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Acid-Catalyzed Intermolecular Hydroarylation of Trifluoromethylated Alpha-Methylstyrenes for New Quaternary Carbon-Containing Compounds and Metal-Catalyzed Hydrogen atom Transfer from Water to Unsaturated C–C Bonds in a Classroom Setting.

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

in

Chemistry and Chemical Biology

by

Jose Alvarenga

Committee in Charge:

Professor Erik J. Menke, Chair

Professor Hrant Hratchian

Professor Rudy M. Ortiz

Professor Ryan D. Baxter, Advisor

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The Dissertaton of Jose Alvarega is approved, and it is acceptable in quality and form for publication on microfilm and electronically:

Professor Erik J. Menke Chair

Professor Hrant Hratchian

Professor Rudy M. Ortiz

Professor Ryan D. Baxter (Advisor)

University of California, Merced

2022

DEDICATION

My Family

Dedicated to the loving memory of my grandparents,

Maria Sandoval de Alvarenga

Abelino Alvarenga

Maria Isabel Rivera de Hernandez

Cecilio Hernandez

Special dedication to Dr. Raymond Garcia and Martha Hernandez

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LIST OF ABBREVIATION

Å	Angstrom
Boc	*tert*-butoxylcarbonyl
br	broad
Bu	butyl (C_4H_9)
C–C	carbon–carbon
d	doublet
DCE	1,2-dichloroethane
DCM	dichloromethane
dd	doublet of doublet
DMF	*N*,*N*-dimethylformamide
EAS	electrophilic aromatic substitution
Equiv	molar equivalent
ESI	electrospray ionization
Et	ethyl
EI	electron impact
FT	Fourier transform
GC	gas chromatography
H	hour
Hex	hexyl (C_6H_{13})
HRMS	high-resolution mass spectrometry
Hz	hertz

LIST OF ABBREVIATIONS (continued)

IR	infrared
J	coupling constant
LC	liquid crystal
M	molarity
m	multiple
Me	methyl
mmol	millimole
Ms	methanesulfonyl
m/z	mass-to-charge
np	nanoparticle
NMR	nuclear magnetic resonance
pen	pentet
Ph	phenyl
ppm	parts per million
Pr	propyl
q	quartet
rt	room temperature
s	singlet
t	triplet
TPFPB	tetrakis(pentafluorophenyl)borate
THF	tetrahydrofuran

LIST OF SCHEMES

LIST OF TABLES

ACKNOWLEDGEMENTS

I would like to express my sincere gratitude to my PhD. advisors, Dr. Ryan Baxter and Dr. Benjamin J Stokes. None of my accomplishments would have been possible without their support, encouragement, motivation, and patience.

I like to thank my dissertation committee members, Professors Erik Menke, Rudy M. Ortiz, and Hrant Hratchian for providing valued feedback during my PhD career.

I like to thank the members of the Stokes and Baxter lab for creating a positive and friendly environment in the lab.

I also wish to thank the UC Merced Chemistry and chemical biology facilities, administrative support, research support staff, and Dr. Rice for their help with NMR instruments.

VITA

Education

December 2020 Ph.D. Candidate in Organic Chemistry (advisor: Prof. Benjamin J Stokes/ Ryan Baxter)
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Publications

(4) "Alvarenga, J.; Stokes, J. B. Metal-Catalyzed H Atom Transfer from Water to Unsaturated C–C Bonds in a Classroom Setting." manuscript in preparation 2020

(3) Alvarenga, J.; Yaghoubi, M.; Villanueva, B.; Stokes, J. B. "Lewis Acid-Catalyzed Hydroarylation for Selective Linear Dimerization of α-Methyl Styrenes Derivatives." manuscript in preparation 2020

(2) Alvarenga, J.; Keshavarz, A.; Stokes, J. B. "Acid-Catalyzed Intermolecular Hydroarylation of Trifluoromethylated α-Alkylstyrenes, for New Quaternary Carbon-Containing Compounds." (manuscript in preparation 2021)

(1) Hoffman-Luca, C. G.; Eroy-Reveles, A. A.; Alvarenga, J; Mascharak, P. K. "NO Donors That Can Be Activated by Near-Infrared Light S Syntheses." *Inorganic Chemistry.* **2009**, 4, 9104.

PATENT APPLICATION (no. PCT/US2020/947044)
Methods of Hydroarylation with Acid *(Inventors: Benjamin J. Stokes, Jose Alvarenga, Amir Keshavarz and Xiao Cai)*.

ABSTRACT

Catalytic hydroarylation of alkenes is an attractive alternative to Friedel–Crafts type reactions of alkyl halides for the alkylative functionalization of aromatic C–H bonds. Many catalytic hydroarylations of alkenes are known, but few of them efficiently afford quaternary carbons from 1,1-disubstituted alkenes. Quaternary carbons are difficult to synthesize due to their sterically congested nature, which can lead to kinetic barriers to formation and thermodynamic instability. Herein, we report an efficient and highly selective methodology to intermolecularly functionalize trifluoromethylated (and other electron-deficient) α-methyl styrenes with a variety of aromatic compounds through the action of a tritylium precatalyst. This method gives access to a wide range of diaryl-dialkyl quaternary centers. Recent research into the reduction of alkene/alkyne to an alkane using B–B bond-containing reagents, such as $B_2(OH)_4$ and catalytic amounts of palladium on carbon, can mediate transition metal-catalyzed H atom transfer from H_2O, leading to the reduction of alkenes and alkynes under mild conditions. Very few experiments for an introductory undergraduate organic chemistry lab demonstrate an alkene/alkyne to alkane reaction using transition metals. For this experiment, Palladium acetate was selected as the catalyst, an electron-rich alkene *trans*-stilbene was selected because of its ease to measure and to ensure the reaction could go to completion within the time constraints of a typical lab, which is 2-MeTHF was used as the solvent to increase the speed of completion of the reaction to an hour.

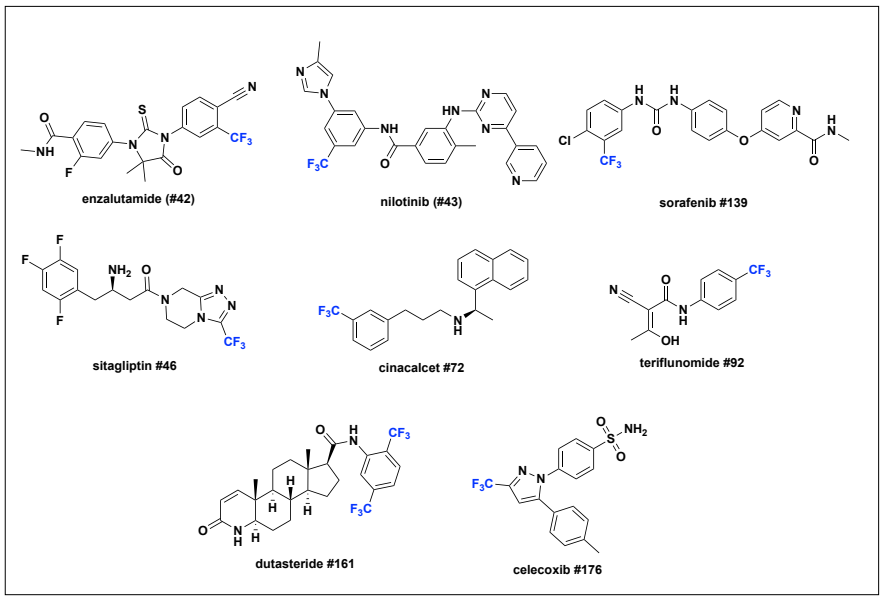
CHAPTER 1

Acid-Catalyzed Intermolecular Hydroarylation of Trifluoromethylated Alpha-Methylstyrenes for New Quaternary Carbon-Containing Compounds

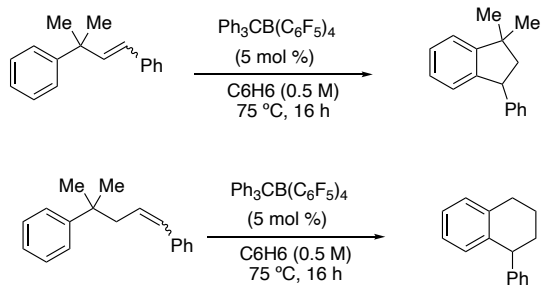
Background

Considerable interest from the pharmaceutical industries has emerged in recent years over the organic molecules that possess a trifluoromethyl group.[1] Aryl trifluoromethyl groups have garnered considerable interest from the pharmaceutical industry in recent years.[3] As of 2016, aryl trifluoromethyl-containing prescription medicines frequented the top 200 in sales, including Astellas's Xtandi® (enzalutamide, #42, $2.3B), Novartis's Tasigna® (nilotinib, #63, $1.7B), and Bayer's Nexavar® (sorafenib, #139, $922M) oncologics, Merck's Janumet® (sitagliptin, #46, $2.2B) for diabetes, Amgen's Sensipar® (cinacalcet, #72, $1.6B) for hormonal imbalance, Sanofi's Aubagio® (teriflunomide, #92, $1.2B) for neurological disorders, Glaxo-Smith Kline Avodart® (dutasteride, #161, $787M) for enlarged prostate, and Pfizer's Celebrex® (celecoxib, #176, $733M) for prescribed mainly for arthritic pain, an anti-inflammatory by inhibiting cox2.

Table 1. Aryl trifluoromethyl-containing prescription medicines in top 200 in sales.

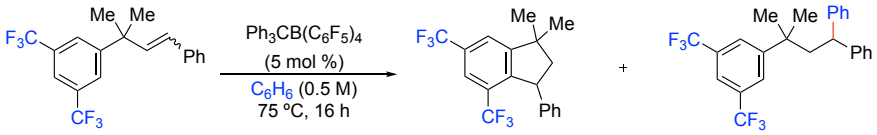


The presence of a highly electron-withdrawing trifluoromethyl group can significantly change the chemical reactivity[2], physical properties of a molecule significantly, and their lipophilicity.[3] These molecules have interesting applications not only in medicine but also in liquid crystals,[4] agrochemicals,[5,] and polymer chemistry.[6] In addition to the trifluoromethyl group, molecules containing the geminal-dialkyl quaternary centers and germinal diaryl-containing compounds are widely present in natural products[7]. Chemists are paying more attention to designing new methods to prepare them.[8] Thus, we decided to synthesize molecules that are composed of both a trifluoromethyl group and a geminal-dimethyl quaternary center in an intermolecular hydroarylation fashion, employing an easily-handled precatalyst, tetrakis(pentafluorophenyl)borate (TPFPB).[9] Recently, our lab has developed a method to construct indane and tetralin backbones through intramolecular hydroarylation of olefins using TPFPB as a precatalyst (Scheme 1) .[10]



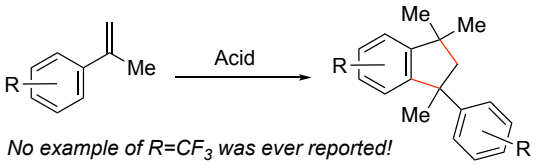
Scheme 1. Depiction of indane and tetralin skeletons.

In the course of this study, our lab reported that substrates containing a trifluoromethyl group were unique in their reluctance to cyclize. Instead, they reacted intermolecularly with solvent (Scheme 2).



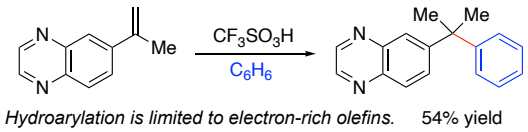
Scheme 2. Solvent addition to the CF_3 containing alkene.

I decided to probe the generality of this phenomenon by simplifying from the indane system to readily available trifluoromethylated α-methylstyrenes. One of the main challenges of these transformations is the formation of byproducts since the reaction is performed under strong acidic conditions. For example, derivatives of alpha-methylsyrenes in the presence of strong acids are prone to undergo dimerization (Scheme 3).[11]



Scheme 3. Dimerization of α -methylstyrenes (Fisher and coworkers, 1958).[11a]

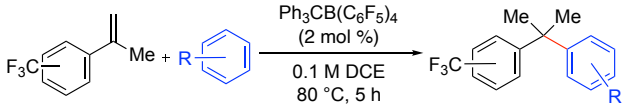
Although there are numerous examples of acid-catalyzed hydroaylation of styrenes reported in the literature[12], no intermolecular hydroarylation reaction for the construction of quaternary carbon-containing compounds has ever been performed on our substrates to the best of our knowledge and the known examples are limited to electron-rich molecules. The Londregan group developed a method using 3-(prop-1-en-2-yl)pyridine styrene (Scheme 4) as their substrate and successfully developed a method to form a carbon-carbon bond between the styrene and the arene in good yields.[14] However, a challenge they reported was that when a second electron-withdrawing group was added to the styrene at any position it formed side products that were not the desired product.



Hydroarylation is limited to electron-rich olefins. 54% yield

Scheme 4. Intermolecular hydroarylation of vinylpyrazine (Klumpp and coworkers, 2011).[12d]

In this novel method, we were able to minimize the dimerization of trifluoromethylated α -methylstyrenes to trace amounts and were successfully made the desired product in a highly regioselective manner in good yield (Scheme 5).

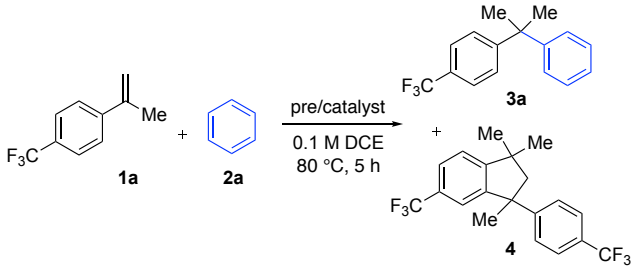


Scheme 5. Intermolecular hydroarylation of trifluoromethylated alpha-methylstyrenes.

Results and Discussion

At the onset of my work, I used **1a** as the model substrate (Table 2). All our olefin substrates could easily be prepared in just one step from commercially available ketones through wittig olefination. With our olefin substrate **1a** in hand, we began the optimization (Table 2) by using benzene **1b** as the source of nucleophile and different acids as precatalysts at various temperatures and concentrations (see the Supporting Information for details).

Table 2. Optimization of the intermolecular hydroarylation of *p*-(trifluoromethyl)-α-methylstyrene



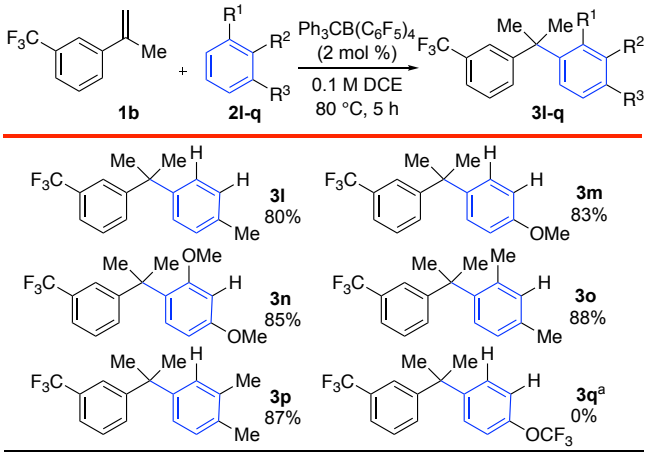
entry	pre/catalyst	pre/catalyst (mol%)	equiv of 2a	conv (%)[a] of 1a	yield (%)[a] of 3a	yield (%)[a] of 4
1	H_2SO_4	10	5	75	0	25
2	TfOH	10	5	100	0	75
3	TfOH	10	20	100	19	80
4	TFA	10	5	100	0	91
5	TFA	10	20	100	8	81
6	$(Tf)_2NH$	10	5	100	18	72
7	$Ph_3CB(C_6F_5)_4$	10	5	100	88	tr
8	$Ph_3CB(C_6F_5)_4$	5	5	100	88	tr
9	$Ph_3CB(C_6F_5)_4$	4	5	100	87	tr
10	$Ph_3CB(C_6F_5)_4$	3	5	100	88	tr
11	$Ph_3CB(C_6F_5)_4$	2	10	100	89	tr
12	$Ph_3CB(C_6F_5)_4$	2	5	100	88	tr
13	$Ph_3CB(C_6F_5)_4$	2	3	100	88	tr
14	$Ph_3CB(C_6F_5)_4$	2	2	100	60	35
15	$Ph_3CB(C_6F_5)_4$	2	1	100	40	55

[a]Determined by ^1H NMR analysis of reaction mixture using 1,3,5 trimethoxy benzene as an internal standard. All reactions were conducted on 0.1 mmol scale.

I first screened different numbers of acids. Only 75% conversion was observed with sulfuric acid (entry 1) and no desired product was formed. The main challenge for optimization was to minimize the formation of cyclic product **2b** and maximize the yield of the desired product **2a**. Switching to stronger acid, like trifluoromethanesulfonic acid (TfOH), we were able to see 19% product but 20 equivalents of **1b** had to be used (entry 3). Lowering the amount of **1b** to 3 equivalents resulted in no desired product but gave 75% yield for **2b** (entry 2). Reaction with trifluoroacetic acid (TFA) behaved similarly as the TfOH (entries 4 and 5). Reaction with 10 mol % of trifluoromethanesulfonimide ($(Tf)_2NH$) only gave 18% of the desired product **2a** (entry 6). We next began screening the reaction with TPFPB as the precatalyst. Our goal was to use the least amount of acid and minimize the formation of the by-product. We were delighted to see that our reaction was highly selective toward our desired product using TPFPB. At 10 mol % precatalyst loading and with 5 equivalents of **2a**, we were able to make **3a** in 88% yield (entry 7). Shortly after, with more optimization, we were able to make **3a** by only using 2 mol % of TPFPB and 3 equivalents of **2a**.

Under the optimal reaction conditions, we began exploring the scope of the intermolecular hydroarylation of *p*-(trifluoromethyl)-α-methylstyrene (Table 3). We were able to isolate **3a** in 88% yield when benzene **2a** was used as the nucleophile. Intermolecular hydroarylation with **2b** was highly selective toward the *para* position of toluene and resulted in 92% yield for **3b**. We observed a similar trend and regioselectivity with substrates **2b–2h**. We were able to isolate the desired products **3c–3e** in good yields

Table 3. Scope of the intermolecular hydroarylation of *m*-(trifluoromethyl)-α-methylstyrene[a]



[a]Isolated yields are reported and the starting material was fully consumed unless otherwise noted.

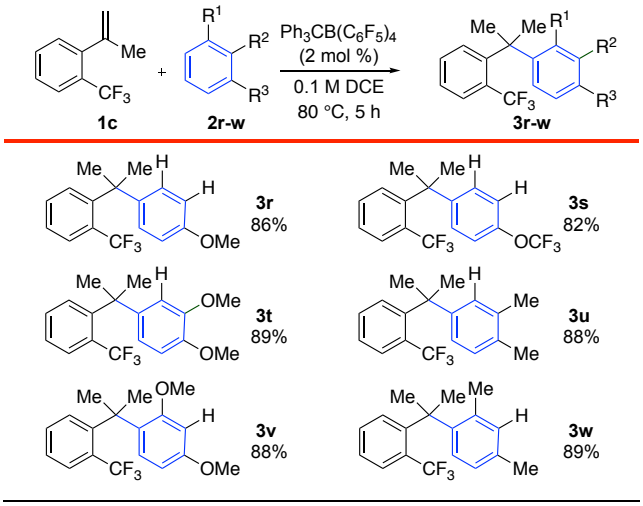
A modest yield was obtained when phenol **2f** was used as the substrate. The relatively low yield could be attributed to the Lewis basicity of the phenolic oxygen. Regardless, the reaction doesn't require *o*-protection of the substrate. Reaction with thiophenol **2g** also did not require *S*-protection of the substrate and resulted in 86% isolate yield for product **3h**. In case of substrate **2h, 2i** and **2j**, again the electronics and sterics dictated the formation of single regioisomers, giving 95% yield for **3h,** 88% yield for **3i** and 87% yield for **3j**. In addition to monoaromatic molecules, bicyclic systems like naphthalene **2k** gave the desired product **3k** in 82% yield.

To further explore the scope of this intermolecular hydroarylation reaction, we next began applying our optimized conditions to *m*-(trifluoromethyl)-α-methylstyrene (Table 3). Interestingly, we observed similar regioselectivity trends for substrates **2i–2p** as the previous table. However, we were not able to make **3q** or its regioisomers when trifluoromethoxybenzene **2q** was used as the nucleophile. These results indicate that

position of trifluoromethyl group will play no role or very little role to the regioselectivity outcomes.

Finally, we investigated the scope of the intermolecular hydroarylation of *o*-(trifluoromethyl)-α-methylstyrene (**Table 4**). We again observed similar regioselectivity trends as **table 2 and 3**. Intermolecular addition to **1c** was favored at the *para* position of anisole **2r** and toluene **2s**. In case of susbtrates 2t–**2u**, the hydroarylation was favored at the less hindered sites, *para* to each methoxy and methyl, respectively. Finally, hydroarylation at the least hindered site and more nucleophilic position of **2v** and **3w** gave **3v** and **3w** in 88% and 89% yield, respectively. Unfortunately, again we were not able to make **3s** or its regioisomers when trifluoromethoxybenzene **2s** was used as the nucleophile.

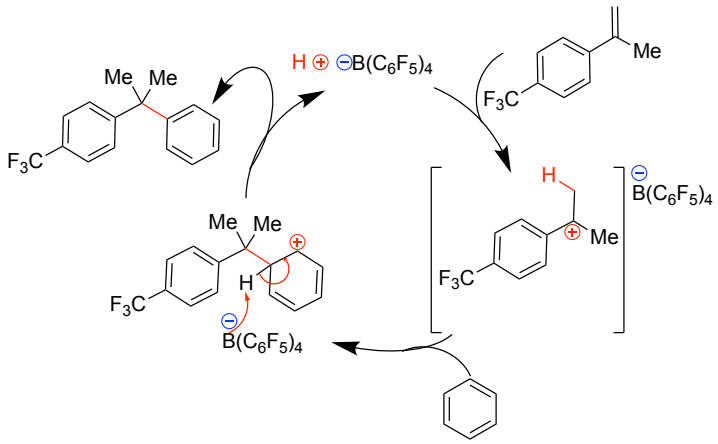
Table 4. Scope of the intermolecular hydroarylation of *o*-(trifluoromethyl)-α-methylstyrene[a]



[a]Isolated yields are reported and starting material was fully consumed, unless otherwise noted.

We hypothesize that the mechanism works in the following sequence in (Scheme 6). First the (TPFPB) adds across the styrene forming a tertiary benzylic carbon cation

intermediate. Then benzene comes in as a nucleophile and attacks the tertiary benzylic carbon cation forming intermediate **a**. $^{-}$BARF then grabs the proton from the benzene intermediate which leads to the rearomatization of the benzene forming product **c**, which was detected by gcms. Also the HBARF catalyst for our reaction is made in this step. HBARF enters the catalytic cycle and attacks **1a** forming a tertiary benzylic carbon cation intermediate. Then the benzene attacks the tertiary benzylic carbon cation forming intermediate **f**. $^{-}$BARF then grabs the proton from the benzene intermediate, which leads to the rearomatization of the benzene forming the desired product **i** and making the HBARF, which returns to the catalytic cycle until **1a** is consumed.



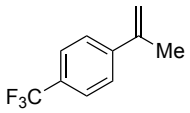
Scheme 6. Hypothesized Brønsted acid-catalyzed mechanism.

In conclusion, we have developed an efficient method for catalytic intermolecular hydroarylation of trifluoromethylated alpha-methylstyrenes by using an easily handled precatalyst, TPFPB. We have demonstrated that our reactions are highly regioselective for the *para* position of monoaromatic nucleophiles. In addition to regioselectivity, interesting and novel molecules with geminal-dimethyl quaternary centers were prepared readily in excellent yields

Experimental

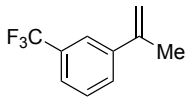
A. Synthesis of Synthesis of alkenes via Wittig olefination

General procedure I: In a dry 125-250 mL round bottom flask was charged with a magnetic stir bar coated with PTFE, methyltriphenylphosphonium bromide (1.6 eq.) was dissolved in 15 mL THF. The round bottom flask was seal with a rubber septum before t-BuOK (1.6 M in THF solution) was syringed into the mixture at room temperature. The reaction turned immediately a yellow color and the reaction was stirred for 30 minutes before the reaction was cold down to 0 °C. A solution of Trifluoromethylated α-Methylstyrene in minimal amount of THF (0.5 mmol-2.5 mmol, 1.0 eq.) was 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 ketone was consumed, the reaction was quenched with saturated aqueous NH_4Cl solution. The alkene was extracted with ethyl acetate three times. The organic layers were collected and dried over sodium sulfate anhydrous before it was concentrated under reduced pressure to afford crude alkene product. Purification by silica gel chromatography using gradient elution afforded pure alkene.



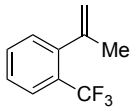
1a

1-(prop-1-en-2-yl)-4-(trifluoromethyl)benzene 1a: General procedure I was followed using 446 mg of 4′-(Trifluoromethyl)acetophenone (2.5 mmol), 1.7 g of methyl triphenyl phosphonium (4.0 mmol) and 2.5 mL of a 1.6 M solution of t-BuOK in THF. Purification by flash column chromatography (100:0 hexanes) afforded **1a** (383 mg, 82%) as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$): 7.59 (M, 5H) 5.43 (s, 1H), 5.19 (s, 1H), 2.17 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 144.1 (C) 142.1 (C), 142.4 (C), 126.2 (CH), 137.1 (CH), 125.2-125.0 (CH), 129.9 (q, J = 273.0 Hz, C), 129.4 (q, J = 32.5 Hz, C), 125.1 (C), 122.2 (q, J = 4.0 Hz, CH), 114.3 (C), 21.4 (CH_3); ^{19}F δ (376 MHz, $CDCl_3$): –62.32(F) ATR-FTIR (neat): 2330, 2100, 1943, 1705, 1365, cm^{-1}; HRMS (EI) *m/z* calculated for $C_{10}H_9F_3[M]^+$: 186.07, found: 186.0656



1b

1-(prop-1-en-2-yl)-3-(trifluoromethyl)benzene 1b: General procedure I was followed using 370mg of 3′-(Trifluoromethyl)acetophenone (2.5 mmol), 1.7 g of methyl triphenyl phosphonium (4.0 mmol) and 2.5 mL of a 1.6 M solution of *t*-BuOK in THF. Purification by flash column chromatography (100:0 hexanes) afforded **1b** (255 mg, 69% yield) as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.59 (M, 5H) 5.43 (s, 1H), 5.19 (s, 1H), 2.17 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 144.1 (C) 142.1 (C), 142.4 (C), 126.2 (CH), 137.1 (CH), 125.2-125.0 (CH), 129.9 (q, J = 273.0 Hz), 129.4 (q, J = 32.5 Hz), 125.1 (C), 122.2 (q, J = 4 Hz), 114.3 (C), 21.4 (CH_3); ^{19}F NMR (376 MHz, $CDCl_3$): δ –58.78 (F); ATR-FTIR (neat): 2247, 2050, 2042, 1935, 1815, 1722, 1275, cm^{-1}; HRMS (EI) *m/z* calculated for $C_{10}H_9F_3[M]^+$: 186.07, found: 186.0656

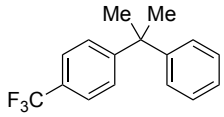


1c

1-(prop-1-en-2-yl)-2-(trifluoromethyl)benzene 1c: General procedure I was followed using 370mg of 2′-(Trifluoromethyl)acetophenone (2.5 mmol), 1.7 g of methyl triphenyl phosphonium (4.0 mmol) and 2.5 mL of a 1.6 M solution of *t*-BuOK in THF. Purification by flash column chromatography (100:0 hexanes) afforded **1c** (255 mg, 69 % yield) as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.59 (M, 5H) 5.43 (s, 1H), 5.19 (s, 1H), 2.17 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 143.7 (C) 143.3 (q, J = 273.0 Hz, C) 142.1 (C), 142.4 (C), 133.1 (CH), 137.1 (CH), 129.9 (CH), 127.9 (q, J = 32.5 Hz, C) 127.7 (q, J = 4.0 Hz, CH), 126.6 (CH), 126.0-125.8 (CF_3), 122.9 (C), 115.1 (C), 25.6 (CH_3); ^{19}F NMR (376 MHz, $CDCl_3$): δ –58.78 (F); ATR-FTIR (neat): 2237, 2060, 2052, 1935, 1920, 1722, 1275, cm^{-1}; HRMS (EI) *m/z* calculated for $C_{10}H_9F_3[M]^+$: 186.07, found: 186.0656.

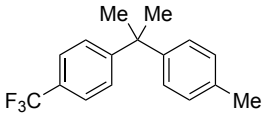
B. Synthesis 1-(2-phenylpropan-2-yl)-3-(trifluoromethyl) benzene derivatives via Catalytic Hydroarylation of β-Benzylstyrenes

General procedure II: In a dry 4 mL glass vial charged with PTFE coated magnetic stir bar, the alkenes were dissolved with 2.0 mL of dichloroethane (DCE) (0.54 M). (1.5 mmol) of the desire arene was added. Then 2.0 mol % Tetrakis(pentafluorophenyl)borate (TPFPB) was added and cap. The reaction mixture was allowed to stir and heated to 80 °C for an 5 hrs. After 1 hour, the reaction solution was then quenched by addition of 1.0 mL of saturated $NaHCO_3$. The 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 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 was flushed with a mixture of hexanes and benzene (100:0 7:3, hexane:benzene) to obtained the pure corresponding product.



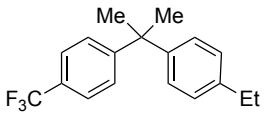
3a

1-(2-phenylpropan-2-yl)-3-(trifluoromethyl)benzene 3a: General procedure II was followed using 93 mg of alkene **1a** (0.5 mmol), 125 mg of **2b** (1.5 mmol), 10 mg of tritylium TPFPB (0.020 mmol) and 2.0 mL of dichloroethane. Purification by flash column chromatography (100% hexanes) afforded **3a** (128 mg, 89% yield) as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.85-7.79 (m, 3H), 7.74-7.72 (d, *J* = 8.0 Hz, 1H), 7.54-7.46 (m, 3H), 7.39-7.37 (d, *J* = 8.1 Hz, 2H), 7.18-7.16 (m, 1H), 7.10-7.08 (d, *J* = 8.0 Hz, 2H), 6.77-6.76 (d, *J* = 8 Hz, 2H), 6.84-6.82 (m, 1H), 6.78-6.76 (m, 1H), 1.68 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 154.3 (C), 146.9 (C), 133.1 (C), 131.8 (CH),127.9 (q, *J* = 273.0 Hz, C), 127.8 (q, *J* = 32.5 Hz, C), 125.6 (q, *J* = 4.0 Hz, CH), 127.4 (CH), 127.2 (CH), 126.3 (CH), 126.1 (CH), 125.7 (CH), 125.08-124.9 (CF), 123.9 (CH), 43.3 (C), 30.4 (CH_3); ^{19}F NMR (376 MHz, $CDCl_3$): δ –53.81; ATR-FTIR (neat): 2231, 2160, 2052, 1935, 1920, 1422, 1275, 120.1 cm^{-1}; HRMS (EI) *m/z* calculated for $C_{11}H_{13}F[M]^+$: 264.1282, found: 264.1285.



3b

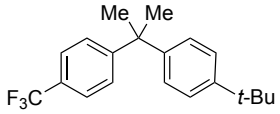
1-methyl-4-(2-(4-(trifluoromethyl)phenyl)propan-2-yl)benzene 3b: General procedure II was followed using 93 mg of alkene **1a** (0.5 mmol), 138 mg of **2b** (1.5 mmol), 10 mg of tritylium TPFPB (0.020 mmol) and 2.0 mL of dichloroethane. Purification by flash column chromatography (100% hexanes) afforded **3b** (128 mg, 93% yield) as a colorless oil. (149 mg, 93 % yield). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.51 (d, *J* = 8.4 Hz, 2H), 7.34 (d, *J* = 8.0 Hz, 2H), 7.10 (s, 4H), 2.32 (s, 3H), 1.68 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 158.5 (C) 150.8 (C), 146.6 (C), 135.5 (C), 128.9 (CH), 127.7 (CH), 127.0 (CH), 126.9 (CH), 126.7 (q, *J* = 273.0 Hz, C), 121.1 (q, *J* = 32.5 Hz, C), 124.9 (q, *J* = 4.0 Hz, CH), 121.0 (C), 42.6 (CH_3), 30.5 (CH_3); 15.5 (C); ^{19}F NMR (376 MHz, $CDCl_3$): δ –62.32; ATR-FTIR (neat): 2971, 1617, 1512, 1408, 1327, 1318, 1172, 1162, 1118, 1084, 1066, 1016, 840 cm^{-1}; HRMS (EI) *m/z* calculated for $C_{11}H_{13}F[M]^+$: 292.1439, found: 292.1441.



3c

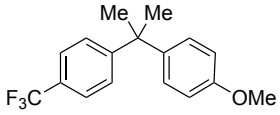
1-ethyl-4-(2-(4-(trifluoromethyl)phenyl)propan-2-yl)benzene 3c: General procedure III was followed using 93 mg of alkene **1a** (0.5 mmol), 159 mg of **2c** (1.5 mmol), 10 mg of

tritylium TPFPB (0.01 mmol) and 2.0 mL of dichloroethane. Purification by flash column chromatography (100% hexanes) afforded **3c** (134 mg, 91% yield) as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.54-7.52 (d, *J* = 8.1 Hz, 2H), 7.36-7.34 (d, *J* = 8.2 Hz, 2H), 7.17 (m, 4H), 2.66-2.61 (q, *J* = 8.2 Hz, 8.0 Hz, 2H), 1.69 (s, 6H); 1.26 (t, *J* = 7.6 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 155.0 (C), 146.9 (C), 141.8 (C), 129.4 (C), 128.3 (C), 127.8 (CH), 127.7 (q, *J* = 273.0 Hz, C), 127.6 (q, *J* = 32.5 Hz, C), 127.5 (q, *J* = 4.0 Hz, CH), 125.0-124.8 (CF), 30.6 (CH_3), 28.3 (CH_2), 21.9 (C), 15.4 (CH_3); ^{19}F NMR (376 MHz, $CDCl_3$): δ –62.31; ATR-FTIR (neat): 3024, 2966, 2932, 2873, 1673, 1617, 1582, 1512, 1493, 1463, 1451, 1409, 1364, 1327, 1252, 1233, 1166, 1126, 1108, 1086, 1067, 1016, 970, 920, 875, 840 cm^{-1}; HRMS (EI) *m/z* calculated for $C_{11}H_{13}F[M]^+$: 292.1139, found: 292.1441.



3d

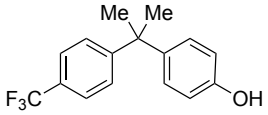
1-(*tert*-butyl)-4-(2-(4-(trifluoromethyl)phenyl)propan-2-yl)benzene 3d: General procedure II was followed using 93 mg of alkene **1a** (0.5 mmol), 201 mg of **2d** (1.5 mmol), 10 mg of tritylium TPFPB (0.01 mmol) and 2.0 mL of dichloroethane. Purification by flash column chromatography (100% hexanes) afforded **3d** (140 mg, 88% yield) as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.53-7.51 (d, *J* = 8.0 Hz, 2H), 7.37-7.35 (d, *J* = 8.0 Hz, 2H), 7.31-7.28 (m, 2H), 7.14-7.12 (d, *J* = 8.0 Hz, 2H), 1.65 (s, 6H), 1.70 (s, 6H), 1.32 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 154.9 (C), 149.9 (C), 148.7 (C), 146.5 (C), 127.1 (CH), 126.8 (q, *J* = 253.0 Hz, C), 126.2 (CH), 125.0 (CH), 126.2 (CH), 125.0 (CH), 124.9-124-8 (CF), 123.9 (q, *J* = 28 Hz, C), 123.6 (q, *J* = 2.8 Hz, CH), 42.7 (C), 34.4(C), 31.3(CH_3), 30.6(CH_3); ^{19}F NMR (376 MHz, $CDCl_3$): δ –62.32; ATR-FTIR (neat): 2966, 2871, 2785, 1327, 1166, 1121, 1066, 1015, 840 cm^{-1}; HRMS (EI) *m/z* calculated for $C_{11}H_{13}F[M]^+$: 320.1752, found: 320.1745.



3e

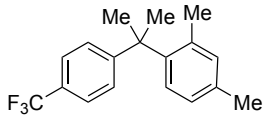
methoxy-3-(2-(4-(trifluoromethyl)phenyl)propan-2-yl)benzene 3e: General procedure II was followed using 93 mg of alkene **1a** (0.5 mmol), 165 mg of **2e** (1.5 mmol), 10 mg of tritylium TPFPB (0.01 mmol) and 2.0 mL of dichloroethane. Purification by flash column chromatography (hexanes:benzene 7:3) afforded **3e** (135 mg, 92% yield) as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.57-7.55 (d, *J* = 8.0 Hz, 2H), 7.40-7.38 (d, *J* = 8.0 Hz, 2H), 7.19-7.17 (d, *J* = 8.0 Hz, 2H), 6.69-6.67 (d, *J* = 8.0 Hz, 2H), 3.83 (s, 3H), 1.73 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 157.7 (C), 155.1 (C), 141.8 (C), 131.2 (q, *J* = 273.0 Hz, C), 128.4 (q, *J* = 4.0 Hz, CH), 128.0 (q, *J* = 32.5 Hz, C), 128.0 (CH), 127.4 (C), 127.1

(CH), 125.0-124.9 (CF), 113.4 (CH), 55.2 (CH_3), 42.5 (C), 30.7 (CH_3); ^{19}F NMR (376 MHz, $CDCl_3$): δ –62.32; ATR-FTIR (neat): 2963, 2932, 2869, 1617, 1454, 1409, 1327, cm^{-1}; HRMS (EI) *m/z* calculated for $C_{11}H_{13}F[M]^+$: 294.1231, found: 294.1217.



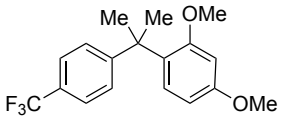
3g

4-(2-(4-(trifluoromethyl)phenyl)propan-2-yl)phenol 3g: General procedure II was followed using 93 mg of alkene **1a** (0.5 mmol), 141 mg of **2g** (1.5 mmol), 10 mg of tritylium TPFPB (0.01 mmol) and 2.0 mL of dichloroethane. Purification by flash column chromatography (hexanes:benzene 5:5) afforded **3g** (90 mg, 64% yield) as a colorless oil. ^1H NMR (400 MHz, $CDCl_3$): δ 7.54-7.52 (d, *J* = 8.0 Hz, 2H), 7.34-7.32 (d, *J* = 8.0 Hz, 2H), 7.09-7.07 (d, *J* = 8.0 Hz, 2H), 6.77-6.75 (d, *J* = 8.0 Hz, 2H), 4.84 (s, 1H), 1.67 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 155.0 (C), 153.5 (C), 142.1 (C), 128.0 (C), 129.7 (q, *J* = 273.0 Hz, C), 128.3 (q, *J* = 32.5 Hz, C), 128.0 (CH), 127.1 (CH), 124.9-124.8 (CF), 114.9 (CH), 42.5 (C), 30.7 (CH_3); ^{19}F NMR (376 MHz, $CDCl_3$): δ –62.32; ATR-FTIR (neat): 3066, 2972, 2881, 2802, 2735,1639,1111 cm^{-1}; HRMS (EI) *m/z* calculated for $C_{11}H_{13}F[M]^+$ 280.1075:, found: 280.1087.



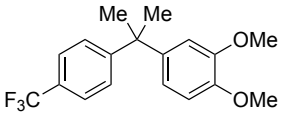
3h

2,4-dimethyl-1-(2-(4-(trifluoromethyl)phenyl)propan-2-yl)benzene 3h: General procedure II was followed using 93 mg of alkene **1a** (0.5 mmol), 159 mg of **2h** (1.5 mmol), 10 mg of tritylium TPFPB (0.01 mmol) and 2.0 mL of dichloroethane. Purification by flash column chromatography (100% hexanes) afforded **3h** (139 mg, 95% yield) as a colorless oil. ^1H NMR (400 MHz, $CDCl_3$): δ 7.73-7.68 (m, 2H), 7.55-7.52 (m, 1H), 7.39-7.35 (m, 1H), 7.00-6.98 (d, *J* = 4.0 Hz, 1H), 6.84-6.80 (m, 2H), 2.22(s, 3H), 2.19 (s, 3H), 1.73 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 148.5 (C), 147.8 (C), 135.8 (C), 133.3 (C), 131.4 (CH),129.4 (C), 129.2 (CH), 129.1 (CH), 126.3 (CH), 128.8-128.6 (CF), 126.3 (q, *J* = 273.0 Hz, C), 125.9 (q, *J* = 4.0 Hz, CH), 123.1 (q, *J* = 32.5 Hz, C), 44.1 (C), 32.3 (CH_3), 20.0 (CH_3), 19.3 (CH_3); ^{19}F NMR (376 MHz, $CDCl_3$): δ –53.02; ATR-FTIR (neat): 2972, 2881, 2802, 2735, 1639, 1576, 1387, 1365, cm^{-1}; HRMS (EI) *m/z* calculated for $C_{11}H_{13}F[M]^+$: 292.1439, found: 292.1441.



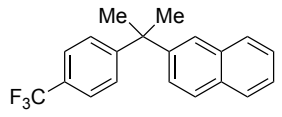
3i

1,2-dimethoxy-3-(2-(4-(trifluoromethyl)phenyl)propan-2-yl)benzene 3i: General procedure II was followed using 91 mg of alkene **1a** (0.5 mmol), 161 mg of **2i** (1.5 mmol), 10 mg of tritylium TPFPB (0.01 mmol) and 2.0 mL of dichloroethane. Purification by flash column chromatography (hexanes:benzene 7:3) afforded **3i** (149 mg, 94% yield) as a colorless oil.^{1}H NMR (400 MHz, $CDCl_3$): δ 7.47-7.45 (d, *J* = 8.0 Hz, 2H), 7.36-7.34 (d, *J* = 4.0 Hz, 1H), 7.25-7.23 (m, 2H), 6.52-6.50 (m, 1H), 6.39-6.37 (m, 1H), 3.82 (s, 3H), 3.33 (s, 3H), 1.64 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 159.8 (C), 159.6 (C), 145.7 (C), 137.1 (C), 134.0 (C), 127.0 (CH), 125.7 (CH), 124.5-124.3 (CF), 123.2 (CH), 124.4 (q, *J* = 273.0 Hz, C), 123.4 (q, *J* = 32.5 Hz, C), 123.2 (q, *J* = 4.0 Hz, CH), 103.8 (CH), 100.1 (CH), 55.2 (CH_3), 55.1 (CH_3), 41.7 (C) 29.6 (CH_3); ^{19}F NMR (376 MHz, $CDCl_3$): δ –62.08; ATR-FTIR (neat): 2967, 2837, 2825, 2236, 1979, 1307, 1209, cm^{-1}HRMS (EI) *m/z* calculated for $C_{11}H_{13}F[M]^+$: 324.1337, found: 324.1340.



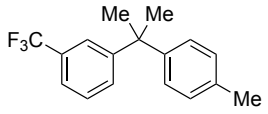
3j

1,2-dimethoxy-3-(2-(4-(trifluoromethyl)phenyl)propan-2-yl)benzene 3j: : General procedure II was followed using 93 mg of alkene **1a** (0.5 mmol), 161 mg of **2j** (1.5 mmol), 10 mg of tritylium TPFPB (0.01 mmol) and 2.0 mL of dichloroethane. Purification by flash column chromatography (hexanes:benzene 7:3) afforded **3j** (143 mg, 88% yield) as a colorless oil. (139 mg, 87 % yield). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.54-7.52 (d, *J* = 8.0 Hz, 2H), 7.37-7.35 (d, *J* = 8.0 Hz, 2H), 6.82-6.80 (d, *J* = 8.0 Hz, 2H), 6.69 (m, 1H), 3.83 (s, 3H), 3.79 (s, 3H), 1.70 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 155.1 (C), 148.5 (C), 147.6 (C), 142.3 (C), 128.3 (CH), 128.0 (q, *J* = 273.0 Hz, C), 127.9 (q, *J* = 32.5 Hz, C), 127.0 (CH), 125.8 (q, *J* = 4.0 Hz, CH), 125.0-124-8 (CF), 118.1 (CH), 110.6 (CH), 55.8 (CH_3), 55.1 (CH_3), 42.3 (C) 30.7 (CH_3); ^{19}F NMR (376 MHz, $CDCl_3$): δ –62.32; ($CDCl_3$): ATR-FTIR (neat): 3062, 3018, 2985, 2909, 2813, 2785, 1616, 1590, 1521, 1507, 1267, 1253, 841 cm^{-1}; HRMS (EI) *m/z* calculated for $C_{11}H_{13}F[M]^+$: 324.1337, found: 324.1348.



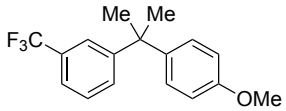
3k

2-(2-(4-(trifluoromethyl)phenyl)propan-2-yl)naphthalene 3k. General procedure II was followed using 93.3 mg of alkene **1a** (0.5 mmol), 192 mg of **2k** (1.5 mmol), 10 mg of tritylium TPFPB (0.01 mmol) and 2.0 mL of dichloroethane. Purification by flash column chromatography (100% hexanes) afforded **3k** (129 mg, 82% yield) as a colorless oil. Our NMR spectra matched those reported by Crudden.[2] ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.87–7.78 (m, 3H), 7.73 (d, *J* = 8.7 Hz, 1H), 7.56–7.44 (m, 4H), 7.38 (d, *J* = 8.8 Hz, 2H), 7.17 (dd, *J* = 8.7, 2.0 Hz, 1H), 1.81 (s, 6H).



3k

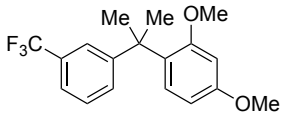
1-(2-(*p*-tolyl)propan-2-yl)-3-(trifluoromethyl)benzene 3k: General procedure II was followed using 92.9 mg of alkene **1b** (0.5 mmol), 137 mg of **2k** (1.5 mmol), 10 mg of tritylium TPFPB (0.01 mmol) and 2.0 mL of dichloroethane. Purification by flash column chromatography (100% hexanes) afforded **3k** (111 mg, 80% yield) as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.58 (s, 1H), 7.49–7.42 (m, 1H), 7.41–7.36 (m, 2H), 7.12 (s, 4H), 2.35 (s, 3H), 1.71 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): 151.9 (C), 146.7 (C), 135.5 (C), 130.7 (C), 130.7 (CH), 130.2 (q, *J* = 31.8 Hz, C), 128.9 (CH), 128.4 (CH), 126.6 (CH), 124.3 (q, *J* = 270.1 Hz, C), 123.0 (q, *J* = 3.8 Hz, CH), 122.5 (q, *J* = 3.9 Hz, CH), 42.8 (C), 30.7 (CH_3), 20.9 (CH_3); ^{19}F NMR (376 MHz, $CDCl_3$): δ –62.31; ATR-FTIR (neat): 3040, 3004, 2965, 2906, 2803, 2784, 1600, 1570, 1501, 1499, 1264, 1252, 840 $cm^{-1}cm^{-1}$; HRMS (EI) *m/z* calculated for $C_{11}H_{13}F[M]^{+}$: 292.1439, found: 292.1441.



3m

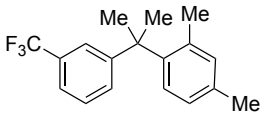
1-(2-(4-methoxyphenyl)propan-2-yl)-3-(trifluoromethyl)benzene. General procedure II was followed using 93 mg of alkene **1b** (0.5 mmol), 163 mg of **2m** (1.5 mmol), 10 mg of tritylium TPFPB (0.01 mmol) and 2.0 mL of dichloroethane. Purification by flash column chromatography (hexanes/benzene, 7:3) afforded **3m** (122 mg, 83% yield) as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ7.60 (s, 1H), 7.50–7.44 (m, 1H), 7.43–7.36 (m, 2H), 7.20–7.15 (m, 2H), 6.90–6.85 (m, 2H), 3.82 (s, 3H), 1.73 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): 157.7 (C), 152.0 (C), 141.8 (C), 130.6 (CH), 130.2 (q, *J* = 30.6 Hz, C), 128.4 (CH), 127.7 (CH), 124.5 (q, *J* = 271.1 Hz, C), 123.0 (q, *J* = 3.8 Hz, CH), 122.5 (q, *J* = 3.8 Hz, CH), 113.5 (CH), 55.2 (CH_3), 42.8 (C), 30.8 (CH_3); ^{19}F NMR (376 MHz, $CDCl_3$): δ –62.3; ATR-FTIR (neat): 3061, 3015, 2982, 2906, 2803, 2765, 1610, 1580, 1521, 1506,

1260, 1253, 845 $cm^{-1}cm^{-1}$; HRMS (EI) *m/z* calculated for $C_{11}H_{13}F[M]^+$: 294.1231, found: 294.1219.



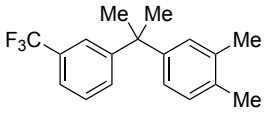
3n

2,4-dimethoxy-1-(2-(3-(trifluoromethyl)phenyl)propan-2-yl)benzene. General procedure II was followed using 93 mg of alkene **1b** (0.5 mmol), 207 mg of **2n** (1.5 mmol), 10 mg of tritylium TPFPB (0.01 mmol) and 2.0 mL of dichloroethane. Purification by flash column chromatography (hexanes/benzene, 7:3) afforded **3n** (135 mg, 83% yield) as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ7.51 (s, 1H), 7.40 (d, *J* = 8.6 Hz, 2H), 7.35–7.28 (m, 2H), 6.55 (dd, *J* = 8.6, 2.6 Hz, 1H), 6.41 (d, *J* = 2.5 Hz, 1H), 3.84 (s, 3H), 3.34 (s, 3H), 1.70 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): 159.7 (C), 158.5 (C), 152.9 (C), 130.0 (C), 129.8 (q, *J* = 31.5 Hz, C), 129.1 (CH), 128.4 (CH), 127.9 (CH), 126.0 (CH), 124.6 (q, *J* = 272.2 Hz, C), 122.1 (q, *J* = 3.9 Hz, CH), 121.6 (q, *J* = 3.9 Hz, CH), 55.2 (CH_3), 54.9 (CH_3), 41.43 (C), 29.6 (CH_3); ^{19}F NMR (376 MHz, $CDCl_3$): δ –62.2; ATR-FTIR (neat): 3080, 3014, 2985, 2909, 2812, 2780, 1616, 1590, 1521, 1507, 1267, 1251, 839 $cm^{-1}cm^{-1}$; HRMS (EI) *m/z* calculated for $C_{11}H_{13}F[M]^+$: 324.1337, found: 324.1313.



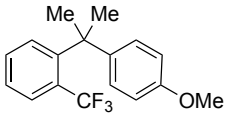
3o

2,4-dimethyl-1-(2-(3-(trifluoromethyl)phenyl)propan-2-yl)benzene 3o: General procedure II was followed using 93 mg of alkene **1b** (0.5 mmol), 159 mg of **2o** (1.5 mmol), 10 mg of tritylium TPFPB (0.01 mmol) and 0.2 mL of dichloroethane. Purification by flash column chromatography (100% hexanes) afforded **3o** (127 mg, 87% yield) as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.59–7.57 (m, 1H), 7.48-7-45 (m, 1H), 7.39–7.37 (m, 2H), 6.87–6.84 (m, 3H). 2.30 (s, 6H); 1.70 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 151.92 (C), 149.64 (C), 143.37 (C), 137.52 (CH), 133.47 (C), 131.2 (q, *J*= 31.5 Hz, C), 128.36 (CH), 128.30 (CH), 127.66 (CH), 124.58 (CH), 124.4 (q, *J* = 270.1 Hz, C), 124.1 (CH), 123.0 (q, *J* = 3.8 Hz, CH), 122.5 (q, *J* = 3.8 Hz, CH), 42.90 (C), 30.70 (CH_3), 21.48 (CH_3); ^{19}F NMR (376 MHz, $CDCl_3$): δ –62.31; ATR-FTIR (neat): cm^{-1}; HRMS (EI) *m/z* calculated for $C_{11}H_{13}F[M]^+$: 292.1439, found:292.1441.



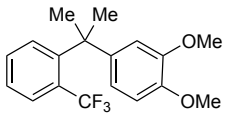
3p

1,2-dimethyl-4-(2-(3-(trifluoromethyl)phenyl)propan-2-yl)benzene. General procedure II was followed using 93 mg of alkene **1b** (0.5 mmol), 159 mg of **3p** (1.5 mmol), 10 mg of tritylium TPFPB (0.01 mmol) and 2.0 mL of dichloroethane. Purification by flash column chromatography (100% hexanes) afforded **3p** (127 mg, 87% yield) as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ7.63 (s, 1H), 7.51–7.45 (m, 1H), 7.44–7.35 (m, 2H), 7.13–7.06 (m, 1H), 7.02 (s, 1H), 7.00–6.95 (m, 1H), 2.28 (s, 3H), 2.27 (s, 3H), 1.73 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): 152.0 (C), 147.2 (C), 136.2 (C), 134.2 (C), 130.7 (CH), 130.2 (q, *J*= 31.5 Hz, C), 129.5 (CH), 128.4 (CH), 128.0 (CH), 125.8 (CH), 124.4 (q, *J* = 270.1 Hz, C), 124.1 (CH), 123.0 (q, *J* = 3.8 Hz, CH), 122.5 (q, *J* = 3.8 Hz, CH), 42.7 (C), 20.0 (CH_3), 19.3 (CH_3); ^{19}F NMR (376 MHz, $CDCl_3$): δ –62.3; ATR-FTIR (neat): 3050, 3052, 2965, 2901, 2822, 2784, 1614, 1591, 1520, 1507, 1267, 1253, 832 $cm^{-1}cm^{-1}$; HRMS (EI) *m/z* calculated for $C_{11}H_{13}F[M]^+$: 292.1439, found:292.1441.



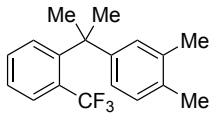
3r

1-(2-(4-methoxyphenyl)propan-2-yl)-2-(trifluoromethyl)benzene 3r: General procedure II was followed using 93 mg of alkene **1c** (0.5 mmol), 151 mg of **2r** (1.5 mmol), 10 mg of tritylium TPFPB (0.01 mmol) and 2.0 mL of dichloroethane. Purification by flash column chromatography (100% hexanes) afforded **3r** (134 mg, 82% yield) as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.74-7.67 (m, 2H), 7.55-7.51 (m, 1H), 7.39-7.35 (m, 1H) 7.01-6.99 (d, *J* = 8.0 Hz, 2H), 6.78-6.76 (d, *J* = 8.0 Hz, 2H), 3.78 (s,3H), 1.73 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 157.3 (C), 147.9 (C), 142.9 (C), 142.8 (C), 131.4 (CH), 128.9 (CH), 128.9-128.7 (CF), 126.7 (CH), 125.8 (q, *J* = 273.0 Hz, C), 125.2 (q, *J* = 32.5 Hz, C), 123.1 (q, *J* = 4.0 Hz, CH), 113.1 (CH), 55.1 (CH_3), 43.8 (C) 32.6 (CH_3); ^{19}F NMR (376 MHz, $CDCl_3$): δ –53.93 (F); ATR-FTIR (neat): 2972, 2836, 2198, 2153, , 1614, 1582, 1503, 1383, 11066, 1038 cm^{-1}; HRMS (EI) *m/z* calculated for $C_{11}H_{13}F[M]^+$: 294.1231, found: 294.1219.



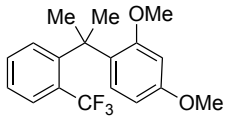
3t

1,2-dimethoxy-3-(2-(4-(trifluoromethyl)phenyl)propan-2-yl)benzene 3t: General procedure II was followed using 93 mg of alkene **1c** (0.5 mmol), 159 mg of **2t**, 10 mg of tritylium TPFPB (0.01 mmol) and 2.0 mL of dichloroethane. Purification by flash column chromatography (hexanes:benzene 7:3) afforded **3t** (141 mg, 89% yield) as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.72-7.68 (m, 2H), 7.55-7.51 (m, 1H), 7.39-7.35 (m, 1H), 6.75-6.73 (m, 1H), 6.66-6.64 (m, 1H), 6.58-6.56 (m, 2H), 3.85 (s, 3H), 3.75(s, 3H), 1.73 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 148.3 (C), 148.0 (C), 146.9 (C), 143.5 (C), 131.4 (CH), 129.4 (q, J = 273.0 Hz, C), 129.0 (CH), 128.9 (q, *J* = 32.5 Hz, CH), 128.2 (q, *J* = 4.0 Hz, C), 126.5 (CH), 117.9-117.7 (CF), 110.5 (CH), 109.9 (CH), 56.1 (CH_3), 56.0 (CH_3), 44.4 (C) 32.3 (CH_3); ^{19}F NMR (376 MHz, $CDCl_3$): δ –53.92 (F); ATR-FTIR (neat): 2966, 2955, 2904, 1512, 1490, 1251, cm^{-1}; HRMS (EI) *m/z* calculated for $C_{11}H_{13}F[M]^+$: 324.1337, found: 324.1313.



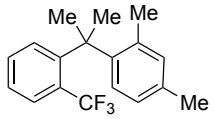
3u

1,2-dimethyl-4-(2-(4-(trifluoromethyl)phenyl)propan-2-yl)benzene 3u: General procedure II was followed using 93 mg of alkene **1c** (0.5 mmol), 159 mg of **2u**, 10 mg of tritylium TPFPB (0.01 mmol) and 2.0 mL of dichloroethane. Purification by flash column chromatography (100% hexanes) afforded **3u** (128 mg, 88% yield) as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.73-7.68 (m, 2H), 7.53-7.50 (m, 1H), 7.39-7.35 (m, 1H), 7.00-6.97 (m, 1H), 6.84-6.79 (m, 2H), 2.20 (s, 3H), 2.18 (s, 3H), 1.73 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 148.4 (C), 147.8 (C), 135.7 (C), 133.3 (C), 131.4 (CH), 129.5 (q, *J* = 273.0 Hz, C), 129.2 (CH), 129.0 (CH), 128.9 (q, *J* = 32.5 Hz, C), 128.7-128.5 (CF), 128.5 (q, *J* = 4.0 Hz, CH), 128.3 (CH), 126.4 (CH), 44.1 (C), 32.4 (CH_3), 19.9 (CH_3); 19.3 (CH_3); ^{19}F NMR (376 MHz, $CDCl_3$): δ –53.81 (F); ATR-FTIR (neat): 2983, 2161, 2054, 1968, 1919, 1455, 1279, 1209, cm^{-1}; HRMS (EI) *m/z* calculated for $C_{11}H_{13}F[M]^+$: 292.1439, found: 292.1441.



3v

2,4-dimethoxy-1-(2-(2-(trifluoromethyl)phenyl)propan-2-yl)benzene benzene 3v: General procedure II was followed using 93 mg of alkene **1a** (0.5 mmol), 162 mg of **2v** 10 mg of tritylium TPFPB (0.01 mmol) and 2.0 mL of dichloroethane. Purification by flash column chromatography (hexanes/benzene 7:3) afforded **3v** (144 mg, 89% yield) as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.62-7.60 (d, *J* = 8.0 Hz, 2H), 7.46-7.44 (m, 1H), 7.30-7.22 (m, 2H), 6.51-6.49 (d, *J* = 8.0 Hz, 1H), 6.33-6.32 (d, *J* = 4.0 Hz, 1H), 3.81 (s, 3H), 3.27 (s, 3H), 1.71 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 159.2 (C), 158.7 (C), 150.1 (C), 143.2 (C), 130.8 (C), 131.2 (CH), 129.4 (CH), 129.2 (q, J = 273.0 Hz, C), 128.8 (q, *J* = 32.5 Hz, C), 128.2 (q, *J* = 4.0 Hz, CH), 128.4 (CH), 127.6-127.4 (CF), 103.5 (CH), 99.6 (CH), 54.8 (CH_3), 42.5 (C) 30.7 (CH_3); ^{19}F NMR (376 MHz, $CDCl_3$): δ –62.32; ATR-FTIR (neat): 2967, 2837, 2825, 2236, 1979, 1307, 1209, cm^{-1} HRMS (EI) *m/z* calculated for $C_{11}H_{13}F[M]^+$: 324.1337, found: 324.1340.



3w

2,4-dimethyl-1-(2-(2-(trifluoromethyl)phenyl)propan-2-yl)benzene 3w: General procedure II was followed using 93 mg of alkene **1c** (0.5 mmol), 159 mg of **2w** 10 mg of tritylium TPFPB (0.020 mmol) and 2.0 mL of dichloroethane. Purification by flash column chromatography (100% hexanes) afforded **3w** (138 mg, 95% yield) as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.54-7.49 (m, 2H), 7.36-7.34 (m, 2H), 7.05-7.01 (m, 1H), 6.93-6.91 (m, 2H), 6.84-6.80 (m, 2H), 2.22(s, 3H), 2.19 (s, 3H), 1.73 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 155.0 (C), 147.1 (C), 136.1 (C), 134.1 (C), 129.3 (CH),128.0 (C), 127.0 (CH), 126.2 (CH), 126.1 (CH), 124.9-124.8 (CF), 126.3 (q, *J* = 273.0 Hz, C) ,125.9 (q, *J* = 4.0 Hz, CH), 123.1 (q, *J* = 32.5 Hz, C), 42.81 (C), 30.02 (CH_3), 20.00 (CH_3), 19.25 (CH_3); ^{19}F NMR (376 MHz, $CDCl_3$): δ –53.20; ATR-FTIR (neat): 2972, 2881, 2802, 2735, 1639, 1576, 1387, 1365, cm^{-1}; HRMS (EI) *m/z* calculated for $C_{11}H_{13}F[M]^+$: 292.1439, found: 292.1441.

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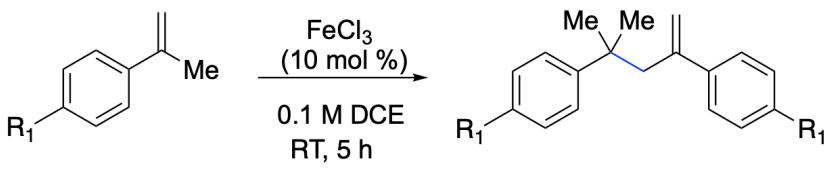
CHAPTER 2

Lewis Acid-Catalyzed Hydroarylation of Styrenes for Linear Dimers

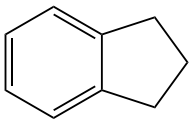
Background

I previously reported an efficient and highly selective methodology to functionalize trifluoromethylation alpha-methylated styrene with a variety of aromatic compounds by utilizing an easily handled precatalyst (tetrakis(pentafluorophenyl)borate) in an intermolecular hydroarylation fashion.[1] In the course of this study, I discovered that trifluoromethylation alpha-methylated styrenes in the presence of iron chloride ($FeCl_3$) gave us the linear product in Scheme. I decided to continue to probe the generality of this phenomenon by studying different alpha-methyl styrenes derivates (Scheme 7).



Scheme 7. Lewis Acid-Catalyzed hydroarylation of styrenes for new linear dimers.

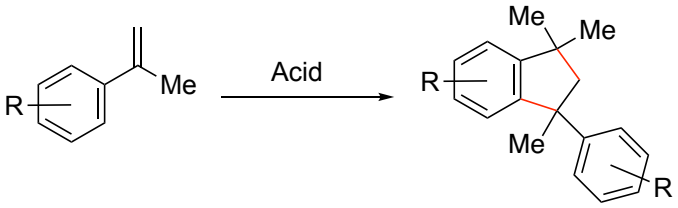
I have a standing interest in both quaternary carbon-containing compounds and hydroarylation reactions. Many metal-catalyzed[2] and acid-catalyzed[3] hydroarylations of alkenes are known, but few of them efficiently afford quaternary carbons from 1,1-disubstituted alkenes.[3] Quaternary carbons are difficult to synthesize due to their sterically congested nature, which can lead to kinetic barriers to the formation and thermodynamic instability.[4] Nonetheless, such molecules are highly sought after in medicines, materials, and synthetic intermediates.[5] Traditional α-methyl styrenes precursors are used via dimerization to make an indane derivative backbone. The indane structure is depicted in structure **1**.



1

Indane derivatives are present in many pharmaceutical drugs and derivatives.[6a,6b] Byproducts are the main challenge for this chemistry because it has been reported that α-methyl styrenes in the presence of a strong acid are prone to dimerization (Scheme 8).[7]

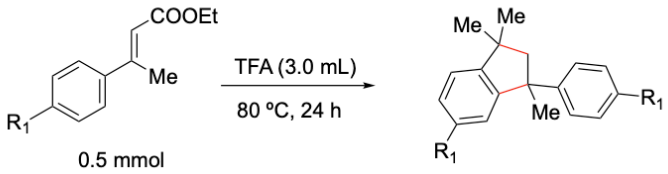
A. Previous work: Dimerization of alpha-methylstyrenes (Fisher and coworkers, 1958).[7]



Scheme 8. Dimerization of α -methyl styrenes (Fisher and coworkers, 1958).[7]

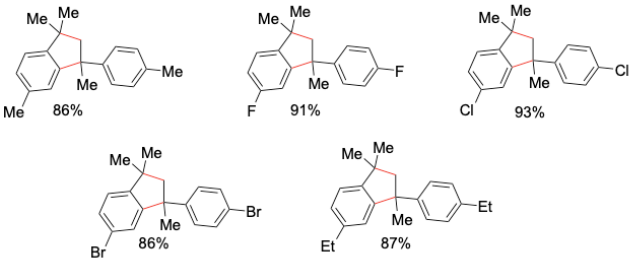
Another drawback from α -methyl styrene dimerization is that functionalization is very hard to obtain after indane backbone is formed.

In related work to α -methyl styrene, Satyanarayana et al. reported metal-free domino one-pot decarboxylative cyclization of cinnamic acid esters toward synthesis of functionalized indanes by employing trifluoroacetic acid (TFA) as a catalyst (Scheme 9).[8]



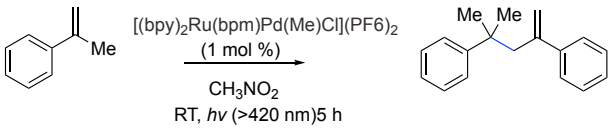
Scheme 9. Decarboxylative cyclization of cinnamic acid esters

Satyanarayana's group applied this methodology to afford many indane derivatives. These derivatives had good yields ranging from 93-86% (Scheme1.)



Scheme 10. Decarboxylative cyclization of cinnamic acid esters to form indane derivatives.

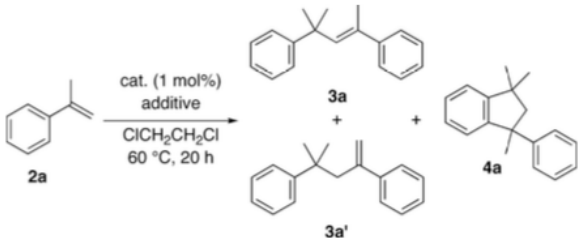
After looking in the literature for examples of styrene reacting with acids, I decided to search for methods that would give the linear dimer product. After looking in the literature I found that there are limited examples to make the linear dimerization, furthermore none for our substrate **2a**. One of the few methods available for linear dimer construction is palladium-ruthenium based chemistry (Scheme 11). [9] Akita and coworkers, employed palladium-ruthenium base catalyst for the formation of the linear dimerization of a-methyl styrene to give the 4-methyl-2,4-diphenyl-1-pentene in 90% yield.



Scheme 11. Previous work: Dimerization of a-methylstyrene by a novel palladium complex with photosensitizing ruthenium(II) polypyridyl moiety (Akita and coworkers, 2005).[9]

In another work, Nishibayashi et al. employed alkanethiolato-bridged diruthenium complexes as a catalyst for the linear dimerization of a-methyl styrene (Table A).[10] This work was a less effective methodology than what Akita [9] had reported earlier. They screened different alkanethiolato-bridged diruthenium complexes catalysts for optimization. When submitting a-methyl styrene to conditions (entry 1) in table 6, 4-methyl-2,4-diphenyl-1-pentene was obtained in 68% yield which was less than the results previously reported by Akita's group. Furthermore, the final product was a mixture of **3a** and **3a'**.

Table 6. Alkanethiolato-bridged diruthenium complexes as a catalyst for the linear dimerization of a-methyl styrene.

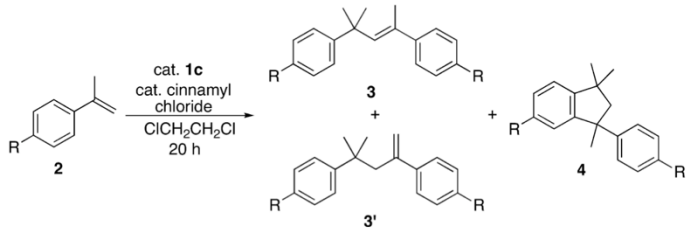


			yield (%)[b]	
entry	cat.	additive (amt (mol %))	dimer (3a/3a′)	4a
1	1c		68 (3/1)	0
2[c]	1c		51 (3/1)	2
3	1a		0	0
4	1b		72 (3/1)	0
5	1c	cinnamyl chloride (2)	0	82
6	1b	cinnamyl chloride (2)	59 (3/1)	0

[a]All reactions of **2a** (1.0 mmol) were carried out in the presence of diruthenium complex (0.010 mmol) and additive in $ClCH_2CH_2Cl$ (3 mL) at 60 °C for 20 h. [b]Isolated yield. [c]For 120 h.

However, Nishibayashi's method was more flexible. The reaction for linear dimerization formation worked well for monosubstituted styrenes (table 7). When substituting the phenyl ring at the *para* position with a methyl group, the linear dimer was formed in (entry 3) was obtained in 56% yield in a 3:1 ratio where the 3 is the major product. By replacing the H with a methoxy in the ortho (entry 4), the reaction preceded in 81% yield in a 1:4 ratio where the **3'** is the major product. Furthermore, when the H was replaced with a phenyl in the ortho position (entry 7), the reaction preceded in 68% yield in a 1:1 ratio where **3** and **3'** were formed.

Table 7. Linear dimerization formation worked well for monosubstituted styrenes.



entry	R	amt of **1c** (mol %)	amt of cinnamyl chloride (mol %)	temp (°C)	yield (%)[b] dimer (3/3')	yield (%)[b] 4
1	H (**2a**)	1		60	68 (3/1)	0
2	H (**2a**)	1	2	60	0	82
3	Me (**2b**)	3		40	56 (3/1)	4
4	Me (**2b**)	3	6	40	0	82
5	MeO (**2c**)	1		40	81 (1/4)	0
6	MeO (**2c**)	1	2	40	0	86
7	Ph (**2d**)	1		60	68 (1/1)	0
8	Ph (**2d**)	1	2	60	9 (2/1)	64

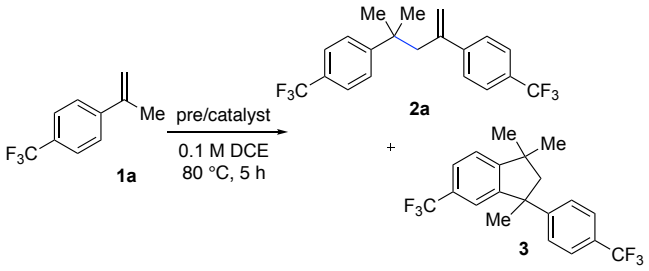
[a]All reactions of **2** (1.0 mmol) were carried out in the presence of **1c** (0.010 mmol) and additive in $ClCH_2CH_2Cl$ (3 mL) for 20 h. [b]Isolated yield.

Nishibayashi's group also used cinnamyl chloride in their reactions as co-catalyst. When substituting the phenyl ring at the *para* position with a methyl group in the presence of cinnamyl chloride the linear dimer was not formed (entry 5**).** Instead, 82% of the indane product was obtained. By replacing the H with a methoxy one (entry 6) the reaction preceded in 86% yield. However, in this case the indane product was the only product formed. Furthermore, when the H was replaced with a phenyl in the ortho position (entry 8) in the presence of cinnamyl chloride the reaction preceded in 64% yield where indane was the major product.

Results and Discussion

At the beginning of my work, I used **1a** as the model substrate. In this chemistry, all the olefin substrates could easily be prepared in just one step from commercially available ketones through Wittig olefination. With my olefin substrate **1a** in hand, I began the optimization (Table 8) using different acids as catalysts at various temperatures and concentrations (see the Supporting Information for details). I first screened different numbers of acids. 80% conversion was observed with iron (III) trifluoromethane (entry 1) and no desired product was formed. 100% conversion was observed with $PdCl_2$ (entry 4) and no desired product was formed. 0% conversion was observed with ruthenium chloride (III) ($RuCl_3$) (entry 2) or any ruthenium base acid. The main challenge for optimization was to minimize the formation of cyclic product **2b** and maximize the yield of the desired product **2a**. Switching to a different Lewis acid, like tin chloride ($SnCl_2$) (entry 3), and trying different metal acids didn't lead to the desired product. I next began screening the reaction with $FeCl_3$ as the catalyst. My goal was to use the least amount of acid and minimize the formation of the by-product. The reaction was highly selective toward our desired product **2a** using $FeCl_3$. At 30 mol % catalyst loading I was able to make **3a** in 91% yield (entry 12). Shortly after, with more optimization, I was able to make **3a** by only using 10 mol % of $FeCl_3$ in 91% yield at room temperature.

Table 8. Optimization of the linear hydroarylation of *p*-(trifluoromethyl)-α-methylstyrene

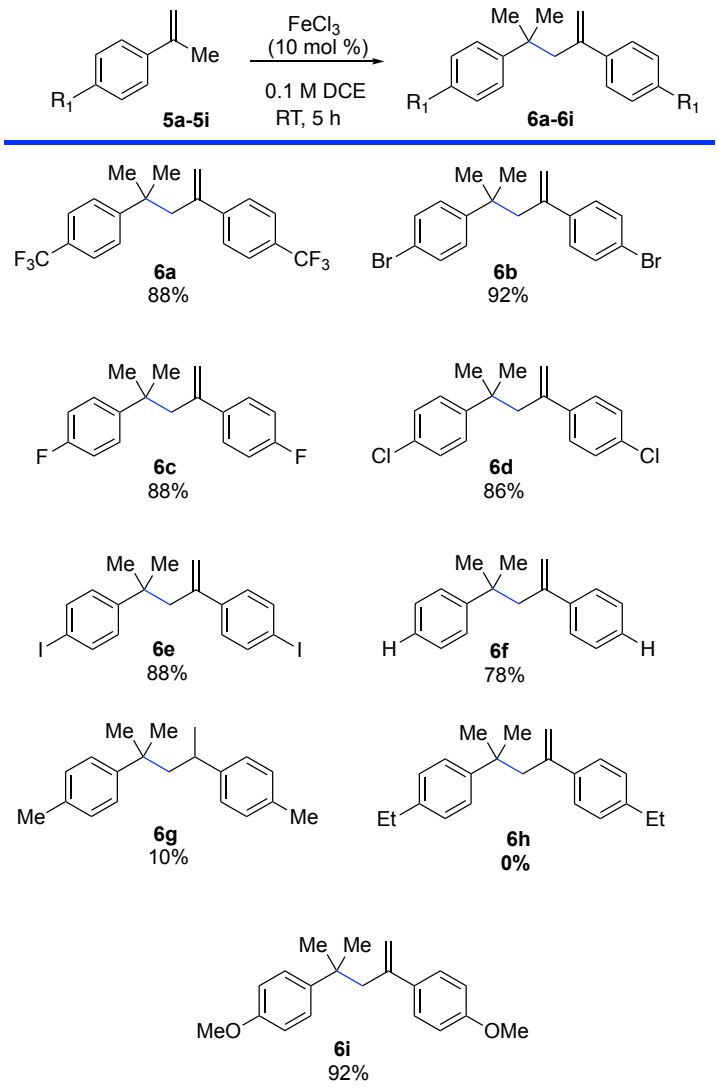


entry	pre/catalyst	pre/catalyst (mol%)	equiv of H_2O	conv (%)[a] of 1a	yield (%)[a] of 3a	yield (%)[a] of 4
1	$RuCl_3$	10	0	0	0	0
2	$RuCl_3$ H_20	20	0	0	0	0
3	TinCl	10	0	0	0	0
4	$PdCl_2$	10	0	100	0	0
5	$Fe(C_5H_7O_2)_3$	10	0	92	88	0
6	Fe(CF3$SO_{3)3}$	10	0	80	0	60
7	$FeCl_2$	10	0	0	0	0
8	$AuCl_3$	10	0	0	0	0
9	$ZnCl_2$	10	0	0	0	0
10	$FeBr_3$	10	0	95	78	0
11	FeF_3	10	0	80	72	0
12	$FeCl_3$	10	0	100	92	0
13	$FeCl_3$	10	1	0	0	0
14	$FeCl_3$	10	5	0	0	0
15[a]	$FeCl_3$	10	0	100	92	0

[a]Determined by ^{1}H NMR analysis of reaction mixture using 1,3, 5 trimethoxy benzene as an internal standard. All reactions were conducted on 0.1 mmol scale.

With the optimal reaction conditions in hand, I began testing the scope of linear hydroarylation by substituting the R_1 position of the α-methylstyrene (Table 2). I was able to isolate **6a** in 88 % yield when CF_3 was at the R_1 position. Substituting the R_1 position from CF_3 to Br substrate resulted in the highest yield of the scope in 92% yield. Similar trends were observed when the R_1 position was substituted with other electron-withdrawing groups. The substrate **5c-5e** led to the desired products with excellent yields for **6c-6e**.

Table 9. Scope of the linear hydroarylation of *p*-α-methylstyrenes[a]



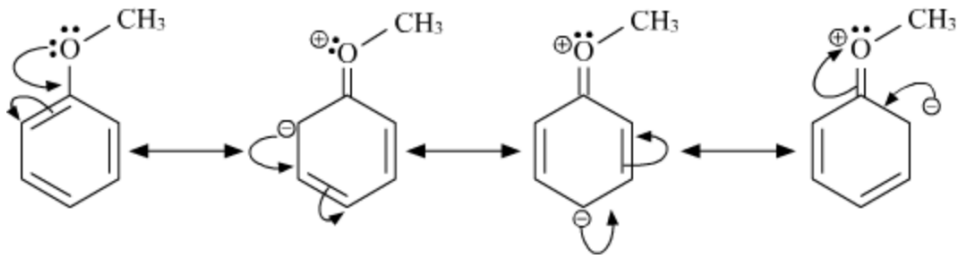
[a]isolated yields are reported and the starting material was fully consumed unless otherwise noted.

For substrate **5f** the CF_3 at the para position was replaced with Hydrogen. With the original conditions, this substrate did not give the desired product **6f**. However, the reaction did go to 100% completion forming a trimer side product. For this substrate, I made an adjustment to the original conditions and reduced the temperature to 0° C, and stopped at 30 min to reduce the side products of the reaction. A 72% isolated yield was obtained when **6f** was used as the substrate at 0° C temperature. The rest of the 28% yield for this substrate formed the trimer side product. I suspect the reduction of yield can be attributed to the absence of the electron-withdrawing group at the para because it reduces the reactivity of the alkene. I hypothesize that replacing the electron-withdrawing group with an electron-donating group at the R_1 will lead to the trimer side product. To test this test hypothesis, I decided to substitute the R_1 with a methyl group an electron-donating group. With the original conditions, this substrate did not give the desired product **6g**. However, the reaction did go to 100% completion forming a trimer side product. For this substrate, I also adjusted the original conditions by reducing the temperature of the reaction to 0° C and stopping at 30 min. The reaction only yielded 10% of **6g** that was detected via by ^{1}H NMR analysis of reaction mixture using 1,3, 5 trimethoxy benzene as an internal standard. I decided to continue testing my hypothesis by substituting the R_1 with an ethyl which is another electron-donating group. With substrate **5h** the reaction went to 100% completion, but 0% was obtained of the desired product **6h** forming a trimer side product. Furthermore, the reaction did go to 100% completion at 0° C. However, at 0° C, only a trimer side product was formed. I decided to continue investigating my hypothesis and I replaced the

R_1 position with a methoxy group that is more electron-donating. With substrate **5i** the reaction went to 100% completion, however to my surprise 50% isolated yield was obtained of the desired product **6i** and the rest was the indane product. I attribute the indane formation to the electron-donating group at R_1, activating the alkene to form the indane product. After obtaining this result, I adjusted the original conditions of the reaction by reducing the temperature to 0° C and stopping at 30 min. In this case substrate **5i** worked well, **6i** was isolated in 87% yield.

This result made me think that maybe the hypothesis could be wrong. However, I remembered the methoxy group has two ways it could affect the benzene electronics of the ring. One is through electron decollation of the methoxy to the benzene ring as represented in Scheme 12. The second one could be through induction where the oxygen is more electronegative than the carbon in the benzene causing the possibility of partially deactivating the ring long enough to stop the reaction in the linear dimer.

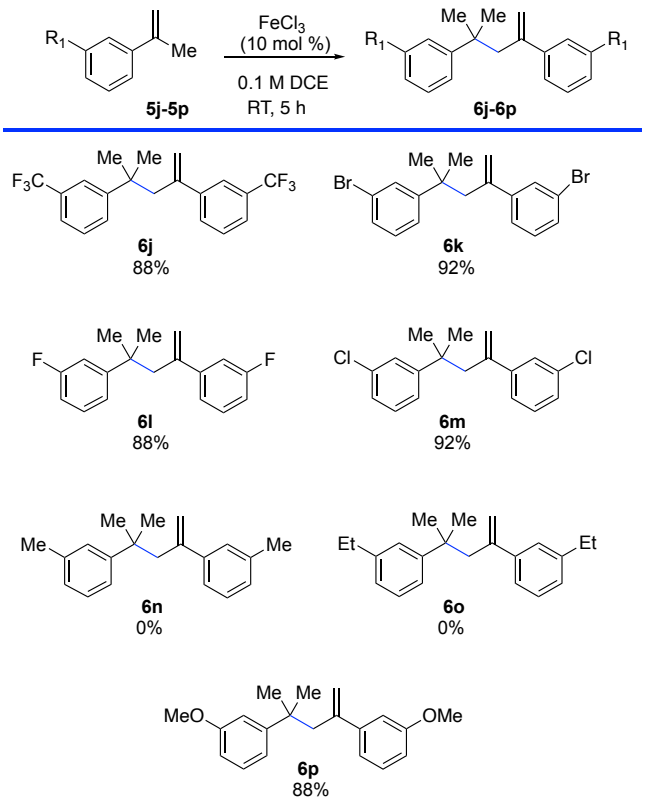
Scheme 12. Electron decollation of the methoxy to the benzene.



I continued to explore the scope of this linear hydroarylation reaction. I continued to apply our optimized conditions to α-methylstyrene by substituting the meta position R_1 with different functional groups (**Table 10**). When I replaced the R_1 position with electron-withdrawing groups I observed similar trends for the substrates **5j–5p** leading to great

isolated yields for products **6i–6o**. Furthermore, I observed similar trends for the substrates **5n** and **5o** . With the original conditions, this substrate did not give the desired products. However, the reaction did go to 100% completion forming a trimer side product. For these substrates, I also made an adjustment to the original conditions by reducing the temperature to 0° C and stopping at 30 min. However, at 0° C only the trimer side product was formed. In the case of the substrate **5p,** which worked well, **6p** was isolated in 88% yield. For this substrate, the reaction temperature was lowered to 0° C and stopped at 30 minutes. I saw the same trend as I saw for the methoxy in the para position. These results indicated that the position of the R1 group played a role in making the linear product.

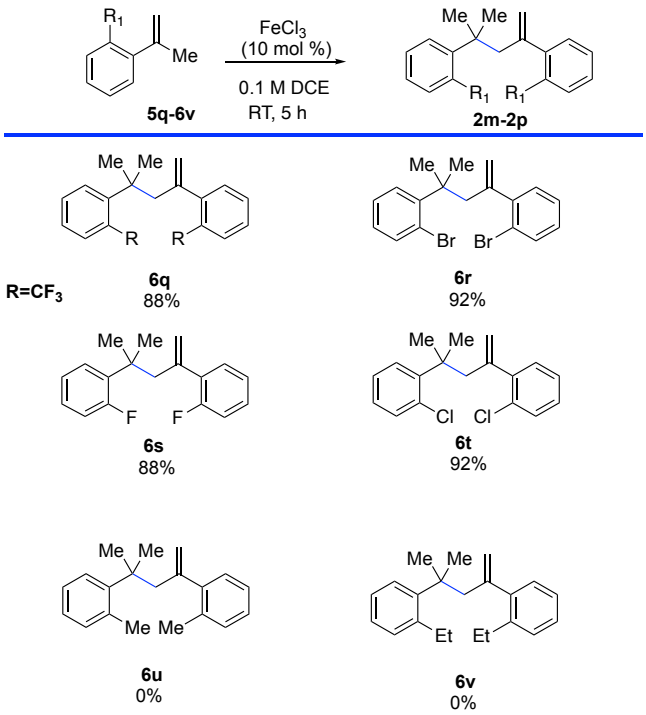
Table 10. Scope of the linear hydroarylation of *p*-α-methylstyrenes[a]



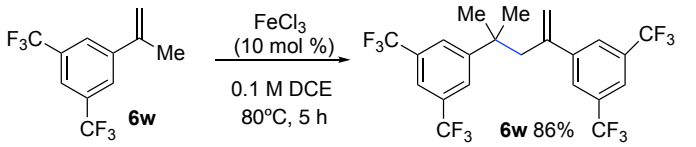
[a]Isolated yields are reported and starting material was fully consumed, unless otherwise noted

Finally, I investigated the ortho position and continued to explore the scope of this linear hydroarylation reaction. I continued to apply the optimized conditions to α-methylstyrene by substituting the ortho position R_1 with different functional groups (**Table 11**). When I replaced the R_1 position with electron-withdrawing groups I observed similar trends for the substrates **5q–5t** leading to great isolated yields for products **6q–6t**. Furthermore, I observed similar trends for the substrates **5u** and **5v**. With the original conditions, this substrate did not give the desired products. However, the reaction did go to 100% completion forming a trimer side product. Finally, linear hydroarylation of **1q** gave an 89% isolated yield.

Table 11. Scope of the intermolecular hydroarylation of *o*-α-methylstyrene[a]

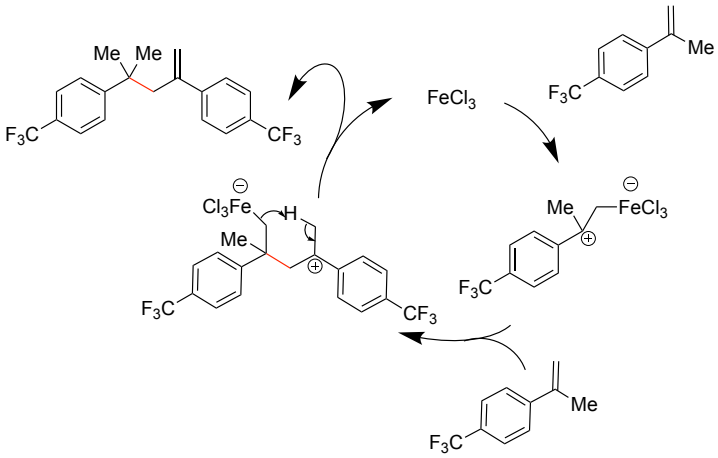


---------- Additional Example ----------



[a]Isolated yields are reported and starting material was fully consumed, unless otherwise noted.

The hypothesized mechanism for the method is described in **Scheme 13**. In step one the $FeCl_3$ adds across the alkene forming a tertiary carbocation. In the second step, another styrene comes in and acts as a nucleophile, attacking the carbon cation, forming a six-member intermediate. In the third step, the electrons that are grabbing the $FeCl_3$ are aligned close enough to grab the H two carbons away and release the $FeCl_3$ and regenerate the catalyst to continue the catalytic cycle.



Scheme 13. Proposed Mechanism

In conclusion, I developed an efficient method for catalytic linear hydroarylation dimerization of α-methylstyrene by using $FeCl_3$. I demonstrated that my reactions work with various styrenes. In addition novel molecules with geminal-dimethyl quaternary centers were prepared readily with excellent yields.

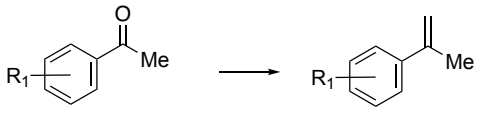
Experimental

I. General Considerations

Tetrakis(pentafluorophenyl)borate (TPFPB) was purchased from Strem or Sigma-Aldrich, and stored in a desiccator when not in use. 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. ^{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 1H NMR acquisition and were otherwise unreferenced. 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).

III. Preparation of *α*-Methylstyrene Derivatives

A. Synthesis of *α*-Methylstyrene Derivatives via Wittig Olefination



General Procedure III: Synthesis of *α*-Methylstyrene via Wittig Olefination of Acetophenone Derivatives.

In a dry 125-250 mL round bottom flask was charged with a magnetic stir bar coated with PTFE, methyltriphenylphosphonium bromide (1.6 eq.) was dissolved in 15 mL THF. The round bottom flask was seal with a rubber septum before t-BuOK (1.6 M in THF solution) was syringed into the mixture at room temperature. The reaction turned immediately a yellow color and the reaction was stirred for 30 minutes before the reaction was cold down to 0 °C. A solution of the desire *α*-Methylstyrene derivatives in minimal amount of THF (0.5 mmol-2.5 mmol, 1.0 eq.) was 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 ketone was consumed, the reaction was quenched with saturated aqueous NH_4Cl solution. The alkene was extracted with ethyl acetate three times. The organic layers was collected and dried over sodium sulfate anhydrous before it was concentrated under reduced pressure to afford crude alkene product. Purification by silica gel chromatography using gradient elution afforded pure alkene.

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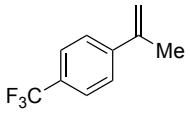
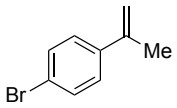


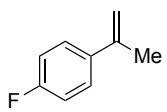
5a

1-(prop-1-en-2-yl)-4-(trifluoromethyl)benzene 5a: General procedure III was followed using 460 mg of **4a** (2.5 mmol), 1.7 g of methyl triphenyl phosphonium (4.0 mmol) and 2.5 mL of a 1.6 M solution of t-BuOK in THF. Purification by flash column chromatography (100:0 hexanes) afforded **5a** (383 mg, 82%) as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$): 7.59 (M, 5H) 5.43 (s, 1H), 5.19 (s, 1H), 2.17 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 144.1 (C) 142.1 (C), 142.4 (C), 126.2 (CH), 137.1 (CH), 125.2-125.0 (CH), 129.9 (q, J = 273.0 Hz, C), 129.4 (q, J = 32.5 Hz, C), 125.1 (C), 122.2 (q, J = 4.0 Hz, CH), 114.3 (C), 21.4 (CH_3); ^{19}F δ (376 MHz, $CDCl_3$): –62.32(F) ATR-FTIR (neat): 2330, 2100, 1943, 1705, 1365, cm^{-1}; HRMS (EI) *m/z* calculated for $C_{10}H_9F_3[M]^+$: 186.0655, found: 186.0656.



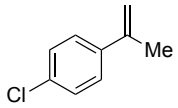
5b

1-bromo-4-(prop-1-en-2-yl)benzene 5b: General procedure III was followed using 489mg of **4b** (2.5 mmol), 1.7 g of methyl triphenyl phosphonium (4.0 mmol) and 2.5 mL of a 1.6 M solution of t-BuOK in THF. Purification by flash column chromatography (100:0 hexanes) afforded **5b** (391.8 mg, 80% yield) as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.46-7.44 (d, J = 8.4 Hz, 2H), 7.34-7.32(d, J = 8.0 Hz, 1H), 5.37 (s, 1H), 5.11 (s, 1H), 2.14 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 142.0 (C) 139.7 (C), 126.2 (CH), 137.1 (CH), 120.8 (C), 112.6 (CH), 21.8 (CH_3); ATR-FTIR (neat): 2338, 2050, 1943, 1705, 1365, 840cm^{-1}; HRMS (EI) *m/z* calcrulated for $C_9H_9Br[M]^+$: 195.9888, found: 195.9886



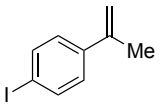
5c

1-fluoro-4-(prop-1-en-2-yl)benzene 5c: General procedure III was followed using 340mg of **4c** (2.5 mmol), 1.7 g of methyl triphenyl phosphonium (4.0 mmol) and 2.5 mL of a 1.6 M solution of t-BuOK in THF. Purification by flash column chromatography (100:0 hexanes) afforded **5c** (255.1 mg, 75% yield) as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.50-7.48 (d, J = 8.4 Hz, 1H), 7.06-7.04 (M, 2H) 5.37 (s, 1H), 5.12 (s, 3H), 2.19 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 163.3 (C) 161.1 (C), 142.4 (C), 126.2 (CH), 137.1 (CH), 112.1 (C), 21.9 (CH_3);, ^{19}F δ -115.04(F) ($CDCl_3$): δ -113.8; ATR-FTIR (neat): 2228, 2040, 1933, 1505 cm^{-1}; HRMS (EI) *m/z* calculated for $C_9H_9F[M]^+$: 136.1694, found: 136.1698.



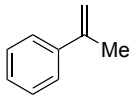
5d

1-chloro-4-(prop-1-en-2-yl)benzene 5d: General procedure III was followed using 380mg of **4d** (2.5 mmol), 1.7 g of methyl triphenyl phosphonium (4.0 mmol) and 2.5 mL of a 1.6 M solution of t-BuOK in THF. Purification by flash column chromatography (100:0 hexanes) afforded **5d** (338.8 mg, 89% yield) as a colorless oil ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.40-7.38 (d, J = 8.4 Hz, 2H), 7.30-7.28 (d, J = 8.0 Hz, 1H), 5.35 (s, 1H), 5.10 (s, 1H), 2.13 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 142.1 (C) 139.6 (C), 133.1 (C), 128.2 (CH), 126.7 (CH), 112.9 (CH), 21.7 (CH_3); ATR-FTIR (neat): 2278, 2030, 1913, 1508 cm^{-1}; HRMS (EI) *m/z* calcrulated for $C_9H_9Cl[M]^+$: 152.6210, found: 152:6218.



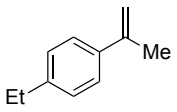
5e

1-iodo-4-(prop-1-en-2-yl)benzen 5e: General procedure III was followed using 609mg of **4e** (2.5 mmol), 1.7 g of methyl triphenyl phosphonium (4.0 mmol) and 2.5 mL of a 1.6 M solution of t-BuOK in THF. Purification by flash column chromatography (100:0 hexanes) afforded **5e** (512.1 mg, 84% yield) as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.66-7.64 (d, *J* = 8.4 Hz, 2H), 7.21-7.19 (d, *J* = 8.0 Hz, 1H), 5.36 (s, 1H), 5.09 (s, 1H), 2.11 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 150.7 (C) 142.2 (C), 137.3 (CH), 131.0 (C), 127.3 (CH), 113.1 (CH), 21.9 (CH_3); ATR-FTIR (neat):): 2218, 2020, 1953, 1538 cm^{-1}; HRMS (EI) *m/z* calcrulated for $C_9H_9I[M]^+$: 243.9749, found: 243.9756.



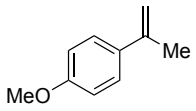
5f

2Prop-1-en-2-ylbenzene 5f: General procedure III was followed using 295mg of **4f** (2.5 mmol), 1.7 g of methyl triphenyl phosphonium (4.0 mmol) and 2.5 mL of a 1.6 M solution of t-BuOK in THF. Purification by flash column chromatography (100:0 hexanes) afforded **5f** (233.2 mg, 79% yield) as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.56-7.54 (d, *J* = 8.4 Hz, 2H), 7.42-7.38(M, 2H), 7.35-7.31 (M, 1H) 5.45 (s, 1H), 5.15 (s, 3H), 2.23 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 143.3 (C) 141.2 (C), 128.2 (CH), 127.4 (CH), 125.5 (CH), 112.4 (C), 21.8 (CH_3); ^{1}ATR-FTIR (neat): 2298, 2030, 1911, 1578 cm^{-1};HRMS (EI) *m/z* calculated for $C_9H_{10}[M]^+$:118.1790, found: 118.1798.



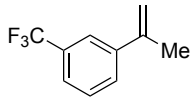
5h

1-ethyl-4-(prop-1-en-2-yl)benzene 5h: General procedure III was followed using 93.2 mg of alkene **4g** (0.5 mmol), 1.7 g of tritylium TPFPB (0.020 mmol) and 2.0 mL of dichloroethane. Purification by flash column chromatography (100% hexanes) afforded **5h** (134.3 mg, 82%) as a colorless oil. (148.8 mg, 93 % yield). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.42-7.40 (d, *J* = 8.4 Hz, 2H), 7.19-7.17 (d, *J* = 8.0 Hz, 1H), 5.35 (s, 1H), 5.10 (s, 1H), 3.69-3.63 (q, *J* = 7.0 Hz, 2H), 2.16 (s, 3H), 1.26-1.24 (t, *J* = 6.0 Hz, 3H),; ^{13}C NMR (100 MHz, $CDCl_3$): δ 143.3 (C) 143.0 (C), 138.5 (C), 127.7 (CH), 125.4 (CH), 111.5 (CH), 28.3 (CH_2); 21.8 (CH_3); 15.5 (CH_3); ATR-FTIR (neat): ?840 cm^{-1}; HRMS (EI) *m/z* calcrulated for $C_{11}H_{14}[M]^{+}$: 146.2330, found: 146.2337



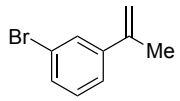
5i

1-methoxy-4-(prop-1-en-2-yl)benzene 5i: General procedure III was followed using 370mg of **4h** (2.5 mmol), 1.7 g of methyl triphenyl phosphonium (4.0 mmol) and 2.5 mL of a 1.6 M solution of t-BuOK in THF. Purification by flash column chromatography (100:0 hexanes) afforded **5i** (255.4 mg, 69% yield) as a colorless oil.^{1}H NMR (400 MHz, $CDCl_3$): δ 7.43-7.41 (d, *J* = 8.4 Hz, 2H), 6.88-6.86 (d, *J* = 8.0 Hz, 1H), 5.26 (s, 1H), 5.01 (s, 1H), 3.79 (s, 3H), 2.16 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 158.6 (C) 142.2 (C), 133.4 (C), 126.7 (CH), 113.0 (CH), 110.2 (CH), 28.3 (CH_2); 54.7 (CH_3); 21.8 (CH_3); ATR-FTIR (neat): ?840 cm^{-1}; HRMS (EI) *m/z* calcrulated for $C_{10}H_1O$ $[M]^{+}$: 148.0888, found: 148.0858,



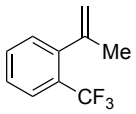
5j

1-(prop-1-en-2-yl)-3-(trifluoromethyl)benzene 5j: General procedure III was followed using 370mg of 3′-(Trifluoromethyl)acetophenone (2.5 mmol), 1.7 g of methyl triphenyl phosphonium (4.0 mmol) and 2.5 mL of a 1.6 M solution of *t*-BuOK in THF. Purification by flash column chromatography (100:0 hexanes) afforded **5j** (255 mg, 69% yield) as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.59 (M, 5H) 5.43 (s, 1H), 5.19 (s, 1H), 2.17 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 144.1 (C) 142.1 (C), 142.4 (C), 126.2 (CH), 137.1 (CH), 125.2-125.0 (CH), 129.9 (q, J = 273.0 Hz), 129.4 (q, J = 32.5 Hz), 125.1 (C), 122.2 (q, J = 4 Hz), 114.3 (C), 21.4 (CH_3); ^{19}F NMR (376 MHz, $CDCl_3$): δ –58.78 (F); ATR-FTIR (neat): 2247, 2050, 2042, 1935, 1815, 1722, 1275, cm^{-1}; HRMS (EI) *m/z* calculated for $C_{10}H_9F_3[M]^+$: 186.0655, found: 186.0656.



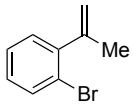
5k

1-bromo-4-(prop-1-en-2-yl)benzene 5k: General procedure III was followed using 370mg of **4k** (2.5 mmol), 1.7 g of methyl triphenyl phosphonium (4.0 mmol) and 2.5 mL of a 1.6 M solution of t-BuOK in THF. Purification by flash column chromatography (100:0 hexanes) afforded **5k** (255.4 mg, 69% yield) as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.56-7.54 (d, J = 8.4 Hz, 1H 5.22) 7.28-7.26 (M, 1H), 7.22-7.18 7.20-7.18 (d, J = 8.4 Hz, 1H), 7.13-7.11 (M, 1H),), 4.94 (s, 1H), 2.10 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 144.3 (C) 142.7 (C), 131.7 (C), 131.7 (CH), 129.7 (CH), 128.5 (CH), 126.0 (CH), 116.1 (CH), 23.3 (CH_3); ATR-FTIR (neat): 2331, 2055, 1933, 1305, 1361, 840cm^{-1}; HRMS (EI) *m/z* calculated for $C_9H_9Br[M]^+$: 195.9888, found: 195.9886



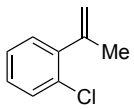
5q

1-(prop-1-en-2-yl)-2-(trifluoromethyl)benzene 5q: General procedure III was followed using 370 mg of 4q (2.5 mmol), 1.7 g of methyl triphenyl phosphonium (4.0 mmol) and 2.5 mL of a 1.6 M solution of *t*-BuOK in THF. Purification by flash column chromatography (100:0 hexanes) afforded **5q** (255 mg, 69 % yield) as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.59 (M, 5H) 5.43 (s, 1H), 5.19 (s, 1H), 2.17 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 143.7 (C) 143.3 (q, J = 273.0 Hz, C) 142.1 (C), 142.4 (C), 133.1 (CH), 137.1 (CH), 129.9 (CH), 127.9 (q, J = 32.5 Hz, C) 127.7 (q, J = 4.0 Hz, CH), 126.6 (CH), 126.0-125.8 (CF_3), 122.9 (C), 115.1 (C), 25.6 (CH_3); ^{19}F NMR (376 MHz, $CDCl_3$): δ –58.78 (F); ATR-FTIR (neat): 2237, 2060, 2052, 1935, 1920, 1722, 1275, cm^{-1}; HRMS (EI) *m/z* calculated for $C_{10}H_9F_3[M]^+$: 186.0655, found: 186.0656.



5r

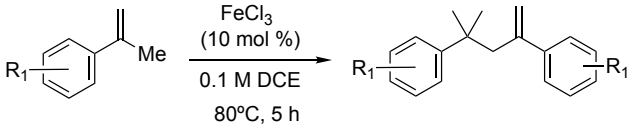
1-bromo-2-(prop-1-en-2-yl)benzene 5r : General procedure I was followed using 370mg of **4r** (2.5 mmol), 1.7 g of methyl triphenyl phosphonium (4.0 mmol) and 2.5 mL of a 1.6 M solution of t-BuOK in THF. Purification by flash column chromatography (100:0 hexanes) afforded **5r** (255.4 mg, 69% yield) as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.56-7.54 (d, J = 8.4 Hz, 1H 5.22) 7.28-7.26 (M, 1H), 7.22-7.18 7.20-7.18 (d, J = 8.4 Hz, 1H), 7.13-7.11 (M, 1H),), 4.94 (s, 1H), 2.10 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 144.3 (C) 142.7 (C), 131.7 (C), 131.7 (CH), 129.7 (CH), 128.5 (CH), 126.0 (CH), 116.1 (CH), 23.3 (CH_3); ATR-FTIR (neat): 2331, 2055, 1933, 1305, 1361, 840cm^{-1}; HRMS (EI) *m/z* calculated for $C_9H_9Br[M]^+$: 195.9888, found: 195.9886



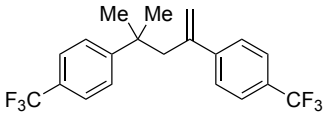
5t

1-chloro-2-(prop-1-en-2-yl)benzene 5t: General procedure I was followed using 380mg of **4t** (2.5 mmol), 1.7 g of methyl triphenyl phosphonium (4.0 mmol) and 2.5 mL of a 1.6 M solution of t-BuOK in THF. Purification by flash column chromatography (100:0 hexanes) afforded **5t** (269.48 mg, 71% yield) as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.37-7.35 (d, J = 8.4 Hz, 1H)), 7.22-7.16 (M, 3H),) 5.23 (s, 1H), 4.97 (s, 1H), 2.12 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 144.5 (C) 142.7 (C), 131.5 (C), 128.7 (CH), 128.6 (CH), 128.1 (CH), 126.0 (CH), 115.9 (CH), 23.2 (CH_3); ATR-FTIR (neat): 2278, 2030, 1913, 1508 cm^{-1}; HRMS (EI) *m/z* calculated for $C_9H_9Cl[M]^+$: 152.6210, found: 152:6218.

General procedure IV: Procedure: Linear Dimerization

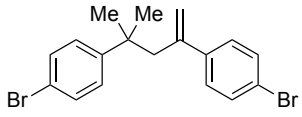


In a dry 4 mL glass vial charged with PTFE coated magnetic stir bar, the alkenes were dissolved with 2.0 mL of dichloroethane (DCE) (0.54 M). (0.5 mmol) of the desire arene was added. Then 10.0 mol% Iron Trichloride (4.0 mmol) was added and cap. The reaction mixture was allowed to stir RT for an 5 hrs. After 1 hour, the reaction solution was then quenched by addition of 1.0 mL of saturated $NaHCO_3$. The 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 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 was flushed with a mixture of hexanes and benzene (100:0 7:3, hexane:benzene) to obtained the pure corresponding product.



6a

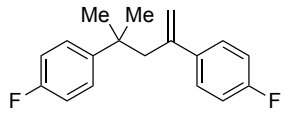
4,4'-(4-methylpent-1-ene-2,4-diyl)bis(fluorobenzene): General procedure IV was followed using 93mg of **5a** (0.5 mmol), Iron Trichloride (4.0 mmol) and 2.0 mL of DCE . Purification by flash column chromatography (100:0 hexanes) afforded **6a** (163 mg, 88% yield) as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.19-7.15 (m, 2H) 7.14-7.10 (m, 2H)), 6.89-6.83 (m, 4H)), 5.08 (s, 1H), 4.78 (s, 1H), 2.77 (s, 2H), 1.23 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 163.8(C) 161.9 (C), 160.5 (C), 159.5 (CH), 136.7(CH), 129.9 (q, J = 273.0 Hz, C), 129.4 (q, J = 32.5 Hz, C), 125.1 (C), 122.2 (q, J = 4 Hz, CH) 127.9 (CH), 127.8(CH), 127.4 (CH), 127.3 (CH), 116.9 (CH), 90.7 (C), 50.3 (CH_2), 37.7 (C), 28.4 (CH_3); ATR-FTIR (neat): 2231, 2160, 2052, 1935, 1920, 1422, 1275, cm^{-1}; HRMS (EI) *m/z* calculated for $C_{20}H_{18}F_6$ $[M]^+$: 372.1313, found:372.1311.



6b

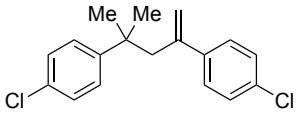
4,4'-(4-methylpent-1-ene-2,4-diyl)bis(bromobenzene): General procedure IV was followed using 97 mg of **5b** (0.5 mmol), Iron Trichloride (4.0 mmol) and 2.0 mL of DCE

. Purification by flash column chromatography (100:0 hexanes) afforded **2b** (179 mg, 92% yield) as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.33-7.29 (M, 4H)), 7.10-7.08 (d, *J* = 8.4 Hz, 2H)), 7.04-7.02 (d, *J* = 8.4 Hz, 2H)),, 5.12 (s, 1H), 4.80 (s, 1H), 2.76 (s, 2H), 1.21 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 147.7(C) 145.2 (C), 141.9 (C), 131.1 (CH), 130.7(CH), 128.1 (CH), 127.7 (CH), 117.8 (CH), 120.7 (C), 119.4 (C), 49.7 (CH_2), 38.4 (C), 28.4 (CH_3); ATR-FTIR (neat): 2231, 2169, 2052, 1935, 1910, 1412, 1275, cm^{-1} ; HRMS (EI) *m/z* calculated for $C_{18}H_{18}Br_2$ $[M]^+$: 391.9775, found:391.9768



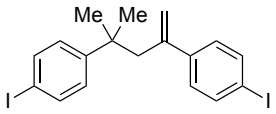
6c

4,4'-(4-methylpent-1-ene-2,4-diyl)bis(fluorobenzene): General procedure IV was followed using 68 mg of **5c** (0.5 mmol), Iron Trichloride (4.0 mmol) and 2.0 mL of DCE . Purification by flash column chromatography (100:0 hexanes) afforded **6c** (120 mg, 88% yield) as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.19-7.15 (m, 2H) 7.14-7.10 (m, 2H)), 6.89-6.83 (m, 4H)), 5.08 (s, 1H), 4.78 (s, 1H), 2.77 (s, 2H), 1.23 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 163.8(C) 161.9 (C), 160.5 (C), 159.5 (CH), 136.7(CH), 127.9 (CH), 127.8(CH), 127.4 (CH), 127.3 (CH), 116.9 (CH), 90.7 (C), 50.3 (CH_2), 37.7 (C), 28.4 (CH_3); ATR-FTIR (neat): 2241, 2160, 2051, 1925, 1925, 1422, 1278, cm^{-1} ; HRMS (EI) *m/z* calculated for $C_{18}H_{18}F_2$ $[M]^+$: 272.1377, found: 273.1255



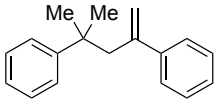
6d

4,4'-(4-methylpent-1-ene-2,4-diyl)bis(chlorobenzene): General procedure IV was followed using 76 mg of **5d** (0.5 mmol), Iron Trichloride (4.0 mmol) and 2.0 mL of DCE . Purification by flash column chromatography (100:0 hexanes) afforded **6d** (130 mg, 86% yield) as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.53-7.51 (d, *J* = 8.4 Hz, 2H)), 7.50-7.48 (d, *J* = 8.4 Hz, 2H)), 6.96-6.94 (d, *J* = 8.0 Hz, 2H)), 6.89-6.87 (d, *J* = 8.0 Hz, 2H)), 5.12 (s, 1H), 4.74 (s, 1H), 2.71 (s, 2H), 1.21 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 147.7(C) 145.3 (C), 141.5 (C), 132.6 (C), 131.3 (C), 128.3 (CH), 127.8 (CH), 127.7 (CH), 127.4 (CH), 117.5 (CH), 49.7 (CH_2), 38.3 (C), 28.7 (CH_3); ATR-FTIR (neat): 2241, 2220, 2012, 1935, 1920, 1422, 1271, cm^{-1} ; HRMS (EI) *m/z* calculated for $C_{18}H_{18}Cl_2$ $[M]^+$: 304.0786, found: 304.0786.



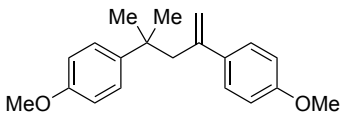
6e

4,4'-(4-methylpent-1-ene-2,4-diyl)bis(iodobenzene): General procedure IV was followed using 121 mg of **5e** (0.5 mmol), Iron Trichloride (4.0 mmol) and 2.0 mL of DCE . Purification by flash column chromatography (100:0 hexanes) afforded **6e** (218 mg, 88% yield) as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.53-7.51 (d, *J* = 8.4 Hz, 1H)), 7.50-7.48 (d, *J* = 8.4 Hz, 1H)), 6.96-6.94 (d, *J* = 8.0 Hz, 1H)), 6.89-6.87 (d, *J* = 8.0 Hz, 1H)), 5.12 (s, 1H), 4.81 (s, 1H), 2.75 (s, 2H), 1.21 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 144.8(C) 145.3 (C), 142.7 (C), 137.0 (CH), 136.7(CH), 128.4 (CH), 128.2 (CH), 115.9 (CH), 92.7 (C), 90.7 (C), 49.6 (CH_2), 38.5 (C), 28.0 (CH_3); ATR-FTIR (neat): 2235, 2168, 2051, 1932, 1928, 1420, 1279, cm^{-1}; HRMS (EI) *m/z* calculated for $C_{18}H_{18}I_2$ $[M]^+$: 487.9498, found:497.9498



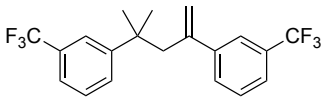
6f

(4-methylpent-1-ene-2,4-diyl)dibenzene): General procedure IV was followed using 59 mg of **5f** (0.5 mmol), Iron Trichloride (4.0 mmol) and 2.0 mL of DCE . Purification by flash column chromatography (100:0 hexanes) afforded **6f** (92 mg, 78% yield) as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.33-7.20 (m, 9H)), 7.15-7.12 (m, 1H)), 5.16 (s, 1H), 4.81 (s, 1H), 2.86 (s, 2H), 1.25 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 149.3(C) 146.7 (C), 143.4 (C), 27.7 (CH), 130.0 (CH), 127.8 (CH), 127.7 (CH), 126.8 (CH), 126.4 (CH), 126.3(CH), 125.9 (CH), 125.8 (CH), 125.4 (CH), 116.9 (CH), 49.3 (CH_2), 38.7 (C), 28.4 (CH_3); ATR-FTIR (neat): 2221, 2160, 2052, 1935, 1920, 1420, 1275, cm^{-1} ; HRMS (EI) *m/z* calculated for $C_{18}H_{20}$ $[M]^+$: 236.1565, found: 236.1563.



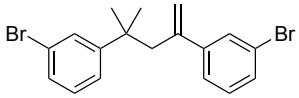
6i

4,4'-(4-methylpent-1-ene-2,4-diyl)bis(methoxybenzene): General procedure IV was followed using 74 mg of **1h** (0.5 mmol), Iron Trichloride (4.0 mmol) and 2.0 mL of DCE . Purification by flash column chromatography (70:30 hexanes/benzene) afforded **6i** (136 mg, 92 % yield) as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.20-7.16 (m, *J* = 8.4 Hz, 4H)), 6.77-6.75 (d, *J* = 8.4 Hz, 1H)), 6.96-6.94 (d, *J* = 8.0 Hz, 1H)), 6.89-6.87 (d, *J* = 8.0 Hz, 1H)), 5.19 (s, 1H), 4.71 (s, 1H), 3.79 (s, 3H), 3.77 (s, 3H), 2.76 (s, 2H), 1.20 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 158.4(C) 157.3 (C), 145.5 (C), 141.8 (C), 135.8 (C-H),127.3 (CH), 126.8(CH), 115.2 (CH), 113.3 (CH), 112.0 (CH), 55.4 (CH_3), 49.8 (CH_2), 38.0 (C), 28.7 (CH_3); ATR-FTIR (neat): 2251, 2160, 2052, 1935, 1928, 1422, 1272, cm^{-1}; HRMS (EI) *m/z* calculated for $C_{20}H_{24}O_2$ $[M]^+$: 296.1776, found: 296.1772.



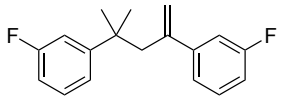
6j

3,3'-(4-methylpent-1-ene-2,4-diyl)bis((trifluoromethyl)benzene): General procedure IV was followed using 93 mg of **1h** (0.5 mmol), Iron Trichloride (4.0 mmol) and 2.0 mL of DCE . Purification by flash column chromatography (100:0 hexanes) afforded **6j** (163 mg, 88% yield) as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.42-7.40 (d, *J* = 8.4 Hz, 1H)), 7.29-7.25 (M, 1H)), 7.17-7.11 (M, 2H)), 6.96-6.88 (M, 3H)), 6.69-6.67 (d, *J* = 8.4 Hz, 1H)), 5.16 (s, 1H), 4.96 (s, 1H), 3.30 (s, 2H), 1.48 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 149.0 (C) 145.4 (C), 143.3 (C), 129.7 (C), 129.2 (CH), 128.7 (CH), 128.6 (CH), 128.1 (CH), 127.7 (CH), 118.7 (), 49.9 (CH_2), 38.5 (C), 28.7 (CH_3); ATR-FTIR (neat): 2231, 2160, 2052, 1935, 1920, 1422, 1275, cm^{-1}; HRMS (EI) *m/z* calculated for $C_{20}H_{18}F_6$ $[M]^+$: 372.1313, found: 372.1311.



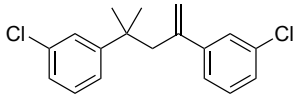
6k

3,3'-(4-methylpent-1-ene-2,4-diyl)bis(bromobenzene): General procedure IV was followed using 97 mg of **5k** (0.5 mmol), Iron Trichloride (4.0 mmol) and 2.0 mL of DCE . Purification by flash column chromatography (100:0 hexanes) afforded **6k** (179 mg, 92 % yield) as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.33-7.29 (M, 4H), 7.11-7.09 (d, *J* = 8.4 Hz, 2H) 7.03-7.01 (, *J* = 8.4 Hz, 2H), 5.12 (s, 1H), 4.80 (s, 1H), 2.76 (s, 2H), 1.48 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 143.9 (C) 140.7 (C), 132.2 (C), 128.7 (CH), 128.3 (C), 125.5 (CH), 123.9(CH), 129.1 (CH), 117.1 (CH), 115.2 (CH), 112.9 (CH), 44.3 (CH_2), 26.8(C), 21.5 (CH_3); ATR-FTIR (neat): 2231, 2160, 2052, 1935, 1920, 1422, 1275, cm^{-1}; HRMS (EI) *m/z* calculated for $C_{18}H_{18}Br_2$ $[M]^+$: 391.9775, found:391.9768



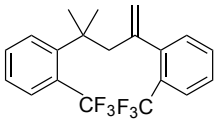
6l

3,3'-(4-methylpent-1-ene-2,4-diyl)bis(fluorobenzene): General procedure IV was followed using 68 mg of **1j** (0.5 mmol), Iron Trichloride (4.0 mmol) and 2.0 mL of DCE . Purification by flash column chromatography (100:0 hexanes) afforded **6l** (120 mg, 88% yield) as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ 6.93-6.90 (M, 3H), 6.84-6.81 (M, 3H), 7.17-7.11 (M, 2H), 6.96-6.88 (M, 3H), 6.78-6.76 (d, *J* = 8.4 Hz, 1H), 6.75-6.73 (d, *J* = 8.4 Hz, 1H), 6.72-6.70 (d, *J* = 8.4 Hz, 1H), 5.10 (s, 1H), 4.87 (s, 1H), 2.78 (s, 2H), 1.33 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 152.3 (C) 150.0 (CH), 145.9 (C), 144.3 (CH), 143.9 (CH), 139.9 (C), 139.5 (C), 131.9-131.6 (CF), 126.1 (CH), 126.0 (CH), 124.0 (CH), 120.5 (CH), 50.2 (CH_2), 38.5 (C), 28.6 (CH_3); ATR-FTIR (neat): 2231, 2160, 2052, 1935, 1920, 1422, 1275, cm^{-1}; HRMS (EI) *m/z* calculated for $C_{18}H_{18}F_2$ $[M]^+$: 272.1377, found: 273.1255



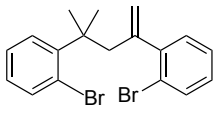
6m

3,3'-(4-methylpent-1-ene-2,4-diyl)bis(Chlorobenzene); procedure IV was followed using 76 mg of **1k** (0.5 mmol), Iron Trichloride (4.0 mmol) and 2.0 mL of DCE . Purification by flash column chromatography (100:0 hexanes) afforded **6m** (139 mg, 92 % yield) as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.42-7.40 (d, *J* = 8.4 Hz, 1H)), 7.18-7.15 (M, 2H), 7.10-7.07 (M, 2H), 7.02 (M, 2H), 5.17 (s, 1H), 4.86 (s, 1H), 2.76 (s, 2H), 1.24 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 155.0 (C) 150.7 (C), 145.3 (C), 144.8 (C), 129.1 (CH), 128.9 (CH), 127.9 (CH), 126.8 (CH), 126.5 (CH), 124.6 (CH), 124.2 (CH), 118.4 (CH), 49.7 (CH_2), 38.6 (C), 28.6 (CH_3); ATR-FTIR (neat): 2231, 2160, 2052, 1935, 1920, 1422, 1275, cm^{-1}; HRMS (EI) *m/z* calculated for $C_{18}H_{18}Cl_2$ $[M]^+$: 304.0786, found: 304.0786.



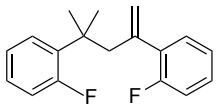
6q

2,2'-(4-methylpent-1-ene-2,4-diyl)bis((trifluoromethyl)benzene): General procedure IV was followed using 93 mg of **5m** (0.5 mmol), Iron Trichloride (4.0 mmol) and 2.0 mL of DCE . Purification by flash column chromatography (100:0 hexanes) afforded **6q** (163 mg, 88 % yield) as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.70-7.68. (d, *J* = 8.4 Hz, 2H), 7.63-7.55 (M, 2H), 7.63-7.55 (M, 2H), 7.49-7.45 (M, 2H)), 7.38-7.34 (M, 2H)), 7.00-6.98 (d, *J* = 8.4 Hz, 2H), 5.16 (s, 1H), 4.96 (s, 1H), 3.27 (s, 2H), 1.44 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 152.3 (C) 150.1 (C), 145.9 (C), 144.3 (CH), 143.9 (CH), 140.1 (C), 135.5 (CH), 131.8-138-4 (CF), 126.0 (CH), 125.8 (CH), 124.0 (CH), 120.8 (C), 50.6 (CH_2), 38.5 (C), 28.4 (CH_3); ATR-FTIR (neat): 2231, 2160, 2052, 1935, 1920, 1422, 1275, cm^{-1}; HRMS (EI) *m/z* calculated for $C_{20}H_{18}F_6$ $[M]^+$: 372.1313, found:372.1311.



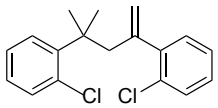
6r

2,2'-(4-methylpent-1-ene-2,4-diyl)bis(bromobenzene): General procedure IV was followed using 97 mg of **5r** (0.5 mmol), Iron Trichloride (4.0 mmol) and 2.0 mL of DCE . Purification by flash column chromatography (100:0 hexanes) afforded **6r** (178 mg, 92 % yield) as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.42-7.40 (d, *J* = 8.4 Hz, 1H)), 7.29-7.25 (M, 1H)), 7.17-7.11 (M, 2H)), 6.96-6.88 (M, 3H)), 6.69-6.67 (d, *J* = 8.4 Hz, 1H)), 5.16 (s, 1H), 4.96 (s, 1H), 3.30 (s, 2H), 1.48 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 147.6(C) 145.5 (C), 141.9 (C), 131.3 (C), 131.1 (CH), 130.8(CH), 130.6(CH), 128.1 (CH), 127.7 (CH), 119.5 (CH), 117.6 (CH), 119.4 (C), 49.7 (CH_2), 38.5 (C), 28.7 (CH_3); ATR-FTIR (neat): 2231, 2160, 2052, 1935, 1920, 1422, 1275, cm^{-1}; HRMS (EI) *m/z* calculated for $C_{18}H_{18}Br_2$ $[M]^+$: 391.9775, found: 391.976.



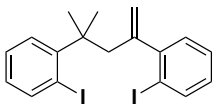
6s

2,2'-(4-methylpent-1-ene-2,4-diyl)bis(fluorobenzene): General procedure IV was followed using 68 mg of **5s** (0.5 mmol), Iron Trichloride (4.0 mmol) and 2.0 mL of DCE . Purification by flash column chromatography (100:0 hexanes) afforded **6s** (120 mg, 88% yield) as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.26-7.24 (d, *J* = 8.4 Hz, 2H)), 7.21-7.19 (d, *J* = 8.4 Hz, 2H)), 7.10-7.07 (M, 2H)), 7.03-6.97 (M, 2H)), 6.95-6.91 (M, 4H)), 6.76-6.74 (d, *J* = 8.4 Hz, 2H)),, 5.17 (s, 1H), 4.97 (s, 1H), 3.28 (s, 2H), 1.45 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 145.9(C) 143.7 (C), 141.9 (C), 139.5 (C), 131.5(CH), 130.2 (CH), 129.3 (CH), 128.9 (CH), 127.6 (CH), 127.5 (CH), 125.9 (CH), 119.9 (CH), 45.4 (CH_2), 39.9 (C), 28.7 (CH_3); ATR-FTIR (neat): 2238, 2160, 2054, 1935, 1920, 1422, 1275, cm^{-1}; ; HRMS (EI) *m/z* calculated for $C_{18}H_{18}F_2$ $[M]^+$: 272.1377, found: 273.1255



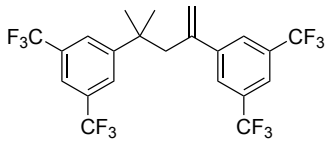
6t

2,2'-(4-methylpent-1-ene-2,4-diyl)bis(chlorobenzene): General procedure IV was followed using 68 mg of **5p** (0.5 mmol), Iron Trichloride (4.0 mmol) and 2.0 mL of DCE . Purification by flash column chromatography (100:0 hexanes) afforded **6t** (120mg, 92 % yield) as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.25-7.23 (d, *J* = 8.4 Hz, 2H)), 7.20-7.18 (d, *J* = 8.4 Hz, 2H)), 7.09-7.06 (M, 2H)), 7.03-6.95 (M, 2H)), 6.94-6.91 (M, 4H)), 6.75-6.73 (d, *J* = 8.4 Hz, 2H)),, 5.16 (s, 1H), 4.96 (s, 1H), 3.27 (s, 2H), 1.44 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 145.8(C) 143.9 (C), 142.0 (C), 139.5 (C), 131.5 (CH), 130.3 (CH), 129.3 (CH), 127.5 (CH), 127.1 (CH), 126.2 (CH), 119.7 (CH), 45.7 (CH_2), 39.9 (C), 29.0 (CH_3); ATR-FTIR (neat): 2231, 2160, 2052, 1935, 1920, 1422, 1275, cm^{-1}; HRMS (EI) *m/z* calculated for $C_{18}H_{18}Cl_2$ $[M]^+$: 304.0786, found: 304.0786.



6u

2,2'-(4-methylpent-1-ene-2,4-diyl)bis(iodobenzene): General procedure IV was followed using 121 mg of **5u** (0.5 mmol), Iron Trichloride (4.0 mmol) and 2.0 mL of DCE . Purification by flash column chromatography (100:0 hexanes) afforded **6u** (197 mg, 81% yield) as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.15-7.10 (M, 4H), 7.02-7.00 (M, 2H)), 6.88-6.85 (M, 2H), 5.09 (s, 1H), 4.97 (s, 1H), 2.78 (s, 2H), 1.66 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 145.8 (C) 143.8 (C), 142.0 (C), 133.8 (C), 131.5 (CH), 130.2 (CH), 129.1 (CH), 129.0 (CH), 127.5 (CH), 127.2 (CH), 126.3 (CH), 126.0 (CH), 119.4 (C), 45.7 (CH_2), 38.9 (C), 28.7 (CH_3); ATR-FTIR (neat): 2231, 2160, 2042, 1935, 1910, 1422, 1235, cm^{-1}; HRMS (EI) *m/z* calculated for $C_{18}H_{18}I_2$ $[M]^+$: 487.9498, found:497.9498



6x

5,5'-(4-methylpent-1-ene-2,4-diyl)bis(1,3-bis(trifluoromethyl)benzene): General procedure IV was followed using 127 mg of **5x** (0.5 mmol), Iron Trichloride (4.0 mmol) and 2.0 mL of DCE . Purification by flash column chromatography (100:0 hexanes) afforded **6** (218 mg, 71% yield) as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.84-7.76 (m, 2H), 7.55 (s,1H), 7.55 (s, 1H), 7.30 (s, 1H), 5.24 (s, 1H), 5.16 (s, 1H), 2.91 (s, 2H), 1.43 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 145.8 (C) 143.8 (C), 142.0 (C), 133.8 (C), 131.5 (CH), 130.2 (CH), 129.1 (CH), 129.0 (CH), 127.5 (CH), 127.2 (CH), 126.3 (CH), 126.0 (CH), 119.4 (C), 45.7 (CH_2), 38.9 (C), 28.7 (CH_3); ^{19}F δ (376 MHz, $CDCl_3$): –62.78 (F), –62.86 (F), –63.09 (F), –63.22 (F), ATR-FTIR (neat): 2231, 2160, 2042, 1935, 1910, 1422, 1235, cm^{-1}; HRMS (EI) *m/z* calculated for $C_{22}H_{16}F1_2$ $[M]^+$: 509.1060, found: 509.1039.

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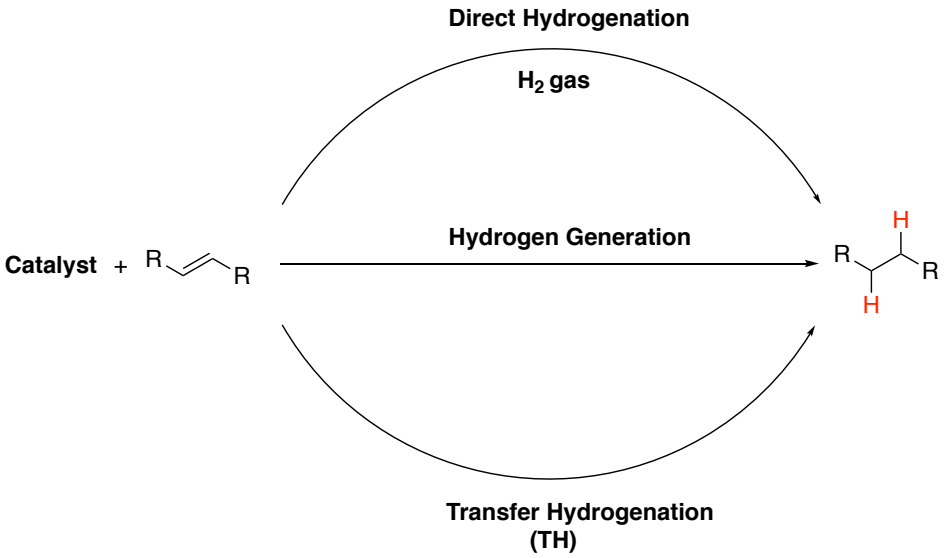
CHAPTER 3

Metal-Catalyzed H Atom Transfer from Water to Unsaturated C–C Bonds in a Classroom Setting.

Background

I was interested and developing a lab that would expose students to research methodology and research techniques. This lab developed will be implemented in our curriculum. I was interested and implementing an organic method that was published in the literature. Also, I wanted to implement scientific techniques that will develop the skills of the students. There are three types of hydrogenations the first one is direct hydrogenation that uses a metal and hydrogen gas to reduce alkenes or alkynes. This chemical reaction involves molecular hydrogen with another compound the presence of a metal is usually needed the metals typically used for this reaction are nickel, palladium, and platinum. Direct hydrogenation is very important in the food industry typical vegetable oils and other oils are usually hydrogenated and they're used produced to make more saturated fats. The way direct hydrogenation works by reducing most of the alkenes in the fat. Oils are produced too solids They can be used to replace butter in many foods. (1) As a result, from going from oils to solid leads to better shelve storage for the industry. Direct hydrogenation it's very important in the industry however in a class setting is not ideal it uses high pressure hydrogen gas for the reaction to proceed leading to conditions that precents dangers of creating fires in a student organic lab. So, for this reason we believe that this method is not suitable for our purpose.

The second type of hydrogenation involves the production of hydrogen gas during the reaction. This method I believe is still not suitable for our lab because of the hydrogen gas production that could lead to fires and other dangers in out setting the lab.



Scheme 14. Types of Hydrogenations.

The third option is transfer hydrogenation a palladium catalyzed transfer hydrogenation to reduce double bonds using tetrahydroxydiboron as a mediator to transfer hydrogen from water as the hydrogen source.[2] This reaction can reduce double bonds that are within rings, terminal and internal double bonds, and double bonds that are next to atoms other than carbons and hydrogen. Diboron species are molecules that contain two boron atoms that are bond together. It can be attached to various hetero-atoms to give them

different chemical properties due to the electronic effects of the functional groups attached to them. They are often used to synthesize boronic acids that are widely used in Suzuki cross-coupling reactions,[3] Diel-Alder reactions,[4]asymmetric amino acid synthesis[5] and carboxylic acid activation.[6] I selected transfer hydrogenation because is safe for a student organic lab. After researching the literature I found no other student organic lab has implemented a transfer hydrogenation reaction.

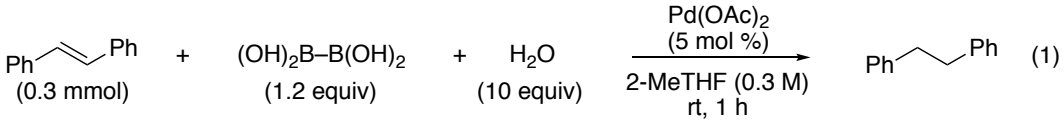
One of the techniques I was interested in implemented is this lab was NMR yields. NMR yields it's a useful technique to determine the ratios in a compound mixture by using and NMR integrals. NMR yields are technique that is important in research in developing new methods in organic chemistry methodology development. The requirements for this kind of technique to be useful the sample must be homogeneous and have sufficient relaxation. H1 NMR and F19 NMR usually doesn't have this kind limitation because they have the capacity of extending the D1 to 5 seconds.

There are two types of NMR's quantitative NMR techniques. The first one is what we call relatively concentration determination for relatively concentration where you are comparing the integrals from compound with another compound or impurity. This allows the possibility to determine if we have any impurities in your samples. The technique we were interested applying to our labs and to our curriculum was the absolute concentration determination. Here we are comparing integrals of interests to determine the concentration

of the desire compound and the purity pressing in sample. In order, to use this technique, we are implementing an internal standard. The internal standard will be used as a reference compound. The concentration of this reference compound will be known and assist to determine the concentration of the desired compound that will be given to the student. Also, the chemical shifts will be known and provided to the students to prevent overlapping with the signals the integral signals of the desire compound. For this experiment to work the nucleus of the standard compound cannot overlap with the signals of the compound we're trying to find the concentration. The internal standard we plan to use for this lab will be prepared by our support staff. This will prevent error gaps from student to student in their data. It's important to weight the standard as accurate as possible. This will allow for better measurements of the unknown concentration. A second important factor is that we must use solvents there are going to dissolve both materials in this case the unknown and internal standard if the materials are not soluble the concentration measurements will be incorrect. There are many internal standards available the one we decided to use for this lab is 1,3,5 trimethoxy benzene. The 1,3,5 trimethoxy benzene produces signals that are not going to overlap with the compound we are going to determine the concentration.

Discussion

The lab I decided to implement was developed from a method that was published in the journal of American chemical society. This method was developed in one our labs at UC Merced by The Stokes lab. In 2016, Stokes lab made their contribution by developing a palladium catalysized transfer hydrogenation to reduce double bonds using tetrahydroxydiboron as a mediator to transfer hydrogen from water as the hydrogen source (scheme 15).[i]



Scheme 15. Direct Hydrogenations.

The Stokes lab transfer hydrogenation method it's a very flexible method. This method is capable of reducing trans alkenes bonds and cis alkenes to alkanes. Also, transfer hydrogenation is capable of reducing mono substituted, di substituted, tri substituted, and tetra substituted alkenes to alkanes in excellent yields as you can see in table 12. Furthermore, this method is capable of reducing internal and external alkynes as you can see in table 13. This gave me flexibility when I designed the lab. I decided to go with trans stilbene alkene because it's an easy starting material that could be handled and measure easily by the students.

Table 12. Reduction of alkenes.

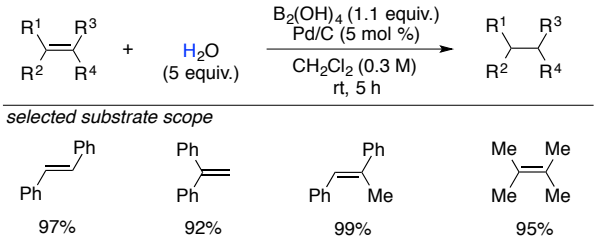
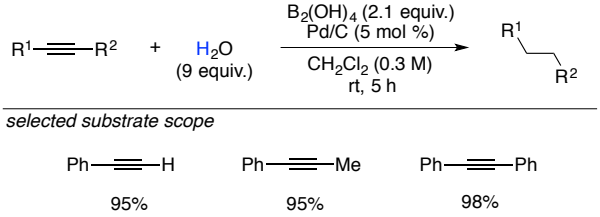


Table 13. Reduction of alkynes.

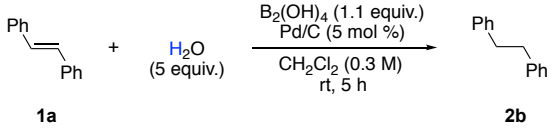


When I was designing this lab a couple of challenges came out during the designed. The first problem that came out is that this lab requires a special piece of equipment called a Slink line in **Figure A**.

Figure A

Unfortunately, our student organic labs don't have this piece of equipment. This piece of equipment is needed because is used to evacuate air out of the reaction. The second challenge that I face was that this reaction took three hours to go into completion. The labs in our school are only three hours long. This type of time will not leave us anytime to carry out any type of analyses.

Table 14. Air sensitive Optimization.



1a **2b**

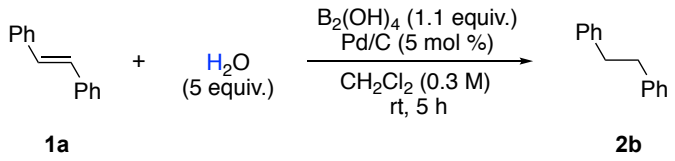
entry	degas H_2O	degas CH_2Cl_2	conv. (%) of 2a	yield (%) of 2b
1	NO	NO	0	0
2	Yes	Yes	100	85
3	Yes	NO	100	84

Reactions were conducted on 0.1 mmol scale in a small capped vial.
Yields were determined by ^1H NMR analysis using 1,3,5-trimethoxybenzene as an internal standard.

With these challenges in mind, I began testing conditions that that could help me solve these challenges. The first part I wanted to investigate was how sensitive was this reaction to air. The first entry in table U was conducted by using all the chemicals straight from the commercial bottles without removing any air or degassing of any chemical. Unfortunately, the reaction didn't work so I knew air was going to be a problem with this reaction. In the second entry I decided to degas water and methylene chloride and use the rest of the chemicals straight from the

commercially available bottles. With these conditions the reaction went to 100% conversion and obtaining 85% of the of the desire product. The third entry in Table 15 I decided to go whit only degas water. With these conditions the reaction went to 100% conversion and obtaining 84%. With these conditions I was headed in the right direction. However, we faced the challenge of the time constraint. Fortunately, we had a meeting with the support staff they brought up couple of concerns. Concern number one was that Palladium on carbon it's flammable and can cause fires easily. Also, methylene chloride is not considered very green reagent. They were concerned that we will be producing a lot of halogenated waste. After this meeting I decided to go back to the drawing board I research the original publication to see what alternative Palladium source was used in their optimization. I noticed that they use Palladium acetate in their optimization and gave good yields. I decided to use Palladium acetate to replace palladium on carbon. Under these conditions the reaction went to 100% conversion and obtaining 87% of the of the desire product. (Scheme 1) after replacing Palladium on carbon I was able to be fixed one of the concerns.

Table 15.

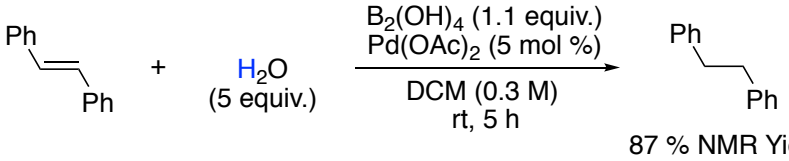


1a **2b**

entry	degas H_2O	degas CH_2Cl_2	conv. (%) of 2a	yield (%) of 2b
1	NO	NO	0	0
2	Yes	Yes	100	85
3	Yes	NO	100	84

Reactions were conducted on 0.1 mmol scale in a small capped vial.
Yields were determined by ^1H NMR analysis using 1,3,5-trimethoxybenzene as an internal standard.

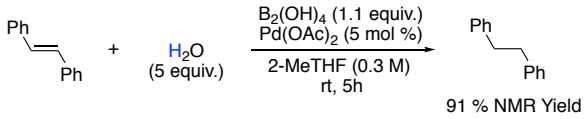
Scheme 16. Palladium acetate to replace palladium on carbon.



87 % NMR Yield

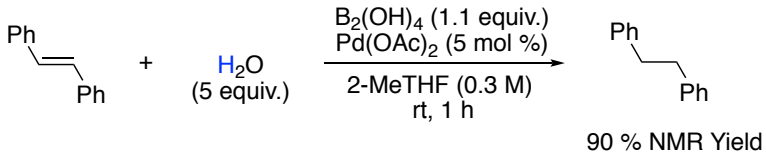
After I addressed palladium on carbon, I decided to tackle the other concern the staff had about methylene chloride. I decided to replace the methylene chloride with 2-methy THF. 2-methy THF is a more green friendly solvent. Under these conditions the reaction went to 100% conversion and obtaining 91% of the of the desire product. (Scheme 17). The staff was happy so I was one step closer to finishing the lab procedure.

Scheme 17. Replacement of methylene chloride with 2-methy THF.



After I addressed the second concerns, I decided to tackle last challenge of time constraint. From experience from working on palladium chemistry I knew that 2-methy THF will accelerate the reaction time. As I predicted, these conditions the reaction went to 100% conversion and obtaining 91% of the of the desire product in 1 hour. (Scheme 18). After optimizing the conditions, I decided it was time to test my procedure with one of my undergraduate student Bridget Villanueva who already had taking both organic lab courses in UC Merced. She was able to reproduce the procedure with no problems in excellent yields in benchtop setting like what the undergraduates will be doing in the organic lab setting.

Scheme 18. Time optimization



Results

Students in the lab section work in groups of two and follow the procedure that can be completed in 2 hours. The students add 4 mg of $Pd(OAc)_2$ directly into a 1-dram vial containing a micro stir bar. They add 32 mg of tetrahydroxydiborane to the vial using a weighting paper, then they add 54 mg of *trans*-stilbene to the vial using a weighting paper. Pour in 1.0 mL of 2-MeTHF into the reaction vial and reseal using a graduated cylinder. The reaction mixture is stirred at, room temperature for one hour. After stirring for one hour, filter the mixture by pipetting it through a pipet plug of Celite® (~0.5 g, retained by glass wool) into a tared 25 mL RBF. Rinse and filter the reaction vial three more times with about 1 mL of 2-methyltetrahydrofuran each time. The Celite® will also absorb any excess water. Evaporate the solvent from the 25 mL RBF using the rotary evaporator and record the mass of your RBF. Students are provided with representative 1H NMR.

The metal-catalyzed H atom transfer from H_2O experiment has been performed by 100-120 students for the past year. This experiment has been performed at the end of the term of the second-semester of undergraduate organic chemistry course that is required for all chemistry, biochemistry, pre-med and biology majors. This experiment is introduced at the end of the semester when the students have already been exposed to GC, IR, and NMR spectroscopy.Product yields generated by the students very in this experiment, ranging from 55-97%. *Trans*-stilbene conversion to bibenzyl was high most

of the time. In rare occasions, the starting material was detected by ^{1}H NMR. The NMR yield was calculated with the assistance of 1,3,5

trimethoxybenzene standard present in the NMR samples that were prepared by the students. It was suspected that sometimes the yields were low because of filtration problems. A second problem we suspected to contribute to low yields was using the wrong concentration of the standard used to calculate the percent yield.

Analysis of a sample $^{1}HNMR$ spectrum of the product (Supporting Information) clearly showed the singlet corresponding to the methylene (δ = 2.90 ppm) of bibenzyl and the absence of ethylene (δ = 6.90 ppm) protons of *trans*-stilbene. From a sample ^{13}C NMR spectrum of the product (Supporting Information), the signal (δ = 39 ppm) was assigned to the methylene carbons of bibenzyl.

Conclusion

The transfer hydrogenation experiment I developed for the students demonstrated that an alkene to alkane conversion without the use of a highly flammable hydrogen gas can be done in a student organic lab setting. The experiment was easy to run and completed successfully in 2 hours. The product of the reduction reaction was analyzed by NMR spectroscopy. The experiment was easily adaptable to an instructional lab setting. This laboratory experiment offered the opportunity for the students to experience a more advanced experiment in organic chemistry and to attract them to the sciences especially chemistry. The students were challenged to developed their problem solving and technical skills.

Experimental

Notes for Instructor:

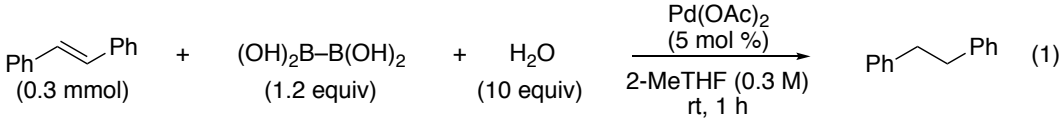
^{1}H NMR spectra were obtained at 400 or 500 MHz and referenced to the residual $CHCl_3$ singlet at 7.26 ppm unless otherwise noted. The abbreviations s, d, t, q, dd, td, qd, and m stand for the resonance multiplicities singlet, doublet, triplet, quartet, doublet of doublet, triplet of doublet, quartet 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.

A Palladium-Catalyzed Transfer Hydrogenation of *trans*-Stilbene
CHEM 100L

written by José Alvarenga, Donna Jaramillo-Fellin, and Benjamin J. Stokes

I. Preview

The reaction you will plan, execute, and study this week is a palladium-catalyzed transfer hydrogenation of an alkene using tetrahydroxydiboron and water (eq 1). This reaction was discovered and developed here at UC Merced (including by undergraduates)[1] and has been cited and used by chemists around the world.



You will use NMR spectroscopy to quantify the percentage of *trans*-stilbene that is consumed and how much is converted to product, as well as to understand structural differences between the starting material and product. Although you have mainly used ^{1}H NMR to identify products and understand molecular structure, it is also a useful technique for quantifying reaction conversions and yields using a crude reaction mixture (i.e., without resorting to isolation). In certain cases, product isolation may be unnecessary due to the desire for high reaction throughput (such as during the optimization of a new reaction method), or impossible due to product volatility, or undesirable when trying to identify reaction byproducts.

Pre-Lab Tasks:
1) Download and read the journal article (ref. 1; see section V below).
2) List three other reactions that could convert an alkene into an alkane.
3) What is "transfer hydrogenation" and how does it differ from direct hydrogenation?
4) How can *trans*-stilbene be distinguished from *cis*-stilbene by ^{1}H NMR?
5) Give two reasons why ^{1}H NMR is more suitable for quantifying reaction yield than ^{13}C NMR.

II. Chemicals
Celite® 545 (Acros® #34967, diatomaceous earth)CAS #91053-39-3
chloroform-d (Acros® #16625, 99.8 atom % 2H) CAS #865-49-6

2-methyltetrahydrofuran (Acros® #16836, 99+%)CAS #96-47-9
palladium acetate (Acros® #44139)CAS #3375-31-3
trans-stilbene (Acros® #16104, 96%) CAS #103-30-0
tetrahydroxydiboron (AKSci® #V2659, 95%) CAS #13675-18-8
1,3,5-trimethoxybenzene (Acros® #16055, 99%)CAS #621-23-8
water (deionized, SE1 house reverse osmosis)

III. Procedure
You will work in pairs on this lab.
1.)Using a metal spatula, weigh 4 mg of palladium acetate directly into a 1 dram vial containing a micro stir bar.
2.)Weigh and add 32 mg of tetrahydroxydiboron to the vial using a weighing paper.
3.)Weigh and add 54 mg of trans stilbene to the vial using a weighing paper.
4.)Pour 1.0 mL of 2 MeTHF into the reaction vial using a graduated cylinder and reseal. Minimize the time that the reaction vial is open to air.

5.)Promptly add 50 μL of H2O to the vial using the calibrated micropipette provided for this task and close the vial.
6.)Secure the reaction vial gently with a three-arm clamp and stir semi-vigorously (at a setting of 3 or 4) at room temperature (no heating!) for one hour. For safety, double check that you are not heating.
7.)Prepare a glass Pasteur pipet that already has a plug of glass wool by adding 2 cm (~0.5 g) of Celite® on top of the glass wool. You will filter your mixture through this pipet.
8.)After stirring for one hour, remove the stir bar. Use a Pasteur pipet to filter the mixture through the prepared Pasteur pipet into a tared 25 mL round bottom flask. Rinse the reaction vial three more times with about 1 mL of fresh 2 methyltetrahydrofuran each time and filter the rinses through the prepared pipet into the same flask. The Celite® will dry any excess water. Dispose of the pipets and their contents in the "Chemical Contaminated Items" container in hood.
9.)Evaporate the solvent from the 25 mL round bottom flask using the rotary evaporator.. As directed by your TA, empty the rotavap collection flask into the "Organic Solutions" bottle.
10.)Weigh the flask with your product. Calculate your percent yield.
11.)Obtain the high field 1H NMR spectrum of your product:
a.Label your NMR tube per your TA's instructions.
b.Dissolve the entirety of your product residue in precisely 1.0 mL of the provided 1,3,5-trimethoxybenzene solution in chloroform-D using the provided calibrated micropipette.
c.Pipet approximately 600 μL of your solution into your labeled NMR tube, which should fill the NMR tube 5 cm.
d.Dispose of the Pasteur pipets in the "Chemical Contaminated Items" container in hood. Return the latex bulbs to the blue bin.
e.Cap the NMR tube. Do not invert the NMR tube since the cap may contain contaminants.

f.Give your labeled NMR tube to your TA, who will collect your 1H NMR spectrum for you and e-mail you your spectrum.
g.When your TA returns your NMR tube, empty its contents into the "Halogenated Solutions" waste bottle in the hood. Rinse the NMR tube and cap with acetone and pour the acetone into a "Halogenated Solutions" bottle. Place the NMR tube back into your section's portion of the NMR tube rack. Place the cap back in the blue bin.

Cleaning up:
Recover and clean the stir bar per your TA's demonstration.
Pour any rinsing acetone into the "Halogenated Solutions" bottles.
Pour the chloroform-d solution from the NMR tube into the "Halogenated Solutions" bottle, along with the acetone used to rinse the NMR tube and cap. After rinsing the NMR tube
and cap with acetone, place the NMR tube in the rack upside down and put the cap back in the bin. Save it for another lab period.
Dispose of the vial and Pasteur pipets in the "Chemical Contaminated Items" container but return the pipet bulb to the bin.

IV. Questions

1) Report your mass-based percent yield and discuss how this could have been improved.
2) Assign the peaks in your ^{1}H NMR spectrum to your substrate (starting material) and product. Are there any peaks you can't explain?
3) Calculate NMR yield using 1,3,5-trimethoxybenzene as your internal standard. Are there any discrepancies between percent yield calculated in (1) and the NMR yield calculated with the 1,3,5-trimethoxybenzene standard? Explain and rationalize.
4) How many equivalents of hydride (relative to equivalents of stilbene) did you use in this lab? Did you generate more hydride equivalents than you used?

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