) and 2.0 mL of dry toluene. Purification by flash column chromatography (100:0→90:10, hexane:benzene) afforded 6-*endo* product **3.2s** (50.0 mg, 69% yield) as a colorless oil. R_f = 0.60 (80:20 hexanes:benzene visualized by 254 nm UV light and *p*-anisaldehyde stain). ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.33–7.25 (m, 2H), 7.18–7.15 (m, 4H), 7.09–6.97 (m, 4H), 6.80 (d, *J* = 1.6 Hz, 1H), 5.29 (d, *J* = 16.0 Hz, 1H), 5.23 (d, *J* = 15.9 Hz, 1H), 4.67 (ddd, *J* = 11.8, 4.8, 1.6 Hz, 1H), 2.16 (appr t, *J* = 12.4 Hz, 1H), 2.09 (dd, *J* = 12.8, 4.7 Hz, 1H), 1.50 (s, 3H), 1.36 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 149.8 (C), 140.5 (C), 138.1 (C), 134.9 (C), 128.9 (CH), 127.7 (CH), 127.1 (CH), 126.7 (CH), 126.3 (C), 124.0 (CH), 123.1 (2CH), 122.8 (CH), 117.0 (C), 113.0 (CH), 107.2 (CH), 50.9 (CH_2), 50.5 (CH_2), 35.8 (CH), 33.5 (C), 30.2 (CH_3), 28.1 (CH_3); ATR-FTIR (neat): 3091, 3071, 3035, 1959, 1813, 1478 cm^{-1}; HRMS (ESI) m/z calculated for $C_{24}H_{24}NS$ $[M+H]^+$: 358.1624, found 358.1622.



3.2t

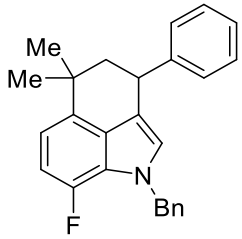
1-benzyl-2,5,5-trimethyl-3-phenyl-1,3,4,5-tetrahydrobenzo[cd]indole 3.2t. The general cyclization procedure was followed using 73.1 mg of alkene **3.1t** (0.2 mmol), 7.9

mg of anhydrous benzenesulfonic acid (0.25 mmol) and 2.0 mL of dry toluene. Purification by flash column chromatography (100:0→90:10, hexane:benzene) afforded 6-*endo* product **3.2t** (51.2 mg, 70% yield) as a colorless oil. R_f = 0.65 (80:20 hexanes:benzene visualized by 254 nm UV light and *p*-anisaldehyde stain). ^{1}H NMR (500 MHz, $CDCl_3$): 7.34–7.20 (m, 8H), 7.15–6.99 (m, 5H), 5.25 (s, 2H), 4.27 (ddd, *J* = 11.7, 4.7, 1.4 Hz, 1H), 2.08 (appr t, *J* = 12.4 Hz, 1H), 1.98 (dd, *J* = 13.1, 4.8 Hz, 1H), 1.73 (d, *J* = 1.3 Hz, 3H), 1.47 (s, 3H), 1.35 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 146.2 (C), 139.8 (C), 138.5 (C), 135.0 (C), 130.4 (C), 128.9 (CH), 128.6 (CH), 128.4 (CH), 127.3 (CH), 126.4 (C), 126.3 (2CH), 121.6 (CH), 112.8 (CH), 112.3 (C), 106.4 (CH), 51.5 (CH_2), 46.8 (CH_2), 38.8 (CH), 35.4 (C), 30.3 (CH_3), 28.2 (CH_3), 11.3 (CH_3); ATR-FTIR (neat): 3091, 3071, 3035, 1959, 1813 1478 cm^{-1} ; HRMS (ESI) m/z calculated for $C_{27}H_{28}N$ $[M+H]^+$: 366.2216, found 366.2215.



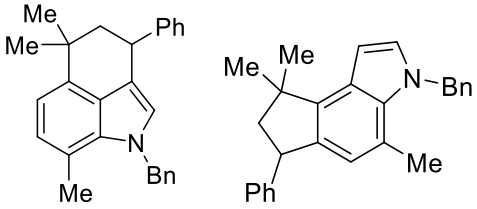
3.2u

1-benzyl-7-chloro-5,5-dimethyl-3-phenyl-1,3,4,5-tetrahydrobenzo[cd]indole 3.2u. The general cyclization procedure was followed using 77.2 mg of alkene **3.1u** (0.2 mmol), 7.9 mg of anhydrous benzenesulfonic acid (0.25 mmol) and 2.0 mL of dry toluene. Purification by flash column chromatography (100:0→90:10, hexane:benzene) afforded 6-*endo* product **3.2u** (55.0 mg, 71 % yield) as a colorless oil. R_f = 0.55 (80:20 hexanes:benzene visualized by 254 nm UV light and *p*-anisaldehyde stain). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.43–7.23 (m, 8H), 7.16–7.06 (m, 3H), 7.02 (d, *J* = 1.5 Hz, 1H), 6.57 (d, *J* = 1.6 Hz, 1H), 5.22 (d, *J* = 16.0 Hz, 1H), 5.15 (d, *J* = 15.9 Hz, 1H), 4.27 (ddd, *J* = 12.3, 4.5, 1.6 Hz, 1H), 2.06 (appr t, *J* = 12.6 Hz, 1H), 1.95 (dd, *J* = 13.0, 4.5 Hz, 1H), 1.47 (s, 3H), 1.36 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 145.4 (C), 142.0 (C), 137.6 (C), 135.1 (C), 129.0 (CH), 128.7 (CH), 128.5 (C), 128.2 (CH), 127.8 (CH), 127.0 (CH), 126.7 (CH), 125.4 (C), 123.3 (CH), 117.5 (C), 114.2 (CH), 107.2 (CH), 50.5 (CH_2), 50.0 (CH_2), 38.2 (CH), 35.8 (C), 30.0 (CH_3), 28.1 (CH_3); ATR-FTIR (neat): 3090, 3071, 3035, 1959, 1813, 1478 cm^{-1}; HRMS (ESI) m/z calculated for $C_{26}H_{25}ClN$ $[M+H]^+$: 386.1670, found 386.1668.



3.2v

1-benzyl-8-fluoro-5,5-dimethyl-3-phenyl-1,3,4,5-tetrahydrobenzo[cd]indole 3.2v. The general cyclization procedure was followed using 73.9 mg of alkene **3.1v** (0.2 mmol), 7.9 mg of anhydrous benzenesulfonic acid (0.25 mmol) and 2.0 mL of dry toluene. Purification by flash column chromatography (100:0→90:10, hexane:benzene) afforded 6-*endo* product **3.2v** (66.5 mg, 90% yield) as a colorless oil. R_f = 0.58 (80:20 hexanes:benzene visualized by 254 nm UV light and *p*-anisaldehyde stain). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.40–7.24 (m, 8H), 7.18 (d, *J* = 7.4 Hz, 2H), 6.87 (m, 2H), 6.55 (s, 1H), 5.45 (d, *J* = 15.8 Hz, 1H), 5.32 (d, *J* = 15.7 Hz, 1H), 4.25 (dd, *J* = 12.3, 4.5 Hz, 1H), 2.03 (t, *J* = 12.6 Hz, 1H), 1.92 (dd, *J* = 12.9, 4.5 Hz, 1H), 1.47 (s, 3H), 1.33 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 148.2 (d, *J* = 242.3 Hz, C-F), 145.6 (C), 138.7 (C), 136.4 (d, *J* = 3.7 Hz, C), 130.4 (d, *J* = 5.9 Hz, C), 128.8 (CH), 128.7 (CH), 128.2 (CH), 127.7 (CH), 127.2 (CH), 126.6 (CH), 124.0 (CH), 118.4 (C), 113.2 (d, *J* = 5.9 Hz, CH), 108.1 (CH), 107.9 (CH), 52.2 (CH_2), 50.1 (CH_2), 38.3 (CH), 35.4 (C), 30.3 (CH_3), 28.4 (CH_3); ^{19} F NMR (376 MHz, $CDCl_3$): δ -138.56; ATR-FTIR (neat): 3063, 3029, 2958, 2924, 1602, 1513, 1452 cm^{-1}; HRMS (ESI) m/z calculated for $C_{26}H_{25}FN$ $[M+H]^+$: 370.1966, found 370.1964.



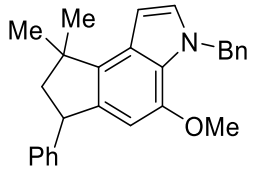
3.2w **3.3w**

1-benzyl-5,5,8-trimethyl-3-phenyl-1,3,4,5-tetrahydrobenzo[cd]indole 3.2w & 3-benzyl-4,8,8-trimethyl-6-phenyl-3,6,7,8-tetrahydrocyclopenta[e]indole 3.3w. The general cyclization procedure was followed using 73.1 mg of alkene **3.1w** (0.2 mmol), 7.9 mg of anhydrous benzenesulfonic acid (0.25 mmol) and 2.0 mL of dry toluene. Purification by flash column chromatography (100:0→90:10, hexane:benzene) afforded 6-*endo* product **3.2w** (31.8 mg, 43.5% yield) and 5-*endo* product **3w** (8.5 mg, 11.6% yield) both as colorless oil. R_f = 0.62 (80:20 hexanes:benzene visualized by 254 nm UV light and *p*-anisaldehyde stain).

Selected spectral data for *6-endo* product **3.2w**: ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.45–7.23 (m, 8H), 7.02–6.89 (m, 4H), 6.53 (d, *J* = 1.6 Hz, 1H), 5.54 (d, *J* = 17.0 Hz, 1H),5.46 (d, *J* = 17.0 Hz, 1H), 4.31 (ddd, *J* = 12.3, 4.4, 1.6 Hz, 1H), 2.52 (s, 3H), 2.10 (appr t, *J* = 12.6 Hz, 1H), 1.96 (dd, *J* = 12.9, 4.5 Hz, 1H), 1.51 (s, 3H), 1.39 (s, 3H); ^{13}C NMR (125 MHz,

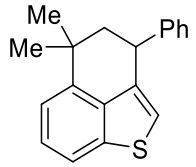
$CDCl_3$): δ 146.0 (C), 140.1 (C), 138.7 (C), 133.6 (C), 128.9 (C, CH), 128.6 (CH), 128.3 (CH), 127.3 (CH), 126.5 (CH), 125.8 (CH), 125.0 (CH), 124.6 (CH), 118.5 (C), 117.3 (C), 113.3 (CH), 51.9 (CH_2), 50.0 (CH_2), 38.3 (CH), 35.3 (C), 30.4 (CH_3), 28.4 (CH_3), 19.1 (CH_3); ATR-FTIR (neat): 3059, 3026, 2957, 2924, 2864, 1602, 1495 cm^{-1}; HRMS (ESI) m/z calculated for $C_{27}H_{28}N$ $[M+H]^+$: 366.2216, found 366.2214.

Selected spectral data for 5-*endo* product **3.3w:** ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.50 (d, *J* = 7.9 Hz, 1H), 7.27 (s, 1H), 7.24–7.16 (m, 5H), 7.13–7.09 (m, 2H), 7.02 (t, *J* = 7.5 Hz, 1H), 6.84 (d, *J* = 7.2 Hz, 1H), 6.67 (dd, *J* = 7.3, 2.1 Hz, 2H), 5.37 (d, *J* = 17.5 Hz, 1H), 4.82 (d, *J* = 17.5 Hz, 1H), 4.28 (dd, *J* = 8.6, 6.0 Hz, 1H), 2.84 (dd, *J* = 13.0, 8.7 Hz, 1H), 2.46 (s, 3H), 2.25 (dd, *J* = 13.0, 6.0 Hz, 1H), 1.56 (s, 3H), 1.45 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 144.9 (C), 144.7 (C), 140.2 (CH), 140.1 (C), 128.7 (2CH), 128.6 (C), 127.8 (CH), 127.0 (CH), 126.6 (CH), 125.3 (CH), 124.2 (C), 124.0 (CH), 121.9 (C), 119.5 (CH), 116.7 (CH), 57.7 (CH_2), 49.4 (CH_2), 44.6 (CH), 39.8 (C), 30.3 (CH_3), 29.8 (CH_3), 19.6 (CH_3); ATR-FTIR (neat): 3061, 3028, 2952, 2861, 1604, 1494 cm^{-1}; HRMS (ESI) m/z calculated for $C_{27}H_{28}N$ $[M+H]^+$: 366.2216, found 366.2213.



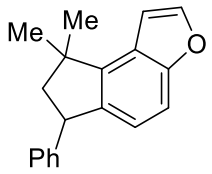
3.3x

3-benzyl-4-methoxy-8,8-dimethyl-6-phenyl-3,6,7,8-tetrahydrocyclopenta[e]indole 3.3x. The general cyclization procedure was followed using 76.3 mg of alkene **3.1x** (0.2 mmol), 7.9 mg of anhydrous benzenesulfonic acid (0.25 mmol) and 2.0 mL of dry toluene. Purification by flash column chromatography (100:0→90:10, hexane:benzene) afforded 5-*endo* product **3.3x** (24.4 mg, 32% yield) as a colorless oil. R_f = 0.58 (80:20 hexanes:benzene visualized by 254 nm UV light and *p*-anisaldehyde stain). ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.32–6.98 (m, 9H), 6.82–6.78 (m, 2H), 6.64–6.61 (m, 1H), 5.73–5.59 (m, 2H), 4.62 (d, *J* = 16.1 Hz, 1H), 4.22 (dd, *J* = 8.6, 6.1 Hz, 1H), 3.78 (s, 3H), 2.80 (dd, *J* = 12.9, 8.6 Hz, 1H), 2.23 (dd, *J* = 13.0, 6.1 Hz, 1H), 1.53 (s, 3H), 1.41 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): ^{13}C NMR (125 MHz, $CDCl_3$): δ 148.0 (C), 144.7 (C), 144.5 (C), 140.3 (C), 129.0 (C), 128.7 (CH), 128.3 (CH), 127.8 (CH), 126.8 (C), 126.7 (CH), 126.6 (CH), 126.4 (CH), 125.3(C), 119.6 (CH), 111.7 (CH), 102.6 (CH), 57.9 (OCH_3), 55.5 (CH_2), 49.8 (CH_2), 44.6 (CH), 39.6 (C), 30.3 (CH_3), 29.8 (CH_3); ATR-FTIR (neat): 2957, 2924, 2858, 1698, 1573, 1495 cm^{-1}; HRMS (ESI) m/z calculated for $C_{27}H_{28}NO$ $[M+H]^+$: 382.2165, found 382.2159.



3.5

5,5-dimethyl-3-phenyl-4,5-dihydro-3H-naphtho[1,8-bc]thiophene 3.5. The general cyclization procedure was followed using 55.7 mg of alkene ***cis*-3.4** (0.2 mmol), 25.3 mg of anhydrous benzenesulfonic acid (0.8 mmol) and 2.0 mL of dry toluene. Purification by flash column chromatography (100% hexanes) afforded inseparable regioisomers **3.5** and **3.6** (**3.5** : **3.6** = 93 : 7, 53.5 mg, brsm 96% yield) as a colorless oil. R_f = 0.66 (80:20 hexanes:benzene visualized by 254 nm UV light and *p*-anisaldehyde stain). Selected spectral data for **3.5**: ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.74 (dd, *J* = 5.6, 3.3 Hz, 1H), 7.55 (dd, *J* = 8.3, 1.3 Hz), 7.4–7.3 (m, 5H), 7.15 (appr s, 1H), 6.68 (d, *J* = 2.0 Hz, 1H), 4.26 (ddd, *J* = 13.1, 4.4, 2.1 Hz, 1H), 2.19 (appr t, *J* = 13.1 Hz, 1H), 1.99 (dd, *J* = 13.0, 4.4 Hz, 1H), 1.54(s, 3H), 1.41(s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 144.3 (C), 143.8 (C), 139.2 (C), 137.7 (C), 136.3 (C), 128.6 (CH), 128.4 (CH), 126.8 (CH), 124.8 (CH), 120.0 (CH), 119.8 (CH), 118.6 (CH), 48.0 (CH_2), 41.3 (CH), 30.4 (CH_3), 28.6 (CH_3); HRMS (ESI) m/z calculated for $C_{19}H_{18}S$ $[M]^+$: 278.1129, found: 278.1096.

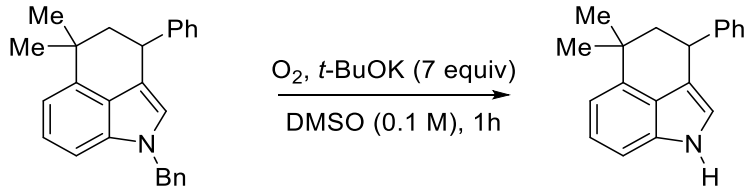


3.8

8,8-dimethyl-6-phenyl-7,8-dihydro-6H-indeno[5,4-b]furan 3.8. Modified The general cyclization procedure was followed using 52.5 mg of alkene ***cis*-3.7** (0.2 mmol), 25.3 mg of anhydrous benzenesulfonic acid (0.8 mmol) and 2.0 mL of dry toluene at 80 °C. Purification by flash column chromatography (100% hexanes) afforded **3.8 (**17.0 mg, 31% yield) as a colorless oil. R_f = 0.50 (80:20 hexanes:benzene visualized by 254 nm UV light and *p*-anisaldehyde stain). Selected spectral data for **3.8**: ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.65 (d, *J* = 2.2 Hz, 1H), 7.36–7.22 (m, 6H), 6.89 (dd, *J* = 2.3, 1.0 Hz, 1H), 6.79 (dd, *J* = 8.4, 1.0 Hz, 1H), 4.48-4.45 (m, 1H), 2.49 (dd, *J* = 12.6, 7.7 Hz, 1H), 2.07 (dd, *J* = 12.6, 9.7 Hz, 1H), 1.59 (s, 3H), 1.39 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 155.3 (C), 145.8 (C), 144.9 (CH), 144.6 (C), 139.1 (C), 128.4 (CH), 128.3 (CH), 126.3 (CH), 122.2 (CH), 121.1 (CH), 109.7 (CH), 104.4 (CH), 53.4 (CH_2), 49.2 (CH), 44.1 (C), 28.9 (CH_3), 27.8 (CH_3); HRMS (ESI) m/z calculated for $C_{19}H_{18}O$ $[M]^+$: 262.1358, found: 262.1368.

Scheme 19. Deprotection of Benzyl Indole

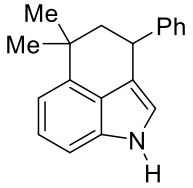
A. Deprotection Procedure



3.2a **3.2h**

To a solution of 71.0 mg of **3.2a** (0.2 mmol) in DMSO (0.2 mL, 10 equiv) was added 0.9 mL (7 equiv) *t*-BuOK (1.6 M in THF) with O_2 purging into the solution. The reaction was allowed to stir and being monitored by TLC. The N-Bn indole was fully consumed after an hour and the reaction was quenched with saturated NH_4Cl solution and the deprotected indole was extraction with EtOAc (3x10.0 mL). The combined organic layers were washed with brine and dried over anhydrous sodium sulfate before concentrated under reduced pressure. The crude product was then transferred to silica gel packed column chromatography (100:0→70:30, hexanes:benzene).

B. Synthesis and Characterization of Deprotected Indole



3.2h

5,5-dimethyl-3-phenyl-1,3,4,5-tetrahydrobenzo[cd]indole 3.2h. The deprotection procedure was followed using 71.0 mg of **3.2a** (0.2 mmol) in DMSO (0.2 mL, 10 equiv) and 0.9 mL *t*-BuOK (1.4 mmol, 1.6 M solution in THF)**.** Purification by flash column chromatography (100:0→70:30, hexane:benzene) afforded pure **3.2h** (24.0 mg, 91% yield) as white wax. R_f = 0.35 (80:20 hexanes:benzene visualized by 254 nm UV light and *p*-anisaldehyde stain). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.93 (br s, 1H), 7.43–7.41 (m, 2H), 7.37–7.34 (m, 2H), 7.29–7.26 (m, 1H), 7.23–7.19 (m, 2H), 7.08–7.04 (m, 1H), 6.65 (t, *J* = 2.0 Hz, 1H), 4.30 (ddd, *J* = 12.3, 4.5, 1.6 Hz, 1H), 2.08 (t, *J* = 12.6 Hz, 1H), 1.95 (dd, *J* = 12.9, 4.4 Hz, 1H), 1.50 (s, 3H), 1.37 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 145.8(C), 140.6 (C), 134.2 (C), 128.6 (CH), 128.3 (CH), 126.6 (CH), 126.2 (C), 122.9 (CH), 118.5 (CH), 118.0 (C), 113.2 (CH), 108.3 (CH), 50.2 (CH_2), 38.4 (CH), 35.7 (C), 30.3 (CH_3), 28.2 (CH_3); HRMS (ESI) m/z calculated for $C_{19}H_{20}N$ $[M+H]^+$: 262.1596, found 262.1589.

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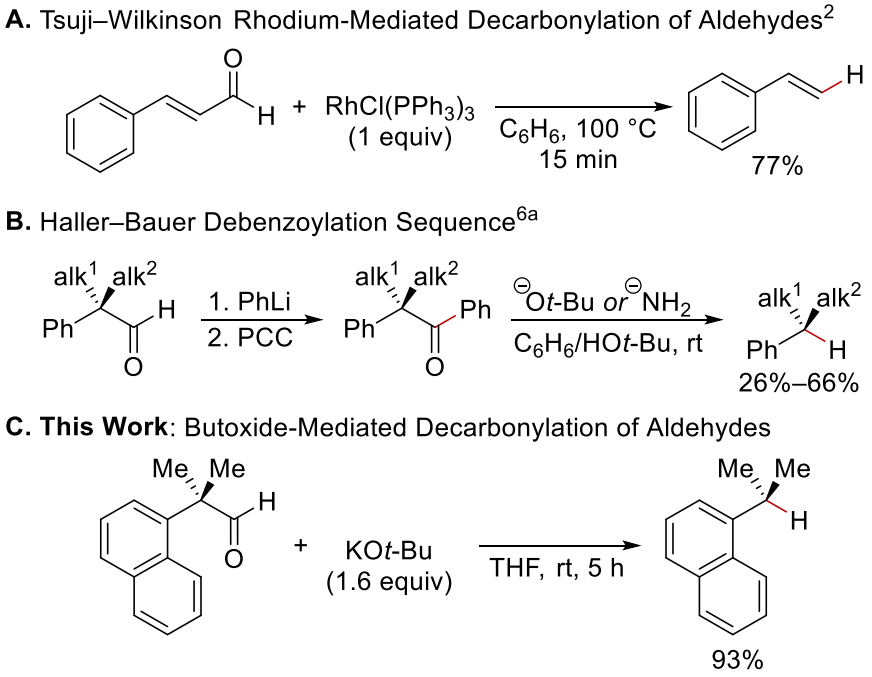
Chapter 4

Ambient Temperature *tert*-Butoxide-Mediated Decarbonylation of α-Quaternary Homobenzaldehydes

Background

The decarbonylation of aldehydes is an important synthetic transformation, as exemplified by its strategic application in natural product total synthesis.[1] However, existing methods are prohibitively expensive. For example, the Tsuji–Wilkinson decarbonylation of alkenyl aldehydes requires a stoichiometric amount of rhodium and high temperature (Scheme 1A),[2,3] while the Haller–Bauer butoxide-mediated debenzoylation must be preceded by a phenylation/oxidation sequence.[4,6] A general, mild, base-mediated aldehyde decarbonylation method has not been developed, perhaps due to competing disproportionation reactions.[5,7,8] In this chapter, a *tert*-butoxide-mediated decarbonylation of quaternary homobenzaldehydes and related arenes and heteroarenes (Scheme 1C) is described. Widely administered as a base and catalyst, the use of *tert*-butoxide as a reactant is somewhat uncommon.[9,10,11]

Scheme 20. Methods for Deformylation

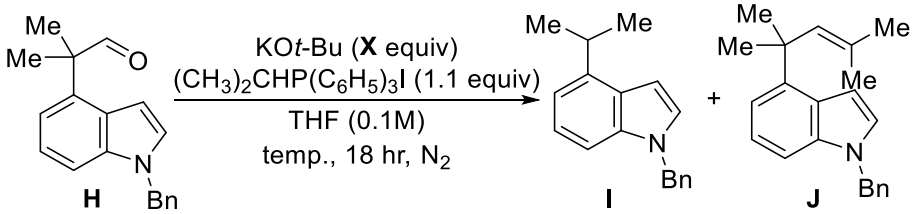


Our group and collabrators have recently started leveraging ***α*-quaternary** homobenzaldehydes as synthetic intermediates and reactants, respectively, which have been presented in previous two chapters in this dissertation. In the course of the development of new alkene functionalization reactions of homobenzylstyrenes (Chapter 3) I observed that indolic aldehyde **H** was inert to Wittig olefination using triphenylisopropylphosphonium iodide under our typical conditions[12] (Table 9, entry 1). Elevating the temperature slightly led to some decarbonylation (entry 2), while additional KO*t*-Bu (1.6 equiv) led to an impressive yield of **I** at ambient temperature (entry 3). We

further scrutinized this outcome using naphthyl analog **4.3b** as a cheaper alternative to indole (Table 10). Absent base, isopropyltriphenylphosphonium iodide did not trigger any conversion (entry 1). No conversion was observed using NaH as base, but decarbonylation again occurred readily with KO*t*-Bu (entry 3). Excitingly, KO*t*-Bu is the sole additive needed for the reaction (entry 4). Decarbonylation is largely prohibited when the reaction is performed open to air (entry 5). Conversion decreases slightly when molecular sieves are used (entry 6), suggesting a possible complementary role for water (see below). NaO*t*-Bu was similarly effective (entry 7), but lithium di-*iso*-propyl amide (LDA) led to decomposition—no Cannizzaro disproportionation was observed, perhaps due to steric encumbrance (entry 8).[13] Potassium hydroxide afforded no reaction in aprotic or protic solvents (entries 9 and 10, respectively). Solvent evaluation revealed that DMF was also well tolerated (entry 11), while HO*t*-Bu inhibited the reaction (not shown).[14] Applying TEMPO as a radical inhibitor decreased the yield slightly (entry 12).[15]

Results and Discussion

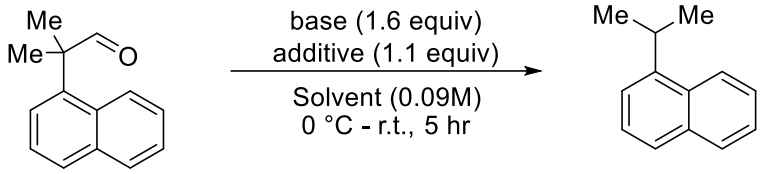
Table 9. Discovery of Quaternary Homobenzladehyde Decarbonylation[a]



entry	**X**	temp. (°C)	conv (%)	yield of **I** (%)	yield of **J** (%)
1	1.1	0-r.t.	<5	n.d.	n.d.
2	1.1	0-45	53	25	<5
3	1.6	0-r.t.	100	72	<5

[a] Conversions and yields were determined by ^{1}H NMR using 1,3,5-trimethoxybenzene as an internal standard.

Table 10. Reaction Optimization of Base Mediated Aldehyde Decarbonylation[a]



4.3b **4.4b**

entry	Base[b]	additive	main solvent	conv. (%)	yield (%)
1	none	$(CH_3)_2CHP(C_6H_5)_3I$	THF	<5	n.d.
2	NaH	$(CH_3)_2CHP(C_6H_5)_3I$	THF	<5	n.d.
3	KO*t*-Bu	$(CH_3)_2CHP(C_6H_5)_3I$	THF	>95	78
4	KO*t*-Bu	none	THF	>95	89
5[c]	KO*t*-Bu	none	THF	100	17
6	KO*t*-Bu	4 Å mol. Sieves[d]	THF	78	70
7	NaO*t*-Bu	none	THF	>95	87
8	LDA	none	THF	>95	<5
9	KOH	none	THF	<5	n.d.
10[e]	KOH	HO*t*-Bu	THF	<5	n.d.
11	KO*t*-Bu[f]	none	DMF	>95	74
12	KO*t*-Bu	TEMPO	THF	>95	62

[a] Reactions were conducted on 0.1 mmol scale and under N_2 atmosphere unless otherwise noted. Conversions and yields were determined by ^1H NMR using 1,3,5-trimethoxybenzene as an internal standard. [b] Base formulations: NaH (60 wt % in oil); KO*t*-Bu (1.6 M solution in THF); KOH and K_2CO_3 (solid); LDA (2.0 M solution); NaO*t*-Bu (2.0 M in THF). [c] Reaction was conducted under air. [d] 100% w/w. [e] Base and 1.6 equiv HO*t*-Bu sonicated for 5 minutes. [f] Used solid KO*t*-Bu.

Turning the attention to reaction scope (Figure 1), simple *gem*-dimethyl homobenzaldehydes (**4.1a**–**4.1c**) afforded lower yield than the aforementioned indole and naphthyl analogs. For instance, **4.2a** was only observed in 11% NMR yield.[16] Methoxy-bearing substrates **4.1b** and **4.1c** were similarly low yielding, but the yield improved significantly with a phenyl substituent in the *para* position, affording **4.2d** in 67% yield and thereby highlighting the reaction's electronic sensitivity. Shifting to cyclic *gem*-dialkyls, *α*-cyclopropyl (**4.1e**) and *α*-cyclobutyl (**4.1f**) substrates were decarbonylated in just 9% and 24% yield, respectively, but cyclopentyl (**4.1g**) and cyclohexyl (**4.1h**) substrates were isolated in increasing yield (44% and 76%, respectively), suggesting that a diminished Thorpe–Ingold effect accelerates these reactions. Other monoaryl substrates evaluated include tetralin **1i** and triphenylacetaldehyde **4.1j**, both of which underwent

deformylation in good yield (61% and 79%, respectively). To our surprise, cyclopentane containing substrate **4.4a** was prepared with doubled efficiency compared to **4.2g**. To investigate the role of water in the reaction, a 1mmol scale using model substrate **4.3b** was conducted with addition of minimal D_2O (5 μL), which maintained excellent yield in deformylation. Pleasantly, it also revealed a proton to deuteron incorporation (2:1). Deformylation proceeded with no restriction at a different position on naphthyl substrate to afford **4.4c** in good yield. In benzofurans, **4.4d** was obtained in good yield as well. Surprisingly, **4.4e** could not be prepared efficiently and a dearomatized side product was detected, which set forth a radical mechanistic hypothesis (Figure 2). Several *α-gem*-dimethyl aryl scaffolds with extended delocalization were also explored. For example, benzyl protected homoindolyl aldehyde could be deformylated with little disruption. Most intriguingly, both EDG and EWG-equipped indole substituents, **4.4g** and **4.4f**, were prepared efficiently recommending radical character of the intermediate. In addition, fragmentation was equally successful for methyl-substituted indoles to achieve **4.4i** and **4.4j**. Deformylation on other heteroarene substrates, such as benzothiophene to afford **4.4k**-**4.4o**, was also fruitful. In most cases, it showed no *regio*-effect except for **4.4l** (27% yield) due to the potential dearomatization as observed with **4.4e**. Our next targets were tri-aromatic frameworks such as carbazole, dibenzothiophene and dibenzofuran and good to excellent yields resulted (**4.6a**-**4.6d**) in all cases.

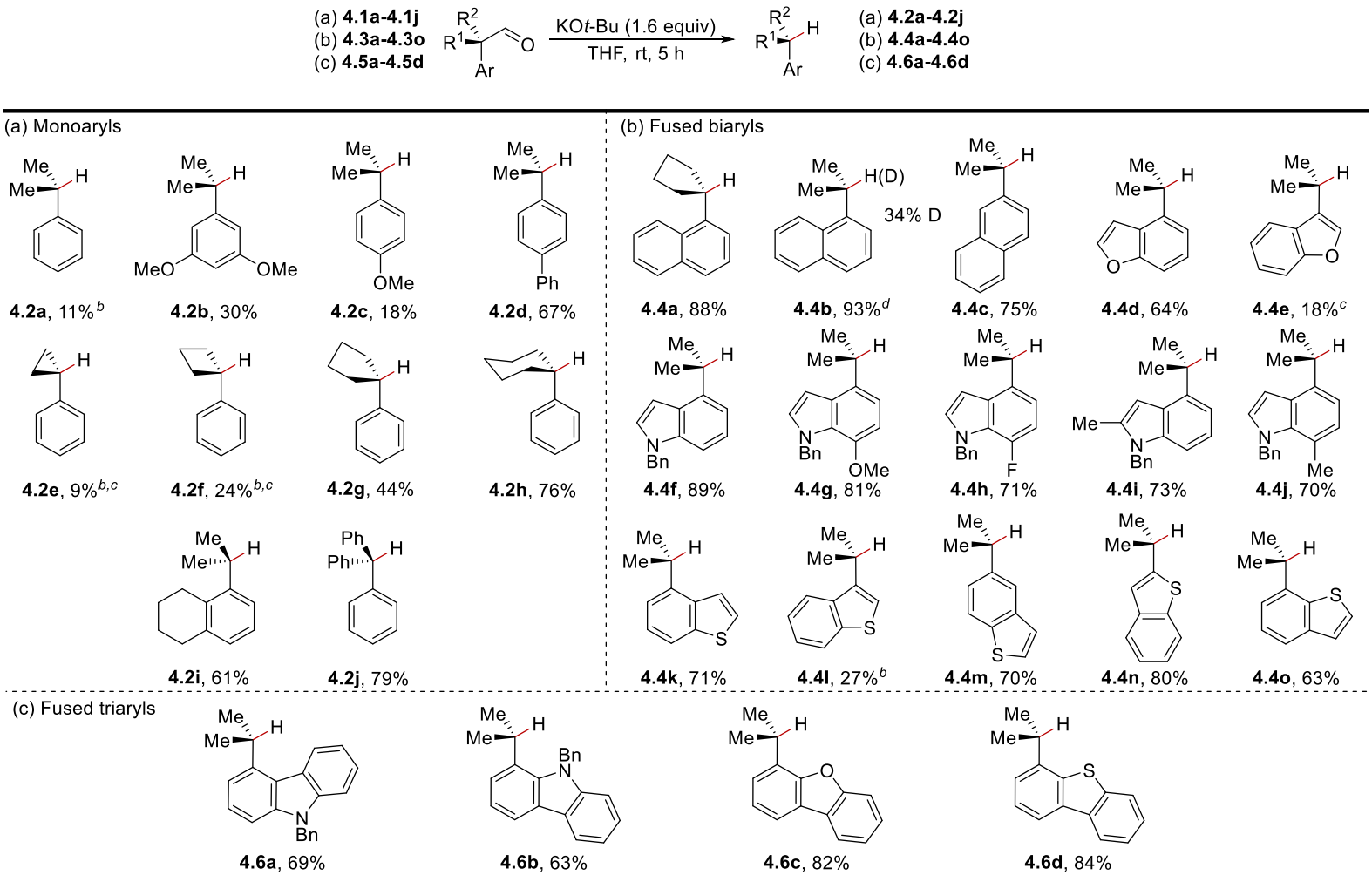
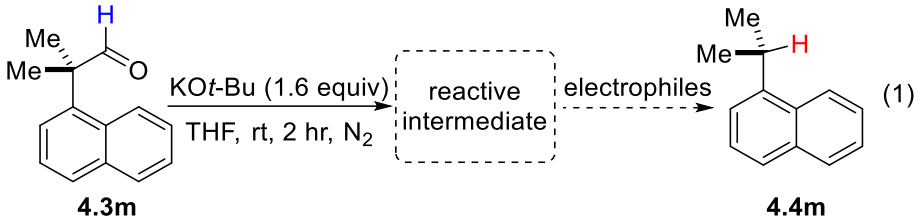
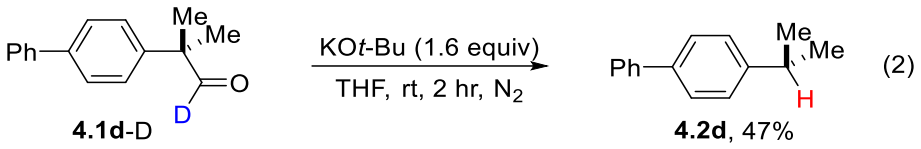


Figure 1. Scope evaluation of decarbonylation on quaternary center containing aldehydes. [a]Reactions were conducted on a 0.3 mmol of aldehyde. Unless otherwise noted, all yields referred to isolated yields. [b]NMR yield using 1,3,5-trimethoxybenzne as an internal standard. [c]product volatile under high-vac. [d]reaction was conducted using 1mmol of **4.3b** with 5 μL of D_2O.

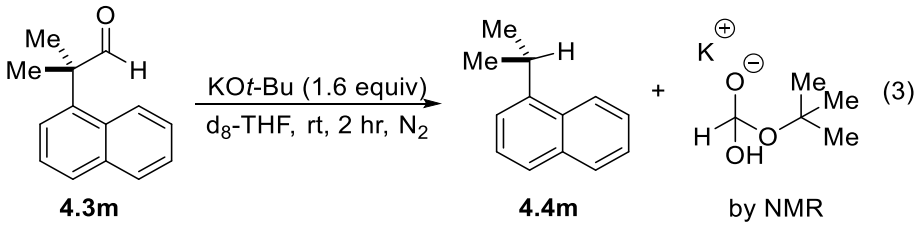
To elucidate the lifetime of the cleaved intermediate, electrophiles, such as selectfluor®, ethyl bromide and D_2O were applied to quench the reaction (eq 1). To our surprise, all resulted the same C-C bond cleavage to provide hydrocarbon. Thus, suggestively, water was involved early in the reaction process.



To eliminate decarbonylation mechanism *via* CO extraction, a deuterated aldehyde **4.1d-D** was prepared. In spite a 20% reduction in yield compared to **4.1d-H**, no deuteron retention was observed in **4.2d** (eq 2).



Furthermore, using d_8-THF yielded no deuteration, and a *tert*-butylformate equivalence was suspected based on ^{1}H NMR analysis (eq 3).



This along with synthesis of **4.4m** (1 mmol) revealed that water was the sole H source. Intriguingly, when α–aryl aldehyde was positioned at C3 on benzofuran, an unexpected dihydrobenzofuran side product **4.7** was isolated (Figure 2). The observation of this kinetic product indicates that radical process is more predominant because dearomatization through anionic process is disfavored when the carbanion is at C2 position in K' (path I). On the other hand, an oxygen radical is likely preferred in L' (path II).

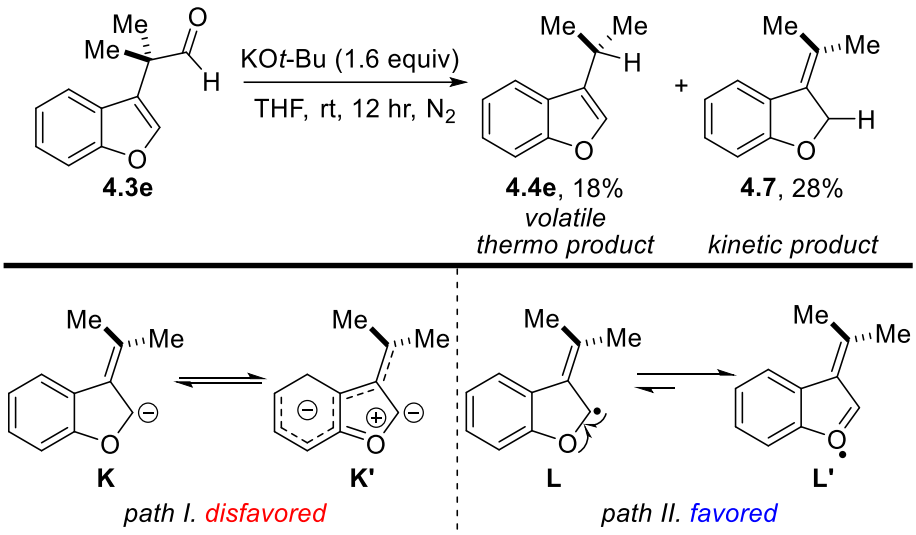
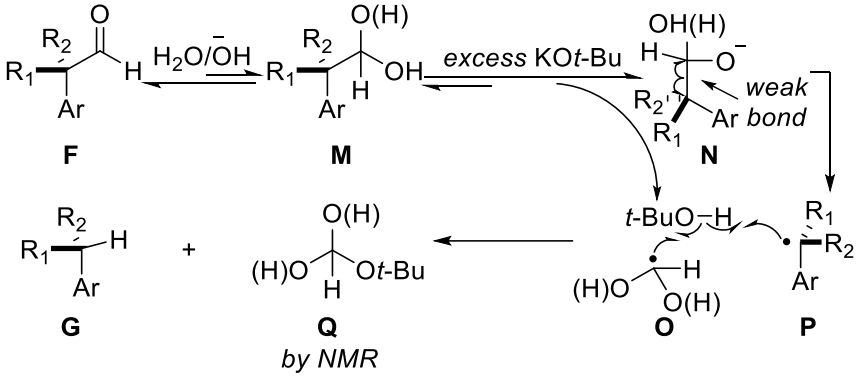


Figure 2. Dihydrobenzofuran formation suggests a radical pathway.

Thus, we hypothesize that the mechanism (Scheme 2) is initiated by a mixture of H_2O/KOH/KO*t*-Bu to form a *gem*-diol intermediate **M** or it's mono-deprotonated equivalence from aldehyde **F**, for which the tetrameric structure of KO*t*-Bu in THF may be accountable.[17]

Scheme 21. A Plausible Mechanism: Water Induced Homolytic Cleavage via Geminal Diol Intermediate



This is consistent with the decomposition result when the reaction was conducted in an open vessel (table 2, entry 5) because **M** is extremely sensitive to oxygen to afford carboxylic acid and peroxide under basic condition. Indeed, a benzylic alcohol product could be isolated through Baeyer-Villiger oxidation. Since KO*t*-Bu is in excess, deprotonation happens promptly according to Le Chatelier's principle to afford *tet*-alkoxide **N** and HO*t*-Bu, which may explain the sluggish reactivity with addition of HO*t*-Bu. It is then followed by a homolysis to provide single electron species **O** and **P**. Then, previously generated HO*t*-Bu is split by the radicals to afford **Q** (detected by NMR in *d*-THF without workup) and hydrocarbon **G**. Notably, both mono- or di-alkoxide as in **N**

likely proceed through fragmentation because less than stoichiometric KO*t*-Bu (1.6 equiv) can be used, which also indicated KOH was not the sole initiator (nucleophile) during **F→M**. Although it has been reported that the ratio between heterolytic and homolytic cleavage is metal- dependent in *tert*-alkoxide **N**,[18] the formation of **4.7** along with TEMPO experiment suggest that the cleavage more likely proceeds through homolytic radical pathway.

Conclusion

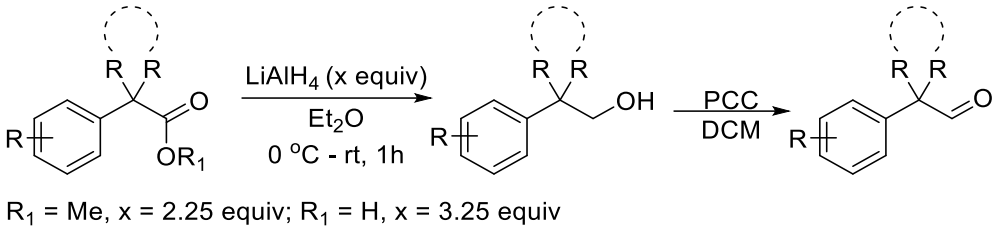
A discovery of an unprecedented MO*t*-Bu/H_2O mediated decarbonylation of non-enolizable quaternary center containing homo-aryl aldehydes has been demonstrated in this chapter, which futures a possible homolytic sp^3-sp^2 C-C bond cleavage. This method overcomes the limitation of C-C bond cleavage of aldehyde groups that are in general, sensitive under strong basic conditions.

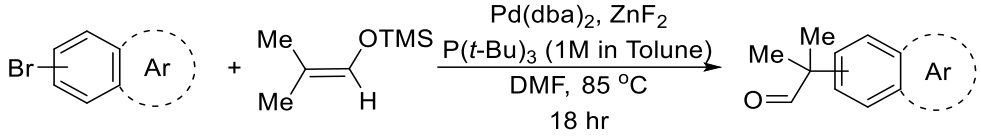
Experimental

General Considerations

Silyl enol ethers were used as purchased from Gelest. A Mettler Toledo XS105 balance (repeatable to 0.1 mg) was used to measure mass. Flash column chromatography was performed using 40–63 μm 60 Å silica. Melting points were obtained on an electrothermal melting point apparatus and are uncorrected. NMR spectra were obtained on Agilent spectrometers. ^{1}H NMR spectra were obtained at 400 or 500 MHz and referenced to the residual $CHCl_3$ singlet at 7.26 ppm unless otherwise noted. The abbreviations s, d, t, q, dd, td, qd, and m stand for the resonance multiplicities singlet, doublet, triplet, quartet, doublet of doublet, triplet of doublet, quartet of doublet, and multiplet, respectively ('app.' denotes apparent). ^{13}C NMR spectra were obtained at 100 or 125 MHz and referenced to the center line of the $CDCl_3$ triplet at 77.2 ppm unless otherwise noted. Carbon atom degree of substitution was determined using ^{1}H–^{13}C HSQC. ^{19}F NMR spectra were obtained at 376 MHz subsequent to ^{1}H NMR acquisition and were otherwise unreferenced. FT-IR analysis was performed on a Thermo-Nicolet 380 using a diamond GladiATR from Pike technologies. APCI/ESI HRMS data were obtained on an Agilent LC-TOF (NSF CHE-0541848); EI HRMS data were obtained on a Waters GCT GC/MS (NSF CHE-0742001). Glassware for all reactions was oven-dried at 145 °C and cooled in a desiccator prior to use.

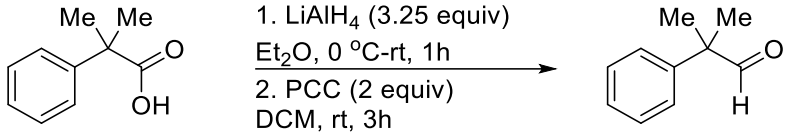
Scheme 22. General Approaches for Aldehydes





Scheme 23. General Procedures for Aldehydes

A. General Procedure 1: Reduction-Oxidation of Carboxylic Acid or Ester

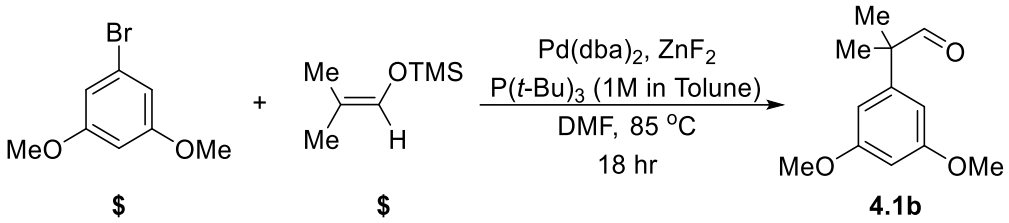


$ **4.1a**

2-methyl-2-phenylpropanal 4.1a. To a dry 250 mL round bottom flask charged with a PTFE coated magnetic stir bar were added 2-methyl-2-phenylpropanoic acid (1.0 g, 6.1 mmol, 1.00 equiv) and diethyl ether (122 mL, 0.05 M). The solution was then cooled to 0 ºC and purged with nitrogen for 5 minutes. To the cold mixture was added LiAlH4 (753.4 mg, 3.25 equiv) in 4 portions over 10 minutes (Caution! Excessive hydrogen gas generation for the first portion!). The reaction was slowly warmed to room temperature and stirred for one hour. Once all carboxylic acid was consumed (monitored by TLC), the reaction was carefully quenched by addition of 1 M aqueous HCl (~10 mL) at 0 ºC. The primary alcohol intermediate was extracted with diethyl ether three times. The ether solution was dried over anhydrous magnesium sulfate before it was concentrated in vacuo. The crude product was then dissolved with DCM (24.5 mL, 0.25 M). The solution was chilled in an ice bath and allowed to purge with argon. To this inert gas-protected mixture, PCC (2.60 g, 2.0 equiv) was added. The reaction was allowed to stir at room temperature for 3 hours until all primary alcohol had been consumed as determined by TLC. The mixture was then diluted with EtOAc (20 mL) and the organic solution was filtered through a pad of Celite®. The combined liquid was dried over anhydrous sodium sulfate. All organic solvents were

removed under reduced pressure and the residue was purified by flash column chromatography on SiO_2 using hexanes:EtOAc (100:0→92:8) to afford aldehyde (701 mg, 77% yield), which was prone to decomposition over time. ^{1}H NMR (400 MHz, CDCl3) δ: 9.50 (s, 1H), 7.40-7.27 (m, 5H), 1.47 (s, 6H); ^{13}C NMR (100 MHz, CDCl3) δ: 202.3, 141.4, 129.0, 127.4, 126.8, 50.6, 22.6. The spectral data matched those reported in the literature.[12a]

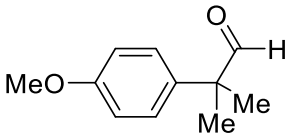
B. General procedure 2: Pd-catalyzed Cross-Coupling



$ $ 4.1b

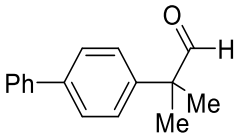
2-(3,5-dimethoxyphenyl)-2-methylpropanal 4.1b. To a dry 50 mL round bottom flask charged with a PTFE-coated magnetic stir bar were added 396.0 mg of zinc fluoride (3.83 mmol, 1.50 equiv) and 146.6 mg of bis(dibenzylideneacetone) palladium (0) (0.26 mmol, 0.10 equiv). The reaction flask was then sealed with a rubber septum, degassed, and back-filled with nitrogen. Then 25.5 mL of DMF (0.1 M) and 553.5 mg of 1-bromo-3,5-dimethoxybenzene (2.55 mmol, 1.00 equiv) were added at room temperature. To this mixture were added 0.8 mL of a 1.0 M solution of tri-*tert*-butylphosphine in toluene (0.80 mmol, 0.31 equiv) and 0.7 mL of trimethyl((2-methylprop-1-en-1-yl)oxy)silane (3.83 mmol, 1.50 equiv) at the same time through syringe. The reaction mixture was heated to 85 °C and was allowed to stir in an N_2 atmosphere overnight. The reaction mixture was cooled to room temperature before filtration through Celite®, and the Celite® cake was washed with 15 mL of ethyl acetate. The filtrate was concentrated under reduced pressure. The crude product was purified by silica gel chromatography (100:0→85:15 hexanes:ethyl acetate) to afford **1b** as colorless oil (419.6 mg, 79%). ^{1}H NMR (400 MHz, CDCl3): δ 9.44 (s, 1H), 6.39 (s, 2H), 6.37 (s, 1H), 3.76 (s, 6H), 1.41 (s, 6H); ^{13}C NMR (100 MHz, CDCl3): δ 201.8 (C=O), 161.1 (C), 143.6 (C), 105.1 (CH), 98.6 (CH), 55.3 (CH3), 50.5 (C), 24.0 (CH3). The spectral data matched those reported in the literature.[12a]

C. Synthesis and Characterization of Aldehydes



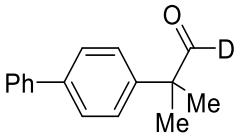
4.1c

2-(4-Methoxyphenyl)-2-methylpropanal 4.1c. General procedure 1 was followed using 2.50 g of methyl 2-(4-methoxyphenyl)-2-methylpropanoate (12.0 mmol) and 1.03 g of $LiAlH_4$ (27.0 mmol) in 120 mL of Et2O. The crude isolate was then oxidized using 5.3 g of PCC (24 mmol) in 60 mL of DCM. Purification by flash column chromatography (100:0→80:20 hexanes:EtOAc) afforded **4.1c** as light yellow oil. (1.65 g, 77% yield over two steps). ^{1}H NMR (400 MHz, CDCl3): δ 9.44 (s, 1H), 7.19 (d, *J* = 8.4 Hz, 2H), 6.91 S13 (d, *J* = 8.6 Hz, 2H), 3.78 (s, 3H), 1.43 (s, 6H); ^{13}C NMR (100 MHz, CDCl3): δ 202.1 (C=O), 158.7 (C), 133.0 (C), 127.8 (CH), 114.2 (CH), 55.2 (CH3), 49.7 (C), 22.5 (CH3). The spectral data matched those reported in the literature.[12a]



4.1d

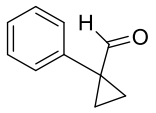
2-([1,1'-Biphenyl]-4-yl)-2-methylpropanal 4.1d. General procedure 1 was followed using 5.62 g of methyl 2-([1,1'-biphenyl]-4-yl)-2-methylpropanoate (22.1 mmol) and 1.89 g of $LiAlH_4$ (49.7 mmol) in 220 mL of Et2O. The crude isolate was then oxidized using 9.7 g of PCC (42.2 mmol) in 89 mL of DCM. Purification by flash column chromatography (100:0→80:20 hexanes:EtOAc) afforded **4.1d** as a light yellow oil (3.0 g, 60% yield over two steps). ^{1}H NMR (400 MHz, CDCl3): δ 9.64 (s, 1H), 7.77-7.65 (m, 3H), 7.55 (t, *J* = 7.5 Hz, 1H), 7.48-7.45 (m, 5H), 1.61 (s, 6H); ^{13}C NMR (100 MHz, CDCl3): δ 202.0 (C=O), 140.6 (C), 140.3 (C), 140.2 (C), 129.0 (CH), 128.5 (CH), 127.7 (CH), 127.3 (CH), 127.2 (CH), 50.3(C), 22.62 (CH3). The spectral data matched those reported in the literature.[12a]



4.1d-D

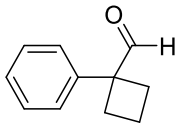
2-([1,1'-biphenyl]-4-yl)-2-methylpropanal-1-d 4.1d. General procedure 1 was followed using 1.12 g of methyl 2-([1,1'-biphenyl]-4-yl)-2-methylpropanoate (4.42 mmol) and 378.5 mg of $LiAlD_4$ (9.94 mmol) in 44.0 mL of Et2O. The crude isolate was then oxidized using 1.94 g of PCC (8.44 mmol) in 17.8 mL of DCM. Purification by flash column chromatography (100:0→80:20 hexanes:EtOAc) afforded **4.1d-D** as a light yellow oil

(408.3 g, 41% yield over two steps). ^{1}H NMR (400 MHz, CDCl3): δ 7.68 – 7.56 (m, 4H), 7.46 (t, *J* = 7.7 Hz, 2H), 7.41 – 7.33 (m, 3H), 1.52 (s, 6H); ^{13}C NMR (100 MHz, CDCl3): δ 201.8 (m, C=O), 140.5 (C), 140.2 (2C), 128.8 (CH), 127.5 (CH), 127.4 (CH), 127.2 (CH), 127.1 (CH), 50.1(m, C), 22.5 (CH_3).



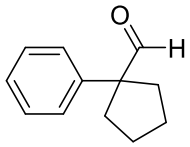
4.1e

1-phenylcyclopropane-1-carbaldehyde 4.1e. General procedure 1 was followed using 486.57 mg of 1-phenylcyclopropane-1-carboxylic acid (3.0 mmol) and 370.01 mg of $LiAlH_4$ (9.75 mmol) in 30 mL of Et_2O. The crude isolate was then oxidized using 1.29 g of PCC (6.0 mmol) in 12 mL of DCM. Purification by flash column chromatography (100:0→95:5 hexanes:EtOAc) afforded **4.1e** as a light yellow oil (179.81 mg, 41% over two steps). ^{1}H NMR (500 MHz, $CDCl_3$): δ 9.31 (s, 1H), 7.83 – 6.64 (m, 5H), 1.73 – 1.54 (m, 2H), 1.49 – 1.35 (m, 2H);^{13}C NMR (100 MHz, CDCl3): δ 201.1 (C=O), 137.5 (C), 130.1 (CH), 128.6 (CH), 127.7 (CH), 37.5 (C), 16.2 (CH_2). The spectral data matched those reported in the literature.[19]



4.1f

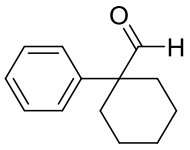
1-Phenylcyclobutane-1-carbaldehyde 4.1f. General procedure 1 was followed using 1.07 g of 1-phenylcyclobutane-1-carboxylic acid (6.1 mmol) and 0.753 g of $LiAlH_4$ (19.8 mmol) in 122 mL of Et_2O. The crude isolate was then oxidized using 2.72 g of PCC (12.2 mmol) in 25 mL of DCM. Purification by flash column chromatography (100:0→95:5 hexanes:EtOAc) afforded **4.1f** as a light yellow oil (723.2 mg, 74% over two steps). ^{1}H NMR (400 MHz, CDCl3): δ 9.55 (s, 1H), 7.41-7.37 (m, 2H), 7.28 (t, *J* = 7.1 Hz, 1H), 7.17 (d, *J* = 7.7 Hz, 2H), 2.78-2.70 (m, 2H), 2.46-2.38 (m, 2H), 2.08-1.88 (m, 2H);^{13}C NMR (100 MHz, CDCl3): δ 199.4 (C=O), 130.9 (C), 128.8 (CH), 127.0 (CH), 126.4 (CH), 57.6 (C), 28.3 (CH2), 15.8 (CH2). The spectral data matched those reported in the literature.[12a]



4.1g

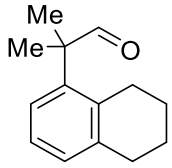
1-Phenylcyclopentane-1-carbaldehyde 4.1g. General procedure 1 was followed using 1.16 g of 1-phenylcyclopentane-1-carboxylic acid (6.1 mmol) and 0.753 g of $LiAlH_4$ (19.8

mmol) in 122 mL of Et2O. The crude isolate was then oxidized using 2.72 g of PCC (12.2 mmol) in 25 mL of DCM. Purification by flash column chromatography (100:0→95:5 hexanes:EtOAc) afforded **4.1g** as a light yellow oil (0.71 g, 67% over two steps). ^{1}H NMR (400 MHz, CDCl3): δ: 9.31 (s, 1H), 7.24–7.28 (m, 2H), 7.15–7.19 (m, 3H), 2.41–2.47 (m, 2H), 1.76–1.83 (m, 2H), 1.64–1.68 (m, 2H), 1.54–1.60 (m, 2H); ^{13}C NMR (100 MHz, CDCl3): δ: 200.6, 140.3, 128.7, 127.6, 127.1, 63.6, 32.3, 24.2. The spectral data matched those reported in the literature.[12a]



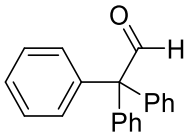
4.1h

1-Phenylcyclohexane-1-carbaldehyde 4.1h. General procedure 1 was followed using 1.25 g of 1-phenylcyclohexane-1-carboxylic acid (6.1 mmol) and 0.753 g of $LiAlH_4$ (19.8 mmol) in 122 mL of Et2O. The crude isolate was then oxidized using 2.72 g of PCC (12.2 mmol) in 25 mL of DCM. Purification by flash column chromatography (100:0→95:5 hexanes:EtOAc) afforded **4.1h** as a light yellow oil (0.90 g, 78% over two steps). ^{1}H NMR (400 MHz, CDCl3): δ 9.38 (s, 1H), 7.41-7.31 (m, 4H), 7.30-7.24 (m, 1H), 2.38-2.26 (m, 2H), 1.91-1.80 (m, 2H), 1.73-1.57 (m, 3H), 1.56-1.43 (m, 2H), 1.37-1.26 (m, 1H); ^{13}C NMR (100 MHz, CDCl3): δ 202.3 (C=O), 139.7 (C), 128.9 (CH), 127.2 (CH), 127.1 (CH), 54.4 (C), 31.3 (CH2), 25.6 (CH2), 22.8 (CH2). The spectral data matched those reported in the literature.[12a]



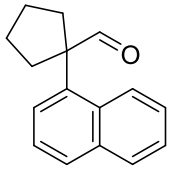
4.1i

2-methyl-2-(5,6,7,8-tetrahydronaphthalen-1-yl)propanal 4.1i. The general cross-coupling procedure 2 was followed using 538.3 mg of 5-bromo-1,2,3,4-tetrahydronaphthalene (2.55 mmol), 396.0 mg of zinc fluoride (3.83 mmol), 146.6 mg of bis(dibenzylideneacetone)palladium(0) (0.26 mmol), 0.8 mL (0.8 mmol) tri-tertbutylphosphine, and 0.7 mL of trimethyl((2-methylprop-1-en-1-yl)oxy)silane (3.83 mmol) in 25.5 mL of DMF. Purification by silica gel chromatography (100:0→70:30 hexanes: benzene) afforded **4.1j** (407.5 g, 79% yield) as a colorless oil. ^{1}H NMR (500 MHz, $CDCl_3$): δ 9.65 (s, 1H), 7.36–7.15 (m, 2H), 7.09 (dd, *J* = 7.4, 1.4 Hz, 1H), 2.83 (t, *J* = 6.3 Hz, 2H), 2.49 (t, *J* = 6.0 Hz, 2H), 1.86 – 1.69 (m, 4H), 1.46 (s, 6H); ^{13}C NMR (126 MHz, $CDCl_3$): δ 204.7 (C=O), 140.3 (C), 139.1 (C), 136.6 (C), 128.9 (CH), 126.1 (CH), 124.1 (CH), 51.1 (C), 30.1 (CH_2), 27.8 (CH_2), 23.4 (CH_3), 23.4 (CH_2), 23.0 (CH_2), 22.4 (CH_2).



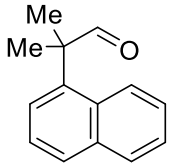
4.1j

2,2,2-triphenylacetaldehyde 4.1j. General procedure 1 was followed using 1.50 g of 2,2,2-triphenylacetic acid (5.2 mmol) and 0.643 g of $LiAlH_4$ (16.9 mmol) in 104 mL of Et2O. The crude isolate was then oxidized using 1.68 g of PCC (7.80 mmol) in 25 mL of DCM. Purification by flash column chromatography (100:0→95:5 hexanes:EtOAc) afforded **4.1j** as a light yellow powder (778.9 mg, 55% over two steps). The ^{1}H NMR data matched those reported by Henderson and Heathcock.[20]



4.3a

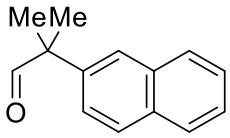
1-(naphthalen-1-yl)cyclopentane-1-carbaldehyde 4.3a. General procedure 1 was followed using 1.20 g of 1-(naphthalen-1-yl)cyclopentane-1-carboxylic acid (5.0 mmol) and 0.62 g of $LiAlH_4$ (16.25 mmol) in 100 mL of Et_2O. The crude isolate was then oxidized using 2.16 g of PCC (10.0 mmol) in 25 mL of DCM. Purification by flash column chromatography (100:0→95:5 hexanes:EtOAc) afforded **4.3a** as a colorless oil (583.2 mg, 52% over two steps); ^{1}H NMR (400 MHz, CDCl3): δ 9.49 (d, *J* = 1.2 Hz, 1H), 7.94 – 7.73 (m, 3H), 7.60 (d, *J* = 7.3 Hz, 1H), 7.54 – 7.44 (m, 3H), 2.66 (dd, *J* = 12.7, 6.4 Hz, 2H), 2.14 (dd, *J* = 13.4, 7.0 Hz, 2H), 1.86 – 1.65 (m, 4H); ^{13}C NMR (100 MHz, CDCl3): δ 201.8 (C=O), 129.1 (CH), 128.7 (CH), 126.1 (CH), 125.6 (CH), 125.4 (CH), 125.2 (CH), 124.7 (CH), 33.2 (CH_2), 24.8 (CH_2), quaternary carbons were interfered.



4.3b

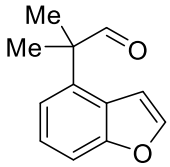
2-methyl-2-(naphthalen-1-yl)propanel 4.3b. General procedure 2 was followed using 528.0 mg of 1-bromonaphthalane (2.55 mmol), 396.0 mg of zinc fluoride (3.83 mmol, 1.5 equiv), 146.6 mg of bis(dibenzylideneacetone)palladium(0) (0.26 mmol), 0.8 mL (0.8 mmol) tri-tertbutylphosphine, and 0.7 mL of trimethyl((2-methylprop-1-en-1-yl)oxy)silane (3.83 mmol) in 25.5 mL of DMF. Purification by silica gel chromatography (100:0→80:20 hexanes: benzene) afforded **4.3m** (429.8 g, 85% yield) as a colorless oil. ^{1}H NMR (400 MHz, CDCl3): δ 9.69 (s, 1H), 7.95 – 7.88 (m, 1H), 7.85 (dt, *J* = 8.1, 1.1 Hz, 1H), 7.80 – 7.74 (m, 1H), 7.58 (dd, *J* = 7.3, 1.4 Hz, 1H), 7.55 – 7.50 (m, 1H), 7.51 – 7.45

(m, 2H), 1.65 (s, 6H); ^{13}C NMR (100 MHz, CDCl3): δ 204.9 (C=O), 138.1 (C), 134.5 (C), 131.3 (C), 129.4 (CH), 128.8 (CH), 126.3 (CH), 125.5 (CH), 125.4 (CH), 124.6 (CH), 124.5 (CH), 51.1 (C), 23.5 (CH3). The spectral data matched those reported in the literature.[21]



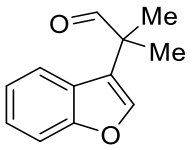
4.3c

2-methyl-2-(naphthalen-2-yl)propanel 4.3c. General procedure 2 was followed using 528.0 mg of 2-bromonaphthalane (2.55 mmol), 396.0 mg of zinc fluoride (3.83 mmol, 1.5 equiv), 146.6 mg of bis(dibenzylideneacetone)palladium(0) (0.26 mmol), 0.8 mL (0.8 mmol) tri-tertbutylphosphine, and 0.7 mL of trimethyl((2-methylprop-1-en-1-yl)oxy)silane (3.83 mmol) in 25.5 mL of DMF. Purification by silica gel chromatography (100:0→80:20 hexanes: benzene) afforded **4.3c** (450.0 g, 89% yield) as a colorless oil. The spectral data matched those reported in the literature.[21]



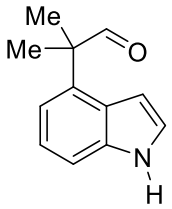
4.3d

2-(Benzofuran-4-yl)-2-methylpropanal 4.3d. The general cross-coupling procedure 2 was followed using 394.1 mg of 4-bromobenzofuran (2.00 mmol), 310.2 mg of zinc fluoride (3.0 mmol), 115.0 mg of bis(dibenzylideneacetone)palladium(0) (0.2 mmol), 0.60 mL of tri-tert-butylphosphine (0.60 mmol), and 0.6 mL of trimethyl(2-methylprop-1-enyloxy)silane (3.0 mmol) in 20.0 mL of DMF. Purification by flash column chromatography (100:0→95:5 hexanes:benzene) afforded **4.3d** (289.0 mg, 77% yield) as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ 9.54 (s, 1 H), 7.60 (appr s, 1H), 7.49 (d, *J* = 8.3 Hz, 1H), 7.33 (t, *J* = 7.9 Hz, 1H), 7.23 (d, *J* = 7.6 Hz, 1H), 6.71 (appr s, 1H), 1.56 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 202.4 (C=O), 155.3 (C), 144.8 (CH), 134.3 (C), 126.0 (C), 124.5 (CH), 120.1 (CH), 111.1 (CH), 105.9 (CH), 50.8 (C), 22.0 (CH_3); HRMS (ESI) m/z calculated for $C_{12}H_{13}O_2$ $[M+H]^+$: 189.0910, found: 189.0903. The spectral data matched those reported in the literature.[12b]



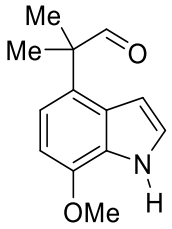
4.3e

2-(Benzofuran-3-yl)-2-methylpropanal 4.3e. The general cross-coupling procedure 2 was followed using 394.1 mg of 3-bromobenzofuran (2.00 mmol), 310.2 mg of zinc fluoride (3.0 mmol), 115.0 mg of bis(dibenzylideneacetone)palladium(0) (0.2 mmol), 0.60 mL of tri-tert-butylphosphine (0.60 mmol), and 0.6 mL of trimethyl(2-methylprop-1-enyloxy)silane (3.0 mmol) in 20.0 mL of DMF. Purification by flash column chromatography (100:0→95:5 hexanes:benzene) afforded **4.3e** (243.9 mg, 65% yield) as a yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ 9.57 (s, 1H), 7.61 – 7.38 (m, 4H), 7.37 – 7.27 (m, 1H), 7.24 (q, *J* = 7.4, 6.4 Hz, 1H), 1.56 (s, 7H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 201.5 (C=O), 155.9 (C), 141.8 (CH), 126.0 (C), 124.6 (CH), 122.7 (CH), 121.7 (C), 120.8 (CH), 111.8 (CH), 45.9 (C), 21.4 (CH_3).



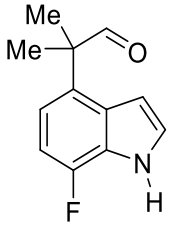
S4.1

2-(1H-Indol-4-yl)-2-methylpropanal S4.1. The general cross-coupling procedure 2 was followed using 535.1 mg of 4-bromoindole (2.55 mmol), 396.0 mg of zinc fluoride (3.83 mmol), 146.6 mg of bis(dibenzylideneacetone)palladium(0) (0.26 mmol), 0.8 mL of tri-*tert*-butylphosphine (0.80 mmol), and 0.7 mL of trimethyl(2-methylprop-1-enyloxy)silane (3.83 mmol) in 25.5 mL of DMF. Purification by flash column chromatography (100:0→80:20 hexanes:benzne) afforded **S4.1** as a colorless oil (405.8 mg, 85%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 9.62 (s, 1H), 8.38 (s, 1H), 7.38 (d, *J* = 8.1 Hz, 1H), 7.26 (app. t, *J* = 7.8 Hz, 1H), 7.18 (m, 1H), 7.14 (d, *J* = 7.4 Hz, 1H), 6.48–6.46 (m, 1H), 1.61 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 204.2 (C=O), 136.4 (C), 133.5 (C), 126.3 (C), 124.4 (CH), 122.3 (CH), 117.4 (CH), 111.2 (CH), 102.2 (CH), 51.2 (C), 22.1 (CH_3); ATR-FTIR (neat): 3409, 2971, 2933, 2809, 2709, 1717, 1611, 1503 cm^{-1}; HRMS (ESI) m/z calculated for $C_{12}H_{14}NO$ $[M+H]^+$: 188.1070, found 188.1072. The spectral data matched those reported in the literature.[12b]



S4.2

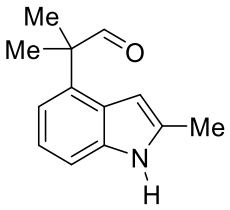
2-(7-Methoxy-1H-indol-4-yl)-2-methylpropanal S4.2. The general cross-coupling procedure 2 was followed using 500.0 mg of 4-bromo-7-methoxy-1H-indole (2.30 mmol), 356.7 mg of zinc fluoride (3.45 mmol), 132.2 mg of bis(dibenzylideneacetone)palladium(0) (0.23 mmol), 0.7 mL of tri-tert-butylphosphine (0.69 mmol), and 0.6 mL of trimethyl(2-methylprop-1-enyloxy)silane (3.45 mmol) in 23.0 mL of DMF. Purification by flash column chromatography (100:0:0→92:3:5 hexanes:benzene:ethyl acetate) afforded **S4.2** (284.8 mg, 57% yield) as a yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ 9.57 (s, 1 H), 8.59 (s, br, 1 H), 7.16 (dd, *J* = 3.2, 2.5 Hz, 1H), 7.03 (d, *J* = 8.0 Hz, 1H), 6.68 (d, *J* = 8.0 Hz, 1H), 6.46 (dd, *J* = 3.2, 2.2 Hz, 1H), 3.98 (s, 3H), 1.58 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 203.8 (C=O), 146.0 (C), 127.3 (C), 126.7 (C), 125.8 (C), 123.7 (CH), 117.6 (CH), 102.5 (CH), 101.5 (CH), 55.3 (OCH_3), 50.4 (C), 22.0 (CH_3); HRMS (ESI) m/z calculated for $C_{13}H_{16}NO_2$ $[M+H]^+$: 218.1176, found 218.1178. The spectral data matched those reported in the literature.[12b]



S4.3

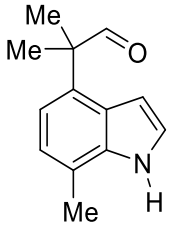
2-(7-Fluoro-1H-indol-4-yl)-2-methylpropanal S4.3. The general cross-coupling procedure 2 was followed using 513.2 mg of 4-bromo-7-fluoroindole (2.44 mmol), 378.4 mg of zinc fluoride (3.66 mmol), 140.3 mg of bis(dibenzylideneacetone)palladium(0) (0.24 mmol), 0.7 mL of tri-tert-butylphosphine (0.73 mmol), and 0.7 mL of trimethyl(2-methylprop-1-enyloxy)silane (3.66 mmol) in 24.0 mL of DMF. Purification by flash column chromatography (100:0→80:20 hexanes:benzene) afforded **S4.3** (345.5 mg, 69% yield) as colorless oil. ^{1}H NMR (500 MHz, $CDCl_3$): δ 9.58 (s, 1H), 8.82 (s, br, 1H), 7.23 (t, *J* = 2.8 Hz, 1H), 7.04–7.01 (m, 1H), 6.96–6.93 (m, 1H), 6.50–6.49 (m, 1H), 1.59 (s, 6H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 203.9 (C=O), 149.5 (d, *J* = 244.4 Hz, C-F), 129.7 (d, *J* = 5.3 Hz, C), 129.1 (d, *J* = 3.6 Hz, C), 125.1 (CH), 124.6 (d, *J* = 13.6 Hz, C), 117.6 (d, *J* = 6.5 Hz, CH), 106.6 (d, *J* = 16.0 Hz, CH), 102.9 (d, *J* = 1.9 Hz, CH), 50.2 (C), 21.68 (CH_3); ^{19} F NMR (470 MHz, $CDCl_3$): δ –136.2; ATR-FTIR (neat): 3318, 3090, 3071, 2970, 1728,

1649, 1619, 1525 cm^{-1}; HRMS (ESI) m/z calculated for $C_{12}H_{13}FNO$ $[M+H]^+$: 206.0976, found 206.0977. The spectral data matched those reported in the literature.[12b]



S4.4

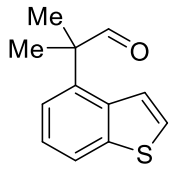
2-Methyl-2-(2-methyl-1H-indol-4-yl)propanal S4.4. The general cross-coupling procedure 2 was followed using 500.0 mg of 4-bromo-2-methyl-1H-indole (2.38 mmol), 369.1 mg of zinc fluoride (3.57 mmol), 136.9 mg of bis(dibenzylideneacetone)palladium(0) (0.24 mmol), 0.7 mL of tri-*tert*-butylphosphine (0.71 mmol), and 0.7 mL of trimethyl(2-methylprop-1-enyloxy)silane (3.57 mmol) in 23.8 mL of DMF. Purification by flash column chromatography (100:0→80:20 hexanes:benzne) afforded **S4.4** as a light yellow oil (273.0 mg, 57%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 9.58 (s, 1 H), 8.06 (s, 1 H), 7.27 (d, *J* = 8.1 Hz, 1H), 7.16 (appr. t, *J* = 7.7 Hz, 1H), 7.08 (dd, *J* = 7.4, 1.0 Hz, 1H), 6.16 (s, 1H), 2.41 (s, 3H), 1.57 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 204.2 (C=O), 136.6 (C), 135.4 (C), 132.4 (C), 127.5 (C), 121.3 (CH), 117.2 (CH), 110.3 (CH), 100.1 (CH), 51.1 (C), 22.0 (CH_3), 13.9 (CH_3); HRMS (ESI) m/z calculated for $C_{13}H_{16}NO$ $[M+H]^+$: 202.1226, found 202.1229. The spectral data matched those reported in the literature.[12b]



S4.5

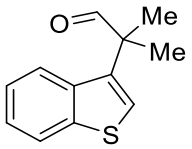
2-Methyl-2-(7-methyl-1H-indol-4-yl)propanal S4.5. The general cross-coupling procedure 2 was followed using 500.0 mg of 4-bromo-7-methyl-1H-indole (2.38 mmol), 369.1 mg of zinc fluoride (3.57 mmol), 136.9 mg of bis(dibenzylideneacetone)palladium(0) (0.24 mmol), 0.7 mL of tri-*tert*-butylphosphine (0.71 mmol), and 0.7 mL of trimethyl(2-methylprop-1-enyloxy)silane (3.57 mmol) in 23.8 mL of DMF. Purification by flash column chromatography (100:0→90:10 hexanes:benzene) afforded **S4.5** as a colorless oil (349.7 mg, 73%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 9.62 (s, 1 H), 8.71 (s, 1 H), 7.19–7.17 (m, 1H), 7.05 (app. s, 2H), 6.50 (dd, *J* = 3.3, 1.9 Hz, 1H), 2.49 (s, 3H), 1.59 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 204.2 (C=O), 135.9 (C), 130.9 (C), 125.7 (C), 124.2 (CH), 122.5 (CH), 120.4 (C), 117.4 (CH), 102.3 (CH), 50.8 (C), 22.0 (CH_3), 16.6 (CH_3); ATR-FTIR (neat): 3472, 2963, 2920, 1711 cm^{-1}; HRMS (ESI) m/z calculated for $C_{13}H_{16}NO$

$[M+H]^+$: 202.1226, found 202.1228. The spectral data matched those reported in the literature.[12b]



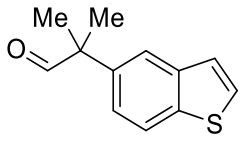
4.3k

2-(Benzo[b]thiophen-4-yl)-2-methylpropanal 4.3k. The general cross-coupling procedure 2 was followed using 485.5 mg of 4-bromobenzo[b]thiophene (2.30 mmol), 356.7 mg of zinc fluoride (3.45 mmol), 132.3 mg of bis(dibenzylideneacetone)palladium(0) (0.23 mmol), 0.7 mL of tri-tert-butylphosphine (0.69 mmol), and 0.6 mL of trimethyl(2-methylprop-1-enyloxy)silane (3.45 mmol) in 23.0 mL of DMF. Purification by flash column chromatography (100:0→90:10 hexanes:benzene) afforded **4.3k** (352.4 mg, 75% yield) as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ 9.58 (s, 1 H), 7.88 (td, *J* = 4.5, 0.9 Hz, 1H), 7.46 (d, *J* = 5.7 Hz, 1H), 7.40(dd, *J* = 4.6, 0.8 Hz, 2H), 7.28 (dd, *J* = 5.7, 1.0 Hz, 1H), 1.59 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 203.5 (C=O), 141.2 (C), 137.6 (C), 136.4 (C), 126.8 (CH), 124.4 (CH), 122.6 (CH), 122.3 (CH), 121.9 (CH), 51.4 (C), 22.4 (CH_3). The spectral data matched those reported in the literature.[12b]



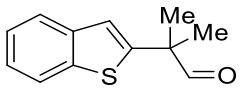
4.3l

2-(Benzo[b]thiophen-3-yl)-2-methylpropanal 4.3l. The general cross-coupling procedure 2 was followed using 485.5 mg of 3-bromobenzo[b]thiophene (2.30 mmol), 356.7 mg of zinc fluoride (3.45 mmol), 132.3 mg of bis(dibenzylideneacetone)palladium(0) (0.23 mmol), 0.7 mL of tri-tert-butylphosphine (0.69 mmol), and 0.6 mL of trimethyl(2-methylprop-1-enyloxy)silane (3.45 mmol) in 23.0 mL of DMF. Purification by flash column chromatography (100:0→90:10 hexanes:benzene) afforded **4.3l** (293.7 mg, 63% yield) as a colorless oil. ^{1}H NMR (400 MHz, Chloroform-*d*): δ 9.54 (s, 1H), 7.99 – 7.77 (m, 1H), 7.75 – 7.54 (m, 1H), 7.41 – 7.30 (m, 3H), 1.60 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 202.5 (C=O), 141.1 (C), 137.2 (C), 136.5 (C), 124.3 (CH), 124.2 (CH), 123.5 (CH), 123.2 (CH), 123.0 (CH), 49.3 (C), 22.0 (CH_3).



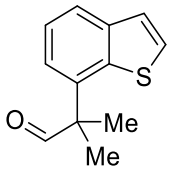
4.3m

2-(Benzo[b]thiophen-5-yl)-2-methylpropanal 4.3m. The general cross-coupling procedure 2 was followed using 485.5 mg of 5-bromobenzo[b]thiophene (2.30 mmol), 356.7 mg of zinc fluoride (3.45 mmol), 132.3 mg of bis(dibenzylideneacetone)palladium(0) (0.23 mmol), 0.7 mL of tri-tert-butylphosphine (0.69 mmol), and 0.6 mL of trimethyl(2-methylprop-1-enyloxy)silane (3.45 mmol) in 23.0 mL of DMF. Purification by flash column chromatography (100:0→90:10 hexanes:benzene) afforded **4.3m** (329.3 mg, 70% yield) as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ 9.54 (s, 1H), 7.99 – 7.77 (m, 1H), 7.75 – 7.54 (m, 1H), 7.41 – 7.30 (m, 2H), 1.60 (s, 6H).^{13}C NMR (100 MHz, CDCl3): δ 202.2 (C=O), 140.1 (C), 138.7 (C), 137.4 (C), 127.3 (CH), 123.9 (CH), 123.2 (CH), 122.9 (CH), 121.6 (CH), 50.4 (C), 22.7 (CH_3).



4.3n

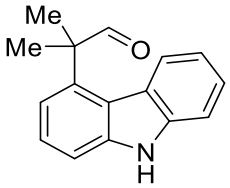
2-(Benzo[b]thiophen-2-yl)-2-methylpropanal 4.3n. The general cross-coupling procedure 2 was followed using 485.5 mg of 2-bromobenzo[b]thiophene (2.30 mmol), 356.7 mg of zinc fluoride (3.45 mmol), 132.3 mg of bis(dibenzylideneacetone)palladium(0) (0.23 mmol), 0.7 mL of tri-tert-butylphosphine (0.69 mmol), and 0.6 mL of trimethyl(2-methylprop-1-enyloxy)silane (3.45 mmol) in 23.0 mL of DMF. Purification by flash column chromatography (100:0→90:10 hexanes:benzene) afforded **4.3n** (277.5 mg, 59% yield) as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ 9.56 (s, 1H), 7.99 – 7.60 (m, 2H), 7.41 – 7.27 (m, 2H), 7.15 (d, *J* = 0.8 Hz, 1H), 1.60 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 199.7 (C=O), 146.6 (C), 139.8 (C), 139.5 (C), 124.5 (CH), 124.3 (CH), 123.4 (CH), 122.2 (CH), 121.4 (CH), 49.4 (C), 23.3 (CH_3).



4.3o

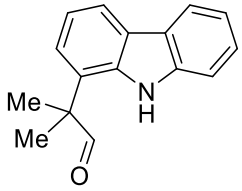
2-(Benzo[b]thiophen-7-yl)-2-methylpropanal 4.3o. The general cross-coupling procedure 2 was followed using 485.5 mg of 7-bromobenzo[b]thiophene (2.30 mmol), 356.7 mg of zinc fluoride (3.45 mmol), 132.3 mg of bis(dibenzylideneacetone)palladium(0) (0.23 mmol), 0.7 mL of tri-tert-butylphosphine (0.69 mmol), and 0.6 mL of trimethyl(2-

methylprop-1-enyloxy)silane (3.45 mmol) in 23.0 mL of DMF. Purification by flash column chromatography (100:0→90:10 hexanes:benzene) afforded **4.3o** (357.0 mg, 76% yield) as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ 9.62 (s, 1H), 7.81 (dd, *J* = 7.8, 1.1 Hz, 1H), 7.55 – 7.28 (m, 4H), 1.64 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 202.3 (C=O), 141.0 (C), 138.1 (C), 136.1 (C), 126.2 (CH), 124.7 (CH), 124.1 (CH), 123.5 (CH), 122.4 (CH), 51.6 (C), 21.3 (CH_3).



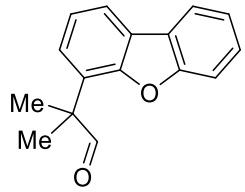
S4.6

2-(9H-carbazol-4-yl)-2-methylpropanal S4.6. The general cross-coupling procedure 2 was followed using 492.2 mg of 4-bromo-9H-carbazole (2.00 mmol), 310.2 mg of zinc fluoride (3 mmol), 115.0 mg of bis(dibenzylideneacetone)palladium(0) (0.2 mmol), 0.60 mL of tri-tert-butylphosphine (0.60 mmol), and 0.6 mL of trimethyl(2-methylprop-1-enyloxy)silane (3.0 mmol) in 20.0 mL of DMF. Purification by flash column chromatography (100:0→95:5 hexanes:benzene) afforded **S4.6** (322.7 mg, 68% yield) as a yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ 9.81 (s, 1H), 8.32 (s, 1H), 7.87 (d, *J* = 8.2 Hz, 1H), 7.55 – 7.36 (m, 4H), 7.33 – 7.10 (m, 2H), 1.73 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 205.1 (C=O), 140.4 (C), 139.5 (C), 137.9 (C), 125.9 (CH) , 125.5 (CH), 124.4 (CH), 121.1 (C), 121.0 (C), 119.5 (CH), 117.8 (CH), 110.5 (2CH). 51.3 (C), 22.8 (CH_3).



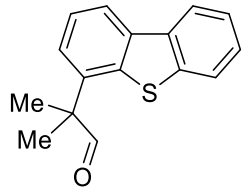
S4.7

2-(9H-carbazol-1-yl)-2-methylpropanal S4.7. The general cross-coupling procedure 2 was followed using 492.2 mg of 1-bromo-9H-carbazole (2.00 mmol), 310.2 mg of zinc fluoride (3 mmol), 115.0 mg of bis(dibenzylideneacetone)palladium(0) (0.2 mmol), 0.60 mL of tri-tert-butylphosphine (0.60 mmol), and 0.6 mL of trimethyl(2-methylprop-1-enyloxy)silane (3.0 mmol) in 20.0 mL of DMF. Purification by flash column chromatography (100:0→95:5 hexanes:benzene) afforded **S4.7** (275.3 mg, 58% yield) as a yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ 9.48 (s, 1H), 8.43 (s, 1H), 8.17 – 8.00 (m, 2H), 7.53 – 7.39 (m, 3H), 7.32 (t, *J* = 7.7 Hz, 1H), 7.28 – 7.21 (m, 1H), 1.68 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 203.3 (C=O), 139.5 (C), 137.7 (C), 126.1 (CH), 124.4 (C), 123.3 (CH), 122.7 (C), 121.2 (C), 120.3 (CH), 120.2 (CH), 119.9 (CH), 119.6 (CH), 111.0 (CH). 49.8 (C), 21.1 (CH_3).



4.5c

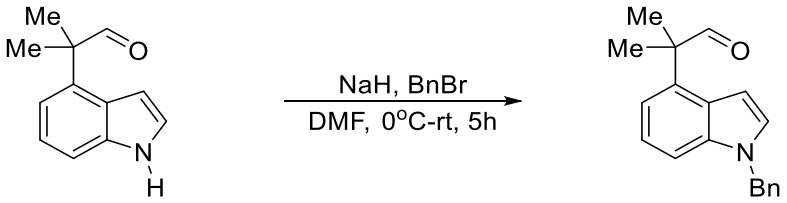
2-(dibenzo[b,d]furan-4-yl)-2-methylpropanal 4.5c. The general cross-coupling procedure 2 was followed using 494.2 mg of 4-bromodibenzo[b,d]furan (2.00 mmol), 310.2 mg of zinc fluoride (3 mmol), 115.0 mg of bis(dibenzylideneacetone)palladium(0) (0.2 mmol), 0.60 mL of tri-tert-butylphosphine (0.60 mmol), and 0.6 mL of trimethyl(2-methylprop-1-enyloxy)silane (3.0 mmol) in 20.0 mL of DMF. Purification by flash column chromatography (100:0→95:5 hexanes:benzene) afforded **4.5c** (367.0 mg, 77% yield) as a colorless oil. ^{1}H NMR (500 MHz, $CDCl_3$): δ 9.90 (s, 1H), 7.97 (dd, *J* = 7.8, 1.3 Hz, 1H), 7.93 (dd, *J* = 6.7, 2.2 Hz, 1H), 7.61 (d, *J* = 8.3 Hz, 1H), 7.48 (ddd, *J* = 8.4, 7.3, 1.4 Hz, 1H), 7.44 – 7.32 (m, 3H), 1.70 (s, 6H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 202.6 (C=O), 155.9 (C), 154.1 (C), 128.4 (C), 127.4 (CH), 126.7 (C), 124.8 (C), 124.7 (CH), 124.0 (C), 123.3 (CH), 123.0 (CH), 120.7 (CH), 120.1 (CH), 111.9 (CH), 49.3 (C), 22.0 (CH_3).



4.5d

2-(dibenzo[b,d]thiophen-4-yl)-2-methylpropanal 4.5d. The general cross-coupling procedure 2 was followed using 526.3 mg of 4-bromodibenzo[b,d]thiophene (2.00 mmol), 310.2 mg of zinc fluoride (3 mmol), 115.0 mg of bis(dibenzylideneacetone)palladium(0) (0.2 mmol), 0.60 mL of tri-tert-butylphosphine (0.60 mmol), and 0.6 mL of trimethyl(2-methylprop-1-enyloxy)silane (3.0 mmol) in 20.0 mL of DMF. Purification by flash column chromatography (100:0→95:5 hexanes:benzene) afforded **4.5d** (371.4 mg, 73% yield) as a light yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ δ 9.66 (s, 1H), 8.42 – 7.97 (m, 2H), 7.83 (dd, *J* = 6.0, 3.2 Hz, 1H), 7.52 (d, *J* = 7.7 Hz, 1H), 7.50 – 7.42 (m, 3H), 1.66 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 202.48 (C=O), 138.9 (C), 138.1 (C), 136.9 (C), 136.4 (C), 135.1 (C), 127.0 (CH), 125.0 (CH), 124.8 (CH), 124.5 (CH), 122.4 (CH), 121.6 (CH), 121.1 (CH), 51.7 (C), 21.3 (CH_3).

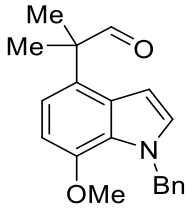
D. General procedure 3: Benzylation of Indole/Carbazole Aldehydes



S4.1 **4.3f**

2-(1-Benzyl-1H-indol-4-yl)-2-methylpropanal 4.3f. To a solution of aldehyde **S4.1** (1.5 g, 8.0 mmol) in DMF (16.0 mL, 0.5M), 60 wt.% NaH (480.0 mg, 1.5 eq.) was added in an ice bath through four portions. The slurry was allowed to stir at room temperature for 30 minutes before it was cooled to 0 °C. Benzyl bromide (2.0 g, 1.5 eq.) was diluted with DMF (1.0 mL) before it was added to the deprotonated indole solution through syringe. The reaction mixture was then allowed to stir at room temperature for overnight. After the complete consumption of the starting material indicated by TLC, the reaction was quenched by addition of saturated $NaHCO_3$ solution (~10mL) at 0 °C. The product was extracted with EtOAc three times and combined organic layers were washed with brine and dried over anhydrous sodium sulfate before it was concentrated under reduced pressure. The crude benzylated aldehyde was flushed through silica gel column with mixture of hexanes and ethyl acetate (hexanes:ethyl acetate , 100:0→90:10) to obtain pure aldehyde **S7** (2.0 g, 89% yield) as light yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ 9.64 (s, 1 H), 7.38 – 7.21 (m, 5H), 7.17 – 7.13 (m, 4H), 6.49 (dd, *J* = 3.3, 0.7 Hz, 1H), 5.33 (s, 2H), 1.62 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 203.8 (C=O), 137.3 (C), 136.8 (C), 133.8 (C), 128.9 (CH), 128.4 (CH), 127.8 (CH), 127.1 (C), 127.0 (CH), 122.0 (CH), 117.2 (CH) , 109.7 (CH), 101.3 (CH), 51.1 (C), 50.3 (CH_2), 22.1 (CH_3); ATR-FTIR (neat): 2970, 2931, 1722 cm^{-1}; HRMS (ESI) m/z calculated for $C_{19}H_{20}NO$ $[M+H]^+$: 278.1539, found 278.1539. The spectral data matched those reported in the literature.[5]

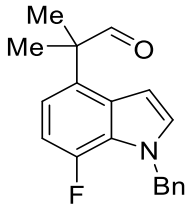
E. Synthesis and Characterization of Benzylated Aldehydes



4.3g

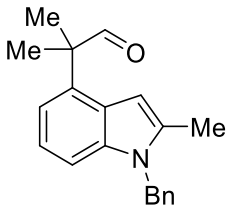
2-(1-benzyl-7-methoxy-1H-indol-4-yl)-2-methylpropanal 4.3g. The general procedure 3 was followed using 434.6 mg of **S4.2** (2.0 mmol), 120.0 mg of 60 wt.% NaH (3.0 mmol) and 514.0 mg of benzyl bromide (3.0 mmol in 1.0 mL DMF) in 10.0 mL DMF. Purification by flash column chromatography (100:0→90:10 hexanes: EtOAc) afforded benzylated

indole **4.3g** (436.5 mg, 71% yield) as colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ 9.57 (s, 1H), 7.33 – 7.24 (m, 3H), 7.16 – 7.10 (m, 2H), 7.06 – 6.97 (m, 2H), 6.66 (d, *J* = 8.1 Hz, 1H), 6.41 (d, *J* = 3.2 Hz, 1H), 5.64 (s, 2H), 3.86 (s, 3H), 1.58 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 204.0 (C=O), 147.4 (C), 139.4 (C), 129.2 (CH), 129.1 (C), 128.5 (CH), 127.2 (CH), 126.8 (CH), 126.1 (C), 126.0 (C), 117.5 (CH), 102.5 (CH), 101.6 (CH), 55.3 (CH_3), 52.6 (CH_2), 50.4 (C), 22.0 (CH_3).



4.3h

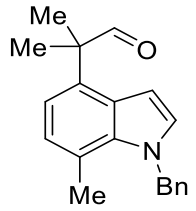
2-(1-benzyl-7-fluoro-1H-indol-4-yl)-2-methylpropanal 4.3h. The general procedure 3 was followed using 410.5 mg of **S4.3** (2.0 mmol), 120.0 mg of 60 wt.% NaH (3.0 mmol) and 514.0 mg of benzyl bromide (3.0 mmol in 1.0 mL DMF) in 10.0 mL DMF. Purification by flash column chromatography (100:0→90:10 hexanes: EtOAc) afforded benzylated indole **4.3h** (455.0 mg, 77% yield) as colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ 9.54 (s, 1H), 7.36 – 7.24 (m, 3H), 7.19 – 7.12 (m, 2H), 7.09 (d, *J* = 3.3 Hz, 1H), 6.98 (dd, *J* = 8.2, 4.2 Hz, 1H), 6.88 (dd, *J* = 12.3, 8.2 Hz, 1H), 6.42 (dd, *J* = 3.3, 2.4 Hz, 1H), 5.48 (s, 2H), 1.55 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 203.4 (C=O), 150.0 (d, *J* = 244.5 Hz, C), 137.9 (C), 130.8 (d, *J* = 5.5 Hz, C), 129.6 (CH), 129.2 (d, *J* = 3.7 Hz, C), 128.7 (CH), 128.1 (d, *J* = 62.3 Hz, C), 127.7 (CH), 126.9 (d, *J* = 0.9 Hz, CH), 117.4 (d, *J* = 6.9 Hz, CH), 107.3 (d, *J* = 18.2 Hz, CH), 102.3 (d, *J* = 1.5 Hz, CH), 52.2 (d, *J* = 6.1 Hz, CH_2), 50.5 (C), 22.0 (CH_3); ^{19} F NMR (376 MHz, $CDCl_3$): δ –136.0.



3.3i

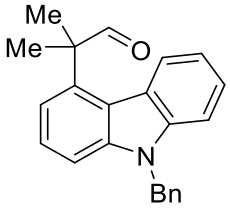
2-(1-benzyl-2-methyl-1H-indol-4-yl)-2-methylpropanal 4.3i. The general procedure 3 was followed using 402.6 mg of **S4.4** (2.0 mmol), 120.0 mg of 60 wt.% NaH (3.0 mmol) and 514.0 mg of benzyl bromide (3.0 mmol in 1.0 mL DMF) in 10.0 mL DMF. Purification by flash column chromatography (100:0→90:10 hexanes: EtOAc) afforded benzylated indole **4.3i** (466.2 mg, 80% yield) as colorless oil. ^{1}H NMR (500 MHz, $CDCl_3$): δ 9.65 (s, 1H), 7.41 (s, 1H), 7.35 – 7.26 (m, 2H), 7.25 – 7.22 (m, 1H), 7.19 (t, *J* = 7.6 Hz, 1H), 7.14 (dd, *J* = 7.2, 1.2 Hz, 1H), 7.02 (dd, *J* = 8.1, 1.4 Hz, 2H), 6.29 (s, 1H), 5.33 (s, 2H), 2.39 (d, *J* = 1.0 Hz, 3H), 1.64 (s, 6H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 203.9 (C=O), 137.6 (C),

136.9 (C), 132.3 (C), 128.8 (CH), 128.4 (C), 127.4 (CH), 126.5 (C), 126.0 (CH), 120.9 (CH), 117.0 (CH), 109.1 (CH), 100.1 (CH), 51.0 (C), 46.6 (CH_2), 21.9 (CH_3), 12.8 (CH_3).



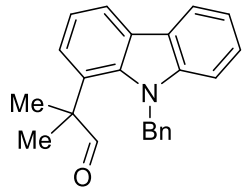
4.3j

2-(1-benzyl-7-methyl-1H-indol-4-yl)-2-methylpropanal 4.3j. The general procedure 3 was followed using 402.6 mg of **S4.5** (2.0 mmol), 120.0 mg of 60 wt.% NaH (3.0 mmol) and 514.0 mg of benzyl bromide (3.0 mmol in 1.0 mL DMF) in 10.0 mL DMF. Purification by flash column chromatography (100:0→90:10 hexanes: EtOAc) afforded benzylated indole **4.3j** (437.1 mg, 75% yield) as colorless oil. ^{1}H NMR (500 MHz, $CDCl_3$): δ 9.64 (s, 1H), 7.37 – 7.23 (m, 3H), 7.13 – 7.01 (m, 2H), 7.02 – 6.90 (m, 3H), 6.49 (d, *J* = 3.3 Hz, 1H), 5.61 (s, 2H), 2.58 (s, 3H), 1.62 (s, 7H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 204.1 (C=O), 139.4 (C), 135.3 (C), 131.6 (C), 130.3 (CH), 128.9 (CH), 128.1 (C), 127.4 (CH), 125.5 (CH), 124.8 (CH), 121.0 (C), 117.4 (CH), 101.4 (CH), 52.3(C), 50.7 (CH_2), 22.0 (CH_3), 19.5 (CH_3).



4.5a

2-(9H-carbazol-4-yl)-2-methylpropanal 4.5a. The general procedure 3 was followed using 474.6 mg of **S4.6** (2.0 mmol), 120.0 mg of 60 wt.% NaH (3.0 mmol) and 514.0 mg of benzyl bromide (3.0 mmol in 1.0 mL DMF) in 10.0 mL DMF. Purification by flash column chromatography (100:0→90:10 hexanes: EtOAc) afforded benzylated indole **4.5a** (576.3 mg, 88% yield) as colorless oi; ^{1}H NMR (500 MHz, $CDCl_3$): δ 9.94 (s, 1H), 8.07 (d, *J* = 8.2 Hz, 1H), 7.61 – 7.47 (m, 4H), 7.42 – 7.16 (m, 7H), 5.60 (s, 2H), 1.85 (s, 6H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 205.1 (C=O), 141.7 (C), 140.8 (C), 138.1 (C), 137.0 (C), 128.9 (CH), 128.5 (C), 127.9 (C), 127.6 (CH), 126.4 (CH), 126.0 (CH), 125.7 (CH), 124.7 (CH), 121.0 (C), 119.4 (CH), 117.8 (CH), 108.9 (2CH), 51.4 (C), 46.6 (CH_2), 23.0 (CH_3).

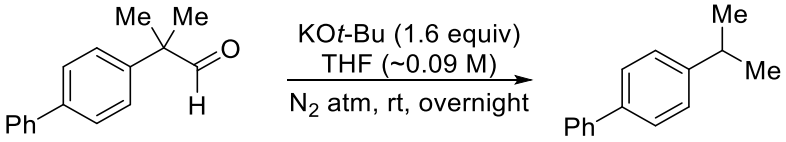


4.5b

2-(9-benzyl-9H-carbazol-1-yl)-2-methylpropanal 4.5b. The general procedure 3 was followed using 474.6 mg of **S4.7** (2.0 mmol), 120.0 mg of 60 wt.% NaH (3.0 mmol) and 514.0 mg of benzyl bromide (3.0 mmol in 1.0 mL DMF) in 10.0 mL DMF. Purification by flash column chromatography (100:0→90:10 hexanes: EtOAc) afforded benzylated indole **4.5b** (589.4 mg, 90% yield) as colorless oi; ^{1}H NMR (400 MHz, $CDCl_3$): δ 9.65 (s, 1H), 8.42 – 7.97 (m, 2H), 7.55 (dd, *J* = 7.7, 1.2 Hz, 1H), 7.39 – 7.32 (m, 2H), 7.26 (td, *J* = 7.4, 1.0 Hz, 1H), 7.20 – 7.12 (m, 4H), 5.60 (s, 2H), 1.62 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 204.5 (C=O), 141.7 (C), 139.4 (C), 137.2 (C), 128.6 (CH), 127.0 (CH), 126.2 (CH), 126.0 (C), 125.9 (C), 125.8 (CH), 125.6 (CH), 123.8 (C), 120.2 (CH), 120.0 (CH), 119.9 (CH), 119.7 (CH), 111.1 (CH), 50.8 (C), 49.7 (CH_2), 24.5 (CH_3).

Scheme 24. Deformylation through C-C Bond Cleavage

A. General procedure 4: KO*t*-Bu Mediated Cleavage



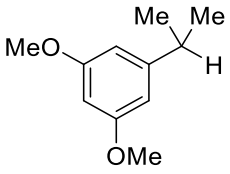
4.1d **4.2d**

In a flame-dried 25 mL round bottom flask charged with a PTFE-coated magnetic stir bar was purged with nitrogen for 10 minutes. To the flask, 0.2 mL KO*t*-Bu solution (1.6M in THF stock solution, 0.32 mmol, 1.6 equiv) was diluted with 1.0 mL dry non-stabilized THF. A pre-nitrogen-purged aldehyde **4.1d** (0.2 mmol, 1 equiv) solution in 1.0 mL THF (0.2M) was then added to the diluted KO*t*-Bu solution dropwise at room temperature. The mixture was then allowed to stir for overnight under positive nitrogen pressure. The reaction was then quenched by addition of aqueous NH_4Cl solution (~5 mL) and EtOAc (~2 mL) and allowed to stir until the color of the solution turned colorless or stabilized. The aqueous layer was extracted with EtOAc (~5 mL) three times and the combined organic layers were washed with brine and dried over sodium sulfate. The dried solution was concentrated under reduced pressure to afford crude deformylated hydrocarbon. The crude oil was then purified by silica gel chromatography.

Notes:

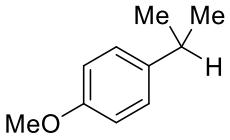
a. For **4.1a**, **4.1b and 4.1c**, a reverse addition (KO*t*-Bu solution added slowly to aldehyde solution in THF) yielded no deformylated hydrocarbon but a total decomposition of the aldehyde.
b. For **4.3a** and **4.3m**, a reverse addition resulted minor to moderate decrease in yields.
c. Decomposition was observed if reaction was conducted under air regardless of the order of the addition.
d. To minimize decomposition, most substrates were mostly conducted using general procedure 4.

B. Synthesis and Characterization of Deformylated Hydrocarbons



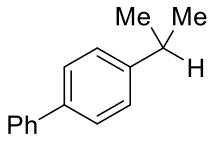
4.2b

1-isopropyl-3,5-dimethoxybenzene 4.2b. The general deformylation procedure was followed using 41.7 mg of **4.1b** (0.2 mmol), 0.2 mL of KO*t*-Bu solution (0.32 mmol) in 2.0 mL THF. Purification by flash column chromatography (100:0→99:1 hexanes:ethyl acetate) to afford **4.2b** as colorless oil (10.82 mg, 30%); ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.46 (d, *J* = 2.4 Hz, 2H), 6.15 (s, 1H), 3.83 (s, 6H), 2.90 (hept, *J* = 6.9 Hz, 1H), 1.30 (d, *J* = 6.9 Hz, 6H). The spectral data matched those reported in the literature.[22]



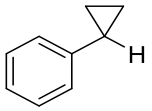
4.2c

1-isopropyl-4-methoxybenzene 4.2c. The general deformylation procedure was followed using 35.6 mg of **4.1c** (0.2 mmol), 0.2 mL of KO*t*-Bu solution (0.32 mmol) in 2.0 mL THF. Purification by flash column chromatography (100:0→99:1 hexanes:ethyl acetate) to afford **4.2c** as colorless oil (5.5 mg, 18%); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.15 (d, *J* = 8.2 Hz, 2H), 6.85 (d, *J* = 8.7 Hz, 2H), 3.79 (s, 2H), 2.87 (hept, *J* = 6.9 Hz, 1H), 1.23 (d, *J* = 6.9 Hz, 6H); ^{13}C NMR (100 MHz, CDCl3): δ 157.6 (C), 141.0 (C), 127.2 (CH), 113.7 (CH), 55.2 (CH_3), 33.3 (C), 24.2 (CH_3). The spectral data matched those reported in the literature.[23]



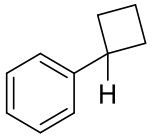
4.2d

4-isopropyl-1,1'-biphenyl 4.2d. The general deformylation procedure was followed using 44.9 mg of **4.1d** (0.2 mmol), 0.2 mL of KO*t*-Bu solution (0.32 mmol) in 2.0 mL THF. Purification by flash column chromatography (100:0→99:1 hexanes:ethyl acetate) to afford **4.2d** as colorless oil (26.3 mg, 67%); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.15 (d, *J* = 8.2 Hz, 2H), 6.85 (d, *J* = 8.7 Hz, 2H), 3.79 (s, 2H), 2.87 (hept, *J* = 6.9 Hz, 1H), 1.23 (d, *J* = 6.9 Hz, 6H); ^{13}C NMR (100 MHz, CDCl3): δ 157.6 (C), 141.0 (C), 127.2 (CH), 113.7 (CH), 55.2 (CH_3), 33.3 (C), 24.2 (CH_3). The spectral data matched those reported in the literature.[24]



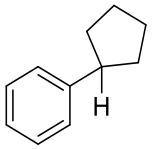
4.2e

cyclopropylbenzene 4.2e. The general deformylation procedure was followed using 23.6 mg of **4.1e** (0.2 mmol), 0.2 mL of KO*t*-Bu solution (0.32 mmol) in 2.0 mL THF. Purification by flash column chromatography (100% hexanes) afforded hydrocarbon **4.2e** (9% NMR yield).



4.2f

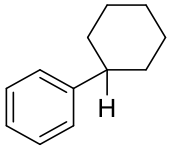
cyclobutylbenzene 4.2f. The general deformylation procedure was followed using 34.85 mg of **4.1f** (0.2 mmol), 0.2 mL of KO*t*-Bu solution (0.32 mmol) in 2.0 mL THF. Purification by flash column chromatography (100% hexanes) afforded hydrocarbon **4.2f** as colorless oil (12.87 mg, 44%); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.37 – 7.12 (m, 5H), 3.55 (p, *J* = 8.8 Hz, 1H), 2.47 – 2.26 (m, 2H), 2.23 – 2.09 (m, 2H), 2.08 – 1.95 (m, 1H), 1.92 – 1.78 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 146.5 (C), 128.2 (CH), 127.1 (CH), 125.6 (CH), 45.9 (C), 34.6 (CH_2), 25.5 (CH_2). The spectral data matched those reported in the literature.[25]



4.2g

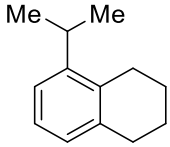
cyclopentylbenzene 4.2g. The general deformylation procedure was followed using 34.85 mg of **4.1g** (0.2 mmol), 0.2 mL of KO*t*-Bu solution (0.32 mmol) in 2.0 mL THF.

Purification by flash column chromatography (100% hexanes) afforded hydrocarbon **4.2g** as colorless oil (12.87 mg, 44%); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.39 – 7.09 (m, 5H), 2.99 (tt, *J* = 9.5, 7.5 Hz, 1H), 2.21 – 1.86 (m, 2H), 1.81 (qdt, *J* = 5.1, 3.2, 1.5 Hz, 2H), 1.74 – 1.65 (m, 2H), 1.60 (dddd, *J* = 12.1, 6.3, 5.0, 3.9 Hz, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 146.5 (C), 128.2 (CH), 127.1 (CH), 125.6 (CH), 45.9 (C), 34.6 (CH_2), 25.5 (CH_2).



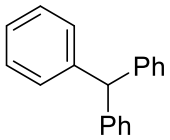
4.2h

cyclohexylbenzene 4.2h. The general deformylation procedure was followed using 37.65 mg of **4.1h** (0.2 mmol), 0.2 mL of KO*t*-Bu solution (0.32 mmol) in 2.0 mL THF. Purification by flash column chromatography (100% hexanes) afforded hydrocarbon **4.2h** as colorless oil (24.36 mg, 76%); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.39 – 7.05 (m, 5H), 2.50 (tt, *J* = 11.4, 3.5 Hz, 1H), 1.95 – 1.81 (m, 4H), 1.49 – 1.21 (m, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 148.1 (C), 128.2 (CH), 126.8 (CH), 125.7 (CH), 44.5(C), 34.5 (CH_2), 26.9 (CH_2), 26.2 (CH_2). The spectral data matched those reported in the literature.[26]



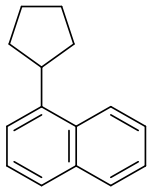
4.2i

5-isopropyl-1,2,3,4-tetrahydronaphthalene 4.2i. The general deformylation procedure was followed using 40.46 mg of **4.1i** (0.2 mmol), 0.2 mL of KO*t*-Bu solution (0.32 mmol) in 2.0 mL THF. Purification by flash column chromatography (100% hexanes) afforded hydrocarbon **4.2j** as colorless oil (21.26 mg, 61%); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.12 (d, *J* = 5.0 Hz, 2H), 6.95 (t, *J* = 4.5 Hz, 1H), 3.17 (hept, *J* = 6.8 Hz, 1H), 2.80 (dt, *J* = 13.4, 6.4 Hz, 4H), 2.05 – 1.63 (m, 4H), 1.24 (d, *J* = 6.8 Hz, 6H) ^{13}C NMR (100 MHz, $CDCl_3$): δ 146.9 (C), 137.2 (C), 134.0 (C), 126.9 (CH), 125.5 (CH), 122.1 (CH), 30.4 (CH_2), 28.2 (C), 25.8 (CH_2), 23.6 (CH_2), 23.4 (CH_3), 22.8 (CH_2).



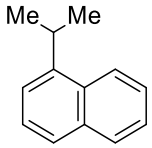
4.2j

triphenylmethane 4.2j. The general deformylation procedure was followed using 54.47 mg of **4.1j** (0.2 mmol), 0.2 mL of KO*t*-Bu solution (0.32 mmol) in 2.0 mL THF. Purification by flash column chromatography (100% hexanes) afforded hydrocarbon **4.2i** as white solid (38.60 mg, 79%).



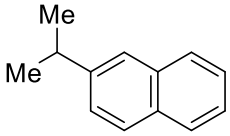
4.4a

1-cyclopentylnaphthalene 4.4a. The general deformylation procedure was followed using 44.86 mg of **4.3a** (0.2 mmol), 0.2 mL of KO*t*-Bu solution (0.32 mmol) in 2.0 mL THF. Purification by flash column chromatography (100% hexanes) afforded hydrocarbon **4.4a** as colorless oil (34.55 mg, 88%); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.24 – 8.13 (m, 1H), 7.86 (dd, *J* = 7.7, 1.7 Hz, 1H), 7.71 (dd, *J* = 5.6, 3.8 Hz, 1H), 7.62 – 7.38 (m, 4H), 3.80 (p, *J* = 7.2, 6.6 Hz, 1H), 2.37 – 2.10 (m, 2H), 2.10 – 1.63 (m, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 142.1 (C), 133.9 (C), 132.2 (C), 128.7 (CH), 126.2 (CH), 125.6 (CH), 125.5 (CH), 125.2 (CH), 123.9 (CH), 122.0 (CH), 41.2 (C), 33.6 (CH_2), 25.3 (CH_2).



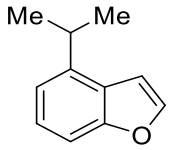
4.4b

1-isopropylnaphthalene 4.4b. The general deformylation procedure was followed using 39.70 mg of **4.3b** (0.2 mmol), 0.2 mL of KO*t*-Bu solution (0.32 mmol) in 2.0 mL THF. Purification by flash column chromatography (100% hexanes) afforded hydrocarbon **4.4b** as colorless oil (31.70 mg, 93%); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.16 (dd, *J* = 8.5, 1.2 Hz, 1H), 7.90 – 7.84 (m, 1H), 7.73 (dt, *J* = 7.8, 1.1 Hz, 1H), 7.62 – 7.38 (m, 4H), 3.79 (hept, *J* = 6.9 Hz, 1H), 1.44 (d, *J* = 6.9 Hz, 6H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 144.6 (C), 133.9 (C), 131.3 (C), 128.9 (CH), 126.3 (CH), 125.7 (CH), 125.6 (CH), 125.2 (CH), 123.30 (CH), 121.7 (CH), 28.5 (C), 23.6 (CH_3). See NMR spectral date 4b-D for Deuterated variation. The spectral data matched those reported in the literature.[27]



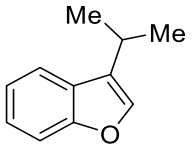
4.4c

2-isopropylnaphthalene 4.4c. The general deformylation procedure was followed using 39.70 mg of **4.3c** (0.2 mmol), 0.2 mL of KO*t*-Bu solution (0.32 mmol) in 2.0 mL THF. Purification by flash column chromatography (100% hexanes) afforded hydrocarbon **4.4c** as colorless oil (25.56 mg, 75%); ^{1}H NMR (400 MHz, CDCl3): δ 7.87 – 7.72 (m, 3H), 7.67 – 7.60 (m, 1H), 7.52 – 7.32 (m, 3H), 3.08 (hept, *J* = 6.9 Hz, 1H), 1.35 (d, *J* = 6.9 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 146.3 (C), 133.6 (C), 132.1 (C), 127.8 (CH), 127.5 (CH), 127.5 (CH), 125.8 (CH), 125.7 (CH), 125.0 (CH), 124.1 (CH), 34.2 (C), 23.9 (CH_3). The spectral data matched those reported in the literature.[28]



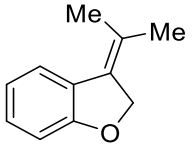
4d

4-isopropylbenzofuran 4.4d. The general deformylation procedure was followed using 37.6 mg of **4.3d** (0.2 mmol), 0.2 mL of KO*t*-Bu solution (0.32 mmol) in 2.0 mL THF. Purification by flash column chromatography (100% hexanes) afforded hydrocarbon **4.4d** as colorless oil (20.51 mg, 64%); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.61 (d, *J* = 2.2 Hz, 1H), 7.35 (dt, *J* = 8.2, 1.0 Hz, 1H), 7.28 – 7.22 (m, 1H), 7.10 (dt, *J* = 7.4, 0.8 Hz, 1H), 6.85 (dd, *J* = 2.2, 1.0 Hz, 1H), 3.27 (hept, *J* = 6.9 Hz, 1H), 1.36 (d, *J* = 7.0 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 155.0 (C), 144.2 (C), 142.0 (C), 124.3 (CH), 118.7 (CH), 108.9 (CH), 105.1 (2CH), 31.7 (C), 23.1 (CH_3).



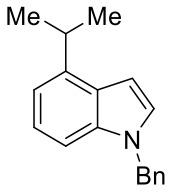
4.4e

3-isopropylbenzofuran 4.4e. The general deformylation procedure was followed using 37.6 mg of **4.3e** (0.2 mmol), 0.2 mL of KO*t*-Bu solution (0.32 mmol) in 2.0 mL THF. Purification by flash column chromatography (100% hexanes) afforded hydrocarbon **4.4e** as colorless oil (5.80 mg, 18%); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.63 – 7.59 (m, 1H), 7.47 (d, *J* = 8.2 Hz, 1H), 7.41 – 7.35 (m, 1H), 7.33 – 7.18 (m, 2H), 3.11 (pd, *J* = 6.9, 1.1 Hz, 1H), 1.38 (d, *J* = 6.9 Hz, 6H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 155.6 (C), 139.7 (CH), 127.6 (C), 127.3 (C), 123.9 (CH), 122.0 (CH), 120.1 (CH), 111.5 (CH), 24.6 (C), 22.4 (CH_3).



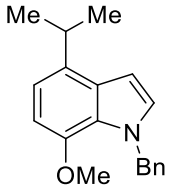
4.7

3-(propan-2-ylidene)-2,3-dihydrobenzofuran 4.7. The general deformylation procedure was followed using 37.6 mg of **4.3e** (0.2 mmol), 0.2 mL of KO*t*-Bu solution (0.32 mmol) in 2.0 mL THF. Purification by flash column chromatography (100:0→80:20 hexanes: benzene) afforded hydrocarbon **4.7** as colorless oil (9.02 mg, 28%); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.48 (dd, *J* = 7.7, 1.2 Hz, 1H), 7.11 (td, *J* = 7.8, 1.3 Hz, 1H), 6.98 – 6.66 (m, 2H), 5.33 – 4.65 (m, 2H), 2.06 (s, 3H), 1.77 (d, *J* = 2.0 Hz, 3H);^{13}C NMR (100 MHz, $CDCl_3$): δ 163.9 (C), 128.9 (C), 128.1 (CH), 126.6 (C), 123.6 (CH), 123.4 (C), 120.33 (CH), 109.9 (CH), 74.6 (CH_2), 23.3 (CH_3), 20.9 (CH_3).



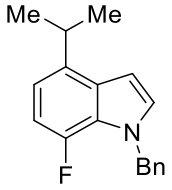
4.4f

1-benzyl-4-isopropyl-1H-indole 4.4f. The general deformylation procedure was followed using 55.47 mg of **4.3f** (0.2 mmol), 0.2 mL of KO*t*-Bu solution (0.32 mmol) in 2.0 mL THF. Purification by flash column chromatography (100:0→90:10 hexanes: EtOAc) afforded hydrocarbon **4.4f** as colorless oil (44.39 mg, 89%); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.41 – 7.22 (m, 4H), 7.21 – 7.09 (m, 4H), 7.02 (dd, *J* = 4.8, 3.4 Hz, 2H), 6.65 (d, *J* = 3.2 Hz, 2H), 5.33 (s, 2H), 3.42 (hept, *J* = 6.9 Hz, 1H), 1.42 (d, *J* = 6.9 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 141.3 (C), 137.6 (C), 137.2 (C), 137.1 (C), 128.7 (CH), 127.6 (CH), 127.5 (CH), 126.9 (CH), 122.0 (CH), 115.2 (CH), 107.4 (CH), 100.1 (CH), 50.2 (CH_2), 31.2 (C), 23.2 (CH_3).



4.4g

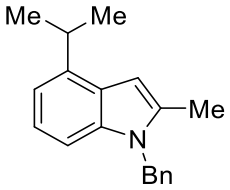
1-benzyl-4-isopropyl-7-methoxy-1H-indole 4.4g. The general deformylation procedure was followed using 61.48 mg of **4.3g** (0.2 mmol), 0.2 mL of KO*t*-Bu solution (0.32 mmol) in 2.0 mL THF. Purification by flash column chromatography (100:0→85:15 hexanes: EtOAc) afforded hydrocarbon **4.4g** as light yellow oil (45.26 mg, 81%); ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.47 – 7.18 (m, 3H), 7.19 – 7.07 (m, 2H), 7.03 (d, *J* = 3.2 Hz, 1H), 6.86 (d, *J* = 7.9 Hz, 1H), 6.68 – 6.47 (m, 2H), 5.64 (s, 2H), 3.82 (s, 3H), 3.30 (hept, *J* = 6.9 Hz, 1H), 1.37 (d, *J* = 6.9 Hz, 6H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 145.9 (C), 139.7 (C), 133.6 (C), 129.4 (C), 128.4 (CH), 127.8 (CH), 127.6 (C), 127.0 (CH), 126.8 (CH), 115.0 (CH), 102.7 (CH), 100.5 (CH), 55.4 (CH_3), 52.4 (CH_2), 30.5 (C), 23.5 (CH_3).



4.4h

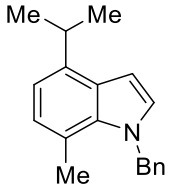
1-benzyl-7-fluoro-4-isopropyl-1H-indole 4.4h. The general deformylation procedure was followed using 59.07 mg of **4.3h** (0.2 mmol), 0.2 mL of KO*t*-Bu solution (0.32 mmol) in 2.0 mL THF. Purification by flash column chromatography (100:0→90:10 hexanes: EtOAc) afforded hydrocarbon **4.4h** as light yellow oil (37.96 mg, 71%); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.37 – 7.26 (m, 2H), 7.20 – 7.04 (m, 4H), 6.87 – 6.75 (m, 2H), 6.60 (dd, *J* = 3.2, 2.4 Hz, 1H), 5.48 (s, 2H), 3.31 (hept, *J* = 7.0 Hz, 1H), 1.35 (d, *J* = 6.9 Hz, 6H) ^{13}C

NMR (100 MHz, $CDCl_3$): δ 148.8 (d, *J* = 240.5 Hz, C), 138.3 (C), 136.8 (C), 131.0 (C), 129.5 (C), 128.8 (CH), 128.7 (CH), 127.5 (CH), 126.9 (CH), 115.09 (d, *J* = 6.7 Hz, CH), 107.26 (d, *J* = 16.3 Hz, CH), 101.1 (CH), 52.2 (CH_2), 30.6 (C), 23.2 (CH_3); ^{19}F NMR (376 MHz, $CDCl_3$): -139.0.



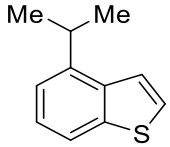
4.4i

1-benzyl-4-isopropyl-2-methyl-1H-indole 4.4i. The general deformylation procedure was followed using 58.28 mg of **4.3i** (0.2 mmol), 0.2 mL of KO*t*-Bu solution (0.32 mmol) in 2.0 mL THF. Purification by flash column chromatography (100:0→90:10 hexanes: EtOAc) afforded hydrocarbon **4.4i** as light yellow oil (38.45 mg, 73%); ^1H NMR (400 MHz, $CDCl_3$): δ 7.36 – 7.18 (m, 3H), 7.12 – 6.94 (m, 5H), 6.46 – 6.33 (m, 1H), 5.30 (s, 2H), 3.35 (hept, *J* = 6.9 Hz, 1H), 2.39 (s, 3H), 1.40 (d, *J* = 6.9 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 140.0 (C), 138.0 (C), 137.2 (C), 135.9 (C), 128.7 (CH), 127.2 (CH), 126.6 (C), 126.0 (CH), 121.0 (CH), 115.3 (CH), 107.0 (CH), 98.9 (CH), 46.6 (CH_2), 31.3 (C), 23.2 (CH_3), 12.8 (CH_3).



4.4j

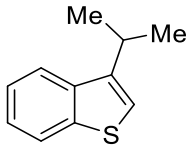
1-benzyl-4-isopropyl-7-methyl-1H-indole 4.4j. The general deformylation procedure was followed using 58.28 mg of **4.3j** (0.2 mmol), 0.2 mL of KO*t*-Bu solution (0.32 mmol) in 2.0 mL THF. Purification by flash column chromatography (100:0→90:10 hexanes: EtOAc) afforded hydrocarbon **4.4j** as light yellow oil (36.87 mg, 70%); ^1H NMR (400 MHz, $CDCl_3$): δ 7.41 – 7.20 (m, 3H), 7.09 (d, *J* = 3.2 Hz, 1H), 7.01 – 6.96 (m, 2H), 6.91 (q, *J* = 7.4 Hz, 2H), 6.68 (d, *J* = 3.3 Hz, 1H), 5.61 (s, 2H), 3.42 (hept, *J* = 6.9 Hz, 1H), 2.54 (s, 3H), 1.43 (d, *J* = 6.9 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 139.7 (C), 139.2 (C), 134.9 (C), 129.5, 128.8, 128.4, 127.3, 125.6 (CH), 124.8 (CH), 118.6, 115.3 (CH), 100.3 (CH), 52.2 (CH_2), 30.7 (C), 23.3 (CH_3), 19.4 (CH_3).



4.4k

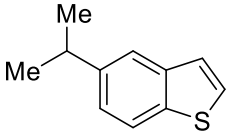
4-isopropylbenzo[b]thiophene 4.4k. The general deformylation procedure was followed using 40.9 mg of **4.3k** (0.2 mmol), 0.2 mL of KO*t*-Bu solution (0.32 mmol) in 2.0 mL THF.

Purification by flash column chromatography (100% hexanes) afforded hydrocarbon **4.4k** as colorless oil (25.03 mg, 71%);[1]H NMR (400 MHz, $CDCl_3$): δ 7.74 (d, *J* = 7.9 Hz, 1H), 7.50 (dd, *J* = 5.6, 0.8 Hz, 1H), 7.44 (d, *J* = 5.6 Hz, 1H), 7.32 (t, *J* = 7.7 Hz, 1H), 7.28 – 7.17 (m, 1H), 3.49 (hept, *J* = 6.9 Hz, 1H), 1.38 (d, *J* = 6.9 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 143.7 (C), 139.9 (C), 138.0 (C), 125.6 (CH), 124.5 (CH), 121.7 (CH), 120.0 (CH), 119.9 (CH), 31.3 (C), 23.3 (CH_3).



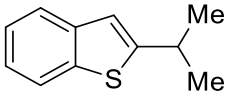
4.4l

3-isopropylbenzo[b]thiophene 4.4l. The general deformylation procedure was followed using 40.9 mg of **4.3l** (0.2 mmol), 0.2 mL of KO*t*-Bu solution (0.32 mmol) in 2.0 mL THF. Purification by flash column chromatography (100% hexanes) afforded impure **4.4l** as colorless oil (16.92 mg, 27%, determined by ^{1}H NMR using 1,3,5-trimethoxybenzene as an internal standard); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.89 – 7.83 (m, 1H), 7.80 (dt, *J* = 8.2, 0.9 Hz, 1H), 7.45 – 7.27 (m, 3H), 7.19 – 7.06 (m, 3H), 3.31 (pd, *J* = 6.9, 1.0 Hz, 1H), 1.38 (d, *J* = 6.8 Hz, 7H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 130.3 (C), 129.1 (C), 127.7 (C), 124.1 (CH), 123.7 (CH), 122.9 (CH), 121.9 (CH), 118.9 (CH), 27.8 (C), 22.8 (CH_3).



4.4m

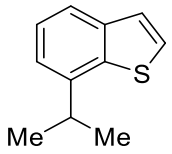
5-isopropylbenzo[b]thiophene 4.4m. The general deformylation procedure was followed using 40.9 mg of **4.3m** (0.2 mmol), 0.2 mL of KO*t*-Bu solution (0.32 mmol) in 2.0 mL THF. Purification by flash column chromatography (100% hexanes) afforded hydrocarbon **4.4m** as colorless oil (24.68 mg, 70%); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.80 (d, *J* = 8.3 Hz, 1H), 7.67 (d, *J* = 1.7 Hz, 1H), 7.41 (d, *J* = 5.4 Hz, 1H), 7.29 (dd, *J* = 5.4, 0.8 Hz, 1H), 7.24 (d, *J* = 1.7 Hz, 1H), 3.04 (hept, *J* = 6.9 Hz, 1H), 1.32 (d, *J* = 6.9 Hz, 7H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 145.1 (C), 139.9 (C), 137.2 (C), 126.4 (CH), 123.7 (CH), 123.7 (CH), 122.2 (CH), 120.8 (CH), 34.1 (C), 24.3 (CH_3).



4.4n

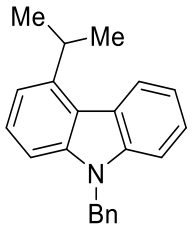
2-isopropylbenzo[b]thiophene 4.4n. The general deformylation procedure was followed using 40.9 mg of **4.3n** (0.2 mmol), 0.2 mL of KO*t*-Bu solution (0.32 mmol) in 2.0 mL THF. Purification by flash column chromatography (100% hexanes) afforded hydrocarbon **4.4n** as colorless oil (28.20 mg, 80%); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.86 – 7.72 (m, 1H), 7.68 (dt, *J* = 7.8, 0.8 Hz, 1H), 7.44 – 7.16 (m, 2H), 7.03 (d, *J* = 1.0 Hz, 1H), 3.26 (heptd, *J* = 6.8, 1.1 Hz, 1H), 1.41 (d, *J* = 6.8 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 154.1 (C), 140.1

(C), 138.8 (C), 124.0 (CH), 123.4 (CH), 122.8 (CH), 122.2 (CH), 118.2 (CH), 30.6 (C), 24.4 (CH_3).



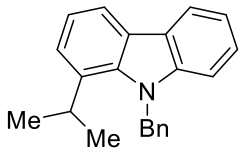
4.4o

7-isopropylbenzo[b]thiophene 4.4o. The general deformylation procedure was followed using 40.9 mg of **4.3o** (0.2 mmol), 0.2 mL of KO*t*-Bu solution (0.32 mmol) in 2.0 mL THF. Purification by flash column chromatography (100% hexanes) afforded hydrocarbon **4.4o** as colorless oil (22.21 mg, 63%); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.68 (dd, *J* = 7.9, 1.1 Hz, 1H), 7.43 (d, *J* = 5.5 Hz, 1H), 7.40 – 7.32 (m, 2H), 7.24 (dd, *J* = 7.4, 1.0 Hz, 1H), 3.27 (hept, *J* = 6.9 Hz, 1H), 1.42 (d, *J* = 6.9 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 142.8 (C), 139.7 (C), 138.8 (C), 125.5 (CH), 124.8 (CH), 124.6 (CH), 121.3 (CH), 119.9 (CH), 33.4 (C), 22.6 (CH_3).



4.6a

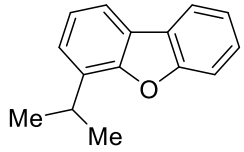
9-benzyl-4-isopropyl-9H-carbazole 4.6a. The general deformylation procedure was followed using 65.49 mg of **4.5a** (0.2 mmol), 0.2 mL of KO*t*-Bu solution (0.32 mmol) in 2.0 mL THF. Purification by flash column chromatography (100:0→90:10 hexanes: EtOAc) afforded hydrocarbon **4.6a** as colorless oil (45.19 mg, 69%); ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.31 (d, *J* = 8.0 Hz, 1H), 7.57 – 7.38 (m, 4H), 7.35 – 7.12 (m, 7H), 5.55 (s, 2H), 4.07 (hept, *J* = 7.0 Hz, 1H), 1.57 (d, *J* = 6.8 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 144.7 (C), 141.0 (C), 140.7 (C), 137.3 (C), 128.8 (CH), 127.4 (CH), 126.4 (CH), 126.0 (CH), 125.1 (CH), 123.2 (CH), 122.8 (C), 120.4 (C), 119.2 (CH), 115.3 (CH), 108.8 (CH), 106.5 (CH), 46.5 (CH_2), 30.4 (C), 22.7 (CH_3).



4.6b

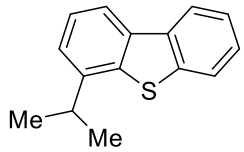
9-benzyl-1-isopropyl-9H-carbazole 4.6b. The general deformylation procedure was followed using 65.49 mg of **4.5b** (0.2 mmol), 0.2 mL of KO*t*-Bu solution (0.32 mmol) in 2.0 mL THF. Purification by flash column chromatography (100:0→90:10 hexanes: EtOAc) afforded hydrocarbon **4.6b** as colorless oil (41.27 mg, 63%); ^{1}H NMR (400 MHz,

$CDCl_3$): δ 8.13 (d, *J* = 7.7 Hz, 1H), 8.02 (dd, *J* = 7.6, 1.3 Hz, 1H), 7.51 – 7.15 (m, 9H), 7.11 – 7.00 (m, 1H), 5.74 (s, 2H), 3.57 (hept, *J* = 6.8 Hz, 1H), 1.27 (d, *J* = 6.8 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 141.9 (C), 138.5 (C), 132.3 (C), 128.8 (CH), 128.7 (C), 127.2 (CH), 125.9 (CH), 125.6 (CH), 124.3 (C), 123.5 (CH), 123.3 (C), 119.9 (CH), 119.7 (CH), 119.4 (CH), 117.9 (CH), 109.0 (CH), 49.1(CH_2), 27.7 (C), 24.5 (CH_3).



4.6c

4-isopropyldibenzo[b,d]furan 4.6c. The general deformylation procedure was followed using 47.66 mg of **4.5c** (0.2 mmol), 0.2 mL of KO*t*-Bu solution (0.32 mmol) in 2.0 mL THF. Purification by flash column chromatography (100:0→90:10 hexanes: EtOAc) afforded hydrocarbon **4.6c** as colorless oil (34.49 mg, 82%); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.96 (ddd, *J* = 7.7, 1.4, 0.7 Hz, 1H), 7.80 (dd, *J* = 7.3, 1.7 Hz, 1H), 7.66 – 7.55 (m, 1H), 7.46 (ddd, *J* = 8.3, 7.3, 1.4 Hz, 1H), 7.39 – 7.24 (m, 3H), 3.59 (hept, *J* = 6.9 Hz, 1H), 1.45 (d, *J* = 6.9 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ ^{13}C NMR (101 MHz, $cdcl_3$) δ 156.0 (C), 154.1 (C), 132.8 (C), 126.8 (CH), 124.6 (C), 124.0 (CH), 123.9 (C), 122.8 (CH), 122.5 (CH), 120.6 (CH), 118.0 (CH), 111.6 (CH), 28.7 (C), 22.6 (CH_3).



4.6d

4-isopropyldibenzo[b,d]thiophene 4.6d. The general deformylation procedure was followed using 50.87 mg of **4.5d** (0.2 mmol), 0.2 mL of KO*t*-Bu solution (0.32 mmol) in 2.0 mL THF. Purification by flash column chromatography (100:0→90:10 hexanes: EtOAc) afforded hydrocarbon **4.6d** as colorless oil (38.03 mg, 84%); ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.22 – 8.09 (m, 1H), 8.01 (dd, *J* = 7.8, 1.2 Hz, 1H), 7.92 – 7.82 (m, 1H), 7.52 – 7.39 (m, 3H), 7.36 (dt, *J* = 7.4, 0.9 Hz, 1H), 3.25 (hept, *J* = 6.9 Hz, 1H), 1.43 (d, *J* = 6.9 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 143.0 (C), 139.0 (C), 138.5 (C), 136.2 (C), 135.6 (C), 126.5 (CH), 125.0 (CH), 124.2 (CH), 122.7 (CH), 122.6 (CH), 121.6 (CH), 119.2 (CH), 33.5 (C), 22.5 (CH_3).

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Conclusion

Gem-dialkyl-containing benzylic quaternary center is important in active pharmaceutical ingredients. In addition, it is also a unique steric biasing tool in organic synthesis, with which my doctoral research studies give rise to three useful methods for the syntheses of medicinal motifs. The catalytic hydroarylation reactions have provided sustainable and convenient access to *gem*-dialkyl-containing carbocycles with quaternary centers with high yield and effective *regio*- selectivity. In addition, the utility of intramolecular π–stacking though non-covalent dispersion interaction in seemingly conventional reactions has rarely been exploited. The direct decarbonylation reaction of *quat*-center containing aldehydes is significantly milder compared to the exsisting methods. Moreover, the suggestive radical mechanism may add insight for future development of useful methods *via* C-C bond cleavage.